Reviewer's report

Title: Changes of Hormone Replacement Therapy in Menopausal Women: An Observational Study in Taiwan

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Reviewer: Virginie RINGA

Reviewer's report:

1. Question posed by the authors
The authors analysed the influence of the publication of the results of the WHI on the decision to use HRT to treat menopausal women in Taiwan.
This is an important question clearly defined, others groups have studied this issue in other countries.

2. Methods
To take into account the decision to use HRT, the authors selected 504 women for whom they had data for the analyses (i.e. women 45 years and older from a representative sample of Taiwan’s general population who consented to the linkage of their personal data and National Health Insurance (NHI) data). These 504 women had NIH records which indicated « they had sought treatment for menopause related problems » 6 months before and 6 months after the publication of the WHI. The dependant variable was the prescription of HRT during an outpatient visit for menopause. It is stated page 10 in the Results section that these 504 women had 2549 outpatient visits (in the one year period studied).
Page 9, in the section Statistical analysis, the authors write that they analyzed « the effect of the WHI on HRT, … on the likelihood that a woman would use HRT in the outpatient visit for menopause ». This sentence is not clear, and the occurrence of a prescription of HRT during an outpatient visit is not the same variable as HRT used by the woman.

The major problem is that we do not know if the analyses considered the number of outpatient visits or the number of women. On page 9, in the section Statistical analysis, it seems that the analyses considered outpatient visits, because the authors report « our reference group of outpatient visits consisted of those visits by unmarried and unemployed … ».

The seven ICD9CM codes used to define menopausal conditions must be detailed.

HRT was defined by estrogen OR progestin. Usually HRT is defined by at least use of estrogen, but progestin alone cannot be considered as HRT.

The source of information for all variables should be mentionned, i.e. interview during the 2001 NHIS or outpatient records.

In the methods section there is a comparison between women who gave their consent to the linkage of their data and NHI data and women who did not, but the results of this comparison, and the differences observed between women is not discussed in the Discussion section, i.e. how these differences may have biased the results observed on prescription of HRT.

The methods used to study the influence of WHI on the prescription of HRT need to be clarified. The
two samples of women, before and after the publication of the WHI, are not independent: among the 504 women, 285 had NHI outpatient record for menopause during the 2 periods. It is not clear how this was taken into account in the statistical analysis. The authors should specify how the methods they used- pooled analysis and random effect- dealt with this, and give references for these methods.

What were the criteria used to include the variables in the logistic regression?

The authors must indicate the statistical software they have used for the analyses.

Table 2 is difficult to understand and its usefulness is not clear.

The term « cases » for the 504 women included in the analyses does not seem appropriate. MP = ? menopausal?

It is not easy to understand the meaning of the 2 groups: 402 before WHI, 360 after. In the text page 10, other numbers are reported (144 before, 102 after). Is it the number of outpatient visits?

Table 3: the overall sample size must be given for the logistic regression because of missing data, and also the size of each group for each variable: for instance, WHI report after, n= before, n= . And also to clarify the point concerning the unit of analysis, outpatient visit or woman.

For the line « Medical care », what is the meaning of the OR 3.27? (no OR is mentioned for the model b)

How can the authors explain the differences between OR obtained with the 2 methods, because for medical care for instance, the ORs are quite different.

Results concerning interactions between for instance level of education and the period (before and after WHI) would be interesting. The results presented here show that on one side the period is related to the prescription of HRT, and that other factors, such as women’s characteristics, are also associated with HRT prescription. It would have been interesting to explore the association of the period and the prescription of HRT in different categories of level of education, or according to the physician’s specialty.

A general remark concerning this study is that the way the methods, the results and the tables are reported should be improved to correspond to the relevant standard of epidemiological analyses.

3. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   yes

4. Are the discussion and conclusions well balanced and adequately supported by the data?

   The sentence « the decision whether to use HRT … was not purely dominated by the physicians » should be modified.

   Concerning the limitations of the study, the authors report that they did not taken into account women who might stop seeking medical treatment for menopause, and so that they have underestimated women’s reaction to the WHI report. Does this mean that they hypothesized that women reported fewer complaints related to menopause after the publication of the WHI?

   Another limitation of the study is that we do not know the proportion of the 144+258 women in the first period who were using HRT.

   The interpretation of the results given in the conclusion should not mention « the different reactions from health providers and the patients », because these reactions can only be indirectly estimated through the data. The sentence « the decision whether to use HRT … was not purely dominated by the physicians » should be modified.

5. Do the title and abstract accurately convey what has been found?
   Yes
6. Is the writing acceptable?
English should be improved.

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No

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