Reviewer’s report

Title: Adherence to hormone therapy among women with breast cancer

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Reviewer: Volker Ziller

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This study aimed to identify the factors associated with adherence to hormone therapy for breast cancer. This aim was reached to some extend but further modification is recommended before publication. The flaws mentioned in the first review have been clarified but not completely solved. The non-expert reader could benefit of some more clarification of the definitions used and the limitation that probably many non-adherent patients were lost is still not adequately discussed. A general comment is that retrospective studies of this type can only reveal associations and coincidences. They are able to create and not to prove hypothesis. The authors therefore should be more careful in interpreting their data – examples are provided in the specific comments. Altogether this is an interesting and important study, the limitations are yet not clear enough discussed and explained.

Specific comments:

“The last included dispensing date was 10/29/2010”

“The study inclusion criteria for women with breast cancer tumors who were enrolled between 2002 and 2008”

How was the overlap delt with – last observation carried forward? Cut at the last dispensing date for all patients? The problem of the used definition is still that a lot of information is lost (even if many well accepted publications did use this “official way” of measuring, I do believe it is rather not the optimal way to define a non-adherence population to investigate the given questions)

“For patients with multiple recorded tumors, we used the more complete observation, the observation with the highest stage if the diagnosis dates were the same or the earliest observation if the diagnosis dates were different. “

This leads to inclusion of patients that received more than one antihormonal treatment? Did this sub-group do better than the others?

“Due to the applied criteria, only women that received drugs at least twice were included in the study. This procedure could have contributed to underestimations in the adherence rates. “

Overestimations! This excludes probably many non-adherent patients! Again:
Why excluding those not returning for second dispensing? – if they can be followed they would provide important information on non-adherence.

“Thus, it is reasonable to believe that the included participants did not differ greatly from the general population.”

To better clarify generalizability comparison to general population based on baseline and demographics could be discussed.

“It is believed that the observed lower adherence rate among young patients in the present study is related to the adverse effects of hormone therapy on the women’s sexuality, which include fertility issues and menopausal symptoms [13]. Moreover, the association between greater compliance and having a partner, which was also found in other studies [22, 26], might be linked to receiving support. This result is consistent with the idea that social support is highly predictive of adherence [1].”

This is not based on the data provided and should be marked as “speculated.”

“The importance of investments in early diagnosis is also supported by the present study; it not only has a direct effect on patient survival [4, 8] but also an indirect effect by facilitating treatment compliance.”

This sounds plausible but is also speculative as no causality is proven by the study, there might be numerous underlying bias that could be discussed here.

“The current study also revealed that patient monitoring by mastologists and oncologists had a positive effect on hormone therapy adherence [19].”

This is the same problem: there is an association of mastologist and adherence – this says that patients that do see their mastologist are adherent – not necessarily that seeing the mastologist is helpful to improve adherence – it is a coincidence and not necessarily a causality.

“However, a more intensive use of health care resources such as chemotherapy, tests and hospitalizations appeared to associate with lower adherence; this result was not directly observed in other studies but may be indirectly related to the association between lower adherence and comorbidities [15, 20] because lower adherence occurs when patients are more severely ill.”

And again, there might a number of explanations why severity of disease or progression might lead to non-adherence or non-persistence – e.g. doctor stops medication due to progression.

The authors should consider to avoid the words “effect” and rather use “association” and other more hypothetic terms.

**Level of interest:** An article of importance in its field
Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests'