Reviewer's report

Title: Effect of vaginal self-sampling on cervical cancer screening rates: a community-based study in Newfoundland.

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Reviewer: Paolo Giorgi Rossi

Reviewer's report:

The paper presents an interesting experience using self sampling in an opportunistic screening. Unfortunately the study design was very subject external factors that could make impossible to establish any causal relation, and actually such an incident occurred.

1. Having a control community in a pre-post study is a good idea, but declaring that in the control community someone other made an intervention may be even stronger than yours makes all the study very weak.

2. Finally, it is not clear to me why you did not designed a factorial 2X2 study. If the reason is that it was impossible to make an intervention with self sampling alone without any kind of advertising about the availability of the new device, it can be reasonable (I think it was possible making a base level of advertising for all the arms).

3. Nevertheless the paper give important insights o the difficulties in adopting self sampling in opportunistic screening. In fact, the authors obtained the same proportion of returned samples observed in many studies mailing directly at home the self sampler only to non responders.

4. Another problem that limits the interest of the paper for other countries is the protocol adopted for screening: one year interval, for both HPV positive/cytology negative and HPV negative women!

5. The authors have all the information needed to compute the impact on total Pap test coverage, even with more reasonable definition than a Pap-test every year.

Specific comments

Abstract

1. Line 5: “major risk factor” does not really explain the relation between HPV and cervical cancer “necessary cause” is much clearer.

2. Lines 10 11: how were the three community allocated to the three interventions? Randomly?

3. Lines 21-22: the sentence is not clear I would say “not had a pap in the last three years” or “the last pap was three year or more”.

Background
4. Lines 35-36: this is not the point. Relative risk estimates are very wide and not meaningful because in many case there are zero cases not exposed, so the OR tends to infinite. This kind of risk is very different from that of smoking. In any case the point is if HPV testing, followed by appropriate triage, colposcopy and treatment protocols, can prevent the incidence of CIN3 and cancer better than Pap test. There are several evidences about this point: Naucler 2012, Bulkman 2007, Ronco 2010, Kitchener 2009, Sankaranarayanan 2009, but most of all the pooled analysis of the European trials Ronco 2014 Lancet. May be these evidence were not sufficient to produce recommendations by the CTFPHC (different protocols used in different trials and doubts on the increase in colposcopies mainly), but the evidences are strong that HPV can protect more than Pap test.

5. Line 40: the sentence is not correct: in fact in many studies conducted in countries with well implemented screening programs the proportion of cancers occurred in correctly screened women is quite high: this could occur for two reasons 1) the coverage is so high that even a 5 fold higher risk cannot invert the ratio (Giorgi Rossi Eur J Cancer Prev 2014 shows a situation like that); 2) some studies includes among screened women also cancers found at first screening round.

6. Line 41: the sentence “suggested … tool that is acceptable to women…” is reasonable only if it is referred to self sampling not to HPV testing in general.

7. Pag 4 line 55: “lower screening rates” is a consequence of all the other factors, cannot be listed together.

8. Line 57: in the study by Giorgi Rossi et al there was an analysis stratified by centres and one centre (the only one in which there was no effect) was rural area. Also in the first paper by Gok (BMJ 2010), large part of the population was rural, I am not sure but stratified analyses have been presented after the first publication.

9. Line 60: What do you mean with “in addition”? women can perform both HPV and Pap in co-testing? This recommendation is somewhat strange: the advantages of self sampling disappears, women cannot receive the message that HPV test has a longer protection… This protocol has no rationale.

Methods

10. Describe how the communities were allocated to interventions.

11. Line 86: please specify better which sampler (producer commercial name, city etc.) and descried it (a photo would be useful).

12. Line 94: what was the appropriate follow up? Why not a direct contact with the positive women to arrange an appointment for Pap or colposcopy?

13. Line 95 -96: what is a custom pamphlet?

14. Line 103: please use two or three words to define “Well Woman appointment”

15. Line 109: “study participants” or “eligible women”

16. Line 110: why the screening history of participants was ascertained only in
Discussion

17. Line 166: “we believe” there are several methods to quantify the impact of Pap test increase in terms of years of life gained, obviously you must distinguish a the gain of a women who have never been screened before and the gain of changing the status from under-screened >than 3-5 years to screened.

18. Line 182: the studies in Mexico are door to door distribution.

19. Line 205: the problem of informed consent is relevant: actually you cannot compare the participation obtained in a setting in which women are asked to sign informed consent with the participation in a real community based intervention. This problem should be explained to Ethical committees: when the test is not experimental anymore and the object of our research is the behaviour of our target population, consent should be reduced to a minimum if any. I know this is not a fault of the researchers, but a serious debate with Ethical committees representative at international level should be done otherwise we will have only clinically oriented research and not public health oriented research.

20. Line 213: while the cost of the sampler is quiet low (well done!) the cost for HPV test is completely out of the screening market: in Europe, the screening programs adopting HPV in routine are paying it 4.5-6 euro (VAT excluded).

21. Lines 226-228: I think the authors may mention the Arbyn systematic review (in press I think but presented at Eurogin 2015) that shows a significant and consistent increase only for mailing at home the device, while any opt in strategy had results not much better than standard recall letter.

Conclusions

22. I am asking if it is possible to talk about increasing Pap test coverage without mentioning an organised program based on the routine invitation of all the target population: there are so many evidences that this is the most effective and cost effective intervention that any other strategy should be taken into account only as e reinforce of an organised call recall program.

References

23. The studies from France (Piana; Sancho-Garnier) have been implemented in a quite non-organised screening (even if they define it a program there is no systematic call recall and no central coordination of the management of positive women) I suggest to include a comparison

24. With these two studies in discussion.

25. Only one study, to my knowledge, used pharmacies to distribute the self sampler, this way of distribution is the most similar to yours (Giorgi Rossi et al 2015 BJC), they had no increase in response compared to recall letter.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

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