Author's response to reviews

Title: Awareness and knowledge of HPV, cervical cancer, and vaccines in young women after first delivery in Sao Paulo, Brazil

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Author's response to reviews: see over
São Paulo, 06 October 2010

To: BMC Women’s Health

Re: REVISED Manuscript Submission

Title: Awareness and knowledge of HPV, cervical cancer, and vaccines in young women after first delivery in São Paulo, Brazil

Dear Sirs

Please find attached the above named revised manuscript which we would be grateful if you would consider for publication. We highlighted (with violet coloured text) all changes in the manuscript.
The responses to the reviewers’ comments are in the text below.

Yours sincerely,

Cristina H Rama (corresponding author)

Version: 2 Date: 24 August 2010
Reviewer: Carrie Nielson

Reviewer’s report:

Major Compulsory Revisions

1. The rationale for studying this population was not given in this manuscript, but is clear from the discussion section in their previous paper (ref 6). This information (i.e., high HPV prevalence but low oncogenic HPV prevalence) is important for readers to consider the utility of offering these women the HPV vaccine after sexual debut.

We added in the Page 4; Background:
For this reason, in some countries, school vaccination programs have been established as a strategy to vaccinate girls against HPV. However, pregnant adolescents and girls of lower socio-economic status are more likely to drop out of school, therefore, opportunities
for catch-up vaccination are valuable to improve coverage among the at risk young female population.

We added in the Page 5; Background:
The rationale for studying this population is that first delivery health care services could represent a suitable opportunity to offer HPV vaccines for adolescents and young women who have not been previously vaccinated.

2. There was some information given to all participants about the HPV vaccine, which led to 100% of them indicating acceptability. This information should be completely described. For example, were its cost, effectiveness, side-effects, and alternatives to vaccination (i.e., regular screening) explained? If they were only told that the vaccine can prevent cervical cancer and genital warts, it is not surprising they would all agree, but this would not be very complete information for decision making purposes.

   In the present study, only explanations on the prevention of illnesses through vaccines and on the HPV prophylactic vaccine were given by the interviewers.

   When the study (including the questionnaire) was approved by the Ethics Committee, HPV vaccine was not yet approved. The present study began 16 days after the first regulatory approval of one of the HPV vaccines by FDA. When the study questionnaire was applied, HPV vaccine was not yet approved in Brazil (until now it has not yet been included in Brazilian public vaccination programs).

   The purpose of our study was to assess the level of awareness and knowledge of HPV infection, cervical cancer prevention and vaccines in adolescents and young mothers. The idea was also to evaluate whether the young mothers, after first delivery, had some type of fear or taboo to receive a new vaccine in this period.

3. Abstract: Does the fact that it is a “public maternity hospital” (in Methods) imply they are “low income” (in Conclusions)? Please clarify the population base and the use of “low income” throughout the manuscript.

   Eligible women of this study were all primiparous women aged between 15 and 24 years who had been living in the metropolitan area of Sao Paulo for at least six months and gave birth at Leonor Mendes de Barros Hospital. This hospital is a public maternity in a poor region of Sao Paulo-Brazil and serves mostly low income people from the adjacent areas. Nevertheless, pregnancies in adolescents and young women are more often observed in underserved populations.

4. The reason for excluding income in the multivariable model is not given. Therefore, I’m not sure the appropriate model and adjusted PRs are presented.

We added in the Page 9; RESULTS:
All selected variables (age, years of schooling, marital status, income and previous STD), were included in the multivariate analysis model. However, when years of schooling and income were included, the model did not converge. Then, the variable income was taken out. In the analysis including the other four variables, years of schooling (P for trend = 0.307) and marital status (P = 0.296) were not significantly associated with HPV awareness. The multivariate analysis revealed that only age (P for trend = 0.021) and previous STD (P < 0.001) were independently associated with HPV awareness. The prevalence ratio of HPV awareness for women aged 19–21 years was 1.32 with a 95% CI
of 0.87–2.01, and for women aged 22–24 years it was 1.63 with a 95% CI of 1.07–2.48 (reference group: women 15–18 years old). Women who reported a previous STD were more likely to be aware of HPV (PR = 2.05; 95% CI: 1.46–2.87) compared to women who had never had any STD.

Minor Essential Revisions

Exclusion criteria should be stated not referred to in a previous publication.

We added in the Page 5; METHODS:
The following exclusion criteria, as previously published [6], were applied: non-Brazilian, inability or refuse to give informed consent or immunodeficiency (including AIDS/HIV infection checked in medical records).

2. Why is it important that women know how cytological tests are performed?
The query was intended to estimate how many women were aware, and whether they were able to distinguish between the taking of smears (cytological tests) and other gynecological examinations.

A requirement for opportunistic screening programs to prevent cervical cancer, based on cytology, is the women performing the Pap smear collection according to time intervals recommended. Therefore, it is important for women to identify when they were subjected to cytology.

3. “Ordinal gynecological test” should probably be “ordinary ...”, although this phrase seems a bit ambiguous. Is the point that women should be asking for a Pap smear when they have their annual gynecologic exam?
Please, see answer above.

4. Include in the background some information about vaccine approval and educational efforts in Brazil that are mentioned in the Discussion.
We added in Discussion:
In Brazil, Quadrivalent and Bivalent HPV vaccines have been approved by regulatory authorities for females aged, respectively, 9 to 26 years and 10 to 25 years but they are not yet included in public vaccination programs [23]

Discretionary Revisions

Is HPV vaccine contraindicated among pregnant women?

HPV vaccine is not recommended for pregnant women. However, women who are breast feeding may get the vaccine.[Vaccines and Immunizations. Centers for Disease and Control. Available at: http://www.cdc.gov/vaccines/vpd-vac/should-not-vacc.htm#HPV]

Presumably these women were not receiving regular health care until they became pregnant but did have some contact with the health care system for prenatal care. Is post-delivery the first opportunity to offer this population a catch-up vaccine?
The majority of these young women do not have regular access to healthcare. However, when they become pregnant, they seek assistance and continue to do so after delivery in order to extend medical care to their babies.
First delivery health care services could represent a suitable opportunity to offer HPV vaccines for adolescents and young women who have not been previously vaccinated.
Reviewers report:
Background
- Paragraph 3: “However, vaccine coverage in adolescents can be low because they generally seek preventive health services less frequently than other age groups [5].”
Please be more clear about this sentence. Also the reference 5 does not help me to fully understand what the authors have stated.
We changed the text in Page 4; Background: However, providing a vaccine “against cancer” to adolescent girls raises several challenges because many young unmarried girls and women face significant challenges in accessing the health care necessary to meet their sexual and reproductive health needs.

[in accordance with ref [5]:
Pollack AE, et al; page 59: Target populations - Adolescent girls – Providing a vaccine “against cancer” to adolescent girls raises several challenges…….Many young unmarried girls and women face significant challenges in accessing the health care necessary to meet their sexual and reproductive health needs. While neither national immunization programmes nor sexual and reproductive health programmes are ideal for providing services to young adolescents, a package of health services should be developed to offer girls an HPV vaccine and other interventions that could have a broader impact on their reproductive health.]

- Please insert some basic information on HPV vaccination strategy in the study setting. It is difficult for me understand the aim of this study without any data about the vaccination programs choosed, the way of vaccine offer, and so on. Some information are present at the end of discussion (and in the cover letter) but they should be anticipated in the background.
It was not the purpose of our study to vaccinate against HPV (HPV vaccine has not been offered to the enrolled young women). Moreover in Brazil HPV vaccines are not available in the publics. Our study therefore aimed only to evaluate if first delivery health care services could represent a suitable opportunity to offer HPV vaccines for adolescents and young women.

Methods
- Paragraph 1: “Detailed exclusion criteria have been previously published [6].”
Please summarize the main exclusion criteria from this study.
We added in the Page 5; METHODS:
The following exclusion criteria, as previously published [6], were applied: non Brazilian, inability or refuse to give informed consent or immunodeficiency (including AIDS/HIV infection checked in medical records).

- Paragraph 4: “A total of 509 women were invited to participate: ……Therefore, 301 primiparous women were included in the analysis.”
No woman had been vaccinated for HPV? HPV vaccine has not been offered to the enrolled young women and no women had been previously vaccinated to HPV.

Discussion
The authors conclude their discussion stressing the need for educational interventions. At the end of the article it is not yet clear for me if the vaccine has
been offered to the enrolled young women or not. If yes, is it been offered free of charge? What is the reached coverage? Their conclusions appear a little obvious without this information.

Please note that in the results is reported: “All participants affirmed that they would accept vaccination after delivery if the HPV vaccine were available (Table 1).”

When the study (including the questionnaire) was approved by the Ethics Committee, HPV vaccine was not yet approved. The present study began 16 days after the first regulatory approval of one of the HPV vaccines by FDA. When the study questionnaire was applied, HPV vaccine was not yet approved in Brazil (until now it has not yet been included in Brazilian public vaccination programs).

The purpose of our study was to assess the level of awareness and knowledge of HPV infection, cervical cancer prevention and vaccines in adolescents and young mothers. The idea was also to evaluate whether the young mothers, after first delivery, had some type of fear or taboo to receive a new vaccine in this period.
Reviewer's report:
This paper is well designed and brings new information essential to a successful implementation of the HPV vaccine in Brasil. There are only some minor changes that the authors might consider (Minor Essential Revisions).
- Background; space between HPV and the type number. Corrected

- Statistical analysis paragraph and Tables 2 and 3M; instead of symbol write Chi-square for trend. Corrected.

- In the text delete the Zero decimal (i.e. 27% instead of 27.0%) and replace “on 08 June 2006” by June 8, 2006. Corrected.

- Results; delete one space before the comma Corrected.

- Discussion; comma before “which” and small letter to “knowledge of HPV can be changing…. Corrected.

- Table 1, define the 301 “participants” in the same manner like in Tables 2 and 3

  Table 2: Prevalence ratios and corresponding 95% confidence intervals (CI) for HPV awareness according to selected socio-demographic characteristics and smoking habits among 301 young primiparous women, Sao Paulo, Brazil, 2006–2007

  Table 3: Prevalence ratios and corresponding 95% confidence intervals (CI) for HPV awareness according to selected sexual behaviours, reproductive characteristics, and history of contraception among 301 young primiparous women, Sao Paulo, Brazil, 2006–2007

- Tables 2 and 3; define the superscript *: statistically significant. The superscript define: Chi-square for trend