Author's response to reviews

Title: Determinants of sexual activity and its relation to cervical cancer risk among South African women

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Author's response to reviews: see over
Dear Dr Edmunds,

Please find the revised manuscript enclosed: as well as a detailed response to the reviewer’s comments (below). We have accepted all of the reviewer’s suggestions and have revised the manuscript accordingly. Thank you for your continued consideration of our manuscript.

We look forward to hearing from you.

Yours sincerely,
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Responses to Review by authors: Responses by authors are in italics

Ref: MS: 1324696400125442 (BMC, Public Health)

Manuscript Title: Determinants of sexual activity and its relation to cervical cancer risk among South African women

Version: 1 Date: 30 April 2007

Reviewer #1: Ron Gray

Major compulsory revisions

1. A table comparing demographic and other important characteristics in cases and controls should be presented.

A table has been added (now labeled as Table 1) comparing demographic and other important characteristics in cases and controls (see highlighted section page 20 of manuscript) and the following paragraph inserted in the text on page 7:

As can be seen in Table 1 showing a comparison of socio-demographic background of cases and controls, women in both groups had similar characteristics: the mean age was 45 and 44 years respectively; urban residence 58% and 54% and having more 8 or more years of schooling, 92% and 91%
respectively; the proportion of married women both 53% and black and coloured women both 25% and 75% respectively.

2. Legends are missing on the tables.

Legends have been added to all tables (see highlighted sections pages 21-23 of manuscript):

(PREVIOUSLY TABLE 1) Table 2: Socio-demographic factors associated with earlier sexual debut

(PREVIOUSLY TABLE 2) Table 3: Socio-demographic factors associated with increased number of sexual partners

(PREVIOUSLY TABLE 3) Table 4: Cervical cancer risk in relation to age of sexual debut

(PREVIOUSLY TABLE 4) Table 5: Cervical cancer risk in relation to the number of lifetime partners.

3. The crude and adjusted relative risk estimates should be presented.

In the revised tables 2-5 both crude and relative risk estimates are now presented (see highlighted section page 21-23 of manuscript).

1. The following addition has been made to the methods section to explain the use of odds ratios and address this issue, (see highlighted section page 6 of manuscript).

Odds ratios as a measure of association are an appropriate measure in case-control studies even when outcomes are common as in Tables 2 and 3. In the instance where the outcome is uncommon, as is the case in Tables 4 and 5 for cervical cancer risk, (estimated incidence of 31/100,000) this they are most likely to be a good estimate of relative risk. We assessed the association of potential cervical cancer risk factors with age at sexual debut using multiple logistic regression
analysis, estimating odds ratios for age at first sex <16 years relative to first sex at a later age.

*And*

The crude and adjusted relative risk estimates were similar and both are presented.

**Reviewer #2: Patti Gravitt**

**Major Compulsory Revisions**

1. The paper will be enhanced with the addition of more detail in the statistical analysis section, which is currently quite difficult to follow. Much has to be inferred from the tables. Please state clearly that the population in Table 1 is restricted to controls.

   *More detail has been added to the statistical analysis section (see response to reviewers 2 & 3 below. The text has been amended to ensure that it is clearly stated that the population in Tables 2 and 3 (previously Table 1 and 2) are restricted to controls. It reads as follows (see highlighted section page 7 of manuscript):*

   Both tables 2 and 3 (PREVIOUSLY TABLES 1 & 2) show socio-economic factors associated with earlier sexual debut and increased number of partners respectively are restricted to controls.

2. Add Table legends and titles which clearly indicate the contents of the table and analysis.

   *Legends and titles have been added to all tables indicating the contents of the table and the analysis (this also addresses the point made under general in reviewer 1’s report). Additions have also been made in the text to make the analysis and content of the tables clearer. They read as follows (see highlighted section page 7 & 8 of manuscript):*

   **Age at sexual debut**  Twenty-three percent of the controls had sex < 16 years. Table 2 (PREVIOUSLY TABLE 1) describes socio-demographic factors
associated with earlier age at first intercourse and gives odds ratios for age at first
sexual intercourse < 16 years relative to first sex at age ≥ 17 among the controls.

(Table 2)

**Number of sexual partners** Thirty-nine percent of controls had had at least three
sexual partners. Table 3 (PREVIOUSLY TABLE 2) describes socio-demographic
factors associated with an increased number of sexual partners, ≥3, relative to 1
partner for among the controls.

(Table 3)

3. Tables 3 & 4 present data that is well-described in the literature, and distracts from
the main analysis of determinants of sexual risk behavior in a population in South
Africa.

   **While the main focus of the paper is determinants of sexual risk behaviour in a
population in South Africa. Tables 3 and 4 add to the analysis in that they indicate
the robustness of this study in confirming that similar risk factors exist for cervical
cancer in this South African population. This is commented on in the discussion,
der under the heading ‘Sexual activity and cervical cancer risk’, page11 of
manuscript.**

The discussion should include some comments to acknowledge that because you
are analyzing controls from an age-matched case-control study of cervical cancer,
you are significantly limited in making inferences about sexual behaviours in
younger women (only 6% of the population was under 30 years).
*The authors agree. The following sentences have been added to the discussion (see highlighted section page 12 of manuscript):*

Controls in this study were age matched cases of cervical cancer, a disease more common in older women. Hence the study is limited in making inferences about younger women since only a small percent of the study population (6%) was under the age of 30 years.

**Reviewer # 3: Paul Hewson**

**Major Compulsory Revisions**

In a number of places, the paper is rather over-assertive. For example it states that “The South African age-standardized incidence is 30/100,000 wherea this is clearly an ‘estimate’ of incidence. Another example is that you find on evidence of a trend in time. I can’t see anything in your results about that.

>This has been corrected in the revised manuscript to read (see highlighted section page 1 of manuscript):…is estimated to be 31/100,000 (see highlighted section page 3 of manuscript)

The evidence showing no evidence in a trend of younger age at first sex over time has been added to the results section (see highlighted section page 7 of manuscript) and reads as follows:
The chi square test for trend, an indicator of changes over time, was 1.33, p=0.25, showing no evidence of a trend of younger sexual debut over time.

2. My concern was in terms of the selection of cases and controls – specifically a wider range of hospitals were used that the two treating cancer. Readers unfamiliar with the arrangements for health care in South Africa need to know a little more about the reasons for doing this, and particularly need to be reassured for example that the cases weren’t taken from a narrower set of patients than may have been the case with the control hospitals. It would be useful to know a little more about how they were ‘judged to be independent of cervical cancer risk, contraceptive use and sexual practice” (some background statistics may help here). And some more detail on matching is needed given the potential for overmatching here.

A section has been added to the methods to address these concerns and clarify the reasons for controls being selected from a wider range of hospitals than cases and indicating that the cases weren’t taken from a narrower set of patients. Clarification has added for how controls were judged to be independent of cervical cancer risk, contraceptive use and sexual use. This section reads as follows (see highlighted section page 4 of manuscript):

Women developing cervical cancer and using public health facilities were all treated at two tertiary care hospitals, in Cape Town….. Controls were treated and recruited in nongynecologic, nonobstetric wards in local hospitals, accounting for
the wider range of hospitals for controls. Cases and controls series-matched in a ratio of 1:3 on decade of age, race and geographic residence (urban or rural areas in same catchment geographical areas). Controls were selected to be representative of the same population from which the cases were identified and were similar in a range of socio-demographic characteristics (see Table 1). Eligible controls were women with primary diagnoses such as trauma or acute infections, that have not been linked in previous studies, either positively or negatively to cervical cancer risk, to contraceptive use (e.g. trauma, appendicitis, disc disease and other major orthopaedic conditions; selective admissions for major surgery for conditions such as inguinal hernia) or to sexual practices: women with conditions such as ischemic heart disease or venous thromboembolism, or gynecologic disorders, were not eligible.

3. There’s a fascinating result, in that you state age of first intercourse is associated with low education and then go on to highlight infection risks being due to ‘higher education level and lower age at first intercourse. I can guess as to what’s going on here, but it needs to be clearly explored in the context of the modelling of results.

The findings related to age at first intercourse and educational level on the one hand and number of sexual partners on the other are explored through the addition of the following paragraph in the discussion (see highlighted section page 10 of manuscript): Women with low educational levels may have poorer
knowledge and a less control over reproductive and sexual decision-making and this may lead to an earlier sexual debut. [11] While it may seem paradoxical that an early sexual debut is associated with lower educational levels while having a greater number of partners is associated with the inverse, this is not necessarily the case. Higher education may increase women’s financial autonomy, allowing her to have greater independence in choice in intimate relationship and hence increase her number of life-time partners.

Minor essential revisions

1. In places you have used ‘data were’ but in others you have used ‘data was’. I prefer the former.

This has been corrected to ‘data were’ throughout.

2. I’m always curious about forcing binary splits within data when you have a continuum (such as examining first intercourse below 16) – if we look at this continuously perhaps it may be the case that another age is more important.

A section has been added to the methods to clarify the use of categorical age at first intercourse variable rather than it being a continuous variable. This section reads as follows (see highlighted section page 5 & 6 of manuscript):
Age at first sex was collected in various categories (<16 years; 16-19 years and ≥20 years) and not as a continuous variable. This binary split was practically necessary to ensure adequate numbers in the by variable categories for analysis. Descriptive associations between the two main sexual activity indices that we created (age at first sex < 16 years and 3+ sexual partners) are presented as odd ratios derived from logistic regression analyses in Tables 2 and 3. Case-control methods were employed for data presented in Tables 4 and 5. Odds ratios as a measure of association are an appropriate measure in case-control studies even when outcomes are common as in Tables 2 and 3. In the instance where the outcome is uncommon, as is the case in Tables 4 and 5 for cervical cancer risk, (estimated incidence of 30/100,000) this they are most likely to be a good estimate of relative risk. We assessed the association of potential cervical cancer risk factors with age at sexual debut using unconditional multiple logistic regression to adjust for confounding and estimated odds ratios for first sex at age <16 years relative to first sex.