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Prostate-specific antigen as a biomarker of condom failure: comparison of three laboratory assays and self-reported condom use problems in a randomized trial of female condom performance^{☆, ☆☆}

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Abstract

Background—Prostate-specific antigen (PSA), a biomarker for semen exposure, may provide a more objective measure of condom failure than subject self-reports. Methods for measuring PSA vary and their comparability with respect to assessing condom performance has not been adequately evaluated. This study compared results from three different PSA assays of vaginal samples collected by subjects in a randomized clinical trial which compared the performance of female condoms.

Study Design—We selected 30 pairs of pre- and post-coital vaginal samples from subjects who reported condom functionality problems or whose original PSA assay was positive. Samples were retested using three different PSA assays [quantitative enzyme-linked immunoassay (EIA), rocket immune-electrophoresis (RIE) and chromatographic immunoassay (CIA)]. We compared the proportion of condom uses where the post-coital PSA result indicated semen exposure for each of the three assays.

Results—Despite varying levels of sensitivity, the results from all three assays were remarkably consistent. Self-reported condom failures did not correlate well with positive PSA results, suggesting that exclusive reliance on either PSA or user self-report may be inadequate for assessing condom functionality.

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Conclusion—In combination with user self-report of condom failure, PSA testing provides a reliable, objective marker of condom functionality. Studies based on PSA testing may improve on conventional contraceptive clinical trials by offering a more direct assessment of a condom product's ability to prevent semen exposure.

Keywords

Prostate-specific antigen (PSA); PSA Assays; Biomarker; Rocket immuno-electrophoresis (RIE); Chromatographic immunoassay (CIA); Condom failure; Condom self-report; Female condom performance; Quantitative enzyme-linked immunoassay (EIA)

1. Introduction

The evaluation of new condoms that are under consideration for FDA approval as Class II or Class III devices typically relies on user-reported problems (e.g., breakage, slippage) to provide a measure of barrier performance, in addition to standard laboratory tests on the condom. There is continuing concern, however, that studies based exclusively on self-reported measures of condom use and condom failure may yield invalid results because of inaccurate reporting of these events by study participants. Objective biomarkers of semen exposure, most notably prostate-specific antigen (PSA), are valid predictors of exposure to semen and may offer a reliable counterpart to user self-report for assessing condom performance during penile-vaginal intercourse [1]. An increasing number of clinical trials have incorporated testing for PSA levels to assess the performance of male and female condoms [2–12].

Recent studies that have compared PSA measurement with self-reported condom use and use problems suggest that PSA provides a more complete measure of condom failure during vaginal intercourse [13–16]. Methods for measuring PSA, however, vary in characteristics, performance and cost, and their comparability with respect to assessing condom performance has not been adequately evaluated. The current study addressed this problem by evaluating results from three different PSA assays and self-reported condom use functionality problems in the same set of remnant specimens from a randomized clinical trial of female condom performance.

2. Methods

2.1. Description of original trial

The vaginal samples available for retesting for PSA were collected by couples who participated in a Phase I clinical trial comparing the performance of an investigational female condom with a commercial female condom. The study was conducted between June and August 2003, and has been described in detail elsewhere (“Comparative Research Study of the Reality Female Condom and Version 5 of the Reddy Female Condom”, final report, CONRAD, 2004). Briefly, 15 low-risk, monogamous adult couples were asked to use three condoms of one female condom type followed by three uses of the other female condom type, for a total of six uses per couple. Couples were randomized to the order in which they used the two condom types. During the trial, couples were asked to abstain from sexual intercourse for at least 24 h preceding the use of each study condom to minimize the

possibility of elevated pre-coital PSA levels. After use of each study condom, couples completed a detailed questionnaire regarding the functional performance of the condom (e.g., breakage, slippage, etc.) and its acceptability during that use. For each coital act, couples also used study-provided cotton swabs to collect a vaginal sample for detection of semen before insertion and after removal of a study condom. After air-drying the swabs, couples placed them in individual plastic tubes capped with a screw-top lid. The samples were stored at room temperature from collection through the extraction process. In total, 180 vaginal samples were collected across the 90 total sex acts reported by the 15 couples. All trial participants were also asked for consent allowing the pre- and post-coital vaginal samples collected to be tested for PSA. The study protocol for the original trial was approved by the institutional review board at the California Family Health Council.

For the present evaluation, we conducted additional laboratory testing for PSA on one-third of the remnant vaginal samples kept in storage. Specifically, three sets of pre- and post-coital vaginal samples that were collected by 10 of the 15 couples were selected for retesting (i.e., 30 pre–post pairs comprising 60 samples). The sets were selected to oversample condom uses where functionality problems were reported: five sets (15 pre–post pairs) involved use of the investigational condom and five involved use of the commercially available female condom. The samples from all selected sets were complete, and each sample had an adequate remnant specimen available for retesting. All post-coital samples obtained from the inside of the condom indicated the presence of semen based on PSA results, suggesting that ejaculation had occurred.

We preferentially included sets in which a condom was reported by the participant to have failed during intercourse (i.e., broke during intercourse or withdrawal, slipped completely out during intercourse or withdrawal, turned inside out, pushed into the vagina) as well as sets in which the original post-coital rocket immune-electrophoresis (RIE) test result from the 2003 trial was positive for PSA. Included sets were also required to have a corresponding condom use self-report form completed by participants for that coital act. Neither the condom type nor assigned order of use was considered when selecting samples for inclusion.

2.1.1. Testing of remnant specimens for PSA—Samples included in this evaluation were retested for the presence of PSA using three different assays: (1) quantitative enzyme-linked immunoassay (EIA), (2) RIE and (3) chromatographic immunoassay (CIA).

The EIA assay employed was the Abbott Architect system (Abbott Laboratories, Abbott Park, IL, USA). The assay, capable of detecting PSA in concentrations well below 1 ng/mL, was performed at the Centers for Disease Control and Prevention.

The RIE and CIA assays were performed at the Serological Research Institute in Richmond, CA, under the direction of the chief forensic serologist. Testing of the RIE assay followed a protocol that has been described in detail elsewhere [4]. This assay yields a positive test result for PSA concentrations greater than 100 ng/mL. The CIA assay (Seratec, Göttingen, Germany) has a reliable lower limit of PSA detection of at least 4 ng/mL [1]. The presence or absence of a line on a CIA card indicates whether PSA was detected in the sample.

2.1.2. Classification of PSA samples—In order to use PSA as an objective marker of condom failure, we needed to assess whether the PSA value from a post-coital vaginal sample could be used to determine exposure to semen and, if so, what PSA amount would constitute a condom failure. Moreover, the PSA result of the post-coital vaginal sample must measure PSA deposited during use of the condom and not residual PSA deposited during prior acts of intercourse. Thus, the PSA level of the pre-coital vaginal sample must be low for the set of PSA results to be evaluable for the condom use. An increase in the PSA level observed in the post-coital vaginal sample that exceeds a predefined threshold can be attributed to semen exposure resulting from condom failure.

For this evaluation, we devised a classification scheme taking into account the varying limits of PSA detection across the three evaluated assays (Table 1). Evaluable results were defined as a pre-coital vaginal PSA result of <5 ng/mL for the EIA assay, of zero for the RIE assay, and either no line or a faint line for the CIA assay. A positive result for semen exposure for the EIA assay (described below) was defined as a net increase of ≥22 ng/mL in PSA concentration between the pre- and post-coital samples. Similarly, a positive test result for semen exposure was defined as a nonzero PSA result for the RIE assay and a distinct line for the CIA assay.

For the EIA assay, we set our threshold for an evaluable pre-coital PSA concentration of <5 ng/mL based on a reanalysis of results from a previous study of 40 women in Alabama where the decay of PSA concentrations was evaluated following vaginal inoculation with measured amounts of semen [3]. As shown in Appendix, most vaginal samples taken between 24 and 48 h after inoculation with semen yielded a PSA value <5 ng/mL. Setting the maximum evaluable pre-coital PSA concentration at 5 ng/mL minimizes the loss of evaluable condom uses due to residual PSA from prior acts of intercourse. At the same time, the <5 ng/mL PSA limit is still low enough that a net increase of ≥22 ng/mL PSA concentration in the post-coital vaginal sample is likely to represent new semen exposure. We defined semen exposure as at least a 22 ng/mL net increase in post-coital vaginal sample over the pre-coital vaginal sample to minimize the chance that a random variation in sampling could be erroneously interpreted as a condom failure (see Appendix).

2.2. Specimen processing

The remnant vaginal specimens from the 2003 trial were transported to Serological Research (Richmond, CA, USA), extracted with 150 µL of phosphate buffered saline and subsequently retested for PSA using both RIE and CIA. Remaining unused extract was forwarded to the laboratories at the Centers for Disease Control and Prevention for further retesting for PSA using EIA. Test results were forwarded to the California Family Health Council for linkage with user-reported performance information specific to each condom use as obtained from participants during the original trial. Thus, PSA testing of specimens was conducted independent of knowledge of the presence or absence of self-reported user problems.

The main aims of this evaluation were (1) to compare the proportion of condom uses that tested positive for semen exposure for each of the three PSA assays employed by comparing pre- and post-coital values, and (2) to compare PSA assay results with participant self-report

of condom functionality problems (break, slip or other reported condom problems). The study protocol for the present evaluation was reviewed for human subjects concerns and approved as exempt research by institutional review boards at the Centers for Disease Control and Prevention and the California Family Health Council.

3. Results

Pre-coital and post-coital results for the three PSA biomarker assays for the 30 selected condom uses are summarized in Table 2, according to the classification parameters of the EIA result as inevaluable or evaluable uses. Four of 30 condom uses had pre-coital vaginal PSA results exceeding 5 ng/mL on the EIA assay and were thus classified as inevaluable. Three of these four uses were also inevaluable according to the CIA results. However, no condom uses were inevaluable according to the less sensitive RIE assay.

Of the remaining 26 evaluable condom uses, 22 uses had post-coital vaginal PSA results that indicated no new semen exposure. The results for all three assays were consistent with one another, with the exception of one RIE result that was unavailable due to laboratory error (Couple 9, Use 1). Additionally, the largest increase observed in PSA between the pre- and post-coital vaginal results for uses classified as no exposure was under 3 ng/mL (Couple 5, Use 3), well below the semen exposure definition of >22 ng/mL for the EIA assay.

Four of the 26 evaluable condom uses had post-coital vaginal PSA results suggesting semen exposure. The results from the three assays were consistent with each other except for one RIE result, which was unavailable due to laboratory error (Couple 10, Use 3). The lowest EIA PSA result indicative of semen exposure was a result of 5309 ng/mL (also for Couple 10, Use 3), far in excess of the predefined 22 ng/mL threshold for semen exposure.

Table 3 compares the PSA semen exposure status with the couple's self-report of condom use functionality problems for the 26 evaluable condom uses. For the 22 condom uses with no PSA evidence of semen exposure, couples reported that no problems had occurred during 15 uses. However, for the remaining seven uses with no evidence of semen exposure, couples reported one or more functionality problems, three of which were classified as condom "clinical failures" [e.g., outer frame pushed in, breakage as defined in World Health Organization's Female Condom Technical Review. Committee report of meeting, 16–18 Jan 2006, Geneva, Switzerland) (Couple 9, Use 1) and (Couple 10, Uses 1 and 2)]. For the four evaluable condom uses with PSA results indicative of semen exposure, two were associated with reported problems (Couple 8, Uses 1 and 2), one use of which involved slippage and thus constituted a condom clinical failure.

4. Discussion

This study is among the first to evaluate multiple PSA assays to determine semen exposure as a result of condom failure. Previously conducted studies [2–4,7,12–16] have typically employed only a single PSA assay. Our findings indicated a remarkable consistency of biomarker results regarding the presence or absence of semen exposure across the three PSA assays. Furthermore, our evaluation also suggests that there was little degradation in PSA levels of vaginal samples that had been stored at room temperature for over 3 years; the EIA

and CIA assays were still able to detect very low levels of PSA, while the RIE assay results were comparable to those obtained in the original study. The relatively long-term stability of PSA in the vaginal samples as evidenced by the consistency of results across the three PSA assays provides reassurance that these tests can be used in studies of remnant specimens.

Our findings are subject to several limitations. First, we evaluated a relatively small, nonrepresentative sample of condom uses from monogamous couples who were not at risk of pregnancy. We also disproportionately selected those condom uses where functionality problems were reported by couples to enable a more meaningful comparison with PSA assay results. As a result, the overall proportion of uses with detectable PSA by one or more assays and the overall proportion of uses with self-reported functionality problems were artificially high. Second, because we evaluated PSA levels from a single comparative trial of two female condom types, our findings may have limited generalizability to the PSA levels that might be observed in different populations. All of the 30 condom uses evaluated had a post-coital PSA increase of either less than 2.9 ng/mL (indicative of no semen exposure) or greater than 5000 ng/mL (indicative of semen exposure). Because all results evaluated were far from the predefined threshold for defining exposure (>22 ng/mL increase in post-coital PSA), misclassification of exposure is unlikely to have occurred. While this study was not designed to meet biological thresholds for conception or sexually transmitted infection (STI), it is important to note that processed semen samples containing fewer than 10×10^6 spermatozoa are unlikely to result in fertilization [17]. Since the median sperm count in fertile men ranges between 70×10^6 /mL and 100×10^6 /mL [18,19], exposure to a volume of ejaculate <0.1 mL is not likely to result in conception. After inoculation of 0.1 mL of semen, the median vaginal PSA is 273 ng/mL (Appendix Table A1). Thus, our threshold increase of 22 ng/mL represents a conservative definition of semen exposure and may exaggerate the risk of conception. On the other hand, the amount of semen exposure needed to establish an STI is difficult to assess and is likely to vary as a function of the large variation in infectivity across STIs. However, for functionality studies that compare an investigational device with a commercially available control device, identification of a biologically relevant threshold may not be essential to assess the relative protection offered by the study devices, as a quantitative comparison of the distribution of post-coital PSA levels in evaluable condom uses would provide valid information on the relative performance of the devices and could support statements about the superiority or noninferiority of a device compared to the other.

However, the varying sensitivity of the three PSA assays revealed inconsistencies in determining whether a condom use was evaluable based on the PSA level of the pre-coital vaginal sample. According to the relatively insensitive RIE assay, all 30 condom uses were evaluable since RIE did not detect any PSA in the pre-coital vaginal sample. In contrast, the highly sensitive EIA assay, using a cutpoint of >5 ng/mL, classified 4 of the 30 condom uses as inevaluable. Three of these four uses would have also been classified as inevaluable according to the CIA results. On the other hand, if the EIA cutpoint had been lowered to the more conventional threshold of >1 ng/mL, five additional condom uses would have been considered inevaluable. Thus, use of a lower threshold could exert a major impact on the assessment of semen exposure.

Other studies have found that, while most vaginal samples collected more than 48 h after reported coitus have PSA concentrations <1 ng/mL, occasional samples may have concentrations as high as 5 ng/mL [1,3]. Setting the maximum PSA concentration allowable in a pre-coital vaginal sample unnecessarily low can have several untoward consequences. First, there is the possible reduction in the sample size and statistical power of the study. Second, true semen exposures could be excluded from the analysis. For example, a pre-coital vaginal sample with a PSA concentration barely above the evaluable limit (e.g., 6 ng/mL) could cause the exclusion of a post-coital vaginal sample with a PSA concentration >100,000 ng/mL, a clear indication that the condom had failed to prevent semen exposure during coitus. This could lower the overall estimate of the frequency of semen exposure. The lowering of the semen exposure estimate would be especially pronounced if couples at greatest risk of semen exposure also had more frequent intercourse which led to a high proportion of their results being excluded from the analysis because of residual PSA from recent coitus. On the other hand, we would not want to include uses where the pre-coital PSA concentration interferes with the ability to detect subsequent semen exposure due to a condom failure. Setting the evaluable pre-coital PSA concentration threshold at 5 ng/mL is a reasonable compromise between the competing factors.

The comparison of the PSA results with self-reported condom use problems suggests that exclusive reliance on either PSA biomarkers or user self-report may be inadequate for assessing condom functionality. Consistent with other studies [4,7], we found that coital acts in which participants reported functionality problems with condoms did not necessarily correspond to those acts with PSA results indicative of semen exposure. This could be due to sampling error, participant noncompliance (e.g., failure to submit vaginal samples for the reported use), the timing/absence of ejaculation, or functionality problems that did not impair the condom's ability to act as an effective barrier to semen (e.g., tear at the rim of the condom). Likewise, coital acts in which participants reported no condom functionality problems did not necessarily correspond with PSA results indicative of no semen exposure. Possible explanations include participants' inability to notice functionality problems and failure to report the problem accurately.

Although this study was limited to two female condom types, our findings suggest a meaningful role for PSA biomarkers in evaluating the clinical performance of any new male or female condom product. In addition to clinical functionality studies (i.e., breakage and slippage) that have served as the standard for assessing condom performance [1–4,7], PSA could be incorporated to further standardize evaluation criteria across condom types and across studies. Specifically, with the advent of novel designs for male and female condoms, our results suggest PSA could be used to help assess the relative importance of various failure modes given that the incidence of self-reported user problems may vary in different populations and settings [11].

5. Conclusion

EIA, RIE and CIA assays yielded consistent results assessing semen exposure following condom use, although the EIA and CIA assays were far more sensitive than the RIE. In combination with conventional self-report of condom problems and failure modes, PSA

offers an objective marker of condom functionality. PSA testing enables detection of semen exposure in the absence of self-reported condom problems, while user self-report enables detection of potentially important condom functionality problems in the absence of semen exposure. Both provide key information for better understanding condom performance for prevention of pregnancy and sexually transmitted infection (STD). Further research should investigate how biomarker and self-reported measures can be jointly incorporated into studies to improve assessment of condom performance. For example, the strength of their combined use may eventually make it feasible to have enhanced functionality studies supplant conventional contraceptive efficacy studies where prohibitively large sample sizes and their associated costs, study duration, recruitment difficulties and low participant compliance pose significant barriers to making improved condom products available to consumers in a timely manner. Finally, measurement of post-coital semen exposure using a highly sensitive PSA assay may be more pertinent to evaluating an experimental condom's capacity to prevent disease or pregnancy than results from a contraceptive clinical trial relying on STI or pregnancy outcomes and self-reported data.

Appendix

Definition of a minimum increase in the PSA concentration in vaginal fluid is desirable to prevent counting false-positive exposures. To illustrate the problem, we have reanalyzed the data from the measured semen exposure study (Ref. [3]). The results of these analyses are displayed in Appendix Tables A1 and A2.

Table A1 confirms that PSA values are very low and usually <5 ng/mL 24 h after exposure and that the mean PSA values increase dramatically immediately after exposure to semen. The variance of PSA measurements increases with the mean value. Thus, while we can expect that PSA will be very low and almost always below 1 ng/mL, if there is a long period of abstinence prior to collecting the pre-coital sample (first row of Table 1), it is possible to detect low PSA values (between 1 and 14.9 ng/mL) in a small proportion of cases when the interval is short and even at 24 h (last row of Table 1). Selecting an evaluability threshold of 5 ng/mL for the pre-coital vaginal PSA minimizes the number of false-positive tests that result in excluding sex acts with true exposure from the analysis.

Table A2 shows the difference in PSA values between two swabs collected by the same woman at the same time. The last row of Table A2 provides the rationale for the minimum 22 ng/mL increase requirement for assessing a new exposure, which corresponds to the 95th percentile of the distribution of differences between PSA values for swabs taken at the same time 24 h after exposure to 1000 mL of semen. Thus, if the last exposure was to a large amount of semen, it is possible that the pre-coital and post-coital swabs will vary by up to 22 ng/mL by chance alone. This criterion was used in evaluating semen exposure in some studies [6,10], while other studies employed a 15 ng/mL difference [9,11]. Changing the minimum difference from 22 to 15 ng/mL would change the probability of a false-positive exposure assessment by a small amount.

It should be noted that the mean increase after a 10- μ L semen exposure was 175. Thus, even a very small volume of semen would be expected to result in an increase in PSA greater than 22.

Table A1
Distribution of PSA (ng/mL) in the extraction fluid of vaginal swab samples collected by 40 women before and after exposure to measured amounts of semen

Exposure and sampling	<i>n</i>	Mean	SD	5th percentile	Median	95th percentile
Before or 48 h after any exposure	444	0.2	0.8	0.0	0.1	0.9
24 h after 10 μ L	80	0.1	0.2	0.0	0.1	0.4
24 h after 100 μ L	76	0.8	2.7	0.0	0.1	4.2
24 h after 1000 μ L	66	2.5	7.9	0.0	0.2	14.9
Right after 10 μ L	80	175.0	322.0	0.1	53.0	905.0
Right after 100 μ L	76	1537.0	2232.0	0.0	273.0	5452.0
Right after 1000 μ L	66	6025.0	4466.0	11.4	5,016.0	10,279.0

Table A2
Distribution of differences in PSA (ng/mL) within pairs of swab samples collected simultaneously

Exposure and sampling	<i>n</i>	Mean	SD	5th percentile	Median	95th percentile
Before or 48 h after any exposure	222	0.26	0.94	0.00	0.03	0.80
24 h after 10 μ L	120	0.08	0.13	0.00	0.03	0.39
24 h after 100 μ L	114	0.42	1.50	0.00	0.04	4.73
24 h after 1000 μ L	99	2.62	9.52	0.02	0.15	21.70

References

1. Mauck CK, Doncel GF. Biomarkers of Semen Exposure Clinical Working Group. Biomarkers of semen in the vagina: applications in clinical trials of contraception and prevention of sexually transmitted pathogens including HIV. *Contraception*. 2007; 75:407–19. Epub 2007 Apr 30. [PubMed: 17519146]
2. Lawson ML, Macaluso M, Bloom A, Hortin G, Hammond KR, Blackwell R. Objective markers of condom failure. *Sex Transm Dis*. 1998; 25:427–32. [PubMed: 9773437]
3. Macaluso M, Lawson L, Akers R, et al. Prostate-specific antigen in vaginal fluid as a biologic marker of condom failure. *Contraception*. 1999; 59:195–201. [PubMed: 10382083]
4. Walsh TL, Freziers RG, Nelson AL, Wraxall BG, Clark VA. Evaluation of prostate-specific antigen as a quantifiable indicator of condom failure in clinical trials. *Contraception*. 1999; 60:289–98. [PubMed: 10717781]
5. Lawson ML, Macaluso M, Duerr A, et al. Partner characteristics, intensity of the intercourse, and semen exposure during use of the female condom. *Am J Epidemiol*. 2003; 157:282–8. [PubMed: 12578797]
6. Macaluso M, Lawson ML, Hortin G, Duerr A, Hammond KR, Blackwell R, et al. Efficacy of the female condom as a barrier to semen during intercourse. *Am J Epidemiol*. 2003; 157:289–97. [PubMed: 12578798]

7. Walsh TL, Freziers RG, Peacock K, et al. Use of prostate-specific antigen (PSA) to measure semen exposure resulting from male condom failures: implications for contraceptive efficacy and the prevention of sexually transmitted disease. *Contraception*. 2003; 67:139–50. [PubMed: 12586324]
8. Walsh TL, Freziers RG, Peacock K, et al. Effectiveness of the male latex condom: combined results for three popular condom brands used as controls in randomized clinical trials. *Contraception*. 2004; 70:407–13. [PubMed: 15504381]
9. Galvao LW, Oliveira LC, Jua D, et al. Effectiveness of female and male condoms in preventing exposure to semen during vaginal intercourse: a randomized trial. *Contraception*. 2005; 71:130–6. [PubMed: 15707563]
10. Macaluso M, Blackwell R, Jamieson DJ, et al. Efficacy of the male latex condom and of the female polyurethane condom as barriers to semen during intercourse: a randomized clinical trial. *Am J Epidemiol*. 2007; 166:88–96. [PubMed: 17420182]
11. Chen MP, Macaluso M, Blackwell R, et al. Self-reported mechanical problems during condom use and semen exposure. Comparison of two randomized trials in the United States of America and Brazil. *Sex Transm Dis*. 2007; 34:557–62. [PubMed: 17417133]
12. Bahamondes L, Diaz J, Marchi NM, et al. Prostate-specific antigen in vaginal fluid after exposure to known amounts of semen and after condom use: comparison of self-collected and nurse-collected samples. *Hum Reprod*. 2008; 23:2444–51. [PubMed: 18664473]
13. Gallo MF, Behets FM, Steiner MJ, et al. Prostate-specific antigen to ascertain reliability of self-reported coital exposure to semen. *Sex Transm Dis*. 2006; 33:476–9. [PubMed: 16865047]
14. Gallo MF, Behets FM, Steiner MJ, et al. Validity of self-reported ‘safe sex’ among female sex workers in Mombasa, Kenya—PSA analysis. *Int J STD AIDS*. 2007; 18:33–8. [PubMed: 17326860]
15. Gallo MF, Steiner MJ, Hobbs MM, et al. Predictors of unprotected sex among female sex workers in Madagascar: comparing semen bio-markers and self-reported data. *AIDS Behav*. 2010; 14:1279–86. [PubMed: 20625928]
16. Minnis AM, Steiner MJ, Gallo MF, et al. Biomarker validation of reports of recent sexual activity: results of a randomized controlled study in Zimbabwe. *Am J Epidemiol*. 2009; 170:918–24. Epub 2009 Sep 9. [PubMed: 19741042]
17. Miller DC, Hollenbeck BK, Smith GD, et al. Processed total motile sperm count correlates with pregnancy outcome after intrauterine insemination. *Urology*. 2002; 60:497–501. [PubMed: 12350496]
18. Irvine DS. Epidemiology and aetiology of male infertility. *Hum Reprod*. 1998; 13(suppl_1):33–44. [PubMed: 9663768]
19. Jørgensen N, Auger J, Giwercman A, et al. Semen analysis performed by different laboratory teams: an intervariation study. *Int J Androl*. 1997; 20:201–8. [PubMed: 9401822]

Table 1
Interpretation criteria for three PSA tests (EIA, RIE and CIA)

Pre-coital test	Evaluable	Inevaluable
EIA ^a	<5 ng/mL	5 ng/mL
RIE ^a	0	>0
CIA ^a	No line, faint line	Clear line
Post-coital test	No exposure	Exposure
EIA	<22 ng/mL above pre-coital	22 ng/mL above pre-coital
RIE	0	>0
CIA	No line, faint line	Clear line

^aEIA, Quantitative enzyme-linked immunoassay; RIE, rocket immuno-electrophoresis; CIA, chromatographic immunoassay.

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Table 2
Listing of pre- and post-coital results of three PSA tests for 30 condom uses

	EIA		RIE		CIA ^a	
	Pre	Post	Pre	Post	Pre	Post
Inevaluable uses (n=4)						
Couple 1 (1) ^b	179.6	128.4	0	0	CL	CL
Couple 1 (2)	191.3	11.54	0	0	CL	CL
Couple 1 (3)	73.8	21.5	0	0	CL	CL
Couple 2 (1)	5.7	0.43	0	0	NL	NL
Evaluable uses (n=26)						
No exposure (n=22)						
Couple 2 (2)	0.4	0.39	0	0	NL	NL
Couple 2 (3)	0.38	0.49	0	0	NL	NL
Couple 3 (1)	0.34	0.47	0	0	NL	NL
Couple 3 (2)	0.44	0.4	0	0	NL	NL
Couple 3 (3)	0.43	0.36	0	0	NL	NL
Couple 4 (1)	0.37	0.39	0	0	FL	FL
Couple 4 (2)	0.37	0.39	0	0	NL	FL
Couple 4 (3)	0.38	0.37	0	0	NL	NL
Couple 5 (1)	0.4	0.51	0	0	NL	NL
Couple 5 (2)	0.38	1.01	0	0	NL	FL
Couple 5 (3)	0.4	3.3	0	0	NL	FL
Couple 6 (2)	0.57	0.75	0	0	NL	NL
Couple 6 (3)	0.51	2.4	0	0	NL	NL
Couple 7 (1)	0.47	0.5	0	0	NL	NL
Couple 7 (2)	0.46	0.47	0	0	NL	NL
Couple 7 (3)	2.03	1.86	0	0	FL	FL
Couple 8 (3)	1.15	2.82	0	0	NL	NL
Couple 9 (2)	0.4	0.41	0	0	NL	NL
Couple 9 (3)	0.41	0.43	0	0	NL	NL
Couple 9 (1)	0.53	0.42	0	^c	NL	NL

	EIA		RIE		CIA ^a	
	Pre	Post	Pre	Post	Pre	Post
Couple 10 (1)	0.47	0.6	0	0	NL	NL
Couple 10 (2)	0.54	1.32	0	0	NL	NL
Exposure ($n=4$)						
Couple 6 (1)	1.7	87,920	0	151,000	NL	CL
Couple 8 (1)	3.98	>100,000	0	168,000	NL	CL
Couple 8 (2)	4.52	>100,000	0	269,000	FL	CL
Couple 10 (3)	0.42	5309	0	<i>c</i>	NL	CL

^aCL, Clear line; NL, no line; FL, faint line.

^bNumber in parenthesis is the sequence of condom use: first, second or third use.

^cDisagrees with EIA result or result unavailable.

Table 3
Evaluable condom uses by PSA exposure and self-reported problems

	PSA exposure status	Self-reported problems
No exposure and no self-reported problem (<i>n</i> =15)		
Couple 2 (2) ^a	No exposure	No problem
Couple 2 (3)	No exposure	No problem
Couple 3 (1)	No exposure	No problem
Couple 3 (2)	No exposure	No problem
Couple 3 (3)	No exposure	No problem
Couple 4 (1)	No exposure	No problem
Couple 4 (2)	No exposure	No problem
Couple 4 (3)	No exposure	No problem
Couple 5 (1)	No exposure	No problem
Couple 5 (3)	No exposure	No problem
Couple 6 (2)	No exposure	No problem
Couple 7 (3)	No exposure	No problem
Couple 8 (3)	No exposure	No problem
Couple 9 (2)	No exposure	No problem
Couple 9 (3)	No exposure	No problem
No exposure and self-reported problem (<i>n</i> =7)		
Couple 5 (2)	No exposure	Pull out
Couple 6 (3)	No exposure	Partial turn inside out and partial slip off during withdrawal
Couple 7 (1)	No exposure	Pullout during withdrawal
Couple 7 (2)	No exposure	Pullout and partial slip out during
Couple 9 (1)	No exposure	Outer frame pushed in and pullout during withdrawal ^b
Couple 10 (1)	No exposure	Broke and outer frame pushed in ^b
Couple 10 (2)	No exposure	Outer frame pushed-in ^b
Exposure and no self-reported problem (<i>n</i> =2)		
Couple 6 (1)	Exposure	No problem
Couple 10 (3)	Exposure	No problem
Exposure and self-reported problem (<i>n</i> =2)		
Couple 8 (1)	Exposure	Slipped out ^b
Couple 8 (2)	Exposure	Pull out and partial slip out

^aNumber in parenthesis is the sequence of condom use: first, second or third condom use.

^bClinical failures.