No Protective Effect of Circumcision on Human Immunodeficiency Virus Incidence

To the Editor—Some troubling points arise from a comparison of the JID article by Lavreys et al. [1] and the report on the same study cohort that was published in AIDS [2]. The introduction does not mention important studies that found no protective role for circumcision (and even a tendency in the opposite direction), such as the study by Laumann et al. [3].

There is a 1-man discrepancy in the number of subjects reported in the 2 articles; the JID article reports 746 subjects plus 10 exclusions, whereas the article in AIDS reports a total of 755 subjects. The multivariate analysis in AIDS gives a 2.3 hazard rate ratio (HRR) with borderline significance for the intact (uncircumcised) subjects ($P = .05; 95\%$ confidence interval [CI], 1.0–5.0). How did it grow to a more significant HRR of 4.0 ($P < .001; 95\%$ CI, 1.9–8.3) in the JID article?

Of the 7 people excluded from the analysis (because of their circumcision status) in the JID article, 6 were partially circumcised. This raises the question of how the authors defined and measured full and partial circumcision. In addition, 1 subject of unknown circumcision status was excluded, raising the question of how a subject’s circumcision status could be unknown. The excluded subjects included 2 seroconverters who should have been analyzed as part of the circumcised group.

In their article in AIDS, the authors wrote, “No sex with men or intravenous drug use was reported.” The reports of no sex with men are unlikely to be accurate, because homosexuality in Kenya—being both an illegal act and a taboo subject—is severely underreported. Nevertheless, homosexuality is fashionable among young men in Kenya, according to the head of the Kenya AIDS Consortium [4], and was also documented among truck drivers [4].

In the JID article, the authors asserted that “no significant correlates of loss to follow-up were identified that were likely to have influenced the results” [1, p. 335]. This statement in the Discussion section of their article contradicts the significant loss to follow-up among drivers and drivers’ assistants (no $P$ value given) mentioned in the Results section. It also contradicts the very significant difference between those who were enrolled in the cohort but were excluded because of lack of any follow-up visit and those who were retained. As stated in AIDS, drivers and drivers’ assistants were more likely to be excluded (32% vs. 20%, $P < .0005$) than were other occupational groups. If 32% means that 32% of the drivers and their assistants who came for the human immunodeficiency virus (HIV) results did not come to any follow-up visit, then the difference is significant at a level $<.0001$. A reader may wonder why the significance level was written as $P < .0005$. According to the multivariate analysis reported in AIDS, the HRR for HIV seroconversion among drivers and drivers’ assistants is 3.9 ($P = .002; 95\%$ CI, 1.7–9.0). In the JID article this HRR is 4.9 ($P < .001; 95\%$ CI, 2.5–9.5). Drivers and their assistants were therefore more likely to be lost to follow-up during all stages of research and were

References


Reprints or correspondence: Dr. Christopher J. Cold, Dept. of Anatomic and Clinical Pathology, Marshfield Clinic, 1000 N. Oak Ave., Marshfield, WI 54449 (coldc@dgabby.mclldclin.edu).

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Christopher J. Cold1 and Hugh Young2

1Department of Anatomic and Clinical Pathology, Marshfield Clinic, Marshfield, Wisconsin; 2Pukerua Bay, New Zealand

any meaningful conclusions. The “law of small numbers” applies. Those 5 or 6 men might have just been unlucky (for example, they might have all patronized the same particularly infectious prostitute). To apply high-powered statistical methods to such a small final subsample with so many unknown variables is to use a sledgehammer to crack a nut. Furthermore, interviewing men at 3-month intervals about their sexual practice exposed the study to unacceptably high levels of faulty memory, even assuming that all subjects tried to tell the whole truth.

Lavreys et al. admit that “because uncircumcised status and ethnicity were so closely correlated, it was not possible to independently assess the effects of circumcision and ethnic origin.” Nor did the authors assess the effects of ethnic origin on other practices that might influence HIV-1 transmission. One such practice is anal sex. Lavreys et al. seem to have assumed that none of the subjects ever had any but vaginal sex and that this is the only means of HIV transmission. An investigation of the truck drivers’ anal sexual (including homosexual) activity and how such activity is affected by ethnicity and religion (both of which affect circumcision status) might cast a completely different light on these results.

Strategies to prevent AIDS are multifaceted and must be implemented in a real world inhabited by fallible humans. For some of the issues involved, see Young [2]. It was irresponsible for Lavreys et al. [1] to “encourage behavioral scientists to conduct acceptability studies...to begin assessing feasibility of circumcision promotion.” Already, and predictably, public media have seized on this recommendation without reference to the many caveats. The average man in the truck will have great trouble understanding that this painful procedure may measurably reduce the rate of transmission of HIV but does not confer significant, let alone complete, protection on him. Given a choice, people prefer to practice unprotected sex and will grasp at any excuse to do so. Promoting circumcision can undo years of safe-sex education and cause HIV rates to skyrocket, whether men are circumcised or not.
also more likely to seroconvert. Drivers and their assistants were more numerous among the circumcised than among the intact (33.3% vs. 12.6%, \( P < .001 \)). Consequently, it seems that the number of seroconverters among the circumcised was artificially lowered and that there is actually no difference between circumcised and intact subjects. The same logic applies to the association of circumcision with genital ulcer disease.

The authors claim that circumcision is not practiced by the Luo, and these people constitute their intact group. In fact the Luo practice a different form of genital mutilation in which the foreskin is retained but the connective tissue (frenulum) between it and the penile shaft is cut [5]. Luos therefore are not intact, and their deformed foreskins cannot be equated with healthy, protective, undamaged foreskins.

Even if the authors were correct in their conclusion, the implementation of their call for circumcision on a massive scale would be both dangerous and unethical. The morbidity and mortality from circumcision in Africa are high [6–9], but this is apparently of no interest to the authors. Their continuous call has already served to justify forced circumcisions in Kenya [10]. The mere idea of cutting off healthy erogenous organs of nonconsenting minors to reduce their risk of getting a disease that is easily preventable by less drastic means is abominable. Will the authors call for the promotion of mastectomies as a population-based intervention to drastically reduce the incidence of breast cancer?

Avshalom Zoossmann-Diskin*

* The Israeli Association against Genital Mutilation, Tel Aviv, Israel

References


* Present affiliation: Department of Haematology and Genetic Pathology, School of Medicine, Flinders University, Adelaide, SA 5001, Australia.

Reply

To the Editor—The inverse association between male circumcision and acquisition of human immunodeficiency virus type 1 (HIV-1) remains controversial, as illustrated by 2 letters in response to our paper [1–3]. Dr. Moench, in a letter published in the February issue, enumerates some of the many reasons that the protective effect of male circumcision on HIV-1 acquisition has gone largely ignored as a potential preventive intervention [4]. We believe that the controversial nature of circumcision is a major reason. Indeed, we stand accused of being irresponsible and unethical in suggesting that circumcision be considered or further studied as a population-based intervention for HIV-1 prevention. We believe that it would be irresponsible to ignore the results of our prospective study showing that uncircumcised men had a 4-fold increased risk of HIV-1 seroconversion.

Our results are consistent with those of other investigators. The majority of studies have found a protective effect of circumcision on acquisition of HIV-1 [5, 6]. Of 38 cross-sectional studies, 27 found a significant relationship, 5 found a trend, 5 found no effect, and 1 found a negative relationship. Of 7 prospective studies, 5 found a significant protective effect of circumcision, and 2 found a trend. Thus, the weight of evidence from studies conducted in a variety of populations in various countries suggests that the protective effect of circumcision on HIV-1 acquisition is real.

Several of Dr. Zoossmann-Diskin’s points concern differences between the 2 articles that reported results from our cohort study of trucking company workers [1, 2, 7]. Our publication in AIDS evaluated correlates of HIV-1 seroconversion, of which circumcision status was one of many variables. Our publication in the JID evaluated the effect of circumcision status on the acquisition of sexually transmitted diseases, including HIV-1. Because these 2 analyses had different aims, the analysis data sets and the biostatistical analysis approaches differed. For example, we excluded men with partial circumcisions \( (n = 6) \) or unknown circumcision status \( (n = 1) \) from our second analysis because we wanted to avoid misclassification for this key variable. Partial circumcision was defined as retention of a portion of the foreskin. We have repeated our analysis after including these 6 partially circumcised men, and our conclu-