



## **Randomized, Controlled Intervention Trial of Male Circumcision for Reduction of HIV Infection Risk: The ANRS 1265 Trial**

### **CITATION**

Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, et al. (2005) Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: The ANRS 1265 trial. *PLoS Med* 2(11): e298.

### **RESEARCH QUESTION**

Does circumcision reduce the risk of young men becoming infected by HIV?

### **THE STUDY DESIGN**

Randomized, controlled, blindly evaluated trial

### **STUDY SETTING**

Orange Farm and surrounding areas, a semi-urban region close to the city of Johannesburg, South Africa

Recruitment took place from July 2002-February 2004

Written informed consent was obtained.

Protocol was reviewed and approved by the University of Wits Human Research Ethics Committee.

Trial was approved by the Scientific Commission of the French National Agency for AIDS research.

### **PARTICIPANTS**

Included: Male between the age of 18 and 24; wished to be circumcised; resided in the Orange Farm area or surrounding areas; understood the nature of the trial; agreed to be randomized to either intervention group or control group; agreed to come to 3 follow-up visits; agreed to answer general health questions and questions related to sexual activity; agreed to have genital examinations; agreed to give blood samples tested for HIV and Syphilis

Excluded: Potential participants with genital ulcerations were temporarily excluded; male to be circumcised; male to have had any contraindication to circumcision

### **INTERVENTIONS**

Intervention Group: Participants were circumcised within a week.

Control: Participants were to wait until the end of the trial to be circumcised.

Participants from both groups had three follow-up visits at the end of M3, M12, and M21. These three follow-up visits defined three sequential periods, M1-M3, M4-M12, and M13-M21, with expected durations of 3, 9, and 9 months respectively. At each visit, participant answered a face-to-face questionnaire, provided a blood sample, had a genital examination and an individual counselling session.

### **OUTCOMES**

Primary: HIV incidence

Secondary: The role of behavioural factors known to be associated with HIV serostatus; Even though not specified as an outcome, syphilis was tested

**RISK OF BIAS** (Risk Scale: Low – Moderate – High)**SELECTION BIAS: Moderate**

Randomisation was described as “Participants requested to participate actively in the random assignment. Each participant was invited by the manager of the centre to choose an envelope containing the group name from a basket of ten envelopes. After each randomisation, a new envelope was added to the basket. This added envelope was taken sequentially from a set of envelopes pre-prepared in such a way that each set of envelopes contained five for the control and five for the intervention arm”. Allocation concealment not reported. Baseline characteristics of participants were similar in both intervention and control groups.

**PERFORMANCE BIAS: Low - Moderate**

*(I.e what else happened that may have affected the result?)*

Participants were unblind. Personnel were blind. At each visit, participants received compensation. Following circumcision, there was a 6-wk period of abstinence.

**DETECTION BIAS: Low - Moderate**

Participants were unblind. Personnel were blind. Three follow-up visits. Face-to-face questionnaire allowed for collection of data on background characteristics and reported sexual behaviour. Face-to-face questionnaire may have resulted in underreporting of sexual behaviour. Genital examination was performed by a trained nurse. Blood samples were tested for HIV-1 and Syphilis. An ELISA screen and two ELISA confirmatory tests were used to test plasma for HIV-1 infection. Samples that were positive on all three ELISAs were regarded as “positive” and all others as “negative”.

**ATTRITION BIAS: Low**

At the interim analysis

	<b>Intervention HIV-</b>	<b>Control HIV-</b>
Started	1546	1582
Completed trial	1446	1431
Loss to follow-up	100 (6.5%)	151 (9.5%)

Analyses were said to have been performed by intention-to-treat.

**STUDY FINDINGS**

Out of 3483 pre-screened 3274 randomised.

**HIV Incidence**

The incidence rate of 0.85 per 100 py in the Intervention group and the incidence rate of 2.1 per 100 py in the Control group gave a RR of 0.40 (0.24-0.68),  $p = 0.00059$ .

When controlling for behavioural factors, including sexual behaviour that increased slightly in the intervention group, condom use, and health-seeking behaviour, the RR was 0.39 (0.23-0.66).

**ADVERSE EVENTS**

Adverse events related to surgery and that occurred in the first month post-surgery were reported for the Intervention group only.

**COMMENTS**

Even though the study shows that the risk of acquiring HIV infection was significantly reduced by 60% in the men who had undergone circumcision, I think more research is needed before we can be sure.

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