

# Circumcision for HIV needs follow-up

The French National AIDS Council (CNS), an independent government advisory body on AIDS issues, last week urged prudence in implementing male-circumcision programmes to reduce the spread of HIV. It cautioned that over-zealous roll out could lead to a false sense of security and exacerbate the problem.

In March, the World Health Organization (WHO) endorsed the promotion of male circumcision as a tool for HIV prevention, alongside condoms and antiretroviral drugs. The move was based on a WHO expert consultation, which concluded that the evidence for the intervention's efficacy was "compelling". Recent criticism of this view has been received with anger (see 'Cutting criticism').

The strongest evidence comes from three recent studies. In 2005, a study<sup>1</sup> of 3,300 heterosexual men living in and around Orange Farm, South Africa, by France's National AIDS Research Agency, showed that circumcising men reduced the risk of infection by 60%. Similar levels of protection were found in 2007 by American-funded studies in Kisumu<sup>2</sup>, Kenya, and Rakai<sup>3</sup>, Uganda.

Taken together with results from observational studies, this is "as convincing evidence as one ever gets in public health," says Helen

Weiss, a statistical epidemiologist at the London School of Hygiene & Tropical Medicine.

But questions remain about the intervention's applicability as a preventative tool on a large scale, says Willy Rozenbaum of the Pierre and Marie Curie University in Paris, who led the CNS study. Rozenbaum questions the speed with which the WHO has acted, and thinks the organization's endorsement — although detailing the caveats — has been misunderstood

in some quarters as saying circumcision is a "miracle solution".

Rozenbaum notes that the effect of circumcision on HIV prevalence in a population will depend on a host of social and cultural factors. There is a real risk, he says, that after circumcising men may have a false sense of security and increase their number of partners, or dispense with condoms. The report also points out that circumcision leaves men more vulnerable to



**Circumcision reduces the spread of HIV, but needs to be combined with public education.**

## Cutting criticism

A controversial recent publication argues that the evidence from cross-country statistics does not support male circumcision as a key intervention against HIV. But according to several angry AIDS researchers, the paper merely shows that the peer-review system of the journal that published it, *PLoS One*, failed on this occasion. The study, they say, is flawed and, moreover, concerns a debate over statistical techniques that, in this instance, have been largely superseded by more powerful clinical trials.

"Size matters: the number of prostitutes and the global HIV/AIDS pandemic," by John Talbott<sup>4</sup>, a former investment banker, was published on 20 June. In a comparison of HIV prevalence across 77 countries, it argues that the effect of male circumcision is overstated, and that the prevalence

of prostitution is the dominant factor. Among other things, Talbott takes issue with the way that some previous studies have 'weighted' circumcision figures according to the size of national populations.

Ecological analyses such as Talbott's, which look for correlations between HIV prevalence and various factors, are useful for generating hypotheses, but don't prove anything, says Anne Buvé, an expert in HIV prevention at the Institute of Tropical Medicine in Antwerp, Belgium. In her opinion, the paper consists of "sweeping generalizations that add nothing substantial to our state of knowledge".

In understanding the effect of male circumcision "we are past this sort of ecological research", says Buvé, pointing to recent randomized clinical trials showing a major protective effect. Talbott's

paper mentions one such study in passing. Talbott declined to comment for publication.

"Our data were never intended to be used in this way," says Buvé, a co-author on the 2006 paper from which Talbott took the preliminary data that he draws many of his

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figures on prostitution from<sup>5</sup>. A host of factors leads to under- and overestimates of the number of prostitutes nationally. There are also problems in using the Muslim proportion of the population as a surrogate for the level of circumcision, experts say.

Nonetheless, the press release made available by *PLoS One*

describes the paper as containing "important findings that should impact policy decisions". It recommends "mandatory" testing and treatment of prostitutes, adding that opposition to such control methods is comparable to "claiming that a rabid dog must be allowed to run free in a neighborhood regardless of how many men women and children he infected and killed".

These are Talbott's words. It is *PLoS One*'s normal practice to publicize any text supplied by the author as a press release, adding a brief disclaimer at the end.

Talbott's paper is a baptism of fire for the young journal, launched in August 2006. The journal is testing a new publishing model, whereby papers are published quickly after being assessed by peer reviewers on technical soundness alone. The idea is that the papers' reliability

infection if they don't refrain from having sex until the wounds have fully healed and that women may find it more difficult to insist on condom use with circumcised men.

Given these concerns, the CNS calls for implementation schemes to be accompanied by public education as well as research that considers the behavioural and cultural factors that affect HIV transmission. Such research is already under

**"The impact of circumcision on HIV prevalence will depend on a host of social and cultural factors."**

way at various sites. At Orange Farm, a 5-year follow-up study of 30,000 people will look at how the implementation of a real circumcision campaign affects risk behaviours, and

overall HIV prevalence in the population.

Tim Farley, an official in the WHO's HIV prevention team in Geneva, says he "absolutely agrees" with the CNS view, and the need for such research. "These are concerns that need to be studied, but they are not a reason to stop," he says. "We must move ahead in the knowledge that there could be riskier behaviour."

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1. Auvert, B. *et al.* *PLoS Med.* **2**, e298 (2005).
2. Bailey, R. C. *et al.* *Lancet* **369**, 643–656 (2007).
3. Gray, R. H. *et al.* *Lancet* **369**, 657–666 (2007).
4. Talbot, J. R. *PLoS One* **2**, e543 (2007).
5. Vandepitte, J. *et al.* *Sex. Transm. Infect.* **82** (Suppl. 3), iii18–iii25 (2006).

and significance will be further ascertained by online comments and discussion by other scientists that are posted on *PLoS One*'s website after publication.

"The paper is total drivel, it should have been picked up in the review process," claims Tim Farley, an official in the World Health Organization's HIV-prevention team in Geneva. "And coming from *PLoS One* gives [the views in the press release] a public perception of validity. In public health there are severe dangers in such stuff getting through."

"There are lessons to be learned from all papers that we publish; we are a young journal," says Chris Surridge, *PLoS One*'s managing editor, adding that its peer-review model is constantly under refinement. "We are feeling our way."

In this case, the paper was reviewed by a member of *PLoS One*'s editorial board and one external referee. The review criteria of *PLoS One* are that "the data are sufficient to be published and the conclusions not radically overstated by the data," Surridge explains. "I hope we get some discussion of this paper [in the online post-publication comments]."

**D.B. and L.O.-S.**



## Plan for bomb design falters

Congress is losing its appetite for the Reliable Replacement Warhead (RRW), a nuclear bomb conceived as a way to allow weapons physicists to ply their trade in a weapons-ban world. Instead, Capitol Hill is calling for a full review of the US nuclear programme.

After its 4 July recess, the House of Representatives will vote on a bill that would eliminate funding for the RRW from the 2008 budget. The Bush administration had requested \$89 million for the project. And committees in both the House and the Senate are drafting legislation that would limit work on the new design to feasibility and cost assessments. That legislation would also call for a review of the need for nuclear weapons.

Until last autumn, the RRW programme enjoyed bipartisan, if tentative, support in Congress. The project, which aims to design a weapon more robust than its predecessors but that requires no testing (see *Nature* 442, 18–21; 2006), was seen by congressional appropriators as a way to cut the cost of maintaining the nuclear stockpile. Some also liked the idea that it could reduce the size of the stockpile.

But a costly plan released in December on the future of the nuclear weapons complex suggested it would be hard to realize any savings from the RRW. And a study showing that existing warheads will last for at least another 50 years (see *Nature* 444, 660–661; 2006) made the new bomb seem less necessary. Billions have been spent on 'stockpile stewardship' to prolong the lives of current warheads, Congressman Pete Visclosky (Democrat, Indiana) said on 19 June. Now, he said, "We are told: 'Let's do something else'."

"I don't think it is asking too much for a comprehensive nuclear strategy before we build a new nuclear weapon," added Visclosky, who chairs the subcommittee that withdrew the RRW funding.

A separate defence bill working its way through Congress might provide such a strategy. Versions of the authorization bill, which would set out policy but not funding, call for a comprehensive review of US nuclear policy. This would assess whether the size of the stockpile is appropriate in the post-cold-war era and whether an RRW would be necessary for a credible deterrent.

Arms-control advocates are elated by the move. "What Congress has done is really stunning," says Philip Coyle, a senior adviser at the Center for Defense Information, a think-tank in Washington DC. The current US stockpile is far too bloated, he adds.

But supporters of the RRW say that Congress has undercut the weapons programme. Expertise will be lost unless a new generation can design weapons, says Paul Robinson, former director of Sandia National Laboratories in Albuquerque, New Mexico. He notes that the House budget for nuclear weapons is also \$400 million lower than that enacted for 2007. "I feel absolutely sure that members of Congress have not looked at the strategic consequences of what they are doing," he says.

The RRW is not done yet. This week, the Senate begins drafting its own version of the appropriations bill. Senator Pete Domenici (Republican, New Mexico) has vowed to win back support for the programme. A final version of the bill, to be worked out between the House and Senate, is expected sometime in the autumn.

**Geoff Brumfiel**

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