# Circumcision and cervical cancer

# Is there a link?

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Castellsagué X, Bosch X, Munoz N, Meijer C, Shah K, De Sanjosé S, et al. Male circumcision, penile human papillomavirus infection, and cervical cancer in female partners. N Engl J Med 2002;346:1105-12.

## Research question

Does circumcision reduce the risk of penile human papillomavirus (HPV) infection in a man and cervical cancer in his female partner?

# Type of article and design

Seven case-control studies.

#### Relevance to family physicians

We are often asked by new parents about the benefit and harm of male circumcision. Some studies have suggested that circumcision reduces risk of urinary tract infections, penile cancer, and HIV infection. Poor cosmetic results, removing too much or too little foreskin, or uneven removal of the foreskin are potential adverse outcomes; occasionally circumcision results in meatal stenosis. Despite the reported benefits of circumcision, the most common reason for doing it is that the father was circumcised.<sup>2</sup>

There is much literature on male circumcision, and several medical organizations have published policy statements on the topic. The Canadian Paediatric Society does not recommend routine neonatal circumcision<sup>2</sup> nor does the American Academy of Pediatrics<sup>3</sup> or the American Academy of Family Physicians.<sup>4</sup> An interesting website, Circumcision Information and Resource Pages (www.cirp.org) provides the policy statements of English-speaking countries and extensive references for physicians and

parents. Non–English-speaking nations have no policy on the subject because they do not routinely circumcise male infants.

In Canada, it is estimated that 48% of men have been circumcised,<sup>2</sup> but it is difficult to get accurate statistics because almost no health insurance plans in Canada pay for circumcision

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any longer. In the United States, 61% pay; in Australia, 70% pay;<sup>2</sup> and in the United Kingdom, 24% pay.<sup>2</sup> While circumcision is the most commonly performed surgical procedure in the United States,<sup>1</sup> it is uncommon in northern European countries, Central and South America, and Asia.

Human papillomavirus is not currently under systematic surveillance in Canada, so its prevalence is unknown.<sup>5</sup> In the United States, an estimated 5.5 million people become infected with HPV each year, and an estimated 20 million are currently infected.<sup>6</sup>

Is there new evidence that will help guide Canadian family physicians and parents in decisions about neonatal circumcision?

#### Overview of study and outcomes

Seven case-control studies, five involving invasive cervical cancer and two involving cervical carcinoma in situ, looked at data on 3790 women to evaluate a connection between circumcision and HPV in men and cervical cancer in their female partners. The studies were conducted in Spain, Colombia, Brazil, Thailand, and the Philippines. Researchers recruited 1896 women with cervical cancer and 1894 controls either from the general population or from the same hospitals as the women with cervical cancer. The men were the husbands or stable partners of these women. Of the 984 partners of study women and 937 partners of controls who were interviewed, 82.0% and 76.5%, respectively, provided cytologic specimens.

Diagnosis of HPV in men was determined by polymerase chain reaction assay from swabs of the distal urethra and external surface of the glans and coronal ring. Diagnosis of cervical cancer in women was determined from cervical swabs. Variables in

> men and women included age at first intercourse, level of education, lifetime number of sexual partners, condom use, and (for men) self-reported frequency of genital washing after intercourse, sexual intercourse with prostitutes, and physician's assessment of men's genital hygiene.

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# CRITICAL APPRAISAL \* ÉVALUATION CRITIQUE

#### Results

Overall prevalence of circumcision was 19.3%: circumcised men had higher levels of education and reported less frequent genital washing compared with uncircumcised men (40.5% vs 23.0%). In all groups, circumcised men had lower prevalence of HPV (5.5% vs 19.6%). With circumcision, the odds ratio (OR) for penile HPV was 0.37 (95% confidence interval [CI] 0.16 to 0.85) after adjusting for age, level of education, age at first intercourse, lifetime number of sexual partners, and frequency of genital washing after sex. This result persisted whether or not female partners had cervical HPV or cancer. Apart from being uncircumcised, the only other significant risk factor for penile HPV was the number of men's sexual partners.

Female partners of circumcised men had a moderate but nonsignificant decrease in risk of cervical cancer (OR 0.72, 95% CI 0.49 to 1.04). This inverse association was not changed by any of the women's variables. Monogamous female partners of circumcised men at high risk of HPV (intercourse before age 17, six or more sexual partners, and history of contact with prostitutes) had a significant reduction in risk of cervical cancer (OR 0.18, 95% CI 0.04 to 0.89). If both male and female partners were at low risk of infection, the women's risk of cervical cancer was similar whether their partners were circumcised or uncircumcised (OR 1.61, 95% CI 0.86 to 3.02)

#### Analysis of methodology

This paper pools a group of case-control studies and has the usual limitations of retrospective studies. By starting with the outcome of cervical cancer and HPV infection and looking back to see whether circumcision was an associated factor, unknown confounding variables might not have been taken into account. Still, I think this is a good epidemiologic study. Numbers of subjects and controls are large, and variables known to be related to HPV and cervical cancer have been measured.

Participants were not from Canada and, therefore, might not be similar to our own population. Circumcision was self-reported: accuracy was assessed by medical examination of 43% of the men and confirmed in 95% of those. The findings in this study are consistent with those of other studies that show an association between male circumcision and reduced risk of HIV infection and other common sexually transmitted diseases.

### Application to clinical practice

Before reading this study, I usually told parents that there is no medical reason for circumcision and that

it is based on parental preference. This paper has made me rethink that stance. If we could predict at birth that a baby boy was likely to engage in highrisk sexual behaviour, I might recommend circumcision. We are also reminded of the protective effect against cervical cancer of low-risk sexual behaviour. A cohort study that looked prospectively at circumcised and uncircumcised boys would help clarify any cause-effect relationship between circumcision and cervical cancer. This would take many years to accomplish. In the meantime, the debate about circumcision continues.

#### **Bottom line**

- Male circumcision is associated with reduced risk of genital HPV infection in men whether or not their female partners have cervical HPV or cervical cancer.
- · Circumcision is associated with reduced risk of cervical cancer in women with high-risk sexual
- In men with low-risk sexual behaviour and monogamous female partners, circumcision makes no difference to the risk of cervical cancer.

#### Points saillants

- La circoncision masculine est associée à une réduction des risques d'infection génitale au papillomavirus chez l'homme, que leur partenaire féminine ait ou non une infection du col au papillomavirus ou un cancer du col de l'utérus.
- La circoncision est associée à une réduction des risques de cancer du col chez la femme ayant des partenaires sexuels à risque élevé.
- Chez les hommes ayant un comportement sexuel à faible risque et une seule partenaire, la circoncision n'influence pas le risque de cancer du col.

#### References

- 1. Pfenninger JL, Fowler GC. Procedures for primary care physicians. St Louis, Mo: Mosby; 1994.
- 2. Fetus and Newborn Committee, Canadian Paediatric Society. Neonatal circumcision revisited. Can Med Assoc J 1996;154(6):769-80.
- American Academy of Pediatrics. Circumcision policy statement (1999). Pediatrics 1999;103(3):686-93.
- 4. American Academy of Family Physicians. Position paper on neonatal circumcision. Leawood, Kan: American Academy of Family Physicians; 2002.
- 5. Health Protection Branch, Laboratory Centre for Disease Control, Sexually transmitted disease surveillance in Canada. Annual report. Ottawa, Ont: Health Canada; 1995.
- 6. Centers for Disease Control and Prevention. Tracking the hidden epidemics: trends in STDs in the United States. Atlanta, Ga: Centers for Disease Control and Prevention: 2000.