

RESEARCH HIGHLIGHT

Circumcision reduces prostate cancer risk

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There is a strong negative correlation between prostate cancer and circumcision rate across 181 countries ($P < 0.0001$). Adding to the large protective effect of circumcision seen in small studies over the past six decades, a recent large study in Seattle has shown a smaller protective effect. If verified by other large studies elsewhere, the finding would add to the wide array of benefits conferred by this safe, simple procedure that is best performed in infancy.

Researchers at the Fred Hutchinson Cancer Research Center in Seattle, WA, USA have reported recently that circumcision reduces the risk of aggressive prostate cancer by 18% and less aggressive prostate cancer by 12%, but only for circumcision prior to sexual debut.¹

The new findings support data from small studies dating back six decades. For example, in 1951, it was reported that of men operated on for prostatic obstruction only 1.8% of obstructions were cancerous in Jews (circumcised), compared with 19% for non-Jews.² Subsequent research in Sweden,³ Southern California⁴ and the United Kingdom⁵ found circumcised men had a 50%–62% lower prevalence of prostate cancer than uncircumcised men. Consistent with these findings, there is an inverse correlation between prevalence of circumcision and prostate cancer incidence in 181 countries for which sufficient data are available ($P < 0.0001$; **Figure 1**). While striking, such geographical comparisons should, of course, be interpreted with caution. Other factors, such as heritability, somatic mutations and a diet high in red meat also contribute to prostate cancer.

While the increase in risk seen in the new study was much lower than reported

previously, its much larger size (1754 cases and 1645 controls) compared with earlier studies (100–300 per group) reinforces the reliability of the association. The findings should prompt additional large studies in other populations. Will these show a level of protection similar to that seen in Seattle, or will they find stronger protection as in older studies?

The finding of protection only in men circumcised in infancy is consistent with the well-known association of history of any sexually transmitted infections (STIs) with a 48% increase in risk of prostate cancer.⁶ The authors suggest that circumcision's ability to protect against STIs may explain this finding. Infections establish a state chronic active inflammation leading to tissue damage. Inflammation has been implicated in various cancers in other organs.⁷ Infections of various kinds are known to be responsible for 17% of cancers worldwide.⁸ Once the STI(s) that contribute to prostate cancer have been identified, this percentage may rise.

A variety of different STIs have been identified in the prostate. One is HPV, which is the cause of virtually all cervical cancers and half of penile cancers.⁹ Uncircumcised men are at increased risk of penile infection by high-risk HPV types and their female sexual partners have a higher risk of cervical cancer.¹⁰ Penile cancer is a disease confined largely to uncircumcised men, affecting approximately 1 in 1000 over the lifetime.⁹ Although high-risk HPV types have been associated with an increased risk of prostate cancer as well, findings have been inconsistent (see review⁹). A history of gonorrhoea and Chlamydia has also been associated with prostate cancer, although sexually transmitted urethritis is not significantly lower in circumcised men. Syphilis and herpes simplex type 2 are associated with prostate cancer and are less prevalent in circumcised men. The polyomavirus BKV and the molony murine leukemia retrovirus homologue XMRV have been reported by some, but not all, researchers to be present

in prostate cancer specimens (see review⁹). The most common bacterial STI, *Trichomonas vaginalis*, was positively correlated with risk of prostate cancer later in life in the US Physicians Health Study,¹¹ risk being twofold higher for advanced prostate cancer and threefold higher for terminal cases. *T. vaginalis* is symptomless in most men infected with it, and a randomized controlled trial found circumcision reduced infection risk by 59%.¹²

Circumcision also protects against infections of the urinary tract (see review¹³), although since this is provided for boys and men, yet the new findings show that men circumcised after sexual debut are not protected against prostate cancer, the bacteria responsible for urinary tract infections would seem not to contribute to prostate cancer. Balanoposthitis and balanitis are inflammatory conditions seen more commonly in uncircumcised males,¹³ and treatment of these is a common reason for circumcision at any age. Whether the yeast fungi species responsible are capable of migrating up the urinary tract to the prostate, and, if so, might then contribute to prostate cancer, remains to be investigated.

Since prostate cancer affects approximately one in six males, based on the new US findings, circumcision should result in a substantial reduction in the 0.3 million cases of prostate cancer in the United States each year. Based on earlier data showing an approximately 60% increase in prostate cancer risk from lack of circumcision and a 40% prevalence of uncircumcised US men at the average age of prostate cancer diagnosis, previous calculations showed that the single risk factor of lack of circumcision contributed 24% (45 000) of cases.¹⁴ It was further predicted that there would be a saving of \$0.8 billion to the US health system for treatment and terminal care of prostate cancer cases if all men in the United States were circumcised.

The Seattle study provides even more reason for parents to opt for this 'surgical vaccine' to protect their baby boy from health

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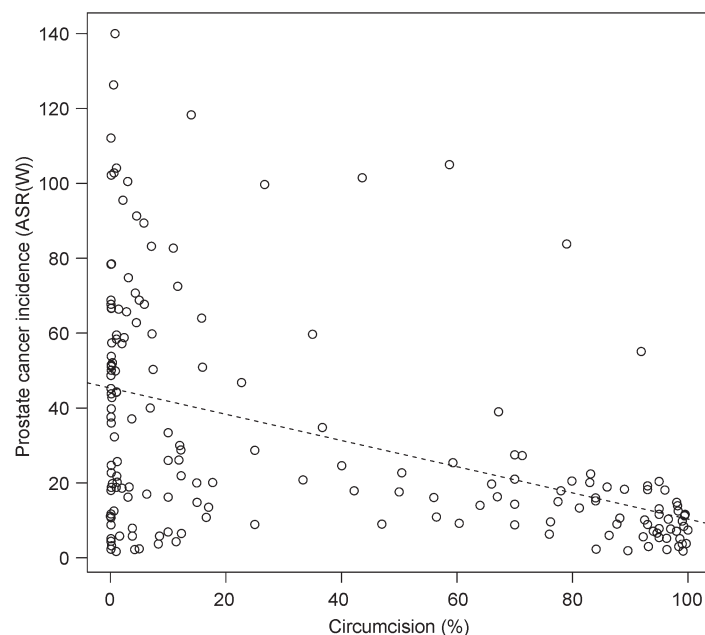


Figure 1 Plot showing association between estimated circumcision prevalence and prostate cancer incidence in 181 countries for which data on each factor are available (obtained on 9 Apr 2012 from <http://globocan.iarc.fr/> and <http://www.circs.org/index.php/Reviews/Rates/Global>). Dashed line shows best fit ($r=0.46$, $P=8.4 \times 10^{-11}$). The analysis involved approximately 900 000 prostate cancer cases.

problems in infancy and over his lifetime. The finding that circumcision in infancy, but not later, reduces prostate cancer risk, adds to the multitude of cogent evidence-based arguments that, in order to confer the greatest lifelong protection, infancy is the optimum time for circumcision.¹⁵

In Asia, there is considerable variability in circumcision rates between different countries. Most males in South Korea and the Philippines get circumcised either in infancy, childhood or adolescence, as is also the case for countries such as Indonesia and Malaysia with large Muslim populations. In China, Japan and many South-east Asian countries, circumcision is uncommon, so presenting males with an increased risk of prostate cancer, penile cancer, various STIs and other conditions that circumcision protects against.¹³ For those countries with low circumcision rates, implementation of circumcision programs, ideally in infancy, will provide greater financial savings to the health system of each, as well as saving lives. Given the high prevalence of prostate cancer, such savings should be enormous. Further savings for lives lost, suffering endured and costs imposed will apply to

women because of the fact that male circumcision reduces their risk of cervical cancer, infertility and various STIs.

The scientific literature on the ability of circumcision to protect against various common conditions is growing at an exponential pace. As a result, prior knowledge and attitudes are quickly being superseded. The new evidence confirming circumcision's protective effect against prostate cancer provides further economic and health grounds for infant circumcision.

- 1 Wright JL, Lin DW, Stanford JL. Circumcision and the risk of prostate cancer. *Cancer*, e-pub ahead of print 12 March 2012; doi: 10.1002/cncr.26653.
- 2 Ravich A, Ravich RA. Prophylaxis of cancer of the prostate, penis, and cervix by circumcision. *NY State J Med* 1951; **51**: 1519–20.
- 3 Apt A. Circumcision and prostatic cancer. *Acta Med Scand* 1965; **178**: 493–504.
- 4 Ross RK, Shimizu H, Paganini-Hill A, Honda G, Henderson BE. Case-control studies of prostate cancer in blacks and whites in southern California. *J Natl Cancer Inst* 1987; **78**: 869–74.
- 5 Ewings P, Bowie C. A case-control study of cancer of the prostate in Somerset and east Devon. *Br J Cancer* 1996; **74**: 661–6.

- 6 Taylor ML, Mainous AG 3rd, Wells BJ. Prostate cancer and sexually transmitted diseases: a meta-analysis. *Fam Med* 2005; **37**: 506–12.
- 7 Correa P. Is prostate cancer an infectious disease? *Int J Epidemiol* 2005; **34**: 197–8.
- 8 de Marzo AM, Platz EA, Sutcliffe S, Xu J, Grönberg H *et al.* Inflammation in prostate carcinogenesis. *Nat Rev Cancer* 2007; **7**: 256–69.
- 9 Morris BJ, Gray RH, Castellsague X, Bosch FX, Halperin DT *et al.* The strong protection afforded by circumcision against cancer of the penis. (Invited Review). *Adv Urol* 2011; **2011**: 812368.
- 10 Castellsagué X, Bosch FX, Muñoz N, Meijer CJ, Shah KV *et al.* Male circumcision, penile human papillomavirus infection, and cervical cancer in female partners. *N Engl J Med* 2002; **346**: 1105–12.
- 11 Stark JR, Judson G, Alderete JF, Mundodi V, Kucknoor AS *et al.* Prospective study of *Trichomonas vaginalis* infection and prostate cancer incidence and mortality: Physicians' Health Study. *J Natl Cancer Inst* 2009; **101**: 1406–11.
- 12 Sobngwi-Tambekou J, Taljaard D, Nieuwoudt M, Lissouba P, Puren A *et al.* Male circumcision and *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Trichomonas vaginalis*: observations in the aftermath of a randomised controlled trial for HIV prevention. *Sex Transm Infect* 2009; **85**: 116–20.
- 13 Morris BJ, Wodak AD, Mindel A, Schrieber L, Duggan KA *et al.* Infant male circumcision: an evidence-based policy statement. *Open J Prevent Med* 2012; **2**: 79–82.
- 14 Morris BJ, Waskett J, Bailis SA. Case number and the financial impact of circumcision in reducing prostate cancer. *BJU Int* 2007; **100**: 5–6.
- 15 Morris BJ, Waskett JH, Banerjee J, Wamai RG, Tobian AA *et al.* A 'snip' in time: what is the best age to circumcise? *BMC Pediatr* 2012; **12**: 20.