LETTER TO EDITOR

Letter to the Editor – Re: Canadian Pediatrics Society position statement on newborn circumcision: a risk-benefit analysis revisited

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Dear Editor,

The Canadian Pediatric Society (CPS) appreciates the chance to respond to "Canadian Pediatrics Society position statement on newborn circumcision: a risk-benefit analysis revisited". Morris et al advocate for routine neonatal male circumcision. We will comment on the main arguments raised:

- 1. The procedure is safe: There is a lack of data on procedural complications in Canada. The most important factor is no doubt the skill of the operator which varies markedly. The 0.5% rate quoted by Morris et al (versus the 1.5% rate in the CPS statement²) is based on billing codes from a United States (US) administrative database study;³ 92% of the complications occurred in hospital which is unexpected and suggests that the methodology did not allow for capture of outpatient complications. Many would argue that the severity of complications is far more important than the rate. Although necrotizing fasciitis, amputation of the penis and death are incredibly rare, some would consider it unethical for the CPS to advocate for an elective procedure that may or may not benefit an individual patient yet has any potential to result in such devastating outcomes.⁴
- 2. Circumcision prevents urinary tract infections (UTIs) in males of all ages: The literature in this area is difficult to interpret because urines obtained via a midstream or catheter specimen from an uncircumcised male are commonly contaminated by organisms under the foreskin. Evidence for this is that 9% of uncircumcised and 0.5% of circumcised asymptomatic males had bacteruria later verified by suprapubic urine collection to be falsely positive.⁵ If one ignores this limitation, the number needed to circumcise (NNTC) to prevent one UTI was 111 in a 2005 systematic review of boys of all ages.⁶ In a more recent systematic review the NNTC was still 73 for studies that included only infants.⁷ Prevention of UTI in infancy remains desirable but there is increasing evidence that UTIs do not cause long term renal damage with a normal urinary tract^{8,9} and can generally be treated with outpatient oral antibiotics.¹⁰

There is a paucity of data on UTIs in older children or adults. A systematic review claimed a 6.6 fold increase in uncircumcised males 1-16 years but it appears that infant data were not able to be excluded from the six studies used to derive this estimate. Evidence for adult males appears to be limited to an observational study of men with urinary symptoms in a Sexually Transmitted Infection (STI) Clinic where 30% of 26 men with UTIs were uncircumcised versus 12% of 50 with other diagnoses. Therefore, there is only very low quality evidence that circumcision prevents UTIs beyond infancy.

The CPS statement says "Using estimates of lifetime risk for male UTI, a recent meta-analysis calculated that, over a lifetime, the relative risk (RR) for UTI was 3.65 for uncircumcised versus circumcised males, with 23% of all UTIs attributed to lack of circumcision." Morris et al claim that this misquotes his systematic review which states "The difference, 23.2 (i.e. 32.1 minus 8.8), represents the percentage of UTIs during the lifetime attributable to the single risk factor of lack of circumcision." We think that these two sentences convey the same meaning.

3. Circumcision prevents STIs: There is high quality data from randomized controlled trials (RCTs) that adult circumcision in Africa decreases the incidence of human immunodeficiency virus (HIV) by approximately 60%¹²⁻¹⁴ with sustained efficacy at 6 years.^{15,16} However, it is not at all clear that routine neonatal circumcision would prevent a large number of cases of HIV in Canada where the incidence of HIV is low and heterosexual sex accounts for a minority of cases.

A recent systematic review of 30 studies with over 12,000 men in each group demonstrated a lower human papillomavirus (HPV) prevalence with circumcision (OR: 0.68; 95% CI: 0.56-0.82) but no difference in HPV incidence or clearance or in the prevalence or incidence of genital warts.¹⁷ Data from the Ugandan HIV RCT showed a statistically significant reduction in the prevalence of high risk HPV genotypes in circumcised males (from 28% to 18%)¹⁸ and their partners (from 39% to 28%)¹⁹ which will hopefully translate into prevention of genital and oral cancers. Pending such data, Morris et al quote a study of 1896 women with cancer of the cervix or carcinoma-in-situ and age-matched controls as evidence that circumcision prevents cancer of the cervix. The odds ratio for cancer of the cervix in the partner was 0.69 (95% CI: 0.43-1.11) for circumcised men. The risk was only statistically significant in the small sub-group of women with a single lifetime partner who reported high risk behavior.²⁰ In Canada, routine HPV vaccine for both genders is likely to be a far more effective cancer prevention strategy than routine male circumcision as vaccine is almost 100% effective in preventing acquisition of high risk genotypes.²¹

With regard to herpes simplex virus (HSV), the incidence was about 30% lower following circumcision in two of the three randomized African HIV trials with no efficacy in the third trial.²² Weaker evidence comes from an observational study where women who had ever had sex with an uncircumcised man were 2.7 times more likely to be seropositive for HSV-2 (95% CI: 1.8-4.0).²³ Follow up to date of the randomized African HIV trials showed that circumcision conferred no benefit for syphilis,¹⁸ gonorrhea²⁴ or chlamydia.²⁴ However, it decreased the incidence of genital ulcers, trichomonas and bacterial vaginosis in female partners.²⁵

A meta-analysis of 53,567 men who have sex with men (MSM) in 15 observational studies demonstrated that circumcision did not decrease the incidence of STIs, including HIV.²⁶ In lieu of mentioning this study, Morris et al quote two studies with annual STI testing of MSM.^{27,28} It is true that the 10% of men who only practiced insertive anal intercourse had a 90% lower risk of syphilis if they were circumcised but the authors fail to mention that there was no difference in the incidence of HSV, self-reported genital warts, urethral gonorrhea or chlamydia based on circumcision status; potential benefit in the whole group was limited to a decreased incidence (but not prevalence) of syphilis. A statistically significant difference for HIV transmission was found only among the one-third of study participants who reported a preference for the insertive role in anal intercourse.

- 4. Circumcision prevents male cancers: Cancer of the penis accounts for approximately 200 cases and 40 deaths annually in Canada.³⁰ The primary risk factor appears to be phimosis.³¹ Over half of cases are HPV-related³² so one would expect the incidence to decrease with our HPV immunization programs. As for cancer of the prostate, the systematic review that Morris et al claim shows benefit from circumcision states "With a sample size of 8633 subjects from seven published case-control studies, this meta-analysis demonstrates an overall small (12%) nonsignificant reduced risk of prostate cancer in circumcised men".³³ It was only with post-hoc omission of outlier studies or sub-group analysis that a statistically significant result was attained.
- 5. Circumcision prevents other sequelae: Morris et al criticize the fact that the table in the CPS guideline on benefits of circumcision is incomplete. Phimosis, balanitis and candidiasis are intertwined and mainly preventable by circumcision or proper care of the uncircumcised penis. Determining the NNTC to prevent them individually is not possible. In an attempt to do so, Morris et al combine the data on balanitis from multiple observational studies; this is low quality data. Their data on penile candidasis were obtained from a phone survey which is unlikely to be an accurate method of collecting such information. ²⁹
- 6. Circumcision is cost effective: It is premature to calculate the cost-effectiveness of routine neonatal circumcision in Canada since the rates of complications and benefits remain speculative.
- 7. The CPS statement is discordant with others: Morris et al imply that the American Academy of Pediatrics (AAP) and the US Centers for Disease Control (CDC) recommend routine neonatal circumcision in the absence of cultural conflicts. The actual wording of the AAP statement is "Although health benefits are not great enough to recommend routine circumcision for all male newborns, the benefits of circumcision are sufficient to justify access to this procedure for families choosing it and to warrant third-party payment for circumcision of male newborns". The CDC states "Parents and guardians should be informed about the medical benefits and risks of neonatal male circumcision. Other considerations, such as religion, societal norms and social customs, hygiene, aesthetic preference, and ethical considerations also influence decisions about male circumcision. Ultimately,

whether to circumcise a male neonate is a decision made by parents or guardians on behalf of their newborn son".³⁴ We do not think that these statements are as pro-circumcision as do Morris et al; like ours, they emphasize the importance of presenting a balanced view to parents and allowing them to decide. As far as we are aware, no country outside of Africa has adopted a national policy promoting routine circumcision and in Europe and Australia, non circumcision remains the norm.³⁵

The two Canadian authors of the Morris et al article operate circumcision clinics which represent a conflict of interest. Neonatal circumcision is a procedure with lifelong consequences performed without patient consent. The deeply disquieting bottom line is that at least three normal infants died in Canada following circumcision in the past 15 years 4^{36,37} and this tragic fact – multiplied many fold in less developed countries – must give grave pause to any recommendation for routine neonatal circumcision. The CPS statement will be revised to promote routine circumcision only if high quality evidence to support that stance becomes available.

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