Canadian Pediatrics Society position statement on newborn circumcision: a risk-benefit analysis revisited

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MORRIS BJ, KLAUSNER JD, KRIEGER JN, WILLCOX BJ, CROUSE PD, POLLOCK N. Canadian Pediatrics Society position statement on newborn circumcision: a risk-benefit analysis revisited. *Can J Urol* 2016;23(5):8495-8502.

Introduction: *The Canadian Pediatrics Society (CPS) recently released a position statement on early infant (newborn) male circumcision (EIMC). It concluded that since benefits do not exceed risks, circumcision should only be performed on boys in high-risk populations or circumstances. This contradicts recommendations by the American Academy of Pediatrics and the Centers for Disease Control and Prevention (CDC) whose policies each support more widespread implementation of EIMC. Here we review the CPS statement, particularly its risk-benefit analysis, to determine the basis for this disparity.*
Materials and methods: *We performed a risk-benefit analysis based on relevant literature retrieved from PubMed reporting frequency of each condition, giving emphasis to data from meta-analyses and randomized controlled trials.*
Results: *Although the CPS recognized some of the benefits of EIMC, its inclusion of weak studies of adverse events led to these being over-estimated, greatly exceeding the figure of < 0.5% found in a recent large, technically robust, CDC study. The CPS under-estimated benefits by omitting balanitis, balanoposthitis, prostate cancer, some sexually transmitted infections and candidiasis, and failing to consider lifetime prevalence of urinary tract infections in uncircumcised males. In contrast, our more inclusive risk-benefit analysis found benefits exceed risks by approximately 100 to 1 and that lack of EIMC contributes to adverse medical conditions, some potentially fatal, in approximately half of uncircumcised males.*
Conclusions: *The 2015 CPS position statement on EIMC is at odds with the evidence. The CPS conclusions stem from errors in its risk-benefit analysis. In light of our findings we recommend the CPS issue a revised statement.*

Key Words: male circumcision, policy, risk-benefit, Canadian Pediatrics Society

Introduction

The 2015 Canadian Pediatric Society (CPS) position statement on early infant (newborn) male circumcision (EIMC) summarizes evidence for and against this procedure.[1] Because the statement fails to find that benefits exceed risks, fails to recommend circumcision of all newborn males except in families having cultural conflicts, and fails to recognize the need for access and third party cost coverage, the CPS recommendations are at odds with the 2012 EIMC policy statement by the American Academy of Pediatrics (AAP).[2] The Centers for Disease Control and Prevention (CDC) 2014 draft recommendations support the conclusions by the AAP.[3] The CDC also recommended circumcision of mature males as well in high-risk populations to help reduce the risk of human immunodeficiency virus (HIV) and other sexually transmitted infections (STIs).

Accepted for publication July 2016

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The CPS concludes that, "while there may be a benefit for some boys in high-risk populations and circumstances where the procedure could be considered for disease reduction or treatment, the [CPS] does not recommend the routine circumcision of every newborn male". The reason for the disparity between the CPS statement and statements by the AAP and CDC can be attributed to the risk-benefit analysis presented in the CPS report. The results of that analysis appear to be the basis for its statement that, "because the medical risk:benefit ratio ... is closely balanced ... it is challenging to make definitive recommendations for the entire male newborn population in Canada." However, the CPS did not estimate the total proportion of boys experiencing adverse events after circumcision, nor the total proportion experiencing adverse medical conditions because of being uncircumcised. Therefore it is difficult to judge the basis for the CPS's sweeping conclusion.

We therefore performed a more thorough risk-benefit analysis in order to better understand why the CPS conclusions conflict with those of the AAP and CDC. As a result of the findings from our more wide-ranging and thorough evidence-based risk-benefit analysis it would be appropriate for the CPS to offer a more open statement on newborn circumcision.

Materials and methods

A risk-benefit analysis was conducted using information obtained after an evaluation of all articles that had been retrieved from PubMed by the first author by way of weekly PubMed email alerts and, prior to the inception of PubMed in 1996, by Medline (US National Library of Medicine) and Current Contents (Institute of Scientific Information) from 1991 onwards. PubMed searches retrieve old articles dating back to the 1930s, not just new ones. On 7 March 2016 the current number of articles on PubMed listed using the keyword circumcision and related terms in combination with 46 key words for relevant specific medical conditions were determined. The total for circumcision was 13,520, whereas a PubMed search by the keyword circumcision by itself generated 6,811 articles, indicating most overlapped. The title of each article and abstract were viewed, and those with original data or meta-analyses of relevant data were read in full. Altogether 49 relevant articles were included, 44 on medical conditions whose prevalence was found to be affected my male circumcision and five involving large studies on adverse events. Wherever possible, the articles we used were recent meta-analyses and randomized controlled trials (RCTs) since quality of well-designed and executed meta-analyses and RCTs are regarded as 1++ and 1+ by a conventional international grading system.[4] The large well-designed landmark RCTs that have been conducted in several countries in sub-Saharan Africa provided high quality data on HIV and other STIs. When level 1++ and 1+ data were not available, data from original studies rated 2++ and 2+ were included. Only articles reporting prevalence data were considered. We excluded low quality observational studies, review articles, case reports, opinion pieces, articles on surgical technique, recovery from surgery, diagnosis, treatment, penile histology, conference abstracts and articles on female genital cutting (often referred to as "female circumcision"). The protective effect conferred by the single risk factor of the foreskin against a particular STI during heterosexual intercourse with a female partner was assumed to differ little between high and low prevalence settings.[5] However, the proportion of men at risk of an STI was influenced by the prevalence of each in Canada and was taken into account after ascertaining prevalence figures for each STI in Canada by Internet searches. We gave preference to data in authoritative sources. If these were not available we relied on figures available for the USA, and then Australia or the UK. Figures for number needed to treat (NNT) and number needed to harm (NNH) were obtained for the various medical conditions that circumcision protects against and adverse events that can occur during the circumcision procedure or subsequently.

Results

The findings from our comprehensive risk-benefit analysis, together with estimates of NNT and NNH, are shown in Table 1. When recent meta-analysis data were available (indicated by "Meta" in Table 1) we considered it unnecessary to cite the original studies as well. Our compilation included common conditions the CPS failed to refer to in its risk-benefit analysis, namely balanitis, balanoposthitis, prostate cancer, several STIs and candidiasis. When we added together the relative protection afforded by circumcision against each of the medical conditions, we found that up to 65% of uncircumcised males might experience at least one of these over their lifetime. Our tally did not include genital ulcer disease, because, in Canada, this is mostly caused by genital herpes,[6] so would have led to double counting.

For adverse events, we found that by considering a more extensive compilation of study data for each than was used by the CPS, the combined frequency of adverse events was 0.4% overall. After comparing the

TABLE 1. **Potential risks and benefits of early infant ('neonatal') circumcision**

Potential risks	**NNH**	**%Affected***	**Reference(s)****
Minor bleeding	1000	0.1-0.2	OS[20,47] 2++
Local infection	1600	0.06	OS[20,47] 2++
Severe infection	3,000	0.03	OS[20] 2++
Partial penile amputation	6,000	0.0002	OS[20] 2++
Correctional procedures	1200	0.08	OS[20] 2++
Death	> 10 million	< 0.00001	OS[47] 2++
Meatal stenosis	> 1000	< 0.01	OS[20,22-24] 2++
	Total affected = approx. 0.4%		
Potential benefits in protection against	**NNT**	**RR†**	**%Affected‡**	**Reference***
Phimosis	10	> 90%	10	OS[48-60] 2+
Balanitis/balanoposthitis	10	68%	6.8	Meta[32] 1+
Urinary tract infection: age 0-1 y	90	90%	1.3	Meta[27] 1+
Urinary tract infection when other risk factors exist	4-6	90%	26	Meta[61] 1+
Urinary tract infection: age 1-16	150	85%	2.7	Meta[27] 1+
Urinary tract infection: age > 16 y	4	70%	28	Meta[27] 1+
Urinary tract infection: lifetime	4.3	3.6	27	Meta[27] 1+
Pyelonephritis (infants)	160	–	0.6	OS[62,63] 2+
Candidiasis (thrush)	25	60%	10	OS[64] 2+
HIV (heterosexually acquired)	298	60%	0.2	OS[33] 2+
	1000	70%	0.1	Meta[65] 1++
Herpes simplex virus type 2	16	30%	4	RCT[66-69] 1++
	32	15%	4	Meta[70] 1+
High-risk human papillomavirus	4	56%	11	Meta[30] 1++
	4	53%-65%	11	Meta[71] 1++
	5	40%	6-10	RCT[72-77] 1++
Trichomonas vaginalis	200	50%	1	RCT[78] 1+
Mycoplasma genitalium	100	40%	0.5	RCT[79] 1+
Treponema pallidum	50	47	1	Meta[70] 1+
	50	40%-55%	1	OS[80,81] 2+
Hemophilus ducreyi	50	50%	< 1	Meta[70] 1+
Genital ulcer disease	50	50%	1	OS[6,82-84] 2+
Penile cancer$^{\chi}$	1000	67%	0.07	Meta[85] 1+
	1000	95%	0.1	OS[86] 2+
	900	95%	0.11	OS[87] 2+
	1400	99%	0.07	OS[88] 2+
Prostate cancer: population-based	5.9	17%	2.1	Meta[89] 1+
black race	2.4	42%	17	Meta[89] 1+
	Total affected = approx. 65% of uncircumcised males			

*% affected by an adverse event is the inverse of the number needed to harm (NNH) value, which is the approx. number of males who need to be circumcised to see one of each particular (mostly minor) adverse effect. **reference(s) and type of study: Meta = meta-analysis; RCT = randomized controlled trial(s); OS = original study(ies) and quality. The meta-analyses provide comprehensive lists of references to individual studies relevant to the topic. Quality rating, based on international grading system,[4] was 1++ and 1+ for well-conducted meta-analysis and RCTs; for the original studies cited above it was 2++ or 2+. When more than one study is cited an overall quality rating is given. †Risk reduction if circumcised. ‡The % of males who will be affected as a result of the single risk factor of retention of the foreskin. Data for STIs were estimated after taking into account the external factor of heterosexual exposure, which is dependent on population prevalence of each STI in Canada and risk reduction conferred by circumcision. The % of males affected were estimated after taking into account potential lifetime risk and risk reduction conferred by circumcision: i.e. lifetime risk of prostate cancer in Canada is 1 in 8 (0.125), so for a 17% risk reduction conferred by circumcision, the % affected is 0.125 x 0.17 x 100 = 2.1%. Canadian data were used as far as possible,[84,90-95] otherwise US figures,[5,33] followed by Australian[64] figures. $^{\chi}$The last two entries for penile cancer are shown because they are the references cited by the AAP and CDC in their respective circumcision policy statements. NNT = number needed to treat

total for benefits with the total for risks we determined that the cumulative frequency of medical conditions attributable to the risk factor of the foreskin was approximately 100-fold higher than the cumulative frequency of adverse events/complications of the circumcision procedure.

Studies have shown that women with circumcised male partners are at significantly lower risk of oncogenic HPV types,[7] cervical cancer[7] and HSV-2.[8,9] The protective effect in women has been confirmed by RCT findings for high-risk HPV types,[10-12] HSV-2,[13] *T. vaginalis*,[14] *M. genitalium*,[14,15] bacterial vaginosis,[14,16] and genital ulceration.[14] In men who have anal intercourse with other men, data from Sydney, Australia, revealed a 90% lower risk of HIV[17] and syphilis[18] for those men who adopt the insertive role exclusively during this sexual practice.

Discussion

Our risk-benefit analysis found benefits of EIMC greatly exceed risks. It would appear that omission of several conditions EIMC protects against, failure to consider protection against UTI beyond infancy, and inflated figures for adverse events in its risk-benefit analysis may have led the CPS to underestimate the benefits and overestimate risk of the procedure. This would explain why the recommendations in its 2015 position statement are at odds with the affirmative policy statements by the AAP and CDC. To help understand the basis for the outcome of the CPS risk-benefit analysis we critically evaluate below the details of data sources used by the CPS.

Procedural risk during EMC

The CPS cites a meta-analysis of global data for medical and traditional circumcisions that, "found a complication rate of 1.5% in neonates or infants".[19] However, it seems odd that the CPS uncritically presented a figure of 1.5% just for risk of minor bleeding. Importantly, the CPS did not present an overall figure for NNH. Rather, it only stated NNH figures for local infection (minor) of 67 and meatal stenosis of 10-50. No NNH figures were provided in the CPS Table for minor bleeding, severe infection, death from unrecognized bleeding or unsatisfactory cosmetic result. Instead extremely rare was stated by the CPS. Based only on the NNH data it does present, the CPS estimates for overall procedural risk would thus vastly exceed the figure obtained by the CDC in a recent study of 1.4 million medical male circumcisions (93% in newborns) in the United States.[20] That study, which the CPS ignored, found that for circumcisions performed during the first 28 days after birth the incidence of total MC adverse events was slightly less than 0.5%.[20] The CDC study found, moreover, incidence of infections, surgical procedures, pneumothorax, penile disorders and gangrene were each significantly higher in uncircumcised males during this period.[20] Total adverse events were, nevertheless, twice as high in circumcised as uncircumcised newborn boys in the CDC study.

A major factor contributing to its overestimation of risk appears to be the use by the CPS of a figure of 2%-10% for meatal stenosis. That estimate came from a small, single author, underpowered case study of 1,009 circumcised and 91 uncircumcised boys that was severely criticized.[21] Diagnosis of meatal stenosis is somewhat subjective. The difference in the diagnosis rate of meatal stenosis between circumcised and uncircumcised boys in that study was, moreover, not statistically significant. In contrast, the large CDC study found the risk of "strictures" during an 180 day period following birth to be similar between circumcised and uncircumcised boys (0.01%).[20] A United Kingdom study found meatal stricture in 0.01% of 66,519 circumcised boys.[22] Iranian studies found prevalence of meatal stenosis to be 0.55% during the 15 months after newborn circumcision of 3,000 boys[23] and 0.9% at ages 6-12 years after circumcision of 3,125 boys, 71% performed on boys older than 2 years, most (86%) by a paramedical or traditional circumciser.[24]

Adhesions may be seen at follow up after an EIMC, and while these can be gently teased away by the physician, it has been suggested that no action is needed because they tend to resolve spontaneously.[25]

Circumcision revision occurred after 16% of EIMCs in the United States, an 119% increase over the period 2004 to 2009.[26] One reason suggested by the authors was changes in parental expectations about what the "normal" appearance of the penis should be following circumcision, revision for excess foreskin being the main reason. Better advice from the physician on improvements to be expected with growth of the penis with age may help address this trend.

Urinary tract infections (UTIs)

The CPS estimate for UTI protection comes from a decade-old meta-analysis in which the impact of circumcision on reducing infant UTIs was diluted by inclusion of data on older boys and men in whom risk reduction is lower.[27] That meta-analysis was severely criticized for including older males and its suggestion that circumcision only be recommended for boys with recurrent UTI or urinary tract abnormalities such as high-grade vesico-ureteric reflux or obstructive uropathy.[28] Nevertheless, the CPS policy followed

the flawed conclusions in that study. The CPS did cite a recent, more extensive, meta-analysis that found 1 in 3 uncircumcised males are likely to experience a UTI over their lifetimes, as compared with 1 in 12 circumcised males,[27] but it did not use those data in their risk-benefit analysis. As a result lifetime risk of UTI was understated. The CPS report, moreover, misrepresents the findings in that meta-analysis by stating that the study found, "23% of all UTIs [were] attributed to lack of circumcision," whereas what the study actually concluded was, "The single risk factor of lack of circumcision confers a 23.3% chance of urinary tract infection during the lifetime." While there are numerous studies of UTI and lack of circumcision in infants, and to a lesser extent older boys, more studies of UTI in men are needed. There have, moreover, been no studies of the relation between circumcision and UTI in elderly men, in whom UTIs are common.

Penile cancer

The risk-benefit analysis Table in the CPS article provides an extraordinarily wide-ranging estimate of 900-322,000 for decreased risk of penile cancer conferred by circumcision. The 322,000 figure is in fact the upper bound of the annual incidence figure, which averages 1 in 100,000 in developed countries,[29] whereas the figure of 900 pertains to lifetime risk and comes from the figure of 1 in 909 for the United States that appeared in the AAP EIMC policy statement.[2] Most penile cancers occur in uncircumcised men and while uncommon in uncircumcised men, penile cancer is only rare in circumcised men.

Oncogenic human papillomavirus (HPV) types are present in half (not 80%) of penile cancers,[30] and, given the 70% frequency of the two oncogenic HPV types targeted by current HPV vaccines, vaccination of boys might lower penile cancer by up to 30%.[31]

The CPS did not cite meta-analyses showing that penile cancer is associated with phimosis (OR = 12.1; 95% CI 5.57-26.2), balanitis (OR = 3.82; 95% CI 1.61-9.06) and smegma (OR = 3.04; 95% CI 1.29-7.16),[29] each of which are much more prevalent in uncircumcised males.

Inflammatory dermatoses

EIMC protects against balanitis and balanoposthitis (OR = 0.32; 95% CI 0.20-0.52 in a meta-analysis[32]). These conditions are common in boys and men, particularly when not circumcised. The CPS did not include penile inflammatory conditions in its risk-benefit analysis.

HIV

Because circumcision strongly protects against HIV infection the CPS statement that, "there may be a benefit for some boys in high-risk populations" seems conservative, especially as the CPS statement noted that in Canada 20.3% of new HIV infections occur in heterosexuals, "not originally from a country where HIV is endemic." Since the spread of HIV to heterosexuals in developed countries is rising, recommending EIMC should help reduce the ongoing risk of continued transmission when the boy becomes sexually active. The CPS noted higher HIV infections in Aboriginal Canadians, 30.2% of these arising from heterosexual exposure. It quotes CDC calculations showing that in the United States reduction in heterosexual transmission of HIV by EIMC ranges from 8% in white males to 21% in black males and is cost-saving for HIV prevention in black and Hispanic males.[33]

Cost-effectiveness

Not only the CDC,[33] but analyses by researchers at Johns Hopkins University and others in the United States have found EIMC to be cost-effective in reducing HIV infections, but in addition reducing other STIs, as well as UTIs.[34-37] The Johns Hopkins study of just infections found that, reducing the [EIMC] rate to 10% in the USA will increase lifetime health care costs by $407 per male and $43 per female and that net expenditure per annual birth cohort (including the procedure and complication costs) is expected to increase by $505 million, reflecting an increase of $313 per foregone [EIMC]. These estimates were for direct costs only. The study further estimated that if EIMC decreased to 10% lifetime prevalence of infant UTIs would increase by 211.8%, high- and low-risk human papillomavirus by 29.1%, herpes simplex virus type 2 by 19.8% and HIV by 12.2%. Among females, lifetime prevalence of bacterial vaginosis would increase by 51.2%, trichomoniasis by 51.2%, high-risk HPV by 18.3% and low-risk HPV by 12.9%. Cost savings may also apply to reduction in penile, prostate and cervical cancer.[31] Further cost-savings will be achieved from prevention of the other conditions listed in Table 1 and avoiding the need for more costly[20] circumcisions in older males to treat foreskin-related medical problems. The Johns Hopkins researchers pointed out that their, "cost increase outcomes [were] highly conservative", stating that just for HIV, "the associated indirect costs may be more than four times the total direct medical expenses"[38] and that claims of psychological consequences, decreased sexual function and sexual pleasure are not supported by results of post-procedure follow up studies.[34] Indirect costs associated with other medical conditions will also be reduced by the reduction in prevalence

of each as a result of EIMC. We expect that cost-effectiveness studies for Canada may confirm these findings.

Cost for circumcision of older boys and men in he USA averages US $1,500,[26] which greatly exceeds the cost of EIMC of US$291[33,39] used in the Johns Hopkins study.

Conclusions

In contrast to the errors we have identified in the CPS statement, the AAP[2] and CDC[3] policy statements, as well as that of the Circumcision Academy of Australia[40] (whose brochure is listed as a resource at the end of the CPS report), concluded that benefits of EIMC exceed risks and recommended education, access and health insurance coverage, as well as government funding to help with affordability. We find that the failure of the CPS to recommend circumcision for all newborns, while stating that the benefits and risks are evenly balanced (with no figure given), stems from an inadequate risk-benefit analysis.

The flawed CPC statement may unfortunately make it more difficult for Canadians to access medical circumcision for newborn males.

To its credit the CPS position statement lists many, but not all, of the benefits of EIMC. It also recognizes the protection conferred to female partners against cervical cancer, several common STIs and bacterial vaginosis. It furthermore appreciates that EIMC as preferable to circumcision of older boys and men. While EIMC is convenient, quick, safe, low-cost and provides immediate and lifelong protections, circumcision later in life takes longer, costs more, includes a 10-20 fold higher risk of adverse events[20] and often involves general anesthesia, so adding to risk and costs. Circumcision later in life means the cosmetic outcome is diminished when sutures are used, often requires time off school or work, means sexual abstinence for 6 weeks, which some males and their sexual partners find undesirable, and presents other barriers, including psychological.[2,3,32]

The CPS policy accurately confirms that, "medical studies do not support circumcision as having a negative impact on sexual function or satisfaction in males or their partners," citing two randomized controlled trials,[41,42] although not recent extensive systematic reviews[43,44] and a meta-analysis,[45] nor a systematic review of histological correlates of penile sexual sensation.[46]

Taken together, our evaluation of the CPS position statement leads us to conclude that the CPS should withdraw its current report and issue a revised position statement. □

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