TITLE: Newborn Male Circumcision for the Prevention of Sexually Transmitted Infections, Urinary Tract Infections, and Cancer: Clinical Effectiveness and Guidelines

DATE: 6 February 2015

RESEARCH QUESTIONS

1. What is the clinical effectiveness of newborn male circumcision for the prevention of sexually transmitted infections (STIs), urinary tract infections (UTIs), and cancer?

2. What are the evidence-based guidelines regarding the medical indications for newborn male circumcisions?

KEY FINDINGS

Seven systematic reviews and 16 non-randomized studies were identified regarding the clinical effectiveness of newborn male circumcision for the prevention of STIs, UTIs, and cancer. In addition, three evidence-based guidelines were identified regarding the medical indications for newborn male circumcisions.

METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2015, Issue 1), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2010 and January 27, 2015. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.
SELECTION CRITERIA

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

<table>
<thead>
<tr>
<th>Population</th>
<th>Newborn males in a North American or Western setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Circumcision</td>
</tr>
<tr>
<td>Comparator</td>
<td>No circumcision</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Clinical effectiveness, benefits and harms (e.g., infection), evidence-based guidelines</td>
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<tr>
<td>Study Designs</td>
<td>Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, evidence-based guidelines</td>
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RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, and evidence-based guidelines.

Seven systematic reviews, 16 non-randomized studies, and three evidence-based guidelines were identified regarding male circumcision for the prevention of infection and disease. No relevant health technology assessments or randomized controlled trials were identified.

Additional references of potential interest are provided in the appendix.

OVERALL SUMMARY OF FINDINGS

Seven systematic reviews were identified regarding male circumcision for the prevention of infection and disease.\(^1\)\(^-\)\(^7\) Of note, some studies included in the systematic reviews may have been conducted in other populations (i.e., in countries outside of North America).

Two systematic reviews\(^1\),\(^4\) examined the evidence regarding the prevalence of urinary tract infections (UTIs) in circumcised males. A 2013 meta-analysis by Morris and Wiswell\(^1\) reported that 8.8% of circumcised males will experience a UTI in their lifetime, compared with 32.1% of uncircumcised males. However, a systematic review from 2012\(^4\) did not identify any relevant randomized controlled trials regarding routine circumcision in neonatal males for the prevention of UTIs in infants.

Three systematic reviews\(^2\),\(^6\),\(^7\) examined the relationship between circumcision and acquisition of sexually transmitted infections. The results of one study\(^2\) showed that the risk of chlamydia, genital herpes, gonorrhea, or human papillomavirus (HPV) was not impacted by circumcision. Low quality evidence showed no association between circumcision and herpes simplex viruses 1 or 2, or syphilis in men who have sex with men.\(^6\) The role of circumcision for the prevention of human immunodeficiency virus (HIV) in men who have sex with men was inconclusive.\(^6\) Circumcision was observed to be protective against viral sexually transmitted infections, and possibly trichomoniasis, in one study.\(^7\)
Two systematic reviews\(^3,^5\) specifically evaluated the association between circumcision and acquisition of HPV, including genital warts. There was no observed relationship between circumcision and genital warts in either study\(^3,^5\). Regarding decreased HPV incidence and increased HPV clearance, one systematic review found no evidence of association\(^3\), while another found weak evidence to support an association\(^5\).

The main findings of the 16 non-randomized studies\(^8-23\) are summarized in Table 2.

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Patient Population</th>
<th>Findings</th>
</tr>
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<tbody>
<tr>
<td>STIs</td>
<td></td>
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<tr>
<td>Albero, 2014(^9) N = 4,033</td>
<td>Circumcised males had lower incidences of HPV types 58, 68, 42, 61, 71, 81, and IS39, but higher incidences of HPV types 39 and 51, compared with uncircumcised males. Median time to clearance of HPV was shorter in circumcised males.</td>
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<tr>
<td>Albero, 2013(^10) N = 4,072</td>
<td>Certain non-oncogenic HPV types (11, 40, 61, 71, and 81) were weakly, negatively associated with circumcision.</td>
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<tr>
<td>Canadas, 2013(^11) N = 706</td>
<td>The prevalence of penile HPV infection was lower in circumcised males (22%) than in uncircumcised males (27%).</td>
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<tr>
<td>Doerner, 2013(^12) N = 1,521 (16.7% circumcised)</td>
<td>There was no association between HIV and circumcision among MSM.</td>
<td></td>
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<tr>
<td>Poynten, 2012(^14) HIV negative N = 1,427; HIV positive N = 245</td>
<td>Among MSM, there was an association between circumcision and decreased HPV 16 seroconversion.</td>
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<tr>
<td>Oster, 2011(^15) N = 5,183</td>
<td>HIV infection was not associated with circumcision status for MSM.</td>
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<tr>
<td>Sanchez, 2011(^16) N = 1,824</td>
<td>Among MSM, circumcision did not have a protective effect for the acquisition of HIV, but may have a reduced risk for those that predominantly are insertive with their partners.</td>
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<tr>
<td>Vanbuskirk, 2011(^17) N = 477</td>
<td>Uncircumcised men were more likely than circumcised men to have HPV detection at multiple genital sites, though overall acquisition of HPV did not differ between groups.</td>
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<tr>
<td>Ferris, 2010(^18) N = 4,290 (58% circumcised)</td>
<td>Circumcision status was unrelated to STI history. History of non-specific urethritis was higher among circumcised males, and history of penile candidiasis was lower among circumcised males.</td>
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<tr>
<td>Gust, 2010(^19) N = 4,889 (86.1% circumcised)</td>
<td>For MSM who have predominantly insertive, unprotected anal sex with their partners, those who were uncircumcised did not have an increased risk of HIV infection.</td>
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<tr>
<td>Hernandex, 2010(^20) N = 357</td>
<td>HPV clearance was faster in circumcised males, but there was no difference in the acquisition of HPV by circumcision status.</td>
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<tr>
<td>Jameson, 2010(^21) Circumcised N = 3,241; Uncircumcised N = 587</td>
<td>HIV infection and STIs did not differ by circumcision status for MSM.</td>
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<tr>
<td>Jozkowski, 2010(^22) N = 26,257</td>
<td>There were no significant differences for STI diagnoses based on circumcision status for MSM.</td>
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<tr>
<td>McDaid, 2010(^23) N = 1,405</td>
<td>There was no association between HIV and circumcision status for MSM.</td>
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</table>
### Table 2: Summary of Included Non-Randomized Studies

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Patient Population</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cancer</strong></td>
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<tr>
<td>Spence, 2014⁹</td>
<td>Prostate cancer cases N = 1,590; Controls = 1,618</td>
<td>Circumcision had a weak protective effect against prostate cancer, when performed before 1 year of age.</td>
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<tr>
<td><strong>UTI</strong></td>
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<tr>
<td>Dubrovsky, 2012¹³</td>
<td>N = 440</td>
<td>Circumcised boys had a lower risk of UTI compared with uncircumcised boys (adjusted OR = 0.07).</td>
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</table>

HIV = human immunodeficiency virus; HPV = human papillomavirus; MSM = men who have sex with men; STI = sexually transmitted infections; UTI = urinary tract infection.

Three evidence-based guidelines²⁴-²⁶ were identified regarding the medical indications for newborn male circumcisions. Guidelines from the Institute for Clinical Systems Improvement²⁴ recommend third-party payment for circumcision if requested by families, given sufficient evidence for its clinical benefits. These guidelines also acknowledge that infant male circumcision is not universally recommended, and the choice to pursue it is often related to personal values and cultural beliefs.²⁴ The American Urological Association Education and Research guidelines²⁵ state that circumcision is protective against UTIs and may be a considered procedure for male infants with vesicoureteral reflux. Guidelines from Spain²⁶ do not recommend circumcision, even though there is evidence for some protection against UTIs.
REFERENCES SUMMARIZED

Health Technology Assessments
No literature identified.

Systematic Reviews and Meta-analyses


Randomized Controlled Trials
No literature identified.

Non-Randomized Studies


Guidelines and Recommendations


Summarized at: http://www.guideline.gov/content.aspx?id=24027
See: Option: Circumcision of the male child… page 7

Summarized at: http://www.guideline.gov/content.aspx?id=46945
See: 7.3 Phimosis as a risk factor for UTI, pages 67 – 69

PREPARED BY:
Canadian Agency for Drugs and Technologies in Health
Tel: 1-866-898-8439
www.cadth.ca
APPENDIX – FURTHER INFORMATION:

Systematic Review – Unclear or Older Age at Circumcision


Randomized Controlled Trial – Unclear or Older Age at Circumcision


Non-Randomized Studies

Unclear or Older Age at Circumcision


Alternate Outcome