A Cost-Utility Analysis of Neonatal Circumcision

Robert S. Van Howe, MD, MS, FAAP

A cost-utility analysis, based on published data from multiple observational studies, comparing boys circumcised at birth and those not circumcised was undertaken using the Quality of Well-being Scale, a Markov analysis, the standard reference case, and a societal perspective. Neonatal circumcision increased incremental costs by $828.42 per patient and resulted in an incremental 15.30 well-years lost per 1000 males. If neonatal circumcision was cost-free, pain-free, and had no immediate complications, it was still more costly than not circumcising. Using sensitivity analysis, it was impossible to arrange a scenario that made neonatal circumcision cost-effective. Neonatal circumcision is not good health policy, and support for it as a medical procedure cannot be justified financially or medically. ***Key words:*** *circumcision; phimosis; cost-utility analysis; circumcision complications; penile cancer.* ***(Med Decis Making 2004;24:584-601)***

Neonatal male circumcision is the most commonly performed procedure on children in the United States. Although the topic has been the subject of heated debate during the past 3 decades, past studies[1–4] have failed to demonstrate the cost-effectiveness of the procedure. Despite these findings, most private insurance and state Medicaid programs in the United States continue to reimburse physicians who perform the procedure. In an era of limited health care funding, close scrutiny of the cost-effectiveness of medical practices has become increasingly important.

Advocates of the surgery claim that the benefits of neonatal circumcision justify its universal implementation[5]; however, currently not a single national medical organization endorses neonatal circumcision.[6–11] The American Academy of Pediatrics' most recent task force on circumcision concluded that "existing scientific evidence demonstrates potential medical benefits of newborn male circumcision; however, these data are not sufficient to recommend routine neonatal circumcision."[11] The recommendation of the task force and the near ubiquity of the practice in the United States appear to be in conflict. In an effort to sort out these differences, the best available tool to determine the financial and health impact of the benefits of neonatal circumcision is a cost-utility analysis.

Since publication of the previous cost-utility and cost-effectiveness studies,[1–4] 3 studies have documented circumcised men to be at greater risk for sexually transmitted diseases,[12–14] and males circumcised at birth have been shown to be at risk for penile cancer,[15] contrary to the popular belief that circumcision eliminated the possibility of this malignancy.[16] *Meatal stenosis* (italicized medical terms are defined in the appendix), which was not included in previously published calculations, has been discovered to frequently affect circumcised males.[17–23] With the publication of these studies, the Canadian Paediatric Society has recommended that a new cost-utility analysis of neonatal circumcision be performed.[7] Using the data currently available in the medical literature, a cost-utility analysis of neonatal circumcision was undertaken.

METHOD

A cost-utility analysis, using the reference case standard developed by the Panel on Cost-Effectiveness in Health and Medicine convened by the US Public Health Service in 1993,[24] was performed. The analysis adopted a societal perspective and included the 72-year life span of an average male because circumcision status is believed to impact health throughout life. Util-

Received 25 February 2004 from the Department of Pediatrics, Michigan State University College of Human Medicine, Marquette, Michigan. Presented as a poster at the 20th annual meeting of the Society for Medical Decision Making, Cambridge, Massachusetts, 27 October 1998. Revision accepted for publication 2 August 2004.

Address correspondence and reprint requests to Robert S. Van Howe, MD, MS, 2083 W. Fair Avenue, Marquette, MI 49855-2340; phone: 906-228-7454; e-mail: vanhowe@lushen.com.

DOI: 10.1177/0272989X04271039

ity was estimated using the Quality of Well-being Scale and values as previously described.[2,25–27]

The Quality of Well-being Scale assigns values in 4 categories: symptom/problem complexes, mobility scale, physical activity scale, and social activity scale. For each condition, a value is assigned for each of the scales. The total of the scale values is the quality of well-being lost by having the condition. This total is multiplied by the duration of the condition to estimate the impact of the condition in quality-adjusted life years. Odds ratios, used as an estimate of relative risk, are expressed as the odds among noncircumcised males divided by the odds among circumcised males. Meta-analyses were performed using a random-effects model (DerSimonian and Laird method) by the Mantel-Haenszel method.[28]

The incidence values, financial costs, utility weights, and durations used in this analysis are listed in Table 1. The values used to calculate costs for urinary tract infection and the costs and well-years lost for immediate complications from neonatal circumcision are listed in Table 2 and Table 3, respectively. All costs have been adjusted to 1999 US dollars using the Consumer Price Index.[29] Incidence values listed in Table 1 are the lifetime, cumulative incidence values. In the analysis, if a condition could occur over a number of years, the yearly incidence was divided over these years, and age-related yearly incidence rates were applied where available.

Costs and utility were discounted at rates of 0%, 3%, and 5%.[30] Previously published age distributions of the onset of penile cancer,[31] HIV,[32] *phimosis*, *balanoposthitis*,[33] and sexually transmitted diseases[34] were employed in this analysis.

Time lost from work for treatment and physician visits were valued using the May 1999 average earning in the private sector of the United States (hourly = $13.19).[35] Duration of time lost from work is used as described in the reference case standard[24] and, with the exception of the hospitalization of normal newborns for which no time lost from work costs were assessed, equaled the length of hospitalization and/or the length of illness of severity enough to prevent return to day care. The time lost from work cost for a physician visit was assumed to be 4 h or a half-day of work.

A Markov analysis model was chosen to accommodate varying ages of onset, chronic disease states, recurrences, and discounting. Calculations were performed using DATA 3.5 for Healthcare for Windows (TreeAge Software, Inc., Williamstown, MA). Cycle length was 1 year with 72 cycles performed. Transition probabilities were determined by disease incidence, the odds ratios as an estimate of relative risk between the 2 groups, and the age-incidence data where available. Sensitivity analysis as well as calculations of the most favorable scenario (MFS; the least costly for circumcision and the most costly for noncircumcision) and the least favorable scenario (LFS; the most costly for circumcision and the least costly for noncircumcision) for neonatal circumcision were performed. A Monte Carlo simulation taking 1000 samples was performed employing the distributions of 24 of the most influential variables.

Articles addressing the impact of neonatal circumcision on health were collected by searching MEDLINE using *circumcision* as a search word, reviewing the citations in pertinent articles, and querying experts in the field. Articles published since 1900 were considered. Preference was given to the most current information.

Sensitivity analysis was performed on 47 variables. The greatest obstacle in performing the analysis was the large number of variables in the decision tree and the wide variation in the medical literature for nearly all of these variables. This necessitated the establishment of the MFS and LFS. The MFS would reflect the opinions of circumcision advocates, who emphasize circumcision's benefits and downplay its risks while emphasizing the *prepuce's* propensity for disease. The LFS would alternatively place neonatal circumcision in the worst possible light. By establishing these scenarios, the most extreme views are accommodated in the analysis. The 95% confidence interval for the analysis would likely be within these extremes.[24] In the absence of a professional consensus, a baseline analysis was developed based on review of the medical literature, taking study design and methods into account.

Cost of Neonatal Circumcision

A median physician reimbursement of $107, derived from a national survey of physicians, was used in the calculations and adjusted for 1999 US dollars.[36] The cost of performing a neonatal circumcision consists of more than the reimbursement to the physician. The time of hospital personnel, use of hospital space, and sterilization and handling of hospital equipment have also to be considered and has been estimated previously to be 82% of the physician costs.[4] The combination of the physician-related costs and hospital-related costs brings the total cost of an inpatient neonatal circumcision to $195. The duration of symptoms following neonatal circumcision was assumed to be 7 days.[37]

Table 1 Assumptions Used to Calculate Cost Utility

	Cumulative Incidence				Well-Years Lost	
	MFS (%)	LFS (%)	Best Judgment (%)	Cost ($)	Multiplier[a]	Duration (days)
Intact genitalia						
Urinary tract infections	1.60	1.43	1.52	Table 2	0.251	10
Hospitalized[b]	34.55	34.35	34.51	Table 2	0.341	5
Urosepsis[b]	4.86	4.86	4.86	2000	0.680	10
Vesicoureteral reflux[b]	10.00	10.00	10.00	1405	0.144	730
Renal disease[c]	2.00	2.00	2.00	500	0.144	Life
Additional hospitalization	18.39	17.87	18.12	3000	0.622	3
Recovery					0.327	7
Phimosis	4.00	0.60	0.90		0.292	7
Topical therapy	0	80	25	90	0.144	7
Topical failure rate		15	15			
Circumcision	100	0	75	1500	0.532	14
Complications	14	0	14	1500	0.622	3
Preputial plasty	0	20	0	2000	0.410	7
Complications		7		2000	0.622	3
Paraphimosis	0.05	0.01	0.05	350	0.605	1
Balanitis	11	4	8	60	0.292	4
First recurrence	20	20	20	40	0.144	7
Second recurrence	15	15	15	20		
Third recurrence	15	15	15			
Smegma	4	1	2	5	0.010	30
Pyoderma	8.22	1.37	2.70	135	0.301	7
STD					0.301	14
Bacterial STD	16.10	10.84	13.31	272	0.301	14
Viral STD	5.81	3.00	4.39		0.301	14
Herpes	1.48	1.12	1.30	303	0.301	14
Warts	4.33	1.88	3.09	213	0.301	14
HIV	0.0559	0.0454	0.0509	As below	As below	
Penile cancer (lifetime risk)	0.0870	0.0870	0.0870	25,000	See text	
Mortality	20	20	20	10,000	See text	
Neonatal circumcision						
Physician's fee	100	100	100	107	0.349	7
Hospital costs	20	100	80	88		
Increased stay	20	100	80	234		
Immediate complications	0.20	6.40	3.10	Table 3	Table 6	
Death from procedure	0.0002	0.01	0.0002		1	Life
Urinary tract infections	0.16	1.14	1.01	Table 2	0.251	10
Hospitalized[b]	15.87	20.12	18.03	Table 2	0.341	5
Urosepsis[b]	4.86	4.86	4.86	2000	0.68	10
Vesicoureteral reflux[b]	10.00	21.00	21.00	1405	0.144	730
Renal disease[c]	2.00	2.00	2.00	500	0.144	Life
Additional hospitalization	25.91	26.57	26.26	3000	0.622	3
Recovery					0.327	7
Phimosis	0.30	1.40	1.00		0.292	7
Surgery	100	100	100	1500	0.532	14
Complications	10	10	10	1000	0.622	3

(continued)

Table 1 (continued)

	Cumulative Incidence				Well-Years Lost	
	MFS (%)	LFS (%)	Best Judgment (%)	Cost ($)	Multiplier[a]	Duration (days)
Balanitis	4	13.9	10	60	0.292	4
First recurrence	20	20	20	40	0.144	7
Second recurrence	15	15	15	40		
Third recurrence	15	15	15	40		
Subpreputial debris	5	15	10	5	0.010	30
Coronal adhesions	8	15	12	10	0.010	90
Surgical correction	1.34	2.50	2.00	500	0.532	7
Pyoderma	5.6	12.6	6.4	135	0.301	7
Circumcision revision	1	5.0	2.8	1500	0.532	7
Complications	5	5	5	1500	0.622	3
Meatitis	10	20	20	5	0.040	30
Meatal stenosis	3	8	5	65	0.292	7
Surgery	50	50	50	1000	0.605	7
Foreskin restoration	0.01	0.2	0.1	50	0.257	4 years
Surgical restoration	2.5	2.5	2.5	1000	0.532	14
STDs					0.301	14
Bacterial STD	11.29	16.56	14.09	272	0.301	14
Viral STD	3.19	6.00	4.61		0.301	14
Herpes	0.92	1.28	1.10	303	0.301	14
Warts	2.27	4.71	3.51	213	0.301	14
HIV mild[d]	0.00236	0.0342	0.0287	5000	0.382	5 years
Moderate				20,000	0.578	2 years
Severe				50,000	0.640	1.25 years
Penile cancer	0.0160	0.0490	0.0290	25,000	See text	
Mortality	20	20	20	10,000	See text	

Note: MFS = most favorable scenario that is the least costly for circumcision and the most costly for noncircumcision; LFS = least favorable scenario that is the most costly for circumcision and the least costly for noncircumcision; STD = sexually transmitted disease.

a. Well-years lost multiplier is the quality of life lost while having the condition with full health being 1.00. A multiplier of 0.382 would mean that illness had subtracted 0.382 from full health of 1.00. The quality-adjusted life years lost would be the multiplier multiplied by the duration of the condition.

b. Percentages are of those with urinary tract infection.

c. Percentages are of those with vesicoureteral reflux. Cost is per year.

d. HIV costs are costs per year.

Rate of Immediate Complications from Neonatal Circumcision

The rate of immediate complications from neonatal circumcision in the medical literature ranges from 0.2%[38,39] to 3.1%[40] to 6.4%.[41] The 0.2% value was derived in 2 separate studies that relied on databases rather than chart reviews to collect information. Since a database is likely to miss a substantial number of complications, the 3.1% value, derived by investigators with the Centers for Disease Control and Prevention after thorough review of more than 1600 charts,[40] was employed for the baseline analysis. The 0.2% value was used for the MFS, whereas the 6.4% value was used for the LFS.

Immediate Complications

Complication costs were estimated using the cost of each complication and its absolute frequency (Table 3). The frequencies were determined by combining the data from 10 published series.[38,40–48] Because circumcision of an infant with *hypospadias* was not included in all of the published studies, the incidence reported by Gee and Ansell[48] was used. Since one or both parents often take time off from work associated with the birth

Table 2 Assumptions Used to Calculate the Cost (in 1999 US Dollars) of Diagnosing and Treating Urinary Tract Infection

	Outpatient	Inpatient
Clinic visit	56	0
Emergency room visit	80	213
Laboratory	284	380
Hospital room	0	1034
Nursing/room	0	634
Medication	15	150
Miscellaneous	26	57
Renal ultrasound	177	177
Voiding cystourethrogram	145	145
Total	783	2790

Source: Adapted from Hoberman and others.[64]

of a child, no cost for additional time of lost work was attributed to the immediate complications following neonatal circumcision.

Prolonged Hospitalization

A large, multicenter study determined that a circumcised boy stayed, on average, 0.26 days longer in the hospital regardless of the route of delivery. This translates into approximately one-fourth of circumcised boys staying in the hospital an extra day when compared to boys not circumcised. The increased length of stay was not attributed to complications from the procedure.[49] The increase in hospitalization costs due to delayed hospital discharge of the mother and newborn was included for all circumcisions performed prior to perinatal discharge.

Death from Circumcision

Similar to children who die of heritable disorders,[50] deaths resulting from complications of neonatal circumcision are often not reported as such on the death certificate. To determine the number of deaths due to circumcision by tabulating the number of cases reported in the medical literature is likewise folly.[51] The most commonly quoted death rate for neonatal circumcision is 1 in 500,000.[52] This incidence was used for calculating both the MFS and the baseline analysis. Alternatively, Gairdner reported between 9 and 12 deaths out of 90,000 circumcisions performed each year in the United Kingdom.[53] This incidence was used in the LFS.

Urinary Tract Infection

Until 1999, urinary tract infection rates have been reported as low as 0.01%[54] and as high as 0.31%[55] in circumcised boys and as low as 0.1%[52] and as high as 4.12%[56] in noncircumcised boys. Larger studies from the US Army dependent population that yielded the 4.12% incidence have subsequently failed to replicate the 4.12% rate.[57] Case-controlled prospective studies have documented odds ratios from 4.02[58] to 4.87.[59]

The assumptions for the baseline analysis rely heavily on a Canadian study published in *The Lancet* in 1999 by To and associates.[60] Although this study was based on a patient database, it avoids several of the flaws that characterized the US Army studies.[38,56,57,61,62] The Canadian study documented that circumcised boys with urinary tract infection were more likely to be treated as outpatients than were noncircumcised boys with urinary tract infection.

The incidence of hospitalized urinary tract infections in the 1st year of life was estimated directly from the Canadian study. To and others also documented the number of outpatient billings for urinary tract infection. The incidence of outpatient urinary tract infections was estimated by taking the number of billings for outpatient urinary tract infection and dividing it by 2.5 (this assumed that each outpatient urinary tract infection had an average of 2.5 billings related to the urinary tract infection). When the number of inpatient and outpatient urinary tract infections are combined, the overall rate is similar or higher than what has been reported in other studies.[63] The costs of inpatient and outpatient treatment of urinary tract infection were adopted from Hoberman and associates[64] as shown in Table 2. The adjustments of the costs estimated by Hoberman and associates reflect that renal scans are currently not part of the standard workup for urinary tract infection[65] and that less expensive antibiotics are more commonly used than those employed in their study.

For the LFS, the lower 95% confidence interval from the Canadian study was used. For the MFS, the urinary tract infection rate for noncircumcised boys was the upper 95% confidence interval value from the Canadian study. The urinary tract infection rate for circumcised boys was assumed to be one-tenth this value (consistent with the odds ratios reported in the US Army studies).

Although weak, evidence in the literature suggests that noncircumcised boys who develop urinary tract infection are less likely to have renal disease than circumcised boys who develop urinary tract infection.[66–69] The assumptions used reflect this.

Table 3 Immediate Complications from Neonatal Circumcision: Their Relative Frequency,[a] Costs, and Impact on Health

	Incidence (%)[a]	Cost per Case ($)	Well-Year Lost Multiplier	Duration (days)
Bleeding	53	500	0.349	2
Reoperation	5[b]	2500	0.349	3
Transfusion	1[b]	1500	0.622	7
Topical infections	30	1250	0.349	2
Sepsis	2	16,500	0.680	10
Meningitis	0.01	77,500	0.680	14
Minor surgical mishaps	8	1000	0.360	3
Anesthesia (hematoma)	3	100	0.118	7
Anesthesia (major)	0.3	2500	0.680	2
Obstructive uropathy	0.4	31,000	0.144	Life
Acute renal failure	0.1	11,000	0.680	7
Chronic renal failure	0.03		0.144	Life
Glans necrosis	4.2	12,000		
Acute			0.457	7
Chronic			0.129	55 years
Glans and penile amputation	1.6	20,000	0.257	Life
Ruptured bladder	0.01	15,000	0.563	30
Heart failure	0.01	20,000	0.530	7
Hypospadias inadvertently circumcised	1.18 per 100,000[c]	9,000	0.499	14

a. Percentage of those who develop complications.
b. Percentage of bleeding complications.
c. Incidence in total population.

The incidence of sepsis coinciding with urinary tract infection varies widely. The highest value (36.3%) was found in the study by Wiswell and Geschke, who also found 2 cases of meningitis.[38] Recently, Hoberman and others found a bacteremia rate of between 3% and 5% in male and female infants with urinary tract infection.[64] Similarly, Craig and colleagues reported concomitant bacteremia in 4.86% of boys.[58] Many of the cases of bacteriuria seen by Wiswell and Geschke can be attributed to the young patient age (younger than 1 month) and boys who were "too sick" to circumcise in whom urinary tract infections and meningitis were sequelae of primary sepsis. The bacteremia rate of 4.86% in the Australian study was used in the baseline analysis.[58]

Hospital Admissions in the 1st Year of Life

In the Canadian database used to determine the rate of urinary tract infection based on circumcision status, it was discovered that circumcised boys were significantly more likely to require hospitalization (excluding hospitalizations for urinary tract infection) during the 1st year of life.[60] The MFS and LFS were determined using the 95% confidence intervals. There is nothing to indicate that these hospitalizations are accounted for elsewhere in the analysis.

Phimosis

One of the major difficulties in dealing with the topic of phimosis is determining what constitutes "pathologic" phimosis as opposed to developmental phimosis. The definition of phimosis has never been precise and is often applied to the normal foreskin.[70] Prospective studies have demonstrated phimosis to be a rare finding in boys. Smith and others found 1 case of phimosis in 1000 boys.[71] In 213 Japanese boys younger than 2 years, only 4 (1.88%) had a "pinhole prepuce."[72] In France, the rate was 2.6%,[73] whereas in England, the incidence of true pathologic phimosis was calculated to be 0.9%.[74] The most recent study from Liverpool found that 0.6% of boys would develop phimosis by 15 years of age.[75]

When only prospective studies with a clear definition of phimosis are considered, the rate of pathologic phimosis, or *preputial stenosis*, is less than 2% in noncircumcised boys[72,74–76] and 0.32%[42] to 1%[44] in circumcised boys.

Although most cases of preputial stenosis in noncircumcised males result from premature, forcible retraction of the prepuce and resolve with a program of stretching by hand,[76–78] new studies have shown that topical therapy with corticosteroids is 75% to 95% effective.[70] Also, *preputial plasty* has superior results compared to circumcision, with half the morbidity and a significantly shorter recovery period.[79] For the MFS, all cases of preputial stenosis underwent circumcision. For the LFS, topical therapy was attempted first, followed by preputial plasty. For the baseline analysis, 25% were treated initially with topical therapy, whereas the remainder were circumcised.

Paraphimosis

The incidence of *paraphimosis*, which is nearly always iatrogenic, is unknown. Gairdner reported in 1949 that 7 (0.88%) out of 800 hospital admissions for male children were for paraphimosis and 10 (0.20%) out of 5000 adult male hospital admissions were for paraphimosis.[53] The incidence of paraphimosis for the population as a whole would be substantially less than these figures. Therapy involves initial decompression followed by treatment of the underlying preputial stenosis.

Balanitis

Balanitis refers to any inflammation of the penis, including conditions known as *posthitis*, balanitis, and balanoposthitis. The rate of balanitis is similar in both groups,[80,81] but the rate of balanitis in noncircumcised boys aged 3 is very low (0.07%).[82] Studies have consistently found that at the ages at which boys are in diapers, the rate of balanitis is lower in noncircumcised boys.[23,80] The rate of balanitis may be lower in circumcised males after toilet training,[80] but one study of adult men found balanitis more commonly in circumcised men (one-third of patients) than would be expected based on the circumcision rate in that community (5% to 10%).[83] The impact of circumcision on the incidence of balanitis in adult men is unknown.

Pyoderma

Studies by Enzenauer and others found that circumcised boys were more likely to have symptomatic topical skin infections, with an incidence of 2.7% in noncircumcised boys and 6.4% in circumcised boys.[84,85] Several previous studies found that staphylococcal *pyoderma* in newborns affected predominantly boys, nearly all of whom were circumcised.[86–88] This finding is consistent with the change in the periurethral bacterial flora following circumcision, which goes from predominantly gram-negative organisms to gram-positive organisms, predominantly staphylococcus.[89–91] MFS and LFS were calculated using 95% confidence intervals from the data of Enzenauer and colleagues.

Coronal Adhesions

Preputial remnants will often adhere to the surface of the *glans* following circumcision. Rates of 8%,[43] 12%, and 15%[92] were used to make calculations, although rates as high as 29.7% have been reported in the literature.[23] Most of these *coronal adhesions* will dissolve spontaneously, but a rate of surgery to lyse the adhesions of 3.3% has been reported and was used in the present calculations.[92]

Subpreputial Debris

A substantial percentage (24.7%) of circumcised boys will have epithelial debris trapped between the glans and overlying skin while they are still in diapers. In older boys, this debris is rarely found.[23] This debris can cause irritation and may signal improper hygiene. In contrast, *smegma*, the epithelial debris found between the glans and foreskin, is a rare finding in noncircumcised infants (0.5%).[82] In the general population of noncircumcised adolescent boys and young men, the rate of substantial smegma accumulation is approximately 2%.[93]

Meatitis and Meatal Stenosis

Studies have found meatal ulcerations in 8% to 31% of circumcised boys.[44,53,94] Traumatic meatitis of the unprotected postcircumcision urethral meatus and/or meatal ischemia following damage to the frenular artery at circumcision may lead to *meatal stenosis*,[17] which is a major contributor to obstructive uropathy.[94,95] The incidence of meatal stenosis following circumcision ranges between 2.9%[21] and 11.1%.[22] The rates of developing meatal stenosis were assumed to be 3%, 5%,[23] and 8%[44] for making calculations. Half were estimated to require *meatotomy*. Boys aged 3 to 7 years were considered most likely to develop meatal stenosis.

Circumcision Revision

Circumcision revision rates of 1%,[43,47] 2.8%,[80] and 9.5%[45] have been reported. These rates were used for the different scenarios.

HIV

Several studies conducted in Africa have shown HIV to be more common in noncircumcised men; other studies have shown the opposite, whereas most have shown little or no difference.[96,97] The HIV pandemic in Africa demonstrates distinct epidemiological differences from the outbreaks in North America or Europe.[97] For example, most infections in Europe and North America are transmitted by nonheterosexual means. Based on World Health Organization 1998 data of First World countries, the United States has the highest rate of HIV as well as the highest rate of infant circumcision.[97–100] Consequently, what little evidence for a role of circumcision in preventing HIV infection in the United States is weak and inconclusive.

For calculation purposes, the baseline analysis used an odds ratio of 1.78, with the extreme cases using the 95% confidence interval of 1.33 and 2.37 derived from performing a meta-analysis of peer-reviewed published studies,[13,97,101–109] using a random effects model.[28] The annual incidence of heterosexually transmitted HIV for men not identified as intravenous drug users in 1998 in the United States was 398 per million.[100] Using the 1.78 odds ratio, the incidence of HIV infection would be 509 and 287 per million in noncircumcised and circumcised men, respectively. The impact of circumcision status on HIV transmission in homosexual men has received little or no study with conflicting results.[110,111] Likewise, the impact of circumcision status on the transmission of HIV in intravenous drug users would be difficult to explain. Consequently, only heterosexually transmitted HIV was considered in this model.

Sexually Transmitted Diseases

Although it has long been assumed that men with foreskins were at higher risk for sexually transmitted diseases, new studies have shown circumcised men to be at increased risk for developing gonorrhea, syphilis, genital warts, nongonococcal urethritis, chlamydial infections, and genital herpes. Many of the older studies failed to control for differences in sexual practices, socioeconomic status, and so forth, whereas several of the newer studies used study design elements to minimize the impact of these factors. Overall, circumcised men may have a greater number of sexually transmitted diseases.[112]

A random-effects model[28] of meta-analysis was applied to available data[107,112–114] to determine the impact of circumcision status on susceptibility to different sexually transmitted diseases. Summary effects were used in the best judgment calculation, whereas the 95% confidence intervals were used for the MFS and LFS. The incidences and age distributions of the various sexually transmitted diseases in American males were provided by the National Health and Social Life Survey conducted by a research team at the University of Chicago.[34]

Penile Cancer

While keeping the incidence of penile cancer in noncircumcised men consistent with the rate reported in northern Europe (lifetime risk of 1 in 1149),[115–117] the rate in circumcised men was reduced using the odds ratio and 95% confidence intervals determined by Maden and others.[15] The cost of treating penile cancer was estimated at $25,000.[2] For the 20% of men expected to die from penile cancer, an additional cost of $10,000 was added to reflect the cost associated with their greater morbidity. Age-of-onset data[31] were used to calculate well-years lost as previously described,[2] with one alteration: Instead of an 8-year delay in loss of life expectancy for all men with penile cancer, the 20% expected to die from the illness were tallied as mortalities, whereas loss of health for 3 years was tallied for the 80% who survived the cancer.

Foreskin Restoration

A growing number of men circumcised at birth have been pursuing foreskin restoration.[118–122] Approximately 0.1% of men circumcised at birth could be expected to pursue foreskin restoration. Of these, only 2.5% would rely on surgical means, with the remainder relying on taping methods and devices that stretch skin over the glans. The average duration of foreskin stretching is about 4 years (Wayne Griffiths, personal communication, March 1997).[120,121]

RESULTS

Markov Analysis

Marginal costs for the different cost scenarios and discount rates are seen in Table 4. In every scenario, it was more costly to circumcise. Using the baseline analysis, neonatal circumcision and its sequelae cost

Table 4 Marginal Costs per Individual Resulting from Neonatal Circumcision Compared to Noncircumcision (in dollars)

	Most Favorable for Neonatal Circumcision	Least Favorable for Neonatal Circumcision	Best Judgment
No discount	99.15	1158.51	778.66
3% discount	304.48	1135.54	828.42
5% discount	356.30	1124.13	837.59

Table 5 Marginal Well-Years Lost per 1000 Resulting from Neonatal Circumcision Compared to Noncircumcision

	Most Favorable for Neonatal Circumcision	Least Favorable for Neonatal Circumcision	Best Judgment
No discount	–11.344	45.082	15.925
3% discount	2.224	26.688	15.300
5% discount	4.845	21.943	14.609

$828.42 (3% discount) to $837.59 (5% discount) more than leaving the genitalia intact. Even for the MFS, circumcision was more costly. In all scenarios, the cost of neonatal circumcision is higher than noncircumcision, regardless of the discount rate.

With one exception, each set of assumptions and discount rates results in neonatal circumcision having an overall lifetime negative impact on health (Table 5). The only exception was the MFS with no discount of costs or utility. When discounting is applied, the positive health effect of this extreme situation cannot be demonstrated. With neonatal circumcision having an overall negative impact on health and failing to save money, noncircumcision was clearly the dominant strategy.

Sensitivity Analysis

Forty-seven variables were subjected to sensitivity analysis. Individually, none of the variables altered the conclusion of the analysis. The impact of the 22 most influential variables is depicted in a tornado diagram (Figure 1). The variables related to the initial circumcision had the most impact. The threshold incidences of various ailments in noncircumcised males necessary to make neonatal circumcision cost-neutral in the baseline analysis (3% discount) are listed in Table 6. For all ailments, the incidence to make neonatal circumcision cost-neutral is far outside the realm of what has been reported in the medical literature.

To make neonatal circumcision cost-neutral, hospitalized urinary tract infections would need to cost $229,564. One-way sensitivity analysis was unable to reach a threshold for the physician fee, for the rate of immediate complications, the death rate, or for the duration of pain following the procedure. Using the baseline analysis (3% discount), if neonatal circumcision were cost-free, were immediate complication-free, had no additional days of hospitalization, and had no immediate negative impact on health, neonatal circumcision would still be more costly (marginal $400.03) and have a negative impact on health (marginal 3.34 well-years/1000).

Table 6 Incidence of Illnesses Afflicting Males with a Foreskin That Would Be Necessary to Make Neonatal Circumcision Either Cost or Health Neutral in the Best Judgment Scenario Compared to Reported Incidences (3% Discount Rate)

Illness	Cost	Health	Reported
Urinary tract infection	38.52%	35.52%	1.50%
Balanitis	>100%	>100%	8.0%
Phimosis	41.49%	53.11%	0.9%
HIV	4.36%	0.49%	0.0398%
Bacterial STDs[a]	17.67×	8.18×	
Viral STDs[a]	58.54×	22.84×	
Penile cancer (lifetime risk)	1 in 9.36	1 in 113	1 in 1735

a. Reported as multiples of best judgment assumptions.

Marginal Cases

The cost to prevent an additional case of various ailments is shown in Table 7. The costs to prevent the marginal case of an illness are excessive.

Monte Carlo Simulation

A Monte Carlo simulation taking 1000 samples using 24 variables yielded a marginal cost per patient of $852.04 ± $175.02 (± standard deviation; 0% discount), $908.65 ± $167.80 (3% discount), and $922.10 ± $165.48 (5% discount). The marginal utility in well-years lost per 1000 individuals was 15.64 ± 6.48 (0%

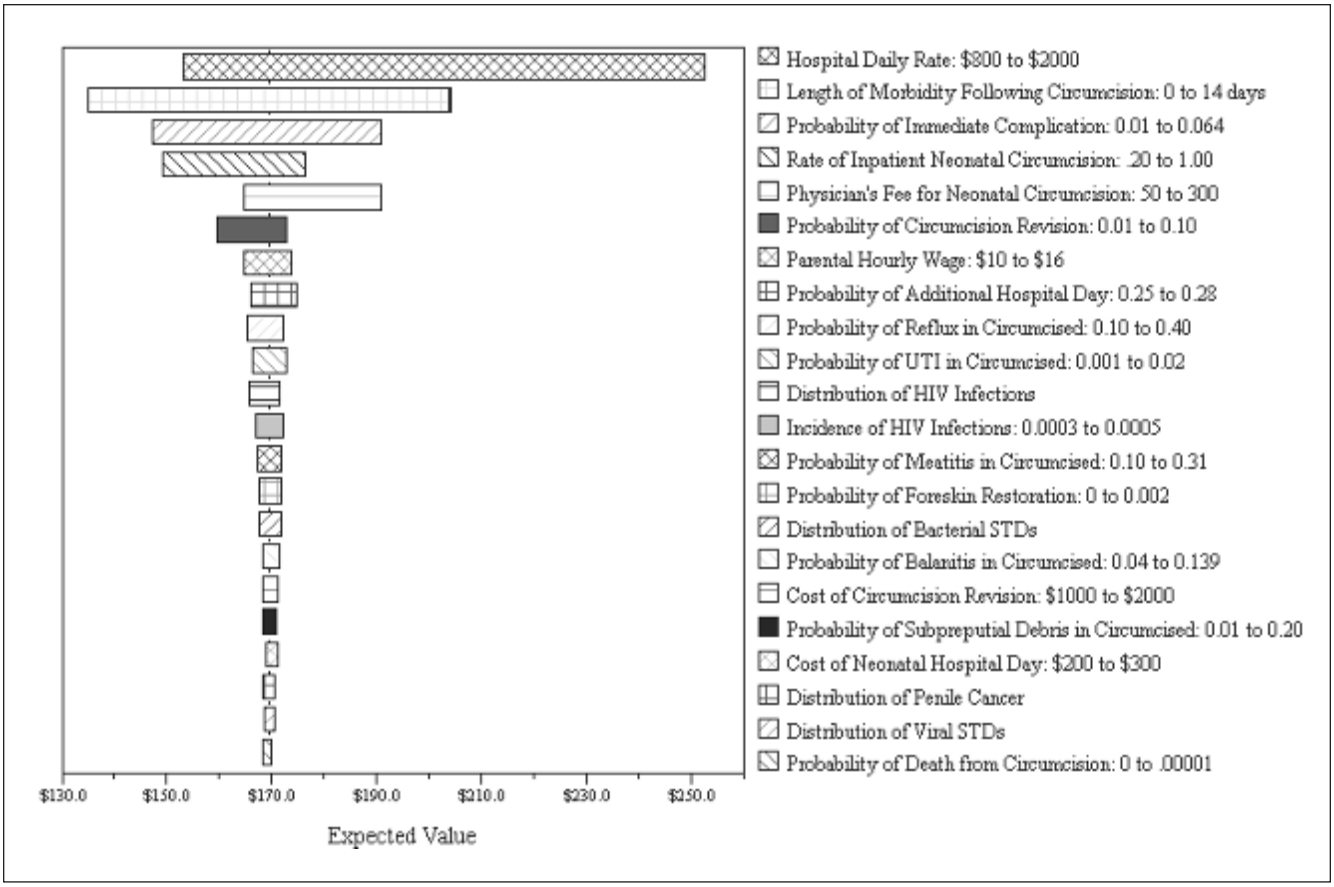

Figure 1 Tornado diagram of most influential variables. UTI = urinary tract infection; STD = sexually transmitted disease.

discount), 16.10 ± 3.81 (3% discount), and 15.47 ± 3.36 (5% discount).

Health Policy Space

Figure 2 displays the results of the analysis in health policy space. The x-axis represents well-years gained or lost per 1000 persons, whereas the y-axis represents net dollars per individual. All the points, with one exception, fall in the right-upper quadrant where wellness is lost and dollars are spent, representing undesirable health policy. The results published by Ganiats and colleagues, discounted at 5%, are included for comparison purposes.[2] Figure 3 displays results of Monte Carlo simulations in health policy space showing the 95% confidence intervals.

DISCUSSION

This analysis demonstrates that regardless of the values placed on the variables in the model, neonatal circumcision is more costly and has more adverse health effects over the lifetime than foregoing the procedure does. This is demonstrated using sensitivity analysis, analysis of extreme scenarios, and Monte Carlo simulations.

The results of the present study are in step with those previously published. The studies by Lawler and colleagues[1] and Ganiats and associates[2] found little difference in lifetime cost between those circumcised at birth and those left intact. Newer, less invasive treatments of preputial stenosis, as well as a better understanding of the penile problems seen in circumcised men (including penile cancer and meatal stenosis) and the cost of longer perinatal stays, have swung the pendulum away from a cost-neutral position. Consistent with the present study, Ganiats and associates found that neonatal circumcision impaired health to the degree that it would take a 28% rate of circumcision later in life to have the same negative impact on health.[2]

Similar to the present analysis, Chessare found that the rate of urinary tract infection among infant boys with foreskins must equal or exceed 29% for neonatal

Table 7 Marginal Cost per Case Averted by Performing Circumcisions (in dollars)

Ailment	Best Judgment Scenario	Most Favorable Scenario	Least Favorable Scenario
Urinary tract infection	69K	22.8K	127.9K
HIV infection	4.75M	1.33M	11.5M
Penile cancer	1.42M	435K	2.95M
Phimosis	76K	22.8K	198K
Paraphimosis	1.66M	609K	2.27M
Syphilis	398K	90K	[a]
Gonorrhea	93K	10.0K	[a]
Genital herpes simplex	452K	66K	[a]
Any ailment	22.4K	4.5K	50.8K

Note: In the least favorable scenario, circumcision increased the likelihood of these ailments.

circumcision to be cost-effective.[3] Similar to previous studies, penile cancer and urinary tract infections played only a small role in total financial analysis because more common penile problems had a much larger impact.

The greatest handicap in the development of this analysis was the poor quality of the vast majority of the studies encountered. Although most studies provided raw data, very few identified, let alone controlled for, confounding factors or effect modifiers. No attempts were made to confirm the validity of ecological data or the accuracy of demographic information from databases. In some studies, subjects were arbitrarily excluded, whereas in others, including prospective studies, circumcision status was not recorded in substantial percentages. The wide range of study results likely reflects this lack of attention to solid methodology.

Because of the large number of variables in the analysis and their additive effects, traditional 2-way and 3-way sensitivity analysis could not adequately address the diversity of available data and would underestimate the confidence interval of the model.[24] By calculating the extreme scenarios favoring circumcision and favoring noncircumcision, knowing that the 95% confidence interval would be well within this range, sensitivity analysis of all variables is simultaneously accomplished. Since the extreme scenario favoring neonatal circumcision found the procedure to cost more in both money and health, it is therefore impossible to manipulate the variables to justify neonatal circumcision on a financial or health basis. Since it is unlikely that the MFS or the LFS reflect reality, the truth lies somewhere in between these 2 extremes. The baseline analysis, especially given the poor quality of the studies to chose from, is a rough estimate. The breadth of the confidence interval of the baseline analysis is more closely estimated using the Monte Carlo simulation. The limitation of this method is its inability to accommodate all of the variables in the model and tendency to center on the baseline result.

Studies from the past century were reviewed to determine their role in this analysis. Although more weight was given to recent studies, in general results were more dependent on study design than on the decade in which the study was performed. The lack of definitive studies is in part due to the rarity of benefits from neonatal circumcision, if they exist at all, and poor study design. In nearly all of the studies consulted, it was impossible to differentiate the impact of circumcision from other characteristics that distinguish circumcised and noncircumcised populations. The 40-fold difference between the low and high value of immediate complication rates is indicative of the difficulty in studying this issue. The low value was compiled by using a database of 136,086 boys born in US Army hospitals worldwide from 1980 to 1985.[38] The charts of these individuals were not reviewed, nor was a sample reviewed to determine whether the database accurately reflected what could be abstracted directly from the charts. Undocumented complications of circumcision are not unusual. As a result, a database would seriously underestimate the complication rate of neonatal circumcision. Despite these methodological flaws, the results from the Wiswell and Geschke study, which were confirmed in a recent study sharing the identical methodology,[39] were used in calculating the MFS.

Likewise, there are a number of obstacles in studying the impact of the presence of a foreskin on urinary tract infections. The most notable is the difficulty in accurately documenting differences regarding rare occurrences. The other major obstacle is the number of confounding risk factors for developing a urinary tract infection that have yet to be controlled for in most of the studies published to date. These include rooming in,[122] breastfeeding,[123–127] parental education and social status,[128] prenatal maternal urinary tract infections,[129] history of urinary tract infection in a 1st-degree relative,[127] maternal fever at the time of delivery, perinatal anoxia,[130] low birth weight,[131] prematurity,[132–134] hygienic practices,[135–138] previous bacterial or viral infection, previous course of antibiotics,[127] race,[139–143] urine collection method,[144–147] and diagnostic criteria.[148,149] Any one of these factors might explain the small (less than 1 per 100) absolute difference in the incidence of urinary tract infection documented in previous studies. To date, only 1 study has adjusted for perinatal

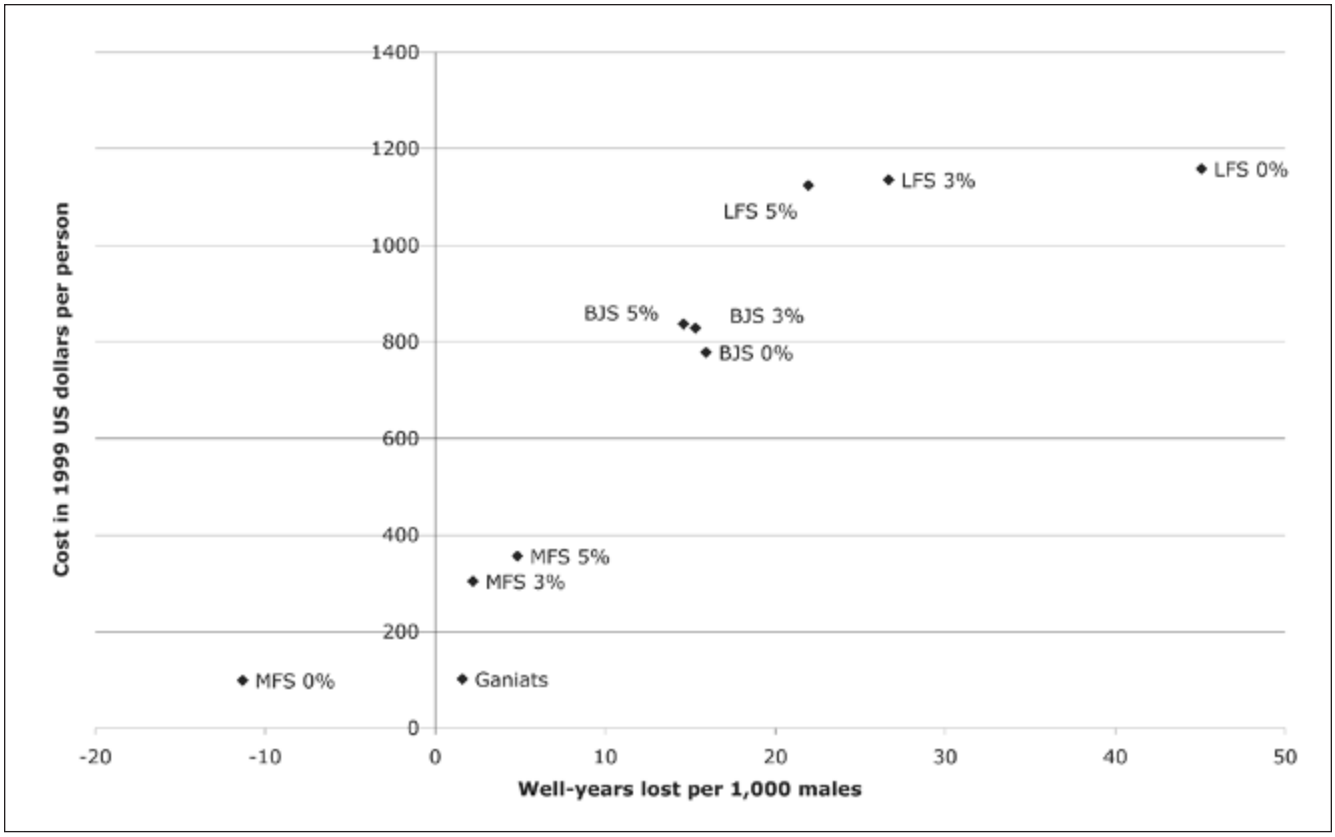

Figure 2 Healthy policy space. LFS = least favorable scenario; BJS = best judgment scenario; MFS = most favorable scenario.

complication and socioeconomic status.[60] Otherwise, none of the other factors have been addressed.

The reasons for using the recent Canadian study by To and associates[60] in estimating urinary tract infection risk are 4-fold. First, To and associates studied the entire population of Ontario, which should be fairly representative of the general population, as opposed to dependents of a volunteer army, which may not be representative of the population as a whole. Second, the Canadian study eliminated from consideration newborns with complicated neonatal courses and controlled for socioeconomic status. In the US Army studies, one-third of the boys not circumcised at birth were too sick to undergo the procedure neonatally.[150] Third, the Canadian study had a nearly even proportion of boys circumcised and not circumcised, whereas the US Army studies had a very high circumcision rate. Thus, the impact of a unidirectional misclassification error, to which database studies are prone and reported to be as high as 15% to 30%,[40,151] would be less in the Canadian study. Finally, the Canadian study tabulated urinary tract infections treated as both outpatients and inpatients, whereas the US Army study considered only urinary tract infections treated as inpatients.

A mathematical model has been developed to assess the potential impact of the confounding variables listed above insofar as they can be differentially attributed to circumcision status. Even when no underlying difference in the incidence of true urinary tract infection is assumed, a 4-fold increase in the diagnosis of urinary tract infection in noncircumcised males can be demonstrated (unpublished data). Other factors, such as breast-feeding, can have a large impact on urinary tract infection rates, but their relative distribution to circumcised and noncircumcised males is unknown. Likewise, adjusting the large urinary tract infection database studies for prematurity or misclassification substantially reduced the odds ratio of the association between the prepuce and urinary tract infections.[152] After accounting for the combined impact of confounding factors and misclassification, the association between the prepuce and diagnosing urinary tract infection may be fatuous. This is suggested by several studies from Israel that have demonstrated that neonatal circumci-

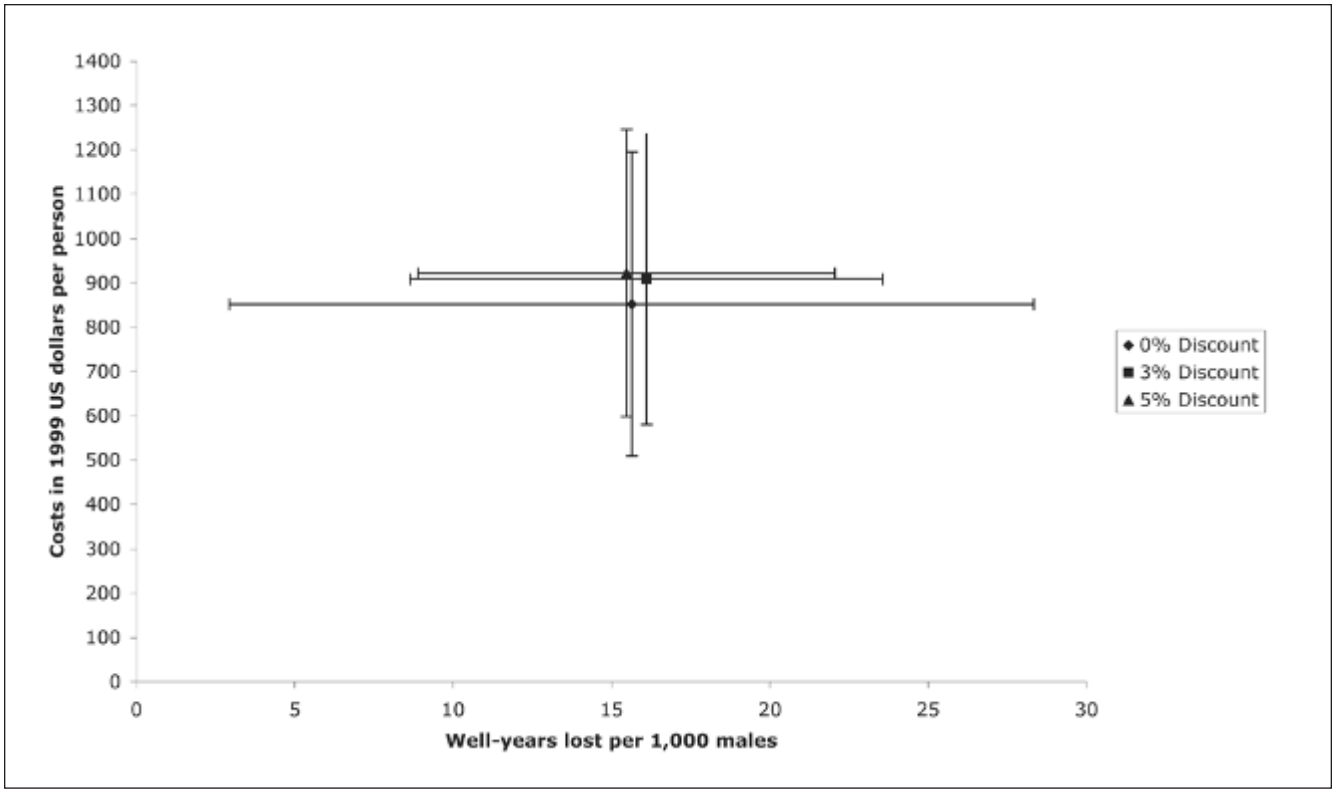

Figure 3 Health policy space, Monte Carlo simulation with 95% confidence intervals.

sion induces an incidence spike of urinary tract infections shortly following the procedure.[55,153,154]

Randomized blinded prospective studies are impossible, so in their absence, methodologically flawed observational studies,[155] showing that the prepuce predisposes to preputial stenosis, urinary tract infections, and penile cancer, were considered valid for purposes of this study. It is reasonable to doubt the role of the prepuce in these conditions. No study has ever demonstrated that neonatal circumcision significantly lowers the incidence of preputial stenosis. The incidences of penile cancer in Denmark,[115] Finland,[117] Norway,[116] and Japan,[156] where less than 1.5% of men are circumcised, are lower than in the United States,[157] where the majority of men are circumcised. If circumcision is believed to decrease the risk of developing penile cancer, it is unclear why these noncircumcising countries with similar standards of living and hygiene have lower incidences of penile cancer. There is inconsistency and a high degree of variation in the studies looking at circumcision status and sexually transmitted diseases,[112] including HIV infection.[97] Nearly all studies of immediate complications from neonatal circumcision are retrospective and may underestimate the number of complications. For example, the only prospective study published to date investigated only bleeding and found that 9.9% of boys who underwent neonatal circumcision had notable bleeding following the surgery.[158]

Although the focus of this analysis is the cost utility of neonatal circumcision given the present medical milieu in North America, HIV data from Africa were included in the analysis because of their availability. Most experts agree that the pandemic in Africa is clearly different than the pandemic in North America.[98] As a result, using African data may overstate the advantage of neonatal circumcision as North American studies have, for the most part, failed to document any advantage for circumcised males.[13,110,159,160] A cost utility of circumcision for males living in Africa would require a different set of assumptions but should be undertaken before implementation of any circumcision policy.

Odds ratios closely approximate relative risks when the incidence of events is small. Since most outcomes for which the odds ratio were relied on occurred in less than 1% of the population, the expected difference between relative risks and odds ratio would be small. For example, the odds ratio of 1.7739 used for HIV infection corresponds to a relative risk of 1.7735. For penile

cancer, the odds ratio of 3.002 corresponds to a relative risk of 3.000. For urinary tract infections, the odds ratio of 1.506 corresponds to a relative risk of 1.505. Clearly, converting odds ratios to relative risks would have a minimal impact on the outcome of the analysis.

There are several factors excluded from the analysis because of the difficulty in quantifying their effect. For example, neonatal pain experts now believe that neonates may feel more pain for a given stimulus than older infants do.[161] Although it is unknown how long neonates suffer from circumcision, it has been demonstrated that circumcised boys cry louder and longer when given their immunizations several months later.[162] No attempt was made to quantify this alteration in pain response. Likewise, no attempt was made to place a value on bodily integrity or the retention of the specialized nerve endings concentrated in the end of the prepuce.[163] These intangibles weigh in favor of leaving the penis alone. Also, the value of the infant to be free from intrusive unnecessary medical and surgical procedures before he has reached the age of full and legal discretion (*Little v Little* 576 S. W. 2d 493-5; *Re Richardson* 284 So 2d 185-7; *Wisconsin v Yoder* (1972) 406 US 205, 234; *Kate's School v Department of Health* (1979) 155 Cal. Rptr. 529; *Valerie N. v Valerie N* (1985) 219 Cal. Rptr. 387; *Prince v Massachusetts* 321 US 158 (1944)[164] was not considered.

Any adjustments in this analysis for the impact of neonatal circumcision on genital hygiene or genital "sameness" would be purely speculative since, other than 2 studies demonstrating an increase in hygiene-related issues in circumcised boys younger than 3 years,[23,80] no study has demonstrated circumcision's impact on hygiene or "being different" from one's cohort, let alone their magnitude, prevalence, or direction. Given this lack of factual evidence, no attempt was made to incorporate these undocumented concerns into the analysis.

The perpetuation of neonatal circumcision cannot be justified financially or medically; therefore, any justification for the practice must be based on religion, culture, or aesthetics. A limitation of cost-utility analysis is the inability to incorporate such factors. Currently in the United States, cultural considerations trump financial and health concerns when deciding to have a newborn male circumcised. Consequently, this cost-utility analysis will have little or no impact on circumcisions performed for cultural reasons. Instead, this cost-utility analysis is aimed at the financial and medical aspects of neonatal circumcision.

Should 3rd-party payers pay for the procedure? Based on this analysis, it would be in their financial interests not to. Still, insurance companies take cultural factors into account when marketing their health plans. This justification has been given by members of the insurance industry for providing neonatal circumcision benefits to their customers. It seems odd, however, that other body modifications, such as ear piercing and tattoos, are rarely covered by medical insurance plans.

The medical community faces a different set of issues. Should medical care providers perform a procedure on a newborn knowing that it is more likely to impair health than improve it? Medical ethical standards, such as "do no harm," appear not to condone such a practice.[165] By performing circumcisions on infants, health care providers venture into the realm of being "cultural brokers." The debate whether this is the proper venue for medical services has not taken place. The analysis is clear: Neonatal circumcision cannot be justified on economic or medical grounds. If the medical community is interested in preserving health and saving money, they should refrain from promoting, encouraging, or presenting neonatal circumcision as a medical option. Third-party payers may want to reassess their current reimbursement policies and possibly consider paying physicians or parents not to perform neonatal circumcisions. Either of these options would result in an overall cost savings.

APPENDIX
Glossary

Balanitis	Inflammation of the glans (head) of the penis.
Balanoposthitis	Inflammation of the glans (head) of the penis and the prepuce (foreskin).
Coronal adhesions	Tissue connections between remnants of the inner layer of the prepuce (foreskin) and the rim (corona) at the base of the glans (head) of the penis.
Glans	Head of the penis.
Hypospadias	An anomaly in which the opening of the urethra is not at the tip of the glans (head) of the penis but opens on the underside.
Meatal stenosis	Narrowing of the opening of the urethra.
Meatitis	Inflammation of the opening of the urethra.

(continued)

Appendix (continued)

Meatotomy	Enlarging the opening of the urethral opening by surgical means.
Paraphimosis	The inability to bring a retracted prepuce (foreskin) proximally (back over the head of the penis). This can lead to a constriction of blood flow and distal swelling.
Phimosis	An inability to retract the prepuce (foreskin) back over the head of the penis. This is often normal in boys through puberty. There is much confusion in the literature regarding what constitutes phimosis and what forms of phimosis are pathologic.
Posthitis	Inflammation of the prepuce (foreskin).
Prepuce	Foreskin.
Preputial plasty	A surgical procedure in which the opening at the distal end of the prepuce (foreskin) is made larger using plastic surgical techniques.
Preputial stenosis	Abnormal narrowing of the opening at the distal end of the prepuce (foreskin).
Pyoderma	Bacterial skin infection, often caused by Staphylococcus.
Smegma	A collection of dead skin, dead white blood cells, and urethral and prostatic secretions that can form under the prepuce (foreskin).
Urosepsis	A systemic infection that results from an infection of the urinary tract.
Vesicoureteral reflux	An abnormal movement of urine from the bladder up the ureters toward the kidneys.
Voiding cystourethrogram (VCUG)	A radiologic evaluation of the lower urinary tract used to detect vesicoureteral reflux.

REFERENCES

1. Lawler FH, Bisonni RS, Holtgrave DR. Circumcision: a decision analysis of its medical value. Fam Med. 1991;23:587–93.
2. Ganiats TG, Humphrey JB, Taras HL, Kaplan RM. Routine neonatal circumcision: a cost-utility analysis. Med Decis Making. 1991;11:282–93.
3. Chessare JB. Circumcision: is the risk of urinary tract infection really the pivotal issue? Clin Pediatr (Phila). 1992;31:100–4.
4. Cadman D, Gafni A, McNamee J. Newborn circumcision: an economic perspective. Can Med Assoc J. 1984;131:1353–5.
5. Schoen EJ, Wiswell TE, Moses S. New policy on circumcision: cause for concern. Pediatrics. 2000;105:620–3.
6. Australian Medical Association. Circumcision deterred. Aust Med. 1997;6:5.
7. Fetus and Newborn Committee, Canadian Paediatric Society. Neonatal circumcision revisited. Can Med Assoc J. 1996;154:769–80.
8. Leditschke JF. Australasian Association of Paediatric Surgeons. Guidelines for Circumcision. Hersion, Queensland (Australia); 1996.
9. General Medical Council (UK). Guidance for Doctors Who Are Asked to Circumcise Male Children. London: General Medical Council; 1997.
10. Australian College of Paediatrics. Position Statement: Routine Circumcision of Normal Male Infants and Boys. Parkville, Victoria: Australian College of Paediatrics; 1996.
11. American Academy of Pediatrics Task Force on Circumcision. Circumcision policy statement. Pediatrics. 1999;103:686–93.
12. Seed J, Allen S, Mertens T, et al. Male circumcision, sexually transmitted disease, and risk of HIV. J Acquir Immune Defic Syndr Hum Retrovirol. 1995;8:83–90.
13. Laumann EO, Masi CM, Zuckerman EW. Circumcision in the United States: prevalence, prophylactic effects, and sexual practice. JAMA. 1997;277:1052–7.
14. Urassa M, Todd J, Boerma JT, Hayes R, Isingo R. Male circumcision and susceptibility to HIV infection among men in Tanzania. AIDS. 1997;11:73–80.
15. Maden C, Sherman KJ, Beckmann AM, et al. History of circumcision, medical conditions, and sexual activity and risk of penile cancer. J Natl Cancer Inst. 1993;85:19–24.
16. Weiss GN, Weiss EB. A perspective on controversies over neonatal circumcision. Clin Pediatr (Phila). 1994;33:726–30.
17. Persad R, Sharma S, McTavish J, Imber C, Mouriquand PD. Clinical presentation and pathophysiology of meatal stenosis following circumcision. Br J Urol. 1995;75:91–3.
18. Frank JD, Pocock RD, Stower MJ. Urethral strictures in childhood. Br J Urol. 1988;62:590–2.
19. Upadhyay V, Hammodat HM, Pease PW. Post circumcision meatal stenosis: 12 years' experience. N Z Med J. 1998;111:57–8.
20. Frank JD. Circumcision, meatotomy and meatoplasty. In: Spitz L, Coran AG, eds. Pediatric Surgery. 5th ed. London: Chapman & Hall Medical; 1995. p 738–44.
21. Griffiths DM, Atwell JD, Freeman NV. A prospective survey of the indications and morbidity of circumcision in children. Eur Urol. 1985;11:184–7.
22. Stenram A, Malmfors G, Okmian L. Circumcision for phimosis: indications and results. Acta Paediatr Scand. 1986;75:321–3.
23. Van Howe RS. Variability in penile appearance and penile findings: a prospective study. Br J Urol. 1997;80:776–82.
24. Gold MR, Siegel JE, Russell LB, Weinstein MC. Cost-Effectiveness in Health and Medicine. New York: Oxford University Press; 1996.

25. Kaplan RM, Bush JW, Berry CC. Health status index: category rating versus magnitude estimation for measuring levels of well-being. Med Care. 1979;17:501–21.

26. Kaplan RM, Anderson JP. A general health policy model: update and applications. Health Serv Res. 1988;23:203–35.

27. Kaplan RM, Bush JW. Health-related quality of life measurement for evaluation research and policy analysis. Health Psychol. 1982;1:61–80.

28. Petitti DB. Meta-Analysis, Decision Analysis, and Cost-Effectiveness Analysis: Methods for Quantitative Synthesis in Medicine. 2nd ed. New York: Oxford University Press; 2000.

29. US Department of Labor. Consumer price index. Available from: URL: ftp:/!ftp.bls.gov/pub/special.requests/cpi/cpiai.txt. Accessed 24 January 2004.

30. Weinstein MC, Siegel JE, Gold MR, Kamlet MS, Russell LB. Recommendations of the panel on cost-effectiveness in health and medicine. JAMA. 1996;276:1253–8.

31. Kochen M, McCurdy S. Circumcision and the risk of cancer of the penis: a life-table analysis. Am J Dis Child. 1980;134:484–6.

32. Centers for Disease Control and Prevention, National Center for HIV, STD, & TB Prevention, Division of HIV/AIDS Prevention. Basic statistics: cumulative cases (through 12/31/98). Available from: URL: http://www.cdc.gov/nchstp/hiv_aids/stats/cumulati.htm. Accessed 3 August 1999.

33. Rickwood AMK. Medical indications for circumcision. BJU Int. 1999;83 Suppl 1:45–51.

34. Laumann EO, Gagnon JH, Michael RT, Michaels S. The Social Organization of Sexuality: Sexual Practices in the United States. Chicago: University of Chicago Press; 1994. p 376–441.

35. US Bureau of Labor Statistics. The employment situation: May 1999. Available from: URL: http://stats.bls.gov/newsrels.htm. ftp://146.142.4.23/publnews.release/empsit.txt. Accessed June 1999.

36. *Medical Economics Pediatrics Edition.* 1995;14(11):34.

37. Dixon S, Snyder J, Holve R, Bromberger P. Behavioral effects of circumcision with and without anesthesia. J Dev Behav Pediatr. 1984;5:246–50.

38. Wiswell TE, Geschke DW. Risks from circumcision during the first month of life compared with those for uncircumcised boys. Pediatrics. 1989;83:1011–5.

39. Christakis DA, Harvey E, Zerr DM, Feudtner C, Wright JA, Connell FA. A trade-off analysis of routine newborn circumcision. Pediatrics. 2000;105:246–9.

40. O'Brien TR, Calle EE, Poole WK. Incidence of neonatal circumcision in Atlanta, 1985-1986. South Med J. 1995;88: 411–5.

41. Moreno CA, Realini JP. Infant circumcision in an outpatient setting. Tex Med. 1989;85:37–40.

42. Kaweblum YA, Press S, Kogan L, Levine M, Kaweblum M. Circumcision using the Mogen clamp. Clin Pediatr (Phila). 1984;23:679–82.

43. Metcalf TJ, Osborn LM, Mariani EM. Circumcision: a study of current practices. Clin Pediatr. 1983;22:575–9.

44. Patel H. The problem of routine circumcision. Can Med Assoc J. 1966;95:576–81.

45. Leitch IO. Circumcision: a continuing enigma. Aust Paediatr J. 1970;6:59–65.

46. Millar AJW, Roberts D. Complications of circumcision using the plastibell device. S Afr Med J. 1987;72:438–9.

47. MacCarthey D, Douglas JQB. Circumcision in a national sample of 4-year old children. Br Med J. 1952;2:755–6.

48. Gee WF, Ansell JS. Neonatal circumcision: a ten-year overview—with comparison of the Gomco clamp and the Plastibell device. Pediatrics. 1976;58:824–7.

49. Mansfield CJ, Hueston WJ, Rudy MA. Neonatal circumcision: associated factors and length of hospital stay. J Fam Pract. 1995;41:370–6.

50. Cunniff C, Carmack JL, Kirby RS, Fiser DH. Contribution of heritable disorders to mortality in the pediatric intensive care unit. Pediatrics. 1995;95:678–81.

51. Wiswell TE. Circumcision circumspection. N Engl J Med. 1997;336:1244–5.

52. Burger R, Guthrie TH. Why circumcision? Pediatrics. 1974;54:362–4.

53. Gairdner D. The fate of the foreskin. Br Med J. 1949;2:1433–7.

54. Altschul MS. Larger numbers needed. Pediatrics. 1987;80:763–4.

55. Cohen HA, Drucker MM, Vainer S, et al. Postcircumcision urinary tract infection. Clin Pediatr (Phila). 1992;31:322–4.

56. Wiswell TE, Smith FR, Bass JW. Decreased incidence of urinary tract infections in circumcised male infants. Pediatrics. 1985;75:901–3.

57. Wiswell TE, Hachey WE. Urinary tract infections and the uncircumcised state: an update. Clin Pediatr (Phila). 1993;32:130–4.

58. Craig JC, Knight JF, Sureshkumar P, Mantz E, Roy LP. Effect of circumcision on incidence of urinary tract infection in preschool boys. J Pediatr. 1996;128:23–7.

59. Crain EF, Gershel JC. Urinary tract infections in febrile infants younger than 8 weeks of age. Pediatrics. 1990;86:363–7.

60. To T, Agha M, Dick PT, Feldman W. Cohort study on circumcision of newborn boys and subsequent risk of urinary-tract infection. Lancet. 1998;352:1813–6.

61. Wiswell TE, Enzenauer RW, Holton ME, Cornish JD, Hankins CT. Declining frequency of circumcision: implications for changes in the absolute incidence and male to female sex ratio of urinary tract infections in early infancy. Pediatrics. 1987;79:338–42.

62. Wiswell TE, Roscelli JD. Corroborative evidence for the decreased incidence of urinary tract infections in circumcised male infants. Pediatrics. 1986;78:96–9.

63. Jakobsson B, Esbjörner E, Hansson S. Minimum incidence and diagnostic rate of first urinary tract infection. Pediatrics. 1999;104:222–6.

64. Hoberman A, Wald ER, Hickey RW, et al. Oral versus initial intravenous therapy for urinary tract infections in young febrile children. Pediatrics. 1999;104:79–86.

65. Committee on Quality Improvement Subcommittee on Urinary Tract Infection. Practice parameter: the diagnosis, treatment, and evaluation of the initial urinary tract infection in febrile infants and young children. Pediatrics. 1999;103:843–52.

66. Rushton HG, Majd M. Pyelonephritis in male infants: how important is the foreskin? J Urol. 1992;148:733–6, 737–8.

67. Weiss R, Tamminen-Mobius T, Koskimies O, et al. Characteristics at entry of children with severe primary vesicoureteral reflux recruited for a multicenter, international therapeutic trial comparing medical and surgical management. The International Reflux Study in Children. J Urol. 1992;148:1644–9.

68. Mueller ER, Steinhardt G, Naseer S. The incidence of genitourinary abnormalities in circumcised and uncircumcised boys presenting with an initial urinary tract infection by 6 months of age [abstract 121]. Pediatrics. 1997;100:580.

69. Sharifian M, Rees L, Trompeter RS. High incidence of bacteriuria following renal transplantation in children. Nephrol Dial Transplant. 1998;13:432–5.

70. Van Howe RS. Cost-effective treatment of phimosis. Pediatrics. 1998;102:e43.

71. Smith GC, Powell A, Reynolds K, Campbell CA. The five year school medical: time for change. Arch Dis Child. 1990;65:225–7.

72. Kayaba H, Tamura H, Kitajima S, Fujiwara Y, Kato T, Kato T. Analysis of shape and retractibality of the prepuce in 603 Japanese boys. J Urol. 1996;156:1813–5.

73. Branger B, Sable A, Picherot G, et al. Examen du prépuce chez 511 enfants en maternelle: rôle des manoeuvres de décalottage. Ann Pediatr Paris. 1991;38:618–22.

74. Rickwood AM, Hemalatha V, Batcup G, Spitz L. Phimosis in boys. Br J Urol. 1980;52:147–50.
75. Shankar KR, Rickwood AMK. The incidence of phimosis in boys. BJU Int. 1999;84:101–2.
76. Øster J. Further fate of the foreskin: incidence of preputial adhesions, phimosis, and smegma among Danish schoolboys. Arch Dis Child. 1968;43:200–3.
77. Rickwood AM, Walker J. Is phimosis overdiagnosed in boys and are too many circumcisions performed in consequence? Ann R Coll Surg Engl. 1989;71:275–7.
78. Beaugé M. Traitement Medical du Phimoseis Congenital de L'Adolescent. Saint-Antoine University, Paris VI, 1990–1991.
79. Cuckow PM, Rix G, Mouriquand PD. Preputial plasty: a good alternative to circumcision. J Pediatr Surg. 1994;29:561–3.
80. Fergusson DM, Lawton JM, Shannon FT. Neonatal circumcision and penile problems: an 8-year longitudinal study. Pediatrics. 1988;81:537–41.
81. Herzog LW, Alvarez SR. The frequency of foreskin problems in uncircumcised children. Am J Dis Child. 1986;140:254–6.
82. Imamura E. Phimosis of infants and young children in Japan. Acta Paediatr Jpn. 1997;39:403–5.
83. Birley HDL, Walker MM, Luzzi GA, et al. Clinical features and management of recurrent balanitis: association with atopy and genital washing. Genitourin Med. 1993;69:400–3.
84. Enzenauer RW, Dotson CR, Leonard T Jr, Brown J III, Pettett PG, Holton ME. Increased incidence of neonatal staphylococcal pyoderma in males. Mil Med. 1984;149:408–10.
85. Enzenauer RW, Dotson CR, Leonard T, Reuben L, Bass JW, Brown J III. Male predominance in persistent staphylococcal colonization and infection of the newborn. Hawaii Med J. 1985;44:389–90, 392, 394–6.
86. Zafar AB, Butler RC, Reese DJ, Gaydos LA, Mennonna PA. Use of 0.3% triclosan (Bacti Stat) to eradicate an outbreak of methicillin resistant *Staphylococcus aureus* in a neonatal nursery. Am J Infect Control. 1995;23:200–8.
87. Thompson DJ, Gezon HM, Rogers KD, Yee RB, Hatch TF. Excess risk of staphylococcal infection and disease in newborn males. Am J Epidemiol. 1966;84:314–28.
88. Gooch JJ, Britt EM. *Staphylococcus aureus* colonization and infection in newborn nursery patients. Am J Dis Child. 1978;132:893–6.
89. Wiswell TE, Miller GM, Gelston HM Jr, Jones SK, Clemmings AF. Effect of circumcision status on periurethral bacterial flora during the first year of life. J Pediatr. 1988;113:442–6.
90. Wijesinha SS, Atkins BL, Dudley NE, Tam PK. Does circumcision alter the periurethral bacterial flora? Pediatr Surg Int. 1998;13:146–8.
91. Serour F, Samra Z, Kushel Z, Gorenstein A, Dan M. Comparative periurethral bacteriology of uncircumcised and circumcised males. Genitourin Med. 1997;73:288–90.
92. Gracely-Kilgore KA. Penile adhesion: the hidden complication of circumcision. Nurse Pract. 1984;9:22–4.
93. Parkash S, Jeyakumar S, Subramanyan K, Chaudhuri S. Human subpreputial collection: its nature and formation. J Urol. 1973;110:211–2.
94. Mackenzie AR. Meatal ulceration following circumcision. Obstet Gynecol. 1966;28:221–3.
95. Eke FU, Eke NN. Renal disorders in children: a Nigerian study. Pediatr Nephrol. 1994;8:383–6.
96. de Vincenzi I, Mertens T. Male circumcision: a role for in HIV prevention? AIDS. 1994;8:153–60.
97. Van Howe RS. Circumcision and HIV-infection: meta-analysis and review of the medical literature. Int J STD AIDS. 1999;10:8–16.
98. Moses S, Nagelkerke NJ, Blanchard J. Analysis of the scientific literature on male circumcision and risk for HIV infection. Int J STD AIDS. 1999;10:626–8.
99. Storms MR. AAFP fact sheet on neonatal circumcision: a need for updating. Am Fam Phys. 1996;54:1216–8.
100. Joint United Nations Programme on HIV/AIDS, World Health Organization. Global HIV/AIDS and STD Surveillance Project: report on the global HIV/AIDS epidemic—June 1998. Available from: URL: http://www.unaids.org/hivaidsinfo/statistics/june98/global_report/index.html
101. Serwadda D, Wawer MJ, Musgrave SD, et al. HIV risk factors in three geographic strata of rural Rakai District, Uganda. AIDS. 1992;6:983–9.
102. Wawer MJ, Sewankambo NK, Serwadda D, et al. Control of sexually transmitted diseases for AIDS prevention in Uganda: a randomised community trial. Rakai Project Study Group. Lancet. 1999;353:525–35.
103. Gilks CF, Otieno LS, Brindle RJ, et al. The presentation and outcome of HIV-related disease in Nairobi. Q J Med. 1992;82:25–32.
104. Lankoande S, Meda N, Sangare L, et al. Líinfection a VIH chez les chauffeurs routiers au Burkina Faso: une enquete de seroprevalence. Med Trop (Mars). 1998;58:41–6.
105. Kapiga SH, Lyamuya EF, Lwihula GK, Hunter DJ. The incidence of HIV infection among women using family planning methods in Dar es Salaam, Tanzania. AIDS. 1998;12:75–84.
106. Gomo E, Chibatamoto PP, Chandiwana SK, Sabeta CT. Risk factors for HIV infection in a rural cohort in Zimbabwe: a pilot study. Cent Afr J Med. 1997;43:350–4.
107. Lavreys L, Rakwar JP, Thompson ML, et al. Effect of circumcision on incidence of human immunodeficiency virus type 1 and other sexually transmitted diseases: a prospective cohort study of trucking company employees in Kenya. J Infect Dis. 1999;180:330–6.
108. Quinn TC, Wawer MJ, Sewankambo N, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. N Engl J Med. 2000;342:921–9.
109. Harrison LH, da Silva AP, Gayle HD, et al. Risk factors for HIV-2 infection in Guinea-Bissau. J Acquir Immune Defic Syndr. 1991;4:1155–60.
110. Kreiss JK, Hopkins SG. The association between circumcision status and human immunodeficiency virus infection among homosexual men. J Infect Dis. 1993;168:1404–8.
111. Grulich AE, Hendry O, Clark E, Kippax S, Kaldor JM. Circumcision and male-to-male sexual transmission of HIV. AIDS. 2001;15:1188–9.
112. Van Howe RS. Does circumcision influence sexually transmitted diseases? A literature review. BJU Int. 1999;83 Suppl 1:52–62.
113. Bailey RC, Neema S, Othieno R. Sexual behaviours and other HIV risk factors in circumcised and uncircumcised men in Uganda. J Acquir Immune Defic Syndr Hum Retrovirol. 1999;22:294–301.
114. Gray RH, Kiwanuka N, Quinn TC, et al. Male circumcision and HIV acquisition and transmission: cohort studies in Rakai, Uganda. Rakai Project Team. AIDS. 2000;14:2371–81.
115. Frisch M, Friis S, Kruger-Kjaer S, Melbye M. Falling incidence of penis cancer in an uncircumcised population (Denmark 1943-90). Br Med J. 1995;311:1471.
116. Iverson T, Tretli S, Johansen A, Holte T. Squamous cell carcinoma of the penis and of the cervix, vulva and vagina in spouses: is there any relationship? An epidemiological study from Norway, 1960-92. Br J Cancer. 1997;76:658–60.
117. Maiche AG. Epidemiological aspects of cancer of the penis in Finland. Eur J Cancer Prev. 1992;1:153–8.
118. Bigelow J. The Joy of Uncircumcising! Exploring Circumcision History, Myths, Psychology, Restoration, Sexual Pleasure and Human Rights. 2nd ed. Aptos (CA): Hourglass; 1995.

119. The joy of uncircumcising. Br Med J. 1994;309:676–7.
120. Schultheiss D, Truss MC, Stief CG, Jonas U. Uncircumcision: a historical review of preputial restoration. Plast Reconstr Surg. 1998;101:1990–8.
121. Goodwin WE. Uncircumcision: a technique for plastic reconstruction of a prepuce after circumcision. J Urol. 1990;144:1203–5.
122. Winberg J, Bollgren I, Gothefors L, Herthelius M, Tullus K. The prepuce: a mistake of nature? Lancet. 1989;1:598–9.
123. Pisacane A, Graziano L, Zona G. Breastfeeding and urinary tract infection. Lancet. 1990;336:50.
124. Pisacane A, Graziano L, Mazzarella G, Scarpellino B, Zona G. Breast-feeding and urinary tract infection. J Pediatr. 1992;120:87–9.
125. Coppa GV, Gabrielli O, Giorgi P, et al. Preliminary study of breastfeeding and bacterial adhesion to uroepthelial cells. Lancet. 1990;335:569–71.
126. Marild S, Jodal U, Hanson L. Breastfeeding and urinary-tract infection. Lancet. 1990;336:942.
127. Mårild S, Jodal U, Mangelus L. Medical histories of children with acute pyelonephritis compared with controls. Pediatr Infect Dis J. 1989;8:511–5.
128. Savage DC, Wilson MI, McHardy M, Dewar DA, Fee WM. Covert bacteriuria of childhood: A clinical and epidemiological study. Arch Dis Child. 1973;48:8–20.
129. Patrick MJ. Influence of maternal renal infection on the foetus and infant. Arch Dis Child. 1967;42:208–13.
130. Littlewood JM. 66 infants with urinary tract infection in first month of life. Arch Dis Child. 1972;47:218–26.
131. Airede AI. Urinary-tract infections in African neonates. J Infect. 1992;25:55–62.
132. Maherzi M, Guignard JP, Torrado A. Urinary tract infection in high-risk newborn infants. Pediatrics. 1978;62:521–3.
133. Eliakim A, Dolfin T, Korzets Z, et al. Urinary tract infection in premature infants: the role of imaging studies and prophylactic therapy. J Perinatol. 1997;17:305–8.
134. Edelmann CM Jr, Ogwo JE, Fine BP, Martinez AB. The prevalence of bacteriuria in full-term and premature newborn infants. J Pediatr. 1973;82:125–32.
135. Malleson P. Prepuce care. Pediatrics. 1986;77:265.
136. Harkavy KL. The circumcision debate. Pediatrics. 1987;79:649–50.
137. Watson SJ. Care of the uncircumcised penis. Pediatrics. 1987;80:765.
138. Cunningham N. Circumcision and urinary tract infections. Pediatrics. 1986;77:267–9.
139. Askari A, Belman AB. Vesicoureteral reflux in black girls. J Urol. 1982;127:747–8.
140. Skoog SJ, Belman AB. Primary vesicoureteral reflux in the black child. Pediatrics. 1991;87:538–43.
141. Shaw KN, Gorelick M, McGowan KL, McDaniel Yakscoe N, Schwartz JS. Prevalence of urinary tract infection in febrile young children in the emergency department. Pediatrics. 1998;102(2):e16. Available from: URL: http: //www.pediatrics.org/cgi/content/full/102/2/e16
142. Kunin CM. The natural history of recurrent bacteriuria in schoolgirls. N Engl J Med. 1970;282:1443–8.
143. Kunin CM. Epidemiology and natural history of urinary tract infection in school age children. Pediatr Clin North Am. 1971;18:509–28.
144. Schlager TA, Hendley JO, Dudley SM, Hayden GF, Lohr JA. Explanation for false positive urine cultures obtained by bag technique. Arch Pediatr Adolesc Med. 1995;149:170–3.
145. Fleiss PM. Explanation for false positive urine cultures obtained by bag technique. Arch Pediatr Adolesc Med. 1995;149:1041–2.
146. Robson WL, Leung AK. Explanation for false positive urine cultures obtained by bag technique. Arch Pediatr Adolesc Med. 1995;149:1042–3.
147. Pylkkänen J, Vilska J, Koskimies O. Diagnostic value of symptoms and clean-voided urine specimens in childhood urinary tract infection. Acta Paediatr Scand. 1979;68:341.
148. Hoberman A, Wald ER. Urinary tract infections in young febrile children. Pediatr Infect Dis J. 1997;16:11–7.
149. Hansson S, Brandström P, Jodal U, Larsson P. Low bacterial counts in infants with urinary tract infection. J Pediatr. 1998;132:180–2.
150. Wiswell TE, Tencer HL, Welch CA, Chamberlain JL. Circumcision in children beyond the neonatal period. Pediatrics. 1993;92:791–3.
151. Wall RL Jr. Routine circumcision? Recent trends and concepts. N C Med J. 1968;29:103–7.
152. Van Howe RS. Effect of confounding in the association between circumcision status and urinary tract infection. J Infect. In press.
153. Amir J, Alpert G, Reisner SH, Nitzan M. Fever in the first year of life. Isr J Med Sci. 1984;20:447–8.
154. Goldman M, Barr J, Bistritzer T, Aladjem M. Urinary tract infection following ritual Jewish circumcision. Isr J Med Sci. 1996;32:1098–102.
155. Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias: dimensions of methodological quality associated with estimates of treatment effects in controlled trials. JAMA. 1995;273:408–12.
156. Muir CS, Nectoux J. Epidemiology of cancer of the testis and penis. Natl Cancer Inst Monogr. 1979:157–64.
157. Wingo PA, Tong T, Bolden S. Cancer statistics, 1995. CA Cancer J Clin. 1995;45:8–30.
158. Sutherland JM, Glueck HI, Gleser G. Hemorrhagic disease of the newborn: breast feeding as a necessary factor in the pathogenesis. Am J Dis Child. 1967;113:524–33.
159. Chiasson MA, Stoneburner RL, Hildebrandt DS, Ewing WE, Telzak EE, Jaffe HW. Heterosexual transmission of HIV-1 associated with the use of smokable freebase cocaine (crack). AIDS. 1991;5:1121–6.
160. Seidlin M, Vogler M, Lee E, Lee YS, Dubin N. Heterosexual transmission of HIV in a cohort of couples in New York City. AIDS. 1993;7:1247–54.
161. Anand KJ, Hickey PR. Pain and its effects in the human neonate and fetus. N Engl J Med. 1987;317:1321–9.
162. Taddio A, Katz J, Ilersich AL, Koren G. Effect of neonatal circumcision on pain response during subsequent routine vaccination. Lancet. 1997;349:599–603.
163. Taylor JR, Lockwood AP, Taylor AJ. The prepuce: specialized mucosa of the penis and its loss to circumcision. Br J Urol. 1996;77:291–5.
164. Van Howe RS, Svoboda JS, Dwyer JG, Price CP. Involuntary circumcision: the legal issues. BJU Int. 1999;83 Suppl 1:63–73.
165. American Medical Association Council on Ethical and Judicial Affairs. The Code of Medical Ethics: Current Opinions with Annotations. 1996-1997 ed. Chicago: American Medical Association; 1997.