

A Cost-Utility Analysis of Neonatal Circumcision

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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 studies¹⁻⁴ 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 implementation⁵; 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-

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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 diseases³⁴ 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 standard²⁴ 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			Cost (\$)	Well-Years Lost	
	MFS (%)	LFS (%)	Best Judgment (%)		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			Cost (\$)	Well-Years Lost	
	MFS (%)	LFS (%)	Best Judgment (%)		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 Ansell⁴⁸ 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 4.02⁵⁸ 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 associates⁶⁴ 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 infection⁶⁵ 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 (exclud-

ing 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 topi-

cal 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 model²⁸ 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 data³¹ 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

\$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 im-

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

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.

mediate 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).

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%

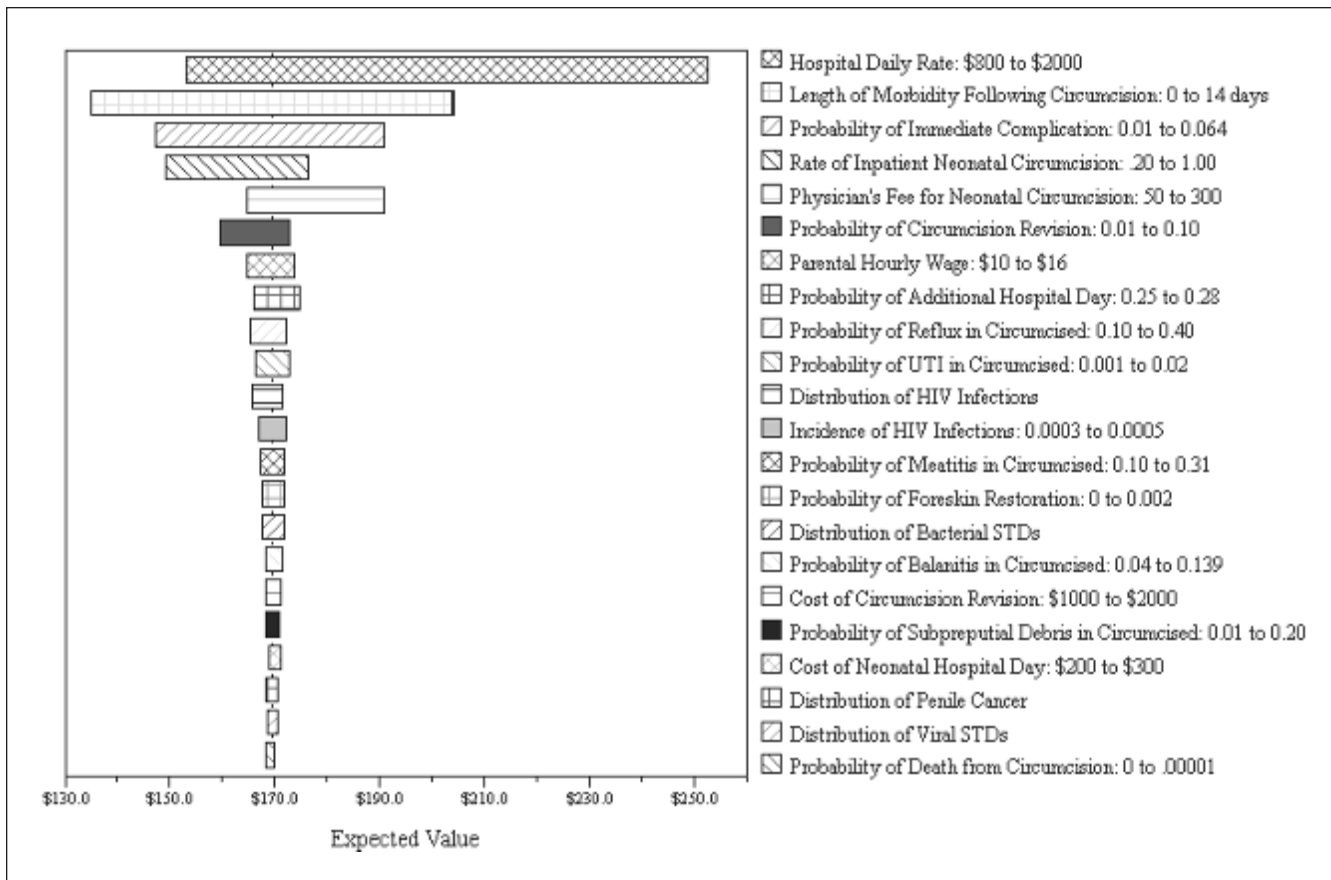


Figure 1 Tornado diagram of most influential variables. UTI = urinary tract infection; STD = sexually transmitted disease.

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 colleagues¹ and Ganiats and associates² 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

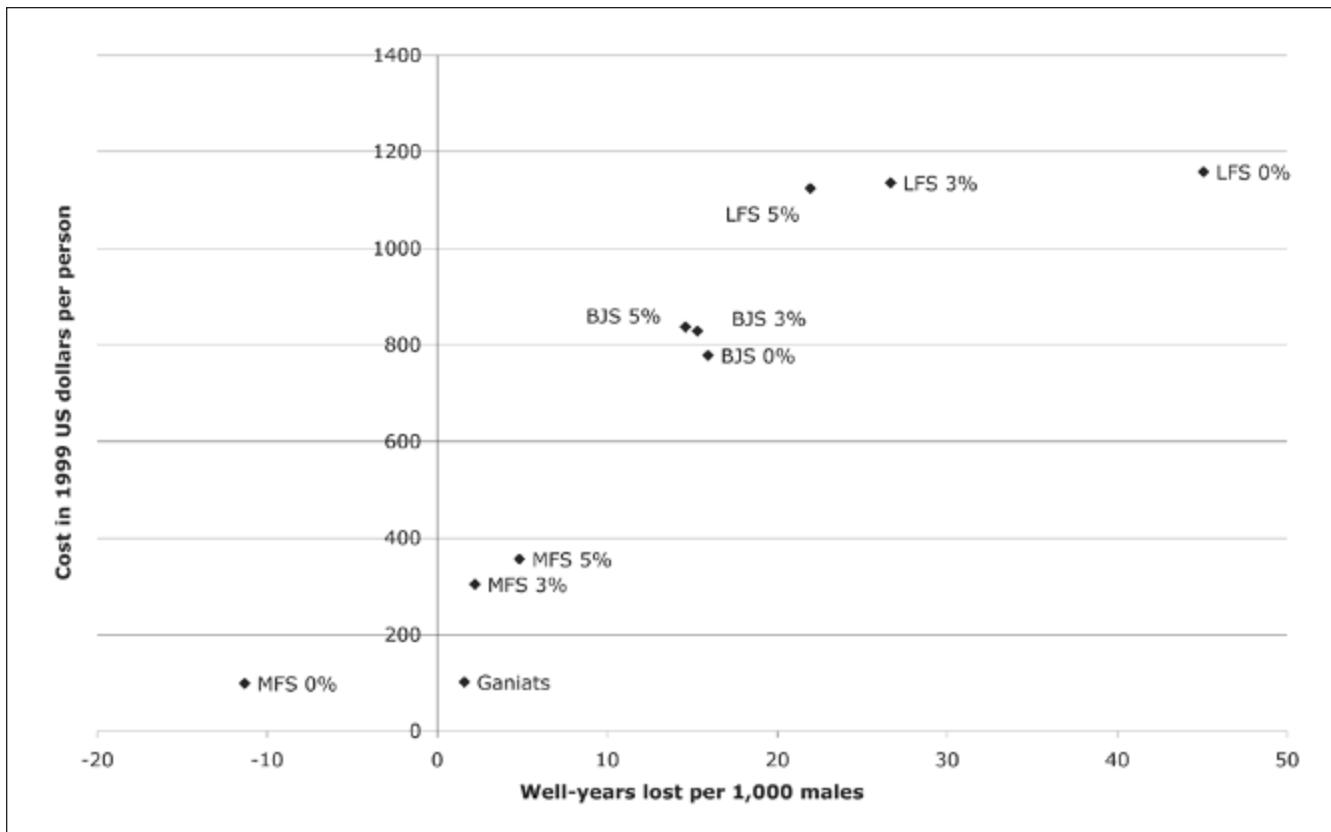


Figure 2 Healthy policy space. LFS = least favorable scenario; BJS = best judgment scenario; MFS = most favorable scenario.

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 associates⁶⁰ 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 in-

patients, 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-

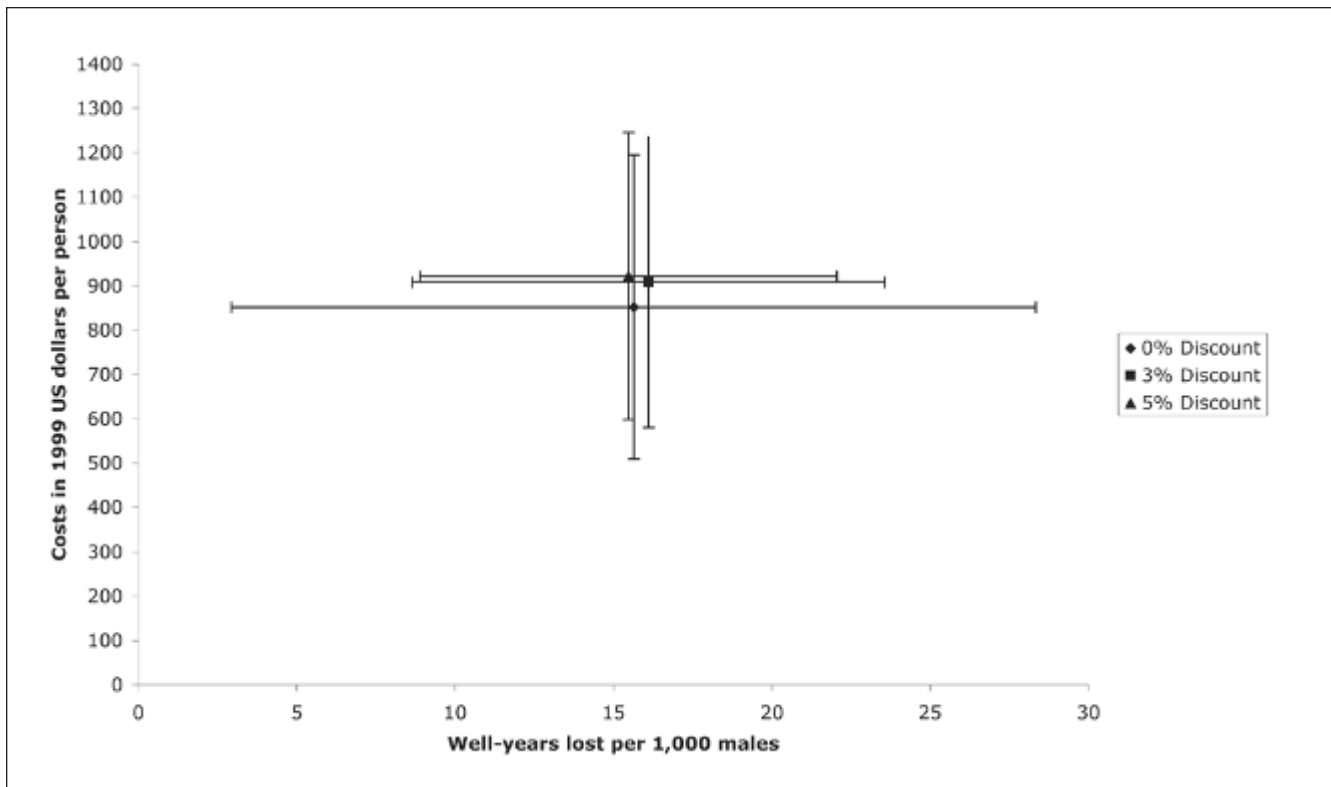


Figure 3 Health policy space, Monte Carlo simulation with 95% confidence intervals.

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 jus-

tification 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

<i>Balanitis</i>	Inflammation of the glans (head) of the penis.	<i>Glans</i>	Head of the penis.
<i>Balanoposthitis</i>	Inflammation of the glans (head) of the penis and the prepuce (foreskin).	<i>Hypospadias</i>	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.
<i>Coronal adhesions</i>	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.	<i>Meatal stenosis</i>	Narrowing of the opening of the urethra.
		<i>Meatitis</i>	Inflammation of the opening of the urethra.

(continued)

Appendix (continued)

<i>Meatotomy</i>	Enlarging the opening of the urethral opening by surgical means.	<i>Preputial stenosis</i>	Abnormal narrowing of the opening at the distal end of the prepuce (foreskin).
<i>Paraphimosis</i>	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.	<i>Pyoderma</i>	Bacterial skin infection, often caused by <i>Staphylococcus</i> .
<i>Phimosis</i>	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.	<i>Smegma</i>	A collection of dead skin, dead white blood cells, and urethral and prostatic secretions that can form under the prepuce (foreskin).
<i>Posthitis</i>	Inflammation of the prepuce (foreskin).	<i>Urosepsis</i>	A systemic infection that results from an infection of the urinary tract.
<i>Prepuce</i>	Foreskin.	<i>Vesicoureteral reflux</i>	An abnormal movement of urine from the bladder up the ureters toward the kidneys.
<i>Preputial plasty</i>	A surgical procedure in which the opening at the distal end of the prepuce (foreskin) is made larger using plastic surgical techniques.	<i>Voiding cystourethrogram (VCUG)</i>	A radiologic evaluation of the lower urinary tract used to detect vesicoureteral reflux.

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