Current Medical Evidence Supports Male Circumcision

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Introduction

Circumcision has a wide array of potential benefits over the lifetime of males, and relatively few risks. Up to one in three males worldwide, if not circumcised, may suffer a medical condition caused by their foreskin [1–3]. In contrast, the risks of the procedure itself are less than 1% in infancy and less than 5% in older children and adults. The benefits have been calculated by some, to exceed risks by over 100 to one [1–3]. Figure 19.1 illustrates why the foreskin represents a risk to health.

Hygiene

Hygiene has always been a major reason for circumcision. It is well known that microorganisms accumulate under the foreskin, and can foster inflammatory processes leading to balanitis/balanoposthitis (see reviews: [1, 2] and discussed in more detail in inflammatory dermatoses section below). Moreover, fimbriated bacteria can migrate up the urethra to cause urinary tract infections (UTIs), especially in infancy.

Smegma tends to accumulate under the foreskin. Smegma is secreted by Tyson's glands and contains neutral lipids, fatty acids, and sterol. Its initial function is lubrication and protection of the glans, but if it is not removed by regular washing it becomes mixed with epithelial cells and infected by bacteria, forming solid aggregates. The bacteria (especially *Mycobacterium smegmatis*) can produce an offensive odor accounting for the common perception that smegma is unclean [4]. The incidence of yeast fungi was found in one study to be 44% in uncircumcised boys and 18% in circumcised boys (ages 8 months to 18 years; mean 6.4 years) [5]. A much lower prevalence of penile candidiasis has also been noted in circumcised men in Australian studies [6–8]. In boys (mean age 5.8 years, range 0.01–13) colonization of the glans penis by yeast was 12% just prior to circumcision and 1% 1 month later [9]. The species found were *Candida albicans* (50%), *Malasserzia furfur* (40%), and *Malassezia sympodialis* (10%).

Inflammatory Dermatoses

Lack of circumcision increases the risk of inflammation of the glans (balanitis) and foreskin (posthitis). In boys the incidence in the uncircumcised is twice as high as in those who are circumcised [10, 11]. In men balanitis is

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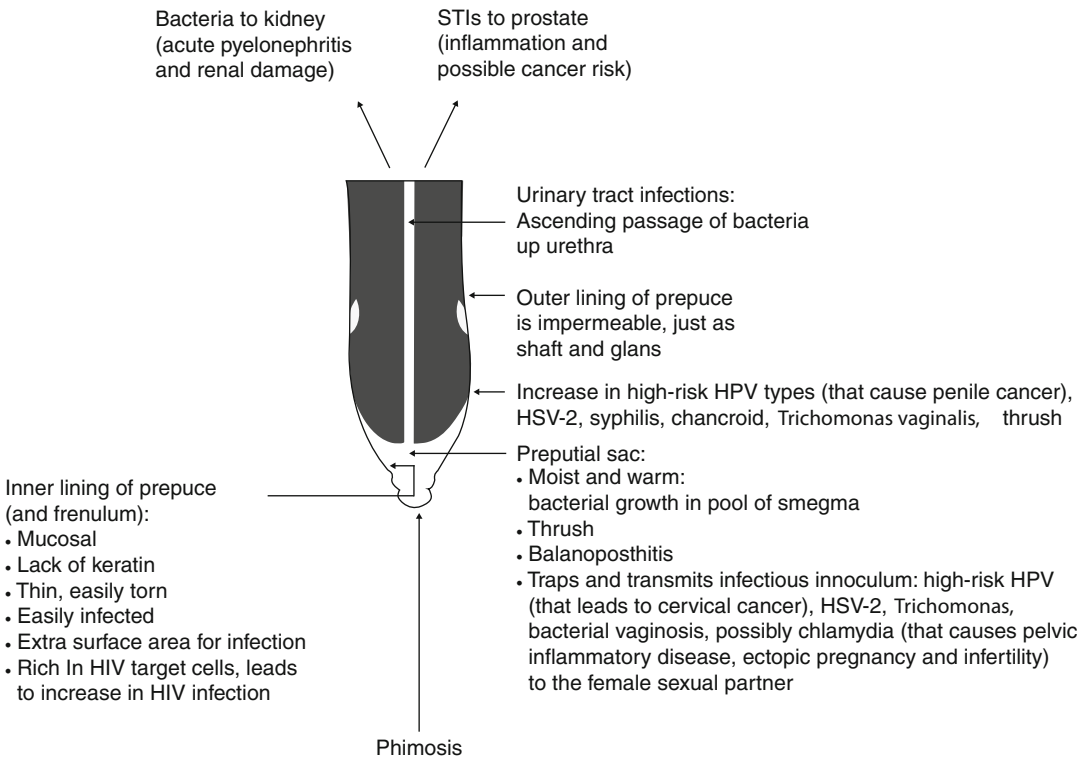

Fig. 19.1 Anatomical relationship of foreskin to the main body of the penis, showing features that lead to increase in infection risk, and the mode of infection by various microorganisms

seen in 11–13% of those not circumcised, but in only 2% of those who are [12, 13]. In uncircumcised diabetic men, the incidence may be as high as 35–40% [13]. In fact, in such men, whose diabetes was previously undiagnosed, a new case of balanoposthitis should alert the practitioner to test for diabetes. During balanoposthitis, the distal penis becomes red, painful, and swollen, and is often accompanied by a purulent discharge [14].

Other penile skin conditions higher in frequency or completely confined to uncircumcised males include psoriasis, ones arising from penile infections, lichen sclerosis, lichen planus, schorrheic dermatitis, plasma cell (Zoon) balanitis, bowenoid papulosis, and nonspecific balanoposthitis [13, 15–17]. *Mycobacterium smegmatis* has been implicated in Zoon balanitis [16], which presents as erythrema (in 100%), swelling (in 91%), discharge (in 73%), dysuria (in 13%), bleeding (in 2%) and ulceration (in 1%) [13].

Phimosis

Historically, protection against phimosis is one of the best known benefits of circumcision. The preputial constriction, in severe cases to a pinpoint, is an impediment to passing urine normally and prevents retraction of the foreskin [18]. Chronic infection and inflammation in men with phimosis may ultimately lead to them having a higher risk of squamous cell carcinoma.

Severe phimosis can in some instances lead to UTIs, localized skin infections, pain when passing urine, retention of urine, kidney stones, and sexual dysfunction [19]. The prevalence of phimosis beyond childhood is approximately 10–30%. This includes "physiological" phimosis (see next paragraph) as well as pathological phimosis. The most common cause of the latter is *balanitis xerotica obliterans* (BXO) or lichen sclerosus et atrophicus. It first presents in boys aged 8–10 years [20] and in the UK it was seen

Table 19.1 Prevalence of phimosis in various studies in different countries

Location	Study group	Prevalence (%)	Reference
UK	5–13 year-olds	20	[26]
UK	Soldiers	14	[27]
New York	Men	9	[28]
Denmark	8 years old	8	[29]
Germany	Youths	9	[30]
Germany	Men	9	[31]
China	3–23 year-olds	12	[32]
China	7–10 year-olds	12	[33]
China	11–18 year-olds	7	[33]
Japan	Men	50	[34]
Japan	11–15 year-olds	23	[35]
Japan	13 year-olds	16	[36]
Taiwan	10–13 year-olds	37	[37]
Bali	Men	50	[38]

in 5% of uncircumcised boys aged under 18 years, and in 6% of uncircumcised boys aged under 15 years [21, 22]. In a study involving men aged 24–70 years with phimosis, lesions were found on the foreskin and glans of 59%, foreskin only in 23%, and glans only in 18% [23]. In pediatric patients, 37% with severe phimosis had *lichen sclerosus* [24]. *Lichen sclerosus* has been found in 4–19% of all foreskins, and, in older patients, progressive *Lichen sclerosus* or other inflammatory changes lead to phimosis [25]. Phimosis in older men is found to be associated with 44–85% of cases of penile cancer [19].

The rates of phimosis (mostly physiological) reported in various studies vary by geography and age, as depicted in Table 19.1.

In a large study in China of 10,421 males aged 0–18 years, apart from the statistics for phimosis itself that are shown in Table 19.1, partial phimosis was seen in a further 20% of the 7–10 year olds and in 9% of the 11–18 year olds [33]. Adhesions were apparent in 29% and 25%, respectively, and a foreskin that could be retracted normally was apparent in only 24% and 42% of each respective age group. The circumcision rate was 15% in the 7–10 year olds and 17% in the 11–18 year olds. Of all of these children, 13% had undergone forced foreskin dilation in the past, 77% of these forced retractions having been performed prior to school age. Despite having had this procedure carried out, in 13% the phimosis persisted and most of these had scar tissue on the distal foreskin.

Urinary Tract Infections

The higher prevalence of UTIs in uncircumcised boys was first noticed in a retrospective analysis in 1982 when 95% of UTIs in boys aged 5 days to 8 months were found to be in those not circumcised [39]. In a series of prospective analyses based on data mining, commencing the same year [40], this was confirmed. In a subsequent study, Wiswell and colleagues found that amongst 5,261 infants born at one US Army hospital, 4% of UTI cases were in uncircumcised males, but in only 0.2% in those who were circumcised [41]. They then went on to examine the records for 219,755 boys born in US Armed Forces hospitals from 1975 to 1979 and found an 11-fold higher incidence of UTIs in the uncircumcised [42]. Then in 1993, their study of infants born between 1985 and 1990 in US Army hospitals worldwide found 496 boys got UTI in their first year of life and 90% of these were uncircumcised [43]. Among

the uncircumcised boys younger than 3 months, 23% had bacteremia caused by the same organism responsible for the UTI. The UTIs were, moreover, recurrent in 19% of uncircumcised boys, but in none of the circumcised [44].

A meta-analysis in 2005 noted 1,222 UTIs in 107,873 uncircumcised infants, that is, 1.1%, and a summary OR for the protective effect of circumcision against UTI of 0.13 (95% CI 0.08–0.20), that is, circumcision reduced UTI 7.7-fold [45]. In Sweden (where infant circumcision is rare), cumulative incidence of UTI was 2.2% by age 2 years [46]. In a study of 2,000 boys circumcised by Plastibell in the first month of life and 1,000 uncircumcised infants, culture of urine obtained by suprapubic bladder catheterization at four time points (1.5, 3, 9, and 15 months) found not one UTI in the circumcised group, but 2% of the uncircumcised boys had a UTI [47]. A meta-analysis published in 2008 found that amongst febrile male infants aged less than 3 months (the age group with highest prevalence of UTI), UTI was the cause of the fever in 20.1% of uncircumcised boys, but only in 2.4% of boys who were circumcised [48]. "Low-risk" criteria were not sufficiently reliable to exclude a serious bacterial infection, which was seen in 19% of febrile neonates, 80% of these having a UTI [49]. The authors recommended that all febrile infants be hospitalized, undergo a full sepsis evaluation, and receive i.v. antibiotics. By the age of 7 years, 2% of boys were confirmed as having had a UTI and another 5% had probably had at least one UTI [50]. In the "Pediatric Research in Office Settings Febrile Infant Study" of 219 US practices, being uncircumcised was the strongest multivariate predictor of UTI, with an odds ratio of 11.6 (95% CI 5.9–22.6) [51].

Imaging studies have shown that 50–86% of children with febrile UTI and presumed pyelonephritis had renal parenchymal defects [52], which persist after treatment and these children may have acquired renal defects. Nuclear scans following the treatment of UTI in febrile infants noted scarring in 10–30% of cases [53]. Of those with acute pyelonephritis, 36–52% will subsequently develop renal scarring [54–57]. In boys with high-grade vesicoureteral reflex not only was UTI reduced by circumcision, but new permanent defects were halved [58].

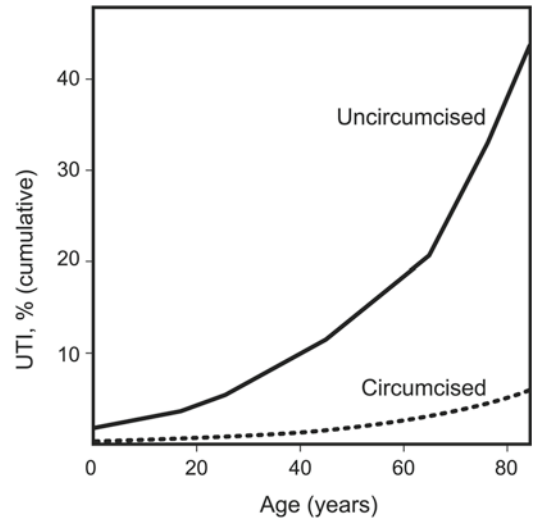

Fig. 19.2 Cumulative prevalence of urinary tract infections over the lifetime of circumcised and uncircumcised males. (Kindly provided by J.H. Waskett, Manchester, UK, from unpublished calculations based on the literature)

The protective effect of circumcision against UTIs continues into adulthood, with a 5.6-fold higher rate of UTI in the uncircumcised having been observed in a study in Seattle of men of average 32 years, and matched for race, age, and sexual activity [59]. Lifetime prevalence of UTI was 13.7% in a large, nationally representative US study of men aged 18–85+ years [60, 61]. Since overall rate of circumcision is 79% in the USA [62], a meta-analysis of all studies has estimated that up to 24% of uncircumcised males, compared with 8% of the circumcised will get a UTI over their lifetime (Fig. 19.2). UTI is the most costly (over $1 billion in men [60]) and resource-intensive urological condition in the USA, and involves 1.8 M physician visits annually [63].

Much is now known about the bacteria and other microorganisms that proliferate under the foreskin (reviewed in [1, 2]). The fact that fimbriated strains of the bacterium *Escherichia coli*, which are pathogenic to the urinary tract and pyelonephritogenic, have been shown to be capable of adhering to the foreskin satisfies one of the criteria for causality [64–69].

Common Sexually Transmitted Infections

Syphilis, Chancroid, HSV-2, Trichomonas, and Sexually Transmitted Urethritis

Reports that circumcision could prevent sexually transmitted infections (STIs) started with syphilis in the mid-1800s [70], though since this involved a comparison of Jews with gentiles the study was not properly controlled. Reports of protection against syphilis and other STIs have continued over the years, including one in 1947 of 1,300 consecutive patients in a Canadian Army unit that showed lack of circumcision to be associated with a ninefold higher risk of syphilis and three times higher gonorrhoea [71]. Many of these studies have been reviewed [1, 2, 72].

A meta-analysis in 2006 of ulcerative STIs that examined 26 research articles (from the USA, UK, Australia, Africa, India, and Peru) found circumcision protected against syphilis (by 39%) and chancroid (by 0–88%), but genital herpes (HSV-2) was only 12% lower in circumcised men [73].

The partial prevention of ulcerative STIs is now supported by data from randomized controlled trials (RCTs), regarded as the "gold standard" in epidemiology. An RCT in Uganda found that the protective effect of circumcision against genital ulcer disease was 48% [74]. Subsequently, large RCTs have found lower genital herpes in men in the circumcised arm of each trial. HSV-2 seroprevalence was 45% lower in a trial involving 2,974 men in South Africa [75] and was 30% lower in an initial trial involving 6,396 men in Uganda [76]. Further Ugandan data from two trials found HSV-2 to be 23% and 41% lower in the men who had been circumcised [77]. But when seroprevalence was examined, a longitudinal study in New Zealand found no difference in HSV-2 between circumcised and uncircumcised men [78]. The twofold higher incidence of genital ulcer disease (GUD), including herpetic lesions, in uncircumcised men led to suggestions that circumcision may reduce the *recurrence* of genital lesions arising from HSV-2 infection [79]. Circumcision also reduced recurrence of genital herpes by 20-fold and prolonged the interval between bouts [80].

An added benefit of circumcision in reducing HSV-2 is that it should also contribute to a lowering of HIV infection [79], even though the latter appeared independent of HSV-2 serostatus [75]. A synergy between HIV and HSV-2 infections has also been reported by the latter group of researchers [81]. In that study, conducted in South Africa, HSV-2 infection per sex act was 0.013 in uncircumcised men, compared with 0.0074 in circumcised men (RR 0.56; $P=0.005$) [81]. HSV-2 suppressive therapy failed to decrease HIV acquisition, as seen in a RCT of female Tanzanian workers, and in a RCT that included women in Africa as well as MSM in Peru and the USA [82]. The persistence and enrichment of HIV receptor-positive inflammatory cells in biopsies from healed genital lesions caused by HSV-2 might explain why anti-HSV-2 therapy does not reduce HIV acquisition [83].

In Black heterosexual men aged 18–25 years who were attending an STI clinic in the USA, HSV-1 seroprevalence was 2.8 times higher in the uncircumcised [84]. HSV-2 seroprevalance did not differ, however.

Circumcision alters the microbiome of the penis [85]. The anoxic microenvironment under the foreskin supports growth of pro-inflammatory anaerobes capable of activating Langerhans cells. These cells present HIV to CD4 cells in draining lymph nodes. Circumcision reduces the anaerobic bacteria, and in so doing helps protect against various STIs, including HIV.

In an RCT in South Africa, the prevalence of gonorrhoea was only 9% lower in circumcised men [86]. In this trial, Chlamydia was 42% lower and *Trichomonas vaginalis* was 46% lower in the men who had been circumcised. In an as-treated analysis, *T. vaginalis* was 51% lower, with an adjusted OR of 0.41 [86]. This explained why women with circumcised male partners have been found to be less at risk of *T. vaginalis* infection [87]. In the Kenyan RCT, however, circumcision did not show protection against either gonorrhoea, Chlamydia or Trichomonas [88]. The data on gonorrhoea and Chlamydia are consistent with most earlier observational findings,

and is to be expected because the preferred host site for these bacterial STIs is the internal urethral cuboidal or columnar epithelium. In this regard, although the Kenyan RCT data differed from the South African RCT data for Chlamydia and Trichomonas, the prevalence of Trichomonas in the Kenyan study was lower than in other African countries.

In men who have sex with men (MSM), a Sydney study found that in those who were circumcised, syphilis was ten times lower in the 33% who only ever engaged in insertive anal intercourse [89]. Similarly, a study of MSM in Seattle, found diagnosis of syphilis to be 2.0 times higher in uncircumcised men, and was completely absent from the 11% who said they were insertive-only [90].

Penile Cancer and HPV Infection

A link between lack of circumcision and penile cancer has been known for a very long time. A report in 1932 noted that not one man with invasive penile cancer had been circumcised neonatally [91], and this was followed by similar findings over the years [92]. In one, involving 213 cases in California, only 2 of 89 men with invasive penile cancer had been circumcised in infancy, and based on these data, the authors calculated that uncircumcised men had a 22 times higher risk of this disease [93, 94].

The predicted lifetime risk of penile cancer for an uncircumcised man is approximately 1 in 600 in the USA and 1 in 900 in Denmark [95]. It accounts for less than 1% of all malignancies in men in the USA and 0.1% of cancer deaths. The 5-year survival rate has been stated as approximately 50% [96] and others point to it being the cause of death in 25–33% of cases [91, 95]. In less-developed countries the rate can be much higher. In Brazil, for example, penile cancer represents 2–6% of all male neoplasias, with 7% of cases being in men aged less than 35 years, and 39% in men older than 66 years [97]. In Balinese men, most of whom being Hindu, are not circumcised, penile carcinoma is the second most frequent carcinoma [38].

In the 1970s, Harald Zur Hausen in Germany identified a link between HPV infection and cervical cancer, and for this discovery he won the Nobel Prize in 2008. HPV is highly infectious. The transmission probability per heterosexual partnership for the 14 common high-risk types ranges from 45% to 94% [98]. The sexually transmitted nature of genital HPV led to the identification of oncogenic HPV types in penile cancers (see review [99]).

In 2002, a large multination study that involved sampling from the urethra and glans penis/coronal sulcus found HPV in 19.6% of 847 uncircumcised men, but only 5.5% of 292 circumcised men (overall odds ratio after adjusting for potential confounding factors = 0.37) [100]. Two Mexican studies are noteworthy: one involving men attending vasectomy clinics found HPV to be five times lower in those who were circumcised [101], and the other, involving healthy military men, found persistent HPV was ten times lower in the circumcised [102].

The distribution of HPV on the penis is important to consider. A study in Hawaii in 2008 of primarily heterosexual men found HPV infection of the glans/coronal sulcus to be higher in uncircumcised men (46%) compared with circumcised men (29%) [103]. The uncircumcised men were 2.5 times more likely to harbor oncogenic HPV types and 3.6 times more likely to be infected with multiple types. In the uncircumcised men, HPV prevalence on the foreskin (44%) was comparable to that on the glans/corona beneath it. A comparison of circumcised and uncircumcised men found the difference between each in HPV prevalence was greater for proximity to the tip of the penis. In the uncircumcised high-risk HPV was 5.3 times higher in the urethra, 1.6 times higher on the glans/coronal sulcus and 1.8 times higher on the shaft [103]. In the HIM study, involving men in the USA, Mexico, and Brazil, high-risk HPV types were lower in circumcised men (OR 0.70), as were low-risk HPV types (OR 0.63) [104]. HPV prevalence ranged from 41% on the shaft to 4.7% in semen [105]. In this study, the strength of the association between circumcision and reduced HPV decreased with distance from the prepuce/urethra. The adjusted OR was

0.17 for the urethra, 0.44 for the glans/corona, 0.53 for the shaft, and there was no difference for scrotum, peri-anal area, anal canal, and semen [105]. In Kisumu, Kenya, high-risk HPV prevalence in 2,705 uncircumcised men aged 17–28 years was glans/coronal sulcus 31% and shaft 12.3% ($P<0.0001$) [106]. HPV16 was the most common type, and 29% were infected with more than one type. Not surprisingly, men with HPV were also more likely to have other STI(s), but genital warts were uncommon (1%).

A meta-analysis in 2009 of 14 studies, involving 5,880 circumcised and 4,257 uncircumcised men, found circumcision to give 1.9-fold protection against high-risk HPV types (95% CI 0.33–0.82) [107]. There was, however, little protection against low-risk HPV types, which manifest as visible warts and tend to occur on the shaft of the penis, a site of infection less likely to be affected by circumcision [107].

Data for two RCTs became available in 2009. One of these, in Rakai, Uganda, found that at 24 months, high-risk HPV in swabs from the coronal sulcus of the penis was 35% lower in circumcised men (18%) compared to uncircumcised (28%) [77]. When confining the analysis to samples certain to contain DNA, HPV was 45% lower in the circumcised men. Protection against acquisition over the 24 months was 42% [108]. Circumcised men were, moreover, 65% less likely to be infected by multiple high-risk HPV types. Another RCT in Uganda found 33% lower acquisition of high-risk HPV over 2 years in the same genital site [109]. Infection by multiple high-risk HPVs was 55% lower, but there was no difference in single infections. An RCT in South Africa found a 34% lower prevalence of high-risk HPV in urethral swabs from the circumcised group at 21 months after surgery [110]. The authors stated, moreover, that owing to the fact that some men would have already been infected with HPV before inclusion in the trial, the true effect of circumcision would have been higher than this. Sampling at the urethra rather than the glans, coronal sulcus or shaft might, moreover, have underestimated the efficacy of circumcision in preventing HPV infection [111]. For HIV-positive men, the RCT found 60% lower acquisition of new high-risk HPV in the men who received a circumcision [112]. High-risk, but not low-risk, HPV is, moreover, associated with a 3.8-fold higher HIV incidence [113]. High-risk HPV is more likely to produce a persistent infection and, by generating an immune response in basal epithelial cells would cause recruitment of HIV target cells, could increase cytokines which stimulate HIV transcription and replication, and could increase inflammation and immune activation, meaning a causal mechanism is possible [113].

As mentioned above for HSV-2, seroprevalence of HPV was also found not to differ according to circumcision status in the same longitudinal cohort of New Zealand men [114]. The explanation for this finding was revealed in another longitudinal study, this time in Tuscon, Arizona, which found that circumcised men clear penile oncogenic (but not non-oncogenic) HPV infections six times faster than uncircumcised men [115]. Interestingly, men who had had 16 or more lifetime sex partners were 4.9 times more likely to clear oncogenic HPV infection. Perhaps their immune system was better primed by years of repeated exposure. Higher clearance from the glans/coronal sulcus of circumcised men was also seen in a Hawaiian study, being 41% for any HPV, 64% for high-risk HPV, and 50% for HPV types other than high-risk ones [116]. In Uganda, an RCT found 39% higher clearance of high-risk HPV over 2 years in HIV-negative men [109]. A parametric frailty model then showed clearance of different types was highly correlated, and was 60% faster if a man was circumcised [117]. In men who were HIV-positive, although circumcision reduced the prevalence and acquisition of high-risk HPV, it did not affect their ability to clear the virus [112]. An editorial discussed these findings [118].

Condoms were found in a US study in 2007 to provide about 50% protection against oncogenic HPV infection of men [119].

Another factor that might be involved is smegma [120–123], possibly by causing chronic inflammation and recurrent infections that lead to preputial adhesions and phimosis [124, 125].

Chronic relapsing balanitis of bacterial, mycotic, or viral origin might increase risk of

invasive penile cancer [126, 127]. A history of balanitis has been reported in 45% of penile cancer patients compared with 8% of controls [94, 128]. Penile lichen sclerosus (BXO) is associated with penile cancer (reviewed in [19]). Incidence of BXO in penile carcinoma patients is 28–50% [129–132]. HPV infection was 2.6 times higher amongst patients with penile lichen sclerosus [133]. Lichen sclerosus is not always associated with the presence of HPV and it could be that lichen sclerosus acts as a catalyst in the onset of penile cancer [134]. Although oncogenic HPV is higher in patients with genital lichen sclerosus (17% vs. 9%), other data suggest that lichen sclerosis is a pre-neoplastic condition unrelated to HPV infection (reviewed in [19]). A review in 2008 suggested that approximately half of penile squamous cell carcinomas (which represent 95% of penile neoplasms) are associated with lichen sclerosus and half with HPV [17].

A co-carcinogenic role of recurrent HSV-2 in penile cancer has also been suggested [135, 136].

There is no correlation between penile cancer and frequency of bathing or method of cleaning the anogenital area before or after sexual intercourse [124].

Invasive penile carcinoma is associated strongly with a history of phimosis (adjusted odds ratio = 16 in one study [124] and 11 in another [137]). Such a history is seen in 45–85% of men with penile cancer [97, 124, 128]. Phimosis causes dysplastic changes in the skin of the preputial sac [125]. Although length of the foreskin had been suggested as a factor, the evidence for this is weak [28]. In the latter study 52% of penile cancer cases with a long foreskin had phimosis. Circumcision in early childhood, by eliminating phimosis, may help prevent the majority of penile cancer cases [137].

Prostate Cancer

Risk of prostate cancer has been found to correlate with a history of STIs [138–145], but the causative agent remains unclear. Such infections may establish in the prostate a state of chronic active inflammation, which is associated with a variety of cancers [143]. Uncircumcised men have a 1.6- to 2.0-fold higher incidence of prostate cancer [138, 146–148]. Because of the high prevalence of prostate cancer, if the association of the protective effect of circumcision were confirmed, circumcision could provide substantial health and economic benefits [149].

HIV: The Virus Responsible for AIDS

Acquired immune deficiency syndrome (AIDS) was first identified in the early 1980s. Unlike other STIs, risk of transmission of the virus responsible (HIV) during a single heterosexual exposure is relatively low [150]. In 1988 a threefold higher rate of positivity for HIV was noted in men in Nairobi who were uncircumcised [151]. In 1989, a further study in Nairobi examining a wide array of variables found HIV prevalence to be tenfold higher in uncircumcised men [152]. Higher HIV in uncircumcised men was reported in the same year in the USA [153]. These early reports were followed by an enormous number of studies in sub-Saharan Africa and elsewhere. A large systematic meta-analysis published in 2000 [154] that examined 27 studies, found that 21 had found risk to be lower in circumcised men. In 15 studies that were adjusted for potential confounding factors, the association with circumcision was 0.42, that is, rate in uncircumcised men was 2.4-fold higher. In high-risk men, the protective effect was 3.7-fold.

The findings have now been confirmed by three large RCTs involving thousands of men. The first, in South Africa, was published in 2005 [155], and the other two, in Kenya and Uganda, were published in 2007 [74, 156]. In each case, so striking was the benefit of circumcision that each trial was stopped by the monitoring boards so that the control group could be offered circumcision without delay. “As-treated” analyses found the protection to be 76% for the South African trial and 61% for the other two. Follow-up of the Kenyan trial has shown a rise in the protective effect to 65% at 3.5 years [157]. A meta-analysis of the RCT results indicated a similar protective effect as seen in observational studies [158]. Over

99% of the men were, moreover, "very satisfied" with their circumcision. Only 1.5% [156] and 3.6% [74] experienced an adverse event and these resolved quickly. In two of the trials there was, moreover, no behavioral risk compensation after circumcision [74, 156].

Circumcision also protects men who engage in insertive-only anal sex with other men. This was fivefold in a study in Soweto, Africa [159], 1.3- and 2.1-fold in Black and Latino men, respectively, in the USA [160], and ninefold in a study in Sydney, Australia [161]. A meta-analysis of 18 studies found HIV was 29% lower in insertive-only MSM [162]. It seems, not surprisingly, that it is only those MSM who are insertive-only who are at lower risk of HIV infection [163]. Modeling by these authors in a resource-rich setting (Sydney, Australia) showed that circumcision of MSM, especially those who were insertive-only, would be cost-effective for HIV prevention, with one infection prevented for every 118 circumcisions for men in the insertive-only category [164].

The risk to women posed by a male infected with HIV is 20% lower if he is circumcised, according to a meta-analysis in 2009 [165]. Later, a study involving seven sites in eastern Africa found a 40% lower risk [166]. An analysis in 2010 found that circumcision provides a 46% protective effect against male-to-female HIV transmission [167]. One study found, moreover, that protection of women is greatest for those whose male partner was circumcised in childhood [168]. If an HIV-infected man gets circumcised and resumes sex before the wound heals properly, the risk he poses to his female partner is, not surprisingly, higher, by 49% [169].

In 2007, the World Health Organization [170] and in 2009 the Cochrane review committee [171] accepted the protective effect of circumcision against HIV infection. Various cost-benefit analyses have pointed to the millions of lives and billions of dollars that will be saved by substantial increases in circumcision [74, 172–185]. The greatest cost-benefit in the long term will come from universal neonatal male circumcision [186]. Neonatal circumcision for HIV prevention is also cost-effective in the USA [187]. The Center for Disease Control & Prevention (CDC) has recognized the need to promote male circumcision for HIV prevention in the USA and to inform parents and physicians of its many benefits [188]. Ethical analyses have concluded that it is unethical to deny safe male circumcision services in high HIV settings [189–192]. Cultural practices have been seen as an impediment, but these do change, especially when there is a survival advantage [193].

The reason why the foreskin is an infection risk is because it retracts up the shaft during an erection, so exposing its thin, mucosal inner surface to HIV during sexual activity [194]. It then traps the infectious inoculum when the penis becomes flaccid again [152]. The mucosal inner lining is only lightly keratinized [195–197] and is rich in Langerhans cells [196]. Dendrites from these project to just under the surface [195]. The susceptibility of the inner lining to infection by live, tagged HIV has been demonstrated in cultured tissue [196]. Internalization of HIV involves the presence on Langerhans cells of the c-type lectin, Langerin, which can bind HIV, internalize it, and is then involved in its transport to regional lymph nodes [198]. In the inner, but not the outer, foreskin, TNF-α can activate Langerhans cells and stimulatory cytokines cause an influx of CD4+ T-cells into the epithelial layer [199]. The higher permeability of the inner foreskin is associated with increased interaction of HIV target cells with external factors, such as HIV. HIV can, moreover, infect T-cells independently of Langerhans cells [200]. HIV's success in establishing a systemic infection might, nevertheless, depend on its early interaction with Langerhans cells [200, 201]. At low viral levels, Langerin is able to clear HIV, shunting it to intracellular granules for degradation, but this mechanism becomes overwhelmed at higher viral loads [202, 203]. By confocal imaging microscopy and mRNA quantification, abundant and superficially present potential HIV target cells (CD3+ and CD4+ T-cells, Langerhans cells, macrophages, and submucosal dendritic cells) has provided anatomical support for the protective effect of circumcision [204]. There was no difference between positive and negative HSV-2 serostatus. In 2010, it was found that HIV infected cells, but

not free HIV, form viral synapses with apical foreskin keratinocytes, followed by rapid internalization by Langerhans cells in the inner foreskin within 1 h [197, 205]. The Langerhans cells then formed conjugates with T-cells, thereby transferring the HIV. The thick keratin layers in the outer foreskin prevented infection [205]. The two novel models established in these experiments led the authors to reject as artifacts earlier claims that there is no difference in keratin thickness [205].

Ulcerative disease and tearing are more common in uncircumcised men, and add to the risk of HIV entry [206]. A large 2-year RCT found significantly lower penile coital injuries amongst men in the circumcised arm of the trial, adjusted odds ratio being 0.71 for soreness, 0.52 for scratches/abrasions/cuts, and 0.62 for bleeding [207]. HSV-2 infection increases HIV risk in men and women by threefold [208]. Men with a higher foreskin surface area are more likely to be infected with HIV [209]. Inflammation of the epithelium of the foreskin is another factor that can increase infection risk and has been noted in 4.2% of men with neither HIV nor HSV-2, 7.8% of men with HSV-2 only, 19% of men with just HIV, and 32% of men with both [210]. For stromal inflammation, the figures were 14%, 30%, 33%, and 61%. Both epithelial and stromal inflammations were more common in men with smegma. Even in the absence of visible lesions, the mucosal tissue can show histological signs of inflammation [204]. Wetness under the foreskin is an indicator of poor hygiene and is associated with a 40% increase in risk of HIV infection [211]. A wet penis may enhance attachment of infectious virions for longer, reduce healing after trauma, or may lead to balanitis under the foreskin and consequent micro-ulcerations [211].

Condoms, when *always* used, reduce HIV infection by 80–90% [212]. Consistent condom use remains unacceptably low, however [169, 213–223]. Even when made available widely, the impact on HIV has been negligible [224]. A review of ten studies from Africa showed there was no association between condom use and reduced HIV infection [225, 226].

Opponents of circumcision have attempted to deny these findings, but such arguments have been refuted in a 48-author commentary [227]. It has been pointed out that "anti-circumcision groups resemble other anti-science and anti-medicine extremists including AIDS denialists who refute public health realities to maintain entrenched belief systems" [228].

Prevention of Cervical Cancer in Women

Cervical cancer is ten times more common than penile cancer. Based on observations such as the rarity of this disease in nuns, but its frequent occurrence in prostitutes, the role of a sexually transmitted agent was long suspected (reviewed by [14]). Moreover, because cervical cancer is less common in populations with high male circumcision rates, a role for lack of circumcision was long suspected.

In 1947, Plaut reported that smegma, found under the foreskin, was capable of causing cervical cancer in mice [229], but the finding remains equivocal [123]. Observational studies in human populations that have implicated the uncircumcised male started in the early 1980s (see review: [72]). In the mid-1980s, as a result of the work of Zur Hausen in Germany, high-risk types of HPV, transmitted during sexual intercourse, were implicated as the causative agents in over 99% of cervical cancer cases [230–232]. These were the same agents responsible for penile intra-epithelial neoplasia (PIN), and in 1987 it was found that women with cervical cancer were more likely to have partners with PIN [233].

It was not until 2002 that strong evidence emerged for a connection between cervical cancer and lack of male circumcision. This large, well-designed, multinational study by the International Agency for Research on Cancer and published in the *New England Journal of Medicine* found that monogamous women were 5.6 times more likely to have cervical cancer if their partner was uncircumcised and had had six or more sexual partners (adjusted odds ratio = 0.42) [100]. For women whose male partner had an intermediate sexual behavior risk index, circumcision was also protective, although not as strongly (odds ratio = 0.50). Penile HPV infection was associated with a fourfold increase in

the risk of cervical HPV infection in the female partner. Although prevalence in condom users (0.83) and nonusers (0.67) differed little [100], a subsequent study of university undergraduates found HPV to be 70% lower in women whose partners always used condoms [234].

In 2006, UNAIDS data from 117 developing countries found a cervical cancer incidence of 35 per 100,000 women per year in 51 countries with a low (<20%) circumcision prevalence compared to 20 per 100,000 women per year in 52 countries with a high (>80%) circumcision prevalence ($P < 0.001$) [235]. Of all factors examined, male circumcision had the strongest association with cervical cancer incidence.

A meta-analysis in 2009 of 14 studies up until September 2007 (5 in the USA, 2 in Mexico, 2 in Australia, and 1 each in South Korea, Denmark, England, Kenya, and the multinational study in Brazil, Columbia, Spain, Thailand, and the Philippines referred to above) found that the risk of cervical cancer in women whose male partner had a high sexual behavior risk index was 5.5 times greater if the man was uncircumcised [107]. In Bali, where most men are not circumcised, cervical carcinoma is the most frequent carcinoma in women [38].

HPV is very common amongst young women. In recent years, a vaccine against 2 of the more than 20 types of HPV that can cause cervical cancer (types 16 and 18) began being used, and since HPV types 16 and 18 account for approximately 70% of cervical cancers, it could theoretically prevent two-thirds of cervical cancers. A large, randomized, placebo-controlled, double-blind trial of women aged 16–24 years found, however, that vaccination reduced the rate of cervical lesions by only 20% over the 3 years of the study [236]. Furthermore, HPV vaccination was found to not be cost-effective, even under favorable assumptions for vaccination programs [237]. Elimination of HPV 16 and 18 from the population might take 20–30 years. In the meantime, at the population level, other oncogenic HPV types not vaccinated against might take over and replace these two types of HPV [238]. Participation has, moreover, been impeded by concerns about promiscuity and by opposition from anti-immunization lobby groups, who point to the real, albeit rare, risks posed by vaccination. Given the high cost of vaccinating all girls compared with the lesser cost and possible higher overall protective effect of universal male circumcision against the many high-risk HPV types, circumcision would appear to be a more logical and more cost-effective strategy. A bonus would, moreover, be to protect against the other conditions seen more commonly in uncircumcised males and their sexual partners.

Prevention of Breast Cancer in Women

In the past decade, ten studies have identified high-risk HPVs in breast tumors [239, 240]. The type(s) found were identical to those in the cervix of each woman [241, 242]. The suggestion that some breast cancers may involve a sexually transmitted agent [243] is supported by findings that women with HPV-positive breast cancer are significantly younger than those with HPV-negative breast cancer [244]. HPV can, moreover, be found in the bloodstream of cervical cancer patients [245] and male blood donors, attached to blood cells [246]. But the actual virus responsible remains to be identified conclusively. Other possible viruses include mouse mammary tumor virus (MMTV) and Epstein-Barr virus (EBV) [240]. Other than for HPV, a role for uncircumcised male partner(s) in any sexual transmission will require further research.

Herpes Simplex Virus Type 2 in Women

In 2003, a history of sexual intercourse with an uncircumcised man (ever) was reported to increase a woman's risk of infection by herpes simplex virus type 2 (HSV-2) by 2.2-fold [247]. This study, in Pittsburgh, Pennsylvania, involved 1,207 women aged 18–30 years, whose overall HSV-2 seroprevalence rate was 25%.

Chlamydia in Women

Chlamydia trachomatis, but not *C. pneumoniae*, was found in 2005 to be 5.6 times more common

in women whose male partner was uncircumcised [248]. The group studied was the same multinational one referred to above for HPV. But a subsequent prospective study in two African countries and Thailand found no significant difference [249]. The multinational study in 2005, however, tested for antibodies to *Chlamydia*, so providing data on lifetime exposure rather than acute infection. The consequences of genital *Chlamydia* infection include pelvic inflammatory disease that may lead to infertility, ectopic pregnancy, and pelvic pain. *Chlamydia* is also a cofactor in HPV-induced cervical cancer and, in both sexes, HIV transmission. In men, just as in women, it can cause infertility, as well as prostatitis and urethral blockage.

To explain the findings it was suggested that the prepuce, by trapping infected cervicovaginal secretions for longer, would increase risk of penile urethral infection and thereby transmission to the vagina during sex [248].

Bacterial Vaginosis and Trichomonas in Women

Bacterial vaginosis (BV), previously termed "Garnerella," is one of the most common infections in women. Its epidemiology is similar to that of established STIs [250] and is associated with cervical intraepithelial neoplasia [251]. A study in 2008 in Pittsburgh of women without BV at enrolment, found that they were twice as likely to develop this condition over the following year if their male partner was uncircumcised [252]. Two earlier studies in the USA did not, however, find an association, but these were small and had limited power [253, 254]. An RCT in Uganda found that bacterial vaginosis of any type was 40% lower, and severe bacterial vaginosis was 61% lower, in the wives of men in the circumcised arm of the trial [87]. It was suggested that the foreskin of males could facilitate survival of BV organisms, such as gram-negative anerobic bacteria, and make an uncircumcised male a more efficient and more prolonged transmitter of infection [87, 250]. Bacterial vaginosis has been regarded recently as a "sexually enhanced disease" rather than an STI, with male circumcision being seen as protective [255].

A study in 2009 of cervical swabs collected in a suburban STI clinic in Sydney found the following microorganisms: *Trichomonas vaginalis* (3.4%), HSV-1 (2.6%), HSV-2 (0.8%), cytomegalovirus (6.0%), Epstein-Barr virus (2.6%), enterovirus (2.1%), varicella-zoster virus (VZV; 0.4%), *Ureaplasma parvum* (57%), *Ureaplasma urealyticum* (6.1%), *Mycoplasma genitalium* (1.3%), *Mycoplasma hominis* (13.7%), *Chlamydia trachomatis* (0.4%), and group B streptococci (0.4%) [256]. In 2010, the entire micobiome under the foreskin was determined. This identified organisms that would cause bacterial vaginosis, including *Anaerococcus* spp., *Finegoldia* spp., *Peptoniphilus* spp., and *Prevotella* spp. [85].

The RCT in Uganda referred to above also demonstrated 48% lower *T. vaginalis* and 22% lower genital ulceration in women whose male partner was in the circumcised arm of the trial [87]. It was suggested that the moist nature of the subpreputial space might enhance the survival of *Trichomonas*.

Effect on Sexual Function, Sensation, Sensitivity, and Satisfaction

The foreskin, just as the rest of the penis, contains sensory nerve receptors. There is, however, no credible scientific evidence that the extra complement of these in uncircumcised men leads to greater sexual pleasure or that circumcision reduces the latter. As to sensitivity, a diminution is desired by many men (and their sexual partners) in order to prevent premature ejaculation and prolong intercourse [257]. Sexual sensation is mediated by a specific class of nerve endings, genital corpuscles, and these are not present in the foreskin [258].

The first scientific study to address the question of penile sensitivity was carried out by Masters and Johnson, who undertook clinical and neurological testing of the ventral and dorsal surfaces, as well as the glans, and detected no difference between circumcised and uncircumcised

men [259]. Sexual pleasure also appeared to be similar.

In 1997, the National Health and Social Life Survey (NHSLS) of 1,410 men in the USA found that uncircumcised men were more likely to experience sexual dysfunctions, especially with age [260]. This was slight at younger ages, but later in life included finding it twice as difficult to achieve or maintain an erection. The survey discovered that circumcised men engaged in a more elaborate set of sexual practices, and their female partners tended to prefer the esthetics of a circumcised penis over an uncircumcised one. The circumcised men received more fellatio and masturbated more.

Greater sexual dysfunction with age was also noted in a telephone-based survey of 10,173 men in Australia in 2006, this being greatest in men over 50, in whom 27% of uncircumcised, but only 15% of circumcised, men reported difficulty maintaining an erection [7]. Physical pain during intercourse was also less common among circumcised men. A later, smaller survey by this group found no difference in erectile problems [8]. The uncircumcised men were, however, more likely to worry that their penis looked unattractive. Both of these surveys have serious shortcomings in breadth, design, and the validity of conclusions reached [261, 262].

Two US studies published in 2002 both found similar or greater sexual satisfaction in men after circumcision as adults [263, 264]. In the smaller survey [263] there was no difference in sexual drive, erection, ejaculation, problem assessment, or satisfaction compared with what the men recalled sex being like prior to foreskin removal. Penile sensitivity was the same. This paper stated that their study was prompted by reports by proponents of "foreskin restoration," in particular the "disparity between the mythology and medical reality of circumcision regarding male sexuality" [263]. In the other study [264], 62% said they were satisfied with having been circumcised and liked their new look, with 50% reporting benefits. Penile sensitivity, although not tested directly, was thought by some of the men in this study to be slightly lower (but not statistically so), which may have contributed to their claims of better sex. Although there was no change in sexual activity, some of the men thought erectile function was slightly less (category scores: 12.3 vs. 11.1, $P=0.05$), which is the opposite of the very much larger NHLS referred to above [260]. As in the latter, oral sex became more frequent, but there was no change in anal sex or masturbation [264]. Their partners were also more likely to initiate sex with the men after they had been circumcised.

Men circumcised for nonmedical reasons in Turkey exhibited increased ejaculatory latency time, which was considered by the men as an advantage in that they could prolong intercourse [265].

A study involving a battery of quantitative somatosensory tests to evaluate the spectrum of small to large axon nerve fiber function found no difference in sensitivity of the glans penis between 43 uncircumcised and 36 neonatally circumcised US men [266]. The authors controlled, moreover, for factors that can alter neurologic testing (age, erectile function status, diabetes, and hypertension).

A study in London of 150 men aged 18–60 years circumcised for benign disease found identical erectile dysfunction scores before and after circumcision [267]. There was no change in libido for 74%; 69% had less pain during intercourse, and 44% of the men, and 38% of the partners thought appearance was better after circumcision. Sensation improved in 38%, was unchanged in 44%, and was worse in 18%. Overall, 61% were pleased and 17% were not, that is, 3.5 times more were happy with their circumcision.

Intravaginal ejaculatory latency time (IVELT; the time from start of vaginal intromission to start of intravaginal ejaculation, recorded by stopwatch and paper diary) in 500 couples, was found to be 6.7 min (range 0.7–44.1) in circumcised men and 6.0 min (0.5–37.4) in those not circumcised [268]. The data were similar for the Netherlands, UK, Spain, and the USA, but in Turkey was 3.7 min (range 0.9–30.4). IVELT decreased significantly with age, being 6.5 min in men aged 18–30 years compared with 4.3 min in men over 51 years ($P<0.0001$). The data were not affected by condom use. The researchers

subsequently repeated the study using a blinded timer device (to reduce any bias) in a different set of 474 men (mean age 38.5 ± 11.4 SD) from the same countries [269]. In circumcised men (excluding Turkey) mean IVELT was 10.3 min (±9.3 SD; range 0.6–52.7) and in uncircumcised men was 8.8 min (±6.9 SD; range 0.3–38.6) ($P = 0.13$). Median was 7.2 and 6.0, respectively (excluding Turkey: 4.4 min). Alcohol users had a higher mean IELT than nonusers (9.0 vs. 7.3; $P = 0.002$). But there was no difference for condom users and nonusers (7.7 vs. 9.0), nor age group (8.2, 9.2, and 7.3 for 18–30, 31–50, and >51 years), and the number of sexual events did not decrease with age category. Erectile dysfunction was 37%, 34%, and 40% in the respective age categories. The men's own estimates of IVELT were 31% higher than the actual recorded values. One-third had an IVELT (averaging 4.9 min) that was shorter than what they would have liked and two-thirds of these were willing to take medication to remedy this.

Age of childhood circumcision had no effect on overall sexual function in men aged 22–44 years (mean 30) in Turkey [270]. Since all men are circumcised in this Muslim country there was no control group of uncircumcised men to compare with. Of the seven areas of sexual function examined, the only difference was higher avoidance seen in those circumcised between ages 0–2 years compared to the 3–5 years and 6–12 years age groups [270]. But had they corrected for small sample size, the significance of this difference would have disappeared.

The quality of the evidence was elevated by the publication of RCT data in 2008. Amongst 4,456 sexually experienced men aged 15–49 years, a trial in Uganda found no difference in sexual satisfaction or clinically significant function between the 2,210 randomized to receive circumcision and the 2,246 who remained uncircumcised over the 2 years of the trial [271]. At 6 months (i.e., the earliest time examined after the procedure), difficulty with penetration was noted in 1.4% of circumcised men and 0.6% of uncircumcised men; pain on intercourse was 0.6% circumcised and 1.2% uncircumcised. And at 12 months and 24 months these were all identical between each group. Sexual satisfaction also did not differ statistically – in circumcised men being 98.5% at enrolment and 98.4% at 2 years, and in uncircumcised men being 98.0% and 99.4%, respectively. The other trial, in Kenya, found that at 24 months, 64.0% of the circumcised men reported that their penis was "much more sensitive" and 54.5% rated their ease of reaching orgasm as "much more" [271, 272]. A large and increasing proportion of the men reported having sex more often compared to before they were circumcised. Risky behavior was decreased in the circumcised men and they found it easier to apply a condom. Although penile sensitivity was increased, this was not associated with premature ejaculation, and it seemed that, overall, the sexual experience for these men was enhanced.

Sensory stimuli from the penis are transmitted by the pudendal nerve. An objective measurement for assessment of sexual satisfaction is, therefore, penile pudendal evoked potential (PEP). In men aged 18–27 years who underwent circumcision, mean PEP latency was 42.0 ms before and 44.7 ms after circumcision, the difference (2.76 ms) being statistically significant [273]. The authors concluded that circumcision may contribute to sexual satisfaction by prolonging PEP latency by 5% and, thus, intercourse time. The study found, moreover, that sexual function was not affected adversely by circumcision.

Concerns about leaving too much mucosa during circumcision, for fear of later premature ejaculation (PE), appear unfounded. A study in Iran found mucosal cuff length was 15.4 mm in men with PE and 14.7 in men without PE [274]. In this study, penis length was 121 and 130 mm in each respective group. A Korean survey of 3,980 men aged 20–59 years found no difference in premature ejaculation by circumcision status [275].

A study in 2007 claiming higher sensitivity of the uncircumcised penis has often been cited by opponents of circumcision. This involved men in the San Francisco Bay Area and was conducted by anti-circumcision identities with funding from National Organization of Circumcision Information Resource Centers (NOCIRC) [276]. It measured "fine-touch pressure thresholds" at 19 locations on the uncircumcised and 11 on the circumcised penis, finding a difference of

borderline significance ($P=0.03$) for the orifice rim. After Bonferroni correction by critics of the study, to eliminate false positives arising from the multiple testing involved, this single statistical difference disappeared [277]. The study contained, moreover, serious design flaws: it listed subjects in Methods who were unaccounted for in Results, contained biased statements, and demonstrated other omissions that cause it to lack credibility [277].

Perhaps the most important parameter is, however, sensation of the penis during arousal. This was tested in a Montreal study using thermal imaging of the penis. It found no difference between circumcised and uncircumcised men aged 18–45 years (mean age 24) [278]. More circumcised participants reported an increase in their level of arousal, while more uncircumcised men reported being unaffected by the erotic stimulus (a movie). Sensitivity to touch on the forearm as compared to the glans penis or shaft decreased during arousal in both groups, as would be required for penetration.

Women's attitudes are also noteworthy. In the USA, a large majority of women preferred the circumcised penis for sexual activity [279]. In this survey, 90% said it looked "sexier," 85% said it felt nicer to touch, and 55% said it smelled more pleasant. Even women who had only ever had uncircumcised partner(s), preferred the appearance of the circumcised penis. Only 2% preferred an uncircumcised penis for fellatio, with 82% preferring the circumcised variety. Preference for intercourse was 71% for the circumcised penis, compared with 6% for the uncircumcised. Manual stimulation was 75% versus 5%, and visual appeal was 76% versus 4%. A similar preference by women for the circumcised penis was noted in Australian magazine survey by Badger [280, 281]. Women's attitudes were also examined in one of the RCTs in Africa, with the overwhelming majority (97%) reporting either no change (57%) or improved (40%) sexual satisfaction after their male partner had been circumcised [282].

Thus, research has revealed that there are no adverse effects of circumcision, there being little or no difference in sensation during arousal, nor sensitivity of the flaccid penis between circumcised and uncircumcised men. Function is no lower and could on average be superior in circumcised men. Satisfaction is very high amongst both men after having been circumcised and their sexual partners. For many men the sexual experience is enhanced after circumcision, the shaft of the penis making closer contact with the walls of the vagina during intercourse.

Rates of Circumcision

Globally, 30% [283] (Fig. 19.3) to 34% (Waskett, Manchester, UK, unpublished) of males are circumcised. The biggest proportion of male circumcisions in the world are a consequence of Islamic tradition or Judaic religious reasons, which are largely immutable. But in the USA, in particular, health reasons and family tradition are the main drivers. Here we discuss recent trends, particularly in countries having a predominantly Anglo-Celtic heritage.

Higher Circumcision Rates in Upper Echelon of Society

Socioeconomic stratification is seen in the USA, with the National Health and Lifestyle Survey finding higher circumcision rates among whites and the better-educated [260]. Rates differed little between Christian denominations. In the National Health and Nutrition Examination Survey (NHANES) of 1999–2004, for those born in the 1970s circumcision rate was 96% in men with an annual household income of greater than US$55,000, 92% for income US$35,000–54,999, and 84% in those below the poverty level [62]. For those born in the 1980s, the corresponding rates were 85%, 85%, and 75%, respectively. This has been the situation in Australia too, where the higher socioeconomic-educated groups in society have higher rates of circumcision [7, 8]. And in the UK, a corresponding class distinction accompanies circumcision practice [284].

In the USA, the withdrawal of Medicaid for circumcision services by 16 states has had a negative impact on the poor [285, 286]. Policy by state health departments is driven in part by

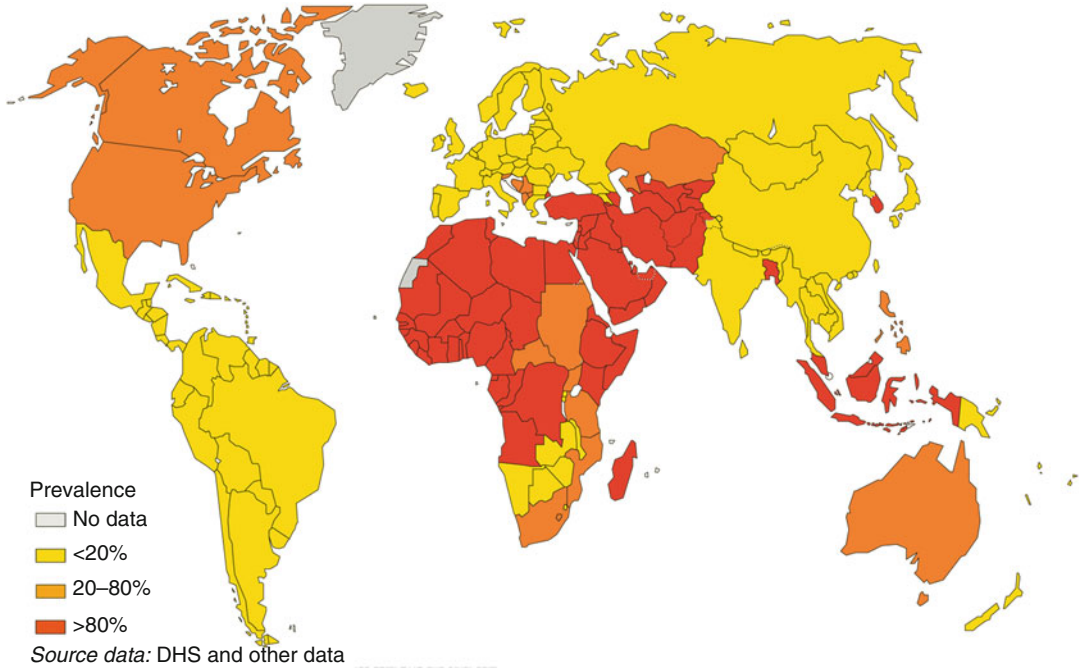

Fig. 19.3 Global circumcision rates in different countries (Kindly provided by the World Health Organization via Kim E.Y. Dickson, with assistance from Helen A. Weiss, London School of Tropical Medicine and Hygiene) (*Source data*: DHS and other data)

American Academy of Pediatrics (AAP) policies. As the AAP policy becomes more positive one would anticipate this disadvantage to be reversed.

Thus, in English-speaking countries of Anglo-Celtic heritage, the upper echelon tend to be circumcised.

Sexual Initiation and Sexuality Do Not Differ by Circumcision Status

In the NHANES survey, sexual initiation occurred at the same age (16.7 and 16.9 years) in uncircumcised and circumcised men [62]. The proportion who had ever had a male partner was also similar (3.4% and 4.9%, respectively). Median number of lifetime sex partners was 5.8 in uncircumcised and 7.0 in circumcised men, a difference that disappeared after stratification by race/ethnicity [62].

Reasons Why Parents Choose to Have Their Boys Circumcised

Although the range, quality, and quantity of medical information on the benefits of circumcision has increased over the years, the reasons given by parents for having their infant boys circumcised have changed little. A survey of new mothers in the USA in 1988 found hygiene and appearance were the two major reasons for choosing to have their newborn son circumcised [279]. Similarly, a Canadian survey found the reasons mothers gave for getting their infant boys circumcised were health or hygiene (44%); to be like their father, siblings, or peers (36%); religion (17%); and other reasons (3%) [287]. Further analysis of the data in this survey shows a strong, significant ($P=0.013$) positive correlation between the mother saying she received enough information about circumcision and the circumcision rates

(Waskett, Manchester, UK, unpublished). A survey in 2007 in Melbourne, Australia, of parents who were having their sons circumcised found that the most common reason was hygiene (96%), followed by family tradition (57%), medical benefit (36%) and aesthetics, with 14% believing it improved sexual performance/enjoyment as an adult, and looked better to women [288]. The most common concern was pain (79%), apparently not realizing that circumcision can be pain-free with local anesthetic as is now recommended by the Royal Australasian College of Physicians (RACP) and AAP. A survey in Mysore, India, of women, 78% of whom were Hindus (who traditionally do not embrace circumcision), 18% were Muslims (who do) and 4% Christians, found that after they were informed actively about the risks and benefits of male circumcision, 81% said they would definitely have their boy(s) circumcised if the procedure were offered in a safe hospital setting, free of charge, and 7% said they would probably get it done, with only 1% saying they would not have their boys circumcised [289].

One of the major developments in recent decades is recognition that infants do feel pain, which has led to local analgesia being recommended. General anesthesia, although recommended by some pediatric bodies is ill-advised, as this carries risks, including those of neuronal damage [290].

Policy Statements and Influence on Rate

In the early 1970s, promotion of infant bonding became popular, and ways of reducing discomfort in newborns were advocated, leading some middle-class families on the East and West coast of the USA to no longer get their boys circumcised. Another factor was a statement by the AAP Committee for the Newborn that there are "no valid medical indications for circumcision" [291]. A slight decline in circumcision ensued. The folly of this trend became evident as a result of research in the years that followed. The research through the 1980s and beyond that showed benefits of circumcision might explain why circumcision rate rose again between 1988 and 2000 in the USA [292, 293]. Interestingly, a study published in 2007 repudiated the 1970s thinking about disruption of infant bonding [294]. This detailed longitudinal study in New Zealand found no adverse effect on breast-feeding outcomes or cognitive ability after comparing a wide range of variables between boys who were circumcised soon after birth in 1974 and those who were not [294]. In the USA today, 86% of parents favor infant male circumcision, those who do not are more likely to be Hispanic [295].

The exact rate of infant circumcision in the USA today is not known precisely owing to lack of universal record keeping, but an analysis by J.H. Waskett and B.J. Morris (2010, unpublished) has found the rate to be steady and high. More reliable data are available for *adult* males, the rate being 88% in whites of Anglo-Celtic extraction, 73% in Blacks, and 43% in Hispanics [105, 296].

In the UK, circumcision rate increased after World War I, just as it did in the USA, but in the mid-1930s it began to decline toward the current overall rate of less than 15% (Waskett and Morris, 2010, unpublished). This fall preceded the adoption by Britain of a nationalized health-care system in 1948, when procedures for which cost was considered to exceed benefit were removed. Circumcision also declined rapidly across Europe after a (misguided) paper by Gairdner in 1949 [26].

Circumcision was fairly much routine in Australia and Canada until the early 1970s, when a similar fall took place in response to statements by the pediatric bodies in each country [297, 298]. These followed the 1971 pronouncement by the AAP referred to above. In Australia, a telephone survey in 2001–2002 of 10,173 men aged 16–59 years found 69% of those born in Australia are circumcised [7]. However, the rate in those aged 16–20 years was only 32%, leading to public health concerns and a call to increase circumcision [261]. Most of the men in this survey had been circumcised in infancy. A later survey in 2005 by the Richters group found circumcision rates of 62–66% for ages 30 through 64 years, but rate was only 35% in 20–29 year olds, and 27%

in those aged 16–19 years [8]. A rate of 66% was found amongst 1,427 homosexual men in Sydney in whom circumcision status was confirmed by clinical examination [299]. For boys aged less than 6 months, the Medicare data show a rise in rate from 10.6% in 1994 to 12.7% in 2004 [300] and then to 18% by 2010 [301]. Medicare data relate to claims and are, thus, underestimates.

In 1975, the AAP statement in the USA was modified to "no absolute valid…" [302], which remained in the 1983 statement, but in 1989 it changed significantly to "New evidence has suggested possible medical benefits" [303]. In its 1999 statement, however, the AAP offered a neutral stance [304]. Although the literature review the AAP conducted was academically weak, it did, nevertheless, mention a vast array of benefits. The major flaw of this document was that it fell short of recommending circumcision, which it would have, had it been based on a more balanced literature survey. This may have been quite understandable, given medico-legal worries in the face of very hostile, politically active anti-circumcision lobby groups. In a joint response, the Chair of the 1989 AAP Taskforce on Circumcision, Edgar Schoen, M.D., and others more expert than those on the 1999 Taskforce, rebutted the 1999 statement [93, 305]. Others also leveled valid criticisms [306, 307]. But surprisingly, in 2005 the AAP reaffirmed its 1999 policy [308], in effect suppressing all of the very strong affirmative evidence published since its 1999 statement. Schoen condemned the AAP for ignoring the 7 years of extensive research findings since 1998 [309]. Further to this, in 2007, when challenged by Schoen [310], a Section Editor of the major journal in the field, *Pediatrics*, called for the AAP to reassess its position in the light of new data [311].

This review is now in progress and news media statements in 2009 and early 2012 suggest that the AAP will move from a neutral to a positive stance, supported by the CDC, that has weighed in on the debate as a result primarily of concern about higher risk of HIV infection in uncircumcised men during heterosexual and insertive homosexual intercourse [188]. In January 2010, a respected pediatric journal published a call for the AAP to advocate neonatal circumcision [168], and this was supported by an editorial commentary by a member of the AAP committee [312]. In that issue, the journal published a brochure for parents that listed health benefits and stated that risks of the procedure were rare and minor [313].

The most recent statement by the Canadian Paediatric Society was in 1996 [314], and by the Royal Australasian College of Physicians (RACP), Division of Paediatrics and Child Health was in 2010 [315]. Although these provide information on the benefits and possibility of rare or minor risks, they too suffered from falling short of drawing the obvious evidence-based conclusion that circumcision is the best choice for lifetime health and sexual well-being. The previous (2004) RACP statement [316] was, in fact, the subject of a damning peer-reviewed critique that demonstrated that it was ideology-based rather than evidence-based [3]. A new, more diverse committee was then formed in 2006, although its chair, once again a pediatrician, has demonstrated in news media comments, placement on the RACP website of an unauthorized statement, and in resistance to recommendations in peer-review of drafts leading up to the final policy statement being released in Sep 2010 considerable resistance to advocating infant circumcision. During this period there was considerable acrimony both within and outside the committee, demonstrating the extremes of emotion that can override sensible implementation of medical evidence attesting to the net benefits of circumcision, especially when performed in infancy when it is lower risk and much simpler to do. The policy that emerged in 2010 can, like its predecessors, be criticized severely for its biased, inaccurate, unscholarly, ideological stance and lack of adherence to evidence-based medicine in reviewing the literature. It led to a petition denouncing it by over 50 professional experts, including Fellows of the RACP and related bodies. A devastating critique in an official journal of the RACP was published in 2012 [316a].

The British Medical Association (BMA) has never made an attempt to review the medical literature on circumcision, producing instead a pompous, paternalistic, and legalistic statement in 2003 [317, 318]. In 2006, it produced a document that recognized the "spectrum of views

within the BMA's membership," stating that the "BMA has no policy," and "the BMA believes that parents should be entitled to make choices about how best to promote their children's interests" subject to limitations imposed by society [319]. In 2007, the *British Medical Journal* (*BMJ*, the official journal of the BMA) published two short "head-to-head" opposing commentaries, one consisting of emotive, legalistic arguments opposing circumcision [320] and the other, by an Editorial staffer, giving a sensible, balanced overview of the many benefits and why "it is far better to help parents to find a competent operator" than comply with the BMA guidelines and make it difficult for them [321]. An article in that issue on medical indications for circumcision distorted and downplayed the benefits by selectively citing publications that supported the negative agenda of its author [322]. It seemed, nevertheless, that at long last the BMA, via the *BMJ*, had begun to address the issues.

The American Urological Association (AUA) has produced statements that are in keeping with the medical evidence, concluding, in 2007, that "circumcision should be presented as an option for health benefits" [323].

In March 2007 the WHO and UNAIDS endorsed circumcision for HIV/AIDS prevention [170] and in 2008 released an extensive document listing the vast array of benefits [324]. Charitable bodies and governments have provided funding to increase circumcision in sub-Saharan Africa, and in 2010, the AUA formed a task force to assist in the rollout.

By and large, the statements of most of these professional bodies have tended to recommend that medical practitioners inform parents fully of the benefits and minor, rare risks associated with having their male children circumcised. Publicly most give the impression that the benefits and harms are very evenly balanced. Indeed, professional bodies have carefully avoided taking sides in the polarized debate, by making noncommittal guidelines and leaving it to the medical practitioner to discuss the matter with the parents [325].

While such bland tolerance has accommodated a broad range of strong and conflicting opinions, the medical profession is today faced with a growing knowledge base that indicates a wide range of health benefits of circumcision and that these exceed any risks, meaning that the time is fast approaching when affirmative statements cannot be avoided [309, 325–328].

Dr Susan Blank, chair of the 2008–2012 AAP Task Force on Circumcision said on ABC News that the Academy noticed some "really very compelling data" and that "it was time to look at the full body of literature and see what is out there." On August 24, 2009 the CDC in the USA announced that it was considering the promotion of routine infant male circumcision for disease prevention. Coinciding with this, Dr Michael Brady, a consultant for the AAP said "The academy is revising its guidelines … and is likely to do away with the neutral tone in favor of a more encouraging policy stating that circumcision has health benefits even beyond HIV prevention, like reducing urinary tract infections for baby boys" [329].

To quote Professor Roger Short: "If we believe in evidence-based medicine, then there can be no debate about male circumcision; it has become a desirable option for the whole world" [330].

The first evidence-based policy statement on infant male circumcision, prepared on behalf of the Circumcision Foundation of Australia, was published in 2012 [331]. Other affirmative evidence-based statements, by the Centers for Disease Control and Prevention and the American Academy of Pediatrics, are anticipated in 2012. The important issue of what is the best age to circumcise has now been addressed by way of a detailed evaluation of the literature [332], finding in favor of infancy.

Conclusion

After a decrease in rate in recent decades, infant male circumcision is rising worldwide. Table 19.2 assembles all of the common risks posed by not circumcising an infant and compares these with the risks inherent in medical circumcision itself, which is the only consideration needed, given that infant circumcision confers virtually no long-term harm to the male.

Table 19.2 The risk of acquiring various medical conditions is more common in uncircumcised males

Condition	Fold increase	NNT
Risks for not circumcising		
Urinary tract infection (infants)	10	50
Urinary tract infections (lifetime)	5	3
Pyelonephritis 5 (infants)	10	100
With concurrent bacteraemia		1,000
Childhood hypertension		1,500
End-stage renal disease		13,000
Candidiasis	2	10
Prostate cancer	1.5–2	6
Balanitis	3	10
Phimosis	Infinite	10
High-risk HPV	5	5
Genital herpes (HSV-2)	1.3	10
Syphilis	3	200
HIV infection	3–8	1,000
Penile cancer	>20	1,000
In female partner:		
Cervical cancer	4	
Chlamydia	4	
HSV-2	2	
Bacterial vaginosis	2	
Note: Thus risk of developing a condition requiring medical attention is over 1 in 3		
Risks associated with medical circumcision in infancy	Proportion	NNH
Local bruising at site of injection of local anaesthetic (if dorsal penile nerve block used)	0.25[a]	4
Infection, local	0.002	600
Infection, systemic	0.0002	4,000
Excessive bleeding	0.001	1,000
Need for repeat surgery (if skin bridges or too little prepuce removed)	0.001	1,000
Loss of penis	Close to 0	One million
Death	0	Virtually zero
Loss of penile sensitivity	0	Zero
Note: Thus risk of an easily-treatable condition = 1 in 500 and of a true complication = 1 in 5,000		

Table 19.2 (continued)

Values are based on statistics for USA (see [3] for refs used for source data
The fold increase in risks is shown relative to number needed to treat (NNT) to prevent that condition. Also shown are risks of the procedure itself, including number needed to harm (NNH)
NNT number needed to treat – i.e., approximate number of males who need to be circumcised to prevent one case of each condition associated with lack of circumcision, *NNH* number needed to harm, i.e., number that need to be circumcised to see one of each particular (mostly minor) adverse effect
aThe minor bruising (from this method only) disappears naturally without any need for medical intervention, so is no included in overall calculation of easily-treatable risks

References

1. Morris BJ. Why circumcision is a biomedical imperative for the 21st century. Bioessays. 2007;29:1147–58.
2. Morris BJ. Circumcision: an evidence-based appraisal – medical, health and sexual [Review]. 2010. http://www.circinfo.net. (over 1,000 references) [accessed Jan 4, 2011].
3. Morris BJ, Bailis SA, Castellsague X, Wiswell TE, Halperin DT. RACP's policy statement on infant male circumcision is ill-conceived. Aust N Z J Public Health. 2006;30:16–22.
4. Wright J. How smegma serves the penis? Sexology. 1970;37:50–3.
5. Iskit S, Ilkit M, Turç-Biçer A, Demirhindi H, Türker M. Effect of circumcision on genital colonization of *Malassezia* spp. in a pediatric population. Med Mycol. 2006;44:113–7.
6. Parker SW, Stewart AJ, Wren MN, Gollow MM, Straton JA. Circumcision and sexually transmissible diseases. Med J Aust. 1983;2:288–90.
7. Richters J, Smith AM, de Visser RO, Grulich AE, Rissel CE. Circumcision in Australia: prevalence and effects on sexual health. Int J STD AIDS. 2006;17:5 47–54.
8. Ferris JA, Richters J, Pitts MK, Shelley JM, Simpson JM, Ryall R, Smith AMA. Circumcision in Australia: further evidence on its effects on sexual health and wellbeing. Aust N Z J Public Health. 2010;34:160–4.
9. Aridogan IA, Ilkit M, Izol V, Ates A, Demirhindi H. Glans penis and prepuce colonisation of yeast fungi in a paediatric population: pre- and postcircumcision results. Mycoses. 2009;52:49–52.
10. Fergusson DM, Lawton JM, Shannon FT. Neonatal circumcision and penile problems: an 8-year longitudinal study. Pediatrics. 1988;81:537–41.

11. Herzog LW, Alvarez SR. The frequency of foreskin problems in uncircumcised children. Am J Dis Child. 1986;140:254–6.
12. Fakjian N, Hunter S, Cole GW, Miller J. An argument for circumcision. Prevention of balanitis in the adult. Arch Dermatol. 1990;126:1046–7.
13. Kohn F-M, Pflieger-Bruss S, Schill W-B. Penile skin diseases. Andrologia. 1999;31 Suppl 1:3–11.
14. Schoen EJ. Circumcision as a lifetime vaccination with many benefits. J Mens Health Gen. 2007;382: 306–11.
15. Mallon E, Hawkins D, Dinneen M, Francis N, Fearfield L, Newson R, Bunker C. Circumcision and genital dermatoses. Arch Dermatol. 2000;136:350–4.
16. English JC, Laws RA, Keough GC, Wilde JL, Foley JP, Elston DM. Dermatoses of the glans penis and prepuce. J Am Acad Dermatol. 1997;37:1–24.
17. Singh S, Bunker C. Male genital dermatoses in old age. Age Ageing. 2008;37:500–4.
18. Schoen EJ. Male circumcision. In: Kandeel FR, Lue TF, Pryor JL, Swerdloff RS, editors. Male sexual dysfunction. Pathophysiology and treatment. New York: Informa; 2007. p. 95–107.
19. Micali G, Nasca MR, Innocenzi D, Schwartz RA. Penile cancer. J Am Acad Dermatol. 2006;54: 369–91.
20. Kiss A, Kiraly L, Kutasy B, Merksz M. High incidence of balanitis xerotica obliterans in boys with phimosis: prospective 10-year study. Pediatr Dermatol. 2005;22:305–8.
21. Griffiths D, Frank JD. Inappropriate circumcision referrals by GPs. J R Soc Med. 1992;85:324–5.
22. Huntley JS, Bourne MC, Munro FD, Wilson-Storey D. Troubles with the foreskin: one hundred consecutive referrals to paediatric surgeons. J R Soc Med. 2003;96:449–51.
23. Kumar B, Narang T, DassRadotra B, Gupta S. Plasma cell balanitis: clinicopathologic study of 112 cases and treatment modalities. J Cutan Med Surg. 2006;10: 11–5.
24. Rossi E, Pavanello P, Franchella A. Lichen sclerosus in children with phimosis. Minerva Pediatr. 2007;59: 761–5.
25. Aynaud O, Piron D, Casanova J-M. Incidence of preputial lichen sclerosis in adults: histologic study of circumcision specimens. J Am Acad Dermatol. 1999; 41:923–6.
26. Gairdner D. The fate of the foreskin: a study of circumcision. Br Med J. 1949;2:1433–7.
27. Osmond TE. Is routine circumcision advisable? J R Army Med Corps. 1953;99:254.
28. Velazquez EF, Bock A, Soskin A, Codas R, Arbo M, Cubilla AL. Preputial variability and preferential association of long phimotic foreskins with penile cancer: an anatomic comparative study of types of foreskin in a general population and cancer patients. Am J Surg Pathol. 2003;27:994–8.
29. Oster J. Further fate of the foreskin: incidence of preputial adhesions, phimosis and smegma among Danish schoolboys. Arch Dis Child. 1968;43:200–3.
30. Saitmacher F. Socialhygienische betrachtungen zu einer routinemassigen zikumzision mannlicher sauglinge. Dtsche Gesundheitwesen. 1960;15: 1217–20.
31. Schoeberlein W. Bedeutung und haeufigkeit von phimose und smegma. Significance and frequency of phimosis and smegma (translated by Kasper JP, 1997; edited by Bailis SA, 1997). Muench Med Wochenschr. 1966;7:373–7.
32. Ben KL, Xu JC, Lu L, Yao JP, Min XD, Li WY, Tao J, Wang J, Li JJ, Cao XM. Promoting male circumcision in China for preventing HIV infection and improving reproductive health (article in Chinese). Zhonghua Nan Ke Xue. 2008;14:291–7.
33. Yang C, Liu X, Wei GH. Foreskin development in 10,421 Chinese boys aged 0–18 years. World J Pediatr. 2009;5:312–5.
34. Ohjimi T, Ohjimi H. Special surgical techniques for the relief of phimosis. J Dermatol Surg Oncol. 1981;7: 326–30.
35. Ishikawa E, Kawakita M. Preputial development in Japanese boys. Hinyokika Kiyo. 2004;50:305–8.
36. Kayaba H, Tamura H, Kitajima S, Fujiwara Y, Kato T, Kato T. Analysis of shape and retractability of the prepuce in 603 Japanese boys. J Urol. 1996;156:1813–5.
37. Su CY, Yin YL. The relationship between preputial condition and personal hygienic practice of senior school boys in two primary schools. J Fam Med ROC. 2001;11:153–63.
38. Boon ME, Susanti I, Tasche MJ, Kok LP. Human papillomavirus (HPV) associated male and female genital carcinomas in a Hindu population. The male as a vector and victim. Cancer. 1989;64:559–65.
39. Ginsburg CM, McCracken GH. Urinary tract infections in young children. Pediatrics. 1982;69:409–12.
40. Wiswell TE, Roscelli JD. Corroborative evidence for the decreased incidence of urinary tract infections in circumcised male infants. Pediatrics. 1982; 69:96–9.
41. Wiswell TE, Smith FR, Bass JW. Decreased incidence of urinary tract infections in circumcised male infants. Pediatrics. 1985;75:901–3.
42. Wiswell TE, Geschke DW. Risks from circumcision during the first month of life compared with those for uncircumcised boys. Pediatrics. 1989;83:1011–5.
43. Wiswell TE, Hachey WE. Urinary tract infections and the circumcision state: an update. Clin Pediatr. 1993;32:130–4.
44. Conway PH, Cnaan A, Zaoutis T, Henry BV, Grundmeier RW. Recurrent urinary tract infections in children: risk factors and association with prophylactic antimicrobials. J Am Med Assoc. 2007;298: 179–86.
45. Singh-Grewal D, Macdessi J, Craig J. Circumcision for the prevention of urinary tract infections in boys: a systematic review of randomized trials and observational studies. Arch Dis Child. 2005;90:853–8.
46. Jakobsson B, Esbjörner E, Hansson S. Minimum incidence and diagnostic rate of first urinary tract infection. Pediatrics. 1999;Part 1:222–6.

47. Simforoosh N, Tabibi A, Khalili SA, Soltani MH, Afjehi A, Aalami F, Bodoohi H. Neonatal circumcision reduces the incidence of asymptomatic urinary tract infection: a large prospective study with long-term follow up using Plastibell. J Pediatr Urol. 2012;8:320–3.
48. Shaikh N, Morone NE, Bost JE, Farrell MH. Prevalence of urinary tract infection in childhood: a meta-analysis. Pediatr Infect Dis J. 2008;27:302–8.
49. Schwartz S, Raveh D, Toker O, Segal G, Godovitch N, Schlesinger Y. A week-by-week analysis of the low-risk criteria for serious bacterial infection in febrile neonates. Arch Dis Child. 2009;94:287–92.
50. Sureshkumar P, Jones M, Cumming RG, Craig JC. Risk factors for urinary tract infection in children: a population-based study of 2856 children. J Paediatr Child Health. 2009;45:87–97.
51. Newman TB, Bernzweig JA, Takayama JI, Finch SA, Wasserman RC, Pantell RH. Urine testing and urinary tract infections in febrile infants seen in office settings: the Pediatric Research in Office Settings' Febrile Infant Study. Arch Pediatr Adolesc Med. 2002; 156:44–54.
52. Rushton HG, Majd M. Dimercaptosuccinic acid renal scintigraphy for the evaluation of pyelonephritis and scarring: a review of experimental and clinical studies. J Urol. 1992;148:1726–32.
53. Hoberman A, Wald ER, Hickey RW, Baskin M, Charron M, Majd M, Kearney DH, Reynolds EA, Ruley J, Janosky JE. Oral versus initial intravenous therapy for urinary tract infections in young febrile children. Pediatrics. 1999;104(Part 1):79–86.
54. Rushton HG. Urinary tract infections in children. Epidemiology, evaluation, and management. Pediatr Clin North Am. 1997;44:1133–69.
55. Jakobsson B, Berg U, Svensson L. Renal scarring after acute pyelonephritis. Arch Dis Child. 1994;71: 386–7.
56. Benador D, Benador N, Slosman D, Mermillod B, Girardin E. Are younger children at highest risk of renal sequelae after pyelonephritis? Lancet. 1997;349: 17–9.
57. Wallin L, Bajc M. Typical technetium dimercaptosuccinic acid distribution patterns in acute pyelonephritis. Acta Paediatr. 1993;82:1061–5.
58. Alsaywid BS, Saleh H, Deshpande A, Howman-Giles R, Smith GH. High grade primary vesicoureteral reflux in boys: long-term results of a prospective cohort study. J Urol. 2010;184(Suppl):1598–603.
59. Spach DH, Stapleton AE, Stamm WE. Lack of circumcision increases the risk of urinary tract infections in young men. J Am Med Assoc. 1992;267:679–81.
60. Griebling TL. Urologic diseases in America project: trends in resource use for urinary tract infections in men. J Urol. 2005;173:1288–94.
61. Griebling TL. Urinary tract infection in men. In: Litwin MS, Saigal CS, editors. Urologic diseases in America. NIH Publication No. 07–5512 ed. Washington, DC: US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; US Government Printing Office; 2007, p. 623–45. http://kidney.niddk.nih.gov/statistics/uda/.
62. Xu F, Markowitz LE, Sternberg MR, Aral SO. Prevalence of circumcision and herpes simplex virus type 2 infection in men in the United States: the national health and nutrition examination survey (NHANES), 1999–2004. Sex Transm Dis. 2007;34: 479–84.
63. Litwin MS, Saigal CS, Beerbohm EM. The burden of urologic diseases in America. J Urol. 2005;173: 1065–6.
64. Fussell EN, Kaak BM, Cherry R, Roberts JA. Adherence of bacteria to human foreskin. J Urol. 1988;140:997–1001.
65. Glennon J, Ryan PI, Keane CT, Rees JPR. Circumcision and periurethral carriage of Proteus mirabilis in boys. Arch Dis Child. 1988;63:556–7.
66. Kallenius G, Moillby R, Svenson SB, Helin I, Hultberg H, Cedergren B, Winberg J. Occurrence of P-fimbriated Escherichia coli in urinary tract infections. Lancet. 1981;2:1369–72.
67. Stull TL, LiPuma JJ. Epidemiology and natural history of urinary tract infections in children [review]. Med Clin N Am. 1991;75:287–97.
68. Kallenius G, Svenson S, Mollby R, Cedergren B, Hultberg H, Winberg J. Structure of carbohydrate part of receptor on human uroepithelial cells for pyelonephritogenic Escherichia coli. Lancet. 1981; 2:604–6.
69. Wiswell TE, Miller GM, Gelston Jr HM, Jones SK. Effects of circumcision status on periurethral bacterial flora during the first year of life. J Paediatr. 1988; 113:442–6.
70. Hutchinson J. On the influence of circumcision in preventing syphilis. Med Times Gazette. 1855;2:542–3.
71. Wilson RA. Circumcision and venereal disease. Can Med Assoc J. 1947;56:54–6.
72. Morris BJ, Castellsague X. The role of circumcision in prevention of STIs. In: Gross GE, Tyring S, editors. Sexually Transmitted Infections and Sexually Transmitted Diseases, chapter 54, Springer, Heidelberg, 2011, pp. 715–739.
73. Weiss HA, Thomas SL, Munabi SK, Hayes RJ. Male circumcision and risk of syphilis, chancroid, and genital herpes: a systematic review and meta-analysis. Sex Transm Infect. 2006;82:101–9.
74. Gray RH, Kigozi G, Serwadda D, Makumbi F, Watya S, Nalugoda F, Kiwanuka N, Moulton LH, Chaudhary MA, Chen MZ, Sewankambo NK, Wabwire-Mangen F, Bacon MC, Williams CF, Opendi P, Reynolds SJ, Laeyendecker O, Quinn TC, Wawer MJ. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. Lancet. 2007;369:657–66.
75. Sobngwi-Tambekou J, Taljaard D, Lissouba P, Zarca K, Puren A, Lagarde E, Auvert B. Effect of HSV-2 serostatus on acquisition of HIV by young men: results of a longitudinal study in Orange Farm, South Africa. J Infect Dis. 2009;199:958–64.

76. Tobian AAR, Charvat B, Ssempijja V, Kigozi G, Serwadda D, Makumbi F, Iga B, Laeyendecker O, Riedesel M, Oliver A, Chen MZ, Reynolds SJ, Wawer MJ, Gray RH, Quinn TC. Factors associated with the prevalence and incidence of herpes simplex virus type 2 infection among men in Rakai, Uganda. J Infect Dis. 2009;199:945–9.
77. Tobian AAR, Serwadda D, Quinn TC, Kigozi G, Gravitt PE, Laeyendecker O, Charvat B, Ssempijja V, Riedesel M, Oliver AE, Nowak RG, Moulton LH, Chen MZ, Reynolds SJ, Wawer MJ, Gray RH. Male circumcision for the prevention of HSV-2 and HPV infections and syphilis. N Engl J Med. 2009;360:1298–309.
78. Dickson N, van Roode T, Paul C. Herpes simplex virus type 2 status at age 26 is not related to early circumcision in a birth cohort. Sex Transm Dis. 2005;32:517–9.
79. Bailey RC, Mehta SD. Circumcision's place in the vicious cycle involving herpes simplex virus type 2 and HIV. J Infect Dis. 2009;199:923–5.
80. Jerath VP, Mahajan VK. Does circumcision influence recurrences in herpes genitalis? Indian J Dermatol Venereol Leprol. 2009;75:575–8.
81. Mahiane SG, Legeai C, Taljaard D, Latouche A, Puren A, Peillon A, Bretagnolle J, Lissouba P, Nguema EP, Gassiat E, Auvert B. Transmission probabilities of HIV and herpes simplex virus type 2, effect of male circumcision and interaction: a longitudinal study in a township of South Africa. AIDS. 2009;23:377–83.
82. Tobian AA, Quinn TC. Herpes simplex virus type 2 and syphilis infections with HIV: an evolving synergy in transmission and prevention. Curr Opin HIV AIDS. 2009;4:294–9.
83. Zhu J, Hladik F, Woodward A, Klock A, Peng T, Johnston C, Remington M, Magaret A, Koelle DM, Wald A, Corey L. Persistence of HIV-1 receptor-positive cells after HSV-2 reactivation is a potential mechanism for increased HIV-1 acquisition. Nat Med. 2009;15:886–92.
84. Van Wagoner NJ, Geisler WM, Sizemore Jr JM, Whitley R, Hook 3rd EW. Herpes simplex virus in African American heterosexual males: the roles of age and male circumcision. Sex Transm Dis. 2010;37:217–22.
85. Price LB, Liu CM, Johnson KE, Aziz M, Lau MK, Jolene Bowers J, Jacques Ravel J, Keim PS, Serwadda D, Wawer MJ, Gray RH. The effects of circumcision on the penis microbiome. PLoS ONE. 2010;5:e8422 (12 pages). doi:10.1371/journal.pone.000842e.
86. Sobngwi-Tambekou J, Taljaard D, Nieuwoudt M, Lissouba P, Puren A, Auvert B. Male circumcision and *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Trichomonas vaginalis*: observations in the aftermath of a randomised controlled trial for HIV prevention. Sex Transm Infect. 2009;85:116–20.
87. Gray RH, Kigozi G, Serwadda D, Makumbi F, Nalugoda F, Watya S, Moulton L, Chen MZ, Sewankambo NK, Kiwanuka N, Sempijja V, Lutalo T, Kagayii J, Wabwire-Mangen F, Ridzon R, Bacon M, Wawer MJ. The effects of male circumcision on female partners' genital tract symptoms and vaginal infections in a randomized trial in Rakai, Uganda. Am J Obstet Gynecol. 2009;200:e1–7.
88. Mehta SD, Moses S, Agot K, Parker C, Ndinya-Achola JO, Maclean I, Bailey RC. Adult male circumcision does not reduce the risk of incident *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, or *Trichomonas vaginalis* infection: results from a randomized, controlled trial in Kenya. J Infect Dis. 2009;200:370–8.
89. Templeton DJ, Jin F, Prestage GP, Donovan B, Imrie JC, Kippax SC, Cunningham PH, Kaldor JM, Mindel A, Cunningham AL, Grulich AE. Circumcision and risk of sexually transmissible infections in a community-based cohort of HIV-negative homosexual men in Sydney, Australia. J Infect Dis. 2009; 200:1813–9.
90. Jameson DR, Celum CL, Manhart L, Menza TW, Golden MR. The association between lack of circumcision and HIV, HSV-2, and other sexually transmitted infections among men who have sex with men. Sex Transm Dis. 2010;37:145–52.
91. Maden C, Sherman KJ, Beckmann AM, Huslop TK, Heh OZ, Ashley RL, Daling JR. History of circumcision, medical conditions, and sexual activity and risk of penile cancer. J Nat Cancer Inst. 1993;85:19–24.
92. Wolbarst AL. Circumcision and penile cancer. Lancet. 1932;1:150–3.
93. Schoen EJ, Wiswell TE, Moses S. New policy on circumcision – cause for concern. Pediatrics. 2000; 105:620–3.
94. Schoen EJ, Oehrli M, Colby CJ, Machin G. The highly protective effect of newborn circumcision against invasive penile cancer. Pediatrics. 2000;105:e36 (34 pages).
95. Kochen M, McCurdy S. Circumcision and risk of cancer of the penis. A life-table analysis. Am J Dis Child. 1980;134:484–6.
96. American Cancer Society. Cancer statistics. 2005. http://www.cancer.org/docroot/CRI/content/CRI_2_4_1X_What_are_the_key_statistics_for_penile_cancer_35.asp?rnav=cri [accessed Jan 4, 2011].
97. Favorito LA, Nardi AC, Ronalsa M, Zequi SC, Sampaio FJ, Glina S. Epidemiologic study on penile cancer in Brazil. Int Braz J Urol. 2008;34:587–91.
98. Bogaards JA, Xiridou M, Coupé VM, Meijer CJ, Wallinga J, Berkhof J. Model-based estimation of viral transmissibility and infection-induced resistance from the age-dependent prevalence of infection for 14 high-risk types of human papillomavirus. Am J Epidemiol. 2010;171:817–25.
99. Morris BJ, Gray RH, Castellsague X, Bosch FX, Halperin DT, Waskett JH, Hankins CA. The strong protection afforded by circumcision against cancer of the penis. Adv Urol. 2011: Article ID 812368 (21pages).
100. Castellsague X, Bosch FX, Munoz N, Meijer CJLM, Shah KV, de Sanjose S, Eluf-Neto J, Ngelangel CA, Chichareon S, Smith JS, Herrero R, Franceschi S. Male circumcision, penile human papillomavirus

infection, and cervical cancer in female partners. N Engl J Med. 2002;346:1105–12.
101. Vaccarella S, Lazcano-Ponce E, Castro-Garduño JA, Cruz-Valdez A, Díaz V, Schiavon R, Hernández P, Kornegay JR, Hernández-Avila M, Franceschi S. Prevalence and determinants of human papillomavirus infection in men attending vasectomy clinics in Mexico. Int J Cancer. 2006;119:1934–9.
102. Lajous M, Mueller N, Cruz-Valdez A, Aguilar LV, Franceschi S, Hernandez-Avila M, Lazcano-Ponce E. Determinants of prevalence, acquisition, and persistence of human papillomavirus in healthy Mexican military men. Cancer Epidemiol Biomarkers Prev. 2005;14:1710–6.
103. Hernandez BY, Wilkens LR, Zhu X, McDuffie K, Thompson P, Shvetsov YB, Ning L, Goodman MT. Circumcision and human papillomavirus infection in men: a site-specific comparison. J Infect Dis. 2008; 197:787–94.
104. Giuliano AR, Lazcano E, Villa LL, Flores R, Salmeron J, Lee JH, Papenfuss M, Abrahamsen M, Baggio ML, Silva R, Quiterio M. Circumcision and sexual behavior: factors independently associated with human papillomavirus detection among men in the HIM study. Int J Cancer. 2009;124:1251–7.
105. Nielson CM, Schiaffino MK, Dunne EF, Salemi JL, Giuliano AR. Associations between male anogenital human papillomavirus infection and circumcision by anatomic site sampled and lifetime number of female sex partners. J Infect Dis. 2009;199:7–13.
106. Smith JS, Backes DM, Hudgens MG, Bailey RC, Veronesi G, Bogaarts M, Agot K, Ndinya-Achola JO, Maclean I, Agingu W, Meijer CJ, Moses S, Snijders PJ. Prevalence and risk factors of human papillomavirus infection by penile site in uncircumcised Kenyan men. Int J Cancer. 2010;126:572–7.
107. Bosch FX, Albero G, Castellsagué X. Male circumcision, human papillomavirus and cervical cancer: from evidence to intervention. J Fam Plann Reprod Health Care. 2009;35:5–7.
108. Gray RH. Infectious disease: male circumcision for preventing HPV infection. Nat Rev Urol. 2009;6: 298–9.
109. Gray RH, Serwadda D, Kong X, Makumbi F, Kigozi G, Gravitt PE, Watya S, Nalugoda F, Ssempijja V, Tobian AA, Kiwanuka N, Moulton LH, Sewankambo NK, Reynolds SJ, Quinn TC, Iga B, Laeyendecker O, Oliver AE, Wawer MJ. Male circumcision decreases acquisition and increases clearance of high-risk human papillomavirus in HIV-negative men: a randomized trial in Rakai, Uganda. J Infect Dis. 2010;201:1455–62.
110. Auvert B, Sobngwi-Tambekou J, Cutler E, Nieuwoudt M, Lissouba P, Puren A, Taljaard D. Effect of male circumcision on the prevalence of high-risk human papillomavirus in young men: results of a randomized controlled trial conducted in orange farm, South Africa. J Infect Dis. 2009;199: 14–9.
111. Gray RH, Wawer MJ, Serwadda D, Kigozi G. The role of male circumcision in the prevention of human papillomavirus and HIV infection. J Infect Dis. 2009;199:1–3.
112. Serwadda D, Wawer MJ, Makumbi F, Kong X, Kigozi G, Gravitt P, Watya S, Nalugoda F, Ssempijja V, Tobian AA, Kiwanuka N, Moulton LH, Sewankambo NK, Reynolds SJ, Quinn TC, Oliver AE, Iga B, Laeyendecker O, Gray RH. Circumcision of HIV-infected men: effects on high-risk human papillomavirus infections in a randomized trial in Rakai, Uganda. J Infect Dis. 2010;201:1463–9.
113. Auvert B, Lissouba P, Cutler E, Zarca K, Puren A, Taljaard D. Association of oncogenic and nononcogenic human papillomavirus with HIV incidence. J Acquir Immune Defic Syndr. 2010;53:111–6.
114. Dickson NP, Ryding J, van Roode T, Paul C, Herbison P, Dillner J, Skegg DC. Male circumcision and serologically determined human papillomavirus infection in a birth cohort. Cancer Epidemiol Biomarkers Prev. 2009;18:177–83.
115. Lu B, Wu Y, Nielson CM, Flores R, Abrahamsen M, Papenfuss M, Harris RB, Giuliano AR. Factors associated with acquisition and clearance of human papillomavirus infection in a cohort of US men: a prospective study. J Infect Dis. 2009;199: 362–71.
116. Hernandez BY, Shvetsov YB, Goodman MT, Wilkens LR, Thompson P, Zhu X, Ning L. Reduced clearance of penile human papillomavirus infection in uncircumcised men. J Infect Dis. 2010;201: 1340–3.
117. Kong X, Archer KJ, Moulton LH, Gray RH, Wang MC. Parametric frailty models for clustered data with arbitrary censoring: application to effect of male circumcision on HPV clearance. BMC Med Res Methodol. 2010;10:40.
118. Viscidi RP, Shah KV. Adult male circumcision: will it reduce disease caused by human papillomavirus? J Infect Dis. 2010;201:1447–9.
119. Nielson CM, Harris RB, Dunne EF, Abrahamsen M, Papenfuss MR, Flores R, Markowitz LE, Giuliano AR. Risk factors for anogenital human papillomavirus infection in men. J Infect Dis. 2007;196: 137–45.
120. Pratt-Thomas HR, Heins HC, Latham E, Dennis EJ, McIver FA. Carcinogenic effect of human smegma: an experimental study. Cancer. 1956;9:671–80.
121. Dennis EJ, Heins HC, Latham E, McIver FA, Pratt-Thomas HR. The carcinogenic effect of human smegma: an experimental study. I. Preliminary report. Cancer Epidemiol Biomarkers Prev. 1956;9:671–80.
122. Heins Jr HC, Dennis EJ. The possible role of smegma in carcinoma of the cervix. Am J Obstet Gynecol. 1958;76:726–33.
123. Reddy DG, Baruah IK. Carcinogenic action of human smegma. Arch Pathol. 1963;75:414.
124. Tsen HF, Morgenstern H, Mack T, Peters RK. Risk factors for penile cancer: results of a population-based case-control study in Los Angeles county (United States). Cancer Causes Control. 2001;12:267–77.
125. Reddy CR, Devendranath V, Pratap S. Carcinoma of penis: role of phimosis. Urology. 1984;24:85–8.

126. Haneke E. Skin diseases and tumors of the penis. Urol Int. 1982;37:172–82.
127. Sayed EI, Viraben R, Bazex J, Daste G, Gorguet B, Rishmann R. Carcinome verruqueux du penis. Nouv Dermatol. 1993;12:112–3.
128. Dillner J, von Krogh G, Horenblas S, Meijer CJ. Etiology of squamous cell carcinoma of the penis. Scand J Urol Nephrol. 2000;205(Suppl):189–93.
129. Powell J, Robson A, Cranston D, Wojnarowska F, Turner R. High incidence of lichen sclerosus in patients with squamous cell carcinoma of the penis. Br J Dermatol. 2001;145:85–9.
130. Perceau G, Derancourt C, Clavel C, Durlach A, Pluot M, Lardennois B, Bernard P. Lichen sclerosus is frequently present in penile squamous cell carcinomas but is not always associated with oncogenic human papillomavirus. Br J Dermatol. 2003;148: 934–8.
131. Velazquez EF, Cubilla AL. Lichen sclerosus in 68 patients with squamous cell carcinoma of the penis: frequent atypias and correlation with special carcinoma variants suggests a precancerous role. Am J Surg Pathol. 2003;27:1448–53.
132. Pietrzak P, Hadway P, Corbishley CM, Watkin NA. Is the association between balanitis xerotica obliterans and penile carcinoma underestimated? BJU Int. 2006;98:74–6.
133. Nasca MR, Innocenzi D, Micali G. Association of penile lichen sclerosus and oncogenic human papillomavirus infection. Int J Dermatol. 2006;45:681–3.
134. Ranjan N, Singh SK. Malignant transformation of penile lichen sclerosus: exactly how common is it? Int J Dermatol. 2008;47:1308–9.
135. Fernando JJ, Wanas TM. Squamous carcinoma of the penis and previous recurrent balanitis: a case report. Genitourin Med. 1991;67:153–5.
136. Zur Hausen H. Herpes simplex virus in human genital cancer. Int Rev Exp Pathol. 1983;25:307–26.
137. Daling JR, Madeleine MM, Johnson LG, Schwartz SM, Shera KA, Wurscher MA, Carter JJ, Porter PL, Galloway DA, McDougall JK, Krieger JN. Penile cancer: importance of circumcision, human papillomavirus and smoking in in situ and invasive disease. Int J Cancer. 2005;116:606–16.
138. Ross RK, Shimizu H, Paganini-Hill A, Honda G, Henderson BE. Case-control studies of prostate cancer in blacks and whites in southern California. J Natl Cancer Inst. 1987;78:869–74.
139. Hayes RB, Pottern LM, Strickler H, Rabkin C, Pope V, Swanson GM, Greenberg RS, Schoenberg JB, Liff J, Schwartz AG, Hoover RN, Fraumeni Jr JF. Sexual behaviour, STDs and risks for prostate cancer. Br J Cancer. 2000;82:718–25.
140. Oliver JC, Oliver RT, Ballard RC. Influence of circumcision and sexual behaviour on PSA levels in patients attending a sexually transmitted disease (STD) clinic. Prostate Cancer Prostatic Dis. 2001; 4:228–31.
141. Dennis LK, Dawson DV. Meta-analysis of measures of sexual activity and prostate cancer. Epidemiology. 2002;13:72–9.
142. Fernandez L, Galan Y, Jimenez R, Gutierrez A, Guerra M, Pereda C, Alonso C, Riboli E, Agudo A, Gonzalez C. Sexual behaviour, history of sexually transmitted diseases, and the risk of prostate cancer: a case-control study in Cuba. Int J Epidemiol. 2005;34:193–7.
143. Correa P. Is prostate cancer an infectious disease? Int J Epidemiol. 2005;34:197–8.
144. Taylor ML, Mainous 3rd AG, Wells BJ. Prostate cancer and sexually transmitted diseases: a meta-analysis. Fam Med. 2005;37:506–12.
145. Radhakrishnan S, Lee A, Oliver T, Chinegwundoh F. An infectious cause for prostate cancer. BJU Int. 2007;99:239–40.
146. Ravich A, Ravich RA. Prophylaxis of cancer of the prostate, penis, and cervix by circumcision. N Y State J Med. 1951;51:1519–20.
147. Apt A. Circumcision and prostatic cancer. Acta Med Scand. 1965;178:493–504.
148. Ewings P, Bowie C. A case-control study of cancer of the prostate in Somerset and east Devon. Br J Cancer. 1996;74:661–6.
149. Morris BJ, Waskett J, Bailis SA. Case number and the financial impact of circumcision in reducing prostate cancer. BJU Int. 2007;100:5–6.
150. Fox J, Fidler S. Sexual transmission of HIV-1. Antiviral Res. 2010;85:267–85.
151. Simonsen JNM, Cameron DW, Gakinya MN, Ndinya-Achola JO, D'Costa LJ, Karasira P. HIV infection among men with STDs. N Engl J Med. 1988;319:274–8.
152. Cameron BE, Simonsen JN, D'Costa LJ, Ronald AR, Maitha GM, Gakinya MN, Cheang M, Dinya-Achola JO, Piot P, Brunham RC, Plummer FA. Female to male transmission of human immunodeficiency virus type 1: risk factors for seroconversion in men. Lancet. 1989;2:403–7.
153. Whittington W, et al. HIV-1 in patients with genital lesions attending a North American STD clinic: assessment of risk factors. Int Conf AIDS. 1989;5:409.
154. Weiss HA, Quigley MA, Hayes RJ. Male circumcision and risk of HIV infection in sub-Saharan Africa: a systematic review and meta-analysis. AIDS. 2000; 14:2361–70.
155. Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, Puren A. Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: the ANRS 1265 trial. PLoS Med. 2005;e298:1112–22.
156. Bailey RC, Moses S, Parker CB, Agot K, Maclean I, Krieger JN, Williams CF, Campbell RT, Ndinya-Achola JO. Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. Lancet. 2007;369:643–56.
157. Bailey RC, Moses S, Parker CB, Agot K, Maclean I, Krieger JN, Williams CF, Ndinya-Achola JO. The protective effect of male circumcision is sustained for at least 42 months: results from the Kisumu, Kenya Trial. Paper presented at: XVII International AIDS conference, Mexico City; 2008.

158. Weiss HA, Halperin D, Bailey RC, Hayes RJ, Schmid G, Hankins CA. Male circumcision for HIV prevention: from evidence to action? (review). AIDS. 2008;22:567–74.
159. Lane T, Raymond HF, Dladla S, Rasethe J, Struthers H, McFarland W, McIntyre J. High HIV prevalence among men who have sex with men in Soweto, South Africa: results from the Soweto Men's Study. AIDS Behav. 2011; 15:626–34.
160. Millett GA, Ding H, Lauby J, Flores S, Stueve A, Bingham T, Carballo-Dieguez A, Murrill C, Liu KL, Wheeler D, Liau A, Marks G. Circumcision status and HIV infection among Black and Latino men who have sex with men in 3 US cities. J Acquir Immune Defic Syndr. 2007;46:643–50.
161. Templeton DJ, Jin F, Mao L, Prestage GP, Donovan B, Imrie J, Kippax S, Kaldor JM, Grulich AE. Circumcision and risk of HIV infection in Australian homosexual men. AIDS. 2009;23:2347–51.
162. Millett GA, Flores SA, Marks G, Reed JB, Herbst JH. Circumcision status and risk of HIV and sexually transmitted infections among men who have sex with men: a meta-analysis. JAMA. 2008;300: 1674–84.
163. Templeton DJ, Millett GA, Grulich AE. Male circumcision to reduce the risk of HIV and sexually transmitted infections among men who have sex with men. Curr Opin Infect Dis. 2010;23:45–52.
164. Anderson J, Wilson D, Templeton DJ, Grulich A, Carter R, Kaldor J. Cost-effectiveness of adult circumcision in a resource-rich setting for HIV prevention among men who have sex with men. J Infect Dis. 2009;200:1803–12.
165. Weiss HA, Hankins CA, Dickson K. Male circumcision and risk of HIV infection in women: a systematic review and meta-analysis. Lancet Infect Dis. 2009;9:669–77.
166. Baeten JM, Donnell D, Kapiga SH, Ronald A, John-Stewart G, Inambao M, Manongi R, Vwalika B, Celum C. Male circumcision and risk of male-to-female HIV-1 transmission: a multinational prospective study in African HIV-1-serodiscordant couples. AIDS. 2010;24:737–44.
167. Hallett TB, Alsallaq RA, Baeten JM, Weiss H, Celum C, Gray R, Abu-Raddad L. Will circumcision provide even more protection from HIV to women and men? New estimates of the population impact of circumcision interventions. Sex Transm Infect. 2010;87:88–93.
168. Tobian AA, Gray RH, Quinn TC. Male circumcision for the prevention of acquisition and transmission of sexually transmitted infections: the case for neonatal circumcision. Arch Pediatr Adolesc Med. 2010;164:78–84.
169. Wawer MJ, Makumbi F, Kigozi G, Serwadda D, Watya S, Nalugoda F, Buwembo D, Ssempijja V, Kiwanuka N, Moulton LH, Sewankambo NK, Reynolds SJ, Quinn TC, Opendi P, Iga B, Ridzon R, Laeyendecker O, Gray RH. Circumcision in HIV-infected men and its effect on HIV transmission to female partners in Rakai, Uganda: a randomised controlled trial. Lancet. 2009;374:229–37.
170. WHO and UNAIDS announce recommendations from expert consultation on male circumcision for HIV prevention. 2007. http://www.who.int/hiv/mediacentre/news68/en/index.html.
171. Siegfried N, Muller M, Deeks JJ, Volmink J. Male circumcision for prevention of heterosexual acquisition of HIV in men. Cochrane Database Syst Rev. 2009;2:CD003362 (38 pp).
172. Gray RH, Li X, Kigozi G, Serwadda D, Nalugoda F, Watya S, Reynolds SJ, Wawer M. The impact of male circumcision on HIV incidence and cost per infection prevented: a stochastic simulation model from Rakai, Uganda. AIDS. 2007;21:845–50.
173. Podder CN, Sharomi O, Gumel AB, Moses S. To cut or not to cut: a modeling approach for assessing the role of male circumcision in HIV control. Bull Math Biol. 2007;69:2447–66.
174. Williams BG, Lloyd-Smith JO, Gouws E, Hankins C, Getz WM, Hargrove J, de Zoysa I, Dye C. The potential impact of male circumcision on HIV in Sub-Saharan Africa. PLoS Med. 2006;3(e262): 1032–40.
175. Hankins C, Hargrove J, Williams B, Raddad LA, Auvert B, Bollinger L, Dorrington R, Ghani A, Gray R, Hallett T, Kahn JG, Lohse N, Nagelkerke N, Porco T, Schmid G, Stover J, Weiss H, Welte A, White P, White R. Male circumcision for HIV prevention in high HIV prevalence settings: what can mathematical modelling contribute to informed decision making? PLoS Med. 2009; 6:e1000109.
176. Kahn JG, Marseille E, Auvert B. Cost-effectiveness of male circumcision for HIV prevention in a South African setting. PLoS Med. 2006;3(e517):2349–58.
177. Bollinger LA, Stover J, Musuka G, Fidzani B, Moeti T, Busang L. The cost and impact of male circumcision on HIV/AIDS in Botswana. J Int AIDS Soc. 2009;12:7.
178. Auvert B, Kahn JG, Korenromp E, Lloyd-Smith J, Helleringer S, Taljaard D, Sitta R, Hargrove J, Williams B, Marseille E. Cost of the roll-out of male circumcision in sub-Saharan Africa. In: 7th International AIDS Society conference, Kuala Lumpur; 2007: WEAC105.
179. Nagelkerke NJ, Moses S, de Vlas SJ, Bailey RC. Modelling the public health impact of male circumcision for HIV prevention in high prevalence areas in Africa. BMC Infect Dis. 2007;7:16(15 pages).
180. Auvert B, Marseille E, Korenromp EL, Lloyd-Smith J, Sitta R, Taljaard D, Pretorius C, Williams B, Kahn JG. Estimating the resources needed and savings anticipated from roll-out of adult male circumcision in Sub-Saharan Africa. PLoS One. 2008;3:e2679 (8 pages).
181. Londish GJ, Murray JM. Significant reduction in HIV prevalence according to male circumcision intervention in sub-Saharan Africa. Int J Epidemiol. 2008;37:1246–53.

182. Moses S. Male circumcision: a new approach to reducing HIV transmission. Can Med Assoc J. 2009;181:E134–5.
183. White RG, Glynn JR, Orroth KK, Freeman EE, Bakker R, Weiss HA, Kumaranayake L, Habbema JD, Buvé A, Hayes RJ. Male circumcision for HIV prevention in sub-Saharan Africa: who, what and when? AIDS. 2008;22:1841–50.
184. Gray RH, Wawer MJ, Kigozi G, Serwadda D. Commentary: disease modelling to inform policy on male circumcision for HIV prevention. Int J Epidemiol. 2008;37:1253–4.
185. Uthman OA, Popoola TA, Uthman MM, Aremu O. Economic evaluations of adult male circumcision for prevention of heterosexual acquisition of HIV in men in sub-Saharan Africa: a systematic review. PLoS One. 2010;5:e9628 (7 pages).
186. Binagwaho A, Pegurri E, Muita J, Bertozzi S. Male circumcision at different ages in Rwanda: a cost-effectiveness study. PLoS Med. 2010;7:e1000211 (10 pages).
187. Sansom SL, Prabhu VS, Hutchinson AB, An Q, Hall HI, Shrestha RK, Lasry A, Taylor AW. Cost-effectiveness of newborn circumcision in reducing lifetime HIV risk among U.S. males. PLoS One. 2010;5:e8723 (8 pages).
188. Smith DK, Taylor A, Kilmarx PH, Sullivan P, Warner L, Kamb M, Bock N, Kohmescher B, Mastro TD. Male circumcision in the United States for the prevention of HIV infection and other adverse health outcomes: report from a CDC consultation. Public Health Rep. 2010;125 Suppl 1:72–82.
189. Benatar M, Benatar D. Between prophylaxis and child abuse: the ethics of neonatal male circumcision. Am J Bioeth. 2003;3:35–48.
190. Lie RK, Emanuel EJ, Grady C. Circumcision and HIV prevention research: an ethical analysis. Lancet. 2006;368:522–5.
191. UNAIDS. Safe, voluntary, informed male circumcision and comprehensive HIV prevention programming: guidance for decision-makers on human rights, ethical & legal considerations. 2008. http://data.unaids.org/pub/Report/2008/JC1552_Circumcision_en.pdf [accessed Jan 4, 2011].
192. Clark PA, Eisenman J, Szapor S. Mandatory neonatal male circumcision in Sub-Saharan Africa: medical and ethical analysis. Med Sci Monit. 2007;12:RA205–13.
193. Hargrove J. Migration, mines and mores: the HIV epidemic in Southern Africa. S Afr J Sci. 2008;104:53–61.
194. Szabo R, Short RV. How does male circumcision protect against HIV infection? Br Med J. 2000;320:1592–4.
195. McCoombe SG, Short RV. Potential HIV-1 target cells in the human penis. AIDS. 2006;20:1491–5.
196. Patterson BK, Landy A, Siegel JN, Flener Z, Pessis D, Chaviano A, Bailey RC. Susceptibility to human immunodeficiency virus-1 infection of human foreskin and cervical tissue grown in explant culture. Am J Pathol. 2002;161:867–73.
197. Ganor Y, Zhou Z, Tudor D, Schmitt A, Vacher-Lavenu MC, Gibault L, Thiounn N, Tomasini J, Wolf JP, Bomsel M. Within 1 h, HIV-1 uses viral synapses to enter efficiently the inner, but not outer, foreskin mucosa and engages Langerhans-T cell conjugates. Mucosal Immunol. 2010;3:506–22.
198. Turville SG, Cameron PU, Handley A, Lin G, Pohlmann S, Doms RW, Cunningham AL. Diversity of receptors binding HIV on dendritic cell subsets. Nat Immunol. 2002;3:975–83.
199. Fahrbach KM, Barry SM, Anderson MR, Hope TJ. Enhanced cellular responses and environmental sampling within inner foreskin explants: implications for the foreskin's role in HIV transmission. Mucosal Immunol. 2010;3:410–8.
200. Boggiano C, Littman DR. HIV's vagina travelogue. Immunity. 2007;26:145–7.
201. Hladik F, Sakchalathorn P, Ballweber L, Lentz G, Fialkow M, Eschenbach D, McElrath MJ. Initial events in establishing vaginal entry and infection by human immunodeficiency virus type-1. Immunity. 2007;26:257–70.
202. de Witte L, Nabatov A, Pion M, Fluitsma D, de Jong MA, de Gruijl T, Piguet V, van Kooyk Y, Geijtenbeek TB. Langerin is a natural barrier to HIV-1 transmission by Langerhans cells. Nat Med. 2007;13:367–71.
203. Schwartz O. Langerhans cells lap up HIV-1. Nat Med. 2007;13:245–6.
204. Hirbod T, Bailey RC, Agot K, Moses S, Ndinya-Achola J, Murugu R, Andersson J, Nilsson J, Broliden K. Abundant expression of HIV target cells and C-type lectin receptors in the foreskin tissue of young Kenyan men. Am J Pathol. 2010;176:2798–805.
205. Ganor Y, Bomsel M. HIV-1 transmission in the male genital tract. Am J Reprod Immunol. 2011;65:284–91.
206. Alanis MC, Lucidi RS. Neonatal circumcision: a review of the world's oldest and most controversial operation. Obstet Gynecol Surv. 2004;59:379–95.
207. Mehta SD, Krieger JN, Agot K, Moses S, Ndinya-Achola JO, Parker C, Bailey RC. Circumcision and reduced risk of self-reported penile coital injuries: results from a randomized controlled trial in Kisumu, Kenya. J Urol. 2010;184:203–9.
208. Freeman EE, Weiss HA, Glynn JR, Cross PL, Whitworth JA, Hayes RJ. Herpes simplex virus 2 infection increases HIV acquisition in men and women: systematic review and meta-analysis of longitudinal studies. AIDS. 2006;20:73–83.
209. Kigozi G, Wawer M, Ssettuba A, Kagaayi J, Nalugoda F, Watya S, Mangen FW, Kiwanuka N, Bacon MC, Lutalo T, Serwadda D, Gray RH. Foreskin surface area and HIV acquisition in Rakai, Uganda (size matters). AIDS. 2009;23:2209–13.
210. Johnson KE, Sherman ME, Ssempiija V, Tobian AA, Zenilman JM, Duggan MA, Kigozi G, Serwadda D, Wawer MJ, Quinn TC, Rabkin CS, Gray RH. Foreskin inflammation is associated with HIV and

herpes simplex virus type-2 infections in Rakai, Uganda. AIDS. 2009;23:1807–15.
211. O'Farrell N, Morison L, Moodley P, Pillay K, Vanmali T, Quigley M, Hayes R, Sturm AW. Association between HIV and subpreputial penile wetness in uncircumcised men in South Africa. J Acquir Immune Defic Syndr. 2006;43:69–77.
212. Halperin DT, Steiner MJ, Cassell MM, Green EC, Hearst N, Kirby D, Gayle HD, Cates W. The time has come for common ground on preventing sexual transmission of HIV. Lancet. 2004;364:1913–5.
213. Beckman LJ, Harvey SM, Tiersky LA. Attitudes about condoms and condom use among college students. J Am Coll Health. 1996;44:243–9.
214. Anderson JE, Wilson R, Doll L, Jones S, Barker P. Condom use and HIV risk behaviors among US adults: data from a national survey. Fam Plann Perspect. 1999;31:24–8.
215. Donovan B, Ross MW. Preventing HIV: determinants of sexual behaviour (review). Lancet. 2000;355:1897–901.
216. Quinn TC, Wawer MJ, Sewankambo N, Serwadda D, Li C, Wabwire-Mangen F, Meehan MO, Lutalo T, Gray RH. Viral load and heterosexual transmission of human immunodeficiency virus type 1. N Engl J Med. 2000;342:921–9.
217. Caballero-Hoyos R, Villasenor-Sierra A. Socioeconomic strata as a predictor factor for constant condom use among adolescents (Spanish). Rev Saude Publica. 2001;35:531–8.
218. Tapia-Aguirre V, Arillo-Santillan E, Allen B, Angeles-Llerenas A, Cruz-Valdez A, Lazcano-Ponce E. Associations among condom use, sexual behavior, and knowledge about HIV/AIDS. A study of 13,293 public school students. Arch Med Res. 2004; 35:334–43.
219. Ferrante P, Delbue S, Mancuso R. The manifestation of AIDS in Africa: an epidemiological overview. J Neurovirol. 2005;11 Suppl 1:50–7.
220. Kang M, Rochford A, Johnston V, Jackson J, Freedman E, Brown K, Mindel A. Prevalence of Chlamydia trachomatis infection among 'high risk' young people in New South Wales. Sex Health. 2006;3:253–4.
221. Sanchez T, Finlayson T, Drake A, Behel S, Cribbin M, Dinenno E, Hall T, Kramer S, Lansky A. Human immunodeficiency virus (HIV) risk, prevention, and testing behaviors – United states, national HIV behavioral surveillance system: men who have sex with men, November 2003-April 2005. MMWR Surveill Summ. 2006;55:1–16.
222. Jadack RA, Yuenger J, Ghanem KG, Zenilman J. Polymerase chain reaction detection of Y-chromosome sequences in vaginal fluid of women accessing a sexually transmitted disease clinic. Sex Transm Dis. 2006;33:22–5.
223. Yahya-Malima KI, Matee MI, Evjen-Olsen B, Fylkesnes K. High potential of escalating HIV transmission in a low prevalence setting in rural Tanzania. BMC Public Health. 2007;7:103 (10 pages).
224. Karim SSA, Karim QA. AIDS research must link to local policy. Nature. 2010;463:733–4.
225. Slaymaker E. A critique of international indicators of sexual risk behaviour. Sex Transm Infect. 2004;80 Suppl 2:ii13–21.
226. Lopman B, Nyamukapa C, Mushati P, Mupambireyi Z, Mason P, Garnett GP, Gregson S. HIV incidence in 3 years of follow-up of a Zimbabwe cohort – 1998–2000 to 2001–03: contributions of proximate and underlying determinants to transmission. Int J Epidemiol. 2008;37:88–105.
227. Wamai RG, Weiss HA, Hankins C, Agot K, Karim QA, Shisana O, Bailey RC, Betukumesu B, Bongaarts J, Bowa K, Cash R, Cates W, Diallo MO, Dludlu S, Geffen N, Heywood M, Jackson H, Kayembe PK, Kapiga S, Kebaabetswe P, Kintaudi L, Klausner JD, Leclerc-Madlala S, Mabuza K, Makhubele MB, Miceni K, Morris BJ, de Moya A, Ncala J, Ntaganira I, Nyamucherera OF, Otolorin EO, Pape JW, Phiri M, Rees H, Ruiz M, Sanchez J, Sawires S, Seloilwe ES, Serwadda DM, Setswe G, Sewankambo N, Simelane D, Venter F, Wilson D, Woelk G, Zungu N, Halperin DT. Male circumcision is an efficacious, lasting and cost-effective strategy for combating HIV in high-prevalence AIDS epidemics: time to move beyond debating the science. Future HIV Ther. 2008;2:399–405.
228. Kalichman SC. Neonatal circumcision for HIV prevention: cost, culture, and behavioral considerations. PLoS Med. 2010;7:e1000219 (2 pages).
229. Plaut A, Kohn-Speyer AC. The carcinogenic action of smegma. Science. 1947;105:391–2.
230. Peto J. Cancer epidemiology in the last century and the next decade. Nature. 2001;411:390–5.
231. Walboomers J, Meijer C. Do HPV-negative cervical carcinomas exist? J Pathol. 1997;181:253–4.
232. Walboomers JM, Jacobs MV, Manos MM, Bosch FX, Kummer JA, Shah KV, Snijders PJ, Peto J, Meijer CJ, Munoz N. Human papillomavirus is a necessary cause of invasive cervical cancer. J Pathol. 1999;189:12–9.
233. Barrasso R, De Brux J, Croissant O, Orth G. High prevalence of papillomavirus associated penile intraepithelial neoplasia in sexual partners of women with cervical intraepithelial neoplasia. N Engl J Med. 1987;317:916–23.
234. Winer RL, Hughes JP, Feng Q, O'Reilly S, Kiviat NB, Holmes KK, Koutsky LA. Condom use and the risk of genital human papillomavirus infection in young women. N Engl J Med. 2006;354: 2645–54.
235. Drain PK, Halperin DT, Hughes JP, Klausner JD, Bailey RC. Male circumcision, religion, and infectious diseases: an ecologic analysis of 118 developing countries. BMC Infect Dis. 2006;6:172 (10 pages).
236. Garland SM, Hernandez-Avila M, Wheeler CM, Perez G, Harper DM, Leodolter S, Tang GW, Ferris DG, Steben M, Bryan J, Taddeo FJ, Railkar R, Esser MT, Sings HL, Nelson M, Boslego J, Sattler C, Barr

E, Koutsky LA. Quadrivalent vaccine against human papillomavirus to prevent anogenital diseases. N Engl J Med. 2007;356:1928–43.
237. de Kok IMCM, van Ballegooijen M, Habbem JDF. Cost-effectiveness analysis of human papillomavirus vaccination in the Netherlands. J Natl Cancer Inst. 2009;101:1083–92.
238. Morris BJ, Rose BR. Cervical screening in the 21st century: the case for human papillomavirus testing of self-collected specimens. Clin Chem Lab Med. 2007;45:577–91.
239. Lawson JS, Gunzburg WH, Whitaker NJ. Viruses and human breast cancer. Future Microbiol. 2006;1:33–51.
240. Amarante MK, Watanabe MA. The possible involvement of virus in breast cancer. J Cancer Res Clin Oncol. 2009;135:329–37.
241. Hennig EM, Suo Z, Thoresen S, Holm R, Kvinnsland S, Nesland JM. Human papillomavirus 16 in breast cancer of women treated for high grade cervical intraepithelial neoplasia (CIN III). Breast Cancer Res Treat. 1999;53:121–35.
242. Widschwendter A, Brunhuber T, Wiedemair A, Mueller-Holzner E, Marth C. Detection of human papillomavirus DNA in breast cancer of patients with cervical cancer history. J Clin Virol. 2004; 31:292–7.
243. Kan CY, Iacopetta BJ, Lawson JS, Whitaker NJ. Identification of human papillomavirus DNA gene sequences in human breast cancer. Br J Cancer. 2005;93:946–8.
244. Lawson JS, Kan CY, Iacopetta BJ, Whitaker NJ. Are some breast cancers sexually transmitted? Br J Cancer. 2006;95:1708.
245. Tseng CJ, Pao CC, Lin JD, Soong YK, Hong JH, Hsueh S. Detection of human papillomavirus types 16 and 18 mRNA in peripheral blood of advanced cervical cancer patients and its association with prognosis. J Clin Oncol. 1999;17:1391–6.
246. Chen AC, Keleher A, Kedda MA, Spurdle AB, McMillan NA, Antonsson A. Human papillomavirus DNA detected in peripheral blood samples from healthy Australian male blood donors. J Med Virol. 2009;81:1792–6.
247. Cherpes TL, Meyne LA, Krohn MA, Hiller SL. Risk factors for infection with herpes simplex virus type 2: role of smoking, douching, uncircumcised males, and vaginal flora. Sex Transm Dis. 2003;30:405–10.
248. Castellsague X, Peeling RW, Franceschi S, de Sanjose S, Smith JS, Albero G, Diaz M, Herrero R, Munoz N, Bosch FX. Chlamydia trachomatis infection in female partners of circumcised and uncircumcised adult men. Am J Epidemiol. 2005;162: 907–16.
249. Turner AN, Morrison CS, Padian NS, Kaufman JS, Behets FM, Salata RA, Mmiro FA, Chipato T, Celentano DD, Rugpao S, Miller WC. Male circumcision and women's risk of incident chlamydial, gonococcal, and trichomonal infections. Sex Transm Dis. 2008;35:689–95.
250. Fethers KA, Fairley CK, Hocking JS, Gurrin LC, Bradshaw CS. Sexual risk factors and bacterial vaginosis: a systematic review and meta-analysis. Clin Infect Dis. 2008;47:1426–35.
251. Nam KH, Kim YT, Kim SR, Kim SW, Kim JW, Lee MK, Nam EJ, Jung YW. Association between bacterial vaginosis and cervical intraepithelial neoplasia. J Gynecol Oncol. 2009;20:39–43.
252. Cherpes TL, Hillier SL, Meyn LA, Busch JL, Krohn MA. A delicate balance: risk factors for acquisition of bacterial vaginosis include sexual activity, absence of hydrogen peroxide-producing lactobacilli, black race, and positive herpes simplex virus type 2 serology. Sex Transm Dis. 2008;35:78–83.
253. Zenilman JM, Fresia A, Berger B, McCormack WM. Bacterial vaginosis is not associated with circumcision status of the current male partner. Sex Transm Infect. 1999;75:347–8.
254. Schwebke JR, Desmond R. Risk factors for bacterial vaginosis in women at high risk for sexually transmitted diseases. Sex Transm Dis. 2005; 32:654–8.
255. Verstraelen H, Verhelst R, Vaneechoutte M, Temmerman M. The epidemiology of bacterial vaginosis in relation to sexual behaviour. BMC Infect Dis. 2010;10:81 (11 pages).
256. McIver CJ, Rismanto N, Smith C, Naing ZW, Rayner B, Lusk MJ, Konecny P, White PA, Rawlinson WD. Multiplex PCR testing detection of higher-than-expected rates of cervical mycoplasma, ureaplasma, and trichomonas and viral agent infections in sexually active Australian women. J Clin Microbiol. 2009;47:1358–63.
257. Burger R, Guthrie T. Why circumcision? Pediatrics. 1974;54:362–4.
258. Rhodin JAG. Histology. London: Oxford University Press; 1974.
259. Masters WH, Johnson VE. Human sexual response. Boston: Little Brown; 1966.
260. Laumann EO, Maal CM, Zuckerman EW. Circumcision in the United States. Prevalence, prophyactic effects, and sexual practice. J Am Med Assoc. 1997;277:1052–7.
261. Morris BJ. Circumcision in Australia: prevalence and effects on sexual health (Critique of Richters et al. Int J STD AIDS 2006;17:547–554). Int J STD AIDS. 2007;18:69–70.
262. Morris BJ, Wodak A. Circumcision survey misleading. Aust N Z J Public Health. 2010;34:636–7.
263. Collins S, Upshaw J, Rutchik S, Ohannessian C, Ortenberg J, Albertsen P. Effects of circumcision on male sexual function: debunking a myth? J Urol. 2002;167:2111–2.
264. Fink KS, Carson CC, de Vellis RF. Adult circumcision outcomes study: effect on erectile function, penile sensitivity, sexual activity and satisfaction. J Urol. 2002;167:2113–6.
265. Senkul T, Iseri C, Sen B, Karademir K, Saracoglu F, Erden D. Circumcision in adults: effect on sexual function. Urology. 2004;63:155–8.

266. Bleustein CB, Fogarty JD, Eckholdt H, Arezzo JC, Melman A. Effect of neonatal circumcision on penile neurological sensation. Urology. 2005;65:773–7.
267. Masood S, Patel HRH, Himpson RC, Palmer JH, Mufti GR, Sheriff MKM. Penile sensitivity and sexual satisfaction after circumcision: are we informing men correctly? Urol Int. 2005;75:62–6.
268. Waldinger MD, Quinn P, Dilleen M, Mundayat R, Schweitzer DH, Boolell M. A multinational population survey of intravaginal ejaculation latency time. J Sex Med. 2005;2:492–7.
269. Waldinger MD, McIntosh J, Schweitzer DH. A five-nation survey to assess the distribution of the intravaginal ejaculatory latency time among the general male population. J Sex Med. 2009;6:2888–95.
270. Aydur E, Gungor S, Ceyhan ST, Taiimaz L, Baser I. Effects of childhood circumcision age on adult male sexual functions. Int J Impot Res. 2007;19:424–31.
271. Kigozi G, Watya S, Polis CB, Buwembo D, Kiggundu V, Wawer MJ, Serwadda D, Nalugoda F, Kiwanuka N, Bacon MC, Ssempijja V, Makumbi F, Gray RH. The effect of male circumcision on sexual satisfaction and function, results from a randomized trial of male circumcision for human immunodeficiency virus prevention, Rakai, Uganda. BJU Int. 2008;101:65–70.
272. Krieger JN, Mehta SD, Bailey RC, Agot K, Ndinya-Achola JO, Parker C, Moses S. Adult male circumcision: effects on sexual function and sexual satisfaction in Kisumu, Kenya. J Sex Med. 2008;5:2610–22.
273. Senol MG, Sen B, Karademir K, Sen H, Saraçoğlu M. The effect of male circumcision on pudendal evoked potentials and sexual satisfaction. Acta Neurol Belg. 2008;108:90–3.
274. Hosseini SR, Khazaeli MH, Atharikia D. Role of postcircumcision mucosal cuff length in lifelong premature ejaculation: a pilot study. J Sex Med. 2008;5:206–9.
275. Son H, Song SH, Kim SW, Paick JS. Self-reported premature ejaculation prevalence and characteristics in Korean young males: community-based data from an internet survey. J Androl. 2010;31:540–6.
276. Sorrells ML, Snyder JL, Reiss MD, Eden C, Milos MF, Wilcox N, Van Howe RS. Fine-touch pressure thresholds in the adult penis. BJU Int. 2007;99:864–9.
277. Waskett JH, Morris BJ. Fine-touch pressure thresholds in the adult penis. (Critique of Sorrells ML, et al. BJU Int 2007;99:864–869). BJU Int. 2007;99:1551–2.
278. Payne K, Thaler L, Kukkonen T, Carrier S, Binik Y. Sensation and sexual arousal in circumcised and uncircumcised men. J Sex Med. 2007;4:667–74.
279. Williamson ML, Williamson PS. Women's preferences for penile circumcision in sexual partners. J Sex Educ Ther. 1988;14:8–12.
280. Circumcision BJ. What you think. Aust Forum. 1989;2(11):10–29.
281. Badger J. The great circumcision report part 2. Aust Forum. 1989;2(12):4–13.
282. Kigozi G, Lukabwe I, Kagaayi J, Wawer MJ, Nantume B, Kigozi G, Nalugoda F, Kiwanuka N, Wabwire-Mangen F, Serwadda D, Ridzon R, Buwembo D, Nabukenya D, Watya S, Lutalo T, Nkale J, Gray RH. Sexual satisfaction of women partners of circumcised men in a randomized trial of male circumcision in Rakai, Uganda. BJU Int. 2009;104:1698–701.
283. World Health Organization/UNAIDS. Male circumcision: global trends and determinants of prevalance, safety and acceptability. http://whqlibdoc.who.int/publications/2007/9789241596169_eng.pdf. Geneva: World Health Organization; 2008 [accessed Jan 4, 2011].
284. O'Farrell N, Quigley M, Fox P. Association between the intact foreskin and inferior standards of male genital hygiene behaviour: a cross-sectional study. Int J STD AIDS. 2005;16:556–9.
285. Leibowitz AA, Desmond K, Belin T. Determinants and policy implications of male circumcision in the United States. Am J Public Health. 2009;99:138–45.
286. Morris BJ, Bailis SA, Waskett JH, Wiswell TE, Halperin DT. Medicaid coverage of newborn circumcision: a health parity right of the poor. Am J Public Health. 2009;99:969–71.
287. Public Health Agency of Canada. What mothers say: the Canadian experiences survey. Ottawa: Public Health Agency of Canada; 2009.
288. Xu B, Goldman H. Newborn circumcision in Victoria, Australia: reasons and parental attitudes. ANZ J Surg. 2008;78:1019–22.
289. Madhivanan P, Krupp K, Chandrasekaran V, Karat SC, Reingold AL, Klausner JD. Acceptability of male circumcision among mothers with male children in Mysore, India. AIDS. 2008;22:983–8.
290. Mancuso T, Burns J. Ethical concerns in the management of pain in the neonate. Paediatr Anaesth. 2009;19:953–7.
291. Committee on the Fetus and Newborn, American Academy of Pediatrics. Standards and recommendations for hospital care of newborn infants. 5th ed. Evanston: American Academy of Pediatrics; 1971.
292. Schoen EJ. Ed Schoen, MD on Circumcision: timely information for parents and professionals from America's #1 expert on circumcision. Berkeley: RDR Books; 2005.
293. Nelson CP, Dunn R, Wan J, Wei JT. The increasing incidence of newborn circumcision: data from the nationwide inpatient sample. J Urol. 2005;173:978–81.
294. Fergusson DM, Boden JM, Horwood LJ. Neonatal circumcision: effects on breastfeeding and outcomes associated with breastfeeding. J Paediatr Child Health. 2008;44:44–9.
295. Wang ML, Macklin EA, Tracy E, Nadel H, Catlin EA. Updated parental viewpoints on male neonatal circumcision in the United States. Clin Pediatr (Phila). 2010;49:130–6.
296. Xu F, Markowitz LE, Sternberg MR, Aral SO. Prevalence of circumcision and herpes simplex virus type 2 in men in the United States: the National Health and Nutrition Examination Survey (NHANES), 1999–2004. Sex Transm Dis 2007;34:479–84
297. Australian Paediatrics Association. Circumcision as a hygiene measure. Circumcision in the newborn period. Med J Aust. 1971;2:175.

298. Foetus and Newborn Committee. Circumcision in the newborn period. Can Paediatr Soc News Bull. 1975;8 Suppl:1–2.
299. Templeton DJ, Jin F, Prestage GP, Donovan B, Imrie J, Kippax SC, Kaldor JM, Grulich AE. Circumcision status and risk of HIV seroconversion in the HIM cohort of homosexual men in Sydney. In: 4th International AIDS Society conference, Sydney; 2007: WEAC103.
300. O'Donnell H. Circumcision incidence in Australia. 2004. http://www.cirp.org/library/statistics/Australia/ [accessed Jan 4, 2011].
301. Teutsch D. More boys go under knife as parents opt for kind cut. Sydney Morning Herald; 2010: 31.
302. Thompson HC, King LR, Knox E. Report of the ad hoc task force of circumcision. Pediatrics. 1975;56:610–1.
303. American Academy of Pediatrics. Task force on circumcision. Report of the task force on circumcision. Pediatrics. 1989;84:388–91.
304. Lannon CM, Bailey AGD, Fleischman AR, Kaplan GW, Shoemaker CT, Swanson JT, Coustan D. Circumcision policy statement. Pediatrics. 1999; 103:686–93.
305. Schoen EJ, Wiswell TE, Moses S. Reply to Carole M. Lannon and the task force on circumcision [letter]. Pediatrics. 2001;108:211.
306. Bailis SA. Circumcision – the debate goes on. Pediatrics. 2000;105:682.
307. Kunin SA. Circumcision – the debate goes on. Pediatrics. 2000;105:683.
308. American Academy of Pediatrics. AAP publications retired and reaffirmed. Pediatrics. 2005;116:796.
309. Schoen EJ. Ignoring evidence of circumcision benefits. Pediatrics. 2006;118:385–7.
310. Schoen EJ. Re: circumcision – are you with us or against us? J. S. Elder J Urol 2006; 176: 1911. J Urol. 2007;178:354–5.
311. Elder JS. Re: circumcision – are you with us or against us? J. S. Elder J Urol 2006; 176: 1911. J Urol. 2007;178:355.
312. Brady MT. Newborn circumcision: routine or not routine, that is the question. Arch Pediatr Adolesc Med. 2010;164:94–6.
313. Moreno MA, Furtner F, Rivara FP. Advice for patients: male circumcision: new information about health benefits. Arch Pediatr Adolesc Med. 2010;164:104.
314. Fetus and Newborn Committee, Canadian Paediatric Society. Neonatal circumcision revisited. Can Med Assoc J. 1996;154:769–80.
315. Royal Australasian College of Physicians, Paediatrics & Child Health Division. Circumcision of infant males. Available at: http://www.racp.edu.au/page/policy-and-advocacy/paediatrics-and-child-health.
316. Beasley S, Darlow B, Craig J, Mulcahy D, Smith G. Royal Australasian College of Physicians. Policy statement on circumcision. 2004. http://www.racp.edu.au/hpu/paed/circumcision/ [accessed Jan 4, 2011].
316a. Morris BJ, Wodak AD, Mindel A, Schrieber L, Duggan KA, Dilley A, Willcourt RJ, Cooper DA. The 2010 Royal Australasian College of Physicians policy statement 'Circumcision of infant males' is not evidence based. Int Med J 2012: in press.
317. British Medical Association. The law and ethics of male circumcision – guidance for doctors. 2003. http://www.bma.org.uk/ap.nsf/Content/malecircumcision2003 [accessed Jan 4, 2011].
318. British Medical Association. The law and ethics of male circumcision: guidance for doctors. J Med Ethics. 2004;30:259–63.
319. British. British Medical Association. The law and ethics of male circumcision. Guidance for doctors. London: BMA, 2006.
320. Hinchley G. Is infant male circumcision an abuse of the rights of the child? (head to head article). Br Med J. 2007;335:1180.
321. Patrick K. Medical aspects of male circumcision (head to head). Br Med J. 2007;335:1181.
322. Malone P, Steinbrecher H. Medical aspects of male circumcision. Br Med J. 2007;335:1206–9.
323. American Urological Association. Circumcision. Available at: http://www.auanet.org/content/guidelines-and-quality-care/policy-statements/c/circumcision.cfm [accessed Jan 4, 2011].
324. WHO and UNAIDS. Male circumcision: global trends and determinants of prevalence, safety and acceptability (42 pp; 191 refs). Geneva: World Health Organization; 2008.
325. Franco EL. Male circumcision and AIDS in Africa. Primum non nocere versus the collective good. Epidemiology. 2004;15:133–4.
326. Flynn P, Havens P, Brady M, Emmanuel P, Read J, Hoyt L, Henry-Reid L, Van Dyke R, Mofenson L. Male circumcision for prevention of HIV and other sexually transmitted diseases. Pediatrics. 2007;119:821–2.
327. Dickerman JD. Circumcision in the time of HIV: when is there enough evidence to revise the American Academy of Pediatrics' policy on circumcision? Pediatrics. 2007;119:1006–7.
328. Mor Z, Kent CK, Kohn RP, Klausner JD. Declining rates in male circumcision amidst increasing evidence of its public health benefit. PLoS One. 2007;2(9):e861 (4 pages).
329. Rabin RC. Officials weigh circumcision to fight H.I.V. risk. New York Times. 2009 (Aug 29) Available at: http://www.nytimes.com/2009/08/24/health/policy/24circumcision.html [accessed Jan 4, 2011].
330. Short RV. Male circumcision: a scientific perspective. J Med Ethics. 2004;30:241.
331. Morris BJ, Wodak AD, Mindel A, Schrieber L, Duggan KA, Dilly A, Willcourt RJ, Cooper DA, Lumbers ER, Russell CT, Leeder SR. Circumcision Foundation of Australia. Infant male circumcision: An evidence-based policy statement. Open J Prevent Med. 2012;2:79–92.
332. Morris BJ, Waskett JH, Banerjee J, Wamai RG, Tobian AAR, Gray RH, Bailis SA, Bailey RC, Klausner JD, Willcourt RJ, Halperin DT, Wiswell TE, Mindel A. A 'snip' in time: what is the best age to circumcise? BMC Pediatr. 2012;12:20 (15 pages).