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Circumcision and Sexually Transmitted Disease Prevention: Evidence and Reticence

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Abstract

Circumcision is one of the oldest surgical procedures and the most common surgical procedure performed on males. It is practiced for three main reasons: ritual or religious meanings, prophylactic hygienic purposes, and therapeutic indications. Male circumcision is advocated as an efficacious prevention strategy against sexually transmitted diseases. One of the main biological mechanisms responsible for the lower human immunodeficiency virus (HIV) infection rate in heterosexual circumcised men is the protective effect of keratinization of the glans. Moreover, male circumcision removes the inner part of the prepuce containing Langerhans cells that are targeted by HIV. Several observational studies showed a protective effect of male circumcision regarding the HIV acquisition in heterosexual men, in women with circumcised partners, and in men who have sex with men with an insertive anal role. Circumcision reduced the infection rate of other sexually transmitted diseases like human papillomavirus (HPV), mycoplasma, and genital ulcer disease. It seems now evident that circumcision has no negative effects on sexual function, sensitivity, sexual sensation, and satisfaction. When performed freely after informed consent, male circumcision is a lawful practice in adults. In children, the lack of an informed consent is overcome by the favorable risk/benefit ratio and the decision whether to circumcise or not pertains to the parents.

Keywords: circumcision, HIV, sexually transmitted diseases, sexual function, ethics

1. Introduction

Male circumcision is advocated as an efficacious prevention strategy against sexually transmitted diseases (STDs), other than scaling-up testing and counseling services, campaigns with messages about abstinence, condom use and reducing multiple partners, and universal human

immunodeficiency virus (HIV) testing with immediate initiation of antiretroviral therapy. Many controversies exist around male circumcision. In fact, if the procedure can bring benefits in relation to the prevention of several STDs, short-term surgical complications and suspected long-term harms, in relation to sexual dysfunction, have been also advocated by those opponents to the procedure.

2. Circumcision

2.1. Circumcision in the history

Circumcision is practiced for three main reasons. First, it can be performed for ritual or religious meanings (e.g., Jews circumcise children after 8 days of life, while Muslims between 4 and 13 years of age). Second, it can be done for a prophylactic purpose to guarantee a correct hygiene. Third, especially in western countries, it has also a therapeutic indication to treat many diseases of the foreskin, the most common of which is phimosis.

The technique of circumcision is very old and the first documented evidences of this practice are dated as early as the third millennium BC. In the ancient Egypt, circumcision was made for hygienic reasons and documented evidences have been found to date to sixth dynasty tomb (2345–2181 BC). The reasons for circumcision between the different cultural people were different: religious, hygienic, rites of passage, and a way to differentiate cultural groups.

According to Jewish religion (Genesis 17:10-14), God commanded Abraham to be circumcised, an act to be followed by his descendants. Male circumcision is performed by a circumciser (mohel) during a ceremony (covenant of circumcision called “brit milah”) on the eighth day of a male infant life.

“Khitan” is the term for male circumcision carried out by Muslims as an Islamic rite. Although the Quran itself does not mention circumcision (and in fact some Quranists are against circumcision adducing that Quran forbids to alter one’s body), male circumcision is widely practiced among Muslims like a rite to symbolize their inclusion into the Islamic community. It is considered obligatory in Shia tradition and not obligatory but highly recommended among the Sunni Islam. There is no fixed time for circumcision. The parents should circumcise their children before the age of 10. The preferred age is seven although some Muslims are circumcised as early as on the seventh day after birth (like Jewish people) and as late as at the puberty.

During the nineteenth century in western countries, especially in the United States and Britain, male circumcision has been largely medically adopted like a method to discourage masturbation and became the most common surgical intervention against masturbation.

2.2. Anatomy and functions of the prepuce

The penis is the male reproductive organ. It is located above and in front of the scrotum, below and in front of the pubic symphysis. Its root is in the perineum, attached to the ischio-pubic branches and the suspensor ligament of the penis. The body of the penis has a flattened cylindrical shape,

formed by the two corpora cavernosa and corpus spongiosum of the urethra. The corona separates the base of the glans from the shaft of the penis. The glans is formed by the swelling of the corpus spongiosum of the urethra in the shape of a cone.

The skin that covers the penis noticeably moves on the layers below. Its blood supply is independent of the erectile bodies and is derived from the external pudendal branches of the femoral vessels. The skin that covers the glans like a hood is called prepuce or foreskin. The prepuce is a fold, half skin and half mucosa that continues in the mucosa of the glans at the balanopreputial sulcus. So the outer surface is continuous with the skin of the penis, while the inner surface is modeled on the glans adhering only at the level of the balanopreputial sulcus and the frenulum. The frenulum is a triangular mucosal fold that tends from the inner surface of the foreskin to the underside of the glans 8–10 mm behind the external urethral meatus. A short frenulum can prevent complete retraction of the foreskin and can make painful erection and tear.

The virtual cavity of the prepuce is lubricated by the smegma secreted from Tyson's glands. In case of poor hygiene, the smegma can accumulate and become infected generating balanoposthitis. Repeated balanoposthitis may form adhesions between the inner surface of the foreskin and the mucosa of the glans. In most cases, the preputial orifice is quite wide and weak to be freely retracted over the glans, and allows the glans discovering during erection. The restriction of the preputial ring, preventing the glans to escape from the preputial cavity either at rest or during erection, is called phimosis. Phimosis can be congenital or acquired, and can cause disturbances to urination and erection, and facilitate the appearance of inflammation and infection. In the newborn boy in the first months of life, the prepuce is contracted around the glans. The retraction of the foreskin is possible in the 50% of cases after 1 year of life, and in the 89% at 3 years of age [1]. Phimosis is then present in the 8% of 6–7-year-old children and in only 1% of 16–18-year-old males [2]. In some cases, the glans can go out the foreskin but then cannot be able to reenter generating a swelling accompanied by pain or ulceration; this process is called paraphimosis and requires an immediate manual reduction maneuver.

2.3. Surgical techniques

Literally from Latin, circumcision means “to cut around.” The procedure aims to expose the glans sufficiently to prevent phimosis or paraphimosis (**Figure 1**). It is one of the oldest surgical procedures, performed since the age of the Egyptians. It is surely the most common surgical procedure performed on males. Over the world, it is estimated that 30% of males are circumcised. In the US, an average of a million newborn males is circumcised yearly. Circumcision rate in US is as high as 70%, while in Britain it is 6%.

Absolute indications for medical circumcision are secondary phimosis at any age, primary phimosis with recurrent balanoposthitis and urinary tract infection, and sexual discomfort. The European Association of Urology (EAU) does not recommend routine neonatal circumcision to prevent penile cancer as a recent meta-analysis could not find any risk in uncircumcised patients without a history of phimosis [1]. On the other hand, contraindications for

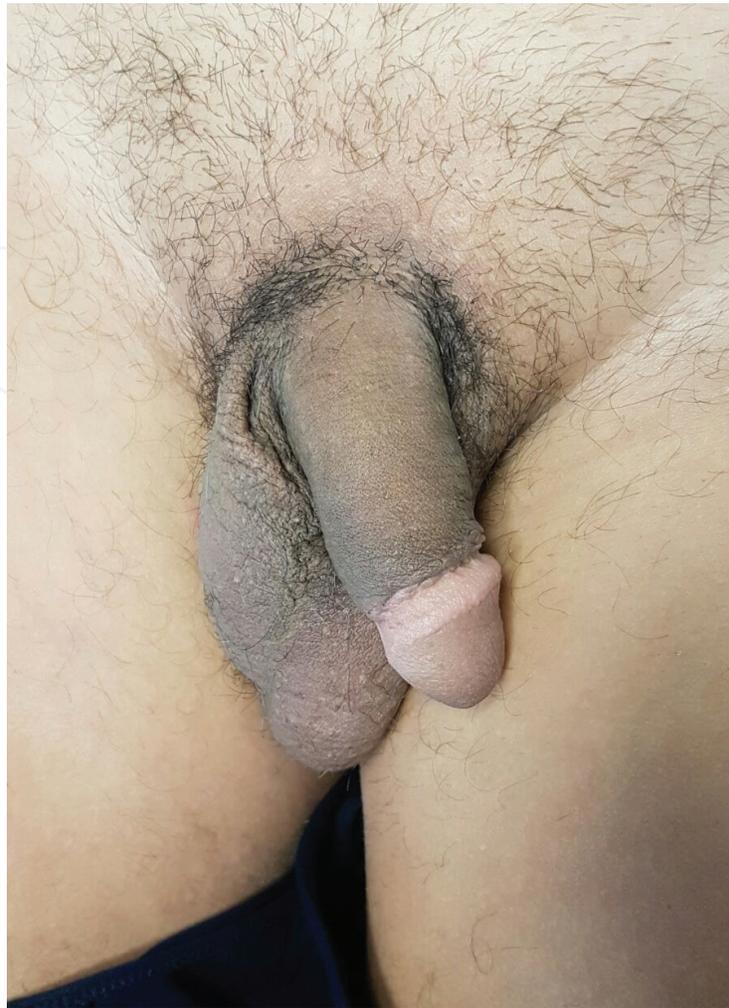


Figure 1. Short-term aesthetic result after circumcision in an adult patient.

circumcision are acute local infection and congenital anomalies of the penis (e.g., hypospadias or buried penis, in which the foreskin may be required for a reconstructive procedure). Asepsis, adequate excision of the outer and inner preputial skin layers, hemostasis, protection of the glans and urethra, and cosmetics are the principles of circumcision.

Circumcision is generally performed under local anesthesia (topical anesthetic cream or anesthetic infiltration at the base of the penis). Different techniques were described depending on the age of the patient and the surgeon's experience. There are device methods and free-hand techniques.

In pediatric settings, the device methods are favored. In this case, the Gomco clamp and its variations, like the Plastibell, are suture-less techniques that use devices that protect the glans, resect the prepuce, and provide hemostasis. The Gomco clamp uses a metal bell placed over the glans after the prepuce is fully retracted. The prepuce is then replaced over it. This is sometimes facilitated by a dorsal slit. A metal plate is placed over the bell and thus the prepuce lies between the two parts. The device is then tensioned to trap the foreskin in position to

be adequately removed after a scalpel incision. The Plastibell is a plastic device with a groove on its back that has to be slipped between the glans and the prepuce. In this case, suture material is looped around in the groove and tied tightly. The foreskin withers and drops off in 7–10 days as the suture cuts off the blood supply distally to the groove.

In adulthood, the Sleeve technique or the dorsal slit technique is preferred. In the first case, the prepuce is retracted over the glans penis and a circumferential incision is made around the shaft, usually distal to the corona. The prepuce is returned to cover the glans and another circumferential incision is made around the shaft at the same position as the first one. The strip of the skin is then removed and the free edges are sutured. When the foreskin cannot be retracted over the glans, a dorsal slit may be suggested. The prepuce is freed from the glans of adhesions and with the aid of forceps, and then a longitudinal incision of both layers of the prepuce is done to some millimeter of the corona. It is cosmetically unacceptable to carry out a dorsal slit alone without excising the prepuce.

Male circumcision has low complication rates when properly performed. The most common complications are bleeding, incomplete removal of the foreskin, infection, urethral meatitis, inclusion cyst, excessive removal of the skin that can lead to severe cosmetic consequences, and functional problems. Injury of the glans, severe scarring, and urethra-cutaneous fistula are major although rare complications of the procedure.

3. Circumcision and HIV infection

3.1. Biological evidence of reduced HIV transmission in circumcised men

Between 75 and 85% of cases of HIV infection worldwide have probably occurred during sexual activity. Two main biological mechanisms are thought to be responsible of the lower HIV infection rate in heterosexual circumcised men [3].

The first is the protective effect of keratinization of the glans and the sulcus following the procedure. Thereafter, male circumcision removes the inner part of the prepuce that is more susceptible to HIV infection. In fact, the inner surface of the foreskin contains Langerhans' cells (LCs) exposing HIV receptors. LCs are antigen-presenting cells (APCs) and are likely to be the primary point of viral entry into the penis of an uncircumcised man [4].

HIV binds to the CD4 and CCR5 receptors on antigen-presenting cells—which include Langerhans' cells and dendritic cells—in the genital and rectal mucosa [5].

A keratinized, squamous epithelium covers the penile shaft and outer surface of the foreskin providing a protective barrier against HIV infection. By contrast, the inner mucosal surface of the foreskin is not keratinized and is rich in LCs making it particularly susceptible to the virus.

A widely accepted model for the sexual transmission of HIV is based on infection of the genital tract of rhesus macaques with Simian immunodeficiency virus (SIV). The same sequence of

cellular events involving the infection of LCs has been experimentally shown in male macaques following the SIV inoculation into the penile urethra or onto the foreskin [6]. Once infected, LCs fuse with adjacent CD4 lymphocytes and migrate to deeper tissues. Within 2 days of infection, the virus can be detected in the internal iliac lymph nodes and shortly thereafter in systemic lymph nodes.

Other mechanisms of increased incidence of HIV infection in uncircumcised men are the ulcerative and inflammatory lesions of the foreskin, and frenulum or glans caused by other STDs. In uncircumcised males, the highly vascular frenulum is particularly susceptible to trauma during intercourse, and ulcerative lesions produced by other STDs increase the ability of HIV to enter in the submucosal layer and link to APCs and CD4 cells. So that circumcision further reduces the risk of infection by lowering the synergy that normally exists between HIV and other STDs.

3.2. Male circumcision and HIV infection

Several observational studies showed a protective effect of male circumcision regarding the human immunodeficiency virus acquisition in heterosexual men (**Table 1**).

In 2000s, three large randomized trials specifically designed to evaluate the effect of male circumcision on the risk of HIV infections were performed in South Africa, in Uganda, and in Kenya [7–9] for a total of more than 11,000 subjects enrolled. Male circumcision showed a

<20% circumcised	Seroprevalence	>80% circumcised	Seroprevalence
(A) Sub-Saharan Africa			
Zimbabwe	25.84	Kenya	11.64
Botswana	25.10	Congo	7.64
Namibia	19.94	Cameroon	4.89
Zambia	19.07	Nigeria	4.12
Swaziland	18.50	Gabon	4.25
Malawi	14.92	Liberia	3.65
Mozambique	14.17	Sierra Leone	3.17
Rwanda	12.75	Ghana	2.38
(B) South/southeast Asia			
Cambodia	2.40	Pakistan	0.09
Thailand	2.23	Philippines	0.06
Myanmar	1.79	Indonesia	0.05
India	0.82	Bangladesh	0.03

Table 1. HIV-1 seroprevalence in relation to circumcision status in some high-incidence areas (A) and low-risk areas (B): June 1998 UNAIDS/WHO percentage estimates.

protective effect with a relative risk (RR) reduction of acquiring HIV infection of 50% after 12 months and 54% after 24 months. All the studies were stopped early due to these significant findings. The results have also been confirmed by a meta-analysis of the studies [10]. The number needed to treat was 56; it means that circumcision prevented 17 HIV infections per 1000 men at 2 years.

According to some mathematical models, the full coverage of male circumcision in those countries at high rate of HIV incidence, like sub-Saharan Africa, could avert 0.3 million deaths in the first 10 years and a further 2.7 million in the next 10 years [11].

The evidences of male circumcision benefits have also been shown from observational studies conducted in the USA and Israel [12], where the HIV burden is lower than Africa, and in low-incidence countries like India [13].

A consultation in Montreux (Switzerland) held on 28 March 2007 and sponsored by the World Health Organization (WHO) and the Joint United Nations Program on HIV/AIDS (UNAIDS) resulted in the recommendation of circumcision as a strategy for the prevention of heterosexually acquired HIV infection in men.

3.3. Effect of male circumcision on the risk of women HIV acquisition

An earlier observational study in Rakai, Uganda, found a relative male-to-female HIV transmission rate ratio of 0.41 (confidence interval (CI): 0.10–1.14) in couples with circumcised versus uncircumcised HIV-infected men. In the same study, for all HIV-positive male partners with viral loads of less than 50,000 copies/ml, no transmissions were observed in circumcised men, compared with a transmission rate of 9.6 per 100 patients (CI: 6.1–13.1, $p = 0.02$) in uncircumcised men [14].

In particular, it was estimated that circumcision may confer a 46% reduction in the rate of HIV transmission from circumcised men to their female partners [15].

Assuming a reduction in male-to-female transmission, the projected impact of circumcision on HIV spread is substantially enhanced, especially for women. Although male circumcision is an intervention applied to men, it brings substantial benefits for women as well.

An increase in the risk of acquisition and transmission of HIV during circumcision wound-healing period is an admitted possibility [16], but it is unlikely to have a major effect on the population. Premature resumption of sexual activity before the wound is healed or “compensatory” increase in risk following circumcision are both unlikely to substantively undermine the benefits of male circumcision on HIV incidence among women or men.

3.4. Infection of men who have sex with men

A Cochrane systematic review and meta-analysis including more than 65,000 participants showed that circumcision may reduce HIV acquisition among men who have sex with men having an insertive anal role but probably have no role among those having a receptive role [17].

4. Male circumcision and other sexually transmitted infections

4.1. Human papillomavirus

Circumcision was shown to decrease human papillomavirus (HPV) infection rates among both HIV-negative and HIV-positive heterosexual men included in a randomized controlled trial (RCT) performed in Uganda (RR 0.40, 95% CI: 0.19–0.84), control event rate 24.7% [18]. Male circumcision decreases also HPV infection rates in female partners especially of circumcised HIV-negative males [19, 20]. It is important to note that female partners of circumcised males have a lower risk of cervical cancer [21].

4.2. Mycoplasma

Circumcision was found to nearly halve the odds of Mycoplasma infection of the genitalia in circumcised men (odds ratio (OR) 0.54; 95% CI: 0.29–0.99) [22]. On the contrary, genital Mycoplasma is not reduced in female partners of circumcised men [23].

4.3. Genital ulcer disease

Two large RCTs showed that male circumcision reduce genital ulcer disease (GUD) incidence with a risk ratio of 0.51 and 0.52 [24]. The risk for GUD is also decreased in female partners of circumcised males as for Chlamydia trachomatis infection [25], bacterial vaginosis, and trichomonas infection [26].

4.4. Syphilis

The relation between male circumcision and new acquisition of syphilis is not clear. In fact, one large RCT showed no significant difference between circumcised and uncircumcised men (adjusted hazard ratio 1.10, 95% CI: 0.75–1.65, $p = 0.44$) [27]. However, another large RCT showed that circumcision was associated with a 42% reduction in the incidence of syphilis (adjusted hazard ratio 0.58, 95% CI: 0.37–0.91). In particular, a 62% reduction of syphilis among HIV-infected men was noted, whereas a nonsignificant reduction in the incidence of syphilis was observed among men without HIV [28].

4.5. Herpes simplex virus

A discrepancy of results exists between the trials conducted in order to evaluate the association of male circumcision and herpes simplex virus (HSV) prevalence. The reason for such a discrepancy is due to the nonunivocal use of the test employed for HSV detection and because of nonhomogeneous characteristics of the subjects and their sexual life.

In fact, two RCTs from Uganda [27] and South Africa [29] showed a significant reduction in HSV infection rates after circumcision. Two other trials conducted in Kenya failed to show such a reduction [24, 30].

4.6. Gonorrhoea and Chlamydia

Male circumcision probably does not interfere with gonorrhoea incidence. In fact, both observational [31] and randomized [32] did not show a risk reduction of gonococcus infection after circumcision.

Similarly, there is no association between Chlamydia infection and circumcision status [32].

5. Circumcision and sexual function

The possible implication of circumcision on sex needs more thorough discussion. The dorsal nerves provide sensory innervation to the penis. These nerves follow the course of the dorsal arteries and richly supply the glans. The prepuce is also a primary sensory part of the penis. In fact, it contains a high concentration of Meissner's corpuscles and sensory cells, which make it a specialized sensory mucosa. The effect of circumcision on sexual sensation is widely discussed and contradictory results have been shown. Some authors reported that the foreskin is important for normal sexual activity and affirm that circumcision removes the most sensitive parts of the penis. In addition to this, the glans of circumcised penis was found to be less sensitive compared to the glans of uncircumcised men, probably due to the subsequent thickening of the glans epithelia. Conversely, other authors showed that there is no substantial difference in sexual pleasure in circumcised and uncircumcised males, but an increased penile sensitivity. The same contradictory results were reported for women partners. In fact, the gliding mechanism, which makes the penis shaft to glide in its own skin covering during intercourse, was thought to add to the comfort of both partners in theory.

However, although one trial conducted in Denmark [33] reported a reduction in sexual satisfaction, more orgasm difficulties, and higher rate of dyspareunia among women partners of circumcised men, the most part of the studies supported the thesis that circumcision does not change or even improve sexual pleasure of women partners.

Krieger et al. [34] assessed, in a randomized trial, the effect of adult male circumcision on men sexual function and pleasure concluding that the procedure did not cause sexual dysfunction. Moreover, using the Brief Male Sexual Function Inventory (BMSFI) and the Intravaginal Ejaculation Latency Time (IELT), after an observational 12-week study, Senkul et al. [35] noted a prolonged mean ejaculatory latency time, which may be considered an advantage, and no substantial differences in the mean BMSFI (**Table 2**).

To analogous conclusions arrived, the studies of Kigozi et al. [36] and Collins et al. [37] use, respectively, the International Index of Erectile Function (IIEF) and the Brief Male Sexual Function Inventory (BMSFI).

On the contrary, the World Health Organization in 2007 [38] stated that there was little evidence to support a negative effect of male circumcision on sexual pleasure.

Author	Study	Sexual assessment	Outcome
Senkul et al. [35]	Observational	BMFI	Increase IELT and no change
Kigozi et al. [36]	Randomized	IIEF	No difference between groups
Collins et al. [37]	Observational	BMFSI	No change
Krieger et al. [34]	Observational	Non-validated questionnaire	No difference (very satisfied)
Frisch et al. [33]	Case-control	Survey	More orgasm difficulties

Table 2. Effects of male circumcision on sexual function.

However, a recent systematic review analyzing the highest quality studies, conducted by Morris and Krieger [39], concluded that male circumcision has no negative effects on sexual function, sensitivity, sexual sensation, or satisfaction.

6. Ethical and legal arguments of male circumcision

6.1. Adults

An ethical argumentation regarding male circumcision should focus on four bioethical principles: autonomy, dignity, integrity, and vulnerability, which are to be understood without giving priority to one principle over another, but according to their mutual connections [40]. Bodily integrity is not a value worthy of respect in his own meaning (*per se*), unless related to dignity and values of a human person under all circumstances concerning health. Integrity, as mentioned in the Barcelona Declaration (1998), is not limited to the body, conversely it concerns the whole life of every person, in its physical, mental, and narrative dimension [41]. Dignity is considered a property of every human being who has dignity if it is the expression of his/her autonomy, at a given moment of his/her life. Strongly related to the notion of autonomy is the obligation of informed consent during the course of health care, with the focus on self-determination [40]. By applying the principle of autonomy in medical ethics, one could even justify the refusal of medical and surgical treatment deemed necessary or, on the contrary, admit the possibility that a competent adult person consent to medical treatment, in spite of the possibility of unwanted negative effects and outcomes. In fact, since last century, patient's informed consent was considered the expression of a wiliness permitting to attempt patient physical integrity and, if it had been missed, any medical act could be understood as "violence."

Some authors opposing to male medical circumcision, skeptical about the Center for Disease Control and Prevention (CDC) guidelines, argued about supposed health benefits of female "circumcision," some forms of which may be even considered as less invasive than male circumcision, trying to balance similarities [42]. This argument is strongly denied by medical classification of the WHO that named "mutilation" as all forms of female circumcision and

consequently no far similarities must be drawn between two practices. Thus, the practices banned by the WHO, as female genital mutilations, even with patient consent, could not be considered lawful [43].

On the point of view of health professionals and physicians duties, by applying the “beneficence” ethical principle, benefits must “simply” exceed predictable risks and complications, all evaluated in the light of scientific evidence principles. Values of integrity and honesty of health professionals are moral aptitudes worldwide mentioned, which must contribute to reach a convinced opinion of the patient [44], with a proper illustration of pros and cons attributable to each medical practice, taking into account all aspects worthy of consideration in patient’s perspective [45–48]. The ratio between risks and benefits, in the case of adult patient, may justify the proposal and adoption of male circumcision, within updated medical guidelines evidence, provided it does not impose to anyone an also minimal genital surgery, even in consideration of absolutely rare frequency of risks and complications related to this practice.

6.2. Children

With regard to health-care decisions for young children, it is generally assumed that their parents should make these. Only when parents make decisions that are very clearly against the interest of their children, an external imposition could be assumed. It is also worthy of consideration for the family that have to live with the results of health decision, and every family has its own set of values; the basis for decision making is related to the model of “surrogate decision-making standard” or, alternatively, the “best interest” standard. Disagreement between the parents’ decision and the health-care professionals involved in the care and the treatment sometime should require legal evaluation in Court.

Criticism related to the Guidelines of the American Academy of Pediatrics (AAP) 2012 policy statement and technical report is yet reported and debated in scientific literature [41]. Basically, this matter regards prophylactic infant male circumcision and parents’ consent, in the view of the best child’s interest and future consequences related to circumcision. One position concludes that, before an age of consent, circumcision is not a desirable health-promotion strategy, given more effective and less ethically problematic alternatives [42]. On the contrary, from a scientific point of view, like infant vaccinations, the benefits of male circumcision exceed risks by a large margin; following these clinical and epidemiological indications, the pro-male circumcision arguments include also legal arguments [49]. Within this favorable approach, parents must make many decisions on behalf of their children. The decision whether to circumcise or not, as for some not obligatory vaccination, is one of those pertaining to parents.

7. Conclusions and key messages on male circumcision

- Male circumcision is effective to reduce HIV infection in heterosexual men, especially in areas at high incidence of the disease.
- Male circumcision should be provided freely after informed consent, ensuring surgical safety and quality.

- Male circumcision is an addition to, not a substitute for, other proven methods for preventing HIV infection, as it provides only partial protection.
- Male circumcision is a preventive measure with an optimal cost/benefit ratio.
- Sex should be resumed at least 6 weeks after circumcision and after a medical examination confirming that the healing process is complete.
- Male circumcision seems to confer protection against HIV infection also in women assuming that sexual intercourses are avoided during the wound-healing period.
- Male circumcision reduces HIV acquisition among men who have sex with men having an insertive anal role.
- Male circumcision reduces the incidence of HPV infection in males and of cervical cancer in women.
- Male circumcision has a protective effect regarding Mycoplasma genitalia infection and genital ulcer disease.
- Conflicting data are available about the benefits of circumcision over the transmission of other sexually transmitted diseases.
- There is no substantial difference in sexual pleasure between circumcised and uncircumcised men.
- Male circumcision is generally well accepted by female partners.
- Several surgical techniques are available, but none has demonstrated superiority over the others.
- Surgical complications are rare in hospital settings.
- When performed freely after informed consent, male circumcision is a lawful practice in adult.
- In children, the lack of an informed consent is overcome by the favorable risk/benefit ratio and the decision whether to circumcise or not pertains to the parents.
- Male circumcision and female genital mutilation are very different things.

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