

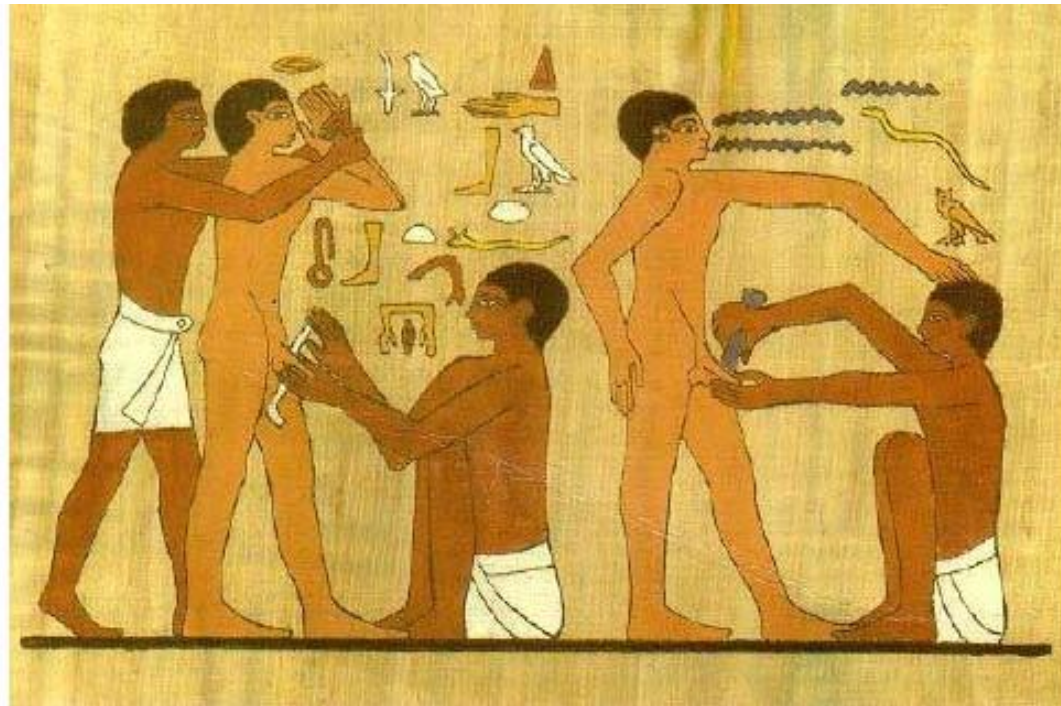
Circumcision



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History

- Dates back to 2300 BC in Egypt
- Was seen as a rite of passage
- Done for cleanliness



History - Judaism

Brit Milah (aka bris): The covenant of circumcision

"Throughout all generations, every male shall be circumcised when he is eight days old...This shall be my covenant in your flesh, an eternal covenant." (Genesis 17:1-14)



History - Islam

Khitan or Khatna

- Circumcision is not listed in the Qur'an, but dates back to the times of Muhammad
- Muhammad was said to have been born without foreskin (aposthetic)
- Not required, but scholars strongly recommend it



Equipment

- Gomco

- Invented by Hiram S. Yellen (Ob/Gyn) and Aaron Goldstein (inventor) in 1934-1935
- **GO**ldstein **M**edical **CO**mpany



- Plastibell

- Invented by Hollister Inc in 1950
- Uses ligature

- Mogen

- Invented by Rabbi Harry Bronstein in 1954
- Comes from Hebrew word *magain*, meaning "shield"

No data comparing these techniques

Morris & Eley. Male Circumcision: an Appraisal of Current Instrumentation. Circlist.
http://en.wikipedia.org/wiki/Gomco_clamp
<http://en.wikipedia.org/wiki/Plastibell>
http://en.wikipedia.org/wiki/Mogen_clamp

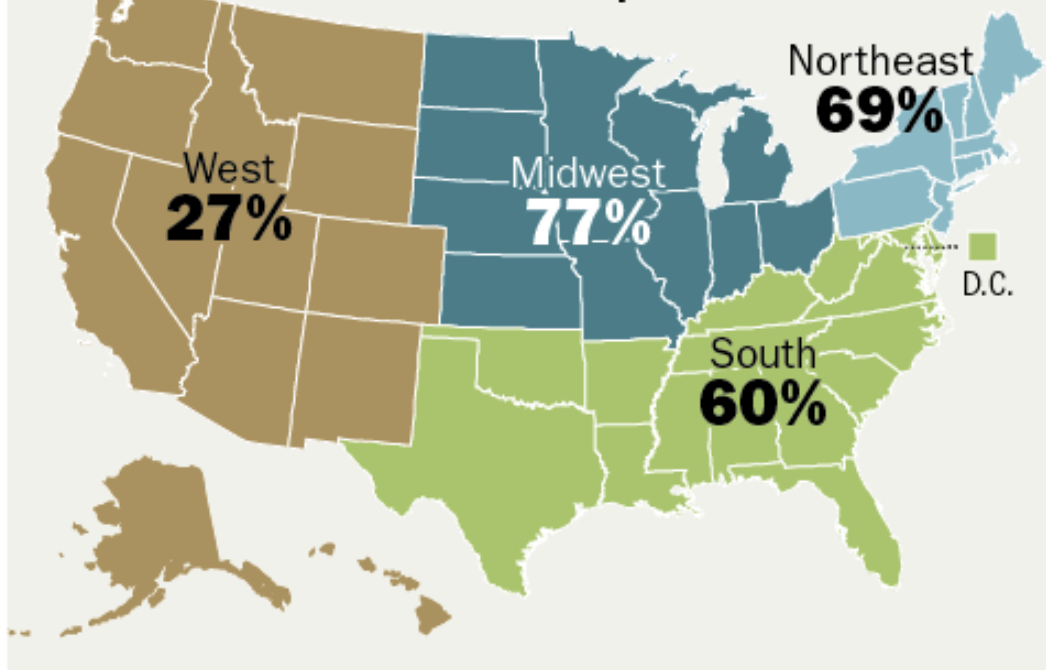


Who gets circumcised in the US?

Circumcision rates vary widely

A January study by UCLA shows circumcision rates are especially low in the West, which has larger groups of Hispanics and Asians, who tend not to be circumcised, and are relatively high in the Midwest. The study found that in the 16 states where Medicaid does not pay for circumcision – Arizona, California, Florida, Idaho, Louisiana, Oregon, Maine, Minnesota, Mississippi, Missouri, Montana, Nevada, North Carolina, North Dakota, Utah and Washington – the circumcision rates were only half what they were in states where coverage was provided.

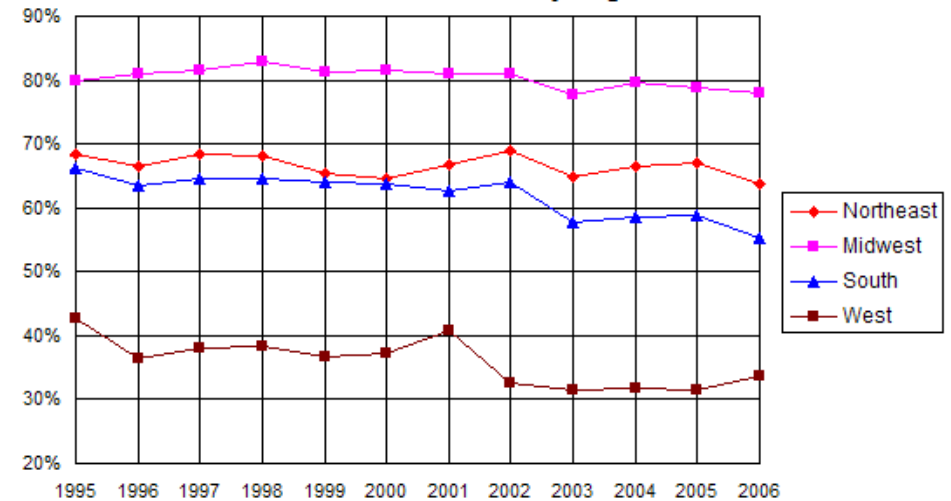
Overall rate: 56 percent



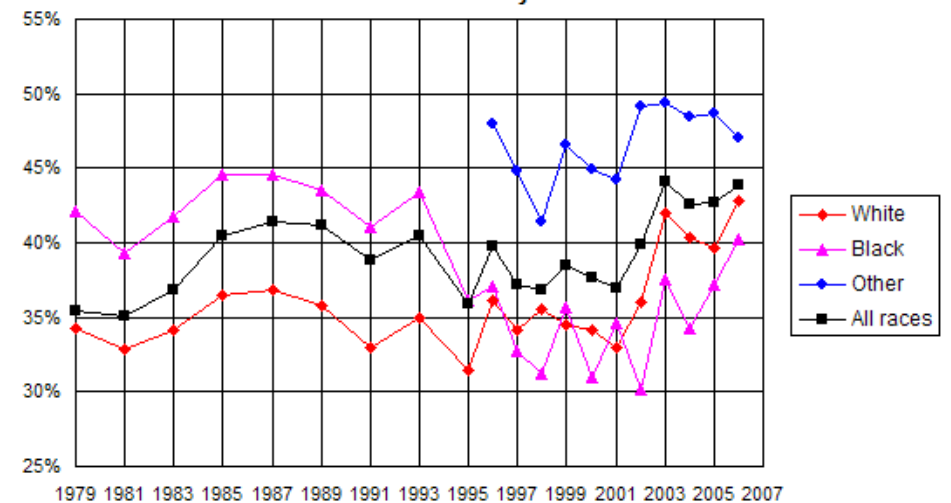
Source: UCLA, nationwide hospital inpatient survey, 2004

Post-Gazette

Circumcision Rate by Region



Intact Rate by Race



1. NHDS (National Hospital Discharge Survey) <http://www.cdc.gov/nchs/about/major/hdasd/nhdsdes.htm>

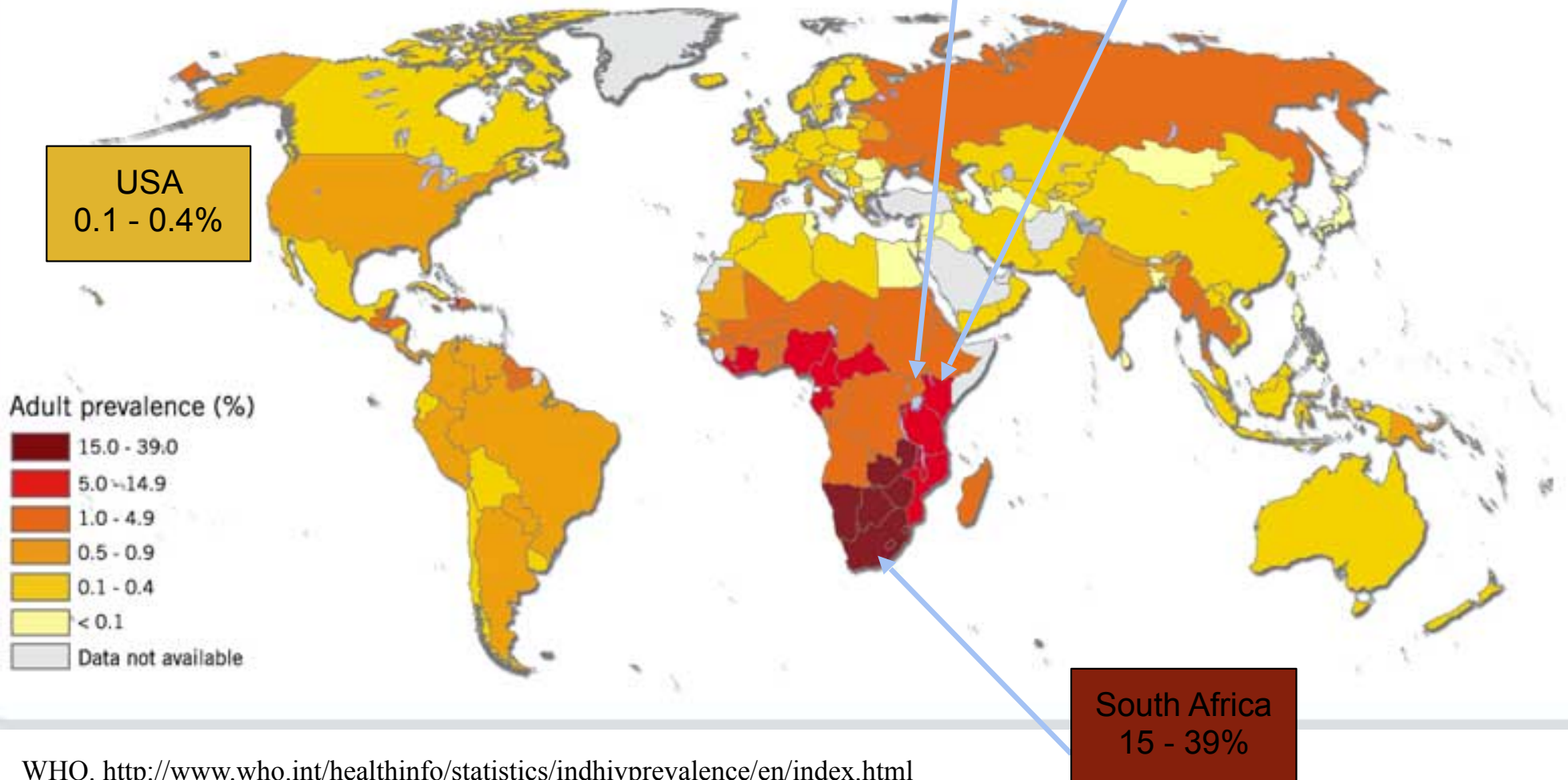
2. <http://www.cirp.org/library/statistics/USA/>

Does circumcision prevent HIV?

Three large RCTs

Prevalence of HIV:

Adults (15-49 years of age) living with HIV (%), end 2003



How is HIV transmitted?

- Outer surface of penis, foreskin is covered by keratinized stratified squamous epithelium which protects against HIV infection
- Inner mucosal layer of foreskin is *not keratinized*, and rich in *Langerhan's cells* which make it susceptible to HIV
- Foreskin then traps inoculum when penis becomes flaccid, keeping contact with area of entry
- Circumcised penis only has mucosal epithelium at distal urethra, with paucity of Langerhan's cells making infection there less likely
- Concomitant penile lesions appear to increase risk of HIV infection

Figure 6. Anatomy of the penis showing areas susceptible to HIV infection

Figure 6a. Flaccid uncircumcised penis

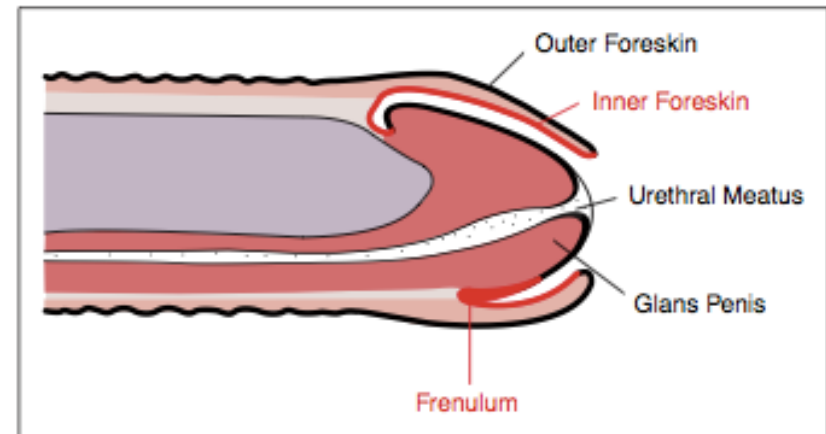
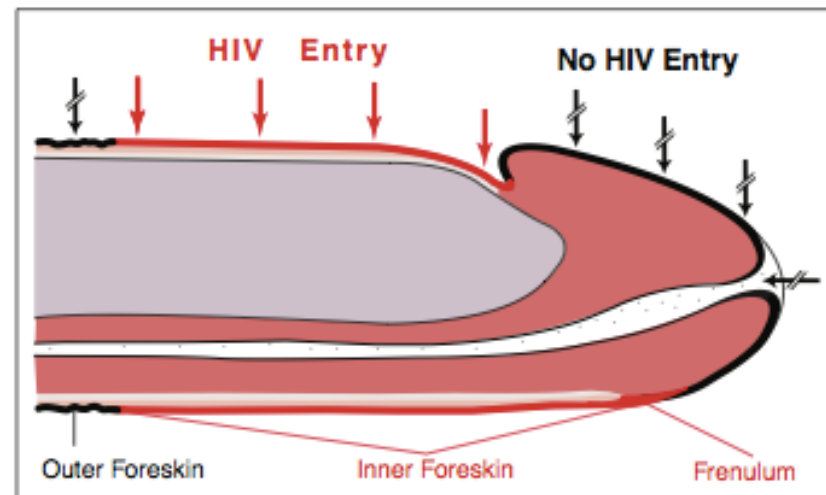


Figure 6b. Erect uncircumcised penis with the foreskin retracted showing likely sites of HIV-1 entry



Source: McCoombe and Short. (98). Permission granted by Lippincott Williams & Wilkins.

1. WHO. Male Circumcision. Global Trends and determinants of prevalence, safety and acceptability. London Schol of Tropical Medicine and Hygeine. 2007. http://www.malecircumcision.org/media/documents/MC_Global_Trends_Determinants.pdf
2. Szabo & Short. How does male circumcision protect against HIV infection? *BMJ*. 2000; 30:1592-4.

#1 Auvert, et al. *PLoS Med* 2005



- n=3274
- HIV *positive or negative* men in South Africa
- Ages 18 - 24
- Immediate circ vs no circ
- F/u at 3, 12, 21 months
- Incidence of HIV infection:
 - Intervention: 0.85 per 100 person-years (20 infections)
 - Control: 2.1 per 100 person-years (49 infections)
- RR of 0.40, or *60% reduction*

This is the first trial to show circumcision protects against HIV infection

#1 Auvert, et al. *PLoS Med* 2005

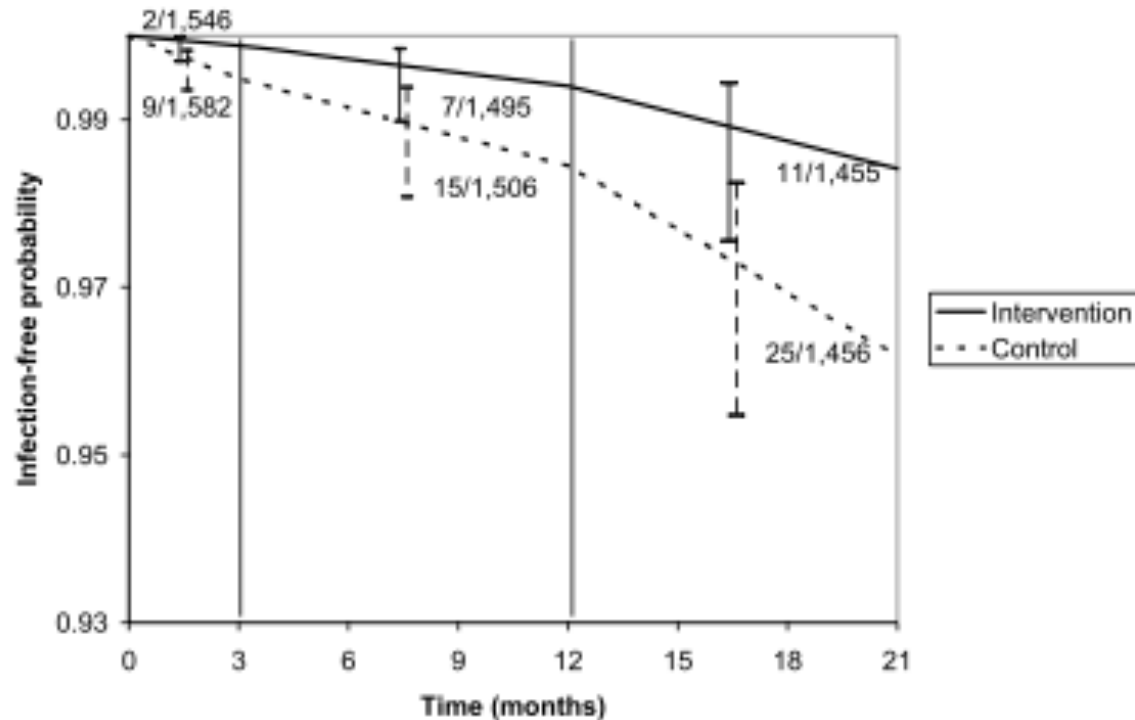
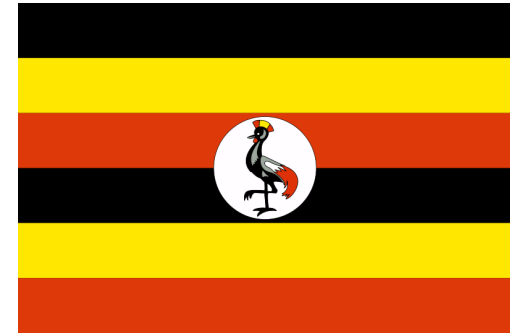


Figure 2. Infection-Free Probability As a Function of Time and of Randomization

This figure represents the infection-free probability using a piecewise exponential distribution with boundaries at M3, M12, and M21 obtained with a Poisson log-linear model (see text). Each segment of exponential has been fitted to the data in each period for each randomization group. The 95% confidence intervals have been represented in the middle of each period. x/y is the number of HIV infections observed in each period (x) and the number of persons at the beginning of the period (y).

DOI: 10.1371/journal.pmed.0020298.g002

#2 Gray, et al. *Lancet* 2007



- n=4996
- HIV negative men in Uganda
- Ages 15 - 49
- Immediate circ vs delayed circ at 24 months
- F/u at 6, 12, 24 months
 - 90% retention in both groups
- Depending on type of intention to treat analysis, showed a reduction of HIV incidence of 50-60%
- Estimate 67 circs to prevent 1 HIV infection

#2 Gray, et al. *Lancet* 2007

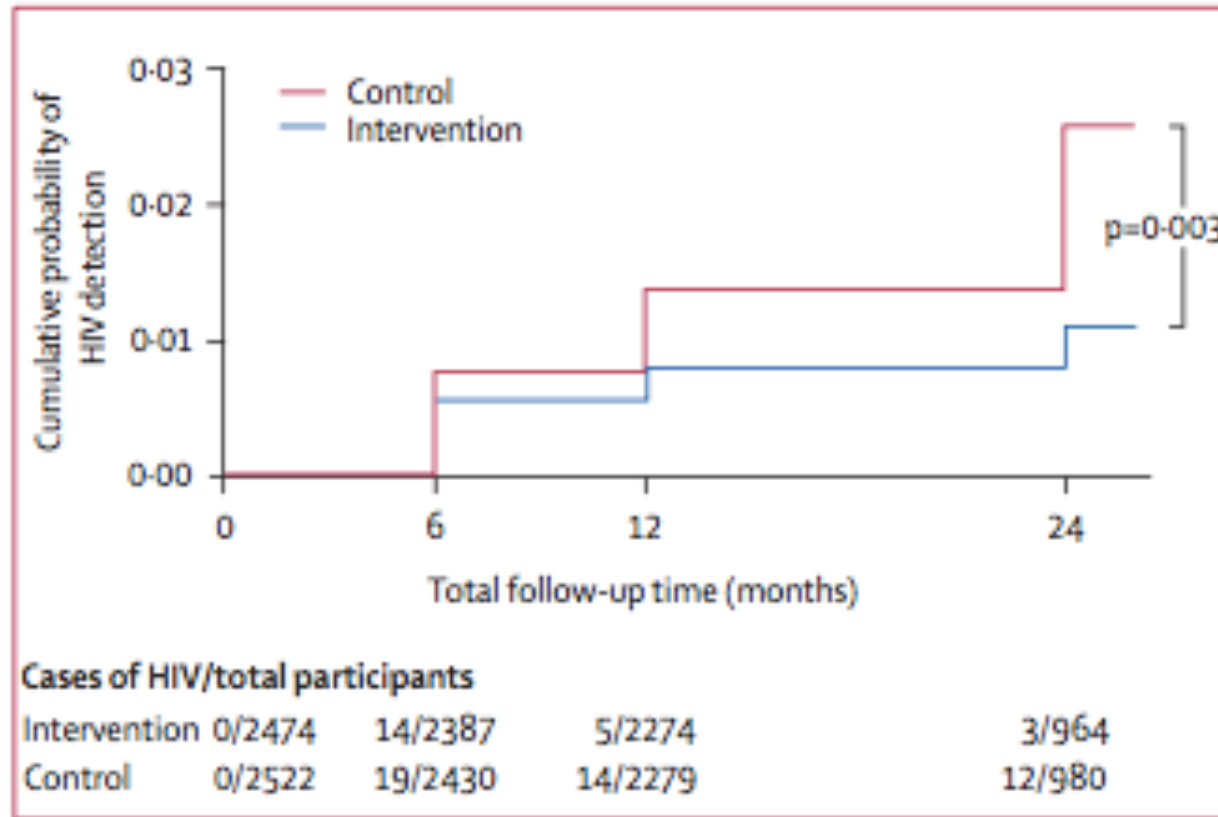


Figure 2: Kaplan-Meier cumulative probabilities of HIV detection by study group

Actual visits grouped by the three scheduled visits at 6 months, 12 months, and 24 months after enrolment. The cumulative probabilities of HIV infection were 1.1% in the intervention group and 2.6% in the control group over 24 months.

#3 Bailey, et al. *Lancet* 2007



- n=2784
- HIV negative men in Kenya
- Ages 18 - 24
- Immediate circ vs no circ
- F/u at 1, 3, 6, 12, 18, 24 months
 - 55% retention in both groups
- Depending on type of intention to treat analysis, showed a reduction of HIV incidence of 53-60%

#3 Bailey, et al. *Lancet* 2007

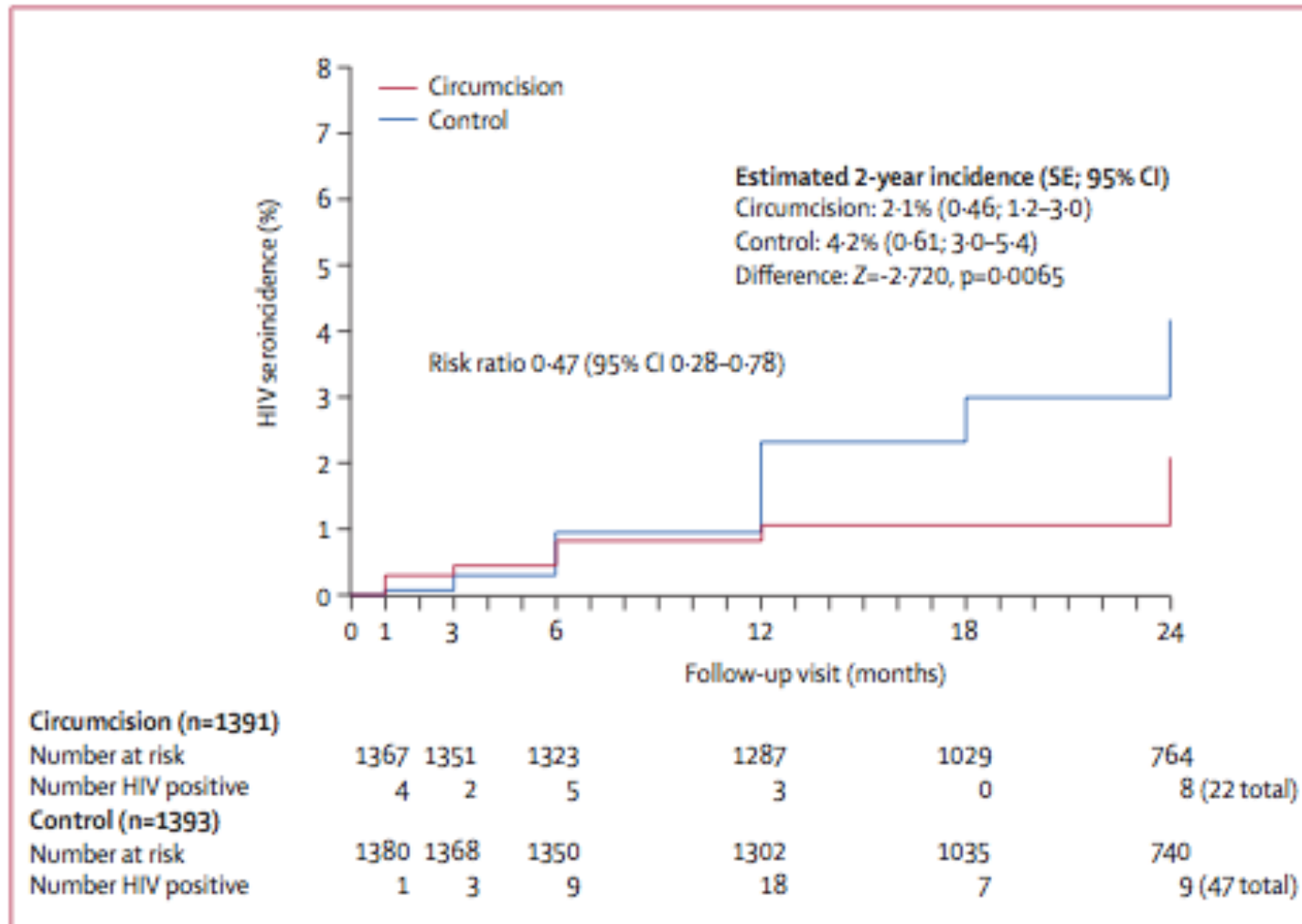


Figure 2: Cumulative HIV seroincidence across follow-up visits by treatment

Time to HIV-positive status is taken as the first visit when a positive HIV test result is noted. Time is credited as the follow-up visit month. Participants without HIV-positive status are censored at the last regular follow-up visit completed where HIV testing was done, credited specifically as months 1, 3, 6, 12, 18, and 24.

Does this apply to US?



That's debated.

- These studies don't address other modalities of HIV transmission (eg MSM and IVDU)
- However, rates of HIV in inner cities (eg Washington DC, 3-5% and 6.5% AA males) approach levels in Africa

Does this apply to US?

- Retrospective
- Baltimore, MD clinic 1993 - 2000
- Heterosexual AA men
- Used multivariable regression to look for association with circumcision and HIV transmission
- Among 394 with known HIV exposure, circumcision was associated with lower HIV prevalence (10.2% vs 22%)
- No difference in group with unknown HIV exposure (35,062 circumcised, 5115 not)

What about other STDs?

Table 3. Association of infections with male circumcision

Infection	Type of study/review	No. of studies ^a	Relative risk (RR) or odds ratio (OR) (95% CI)	Strength of evidence
Urinary tract infections (115)	Randomized controlled trial	1	OR = 0.13 (0.01–2.63)	+++
	Systematic review and meta-analysis	12	OR = 0.13 (0.08–0.20)	
Chancroid (100)	Systematic review	7	RRs from 0.12 to 1.11 ^b	++
Syphilis (100)	Systematic review and meta-analysis	14	RR = 0.67 (0.54–0.83)	++
HIV (130–134)	Randomized controlled trial	3	RRs from 0.40 to 0.52	+++
	Systematic review and meta-analysis of observational data	15	RR = 0.52 (0.40–0.68)	
	Systematic review of observational data	19	RRs from 0.12 to 1.25 ^c	
HSV-2 (100)	Systematic review and meta-analysis of observational data	7	RR = 0.88 (0.77–1.01)	+
HPV (135)	Systematic review and meta-analysis of observational data	8	OR = 0.57 (0.39–0.82)	+++



Also:

- There are some data that show a reduced risk of gonorrhea in circumcised men
- There is a significant reduction in chlamydia infections in females with circumcised male partners
- Men more likely to clear HPV infection, unclear if it decreases transmission to women

1. WHO. Male Circumcision. Global Trends and determinants of prevalence, safety and acceptability. London Schol of Tropical Medicine and Hygeine. 2007. http://www.malecircumcision.org/media/documents/MC_Global_Trends_Determinants.pdf

2. Tobian, *et al.* Male Circumcision for the Prevention of Acquisition and Transmission of Sexually Transmitted Infections. *Arch Ped Adol Med.* Jan 2010;164(78-84).

What about penile cancer?

Schoen, *et al*:

- Retrospective review
- Of 89 with invasive penile cancer, 2 (2.3%) had been circumcised as newborns
- Of 118 with carcinoma in situ, 16 (15.7%) had been circumcised as newborns

Daling, *et al*:

- Population-based case-control study
- Cases n=137, controls n=671
- Men not circumcised *in early childhood* had a 1.5 fold increase in the risk of penile cancer
- Men not circumcised *in childhood* (mostly neonatal) showed 2.3% increased risk of invasive penile cancer, no increased risk for in situ

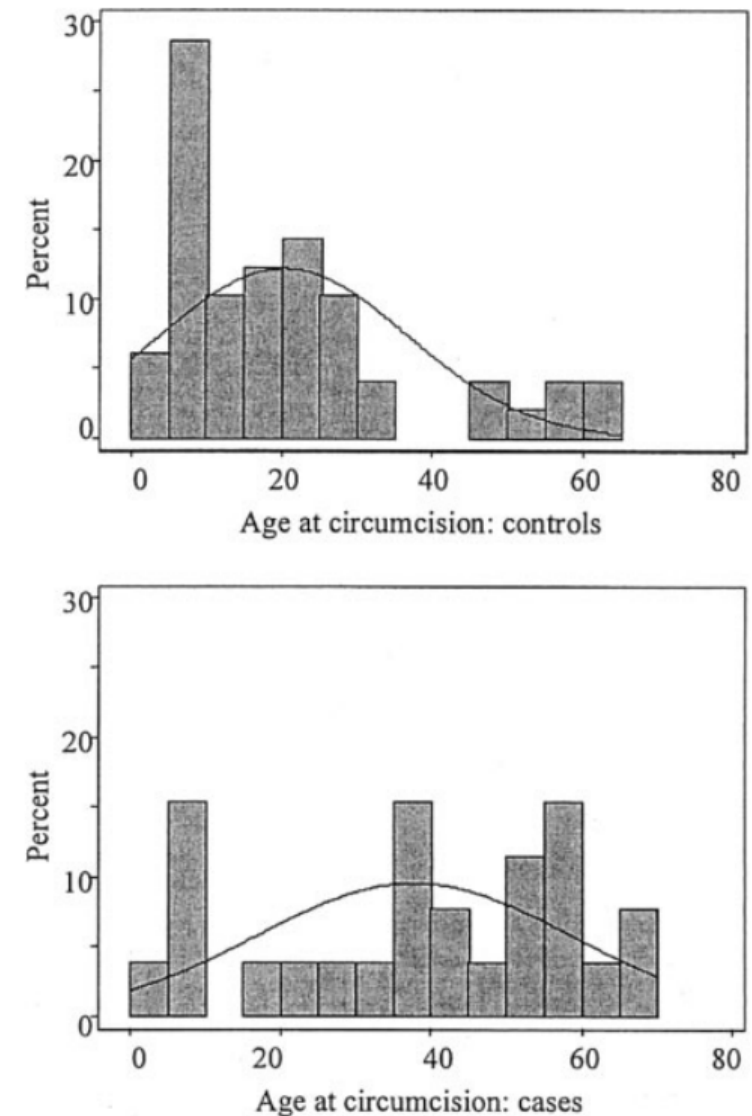


FIGURE 1 – Age at circumcision for cases and controls.

1. Schoen, *et al*. The Highly Protective Effect of Newborn Circumcision Against Invasive Penile Cancer. *Pediatrics*. 2000;105, e36.
2. Daling, *et al*. Penile cancer: importance of circumcision, human papillomavirus and smoking in in situ and invasive disease. *Int J Cancer*. 2005;116.606-16.

Does it affect sexual function?

- Surveyed participants in Kenyan trial (#3)
- Circumcised males reported:
 - increased penile sensitivity
 - enhanced ease of reaching orgasm

Some other much smaller trials offer conflicting evidence.

What data is behind analgesia?

- RCT, n=30
- Used two groups with painful procedures:
 - blood collection via heel
 - circumcision

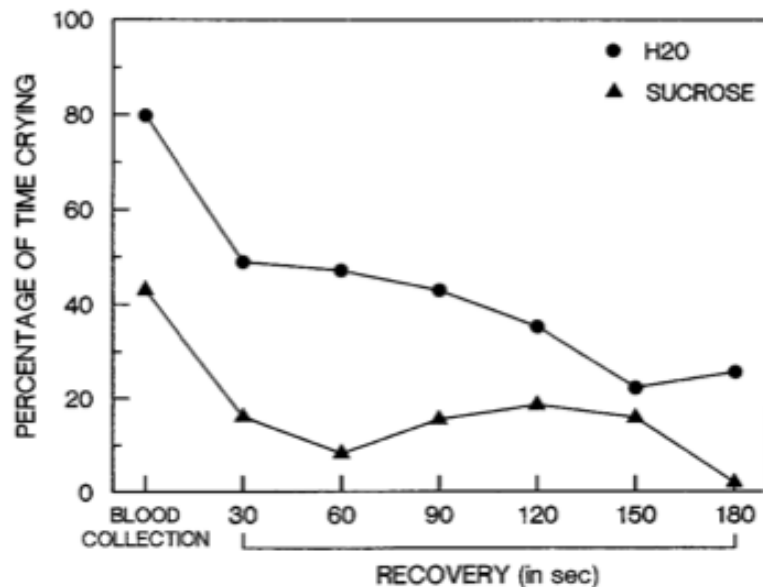


Fig 1. Percentage of time spent crying during blood collection and for 3-minute intervals following collection via heel lance in 2- to 3-day-old infants who received either 2 mL of sucrose or distilled water prior to procedure.

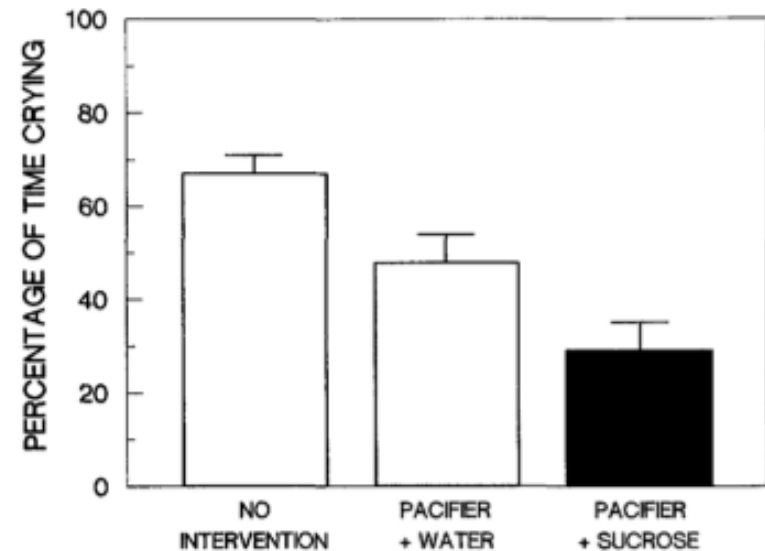


Fig 2. Percentage of time spent crying during circumcision by control infants and those sucking water- or sucrose-flavored pacifier.

What data is behind analgesia?

- RCT, n=44
- All circumcisions, same surgeon
- Everyone gets Tylenol and dorsal penile block
- Primary outcome: heart rate
- Also evaluated: crying time, salivary cortisol
- Results:
 - No difference in HR
 - Significant reduction in crying time and 90-minute post-procedural salivary cortisol level

Aren't we spending too much?

- Computer analysis by the CDC
 - HIV lifetime risk, heterosexual from 2005-6 data
 - Assumed 60% efficacy of circumcision
 - Expected HIV treatment costs
 - Estimated QALYs
- Results:
 - Overall
 - Lowered expected HIV-related treatment costs
 - Slight increase in QALYs
 - Reduced 1.87% lifetime risk by 16%
- Newborn circumcision for White males did not generate cost savings (high existing circumcision prevalence 88%, low lifetime risk of HIV 0.96%)
- Reduced costs were seen more in Hispanic and Black groups (lower existing circumcision prevalence 42% and 73%, higher lifetime risk of HIV 7.5% and 6.7% respectively)

What is the AAP's stance?



- Existing data demonstrates potential benefit
- Not sufficient to recommend routine neonatal circumcision
- Parents should determine what's best for their child, taking into account cultural, religious and ethnic considerations
- Analgesia is safe and effective
- If it is to be performed, use analgesia and only on stable and healthy infants

Access this talk again at:
<http://keithmurphy.org/talks>



