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Clinical performance of ShangRing and PrePex devices

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World Health Organization

WHO Technical Advisory Group (TAG)

- Advisory panel to WHO on technological innovations in male circumcision
- Reviews clinical data on safety and efficacy of circumcision devices considered for potential pre-qualification
- One of several key elements of WHO's pre-qualification and guidelines development processes
- TAG's summary of data on Shang Ring and PrePex devices presented here

Adverse Event Classification adopted by TAG

Adverse Event (AE)

Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs, excluding those definitely not related to the procedure or device

Serious Adverse Event (SAE)

An AE that resulted in medical or surgical intervention to prevent permanent impairment to body structure or a body function, *even if no permanent impairment occurred*

Moderate AE

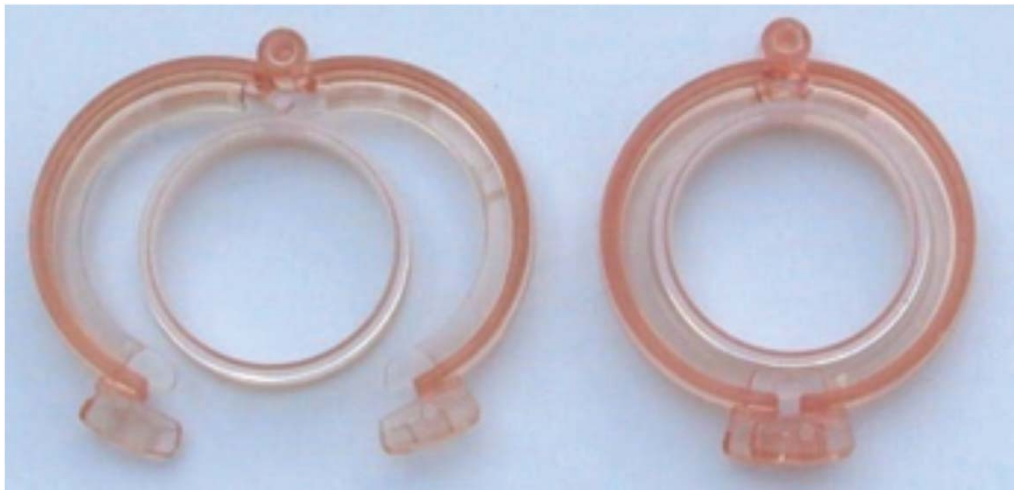
Any AE not classified as an SAE but that required an intervention by a health care provider or medication (parenteral, oral or topical)

Mild AE

All other AEs

Shang Ring Device

- Developed in China; Studied in China and Africa



Shang Ring Studies Reviewed

Study (type)	Location	Clients	Type of providers
Safety Study	Kenya	40 healthy HIV-negative men	Physicians and nurses experienced in conventional surgical circumcision
Spontaneous Detachment	Kenya	50 healthy HIV-negative men	Physicians and nurses experienced in conventional surgical circumcision
Randomized Comparison with Surgery	Kenya and Zambia	200 Shang Ring, 200 surgery, healthy HIV-negative men	Physicians and non-physicians, all with extensive experience with surgical male circumcision
Field Studies	Kenya and Zambia	1256 healthy HIV-negative men	Physicians and non-physicians, all with extensive experience with surgical male circumcision
Acceptability and Safety	Uganda	621 healthy HIV-negative men, 508 of whom chose Shang Ring	Clinical officers in sterile conditions in outpatient operating rooms

Shang Ring Outcomes (1,983 placements)

- High proportion of successful device placements
  - 98.8% of men eligible for device circumcision and device successfully placed
  - Small number of men considered unsuitable for Shang Ring circumcision due to minor foreskin abnormalities
  - Device could not be placed in 15 men (0.8%)
    - Correct ring size not available (8)
    - Foreskin slipped from outer ring (3), damaged (2), too short (1)
    - Outer ring could not be closed (1)
- High proportion with successful circumcision by device alone
  - 1,980 (99.8%) foreskin successfully removed by device alone
  - 3 (0.2%) had insufficient skin removed

Shang Ring Adverse Events (TAG Classification)

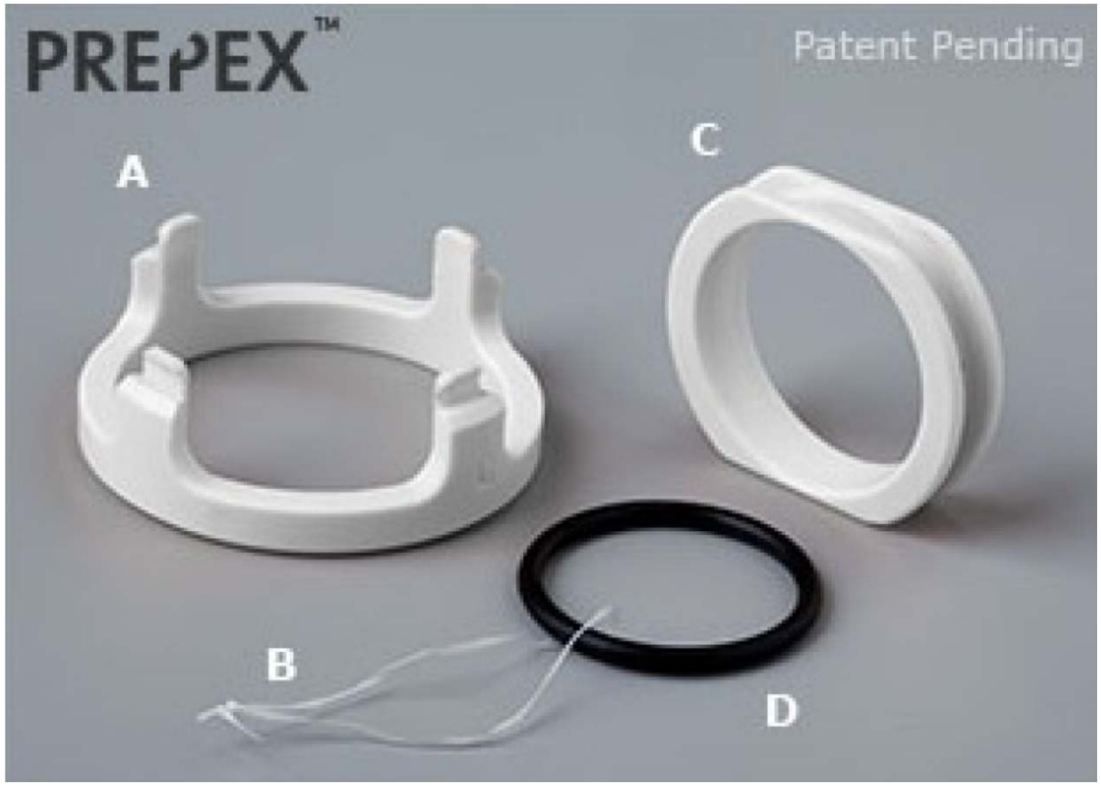
Type of Event	Number	Per cent [95% CI]
Total placements	1,983	
Serious AEs	**0**	**0.0% [0.0%, 0.2%]**
Moderate AEs	**20**	**1.0% [0.6%, 1.6%]**
Pain placement (8) Infection (4) Insufficient skin removed (3) Pain leading to early removal (2) Wound disruption (2) Bleeding (1)		
Mild AEs	**43**	**2.2% [1.6%, 2.9%]**

Shang Ring Outcomes

- Procedure times (shorter than surgery)
  - Placement time 6.4 (SD 3.8) mins
    - Excludes time for injection and induction of local anaesthesia
  - Removal time 3.1 (SD 1.8) mins
  - Total time 10.3 mins (placement and removal)
    - Comparison: mean time for surgical circumcision 20.3 minutes (Kenya and Zambia studies)
    - Excludes time for injection and induction of local anaesthesia
- Healing times (longer than surgery)
  - Comparative study, mean time to complete healing
    - Shang Ring: 44.1 (SD 12.6) days from date of placement
    - Surgery: 38.9 (SD 12.6) days from date of surgery
    - Average 5.2 (2.7–7.7) days longer
  - Healing by secondary intention with ring circumcision

PrePex Device

Developed in Israel; Studied in Africa



PrePex Studies Reviewed

Study (type)	Location	Clients	Type of providers
Safety Study	Rwanda	50 healthy HIV-negative men	Physicians and nurses
Randomized Comparison with Surgery	Rwanda	144 PrePex, 73 surgery	Physicians and nurses
Pilot Study	Rwanda	49 healthy HIV-negative men age 21–54 years	Nurses
Field Study	Rwanda	666 generally healthy men [5 HIV-positive]	Lower cadre nurses
Safety Study	Zimbabwe	53 HIV-negative men	Physicians and nurse assistants
Randomized Comparison with Surgery	Zimbabwe	240 HIV-negative men	As above
Field Study	Zimbabwe	641 HIV-negative men	Nurses with physician back-up support
Field Study	Uganda (IHK)	634 healthy men	Surgeons, medical officers, clinical officers and nurses
Field Study	Uganda (Rakai)	187 HIV-negative men	Not stated

PrePex Outcomes (2,417 placements)

- High proportion of successful device placements
  - 92.6% of men eligible for device circumcision and device successfully placed
  - 5.9% of men considered unsuitable for PrePex circumcision due to phimosis, narrow foreskin opening, tight frenulum, other penile abnormalities
  - Device could not be placed in 38 men (1.3%)
    - Narrow, tight or short foreskin (31)
    - Adhesions (4)
    - Penis circumference outside the range of available ring sizes (3)
- High proportion with successful circumcision
  - 2,405 (99.5%) foreskin successfully removed by device alone
    - Surgery after: self-removal (4), requested early removal (2), displacement (5), device and foreskin removed surgically under local anaesthesia (1)

PrePex Adverse Events (TAG Classification)

Type of Event	Number	Per cent [95% CI]
Total placements	2,417	
Serious AEs	**9**	**0.4% [0.2%, 0.7%]**
See details on next slide *All required prompt surgical intervention to prevent permanent injury or damage*		
Moderate AEs	**18**	**0.7%% [0.4%, 1.2%]**
Premature removal (8), Bleeding (5) Displacement (2), Infection (2), Difficult removal (1) *All required medical intervention to manage*		
Mild AEs	**15**	**0.6% [0.3%, 1.0%]**

PrePex Serious Adverse Events (Total 9)

- Device displacements following sexual activity, masturbation, erection, possible placement error, or accidental dislodging by another person (4)
- Premature self-removal secondary to pain (1);
- Meatal injury at removal (1)
- Difficult removal due to necrotic tissue everted over elastic ring requiring surgical intervention (1)
- Wound disruption or dehiscence (2)

- **Displacements associated with pain, oedema and blistering required prompt surgical intervention to avoid serious infection or permanent injury to penis**

PrePex Outcomes

- Procedure times (faster than conventional surgery)
  - Placement preparation 2.0 (SD 0.8) min
  - Placement procedure 1.5 (SD 1.0) min
  - Removal preparation 0.4 (SD 0.2) min
  - Removal procedure 2.0 (SD 1.1) min
  - In comparative study total placement and removal times 5.7 (SD 1.4) min, compared with 19.2 (SD 3.9) min for surgery
- Healing (longer than conventional surgery)
  - Comparative study, mean time to complete healing
    - PrePex: 38.0 (SD 12.1) days from placement
    - Surgery: 23.0 (SD 7.5) days from date of surgery
    - Average 15 (12 - 18) days longer
  - Healing by secondary intention following ring circumcision

PrePex Outcomes

- Pain
  - Greatest pain and discomfort 3-6 hours after placement
  - 5% lidocaine topical anaesthetic cream applied immediately before placement, oral analgesics given to take as required
  - Appears to be somewhat less pain while device worn than at comparable times following surgery
  - Transient (short duration but quite severe) pain during device removal
- Odour
  - Complaints of bad odour after 3-4 days