Clinical performance of Adult Circumcision Devices Compared with Surgery

Entebbe Uganda, 13 November 2013
Framework for Clinical Evaluation of Devices

- Safety study(ies) in country(ies) of intended final use
- Formal randomised comparison with established method(s) of circumcision
- Acceptability studies in country of intended final use
- Field studies in settings of intended final use

At least two independently conducted series of studies
Collar Clamp Device

• Only one example for which data available
• Shang Ring, developed in China and studied in China and Africa
# Shang Ring Studies Reviewed

<table>
<thead>
<tr>
<th>Study (type)</th>
<th>Location</th>
<th>Clients</th>
<th>Type of providers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Safety Study</strong></td>
<td>Kenya</td>
<td>40 healthy HIV-negative men</td>
<td>Physicians and nurses experienced in conventional surgical circumcision</td>
</tr>
<tr>
<td>Spontaneous Detachment</td>
<td>Kenya</td>
<td>50 healthy HIV-negative men</td>
<td>Physicians and nurses experienced in conventional surgical circumcision</td>
</tr>
<tr>
<td><strong>Randomized Comparison with Surgery</strong></td>
<td>Kenya and Zambia</td>
<td>200 Shang Ring, 200 surgery, healthy HIV-negative men</td>
<td>Physicians and non-physicians, all with extensive experience with surgical male circumcision</td>
</tr>
<tr>
<td>Field Studies</td>
<td>Kenya and Zambia</td>
<td>1256 healthy HIV-negative men</td>
<td>Physicians and non-physicians, all with extensive experience with surgical male circumcision</td>
</tr>
<tr>
<td>Acceptability and Safety</td>
<td>Uganda</td>
<td>621 healthy HIV-negative men, 508 of whom chose Shang Ring</td>
<td>Clinical officers in sterile conditions in outpatient operating rooms</td>
</tr>
</tbody>
</table>
Shang Ring Priority Outcomes (1,983 placements)

• High proportion of clients eligible and device successfully placed
  – 98.8% of men eligible for device circumcision and device successfully placed
  – 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
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 Adverse Events (TAG Classification)

<table>
<thead>
<tr>
<th>Type of Event</th>
<th>Number</th>
<th>Per cent [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total placements</td>
<td>1,983</td>
<td></td>
</tr>
<tr>
<td><strong>Serious AEs</strong></td>
<td></td>
<td></td>
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<tr>
<td>Pain placement (8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection (4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insufficient skin removed (3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain leading to early removal (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wound disruption (2)</td>
<td></td>
<td></td>
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<tr>
<td>Bleeding (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Moderate AEs</strong></td>
<td>20</td>
<td>1.0% [0.6%, 1.6%]</td>
</tr>
<tr>
<td><strong>Mild AEs</strong></td>
<td>43</td>
<td>2.2% [1.6%, 2.9%]</td>
</tr>
</tbody>
</table>
Shang Ring Priority Outcomes

• 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
Shang Ring Priority Outcomes

• Pain
  – Local injectable anaesthesia required for placement
  – Some pain while wearing and somewhat higher during erection than at comparable times following surgery
  – Short, transient discomfort or pain during device removal
Shang Ring Priority 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
Elastic Collar Compression Device

• Only one example for which data are available
• PrePex Device, developed in Israel and studied in Africa
### PrePex Studies Reviewed

<table>
<thead>
<tr>
<th>Study (type)</th>
<th>Location</th>
<th>Clients</th>
<th>Type of providers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safety Study</td>
<td>Rwanda</td>
<td>50 healthy HIV-negative men</td>
<td>Physicians and nurses</td>
</tr>
<tr>
<td>Randomized Comparison with Surgery</td>
<td>Rwanda</td>
<td>144 PrePex, 73 surgery</td>
<td>Physicians and nurses</td>
</tr>
<tr>
<td>Pilot Study</td>
<td>Rwanda</td>
<td>49 healthy HIV-negative men age 21–54 years</td>
<td>Nurses</td>
</tr>
<tr>
<td>Field Study</td>
<td>Rwanda</td>
<td>666 generally healthy men [5 HIV-positive]</td>
<td>Lower cadre nurses</td>
</tr>
<tr>
<td>Safety Study</td>
<td>Zimbabwe</td>
<td>53 HIV-negative men</td>
<td>Physicians and nurse assistants</td>
</tr>
<tr>
<td>Randomized Comparison with Surgery</td>
<td>Zimbabwe</td>
<td>240 HIV-negative men</td>
<td>As above</td>
</tr>
<tr>
<td>Field Study</td>
<td>Zimbabwe</td>
<td>641 HIV-negative men</td>
<td>Nurses with physician back-up support</td>
</tr>
<tr>
<td>Field Study</td>
<td>Uganda (IHK)</td>
<td>634 healthy men</td>
<td>Surgeons, medical officers, clinical officers and nurses</td>
</tr>
<tr>
<td>Field Study</td>
<td>Uganda (Rakai)</td>
<td>187 HIV-negative men</td>
<td>Not stated</td>
</tr>
</tbody>
</table>
PrePex Priority Outcomes (2,417 placements)

- High proportion of clients eligible and devices successfully placed (92.6%)
  - 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)

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

• 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 Priority Outcomes

- Pain
  - Greatest pain and discomfort 3-6 hours after placement
  - Pain control protocols evolved during initial studies in Rwanda
  - 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 but intense pain reported by some men as necrotic foreskin and device removed
PrePex Priority 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
Balance of Benefits and Harms

• Eligibility
  – Standard contraindications to medical circumcision apply to devices (active infection, congenital anomalies, ...)
  – A small proportion of men not eligible for device circumcision (require conventional surgical circumcision)
  – Approximately 5% - 7% not suitable for circumcision with elastic collar compression device

• Successful circumcision
  – Similar proportion of successful circumcisions as with conventional surgery (> 99.5%)
Balance of Benefits and Harms

• Healing times
  – About 1-2 weeks longer on average following circumcision by device compared with surgery

• Safety
  – AE rate comparable to (and possibly lower than) conventional surgery
  – A few SAEs required prompt skilled intervention to prevent serious sequelae
Balance of Benefits and Harms

• Pain
  – Similar to or lower than levels reported following conventional surgery

• Procedure times
  – Shorter than conventional surgery (even if including time for removal), particularly for elastic collar compression device
Values and Preferences of Clients

• Cosmetic result
  – High level of satisfaction following device and surgical circumcision
  – Devices leave neat circumferential wound with no suture marks
  – Comparative cosmetic results 1 year or more following procedure not available

• Odour
  – Some complaints of bad odour reported by clients and noticed by health care providers during removal of necrotic foreskin and elastic collar compression device
Values and Preferences of Clients

• Period of Sexual Abstinence
  – Healing times on average 1-2 weeks longer with device than conventional surgical circumcision
  – Healing may take up to 8-9 weeks in rare cases

• Interference with work and daily activities
  – Direct comparative data lacking
  – Minimal interference with work and daily activities while wearing devices
  – Some interference with urination reported with elastic collar compression device
Values and Preferences of Clients

• Anaesthesia
  – Avoiding injection of local anaesthesia cited as major factor in expressed preferences for elastic collar compression device

• Mandatory Second Visit
  – Unclear whether has any impact on acceptability
Values and Preferences of Providers

• Large proportion of physicians and non-physicians expressed preference for device over conventional surgical circumcision
  – Easy to perform and faster
  – Better cosmetic results
  – Fewer complications
  – No need for suturing
  – Less bleeding
  – No need for routine injectable anaesthesia with elastic collar compression device