Technical updates on Voluntary Medical Male Circumcision:

device methods, tetanus-toxoid containing vaccination

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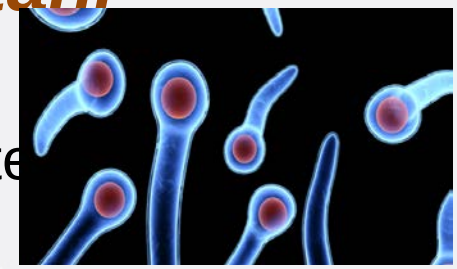
World Health Organization

WHO Prequalification status on devices for adolescent and adult male circumcision for HIV prevention

- ShangRing: prequalified to 13 years and older
  - METHOD CHANGES pending data review: age to 10 years, topical anaesthetic cream, no flip technique, fewer device sizes.
    - Anticipated Q2 2017
- PrePex: prequalified to 13 years and older
  - NEW RISK and MANAGEMENT
    - use only with evidence of sufficient protection through vaccination or provision of doses(s) as needed.
    - tetanus --30 fold increased risk compared to conventional surgical
  - CHANGES REQUESTED: pending review, age to 10 under review
  - NEW METHOD : foreskin removal at Day 0
    - Requires series of studies and data per *Framework for Clinical Evaluation*
- UniCirc: no full submission on PQ

Tetanus and *Clostridium tetani*



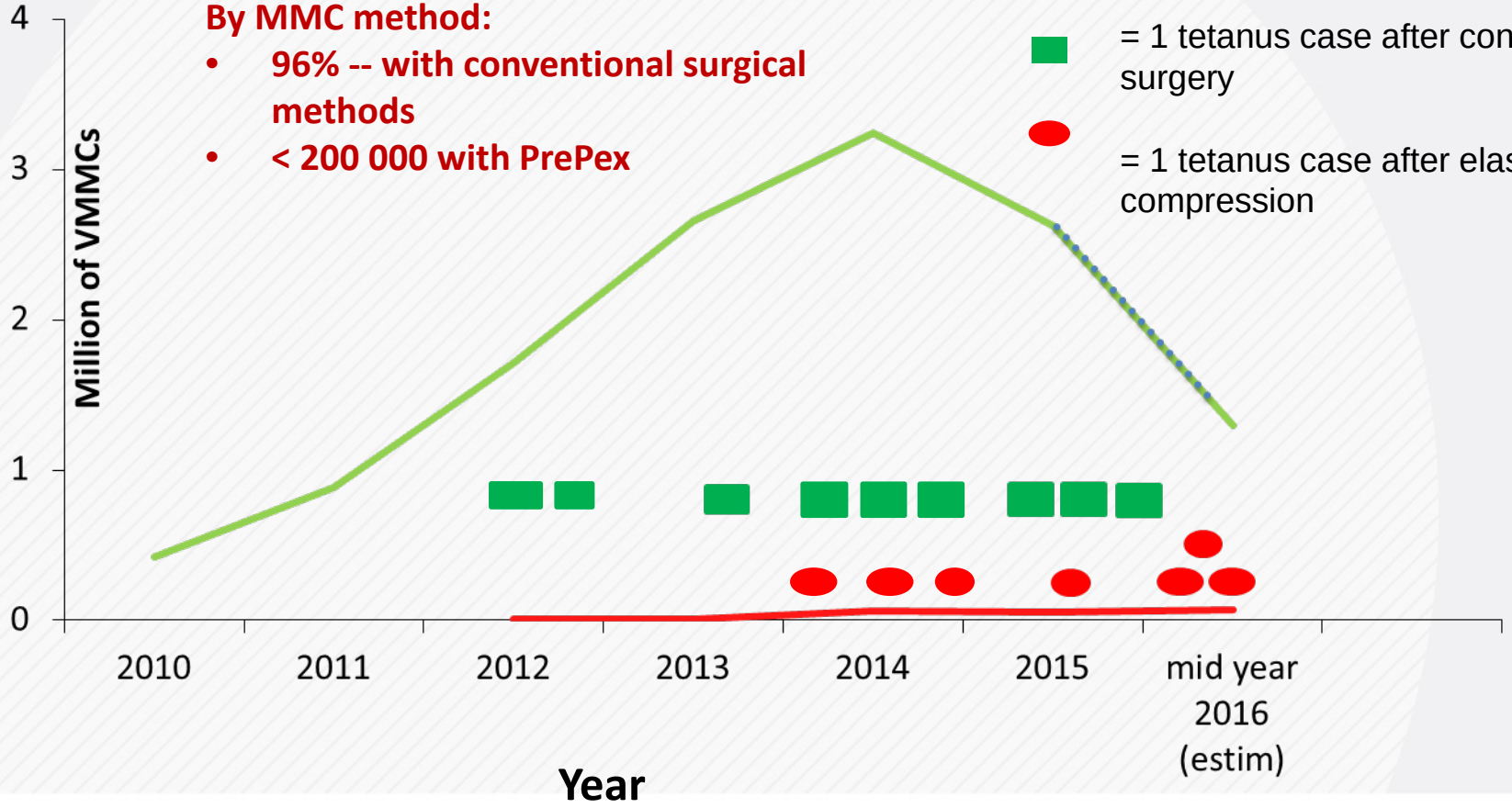
- Causes spastic paralysis – suffering requiring inte
  - Often fatal in low resource setting (40-70%)
- Caused by neurotoxin produced by *Clostridium tetani*
- Spores widespread in nature: dust, soil, faeces
  - Spores can survive extreme conditions such as
    - Boiling for 10-15 minutes
    - Disinfectants such as alcohol, phenol or formalin
  - Spores killed by iodine, bleach, H_2O_2, extreme heat
- Vegetative bacteria thrive in anaerobic conditions
- Any break in the skin can serve as entry point
- Effective cheap vaccine. Not communicable so no herd immunity.
- Incubation period average ~7 days

Annual VMMCs in East and Southern Africa by method and reported tetanus cases by year (n = 16) (cases identified through VMMC programmes)

Over 12 million men reached in 14 countries

By MMC method:

- **96% -- with conventional surgical methods**
- **< 200 000 with PrePex**



Epidemiology: Tetanus incidence and incidence rate ratio by circumcision method, 2014 – June 2016

Countries	Elastic collar compression device cases/circs	Incidence per 100,000 (95% CI)	Surgery cases/circs	Incidence per 100,000 (95% CI)	Incidence rate ratio (95% CI)
Kenya, Rwanda, Uganda and the United Republic of Tanzania	6 / 113,662	5.28 (1.94, 11.5)	6 / 3,717,338	0.161 (0.059, 0.351)	32.7 (8.74, 122)
Rwanda and Uganda only	6 / 110,800	5.45 (1.99, 11.8)	3 / 1,986,443	0.151 (0.031, 0.441)	35.9 (7.66, 222)

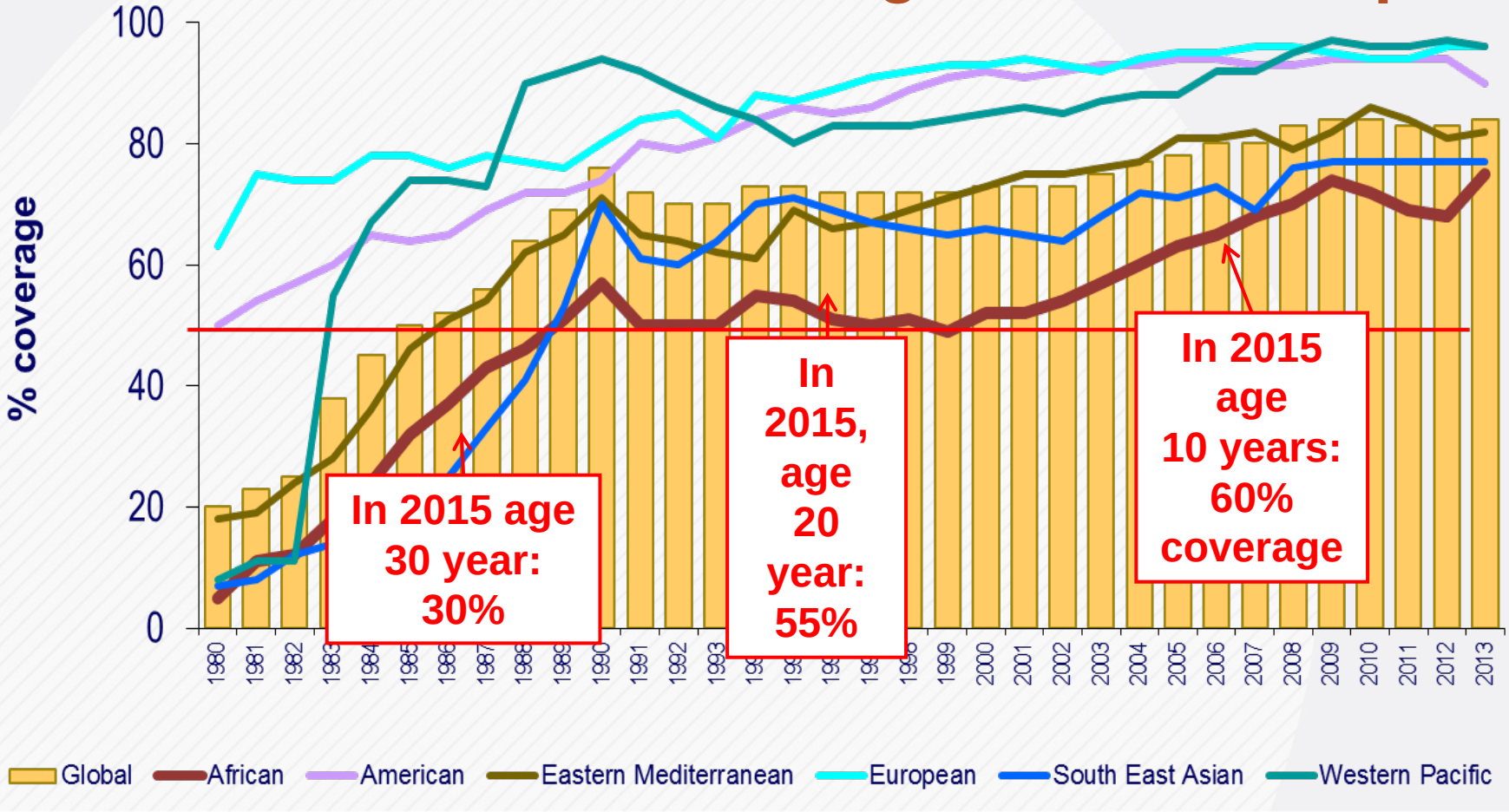
Countries included based on reports of Tetanus case by June 2016; Zimbabwe case not included but IRR remains similar

Biological plausibility on greater risk of tetanus with elastic collar compression method

- All cases were generalized and fit association criteria A or B
- Potential contamination before and while wearing
  - Spores widespread in environment
- Germination of spores and multiplication
  - Anaerobic environment, necrotic tissue with PrePex
    - **Inherent method difference**
  - Incubation 1 -112 days – all cases 9-12 days post placement
  - Presence of flagella
    - migration possible
- Toxin entry possible:
  - microabrasions, bleeding at removal, granulation tissue friable

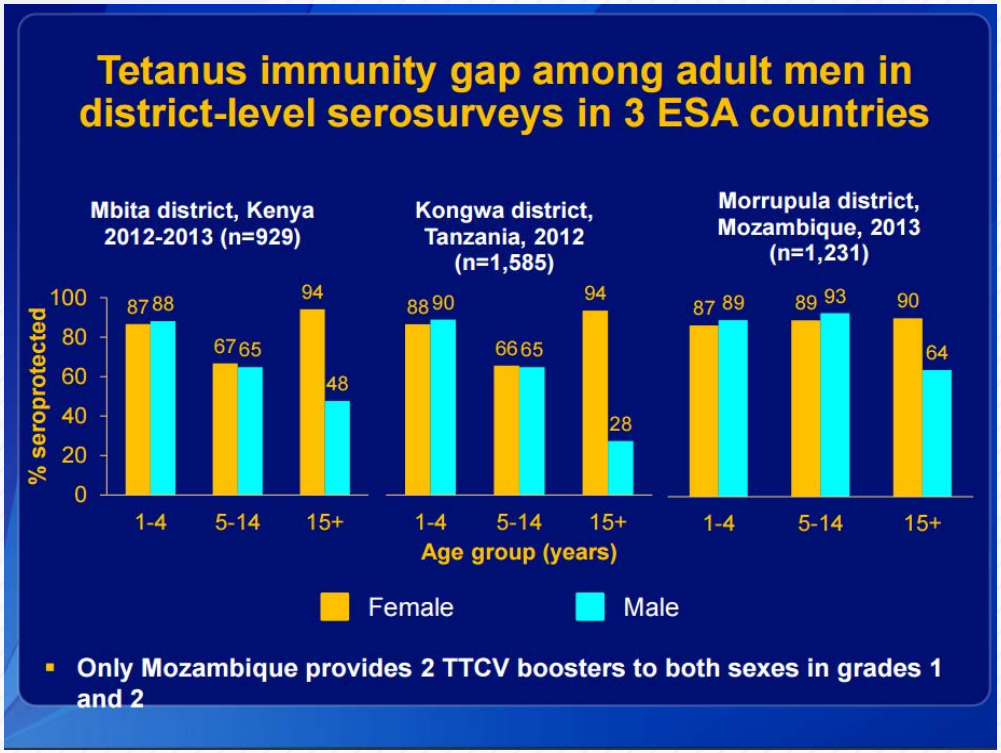
Tetanus toxoid-containing vaccination and sero protection

Global and regional diphtheria-tetanus-pertussis 3 (DTP) immunization coverage, 1980–2013, and VMMC age cohort examples



Gender differential in sero protection

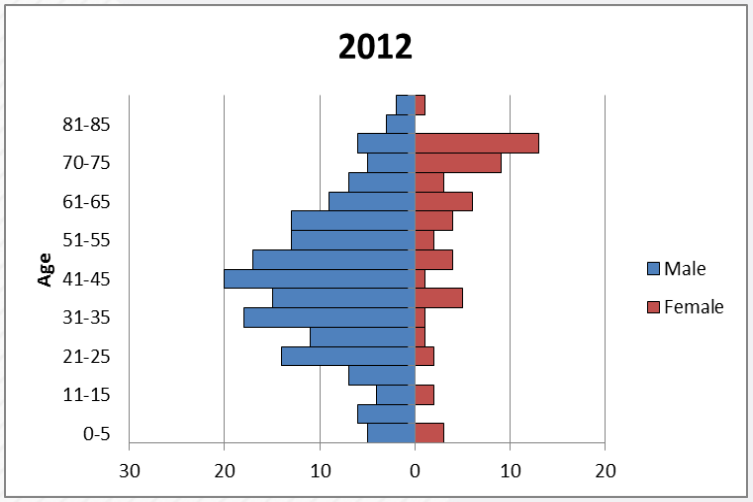
Tetanus sero protection Africa

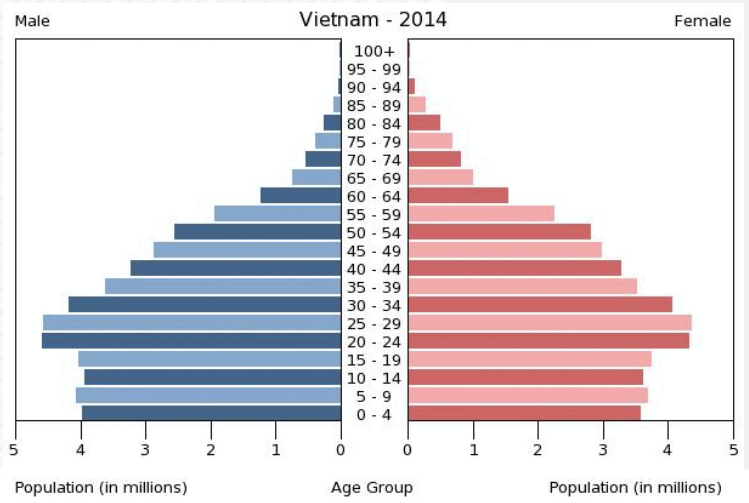


Summary of hospital studies of non-neonatal tetanus in sub-Saharan Africa published 2003-2014

– 71% males, 32.7 years

Tetanus cases by age and sex in Viet Nam





2 paces of implementing WHO recommendations on prevention of HIV and tetanus in ESA

Aristotle described tetanus

V B.C.

Passive massive immunization in humans

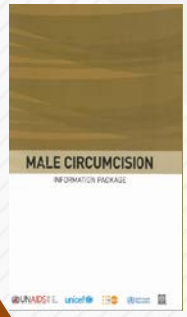
1914

1924

First Tetanus toxoid vaccine

2006

2007



VMMC for men in high HIV prevalence settings.
~ 12 million MCs in 14 countries

2016

WHO: Tetanus toxoid containing vaccination for general population in addition to maternal and infant schedules

1-2 countries with post-infant booster dose policy

Some key points

- **Exponential expansion of medical male circumcision services to men** in 5 years
- **Gender differential on tetanus protection –**
  - men not reached systematically with TTCV vaccination – policy and practice of boosters limited or lacking
- **VMMC is safe with low numbers of adverse events** despite large numbers of circumcisions performed in resource limited settings
  - tetanus rare after VMMC, but risk exists with wound and is preventable
- **Risk differs by method so risk mitigation will differ**

WHO Advice - July and September 2016

- F**or conventional surgical methods** in which the foreskin was removed at the time of the surgery, **no modification to the 2015 consultation advice on vaccination:**

- Ministries of health were advised to develop and phase-in effective and practical delivery strategies for providing tetanus vaccination in the context of their programmes (VMMC and vaccination).
  - strategies depend on the country's TTCV schedule and practices, and its tetanus burden.
  - unless an individual has documented evidence of received of a full five-dose TTCV series, it is advised that a single TTCV dose be administered before or at the time of circumcision.

WHO Advice: July and September 2016
TTCV Differential Mitigation

- **Circumcision with a device method where the foreskin is left in situ and removed several days after application should be undertaken only if the client is adequately protected** against tetanus by immunization with tetanus-toxoid-containing vaccine (TTCV):
  - two TTCV doses at least 4 weeks apart, with the second dose at least 2 weeks before device placement; or
  - if received three infant doses, or one dose during adolescence or adulthood, a TTCV booster at least 2 weeks before device placement (a booster at the time of placement provides only limited protection as it takes 7–14 days for antibodies to rise to protective levels); or
  - a series of five doses of TTCV.

July and September 2016 reports

- **A clean care approach** for all circumcision methods:
  - Encourage personal cleanliness, asking the client to wash his genital area, including under the foreskin, before circumcision and encouraging him to wear clean undergarments.
  - Follow standard surgical protocols on skin preparation
- **Enhance individual and community education** on clean wound care
  - clear and understandable instructions on wound care and genital hygiene
  - clean or sterile dressings to use at home
  - when to return to the health-care facility for post-procedure care
  - educate on benefits of vaccination against tetanus and educate on dangers of applying substances that may contain *Clostridium tetani* (e.g. animal dung poultices or herbal remedies).

Tetanus toxoid-containing vaccination recommendation

WER NO 6., Feb 2017, WHO SAGE recommendations and advocacy for TTCV for adolescent boys

- Inputs from VMMC and gender difference
- 6 doses – 3 primary doses plus 3 booster doses (12-23 mo, 4-7 y, 9-15 y)
- 5 doses if start any time after infancy
  - Adolescents. 9 – 15 years. Aligned with HPV.
    - Pre-adolescent and adolescent boosters are also programmatically feasible and align with the human papillomavirus immunization schedule (girls 9 – 14 years)
- Catch up boosters: military, synergies with adolescent VMMC, method specific
- Provide vaccination cards
- Preferably Td
- Cost 0.10 USD per dose
- Other prevention efforts needed:
  - community education on clean wound care

PRIMARY PREVENTION
Girls 9–13

HPV vaccination
Girls and boys, as appropriate

- Health information and warnings about tobacco use*
- Sexuality education tailored to age and culture
- Condom promotion/provision for those engaged in sexual activity
- Male circumcision

- Collaborate with MoEd

Potential issues on implementation

- Resources - Stock of vaccine available? Funding?
- Safety monitoring strengthening within national programmes -- reporting tetanus and other adverse events. Only Uganda reports non-neonatal tetanus
- Immediate and longer term method perspectives:
  - Maintain high quality essential surgical skills for other interventions
  - Will method choice make difference to accelerate for 15 – 29 yo through 2020
  - Adolescents - younger adolescents need another method as not eligible for ECC method
  - ShangRing of interest?

Thank You