

Broader tetanus prevention:
Impact of current tetanus immunization
programmes and need for acquiring
broader tetanus prevention

SAGE Working Group on Maternal and Neonatal Tetanus
Elimination and Broader Tetanus Prevention

Presented by Robert Steinglass
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Outline

- existing WHO recommendation for TTCV, including infant and booster doses
- immunity gaps identified
- opportunities for improved routine infant programs and delivery of booster doses
- proposed modification to vaccination schedule



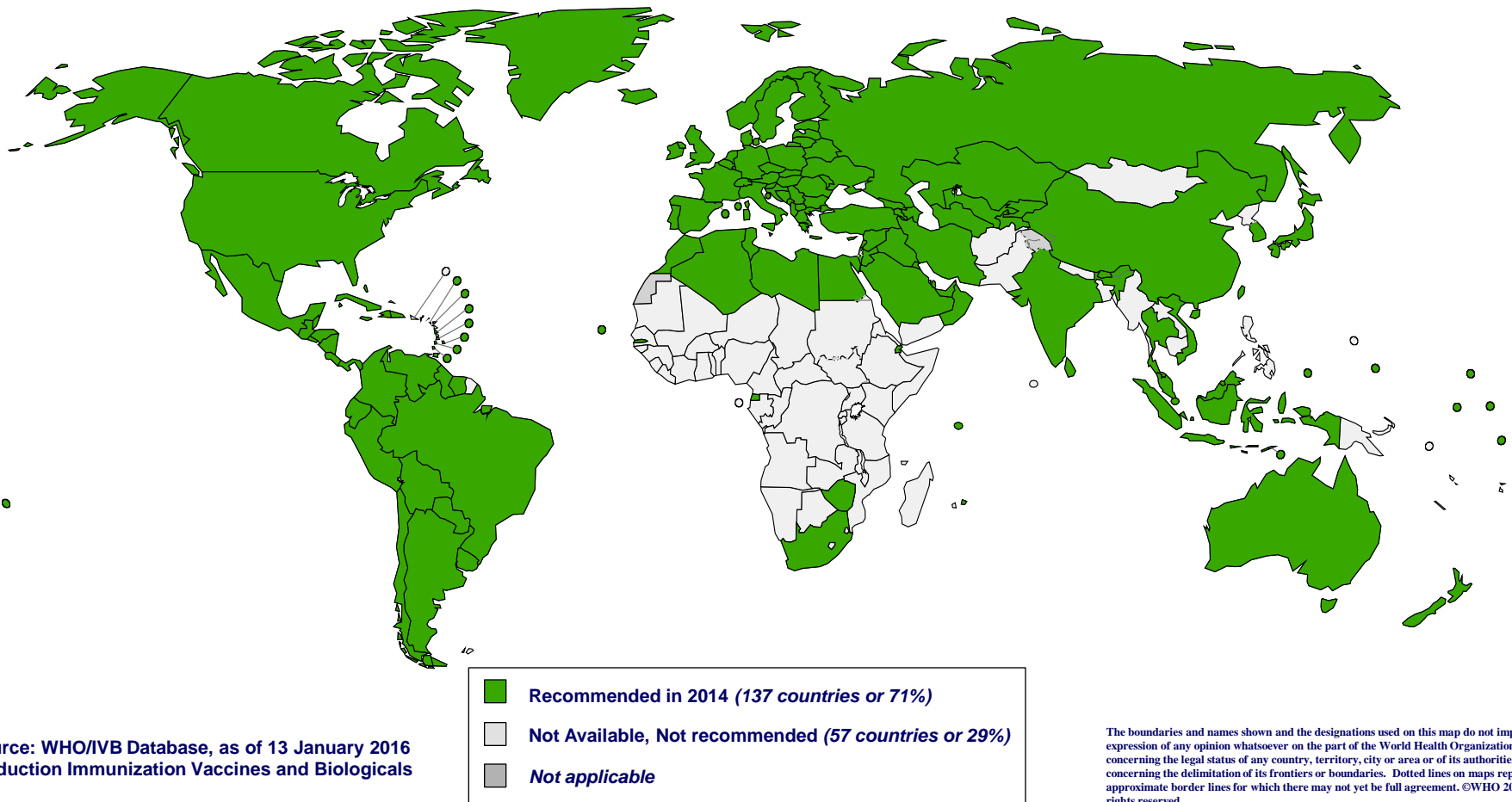
Existing WHO recommendations for TTCV

- 3 TTCV doses in infancy (commonly at 6, 10, 14 weeks; or 2, 3, 4 months)
- 3 TTCV boosters (Td) at 4-7 years, 12-15 years and in early adulthood
- TTCV included in routine antenatal care
- TTCV available as monovalent TT [or in combination with other antigens: D, d, P, aP, IPV, Hep B, Hib (e.g., DTP, Td, DTPHepB, DTPHepBHib, DTaPIPVHib, DTaPIPVHibHepB, Tdap)]

Vaccination schedules are also included for:

- adolescents/adults with no previous vaccination
- pregnant women with no previous vaccination (or unreliable info)
- pregnant women with 3 childhood DTP doses
- pregnant women with 4 childhood DTP doses
- supplementary campaigns in high-risk areas (reproductive-aged women)

136 Countries recommend a 4th dose of DTP-containing vaccines (DTPCV4), 2014



Data source: WHO/IVB Database, as of 13 January 2016
Map production Immunization Vaccines and Biologicals (IVB),
World Health Organization

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. ©WHO 2016. All rights reserved.

Coverage and immunity gaps identified

- global DTP3 coverage is 86% (2015)
- global tetanus protection at birth, based on TTCV coverage in pregnant women, is 83% (2015)
- 49 (25%) Member States don't offer TTCV booster doses in childhood or adolescence (or for adult males) in schedules
- >80% of population in some WHO regions reside in countries with no diphtheria vaccination past 5-6 years of age
- coverage with childhood and adolescent TTCV booster doses frequently not tracked
- tetanus cases following voluntary medical male circumcision
- reviews: of recent serologic data; of systematic reviews on duration of continued protection from various schedules

Tetanus following VMMC circumcision reveals evidence of male immunity gap

- 13* tetanus cases (from 4/12 to 3/16) with 5 deaths within 14 days after VMMC in 5 SE Africa countries highlight gender gap in tetanus morbidity
- 12 of 13 were deemed causally associated with circumcision
- 9 of 13 were 10-19 years old
- most of the 14 priority countries for VMMC have no policy for vaccinating males against tetanus after infancy
- “Incorporating tetanus vaccination into VMMC programmes should be seen as a priority.”
- “The convergence of CE solutions to 2 public health problems affecting men – HIV and tetanus – offers an opportunity for service synergies and enhanced health equity.”

Source: “Tetanus disease and deaths in men reveal need for vaccination” Shona Dala, Julia Samuelson, Jason Reed, Ahmandu Yakubu, Buhle Ncube, and Rachel Baggaley. *Bull World Health Organ* 2016; 94).

*15 cases of tetanus were reported from 2012 through August 2016

Review of studies of hospitalized tetanus cases (2003-14), Sub-Saharan Africa

- non-neonatal tetanus cases comprised 0.3-10.7% of all admissions
- median of 71% of non-neonatal tetanus cases were in men
- median age of tetanus patients across both sexes was 32.7 years

Source: "Tetanus disease and deaths in men reveal need for vaccination" Shona Dala, Julia Samuelson, Jason Reed, Ahmandu Yakubu, Buhle Ncube, and Rachel Baggaley. *Bull World Health Organ* 2016; 94:613-621).

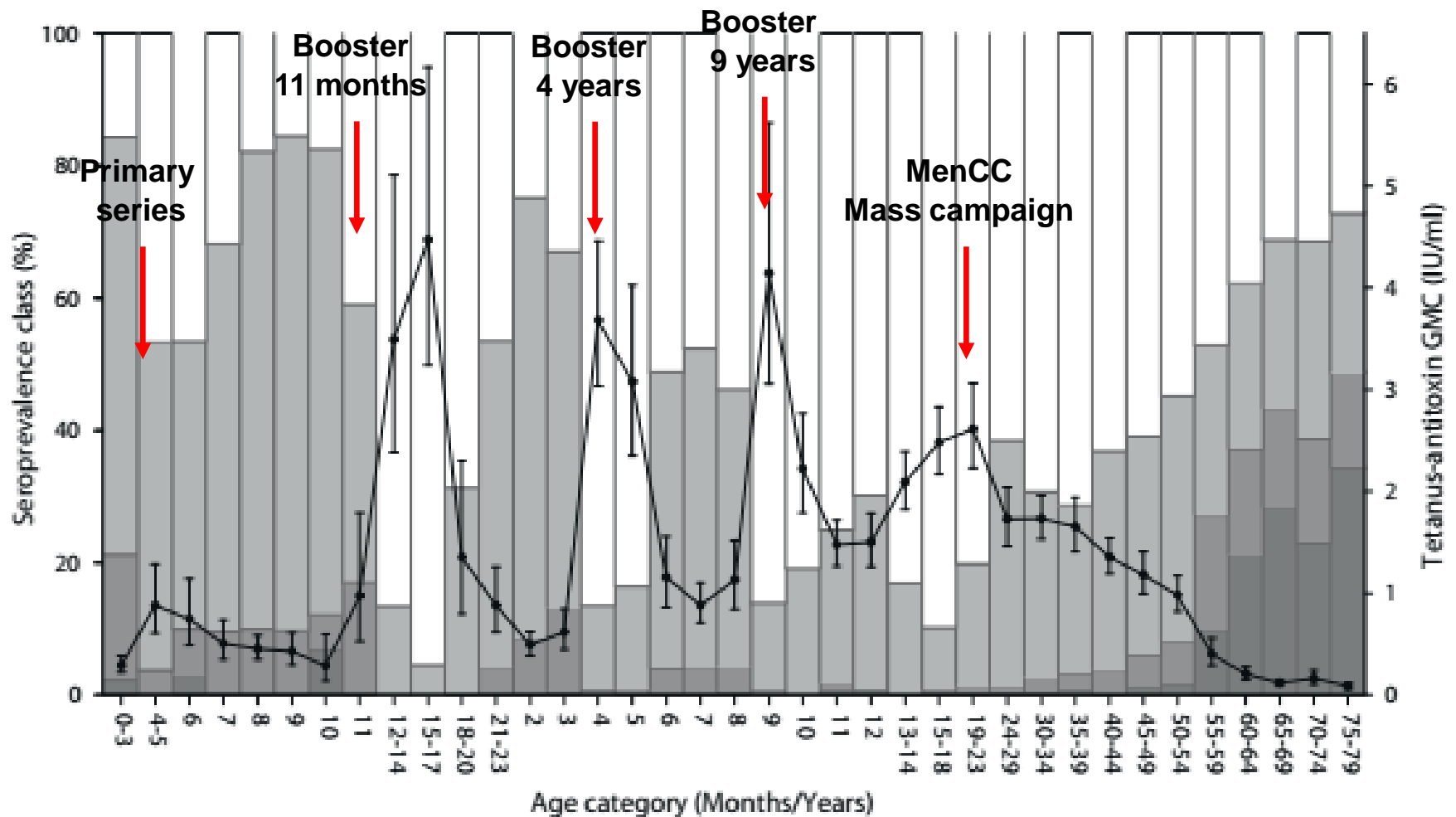
Serologic evidence of immunity

Serologic evidence of robust immunity across age groups and persisting 20–30 years after last vaccination related to schedules containing 6 TTCV doses in Netherlands (3, 4, 5 and 11 months; 4 and 9 years), Australia (2, 4, 6 and 18 months; 4 and 10–15 years), and England (2, 3 and 4 months; 12 months [Hib-Men C-TT conjugate]; 3.5–5 years and 13–18 years).

Booster vaccination during the second year of life after a 3-dose primary series substantially increases antitoxin titers.

Source: Systematic review of literature, WHO's Optimizing Immunization Schedules Project

Tetanus IgG seroprevalence in the Netherlands 2006-2007 (Pienter2)

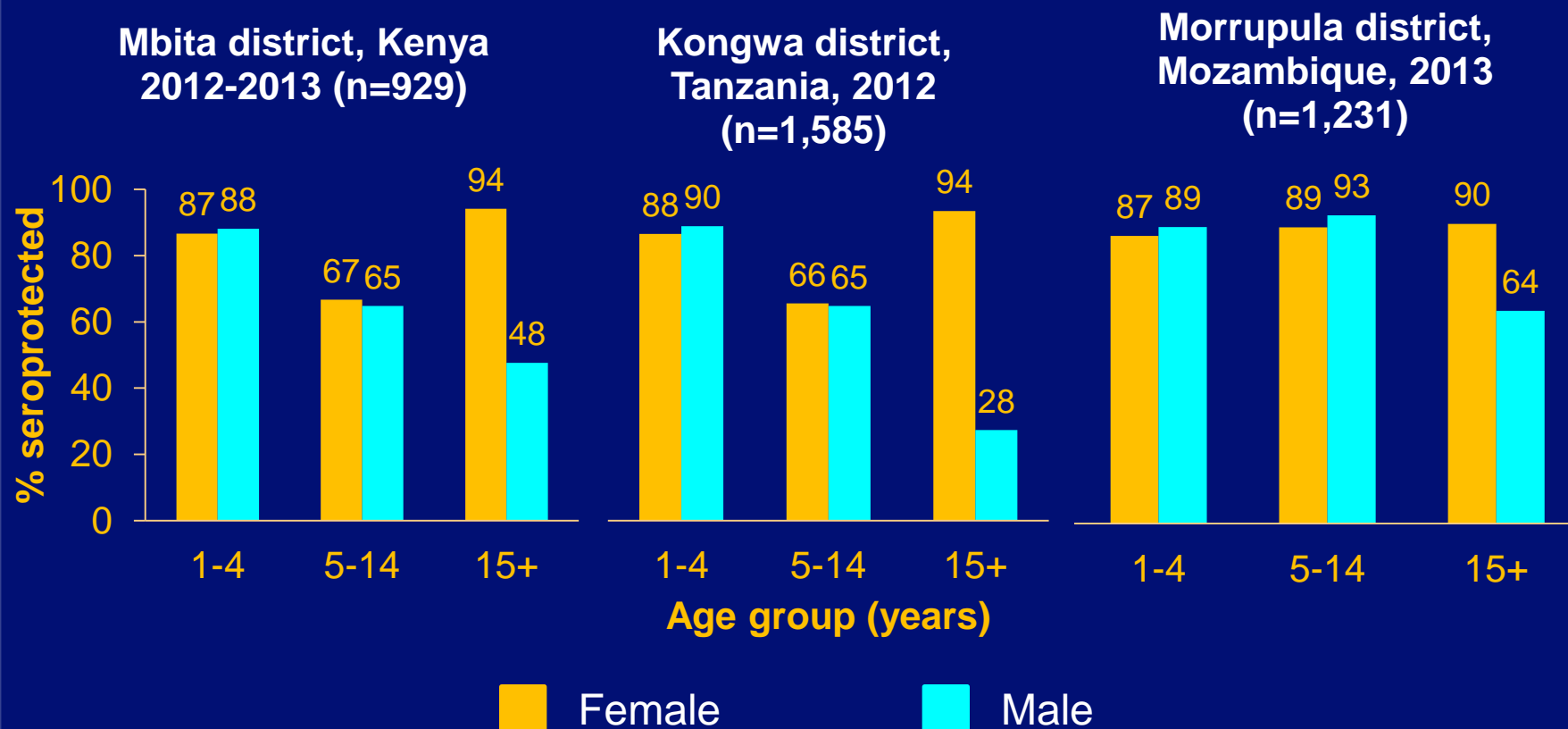


Sero-survey data from multiple African countries

- recent serologic findings from cross-country study (KEN, TAN, MOZ)
- declining sero-protection rates in older children (5-15 years) in absence of booster doses
- disproportionately high immunity gaps for males >15 yrs
- since early 2000s, MOZ included a TTCV booster in 1st and 2nd grades of primary school to boys and girls (KEN and TAN do not)
- MOZ has high seroprotection rates in children 5-14 years versus KEN and TAN
- findings support need for TTCV booster at 2YL and age of school entry to improve sero-protection in younger children and prevent drop in sero-protection at ≥ 5 years

Source: “Results of percentage of sero-protected individuals at district level in three eastern and southern African countries.” Scobie et al, in press

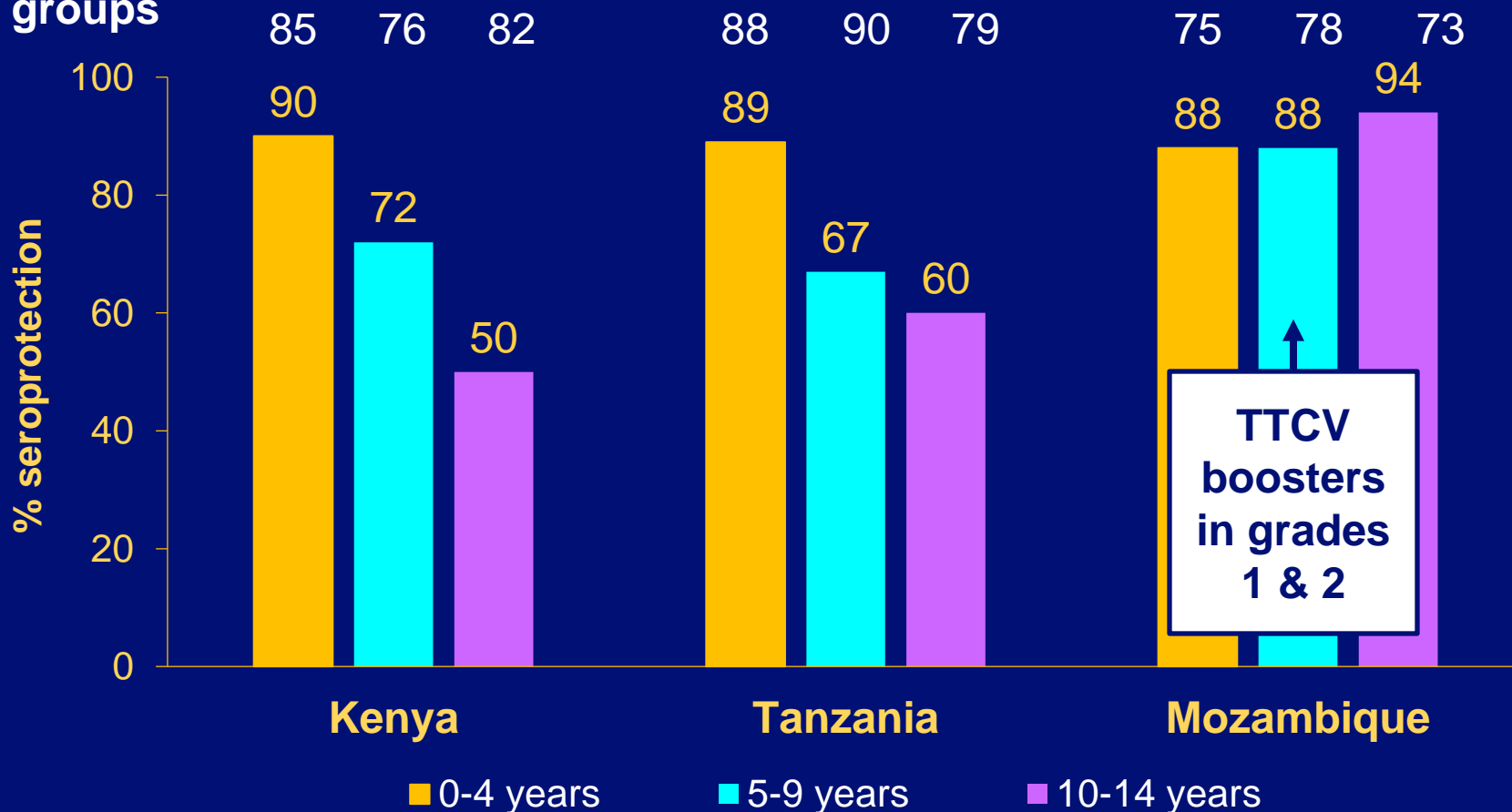
Tetanus immunity gap among adult men in district-level serosurveys in 3 ESA countries



- Only Mozambique provides 2 TTCV boosters to both sexes in grades 1 and 2

Tetanus immunity gap among older children in Kenya and Tanzania district-level serosurveys

Median national WHO-UNICEF estimate of DTP3 coverage (%) for age groups



Scientific and program rationale for early school-age boosters (Td) as a long-term and complementary prevention strategy

- Each booster extends duration of protection from earlier doses
- Takes advantage of high (>90%) enrollment of girls in early grades of primary school, before drop-out, in most low-resource countries
- Achieves “catch-up” immunization of both sexes not reached in infancy (primes them, closes immunity gap, improves equity across sexes)
- Increases likelihood that females enter peak reproductive years immune, especially where ANC coverage and institutional delivery is low
- Reduces # doses needed when females are hard to reach later as adults
- Sustains gains being achieved now during mass campaigns by channeling political interest into sustained follow-up action
- Can be integrated into a comprehensive package of school health interventions to share costs and benefits

Schools are becoming platforms for integrated basket of services

- De-worming
- Neglected tropical disease screening and treatment: Schistosomiasis, Onchocerciasis, Filariasis, Trachoma
- Supplementation: iron, iodine, vitamin A
- Health education: hygiene, tobacco, life skills
- Vaccination: HPV, typhoid, measles, dengue (?)

On its own, tetanus prevention is unlikely to attract sustained and adequate resources.

Modifications proposed to vaccination schedule

- adjust existing TTCV booster dose schedule to include 3 booster doses -- preferably during 2YL, between 4-7 years, between 9-15 years (with 4-5 year minimum interval between doses preferred)

3 doses:	in infancy	in infancy
4th dose:	4-7 years	->2YL
5th dose:	12-15 years	->4-7 years
6th dose:	Early adult	->9-15 years
7th dose:	X	->late in life, if waning immunity
- use 2YL as a platform for also vaccinating against pertussis, measles, and meningitis A
- stress tetanus antigen combined with low-dose diphtheria antigen (Td) is preferred for children 4 years and older
- booster doses late in life may be needed due to waning immunity

Thank you!

