Training Course in Sexual and Reproductive Health Research 2014
Module: Principles and Practice of Sexually Transmitted Infections Prevention and Care

Dual elimination of mother-to-child transmission (MTCT) of HIV and syphilis

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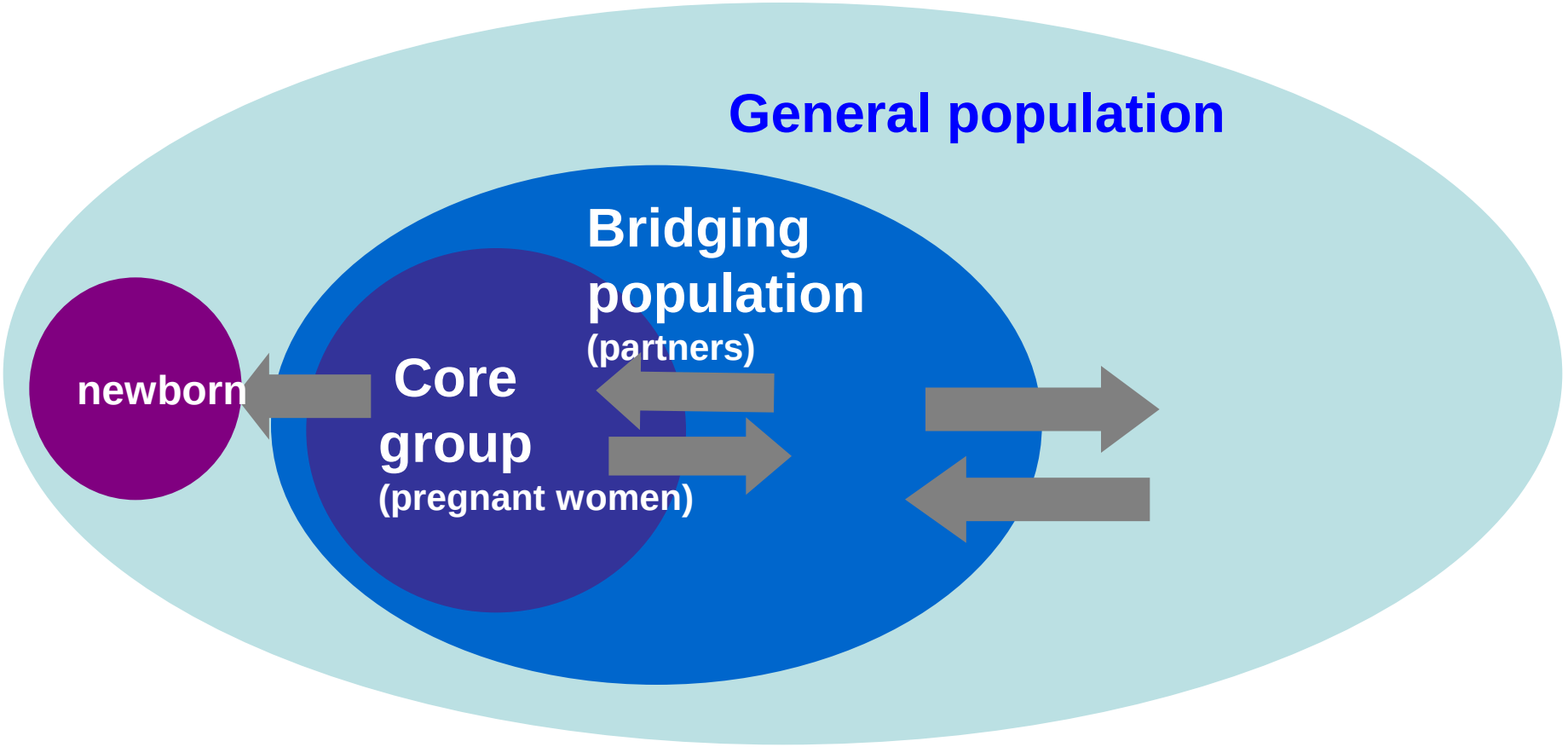
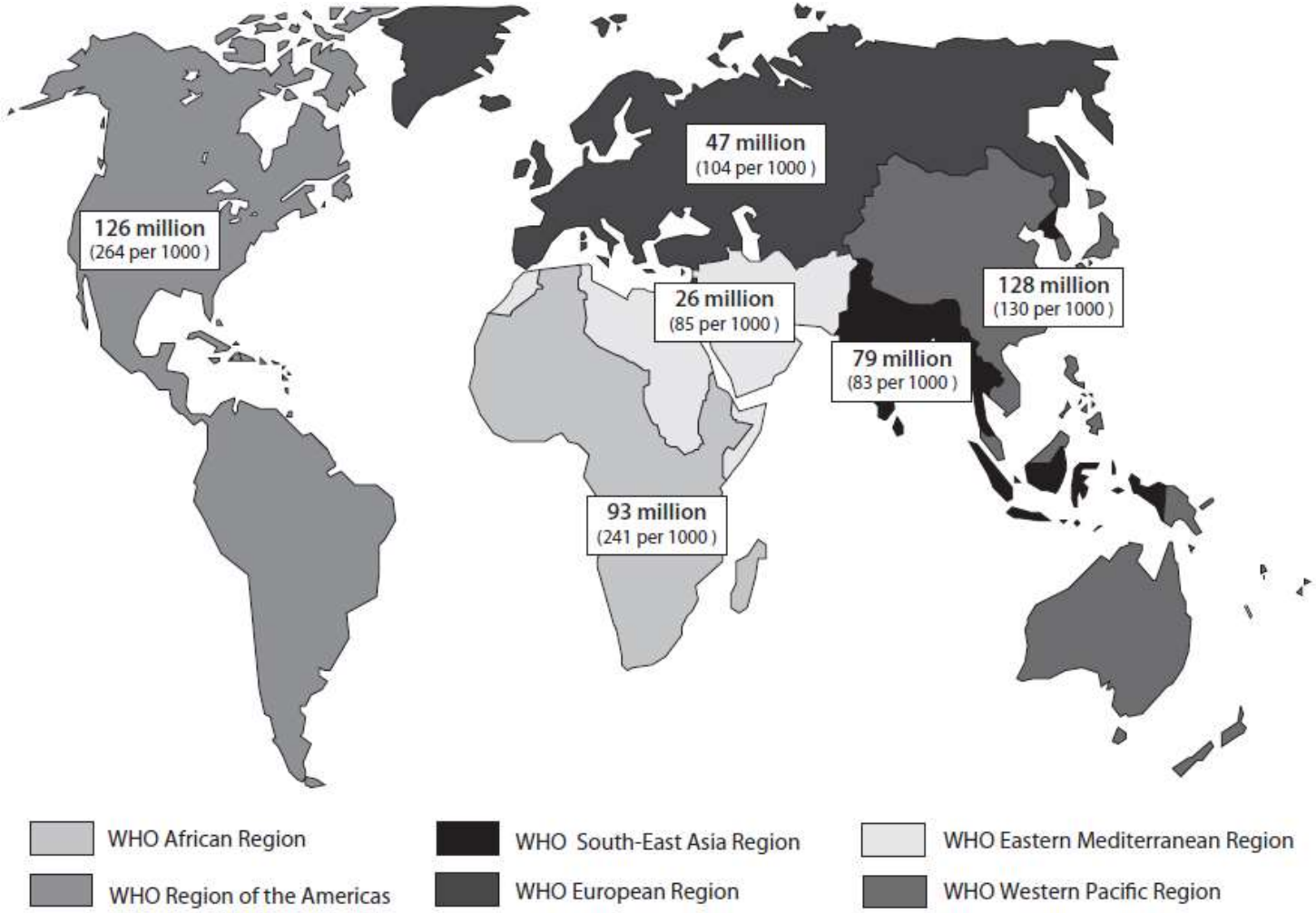
Overview

- Rationale and importance
- Strategies
- Next steps

Syphilis and HIV transmission dynamics



499 million new cases of curable sexually transmitted infections* in 2008

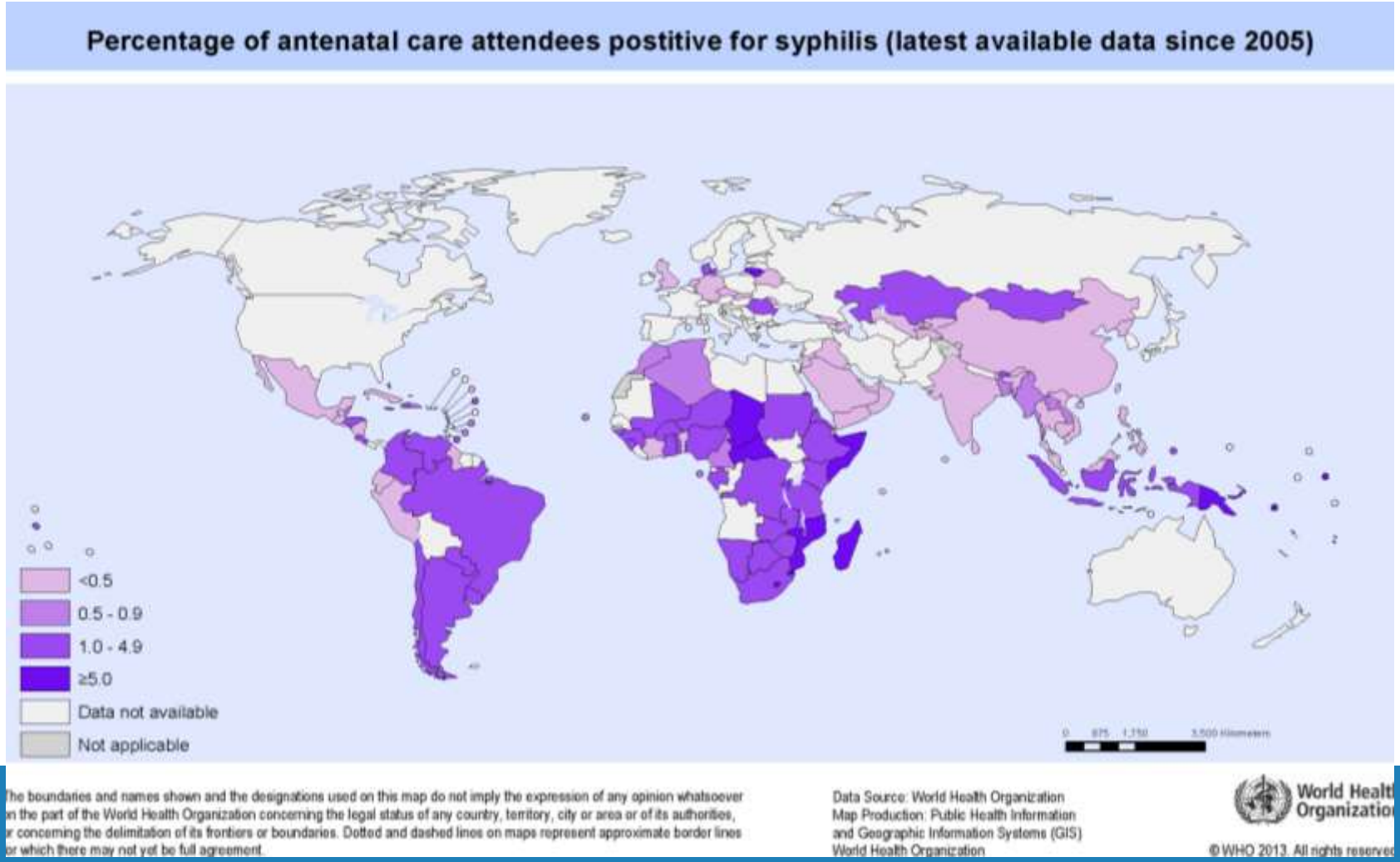


Chlamydia: 106 million, gonorrhea: 106 million, syphilis: 11 million, trichomonas: 276 million

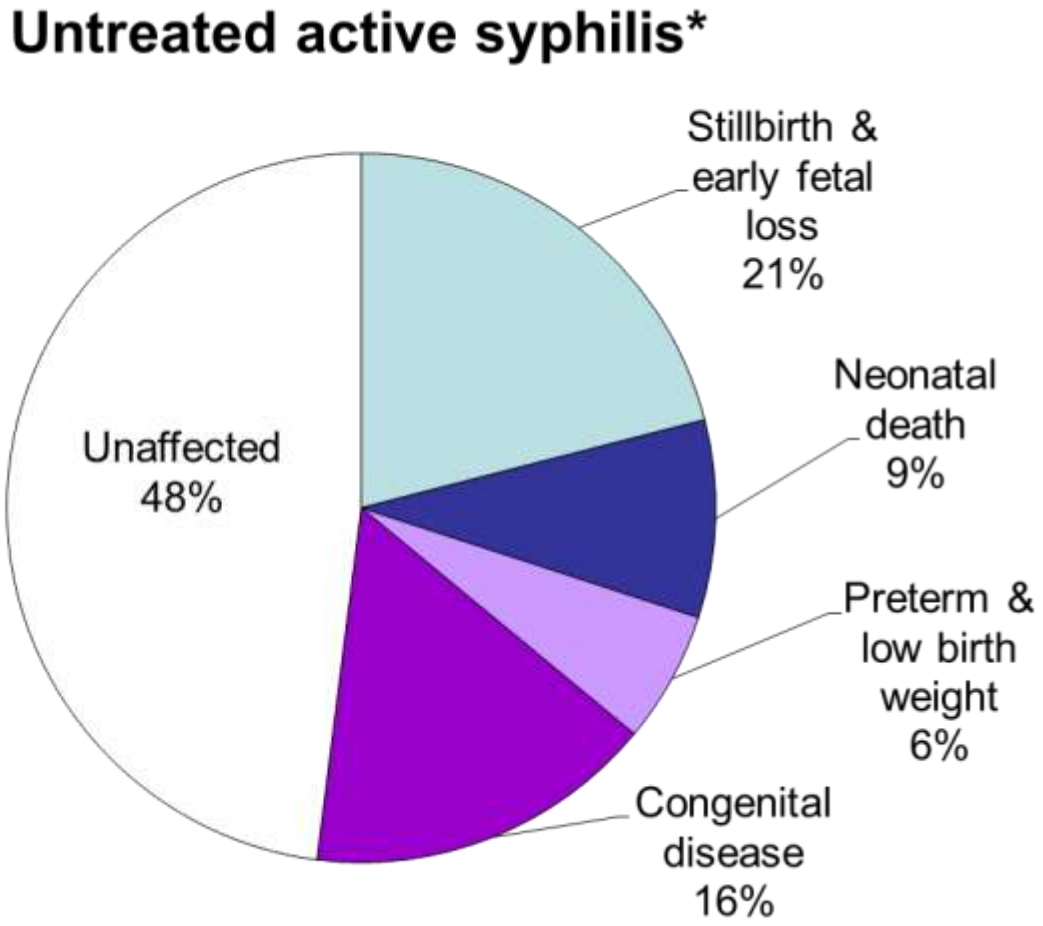
Source: WHO, 2012. Global incidence and prevalence of selected curable sexually transmitted infections – 2008.

10.4 million new cases of syphilis each year

- 1.4 million pregnant women with syphilis



Syphilis is devastating for the majority of fetuses



2008 estimates**

- **215,000 *stillbirths / fetal losses***
- **90,000 *neonatal deaths***
- **65,000 *preterm* or *low birth-weight* infants**
- **150,000 infants with *congenital disease***

*Gomez G et al, WHO Bulletin, 2013.
**Newman L et al, PLOS Medicine 2013.

Congenital syphilis is preventable and treatable

- Inexpensive test *less than US $1.00*
  - Traditional tests require laboratory
  - Rapid tests do not require laboratory
- Treatment
  - Widely available
  - *Penicillin* (one dose) = *US $0.50*
- Treatment given early in pregnancy is more likely to avoid bad outcomes – should test at *first ANC visit*!

**Source: The global elimination of congenital syphilis: rationale and strategy. WHO, 2007.*

Syphilis testing and treatment in ANC is cost-saving or very cost effective in all settings

Table 1.4
Estimated net cost (in US$) over 4 years, number of DALYs averted over 4 years and cost per DALY averted for eight country scenarios varying by burden of disease, syphilis testing and treatment coverage, and health-care costsa

Country scenario	Prevalence of syphilis in pregnant women	Proportion of all pregnant women tested and treated	Health-care cost structure	Net cost (savings) of intervention (4 years) (cost of intervention minus disease costs averted), US$	Number of DALYs averted (4 years)	Cost per DALY averted, US$
A	High	Low	Low	(1 943 017)	106 042	Cost saving[b]
B	High	Low	High	(12 261 250)	106 042	Cost saving
C	High	High	Low	(765 563)	39 155	Cost saving
D	High	High	High	(4 587 778)	39 155	Cost saving
E	Low	Low	Low	1 736 807	17 678	98.25
F	Low	Low	High	543 472	17 678	30.74
G	Low	High	Low	593 188	6527	90.88
H	Low	High	High	140 282	6527	21.49

**Source: Investment Case for Elimination of MTCT of Syphilis – promoting better maternal and child health and stronger health systems. WHO, 2012.*

Elimination of congenital syphilis helps reach global goals

Millennium Development Goals

- **4:** Prevention of congenital syphilis reduces neonatal mortality
- **5:** Early antenatal care and fewer spontaneous abortions and stillbirths improve maternal health
- **6:** Women with syphilis are at greater risk of acquiring and transmitting HIV
  - Ulcerative STDs increase risk of HIV acquisition
  - Ulcerative STDs increase shedding of HIV
  - Syphilis may increase HIV viral load of HIV-infected persons*
  - Syphilis in HIV-infected mothers may increase risk of MTCT of HIV**

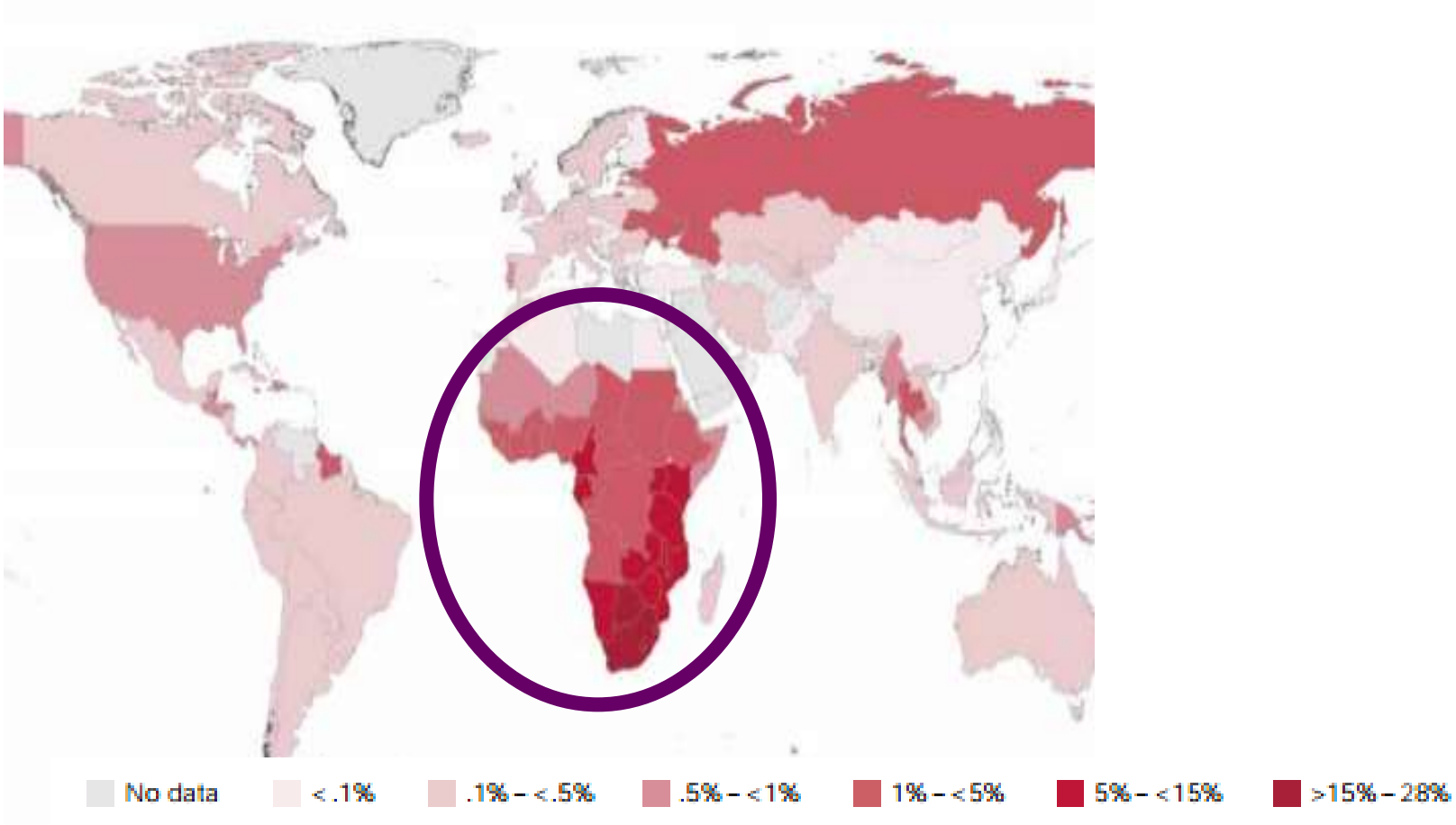
Secretary General's Global Strategy for Women's and Children's Health

- Ensure universal access for women and children to a comprehensive, integrated package of essential interventions & services

** Buchasz et al. AIDS 2004;18:2075-2079.*
*** Mwapasa et al. AIDS 2006;20:1869-1877.*

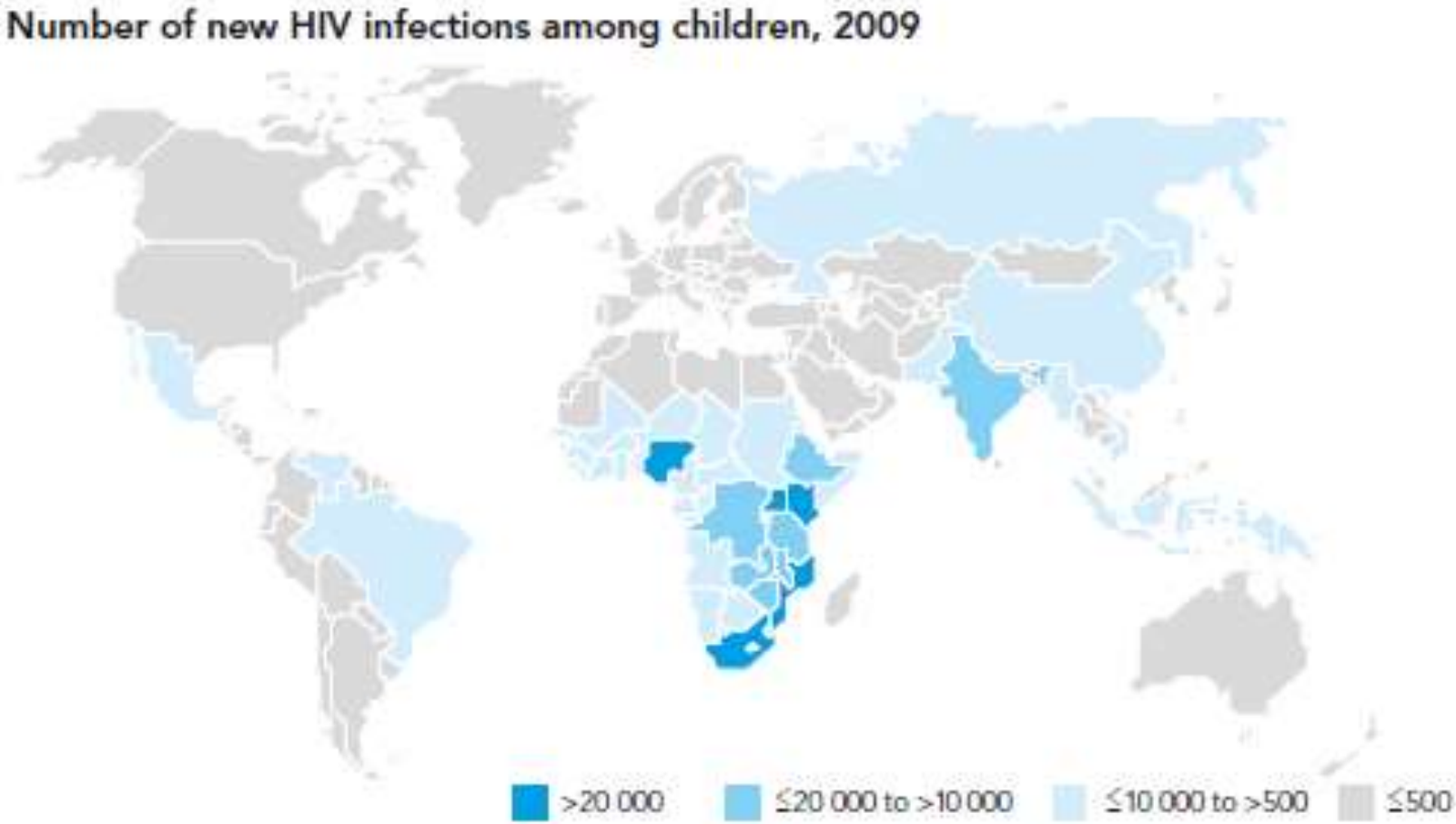
Syphilis rates in pregnancy are high where there is a high HIV burden

Global prevalence of HIV, 2009



Source: UNAIDS Global Report 2010

Number of new perinatal HIV infections, 2009



UNAIDS, Global Plan. Available at: http://www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2011/20110609_ JC2137_ Global-Plan-Elimination-HIV-Children_en.pdf

Maternal syphilis increases HIV transmission

- 1147 HIV-infected pregnant women had syphilis test results, of whom 92 (8.0%) had syphilis
  - ***Maternal syphilis was associated with in utero HIV transmission*** after adjusting for maternal HIV-1 viral load and low birth weight, ARR = 2.77 (1.40-5.46)
  - ***Maternal syphilis was associated with intra/post partum HIV transmission*** ARR = 2.74 (1.58-4.74) after adjusting for recent fever, breast infection, low birth weight and maternal HIV-1 viral load

Characteristic	*In utero* HIV-1 MTCT [ARR (95% CI)]	*P*	Intrapartum/postnatal HIV-1 MTCT [ARR (95% CI)]	*P*
Syphilis infection				
No	Reference		Reference	
Yes	2.77 (1.40–5.46)	0.003	2.74 (1.58–4.74)	0.0003
Log_{10} HIV viral load				
< 3.993	Reference		Reference	
3.993 to < 4.547	1.98 (0.63–6.29)	0.24	1.54 (0.64–3.69)	0.34
4.557 to < 5.036	2.77 (0.91–8.40)	0.07	2.41 (1.07–5.43)	0.03
> 5.036	3.80 (1.31–11.02)	0.01	2.62 (1.16–5.90)	0.02
Low birth weight				
No	Reference		Reference	
Yes	1.52 (0.82–2.79)	0.18	1.88 (1.17–3.05)	0.01
Recent fever[a]				
No	NI		Reference	
Yes	NI		1.73 (1.09–2.74)	0.02
Breast infection				
No	NA	NA	Reference	
Yes	NA	NA	2.09 (1.06–4.12)	0.03

[a]Includes women with fever 1 week prior to enrolment and those with temperature > 37.5°C at enrolment. ARR, Adjusted relative risk; CI, confidence interval; NI, variable not included in the multivariate model.; NA, since breast infection was determined at least 6 weeks postnatally, this variable was not assessed as a predictor of *in utero* HIV-1 MTCT.

Mwapasa et al. AIDS 2006;20:1869-1877.

What is elimination?

- *Eradication* of disease is the abrogation of disease throughout the world
  - For example, small pox & polio

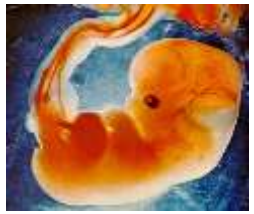
- *Elimination* of disease is the reduction in disease incidence below a threshold of public health importance in a geographic area
  - Current strategies for HIV and syphilis prevention are not sufficiently effective to eradicate disease from the adult population
  - However, elimination of MOTHER-TO-CHILD TRANSMISSION of HIV and syphilis is felt to be feasible

Prevention of mother-to-child transmission of HIV and syphilis infections

Primary Prevention: prevent maternal infection happening

- ***Health education to change sexual behaviors, e.g., condom use***

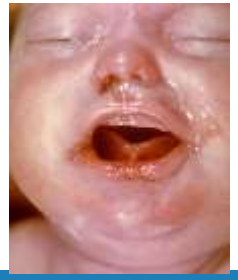
Secondary Prevention: early detect the infection and apply interventions to prevent its transmission to fetus



- ***Screening for infection***
- ***Treatment of infection***

Tertiary Prevention: intervene infections due to the transmission

- ***Testing***
- ***Treatment***
- ***Follow-ups***



The Global Plan towards the Elimination of New HIV Infections among Children by 2015 and Keeping their Mothers Alive

- Global targets
  - Reduce the number of new HIV infections among children by 90%
  - Reduce the number of AIDS-related maternal deaths by 50%
- Four overarching principles for success
  - Women living with HIV at the centre of the response
  - Country ownership
  - Leveraging synergies, linkages and integration for improved sustainability
  - Shared responsibility and specific accountability

The Programme Framework

- Prong 1: prevention of HIV among women of reproductive age
- Prong 2: meeting unmet need for family planning
- Prong 3: For pregnant women living with HIV, ensure HIV testing and counselling and access to ARVs to prevent MTCT
- Prong 4: HIV care, treatment and support for women and children living with HIV and their families

10 point plan for country implementation

1. Conduct strategic assessment of key barriers to EMTCT
2. Develop costed nationally-owned plan for EMTCT
3. Assess available resources for EMTCT and develop a strategy to address unmet needs
4. Implement and create demand for a comprehensive, integrated package of prevention and treatment services
5. Strengthen synergies and integration to improve MCH health outcomes
6. Enhance supply of human resources for health
7. Evaluate and improve access to essential medicines and diagnostics
8. Strengthen community involvement and communication
9. Better coordinated technical support to enhance service delivery
10. Improve outcomes assessment, data quality, and impact assessment

WHO Global Elimination of Congenital Syphilis Initiative

- Objective
  - To eliminate congenital syphilis (ECS) as a *public health problem*
    - Prevent transmission of syphilis from mother to child
- Targets by 2015
  - *Screen >90%* of first ANC attendees for syphilis
  - *Treat >90%* of syphilis-seropositive ANC attendees
- Overarching principles
  - The process should be *country-driven*
  - Integrated approach to *link* with other maternal and newborn health services and sexual and reproductive health initiatives
  - A *rights-based* approach should be applied
  - *Partnership* and collaboration are essential

Available at: http://whqlibdoc.who.int/publications/2007/9789241595858_eng.pdf

The four pillars for Elimination of Congenital Syphilis

I. Ensure sustained political commitment and **advocacy**

II. Increase access to, and quality of, **maternal** and **newborn health services**

III. **Screen** all pregnant women and **treat** all positives

IV. Surveillance, **monitoring** and evaluation systems

Available at: http://whqlibdoc.who.int/publications/2007/9789241595858_eng.pdf

Elimination of MTCT of HIV and syphilis: Why do this together?

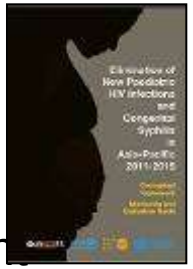
- Both are *sexually transmitted infections* that cause substantial global health burden to *mothers and infants*
  - *Prevention* in general population underlies success
- Both have evidence-based, scalable interventions using *ANC platform*
  - *Early access to ANC*
  - *Early testing*
- Both have *affordable point-of-care tests* feasible for use in basic settings
  - *Prompt test results & treatment,* ideally **"STAT"** (*Same-visit Testing and Treatment*)
  - *Testing at all ANC facilities* - not just those with laboratory capacity
- Both require *reaching out to partners* of pregnant women
- Comprehensive services may be more attractive to women
  - Preliminary evidence from Zambia & Uganda suggested positive impact on HIV testing, ARV, and referral when dual testing provided*

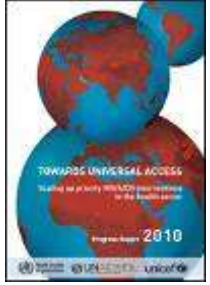
***Source: Strasser et al, 2012.**

WHO Integrated Strategy

- **Advocacy**
  - Pro-active support for dual elimination of MTCT of HIV & syphilis
  - Regional initiatives for dual elimination: Americas, Asia/Pacific, Africa
  - **Programmatic**

    -- Pilot projects to assess impact of integrated services on pregnant women & their partners
  - Work with *priority countries*
    - Identify in-country partners, strengthen policy support , procurement processes and laboratory supply chain
  - Increase quality & coverage of antenatal care
  - Coordinated country support for dual screening to prevent infection
    - Encourage procurement of syphilis tests through PEPFAR, Global Fund
    - Integrate training & guidelines for health workers
    - Jointly strengthen pharmacy/laboratory supply chain & QA systems
    - Support field trials of dual rapid HIV/syphilis tests



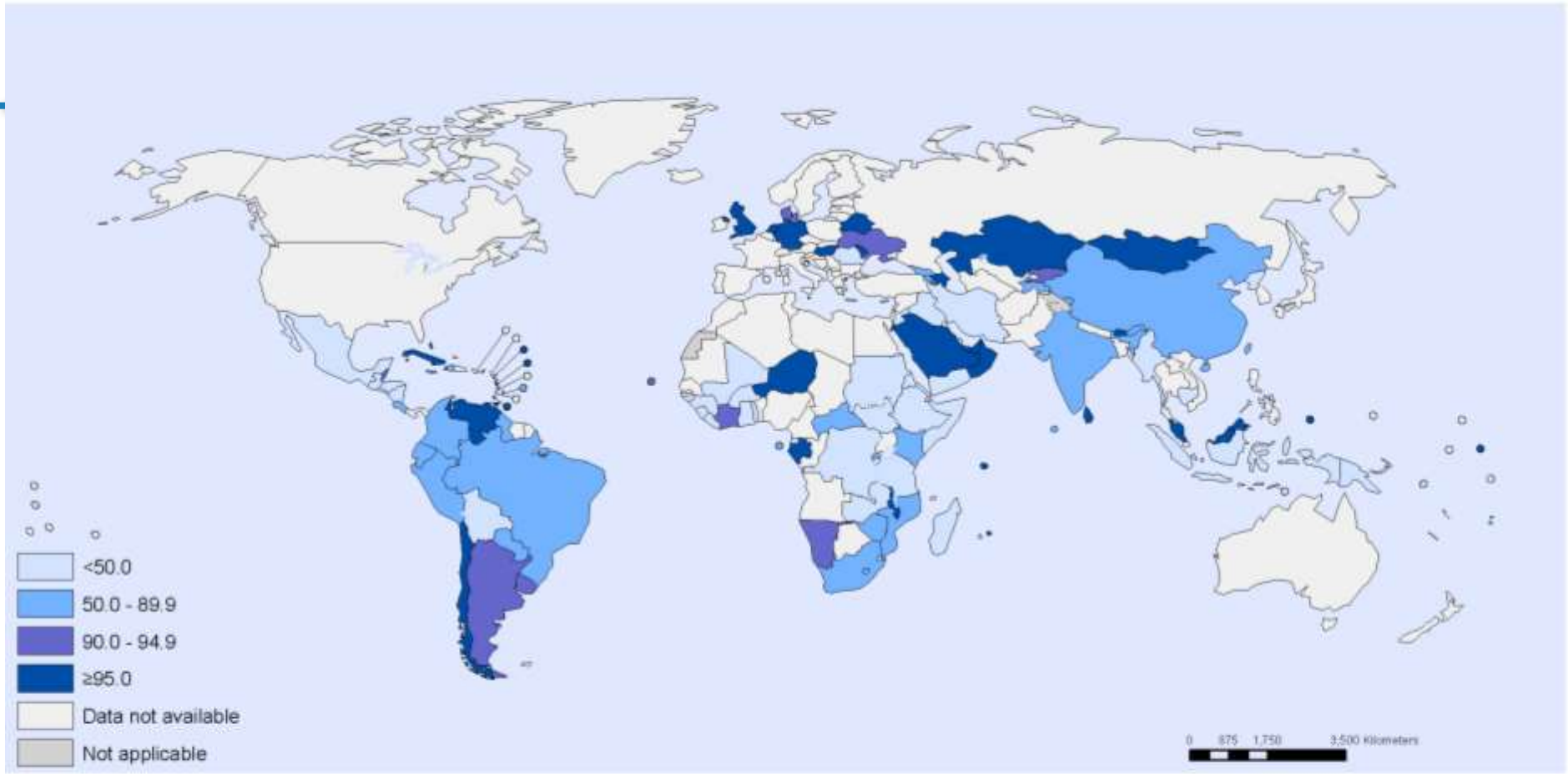


WHO Integrated Strategy

- **Surveillance & monitoring**
  - Lead global process to identify criteria and process for validation/certification of elimination of MTCT of HIV and syphilis
    - Motivation to improve quality of data
    - Motivation to reach even the hardest-to-reach populations
  - Improve quality of M&E data for HIV and STI
  - Include STI in agendas for surveillance, M&E trainings
  - Increase availability of data
    - Global database, web, publications

- **Implementation research**
  - Field testing of dual HIV/syphilis rapid tests
  - How to integrate syphilis and HIV interventions within ANC
  - How to optimally measure impact of ECS interventions – similar methods as eMTCT?

Percentage of antenatal care attendees test for syphilis at first visit (latest available data since 2005)



Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

Source: WHO Global Health Observatory: http://apps.who.int/gho/data

Rationale for establishment of process for validation of EMTCT of HIV and syphilis

- EMTCT Global Plan has been launched and countries are *scaling up* efforts
- Several countries may have *successful programs* to eliminate MTCT of HIV and/or syphilis.
- Currently there is *no standardized process and criteria* to assess and validate EMTCT
- Need credible, systematic approach to allow *monitoring of progress* towards elimination
- Several countries have asked WHO to validate EMTCT achievement
- Successful examples should be celebrated

Global Processes and Criteria for Validation of EMTCT of HIV and Syphilis

- ***Technical consultation*** held 6-8 June 2012
  - To identify appropriate and feasible criteria & processes for validation of EMTCT of HIV and syphilis and next steps
- Decision points
  - ***Common process*** to support, but not require, DUAL elimination
  - **HIV:** Global Plan is the reference (10 targets)
    - Proposal to add case rate (e.g. 0.5 new child HIV infections per 1,000 live births) to provide an absolute target for high & low burden countries
  - **Syphilis:** consensus on case definition for congenital syphilis
    - Criteria for validation: **95%** ANC1 coverage, **95%** tested, 95% treated, **CS rate <= 50 /100,000 live births**)
  - WHO recommended to serve as Secretariat (global and regional)
  - ***Global guidance*** to be released in Q2 2013
  - Majority of validation dialogue to occur between region and country

Qualifying Requirements to Apply for Validation

1. National-level evidence of **achievement of the EMTCT validation process indicator targets** for two (2) years and **achievement of validation impact indicator targets** for one (1) year

2. Evidence that EMTCT of HIV and/or syphilis has been achieved **in at least one of the lowest-performing sub-national administrative units**

3. Existence of an **adequate "validation standard" national monitoring and surveillance system** that can capture service delivery and outcome data and detect the majority of cases of MTCT of HIV and/or syphilis, from **both** the public and private health sectors

4. Validation criteria must have been met in a manner consistent with basic **human rights considerations**

Box 1
Required indicators for global validation of EMTCT of HIV and/or syphilis

HIV
Impact indicators
Mother-to-child transmission (MTCT) HIV case rate of ≤50 new paediatric HIV infections per 100 000 live births
MTCT of HIV of <5% in breastfeeding populations
OR
MTCT of HIV of <2% in non-breastfeeding populations
Process indicators
Antenatal care (ANC) coverage (at least one visit) of ≥95%
Coverage of pregnant women who know their HIV status of ≥95%
Antiretroviral (ARV) coverage of HIV-positive pregnant women of ≥90%

Congenital syphilis
Impact indicator
Incidence of congenital syphilis ≤50 cases per 100 000 live births
Process indicators
ANC coverage (at least one visit) of ≥95%
Coverage of syphilis testing of pregnant women of ≥95%
Treatment of syphilis-seropositive pregnant women ≥95%

Box 3
Summary of procedures for EMTCT of HIV and/or syphilis

Country pre-validation	• MOH submits a validation request to the regional secretariat. • MOH and the RVC jointly establish an NVC. • NVC decides whether to establish an NVT. • NVC (or NVT where active) collects, assesses, and summarizes national data for pre-validation report. • NVC reviews pre-validation report and submits to the RVC.
Country validation	• RVC selects RVT for each candidate country. • RVT reviews country pre-validation report. • RVT and NVT conduct in-country validation visit and interviews with key stakeholders. • RVT prepares and submits national validation report to the regional secretariat.
Regional validation	• Regional secretariat convenes RVC. • RVC reviews national validation report for compliance with minimum regional and global criteria. • If approved, RVC prepares and submits regional validation report to the global secretariat. • If not approved, RVC notifies NVC and provides clear recommendations.
Global validation	• Global secretariat convenes GVC. • GVC reviews regional validation report for compliance with minimum global criteria. • GVC prepares global validation report and submits to global secretariat.
Official validation	• Global secretariat issues letter officially notifying the candidate country of validation status and recommending follow-up actions for maintenance of validation status.
Maintenance of validation	• Global secretariat monitors maintenance of validation indicators through existing annual global reporting systems. • Global secretariat reports any concerns noted to RVC for follow-up and more in-depth assessment.

Summary of opportunities to promote dual elimination

- Advocacy
  - Pro-active support for dual elimination of MTCT of HIV & syphilis
- Improving early access to quality ANC services
  - Pilot projects/IR to assess impact of integrated services on pregnant women & their partners
- Coordinated country support for dual screening to prevent infection
  - Integrate training & guidelines for health workers
  - Jointly strengthen pharmacy/laboratory supply chain & QA systems
  - Support field trials of dual rapid HIV/syphilis tests and other promising tools
- Strengthen surveillance, monitoring, & evaluation
  - Overtly include STI in agendas for surveillance, M&E trainings
  - Improve methods for assessment impact of elimination
- Identify countries ready to request validation of elimination

Questions?

For more information: newmanl@who.int

Acknowledgments: Nathalie Broutet, Xiang-Sheng Chen, Sarah Hawkes, Mary Kamb, Gabriela Gomez, Jeffrey Klausner

www.who.int/reproductivehealth/topics/rtis/syphilis/en/index.html