A Decade of Progress in Global Congenital Syphilis Elimination, 2007 - 2016

Mary Kamb¹, Melanie Taylor¹,², Lori Newman¹,², Sarah Hawkes³, Nathalie Broutet¹

¹. CDC, Division of STD Prevention, Atlanta
². WHO, Department of Reproductive Health Research, Geneva
³. University College London, London
Global Elimination of Congenital Syphilis (CS)

After years of discussion with global experts and >3 years preparation of a Rationale and Strategy, in 2007, WHO and partners launched global elimination of congenital syphilis (CS) as a public health problem using justifications of:

- SEVERE & COMMON CONDITION
- COST EFFECTIVE INTERVENTION
- PROGRAMATICALLY FEASIBLE
- FIT GLOBAL CONTEXT
- REGIONAL EXAMPLE
Rationale and Strategy for Global CS Elimination is based on 4 pillars

I. Ensure sustained political commitment and advocacy

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

III. Screen and treat all pregnant women

IV. Surveillance, monitoring and evaluation systems
The Global Elimination Strategy recognizes the CS prevention cascade, and focuses especially on certain elements.

- **Pregnant women with syphilis**
- **Access ANC**
- **Early ANC**
- ***Syphilis test**
- **Test result**
- ***Treated**
- **Prevent CS**

Syphilis control in a community… *Elimination mathematically impossible at >1% community prevalence*

ANC accessible and affordable, with high 1st visit rates in almost every country… *but not always early enough to prevent CS*

- On-site, point-of-care testing
  - Same-visit testing & treatment (STAT)
  - Any therapy? One dose of penicillin or three? : **At least SD of 2.4 μg IM BPG, ideally before 24 weeks gestation**
  - Partner notification to avoid reinfection
  - Screening at delivery if high risk, high prevalence

*Reporting indicator data to GAM*
**STEP 2: Identifying Key Collaborating Partners**

**WHO HQ and Regional Offices**
- Coordinate overall and regional vision and implementation of the initiative
- Define evidence base for interventions
- Provide technical support

**Special Program for TDR**
- Support development, evaluation & scale up of ASSURED diagnostics

**UN Agencies**
- Support implementation, scale-up, capacity-building and logistics management
- Support countries to integrate adequate programmes into national budgets (costing, budgeting)
- Support advocacy for women, linkages between programmes (STI, HIV, MCH and sexual and reproductive health programmes)

**CDC**
- Synthesizing background evidence, implementation research
- Technical support to WHO
- Monitoring & evaluation of global progress

**Health Ministries**
- Commitment, implementation, reporting of data, validation of elimination

**Academic Institutions**
- Synthesizing background evidence, implementation research, evaluation of tools

**Foundations, NGOs & Consortia**
- Support special evaluations & assessments, implementation research
- Studies addressing critical research and operational questions
STEP 3: Develop rigorous baseline estimates of global Congenital Syphilis

- Rigorous estimates based on country reports and backed-up by representative survey data identified on systematic reviews
- Included newly published data on transmission risk (systematic meta-analysis results)
- Took into account previously treated infections, ANC attendance and CS cases averted by programs
- Reviewed by CHERG and IHME mathematicians

RESEARCH ARTICLE
Global Estimates of Syphilis in Pregnancy and Associated Adverse Outcomes: Analysis of Multinational Antenatal Surveillance Data
Lori Newman, ML Kamb, S Hawkes, G Gomez, L Say, A Seuc, N Broutet
Step 4: Develop the Necessary Guidance, Criteria and Processes and Tools

Agreement for Joint Validation of EMTCT of HIV & Syphilis using similar processes and criteria (2012)
STEP 5: Collecting key indicator data for Elimination of Congenital Syphilis using existing HIV Surveillance Systems

Global AIDS Response Progress Reporting (GARPR), renamed Global AIDS Monitoring system (GAM) in 2016

Negotiated inclusion of 4 CS program & impact indicators reported by countries starting in 2008

1. % of ANC attendees tested for syphilis
2. Syphilis sero-positivity in ANC attendees
3. % syphilis seropositive ANC attendees treated
4. Congenital Syphilis case rate*

* Earlier lack of consistency on CS surveillance case definition has improved over time with publication of EMTCT guidance in 2014 and 2017
UNAIDS GAM: Nationally-reported CS Data: Publicly available on the WHO Global Health Observatory

Interactive and Static Maps

- Static maps on (1) ANC seropositivity, (2) ANC screening coverage, (3) treatment coverage – updated yearly
- Interactive maps
- Country data on 4 indicators over time (since 2008)
- [http://apps.who.int/gho/data/?theme=main](http://apps.who.int/gho/data/?theme=main) under STIs

Investment Case Target Countries (12 + 2)

- Bangladesh
- CAR
- China
- Ghana
- Honduras
- India
- Indonesia
- Madagascar
- Mozambique
- Myanmar
- Papua New Guinea
- Tanzania
- Uruguay
- Zambia
STEP 7: Advances in practical syphilis testing technologies in low income settings

- Developing & evaluating rapid diagnostics that are ASSURED
- Standardized guidance and algorithms
- Training workshops & tools
- Field evaluations studies
- Ensuring quality of tests and testing
- Scaling up dual HIV/syphilis tests in ANC
STEP 8: Updating global guidance on management of syphilis in pregnancy, congenital syphilis

- Updated guidance on managing syphilis in pregnancy
  - Recommended screening
  - Use of penicillin to ensure treatment of the fetus
  - Recognition of global penicillin shortages
  - Clarification on treatment of exposed infants
  - Identification of challenges to using IM penicillin in some regions
  - Evaluating alternative treatment
STEP 9: Criteria and Processes for Validation of EMTCT of HIV and syphilis

- In 2014, 1st guidance establishing criteria & processes for validation of EMTCT of HIV & syphilis (Orange Book)
  - For Congenital Syphilis, 2+ years of quality data establishing
    - > 95% ANC attendance
    - >95% maternal syphilis screening in ANC
    - >95% of positive cases “adequately” treated
    - CS case rate < 50 per 100,000 live births
    - Evidence of program quality even in low performing/high burden areas

- In 2017, updated Orange Book
  - Clarification of certain areas and/or tools
    - CS surveillance case definition
    - Concrete guidance on laboratory quality and human rights, gender and community involvement
  - Establishment of Path to Elimination
STEP 10: Expanded utilization of integrated platforms for service delivery and monitoring

- UNAIDS: Global AIDS Monitoring
- US PEPFAR
- Countdown 2030
- RMNCAH platforms
- Technology: rapid dual HIV/syphilis tests
- Universal Health Care (UHC)
- Gender Equality and Human rights

http://www.who.int/reproductivehealth/test/Linkages-STIs-HIV.pdf?ua=1
Regional EMTCT Successes

Americas Region (PAHO)

• A pioneering region supporting ECS since 1995
• In 2017, renewed commitment to improve and expand through “EMTCT Plus”, leveraging MCH platform to eliminate preventable conditions including MTCT of HIV, syphilis, hepatitis B and Chagas.
Regional EMTCT Successes

Asia-Pacific Region (WPRO/SEARO)

• Several committed countries, including Thailand (1st country in region to achieve elimination in 2016) and China (accounts for many cases globally due to large population)

• In 2017, the WPRO member states endorsed Asia Pacific Regional Framework for Triple EMTCT of HIV, Hepatitis B and Syphilis 2018-2030,
Regional EMTCT Successes

- Africa Region (AFRO)
  - Contributes largest numbers globally, still low coverage of testing and treatment
- “Path to Elimination”
  - Recognition of high burden countries that have made significant progress on the path to elimination for EMTCT of HIV, syphilis or both
Program Data: Antenatal syphilis testing coverage in priority countries, 2008 and 2016

Key CS Elimination Indicator:
Coverage of syphilis testing in ANC > 95%

* Data not reported in 2008 or 2016, thus closest data point used
Program Data: Treatment coverage among syphilis-seropositive pregnant women in priority countries, 2010 and 2016

**Key CS Elimination Indicator:**
Treatment coverage in positive mothers ≥ 95%
(IM benzathine penicillin)

* Data not reported in 2010 and/or 2016, thus closest data point used
Draft 2016 Congenital Syphilis Case Estimates
(with recalculation of 2012)

Draft 2016 CS-Related Adverse Birth Outcome Estimates (with recalculation of 2012)

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ANC-tested and treated
ANC-tested but not treated
In ANC, not tested
Not in ANC

Interim analysis:
Percentage of ANC attendees positive for syphilis, 2016

- 1.04 million pregnant women with syphilis
- 368,000 adverse birth outcomes (ABOs)
The Ultimate Prize: Validation of EMTCT of Syphilis

10 Countries

- 2015
  - Cuba

- 2016
  - Thailand
  - Belarus
  - Moldova

- 2017
  - Anguilla
  - Antigua & Barbuda
  - Bermuda
  - Cayman Islands
  - Montserrat
  - St. Christopher & Nevis

- 2018
  - 4 countries in pipeline
Step-by-step progress toward elimination of MTCT of syphilis as a public health problem

- **Clear progress in several areas**
  - Establishment of CS surveillance, testing quality and coverage, elimination benchmarks and validation framework
  - Integration with HIV and MNCH programs and partners
  - Elimination as a public health problem in 10 countries

- **Challenges to EMTCT of syphilis over the next decade**
  - CS is still low on political agendas (particularly compared with HIV)
  - Logistical challenges (e.g., penicillin shortages, lack of test kits)
  - Still very little progress in Africa, the region with highest burden
  - Maternal syphilis prevalence (0.71% > 0.73%), minimal declines in CS
First step: Global Call to Action

“We largely know what to do to prevent congenital syphilis And we have had the tools to do this for decades…

The problem is simply doing it.”

George Schmid, 2005
EXTRA SLIDES
What concrete progress has been made in reducing the global burden of Congenital Syphilis?

Process and Impact data

Program data/Surveillance

- Country reports on 4 CS Indicators
- Interactive maps updated annually

- **Global Estimates**
  - Modeled data based on country-reports to GAM and available data from published and unpublished ANC and population-based surveys
  - Congenital syphilis estimation tool

- **Data from Candidate Countries for Elimination**
  - Country Reports
  - Regional Validation Team/Committee Reports/Include CS case rates
Program Data: Antenatal syphilis testing coverage in priority countries, 2008 and 2016

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Global Elimination of Congenital Syphilis

We have no vaccine against syphilis. We are unlikely to stop transmission in any region.

Why call this “elimination” and not simply better control?

Because a spotlight was, and is still, needed

- CS is grossly underestimated in global estimates
- While universally recommended, syphilis testing in pregnancy is still not done in high-burden countries
- MNCH focus of the MDGs offered opportunity to refocus on CS, a low-hanging fruit causing substantial, preventable stillbirths, neonatal & infant deaths
- Rapid syphilis testing offered new options for settings with limited lab capacity
- “Elimination” is a goal that inspires and excites countries, partners and funders... and strengthens overall MCH services
STEP: Better understanding of prevalence and risk of MTCT of syphilis compared with MTCT of HIV: Potential synergy?

Estimated New Congenital Syphilis Cases versus HIV Cases Age < 15 Years, by Region, 2006

*Klausner J, Schmid G, Stoner B, Hawkes S, Broutet N. ISSTDR, 2007*
Revised (Baseline) estimates on syphilis in pregnancy and resulting adverse birth outcomes, 2008

- 1.36 million pregnant women with syphilis
- 521,000 adverse birth outcomes (ABOs)

Syphilis seropositivity among ANC Attendees, 2008

- >= 5%
- >= 1.0 to 4.9%
- >= 0.5 to 0.9%
- <= 0.5%
- data not available
Some key findings of 2008 estimates of syphilis in pregnancy and adverse birth outcomes (ABOs)

Lack of adequate services in ANC

- Among 1.36 million pregnant women with syphilis, 80% attended at least 1 ANC visit
- 66% of ABOs were in ANC attendees not tested or treated
- Clinical services likely averted only 26% of all ABOs

Substantial morbidity/mortality were usually not recognized as due to syphilis

- 521,000 ABOs per year due to untreated syphilis
  - 212,000 stillbirths
  - 92,000 early neonatal deaths
  - 65,000 preterm/LBW infants at risk for death
  - 152,000 infected newborns
  - 304,000 deaths
Global Congenital Syphilis Elimination: Step-by-step, several early challenges have been met.

Important Early Steps

- Increasing recognition of burden and severity
- Showing that CS control & elimination is programmatically feasible
- Identifying funding or other means of supporting programs
- Operationalizing congenital syphilis elimination
  - Setting program standards and norms
  - Setting global targets
  - Ensuring surveillance of key variables
  - Ongoing monitoring & evaluation to ensure coverage and quality of programs – especially in highest burden countries
STEP: Collaborations with trusted stakeholders: Getting the word out that syphilis in pregnancy causes catastrophic – but PREVENTABLE – health outcomes

Estimated infant deaths annually (2008):
- HIV: 440,000
- Syphilis: 300,000
- Neonatal tetanus: 168,000
- Malaria: 150,000

- Inclusion of CS in global estimates of adverse birth outcomes
- Syphilis screening/treatment in pregnancy included in “Lives Saved Tools”
- Inclusion of CS within the Lancet Stillbirth Series
Impact Data: Congenital Syphilis Case Rates in 14 Priority Countries, 2016

CS surveillance case definition:
- Live or stillborn infant born to a seropositive pregnant woman who did not receive adequate treatment at least 30 days prior to delivery, OR
- An infant or child < 2 years with clinical, radiographic or laboratory data consistent with CS

Adequate treatment is at least 2.4 μg IM benzathine penicillin G (single dose)

- **Target: CS case rate ≤ 50 per 100,000 live births (LB)**
- **4 of 14 priority countries have reported CS case rates**
  - **Honduras**: 16.4 in 2016 (unclear quality of data, per PAHO, case definition not aligned)
  - **China**: 61.6 in 2014 and 40.7 in 2015 (believed high quality data using WHO case definition)
  - **Uruguay**: 233.6 in 2015 (believed adequate quality data using WHO case definition)
  - **Mozambique**: in 2014: 417.5 (unclear quality of data or alignment of case definition)
Global maternal syphilis infections, adverse pregnancy outcomes, and perinatal deaths in 2008, 2012 and 2016 interim analyses

Number of countries reporting data

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<td>122</td>
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Cases in thousands

- Maternal Syphilis Infections (in thousands)
- Adverse Pregnancy Outcomes (in thousands)
- Perinatal Deaths (in thousands)
- CS case rate per 100,000 LBs