



# Sexually transmitted infections in pregnancy

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## Global burden of curable STIs (1)

- **WHO estimates:** 357 million new cases of curable STIs in 2012 (**chlamydia, syphilis gonorrhea, trichomoniasis**)
- Every day **more than 1 million STIs** are acquired
- The majority of STIs have **no or mild symptoms**
- **Lack of recent data** on curable STI prevalence among pregnant women in many parts of the world



## Combined evaluation of sexually transmitted infections in HIV-infected pregnant women and infant HIV transmission.

Adachi K<sup>1</sup>, Xu J<sup>2</sup>, Yeganeh N<sup>1</sup>, Camarca M<sup>2</sup>, Morgado MG<sup>3</sup>, Watts DH<sup>4</sup>, Mofenson LM<sup>5</sup>, Veloso VG<sup>3</sup>, Pilotto JH<sup>6</sup>, Joao E<sup>7</sup>, Gray G<sup>8</sup>, Theron G<sup>9</sup>, Santos B<sup>10</sup>, Fonseca R<sup>11</sup>, Kreitchmann R<sup>12</sup>, Pinto J<sup>13</sup>, Mussi-Pinhata MM<sup>14</sup>, Ceriotta M<sup>15</sup>, Machado DM<sup>16</sup>, Bryson YJ<sup>1</sup>, Grinsztejn B<sup>3</sup>, Move J<sup>17</sup>, Klausner JD<sup>1,18</sup>, Bristow CC<sup>19</sup>, Dickover R<sup>20</sup>, Mirochnick M<sup>21</sup>, Nielsen-Saines K<sup>1</sup>; NICHD HPTN 040 Study Team.

- **899 mother-infant pairs from Argentina, Brazil, South Africa and USA: 30% with a STI at delivery**  
-> ***C. trachomatis* (17.8%), *T. pallidum* (8.7%), *N. gonorrhoeae* (4%)**

## Sexually Transmitted Diseases Among Pregnant Women: 5 States, United States, 2009-2011.

Williams CL<sup>1,2</sup>, Harrison LL<sup>3</sup>, Lata E<sup>4</sup>, Smith RA<sup>3</sup>, Meites E<sup>4</sup>.

- **Self-reported data from 12,948 pregnant women -> 3.3% with 1 or more curable STIs: *C. trachomatis* (2.4%), *N. gonorrhoeae* (0.5%), *T. pallidum* (0.2%)**
- **Risk factors:** <25 yo, black, unmarried, no college education, no health insurance, income < \$25,000 py

# Guidelines for STI screening in pregnancy

Tick the right answers:

1. WHO recommends screening during pregnancy for HIV, syphilis, chlamydia and gonorrhoea.
2. WHO recommends screening during pregnancy for HIV and syphilis only.
3. WHO recommends a syndromic approach for STI during pregnancy.

# Guidelines for STI screening in pregnancy (1)

**WHO:** no clear screening guidelines and policies for STI in pregnancy, other than for syphilis and HIV.

Country	Type	Pregnant women
<b>Syphilis</b>		
Europe, USA, Canada	systematic	- Serological screening early in pregnancy (1 <sup>st</sup> trimester) - Retest early in the third trimester and at delivery if at high risk
WHO	systematic	1 <sup>st</sup> antenatal care visit screening
<b><i>C. trachomatis</i> and <i>N. gonorrhoeae</i></b>		
France		Not recommended or not specified
Europe		Not specified

## Guidelines for STI screening in pregnancy (2)

Country	Type	Pregnant women
<b><i>C. trachomatis</i> and <i>N. gonorrhoeae</i></b>		
USA, Canada	systematic	<p><b>CT</b></p> <ul style="list-style-type: none"> <li>- All women &lt;25 yo (1st antenatal visit)</li> <li>- Women 25 and older if at increased risk</li> <li>- Retest during the 3rd trimester for women &lt;25 yo or at risk</li> <li>- Test-of-cure 3-4 weeks after treatment and retest within 3 months</li> </ul> <p><b>NG</b></p> <ul style="list-style-type: none"> <li>- All women &lt;25 yo and older women if at increased risk (1st antenatal visit)</li> <li>- Retest 3 months after treatment</li> </ul>
WHO		<ul style="list-style-type: none"> <li>- Screening not recommended</li> <li>- Syndromic approach</li> </ul>

# Antenatal syphilis

Tick the right answers:

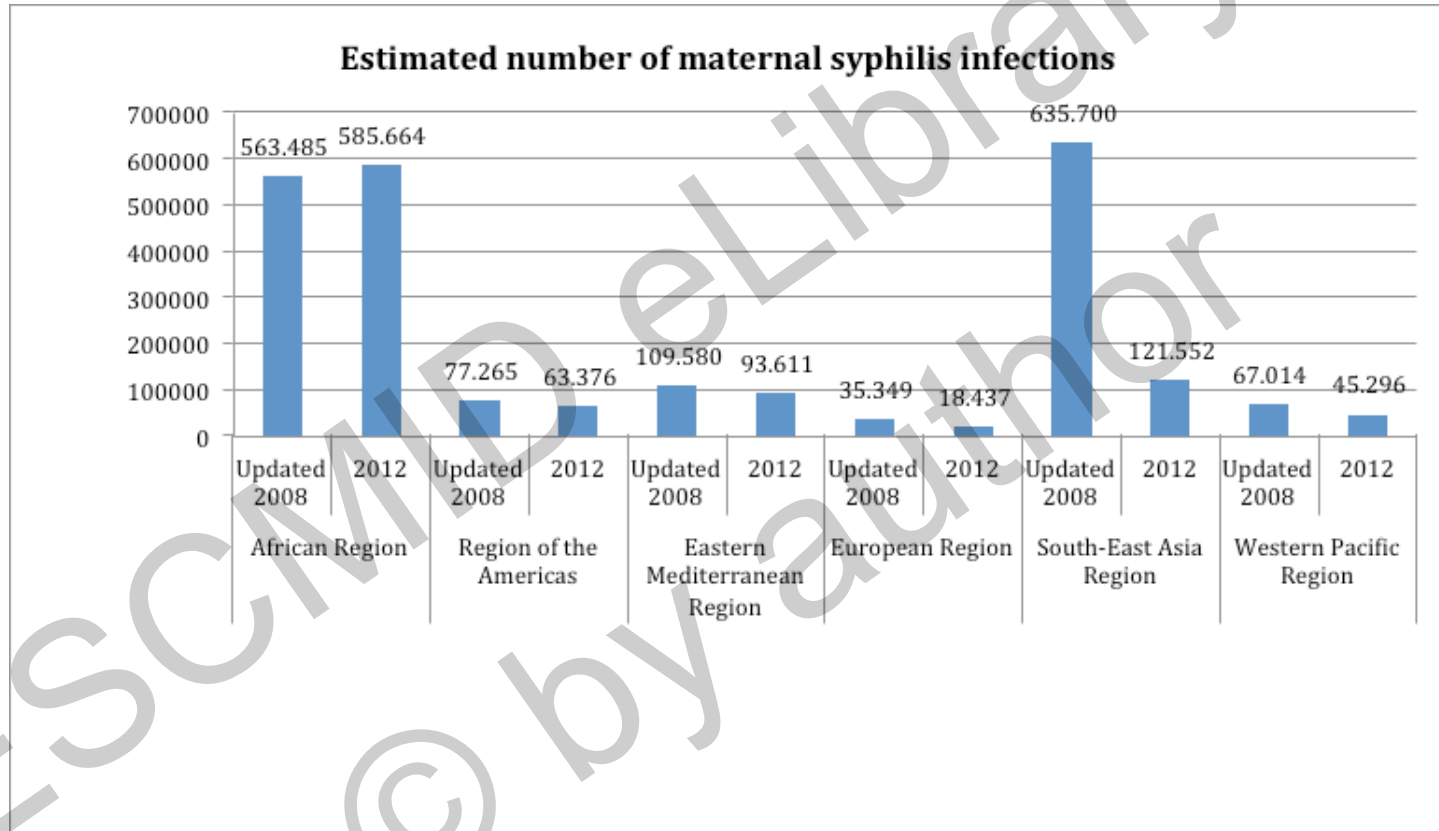
1. **>70% of infants are infected in case of untreated maternal syphilis.**
2. **According to the WHO report on global STI surveillance, the median syphilis prevalence is 7% in the reporting countries.**
3. **Early syphilis is treated by benzathine penicillin 2.4 million unit IM once weekly for 3 consecutive weeks.**

# Antenatal syphilis (1)

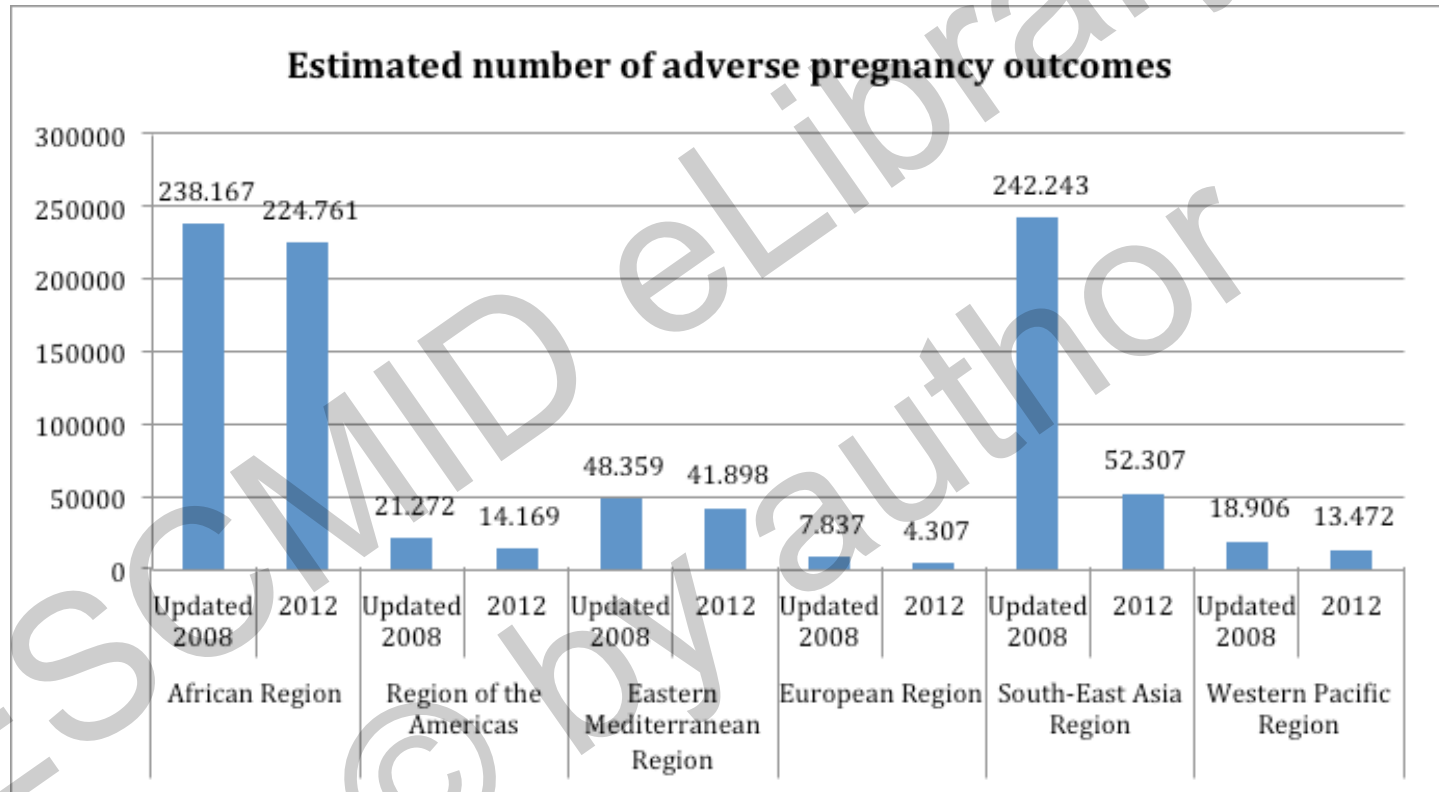
- **Pregnant women with untreated early syphilis:** 70-100% of infants infected with stillbirths in 30% of cases.
- **Pregnancy outcomes:** fetal deaths, still birth, neonatal deaths, preterm/low weight births, infected infants.
- **WHO:**
  - 2012: estimated 930,000 maternal syphilis infections resulted in 350,000 adverse pregnancy outcomes.
  - 90% of maternal infections and adverse outcomes in low-and middle-income countries.
  - Antenatal syphilis screening coverage increased globally.
  - Syphilis seropositivity among pregnant women decreased by 50% between 2008 and 2014.



# Antenatal syphilis (1)



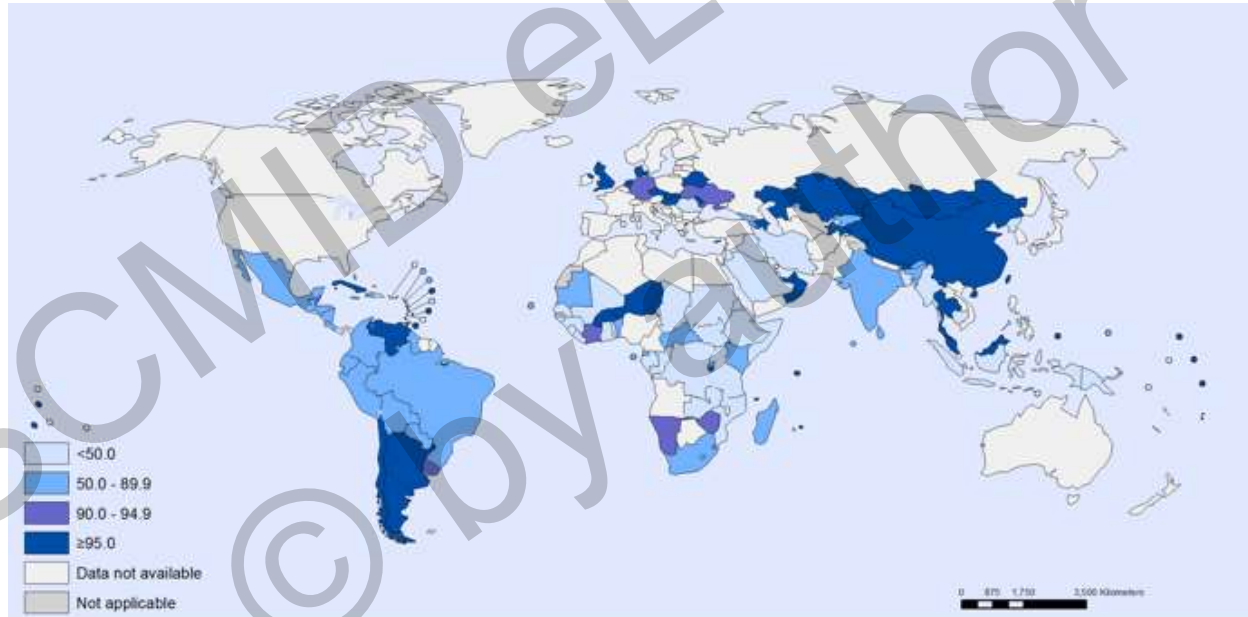
# Antenatal syphilis (1)



## Antenatal syphilis (2)

- WHO, report on global STI surveillance, 2015:
  - 85.5% of ANC attendees tested for syphilis (0.7-100%)

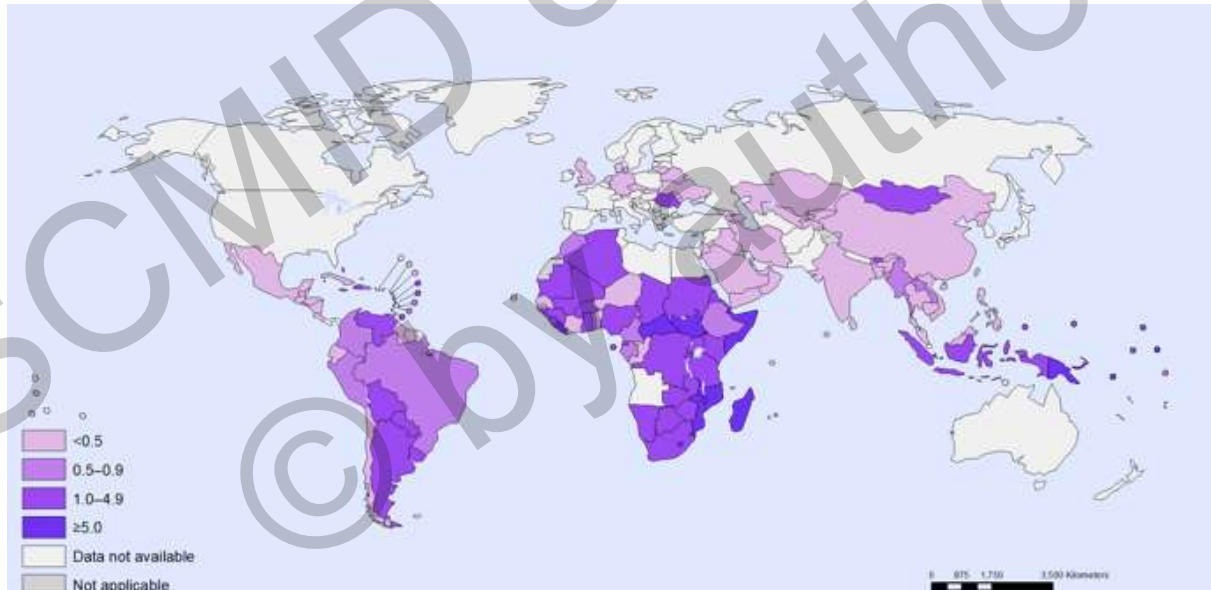
**% of ANC attendees tested for syphilis at 1<sup>st</sup> visit in 2015**



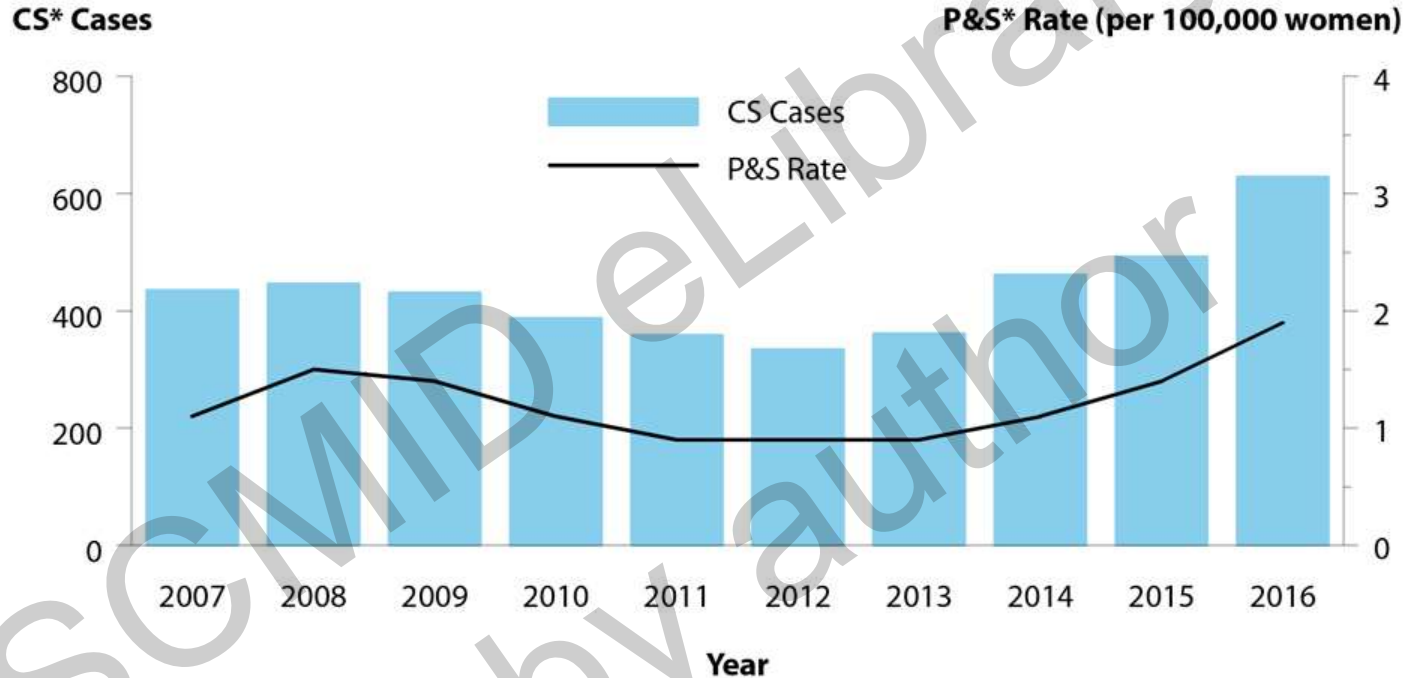
## Antenatal syphilis (2)

- **WHO, report on global STI surveillance, 2015:**
  - 85.5% of ANC attendees tested for syphilis (0.7-100%)
  - Median syphilis prevalence 0.7% (0-13.5%), 45% countries reported more than 1% seroprevalence.

### % of ANC tested positive for syphilis in 2015



- **487 cases of congenital syphilis in 2015 in USA:**  
12 cases for 100,000 live births



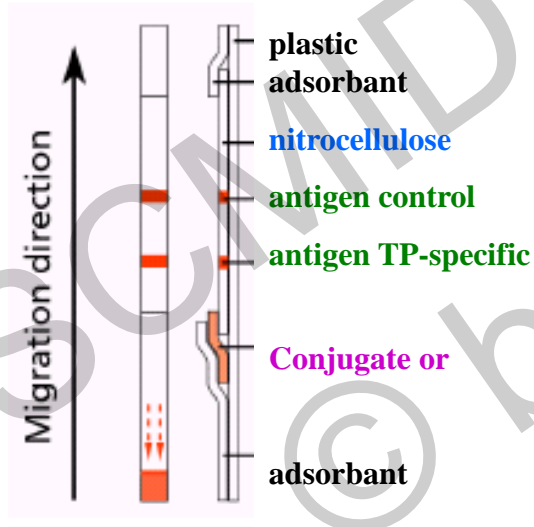
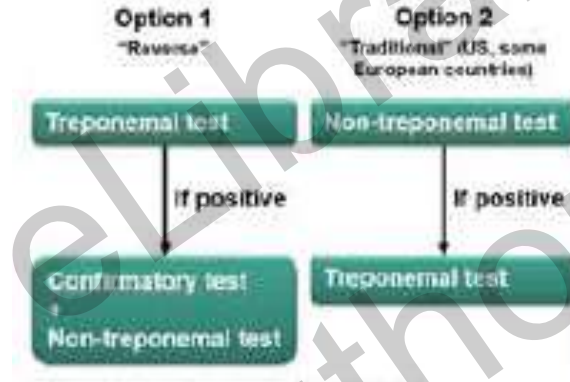
CDC, 2017

- **10-15 cases of CS in France:** <1 case /100,000 live births

# Antenatal syphilis: diagnostic

- Serology +++

- Different algorithms:



- Rapid on-site tests: POC

To increase ANC testing coverage

In settings with low coverage of syphilis screening and treatment for pregnant women

# Antenatal syphilis: treatment

- **WHO, Europe, CDC**
  - **Early syphilis:** benzathine penicillin 2.4 million unit IM single dose
  - **Late or unknown stage syphilis:** benzathine penicillin G 2.4 million units IM once weekly for 3 consecutive weeks
  - **BPG cannot be used:** ceftriaxone 1 g IM once daily for 10 –14 days or erythromycin 500 mg orally 4 times daily for 14 days or azithromycin 2 g once orally

## ***C. trachomatis* and *N. gonorrhoeae* infections during pregnancy**

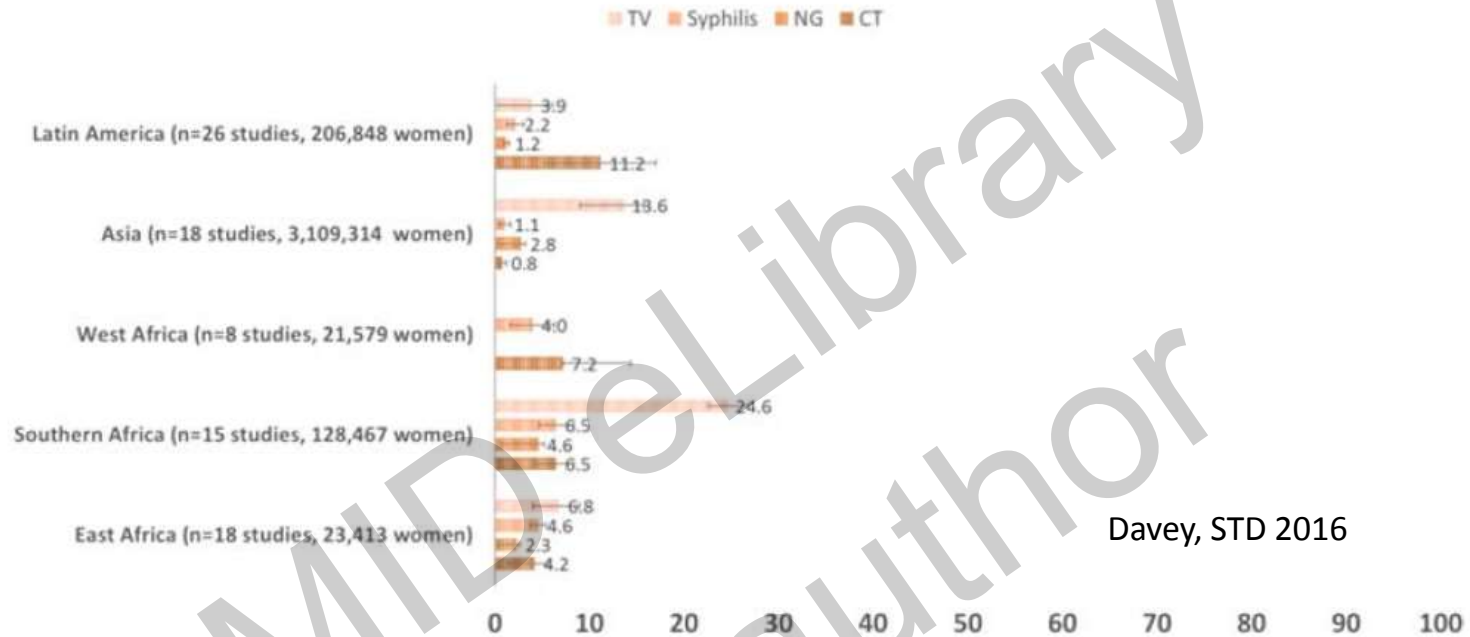
**Tick the right answers:**

- 1. Most of the CT and NG infections are symptomatic in pregnant women.**
- 2. NAATs are widely used for the diagnosis of CT and NG infections.**
- 3. Azithromycin 1g single dose is recommended for the treatment of CT and NG infections during pregnancy.**



## ***Chlamydia trachomatis***

- **>50% *C. trachomatis* infections asymptomatic** during pregnancy in a South African study of 1480 women (Moodley, STD 2015)
- **Pregnant women with untreated chlamydial infections:**  
50-70% of infants infected with:
  - 30-50% developing conjunctivitis
  - 10-20% developing pneumonia
- **Pregnancy outcomes:** miscarriage, still birth, preterm/low weight births, infected infants
- **Worldwide prevalence studies of *C. trachomatis* in pregnant women:**
  - limited data
  - Similar to non pregnant women
  - High in low-resource settings in Sub-Saharan Africa and Asia



Davey, STD 2016

Figure 2. Adjusted mean STI prevalence by region (N=75 studies of STI prevalence among 3,489,621 pregnant women 2010–2015).

- **Australia 2001-2012**, population-based cohort study of 21,267 women tested for *C. trachomatis* during pregnancy (Reekie, Lancet, 2018):  
**6.4% *C. trachomatis* (+)**

- **USA 2005-2008, 1,293,423 pregnant women tested** (Blatt, AJOG 2012):
  - **59% tested at least once for *C. trachomatis***
  - **3.5% *C. trachomatis* (+)**

Matern Child Health J. 2018 Apr;22(4):538-545. doi: 10.1007/s10995-017-2422-9.

### **Sexually Transmitted Diseases Among Pregnant Women: 5 States, United States, 2009-2011.**

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- **Self-reported data from 12,948 pregnant women -> 3.3% with 1 or more curable STI: *C. trachomatis* (2.4%), *N. gonorrhoeae* (0.5%), *T. pallidum* (0.2%)**

# The MATIST project

## Prevalence and risk factors associated with *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and *Mycoplasma genitalium* infections in French pregnant women

Bordeaux University hospital - January to June 2011: 1006 pregnant women

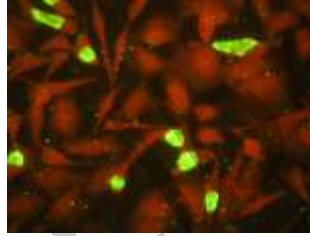
Age (yo)	No. specimens tested	Prevalence of infection with		
		<i>C. trachomatis</i>	<i>M. genitalium</i>	<i>N. gonorrhoeae</i>
18-44	1006	<b>2.5 %</b>	0.8 %	0 %
18-24	166	<b>7.9 %</b>	2.4 %	0 %
25-29	317	1.3 %	0.6 %	0 %
≥ 30	523	1.5 %	0.4 %	0 %

### Risk factors for *C. trachomatis* infection:

- age < 25 yo (OD = 6.7,  $P < 0.001$ )
- single (OD = 4.3,  $P = 0.005$ )
- number of sexual partners > 5 (OD = 6.5,  $P < 0.001$ )

## Diagnostic of *C. trachomatis*

- Intracellular bacteria



- Direct diagnosis

- **NAAT** (real-time PCR, TMA, SDA) +++

High throughput automatized platforms (Roche, Hologic, Abbott, BD, Cepheid, etc.)

Sensitivity and specificity >95%

Dual test *C. trachomatis*-*N. gonorrhoeae*

- **Non invasive specimens:** self-collected vaginal swabs or urines

- **Current available POC tests** not recommended (poor sensitivities):  
optical immunoassays or immunochromatographic tests

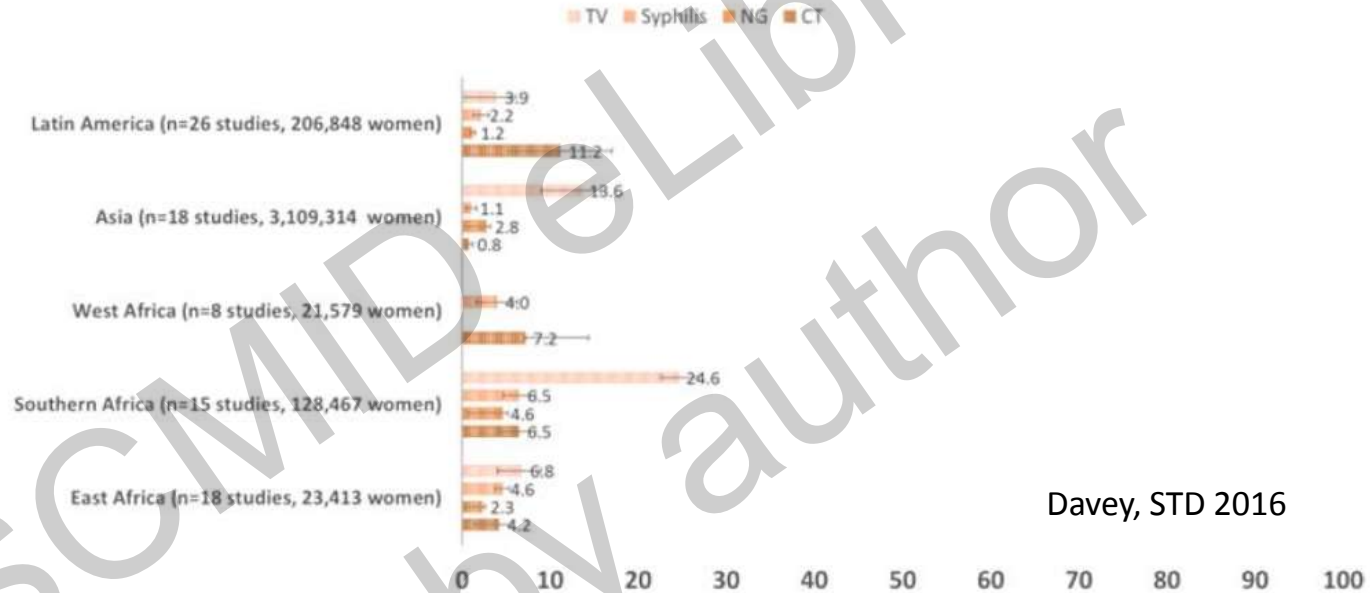
## Treatment of *C. trachomatis* in pregnancy

- **Treatment (Europe, CDC, WHO)**
  - **1<sup>st</sup> line:** Azithromycin 1g orally single dose
  - **Alternatives:** amoxicillin 500 mg 3 times a day for 7 days or erythromycin 500 mg 2 or 4 times a day for 7 days
  - **Test-of-cure recommended in pregnancy:** using NAATs 4 weeks after completion of treatment
- **Topical ocular prophylaxis** for the prevention of gonococcal and chlamydial ophthalmia neonatorum

## *Neisseria gonorrhoeae*

- **Largely asymptomatic infections**
- **Pregnancy outcomes:** spontaneous abortion, still birth, preterm/low weight births, neonatal infections (conjunctivitis, disseminated infection)
- **Worldwide prevalence studies of *N. gonorrhoeae* in pregnant women:**
  - Limited data
  - High in low-resource settings in Sub-Saharan Africa and Asia

# *Neisseria gonorrhoeae*



Davey, STD 2016

Figure 2. Adjusted mean STI prevalence by region (N=75 studies of STI prevalence among 3,489,621 pregnant women 2010–2015).



- **USA 2005-2008, 1,293,423 pregnant women tested** (Blatt, AJOG 2012):
  - **57% tested at least once for *N. gonorrhoeae***
  - **0.6% *N. gonorrhoeae* (+)**

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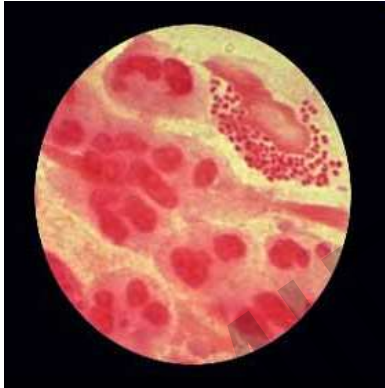
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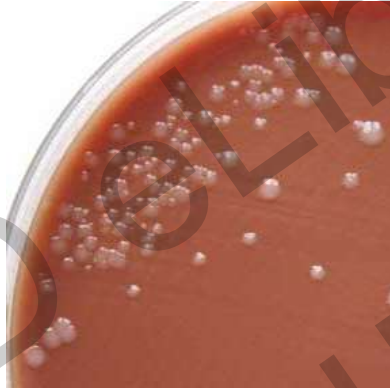
Peuchant, Diagn Microbiol Infect Dis. 2015

# *Neisseria gonorrhoeae*: diagnostic



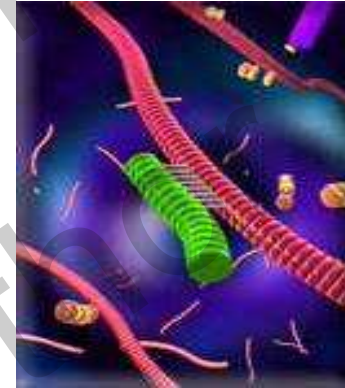
## Microscopy

Rapid  
Poor sens. on vaginal swabs



## Culture

> 2 days  
Symptomatic patients  
Self-collected vaginal swabs, urines  
AST



## NAAT

Sensitivity and specificity >90%  
Asymptomatic patients  
Self-collected vaginal swabs, urines  
Duplex CT/NG

POC immunologic assays not recommended (poor sensitivity)

# Treatment of gonorrhoea in pregnancy

- **Treatment (Europe, CDC, WHO)**
  - **1<sup>st</sup> line:** Ceftriaxone 500 mg IM single dose or  
Ceftriaxone 250 mg IM plus azithromycin 1 g single dose (CDC)
  - **Alternatives:** spectinomycin 2g IM as single dose
  - **Test-of-cure recommended** in all cases to identify persisting infection and emerging resistance
- **Topical ocular prophylaxis** for the prevention of gonococcal and chlamydial ophthalmia neonatorum

## *Mycoplasma genitalium*

- Emerging STI pathogen
- Association between *M. genitalium* and female disease: metanalysis 1980-2014 (Lis et al, Clin Infect Dis 2015)
  - *M. genitalium* infection significantly associated with 2-fold increased risk of:
    - Cervicitis (20 included studies): pooled OR, 1.66
    - PID (10 studies): pooled OR, 2.14
    - Pre-term birth (6 studies): pooled OR 1.89
    - Spontaneous abortion (3 studies): pooled OR 1.82
- Recent metanalysis on the prevalence of *M. genitalium* in different population groups: **pregnant women 0.9%** (4 studies, 3472 women) (Baumann, STI 2018)
- **More research needed for adverse pregnancy outcomes**

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### Risk factors for *M. genitalium* infection:

- Younger age (OD = 9, p = 0.01)
- History of abortion (OD = 8.6, p = 0.01)
- Having 1st sexual intercourse after 20 yo (OD = 7.1, p = 0.03)

## Diagnostic and treatment of *M. genitalium* in pregnancy

- **Diagnostic:** NAAT on non-invasive specimens
- **Treatment (IUSTI Europe, Jensen, JEADV 2016)**
  - a 5-day-course of azithromycin is acceptable
  - **Macrolide-resistant *M. genitalium*:**
    - Pristinamycin is considered safe during pregnancy.
    - Treatment may be considered postponed until after delivery.

# Conclusion

- **Lack of necessary prevalence data on curable STI prevalence** among pregnant women in many parts of the world with still limited focus on CT and NG.
- Continued efforts **to increase ANC testing coverage for syphilis**, especially in African regions.
- Urgent need to elucidate the **necessity of screening and treatment of CT and NG during pregnancy** especially in regions of the world with both a high prevalence of infections and of adverse pregnancy outcomes.
- Necessity to develop **sensitive POC for CT/NG testing**.