

Reflections on 100 years of STD Control and Prevention: What can history teach us about the future?

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Los Angeles STD Summit 2018

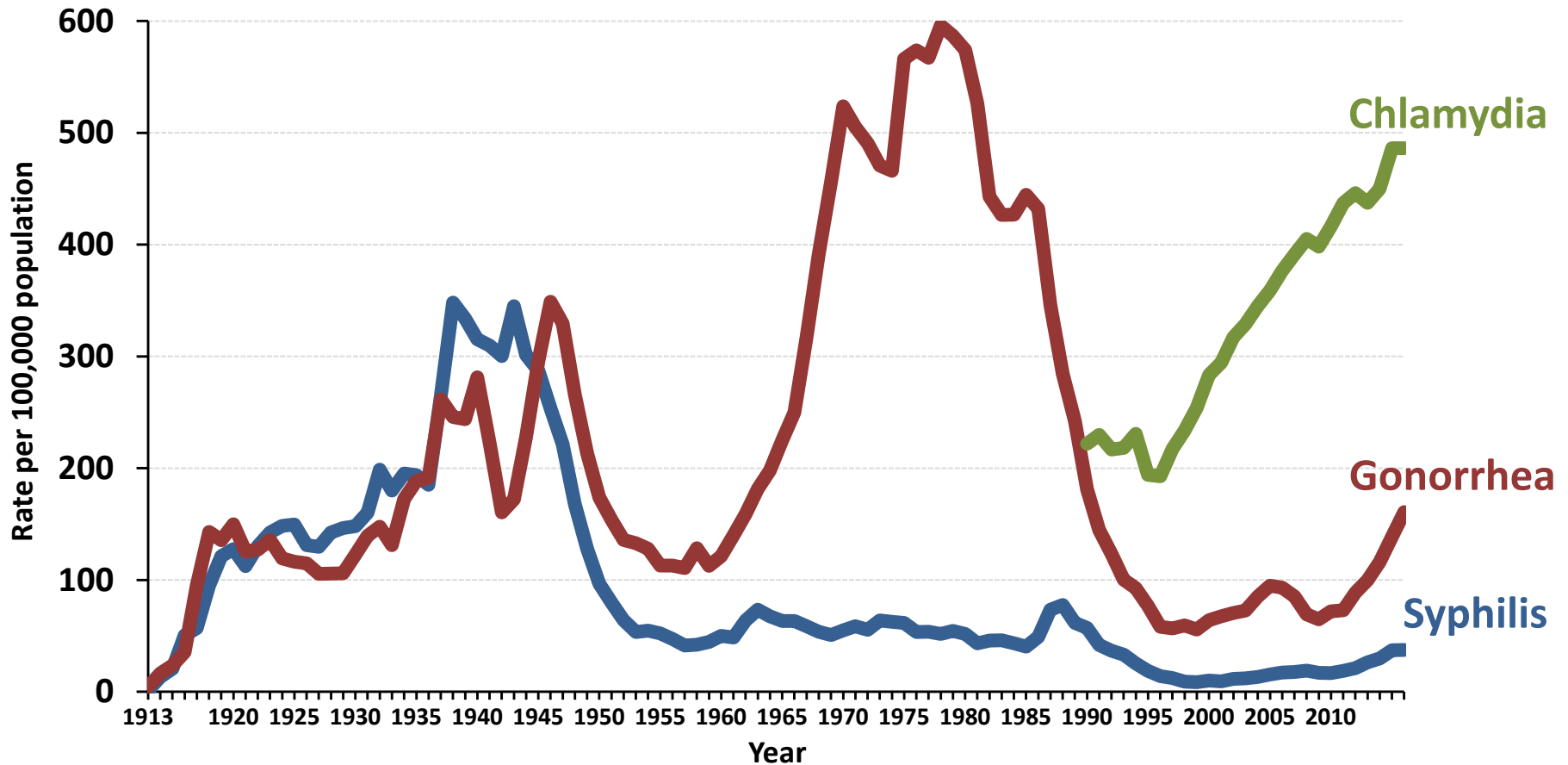
Disclosures

- I have no financial conflicts of interest to declare.
- Reference to product names is not an endorsement.
- This presentation includes off-label uses of diagnostic tests.

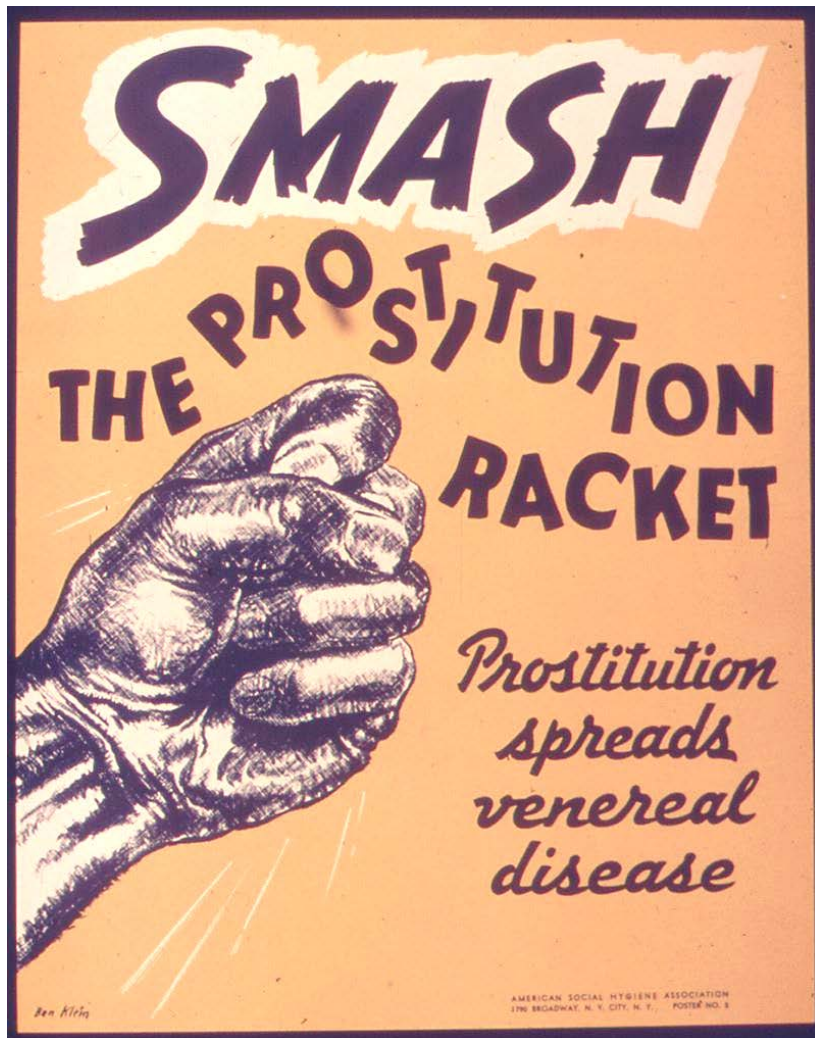
Overview of the Presentation

- Historical recap: the first 100 years
- What STDs share, what they don't
- Public health – health care partnership
key priorities for STD prevention

Syphilis, Gonorrhea and Chlamydia Incidence in California, 1913–2017



Early 20th Century: Pre-Antibiotic Social Hygiene Era



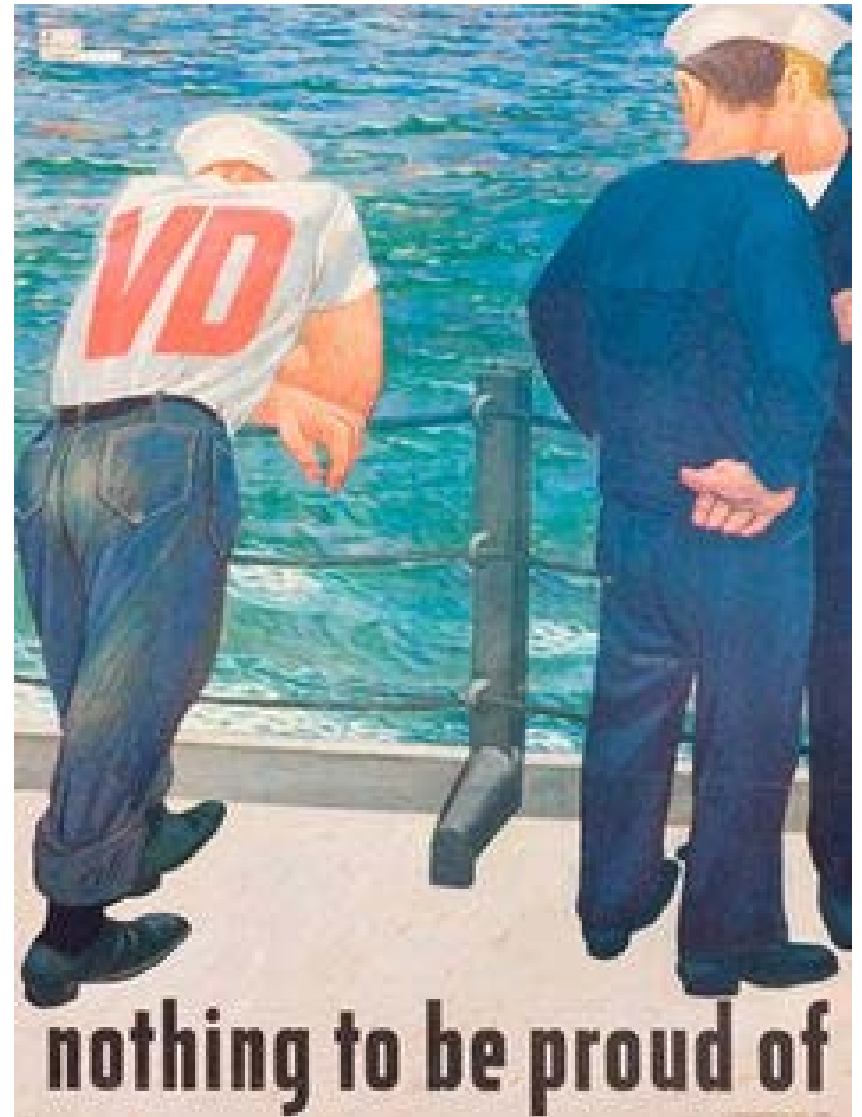


PICK-UPS
"GOOD TIME" GIRLS
PROSTITUTES

SPREAD SYPHILIS AND GONORRHEA

You can't beat the Axis if you get VD

VDgraphic - 9



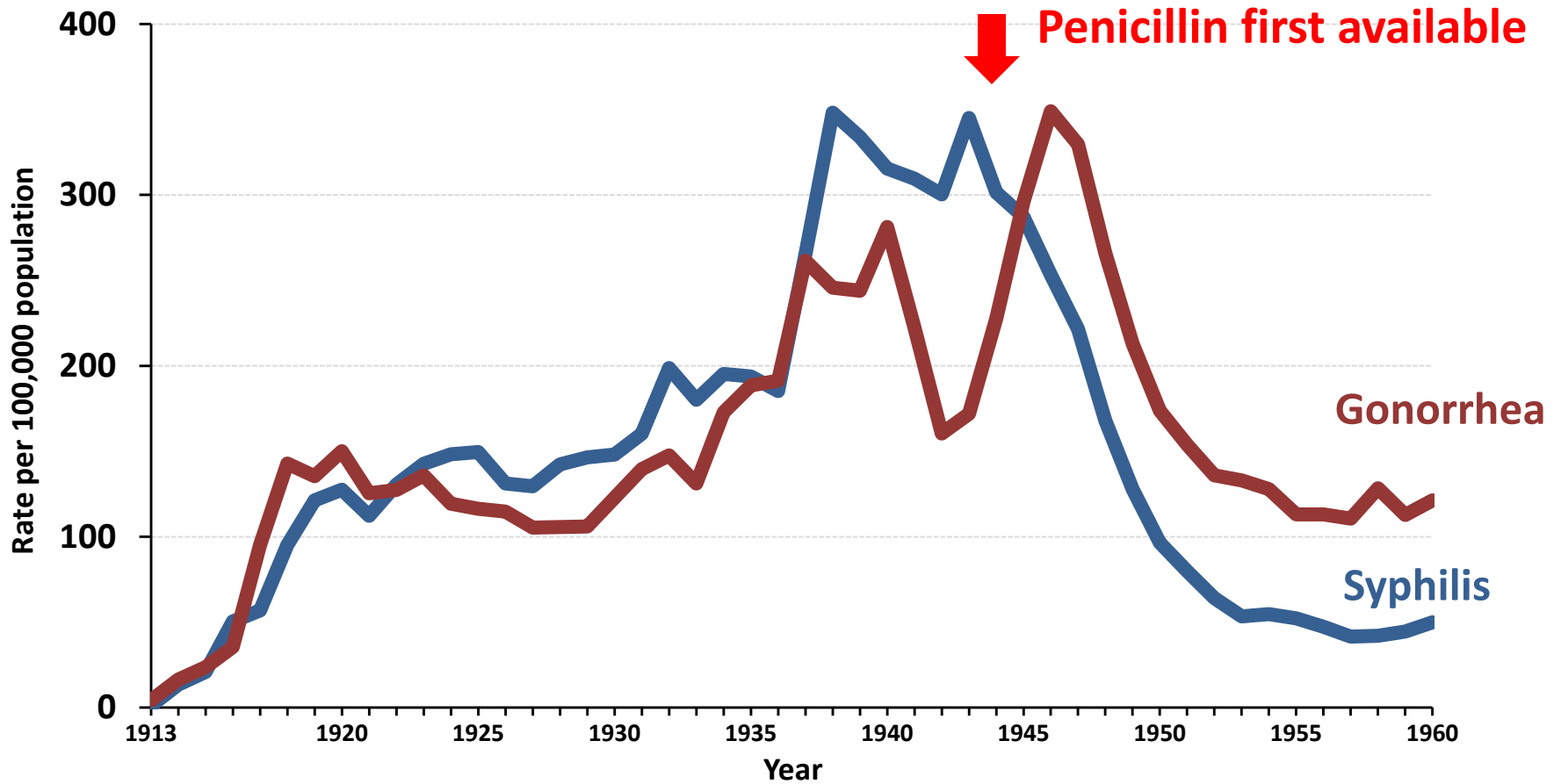
QUESTION: WHICH OF THE FOLLOWING WAS A “GAME CHANGER” IN THE HISTORY OF STD CONTROL?

- A. Latex condoms
- B. Education
- C. Antibiotic treatment
- D. Quarantine
- E. Sadly, there have been NO game changers



Syphilis & Gonorrhea

Reported case rates in California, 1913–1960



QUESTION: WHICH IS YOUR FAVORITE STD?

✧ *Haemophilus ducreyi* (Chancroid)

✧ Chlamydia

✧ Gonorrhea

✧ Syphilis

✧ HPV

✧ HSV

✧ Trichomonas

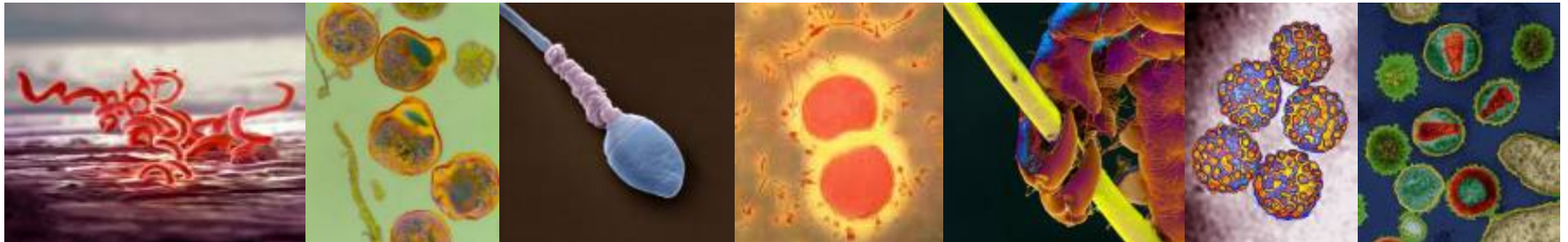
✧ HIV

✧ *Mycoplasma genitalium*

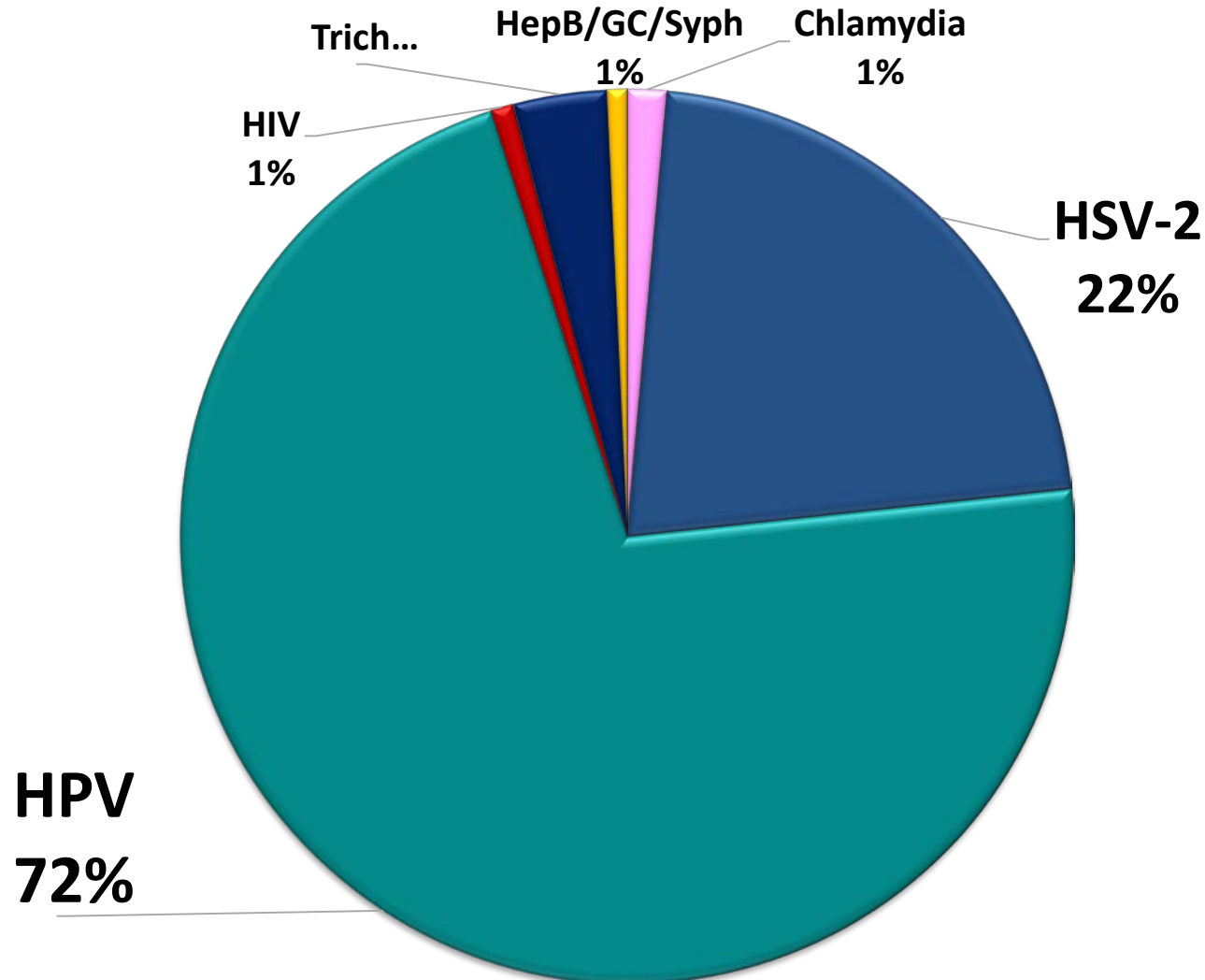


SEXUALLY TRANSMITTED INFECTIONS

- Syphilis
 - Gonorrhea
 - Chlamydia
 - HIV / AIDS
 - Hepatitis B
 - Hepatitis C
 - Chancroid
 - Trichomonas
 - Lympho-
granuloma
venerium (LGV)
 - Granuloma
inguinale
 - Mycoplasma
genitalium
 - HPV
 - Genital herpes
 - Pubic lice
 - Scabies
 - Bacterial vaginosis
 - Shigella
 - Hepatitis A
 - Ebola
 - Zika
- ... MORE



Distribution of Prevalent STDs in the U.S., 2008



Source: Satterwhite, C et al. Sexually Transmitted Infections Among US Women and Men: Prevalence and Incidence Estimates, 2008. *STD* 2013; 40(3): 187-193.



The Story of **Chlamydia**



QUESTION: WHICH ADVANTAGES HAS “CHLAMYDIA CONTROL” HAD OVER OTHER STDs?

- A. Single-dose oral treatment
- B. Research showing screening reduces PID
- C. Advocacy by women’s health and family planning groups
- D. Routine screening supported by USPSTF
- E. Rapid development of molecular tests
- F. Adoption as a national HEDIS measure
- G. Political support along with federal and state funding
- H. All of the above



Chlamydia Key Events, Past 100 years

1900

1925

1950

1975

2000



Chlamydia trachomatis
discovered, 1907

Doxycycline, 1949



Tissue culture, 1970s



Azithromycin, 1980



DNA probe tests, 1980s



Made reportable, 1990



NAATs, 1990s



HEDIS, 2000



Chlamydia
worth talking about

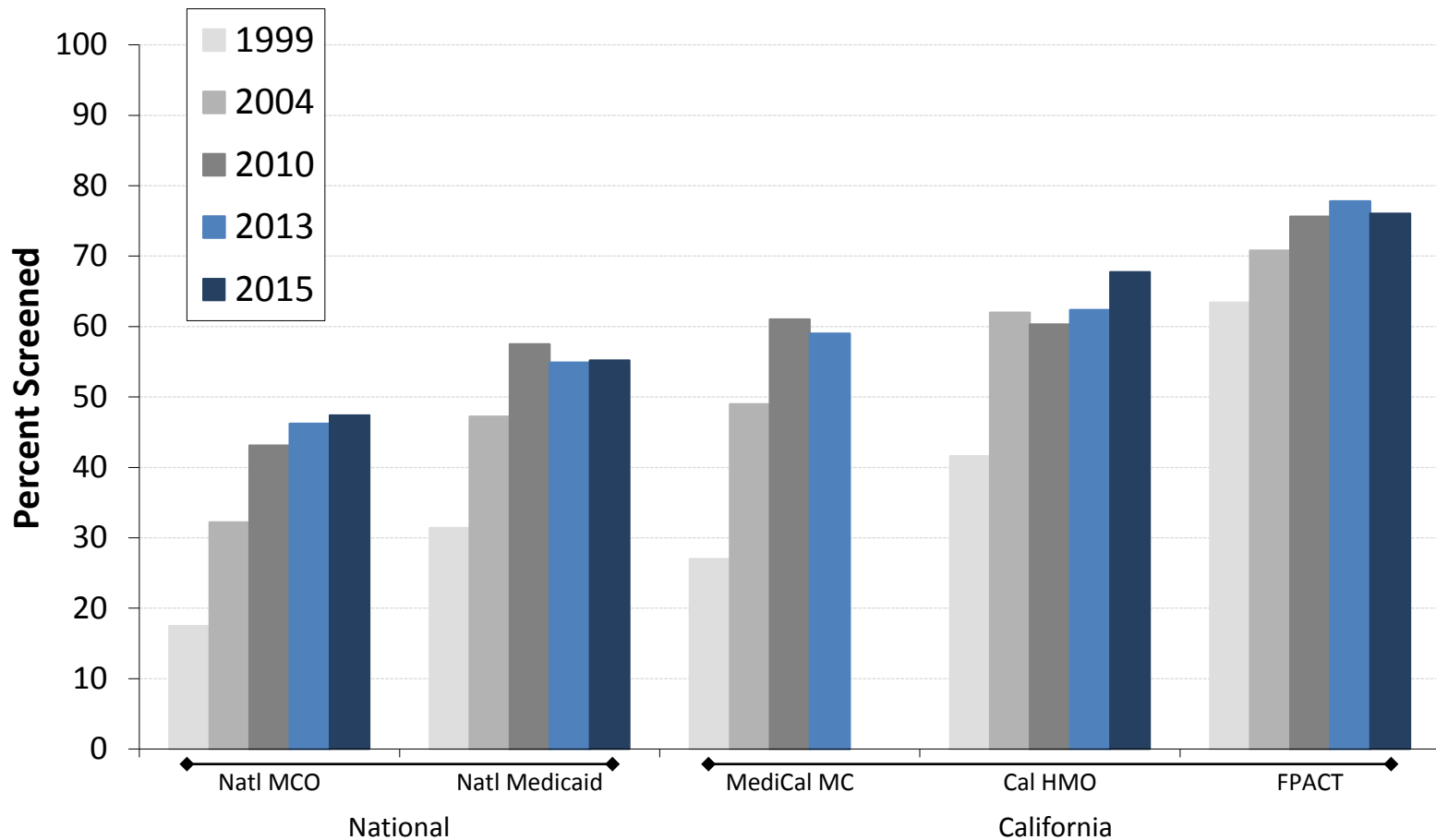
Sponsored by Sacramento County Public Health



I know.
Chlamydia and gonorrhea are curable,
but I need to get tested.

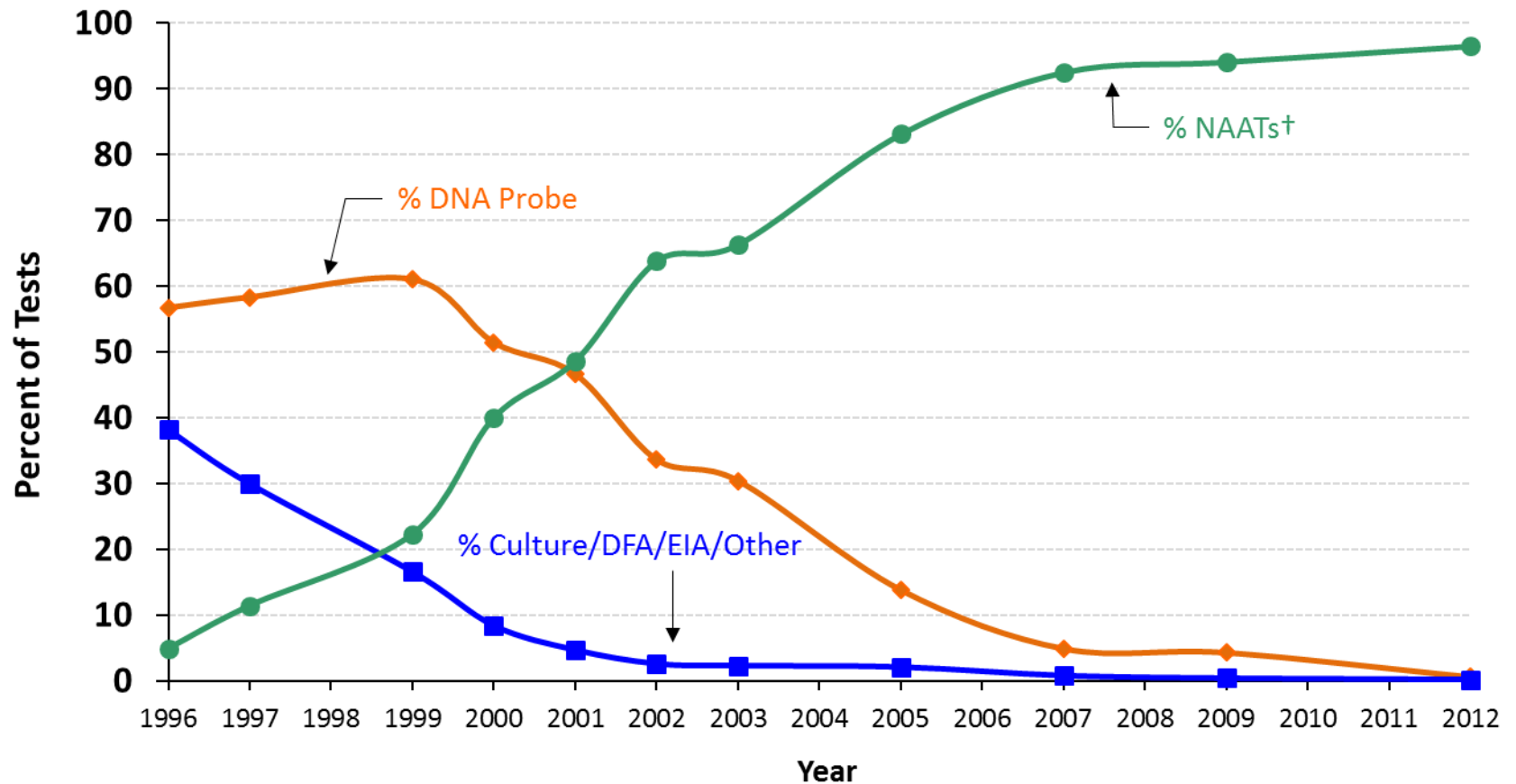
Order a **FREE** home test kit
or find a low-cost clinic at: DontThinkKnow.org
(916) 875-KNOW (5669)

Estimated Chlamydia Screening Coverage (HEDIS), Females Age 15–24, USA and California, 1999–2015



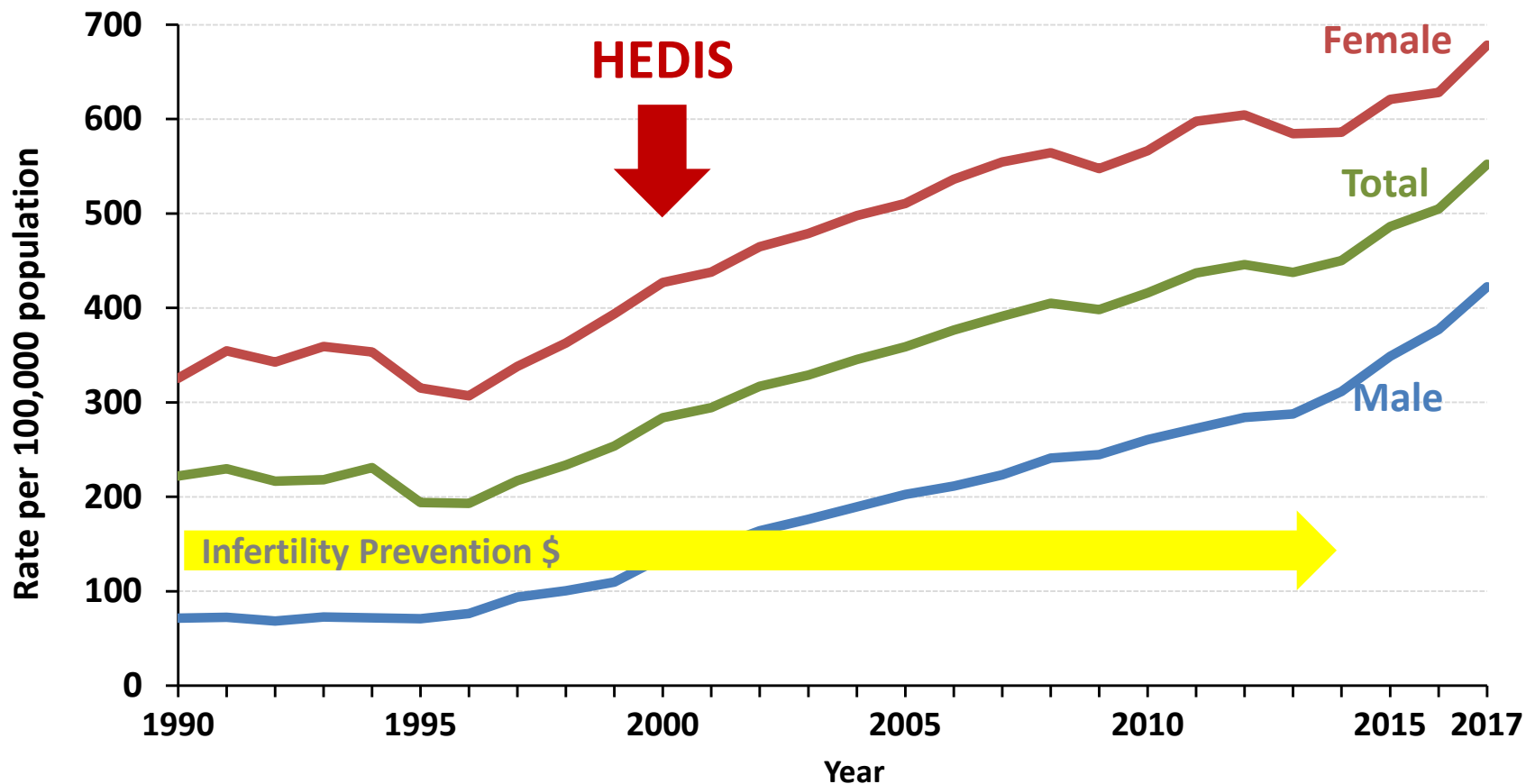
Source: National Committee on Quality Assurance; California DHCS Division of Medi-Cal Managed Care (2015 data not available); Kaiser Permanente Northern CA; California DHCS Office of Family Planning

Percent of Chlamydia Tests by Test Type California Annual Lab Survey, 1996–2012



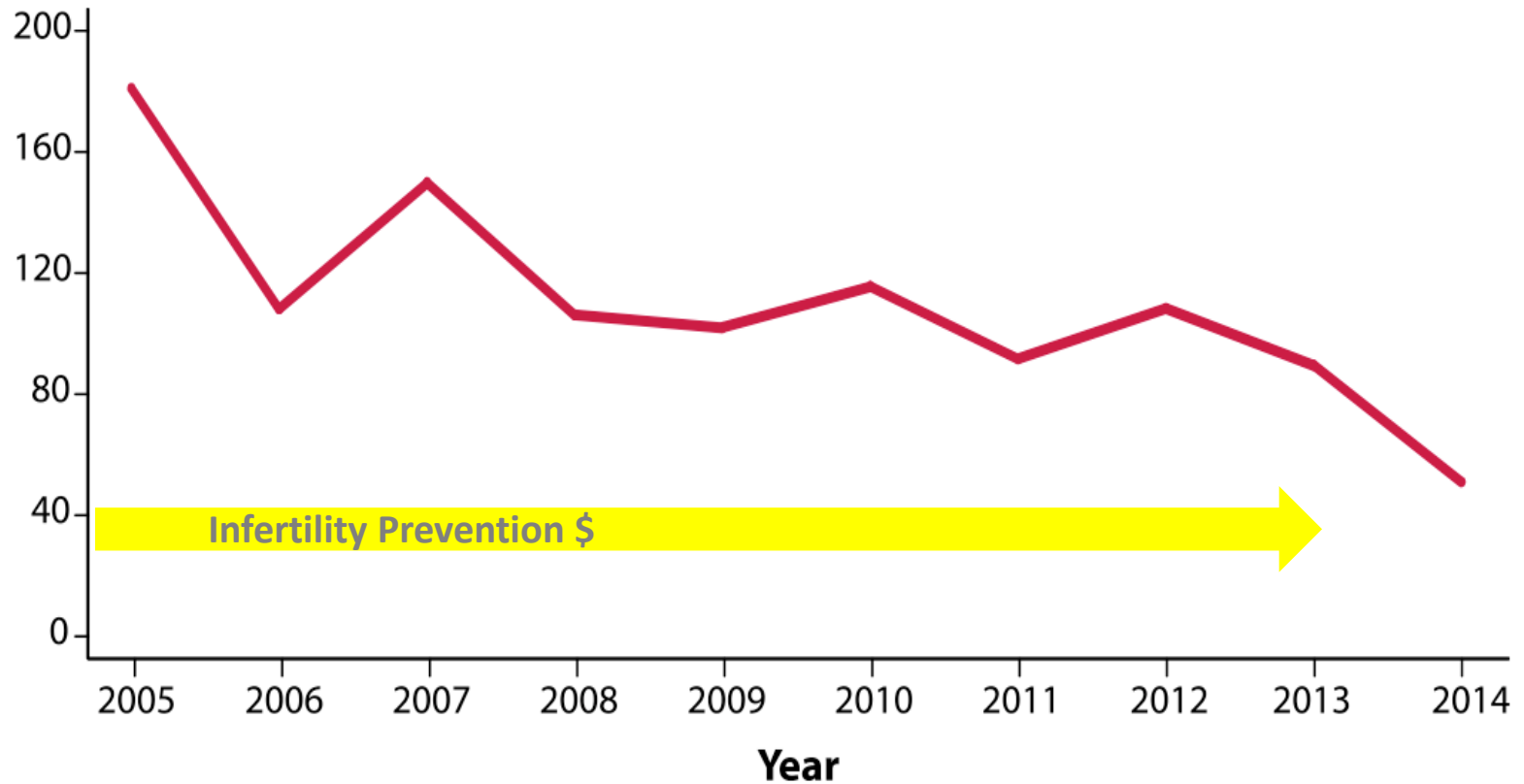
† NAATs: Nucleic acid amplification tests

Chlamydia, Incidence Rates by Gender California, 1990–2017



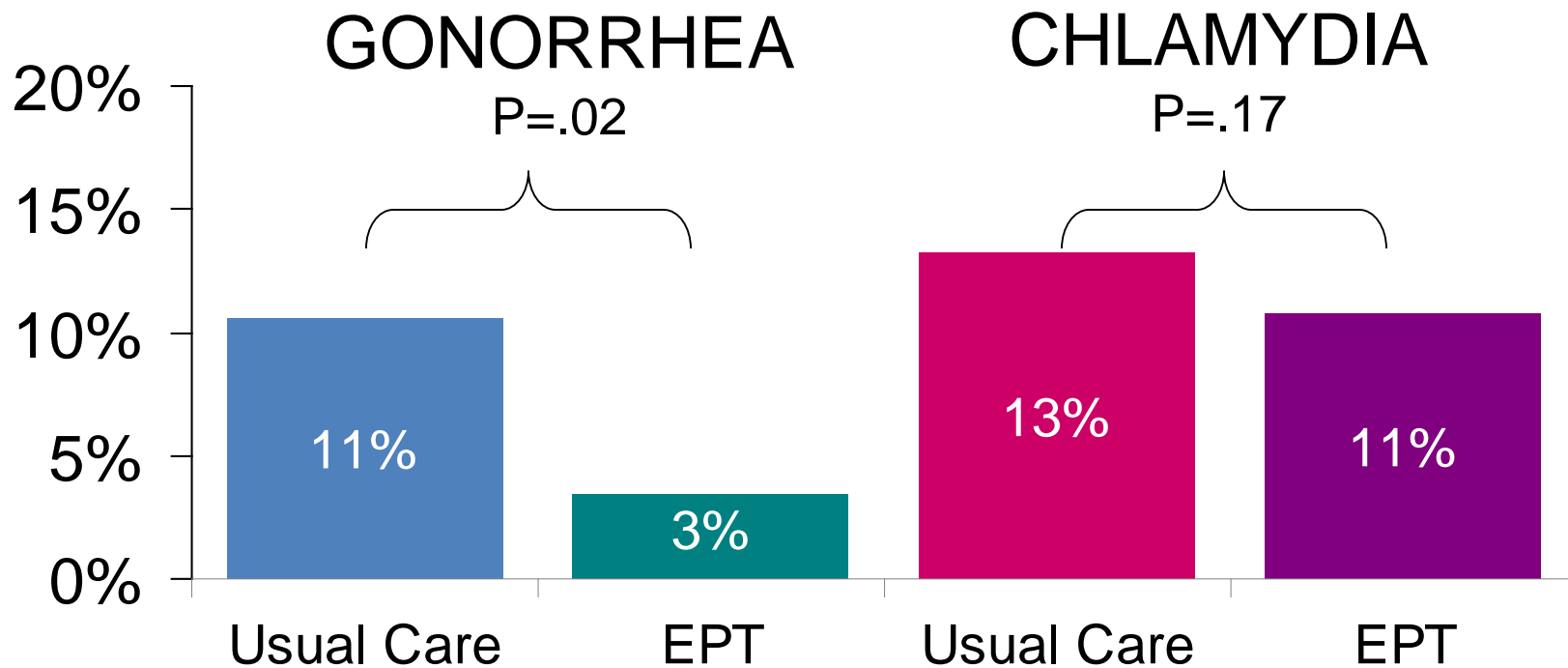
Pelvic Inflammatory Disease – Initial Visits to Physicians’ Offices among Women 15-44 year, US, 2005-2014

Visits (in thousands)



NOTE: The relative standard errors for these estimates are 16%-23%.

The Effectiveness of Expedited Partner Treatment on Re-Infection Rates



Chlamydia: Key Priorities

- Screening in primary care
- Rectal testing
- Expedited partner treatment
- Re-testing @ 3 months
- Youth access to information, prevention and sexual health care

Each STD has a Unique Story...

✧ Chancroid

✧ HPV

✧ HSV

✧ Trichomonas

✧ HIV

✧ Mycoplasma genitalium



The Story of
Gonorrhea



Gonorrhea Key Events, Past 200 years

1800

1850

1900

1950

2000

Neisseria gonorrhoeae
discovered, 1879



Silver/mercury, 1883



Gram stain, 1884



Penicillin/sulfa, 1942



Thayer-Martin culture, 1964



Combo DNA probe tests, 1980s



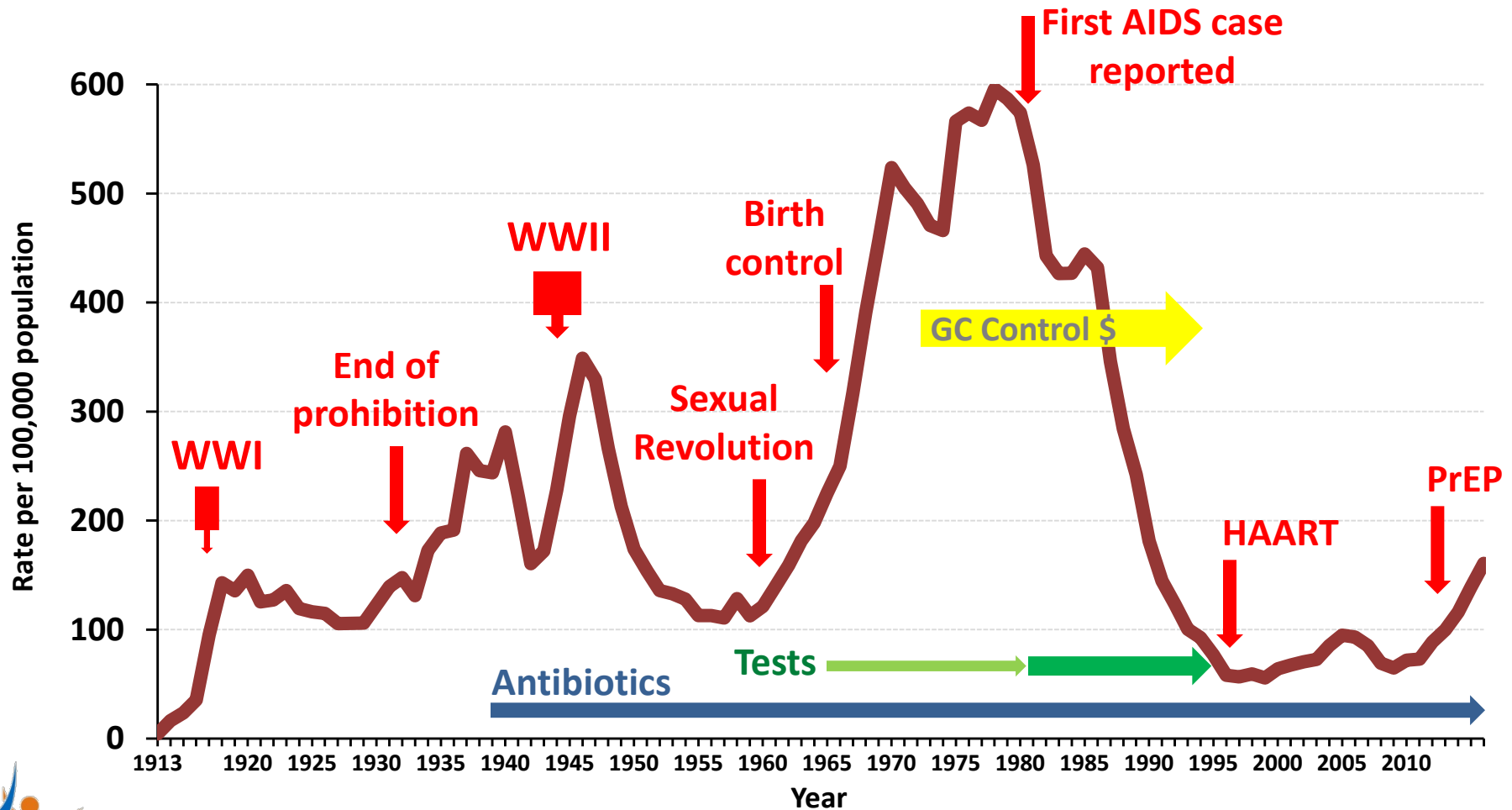
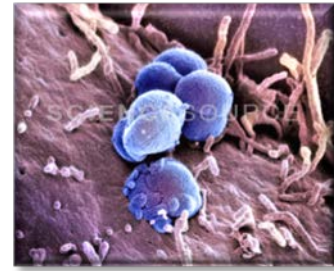
Combo NAATs, 1990



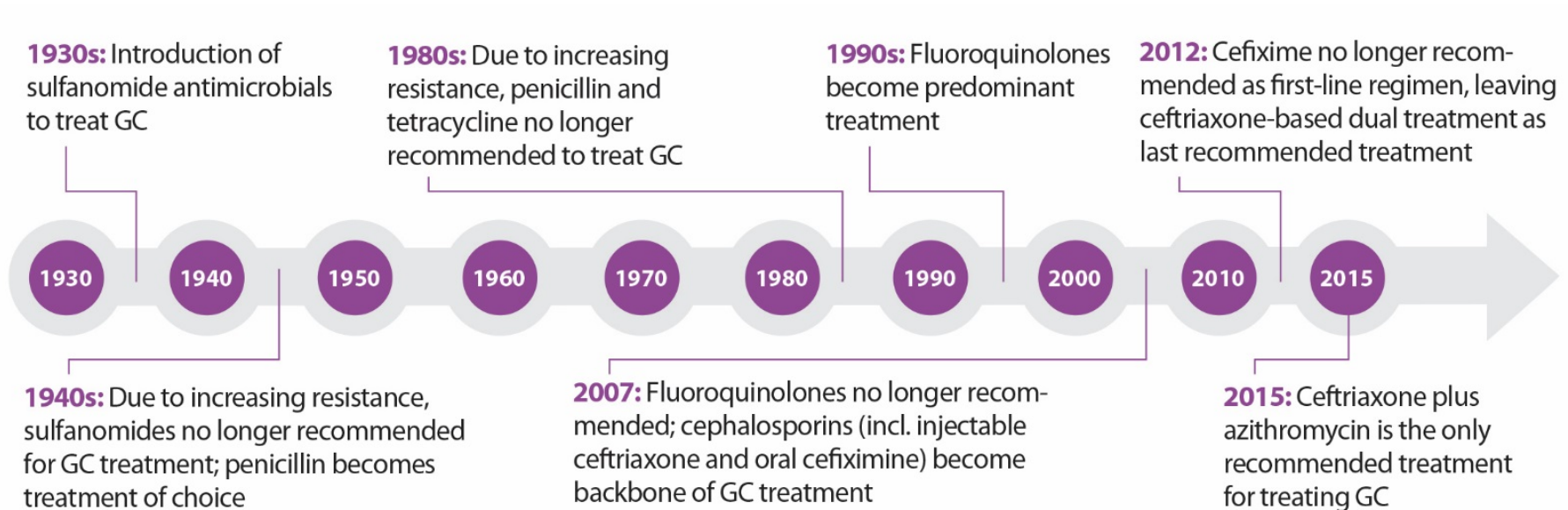
USPSTF "B", 2005



Gonorrhea Incidence in California, 1913–2016



Antibiotic Resistance Development over Time for Gonorrhea

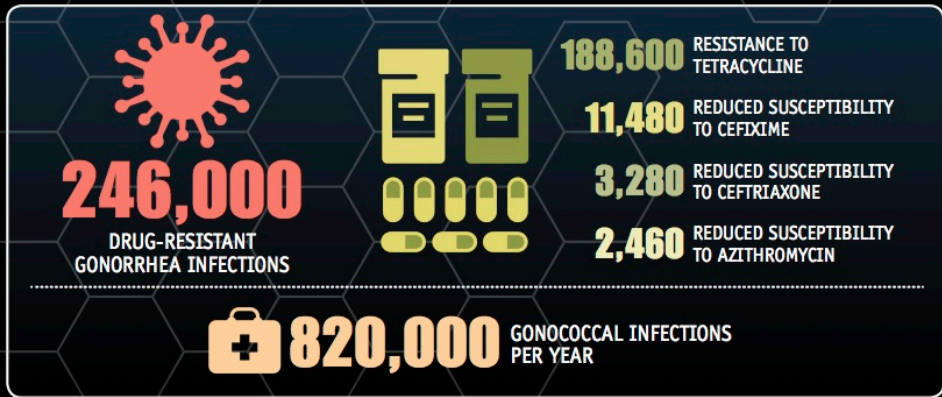




DRUG-RESISTANT NEISSERIA GONORRHOEAE

THREAT LEVEL
URGENT 

This bacteria is an immediate public health threat that requires urgent and aggressive action.



Neisseria gonorrhoeae causes gonorrhea, a sexually transmitted disease that can result in discharge and inflammation at the urethra, cervix, pharynx, or rectum.

RESISTANCE OF CONCERN

N. gonorrhoeae is showing resistance to antibiotics usually used to treat it. These drugs include:

- cefixime (an oral cephalosporin)
- ceftriaxone (an injectable cephalosporin)
- azithromycin
- tetracycline

PUBLIC HEALTH THREAT

Gonorrhea is the second most commonly reported notifiable infection in the United States and is easily transmitted. It causes severe reproductive complications and disproportionately affects sexual, racial, and ethnic minorities. Gonorrhea control relies on prompt identification and treatment of infected persons and their sex partners. Because some drugs are less effective in treating gonorrhea, CDC recently updated its treatment guidelines to slow the emergence of drug resistance. CDC now recommends only ceftriaxone

plus either azithromycin or doxycycline as first-line treatment for gonorrhea. The emergence of cephalosporin resistance, especially ceftriaxone resistance, would greatly limit treatment options and could cripple gonorrhea control efforts.

In 2011, 321,849 cases of gonorrhea were reported to CDC, but CDC estimates that more than 800,000 cases occur annually in the United States.

	Percentage	Estimated number of cases
Gonorrhea		820,000
Resistance to any antibiotic	30%	246,000
Reduced susceptibility to cefixime	<1%	11,480
Reduced susceptibility to ceftriaxone	<1%	3,280
Reduced susceptibility to azithromycin	<1%	2,460
Resistance to tetracycline	23%	188,600

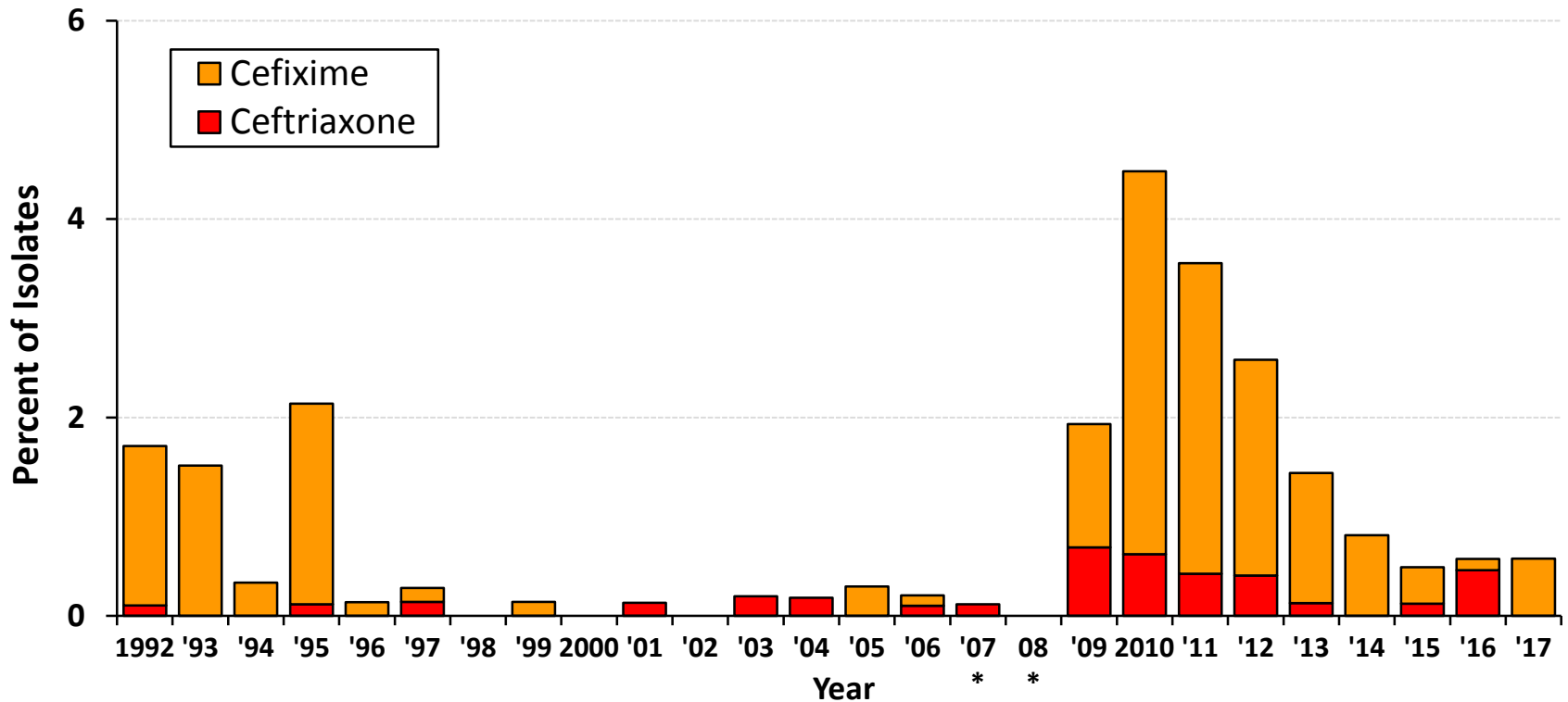
Source: The Gonococcal Isolate Surveillance Project (GISP)—5,900 isolates tested for susceptibility in 2011. For more information about data methods and references, please see technical appendix.

2013



U.S. Department of Health and Human Services
 Centers for Disease Control and Prevention

Gonococcal Isolate Surveillance Project (GISP), Percent of *Neisseria Gonorrhoeae* Isolates with CDC "Alert" Values for Selected Cephalosporins in California GISP STD Clinic Sites, 1992–2017



* Cefixime susceptibility was not run in 2007-2008.

Note: "Alert" values are set by CDC as markers to look at possible decreased susceptibility. Cefixime alerts have MICs $\geq 0.25 \mu\text{g/mL}$. Ceftriaxone alerts have MICs $\geq 0.125 \mu\text{g/mL}$.

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STD Clinic Sites: Long Beach (ended participation in 2007), Los Angeles (added in 2003), Orange, San Diego, San Francisco

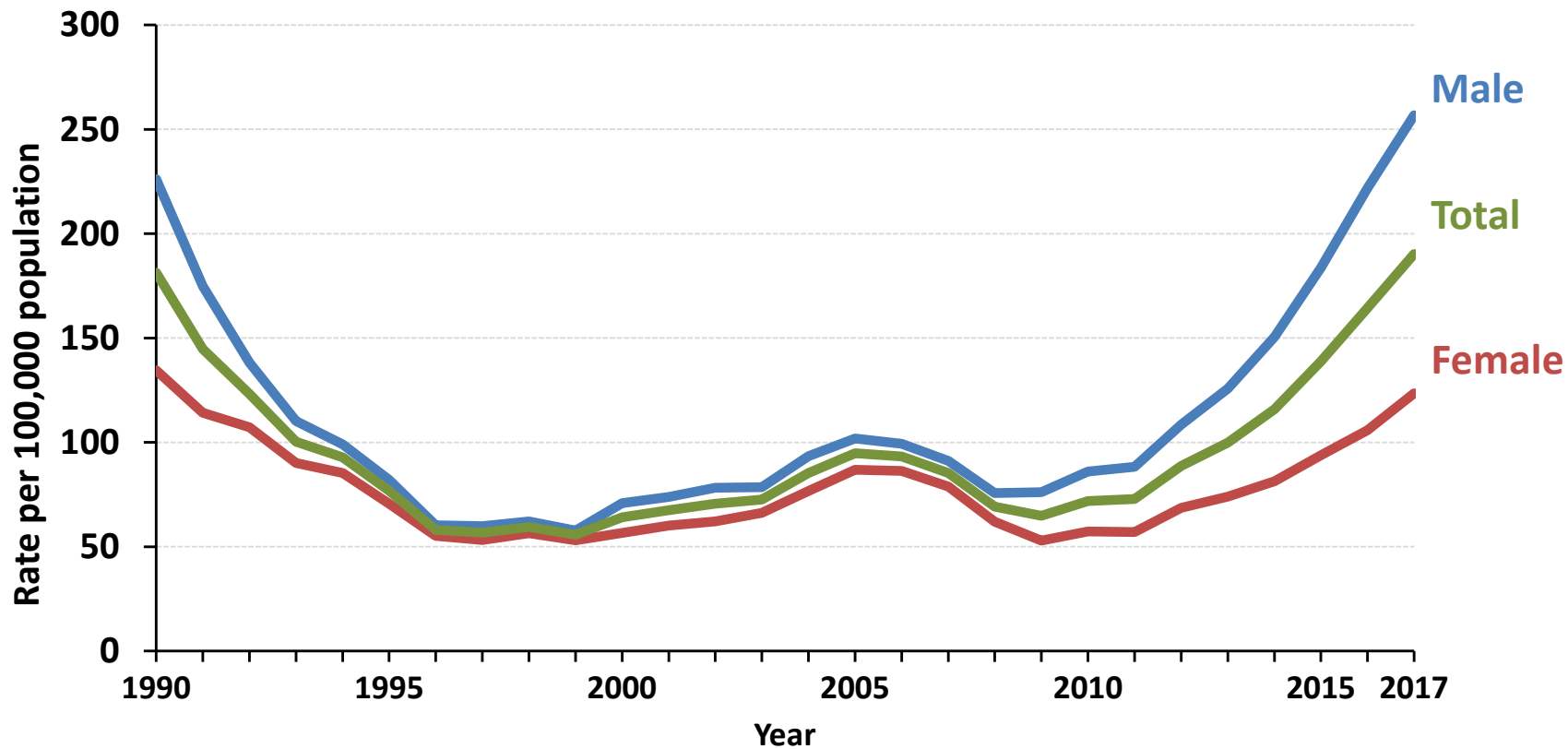


QUESTION: HOW WORRIED ARE YOU ABOUT UNTREATABLE GONORRHEA?

- A. Very – development of ARNG is inevitable. Once it emerges, it will spread rapidly
- B. Somewhat, but better tests will detect drug resistance and guide treatment
- C. Not so much – more antibiotics will be developed soon
- D. Nah – it's all hype. ARNG comes and goes

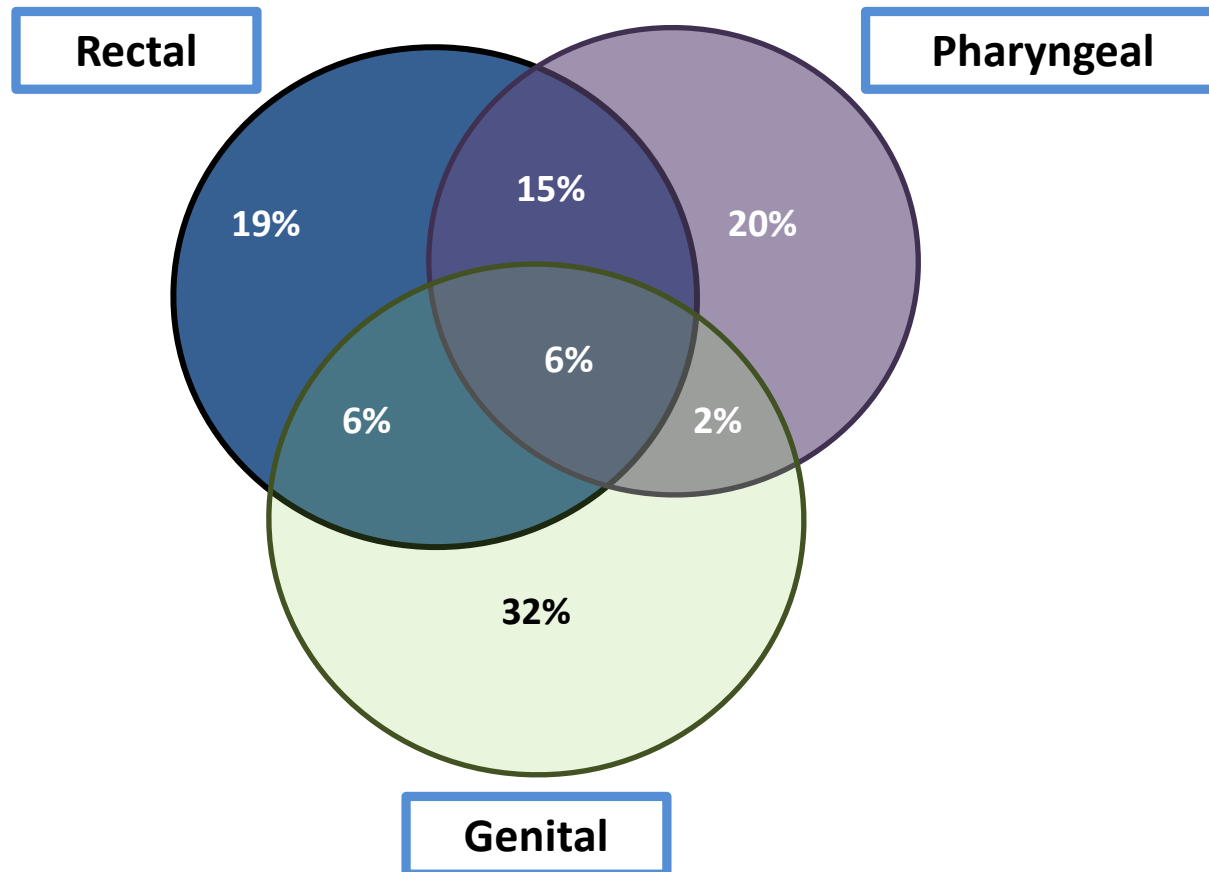


Gonorrhea, Incidence Rates by Gender California, 1990–2017



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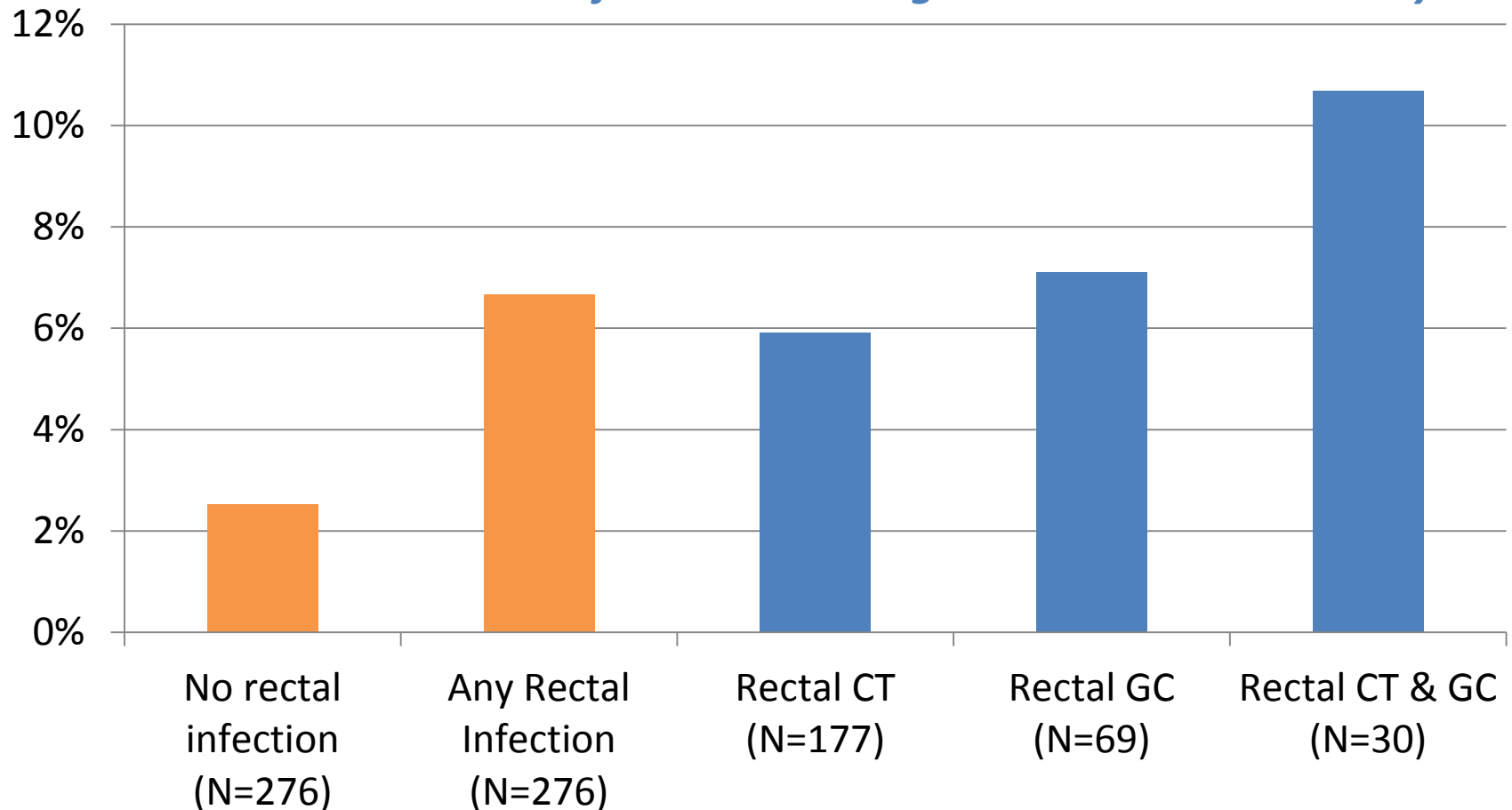
Percent of Gonorrhea Cases by Anatomic Site of Infection among MSM, California Gonococcal Surveillance System (CGSS), 2017



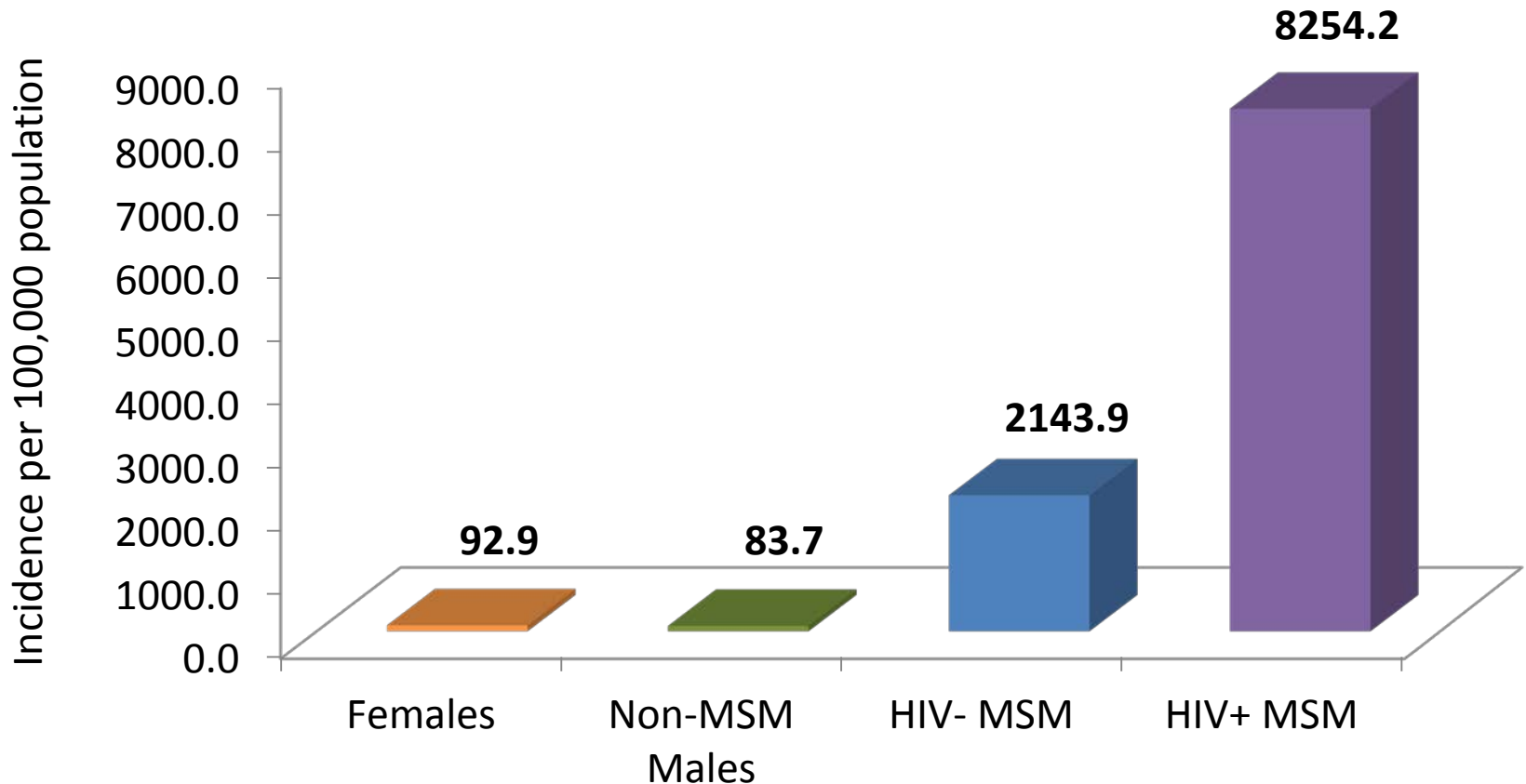
* The California Gonococcal Surveillance System (CGSS) is derived from a 2.5% random sample of Gonorrhea cases reported in a given year.

Rectal gonorrhoea/chlamydia associated with increased HIV Incidence among MSM @ NYC STD Clinics, 2008-10

1 in 15 MSM w rectal infections was diagnosed with HIV within a year



Gonorrhea Incidence Rates* by Sex, Gender of Sex Partners, and HIV Status, California, 2016



* Using HIV denominator data from the Office of AIDS 2015 surveillance report and California (including Los Angeles) and San Francisco STD Surveillance Network sampled and interviewed case data from 2016 as a proxy for incidence, weighted to population using $1/((\text{sample fraction}) * (\text{interview rate}))$.

Gonorrhea: Key Priorities

- Throat and rectal testing
- Dual treatment
- ARNG diagnosis and reporting
- HIV prevention opportunities
- (Expedited partner treatment)

The Story of
Syphilis





“The Great Pox”

“Lues” (venereal plague)

“The Great Imitator”

“Bad Blood”


Medieval Syphilis, Woodcut 1497

Syphilis Key Events, Past 100 years

1900 1925 1950 1975 2000





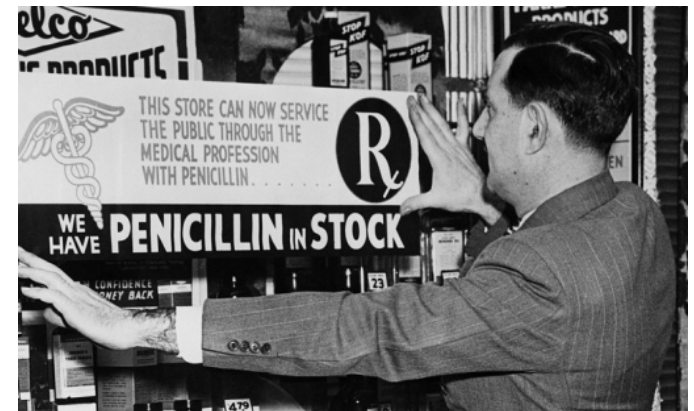
Testing

-  *T. pallidum* discovered 1905 (Shaudinn & Hoffmann)
-  Darkfield & early serology 1906
-  First trep serology 1949
- First rapid trep test 2014 

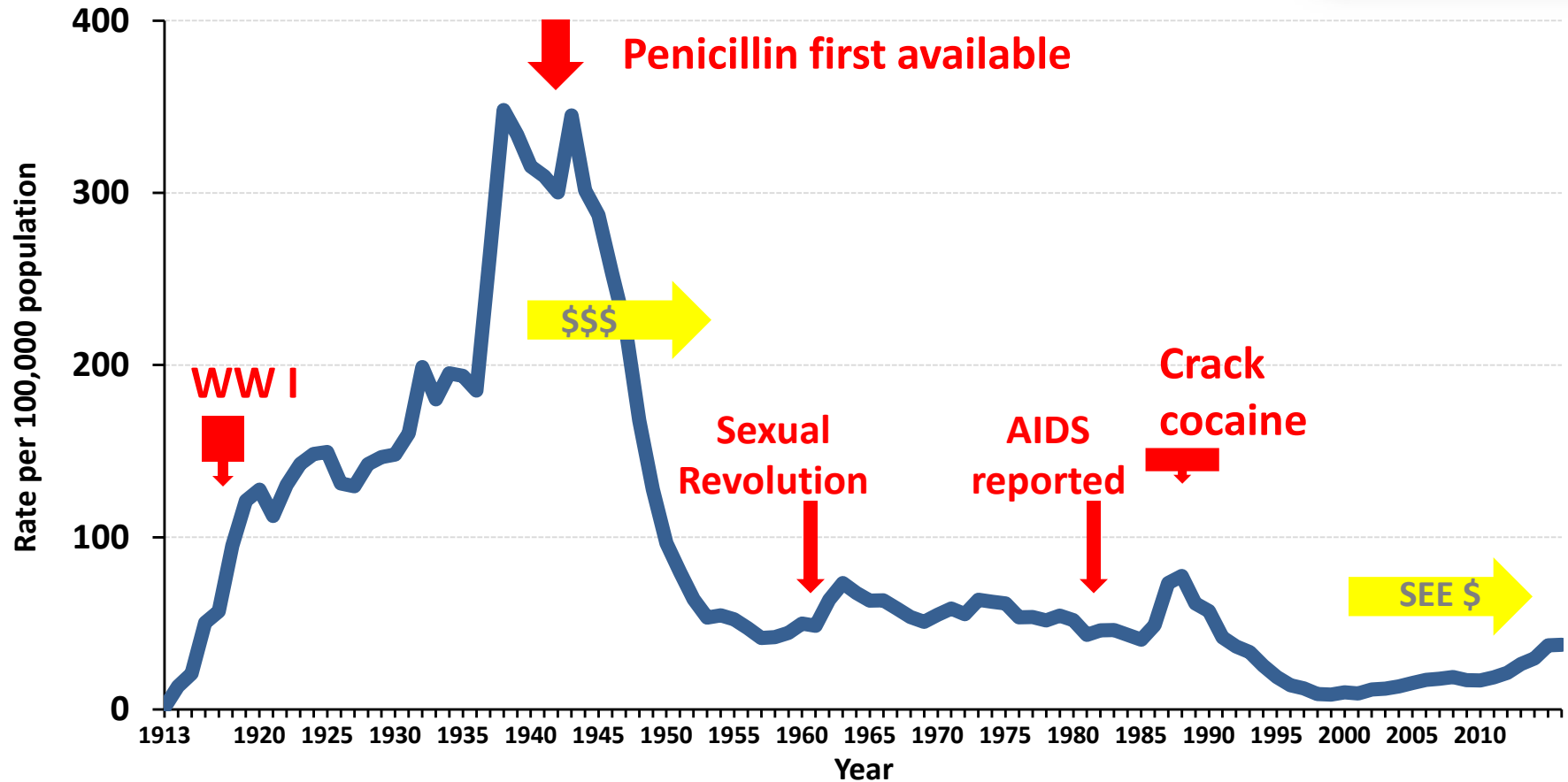
Tuskegee Syphilis Study, 1932-72

Treatment

-  Salvarsan 1910
-  Penicillin 1942



Syphilis Incidence in California, 1913–2016





*“He who
knows syphilis
knows
medicine.”*

- Sir William Osler

Stereoscopic views of syphilis (1910) by S.I. Rainforth, MD

Earliest Syphilis Testing and Treatment



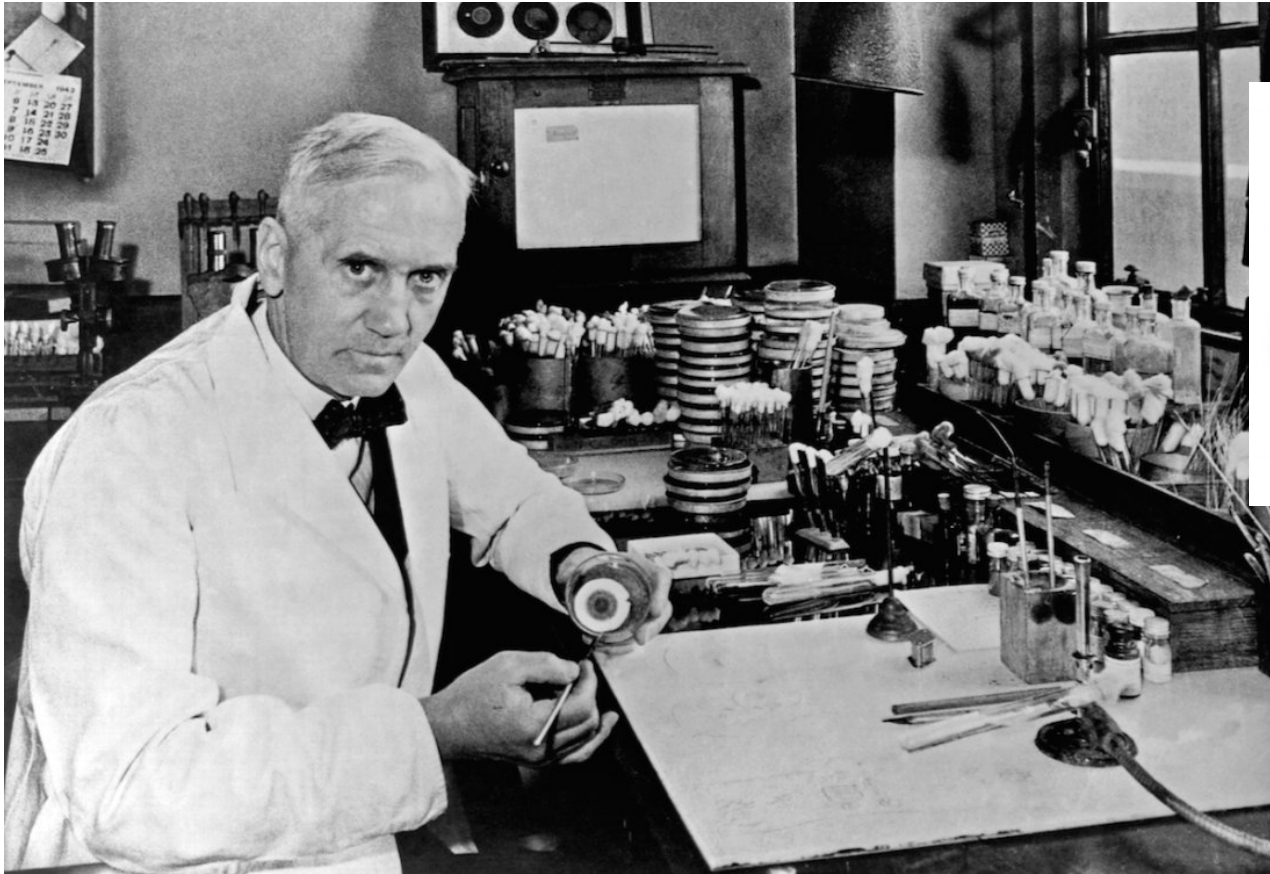
Venereal Disease Research Lab (VDRL),
non-treponemal serology slide test, 1906



Salvarsan: First Effective Treatment



Penicillin -- Game Changer!

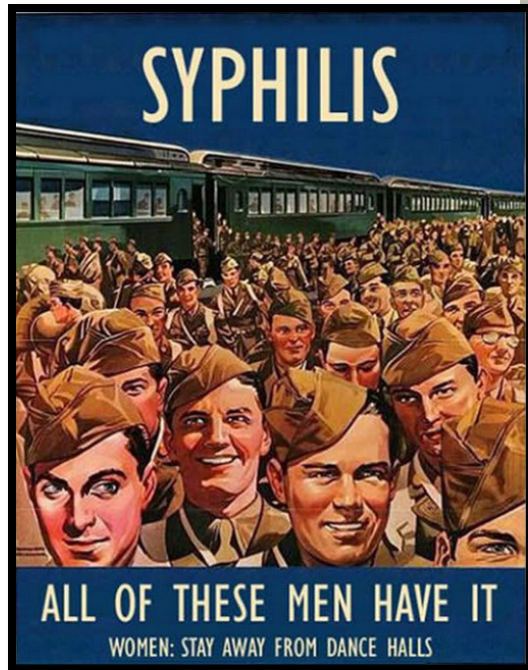


wiseGEEK

Sir Alexander Fleming, 1881-1955

Nobel Prize 1945 for the discovery of penicillin in 1928

“1 in 10”



a Blood Test for all



PROTECTS YOU
against Syphilis

BLACKSTONE THEATRE
NOW
PLAYING

60 EAST BALBO - TELEPHONE HARRISON 6609

FEDERAL
THEATRE
PRESENTS

Spirochete

By
ARNOLD
SUNDGAARD
Produced by
HARRY MINTURN

A
LIVING
NEWSPAPER





Direction of
ADDISON PITT
Settings by
CLIVE
RICKABAUGH

PRICES
83¢ 55¢
40¢ 25¢



EVERY NITE EXCEPT MONDAY - CURTAIN 8:30
WORKS PROGRESS ADMINISTRATION



-  30 states require blood test for syphilis
-  3 states require examination by physician (to determine if free from venereal diseases)
-  3 states prohibit marriage of persons who have had syphilis (require personal affidavit of no infection, or examination specified)
-  12 states grant marriage licenses to persons with syphilis (if no infection)

HOW DOES YOUR STATE REQUIRE BLOOD TESTS?
 WHEN DOES YOUR LICENSE REQUIRE AN EXAMINATION?
 WHAT PLANS ARE THERE TO PREVENT INFECTION?

know for sure-

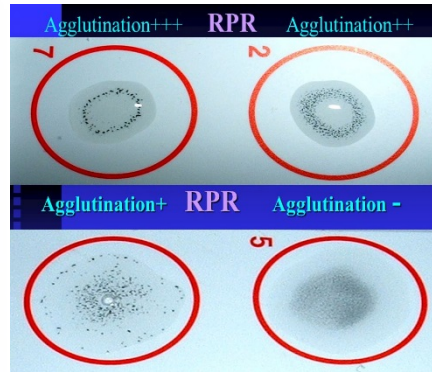


get blood tests *before* marriage

QUESTIONS IN YOUR STATE?

American Social Hygiene Association, Inc.
 1790 Broadway, New York 19, N. Y.

Advances in Syphilis Testing & Treatment



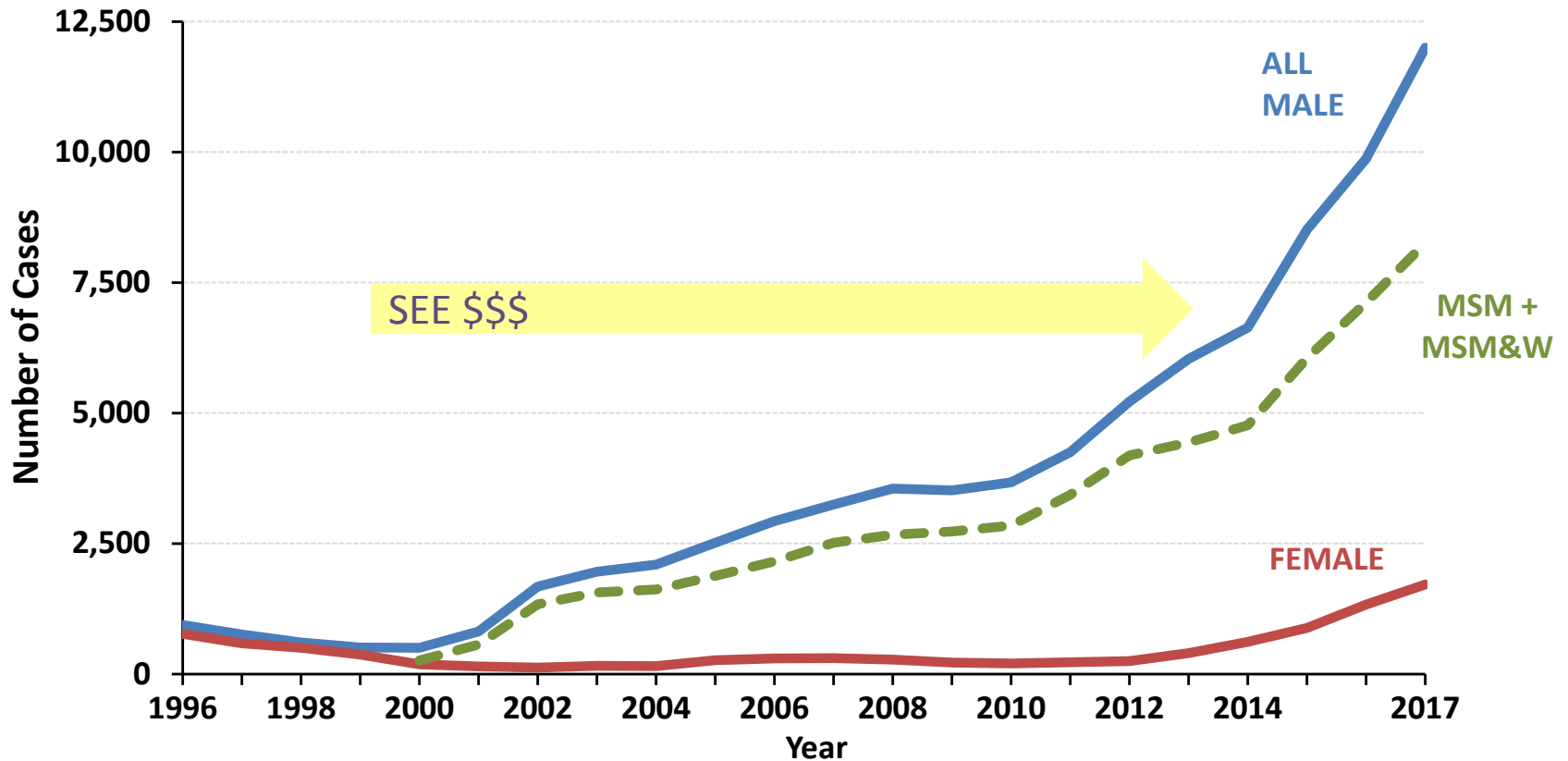
Stat RPR Card



Syphilis Health Check



Early Syphilis*, Cases by Gender California, 1996–2017



* Includes primary, secondary, and early latent syphilis.

Rev. 7/2018

A test that aims to help the homeless

By Lori Gilbert

Posted Oct 3, 2017 at 4:36 PM

Updated Oct 3, 2017 at 5:02 PM



San Joaquin County Health nurse Jenny Malone, left, takes blood sa... ▲

STOCKTON — John wasn't really worried, but he wanted to be sure.

The 26-year-old was one of the homeless who lined up on the sidewalk outside of the St. Mary's Dining Room/Stockton Shelter for the Homeless last week to have his finger pricked for a rapid syphilis blood test.

Unsafe sexual activity is prevalent on the streets, John said, and everyone should be tested.

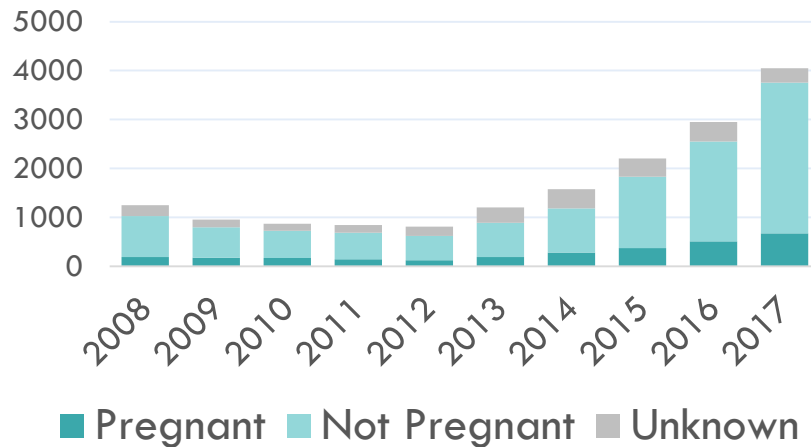
"It sucks they have to give (a \$10 gift card for McDonald's) as an incentive," John said.



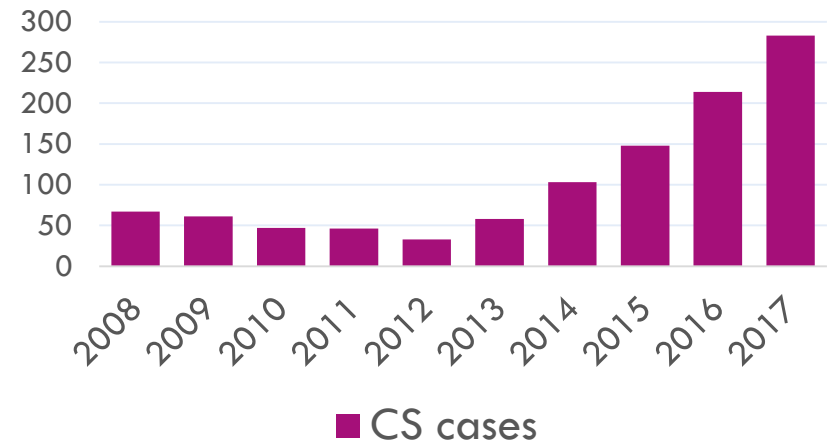
San Joaquin, 2017

Syphilis in females and infants has been increasing in California since 2012

Female syphilis cases (all stages)



Congenital syphilis cases



Syphilis: Key Priorities

- Expanded screening
- Rapid on-site treatment
- Report to health department
- HIV prevention opportunities
- Prevention of complications of neuro and ocular syphilis, and congenital syphilis

The Story of

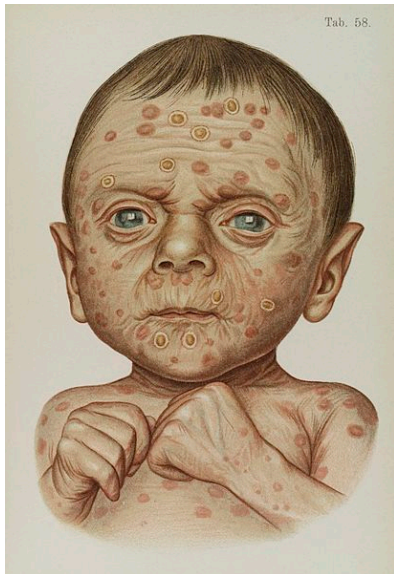
Congenital Syphilis



**Rembrandt's
portrait of Gerard de
Lairesse at age 25**

**Oil on canvas, ca. 1665-67
Metropolitan Museum of Art**

Edvard Munch “The Inheritance” 1897-99



A lithograph from 1898
of an infant with
congenital syphilis
Image: Wellcome Library,
London



Congenital Syphilis Key Events, Past 250 years

1750

1800

1850


1900

1950

2000




1780: Mercury used in specialized infant hospital in Paris


*1905: *T. pallidum* discovered (Shaudinn & Hoffmann)*



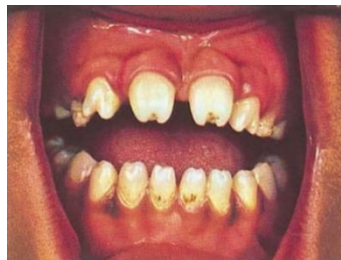

1789: Snuffles





1810: Periosteal bone disease

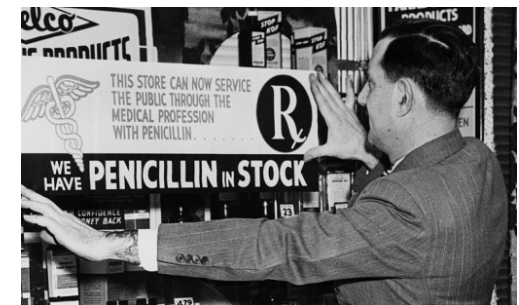



1863: Late CS



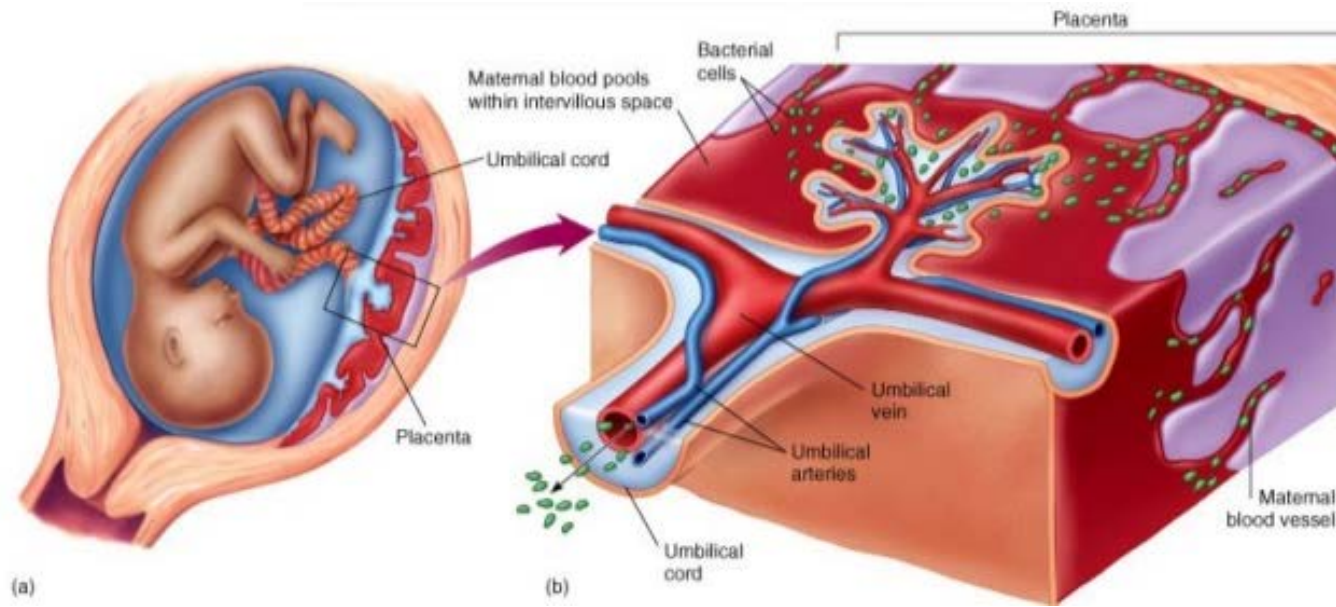

1910: Salvarsan (Erlisch)


1942: Penicillin (Fleming; Lentz & Ingraham)



M. Obladen. 2013 Neonatology 103:274-80.

Mother to child transmission of syphilis can occur anytime during pregnancy



- Increased risk with early maternal stage of disease, spirochetemia (bacteria in the blood), and higher maternal titers
- Latent including late latent infection can be transmitted vertically
- Earliest possible treatment is key to prevention

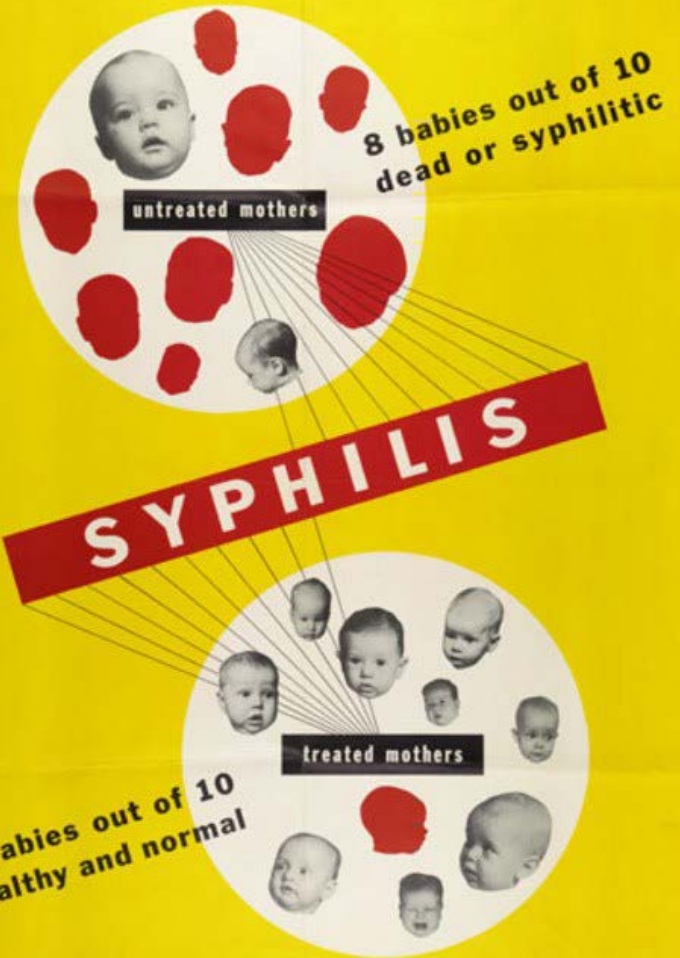


CONGENITAL SYPHILIS IS PREVENTABLE

IF SYPHILITIC MOTHERS WILL TAKE
ADEQUATE TREATMENT DURING THE
LAST FIVE MONTHS OF PREGNANCY

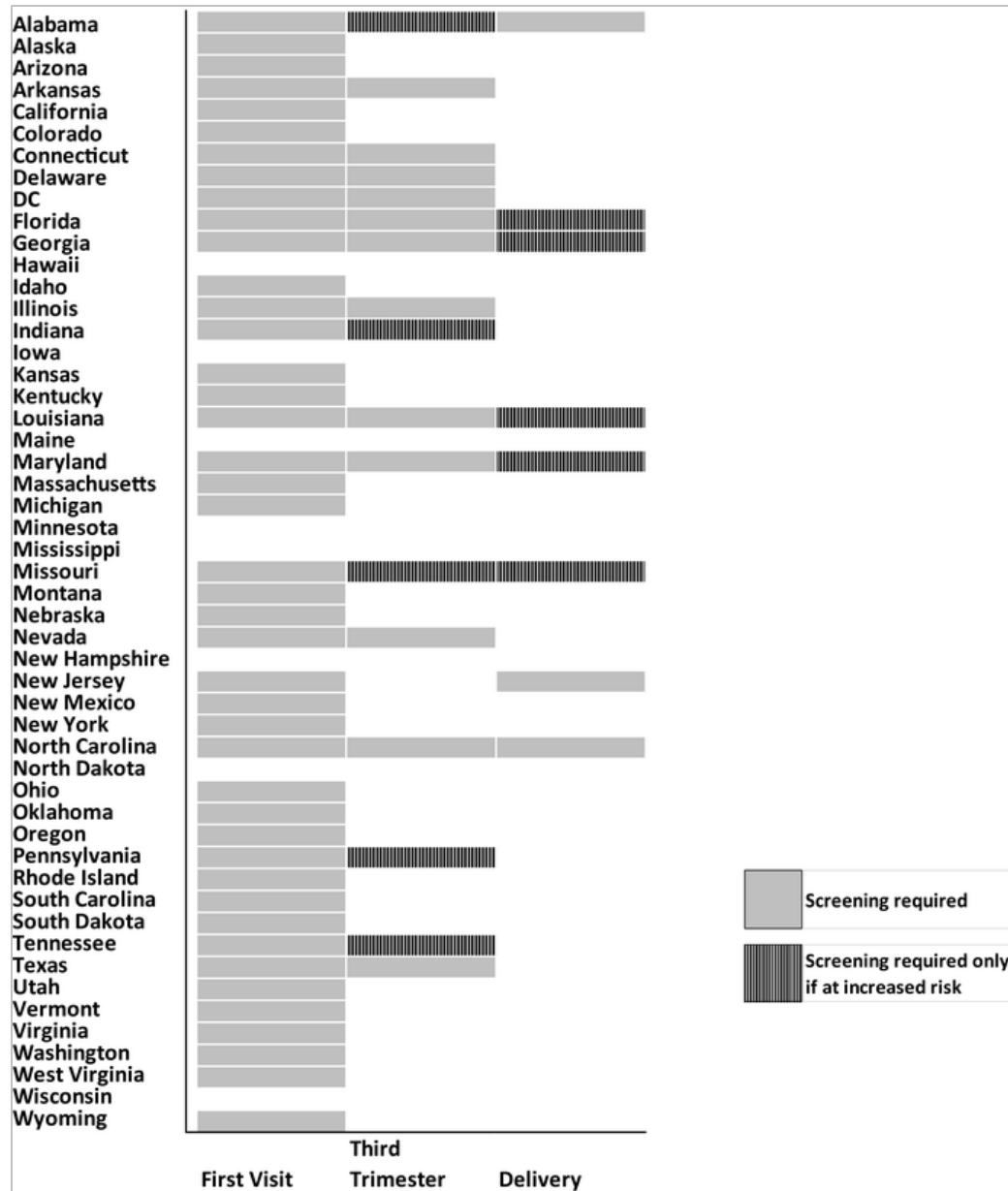
NEW YORK STATE DEPARTMENT OF HEALTH

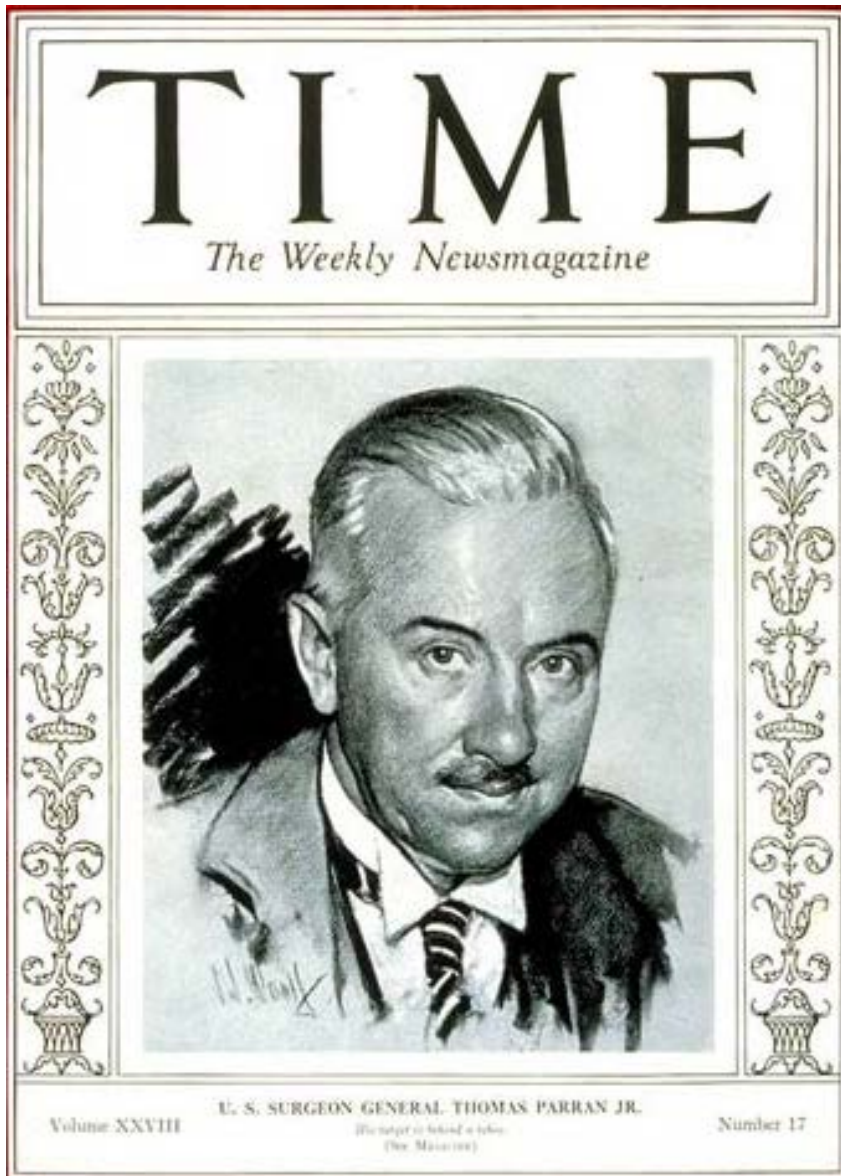
MADE BY WORKS PROGRESS ADMINISTRATION - FEDERAL ART PROJECT NYC



NEW YORK STATE DEPARTMENT OF HEALTH

Prenatal Syphilis Testing Laws by State as of 2016





Thomas Parran, Jr
U.S. Surgeon General 1936-48

“The first thing to do completely, is to *wipe out congenital syphilis.* That is one job that doesn’t need to take a generation.”

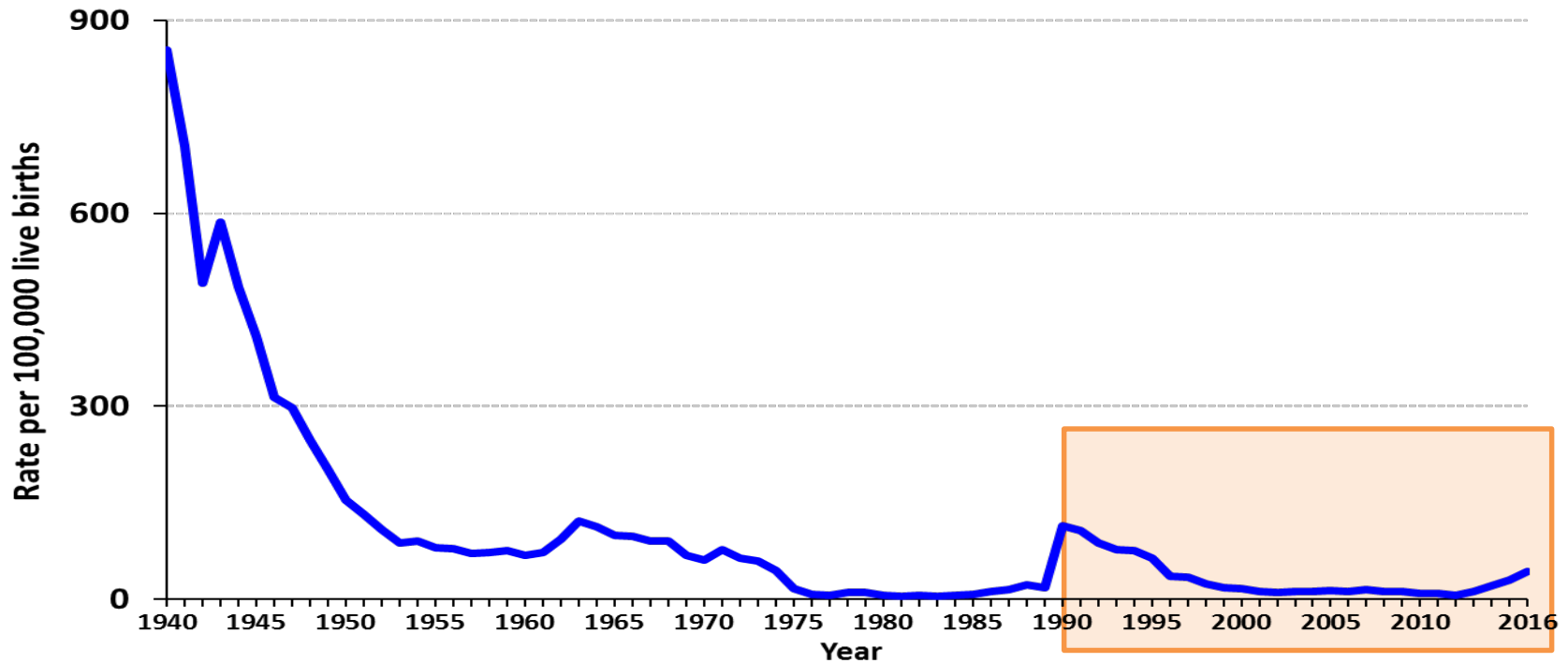
Thomas Parran. **1937.**
Shadow on the Land: Syphilis.
New York, NY: Reynal & Hitchcock

Tuskegee Syphilis Study, 1932-1972

- 28 dead from syphilis
- 100 dead from related complications
- 40 wives infected
- 19 children born with congenital syphilis



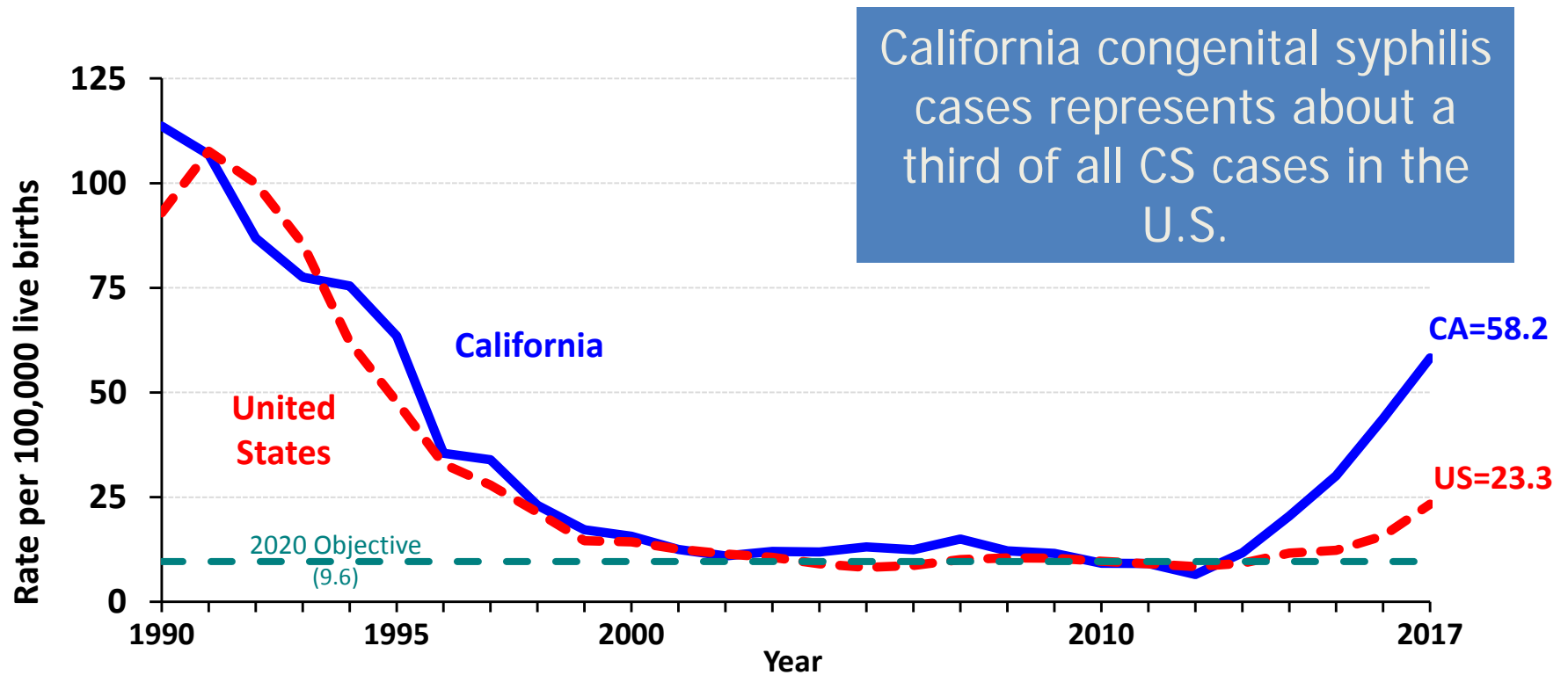
Congenital Syphilis California Incidence Rates, 1940–2016



Note: The Modified Kaufman Criteria were used through 1989. The CDC Case Definition (MMWR 1989; 48: 828) was used effective January 1, 1990.

Rev. 6/2017

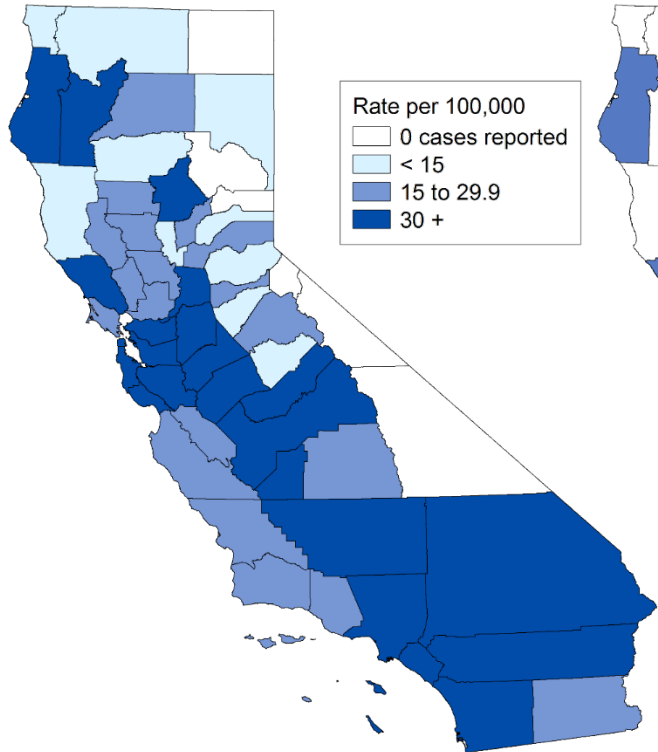
Congenital Syphilis, California versus United States Incidence Rates, 1990–2017



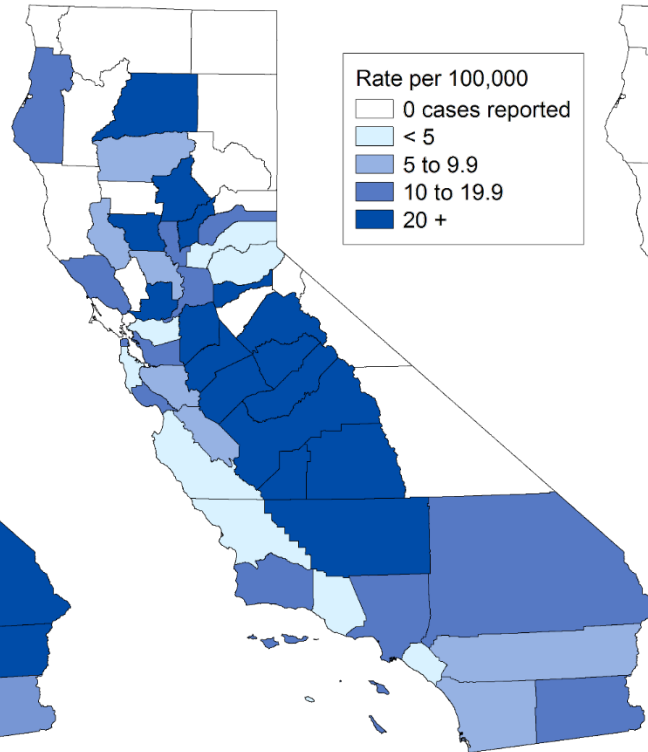
Rev. 7/2018

Early Syphilis* Incidence by County among Males, Females of Childbearing Age (15-44) & Congenital Syphilis, California, 2017

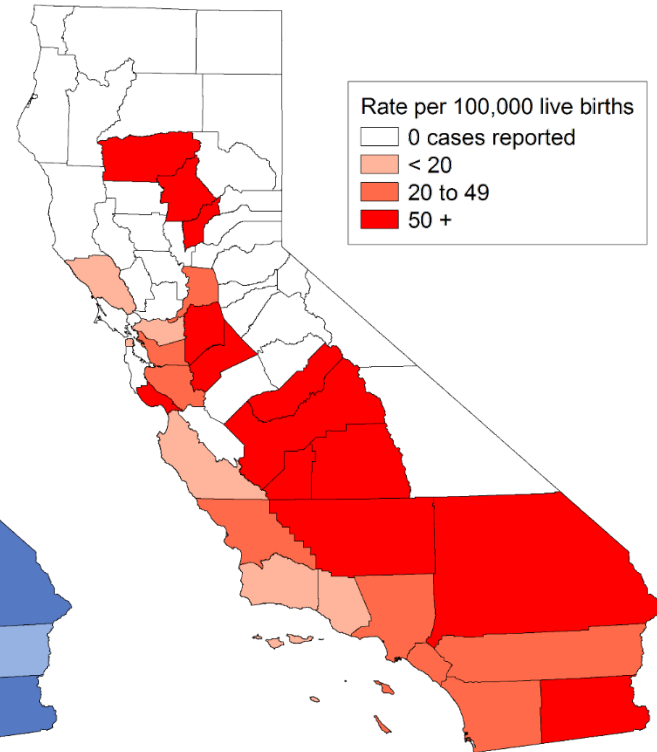
MALE Early Syphilis Rates



FEMALE Early Syphilis Rates



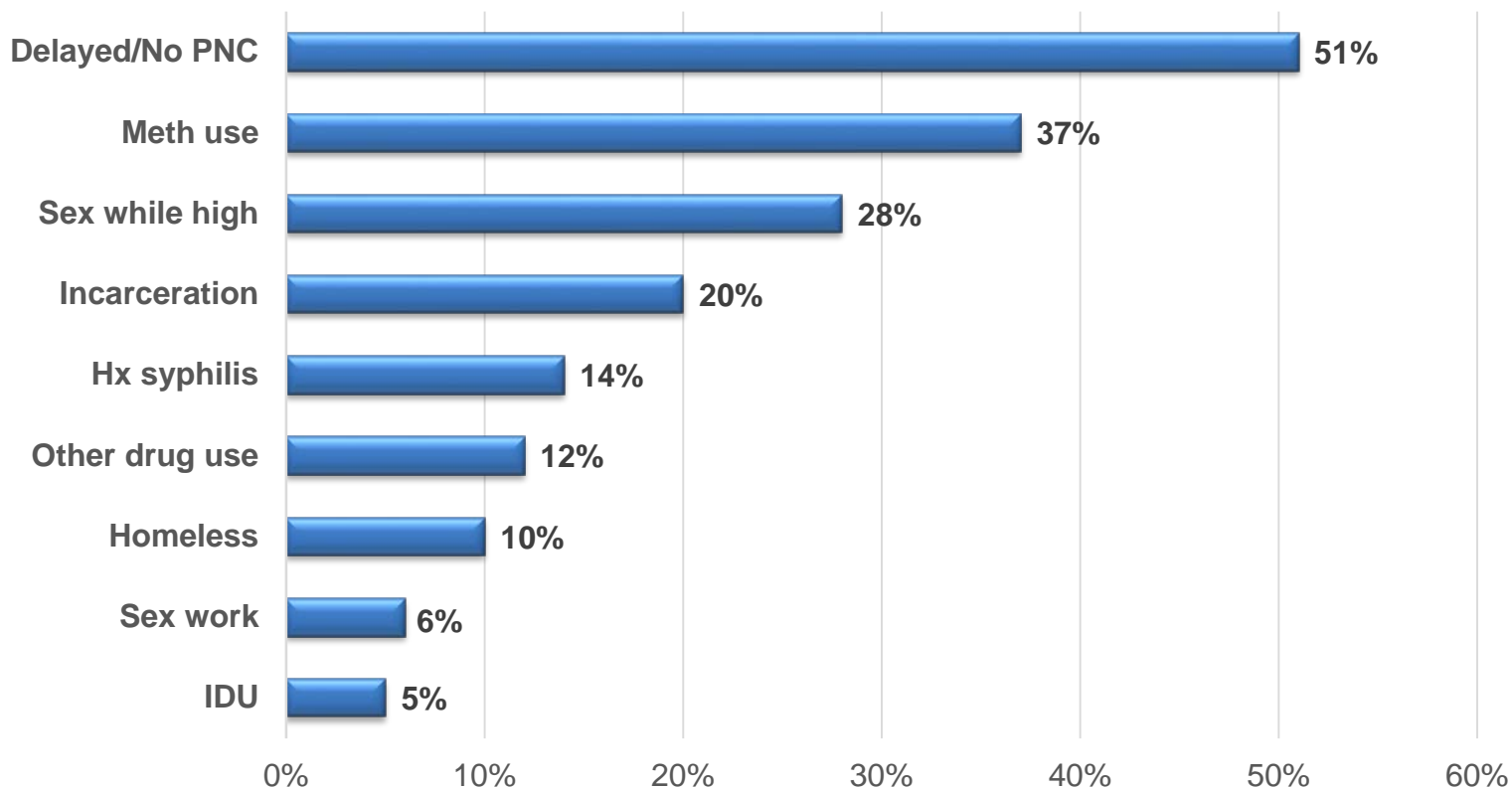
Congenital Syphilis Rates



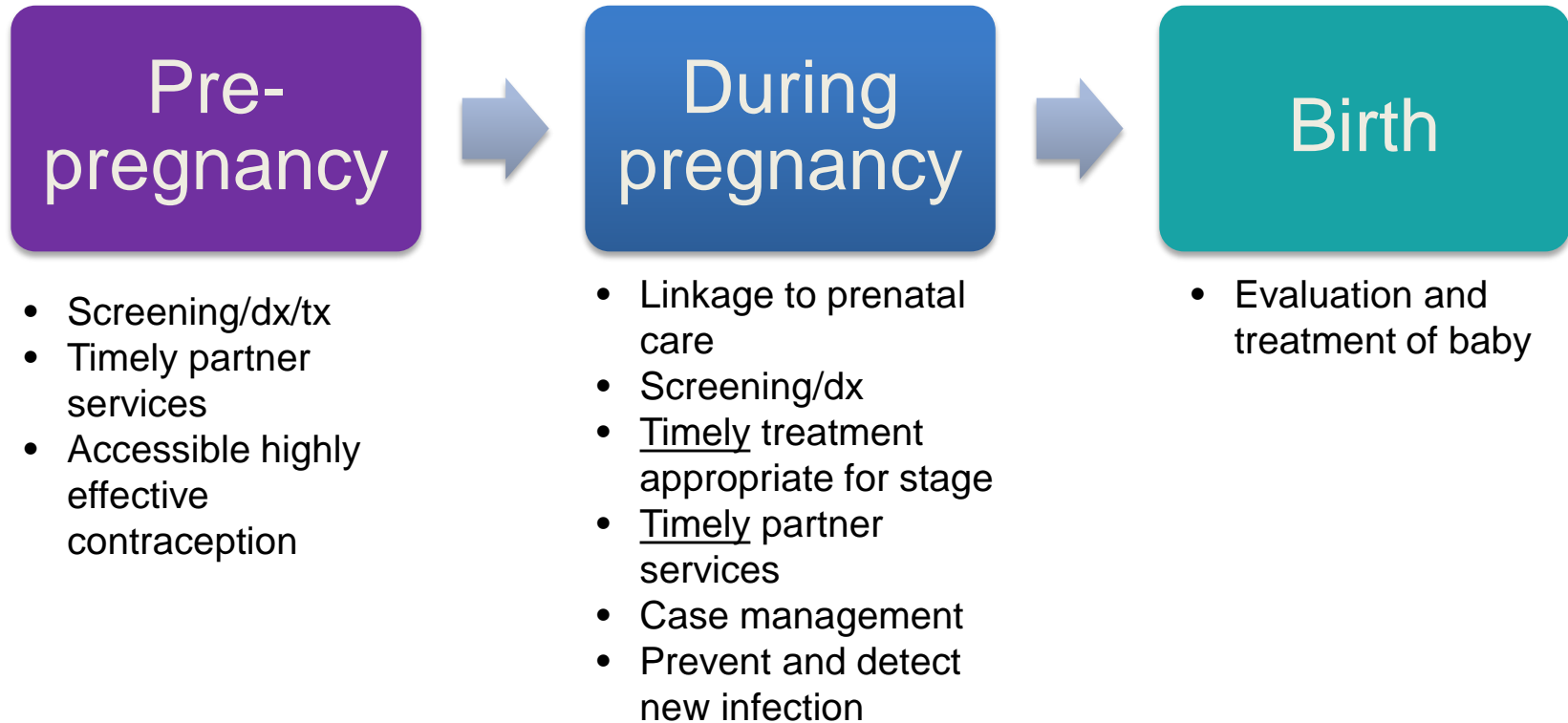
* Includes primary, secondary, and early latent syphilis.

Rev. 7/2018

Maternal Risk Factors, interviewed mothers of CS infants, 2016-2017



Congenital Syphilis Prevention Framework



ADDRESS SOCIAL DETERMINANTS OF HEALTH



U.S. Preventive Services
TASK FORCE

US Preventive Services Task Force | Evidence Report

September 4, 2018

Screening for Syphilis Infection in Pregnant Women Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

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Abstract

Importance The incidence of syphilis and congenital syphilis in the United States has increased after reaching historic lows in the early 2000s.

Objective To systematically review literature on the effectiveness and harms of screening for syphilis in pregnancy and the harms of penicillin treatment in pregnancy to inform the US Preventive Services Task Force.

Data Sources MEDLINE, PubMed, and the Cochrane Central Register of Controlled Trials for relevant English-language literature, published from January 1, 2008, to June 2, 2017. Ongoing surveillance was conducted through November 22, 2017.

Study Selection Studies conducted in countries categorized as “high” or “very high” on the Human Development Index that explicitly addressed 1 of 3 a priori-defined key questions.

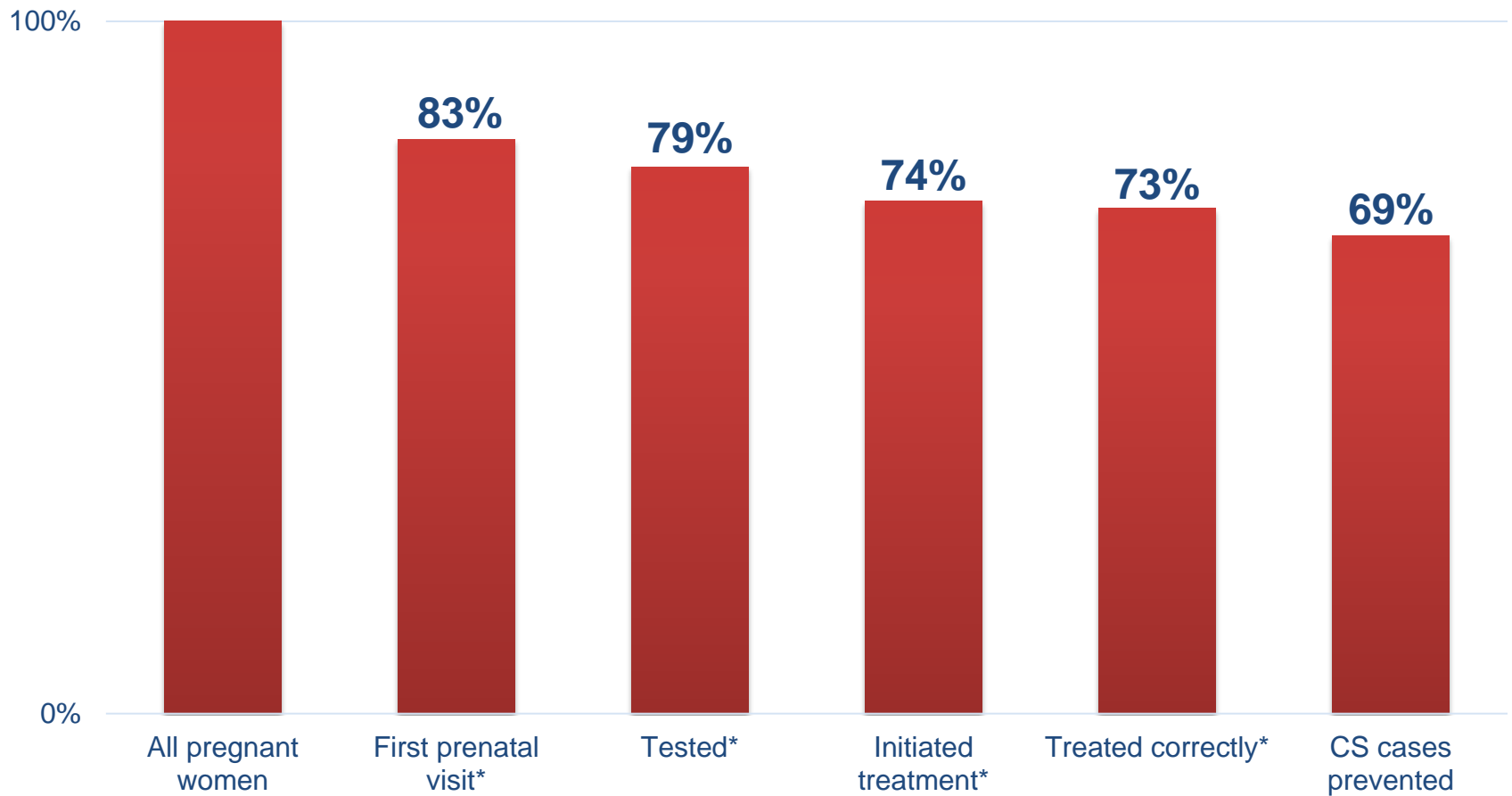
Extraction and Synthesis Independent critical appraisal and data abstraction by 2 reviewers. Data from included studies were narratively synthesized without pool-

and Measures Incidence of congenital syphilis; any harms of screening or penicillin treatment in pregnancy.

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Congenital Syphilis Prevention Cascade, 2017



* ≥ 30 days prior to delivery

Source: Nicole Burghardt, 2017 CPA surveillance data

Congenital Syphilis: Key Priorities

- Address barriers to prenatal care
- Testing and treatment in pregnancy
- Case review
- Prevention at delivery
- Pre-pregnancy prevention opportunities

Where are we now with STDs?



- Surveillance vastly improved
 - Sensitive diagnostic tests & effective treatments are available
 - Reduced stigma around sex and sexuality
-
- Dramatic increases in congenital syphilis
 - Threat of drug resistant gonorrhea
 - Drugs, poverty, barriers to care
 - Gaps in access to testing and treatment

Thank You

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