

Dutch STD control in the coming 10 years

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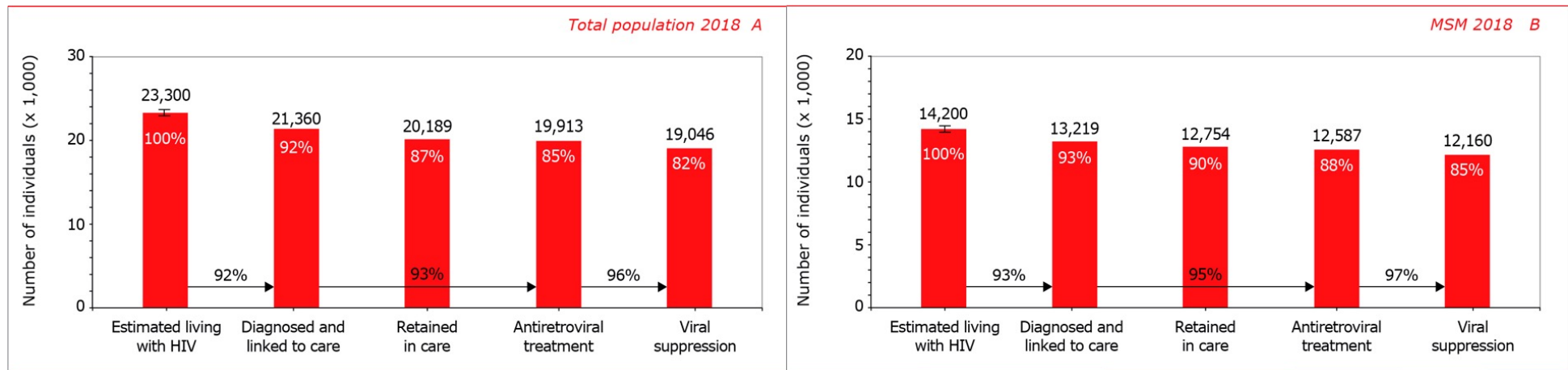
Disclosure

- Gilead: medication and funding for a PrEP cohort study
- MSD: HPV vaccines for a clinical trial

Overview

- Goals of the Dutch STI, HIV and Sexual Health Action Plan 2017-2022
- Test and treat paradigm for STD
- From secondary to primary prevention
- Imminent antibiotic shortages

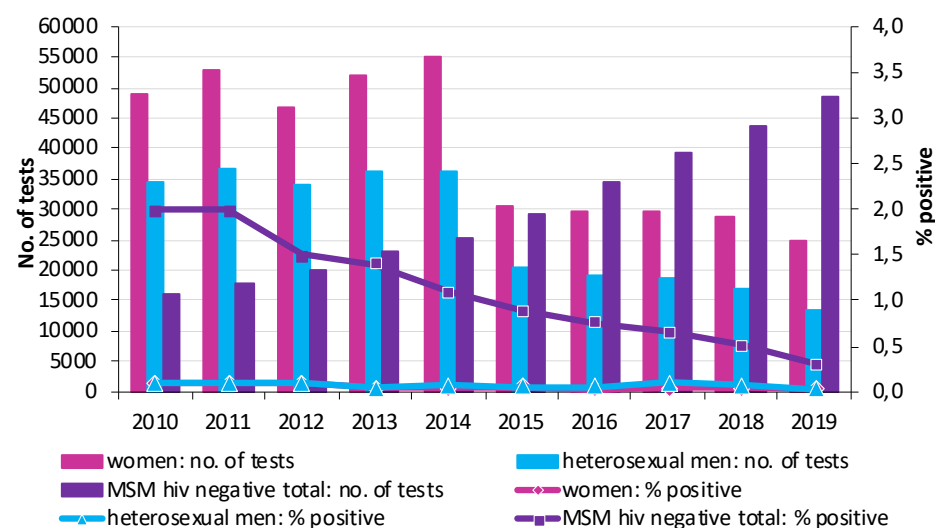
Continuum of HIV care for the total estimated HIV-positive population and for men who have sex with men 2018



Stichting HIV monitoring year report 2019

National Action plan *std, hiv en sexual health* 2017-2022

- HIV goals
 - Zero AIDS deaths
 - The annual number of new HIV diagnoses at least halved
 - (index 2015: 900).
 - 95-95-95 goal reached



Sexually transmitted infections in the Netherlands in 2019, RIVM 2020

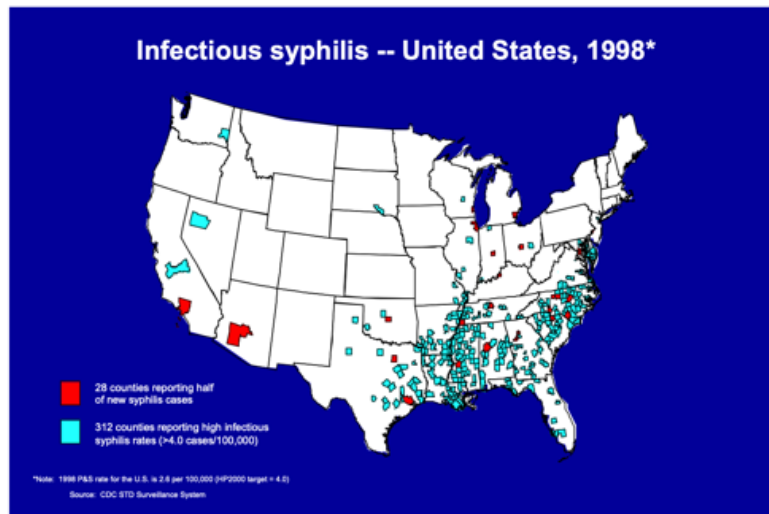
STD elimination?

Eliminating Syphilis from the United States

The U. S. has a unique but narrow window of opportunity to eliminate syphilis while cases are still declining.

Why is Syphilis Elimination in the U.S. within our reach now?

- Syphilis is a preventable and curable sexually transmitted disease (STD).
- Infectious syphilis is at the lowest rate ever reported: 2.6 cases/100,000 population (6,993 total cases).
- Syphilis is now very concentrated.
 - \$ Half of all new cases in 1998 were reported from only 28 counties, which represent less than 1% of all U.S. counties.
 - \$ Counties with high infectious syphilis rates (>4.0 cases/100,000 population) are clustered in the Southeastern U.S.
- Other industrialized countries have already eliminated syphilis.



Efforts to eliminate syphilis

✧ Ideal disease for elimination

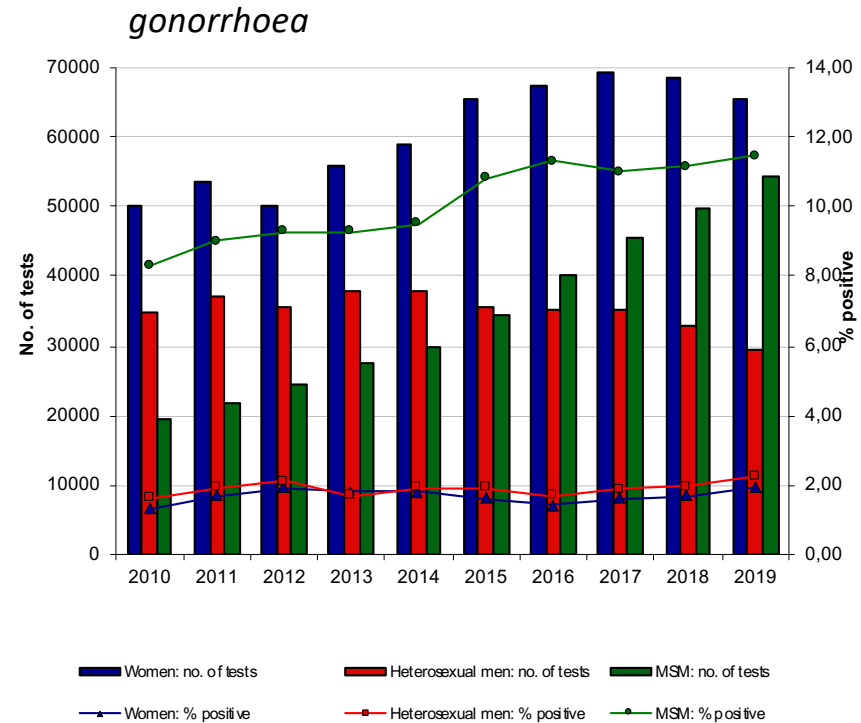
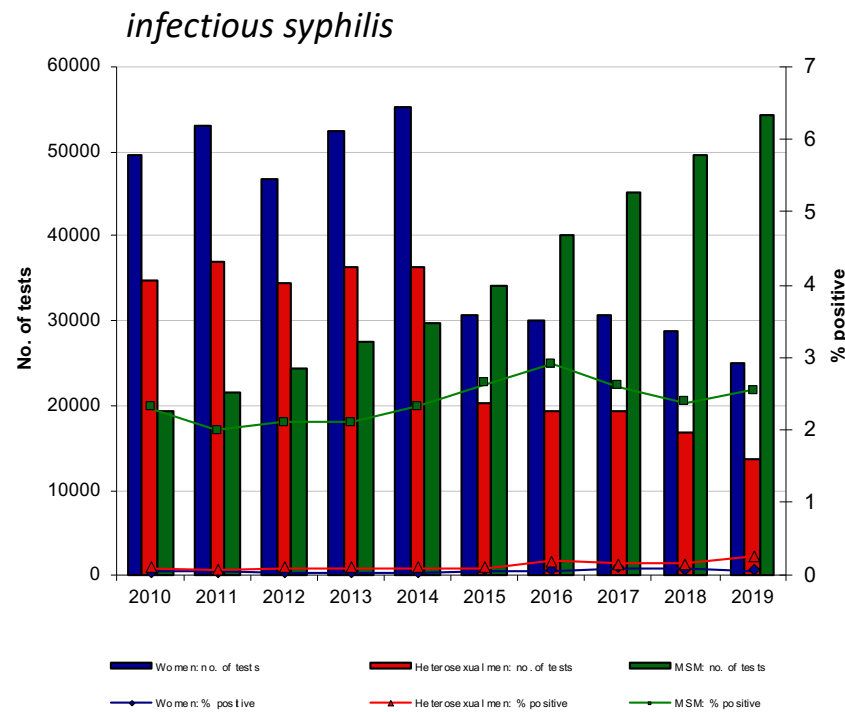
- ◆ Lacks an animal reservoir
- ◆ Long incubation period allows treatment before transmission
- ◆ Remains very susceptible to PCN
- ◆ Other industrialized nations have eliminated syphilis

✧ All time low hit in 2000 (5979 U.S. cases of primary & secondary syphilis)

National Action plan *std, hiv en sexual health* 2017-2022

- Halving the number of new syphilis infections to less than 500 per year (2016: 1,200).
- Halving the number of new gonorrhea infections (2016: 14,000).
- Development of an effective strategy to reduce the burden of disease of chlamydia.
- Decrease in the number of acute HBV and HCV infections to zero.
- Broad social acceptance of sexual diversity and of chronic STIs.

Positivity rates syphilis & gonorrhoea, STI outpatient clinics 2010- 2019 by gender and type of sexual contact



Sexually transmitted infections in the Netherlands in 2019, RIVM 2020

Sustainable development goals (SDG) en SOA/HIV



Chersich et al. Globalization and Health (2018) 14:6

Why do HIV ambitions seem feasible, but (bacterial) STD ambitions do not?

- You can only get HIV once, whereas bacterial STIs repeatedly
- HIV is a focused epidemic in the Netherlands
- Condom use protects against HIV, yet much less against bacterial STD
- There are effective biomedical prevention interventions for HIV:
 - Treatment as Prevention (TasP)
 - Pre-Exposure Prophylaxis (PrEP)
- There are no effective biomedical prevention interventions for STIs:
 - many side effects
 - antibiotic resistance

More testing to fight bacterial STD?

- Doesn't seem to work for chlamydia yet
- 30% decrease in pelvic inflammatory disease (PID) in countries without chlamydial screening efforts

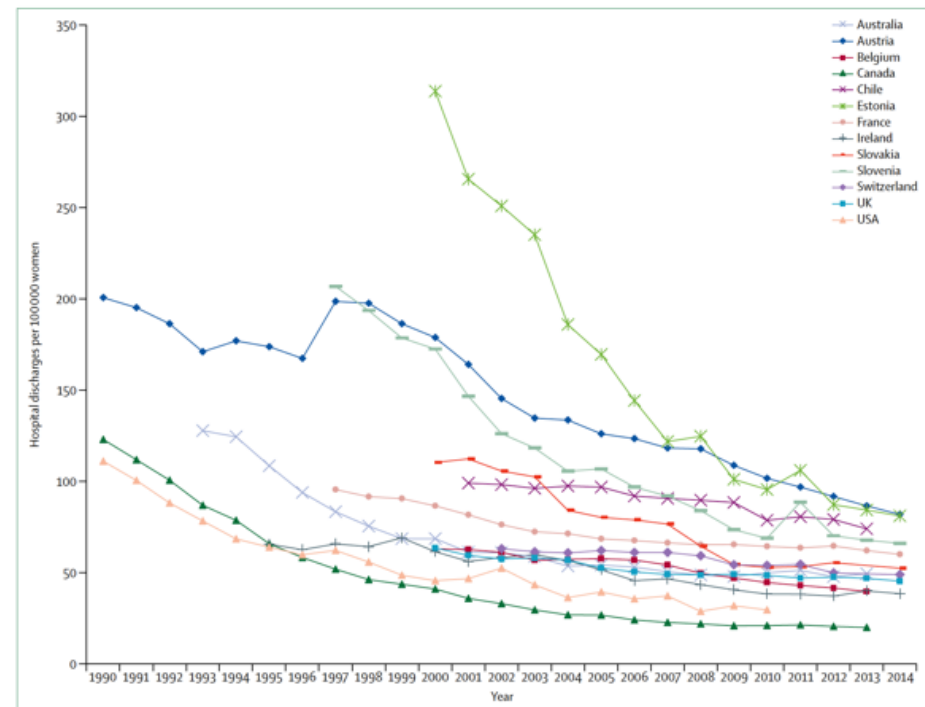
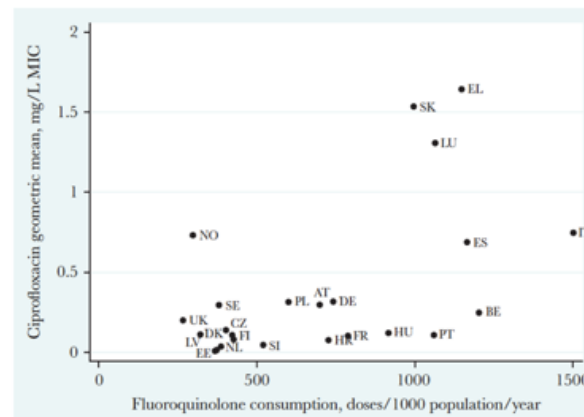
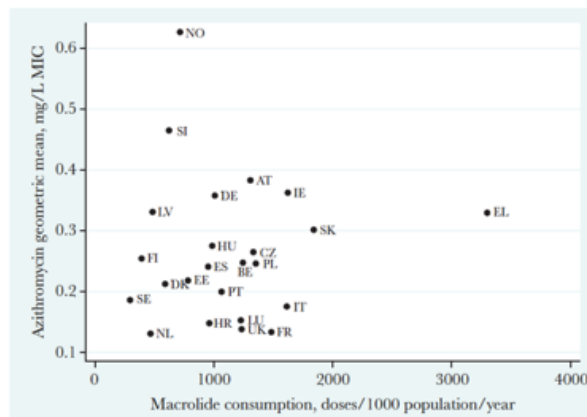
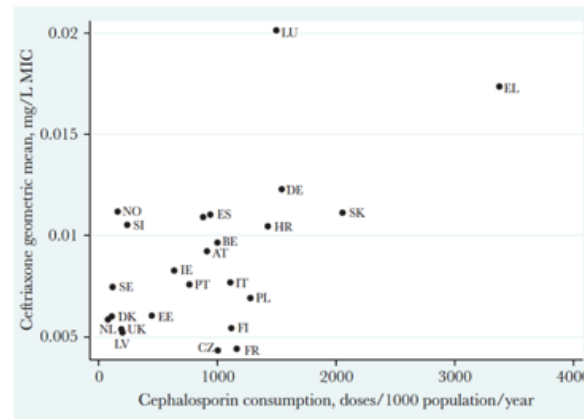
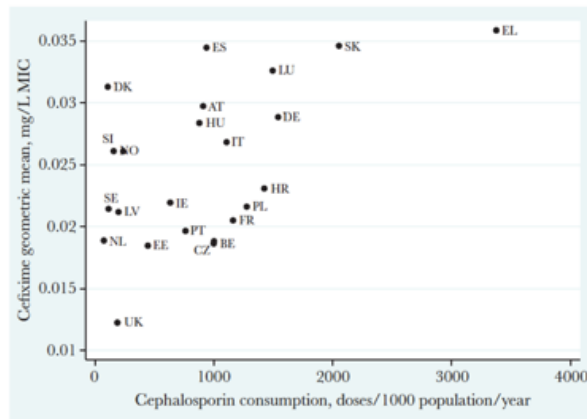


Figure 5: Hospital discharge rates for inflammatory disease in female pelvic organs
Data are from the Organisation for Economic Co-operation and Development.¹⁰¹ See the appendix for further details.

Test and treat paradigm for STD

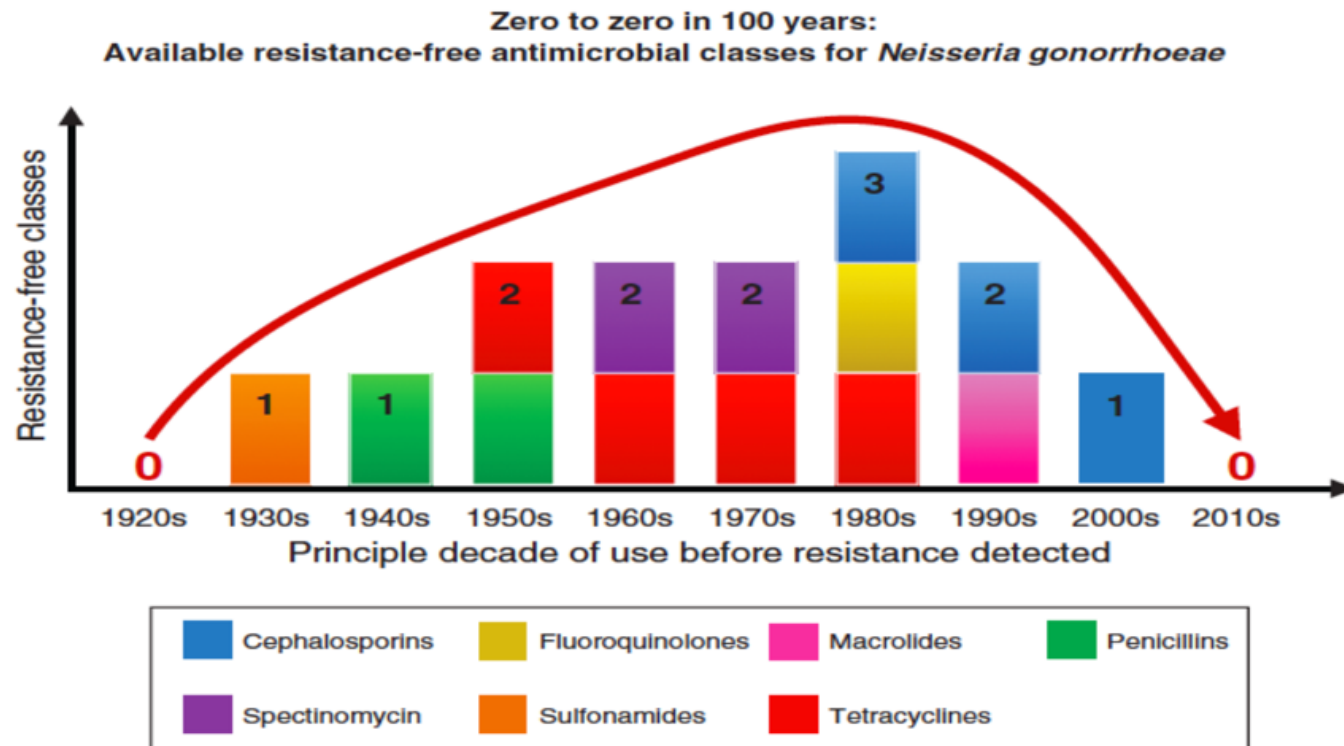
- Highly effective for HIV
 - > 99% of people with HIV fall ill
- Effective with chlamydia?
 - <1% women with chlamydia become infertile or develop pelvic inflammatory disease
- Numbers needed to treat
- Antibiotic resistance due to antibiotic over-consumption
- Fighting infections vs fighting infectious diseases

Antibiotics consumption is associated with reduced antimicrobial susceptibility in gonorrhea



Kenyon C et al. J Inf Dis, April 2019

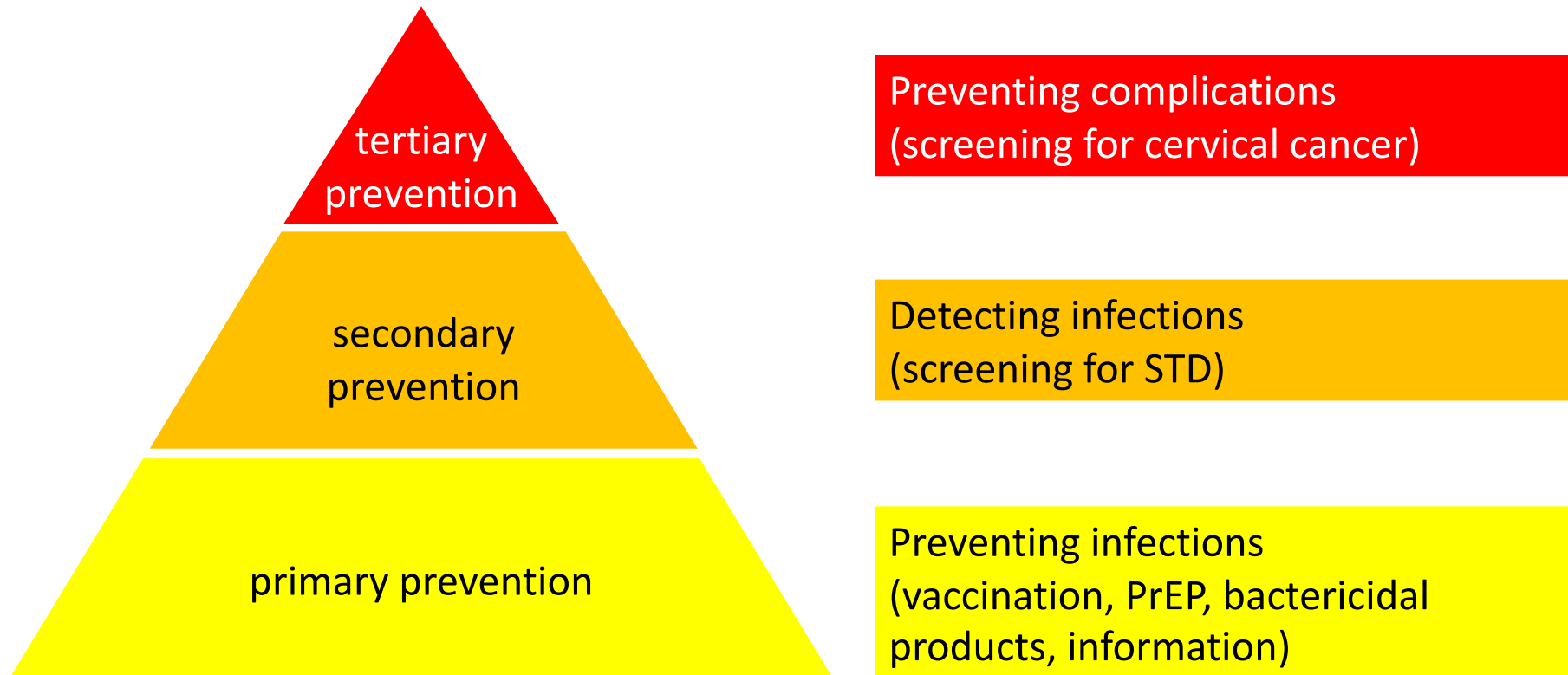
100 years of treatment options for gonorrhea



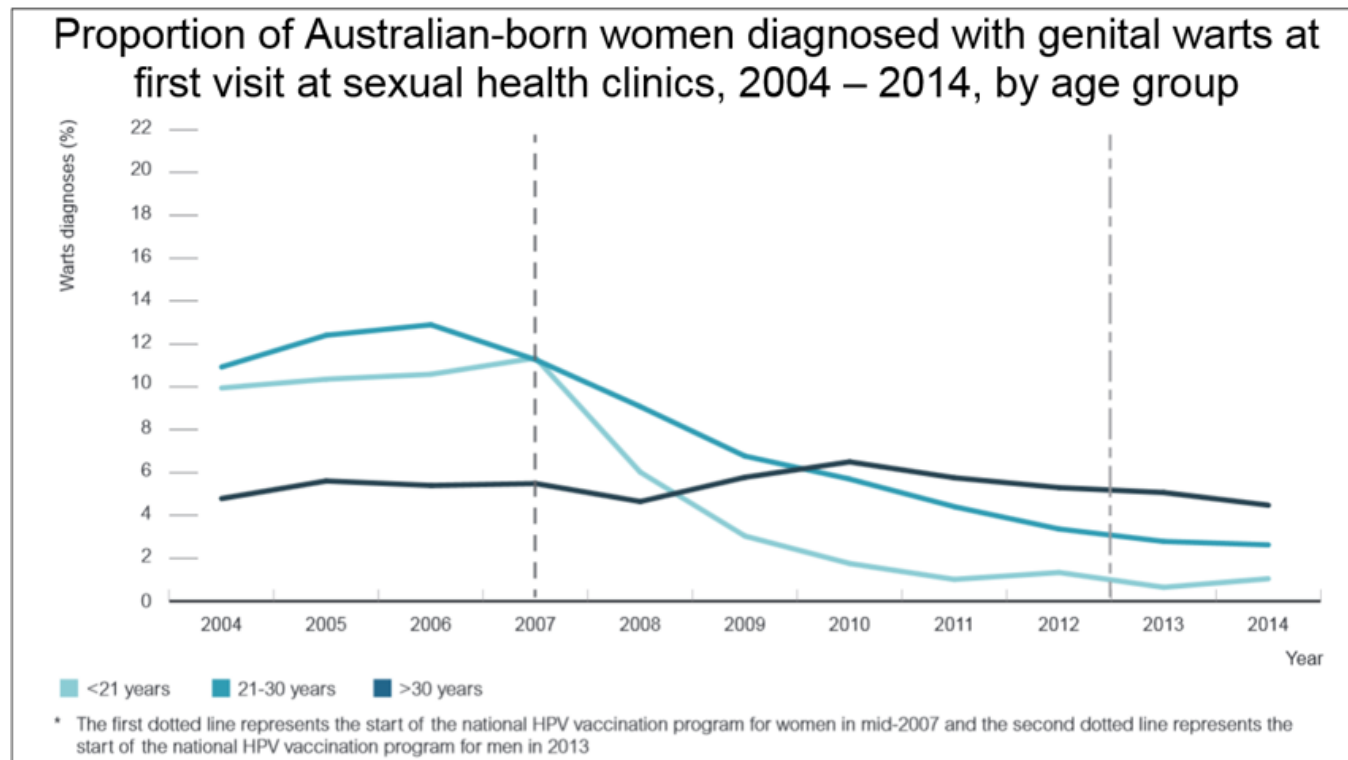
Re-evaluate of test and treatment paradigm

- Detection and treatment asymptomatic chlamydia infections?
 - *Mycoplasma genitalium* infections?
- Blind treatment based on complaints?
 - when a result can be available within 24 hours
- Blind treatment based on partner notification?
 - about 1 in 3 does not require treatment

From secondary to primary prevention



Potential effect of STD vaccines



Oral gargles against gonorrhea transmission

- Role of oral sex in gonorrhea transmission
- OMEGA study: gargling with bactericidal mouthwash against gonorrhea (Australia)
- Most gonorrhea infections ano-rectally
- Douching as a primary prevention?
 - Microbicide Trials Network (MTN)



Point of care testing, results while you wait

- Result <30 minutes
 - more receptive to counseling
 - chain of transmission instantly broken
 - no more “no show”
 - efficiency
- Already available as antibody tests for systemic infections (syphilis, HIV, hepatitis)
- For chlamydia and gonorrhea now 90 minutes waiting time.

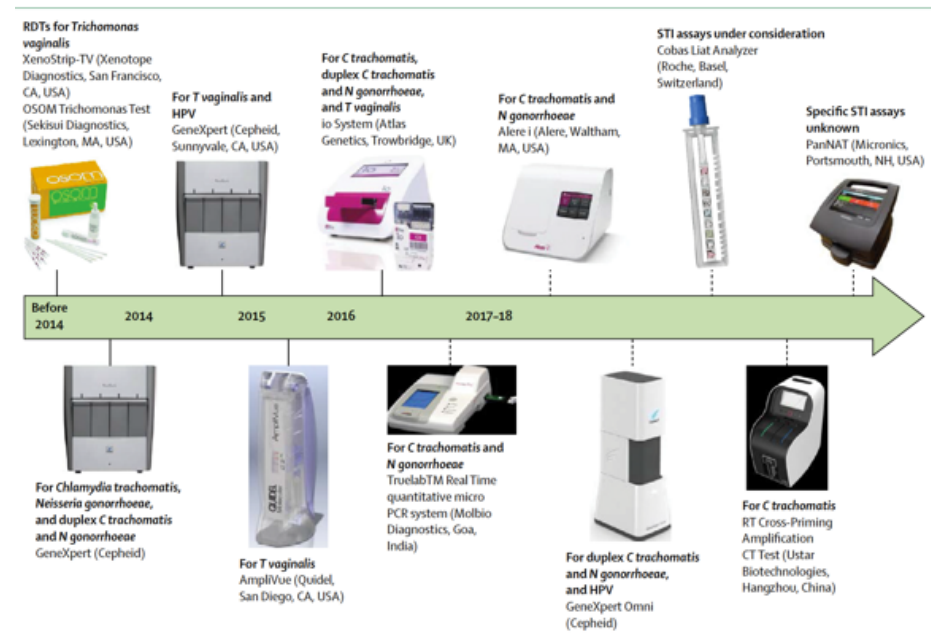
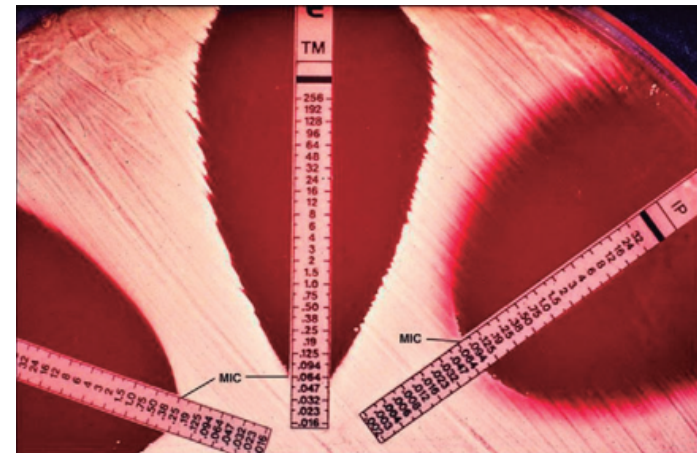


Figure 7: Point-of-care tests or near-point-of-care tests for STIs. These tests are either available or in the pipeline. The dotted line indicates that no market launch date has been set by the manufacturer for these tests.¹⁰ RDTs=rapid diagnostic tests. HPV=human papillomavirus.

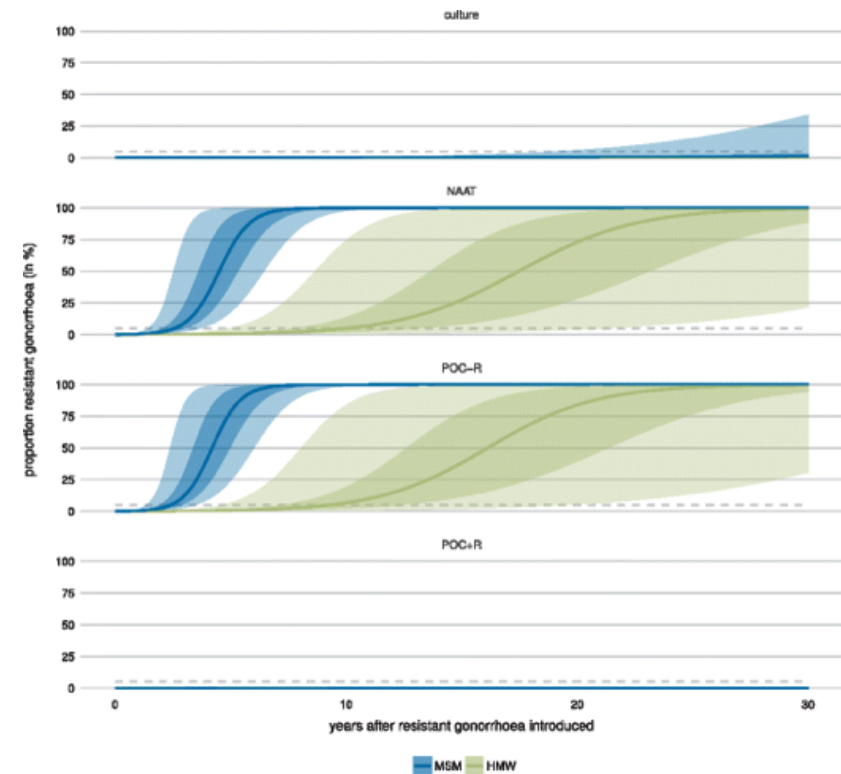
Antimicrobial Resistance (AMR) Testing for Gonorrhea

- WHO considers gonorrhea resistance as a top priority.
- Culture and susceptibility testing are increasingly rare
 - Requires same day sample transportation
 - Results take days
 - Displaced by PCR tests



Gonorrhea point of care diagnostics can accelerate antimicrobial resistance (AMR) induction

- WHO recommends to disband an antibiotic for an indication in case of > 5% resistance
- Culture diagnostics enables targeted treatment, thus impeding AMR
- In contrast to NAAT diagnostics
- Point of care diagnostics WITHOUT resistance determination won't affect AMR induction
- Point of care diagnostics WITH resistance determination can impede AMR



Fingerhuth, BMC Med 2017

Molecular tests for gonorrhoea susceptibility

QuantuMDx

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STI Panel Test

Preventing the spread of sexually transmitted infections



Providing diagnostic and drug sensitivity testing in less than 30 minutes will enable patients to immediately receive the treatment they need.

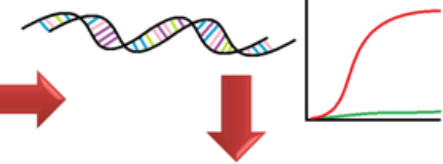
Validation of a Molecular Assay for the Detection of Antimicrobial Resistance in *Neisseria gonorrhoeae* Isolates and Matched Clinical Nucleic Acid Amplification Tests (NAAT) Specimens

S. Peterson*, I. Martin, W. Demczuk, L. Hoang, P. Naidu, D. Haldane, M. R. Mulvey

NAAT Specimens



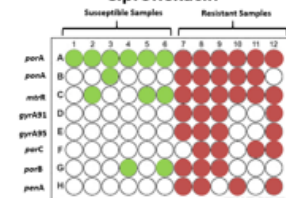
Real-Time PCR



Phenotypic Antimicrobial Susceptibility Testing



Molecular Antimicrobial Susceptibility Prediction for Cephalosporins and Ciprofloxacin



cdc.gov

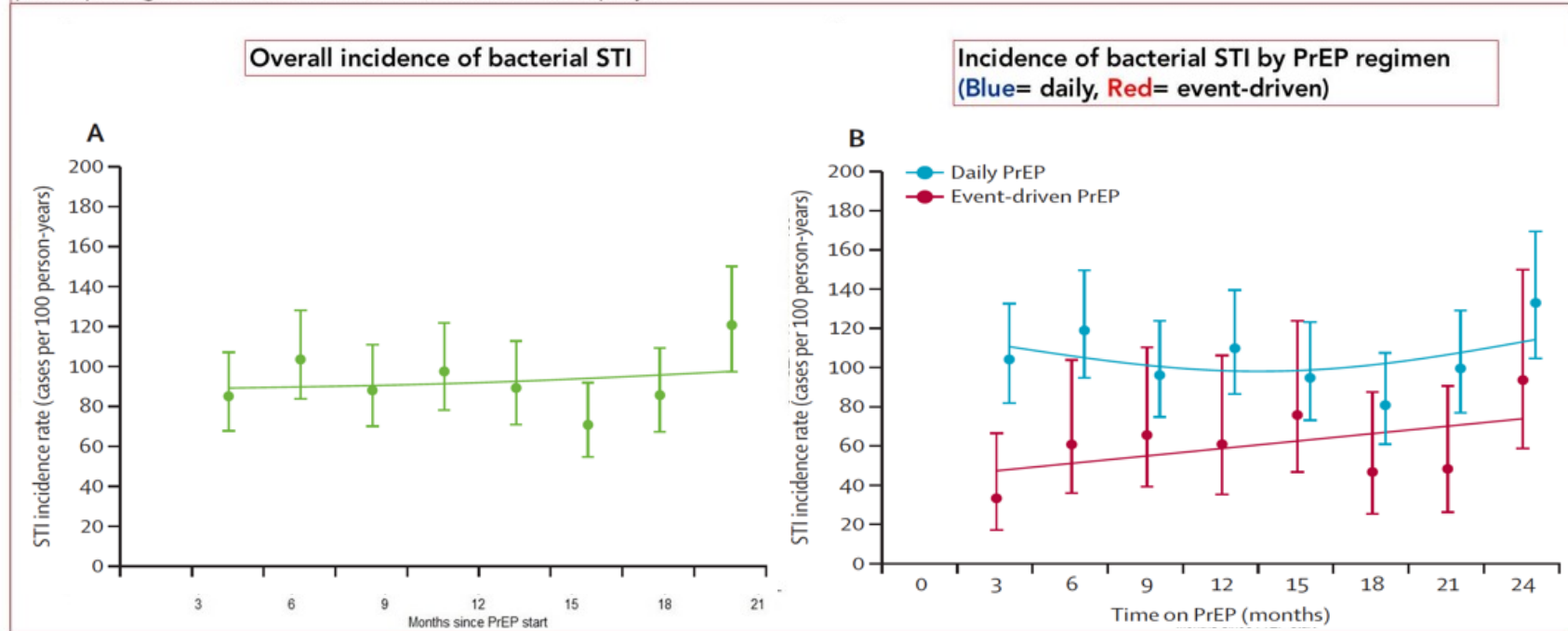
PrEP and STD screening

- Fear of an increase in unsafe sex among PrEP users
- Fear of an increase in the STD incidence
- 3 monthly STD screening



STI incidence in AmPrEP cohort, Amsterdam

Figure 1. Modeled incidence rate of any bacterial STI over time since PrEP start among daily or event-driven PrEP users (n=372) participating in the Amsterdam PrEP demonstration project.



Hoornenborg et al, Lancet HIV 2019

Shortages of out-of-patent antibiotics

- Global shortage of BENZATHINE penicillin G since 2015,
 - first-line treatment option for syphilis
 - profit margins are small and production costs are high
 - produced in only three factories, all located in China
 - two discontinued production due to regulatory / environmental issues.
- BENZATHINE penicillin G is the only safe option for pregnant women to prevent congenital syphilis.
- WHO initiates a public-private program to ensure quality, safety and efficacy standards
- Confusion about BENZATHINE penicillin G and sodium penicillin G

Nurse-Findlay S, Plos Med 2017
Nieuwenburg, STI 2020

Conclusions STD control coming 10 years

- HIV goals in Dutch action plan are realistic, STD targets are not
 - STD test policy more focussed
 - danger of antibiotic resistance
 - from infection control to infectious disease control
 - screening frequency: when no complaints?
 - point of care testing
- From secondary to primary prevention
 - vaccines?
 - biomedical interventions against STD?
- Investment in antibiotic treatment
 - development of new antibiotics
 - availability of out of patent antibiotics



STI & HIV World Congress
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RAI Congress Centre
Amsterdam, the Netherlands



www.stihiv2021.org