The potential impact of vaccination on the prevalence of gonorrhea

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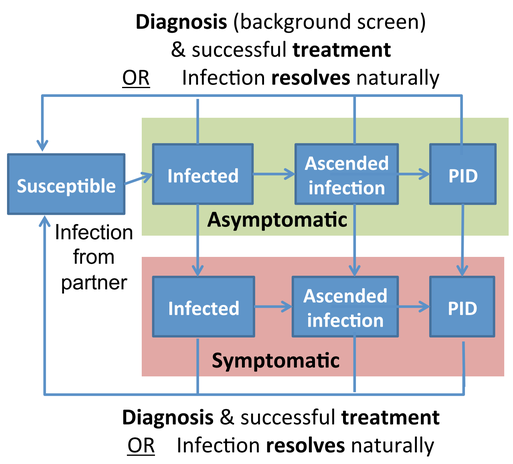
Introduction

- Gonorrhea, one of the most common STIs worldwide, can lead to serious sequelae, including infertility and increased HIV transmission. In the absence of new antibiotics, and given the rapid emergence of resistance to all previously used antibiotics, development of a vaccine would be the ideal solution to this public health emergency.
- Understanding the desired characteristics, target population, and expected impact of an anti-gonococcal vaccine is essential to facilitate vaccine design, assessment, and implementation.
- The modeling presented aims to fill these conceptual gaps and inform future gonococcal vaccine development.

Methods

- Using an individual-based, epidemiological simulation model, gonococcal prevalence was simulated in a heterosexual population after the introduction of various hypothetical vaccines.
- The model was adapted from *Gray et al., JID, 2009,* and is fully described in *Craig et al., Vaccine, 2015*. An overview of the model (**1**) and a subset of parameters used (**2**) are shown.
- A vaccine is considered to have constant protective efficacy until its duration is reached, after which it has no efficacy.
- A 50% efficacious vaccine would halve the probability of infection after sex with an infected partner.
- Simulations were run until prevalence becomes stable or infection disappears from the population.

1 Model Overview

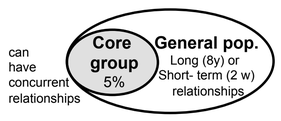


2 Model Parameters

Population parameters

- 100,000 sexually active heterosexuals
- 1:1 ratio of men to women
- constant size: enter on sexual debut (>13y, av 17y) & leave as they age out/ no new partners (av 50y)
- ~1.7% gonorrhea prevalence

Sexual behavior



- Model tracks relationship dynamics
  - Formation / break-up of short- and long-term relationships; Duration of &b/w relationships
- Sex acts per week
- Condom use / effectiveness

Infection parameters

Min. infectious dose	250 CFU
Initial load	10^3
Peak load	10^7
Doubling time	3.4 hr

Clinical parameters

Symptomatic	34%(F)	64%(M)
Av. Infectivity	0.5	0.28
Asym. testing	0.04	0.025
Test sensitivity	90%	
Natural immunity	0	

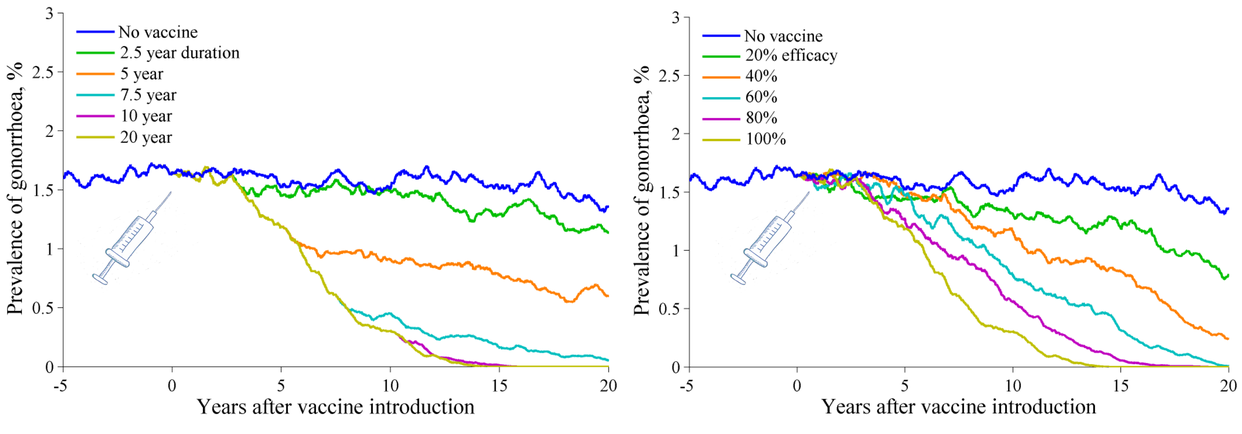
Results

What would be the impact of vaccines with varying efficacy?

- Does a vaccine need to induce sterilizing immunity?
- Would a modest decrease in transmission have an impact?
- What duration of protection is needed?

3 Prevalence of gonorrhea with 100% coverage of 13 year olds with vaccines of:

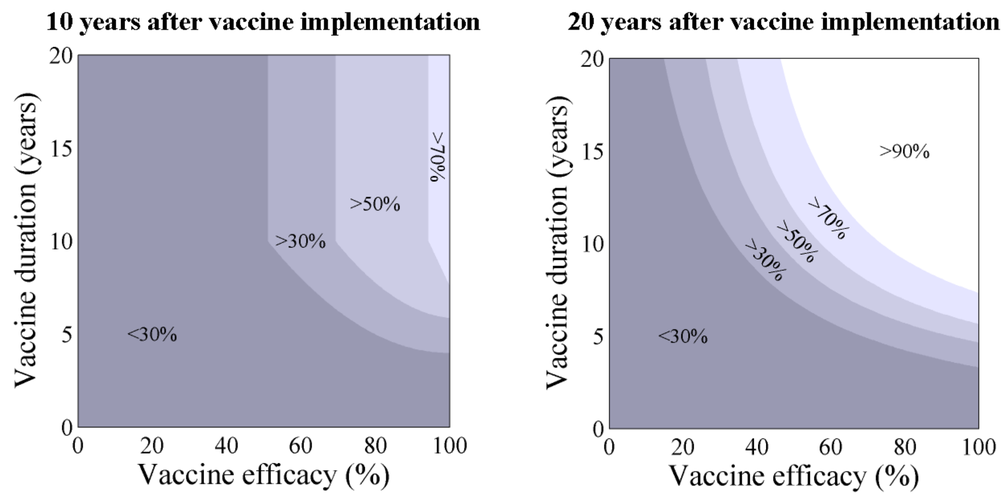
100% efficacy & differing durations | **Differing efficacies & 20 yrs duration**



Model simulations predicted that gonococcal prevalence could be reduced by:

- >90% within ~15 years, using a vaccine of 100% efficacy and 10-20y duration.
- >90% within ~20 years, using a vaccine of 100% efficacy and 7.5 y duration.
- >90% within 20y, with a non-waning vaccine of 60-100% efficacy.
- ~40% within 20y, with a non-waning vaccine of just 20% efficacy.

4 The reduction in gonorrhea prevalence expected



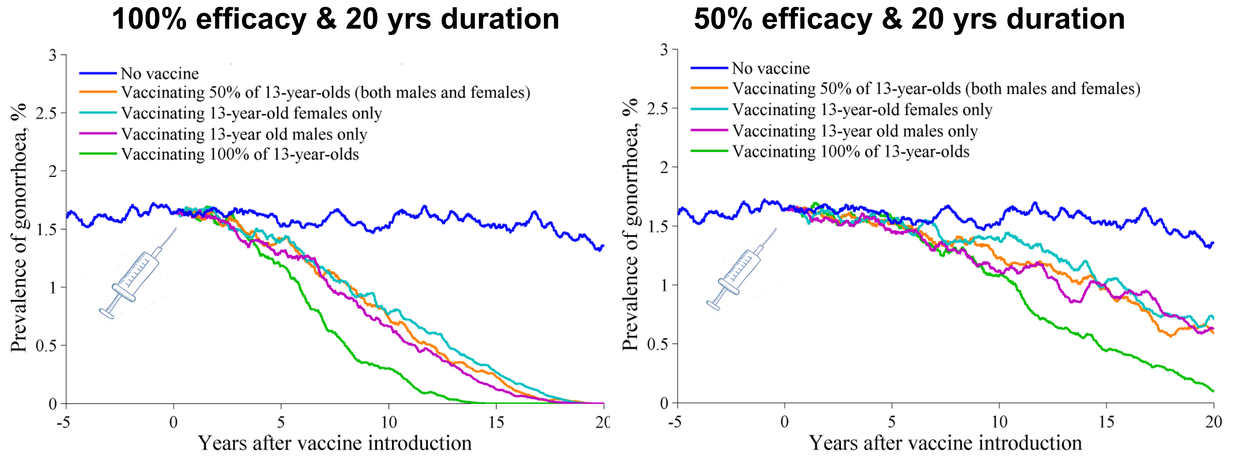
Simulations were run for combinations of efficacy and duration in 10% and 2.5 yr increments, and curves fit to obtain smooth region boundaries. Reduction is relative to prevalence in the no-vaccine scenario. In the left panel, vaccines with ≥10 yr duration are indistinguishable from one another as there has only been 10 years of vaccination.

What should the target population be?

- Should vaccines target specific age, gender, high risk / vulnerable, or other groups?

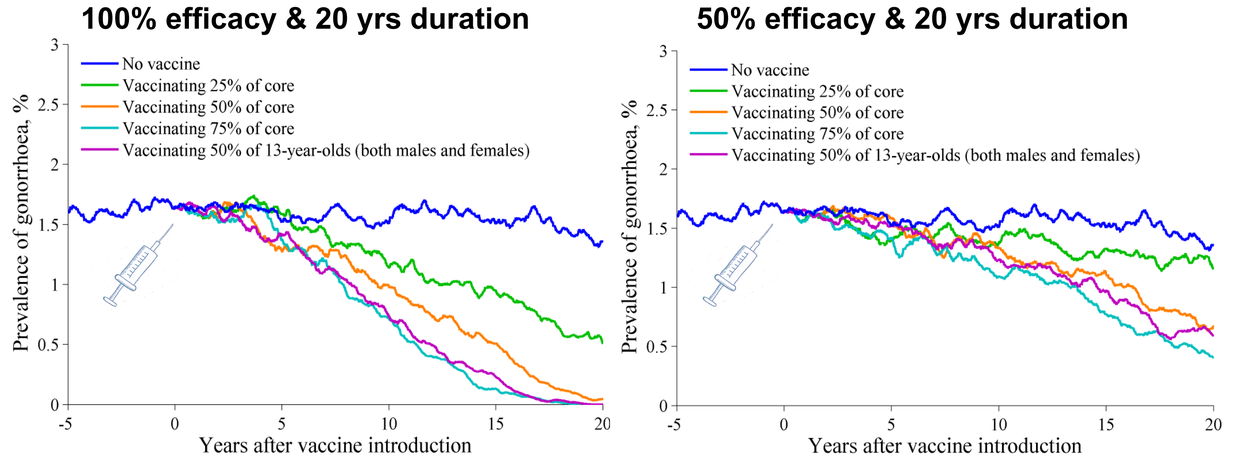
5 Prevalence of gonorrhea with coverage of either males or females with vaccines of:

100% efficacy & 20 yrs duration | **50% efficacy & 20 yrs duration**



6 Prevalence of gonorrhea with coverage of the high-risk "core group" with vaccines of:

100% efficacy & 20 yrs duration | **50% efficacy & 20 yrs duration**



Model simulations predicted that:

- The sex of those vaccinated was unimportant as long as 50% of the eligible population are vaccinated.
- Vaccinating 75% of incoming core group individuals is about as effective, at a population level, as vaccinating 50% of all 13-year-olds.

Conclusion

- A vaccine of moderate efficacy and duration could have a substantive, and rapid, impact on gonococcal prevalence and disease sequelae, if coverage is high and protection lasts over the highest risk period (*i.e.*, most sexual partner change) among youths.
- Targeting specific groups (*e.g.*, high risk 'core' groups, or males/females only) would also have a substantive impact on gonococcal prevalence.

Vaccine efficacy	Vaccine duration	Reduction in GC prevalence	Population coverage
100%	20 y	50% in 7 y	100% All 13 year olds
		> 90% in 13 y	
>70%	10 y	50% in 10 y	
100%	7.5 y	> 90% in 20 y	100% All 13 year olds
80%	10 y		
50%	20 y		
100%	20 y	> 90% in 20 y	50% All 100% Male 100% Female 75% Core (5%)
50%	20 y	50% in 20 y	

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