Deterministic Compartmental Models

Application: Modeling the Potential Benefit of HPV Vaccines

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HIV VACCINE TRIALS NETWORK

Outline

- **Human papillomavirus and cervical cancer**
- **Infectious disease epidemiology – mathematical modelling of sexually transmitted infections (STIs)**
- **Models of a single HPV type and vaccination**
- **SIR vs. SIS models**

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HPV and cervical cancer

- **Human Papillomavirus (HPV) - a necessary cause of cervical cancer (CC)**
- **500 000 new cases of cervical cancer annually worldwide**
- **2nd most common cancer in women in the developing world**
- **HPV - ubiquitous sexually transmitted infection**
- **Most infections resolve spontaneously**
- **A minority go on to develop carcinoma of the cervix over years**

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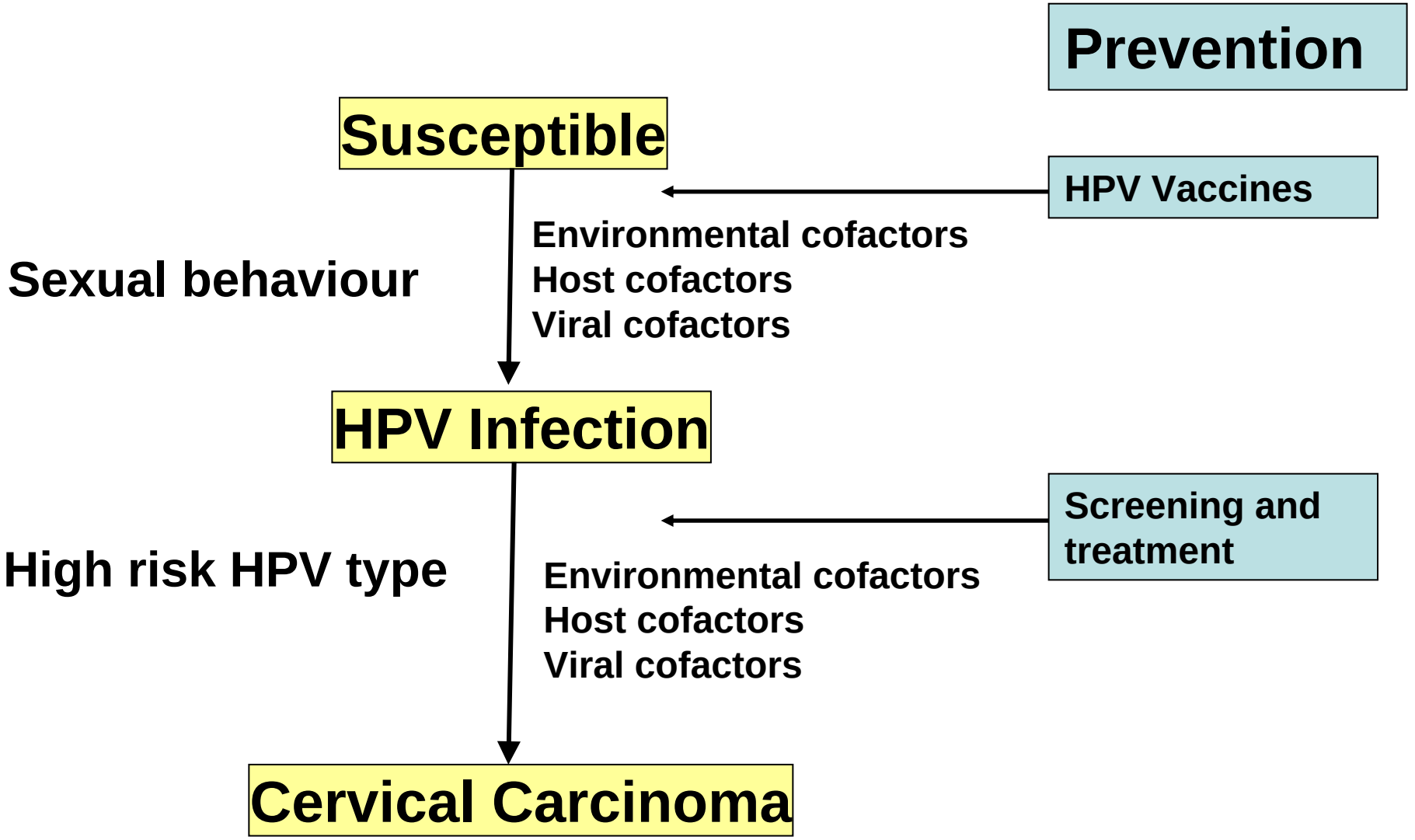
Risk factors for HPV and CC



Questions about HPV vaccines

- **Who should be immunised?**
- **How do vaccine delivery characteristics (such as coverage and age at vaccination) affect effectiveness?**
  - **Coverage: the percentage of the target population that is immunised**

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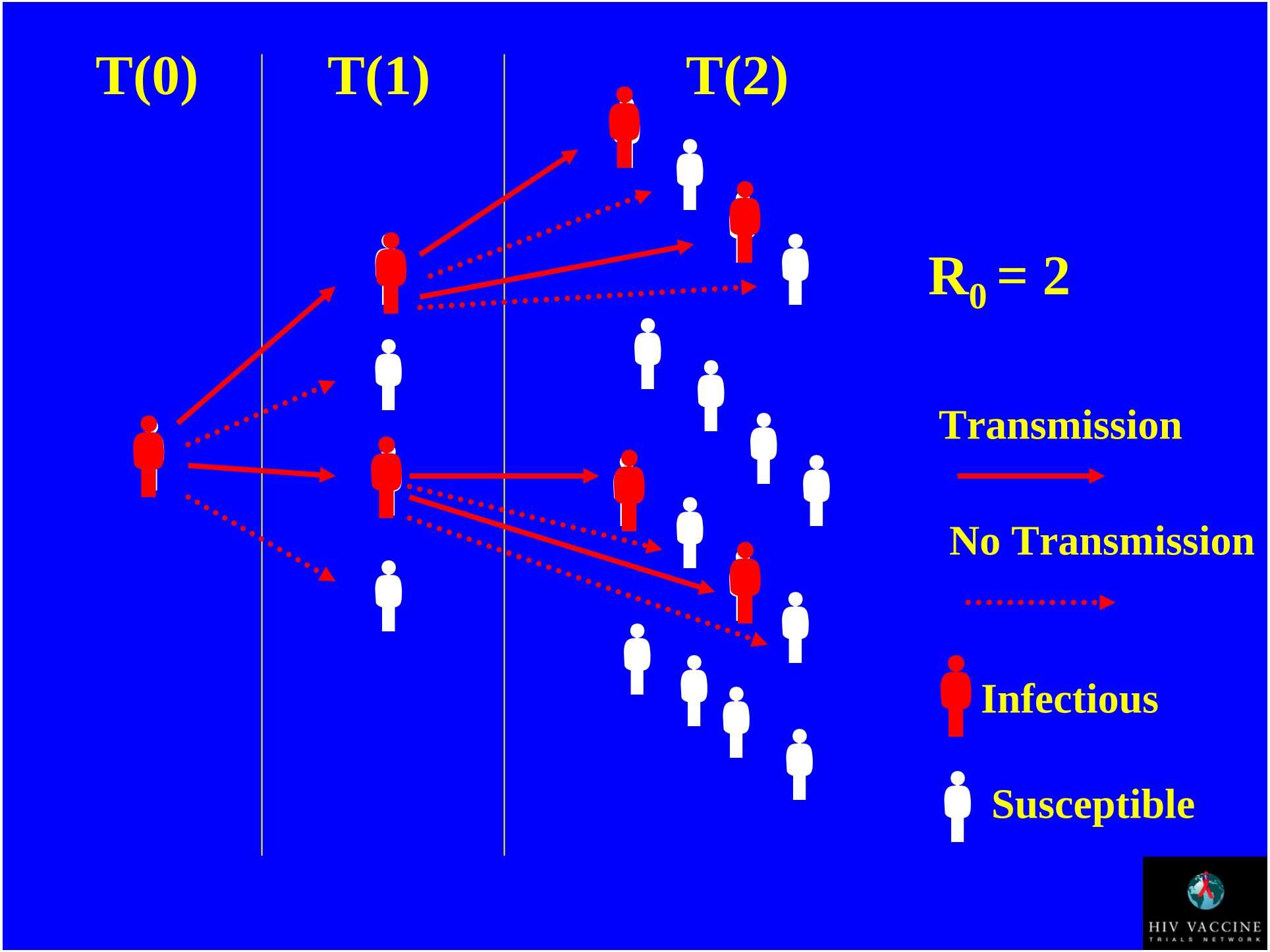
T(0)
T(1)
T(2)
$R_0 = 2$
Transmission
No Transmission
Infectious
Susceptible
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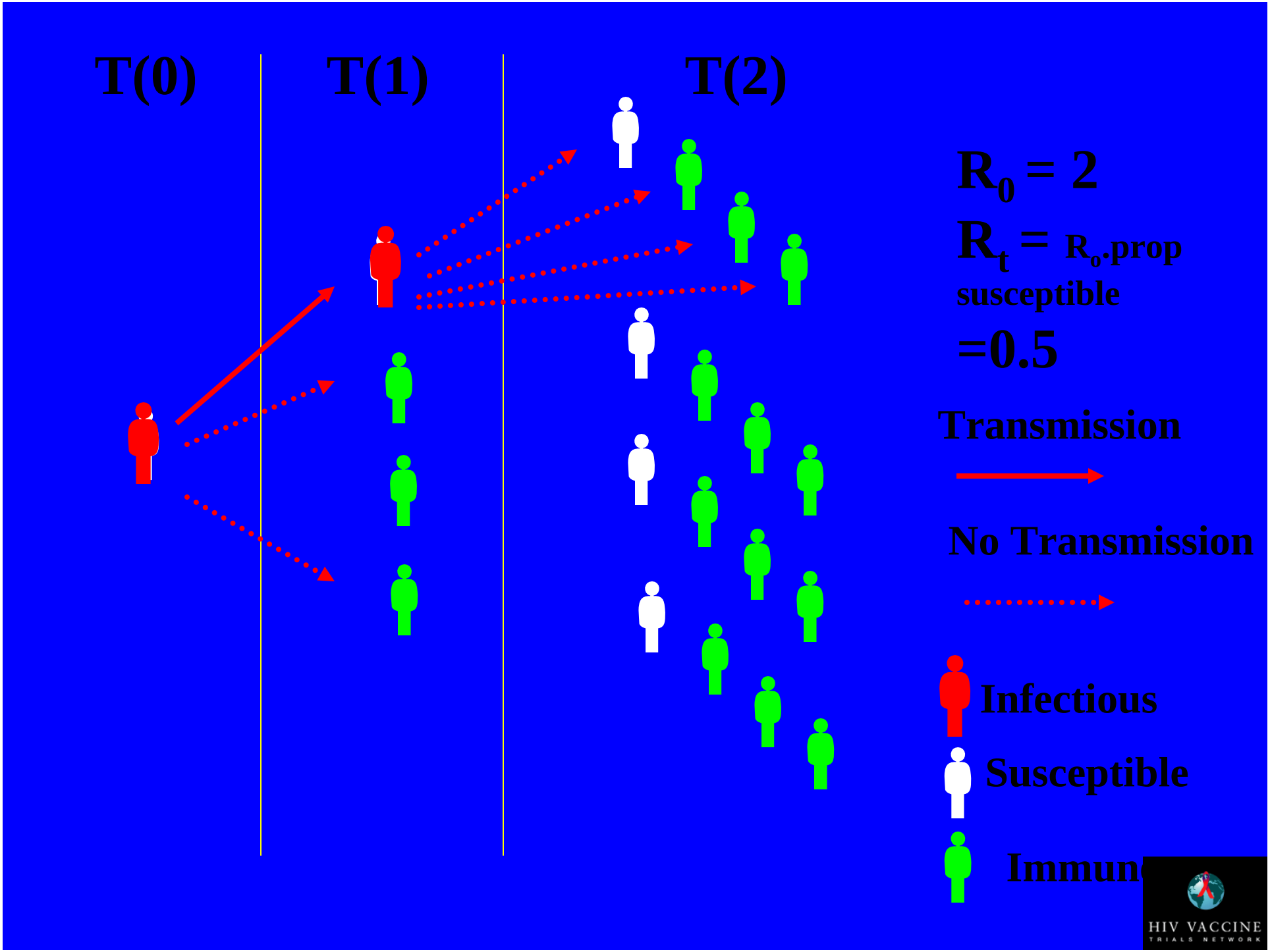
T(0)
T(1)
T(2)
$R_0 = 2$
$R_t = R_o.prop$ susceptible
=0.5
Transmission
No Transmission
Infectious
Susceptible
Immun
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An introduction to mathematical models

- **Models are a framework for understanding and communicating infectious disease**
- **Explicit assumptions help delineate which parameters are based on evidence**
- **Quantitative or qualitative results are compared with observed or experimental data**
- **Validated models can be used to estimate the potential impact of interventions (e.g. vaccination)**

Garnett, G. P. (2002). Sex Transm Infect 78(1): 7-12.

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An introduction to mathematical models

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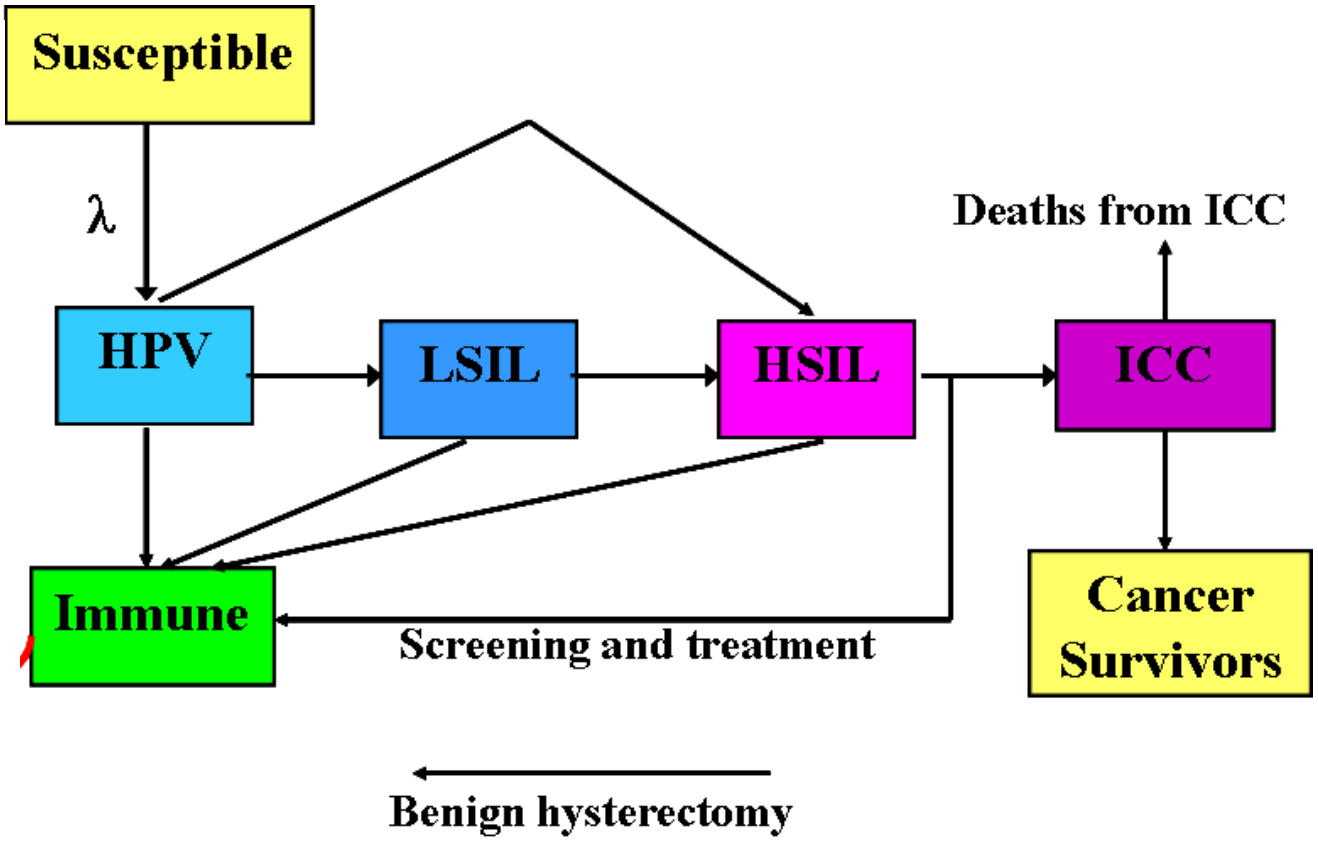

An introduction to mathematical models

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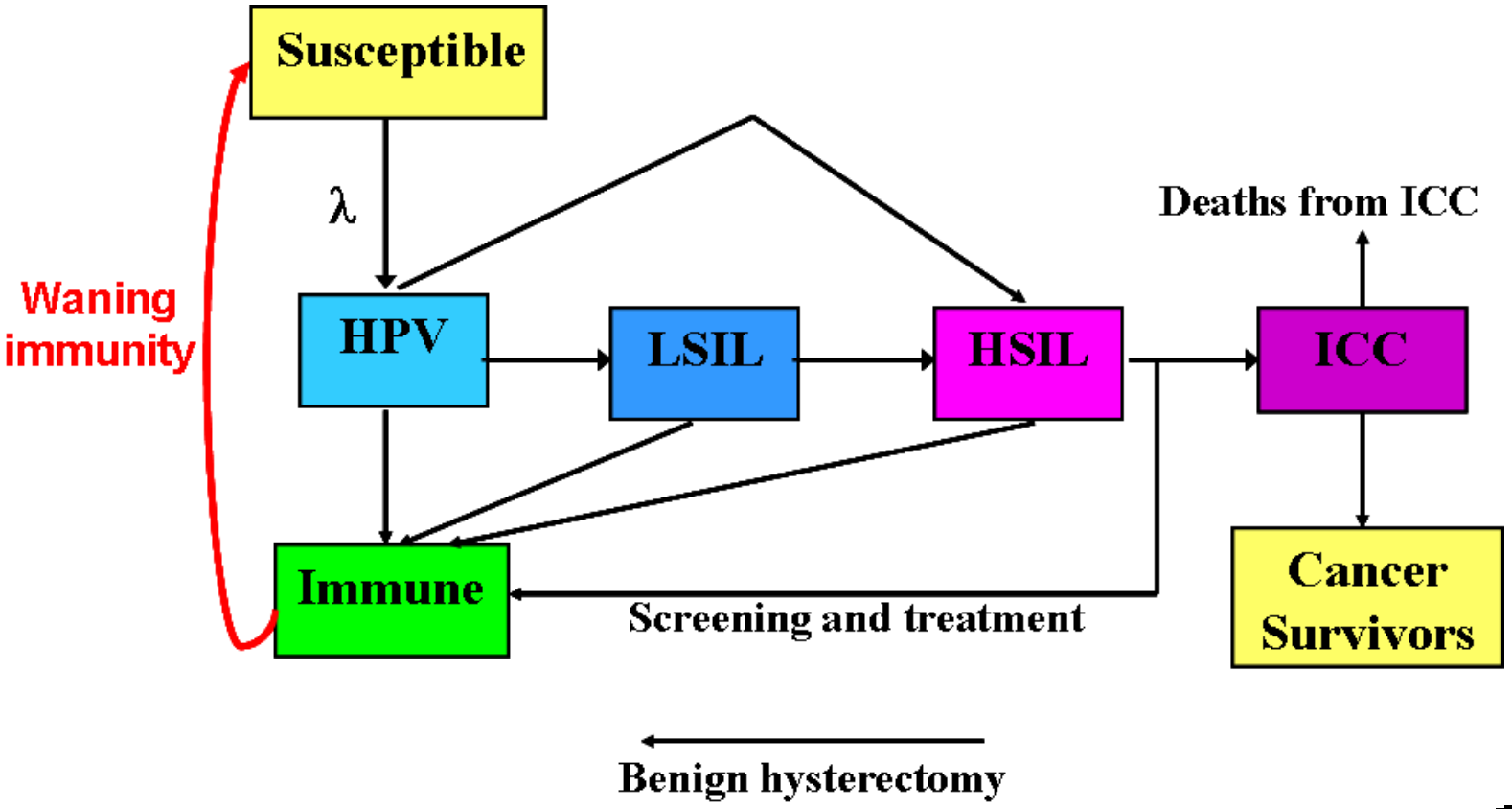

Barnabas, RV et al; The potential impact of HPV vaccination; PLoS Med; 2006

Model description & assumptions

- **Compartmental & deterministic**
- **Model population stratified for age & sexual activity (important for indirect vaccine effects)**
- **Model parameterised using demographic, sexual behaviour, smoking trends & HPV-16 serological data from Finland & HPV progression & regression rates from the literature**
- **Model HPV type 16 only**
- **Heterosexual mixing**
- **Validated against HPV 16 ICC incidence**
- **Explores the impact of waning immunity**

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An introduction to mathematical models

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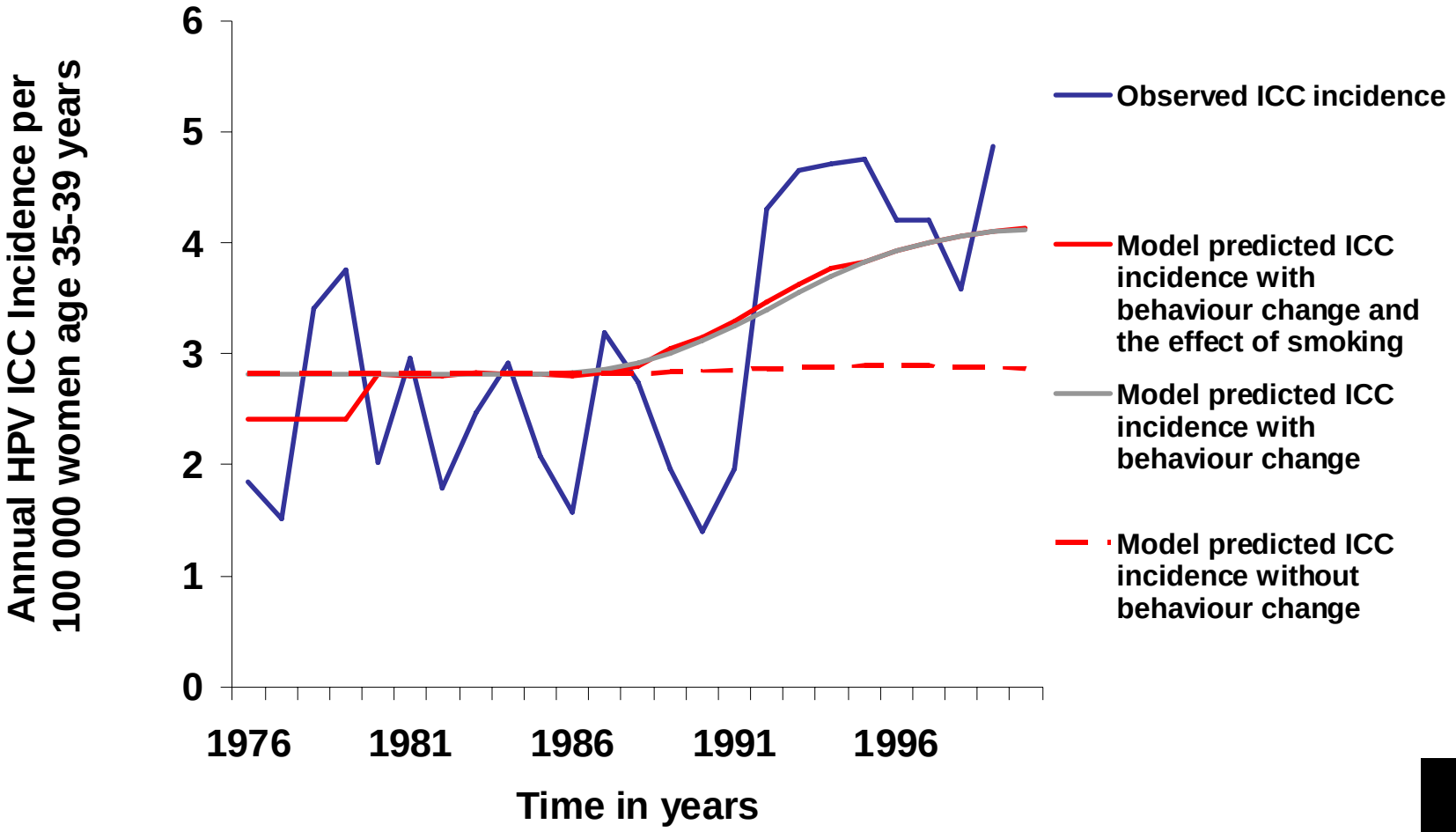

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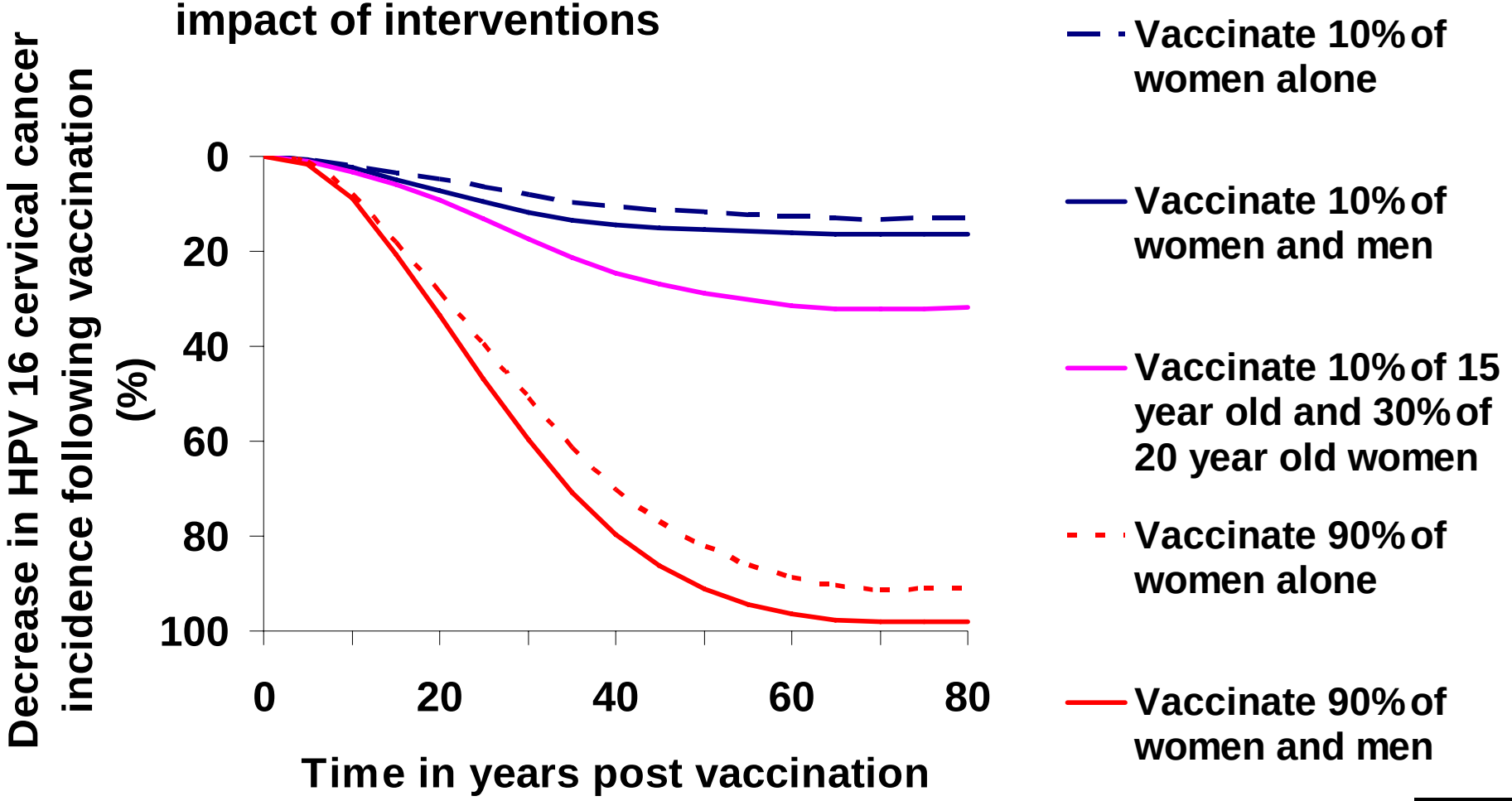
An introduction to mathematical models

- Validated models can be used to estimate the potential impact of interventions



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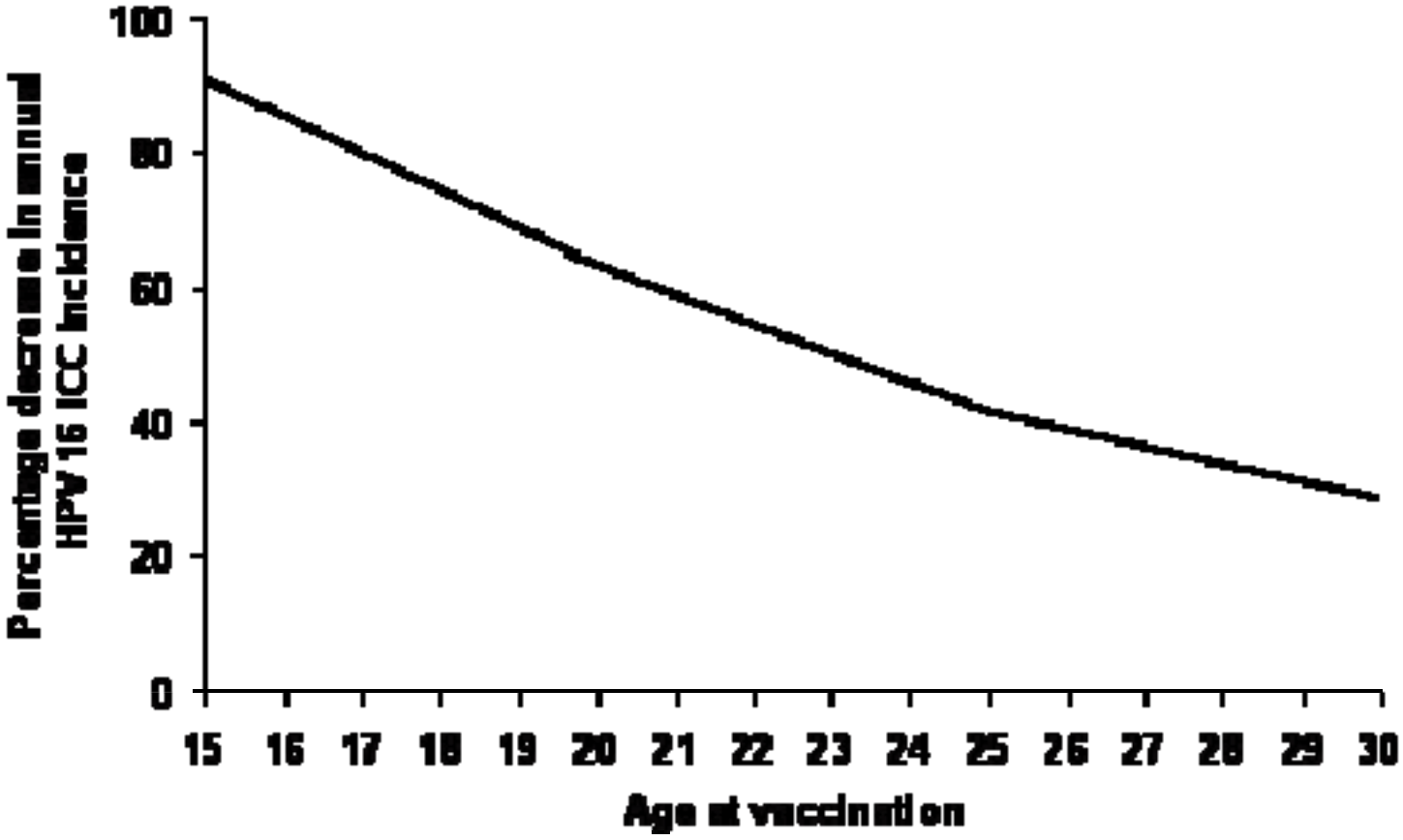
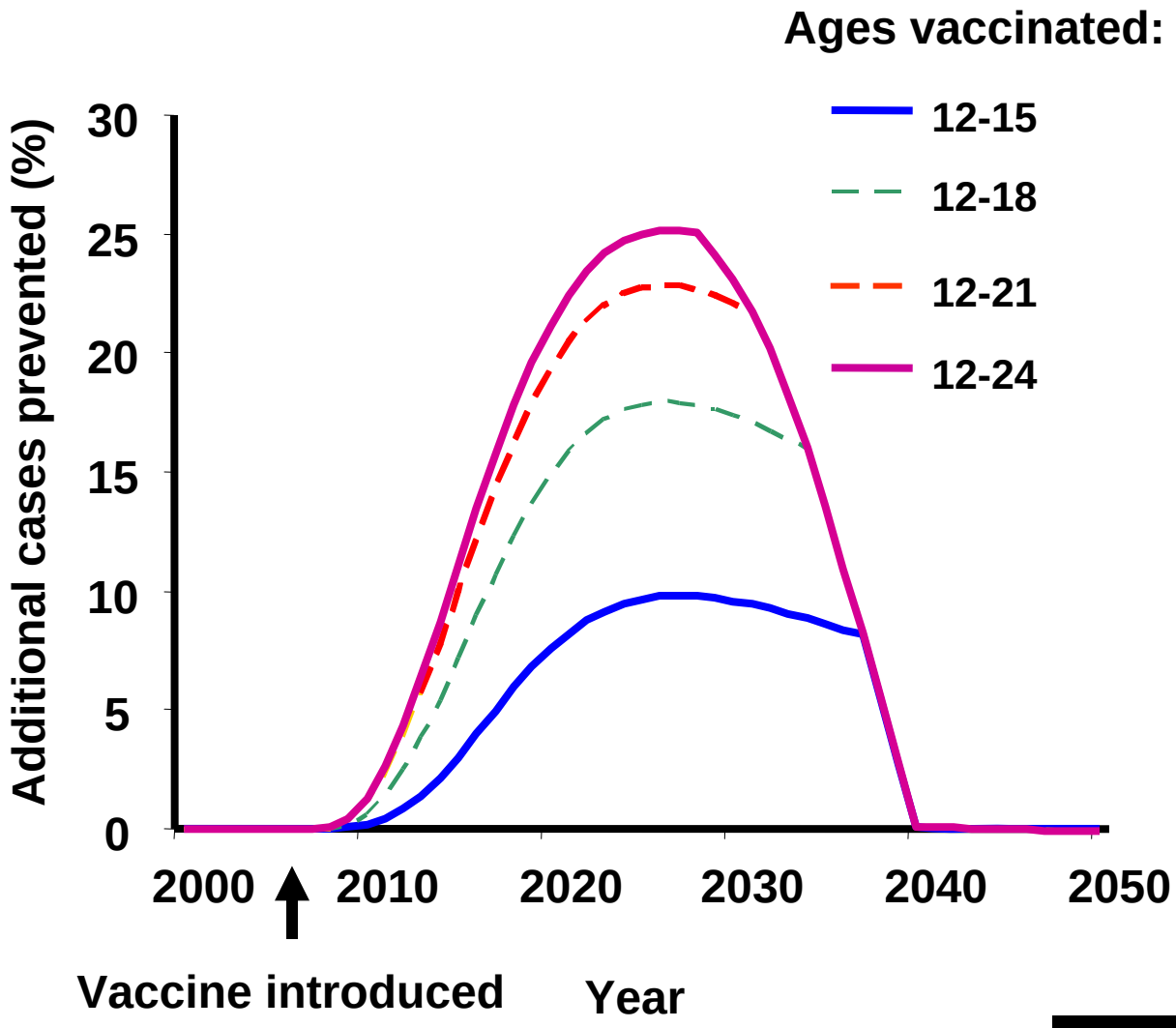
Results: Age at vaccination
Vaccinating 90% of women alone



Catch-up vaccination

- Vaccinating females at age 12 with different catch-up scenarios
- Vaccinating more than 6 years catch-up gives little additional benefit (French et al, 2007)
- Catch up can substantially reduce disease in the short term (Elbasha et al, 2007)



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Should boys be vaccinated?

- **Would the indirect effects of vaccinating boys further reduce cervical cancer incidence among women?**
- **Different assumptions about model structure change the cost effectiveness of vaccinating boys**

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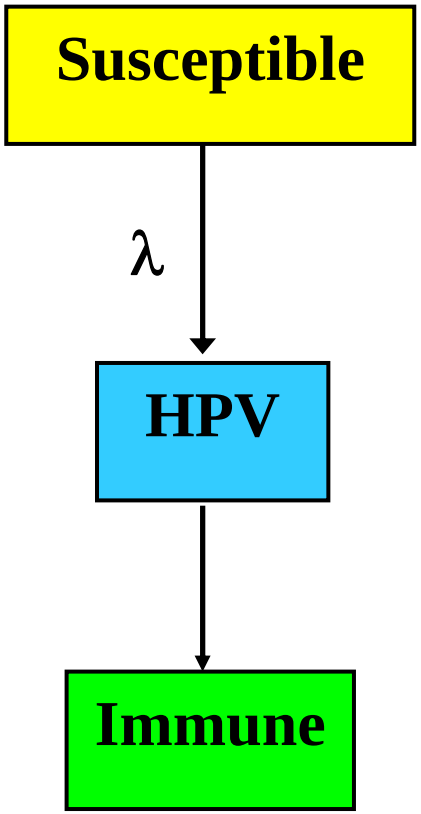
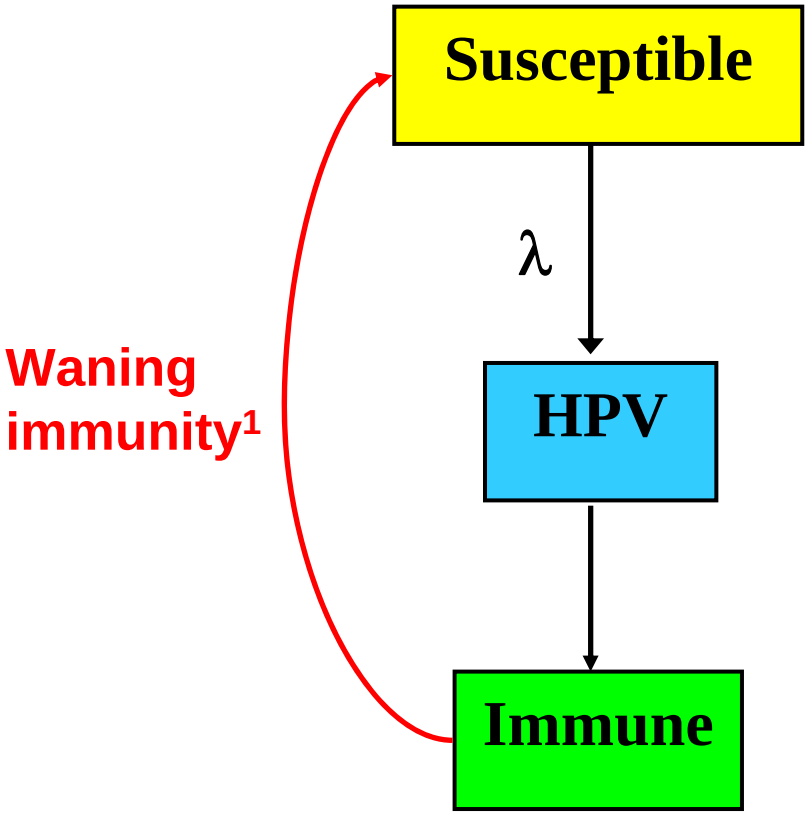
HPV model: men



Susceptible-Infected-Resistant (SIR) model

HPV model: men



Susceptible-Infected-Resistant-Susceptible (SIRS) model

1. Van Velde et al; Modeling HPV vaccine effectiveness; AME; 2001

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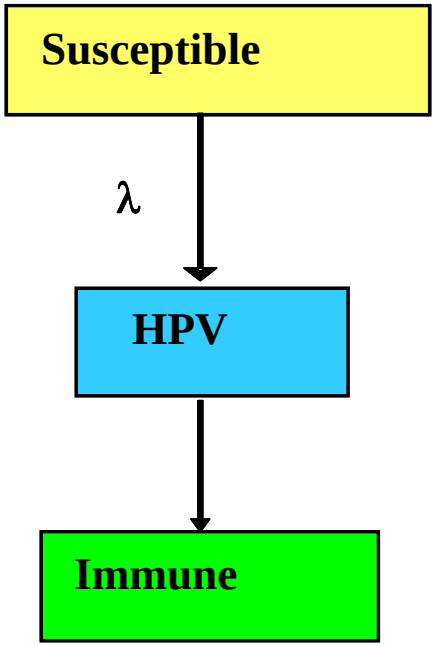
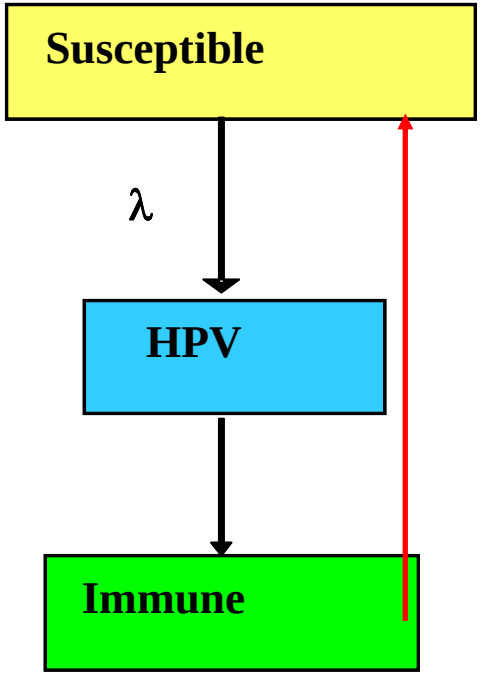
SIR vs SIRS

SIR: Higher transmission probability



SIRS: Lower transmission probability



Transmission probabilities are different for each model design

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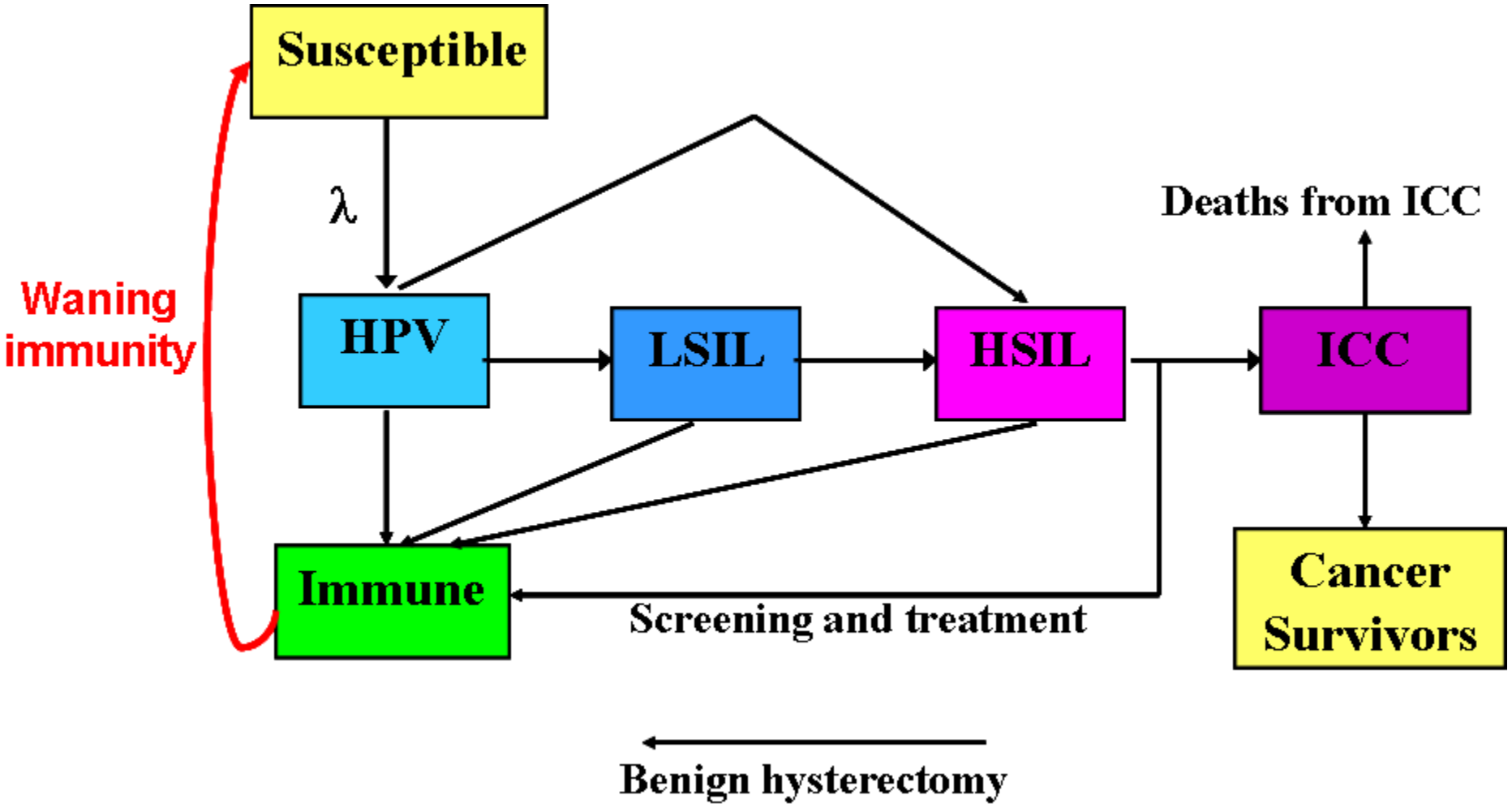
HPV model: women



French K, et al; Modeling the optimum age- & sex-specific pattern of vaccination in Finland; BJC; 2007

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Vaccinating boys can increase % cervical cancer cases prevented

% of males vaccinated in addition to 70% of girls	% of cervical cancers prevented
0%	71%
30%	76%
70%	85%

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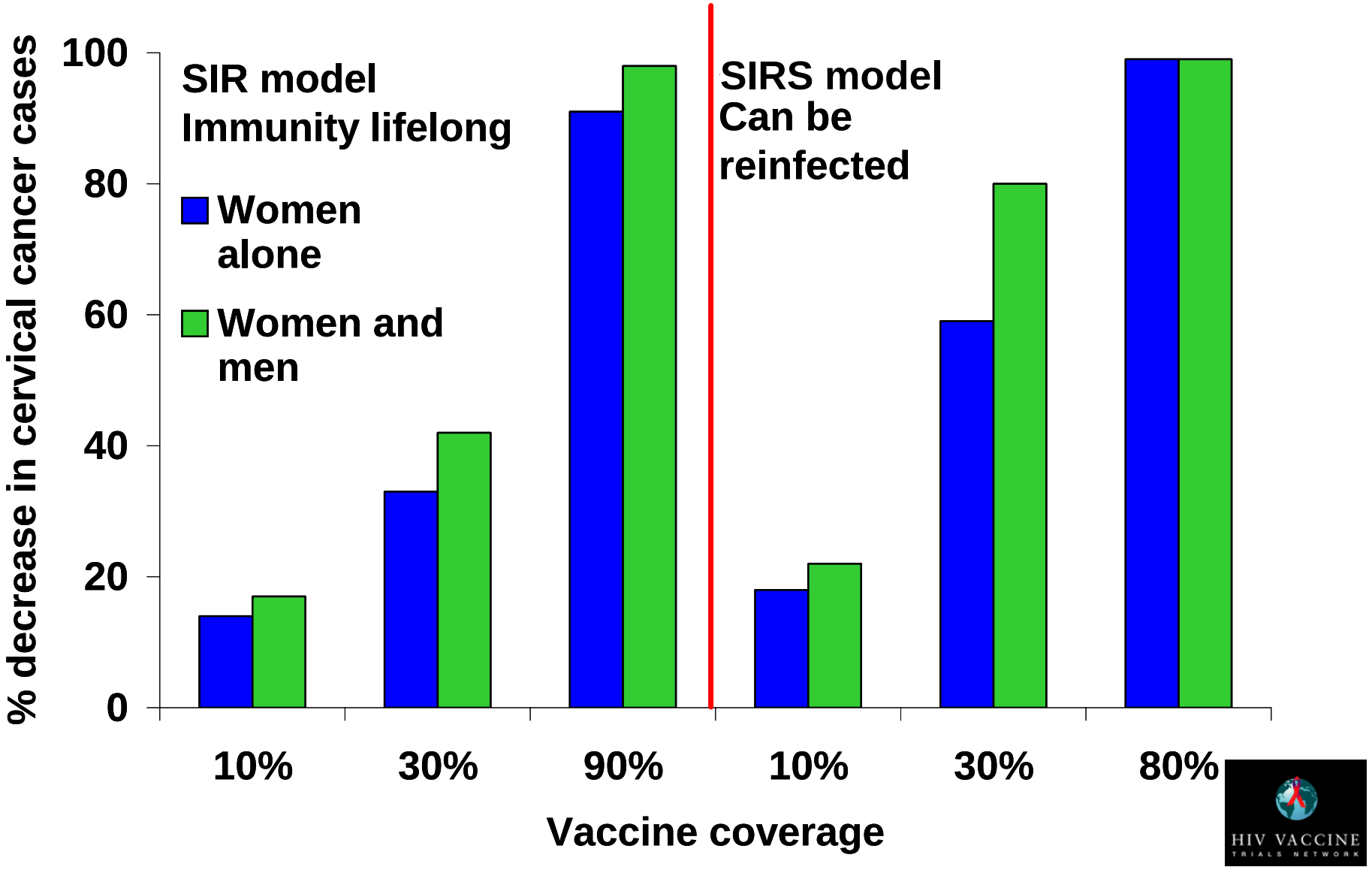
Impact of varying coverage changes with model structure



Cost effectiveness of vaccinating boys

- **Results depend on model assumptions**
- **To prevent HPV 16/18 infection & disease in women (SIS model, low heterogeneity)[1]:**
  - **Vaccination of 12 y/o girls - $14 583/QALY**
  - **Including boys ICER - $442 039/QALY**
- **To prevent HPV 6/11/16/18 infection & disease in women & men (SIR model, more heterogeneity)[2]**
  - **Vaccination of 12-24 y/o females & males - ICER of $45 056/QALY (compared to $4 666/QALY for 12-24 y/o females)**
  - **Impact of vaccinating boys increased at lower coverage of girls**

1. Taira AV et al; Evaluating HPV vaccination programs; Emerging Infect Dis; 2004
2. Elbasha et al; Model for assessing HPV vaccination strategies, Emerging Infect Dis; 2007

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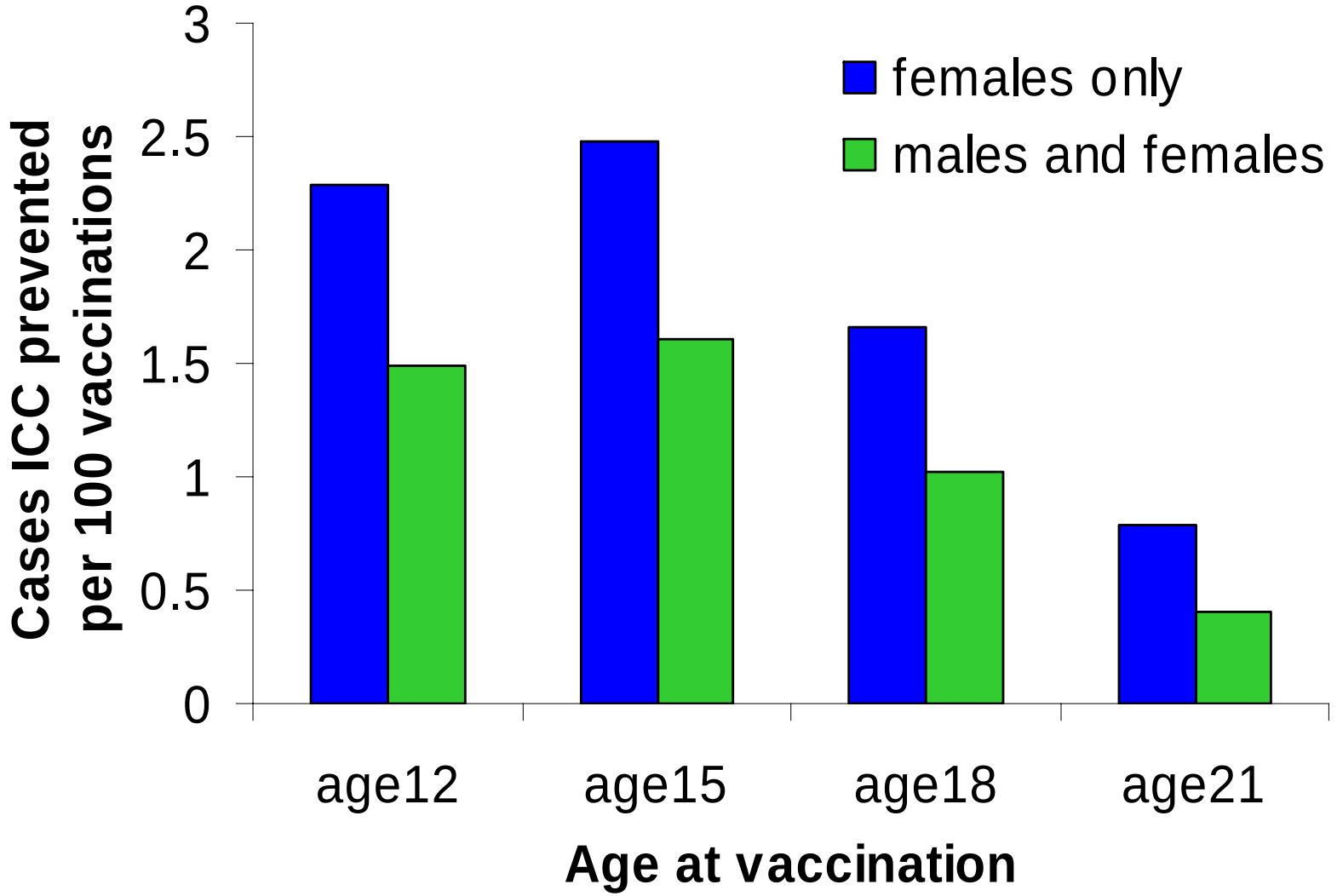
At high coverage, vaccinating women alone prevents more cancers per 100 000 vaccines



Summary

- For transmission models to better assess the impact of vaccination data is needed on
  - HPV infection in older women
  - Natural history of HPV in men
  - Immunity to HPV infection over time
- Models differ widely in their structure, design and assumptions – conclude that widespread HPV vaccination of girls, before sexual debut, with sufficient duration of protection has the potential to substantially reduce HPV precancer and cancer
- Underlying SIS or SIR model structure impacts cost effectiveness analyses
- Understanding model structure, assumptions and how uncertainties are handled helps interpret their results

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