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Introduction to HIV/AIDS modelling

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Overview

1. How are HIV/AIDS models typically structured?
2. What inputs do HIV/AIDS models typically require?
3. Why is HIV/AIDS modelling important?
4. What are the most common messages in published analyses of HIV/AIDS models?
5. Careers in HIV/AIDS modelling

Part 1: How are HIV/AIDS models typically structured?

The basic reproductive number (R_0)

- This is defined as the average number of secondary cases of infection generated by one primary case in a susceptible population.
- This is a measure of the infectiousness of a disease:
  - If $R_0 > 1$, the disease will spread and there will be an epidemic.
  - If $R_0 < 1$, the disease will die out.
- The measure is defined at the time that the disease enters the population (time 0), when it is assumed that all individuals (except the first infected individual) are susceptible.

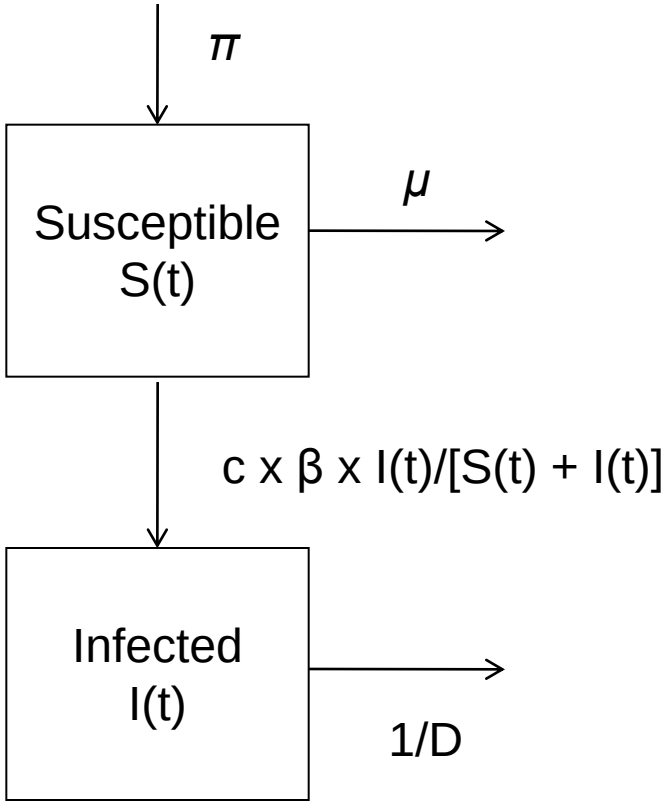
Calculating R_0 for HIV

- R_0 can be thought of as the average probability of transmitting the infection per period, multiplied by the average duration of infection.
- In the case of HIV, this can be written as $R_0 = \beta \times c \times D$, where
  - β is the probability of transmission from an HIV-positive individual to an HIV-negative partner
  - c is the rate at which new sexual partnerships are formed, per annum
  - D is the average duration of HIV infection (in years)

The SIR model

- In the basic SIR model, individuals are categorized as susceptible (S), infected (I) or resistant (R) after recovery from infection.
- In the case of HIV, there is no recovery, and hence it is not necessary to include the R state.
- Hence the most basic HIV model we can construct is a simple 'SI' (susceptible-infected) model.
- Suppose π is the annual number of people entering the population and μ is the annual rate at which people would leave the population in the absence of HIV.
- Let I(t) and S(t) represent the numbers of infected and susceptible people at time t, respectively.

An SI model for HIV



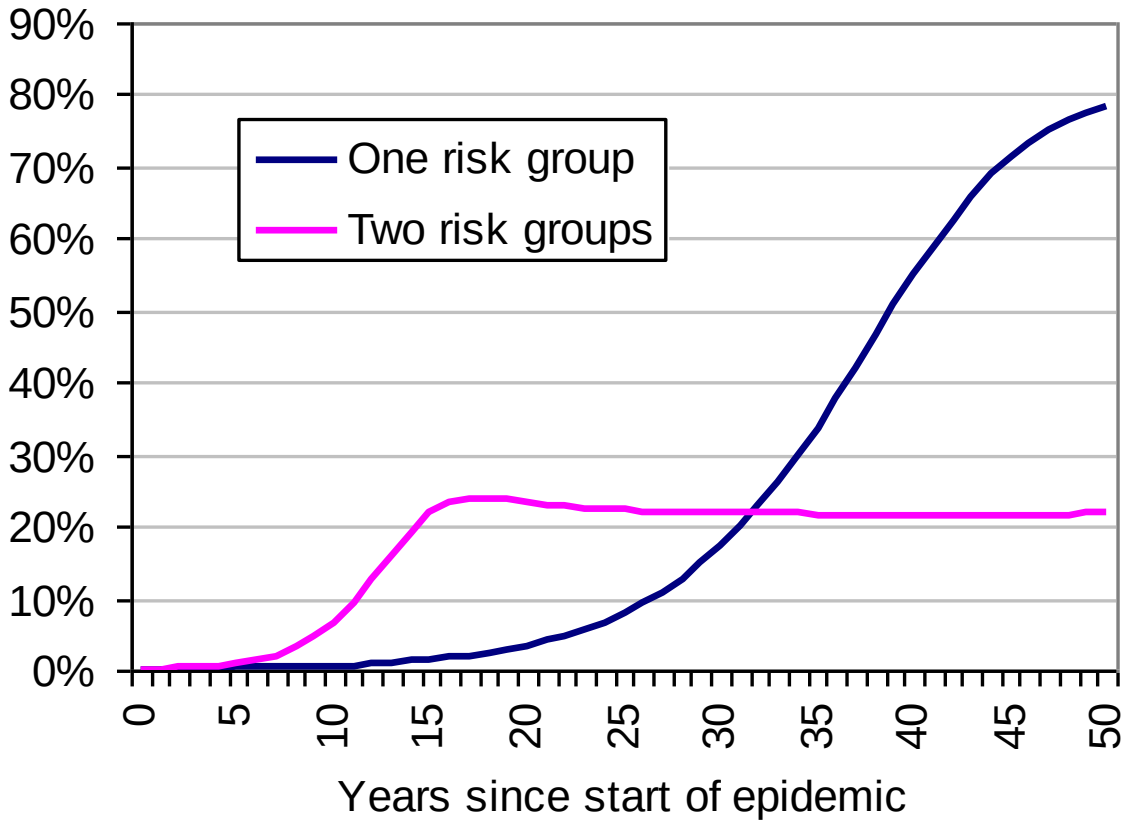
Problems with the SI model

- It's not realistic to assume that everyone has the same sexual risk behaviour.
- It's not realistic to assume that all infected individuals have the same level of infectiousness.
- It's not realistic to assume a constant rate of AIDS mortality in infected individuals.
- The model doesn't allow for stratification of the population by age and sex, which are important determinants of sexual risk behaviour and mortality, as well as being of demographic interest.

Extending the model to allow for heterogeneity in sexual risk behaviour

- The most common approach to allow for heterogeneity in risk behaviour is to divide the population into 'risk groups' representing individuals with different average levels of risk behaviour.
- The 'core group' of individuals with the highest levels of risk behaviour is usually defined as sex workers and their regular clients.
- Although risk groups are often defined in terms of average annual numbers of sexual partners, they could also be defined in terms of factors such as marital status and consistency of condom use.
- Some models allow for movements between risk groups over time.

Prevalence trends in models with one risk group and two risk groups



Model with one risk group:

c = 1.5

Model with two risk groups:

Group 1: 1/3 of population

$c_1 = 3.5$

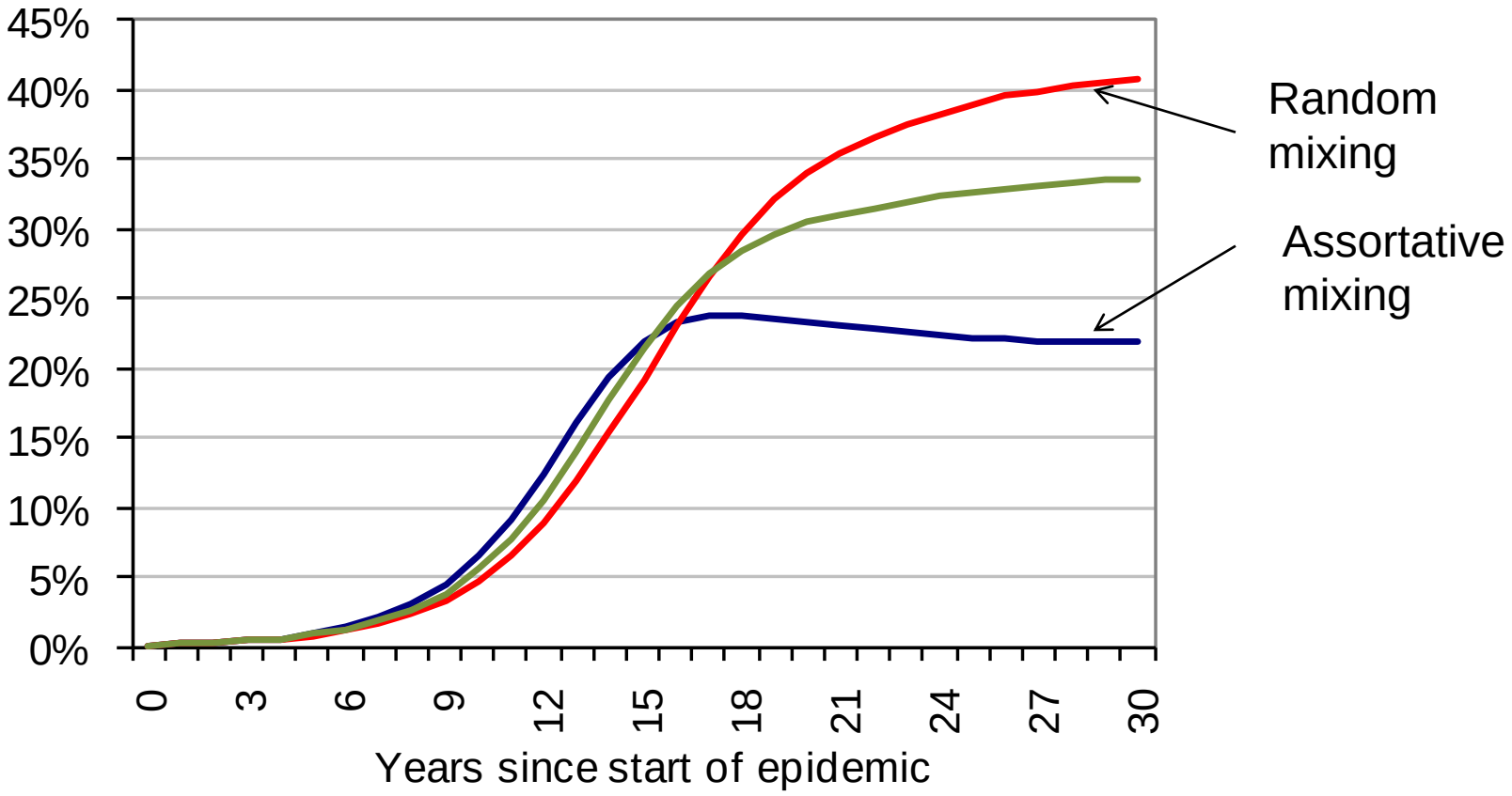
Group 2: 2/3 of population

$c_2 = 0.5$

Modelling heterogeneity

- As shown in previous slide, models with different assumptions about heterogeneity in risk behaviour produce very different forecasts, even when they assume the same average rate of partner acquisition.
- Models that allow for heterogeneity in sexual risk behaviour are also very sensitive to the assumed form of sexual mixing:
  - Assortative mixing: people tend to select their partners from their own risk group
  - Disassortative mixing: people tend to select their partners from outside of their own risk group
  - Random mixing: people have no preferences regarding the risk group of their partners

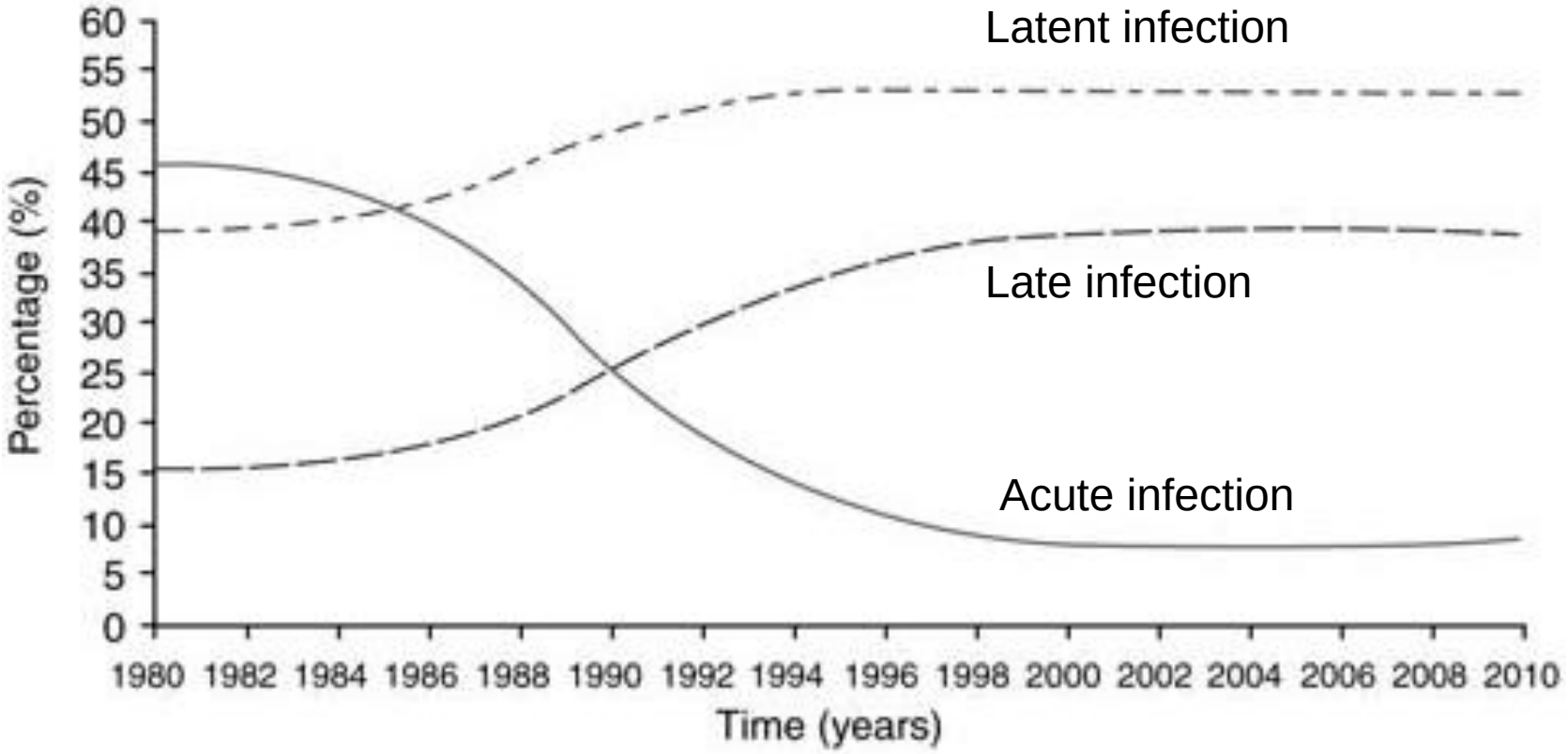
HIV prevalence trends in model with two risk groups



Extending the model to allow for heterogeneity in infectivity

- Many HIV models allow for the infectiousness of the HIV-positive individual to vary over the course of infection:
  - Very high during the first 2-3 months of infection (acute HIV)
  - Low during the asymptomatic phase (latent infection)
  - High during the symptomatic phase (late disease, WHO clinical stages III and IV)
- Some models also allow for changes in sexual activity over the course of disease (e.g. some models assume people cease to acquire new sexual partners after having progressed to AIDS).

% of HIV transmission from individuals in different stages, Kenya

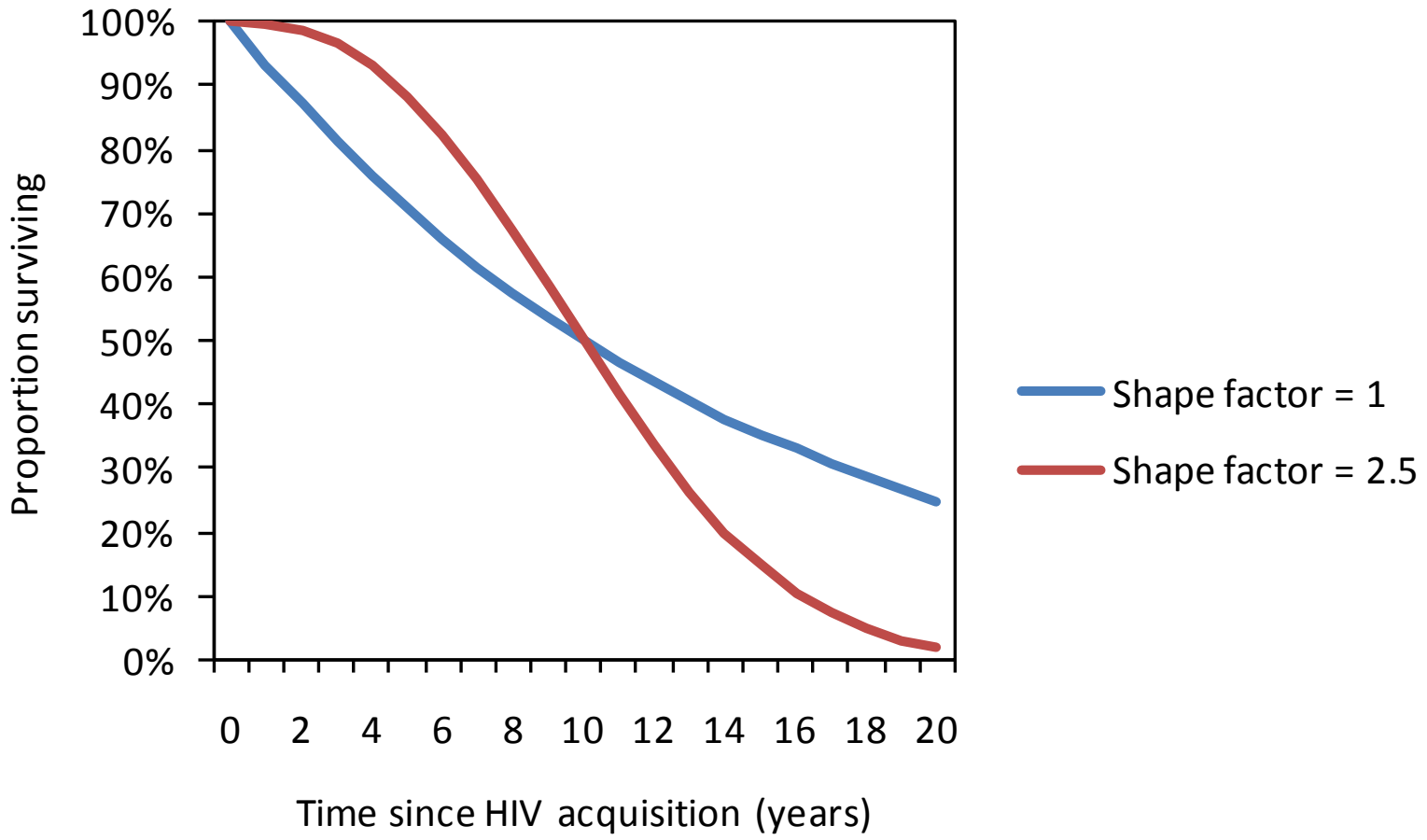


Source: Abu-Raddad et al, *AIDS*, 2008, 22:1055-61

Extending the model to allow for heterogeneity in AIDS mortality

- In reality, mortality of infected adults is typically low during the first few years of HIV infection, then increases as the duration of infection increases.
- Modellers often use a Weibull distribution to model this pattern of increasing mortality.
- The shape parameter of the Weibull distribution, ϕ, represents the extent to which mortality increases with respect to the duration of infection
  - $\phi = 1$ implies constant mortality (not realistic)
  - $\phi > 1$ implies mortality increases with respect to the duration of infection (realistic for adults).

Effect of shape factor on survival rates



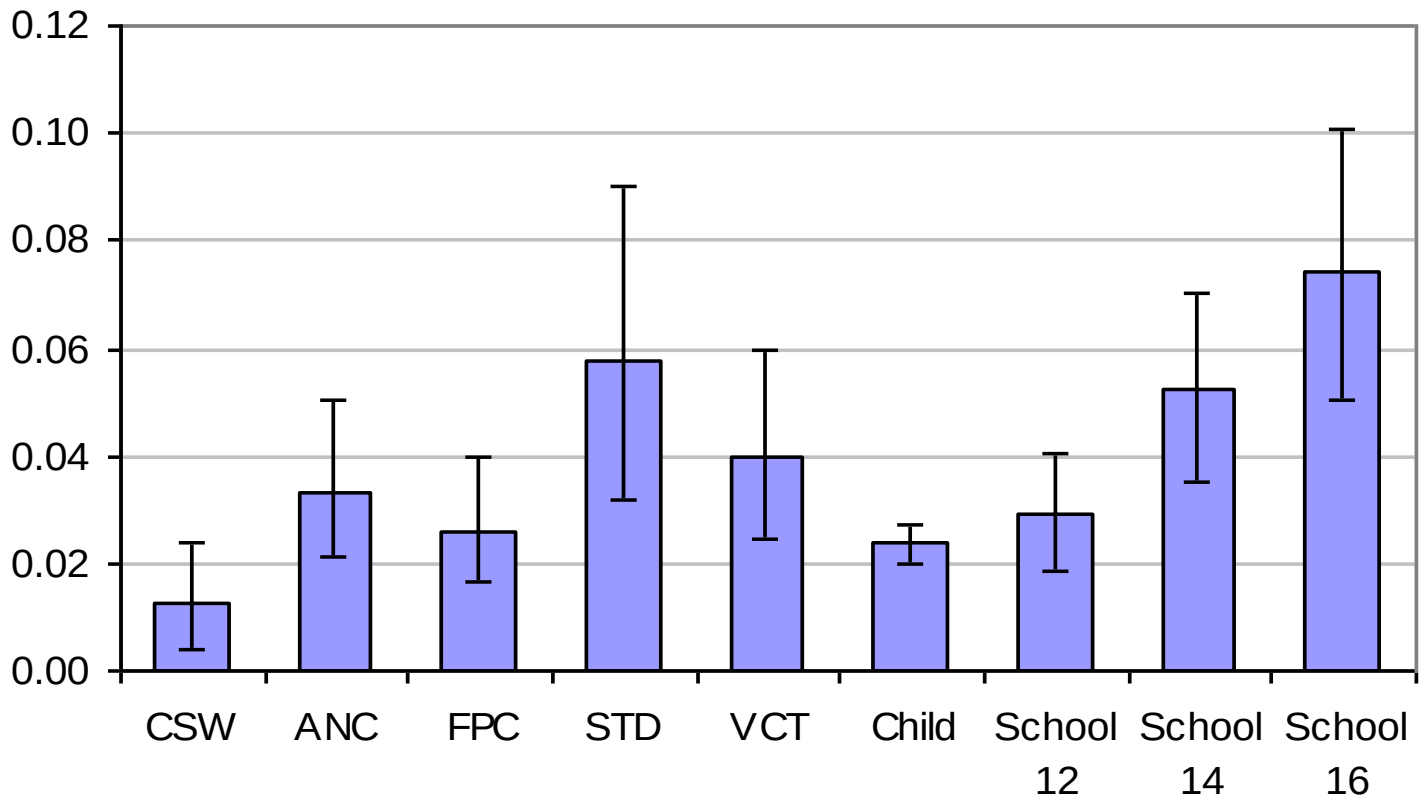
Extending model to allow for age

- Many model parameters vary with age:
  - Rates of partner acquisition (c)
  - Rates of progression to disease (infection at older ages is associated with more rapid disease progression)
  - Non-AIDS mortality rates
- Mathematical models that are age-structured also require assumptions about patterns of age mixing.
- Most models that are age-structured also separate the population into males and females, with separate assumptions about sexual behaviour and transmission probabilities.

Why is the age-structured approach useful?

- Age variation in behavioural and sexual mixing patterns is crucial to understanding HIV transmission.
- Often we want to assess the effect of targeting interventions in particular age groups.
- For example, if we wanted to assess the efficiency of different strategies for distributing a hypothetical HIV vaccine in 2015, we might consider
  - vaccinating commercial sex workers (CSWs)
  - Vaccinating women in antenatal clinics (ANCs) or family planning clinics (FPCs)
  - Vaccinating adults attending STD clinics
  - Vaccinating individuals seeking voluntary counselling and testing (VCT)
  - Vaccinating children at birth
  - Vaccinating children in schools (at ages 12, 14, 16)

Infections averted per vaccinated individual, 2015-2025, South Africa



Source: Johnson et al, *Vaccine*, 2007, 25: 7502-9

Part 2: What inputs do HIV/AIDS models typically require?

Data requirements

1. Demographic information
2. HIV transmission probabilities
3. Sexual behaviour
4. Mortality of infected individuals
5. HIV prevalence data, AIDS mortality data, or reported numbers of AIDS cases

Demographic information

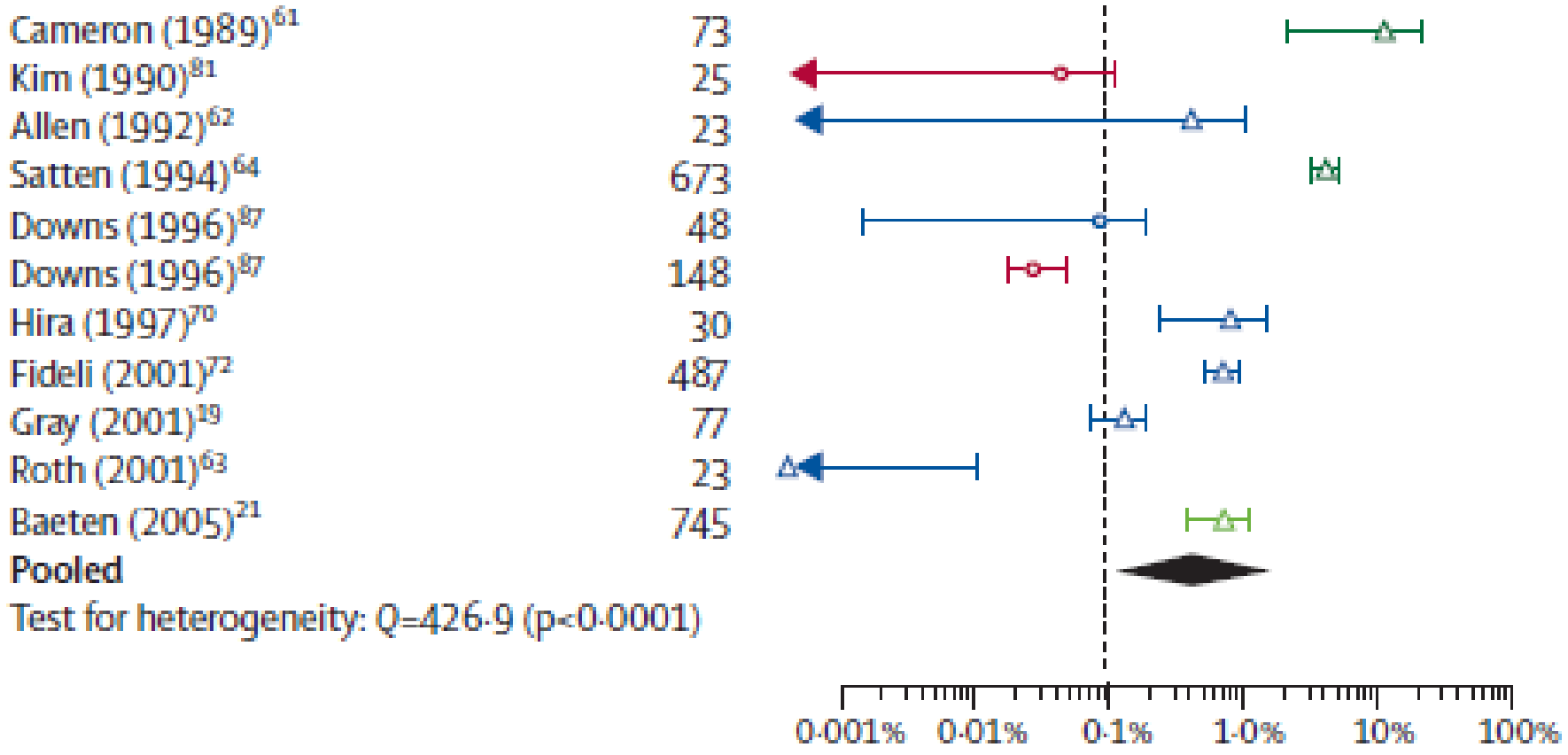
- Size of the population
- Fertility levels
- Non-AIDS mortality
- Migration (usually only a significant issue if one is modelling small sub-national populations)

If the model is stratified by age and sex, all of these variables should be estimated by age and sex.

HIV transmission probabilities

- Some models make assumptions about the probability of transmission **per act of unprotected** sex with an HIV+ partner, other models make assumptions about the probability of transmission **per partnership** with an HIV+ partner.
- Most models require information on relative levels of transmission risk in different stages of HIV disease.
- Most models require information on relative risk of female-to-male and male-to-female transmission.
- Assumptions about transmission probabilities are difficult to set because of extreme variability between different settings.

Female-to-male transmission probabilities, per act of sex



Source: Boily et al, *Lancet Infect Dis*, 2009, 9:118-29

Factors affecting transmission

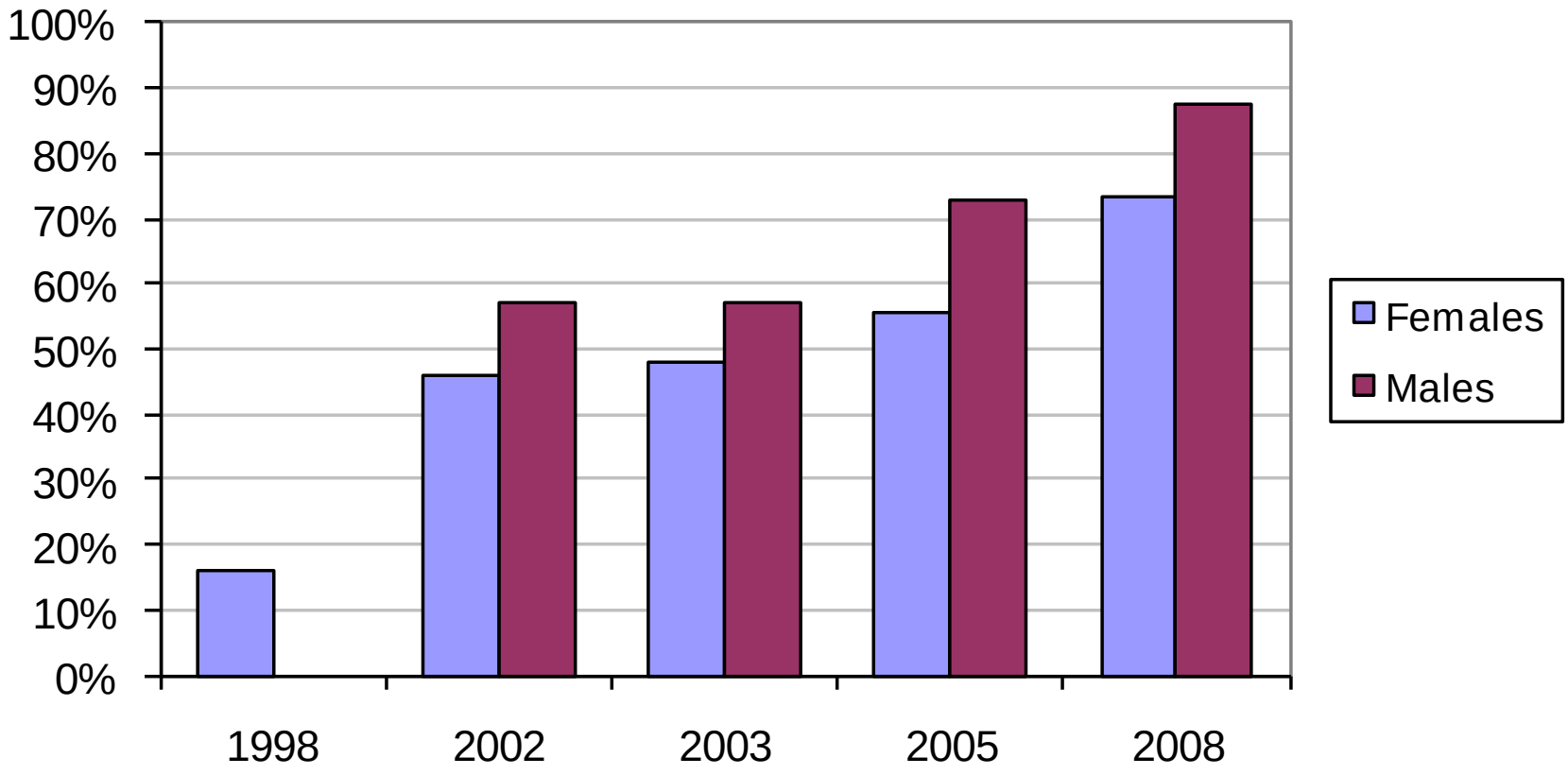
- Models often consider the effect of STDs on the HIV transmission risk – requiring information on both the effect of STDs in the HIV-negative partner and the effect of STDs in the HIV-positive partner.
- Models of prevention programmes also require data on the extent to which transmission probabilities are reduced by
  - Condoms
  - Male circumcision
  - Microbicides and pre-exposure prophylaxis
  - Antiretroviral treatment (ART)

Sexual behaviour

- Rates of partner acquisition
- Frequency of sex
- Levels of condom use
- Patterns of age mixing and mixing between risk groups
- Frequency of contact with commercial sex workers
- Rates of marriage and divorce
- Rates of ‘sexual debut’

Assumptions about sexual behaviour are difficult to set because of social desirability bias and recall bias.

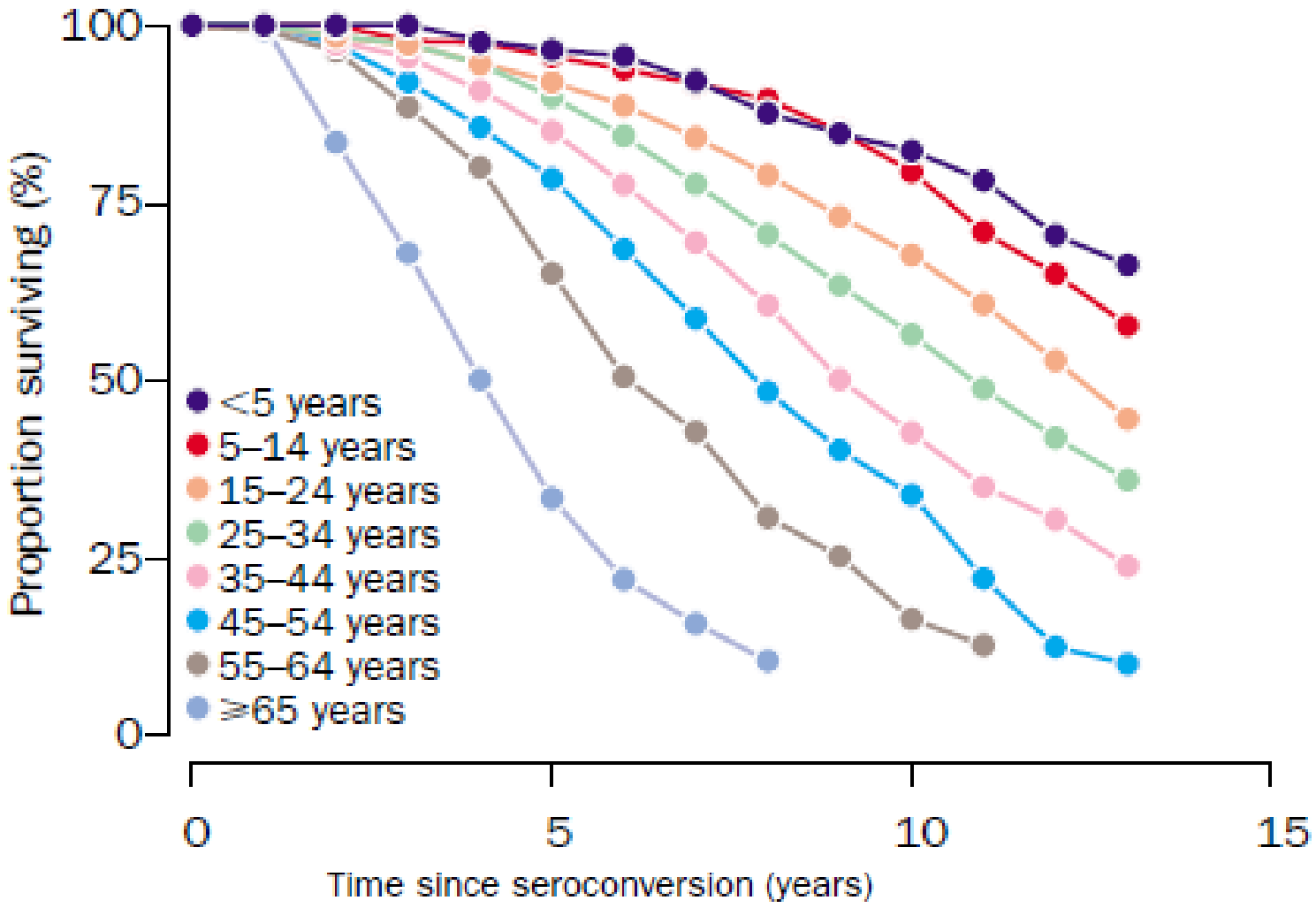
Condom use at last sex, as reported by youth aged 15-24



Mortality of infected individuals

- Typically we need to know:
  - Mortality in untreated individuals (according to duration of infection)
  - Timing of ART initiation
  - Mortality in treated individuals (according to length of time on ART)
  - Average length of time spent in different stages
- Often we require separate assumptions about survival of infected children (high mortality in first year of life, lower thereafter).

% surviving by age at HIV infection, pre-ART



Source: CASCADE, *Lancet*, 2000, 355:1131-7

Other data requirements

- Because of the uncertainties regarding the model parameters (especially those relating to HIV transmission and sexual behaviour), it is important to check that model outputs are consistent with
  - Observed HIV prevalence trends
  - Observed AIDS mortality trends
  - Reported numbers of AIDS cases
- Reported numbers of AIDS cases and AIDS deaths are likely to be unreliable in most developing countries, although information on trends in overall mortality in young adults may be informative.

Part 3: Why is HIV/AIDS modelling important?

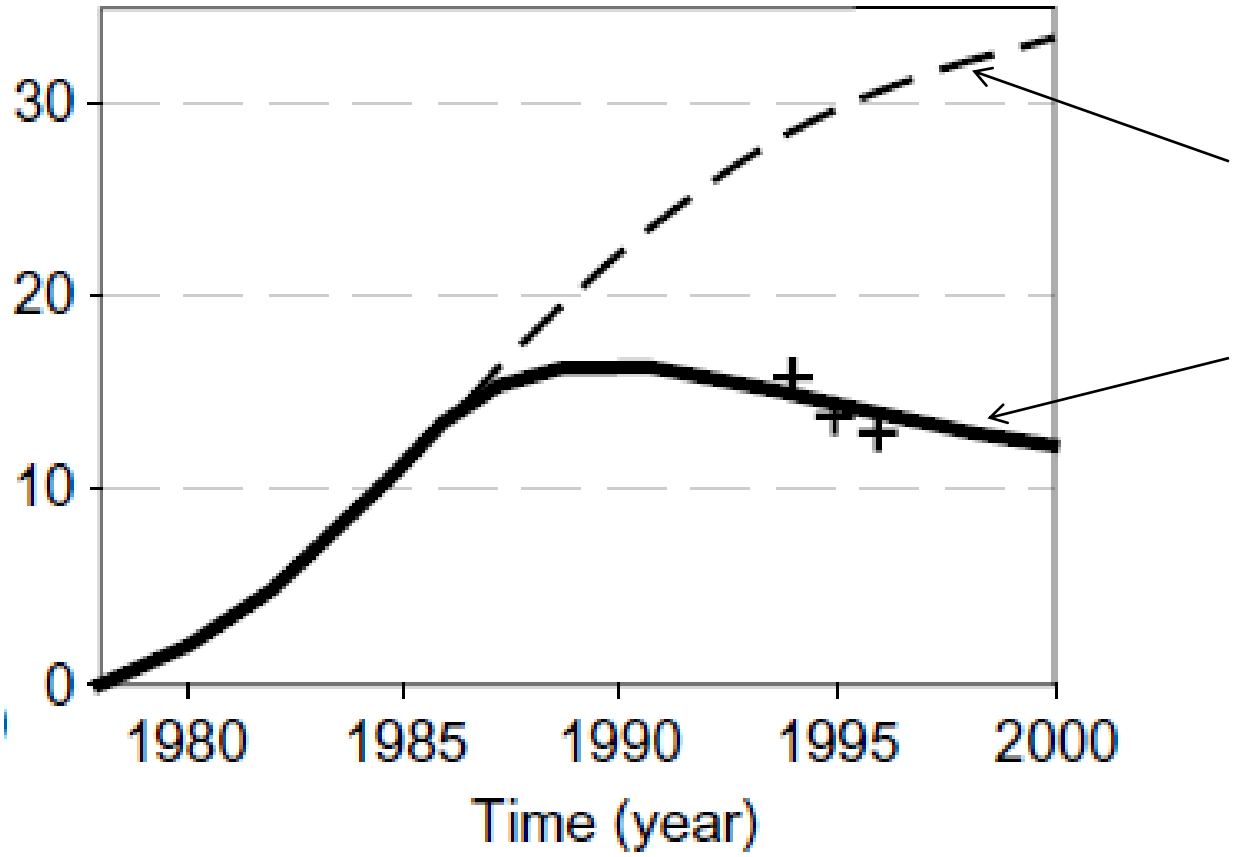
1. Models can be used to interpret trends in HIV prevalence data

- Models show that in mature epidemics, HIV prevalence can be expected to decline **in the absence of interventions**.
- Hence models need to be used to assess the extent to which observed reductions in HIV prevalence can be attributed to behaviour change or interventions.
- In early epidemics, HIV prevalence will tend to rise, even if there are partially effective prevention programmes in place.
- So if HIV prevalence is stable/rising, models might be used to demonstrate that interventions are having an impact.
- We typically compare observed HIV prevalence trends with model estimates of what would have happened in the absence of interventions ('counterfactual' scenario).

e.g. To what extent are the reductions in HIV prevalence in Uganda attributable to behaviour change?

- Korenromp et al (2002) simulated the evolution of the epidemic in the Rakai district of Uganda, using detailed data on sexual behaviour, demographics, HIV and STD prevalence.
- They showed that observed reductions in HIV prevalence and syphilis prevalence could be matched by the model if it was assumed that there were significant reductions in risk behaviour after the end of the Ugandan Civil War in 1986.

Adult HIV prevalence in Rakai, Uganda



Counterfactual scenario (no behaviour change)

Assuming behaviour change starting in 1986

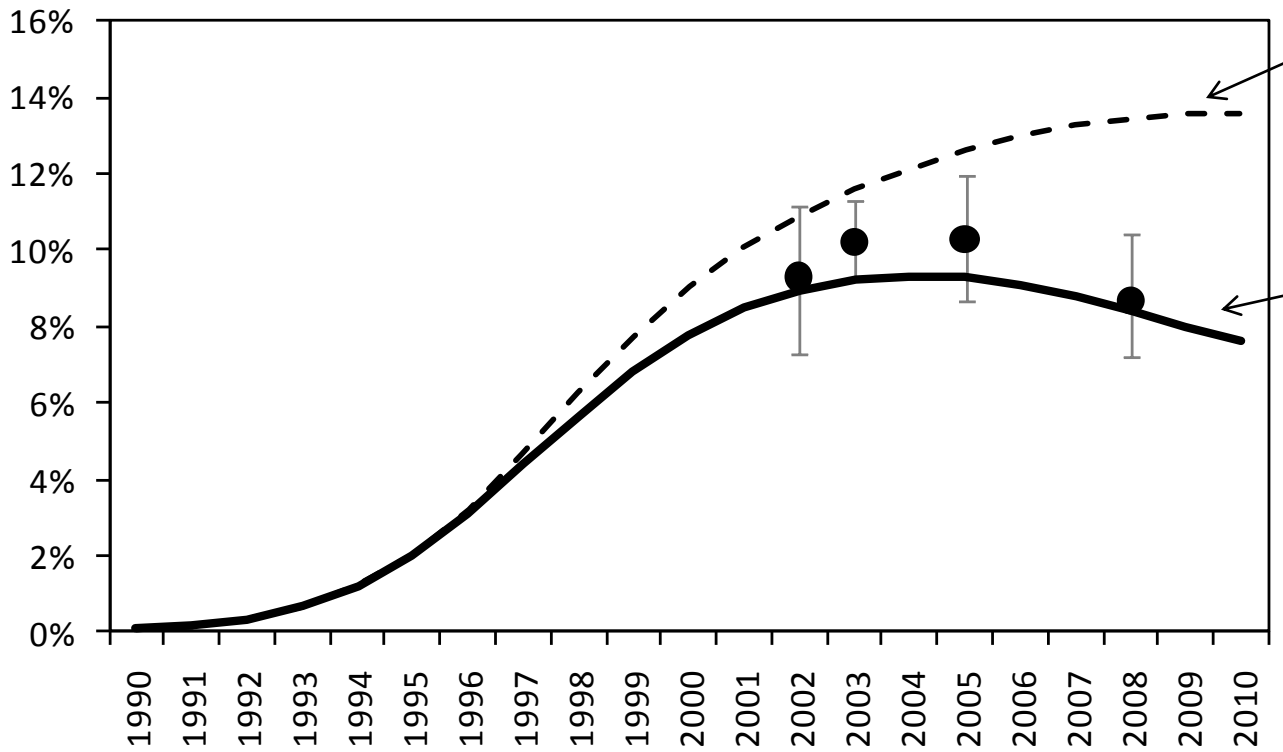
Crosses represent observed adult HIV prevalence levels.

Source: Korenromp et al, *AIDS*, 2002, 16:2209-18

e.g. Have HIV prevention programmes had an impact on HIV prevalence in South African youth?

- We could try to answer this question using the ASSA2008 AIDS and Demographic model, a publicly available model of the South African AIDS epidemic (www.actuarialsociety.org.za).
- Compare model estimates of HIV prevalence in 15-24 year olds in two scenarios:
  - Default model scenario
  - Scenario in which we assume no prevention programmes
- Compare with data from the 2002, 2005 and 2008 HSRC surveys and the 2003 loveLife survey.

HIV prevalence in 15-24 year olds, RSA



Counterfactual scenario (no prevention)

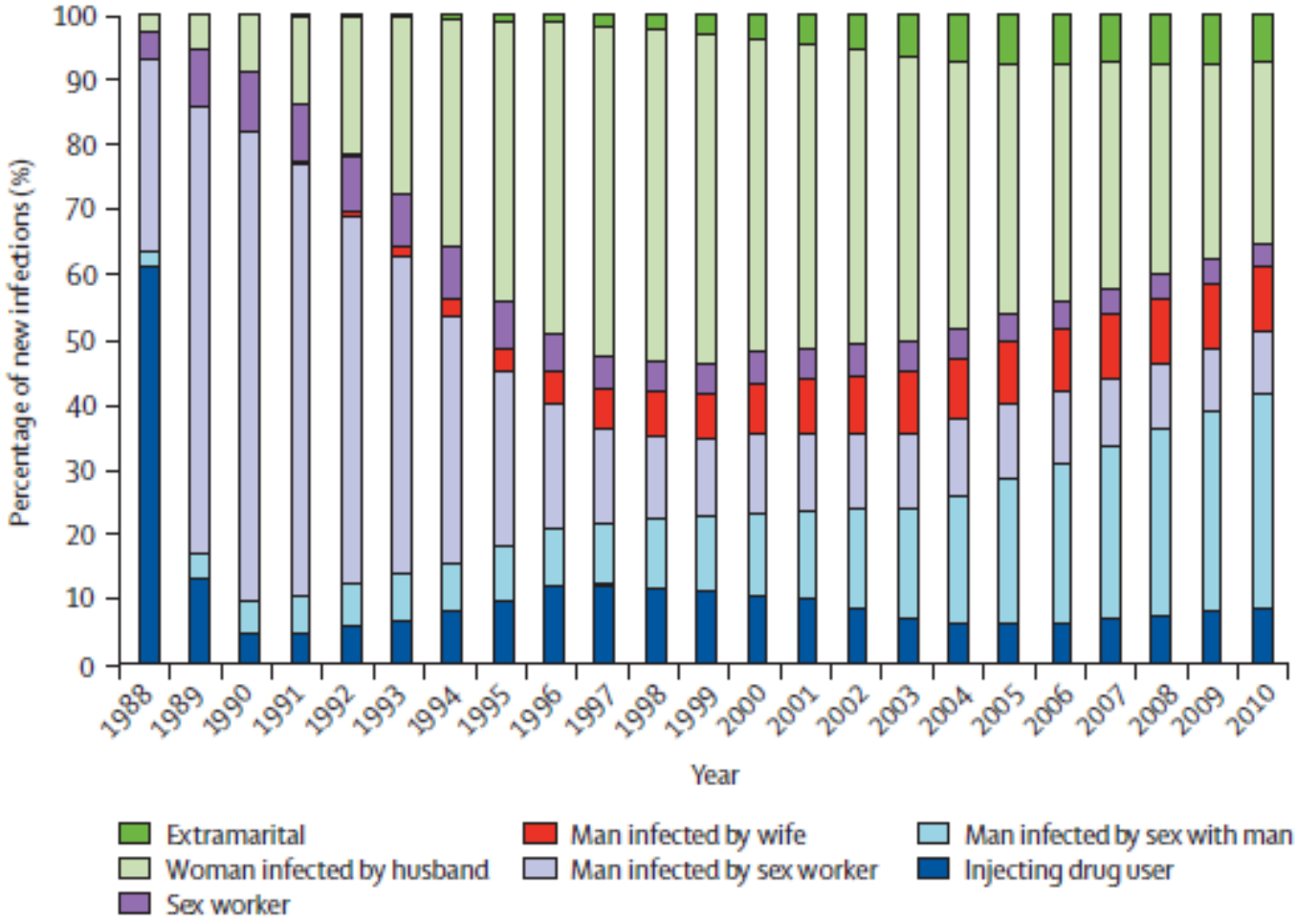
Default scenario

Dots (with 95% CIs) represent observed prevalence in surveys.

2. Models can be used to determine in which risk groups most HIV transmission is occurring

- This is important for policymakers in deciding where to focus their HIV prevention efforts.
- For example, the Asian Epidemic Model (Brown & Peerapatanopokin, 2002) has been used to assess the relative significance of different risk behaviours in Thailand, where there is a mix of heterosexual, MSM (men who have sex with men) and IDU (intravenous drug user) transmission.
- In South Africa, we also have models that can be used to assess the relative significance of transmission in short-term (ST) and long-term (LT) relationships.

% of new infections in Thailand due to different risk behaviours



Source: Bertozzi et al, *Lancet*, 2008, 372: 831-44

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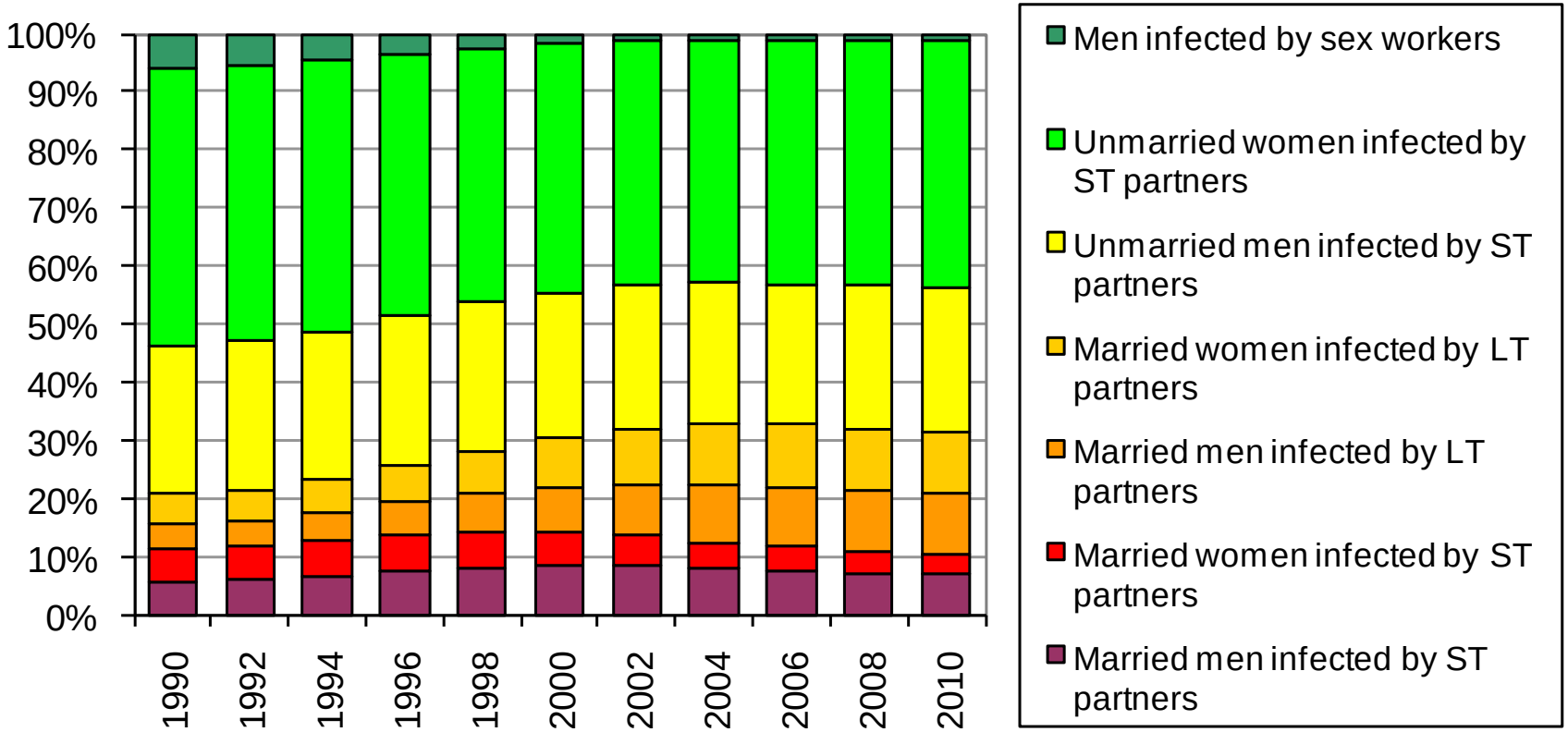
% of new infections in South Africa due to different risk behaviours



Source: Johnson et al, *Demographic Research*, 2009, 21:289-340

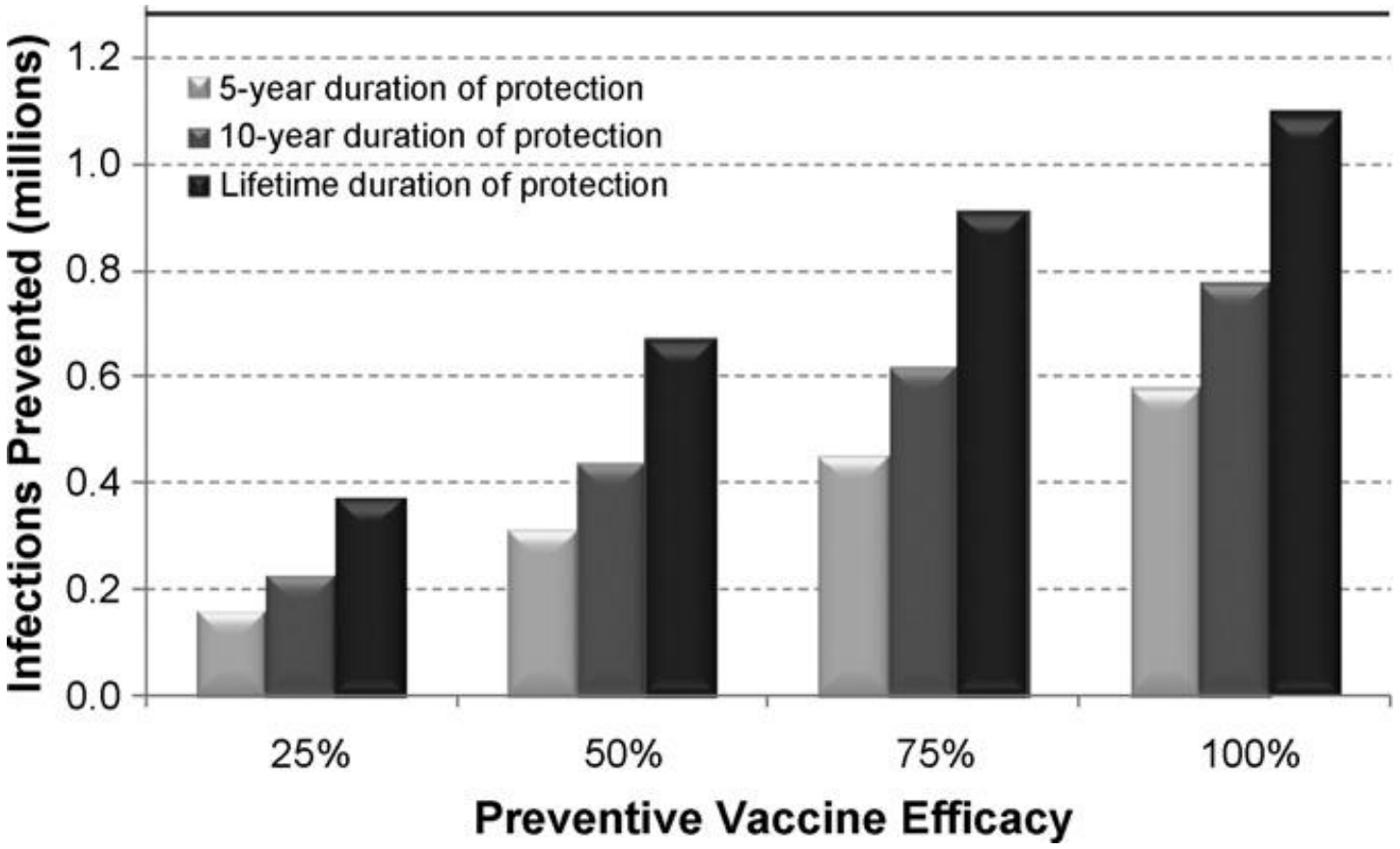
3. Models can be used to assist in the interpretation of randomized controlled trials (RCTs)

- Policy decisions are likely to be strongly influenced by RCT results, but RCTs by themselves don't tell policymakers everything they need to know.
- Models can assist in RCT interpretation by
  - Translating individual-level efficacy to effectiveness at a population level, taking account of local conditions.
  - Extrapolating from community RCTs to predict long-term intervention impact.
  - Setting criteria for evaluating trial success.

e.g. Translating individual-level efficacy to population-level impact

- Long et al (2009) assessed the potential impact of a hypothetical vaccine in the United States, modelling transmission in heterosexuals, MSM and IDUs.
- Over a 20-year period they estimated that approximately 1.3 million new infections would occur, in the absence of a vaccine.
- If a vaccine were introduced with 75% efficacy, reaching 75% of the population, with immunity lasting for an average of 5 years, approximately 450 000 infections would be averted over 20 years (a 35% reduction in incidence).
- Sensitivity testing was conducted to assess the effect of different efficacy and duration of immunity parameters.

HIV infections averted by an HIV vaccine in the USA, over 20 years

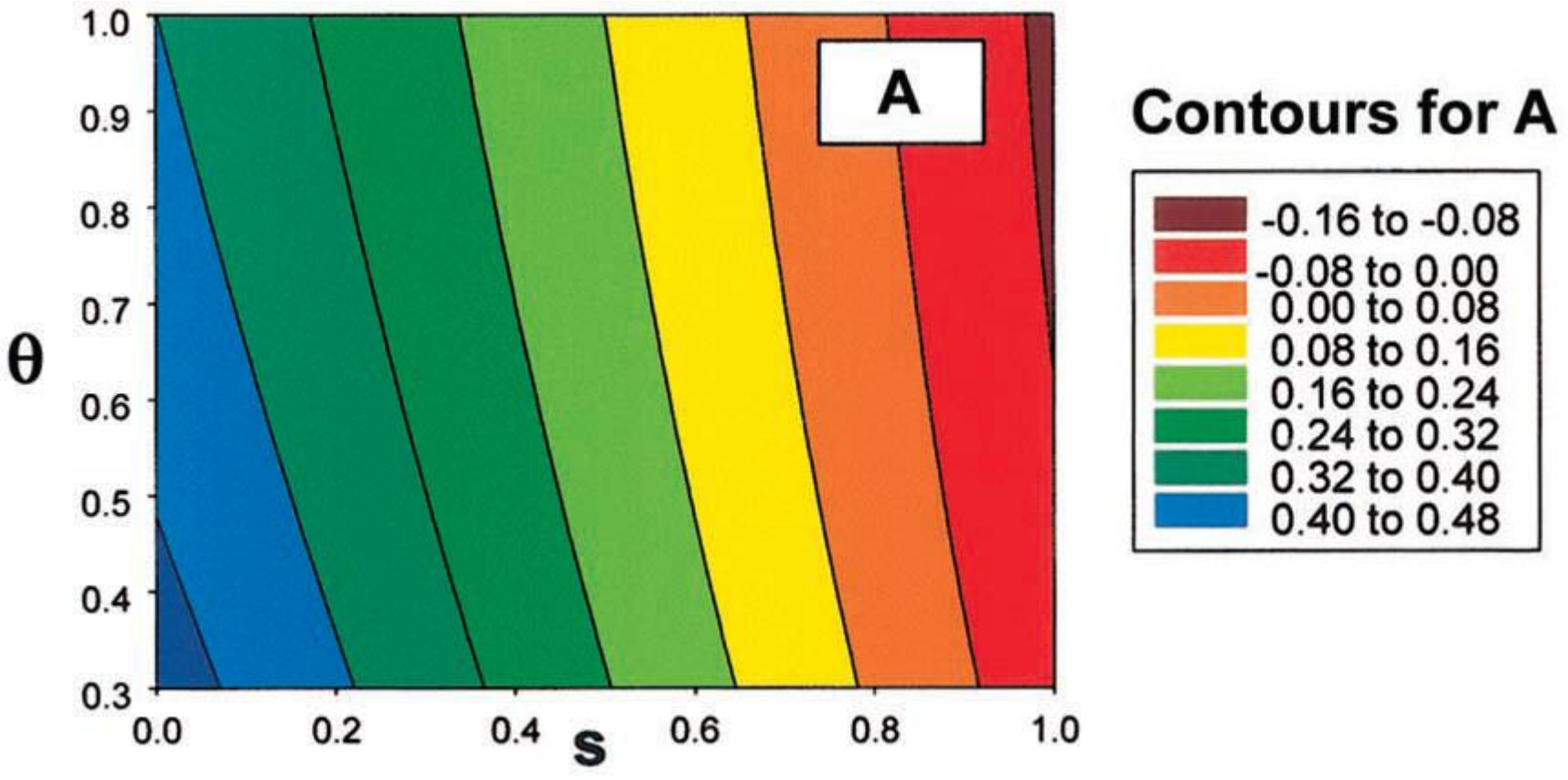


Source: Long et al, *Vaccine*, 2009, 27:5402-10

e.g. Setting criteria for evaluating trial success

- RCTs of HIV vaccine candidates often focus on measuring the effect of the vaccine on susceptibility to HIV.
- But could vaccines be beneficial (in terms of reducing mortality) even if they don't reduce susceptibility to HIV?
- Anderson & Hanson (2005) created a contour plot to show how the number of AIDS deaths averted per vaccine dose would vary according to
  - The ratio of infectiousness of infected vaccinated individuals to that of infected unvaccinated individuals (S)
  - The ratio of the rate of progression to AIDS in infected vaccinated individuals to that in infected unvaccinated individuals (θ)

AIDS deaths averted per dose of non-sterilizing vaccine



Source: Anderson & Hanson, *J Infect Dis*, 2005, 191(Suppl 1):S85-96

Implications

- So even if the vaccine is completely non-sterilizing (i.e. it has no effect of susceptibility to HIV in vaccinated individuals), it could have a significant impact on AIDS mortality at a population level, provided that it reduces the infectiousness of people who become infected after having received the vaccine (low S values).
- This suggests that RCTs should evaluate not only the effect of vaccines on susceptibility to HIV, but also the effect of vaccines on infectiousness of individuals who become infected after having been vaccinated.
  - Viral loads in infected individuals may serve as a reasonable proxy.

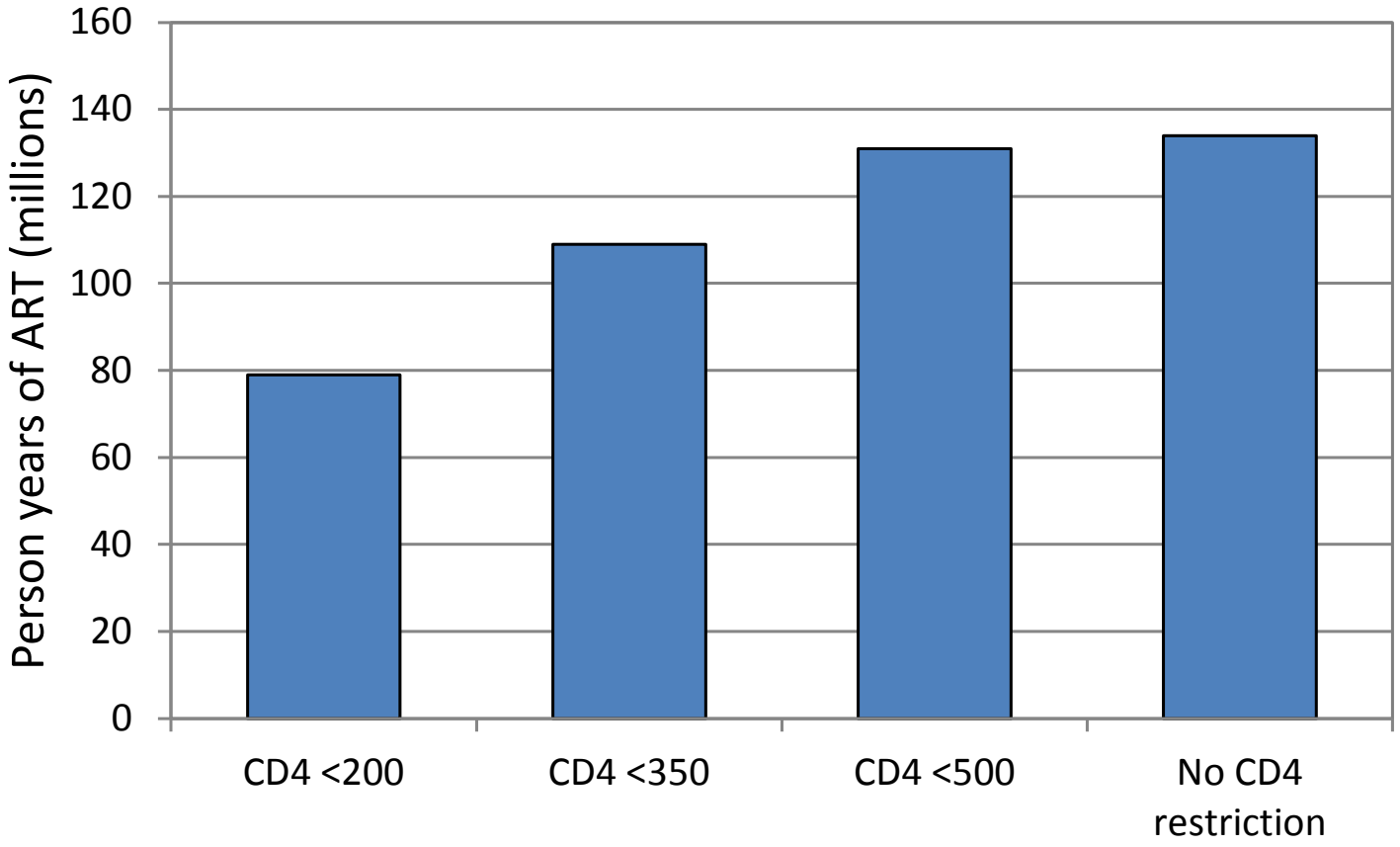
4. Models can be used to make projections of the future impact of the HIV/AIDS epidemic

- Often there is uncertainty about how the impact of the epidemic is likely to evolve in future.
- Models are important in making projections of the resources required to deal with the HIV/AIDS epidemic in future.

e.g. Projecting the number of patients on ART in South Africa

- Granich et al (2012) developed a model to assess the impact of a "test and treat" strategy in South Africa, with HIV testing reaching 90% of the population annually, and ART initiation at different CD4 thresholds (200, 350, 500 vs no CD4 restriction).
- The model was used to project the number of person years of ART provision in South Africa, over the period from 2011 to 2050.
- Results suggest that costs of providing ART in future will be sensitive to the CD4 threshold for ART provision.

Number of person years of ART provision in South Africa, 2011-2050

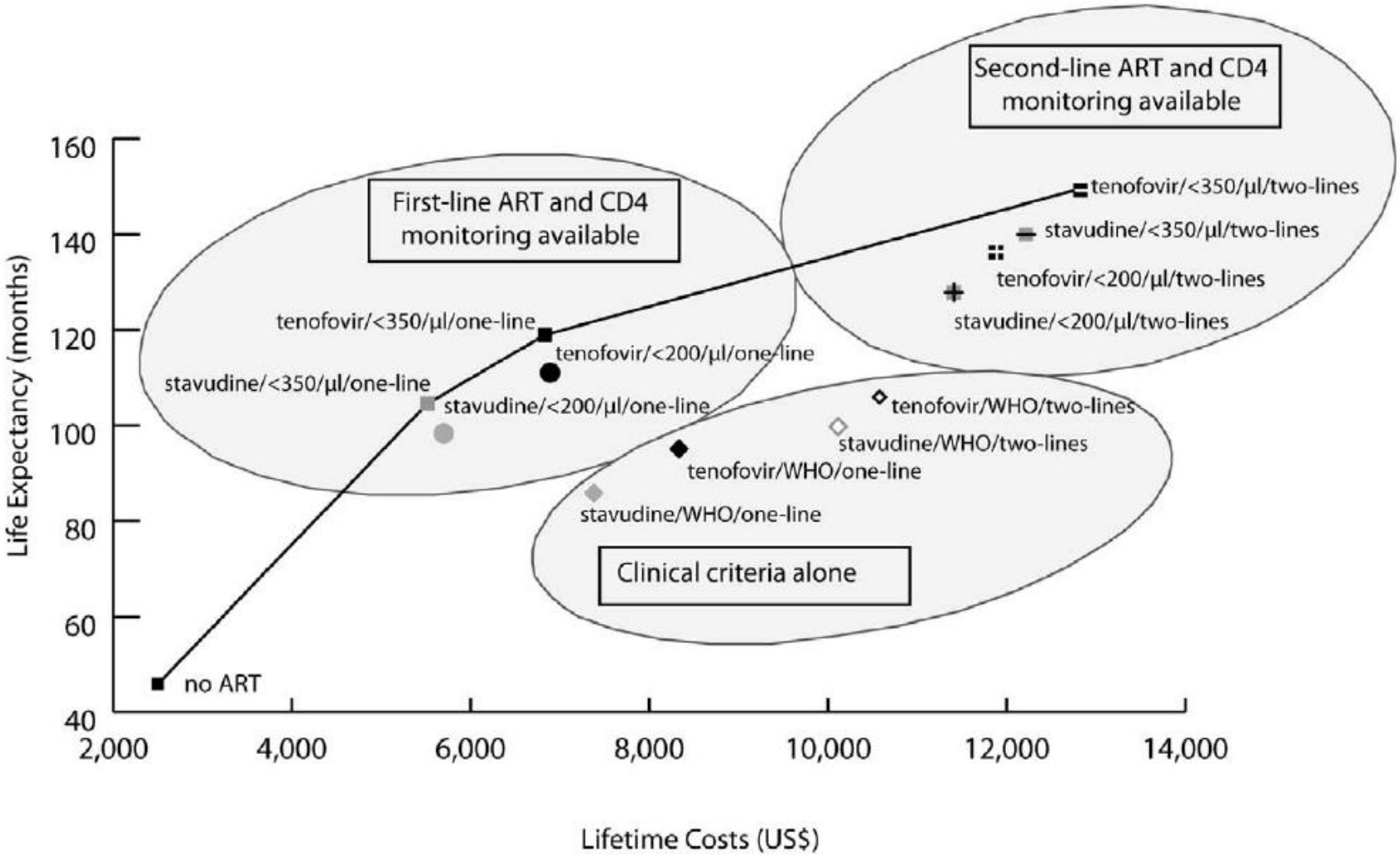


Source: Granich et al, *PLoS One*, 2012, 7:e30216

5. Models can be used to compare the effectiveness and cost-effectiveness of different interventions

- When resources are limited, it is important to focus on those interventions that are likely to be most cost-effective.
- When comparing effectiveness of different interventions it is important to use consistent assumptions and consistent measures of intervention impact.
- For example, Walensky et al (2010) evaluated what would be the most cost-effective ways to increase life expectancy in an African country with limited ART provision:
  - Change ART initiation from WHO stage-based to CD4 200 or 350
  - Introduce second-line ART
  - Replace stavudine with tenofovir in first-line ART

Cost-effectiveness of different ART strategies



Source: Walensky et al, *PLoS Med*, 2010, 7:e1000382

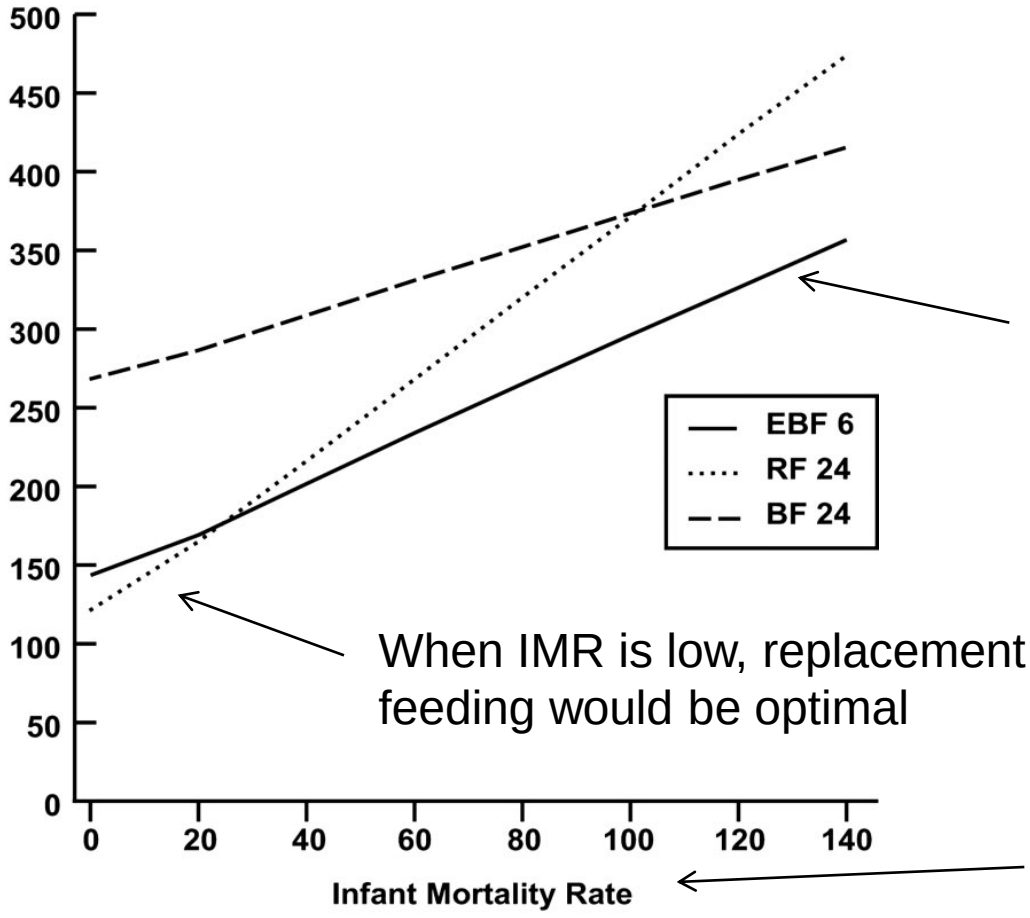
6. Models can be used to identify threats to programme success

- Often interventions fail to have a positive impact at a population level because the ideal conditions that exist in the RCT setting do not exist in the real world.
- Models can be used to quantify the role of factors that threaten programme success.
- Even when programmes have a positive impact on the outcome of interest, they may have unintended negative consequences for other outcomes.
- Models can be used to assess the impact of programmes on these other outcomes.

e.g. The effect of breastfeeding on non-AIDS mortality

- Because of the risk of mother-to-child transmission of HIV associated with breastfeeding, many PMTCT programmes have offered HIV-positive mothers free formula milk.
- However, breastfeeding has been shown to reduce mortality due to other infectious diseases significantly.
- Piwoz & Ross (2005) assessed the effect of three different feeding recommendations for HIV-positive mothers:
  - Exclusive breastfeeding (EBF) for 6 months
  - Replacement feeding (RF)
  - Mixed breastfeeding for 24 months
- They examined the effect on a composite outcome (deaths + HIV infections).

Deaths + HIV infections per 1000 children born to HIV-positive mothers



When infant mortality rate (IMR) is high, exclusive breastfeeding for 6 months would be optimal

When IMR is low, replacement feeding would be optimal

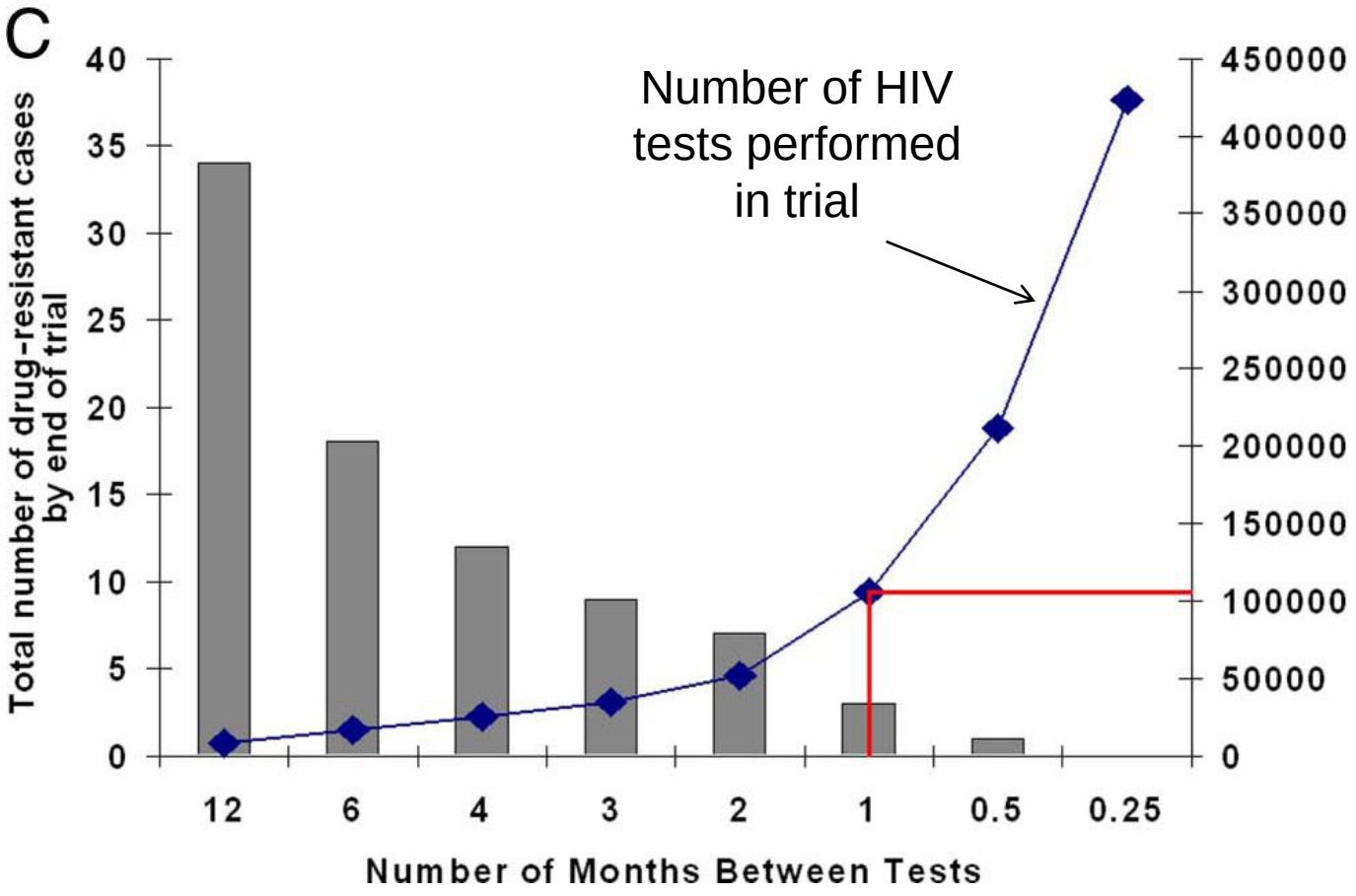
IMR that would be expected in the absence of HIV

Source: Piwoz & Ross, *J Nutr*, 2005, 135:1113-9

e.g. Antiretroviral-based microbicides and drug resistance

- Antiretroviral-based microbicides could be introduced as a new strategy for preventing HIV in women in the near future.
- However, there is the danger that women receiving an ARV-based microbicide could rapidly develop drug-resistant HIV if they become infected while on the microbicide.
- In the context of an RCT this risk is minimal because women are tested frequently, and would be taken off the microbicide immediately if they became infected.
- But in a "real world" setting, where HIV testing is less frequent, the risk is greater.
- Wilson et al (2008) showed this using a mathematical model.

Emergence of drug resistance in RCTs of ARV-based microbicides



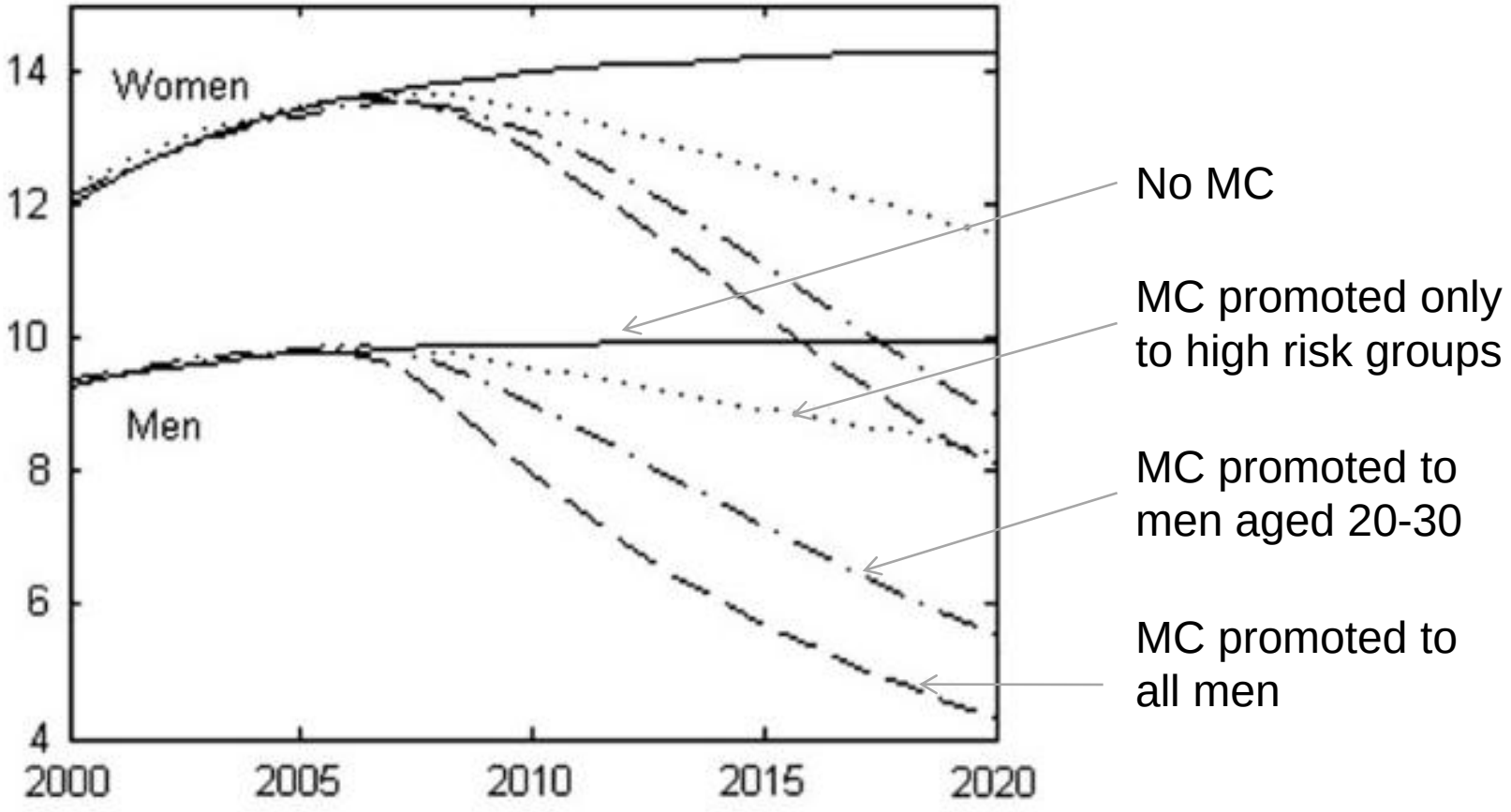
Source: Wilson et al, *Proc Natl Acad Sci USA*, 2008, 105:9835-40

Part 4: What are the most common messages in published analyses of HIV/AIDS models?

1. The positive effects of interventions go beyond the group in which they are introduced

- This is an important point when considering interventions that may appear to favour one interest group over others.
- For example, it is often stated that male circumcision (MC) programmes would only benefit men.
- However, mathematical modelling shows that MC programmes would probably benefit women indirectly, by reducing the chance that their partners are infected.
- e.g. Londish & Murray (2008) considered what would happen if MC was promoted, starting in 2007, in a typical African country.

Effect of MC on adult HIV prevalence

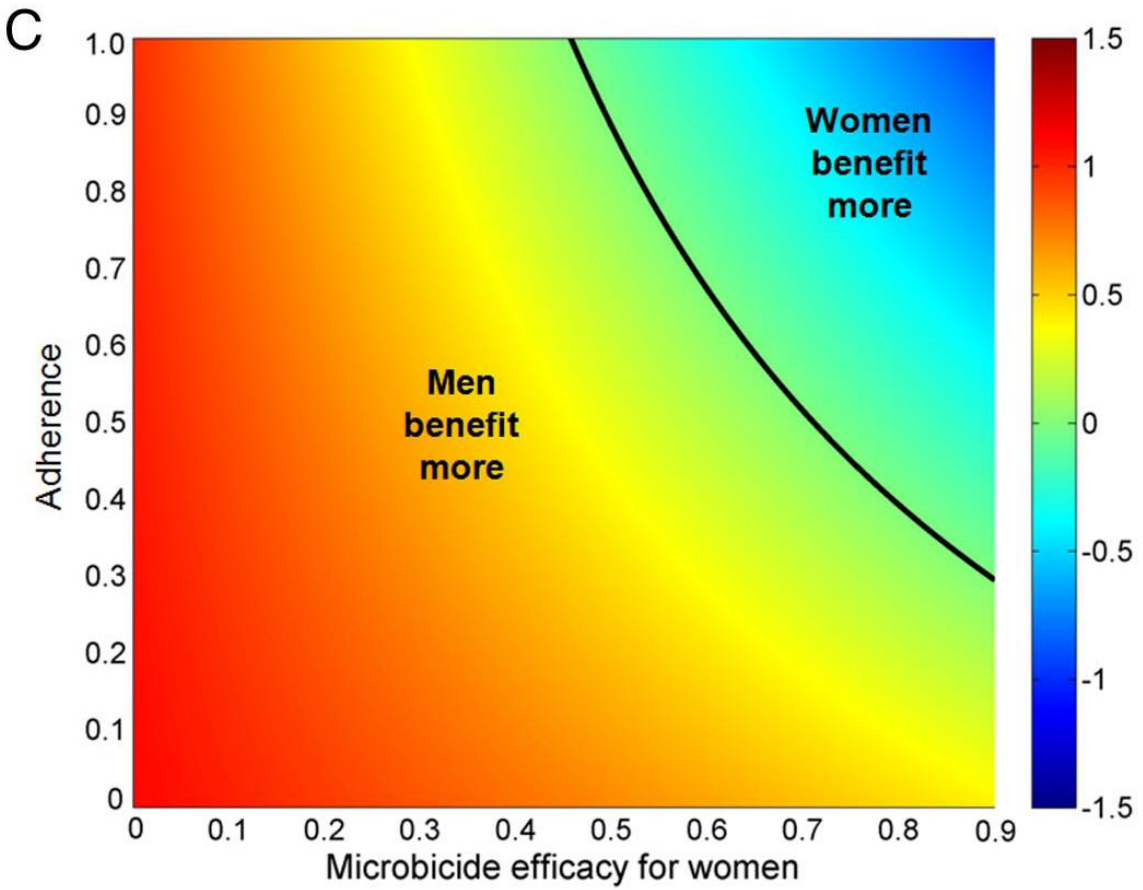


Source: Londish & Murray, *Int J Epidemiol*, 2008, 37:1246-53

e.g. Effect of antiretroviral-based microbicides on HIV incidence in men

- Similarly, it is often stated that microbicides would only benefit women.
- However, men may benefit indirectly due to their partners having a lower HIV risk.
- In addition, if the microbicide is antiretroviral-based, men might benefit because women who become infected while on the microbicide would be less likely to transmit HIV:
  - Antiretroviral drugs suppress virus in female partner.
  - If the virus mutates it is likely to be less transmissible.
- Paradoxically, this may lead to men benefiting MORE than women from an antiretroviral-based microbicide, as shown by Wilson et al (2008).

Impact of an antiretroviral-based microbicide on HIV incidence



Source: Wilson et al, *Proc Natl Acad Sci USA*, 2008, 105:9835-40

e.g. The effect of harm reduction for IDUs on the non-IDU population

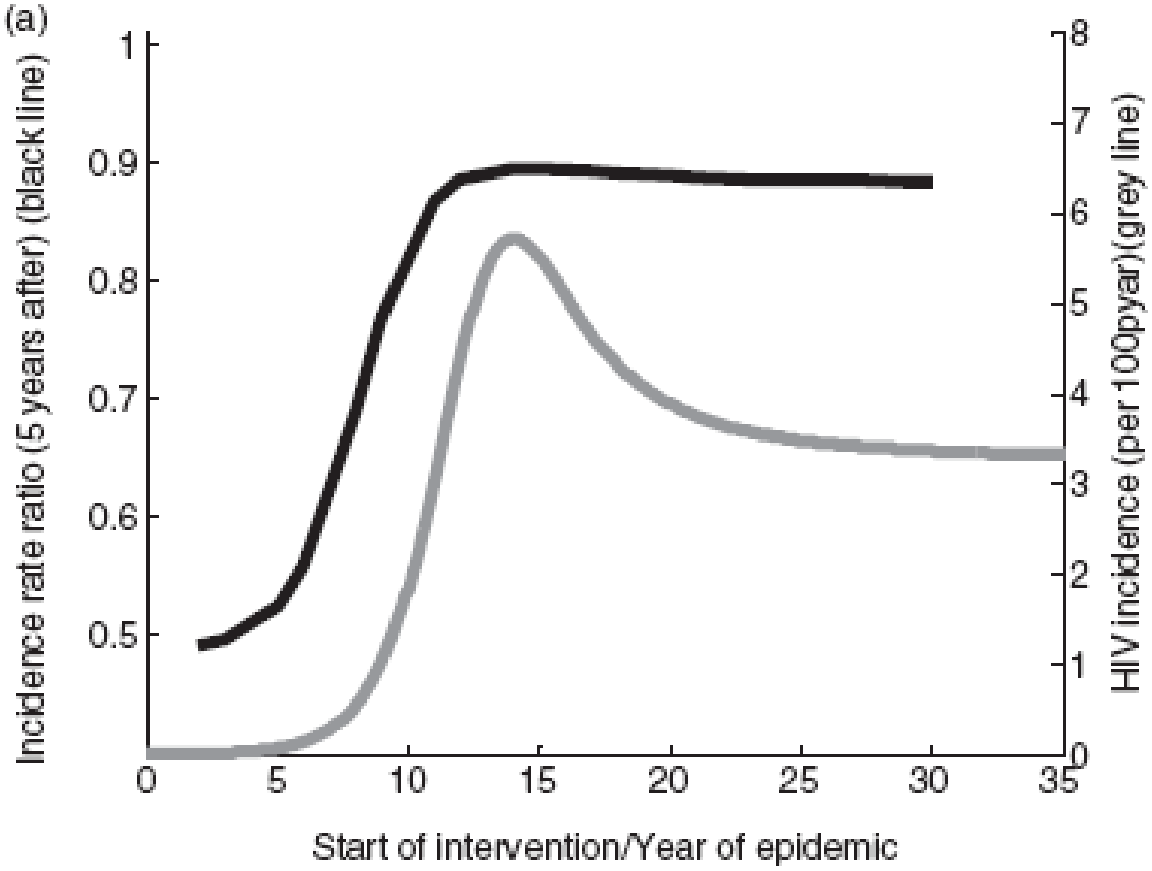
- Foss et al (2006) modelled the effect of a programme in Bangladesh, which involved the provision of syringes and condoms to IDUs.
- In the short term (1st 3 years after start of the programme), the majority of the infections averted were in IDUs.
- However, by 8 years after the start of the intervention, the cumulative number of infections averted in non-IDUs (6010) exceeded the number averted in IDUs (5521).

Source: Foss et al, *Addiction*, 2006, 102:114-25

2. Prevention programmes work better the earlier that they are introduced

- In other words, it is harder to contain an epidemic when it has spread extensively than when the epidemic is in its early stages.
- e.g. Hallett et al (2008) simulated the impact of an intervention targeting sex workers in Zimbabwe, and calculated what the impact would have been if the same intervention had been introduced at different stages in the Zimbabwean epidemic.
- Impact calculated as ratio of HIV incidence post-intervention to HIV incidence that would have been expected in absence of intervention (ratio = 1 implies no impact).

The impact of a behaviour change intervention that targets CSWs

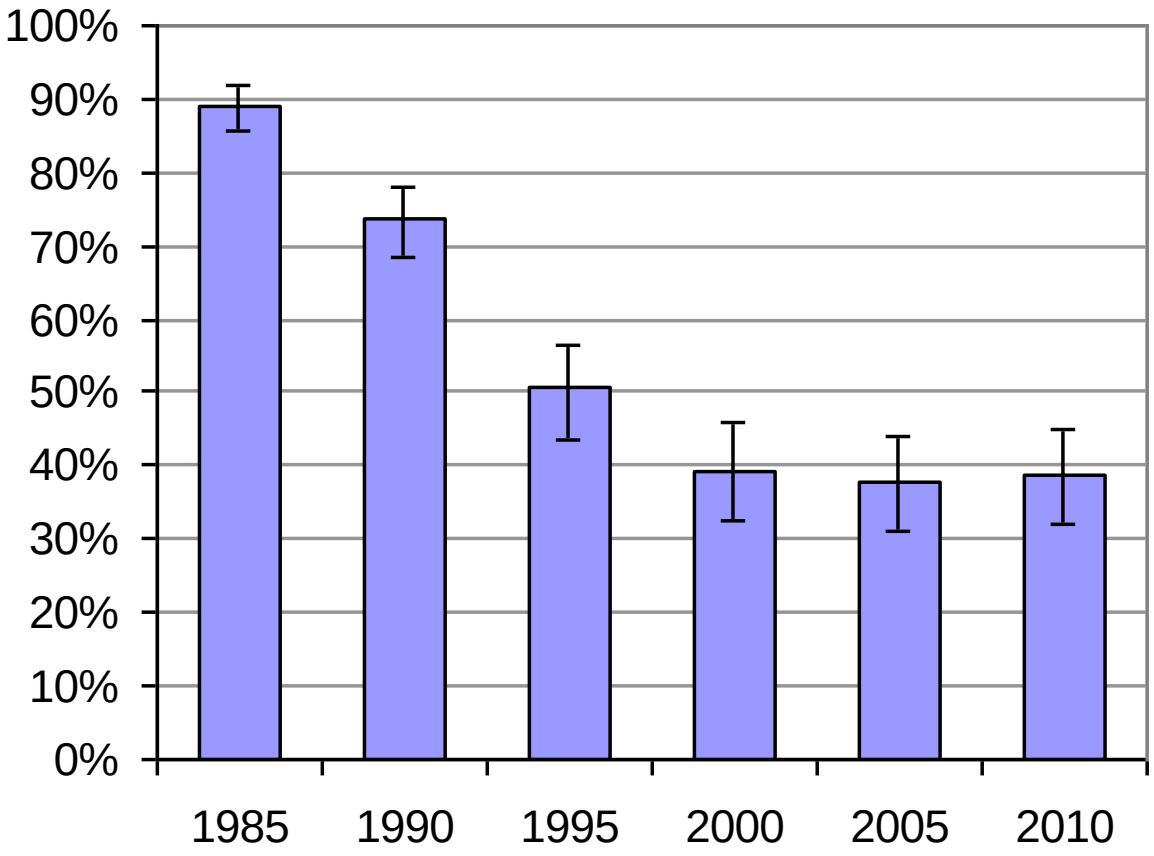


Source: Hallett et al, *Int J Epidemiol*, 2008, 37:77-87

e.g. The impact of eliminating concurrent partnerships in South Africa

- Using a detailed model of sexual behaviour patterns in South Africa, we assess what would have happened if the rate at which secondary patterns are acquired was reduced to zero, at different stages in the epidemic.
- This means assessing what would have happened if nobody had more than one partner at the same time (no concurrent partnerships).
- Note that we are assuming that the rate of primary partner acquisition and frequency of sex with primary partner would remain unchanged (which might lead to the impact being overstated).

% reduction in HIV incidence if con-currency is eliminated at different times

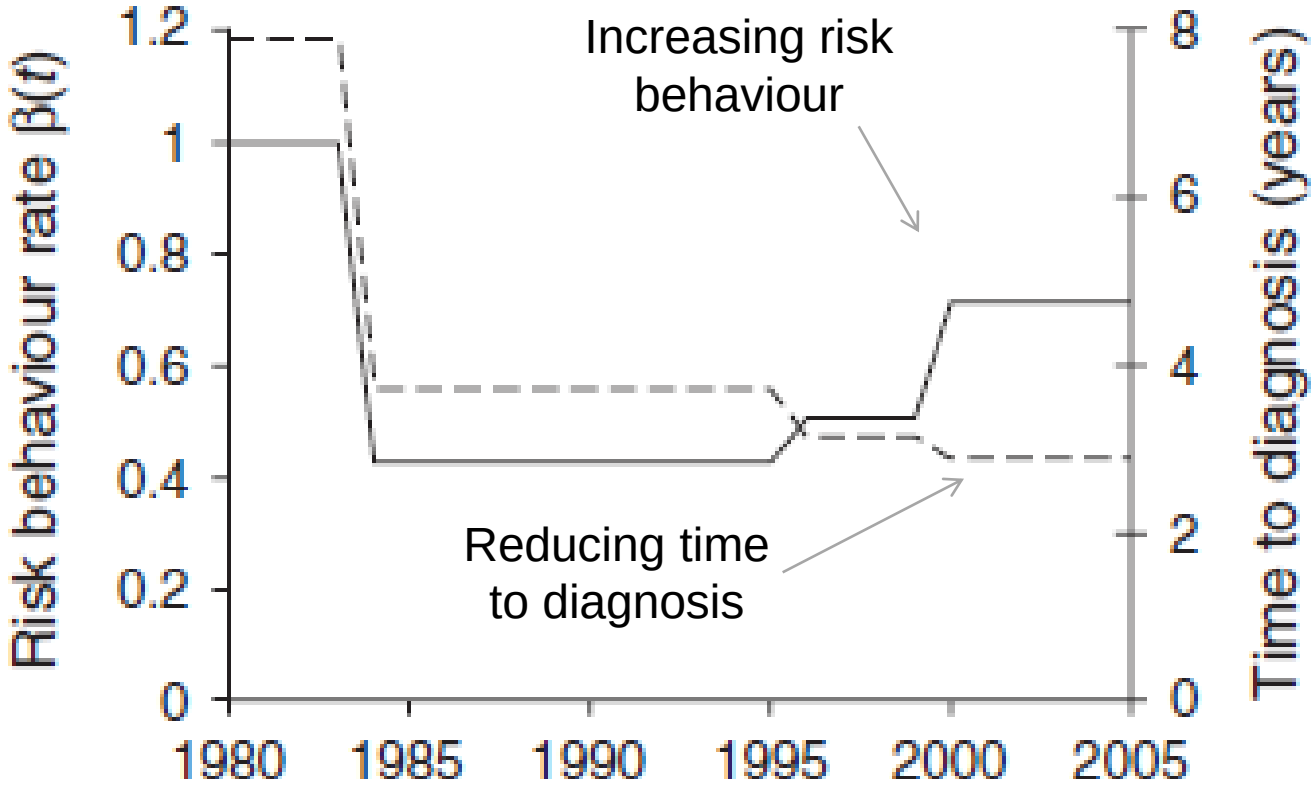


Source: Johnson & White, *STIs*, 2011, 87:629-34

3. Risk compensation can reverse gains made in HIV prevention

- e.g. There has been much concern that HIV incidence in men who have sex with men (MSM) is increasing in industrialized countries due to increased levels of risk behaviour following the introduction of highly active ART (around 1996).
- Bezemer et al (2008) fitted a model to trends in reported numbers of new HIV diagnoses and reported AIDS cases in MSM in the Netherlands.
- The model allows for changes over time in (a) the time to diagnosis, and (b) the rate of risk behaviour.
- The best fits to the data were obtained when assuming reducing time to diagnosis and increasing risk behaviour post-1996 (evidence of risk compensation).

The impact of ART on risk behaviour in MSM

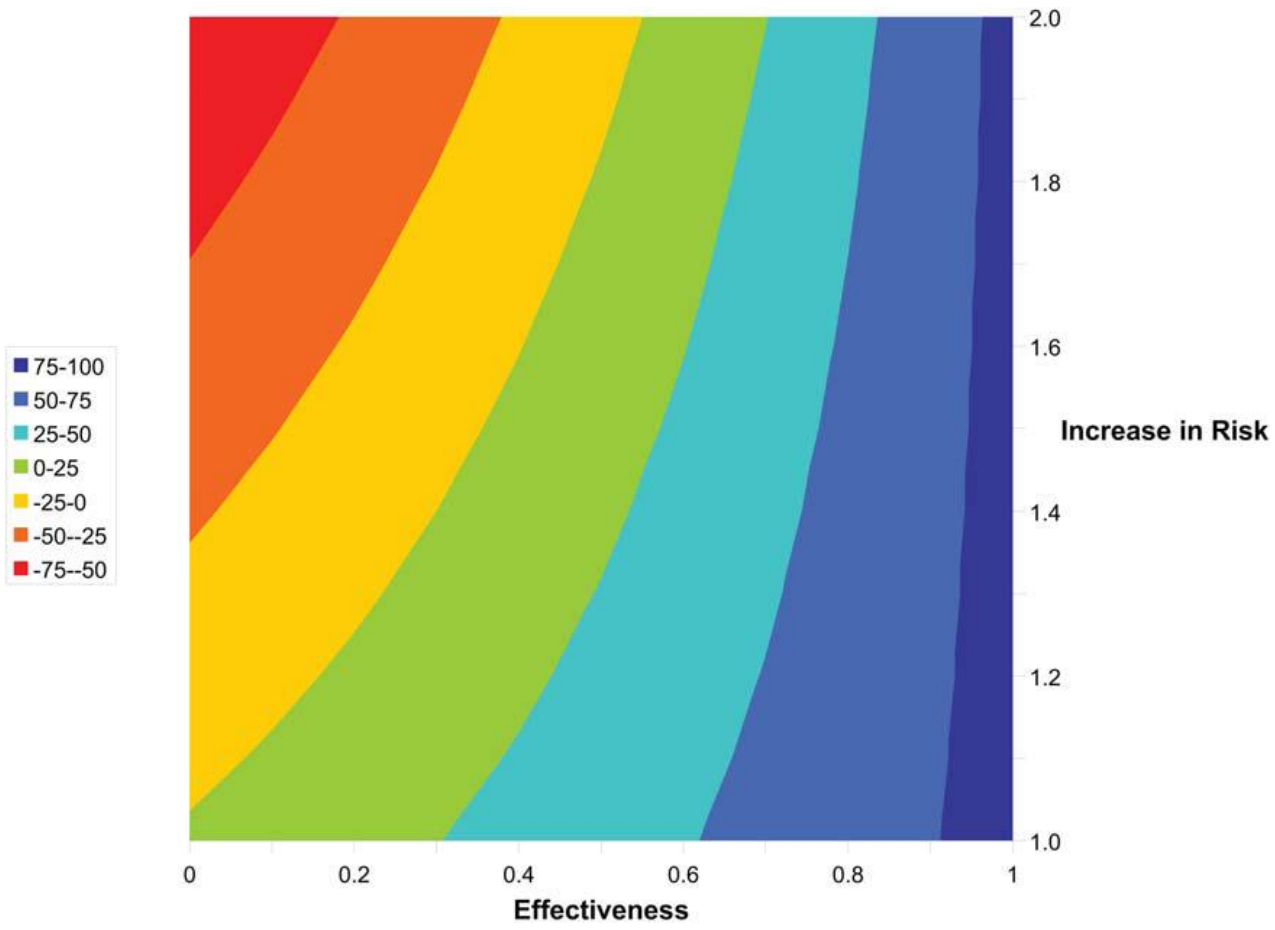


Source: Bezemer et al, *AIDS*, 2008, 22:1071-7

e.g. The impact of pre-exposure prophylaxis (PrEP) on HIV incidence

- Pre-exposure prophylxis (antiretroviral drugs taken before exposure to reduce risk of HIV acquisition) is currently being tested in various trials.
- Abbas et al (2007) modelled what might happen in Zambia if PrEP were effective and it were offered on a large scale.
- They created a contour plot to assess how the % reduction in HIV incidence might be affected by PrEP effectiveness and the relative increase in risk behaviour in individuals receiving PrEP.
- At high levels of PrEP efficacy, % reduction in incidence is not very sensitive to risk compensation, but at low efficacy levels, risk compensation could have a significant impact.

% reduction in HIV incidence due to PrEP in Zambia

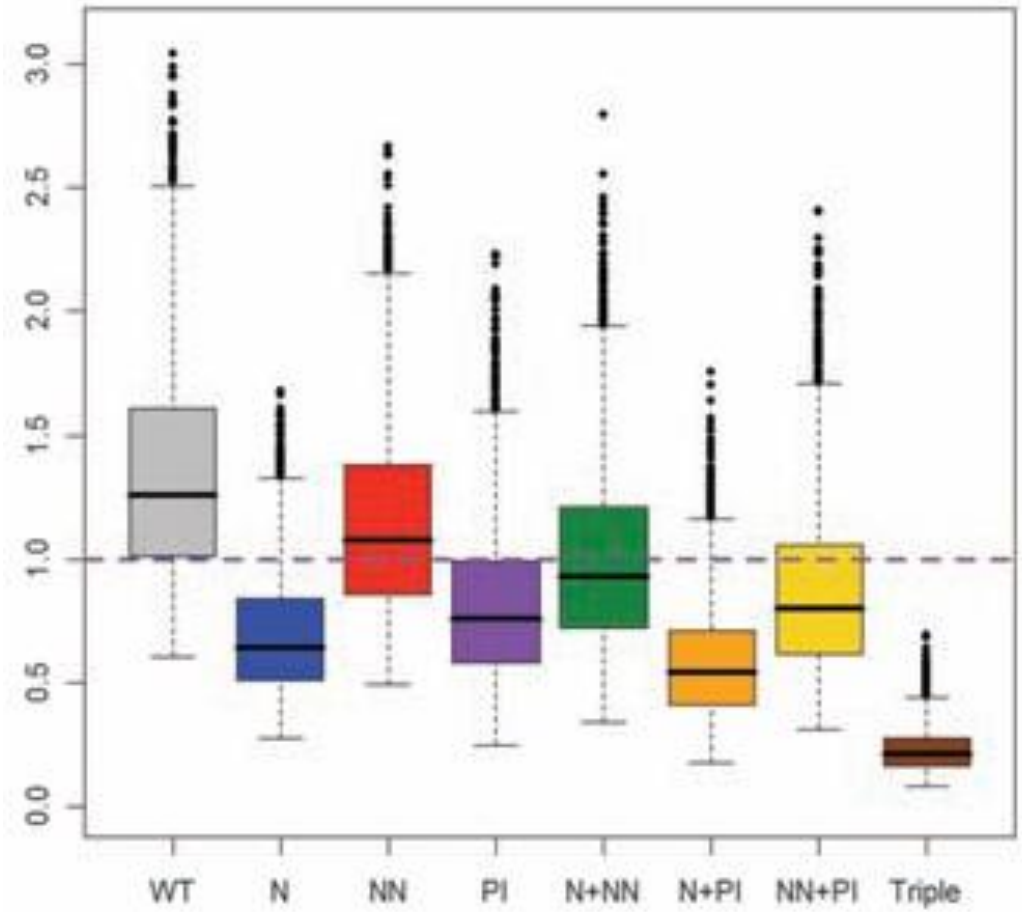


Source: Abbas et al, *PLoS ONE*, 2008, 2:e875

4. Drug resistance is likely to limit the impact of many interventions

- e.g. Smith et al (2010) evaluated the likely evolution of ARV drug resistance in San Francisco, using historic data on drug resistance patterns.
- They calculated the basic reproductive number separately for each HIV strain:
  - Wild-type (WT): not drug-resistant
  - Resistant to nucleoside reverse transcriptase inhibitors (N)
  - Resistant to non-nucleoside reverse transcriptase inhibitors (NN)
  - Resistant to protease inhibitors (PI)
  - And strains resistant to combinations of the above
- Results suggest that there is a significant risk of a self-sustaining epidemic of drug-resistant HIV (R_0 >1), especially for non-nucleoside reverse transcriptase inhibitors.

Basic reproductive numbers for different HIV strains in San Francisco

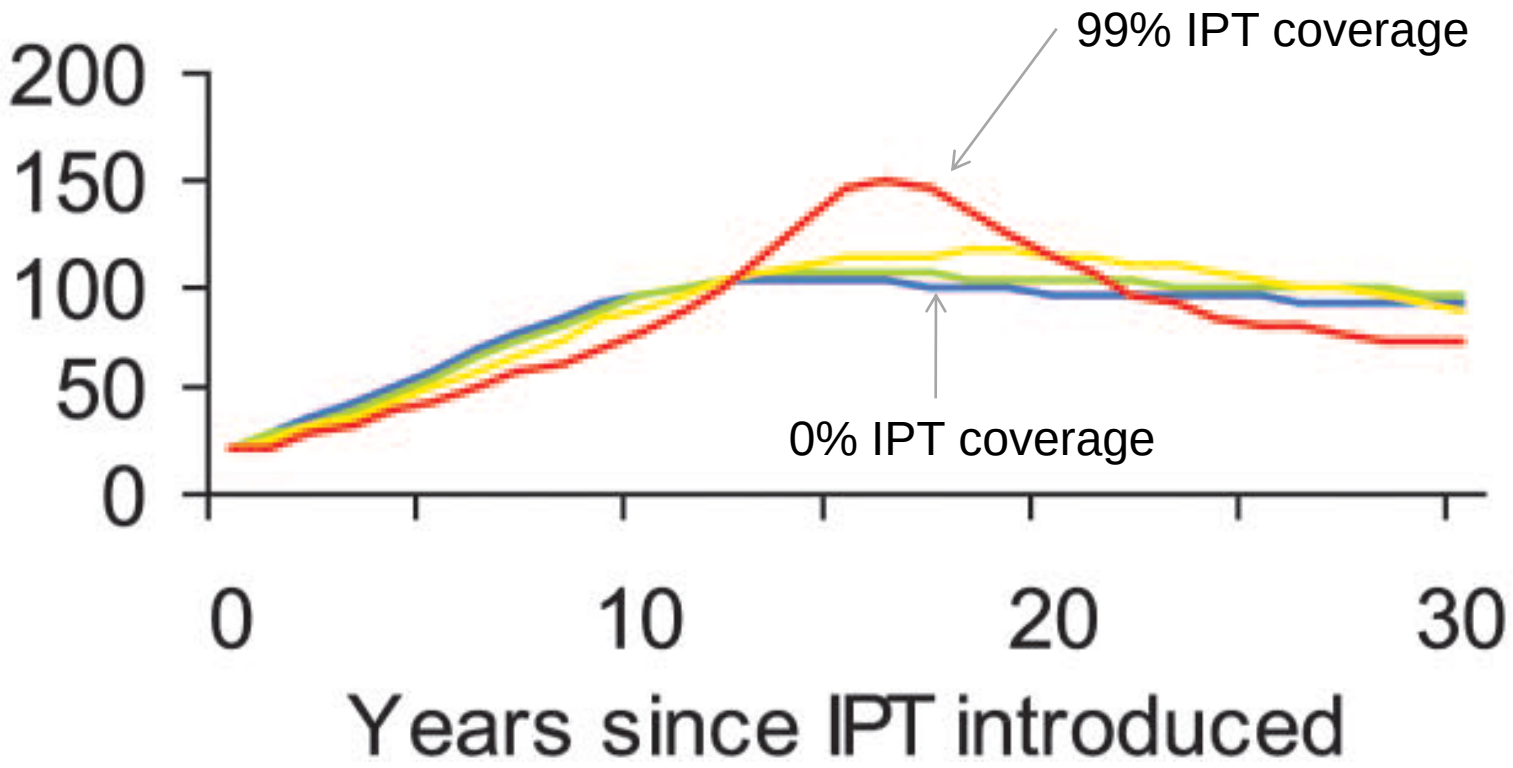


Source: Smith et al, *Science*, 2010, 327:697-701

e.g. Impact of isoniazid preventive therapy (IPT)

- Isoniazid preventive therapy (IPT) is recommended for HIV-infected adults, to reduce the risk of developing TB.
- However, there is concern that the widespread use of isoniazid could lead to the accumulation of drug resistance.
- Cohen et al (2006) assessed the impact of IPT on HIV-related deaths in a typical African country.
  - They assumed drug-sensitive and drug-resistant TB strains compete with one another.
  - They assumed sensitive and resistant TB strains had the same fitness.
- Results suggest IPT may have a significant benefit in the short term, but would have limited net benefit in long term, due to accumulation of substantial resistance.

HIV-associated deaths per 1000 HIV cases, with and without IPT

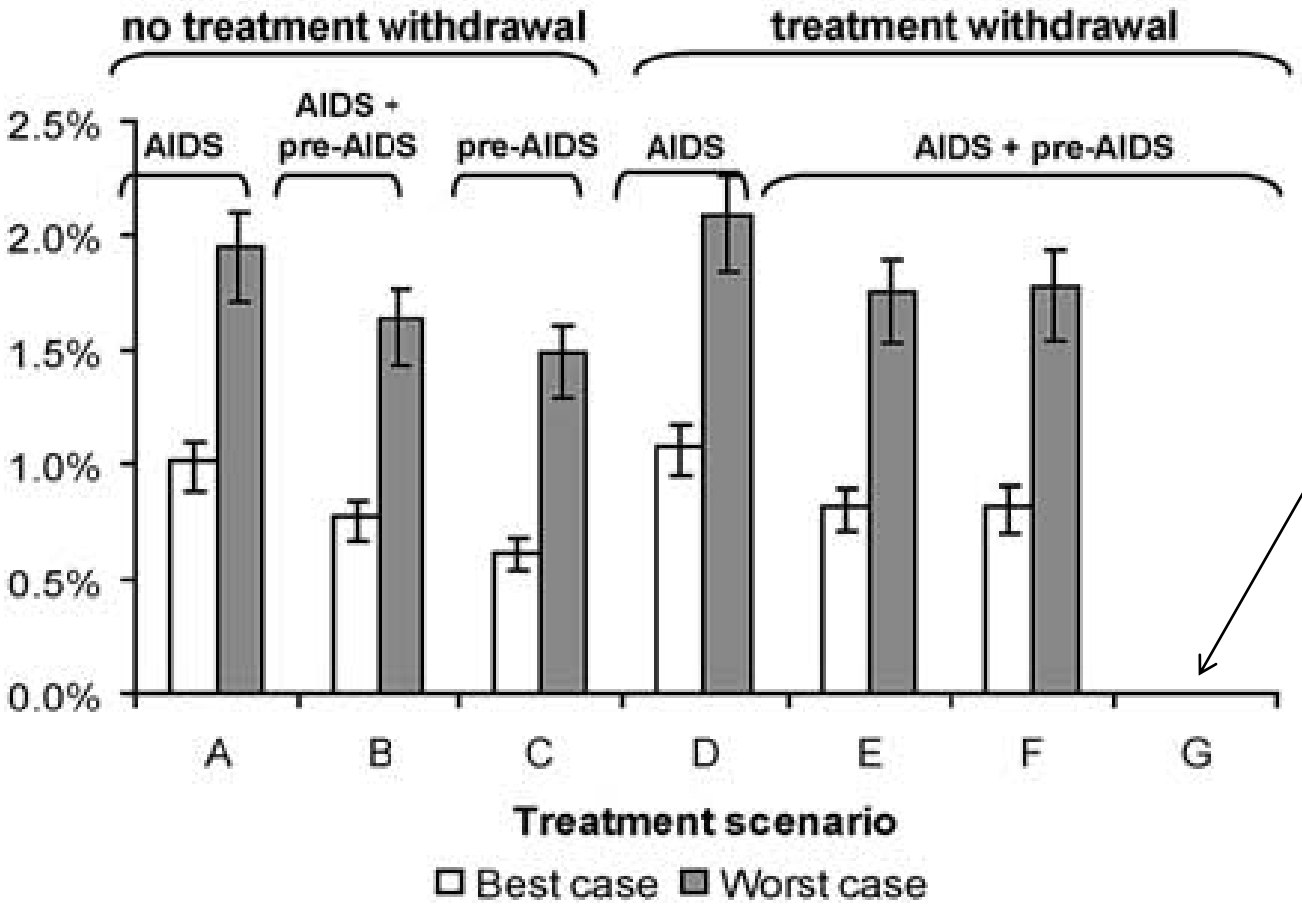


Source: Cohen et al, *Proc Natl Acad Sci USA*, 2006, 103:7042-7

Importance of laboratory monitoring

- Mathematical models can be used to demonstrate the importance of laboratory monitoring in reducing the incidence of drug resistance.
- e.g. Baggaley et al (2006) assessed the effect of different strategies for initiating, monitoring and discontinuing ART:
  - Starting ART only in patients with AIDS (scenarios A & D) compared to starting earlier (B, E-G)
  - No switching of antiretroviral drugs (A-C) vs switching after clinical failure (D-F) vs switching after viral load test shows virological failure (G)
- Results suggest that the % of HIV infections that are drug-resistant would be lowest if there was regular viral load testing to guide ART changes (scenario G).

% of HIV infections that are drug-resistant, under different strategies



Zero resistance in viral load testing scenario

Source: Baggaley et al, *PLoS Med*, 2006, 3:e124

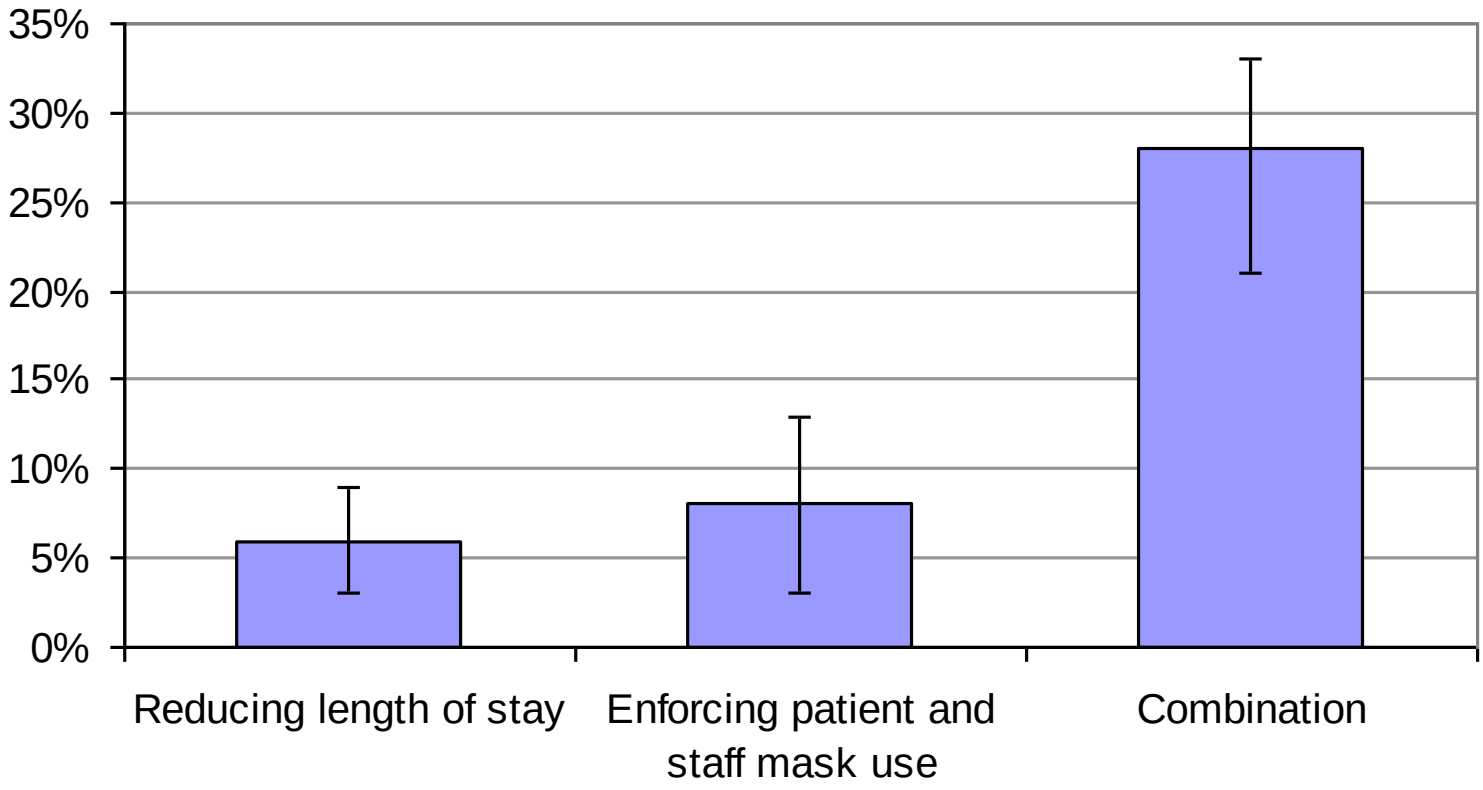
5. Interventions can be synergistic or antagonistic

- In some situations, there will be synergies between interventions.
- In other situations, the impact of an intervention may be reduced if other interventions are in place.
- The question of whether interventions are subject to increasing or decreasing marginal returns depends on the epidemic setting and the nature of the interventions considered.
- Hence, policymakers need to use models that are calibrated to local data and that take account of the interventions that are already in place locally.

e.g. of synergies: interventions to control XDR TB

- Basu et al (2007) simulated the effect of different strategies for controlling extensively drug-resistant TB (XDR TB) in Tugela Ferry (KwaZulu-Natal), a setting in which there is high nosocomial transmission of XDR TB.
- Results suggest that reducing patient length of stay and forcing staff and patients to use masks would each reduce transmission by 5-10% individually.
- However, combining the two interventions would lead to an almost 30% reduction in XDR TB incidence (> the sum of the effects of the individual interventions).

The effect of infection control on XDR TB incidence



Source: Basu et al, *Lancet*, 2007, 370:1500-7

Part 5: Careers in HIV/AIDS modelling

Advantages of working in HIV/AIDS modelling

- Interesting, stimulating work
- Opportunities to work with people from a wide range of different fields (clinicians, economists, policymakers, activists, microbiologists …)
- Many opportunities for international travel and collaboration
- Work is highly relevant in SA and other developing countries.

Disadvantages of working in HIV/AIDS modelling

- Research in disease modelling is not well paid relative to what most mathematically-skilled graduates can earn in the financial services industry.
- Lack of security in research funding
- Dangers of becoming too specialized. To avoid this, you need to gain experience in
  a) Modelling of other diseases
  b) Other disciplines related to infectious disease modelling

Disciplines related to infectious disease modelling

- Epidemiology: the study of the distribution and determinants of disease, including the study of the efficacy of strategies for preventing and treating disease
- Biostatistics: statistical techniques for estimating survival, incidence of disease, factors affecting risk of disease
- Burden of disease: quantifying the impact of different diseases at a population level in terms of “healthy years of life lost”
- Health economics: assessing the cost of health interventions, ranking different interventions in terms of cost per healthy year of life gained

Where do people with these skills end up working?

- Disease modellers: research centres
- Epidemiologists: research centres, govt health departments, other govt agencies, NGOs delivering health interventions
- Biostatisticians: research centres, drug companies, medical schemes
- Burden of disease experts: research centres
- Health economists: research centres, drug companies, govt health departments

Organizations to approach if you are interested in doing a masters/PhD

- Disease modelling: SACEMA
- Epidemiology: UCT School of Public Health (Masters in Public Health programme)
- Biostatistics: UCT Department of Statistics (Masters in Biostatistics programme)
- Burden of disease: Medical Research Council Burden of Disease Research Unit
- Health economics: UCT Health Economics Unit (specialization within the Masters in Public Health programme)
- Demography: UCT Centre for Actuarial Research (MPhil programme)