

Trend in antiretrovirale therapie (ART) regimes: Draagt ART bij aan de preventie van HIV-infectie?

Frank de Wolf

Stichting HIV Monitoring

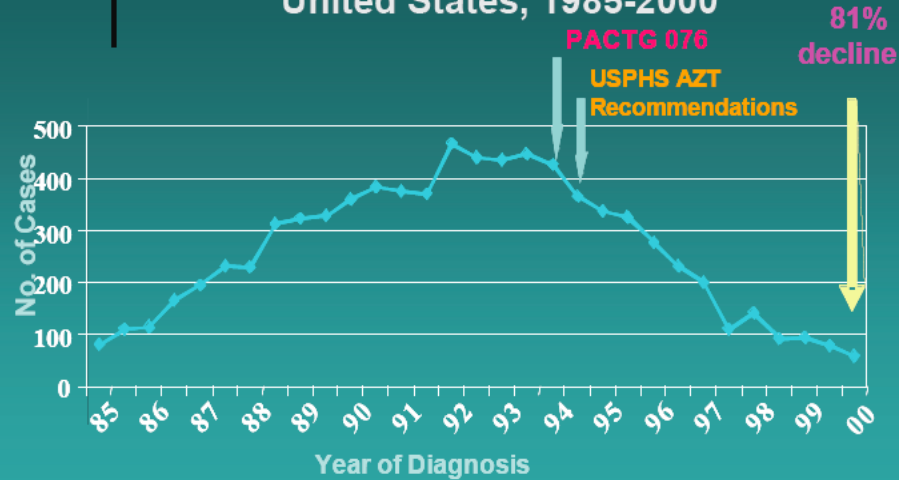
Amsterdam

Draagt ART bij aan de preventie van HIV-infectie?

- MTCT

MTCT

Incidence of Perinatally-Acquired AIDS United States, 1985-2000*

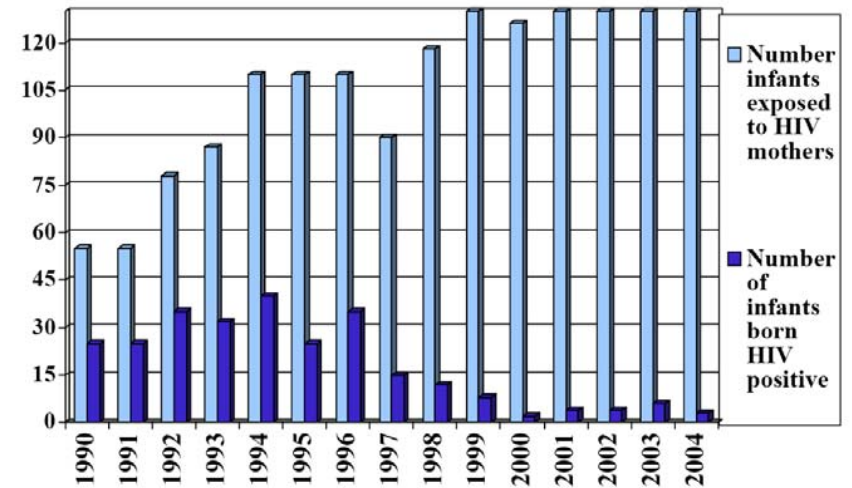


* Reported through December 2000
Slide credit: L. Mofenson

USA, 1985 - 2000

Canada, 1990 - 2004

Canada: Infants Exposed to HIV and Born HIV Positive



Draagt ART bij aan de preventie van HIV-infectie?

- MTCT
- Discordant couples

PVL and HIV Transmission in Serodiscordant Heterosexual Couples

Author	Year	Site	Participants	ART?	Key findings
Porco	2004	San Francisco	534 men who have sex with men (MSM)	Yes	Estimated perpartner HIV transmission risk falls from 0.120 before HAART to 0.048 with widespread HAART
Fang	2004	Taiwan	4390 prevalent HIV cases	Yes	Estimated HIV transmission rate falls from 0.391 to 0.184 new cases per prevalent caseyear with introduction of free HAART
Castilla	2005	Spain	393 heterosexual couples	Yes	HIV rate 8.6% when partner not taking ART vs 0% when partner taking ART; HIV prevalence falls from 10% preHAART (1991-95) to 2% with HAART (199903)

Draagt ART bij aan de preventie van HIV-infectie?

- MTCT
- Discordant couples
- Populatie?

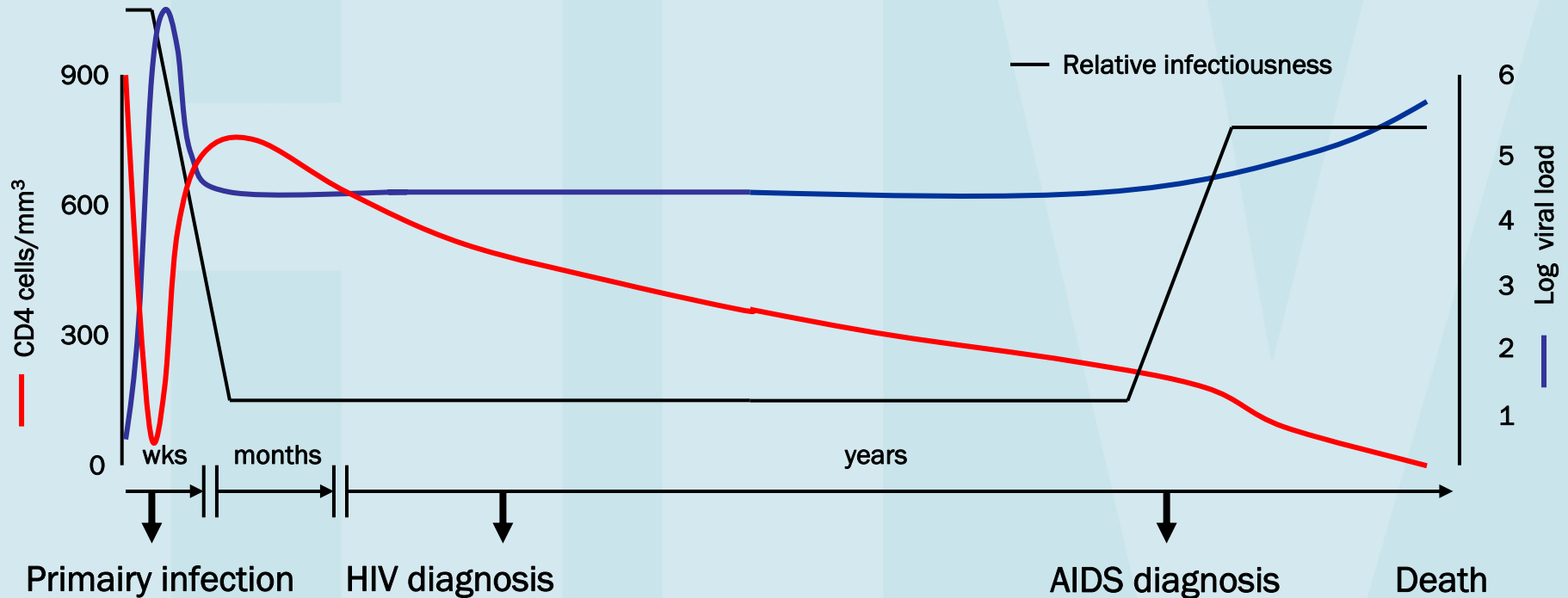
Controlling the HIV epidemic in the Netherlands

Frank de Wolf

HIV Monitoring Foundation

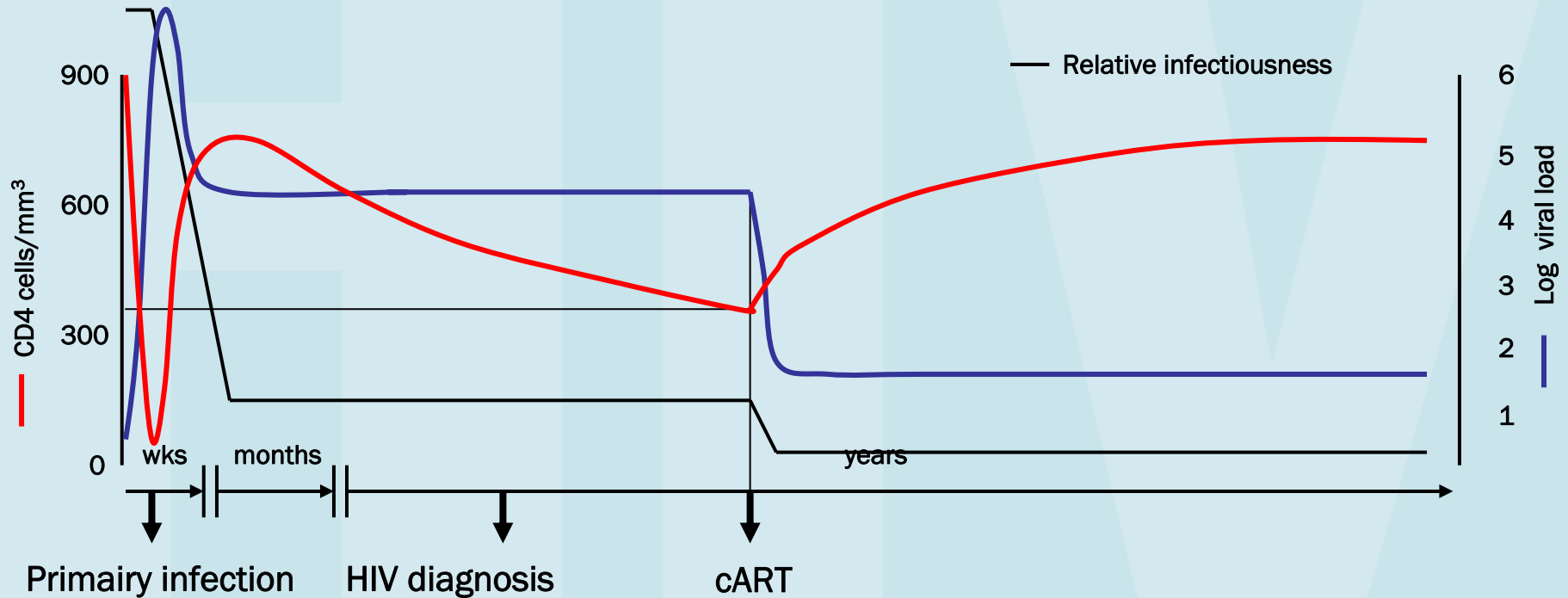
Amsterdam, The Netherlands

Background: HIV infection untreated



The amount of HIV circulating in a infected untreated person varies over time, peaking to levels between $10^5 - 10^7$ RNA cps/ml plasma during primary infection, being around set-point ($10^4 - 10^5$ cps/ml) during the years lasting asymptomatic phase and increasing again during the months to years lasting symptomatic phase until death

Background: HIV infection treated



The response to combination antiretroviral therapy:

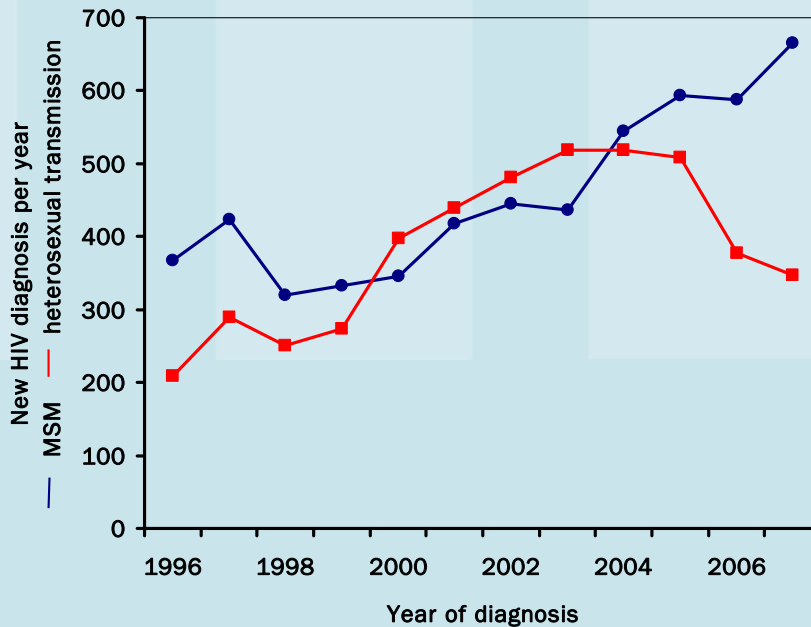
- Plasma viral load levels >50 cps/ml in 50% 40 days and in 90% 80 days after start of cART
- When on treatment, in over 90% of the population levels are below 50 cps/ml for years
- Therapy failure rates are between 6 to 9% per year
- Rate of transmission of intermediate and high-level drug-resistant HIV-1 is 3 to 4%
- Patients live longer and suffer less from AIDS

Impact of cART on the HIV epidemic?

Infectiousness is shown to be strongly correlated to viral load

(Quinn *et al.*, 2000 ; Fideli *et al.*, 2001)

Decrease of new infections since the introduction of cART?



80% of the registered population on cART

20% cART failure

Background

Three factors with substantial impact on transmission of HIV:

- The amount of virus circulating in the donor:
 - Varies, depending on the phase of infection, being highest at primary infection and full blown AIDS *Waver, et al, 2005*
 - Change when on cART with a potential epidemiological impact
- Testing behaviour of those at risk for HIV, having an impact on transmission risk *Marks et al., 2005; Van Griensven et al., 1988*
- Transmission risk behaviour

Study

Quantify the impact of

- cART
- Risk behaviour
- Time to diagnosis

Use a mathematical model to obtain information from data available

Blower et al 2000; Law et al 2001; Nagelkerke et al 2002; Velasco-Hernandez et al 2002; Hosseinipour et al 2002; Xiridou et al 2003; Clements et al 2004; Bezemer et al 2008

Calculate the reproductive number $R(t)$: Average number of people that a donor at time t would infect over his whole infectious lifespan if conditions remained the same as at time t

- If $R(t) > 1$ the epidemic will grow exponentially, driven by local transmission
- If $R(t) < 1$ the epidemic will contract and reflect number of imported cases

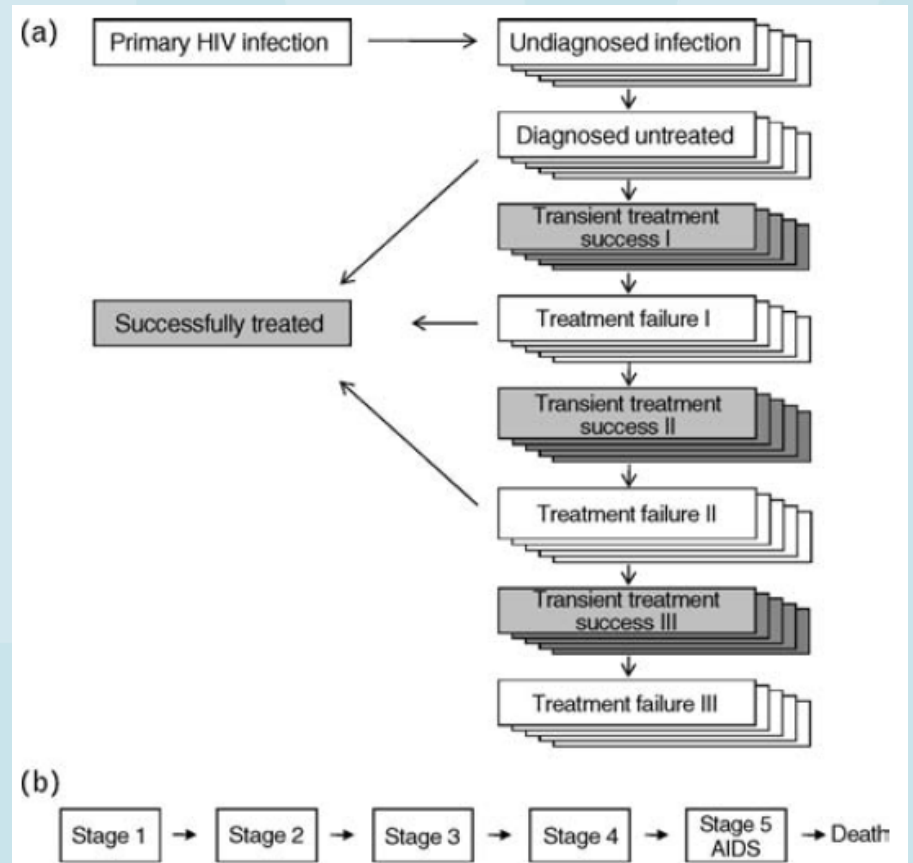
Data: The ATHENA cohort

A national cohort of all HIV infected patients followed in one of the 24 HIV treatment centers in the Netherlands

- Year of HIV-1 diagnosis
- Year of AIDS diagnosis
- Country of infection
- CD4 counts
- Time between diagnosis and cART
- Time to cART success
- Time to cART failure

Model

- Start: primary infection
- After diagnosis, risk behaviour can be reduced
- cART is available after 1996 and can be long term successful or transiently fail
- When successful: not infectious; no disease progression
- Infectiousness highest during primary infection and AIDS
- Mean stay in each of 5 compartments: 1.89 years (fitting an Erlang survival distribution to data of 130 pre-cART seroconverters).
- Stay in primary infection compartment: 0.24 year
- Imported infections flow into primary and undiagnosed compartments



Bezemer, et al; AIDS 2008, 22:1071-1077

Assumptions and estimates

Assumptions:

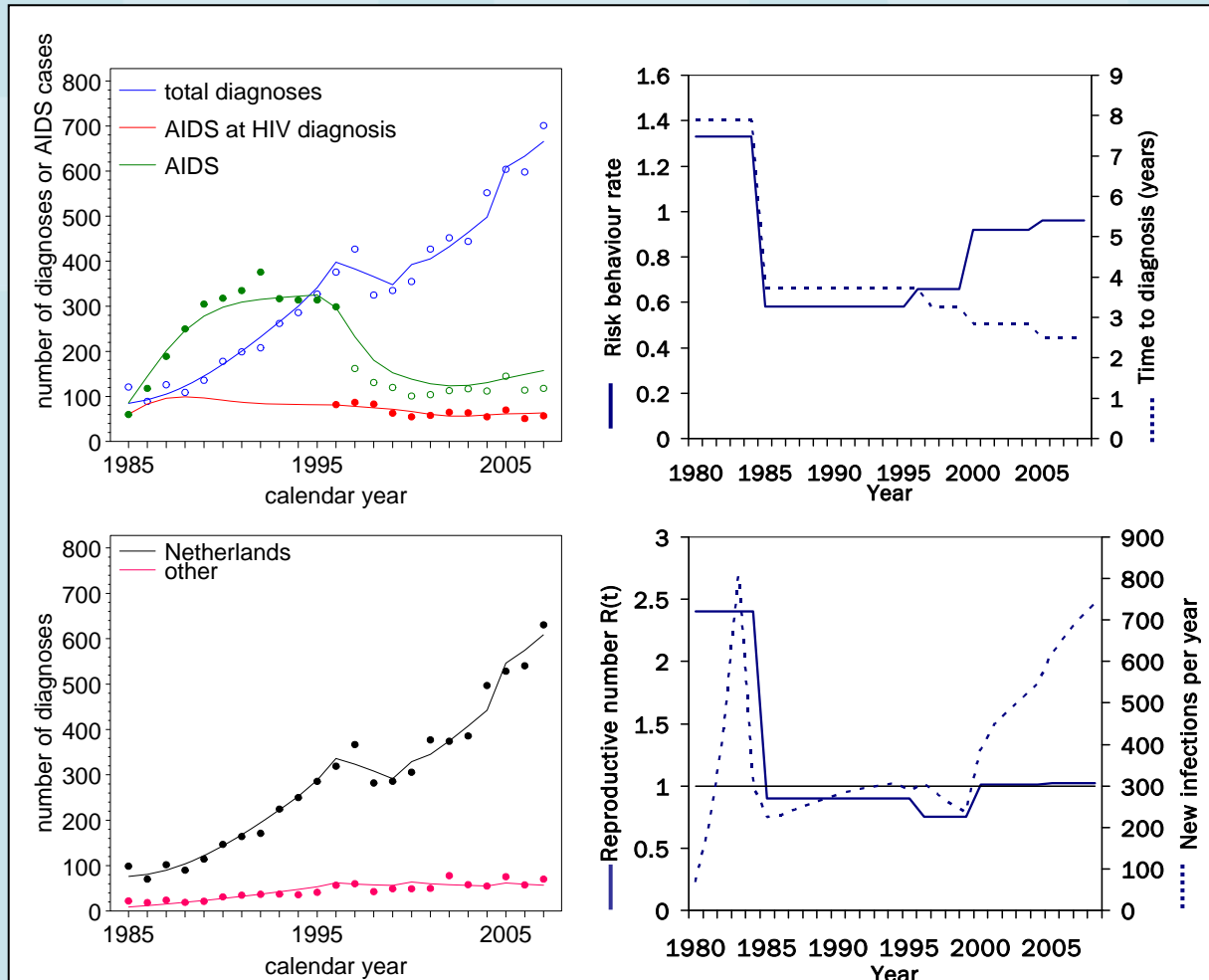
- During successful cART transmission is blocked; during failure there is viral rebound and infectiousness. There are 3 treatment opportunities

Estimate by simultaneous fit to the data on number of new HIV and new AIDS diagnoses per year:

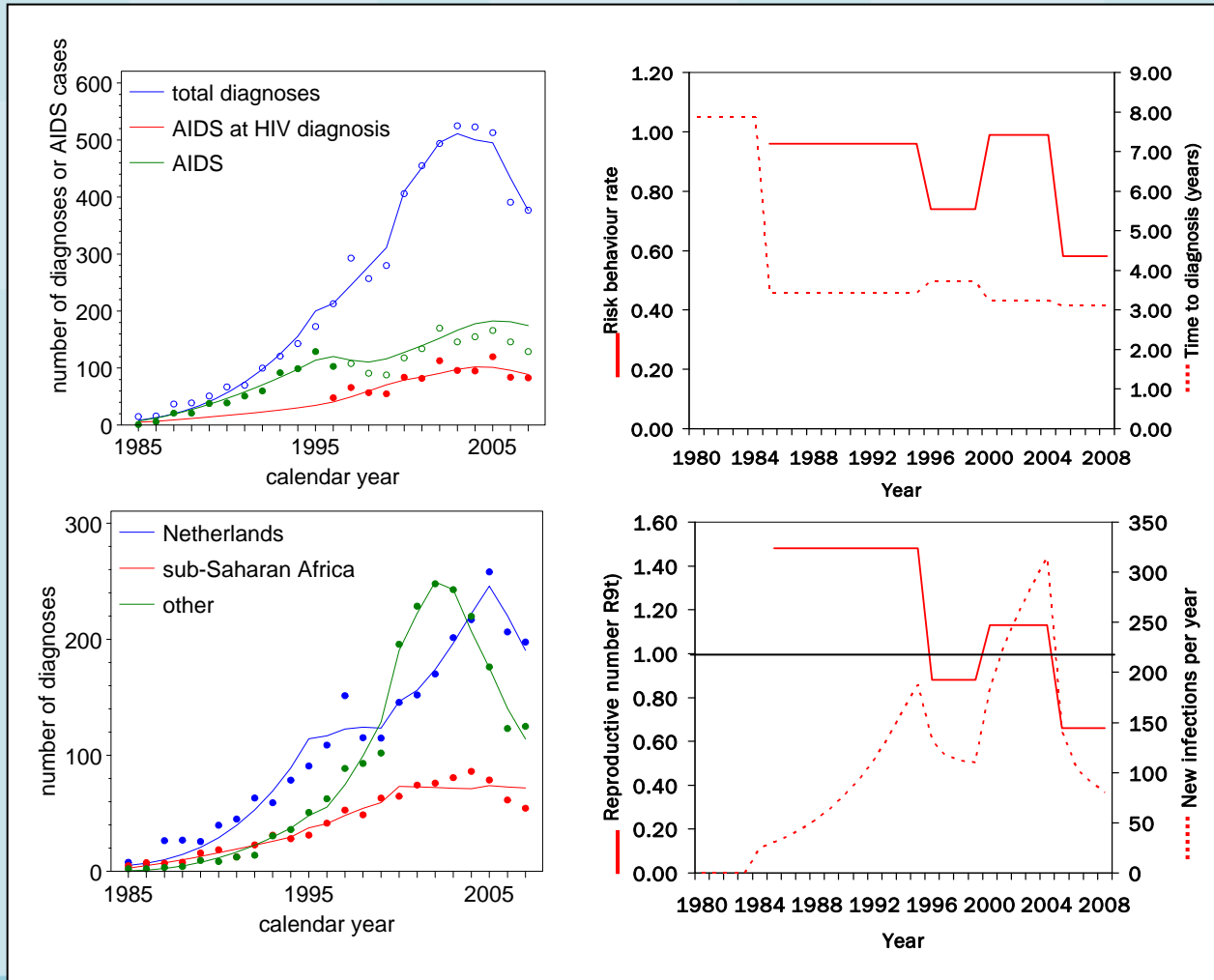
- Relative risk-behaviour parameter: Decreases as number and level of unsafe sex acts between HIV+ and HIV- decreases
- Time from infection to diagnosis: Decreases as testing behaviour increases

What was the relative risk and what was the average time to diagnosis needed to explain our HIV and AIDS diagnosis data?

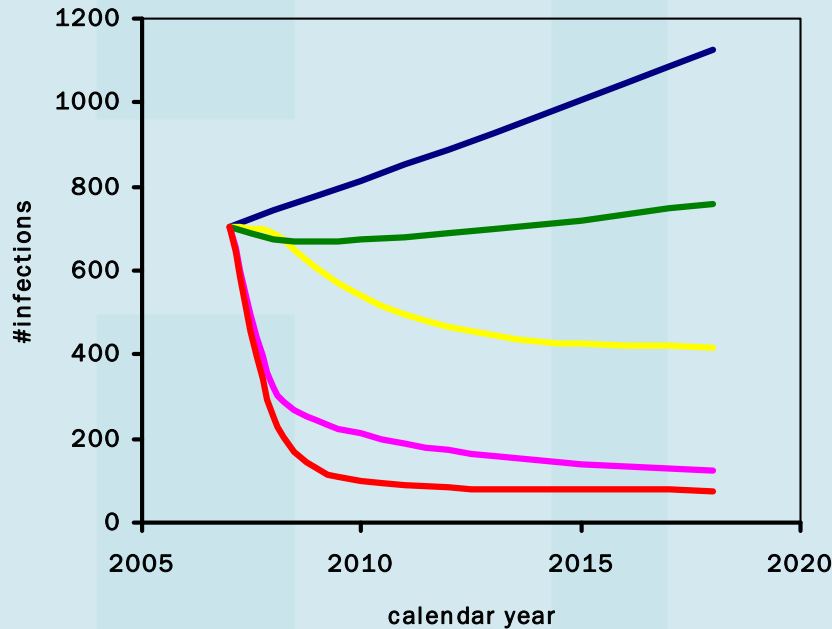
Data & model estimates homosexual men



Data & model estimates heterosexuals



Scenarios MSM epidemic



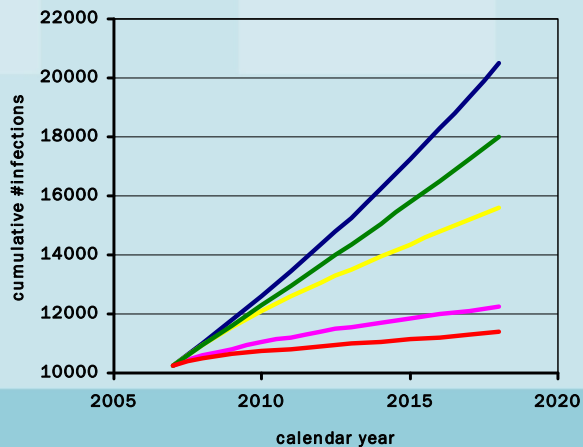
No changes compared to 2007: $N=1125$; $R_m=1.02$

Start cART immediate after diagnosis: $N=760$; $R_m=0.97$

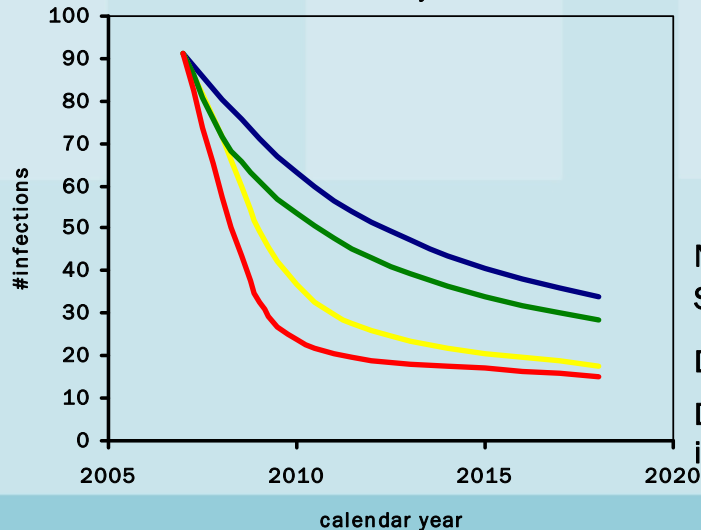
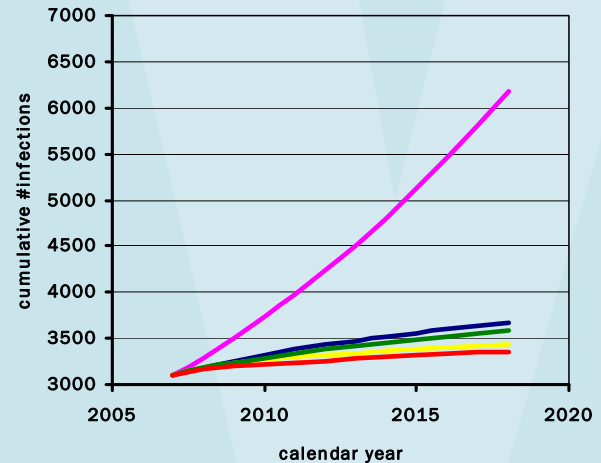
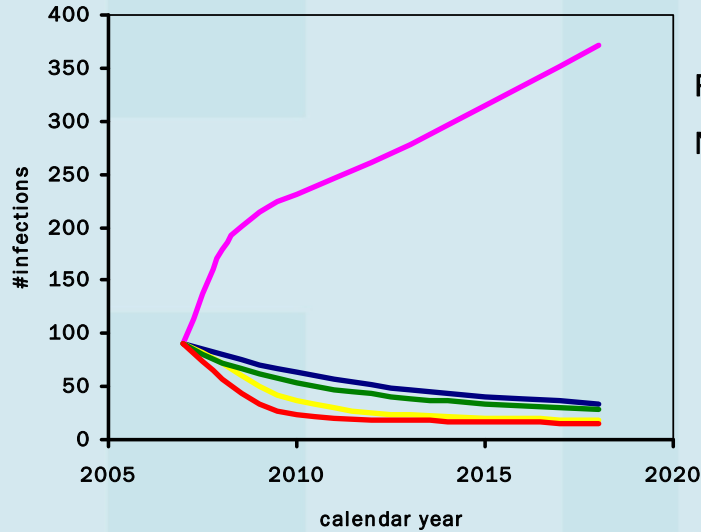
Diagnosis 1 year after infection: $N=418$; $R_m=0.87$

Risk behaviour rate down to pre-cART level: $N=126$; $R_m=0.61$

Decreased risk behaviour, diagnosis one year after infection and cART immediate after diagnosis: $N=78$; $R_m=0.49$



Scenarios heterosexual epidemic



Trends in transmission (summary)

Until 2008:

- Amongst men having sex with men, the ongoing increase in the number of HIV diagnoses (prevalent cases) indicate a growing epidemic, although the time between infection and diagnosis has become shorter in recent years, implicating that increased risk behaviour is still playing a role
- Our best fit to the data indicate that around 21% of all positive MSM are unaware of their positive HIV status and that they account for 90% of the new infections amongst MSM.
- In the heterosexual risk group, the number of diagnoses seems to decrease, indicating a shrinking epidemic, with a reproductive ratio (R_t) firmly below 1 amongst infections that are locally acquired.

Transmission scenarios

- For MSM reducing the net transmission rate (or risk behaviour rate) to pre-cART levels has the biggest impact on the epidemic
- For heterosexuals, having a higher pre-cART transmission rate than MSM, reduction of the time from infection to diagnosis results in the biggest reduction in the number of new infections
- The best strategy is a combination of reduced transmission rates, earlier diagnosis and immediate treatment, although the additional contribution of immediate treatment is limited

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