Poster # 1019

Modelling 27 Years of the HIV-1 Epidemic amongst Men Having Sex with Men: The Netherlands

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ABSTRACT

Background

By fitting extensive national surveillance data to a mathematical model we previously reported a resurging HIV-1 epidemic amongst MSM in the Netherlands between 2002 and 2004 after a period where we found evidence for a retracting epidemic after the introduction of cART in 1996. It appeared that the epidemiological benefits of cART and diagnosis earlier in the course of infection on the HIV incidence was entirely offset by an increase in risk behaviour. Here we present an extended analysis including new data obtained in 2004-2006, validating our model outcome against annual changes in CD4 count at diagnosis over the time period 1980 - 2006.

Methods

Using our mathematical model framework we estimate average changes in unsafe sex and time from infection to diagnosis by fitting to annual HIV-1 and AIDS diagnosis data, and calculate R(t), the average number of new infections generated by each infected person. R(t) > 1, indicates an increasing epidemic.

Results

Between 2004-2006, R(t) appeared to be 1.00 (95% CI 0.91 – 1.05), indicating a stable growing HIV-1 epidemic among men having sex with men, despite the further decrease in time to diagnosis to 2.47 years (2.21 – 2.73). A qualitative comparison of CD4 cell counts at diagnosis obtained from the model *versus* the data showed similar temporal trends. The recent increase in the proportion of newly diagnosed individuals with high CD4 cell counts corroborates our model inferences that the recent increase in annual number of new HIV diagnoses reflects a recent rise in HIV transmission. We estimated that 20% of HIV positives were unaware of their infection at the beginning of 2007 taking account for 89% of the new infections.

Conclusions

Sexual risk-behaviour of MSM unaware of their infection drives the continuous epidemic spread of HIV-1 in The Netherlands. Our model has shown to be a robust and valuable tool for studying HIV epidemics in times of combination anti-retroviral treatment.

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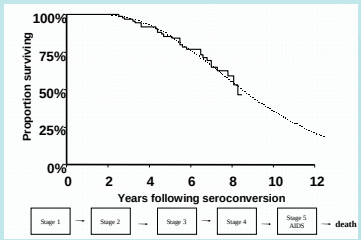
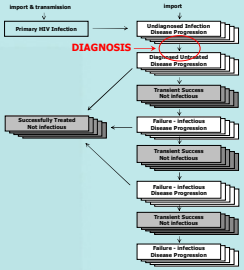
Fig 1. Infectious disease progression



An Erlang survival distribution was fitted to data from 130 MSM seroconverters before the cART era in the Amsterdam Cohort Studies. The maximum likelihood estimate was for an Erlang distribution of degree 5 and rate 1/1.89 per year. This best fit survival distribution can be modelled using a compartmental model, with unidirectional flow through five compartments with mean stay in each of 1.89 years

Fig 2. The model



With the incorporated infectious disease progression, with changing infectiousness, and the parameters on cART use and failure, we can estimate the changes in **time to diagnosis** and **risk behaviour** needed to explain the number of HIV and AIDS diagnosis over calender time.

Fig 3. Model Framework

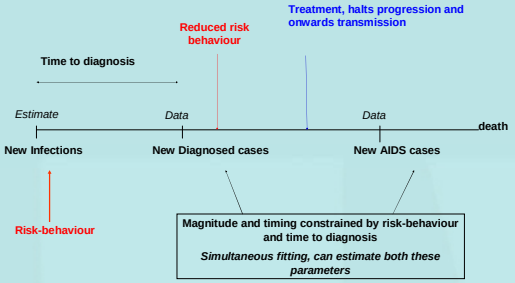
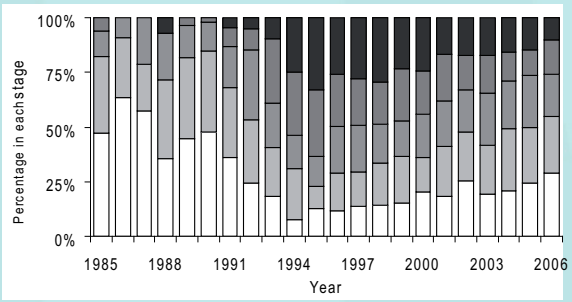


Fig 4. Using CD4 count at diagnosis as a surrogate of the time since infection at diagnosis. We defined five CD4 cell count intervals for every model stage of infection, and show these plotted for MSM in ATHENA as a function of year of diagnosis in **a**, where the proportion of people diagnosed in each stage is shown ranging from earliest (lightest) to last (AIDS, darkest). These estimates are biased by the fact that that only people who survive until 1996 are included in our study. The subsequent figure **b** shows the estimated proportion of newly diagnosed patients in each disease stage as estimated by our best fit model. b includes the same process of truncation which generates bias prior to 1996 as the data (and is thus to be compared to a).

a



b

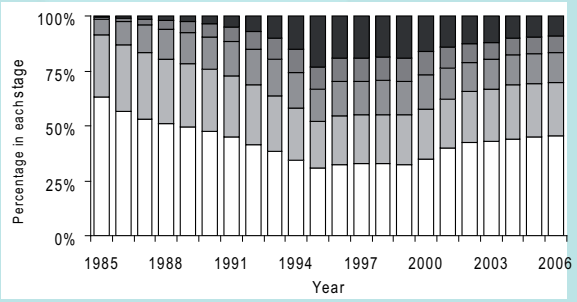


Fig 5. Modelfit, black lines are best model fit to filled symbols. **left**: Number of annual diagnosis separated for infected in the Netherlands in dots, and infected abroad in triangles. We let the model estimate the number of HIV diagnosis among MSM who were not included in the data as they died before 1996, dotted lines. **right**: Annual number of new AIDS cases in blue dots, and simultaneous HIV and AIDS diagnosis in red triangles.

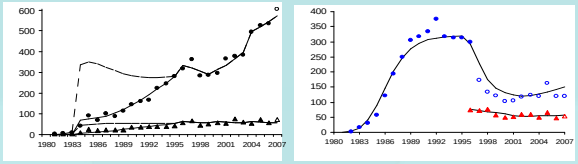


Fig 6. left: Fitting parameters with confidence intervals, on left axis in red is the risk behaviour rate, in blue in years on the right axis is the average time from infection to diagnosis. **right**: Resulting estimated Reproduction number, R(t) over the whole study period, including the confidence interval.

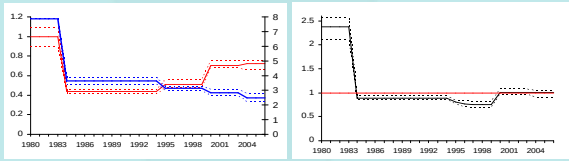


Fig 7. Syphilis diagnoses show a very similar picture as our estimated new HIV infection curve.

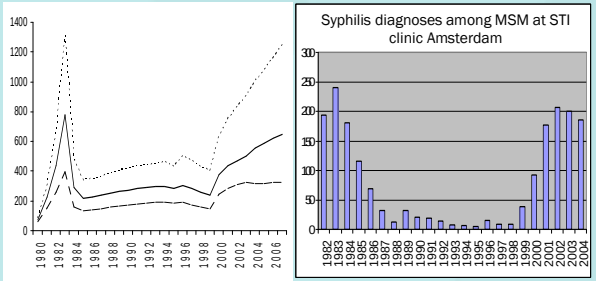
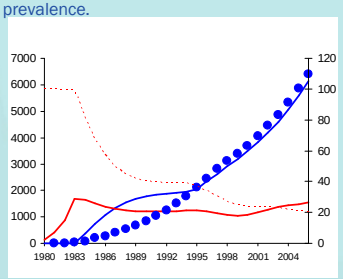


Fig 8. Blue dots is the living diagnosed MSM population, and the blue line the model estimation, The red line is the model estimation for the undiagnosed HIV infected MSM population, and the dotted red line is the percentage undiagnosed of the total prevalence.



The percentage of the undiagnosed of the total infected population has decreased to 24%, but only so due to an increase in survival of the diagnosed population. In absolute numbers around 1600 MSM were undiagnosed at the end of 2006, estimated to be responsible for 90% of new HIV transmissions.