The contribution of steady and casual partnerships to the incidence of HIV infection among homosexual men in Amsterdam

Maria Xiridou\textsuperscript{a}, Ronald Geskus\textsuperscript{a}, John de Wit\textsuperscript{a,b}, Roel Coutinho\textsuperscript{a,c} and Mirjam Kretzschmar\textsuperscript{d}

Objective: To assess the relative contribution of steady and casual partnerships to the incidence of HIV infection among homosexual men in Amsterdam, and to determine the effect of increasing sexually risky behaviours among both types of partners in the era of highly active antiretroviral therapy (HAART).

Methods: A mathematical model was developed for the spread of HIV infection among young homosexual men in Amsterdam after the introduction of HAART. The model describes the formation of both steady and casual partnerships. Behavioural parameters were estimated separately for steady and casual partners from the Amsterdam Cohort Study among young homosexual men. HIV incidence and the fraction of new infections attributed to casual contacts were calculated from the model, allowing for uncertainty in the increases in risky behaviour, the effect of HAART, and levels of HIV testing and HAART administration.

Results: Currently, 86% (range 74–90%) of new HIV infections occur within steady partnerships. A reduction of 75–99% in infectivity caused by HAART will be counter-balanced by increases of 50% (range 30–80%) in risky behaviour with steady partners, but not by increases of up to 100% with casual partners. If HIV testing is increased from 42 to 80% and HAART administration from 70 to 85%, then even an increase of 100% in risk-taking with steady partners will not outweigh the effect of HAART.

Conclusion: Most new HIV infections among homosexual men in Amsterdam occur within steady relationships. Prevention measures should address risky behaviour, specifically with steady partners, and the promotion of HIV testing.

© 2003 Lippincott Williams & Wilkins

AIDS 2003, 17:1029–1038

Keywords: Antiretroviral therapy, HIV incidence, homosexual men, infectious diseases, mathematical models, sexual behaviour, steady and casual partners

Introduction

Data from the Amsterdam Cohort Study (ACS) among young homosexual men suggest that a substantial proportion of new HIV infections occur within steady partnerships [1]. Despite the intensive campaigns promoting safe sex practices among homosexual men in Amsterdam, risk-taking remains at substantial levels,
especially among steady partners. Such behaviour has increased recently [2,3], and there are worries that it may even counterbalance the beneficial effect of highly active antiretroviral therapy (HAART) in reducing HIV viral load and infectivity [4].

Results from previous mathematical models have shown that the transmission dynamics of HIV differ significantly depending on whether sexual contact, and thus transmission, occurs within long steady relationships or within short casual partnerships [5,6]. Therefore, the effect of increasing risky behaviours may likewise differ according to how risk taking increases with steady partners as compared with casual partners. In this paper, we construct a mathematical model that describes the spread of HIV among young homosexual men, taking account of differences in risky behaviour with steady and casual partners. Estimates of parameters relating to risky behaviour and partnership formation were obtained from the ACS. The calculation of HIV incidence from the model was accompanied by uncertainty analysis. We investigate how HIV incidence is affected by changes in risky behaviour with steady partners, risky behaviour with casual partners, and different levels of HIV testing and HAART administration.

Methods

The model

Our mathematical model describing the spread of HIV in the population of homosexual men in Amsterdam after the introduction of HAART is based on that developed by Kretzschmar and Dietz [6]. In their model, (i) sexual contact is assumed to take place only within steady non-concurrent partnerships; (ii) HIV infection is seen as a two-stage process, with infectiousness being high in the first stage (primary infection) and much lower in the second stage (long, asymptomatic secondary infection); (iii) individuals are recruited into the model population when they become sexually active and are removed from the population when they cease sexual activity. This model was extended as follows:

- Men in the second stage of infection are removed earlier from the population, because sexual activity is assumed to cease after the development of AIDS.
- During or between steady relationships men can also be involved in casual partnerships involving only one sexual contact per partner. Casual partnerships can be formed between any two individuals of the population, but men with a steady partner have fewer casual partners than single men. Steady partners who have both been tested HIV negative may make negotiated safety (NS) agreements to be monogamous or to have no unprotected anal intercourse (UAI) outside the relationship, thus reducing their risky behaviour with casual partners.
- A proportion of the men in the second stage of the infection know that they are HIV infected and reduce their risky behaviour. A proportion of those diagnosed are successfully treated, after allowing for non-compliance and treatment failure. Their infectivity is reduced and AIDS survival time is increased.
- The number of new infections depends on the numbers of infected and uninfected men in the population, the probability of transmission per UAI act, and the number of UAI acts. The transmission probability for sexual acts other than UAI is assumed to be negligible [7–10]. The frequency of UAI is different for steady versus casual partners and is influenced by whether NS agreements are made between steady partners or the HIV-positive partner is aware of his serostatus. The risk of becoming infected depends on the type of UAI act (receptive or insertive, denoted URAI and UIAI, respectively), the partner’s stage of the infection, and whether he receives treatment or not.

Our model is described by the set of differential equations (2) given in the Appendix. The parameters are defined in Table 1. In this paper, we use the term ‘risky behaviour’ for the frequency of UAI, and treat it separately for steady and casual partnerships.

Parameter estimation

The ACS among young homosexual men was initiated in 1995 [1–3,11]. The cohort is comprised of young (≤ 30 years) homosexual men living in the Amsterdam metropolitan area. Every 6 months, the participants complete self-administered questionnaires as to sexual behaviour with steady and casual partners during the preceding 6 months (the participants classify their partners as steady or casual according to their own judgement). Estimates of the behavioural parameters were obtained from the first data wave (end of 1995, shortly before HAART was introduced in Amsterdam) or from the third wave (end of 1996) if the necessary data were not available in the first or second wave, as detailed below.

Frequency of unprotected receptive or insertive anal intercourse

UAI between serodiscordant men is denoted as ‘a’ or ‘b’, depending on whether the role of the HIV-negative man is receptive (URAI) or insertive (UIAI). Participants reported their serostatus and that of their steady partner, if they had one, as negative, positive, or unknown. In the third wave, participants were asked the number of times they had URAI and UIAI with their steady partners. For undiagnosed HIV-positive men, the frequency of UAI with their steady partners was estimated based on the frequency of URAI and
UIAI, when steady partners were either both unaware of their serostatus or one was unaware and the other was negative (7.5 URAI and 7.5 UIAI acts in 6 months, giving \( \frac{1}{C_46} = 15 \) acts annually). Study participants were also asked the number of casual partners they had in the preceding 6 months and the number of those partners with whom they had URAI and UIAI. The proportions of casual contacts over one year that were URAI and UIAI among respondents with unknown serostatus were \( \alpha_a = \alpha_b = 5\% \).

**Negotiated safety agreements (\( \theta \))**

Among HIV-negative seroconcordant couples, a proportion \( q_1 \) is couples of men who have both tested HIV-negative. A proportion \( \theta_0 \) of these couples has made no NS agreements. The remaining have made such agreements, but a proportion \( \theta_1 \) of them does not always comply with them. Therefore, for uninfected men with an uninfected steady partner, the proportion of their casual contacts that are URAI and UIAI is reduced to \( \theta_a \) and \( \theta_b \), respectively, where

\[
\theta = (1 - q_1) + q_1 \left[ \theta_0 + (1 - \theta_0) \theta_1 \right]
\]

From 1991 to 1996, approximately 45% of the HIV-negative homosexual men who visited the Amsterdam STI clinic were aware of their serostatus [12]. Therefore we assumed that among couples of uninfected men, the proportion aware that they are both unin-

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Definition</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \rho_s )</td>
<td>2 year</td>
<td>Rate at which singles acquire casual partners</td>
<td>ACS*</td>
</tr>
<tr>
<td>( \rho_m )</td>
<td>8 year</td>
<td>Rate at which men with a steady partner acquire casual partners</td>
<td>ACS</td>
</tr>
<tr>
<td>( \alpha_a, \alpha_b )</td>
<td>5%</td>
<td>Proportion of casual contacts that are URAI, UIAI</td>
<td>ACS</td>
</tr>
<tr>
<td>( \theta )</td>
<td>84%</td>
<td>Reduction factor in risky behaviour with casual partners for uninfected men with an uninfected steady partner as a result of NS agreementsb</td>
<td>ACS, [12]</td>
</tr>
<tr>
<td>( \rho )</td>
<td>0.73/year</td>
<td>Rate of acquiring steady partners</td>
<td>ACS, [6]</td>
</tr>
<tr>
<td>( 1/\alpha )</td>
<td>1.5 years</td>
<td>Duration of steady partnerships</td>
<td>ACS</td>
</tr>
<tr>
<td>( \phi )</td>
<td>73/year</td>
<td>Frequency of all types of sexual intercourse between steady partners</td>
<td>[25]</td>
</tr>
<tr>
<td>( \phi_a, \phi_b )</td>
<td>15/year</td>
<td>Frequency of URAI and UIAI between steady partners</td>
<td>ACS</td>
</tr>
<tr>
<td>( \delta )</td>
<td>42%</td>
<td>Proportion of infected at stage 2 who know they are HIV positive</td>
<td>[12]</td>
</tr>
<tr>
<td>( \tau )</td>
<td>70%</td>
<td>Proportion of those diagnosed who are successfully treated</td>
<td>[11]</td>
</tr>
<tr>
<td>( f_d )</td>
<td>75%</td>
<td>Reduction factor in risky behaviour as a result of HIV diagnosisb</td>
<td>[12]</td>
</tr>
<tr>
<td>( f_c )</td>
<td>74.5%</td>
<td>Percentage reduction in transmission probabilities as a result of HAART</td>
<td>[13–24]</td>
</tr>
<tr>
<td>( n )</td>
<td>20 000</td>
<td>Initial population size</td>
<td>[26]</td>
</tr>
<tr>
<td>( \mu )</td>
<td>30 years</td>
<td>Length of time during which men are sexually active</td>
<td>[25]</td>
</tr>
<tr>
<td>( 1/\mu + \mu_n )</td>
<td>13 years</td>
<td>Time from infection until development of AIDS for those untreated</td>
<td>[27–29]</td>
</tr>
<tr>
<td>( 1/\mu + \mu_k )</td>
<td>22.5 years</td>
<td>Time from infection until development of AIDS for those treated</td>
<td>[30–34]</td>
</tr>
<tr>
<td>( 1/\gamma )</td>
<td>3 months</td>
<td>Duration of the first stage of HIV infection</td>
<td>[35–37]</td>
</tr>
<tr>
<td>( p_{1a} )</td>
<td>0.22</td>
<td>Probability of transmission per URAI act (with infective at stage 1)</td>
<td>[38–40]</td>
</tr>
<tr>
<td>( p_{2a} )</td>
<td>0.011</td>
<td>Probability of transmission per URAI act (with infective at stage 2)</td>
<td>[38–40]</td>
</tr>
<tr>
<td>( p_{1b} )</td>
<td>0.044</td>
<td>Probability of transmission per UIAI act (with infective at stage 1)</td>
<td>[38–40]</td>
</tr>
<tr>
<td>( p_{2b} )</td>
<td>0.0022</td>
<td>Probability of transmission per UIAI act (with infective at stage 2)</td>
<td>[38–40]</td>
</tr>
<tr>
<td>( R_a )</td>
<td>Percentage change in risky behaviour with steady partners</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( R_c )</td>
<td>Percentage change in risky behaviour with casual partners</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 1. Definitions of parameters and their values.**

<table>
<thead>
<tr>
<th>Parameter Value</th>
<th>Definition</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>( r_s )</td>
<td>2/2/year</td>
<td>Rate at which singles acquire casual partners</td>
</tr>
<tr>
<td>( r_m )</td>
<td>8/2/year</td>
<td>Rate at which men with a steady partner acquire casual partners</td>
</tr>
<tr>
<td>( \alpha_a, \alpha_b )</td>
<td>5%</td>
<td>Proportion of casual contacts that are URAI, UIAI</td>
</tr>
<tr>
<td>( \theta )</td>
<td>84%</td>
<td>Reduction factor in risky behaviour with casual partners for uninfected men with an uninfected steady partner as a result of NS agreementsb</td>
</tr>
<tr>
<td>( \rho )</td>
<td>0.73/year</td>
<td>Rate of acquiring steady partners</td>
</tr>
<tr>
<td>( 1/\alpha )</td>
<td>1.5 years</td>
<td>Duration of steady partnerships</td>
</tr>
<tr>
<td>( \phi )</td>
<td>73/year</td>
<td>Frequency of all types of sexual intercourse between steady partners</td>
</tr>
<tr>
<td>( \phi_a, \phi_b )</td>
<td>15/year</td>
<td>Frequency of URAI and UIAI between steady partners</td>
</tr>
<tr>
<td>( \delta )</td>
<td>42%</td>
<td>Proportion of infected at stage 2 who know they are HIV positive</td>
</tr>
<tr>
<td>( \tau )</td>
<td>70%</td>
<td>Proportion of those diagnosed who are successfully treated</td>
</tr>
<tr>
<td>( f_d )</td>
<td>75%</td>
<td>Reduction factor in risky behaviour as a result of HIV diagnosisb</td>
</tr>
<tr>
<td>( f_c )</td>
<td>74.5%</td>
<td>Percentage reduction in transmission probabilities as a result of HAART</td>
</tr>
<tr>
<td>( n )</td>
<td>20 000</td>
<td>Initial population size</td>
</tr>
<tr>
<td>( \mu )</td>
<td>30 years</td>
<td>Length of time during which men are sexually active</td>
</tr>
<tr>
<td>( 1/\mu + \mu_n )</td>
<td>13 years</td>
<td>Time from infection until development of AIDS for those untreated</td>
</tr>
<tr>
<td>( 1/\mu + \mu_k )</td>
<td>22.5 years</td>
<td>Time from infection until development of AIDS for those treated</td>
</tr>
<tr>
<td>( 1/\gamma )</td>
<td>3 months</td>
<td>Duration of the first stage of HIV infection</td>
</tr>
<tr>
<td>( p_{1a} )</td>
<td>0.22</td>
<td>Probability of transmission per URAI act (with infective at stage 1)</td>
</tr>
<tr>
<td>( p_{2a} )</td>
<td>0.011</td>
<td>Probability of transmission per URAI act (with infective at stage 2)</td>
</tr>
<tr>
<td>( p_{1b} )</td>
<td>0.044</td>
<td>Probability of transmission per UIAI act (with infective at stage 1)</td>
</tr>
<tr>
<td>( p_{2b} )</td>
<td>0.0022</td>
<td>Probability of transmission per UIAI act (with infective at stage 2)</td>
</tr>
<tr>
<td>( R_a )</td>
<td>Percentage change in risky behaviour with steady partners</td>
<td></td>
</tr>
<tr>
<td>( R_c )</td>
<td>Percentage change in risky behaviour with casual partners</td>
<td></td>
</tr>
</tbody>
</table>

HAART, Highly active antiretroviral therapy; NS, negotiated safety; UIAI, unprotected insertive anal intercourse; URAI, unprotected receptive anal intercourse.

*aEstimated from the Amsterdam Cohort Study (ACS) among young homosexual men.

bA factor \( \epsilon \) is a reduction factor in risky behaviour if \( \alpha_j \) or \( \phi_j \) are reduced to \( \epsilon \alpha_j \) or \( \epsilon \phi_j \), respectively.

*cBased on the assumption that in the absence of HIV infection and AIDS, the number of sexually active homosexual men remains more or less stable.

UIAI, when steady partners were either both unaware of their serostatus or one was unaware and the other was negative (7.5 URAI and 7.5 UIAI acts in 6 months, giving \( \phi_a = \phi_b = 15 \) acts annually). Study participants were also asked the number of casual partners they had in the preceding 6 months and the number of those partners with whom they had URAI and UIAI. The proportions of casual contacts over one year that were URAI and UIAI among respondents with unknown serostatus were \( \alpha_a = \alpha_b = 5\% \).
fected is \( q_1 = 0.45^2 \approx 20\% \). Approximately 10% of the participants in an HIV-negative seroconcordant relationship had no NS agreements with their steady partner (\( \theta_0 = 10\% \)). Of those who did, approximately 12.5% reported having UAI with casual partners in the same interval, so non-compliance was estimated to be \( \theta_1 = 12.5\% \). Then \( \theta \) is calculated to be 84%.

**Rates of acquiring steady (\( \rho_s \)) and casual partners (\( \rho_u, \rho_m \))**

In an article by Kretzschmar and Dietz [6] it was shown that the proportion of the population involved in a steady relationship is \( Q = \rho/(\rho + \sigma + 2\mu) \) and hence \( \rho = (\sigma + 2\mu)/Q(1-Q) \) (see Table 1). In the first wave, approximately half of the participants reported having a steady partner at the time they completed the questionnaire. Therefore \( Q = 0.5 \) and \( \rho = \sigma + 2\mu \). Those with a steady partner and those without reported having an average of \( \rho_u = 8 \) and \( \rho_s = 22 \) casual partners per year, respectively.

**Reduction in transmission probabilities as a result of treatment (\( f_t \))**

Several studies of various antiretroviral regimens have shown mean reductions in seminal HIV-1 RNA concentrations varying from 0.6 to 3.28 \( \log_{10} \) copies/ml [13–18]. Antiretroviral treatment can thus be expected to decrease infectiousness, because the probability of sexual transmission increases with the viral load [19–24]. According to Quinn et al. [19], the rate ratio for the risk of transmission associated with each log increment in viral load is 2.45 [95% confidence interval (CI) 1.85–3.26]. Here we assumed that treatment can result in a two to 100-fold reduction in transmission probabilities.

**Uncertainty analyses**

To reflect uncertainty in baseline parameters, each uncertain parameter was assigned a probability density function, and we used Latin Hypercube Sampling (see Blower and Dowlatabadi [41] for details) to sample 100 sets of values for these parameters. The following parameters were included in the uncertainty analysis and sampled from the uniform distribution:

- the mean rate of acquiring casual partners (range 16–28 for singles and 6–10 for men with a steady partner);
- the mean frequencies of URAI and UIAI among casual partners (\( \alpha_u, \alpha_s \), range 2.5–7.5%) and among steady partners (\( \phi_u, \phi_s \), range 7.5–22.5);
- the mean duration of steady partnerships (0.75–2.25 years) and then the rate of acquiring steady partners was calculated as \( \rho = \sigma + 2\mu \);
- the proportion of HIV-infected men aware of their serostatus (range 32–52%);
- the percentage reduction in risky behaviour as a result of HIV diagnosis (1–\( f_t \), range 0–50%);
- and the reduction in risky behaviour as a result of

NS agreements, calculated from equation (1), with \( q_1, \theta_0 \), and \( \theta_1 \) in the ranges 10–30%, 5–15%, and 6–20%, respectively.

The system of equations (2) was solved numerically 100 times, each time with one of the 100 sets of parameter values sampled, and the other parameters as shown in Table 1, but without treatment (\( f_t = 0\% \)) or changes in risky behaviour (\( R_s = R_u = 0\% \)). As the parameters were taken from the period 1995–1996 and HIV incidence and prevalence were more or less stable at that time [11,12,42], the endemic equilibrium state of the system corresponds to the situation just before HAART was introduced (see results later). We then used the average of the 100 values of the state variables at equilibrium as the initial conditions for the uncertainty analyses after the introduction of HAART.

For the period after HAART we performed five different uncertainty analyses (corresponding to five different scenarios), allowing for uncertainty in the increase in risky behaviour and the parameters related to HIV testing and HAART. The uncertain parameters and their distributions are shown in Table 2; the other parameters were as in Table 1. For all five scenarios, the time until the development of AIDS for those treated was assumed to be 15–30 years [30–34], the percentage reduction in infectiousness as a result of HAART was 50–99% [13–24], and the percentage reduction in risk taking as a result of HIV diagnosis was 0–50%. The scenarios A, B1, and B2 correspond to the current situation in Amsterdam, with mean levels of HIV testing and HAART administration 42% and 70%, respectively [11,12]. For scenario A we assumed that risky behaviour does not change (\( R_s = R_u = 0\% \)), for B1 that only risk with steady partners increases (range 0–100%), and for B2 only risk with casual partners increases (range 0–100%), assuming that the increases in risky behaviour coincide with the introduction of HAART. The analyses with increases in risky behaviour were repeated with higher levels of HIV testing and HAART administration (means 80% and 85%) in order to examine a hypothetical situation reflecting a more intensive healthcare policy (scenarios C1, C2).

For the analyses after the introduction of HAART we calculated the fraction of new infections resulting from sexual contacts between casual partners and the percentage change in incidence after 5 years, calculated by comparison with the value that incidence would have had at that point if HAART had not been introduced and risky behaviour had not changed.

**Results**

From the uncertainty analysis for the baseline para-
meters (before the introduction of HAART) the incidence of HIV was calculated to be 0.67 infections per 100 person-years (PY) (95% CI, 0.52–0.82 infections/100 PY) and the prevalence was 8.84% (95% CI, 6.90–10.78%). These results are fairly consistent with those from the data. HIV incidence among the cohort’s participants was estimated to be one infection/100 PY for the first data wave and it has been fluctuating between 0.34 and 1.93 infections/100 PY from 1995 to 2000 [3,11,43]. HIV prevalence among participants of the first wave was 5% (95% CI 3.2–7.7%) [43].

Results from the uncertainty analyses 5 years after the introduction of HAART are shown in Fig. 1, Fig. 2, Fig. 3 and Table 2. Fig. 1 shows the percentage change in incidence for scenario A (risky behaviour does not change). Over the range of parameter values used, the average percentage decrease in incidence is 28.91% (see Table 2). The reduction in incidence increases as the infectivity decreases as a result of treatment. If HAART reduces infectiousness by at least 80%, then incidence is reduced by more than 20%.

Fig. 2 shows the fraction of new infections that can be attributed to casual partners for scenarios B1 and B2. If risky behaviour increases by an average of 50% only among steady partners, then 12% (range 10–15%) of the new infections can be attributed to casual partners and the remaining to steady partners. This proportion is 20% (range 14–26%), if risk with casual partners increases by 50% on average. Therefore, steady partners contribute to incidence more than casual partners. This can mainly be explained by the fact that risky behaviour with steady partners is much greater than that with casual partners (30 versus 1.5 UAI acts annually, see Table 1) and even if risk with casual partners increases by 100%, it still remains much lower than that with steady partners.

Fig. 3a and 3b show the percentage change in incidence as a function of the level of increase in risky behaviour with steady or casual partners for scenarios B1 and B2. Increases in risky behaviour with steady partners affect the incidence more than the equal (in percentage) increases with casual partners. A reduction of 75–99% in infectivity as a result of HAART will be counterbalanced by an increase of 50% (range 30–80%) in risky behaviour with steady partners, but risk with casual partners must increase by more than 100% in order to outweigh the benefits of HAART (see also Table 2).

The percentage change in incidence for scenarios C1 and C2 (increased levels of HIV testing and HAART administration) is shown in Fig. 3c and 3d. Comparing the top with the bottom graphs in Fig. 3, shows that

<table>
<thead>
<tr>
<th>Scenario</th>
<th>A</th>
<th>B1</th>
<th>B2</th>
<th>C1</th>
<th>C2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
<td>U(32, 52)</td>
<td>U(32, 52)</td>
<td>U(32, 52)</td>
<td>U(70, 90)</td>
<td>U(70, 90)</td>
</tr>
<tr>
<td>δ</td>
<td>U(50, 100)</td>
<td>U(50, 100)</td>
<td>U(50, 100)</td>
<td>U(50, 100)</td>
<td>U(50, 100)</td>
</tr>
<tr>
<td>τ</td>
<td>U(50, 99)</td>
<td>U(50, 99)</td>
<td>U(50, 99)</td>
<td>U(50, 99)</td>
<td>U(50, 99)</td>
</tr>
<tr>
<td>f&lt;sub&gt;c&lt;/sub&gt;</td>
<td>U(15, 30)</td>
<td>U(15, 30)</td>
<td>U(15, 30)</td>
<td>U(15, 30)</td>
<td>U(15, 30)</td>
</tr>
<tr>
<td>R&lt;sub&gt;c&lt;/sub&gt;</td>
<td>0</td>
<td>0</td>
<td>U(0, 100)</td>
<td>0</td>
<td>U(0, 100)</td>
</tr>
<tr>
<td>R&lt;sub&gt;c&lt;/sub&gt;</td>
<td>0</td>
<td>0</td>
<td>U(0, 100)</td>
<td>0</td>
<td>U(0, 100)</td>
</tr>
</tbody>
</table>

Table 2. Uncertainty analyses after the introduction of highly active antiretroviral therapy.

---

U(α, β), Uniform distribution on the interval (α, β); 95% LCL, UCL, lower and upper limits of the 95% confidence interval.

Fig. 1. The effect of the reduction in infectivity as a result of highly active antiretroviral therapy (HAART) on HIV incidence, 5 years after the introduction of HAART, as calculated for uncertainty analysis A.
increasing HIV testing and HAART administration can boost the effect of treatment, so that even if risk taking increases, the incidence will not increase. With an average increase of 50% in risky behaviour only with steady partners or only with casual partners, the percentage change in incidence is −38.60% and −53.45%, respectively (see Table 2). An increase of 100% in risky behaviour with steady (or with casual) partners will not diminish the effect of HAART if infectivity is reduced by at least 75% (or 50%, respectively).

Discussion

The mathematical model presented in this paper suggests that the majority of new infections among young homosexual men in Amsterdam can be attributed to steady partners. Changes in risky behaviour with steady partners thus have a greater impact on HIV incidence than the equivalent changes among casual partners. The model also shows that increases in risky behaviour may counterbalance the positive effect of HAART, although such increases could be outweighed by increased HIV testing and HAART administration.

Our results agree with those from behavioural studies and other mathematical models. An analysis of data from seroconverters of the ACS revealed that between 1994 and 2000, young seroconverters were more likely to have contracted HIV from their steady partner than from casual partners [1]. Kretzschmar et al. [5] developed a model that describes the formation of two types of partnership with different duration, and showed that under certain conditions targeting only one of these may be enough to control the spread of a sexually transmitted infection. Blower et al. [44] developed a model for the spread of HIV among homosexual men in San Francisco, and showed that a 10% increase in risk taking could counterbalance the benefits of HAART, although the increased usage of HAART could overcome the effect of such increased risky behaviour. With the use of a mathematical model, Law et al. [4] calculated that an increase of 70% in risky behaviour among homosexual men in Australia could counterbalance a 90% reduction in infectivity as a result of HAART. Our prediction of a 50% increase in risk taking with steady partners and more than 100% with casual partners counterbalancing a 75–99% reduction in infectivity as a result of HAART is higher than that from Blower et al. [44], but more consistent with that from Law et al. [4].

These differences in the model predictions result mainly from differences in the modelling assumptions. The model of Blower et al. [44] accounted for the emergence of drug resistance, which reduces the effectiveness of HAART and thus smaller increases in risk taking could counterbalance the benefits of HAART. Also, in our model the level of HAART administration increased instantaneously from zero to its current value. In Blower et al. [44] it increased gradually over time and thus it requires more time to observe the full effect of HAART. Therefore, the predictions of Blower et al. [44] (corresponding to the first year after HAART became available) would be lower than those presented here (corresponding to the fifth year after HAART introduction). Our predictions for the increases in risk taking with casual partners required to counterbalance the effect of HAART are higher than those of Law et
al. [4], a difference resulting mainly from the fact that sexual behaviours with steady and casual partners are separately formulated in our model, but not in Law et al. [4]. As engagement in unsafe sex is much more rare among casual partners, a higher increase in risk taking with casual partners will be required to outweigh the effect of HAART.

Certain limitations to our modelling study should be noted. Sexual behaviour and partnerships are described in a rather simple way in our model. We distinguish between long-lasting partnerships and incidental contacts, therefore neglecting the spectrum of possible behaviours in between. Also, our model captures only the most important aspects of heterogeneity in behaviour, namely the differences between those with and those without a steady partner. We do not consider heterogeneity in the sense of core groups, i.e. groups that consistently display high-risk behaviour. Heterogeneity in that sense can lead to different estimates for the incidence, but it would not change our main conclusions for the contribution of steady partnerships to disease dynamics. Only if turnover in steady partnerships was too low to sustain an epidemic would incorporating a core group lead to a qualitatively different model behaviour. Second, we chose to work with a deterministic model, instead of a more detailed individual based stochastic model, because our main aim was not the quantitative predictions of incidence, but the elucidation of the role of different types of partnerships in the transmission process. Although the results were obtained through numerical solution of the model equations because of the complexity of the model, in principle it is possible to compute an explicit expression for the basic reproduction ratio \( R_0 \) and investigate its dependence on the parameters. For a

Fig. 3. The percentage change in incidence, 5 years after the introduction of highly active antiretroviral therapy, for different levels of increase in risky behaviour with steady partners (left panels) or with casual partners (right panels). (a) and (b) Results for scenarios B1 and B2, respectively, with mean levels of HIV testing and highly active antiretroviral therapy (HAART) administration \( \delta = 42\% \) and \( \tau = 70\% \). (c) and (d) Results for scenarios C1 and C2, respectively, with mean values of \( \delta = 80\% \) and \( \tau = 85\% \). Each datum represents an individual run, drawn with a circle if the reduction in transmission probabilities as a result of HAART is \( 50\% \leq f_\gamma < 75\% \) or with a triangle if \( 75\% \leq f_\gamma < 99\% \).
network without long-lasting concurrent partnerships, a deterministic model has been shown to agree well with a stochastic counterpart [45].

The uncertainty analyses performed in this study can assess the imprecision of our predictions that results from the uncertainty in the parameter estimates. Nevertheless, they cannot embrace all the uncertainty in the system. Moreover, the ranges of parameter values used were centred around the estimates from ACS. Therefore, the dependence of the results on the parameter estimates should be kept in mind. For instance, the proportions of casual contacts that were URAI and UIAI were calculated from the proportions of casual partners with whom men engaged in URAI and UIAI, respectively. This was based on the assumption that there is one sexual encounter per partner, because the participants reported 13 casual partners and 11 anal/oral acts with these partners on average per year. Nevertheless, if there is more than one UIAI encounter per partner, then the proportion of casual partners to HIV incidence has been underestimated here.

The aim of our model was to assess the shares of steady and casual partners as sources of HIV infection among young homosexual men in Amsterdam, and the implications of these on the further development of the HIV epidemic. Our results show that steady and casual partnerships form two different routes of transmission of HIV, and that the former is currently the predominant one. Although these results are specific for Amsterdam, the methodology can be used for other communities as well. In fact, our results for the effect of increasing HAART usage and for the increasing risky behaviours counterbalancing the benefits of HAART have been shown to hold for other populations (see Blower et al. [44] for San Francisco, and Law et al. [4] for Australia). In addition, studies from other risk groups have also shown that risk-taking is more prevalent among steady than among casual partners [46–48]. Therefore, for these communities, similar qualitative results would be expected for the relative contribution of steady and casual partners to the incidence of HIV (see also Stall et al. [49] for reviews of other cohort/survey studies among homosexual men).

The results from this study imply that the promotion of safe-sex practices should undoubtedly be continued with respect to both steady and casual partners, but there is a need to target risky behaviour specifically with steady partners. Different health policies and prevention measures may have to be adopted in targeting each type of partnership, because the appraisal of risk is different according to whether a steady or a casual partner is concerned. The mentality specific to each type of partnership that facilitates the decision to take the risk should be addressed, and prevention measures such as partnership counselling, partner notification and testing should be considered. In particular, the promotion of HIV testing and HAART administration can outweigh the increase in risky behaviours and prevent increases in incidence. The availability of effective medical therapy can now enhance the motivation for testing, because HAART considerably improves the management of the infection for the infected individual.

Acknowledgements

The authors wish to express their gratitude to the participants of the Amsterdam Cohort Studies for their contribution; Nel Albrecht and Dieuwke Ram for the cohort management; Anneke Krol and Marja Dekker for the data management; Udi Davidovich for his assistance and advice on the behavioural data; Nicole Dukers, Ineke Stolte, Liselotte van Asten, and Jacco Wallings for their assistance and suggestions on various aspects of this project; Lucy Phillips for editorial review; and two anonymous referees for many helpful comments. Part of this research was carried out at the Dutch National Institute of Public Health and the Environment (RIVM), where the first author was hosted as a guest.

Sponsorship: This study was supported by a grant from the Dutch AIDS Fund (project 2675). It was performed as part of the Amsterdam Cohort Studies on HIV infection and AIDS, a collaboration between the Municipal Health Service, the Academic Medical Centre, and the Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, Sanquin Division, Amsterdam, the Netherlands.

References


37. Stall R, Hays R, Waleco C, Eksland M, McFarland W. The gay ‘90s: a review of research in the 1990s on sexual behaviour and...


Appendix

The population is divided into nine groups: \(X_0, X_1, X_2, P_{00}, P_{01}, P_{02}, P_{11}, P_{12}, P_{22}\), where \(X\) denotes singles, \(P\) denotes pairs of steady partners, and the subscripts 0, 1, and 2 denote uninfected, infected at stage 1, and infected at stage 2, respectively. The model is described by the following differential equations:

\[
\frac{dX_0}{dt} = v - (\mu + \rho)X_0 + (\sigma + \mu)(2P_{00} + P_{01} + P_{02}) - \rho_s X_0 \frac{I_h}{N} + [(1 - \delta \tau)\mu_A + \delta \tau \mu_e]P_{02}
\]

\[
\frac{dX_1}{dt} = -(\gamma + \mu + \rho)X_1 + (\sigma + \mu)(2P_{11} + P_{01} + P_{12}) + \rho_s X_0 \frac{I_h}{N} + [(1 - \delta \tau)\mu_A + \delta \tau \mu_e]P_{12}
\]

\[
\frac{dX_2}{dt} = \gamma X_1 - (\mu + \rho)X_2 + (\sigma + \mu)(2P_{22} + P_{02} + P_{12}) - [(1 - \delta \tau)\mu_A + \delta \tau \mu_e]X_2 + 2[(1 - \delta \tau)\mu_A + \delta \tau \mu_e]P_{22}
\]

\[
\frac{dP_{00}}{dt} = -(\sigma + 2\mu)P_{00} + \frac{1}{2} \rho \frac{X_0^2}{X} - 2\rho_m \frac{P_{00}I_h}{N}
\]

\[
\frac{dP_{01}}{dt} = -(\sigma + 2\mu + \gamma + \beta_1)P_{01} + (1 - h_1)\rho \frac{X_0 X_1}{X}
\]

\[
+ 2\rho_m \frac{P_{00}I_h}{N} - \rho_m \frac{P_{01}I_h}{N}
\]

(2)

\[
\frac{dP_{02}}{dt} = \gamma P_{01} - (\sigma + 2\mu + \beta_2)P_{02} + (1 - h_2)\rho \frac{X_0 X_2}{X}
\]

\[
- \rho_m \frac{P_{02}I_h}{N} - [(1 - \delta \tau)\mu_A + \delta \tau \mu_e]P_{02}
\]

\[
\frac{dP_{11}}{dt} = \beta_1 P_{01} - (2\gamma + \sigma + 2\mu)P_{11} + \frac{1}{2} \rho \frac{X_1^2}{X}
\]

\[
+ h_1 \rho \frac{X_0 X_1}{X} + \rho_m \frac{P_{01}I_h}{N}
\]

\[
\frac{dP_{12}}{dt} = 2\gamma P_{11} + \beta_2 P_{02} - (\gamma + \sigma + 2\mu)P_{12} + \rho \frac{X_1 X_2}{X}
\]

\[
+ h_2 \rho \frac{X_0 X_2}{X} + \rho_m \frac{P_{02}I_h}{N} - [(1 - \delta \tau)\mu_A + \delta \tau \mu_e]P_{12}
\]

\[
\frac{dP_{22}}{dt} = \gamma P_{12} - (\sigma + 2\mu)P_{22} + \frac{1}{2} \rho \frac{X_2^2}{X}
\]

\[
- 2[(1 - \delta \tau)\mu_A + \delta \tau \mu_e]P_{22}
\]

where \(X = X_1 + X_2 + X_3\) is the total number of singles, \(N\) is the total population size, \(I_h = I_{h1} + I_{h2}\), \(I_1 = X_1 + P_{01} + P_{12} + 2P_{11}\), \(I_2 = X_2 + P_{02} + P_{12} + 2P_{22}\), and

\[
\beta_1 = \sum_j \beta_{1j} p_j \Phi_j
\]

\[
\beta_2 = [(1 - \delta) + \delta(1 - \nu) f_d + \delta \tau (1 - f_s) f_d] \sum_j p_{2j} \Phi_j
\]

\[
h_1 = \sum_j p_{1j} \frac{\Phi_j}{\Phi}
\]

\[
h_2 = [(1 - \delta) + \delta(1 - \nu) f_d + \delta \tau (1 - f_s) f_d] \sum_j p_{2j} \frac{\Phi_j}{\Phi}
\]

\[
h'_1 = \sum_j p_{1j} \alpha_j
\]

\[
h'_2 = [(1 - \delta) + \delta(1 - \nu) f_d + \delta \tau (1 - f_s) f_d] \sum_j p_{2j} \alpha_j
\]

Infection from a casual partner is described by the terms \(\rho_s X_0 I_h/N\) (for singles) and \(\rho_m (2\theta P_{00} + P_{01} + P_{02}) I_h/N\) (for men with a steady partner). The terms \(h_1 \rho X_0 X_1/X\), \(h_2 \rho X_0 X_2/X\) correspond to infection from a steady partner during their first sexual contact and the terms \(\beta_1 P_{01}, \beta_2 P_{02}\) during the course of the relationship.