HIV INCIDENCE IN MSM IS CONTINUING TO RISE IN THE UNITED KINGDOM DESPITE HIGH LEVELS OF ART-INDUCED VIRAL SUPPRESSION

Two valuable papers that significantly improve our understanding of HIV transmission in MSM at the population level in the United Kingdom are attached here 1,2, together with short summaries of each and also editorial commentary which helps to contextualise the findings.

Combination antiretroviral therapy was introduced in 1996 in the United Kingdom, and annual HIV diagnoses in MSM began to rise three years later in 1999, and at the same time increased annual diagnoses of gonorrhoea, NSU, genital warts, genital chlamydia and infectious syphilis were also recorded there. Unfortunately the trend of increased annual diagnoses for most of these conditions has continued unabated up to the present.

The alarming nature of the current STI situation for MSM in England was spelled out very clearly this month by Lisa Power from the Terence Higgins Trust 3.

In 1998 a new community HIV and AIDS prevention strategy called ‘Making it Count’ was produced for MSM in England, and was recommended to the Department of Health as the framework for local HIV commissioning. This strategy replaced universal condom use for anal sex (ie: primary prevention) with an approach where condom use was required only in the case of HIV discordancy or when the HIV status of one or the other partner was unclear. In other words, condom use was reframed as a secondary prevention strategy, and HIV testing became the suggested starting point for HIV prevention. This approach - which is completely different to the one that we have adopted in New Zealand - has clearly not worked.

Our experience suggests that universal condom use for anal sex in sexually active populations of MSM is essential if HIV and STI transmission is to remain under control. Evidence now available from a range of sources also indicates that early treatment has the capacity to reduce somewhere between 25-33% of new HIV diagnoses in MSM, but only if there is no associated decline in condom use for anal sex, ie: condoms must continue to be used for
anal sex irrespective of assumed HIV and STI status, even when both partners are known to be HIV positive (which will limit STI transmission as well as the risk of HIV superinfection)

If condom use erodes, the HIV prevention benefits of ART will be progressively lost in MSM, and - even worse than that - if condom use drops significantly we will face alarming increases in both HIV and STI transmission in this population group. The modelling paper by Andrew Phillips (see attached; Figure 3 and Table 1) suggests that complete cessation of condom use by MSM could result in a 425% increase in new HIV diagnoses in the United Kingdom over the ensuing five year period, which would be a catastrophic outcome.

Tony Hughes
Research Director
12 June 2013

References:

Increased HIV incidence in MSM despite high levels of ART-induced viral suppression in the United Kingdom

- “Promotion of condom use remains a critically important and effective element of prevention polices as it is undoubtedly acting to prevent much more dramatic increases in incidence.”

- In one counter-factual all condom use ceased in 2000, but the level of anal sex and ART coverage remained unchanged. This resulted in 425% increase in HIV incidence after five years.

- “The promotion of condom use among negative as well as HIV positive MSM remains vital to ensure the benefits of ART in reducing transmission of HIV are not undermined.”

New research explores driving forces behind HIV epidemic in men who have sex with men in the UK

18 February 2013

New HIV infections rose in men who have sex with men (MSM) between 1990 and 2010 in the UK, driven by a 26 per cent increase in the proportion having condomless sex, according to new research by the Health Protection Agency and UCL. However, the findings suggest the increase in new infections would have been 68 per cent greater without the introduction of antiretrovirals (ART) in the same period, and 400 per cent greater if MSM condom use had ceased entirely from 2000 onwards. Published in PLOS ONE, the study received funding from the National Institute for Health Research.

Professor Andrew Phillips, lead investigator at UCL, said: “We created a model reconstructing the HIV epidemic in men who have sex with men in the UK. In doing so, we were able to explore the interplay between HIV testing rates, antiretroviral treatment and sexual behaviour on HIV transmission and incidence. By better understanding the driving forces behind the trends we’ve seen in the past, it will allow us to make informed choices to reduce new HIV infections in the future.”

Dr Valerie Delpech, head of HIV surveillance at the HPA, said: “Our research provides important evidence to support current UK public health recommendations on expanded HIV testing and higher levels of ART coverage, to reduce new infections among men who have sex with men. However, we see it is also vital condom use education continues as not only does this have a strong limiting effect on the HIV epidemic, but only a modest increase in unprotected sex is enough to erode the benefits of other interventions”.

Estimated HIV incidence rose from 0.30 per 100 person years (1990-1997) to 0.53 (2006-2010), associated with increased condomless sex following the introduction of effective ART. However, exploring other scenarios, the research found incidence would have reduced during this period if HIV testing levels had been higher (25 per cent lower incidence), if ART had been prescribed at diagnosis (32 per cent lower incidence) or these interventions had been combined (62 per cent lower incidence). Effective ART therapy reduces the infectivity of HIV positive individuals, lowering transmission risk.

Dr Delpech, HPA, continued: “Everyone should use a condom when having sex with new or casual partners, until all partners have had a sexual health screen. We also encourage men who have sex with men to get an HIV and STI screen at least annually, and every three months if having condomless sex with new or casual partners – and clinicians to take every opportunity to recommend HIV testing to this group. Through combining earlier and more frequent HIV testing, programmes that reduce unsafe sexual behaviour and higher levels of ART coverage for those requiring it, we could substantially reduce HIV transmission in this group.”

Ends

Notes to editors


For more information please contact the national HPA press office at Colindale on 0208 327 7901 or email colindale-pressoffice@hpa.org.uk. Out of hours: 0208 200 4400.

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Increased HIV Incidence in Men Who Have Sex with Men Despite High Levels of ART-Induced Viral Suppression: Analysis of an Extensively Documented Epidemic

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Abstract

Background: There is interest in expanding ART to prevent HIV transmission, but in the group with the highest levels of ART use, men-who-have-sex-with-men (MSM), numbers of new infections diagnosed each year have not decreased as ART coverage has increased for reasons which remain unclear.

Methods: We analysed data on the HIV-epidemic in MSM in the UK from a range of sources using an individual-based simulation model. Model runs using parameter sets found to result in good model fit were used to infer changes in HIV-incidence and risk behaviour.

Results: HIV-incidence has increased (estimated mean incidence 0.30/100 person-years 1990–1997, 0.45/100 py 1998–2010), associated with a modest (26%) rise in condomless sex. We also explored counter-factual scenarios: had ART not been introduced, but the rise in condomless sex had still occurred, then incidence 2006–2010 was 68% higher; a policy of ART initiation in all diagnosed with HIV from 2001 resulted in 32% lower incidence; had levels of HIV testing been higher (68% tested/year instead of 25%) incidence was 25% lower; a combination of higher testing and ART at diagnosis resulted in 62% lower incidence; cessation of all condom use in 2000 resulted in a 424% increase in incidence. In 2010, we estimate that undiagnosed men, the majority in primary infection, accounted for 82% of new infections.

Conclusion: A rise in HIV-incidence has occurred in MSM in the UK despite an only modest increase in levels of condomless sex and high coverage of ART. ART has almost certainly exerted a limiting effect on incidence. Much higher rates of HIV testing combined with initiation of ART at diagnosis would be likely to lead to substantial reductions in HIV incidence. Increased condom use should be promoted to avoid the erosion of the benefits of ART and to prevent other serious sexually transmitted infections.

Introduction

Epidemics of HIV in men who have sex with men (MSM) started in the late 1970s and early 1980s and the numbers of new diagnoses continue to increase in several countries [1–7]. In the UK, for example, over 3000 MSM were diagnosed with HIV in 2010, the highest number since the start of the epidemic [1]. If we are to make informed choices on how to reduce new infections it is important to understand past trends in the epidemic and the factors which shaped them. Changes in self-reported condomless anal sex with persons of unknown or serodiscordant HIV status are clearly one key potential factor. Another potential factor is use of antiretroviral therapy (ART), which reduces transmission risk as well as reversing HIV progression [8–9]. The relative impact of these two factors on the MSM HIV epidemic are uncertain. Ecological analyses have observed correlations between ART use and trends in HIV diagnosis [10–11] (albeit one in the context of a mainly IDU epidemic) but these are difficult to interpret without an underlying model of transmission. There is great interest in the possibility of extending ART use in order to help to reduce HIV incidence [12–14], but a cautionary consideration is that the rise in incidence observed in MSM has occurred during a period in which ART use has expanded and the proportion of people with viral suppression has increased [1,15–16]. Here we aim to use a comprehensive model of HIV transmission, progression and the
effect of ART to reconstruct the HIV epidemic among MSM in the UK using comprehensive HIV surveillance data and behaviour data on self-reported condom use among MSM. The model aims to help us understand the relative influences of sexual risk behaviour change, rates of HIV testing, and ART-induced virologic suppression on HIV incidence over the past 15 years. While we focus on the UK our findings are likely to have broad implications for epidemics among MSM globally in resource rich settings.

Methods

Here we describe the modelling briefly. Further details of the model are given in Supporting Information S1. Description of the current analyses are given in Supporting Information S2. We reconstruct sexual risk behaviour, HIV transmission, HIV progression and the effect of ART for the population of MSM in the UK from 1980–2010 using an individual-based stochastic computer simulation model which captures the key underlying mechanisms which determine these processes (model adapted from that used in ref 17, itself developed from models used in refs 16, 18–19). We assume all transmission takes place via condomless anal sex and sexual risk behaviour was modelled as the number of short term (e.g. casual) and long term condomless sex partners which, as for all variables modelled, was updated in 3 month periods.

We consider a range of possible values (i.e. distributions) for the parameters that determine levels of condomless sex and, as for all other parameters, these are sampled from distributions of potential values that reflect uncertainty in the value. For example, it is assumed that a proportion of men (mean 0.5, defined by a beta distribution beta(7,7)) substantially reduce condomless sex with short term partners after HIV diagnosis (the proportion is much higher for long term partners). For each run of the simulation model we sample from each of these distributions to obtain a set of parameter values to be used and generate a full reconstructed epidemic scenario for 1980–2010. We then consider the parameter sets for runs that provide the closest fit to the observed data (as described in detail in Supporting Information S2). We ran the model 10,000 times in order to search for these best fitting parameter sets. Details of distributions for all parameters are given in Supporting Information S2. The sampling from distributions for the parameters relating to sexual risk behaviour and transmission rate means that we explore a range of possible scenarios, including ones in which the ratio of short to long term partners increases or decreases or the number of short term partners occurring in the same period as a man has a longer term partner (concurrency) increases or decreases.

In any given period, the probability of an uninfected person having a condomless sex partner who is infected with HIV depends on their number of partners and on the prevalence of HIV amongst partnerships formed by other men in the population, accounting for patterns of age mixing. The probability of transmission on exposure to an infected partner, depends on the viral load level of the partner (obtained by sampling from the distribution of viral load levels in partnerships formed by HIV infected people, accounting for age), the estimated risk of transmission at that viral load and presence of a concurrent sexually transmitted infection. We assume a low rate of transmission when the viral load is undetectable (although there is little direct evidence to support this, for anal sex) but, again, we consider a distribution of possible values. For people who have become infected with HIV the variables modelled include; primary infection (a period of raised infectivity of duration 3 months), viral load, CD4 count, adherence to ART, risk of AIDS and death. Resistance acquisition and transmission is also incorporated, and its effects accounted for, although this is not a focus in the present paper. The model of progression of HIV and the effect of ART has been shown to provide a generally close fit to observed data relating to natural progression of HIV infection and the effect of ART [16–19]. Based on data from NATSAL [20], we assume that the population of MSM aged over 15 was approximately 500,000 in 1980 and, as for the UK as a whole, has increased in size by 10% up to 2010. We compared model outputs with a wide array of available data [1,20–26].

Results

The model outputs are generally consistent with a range of observed data collected as part of routine surveillance of HIV (Figure 1). A series of other model outputs are shown in Supporting Information S2. Implicit in this reconstruction is the underlying trend in incidence of new HIV infections and in sexual risk behaviour required to be consistent with the observed data. These are shown in figure 2, along with 90% uncertainty bounds reflecting parameter uncertainty.

The model suggests that after an initial period of high HIV incidence in the early 1980 s incidence declined in response to the decline in sexual risk behaviour. However, after the introduction of effective ART, the model shows an increase in sexual risk behaviour (from an estimated 35% of men having condomless anal sex with a partner of unknown or negative HIV status in the past year to 44% in 2010; a 26% increase) and this is associated with a rise in incidence, from a mean 0.30 per 100 person years from 1990–1997 to 0.45 from 1998–2010; p<0.0001. For the most recent five year period (2006–2010) the mean HIV incidence was 0.53. The breakdown of the source of new infections in 2010 according to the diagnosis, primary infection and ART status was calculated. Median proportions with 90% uncertainty bounds are: undiagnosed primary 0.48 (0.34–0.62), undiagnosed not primary 0.34 (0.22–0.46), diagnosed ART naive 0.10 (0.04–0.19), diagnosed ART experienced 0.07 (0.02–0.17). This indicates that a very high proportion of new infections derive from men who are undiagnosed, particularly men in primary HIV infection.

This detailed characterization of the course of the epidemic with a mechanistic model allows us to explore counter-factual scenarios which can help us understand the separate influences of HIV testing, ART use and of condom use on HIV incidence (Table 1). The model was re-run for a scenario in which ART was never introduced, but patterns of testing and sexual risk behaviour change were left unchanged (i.e. with an increase in sexual risk behaviour after 1998 - this is done in order to separate the direct effect of ART on incidence via lower viral load from its effect on increased condomless sex). Figure 3a shows the HIV incidence curve in this scenario, which shows a substantially greater increase in incidence than has been observed for the 2006–2010 period (0.53 to 0.89/100 pyrs in 2006–2010, a 68% increase (95% confidence interval 62%–74%; p<0.0001).

Next, we considered what would be the predicted effect on HIV incidence if in 2000 all condom use had ceased but changes in levels of anal sex and ART coverage in those diagnosed remained unchanged. This was done by assuming that levels of sexual risk behaviour increase such that the proportion of men having condomless anal sex in the past year is set closer to the reported levels of (condom-protected plus condomless) anal sex [20] such that 63% have condomless sex in past year. Here we see very large increases in incidence. We also considered what would have been the pattern of HIV incidence had ART, from 2001 onwards, been
provided to all people with diagnosed HIV, with all else having remained the same, resulting in a predicted lower incidence for 2006–2010 (0.36/100 pyrs; a 32% (95% CI 27%–37%; p<0.0001) reduced incidence. Had rates of testing been greater then there would be expected to have been a lower incidence as a result of the fact that more people eligible for ART would be

Figure 1. Comparison of model outputs with surveillance data. (a) Number of people diagnosed with HIV by year. Data points (black squares) from new HIV diagnoses database 1, (b) Number seen for HIV care by year. Data from SOPHID 1, (c) Number of deaths in people with HIV. Data from HPA death reporting system and Office of National Statistics data 1, (d) Number on ART. Observed data from SOPHID 1, (e) Median CD4 count at diagnosis. Observed data from HPA CD4 laboratory surveillance 1, (f) Proportion of men on ART with Viral load < 500 copies/mL. Observed Data (black squares) from SOPHID 10. Model: median and 90% interval (dark and light grey lines, respectively). For details and further comparisons with data see Supporting Information S2.

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treated, and that diagnosis leads a proportion of men reducing or eliminating condomless sex with men of unknown or negative HIV status. We estimated that had testing rates been considerably higher (such that by 2010 68% of all men were tested each year and 49% tested in any one 3 month period, with targeting of men having condomless sex in the past 6 months, compared with the figures of 25% and 6%, respectively, in the observed scenario), then incidence would have been 0.40/110 pyrs, a 25% (95% CI 20%–28%; p<0.0001) reduction. Finally, with both higher rates of testing and ART initiation at diagnosis predicted incidence was 0.20/100 pyrs; a 62% (95% CI; 58%–66%; p<0.0001) reduction.

Discussion

This reconstruction of an HIV epidemic in MSM based upon multiple rich data sources allows us to understand the influences that condom use, HIV testing and ART have had on HIV incidence at a population level. Our analysis suggests that use of ART, even under a policy of ART initiation only when the CD4 count is below 200 or, latterly, below 350 and in the context of only a modest rate of HIV diagnosis, has had an appreciable impact on HIV incidence in the UK, resulting in most new infections being from people who are yet to be diagnosed. We estimate that incidence would have been 68% higher than that actually observed had ART not been introduced (but sexual risk behaviour changes remaining unchanged) and more than five times higher than the observed had “safer” sex messages been ignored and condom use ceased.

Our study throws light on the apparent paradoxical increase in HIV incidence in MSM epidemics over a period in which ART coverage and viral suppression has been increasing. Our analysis suggests it is the counter-effect of concomitant increases in condomless sex amongst MSM as a whole that has resulted in a net increase in incidence; the model did not fit the data unless we assume such a rise. There is direct evidence of increases in condomless sex due to increases in other STIs as well as from self-report survey data [21,23–27]. A recent paper based on the MSM epidemic in the Netherlands reached a similar conclusion [6]. It is noteworthy that only modest increases in condomless sex are enough to overcome the beneficial effects of ART, highlighting the vulnerability of any new prevention initiative, such as ART initiation at HIV diagnosis, if it leads to increases in condomless sex. While our modelling and empirical evidence strongly suggest that increases in the number of men having condomless sex are the key underlying reason for the increase in incidence we should consider other possible explanations. It might be suggested that this could be accounted for by increases in other sexually transmitted infections which facilitate HIV transmission, but any such increases are likely to be themselves the result of increases in condomless sex. Our model takes account of the fact that presence of such STIs facilitates transmission risk but does not explicitly model transmission of the other STIs. Other explanations that seem unlikely are that HIV has become more infectious over time or that transmission through oral sex is significant and has increased over time. Our model does not inform us of the transmission risk with oral sex.

A key implication of our results is that extension of ART coverage, by increasing rates of diagnosis and with initiation of ART at higher CD4 counts, is likely to have an appreciable effect on reducing HIV incidence in MSM epidemics, so long as this is not accompanied by further general increases in condomless anal sex in the MSM population. Our model allowed us to explore the counterfactual scenario in which from 2001 there was a policy of ART initiation of all people with HIV diagnosed, and it was predicted that this would have resulted in 32% lower HIV incidence in the years 2006–2010 than was estimated to actually be the case. This was based on the key assumption that introduction of this policy would not have resulted in any additional increases in condomless sex ("risk compensation"), either in the individuals treated or the general population. On an individual level, there is thus far no evidence that ART initiation leads to increases in sexual risk behaviour (i.e. greater likelihood of having condomless sex) but there is a clear possibility that this might be the case in future as the effects of ART on infectivity become more widely known [8,9,29]. There could also be a continued population level effect such that with a greater feeling of HIV as a benign and manageable condition, condomless sex generally increases further. However, it does not seem likely that a decision whether to use a condom would be directly dependent on policy on HIV testing and earlier ART initiation, so introduction of such a policy should not in itself have a negative effect on condom use.

Thus, we consider that key public health policy implication of this work is the need to promote frequent HIV testing, and to offer...
Figure 3. Reconstruction of incidence for counter-factual situations; (a) a scenario in which ART was never introduced, but patterns of sexual risk behaviour changes still occurred, (b) a scenario in which all condom use ceased in 2000, but with levels of anal sex as observed, (c) a scenario in which ART was provided at diagnosis from 2000, (d) a scenario in which testing rates increased (such that the proportion testing in the past year was 68% in 2010 compared with 25% as modelled for the actual incidence), and (e) a scenario of both higher testing and ART at diagnosis.

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ART for the purposes of reduction in infectivity. Such an offer would involve an explanation that plasma HIV suppression with ART is likely to be associated with markedly reduced infectivity, although this has not been directly shown in couple studies in MSM (while there is little reason to suggest that this will not be the case, the exact magnitude of the effect could well be different and ongoing studies of this are critical - our analysis does not in itself provide new evidence for the effect of ART on an individual level) [30]. The offer of ART to people with CD4 count above 350/ mm³ should in our view be accompanied by an explanation of the fact that health risks associated with ART initiation have not been reliably shown in a randomized trial to be outweighed by the benefits, although trials are ongoing [31]. This is the position adopted in the British HIV Association guidelines, although some guidelines currently recommend initiation of ART in people with high CD4 count based on observational studies, arguments for a compelling rationale, and extrapolation from existing trials [32,33]. If shown to have individual health benefits, a policy of ART in all people with diagnosed HIV would involve an explanation that plasma HIV suppression with ART at diagnosis would be cost-effective, despite the low absolute risk of clinical disease in people with high CD4 count, due to the effect in reducing HIV incidence, but this should be evaluated formally in models that closely fit to observed data for a given specific setting. At first sight, our finding - consistent with data and some other models [34–40] - of a high proportion of new infections emanating from men who are in primary infection, suggests a limit to the extent of the potential impact of use of ART on HIV incidence. As Koopman has pointed out [37], the key role of primary infection arises not only due to the high levels of infectiousness in this period, but because the variation over time in partnership formation rate means that people tend to get infected in a period in which the condomless sex partner acquisition rate is higher and thus the probability of onward transmission will tend to be higher soon after infection than later. This results in periods in which the effective reproductive number for primary infection is above 1, so “outbreaks” of primary infection are seen. Relatively few men are diagnosed with HIV at this early stage but there is potential for improvement [41] and this requires close attention. However, our modeling predicts that HIV incidence would be reduced substantially with a substantial increase in HIV testing (both in coverage of who is tested and frequency of testing in those tested) and immediate ART initiation in those diagnosed, despite the fact that diagnosis of HIV and treatment initiation cannot be achieved within the period of primary infection. This is likely because many chains of transmission are likely to contain links which involve transmission from people who have been infected for many months or years and these links can feasibly be broken with a policy of high levels of testing and immediate ART initiation, thus reducing the frequency of outbreaks of primary infection.

A second important message is the fact that promotion of condom use remains a critically important and effective element of prevention policies as it is undoubtedly acting to prevent much more dramatic increases in incidence. There is known to be selective condom use according to known or assumed partner HIV serostatus [42]. The message regarding condom use may need to become more nuanced as evidence concerning the effectiveness of virally suppressive ART grows [8,9,30]. Under certain strict conditions regarding viral suppression and lack of current STIs, the risk that HIV will be transmitted to a negative person through condomless sex could be lower than that with use of condoms, given the non-negligible risks of failure to use a condom effectively [43]. However, in general, condom use remains critical to control of HIV epidemics and to reduce risk of acquisition of other sexually transmitted infections such as hepatitis C virus.

Recent modelling of HIV incidence in MSM based on a Bayesian evidence synthesis approach also found evidence of increases in incidence between 2002–2007 [44]. In order to help to predict future trends in incidence it will be helpful to obtain serial annual data on condomless anal sex on representative samples of MSM. Currently, the NATSAL data are the only data based on a random sample, but are only available every 10 years and numbers of MSM included are small. Interpretation of trends from the Gay Men’s Sex Surveys [20] is hampered by the opportunistic self-selecting sampling approach but nevertheless the data are of critical importance in the absence of other sources, as are the series of studies in gyms and bars and online samples [23–26]. Other models of MSM epidemics [45–47] have evaluated the potential effect of ART on transmission.

In conclusion, it seems likely that modest increases in condomless sex in the era of effective ART in the UK have resulted in an increase in HIV incidence in MSM, but that the effects of ART in reducing infectivity have substantially attenuated

Table 1. Summary of estimated difference in HIV incidence according to counter-factual scenarios.

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Mean incidence 2006–10 (/100 prs)</th>
<th>% difference (vs actual)</th>
<th>95% confidence interval</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actual</td>
<td>0.53</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>No ART*</td>
<td>0.89</td>
<td>+68%</td>
<td>+62%–74%</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>No condoms**</td>
<td>2.78</td>
<td>+425%</td>
<td>+406%–442%</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>ART at diagnosis***</td>
<td>0.36</td>
<td>–32%</td>
<td>–27%–37%</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Higher test rate****</td>
<td>0.40</td>
<td>–25%</td>
<td>–20%–28%</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Higher test rate and ART at diagnosis*****</td>
<td>0.20</td>
<td>–62%</td>
<td>–58%–66%</td>
<td>p&lt;0.0001</td>
</tr>
</tbody>
</table>

*scenario in which no ART was introduced, but sexual risk behaviour change still occurred (this is in order to separate the direct effect of ART on incidence via lower viral load from its effect on increased condomless sex).
**scenario in which in 2000 all condom use had ceased but levels of anal sex remained the same. This was done by assuming that levels of sexual risk behaviour increase such that the proportion of men with a condomless sexual partner is set to the reported levels of sex, including condom-protected sex.
***scenario in which policy from 2000 was to initiate ART in all people with diagnosed HIV.
****scenario in which testing rates were much higher from 2000, such that by 2010 68% of all men were tested each year (49% per 3 months, with targeting of men having condomless sex in the past 6 months) compared with the figure of 25% used in modelling (6% per 3 months).
*****scenario with both higher rates of testing and ART initiation at diagnosis.
this effect. More frequent HIV testing and better penetration of regular testing to all MSM is critical. This would be likely to be more effective if clinical practice moves towards ART being prescribed at diagnosis. The promotion of condom use among negative as well as HIV positive MSM remains vital to ensure the benefits of ART in reducing transmission of HIV are not undermined.

Supporting Information

Supporting Information S1 Model Details.

Supporting Information S2 Supplementary Analytical Methods and Results.

References

31. Babiker AG, Emery S, Falインターナショナルに関する注意および療法：部的に一致する。HIVIncidence in Men Who Have Sex with Men

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Author Contributions

Contributed to the formulation of the research questions, had critical input into interpretation of results, and had substantial input into the drafting of the manuscript: AP VC FN AB FL AR AM JE GH AJ JL VD. Led on collection of the HIV surveillance data used in the analysis: VD AB. Worked on development and programming of the HIV Synthesis model: AP VC FN. Performed the model/analysis: AP. Conceived and designed the experiments: AP VC FN AB FL AR AM JE GH AJ VD JL. Performed the experiments: AP VC FN. Analyzed the data: AP VC VD. Wrote the paper: AP VC FN AB FL AR AM JE GH AJ VD JL.


Increased HIV incidence in MSM despite high levels of ART-induced viral suppression in the United Kingdom

- “Promotion of condom use remains a critically important and effective element of prevention polices as it is undoubtedly acting to prevent much more dramatic increases in incidence.”

- In one counter-factual all condom use ceased in 2000, but the level of anal sex and ART coverage remained unchanged. This resulted in 425% increase in HIV incidence after five years.

- “The promotion of condom use among negative as well as HIV positive MSM remains vital to ensure the benefits of ART in reducing transmission of HIV are not undermined.”

One in 20 gay and bisexual men in the UK now has HIV

“Unsafe sexual behaviour” and a lack of testing is being blamed for a failure to cut the number of cases of HIV among gay and bisexual men in the last decade.

Huge improvements in treating and testing for HIV have failed to curb infections, scientists, writing in the Lancet Infectious Diseases, have suggested, with a return of risky sexual practices.

New infections were static at about 2,300 a year between 2001 and 2010, despite rises in early diagnosis and far more people taking medication.

One in 20 gay and bisexual men in the UK now has HIV, rising to one in 12 in London, according to the Medical Research Council (MRC) and Health Protection Agency (HPA), which carried out the research.

Undiagnosed HIV infections in gay and bisexual men increased from 7,370 in 2001 to 7,690 in 2010.

Over the same time period HIV testing of gay men and bisexual men increased by 370% to 59,300 per year and the number receiving HIV care rose from 69% to 80%.

Despite a 20% reduction in the average time between infection and diagnosis, from four years to 3.2 years, 38% of infections in 2010 were still diagnosed after the time patients should have started antiretroviral (ARV) treatment.

Dr Valerie Delpech, the HPA’s head of HIV surveillance, said: “We are seriously concerned about the level of ongoing HIV transmission and the significant impact this is having within the MSM [men who have sex with men] community.
“The most plausible explanation for these results is continuing unsafe sexual behaviour coupled with insufficient HIV testing, showing us just how vital safe sex programmes engaging MSM remain.”

Sir Nick Partridge, the chief executive at Terrence Higgins Trust, the UK’s largest HIV and sexual health charity, said: “These findings highlight the real challenges faced by HIV prevention work, which need much greater attention. Spending on safer sex campaigns for gay men has fallen dramatically over the past ten years. Much greater priority needs to be given to HIV prevention by the NHS, local government and the gay community.”

Yusef Azad, the director of policy at the National AIDS Trust, said: “The Medical Research Council and the Health Protection Agency research which shows a failure to reduce HIV transmission amongst men who have sex with men despite a decade of prevention work makes for depressing reading.”
HIV incidence in gay men unchanged in England and Wales, despite more testing

Treatment on diagnosis may be needed, say researchers

Gus Cairns
Published: 04 February 2013

A paper in *The Lancet Infectious Diseases* by scientists from the UK’s Medical Research Council and the Health Protection Agency (HPA) has calculated that the number of gay men in England and Wales who become infected with HIV each year remained unchanged between 2001 and 2010. This is despite a considerable increase in testing and, they estimate, a 40% reduction in the proportion of gay men with HIV who are undiagnosed.

The paper concludes that, in England and Wales at least, the proportion of gay men with HIV who are on treatment and with undetectable viral loads is currently too low to bring about a decline in annual HIV incidence in this population. This is in contrast to declines in diagnosis, and claims of declines in incidence, seen in places such as San Francisco, the province of British Columbia in Canada, and some locales in South Africa.

As well as extending HIV testing to non-traditional settings and urging gay men to test more frequently, the authors conclude that “the initiation of treatment on diagnosis, regardless of CD4 count might well be necessary to achieve control of HIV transmission”, and welcome the new BHIVA treatment guidelines’ recommendation “that clinicians discuss the benefits of early treatment uptake as a prophylaxis to protect sexual partners” as a step towards this.

**Calculating incidence**

The paper is a mathematical model. It uses available data on diagnoses, CD4 counts at diagnosis, and the proportion of people on antiretroviral therapy (ART) to make estimates of the true annual number of infections (annual incidence) in gay men, the number undiagnosed, average time gap between infection and diagnosis,
the distribution of CD4 counts among diagnosed and undiagnosed men and the proportion who are on treatment and with an undetectable viral load.

Although mathematical models are always estimates, in this case surveillance data from the UK are of good enough quality to make them quite robust, though because by definition fewer very recent infections are diagnosed, incidence estimates for the last two years are less certain than for previous years.

The incidence rate is not the same as the new diagnosis rate in HIV, because of the time lag between infection and diagnosis. If the number or frequency of HIV tests go up, the number of diagnoses will tend to go up, since more long-term undiagnosed infections will be identified. The researchers got round this problem by using CD4 count at diagnosis –available for the majority of diagnosed people in England and Wales – as a surrogate for the time delay between infection and diagnosis, given that CD4 counts in people with untreated HIV tend to decline at an even rate over time.

**Results – diagnosed and undiagnosed**

The number of diagnoses in gay men in England and Wales increased from about 1800 in 2001 to 2600 in 2010. However by adjusting this for CD4 count at diagnosis, the researchers estimated that the true annual total of HIV infections in gay men had remained virtually unchanged, from 2200 in 2001 to about 2300 in 2010. There was an increase in incidence to about 2700 a year in 2003-4, due to increased rates of sex without condoms in gay men, but this has reduced since.

This reduction is due, the researchers say, to more gay men taking tests and to a shorter period between HIV infection and diagnosis. The number of HIV tests taken by gay men in sexual health clinics has grown nearly fourfold, from 16,000 in 2001 to 59,300 in 2010. As a result, the estimated time between infection and diagnosis has shrunk from four years to 3.2 years during this time, and the proportion of gay men with HIV who are undiagnosed from 37 to 22%.

The reason it has not shrunk more, say the authors, is due to gay men not testing often enough. Last year, study co-author Valerie Delpech of the HPA told the IAPAC Prevention Summit that only an estimated 10 to 15% of gay men took an HIV test every year, and that two-thirds of gay men who had had a test at a clinic had, two years later, not returned to that clinic for another one.

Because there are (as of 2010) 3.2 years’ worth of undiagnosed infections in the population, the total number of gay men with HIV who are undiagnosed in England and Wales was estimated as 7690 in 2010. This was only a small increase from 7370 in 2001 and represents a 16% decline from 9140 in 2004-5, again due to more testing.

The proportion of gay men with HIV who are undiagnosed has gone down by 40% while the number has scarcely changed because total HIV prevalence and the number of UK gay men living with HIV has grown over the same period.

**Results – implications for treatment**

In 2001, at HIV diagnosis, about 65% of gay men had a CD4 count under 500 cells/mm$^3$, 40% under 350 cells/mm$^3$, and 18% under 200 cells/mm$^3$. Ten years
later, the proportion in these three categories had only fallen by about 5%. This means that less than 40% of gay men would currently be advised, under treatment guidelines, to begin taking antiretroviral therapy (ART) for treatment reasons as soon as they are diagnosed.

The researchers calculated that, because more undiagnosed infections are recent ones, only 20% of undiagnosed gay men had a CD4 count under 350 cells/mm\(^3\) and only 45% under 500 cells/mm\(^3\). Further decreasing the proportion of gay men with HIV who are undiagnosed, and raising or abolishing the CD4 threshold for treatment initiation, would therefore have considerable cost implications for the National Health Service in England and Wales.

**Conclusions**

In many ways, the UK’s response to HIV has been excellent. The proportion of gay men with a CD4 count under 350 cells/mm\(^3\) who are on ART has increased from 75% in 2001 to 84% in 2010; 65% of all patients in care, including the untreated, have undetectable viral loads; and annual loss to follow-up of those attending care is under 5%.

In the US, in contrast, it is estimated that there are more gay men who are diagnosed but not taking ART than there are undiagnosed, and that only 28% of people with HIV are virally suppressed. But gay men in other countries test more frequently: as an accompanying editorial by Reuben Granich of UNAIDS points out, the 22% of gay men who remain undiagnosed in the UK is not as good as an estimated 14% in Vancouver and only 6% in San Francisco.

Because most of those with detectable viral loads in the UK are undiagnosed, it is estimated by the HPA that up to 50% of HIV infections in gay men here could be being transmitted by men in primary HIV infection and another 35% by undiagnosed men with long-term infection. The authors conclude that treatment initiation at diagnosis, earlier, more targeted testing, and better primary HIV prevention all need to be part of any national HIV prevention plan for England and Wales.

**References**


**The Information Standard Certified Member**
HIV in MSM in England and Wales: back to the drawing board?

The fight to confront HIV has benefited from unprecedented scientific advances. This success has been dependent on innovation derived from trial and error and from necessity. For example, the routes of HIV transmission were elaborated very rapidly, and although prejudice slowed and damaged our response, the progress made was rapid compared with that of many other infectious diseases. We now have five classes of treatment for HIV, and understand that treatment can reduce transmission of HIV to sexual partners and children. Although there is still debate over when to start treatment, we know that waiting too long is risky and leads to irreversible health damage and increased risk of transmission. Stigma and other societal issues pose substantial obstacles to seeking treatment, yet we have a good understanding of the behavioural changes and social support that can help people avoid infection. However, despite rapid advances and an aggressive attitude towards action in the face of potential failure, after more than 30 years, we still struggle to control an HIV pandemic in which over 30 million people have already died, and an estimated 34 million people were living with the virus in 2011.

In The Lancet Infectious Diseases, Paul Birrell and colleagues’ analyse national HIV surveillance data from England and Wales to derive trends in HIV incidence among men who have sex with men. By use of a CD4 staged back calculation model of HIV incidence they disentangled the competing contributions of time-varying rates of diagnosis and HIV incidence to the observed diagnoses. Their methods are sophisticated, rely on well elaborated assumptions and caveats, and will be of great interest for those working to use surveillance data to understand trends in the epidemic. With the use of several different data sources, they also compare the trends against the backdrop of increased HIV testing rates and coverage of antiretroviral therapy (ART). Their results are sobering. Despite substantial investment in HIV prevention, including increased access to HIV testing and treatment, around 2500 men are infected every year and there is no statistical evidence that this rate is decreasing over time. These findings contradict the significant trend towards earlier diagnosis, as shown by a decline in mean time to diagnosis from 4 years to 3 years and more men diagnosed with CD4 counts above the treatment threshold of 350 cells per μL. Additionally, during this time frame, testing for HIV in sexual health clinics increased from around 16 000 to around 59 300 people, diagnoses increased to around 2500 in 2010, an estimated 78% of men who have sex with men living with HIV knew their status, the number of men in care rose to 27 900 (80%) and the proportion of men in care who received ART rose to 80%. Although we could safely conclude that these are favourable outcomes and that without prevention efforts the situation would be far worse, the study findings regarding the flatlining HIV incidence, despite increased HIV testing and treatment rates, should be of considerable concern to men who have sex with men, their partners and families, the community, public health authorities, and policy makers. Innovation in the current response is clearly needed.

The researchers suggest that social context has changed, and conclude the national HIV testing strategy should expand beyond sexual health clinics to reach more people earlier. In view of what we know about health-seeking behaviour this approach makes sense—undoubtedly there are creative national and local solutions to helping people learn their HIV status earlier. While expanding access to testing, monitoring the proportion of estimated people living with HIV who know their status can provide a key indicator of progress—the 78% reported by the authors compares with 94% of gay and bisexual men in San Francisco and 86% in Vancouver, where there is earlier access to testing and treatment. ART prevents HIV transmission—the degree of impact for men who have sex with men is unknown but is likely to be high. With this in mind, the high treatment coverage achieved with current testing strategies and eligibility criteria of a CD4 counts threshold of 350 cells per μL might be insufficient to reduce HIV transmission. Birrell and colleagues’ call for earlier treatment initiation irrespective of CD4 cell count. This is a bold conclusion—the conceptual shift to offering treatment initiation to all those with a positive diagnosis would be a significant innovation. This also makes sense, since turning someone away who has carefully considered the risks and benefits and is eager to start treatment could represent a lost individual and public health opportunity.

With the understanding that viral suppression is linked to improved health outcomes and decreased...
transmission, this approach could translate into improved surveillance to include monitoring trends in the proportion of the diagnosed and undiagnosed people living with HIV who are virally suppressed. However, although Birrell and colleagues mainly discuss the evidence regarding HIV testing and treatment, the analysis also clearly shows that increased testing and earlier treatment is no quick and easy solution. Given the complexity of the epidemic, a comprehensive response including the full range of societal and public health interventions will be necessary to reduce incidence. Although many of the innovative and breakthrough strategies that will ultimately succeed are still on the drawing board, this outstanding article provides some important and simple answers to complex questions regarding potential options that are available to address the UK’s serious HIV epidemic.

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I declare that I have no conflicts of interest. The opinions and statements in this article are those of the authors and do not represent the official policy, endorsement or views of UNAIDS.

HIV incidence in men who have sex with men in England and Wales 2001–10: a nationwide population study

Paul J Birrell, O Noel Gill, Valerie C Delpech, Alison E Brown, Sarika Desai, Tim R Chadborn, Brian D Rice, Daniela De Angelis

Summary

Background Control of HIV transmission could be achievable through an expansion of HIV testing of at-risk populations together with ready access and adherence to antiretroviral therapy. To examine whether increases in testing rates and antiretroviral therapy coverage correspond to the control of HIV transmission, we estimated HIV incidence in men who have sex with men (MSM) in England and Wales since 2001.

Methods A CD4-staged back-calculation model of HIV incidence was used to disentangle the competing contributions of time-varying rates of diagnosis and HIV incidence to observed HIV diagnoses. Estimated trends in time to diagnosis, incidence, and undiagnosed infection in MSM were interpreted against a backdrop of increased HIV testing rates and antiretroviral-therapy coverage over the period 2001–10.

Findings The observed 3.7 fold expansion in HIV testing in MSM was mirrored by a decline in the estimated mean time-to-diagnosis interval from 4.0 years (95% credible interval [CrI] 3.8–4.2) in 2001 to 3.2 years (2.6–3.8) by the end of 2010. However, neither HIV incidence (2300–2500 annual infections) nor the number of undiagnosed HIV infections (7370, 95% CrI 6990–7800, in 2001, and 7690, 5460–10 580, in 2010) changed throughout the decade, despite an increase in antiretroviral uptake from 69% in 2001 to 80% in 2010.

Interpretation CD4 cell counts at HIV diagnosis are fundamental to the production of robust estimates of incidence based on HIV diagnosis data. Improved frequency and targeting of HIV testing, as well as the introduction of ART at higher CD4 counts than is currently recommended, could begin a decline in HIV transmission among MSM in England and Wales.

Introduction UK Medical Research Council, UK Health Protection Agency.

Introduction

High levels of HIV testing combined with prompt antiretroviral therapy (ART) might substantially reduce HIV transmission, especially if high levels of engagement and retention in care can bring about a large reduction in community viral load (the aggregate viral load within a given population or risk group). Various models have investigated the effect of different thresholds for the initiation of treatment, treatment uptake, and adherence rates and suggest that widespread ART coverage could have a population-level prevention effect, thereby reducing HIV transmission.

Two studies of routinely collected surveillance data have shown an association between increases in ART coverage and declines in new HIV diagnoses and community viral load, one in British Columbia, Canada, and another among men who have sex with men (MSM) in San Francisco, USA. The authors concluded that these results support the postulated secondary population-level benefits of ART. In England and Wales, MSM have the highest prevalence of HIV (9% in London and 3% elsewhere). Most MSM are tested and diagnosed in free and confidential dedicated sexually transmitted infection (STI) clinics. Link to HIV care after diagnosis is prompt (more than 95% within 3 months) and retention in care is high (more than 95% a year). The initiation of ART is recommended in patients with a CD4 count below 350 cells per μL. New diagnoses in MSM have continued to rise over the past decade despite the high and rising coverage of ART.

Although trends in new diagnoses remain a crucial measure of the HIV epidemic, they are a suboptimum measure of changes in HIV incidence. An HIV diagnosis is the outcome of three interacting processes: transmission, infection progression, and diagnosis. Consequently, the number of new diagnoses is a dynamic mixture of long-standing and recent infections, and is, therefore, not necessarily synonymous with the number of new infections. Only by reconstructing the complex mechanism underlying observed data can we disentangle the contribution of changes in testing patterns and in incidence to the recorded trends in HIV diagnoses and interpret them appropriately. We used a novel and simple CD4-staged back-calculation approach, incorporating CD4 counts at diagnosis and information on the natural history of HIV infection, to simultaneously estimate HIV incidence and trends in diagnosis rates in MSM in England and Wales for the decade 2001–10. From these estimated trends, we derived estimates of the number of undiagnosed infections over time and trends in the time from infection to diagnosis, giving additional insight into the effect of HIV testing practices over the past decade. We present model outputs alongside comprehensive data.
for HIV testing rates and ART coverage to examine whether increases in testing rates and ART coverage in England and Wales have corresponded to the control of HIV transmission in MSM, where control is defined as a sustained decline in incident HIV infections.

Methods

Data for the back-calculation model

The model uses reports of new HIV and AIDS diagnoses and information on CD4 counts around diagnosis among MSM in England and Wales. Specifically, the model uses quarterly aggregated counts of new AIDS-free and late HIV diagnoses from the early 1980s to the end of 2010. AIDS-free HIV diagnoses are those with no accompanying clinical AIDS diagnosis within 3 months, whereas a late HIV diagnosis refers to a clinical AIDS diagnosis that occurs before or within 3 months of HIV diagnosis. From 1991, the national HIV database has been linked (using soundex code, date of birth, and sex) to CD4 count laboratory reports from haematology laboratories. From this linkage, data are available for the distribution of CD4 counts at diagnosis. Here, a CD4 count is interpreted to be at diagnosis if it is the first recorded CD4 count for a patient taken within 3 months of their initial diagnosis. Between 1991 and 2010 these counts are available in 76% of all new diagnoses, rising to 91% in 2010.

Other data sources

Coverage of ART, defined as the proportion of all people in HIV care who received ART at the date they were last seen, was obtained from the annual census of patients accessing care in all HIV outpatient services in England and Wales. Information relating to ART is complete for 99% of patients. HIV testing data for MSM attending all STI clinics in England and Wales were extracted from quarterly clinic returns for the years 2001–10. The high completeness of surveillance data is ensured through mutual supplementation of information between different systems; additionally, data are necessarily of high quality, because surveillance data directly inform the commissioning and funding of HIV services. Annual loss to follow-up rates for MSM accessing HIV care are very low (<5%).

The CD4 staged back-calculation HIV transmission model

The processes of infection, disease progression, and diagnosis of HIV-infected MSM are described through a discrete multistate model, with time steps every calendar quarter and disease states defined by CD4 count and diagnosis status (appendix). After infection, transition between CD4 states is expressed through assumed known parameters representing the proportion of individuals progressing to the next CD4 state in each quarter, informed from the analysis of longitudinal CD4 counts in HIV-infected people for whom the date of infection is well estimated. In each quarter, a CD4-specific proportion of MSM is diagnosed. These proportions are allowed to vary over calendar time to reflect changing testing patterns throughout the epidemic. Using the data described above, the model permits the simultaneous estimation of HIV incidence and quarterly proportions diagnosed, from which we can quantify the changes in the time-to-diagnosis (appendix) and estimate the number of undiagnosed infections in each CD4 state, both with appropriate statements of uncertainty, expressed in terms of 95% credible intervals (CrI).

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Between 2001 and 2010, the estimated number of new infections oscillated between 2200 and 2800 infections a year (figure 1). Incidence increased to a peak in 2003–04, but, after a slight decline, stabilised at 2300–2500 infections a year from 2006 to the end of 2010. From 2007 onwards, the CrIs attached to the estimates of incidence are of steadily increasing width. This uncertainty arises because the data are less informative about the most recent infection numbers due to only a small proportion of these infections having had sufficient time to be diagnosed and thus appear in the data. However, there is no statistically significant...
change in incidence between any 2 years over the interval and no suggestion of an increasing or decreasing trend (see appendix).

The proportion of undiagnosed individuals who are diagnosed each quarter from the two high CD4 count states (≥350 cells per μL) increased steadily over time (figure 2), with a similar trend seen for the lower CD4 counts (results not shown). As a result, the estimated snapshot time-to-diagnosis distributions (see appendix) indicate a trend towards earlier diagnosis over the decade (figure 2). The mean time-to-diagnosis interval declined from 4·0 years (95% CrI 3·8–4·2) at the beginning of 2001 to 3·2 years (2·6–3·8) by the end of 2010 (figure 2). Furthermore, the total proportion of MSM diagnosed with a CD4 count greater than the recommended treatment threshold (≥350 cells per μL) increased from a low of 48% (45–52%) in the fourth quarter of 2001 to a high of 65% (57–74%) in the third quarter of 2010 (figure 2B). Despite these developments, at 2010 rates of diagnosis, 38% of new infections will not be diagnosed until after the time at which they would have qualified for treatment (figure 2).

The estimated number of undiagnosed HIV infections increased steadily from the beginning of 2001 to a peak of 9140 (95% CrI 8720–9620) infections in the first quarter of 2005 (figure 3). Since this time, there has been a quarter-on-quarter decline in the estimated number of undiagnosed infections, although, similarly to the estimation of incidence, these estimates, from 2007 onwards, are characterised by increasing uncertainty. By the end of 2010 the estimated number of undiagnosed infections in MSM was 7690 (95% CrI 7160–8220), similar to the 7370 (6990–7800) 10 years earlier.

The estimated CD4 count distribution across the undiagnosed HIV infections has changed very gradually over time (figure 3). Undiagnosed HIV infections with a CD4 count of 500 cells per μL or higher consistently account for around 50% of the undiagnosed population, with the general trend following the number of incident infections in each year. These distributions contrast starkly with the observed CD4 count distributions at diagnosis, which are more evenly distributed across the CD4 count states, although diagnoses with CD4 counts higher than 500 cells per μL are still the most common (figure 3). At the other end of the scale, the estimated number of undiagnosed HIV-infected MSM with a CD4 count of less than 350 cells per μL (and thus, in principle, eligible for treatment) remains unchanged from 1490 (95% CrI 1410–1570) at the start of 2001, to 1490 (1240–1770) at the end of 2010, although this change does represent a decrease from a peak in 2007 of 1790 (1700–1880) undiagnosed infections.

These trends in HIV incidence and prevalence can be interpreted against contemporaneous data for uptake of ART, HIV tests done in STI clinics, and numbers of new HIV diagnoses among MSM (table). The annual number of new diagnoses rose from 1640 in 2001 to 2450 in 2005 and levelled off at around 2500 in 2010, whereas the number of men who presented with clinical AIDS at the time of their HIV diagnosis remained fairly stable (125 in 2001 to 177 in 2010). The proportion of diagnoses occurring at high CD4 counts (≥500) has increased over the past 10 years, though not substantially (figure 3). Around 16 000 men were tested for HIV in STI clinics in 2001, a figure that increased 3·7 fold over the decade to 59 300, a substantial growth in testing effort (table). The number of HIV-diagnosed MSM receiving care rose steadily from 12 500 in 2001 to 27 900 in 2010, and the proportion receiving ART, already at 69% in 2001, increased to 80% in 2010. In

Figure 2: Estimated trends in diagnosis by CD4 count
Proportions of HIV-infected MSM in each of the two high CD4 count states that are diagnosed per quarter (A). Estimated expected time to diagnosis and proportion diagnosed at CD4 count of more than 350 (B). Lighter coloured lines indicate 95% credible interval.
2001, 75% of MSM with a CD4 count of less than 350 cells per μL were in receipt of ART, compared with 84% in 2010.

Discussion

Our analysis of 20 years of a comprehensive population-wide surveillance dataset using a CD4-based back-calculation model shows that, over the past decade, there is no evidence of a decline in incidence among MSM, with new infections continuing at around 2300–2500 a year. There is a significant declining trend in the estimated number of undiagnosed HIV infections between a peak at the end of 2004 to the end of 2008, and there is the suggestion that this trend may continue into 2010 (figure 3A), although the uncertainty attached to the most recent estimates makes this decrease difficult to detect. By the end of 2010 we estimate that around 7700 MSM with HIV remained undiagnosed, corresponding to 22% of the total number of MSM with HIV, a decrease from 37% of the total number of infections in 2001.

Our results confirm previous speculations about the high level of continuing HIV transmission in MSM and are consistent with earlier estimates of undiagnosed prevalence obtained using a multiparameter evidence synthesis approach, where a complex dynamic model is used to synthesise the information contained in several datasets. 21, 22 Over the past decade, the estimated diagnosed proportions from each CD4 state all steadily increased, resulting in a shortening of the mean time to diagnosis by 20% from 4.0 to 3.2 years. Through our back-calculation approach we estimated that, since 2001, the CD4 count of almost a third of the undiagnosed individuals was between 350 cells per μL and 500 cells per μL, and in half the count was above 500 cells per μL.

Our modelling approach has several advantages. First, the model takes into account the interaction of three distinct processes (infection transmission, progression, and diagnosis), allowing the estimation of both rates of infection and diagnosis. Ignoring the propensity for individuals to be diagnosed, and temporal changes in this propensity, will lead to estimates for incidence that are based solely on CD4 cell counts and the natural history of HIV infection. Such estimates will typically be biased because of an overestimation of the time since infection as the time at risk of a diagnosis is completely ignored. Second, estimates of the number of undiagnosed infections in the various CD4 states are automatically generated and are consistent with the available information, without need for simplifying, untestable, assumptions (eg, similarity of the CD4 population profile of newly diagnosed and undiagnosed infections). Third, we use observed data from multiple sources, thus reducing the likelihood of biases that might be inherent in individual databases. Other researchers have also made use of multiple data sources, but they have referred to situations where, unlike here, there was no linkage between the new HIV and AIDS diagnoses, 23 the data sources have been used independently with a comparison of the resulting estimates, 24 or the additional data are simply used for model validation. 25 Finally, the coherent, joint estimation of the time-varying incidence and diagnosis rates obtained through applying our back-calculation method strengthens the argument that CD4 counts at diagnosis should be an integral part of national HIV surveillance systems. The availability and completeness of these data in new diagnoses databases in developed countries are poor. 26

This work represents only the first step of a more comprehensive model, which could incorporate many
more complexities (eg, a primary infection stage, or heterogeneity in risk behaviours), allowing the comprehensive investigation of scenarios that might explain the lack of transmission control. Some relevant ideas have already been explored in the analysis of the Dutch HIV epidemic.25

In conclusion, although there is incontestable evidence regarding the benefits of treatment as prevention at an individual level, there is no indication so far that the increased rates of testing and widened access to treatment have controlled HIV transmission in MSM in England and Wales (panel). The most plausible explanation for lack of HIV transmission control (ie, the lack of any sustained decline in incidence) during this period is a resurgence in unsafe sexual behaviour (largely because of treatment optimism),27 and insufficiently frequent HIV testing among this population. The resurgence in unsafe sexual practices is evident through a concomitant epidemic of bacterial STIs and may have been amplified through social media accelerating wider partnership formation.18,28,29 There is strong evidence of a multiple-fold increase over time in the numbers of HIV tests administered to at-risk population and to start treatment earlier if a sustained decline in testing of the at-risk population and to start treatment earlier if a sustained decline in diagnosis.1,3,5,7 These modelling studies were augmented by browsing related citations, identifying three further modelling studies.6,8,25 Since this is a highly active area of current research, further references came to our attention during the lifespan of this work.8,13 None of these studies were directly relevant to a health-care system like that of England and Wales, where HIV is hyperendemic, retention in care is high and treatment is prescribed to many HIV infected individuals with a CD4 count less than 350 cells per μL.

Interpretation

Using the rich array of HIV surveillance data available in England and Wales, we have adopted a novel, relatively parsimonious, CD4-based back-calculation model to estimate simultaneously HIV incidence and CD4-specific diagnosis rates among MSM over the period 2001–2010.30 Furthermore, this work results in the estimation of the number of undiagnosed infections by CD4 count. We did not find any clear evidence for declining incidence despite an estimated shortening of the time-to-diagnosis from 4.0 years to 3.2 years. The number of undiagnosed infections declined only slightly from the middle of the decade, returning to 2001 levels. These results are set alongside data highlighting expanded testing effort and greater treatment coverage over the period. Modelling studies have raised great enthusiasm for the potential of test-and-treat practices to provide control of HIV transmission.27 However, a few studies have identified situations where such practices have only a modest or short-lived benefit and discuss their limitations.8,10,25 In this work we demonstrate how expanding testing and high (and rising) treatment coverage have not corresponded to a decline in HIV transmission. We suggest that healthcare services in England and Wales will need to provide more targeted testing of the at-risk population and to start treatment earlier if a sustained decline in HIV incidence is to be brought about.

<table>
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<th>Year</th>
<th>Total number of infected individuals in HIV care</th>
<th>Total number of infected individuals receiving ART</th>
<th>Percentage of infected individuals in HIV care in receipt of ART</th>
<th>Number of HIV tests in STI clinics</th>
<th>New HIV diagnoses</th>
<th>New HIV diagnoses presenting as AIDS</th>
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<td>27 855</td>
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ART=antiretroviral therapy. STI=sexually transmitted infection.

Panel: Research in context

Systematic review

A search of PubMed using (“antiretroviral therapy” OR “HIV testing”) AND (“HIV diagnoses” OR “HIV incidence” OR “HIV prevalence”) AND “HIV prevention” yielded 19 articles. We selected a subset of these articles, choosing those that investigated the (in some cases, potential) impact of expanded testing and/or treatment upon HIV incidence and that included a significant mathematical or statistical modelling component.8,10,25 These modelling studies were augmented by browsing related citations, identifying three further modelling studies.6,8,25 Since this is a highly active area of current research, further references came to our attention during the lifespan of this work.8,13 None of these studies were directly relevant to a health-care system like that of England and Wales, where HIV is hyperendemic, retention in care is high and treatment is prescribed to many HIV infected individuals with a CD4 count less than 350 cells per μL.

shows that around 35% of patients, most of whom are not in receipt of treatment, have viral loads of greater than 1500 copies per mL and are therefore at risk of transmitting the infection.31 By contrast with the treatment cascade in the USA, where there is a lower retention in care, albeit with a higher proportion of these patients on antiretroviral therapy,32 our estimates of the number of undiagnosed MSM in England and Wales are higher than the observed number of diagnosed MSM.
who remain untreated (table). This finding strongly suggests that the undiagnosed infections represent the principal part of the community viral load reservoir driving HIV transmission.\textsuperscript{3,15,16}

The findings in our paper should alert policy makers and public health authorities to the limited effect of the national HIV Strategy (England),\textsuperscript{7} which aimed to reduce transmission through increasing the uptake of HIV testing in STI clinics, and to the fact that high antiretroviral coverage alone might not be sufficient to eliminate HIV transmission. Primary prevention and, earlier, more targeted, testing must continue to be prioritised as part of any national HIV prevention plan.

In view of the profile of CD4 counts in newly diagnosed patients, showing that around 60% are not immediately eligible for antiretroviral therapy, the initiation of treatment on diagnosis of HIV infection, irrespective of CD4 count, might well be necessary to achieve control of HIV transmission. To this extent, we welcome the new British HIV Association guidelines recommending that clinicians discuss the benefits of early treatment uptake as a prophylactic to protect sexual partners.\textsuperscript{12}

Contributors

PJB contributed to model development, data analysis, interpretation of data and results, writing, and figures. ONG contributed to the writing and the interpretation of results. VCD contributed to the planning and design of the paper, reviews of manuscripts, and writing. AEB contributed to the writing and data management. SD contributed a literature search and to the data management. TRC contributed to the interpretation of results and model development. BDR contributed to data management. DDA initiated and supervised the work, contributing to model development, data analysis, data interpretation, and writing.

Conflicts of interest

We declare that we have no conflicts of interest.

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STI rates are rising to alarming levels in gay men in England

- Lisa Power, Policy Director at the Terrence Higgins Trust said: “The rising numbers of almost every STI among gay men should act as a wakeup call to us all. Unlike heterosexuals, where most infections are in young people aged 15-24, gay men are most likely to get STIs in their late 20s and 30s and high levels continue in their 50s. This is due to different patterns of sexual behaviour, and more frequent partner change.”

- “We need to remind ourselves that treatment as prevention works to reduce transmission of HIV, but it doesn’t do anything to prevent other STIs – and sexually transmitted infections like gonorrhoea and chlamydia actually increase the risk of HIV transmission, even when someone is on treatment. As such, condoms remain a key ingredient not just in protecting against STIs, but also in controlling the spread of HIV.”

- “Gonorrhoea in particular has increased by a third in the last year in gay men and has tripled since 2009. In the context of new reports of drug-resistant strains of the infection, it is vital that gay men use condoms and go for regular sexual health check-ups to control the outbreak.”

Terrence Higgins Trust says high gonorrhoea rates among gay men are a ‘wakeup call’

by Scott Roberts for PinkNews.co.uk
5 June 2013, 11:18am

Sexual health charity the Terrence Higgins Trust has described latest figures showing rates of gonorrhoea among gay men up by a third as a “wakeup call”.

According to Public Health England, more sexually transmitted infections (STIs) were being diagnosed and treated than ever before last year, with improvements in screening particularly for gonorrhoea and chlamydia among young adults and men who have sex with men (MSM).

Increases in STI diagnoses were seen in men who have sex with men, including a 37% increase in gonorrhoea diagnoses.

Chlamydia and genital warts are 8% higher and syphilis diagnoses have risen by 5%.
Dr Gwenda Hughes, head of STI surveillance, said: “Ongoing investment in programmes to increase sexual health awareness, condom use and testing, particularly for groups at most risk, is vital.”

Lisa Power, policy director at the Terrence Higgins Trust (THT), said: “The rising numbers of almost every STI among gay men should act as a wakeup call to us all. Unlike heterosexuals, where most infections are in young people aged 15-24, gay men are most likely to get STIs in their late 20s and 30s and high levels continue into their 50s. This is due to differing patterns of sexual behaviour, and more frequent partner change.”

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She added: “Gonorrhoea in particular has increased by a third in the last year in gay men and has tripled since 2009. In the context of new reports of drug-resistant strains of the infection, it is vital that gay and bisexual men use condoms and go for regular sexual health check-ups to control the outbreak.”

Health experts in the UK remain concerned by the increasingly aggressive nature of gonorrhoea, which is becoming harder and harder to treat, certain strains in Britain may eventually become untreatable within the next few years.