‘Treatment as prevention’ to reduce HIV transmission in the MSM population: Will it work?

Tony Hughes
Research Director
New Zealand AIDS Foundation

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MSM have a 140 fold higher risk for newly diagnosed HIV and syphilis compared with heterosexual men in New York City.

- “The average prevalence of male same-sex behaviour for years 2005-2008 (5.0%; 95% CI: 4.5 to 5.6) was highest among men aged 40-49 years (8.0%) and lowest among men aged 18-29 years (3.9%).”

- “During 2005-2008, there were 9571 new HIV cases among MSM and 1249 among MSW, resulting in an MSM HIV case rate that was 140.4 times as high (95% CI: 132.1 to 148.7) as the rate among MSW (2526.9/100,000 vs 18.0/100,000).”

- “The total number of [primary and secondary] syphilis cases over four years was 2678 among MSM and 334 among MSW, resulting in an MSM syphilis case rate that was 147.3 times as high (95% CI: 130.5 to 163.2) as the rate among MSW (707.0/100,000 vs 4.8/100,000).”
Global prevalence of HIV in MSM compared with adult prevalence, UNAIDS 2010.

HIV risk for different male-to-male sexual activities relative to receptive anal sex without condoms

HIV transmission risk for receptive anal and vaginal intercourse without condoms in developed countries

Global epidemiology of HIV infection in men who have sex with men

- “Our findings show that the high probability of transmission per act through receptive anal intercourse has a central role in explaining the disproportionate disease burden in MSM.”

- “HIV can be transmitted through large MSM networks at great speed. Molecular epidemiological data show substantial clustering of HIV infections in MSM networks, and higher rates of dual-variant and multi-variant HIV infection in MSM than in heterosexual people in the same populations.”
"The greatest reductions were associated with the scenarios that entailed reducing transmission probabilities to those of vaginal intercourse; in all settings, this quickly reduced incidence by greater than 80%, and in some by as much as 98%. This emphasises that biological factors specific to anal sex have a fundamental effect in driving HIV epidemics in MSM worldwide."

Treating HIV-infected people with antiretrovirals significantly reduces transmission to partners (HPTN 052)

- Study of 1,763 serodiscordant couples, 97% were heterosexual and most were married. At enrolment HIV infected partners had CD4+ T cell levels between 350 and 550 cells/mm³.

- There were two study groups: In the first antiretroviral therapy was started immediately and in the second it was postponed until 250 cells/mm³, or until AIDS symptoms appeared.

- Condom use was encouraged. Those reporting 100% condom use had a significantly lower likelihood of acquiring HIV than those reporting less frequent condom use.

- Thirty nine new HIV infections were found in the previously uninfected partners. Of those 28 were genetically linked to an infected partner. The other 11 were not clearly partner linked.

- Of the 28 partner linked infections, 27 occurred in the group where treatment was delayed, only one occurred in the early treatment group. Twenty three of the linked infections (82%) occurred in couples from sub-Saharan Africa.

- The overall finding is that early initiation of antiretroviral therapy lead to a 96% reduction in HIV transmission to uninfected partners in this trial.
“Some biological and epidemiological evidence suggests that ART for preventing transmission via anal intercourse may have more limited efficacy than via vaginal intercourse.”

“While the results of HPTN 052 demonstrated the capacity of ARVs to markedly reduce the risk of penile-vaginal transmission… we cannot be certain that this will be the case for anal intercourse given the much higher transmission probability in the absence of ART.”

“The impact of ART on HIV transmission via anal intercourse requires further evaluation… given the inconclusive observational data currently available for MSM and the challenging biological and behavioural risk factors that may present.”
Antiviral agents and HIV prevention: Controversies, conflicts and consensus

Myron S. Cohen, a,h, b, Kathryn E. Muessig, a, h, M. Kumi Smith, b, Kimberly Powers, a, b and Angela D. M. Kashuba, d

Antiviral agents can be used to prevent HIV transmission before exposure as pre-exposure prophylaxis (PrEP), after exposure as post-exposure prophylaxis (PEP), and as treatment of infected people for secondary prevention. Considerable research has shed new light on antiviral agents for PEP and for prevention of secondary HIV transmission. While promising results have emerged from several PEP trials, the challenges of poor adherence among HIV-negative clients and possible increase in sexual risk behavior remain of concern. In addition, a broader pipeline of antiviral agents for PEP that focus on genital tract pharmacology and safety and resistance issues must be developed. Antiretroviral drugs have also been used to prevent HIV transmission from HIV infected patients to their HIV discordant sexual partners. The HPTN 052 trial demonstrated nearly complete prevention of HIV transmission by early treatment of infection, but the generalizability of the results to other risk groups— including injecting drug users and men who have sex with men— has not been determined.

Most importantly, the best strategy for use of antiretroviral agents to reduce the spread of HIV at either the individual level or the population level has not been developed, and remains the ultimate goal of this area of investigation.

Additionally, combination prevention strategies will need the continued efforts of behavioral interventions to increase condom use, reduce high-risk behaviors, and address suboptimal ARV adherence and risk compensation.


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- Additionally, combination prevention strategies will need the continued efforts of behavioral interventions to increase condom use, reduce high-risk behaviors, and address suboptimal ARV adherence and risk compensation.
HIV diagnosis rate among MSM in major Western European countries plus Australia, Canada and New Zealand

Diagnoses of HIV and selected STIs among MSM in the United Kingdom, 1997-2006

1 Rates of new HIV diagnoses from 2003 onwards are adjusted for reporting delays

STI data from genitourinary medicine clinics and HIV/AIDS diagnoses

A resurgent HIV-1 epidemic among MSM in the era of potent antiretroviral therapy in the Netherlands

A resurgent HIV-1 epidemic among men who have sex with men in the era of potent antiretroviral therapy

Daniela Bezemer\textsuperscript{a}, Frank de Wolf\textsuperscript{b}, Maarten C. Boerlijst\textsuperscript{c}, Ard van Sighem\textsuperscript{d}, T. Deirdre Hollingsworth\textsuperscript{b}, Maria Prins\textsuperscript{d,e}, Ronald B. Geskus\textsuperscript{d},\textsuperscript{f}, Luuk Gras\textsuperscript{g}, Roel A. Coutinho\textsuperscript{d},\textsuperscript{h} and Christophe Fraser\textsuperscript{b}

Objective: Reducing viral load, highly active antiretroviral therapy has the potential to limit onwards transmission of HIV-1 and thus help contain epidemic spread. However, increases in risky behaviour and resurgent epidemics have been widely reported post-haart. This study seeks to quantify the potential for an increase in risk behaviour to offset the benefits of HAART in reducing transmission.

Design: We focus on the HIV-1 epidemic among men who have sex with men in the Netherlands, which has been well documented over the past 20 years within several long-standing national surveillance programs.

Methods: We used a mathematical model including highly active antiretroviral therapy use and estimated the impact of changes in risk behaviour and diagnostis rate needed to explain annual data on HIV and AIDS diagnoses.

Results: We show that the reproduction number R(0), a measure of the state of the epidemic, declined early on from initial values above two and was maintained below one from 1996 to 2003. Since 1996, when highly active antiretroviral therapy became widely used, the reproduction rate has increased to 1.06, roughly an increase of 66% in the latest period 2000–2004. 95% confidence interval 0.99–1.25, just above the threshold for a self-sustaining epidemic. Hypothetical scenarios analysis shows that the epidemiological benefits of highly active antiretroviral therapy, and earlier diagnosis on incidence have been entirely offset by increases in risk behaviour rate.

Conclusion: We provide the first detailed quantitative analysis of the HIV epidemic in a well-defined population and find a resurgent epidemic in the era of highly active antiretroviral therapy, most likely predominantly caused by increases in sexual risk behaviour.

Keywords: antiretroviral therapy, homosexual men, infectious diseases, mathematical models, model predictions, sexual behaviour. surveillance

Since 1996, when HAART became widely used in the Netherlands, the risk behaviour rate has increased by 66% in MSM.

“In conclusion, there is an increase in HIV transmission among MSM in the Netherlands, in spite of earlier diagnosis and subsequent effective treatment. The most effective intervention is to bring risk behaviours back to pre-HAART levels.”

## Impact of ART on HIV transmission at population level

<table>
<thead>
<tr>
<th>First author</th>
<th>Key comments and conclusions on sexual behaviour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blower 2000</td>
<td>Significant efforts should be made to prevent risk behaviour increasing because even small increases will overcome the effect of ART on reducing HIV transmission.</td>
</tr>
<tr>
<td>Law 2001</td>
<td>Apparently large decreases in infectiousness as a result of treatment can be counterbalanced by much more modest increases in unsafe sex.</td>
</tr>
<tr>
<td>Katz 2002</td>
<td>Any decrease in per-contact risk of HIV transmission due to ART use appears to have been counterbalanced or overwhelmed by increases in the number of unsafe sexual episodes.</td>
</tr>
<tr>
<td>Velasco-Hernandez 2002</td>
<td>HIV spread is extremely sensitive to changes in risky sex. It is imperative that the usage of ART should be tightly coupled with effective risk-reduction strategies and that levels of risky sex are substantially reduced.</td>
</tr>
<tr>
<td>Xiridou 2003</td>
<td>A reduction of 75-99% in infectivity caused by ART will be counterbalanced by increases of 50% (range 30-80%) in risky behaviour with steady partners. Prevention measures should address unsafe behaviour.</td>
</tr>
<tr>
<td>Boily 2004</td>
<td>Because ART modifies the natural history of HIV infection it will change the transmission dynamics of the epidemic, and has the potential to increase the aggregate level of risky sexual behaviour in the population over time.</td>
</tr>
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<tr>
<td>McCormick 2007</td>
<td>These results indicate that ART must be accompanied by effective HIV risk reduction interventions. Prevention programmes that decrease HIV transmission are crucial to epidemic control.</td>
</tr>
<tr>
<td>Wilson 2008</td>
<td>The risk of HIV transmission in male homosexual partnerships is high over repeated exposures. If the claim of non-infectiousness in effectively treated patients is widely accepted, and condom use subsequently declines, there is potential for a substantial increase in HIV incidence.</td>
</tr>
<tr>
<td>Hallet 2010</td>
<td>The key message to patients should remain that always using condoms when receiving treatment is the best way to protect partners from the risk of HIV transmission.</td>
</tr>
<tr>
<td>Bezemer 2010</td>
<td>This model showed that if nothing changes, twice as many MSM in the Netherlands will be in need of healthcare for HIV infection in the coming decade than at present. The most effective way to prevent this is to decrease risk behaviour.</td>
</tr>
<tr>
<td>Long 2012</td>
<td>Even substantial expansion of HIV screening and treatment programmes is not sufficient to reduce the HIV epidemic markedly in the United States without substantial reductions in risk behavior.</td>
</tr>
<tr>
<td>Phillips 2012</td>
<td>This analysis suggests that HIV incidence increased as the United Kingdom after ART was introduced as a result of a modest (26%) rise in unprotected anal sex, and that in 2010, 48% of new transmissions came from undiagnosed men with primary HIV infection.</td>
</tr>
</tbody>
</table>

(b) Cessation of all condoms in 2000 would have resulted in a 400% increase in incidence

Why is HIV infection difficult to manage in the MSM population?

(a) Extremely high biological risk of HIV acquisition through unprotected receptive anal sex.
(b) Effect of symptomatic and asymptomatic STI infections on HIV acquisition and transmission risk.
(c) Role of primary HIV infection (PHI) in forward transmission and the great difficulty identifying people with PHI.
(d) Complex relationship between HIV viral load levels in blood, semen and rectal tissue.
(e) Differences in HIV acquisition and transmission risk in the seminal and rectal compartments.
(f) Specific impact of high sexual role flexibility on baseline HIV transmission rates in MSM.
(g) Extent to which HIV transmission in anal intercourse occurs through direct cell-to-cell transfer rather than arising from the spread of cell free virus.
(h) Effects of large and complex sexual network structure – frequent multi-partnering, group sex, concurrency and the impact of the internet – on HIV transmission.
(i) Likelihood that there is a core group of undiagnosed MSM that will be very difficult to locate.
(j) Complex challenge provided by a minority of individuals with HIV infection who resist using condoms and are highly sexually active.
(k) Impact of unresolved alcohol, drug use and mental health issues on sexual risk behaviour.
(l) Damaging effects of social marginalisation and homophobia on MSM who are at high risk.
What are the main limitations of TasP in the MSM population?

(a) High cost of regular and widespread HIV testing and ART provision.
(b) Frequency and extent of population coverage of HIV testing initiatives.
(c) Specific problem of late HIV diagnosis in some parts of the MSM population.
(d) Consistency and durability of adherence to ART treatment schedules, especially in healthier individuals earlier in the course of HIV infection.
(e) Requirement for stability of viral load suppression on ART over many decades.
(f) Long term toxicities and side effects of various ART combinations.
(g) Emergence and spread of drug resistant HIV variants in the MSM population.
(h) Near impossibility of delivering treatment to MSM with primary HIV infection.
(i) Fact that HIV treatment does not become optimally effective in most people for several months after it has been commenced.
(j) Degree to which particular ART combinations achieve maximum viral suppression in different body compartments – blood, seminal and rectal.
(k) Increase in unprotected anal sex occurring as a direct result of ART – behavioural disinhibition and risk compensation.
(l) Difficulty of catching up with the large pool of MSM who are already infected and need priority treatment at the same time as managing newly acquired infections.
(m) Inevitability that ‘treatment for prevention’ is a complex and expensive multi-stage process, and that most of the operational demands will fall on already stretched clinical services.
Why does individual level protection not automatically result in population level protection?

- Protecting one individual from HIV infection has an indirect protective effect on others.
- The **efficacy** of a prevention intervention is the extent to which it benefits the individual directly using it.
- The **effectiveness** of a prevention intervention includes the far-reaching population effects of applying the intervention to a large number of individuals.

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**Modelling sexual transmission of HIV: testing the assumptions, validating the predictions**

Rebecca F. Baggaley and Christophe Fraser

**Purpose of review**

To discuss the role of mathematical models of sexual transmission of HIV in their methods and their impact.

**Recent findings**

We use mathematical modeling of ‘universal test and treat’ as a case study to illustrate wider issues relevant to all modeling of sexual HIV transmission.

**Summary**

Mathematical models are used extensively in HIV epidemiology to deduce the logistical conclusions arising from one or more sets of assumptions. Simple models lead to formal qualitative understanding, whereas complex models can encode more realistic assumptions and, thus, be used for predictive or operational purposes. An overemphasis on model analysis in which assumptions are untested and input parameters cannot be estimated should be avoided. Simple models providing bold assertions have provided compelling arguments in not just public health policy, but may not adequately reflect the uncertainty inherent in the analysis.

**Keywords**

mathematical modelling, sexual transmission, test and treat

**Introduction**

Mathematical models have played important roles facilitating understanding of HIV epidemiology, and evaluating the performance of prevention interventions [1]. From the earliest models examining the interaction between HIV and other sexually transmitted infections (STIs) [2], the effects of sexual mixing patterns among individuals by age [3] and predicting the future course of HIV epidemics [4], modelling has assisted in making projections [5], explaining past and future trends [6-8], as well as predicting the impact of existing and proposed HIV prevention measures [9-13]. Such analyses, in which model input parameters are believed to be estimated with sufficient accuracy, can provide quantitative predictions, often being combined with economic analyses to provide cost-effectiveness or cost-benefit projections [14-15]. When such predictions are not attainable, modelling can explore more qualitative outcomes, able to open up new directions of enquiry, such as predicting the impact of HIV prevention technologies yet to be developed (e.g. vaccines and microbicides).

Both qualitative models (used for broad insights) and detailed models (developed for operational purposes) may influence HIV prevention and treatment policies, yet there may also be a lack of trust due to the opaque nature of modelling methods that are used (often quite complex and technical), or conversely, overconfidence and reliance on certain methods or research groups because of lack of understanding of mathematical models in the wider stakeholders community [11]. In this review, we include a case study that has recently received a lot of attention and in which models have been used to influence the research community, policy and beyond. Mathematical models of HIV testing and antiretroviral treatment as prevention (‘test and treat’).

From efficacy to effectiveness

Mathematical models have proven especially useful for assessing interventions such as ‘test and treat’ or multi-circumcision, because their effect is to prevent transmission, and these interventions have individual, pairwise and population level benefits, which are very hard to estimate using empirical field studies alone. Protecting one individual from acquiring infection has an indirect protective effect on others (Fig. 1a). The efficacy of an HIV prevention intervention depends the degree of protection against infection experienced by one individual benefiting directly from the intervention, such as the protection afforded to a man who is circumcised. Effectiveness of infectious disease interventions is more complex, as it includes the far-reaching population effects of applying the intervention to each of these individuals (as shown by the concept of herd immunity).
Efficacy: Sharply increased transmission risk in primary HIV infection

High rates of forward transmission events after acute/early HIV infection in Canada

- “Acute/infection is characterized by high viremia and high viral set points in the absence of treatment. Acute/early infections are often undiagnosed…”

- “Our results show that 49% of all primary HIV infection strains in the Quebec HIV population from phylogenetic clusters, indicating that early infection may account for a major proportion of onward transmissions.”

- “[P]rimary/early infection, representing <10% of the total sequenced samples in the provincial genotyping programme, disproportionately accounted for approximately half of onward transmission events.”


Note: This means that out of 1.2 million people living with HIV in the United States in 2008, 850,000 individuals did not have suppressed viral load (ie: 72%).
Natural experiments highlight limits of antiretroviral treatment as HIV prevention

**The efficacy of treatment in reducing transmission has been demonstrated for heterosexual transmission in the HPTN 052 trial, with supporting evidence from other types of studies. However, this does not imply that increased ART coverage will result in substantial declines in incidence in real world populations.**

**One way to consider the problem is that there is a series of barriers to overcome for treatment to be effective in reducing infectiousness.**

**It is not uncommon for people to drop out at any of these barriers. Idealised conditions for a treatment-as-prevention strategy may involve setting targets of 90% of all people at each barrier progressing to the next stage. However, as pointed out by Gardner et al. (2011), this would result in a maximum of just 66% of HIV-infected people in the population having suppressed virus.”

Summary: Key drivers of HIV spread in the MSM population

(a) Very high HIV acquisition risk from unprotected receptive anal intercourse.
(b) Extreme infectiousness in the acute/early HIV infection stage.
(c) Strong effect of high HIV prevalence levels on rates of HIV spread.
(d) Significant role of sexual network structure – frequent multi-partnering, concurrency and group sex.
(e) Influence of the internet in sharply increasing partner availability since 2000.
(f) Importance of a small group of superspreaders in accelerating HIV and STI transmission.
(g) Presence of a diffused subset of individuals with undiagnosed HIV infection.
(h) Heightened risk of HIV acquisition and transmission in presence of STI co-infections.
Increased HIV transmission risk in the presence of STIs

Effect of early syphilis infection on plasma viral load in Human Immunodeficiency Virus-infected men

- "In HIV-infected men, syphilis was associated with... an increase in viral load, which implies that syphilis may increase the risk of HIV transmission, even in patients receiving antiretroviral therapy and with a viral load of less than 500 copies/ml."

- "The present study population consisted mainly of MSM infected by syphilis... This population is not covered by the Swiss guideline regarding HIV transmission during effective ART, which concerns couples in stable relationships and who have no other sexually transmitted infections."

- "The present results indicate that populations with high-risk sexual behavior, in which syphilis reinfection is relatively common, must be warned of the risk of HIV transmission and be advised to use condoms."
Highly active antiretroviral therapy does not completely suppress HIV in semen of sexually active HIV-infected MSM

“STIs and genital inflammation can partially override the suppressive effect of HAART on seminal HIV shedding in sexually active HIV-infected MSM. Low seminal HIV titers could potentially pose a transmission risk in MSM, who are highly susceptible to HIV infection.”

“Until more information on transmission risk for MSM is available, it would be prudent to advise sexually active HIV-infected MSM to use condoms and other risk-reduction strategies throughout all stages of HIV disease regardless of HIV treatment status, and to promote the aggressive diagnosis and treatment of STIs.”
## Protective effect of condoms for HIV and STI prevention

<table>
<thead>
<tr>
<th>Sexually Transmitted Infection</th>
<th>Protective effect of condoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>High</td>
</tr>
<tr>
<td>Gonorrhoea</td>
<td>High (unless pharyngeal)</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>High</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>High</td>
</tr>
<tr>
<td>Syphilis</td>
<td>High (if lesions covered by condom)</td>
</tr>
<tr>
<td>Epididymitis</td>
<td>High (where sexually transmitted)</td>
</tr>
<tr>
<td>Chancroid</td>
<td>Probably high</td>
</tr>
<tr>
<td>Lymphogranuloma venereum</td>
<td>Probably high</td>
</tr>
<tr>
<td>Mycoplasma genitalium</td>
<td>Probably high</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>Probably high</td>
</tr>
<tr>
<td>Herpes</td>
<td>Moderate (depends on site of lesions)</td>
</tr>
<tr>
<td>Warts</td>
<td>Moderate</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>Unknown</td>
</tr>
<tr>
<td>Donovanosis</td>
<td>Probably low</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Very low (transmission is faecal-oral)</td>
</tr>
</tbody>
</table>

Universal primary prevention response to HIV and other sexually transmitted infections in MSM
Conclusion

(a) Actively promote consistent condom use for anal sex to prevent HIV and STI spread in the MSM population.

(b) Encourage regular testing for HIV and STIs in the MSM population.

(c) Facilitate early HIV and STI treatment in the MSM population.

(d) Support vaccination for STIs in the MSM population where available.
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Per-contact probability of HIV transmission in homosexual men in Sydney in the era of HAART

Fengyi Jin, James Janssens, Matthew Law, Garrett P. Prestage, Iryna Zablotska, John C.G. Imrie, Susan C. Kippax, John M. Kaldor, Andrew E. Grulich and David P. Wilson

Objective: The objective of this study is to estimate per-contact probability of HIV transmission in homosexual men due to unprotected and inconsistent use of HAART.

Methods: Data were collected from a longitudinal cohort study of community-based HIV-affected homosexual men in Sydney, Australia.

Results: A total of 5417 participants were recruited from June 2001 to December 2006. They were followed up with weekly detailed behavioral interviews and annual testing for HIV. UNAIDSSAU 2007. Data were used in a bootstrapping method, coupled with a statistical analysis that optimized a likelihood function for estimating the per-contact risk of HIV transmission due to various forms of UNAIDSSAU.

In the study, 53 HIV seroconversion cases were identified. The estimated per-contact probability of HIV transmission for receptive UAI was 1.43% (95% confidence interval: 0.48-2.35) if ejaculation occurred inside the rectum, and it was 0.63% (95% CI: 0.15-1.51) if withdrawal prior to ejaculation was involved. The estimated transmission rate for insertive UAI in participants who were circumcised was 0.11% (95% CI: 0.04-0.29), and it was 0.62% (95% CI: 0.07-1.43) in uncircumcised men. Thus, receptive UAI with ejaculation was found to be approximately twice as risky as receptive UAI with withdrawal or insertive UAI in uncircumcised men and over 10 times as risky as insertive UAI for circumcised men.

Conclusion: Despite the fact that a high proportion of HIV-infected men are on antiretroviral treatment and have undetectable viral load, the per-contact probability of HIV transmission due to UAI in this study is similar to estimates reported from developed country settings in the pre-HAART era.

Keywords: Australia, cohort study, HIV, homosexuality, male, per-contact probability, transmission risk

Introduction

Most studies of per-contact probability of sexual HIV transmission have been in heterosexual people [1-4], and few estimates have been made for sex between homosexual men [5,6]. The estimation of per-contact risk in homosexual men is more complex than that of heterosexual transmission. First, sexual monogamy is more common in heterosexuals, and thus non-monogamous monogamous couples are more readily available for study.

In Australia, homosexual men have very high rates of recent HIV testing, about 70% of [diagnosed] HIV positive men are receiving HAART, and 75% of those on treatment have undetectable viral load.

It is therefore surprising that estimates of HIV transmission risk through unprotected anal intercourse in the post-HAART era were similar to those when few HIV positive men had an undetectable viral load.

There are several potential explanations: Primary HIV infection may have a bigger role in population spread than expected; the number of undiagnosed HIV infections may be higher than expected; HIV transmission risk by anal intercourse may not be as closely related to viral load as it is in vaginal intercourse; and STI prevalence may be higher now than in the pre-HAART era.

Strategic limitations of HPTN 052

- Almost all of the study sample was comprised of serodiscordant heterosexual couples, most were also married and all received counselling on behaviour modification and condom use. This means that direct conclusions cannot be drawn from these results about the likely impact of antiretroviral treatment on HIV prevention in the MSM population.

- Prevention effectiveness outside a tightly controlled clinical trial environment that involves monthly monitoring cannot be reliably assumed. The observed virologic failure rates in HTPN 052 were less than 5%, which is far lower than is generally observed in patients on antiretroviral therapy.

- Because the median duration of follow-up in HPTN 052 at report was only 1.7 years, it is not known if the levels of treatment adherence observed here can be sustained over the long term. The low levels of observed virologic failure suggest that adherence was artificially high and this may reflect a strong motivation to protect uninfected long-term partners.

- The extent to which antiretroviral treatment will be accompanied in practice by reductions in condom use over time is also undetermined, and treatment of HIV infected partners does not – of course – limit the risk of HIV acquisition from other sexual contacts or risk from other STIs.

Alcorn, K. Treatment is prevention! HATIP; 180: 29 July 2011.
Increasing sexual risk behaviour amongst Dutch MSM: Mathematical models versus prospective cohort data

-The imputation from this is clear: risk behaviour reduced by approximately half from the mid-1980s through to the mid-1990s, which contributed to the self-limiting nature of the early HIV epidemic.

-The resurgent epidemic in the Netherlands as a whole can be satisfactorily, although not exclusively, explained by increased risk behaviour, predominantly in undiagnosed individuals.

-In terms of incidence, increasing risk behaviour between MSM is offsetting benefits offered by enhanced testing and treatment.
Higher concentrations of HIV RNA in rectal secretions than in blood and semen

- High levels of HIV in rectal secretions are likely to increase the risk of HIV transmission in unprotected anal sex.

- It was found here that regardless of HAART use, median HIV RNA levels were higher in rectal secretions (4.96 log₁₀ copies/mL) than in blood plasma (4.24) or seminal plasma (3.55) (p<0.05 each comparison).

- When controlling for plasma HIV RNA, HAART had an independent effect on seminal HIV levels, but not on those in the rectal compartment.
Classical sexually transmitted diseases drive the spread of HIV-1: Back to the Future

- "Perhaps ironically, this past year was filled with great optimism in HIV-1 prevention, leading The Economist to focus on ‘The End of AIDS’ and Secretary of State Hillary Clinton to describe an ‘AIDS-Free Generation’.”

- "But the ‘hidden epidemic’ of classical STDs is squarely blocking optimal prevention of HIV-1 transmission. These STDs – symptomatic or asymptomatic – simply cannot be ignored.”

- "Surely this problem is no more impossible to attack or less important than any other part of the HIV-1 pandemic."