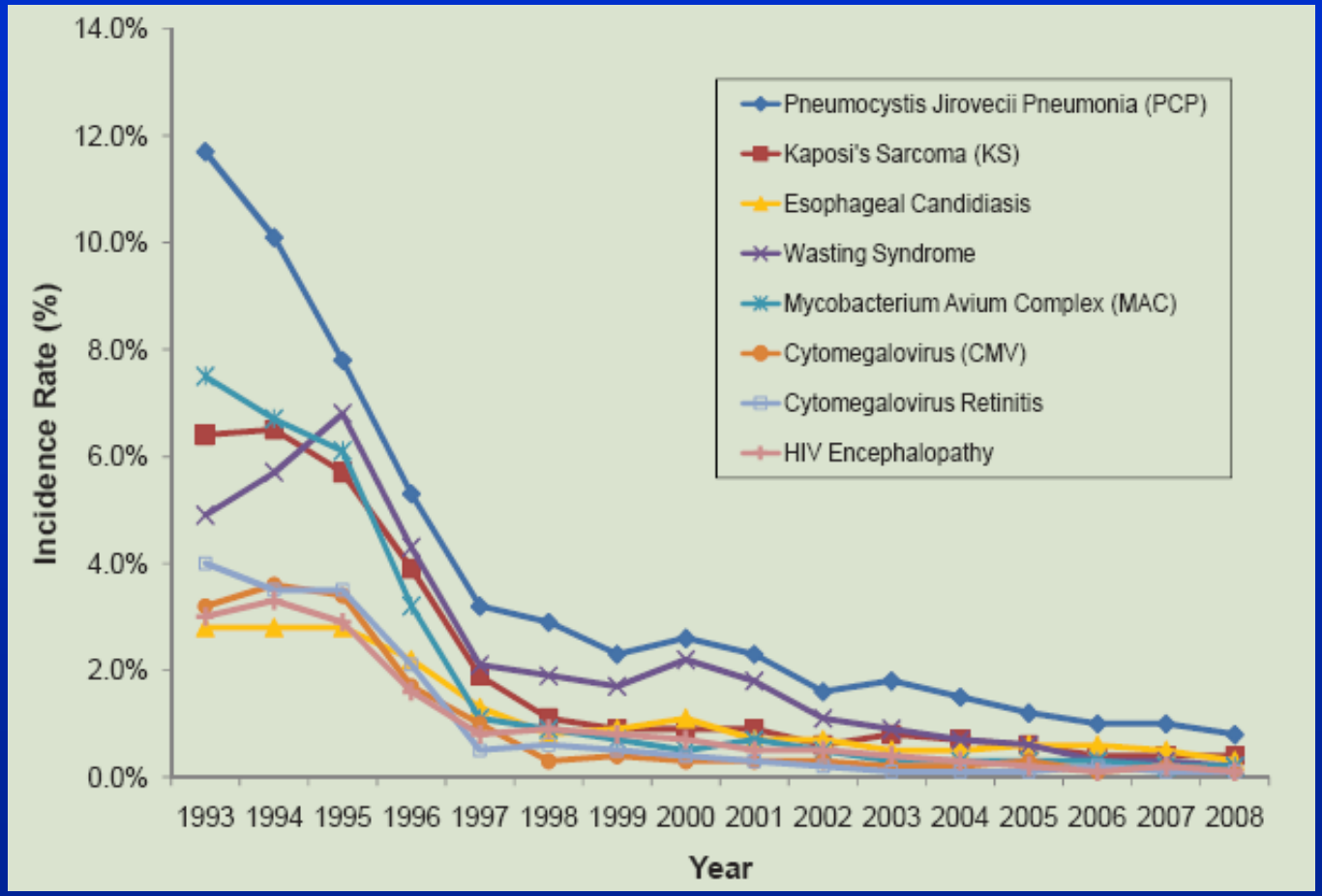
Maximising condom use *and* ensuring early treatment for care in the MSM population

Tony Hughes
Research Director
New Zealand AIDS Foundation

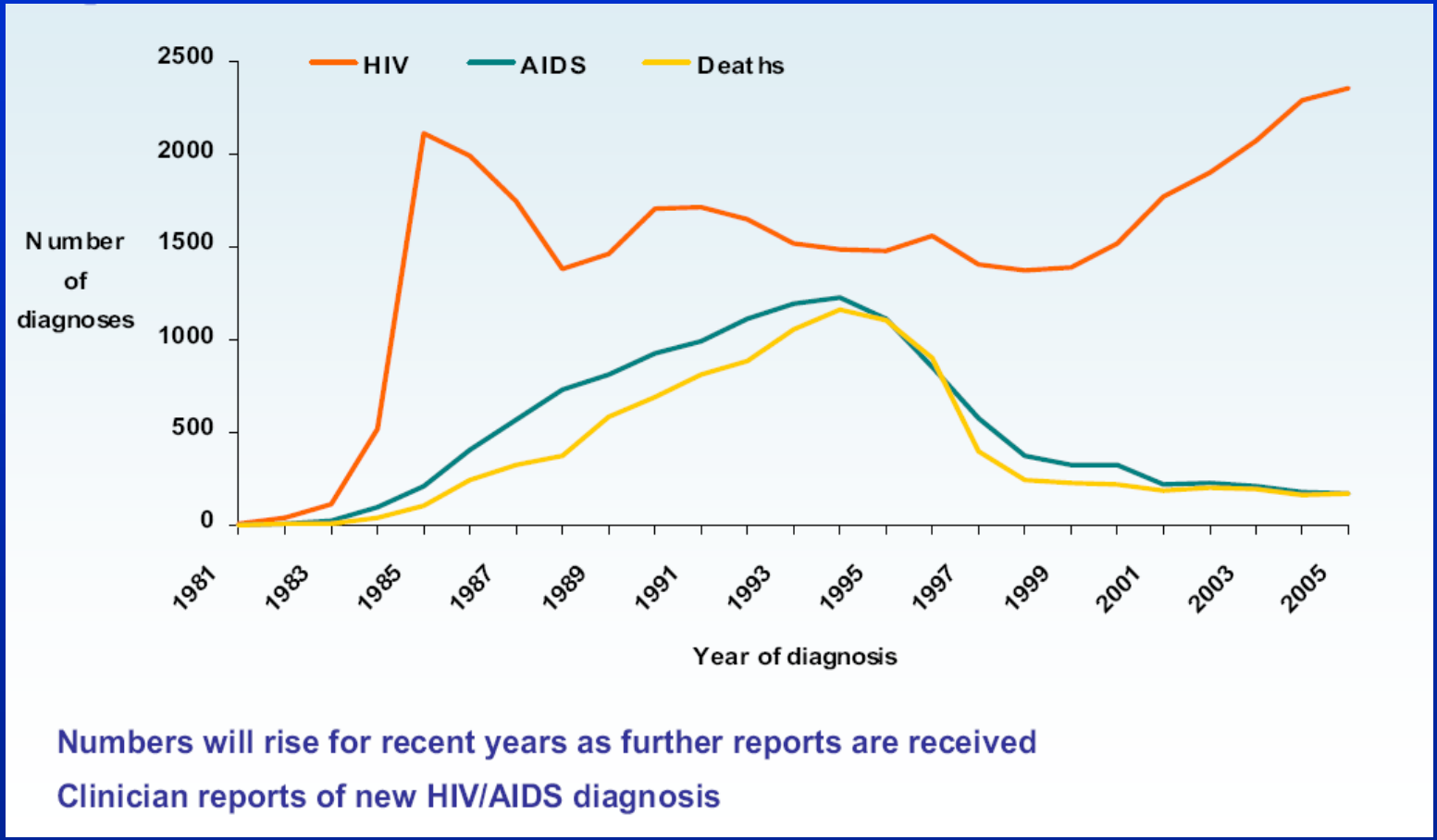
National HIV and AIDS Forum, St Columba Centre, Ponsonby, Auckland, 22 September 2011

Incidence rate of opportunistic illnesses among adults and adolescents with AIDS in San Francisco, 1993-2008



"HIV/AIDS epidemiology annual report 2010." Department of Public Health, San Francisco 2011, Fig 6.1.

Annual HIV diagnoses and deaths for MSM in the United Kingdom, 1981-2005



Hart, G. "Epidemiology of HIV acquisition and transmission in MSM." Expert seminar: 'Partnership patterns and HIV prevention amongst MSM.' National AIDS Trust, June 2009.

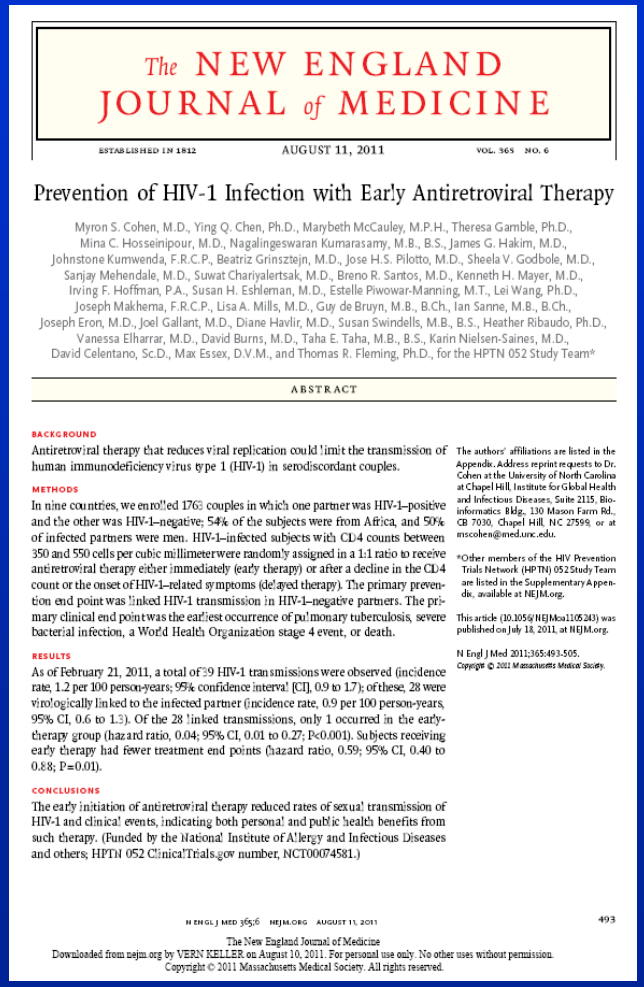
Can treatment prevent transmission?

(a) Does viral load determine the risk of HIV transmission?

(b) Can ART prevent HIV transmission by reducing viral load?

(c) Can reducing viral load with ART to ‘undetectable’ levels stop HIV transmission in the population?

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



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Prevention of HIV-1 Infection with Early Antiretroviral Therapy

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ABSTRACT

BACKGROUND

Antiretroviral therapy that reduces viral replication could limit the transmission of human immunodeficiency virus type 1 (HIV-1) in serodiscordant couples.

METHODS

In nine countries, we enrolled 1763 couples in which one partner was HIV-1–positive and the other was HIV-1–negative; 54% of the subjects were from Africa, and 50% of infected partners were men. HIV-1–infected subjects with CD4 counts between 350 and 550 cells per cubic millimeter were randomly assigned in a 1:1 ratio to receive antiretroviral therapy either immediately (early therapy) or after a decline in the CD4 count or the onset of HIV-1–related symptoms (delayed therapy). The primary prevention end point was linked HIV-1 transmission in HIV-1–negative partners. The primary clinical end point was the earliest occurrence of pulmonary tuberculosis, severe bacterial infection, a World Health Organization stage 4 event, or death.

RESULTS

As of February 21, 2011, a total of 39 HIV-1 transmissions were observed (incidence rate, 1.2 per 100 person-years; 95% confidence interval [CI], 0.9 to 1.7); of these, 28 were virologically linked to the infected partner (incidence rate, 0.9 per 100 person-years, 95% CI, 0.6 to 1.3). Of the 28 linked transmissions, only 1 occurred in the early-therapy group (hazard ratio, 0.04; 95% CI, 0.01 to 0.27; P<0.001). Subjects receiving early therapy had fewer treatment end points (hazard ratio, 0.59; 95% CI, 0.40 to 0.88; P=0.01).

CONCLUSIONS

The early initiation of antiretroviral therapy reduced rates of sexual transmission of HIV-1 and clinical events, indicating both personal and public health benefits from such therapy. (Funded by the National Institute of Allergy and Infectious Diseases and others; HPTN 052 ClinicalTrials.gov number, NCT00074581.)

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N Engl J Med 2011;365:493-505.

- Study of 1,763 serodiscordant couples, 97% were heterosexual. Definitive conclusions about MSM cannot be drawn from these results. At enrolment HIV infected partners had CD4+ T cell levels between 350 and 550 cells/mm^3.
- There were two study groups: In the first antiretroviral therapy was started immediately and in the second it was postponed until 250 cells/mm^3, 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 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.

Cohen, M. S. et al. N Engl J Med 2011; 365: 493-505.

Strategic limitations of HPTN 052

- Definite conclusions about MSM cannot be drawn from these results as almost all of the sample was heterosexual. This matters because anal sex entails a far higher risk of HIV transmission than vaginal sex.
- Prevention effectiveness in real world situations outside the highly controlled clinical trial environment is not addressed, and it is not known if the levels of treatment adherence observed here can be sustained over the long term.
- The extent to which early treatment will be accompanied in practice by reductions in condom use is undetermined, and treatment of HIV infected partners does not - of course - limit the risk of HIV acquisition from other sources.
- The extremely high infectivity in the acute stage of HIV disease also means that treatment-based HIV prevention cannot control HIV transmission on its own because extensive opportunities for HIV spread exist in the first few weeks after infection.

Per-contact probability of HIV transmission in homosexual men in Sydney in the era of HAART

Per-contact probability of HIV transmission in homosexual men in Sydney in the era of HAART

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Objective: The objective of this study is to estimate per-contact probability of HIV transmission in homosexual men due to unprotected anal intercourse (UAI) in the era of HAART.

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

Methods: A total of 1427 participants were recruited from June 2001 to December 2004. They were followed up with 6-monthly detailed behavioral interviews and annual testing for HIV till June 2007. Data were used in a bootstrapping method, coupled with a statistical analysis that optimized a likelihood function for estimating the per-exposure risks of HIV transmission due to various forms of UAI.

Results: During 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 (CI) 0.48–2.85] if ejaculation occurred inside the rectum, and it was 0.65% (95% CI 0.15–1.53) if withdrawal prior to ejaculation was involved. The estimated transmission rate for insertive UAI in participants who were circumcised was 0.11% (95% CI 0.02–0.24), and it was 0.62% (95% CI 0.07–1.68) in uncircumcised men. Thus, receptive UAI with ejaculation was found to be approximately twice as risky as receptive UAI with withdrawal or insertive UAI for 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 is similar to estimates reported from developed country settings in the pre-HAART era.

AIDS 2010, **24**:907–913

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 serodiscordant monogamous couples are more readily available for study

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- "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 that 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.

Jin, F. et al. AIDS 2010; 24: 907-13.

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

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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 risk behaviour and resurgent epidemics have been widely reported post-highly active antiretroviral therapy. The aim of this study was to quantify the impact that highly active antiretroviral therapy had on the epidemic.

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 changes in risk behaviour and diagnosis rate needed to explain annual data on HIV and AIDS diagnoses.

Results: We show that the reproduction number $R(t)$, a measure of the state of the epidemic, declined early on from initial values above two and was maintained below one from 1985 to 2000. Since 1996, when highly active antiretroviral therapy became widely used, the risk behaviour rate has increased 66%, resulting in an increase of $R(t)$ to 1.04 in the latest period 2000–2004 (95% confidence interval 0.98–1.09) near or just above the threshold for a self-sustaining epidemic. Hypothetical scenario analysis shows that the epidemiological benefits of highly active antiretroviral therapy and earlier diagnosis on incidence have been entirely offset by increases in the 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 increasing sexual risk behaviour.

AIDS 2008, **22**:1071–1077

Keywords: antiretroviral therapy, homosexual men, infectious diseases, mathematical models, models/projections, sexual behaviour, surveillance

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- "The joint effect of HAART and risk behaviour on HIV incidence has been previously studied using mathematical models and empirical data. Although based on different assumptions, all these studies come to the same conclusion regarding the potential for an increase in risk behaviour to offset the benefits of HAART in reducing transmission."
- 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."

Bezemer, D. et al. AIDS 2008; 22: 1071-77.

Modelling sexual transmission of HIV: Testing the assumptions, validating the predictions

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

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Current Opinion in HIV and AIDS 2010, 5:269–276

Purpose of review
To discuss the role of mathematical models of sexual transmission of HIV: the methods used and their impact.
Recent findings
We use mathematical modelling of 'universal test and treat' as a case study to illustrate wider issues relevant to all modelling of sexual HIV transmission.
Summary
Mathematical models are used extensively in HIV epidemiology to deduce the logical conclusions arising from one or more sets of assumptions. Simple models lead to broad qualitative understanding, whereas complex models can encode more realistic assumptions and, thus, be used for predictive or operational purposes. An overreliance 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 recent public health policy, but may not adequately reflect the uncertainty inherent in the analysis.

Keywords
male circumcision, mathematical modelling, sexual transmission, test and treat

Curr Opin HIV AIDS 5:269–276

1746-630X

Introduction

Mathematical models have played important roles facilitating understanding of HIV epidemiology and evaluating the performance of prevention initiatives [1]. From the earliest models examining the interaction between HIV and other sexually transmitted infections (STIs) [2], the effects of sexual mixing patterns between 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 initiatives [9–11]. 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 [12**,13]. When such precision is 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 (such as 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 stakeholder community [1]. 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 male 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 denotes 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, vaccination of a

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- 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.
- "The relationship between *individual level efficacy and population level effectiveness* is not straightforward because of the indirect benefits of prevention, but also because people may be exposed to HIV multiple times in a lifetime."
- "Mathematical models are ideal tools for exploring these complex relationships between different scenarios, and therefore for relating individual efficacy to population effectiveness in different settings."

Baggaley, R.F. Fraser, C. Curr Opin HIV AIDS 2010; 5: 269-76.

Modelling trends in HIV incidence among homosexual men in Australia, 1995-2006

EPIDEMIOLOGY AND SOCIAL SCIENCE

Modeling Trends in HIV Incidence Among Homosexual Men in Australia 1995–2006

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Background: Previous mathematical models have indicated that any decrease in HIV incidence in homosexual men due to decreased infectiousness from antiretroviral treatment (ARV) may be offset by modest increases in unsafe sex. The aims of this study were to assess the effects of ARV use and increasing unprotected anal intercourse with casual partners (UAIC) in homosexual men on HIV incidence during 1995–2001 and to project HIV incidence depending on trends in ARV use and UAIC.

Methods: A mathematical model of HIV transmission among homosexual men in Australia was developed. HIV incidence during 1995–2001 was estimated assuming that 70% of men in whom HIV was diagnosed received ARVs and assuming a 10% annual increase in UAIC. For 2001–2006, scenarios included ARV levels remaining at 70% or declining to 50% by 2006, combined with UAIC levels remaining at the 2001 level or continuing to increase annually by 10%.

Findings: The number of incident HIV cases per year was predicted to have declined during 1996–1998 due to the introduction of effective ARVs, with a slow increase during 1998–2001 due to increased levels of UAIC when use of therapies was fairly stable. From 2001, a continued increase in UAIC was predicted to lead to a rise in HIV incidence. A rise in UAIC combined with a moderate decline in ARV use could lead to a 50% increase in HIV incidence by 2006.

Interpretation: These models suggest that widespread ARV use has had some effect in reducing HIV incidence among homosexual men in Australia. However, if current trends in UAIC and ARV use continue, a resurgent HIV epidemic is predicted.

Key Words: antiretroviral therapy, HIV incidence, homosexual men, mathematical models, sexual behavior

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Conflict of interest: None.

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Previous mathematical models of HIV incidence in homosexual men have indicated that any decrease in HIV transmissions due to decreased infectiousness of men receiving antiretroviral treatment (ARV) may be offset by relatively modest increases in unsafe sex.[1–4] However, it has been recently suggested, again based on mathematical models, that widespread ARV treatment could be a method for eradicating HIV.[4]

There is evidence among homosexual men in Australia of increasing rates of unprotected anal intercourse with casual partners (UAIC) over the period 1996–2001.[5,6] Among homosexually active men participating in periodic surveys, reported rates of UAIC increased in Sydney from 14% in 1996 to 26% in 2001, in Brisbane from 14% in 1998 to 19% in 2001, and in Melbourne from 13% in 1998 to 17% in 2001. Uptake of ARV treatment among homosexual men was very rapid during 1996 and 1997 and reached a plateau with about 70% of men in whom HIV was diagnosed receiving treatment.[7] However, with increasing data regarding the efficacy and long-term toxicities of ARVs, an increasing number of men with HIV are either interrupting treatment or initiating ARVs at a later time in the disease, leading to a lower proportion of all HIV-infected persons receiving ARVs.[5,8]

In this paper we use a mathematical model of HIV transmission among homosexual men in Australia to assess 2 research questions. First, what were the competing effects of widespread ARV usage but increasing UAIC in homosexual men on HIV incidence? Second, what trends in HIV incidence in homosexual men are projected depending on future use of ARVs and trends in UAIC?

METHODS

Our previous mathematical models[3,9] of HIV transmission among homosexual men in Australia were extended to cover the period 1995–2006. Model states were included for those uninfected with HIV together with states for those infected with HIV by immunologic status (CD4 > 500 cells/mm^3, 200 ≤ CD4 ≤ 500, CD4 < 200, AIDS) by those being undiagnosed, diagnosed and not on treatment, or diagnosed and on treatment (Fig. 1). Transitions between states includes infection with and without early diagnosis, a decline

- This model aims to assess the effects of ARV use and steadily increasing levels of unprotected anal sex with casual partners (UAIC) on HIV incidence in homosexual men.
- A continued increase in UAIC is predicted to lead to a rise in HIV incidence.
- A rise in UAIC combined with a moderate decline in ARV use could lead to a substantial increase in HIV incidence.
- This model suggests that "widespread ARV use has had some effect in reducing HIV incidence among homosexual men in Australia. However, if current trends in UAIC and ARV use continue, a resurgent HIV epidemic is predicted."

Clements, M.S. et al. J Acq Imm Def Syn 2004; 35: 401-06.

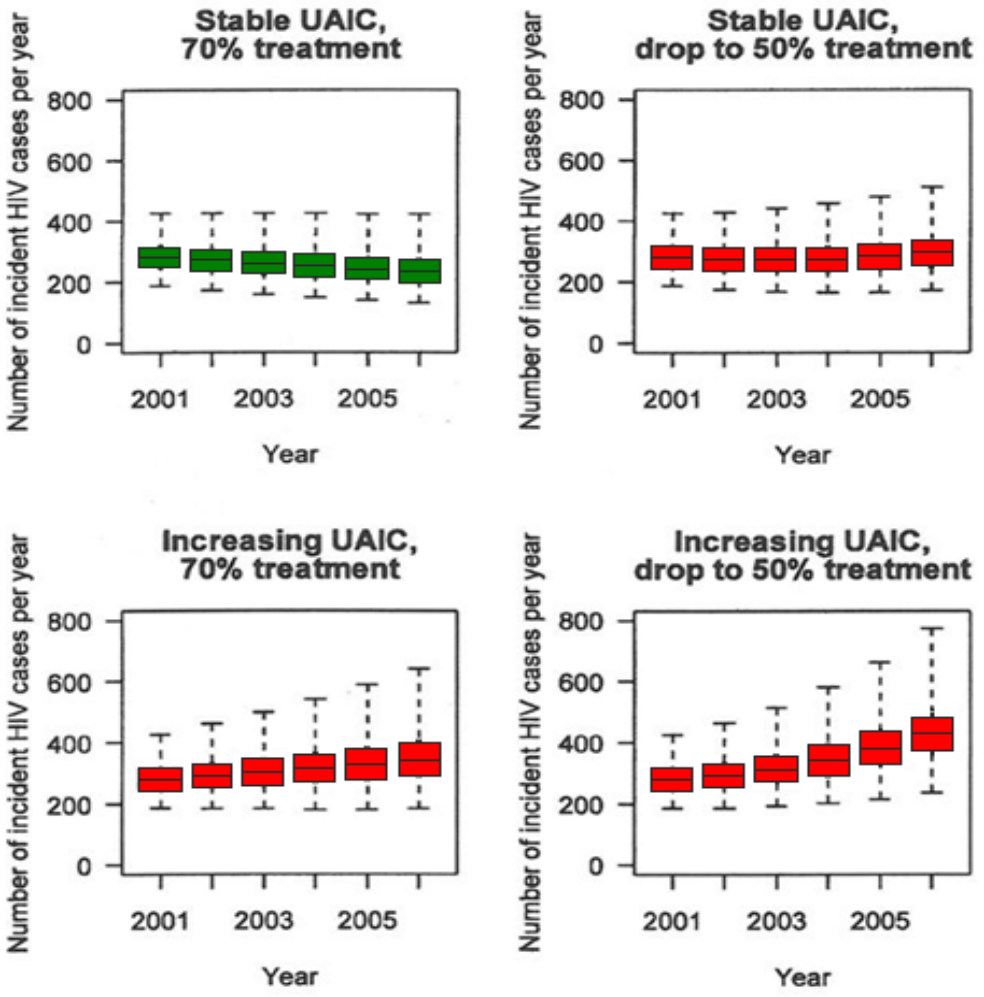
Modelling of HIV incidence among MSM in Australia

HIV incidence ↓ 17%

HIV incidence ↑ 5%

HIV incidence ↑ 22%

HIV incidence ↑ 53%



Clements, M.S. et al. J Acq Imm Def Syn 2004; 35: 401-06.

Models of the impact of ART on HIV transmission

First author	Key comments and conclusions
Velasco-Hernandez 1994	If HIV infected persons are detected and treated, but the sexual behaviour of high risk individuals does not change, a high prevalence of HIV in the population will be maintained.
Law 2001	Apparently large decreases in infectiousness as a result of treatment can be counterbalanced by much more modest increases in unsafe sex.
Law 2002	Even small increases in STI (as a result of more unprotected anal sex) could have an important multiplicative effect on HIV incidence.
Katz 2002	Any decrease in per-contact risk of HIV transmission due to HAART use appears to have been counterbalanced or overwhelmed by increases in the number of unsafe sexual episodes.
Xiridou 2003	A reduction of 75-99% in infectivity caused by HAART will be counterbalanced by increases of 50% (range 30-80%) in risky behaviour with steady partners.
Boily 2004	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 sexual behaviour in the population.
Porco 2004	The benefit of reduced HIV transmission in the community due to widespread use of HAART can be offset by increases in unsafe sexual encounters. Continued emphasis on the avoidance of exposure is essential for success at population level.

First author	Key comments and conclusions
Abbas 2006	The impact of therapy is greater when introduced earlier in the course of the epidemic, but the benefit can be lost by residual infectivity and by sexual disinhibition of the at risk population.
Baggaley 2006	Counselling of patients to promote safe sexual practices is essential. This must aim to effect long term change and prevent behavioural disinhibition, not only for ART patients but for all individuals at risk.
McCormick 2007	These results suggest that ART must be accompanied by effective HIV risk reduction interventions. Prevention programmes that decrease HIV transmission are crucial to epidemic control.
Wilson 2008	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.
Salomon 2008	Treatment alone should not be expected to alter the population-level incidence of new infections dramatically in generalised epidemics, in absence of changes including behavioural responses among both uninfected persons and infected persons who are not on treatment.
Hallet 2010	The main message for patients is that always using condoms during treatment is the best way to protect their partners from the risk of HIV transmission.
Bezemer 2010	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. The most effective way to prevent this is to decrease risk behaviour.

Risk of transmission in discordant couples

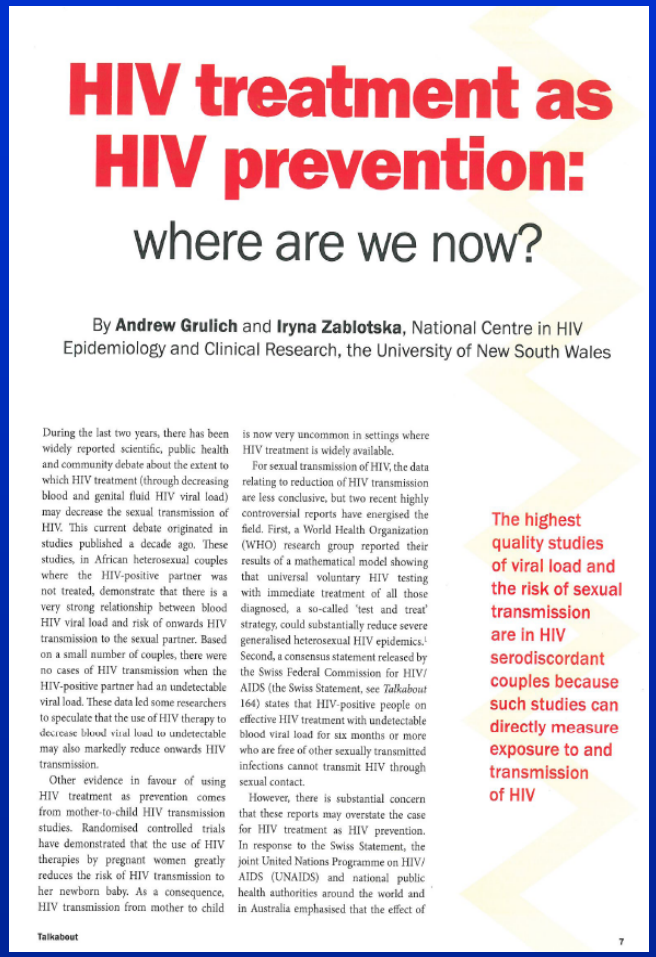
- "We need to separate out the role of treatment for a couple and effects of treatment in the population as a whole. At a population level, there has been an upsurge of risk in some communities, identified by an increasing incidence in other sexually transmitted infections and an increasing incidence of HIV. However, much of this upsurge will be due to risk-taking behaviour, influenced indirectly by the availability of antiretrovirals, by those who are susceptible or infected without being aware of it."

- "The use of antiretrovirals should directly decrease the incidence of infection, but this population-level effect will be limited unless diagnosis is more timely and treatment is used much earlier during infection for public-health reasons rather than necessarily for clinical care."

- "We should [also] be concerned about the spread of other sexually transmitted infections if condoms are not used…asymptomatic sexually transmitted infections might, though local HIV replication, reintroduce a risk of transmission in a discordant couple."

Garnett, G.P. Gazzard, B. Lancet 2008; 372: 270-71.

HIV treatment for prevention: Where are we now?



HIV treatment as HIV prevention:

where are we now?

By **Andrew Grulich** and **Iryna Zablotska**, National Centre in HIV Epidemiology and Clinical Research, the University of New South Wales

During the last two years, there has been widely reported scientific, public health and community debate about the extent to which HIV treatment (through decreasing blood and genital fluid HIV viral load) may decrease the sexual transmission of HIV. This current debate originated in studies published a decade ago. These studies, in African heterosexual couples where the HIV-positive partner was not treated, demonstrate that there is a very strong relationship between blood HIV viral load and risk of onwards HIV transmission to the sexual partner. Based on a small number of couples, there were no cases of HIV transmission when the HIV-positive partner had an undetectable viral load. These data led some researchers to speculate that the use of HIV therapy to decrease blood viral load to undetectable may also markedly reduce onwards HIV transmission.

Other evidence in favour of using HIV treatment as prevention comes from mother-to-child HIV transmission studies. Randomised controlled trials have demonstrated that the use of HIV therapies by pregnant women greatly reduces the risk of HIV transmission to her newborn baby. As a consequence, HIV transmission from mother to child is now very uncommon in settings where HIV treatment is widely available.

For sexual transmission of HIV, the data relating to reduction of HIV transmission are less conclusive, but two recent highly controversial reports have energised the field. First, a World Health Organization (WHO) research group reported their results of a mathematical model showing that universal voluntary HIV testing with immediate treatment of all those diagnosed, a so-called 'test and treat' strategy, could substantially reduce severe generalised heterosexual HIV epidemics.[1] Second, a consensus statement released by the Swiss Federal Commission for HIV/AIDS (the Swiss Statement, see *Talkabout* 164) states that HIV-positive people on effective HIV treatment with undetectable blood viral load for six months or more who are free of other sexually transmitted infections cannot transmit HIV through sexual contact.

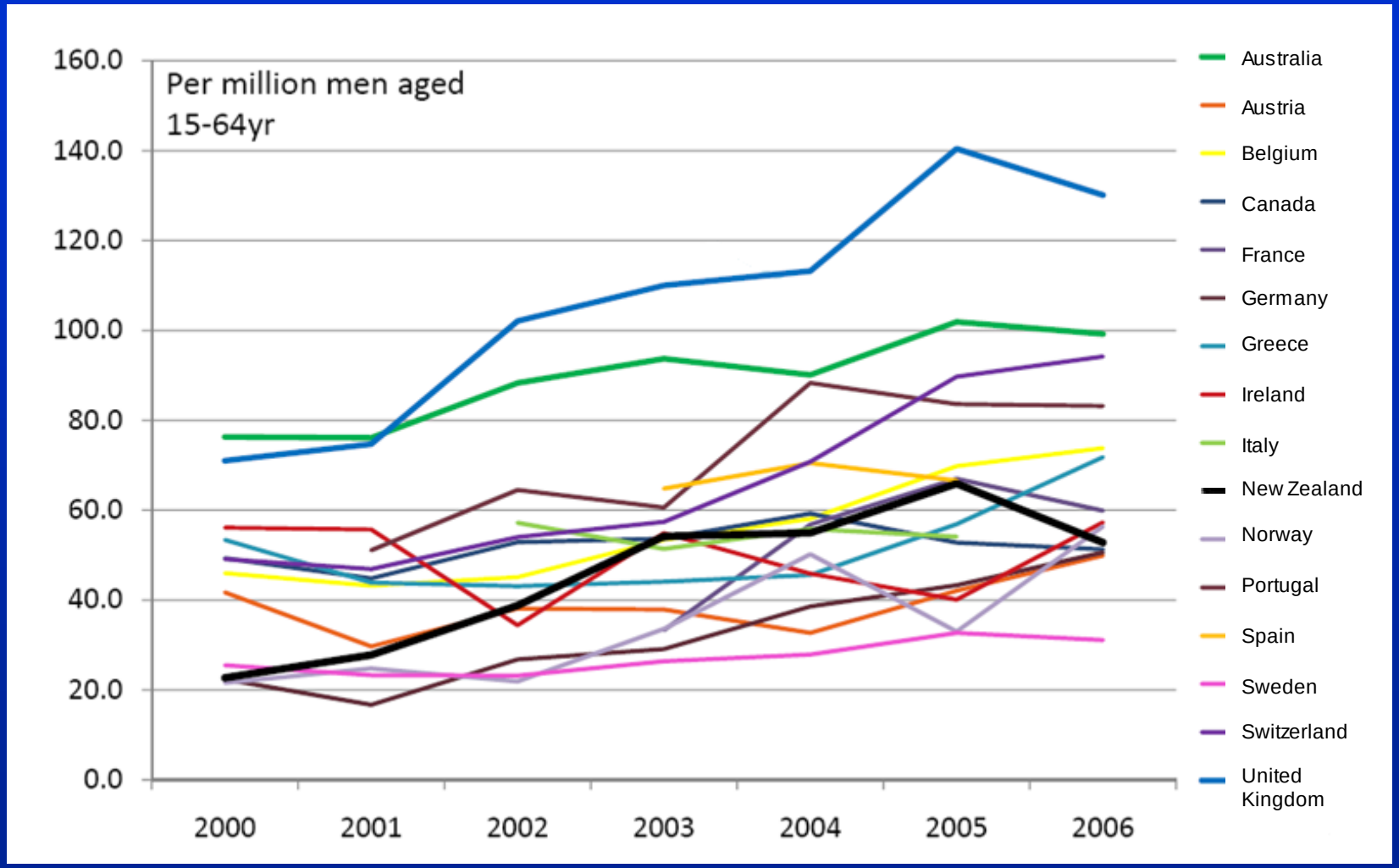
However, there is substantial concern that these reports may overstate the case for HIV treatment as HIV prevention. In response to the Swiss Statement, the joint United Nations Programme on HIV/AIDS (UNAIDS) and national public health authorities around the world and in Australia emphasised that the effect of

The highest quality studies of viral load and the risk of sexual transmission are in HIV serodiscordant couples because such studies can directly measure exposure to and transmission of HIV

- "While the data from heterosexual couples are sparse, they are virtually non-existent in homosexual male couples."
- "Given that transmission risk in anal intercourse is around 20-fold higher than vaginal intercourse, it is quite plausible that the relationship between undetectable viral load and HIV transmission is substantially less strong in homosexual men."
- "In Australia, as in most of the developed world, HIV transmission has recently increased markedly in homosexual men, despite the increasingly large majority of HIV-positive men on HIV therapy with undetectable viral load."
- "This is suggestive - although by no means conclusive - evidence that HIV therapy is substantially less than 100% effective in preventing HIV transmission between homosexual men."

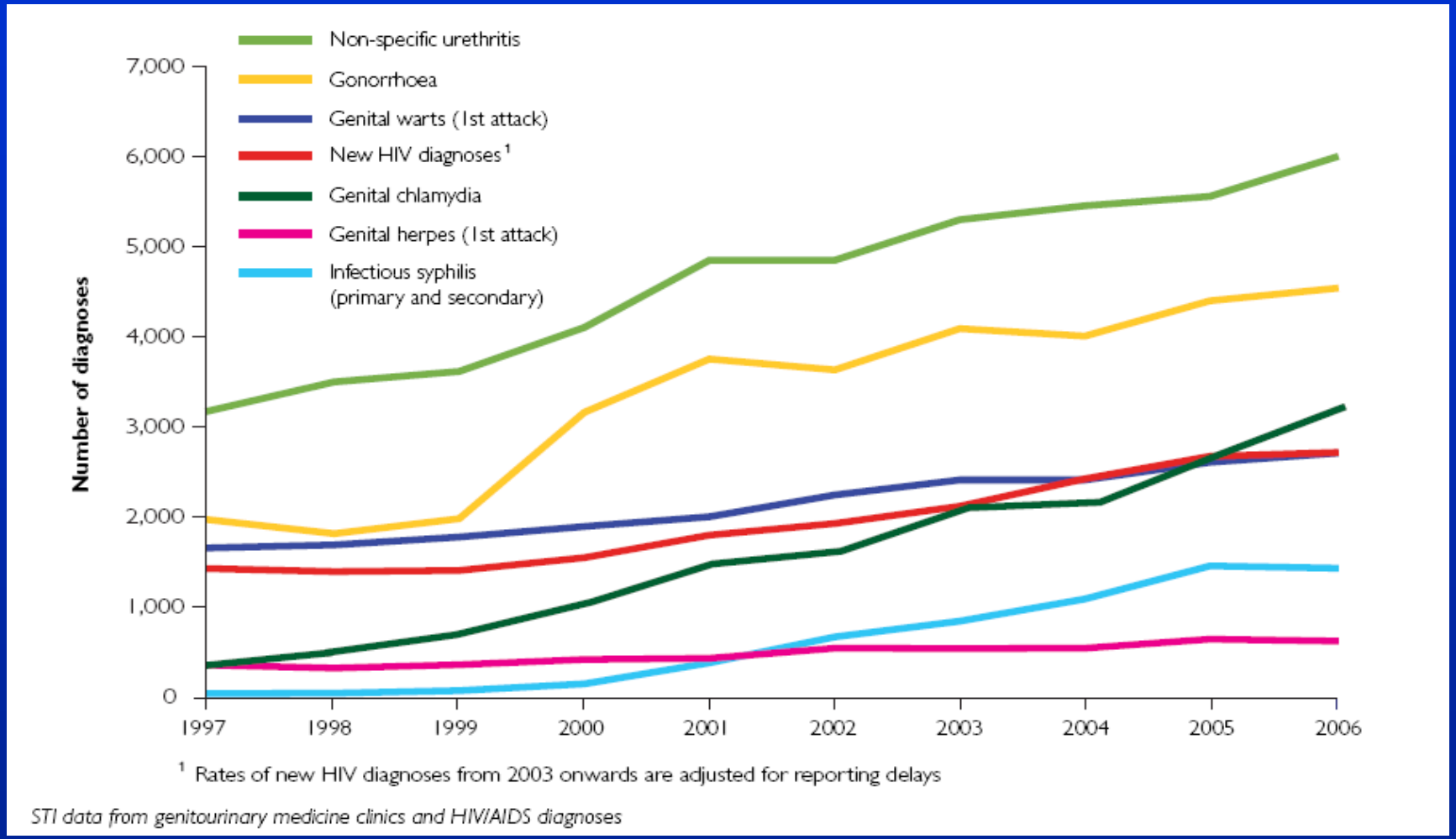
Grulich, A. Zablotska, I. Talkabout, Sept-Nov 2010.

HIV diagnosis rate among MSM in major Western European countries plus Australia, Canada and New Zealand



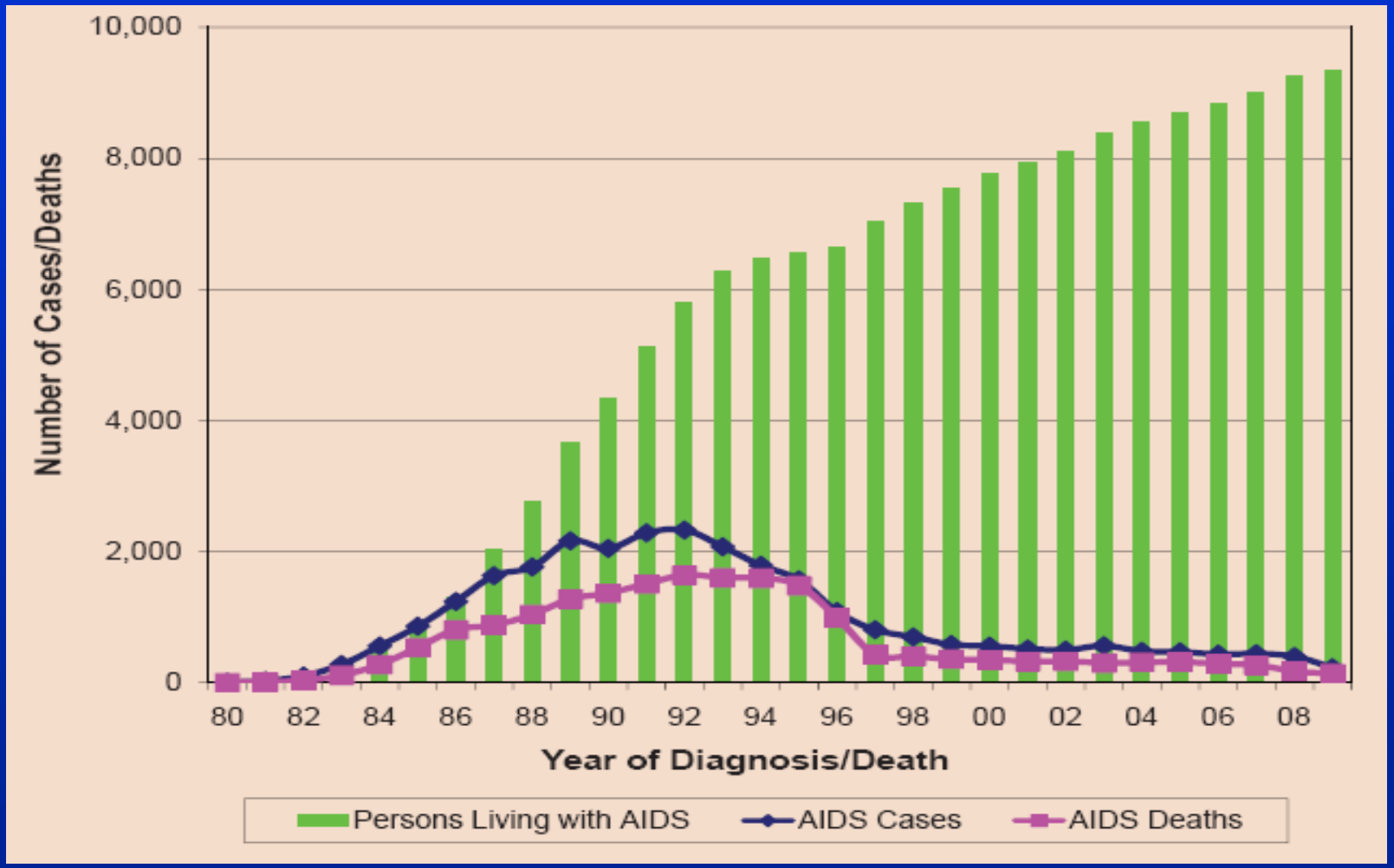
Adapted from: Dickson, N.P. "HIV/AIDS epidemic update." Presented at: 'HIV clinical update meeting.' Auckland City Hospital, 20 Feb 2009.

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



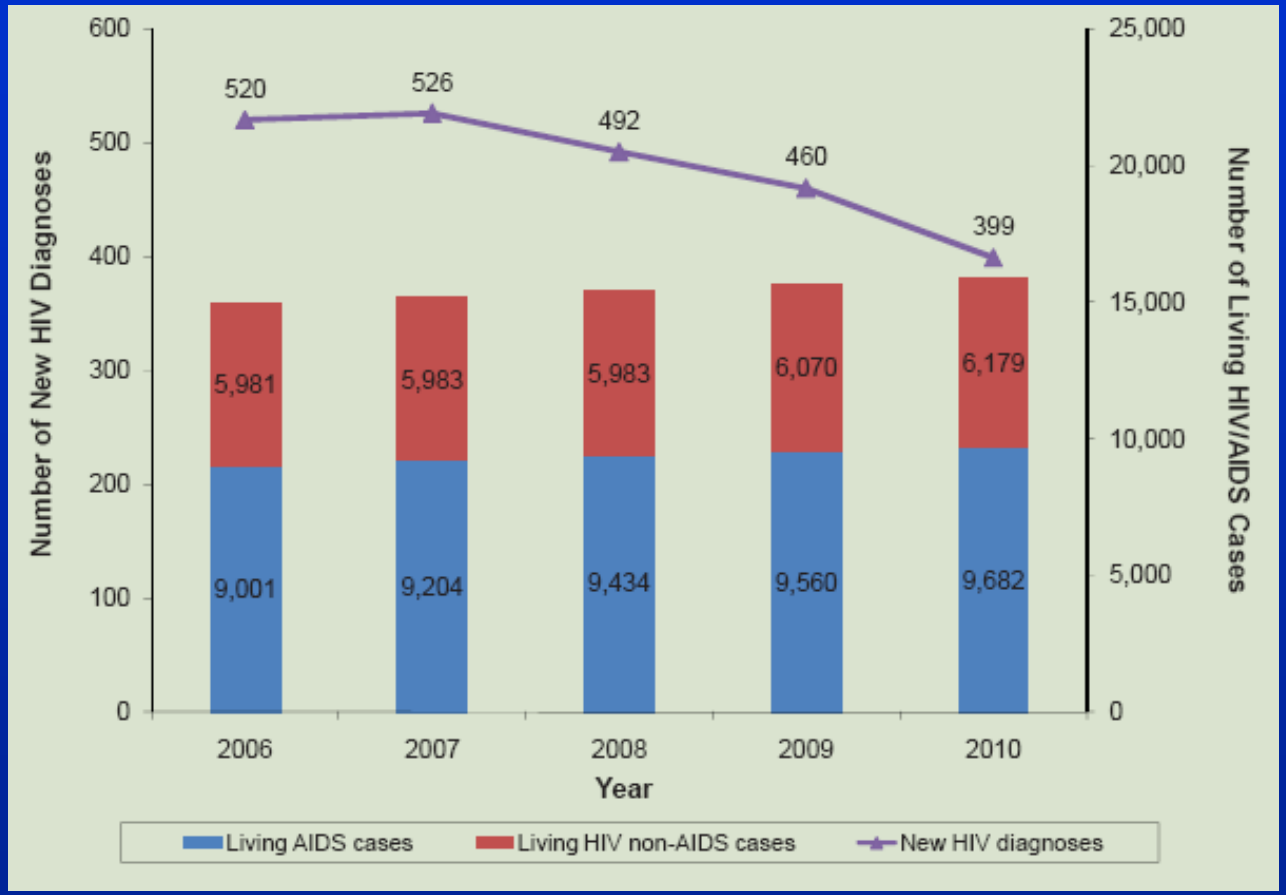
Health Protection Agency. "Testing times, HIV and other sexually transmitted infections in the United Kingdom", 2007.

Total number of people living with AIDS in San Francisco



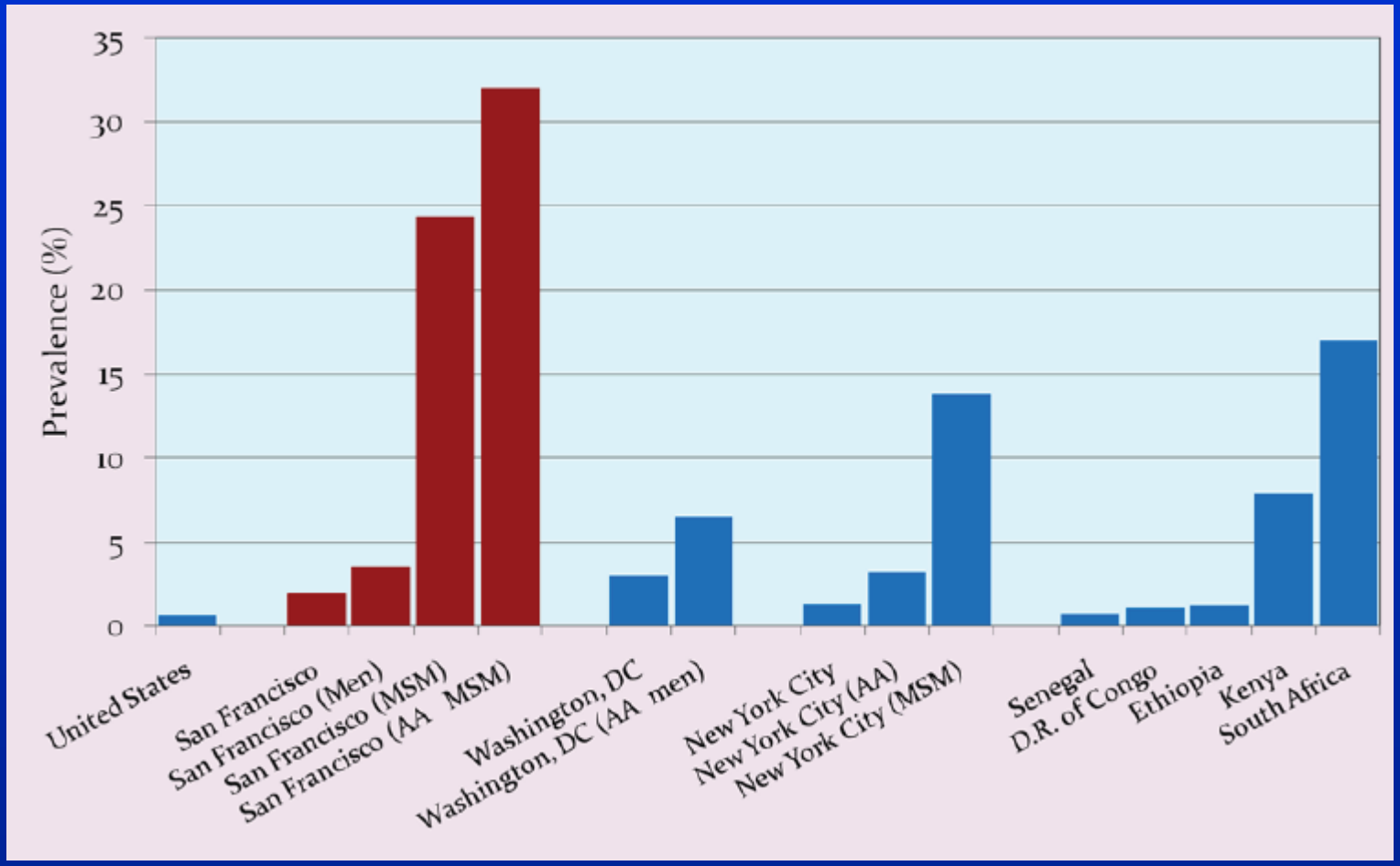
"HIV/AIDS epidemiology annual report 2009." Department of Public Health, San Francisco 2010, Fig 1.1.

Number of cases diagnosed with HIV infection and HIV/AIDS prevalence in San Francisco, 2006-2010



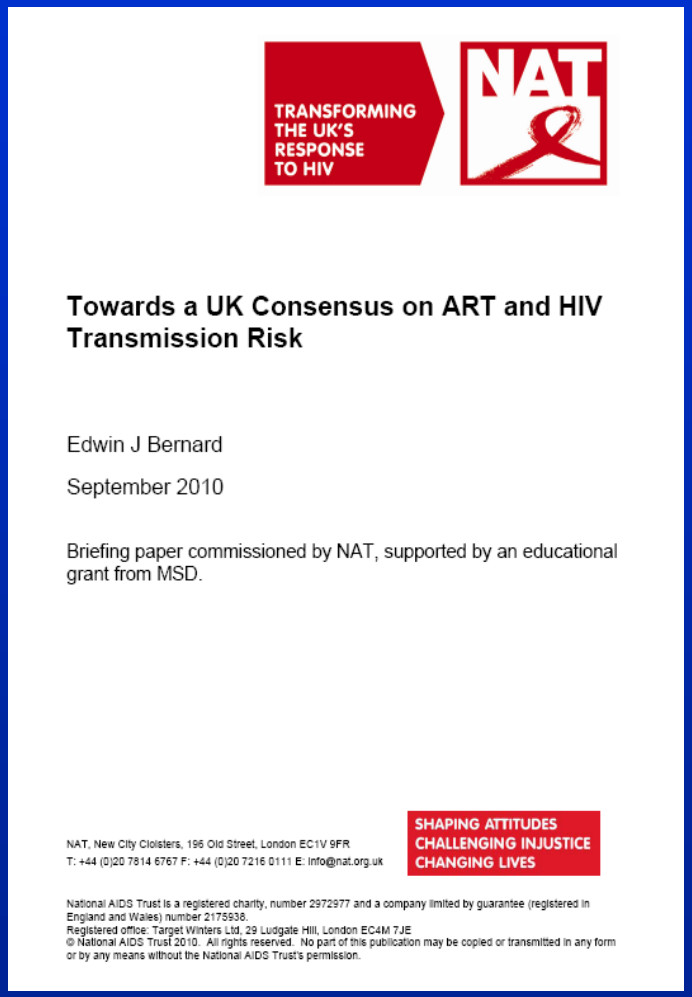
"HIV/AIDS epidemiology annual report 2010." Department of Public Health, San Francisco 2011, Fig 1.2.

HIV prevalence in MSM in San Francisco, 2007



Colfax, G. "HIV prevention update," Community and Public Health Committee, San Francisco Department of Health, 16 March 2010.
Data from: El-Sadr, W.M. "AIDS in America – forgotten but not gone." N Engl J Med 2010; 362: 967-70.

Four different strategic approaches to ART use in HIV positive populations


TRANSFORMING THE UK'S RESPONSE TO HIV

NAT

Towards a UK Consensus on ART and HIV Transmission Risk

Edwin J Bernard

September 2010

Briefing paper commissioned by NAT, supported by an educational grant from MSD.

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SHAPING ATTITUDES
CHALLENGING INJUSTICE
CHANGING LIVES

There are currently four different strategic approaches to ART use in combination with existing prevention methods:

(a) 'Test and link' – strategy to increase regular HIV testing for those at high risk and ensure ongoing linkage to clinical services for all positive people.

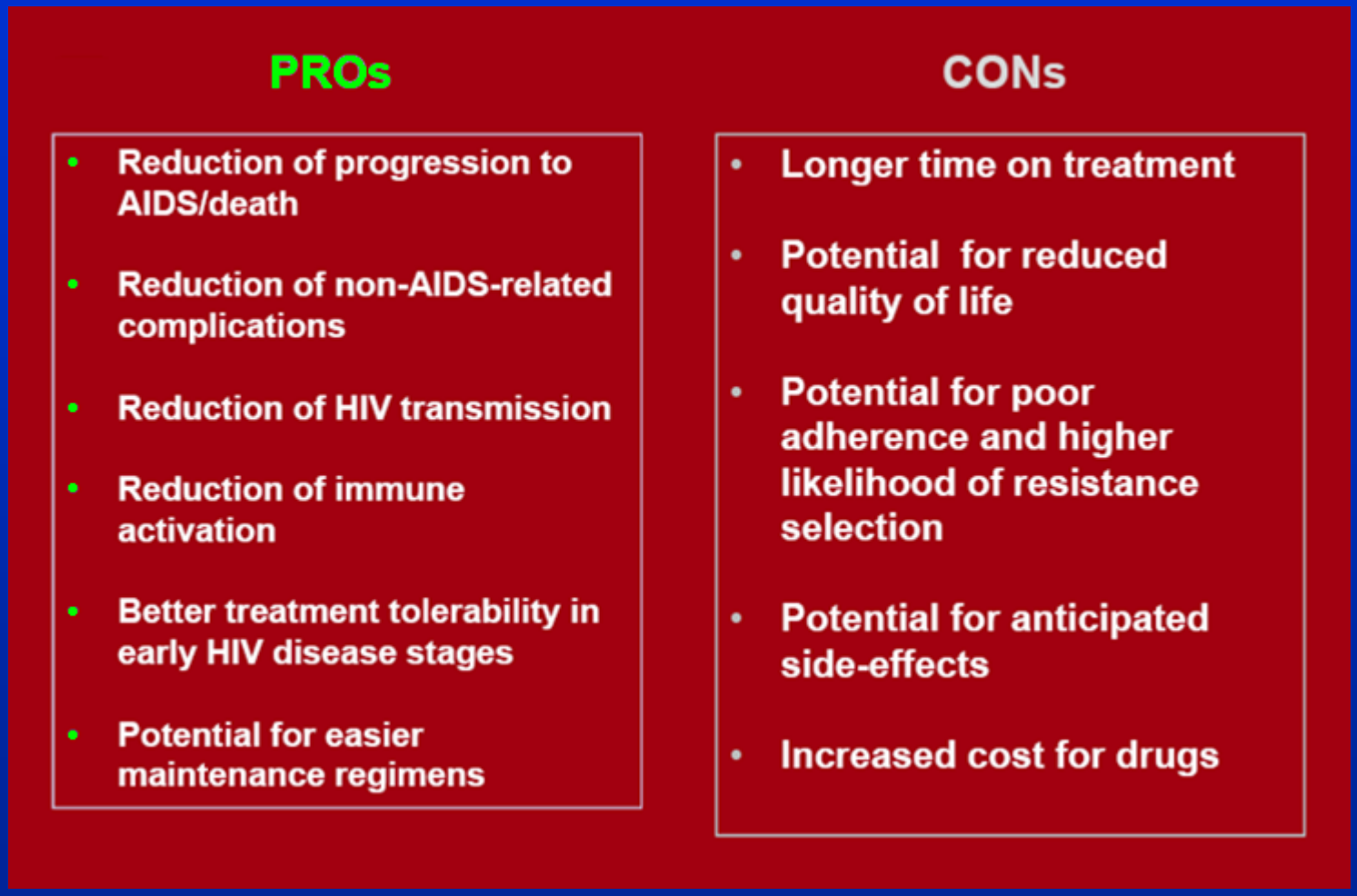
(b) 'Seek and treat' – strategy to increase treatment uptake across the whole population of HIV positive people with low CD4+ levels.

(c) 'Treat for care' – strategy to begin HIV treatment at the earliest stage that will benefit patient care.

(d) 'Test and treat' – strategy to maximize testing and begin HIV treatment immediately for public health benefit.

Bernard, E.J. National AIDS Trust, 2010.

Early HIV treatment for care: Pros and cons



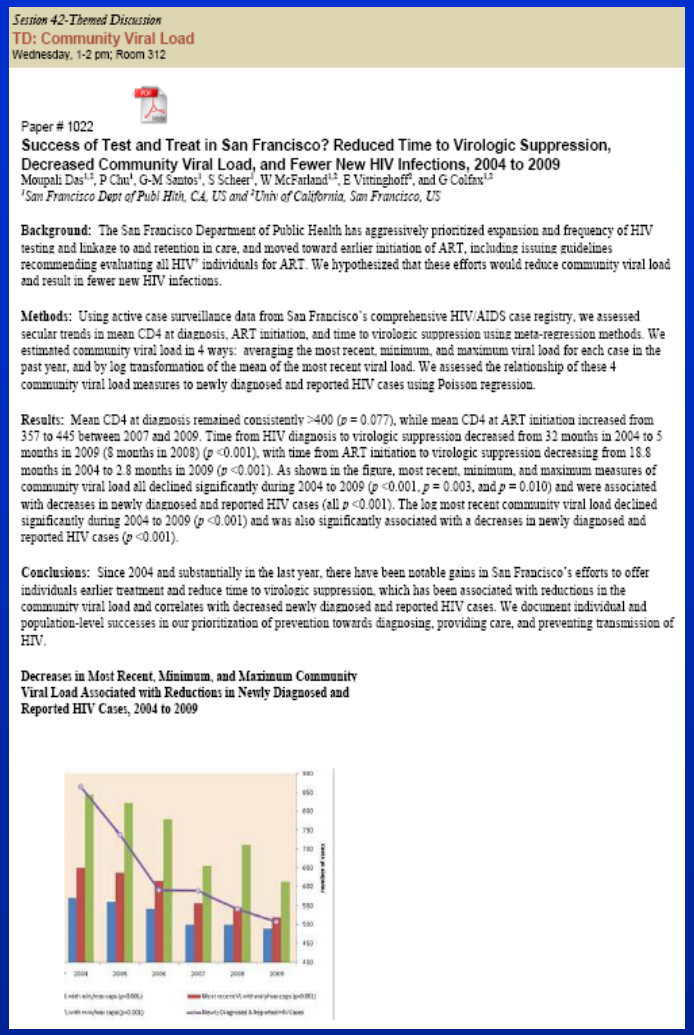
Di Perri, G. "Managing HIV treatment in 2011." Presentation: 6th International AIDS Society conference on HIV Pathogenesis, Treatment and Prevention. 17-20 July, Rome, Italy 2011.

United States DHHS treatment guidelines: CD4 count

- **1996** – all with CD4+ < 500 cells/mm^3 or CD4+ ≥ 500 and VL > 30,000 copies/mL
- **1997** – initiate if VL > 10,000 copies/ml
- **2000** – CD4+ < 350 cells/mm^3, or VL > 30,000 copies/mL, or CD4+ 350-500 cells/mm^3 and VL 5,000-30,000 copies/mL
- **2002** – definitive if CD4+ < 200 cells/mm^3, otherwise clinical judgment
- **2003** – definitive if CD4+ < 200, offer 200-350, some treat and some defer >350 cells/mm^3 and VL >55,000, and most defer if VL <55,000
- **2004** – definitive if CD4+ < 200, offer 200-350, most defer >350 cells/mm^3 and VL >100,1000, and should defer if VL <100,000
- **2008** – definitive if CD4+ < 350 cells/mm^3, otherwise consider
- **2009** – definitive if CD4+ < 500 cells/mm^3, otherwise consider

Di Perri, G. "Managing HIV treatment in 2011." Presentation: 6th International AIDS Society conference on HIV Pathogenesis, Treatment and Prevention. 17-20 July, Rome, Italy 2011.

Expanded HIV testing in San Francisco, 2004-2009



Session 42-Themed Discussion
TD: Community Viral Load
Wednesday, 1-2 pm; Room 312

Paper # 1022

Success of Test and Treat in San Francisco? Reduced Time to Virologic Suppression, Decreased Community Viral Load, and Fewer New HIV Infections, 2004 to 2009

Moupali Das[1,2], P Chu[1], G-M Santos[1], S Scheer[1], W McFarland[1,2], E Vittinghoff[3], and G Colfax[1,2]
[1]*San Francisco Dept of Publ Hlth, CA, US and* [2]*Univ of California, San Francisco, US*

Background: The San Francisco Department of Public Health has aggressively prioritized expansion and frequency of HIV testing and linkage to and retention in care, and moved toward earlier initiation of ART, including issuing guidelines recommending evaluating all HIV+ individuals for ART. We hypothesized that these efforts would reduce community viral load and result in fewer new HIV infections.

Methods: Using active case surveillance data from San Francisco's comprehensive HIV/AIDS case registry, we assessed secular trends in mean CD4 at diagnosis, ART initiation, and time to virologic suppression using meta-regression methods. We estimated community viral load in 4 ways: averaging the most recent, minimum, and maximum viral load for each case in the past year, and by log transformation of the mean of the most recent viral load. We assessed the relationship of these 4 community viral load measures to newly diagnosed and reported HIV cases using Poisson regression.

Results: Mean CD4 at diagnosis remained consistently >400 ($p = 0.077$), while mean CD4 at ART initiation increased from 357 to 445 between 2007 and 2009. Time from HIV diagnosis to virologic suppression decreased from 32 months in 2004 to 5 months in 2009 (8 months in 2008) ($p < 0.001$), with time from ART initiation to virologic suppression decreasing from 18.8 months in 2004 to 2.8 months in 2009 ($p < 0.001$). As shown in the figure, most recent, minimum, and maximum measures of community viral load all declined significantly during 2004 to 2009 ($p < 0.001$, $p = 0.003$, and $p = 0.010$) and were associated with decreases in newly diagnosed and reported HIV cases (all $p < 0.001$). The log most recent community viral load declined significantly during 2004 to 2009 ($p < 0.001$) and was also significantly associated with a decreases in newly diagnosed and reported HIV cases ($p < 0.001$).

Conclusions: Since 2004 and substantially in the last year, there have been notable gains in San Francisco's efforts to offer individuals earlier treatment and reduce time to virologic suppression, which has been associated with reductions in the community viral load and correlates with decreased newly diagnosed and reported HIV cases. We document individual and population-level successes in our prioritization of prevention towards diagnosing, providing care, and preventing transmission of HIV.

Decreases in Most Recent, Minimum, and Maximum Community Viral Load Associated with Reductions in Newly Diagnosed and Reported HIV Cases, 2004 to 2009

- "The San Francisco Department of Health has aggressively prioritised expansion and frequency of HIV testing and linkage to and retention in care, and moved toward earlier initiation of ART, including issuing guidelines recommending evaluating all HIV+ individuals for ART"
- "Time from HIV diagnosis to virological suppression decreased from 32 months in 2004 to 5 months in 2009 (8 months in 2008) (p <0.001)."
- "[M]ost recent, minimum, and maximum measures of community viral load all declined significantly during 2004 to 2009 (p <0.001, p = 0.003, and p = 0.010) and were associated with decreases in newly diagnosed and reported HIV cases (all p <0.001)."
- "Since 2004 and substantially in the last year, there have been notable gains in San Francisco's efforts to offer individuals earlier treatment and reduce time to virologic suppression, which has been associated with reductions in the community viral load and correlates with decreased newly diagnosed and reported HIV cases."

Das-Douglas, M. et al. "Success of test and treat in San Francisco?" Abstract: 18th Conference on Retroviruses and Opportunistic Infections (CROI). Boston: 2011, 27 Feb – 2 March.

Early HIV treatment for care: The current San Francisco General Hospital strategy

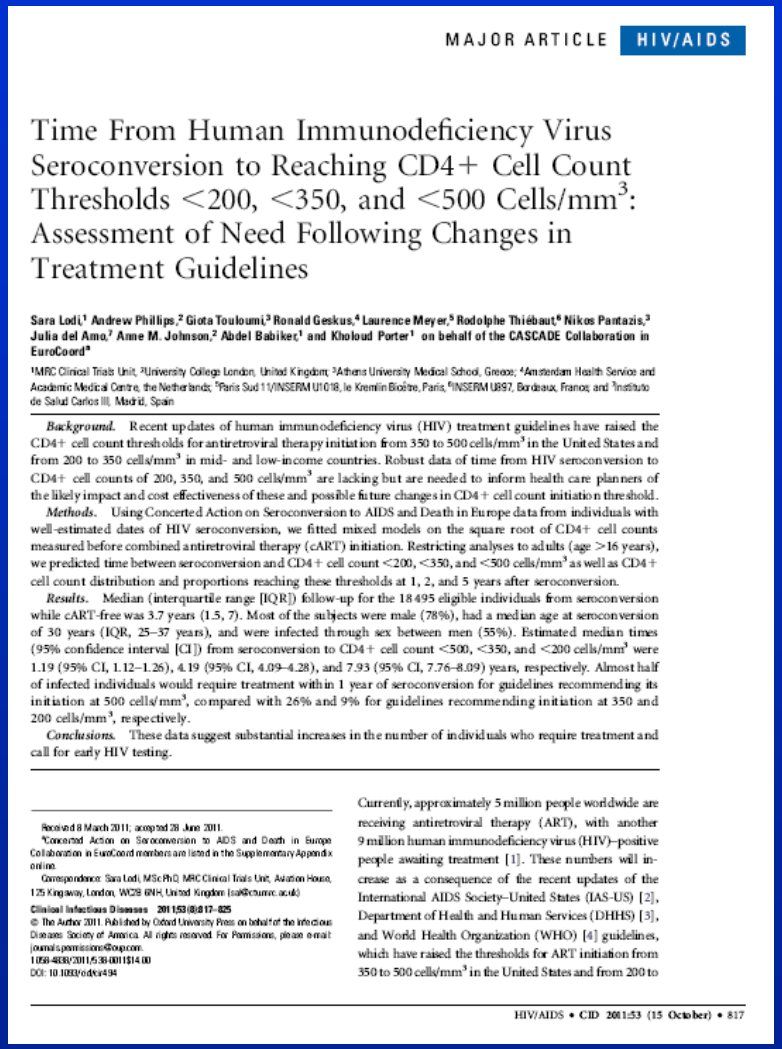
"Our clinicians recommended initiating antiretroviral therapy [for] all of our HIV-positive patients based on our assessment that delaying treatment allows the virus to do damage to major organs systems and would lead to poorer outcomes for patients. It is too early to tell if this shift in treatment strategy last year by our clinic and the Department of Health has had any impact in preventing HIV infections."

"Notwithstanding the community benefit from reduced rates of new infections – which we view as an added gain – we strongly believe that the primary reason HIV patients should start antiretroviral therapy upon diagnosis is so that they will experience better health and will have a longer life span than if they waited."

Dr Diane Havlir, Chief of the UCSF Division of HIV/AIDS at San Francisco General Hospital

Bajko, M. "HIV study: 76% drop in cases with expanded treatment." Bay Area Reporter Online. 14 April 2011.

Time from HIV seroconversion to CD4 count thresholds



MAJOR ARTICLE HIV/AIDS

Time From Human Immunodeficiency Virus Seroconversion to Reaching CD4+ Cell Count Thresholds <200, <350, and <500 Cells/mm^3: Assessment of Need Following Changes in Treatment Guidelines

Sara Lodi,[1] Andrew Phillips,[2] Giota Touloumi,[3] Ronald Geskus,[4] Laurence Meyer,[5] Rodolphe Thiébaut,[6] Nikos Pantazis,[3] Julia del Amo,[7] Anne M. Johnson,[2] Abdel Babiker,[1] and Kholoud Porter[1] on behalf of the CASCADE Collaboration in EuroCoord[a]

[1]MRC Clinical Trials Unit, [2]University College London, United Kingdom; [3]Athens University Medical School, Greece; [4]Amsterdam Health Service and Academic Medical Centre, the Netherlands; [5]Paris Sud 11/INSERM U1018, le Kremlin Bicêtre, Paris, [6]INSERM U897, Bordeaux, France; and [7]Instituto de Salud Carlos III, Madrid, Spain

Background. Recent updates of human immunodeficiency virus (HIV) treatment guidelines have raised the CD4+ cell count thresholds for antiretroviral therapy initiation from 350 to 500 cells/mm^3 in the United States and from 200 to 350 cells/mm^3 in mid- and low-income countries. Robust data of time from HIV seroconversion to CD4+ cell counts of 200, 350, and 500 cells/mm^3 are lacking but are needed to inform health care planners of the likely impact and cost effectiveness of these and possible future changes in CD4+ cell count initiation threshold.

Methods. Using Concerted Action on Seroconversion to AIDS and Death in Europe data from individuals with well-estimated dates of HIV seroconversion, we fitted mixed models on the square root of CD4+ cell counts measured before combined antiretroviral therapy (cART) initiation. Restricting analyses to adults (age >16 years), we predicted time between seroconversion and CD4+ cell count <200, <350, and <500 cells/mm^3 as well as CD4+ cell count distribution and proportions reaching these thresholds at 1, 2, and 5 years after seroconversion.

Results. Median (interquartile range [IQR]) follow-up for the 18 495 eligible individuals from seroconversion while cART-free was 3.7 years (1.5, 7). Most of the subjects were male (78%), had a median age at seroconversion of 30 years (IQR, 25–37 years), and were infected through sex between men (55%). Estimated median times (95% confidence interval [CI]) from seroconversion to CD4+ cell count <500, <350, and <200 cells/mm^3 were 1.19 (95% CI, 1.12–1.26), 4.19 (95% CI, 4.09–4.28), and 7.93 (95% CI, 7.76–8.09) years, respectively. Almost half of infected individuals would require treatment within 1 year of seroconversion for guidelines recommending its initiation at 500 cells/mm^3, compared with 26% and 9% for guidelines recommending initiation at 350 and 200 cells/mm^3, respectively.

Conclusions. These data suggest substantial increases in the number of individuals who require treatment and call for early HIV testing.

Received 8 March 2011; accepted 28 June 2011.

[a]Concerted Action on Seroconversion to AIDS and Death in Europe Collaboration in EuroCoord members are listed in the Supplementary Appendix online.

Correspondence: Sara Lodi, MSc PhD, MRC Clinical Trials Unit, Aviation House, 125 Kingsway, London, WC2B 6NH, United Kingdom (sara@ctu.mrc.ac.uk).

Clinical Infectious Diseases 2011;53(8):817–825

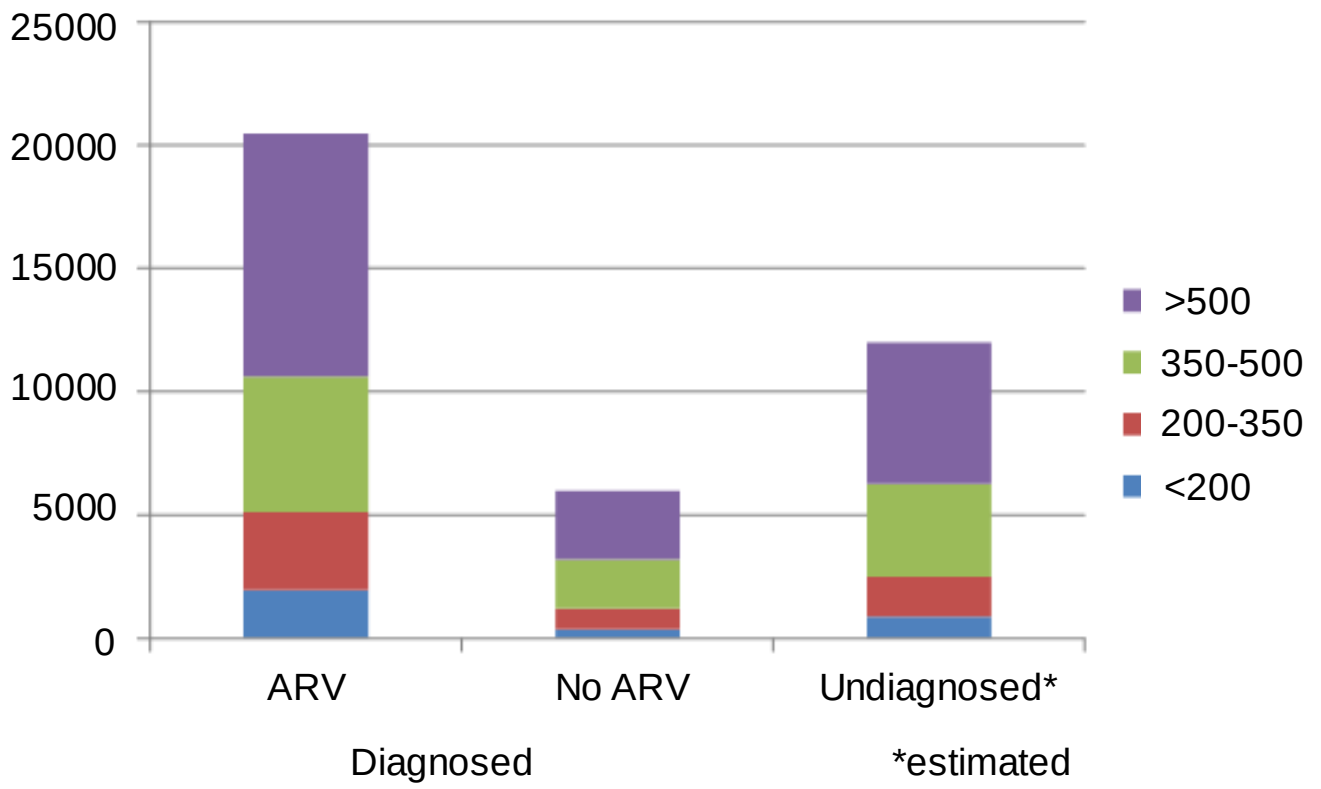
1058-4838/2011/5308-0011$14.00
DOI: 10.1093/cid/cir494

Currently, approximately 5 million people worldwide are receiving antiretroviral therapy (ART), with another 9 million human immunodeficiency virus (HIV)–positive people awaiting treatment [1]. These numbers will increase as a consequence of the recent updates of the International AIDS Society–United States (IAS-US) [2], Department of Health and Human Services (DHHS) [3], and World Health Organization (WHO) [4] guidelines, which have raised the thresholds for ART initiation from 350 to 500 cells/mm^3 in the United States and from 200 to

- Median times from seroconversion to CD4 count <500, <350 and <200 cells/mm^3 were 1.19, 4.19 and 7.93 years respectively.
- Almost half of PLWHIV would require treatment within a year of seroconversion if treatment commenced at 500 cells/mm^3, compared to 26% at 350 cells/mm^3 and 9% at 200 cells/mm^3.
- It is clear that there will be a substantial increase in the number of people requiring ARV treatment if it is started at 500 cells/mm^3.
- These findings also provide strong support for public health campaigns to encourage early HIV testing in populations at increased risk, which will enable treatment to be initiated at the optimum time for patient care.

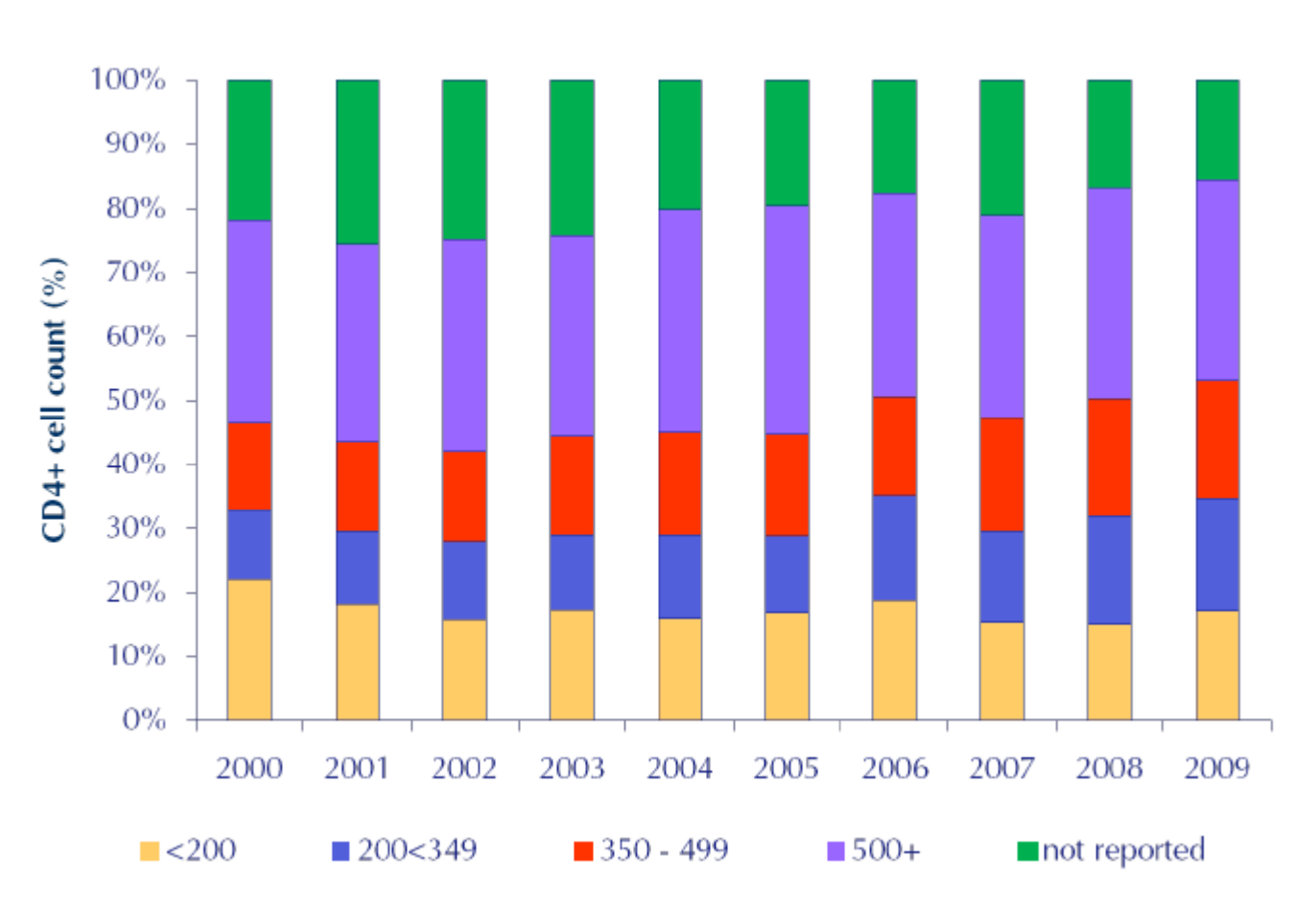
Lodi, S. et al. Clin Infect Dis 2011; 53: 817-825.

Number of HIV-infected MSM by CD4 count in the United Kingdom, 2009



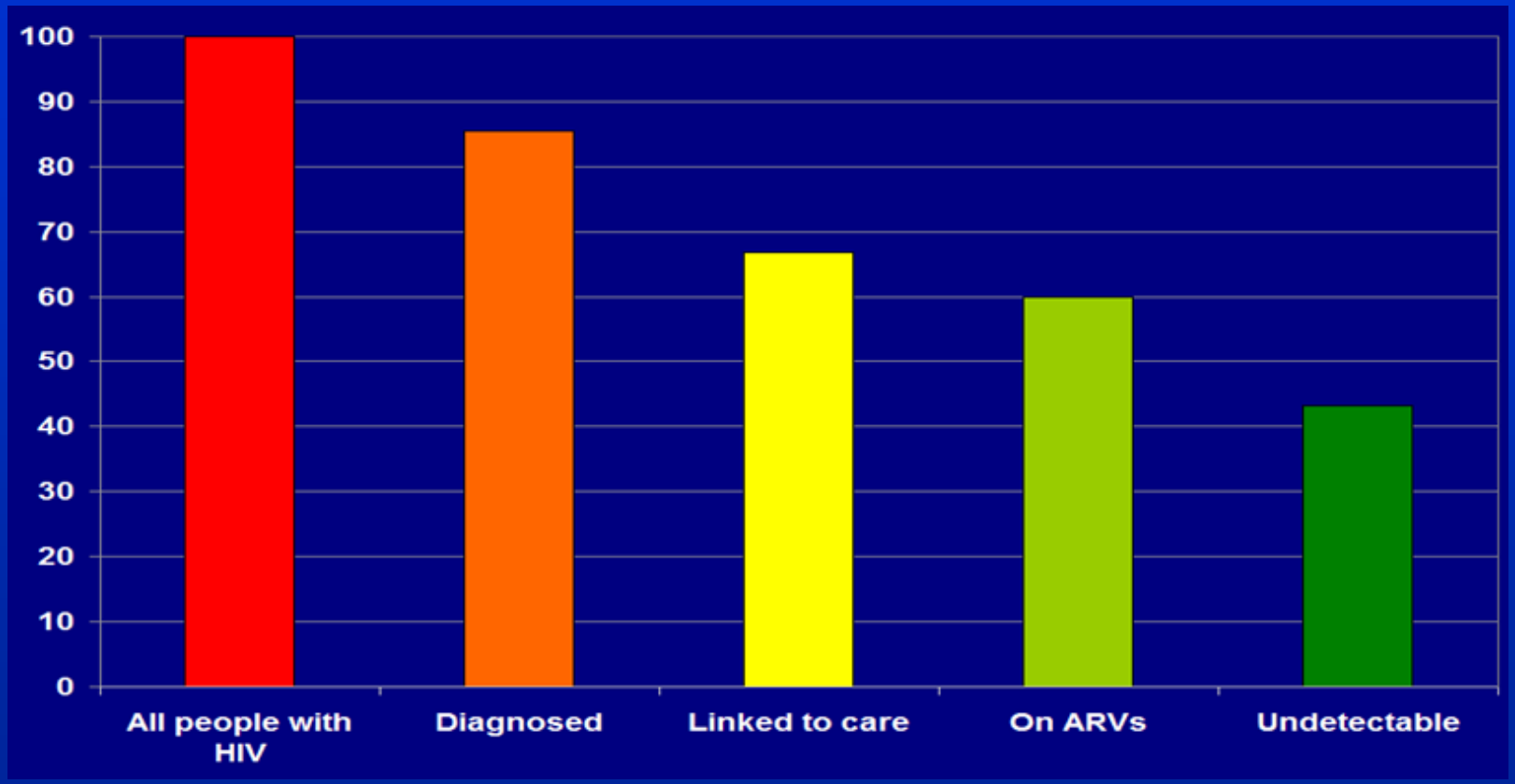
Delpech, V. Brown, A. "The current efficacy of ARV in keeping viral loads down, the population perspective." Seminar on 'treatment as prevention.' National AIDS Trust, November 2010.

CD4 count at HIV diagnosis in Australia, 2000-2009



"HIV/AIDS, viral hepatitis and sexually transmissible infections in Australia." Annual surveillance report 2010: Slide set (PDF).

Total HIV positive population in San Francisco, 2009

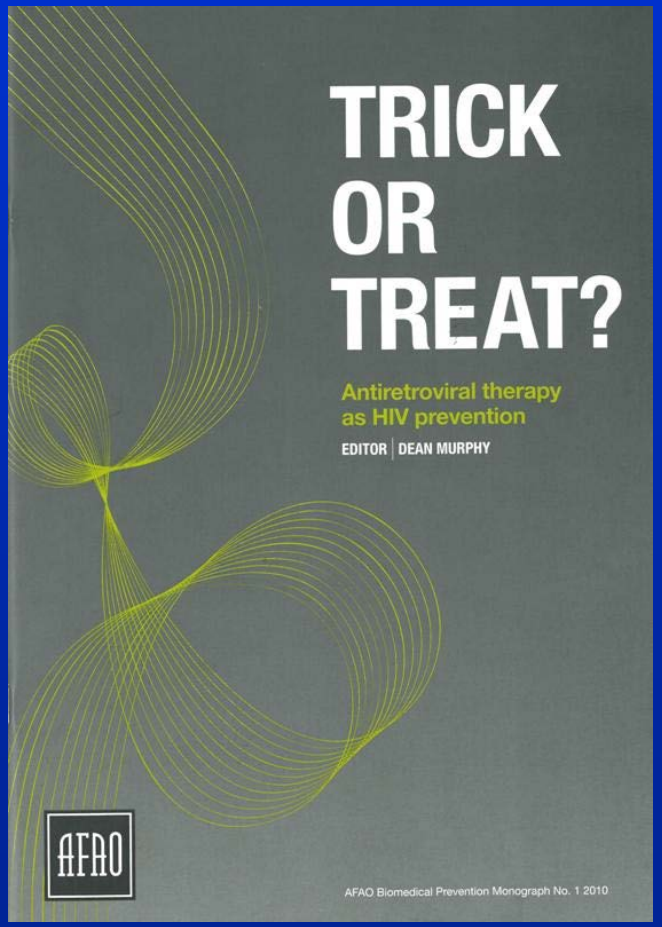


In San Francisco **85.5%** are diagnosed, of whom 78% are linked to care, of whom 90% are on ARV's, of whom 72% are undetectable = **43.2%** of people with HIV in San Francisco have an undetectable viral load due to treatment.

Cairns, G. "Treatment as prevention: why?" Expert seminar on 'treatment as prevention.' National AIDS Trust, November 2010.

Charlebois, E.D. et al. "The effect of expanded antiretroviral treatment strategies on The HIV epidemic among men who have sex with men in San Francisco." Clin Infect Dis 2011; 52: 1046-93.

Effectiveness of early treatment strategies depend on a large number of different factors



"Some of these relate to the capacity of health systems to provide the necessary treatment, monitor viral load, respond to treatment resistance, and decrease rates of sexually transmissible infections in [the] population…"

Susan Kippax, 2010.

The biggest challenge will be to ensure that drug treatment schedules are adhered to over the long term *and* consistent condom use is maintained to guarantee epidemic control at population level.

Kippax, S. "Treatment as prevention: A social science voice." In: "Trick or treat? Antiretroviral therapy as HIV prevention" Murphy, D. Ed. AFAO HIV Biomedical Prevention Series, January 2010.

Pre-exposure prophylaxis for HIV prevention in negative men who have sex with men (iPrEx)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

Robert M. Grant, M.D., M.P.H., Javier R. Lama, M.D., M.P.H., Peter L. Anderson, Pharm.D., Vanessa McMahan, B.S., Albert Y. Liu, M.D., M.P.H., Lorena Vargas, Pedro Goicochea, M.Sc., Martín Casapía, M.D., M.P.H., Juan Vicente Guanira-Carranza, M.D., M.P.H., Maria E. Ramirez-Cardich, M.D., Orlando Montoya-Herrera, M.Sc., Telmo Fernández, M.D., Valdilea G. Veloso, M.D., Ph.D., Susan P. Buchbinder, M.D., Suwat Chariyalertsak, M.D., Dr.P.H., Mauro Schechter, M.D., Ph.D., Linda-Gail Bekker, M.B., Ch.B., Ph.D., Kenneth H. Mayer, M.D., Esper Georges Kallás, M.D., Ph.D., K. Rivet Amico, Ph.D., Kathleen Mulligan, Ph.D., Lane R. Bushman, B.Chem., Robert J. Hance, A.A., Carmela Ganoza, M.D., Patricia Defechereux, Ph.D., Brian Postle, B.S., Furong Wang, M.D., J. Jeff McConnell, M.A., Jia-Hua Zheng, Ph.D., Jeanny Lee, B.S., James F. Rooney, M.D., Howard S. Jaffe, M.D., Ana I. Martinez, R.Ph., David N. Burns, M.D., M.P.H., and David V. Glidden, Ph.D., for the iPrEx Study Team*

ABSTRACT

BACKGROUND

Antiretroviral chemoprophylaxis before exposure is a promising approach for the prevention of human immunodeficiency virus (HIV) acquisition.

METHODS

We randomly assigned 2499 HIV-seronegative men or transgender women who have sex with men to receive a combination of two oral antiretroviral drugs, emtricitabine and tenofovir disoproxil fumarate (FTC–TDF), or placebo once daily. All subjects received HIV testing, risk-reduction counseling, condoms, and management of sexually transmitted infections.

RESULTS

The study subjects were followed for 3324 person-years (median, 1.2 years; maximum, 2.8 years). Of these subjects, 10 were found to have been infected with HIV at enrollment, and 100 became infected during follow-up (36 in the FTC–TDF group and 64 in the placebo group), indicating a 44% reduction in the incidence of HIV (95% confidence interval, 15 to 63; P=0.005). In the FTC–TDF group, the study drug was detected in 22 of 43 of seronegative subjects (51%) and in 3 of 34 HIV-infected subjects (9%) (P<0.001). Nausea was reported more frequently during the first 4 weeks in the FTC–TDF group than in the placebo group (P<0.001). The two groups had similar rates of serious adverse events (P=0.57).

CONCLUSIONS

Oral FTC–TDF provided protection against the acquisition of HIV infection among the subjects. Detectable blood levels strongly correlated with the prophylactic effect. (Funded by the National Institutes of Health and the Bill and Melinda Gates Foundation; ClinicalTrials.gov number, NCT00458393.)

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Grant at the J. David Gladstone Institutes, University of California at San Francisco, 1650 Owens St., San Francisco, CA, 94158, or at robert.grant@ucsf.edu.

*Other members of the Preexposure Prophylaxis Initiative (iPrEx) study team are listed in the Supplementary Appendix, available at NEJM.org.

This article (10.1056/NEJMoa1011205) was published on November 23, 2010, at NEJM.org.

N Engl J Med 2010.

- In this randomised controlled trial, the HIV infection rate in HIV negative gay men given a daily preventive pill with two HIV drugs was reduced by 44% compared to the placebo arm.
- The HIV infection rate in those who took the drugs more than 90% of the time was reduced by 73%.
- Note that **93%** of trial subjects reported taking their pills correctly, but on the basis of drug level monitoring in blood, only **51%** actually did so.
- The investigators calculated that if all participants had taken their pills consistently, the efficacy of the drug treatment regimen would have increased to around 92%.

Grant, R.M. et al. N Engl J Med 2010; 363: 2587-99.

Pre-exposure prophylaxis and predicted condom use among high risk HIV negative men who have sex with men

EPIDEMIOLOGY AND PREVENTION

Preexposure Prophylaxis and Predicted Condom Use Among High-Risk Men Who Have Sex With Men

Sarit A. Golub, PhD, MPH,†‡§ William Kowalczyk, MA,†§ Corina L. Weinberger, PhD,† and Jeffrey T. Parsons, PhD*†‡*

Objectives: Preexposure prophylaxis (PREP) is an emerging HIV prevention strategy; however, many fear it may lead to neglect of traditional risk reduction practices through behavioral disinhibition or risk compensation.

Methods: Participants were 180 HIV-negative high-risk men who have sex with men recruited in New York City, who completed an Audio Computer Assisted Self Interview-administered survey between September 2007 and July 2009. Bivariate and multivariate logistic regression models were used to predict intention to use PREP and perceptions that PREP would decrease condom use.

Results: Almost 70% (n = 124) of participants reported that they would be likely to use PREP if it were at least 80% effective in preventing HIV. Of those who would use PREP, over 35% reported that they would be likely to decrease condom use while on PREP. In multivariate analyses, arousal/pleasure barriers to condom use significantly predicted likelihood of PREP use (odds ratio = 1.71, $P < 0.05$) and risk perception motivations for condom use significantly predicted decreased condom use on PREP (odds ratio = 2.48, $P < 0.05$).

Discussion: These data provide support for both behavioral disinhibition and risk compensation models and underscore the importance of developing behavioral interventions to accompany any wide-scale provision of PREP to high-risk populations.

Key Words: HIV/AIDS, MSM, preexposure prophylaxis, condom use, behavioral disinhibition, risk compensation

(*J Acquir Immune Defic Syndr* 2010;00:000–000)

INTRODUCTION

Preexposure prophylaxis (PREP) represents a new biomedical approach to HIV prevention with the potential to become a powerful tool within the HIV prevention arsenal. Research on perinatal transmission and postexposure antiretroviral treatment[1–4] and data from animal models,[5–7] suggests that daily administration of antiretroviral therapy can significantly reduce or delay the risk of HIV infection. Preliminary results from a randomized controlled trial of PREP among humans[8] provided data on safety of PREP use but did not have sufficient power to conduct planned efficacy analyses. At present, clinical trials of PREP are underway in 13 countries and the Centers for Disease Control and Prevention has called PREP "one of the most important new prevention approaches being investigated today."[9]

Although there is optimism about PREP as a prevention strategy, many worry that the availability of PREP may encourage reliance on "chemical prevention" in place of traditional risk reduction strategies such as condom use or reducing numbers of sexual partners.[10] Some warn that such increases in high-risk behavior may actually undermine the potential benefits of PREP in reducing transmission rates.[11] There are 2 widely accepted models that describe mechanisms through which PREP might increase risk taking. The first model, Behavioral Disinhibition, argues that PREP availability will increase risk taking by reducing self-imposed constraints on high-risk behavior.[10] Behavioral Disinhibition focuses on affective and pleasure-driven aspects of risk taking and argues that individuals who desire condomless sex will view PREP as a substitute for exercising behavioral control.[12] Behavioral Disinhibition is particularly relevant in the context of substance use, as substance use itself is often associated with disinhibitory effects that may lead to increased sexual risk taking.[12] The second model, Risk Compensation, suggests that PREP availability will decrease condom use by decreasing individuals' perceptions of transmission risk.[11] Risk Compensation focuses on the cognitive aspects of risky decision making and argues that individuals who base decisions about condom use on the perceived risk of a given encounter will view unprotected sex as an acceptable risk in the context of PREP.[13]

Cost-effectiveness models of PREP impact have considered these factors and included behavioral impacts that might decrease its effectiveness, including reduced condom use and increased number of sexual partners. These models demonstrate significant reductions in infection risk with adoption of PREP but conclude that the positive impact of

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From the *Department of Psychology, Hunter College, City University of New York (CUNY), New York, NY; †Center for HIV/AIDS Educational Studies and Training (CHEST), New York, NY; ‡Social & Personality Psychology Doctoral Subprogram, The Graduate Center, CUNY, New York, NY; and §Neuropsychology Doctoral Subprogram, The Graduate Center, CUNY, New York, NY.

Collection of these data was supported by a grant from the National Institute on Drug Abuse (NIDA) (R01-DA020366, J.T.P., Principal Investigator).

Correspondence to: Sarit A. Golub, PhD, MPH, Department of Psychology, Center for HIV Educational Studies and Training, Hunter College, City University of New York; 695 Park Avenue, Room 714N, New York, NY 10065 (e-mail: sarit.golub@hunter.cuny.edu).

- Study of 180 high risk HIV negative men who have sex with men (MSM) in New York City.
- Almost 70% reported they would be likely to use PrEP if it was at least 80% effective in preventing HIV transmission.
- Of those who would use PrEP, over **35%** reported they would be likely to decrease their condom use while on PrEP.
- "Risk perception motivations for condom use significantly predicted decreased condom use on PrEP (odds ratio = 2.48, P<0.05)."

Golub, S.A. et al. J Acq Imm Def Syn 2010; 54: 548-55.

Current cost of PrEP for HIV prevention in New Zealand

	Condoms and Lube NZAF	Condoms and Lube retail	ARV treatment/ PrEP
1 week	72 cents	$2.22	$321.11
6 months	$17.28	$57.72	$8,349.00
1 year	$34.56	$115.44	$16,698.00
10 years	$345.60	$1154.40	$166,980.00
50 years	**$1728.00**	**$5772.00**	**$834,900.00**

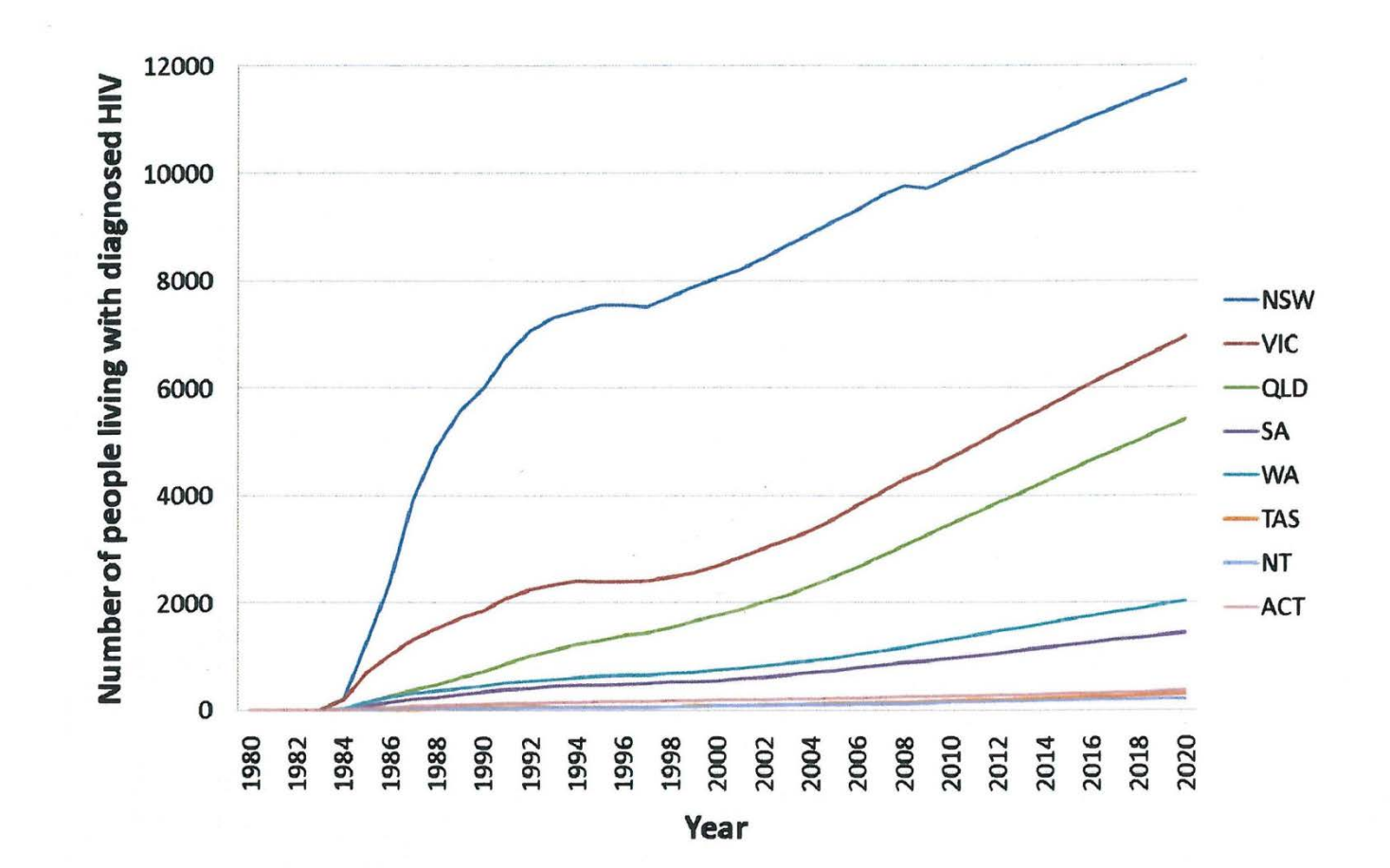
*'*Condoms and Lube NZAF*' based on PHARMAC subsidised condom price and established supplier agreement for lube and calculated for 2 safe sex episodes per week

*'*Condoms and Lube retail*' based on online purchase price for NZAF equivalent condoms and lube and calculated for 2 safe sex episodes per week

* 'ARV treatment/*PrEP*' is average cost of ARVs per HIV-positive person on treatment in 2010

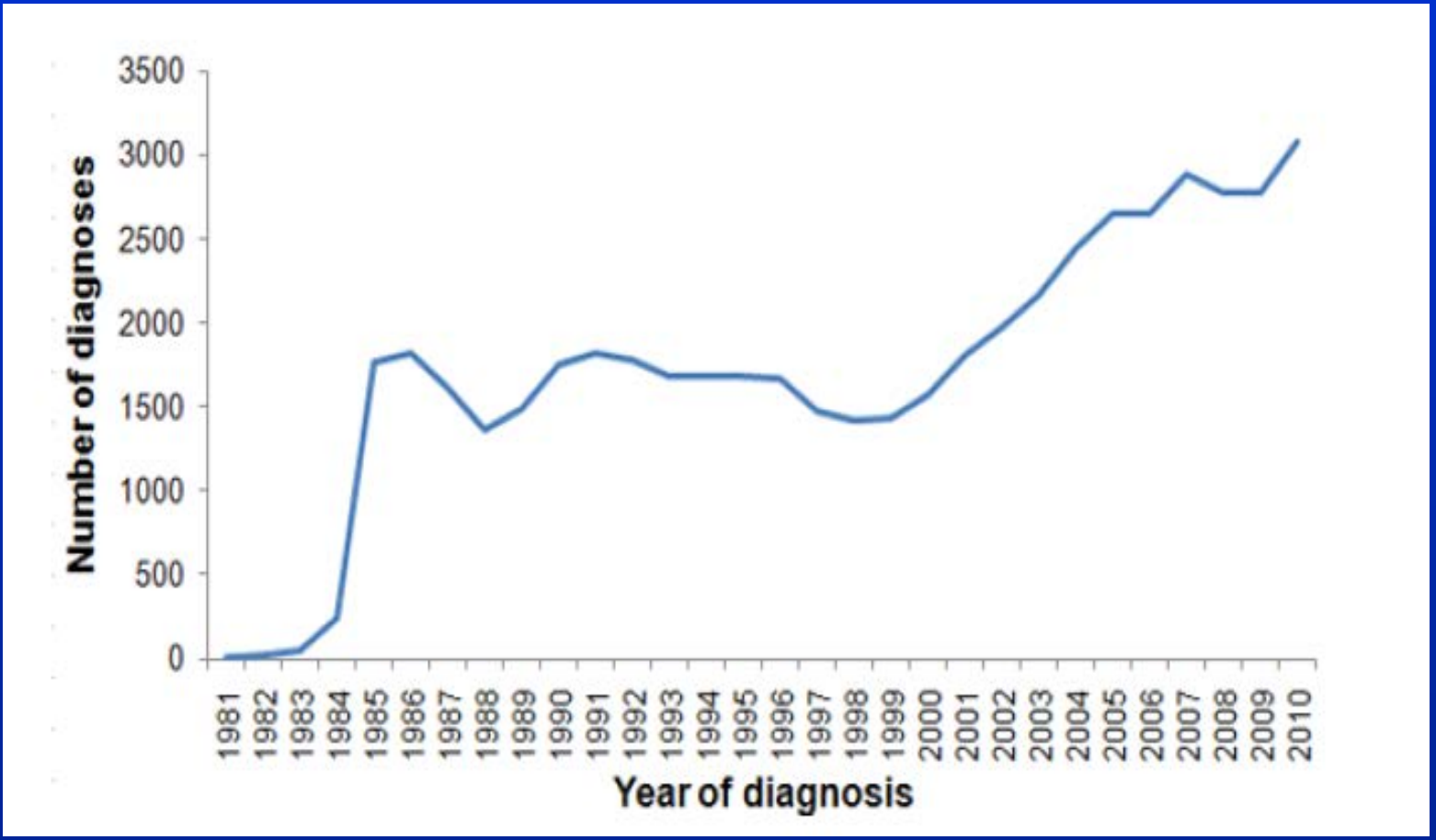
Myers, J. "PEP and PrEP for HIV prevention in New Zealand." Presented: Gay Community Forum, Wellington 14 June 2011.

Number of people living with diagnosed HIV infection in each Australian state (estimated 2010-2020)



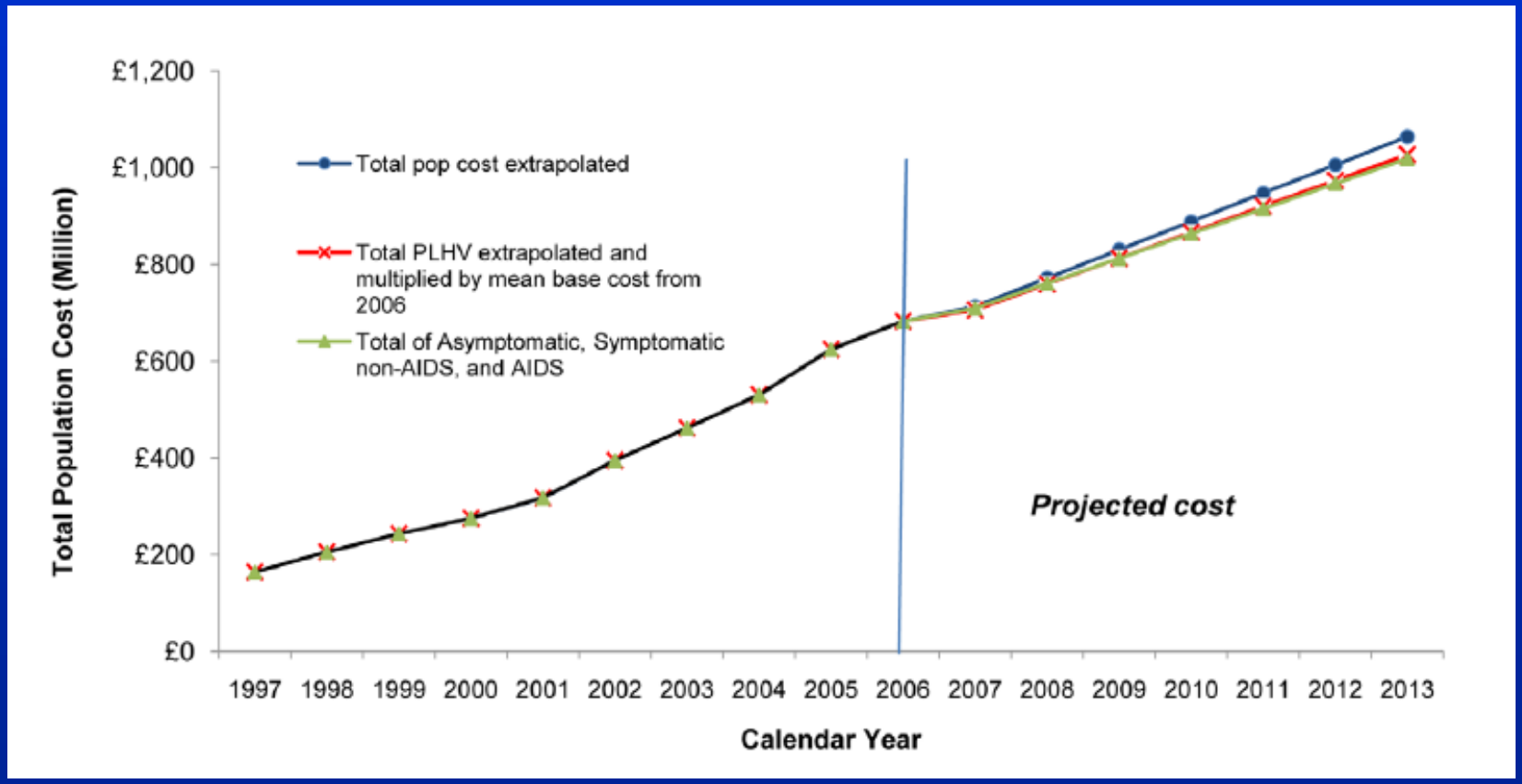
Wilson, D. Jansson, J. and Watson, J. "Mapping HIV outcomes: geographical and clinical forecasts of numbers of people living with HIV in Australia", National Centre in HIV Epidemiology and Clinical Research, and National Association of People Living with HIV/AIDS; 2010.

Annual HIV diagnoses among MSM in the United Kingdom, 1981-2010



Health Protection Agency. "30 years on: People living with HIV in the UK about to reach 100,000." Health Protection Report 2011; 5: No 22.

Annual United Kingdom population HIV costs 1997-2006 and projections 2007-2013, including community care



Sundhiya, M. et al. PLoS One 2010; 5: e15677.

Rising population cost for treating people living with HIV in the United Kingdom, 1997-2013

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PLoS one

Rising Population Cost for Treating People Living with HIV in the UK, 1997-2013

Sundhiya Mandalia[1,2,3], Roshni Mandalia[1], Gary Lo[1,3], Tim Chadborn[4], Peter Sharott[5], Mike Youle[1,6], Jane Anderson[7], Guy Baily[8], Ray Brettle[9], Martin Fisher[10], Mark Gompels[11], George Kinghorn[12], Margaret Johnson[6], Brendan McCarron[13], Anton Pozniak[3], Alan Tang[14], John Walsh[15], David White[16], Ian Williams[17], Brian Gazzard[1,2,3], Eduard J. Beck[1,3,18]*, for the NPMS-HHC Steering Group

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Abstract

Background: The number of people living with HIV (PLHIV) is increasing in the UK. This study estimated the annual population cost of providing HIV services in the UK, 1997–2006 and projected them 2007–2013.

Methods: Annual cost of HIV treatment for PLHIV by stage of HIV infection and type of ART was calculated (UK pounds, 2006 prices). Population costs were derived by multiplying the number of PLHIV by their annual cost for 1997–2006 and projected 2007–2013.

Results: Average annual treatment costs across all stages of HIV infection ranged from £17,034 in 1997 to £18,087 in 2006 for PLHIV on mono-therapy and from £27,649 in 1997 to £32,322 in 2006 for those on quadruple-or-more ART. The number of PLHIV using NHS services rose from 16,075 to 52,083 in 2006 and was projected to increase to 78,370 by 2013. Annual population cost rose from £104 million in 1997 to £483 million in 2006, with a projected annual cost between £721 and £758 million by 2013. When including community care costs, costs increased from £164 million in 1997, to £683 million in 2006 and between £1,019 and £1,065 million in 2013.

Conclusions: Increased number of PLHIV using NHS services resulted in rising UK population costs. Population costs are expected to continue to increase, partly due to PLHIV's longer survival on ART and the relative lack of success of HIV preventing programs. Where possible, the cost of HIV treatment and care needs to be reduced without reducing the quality of services, and prevention programs need to become more effective. While high income countries are struggling to meet these increasing costs, middle- and lower-income countries with larger epidemics are likely to find it even more difficult to meet these increasing demands, given that they have fewer resources.

Citation: Mandalia S, Mandalia R, Lo G, Chadborn T, Sharott P, et al. (2010) Rising Population Cost for Treating People Living with HIV in the UK, 1997-2013. PLoS ONE 5(12): e15677. doi:10.1371/journal.pone.0015677

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Competing Interests: During 2008/2009, the NPMS-HHC was financially supported through a non-restrictive grant from Tibotec, with no influence on the independence of the Steering Group and its editorial policy. This does not alter the authors' adherence to all the PLoS ONE policies on sharing data and materials.

* Email: becke@unaids.org

Introduction

The UK has the fastest growing HIV epidemic in Western Europe [1]. The number of PLHIV alive and using NHS services have increased, partly due to more effective ART regimens resulting in their longer survival [2], partly due to uninfected people continuing to be infected with HIV either in the UK or abroad [3]. This combination has resulted in increasing number of PLHIV using NHS services [4] which is likely to have resulted in increased population costs for HIV treatment and care. The aim of this study was to estimate the treatment and care costs for PLHIV in the UK population by stage of HIV infection and type of ART between 1997 and 2006 and project costs for 2007–2013.

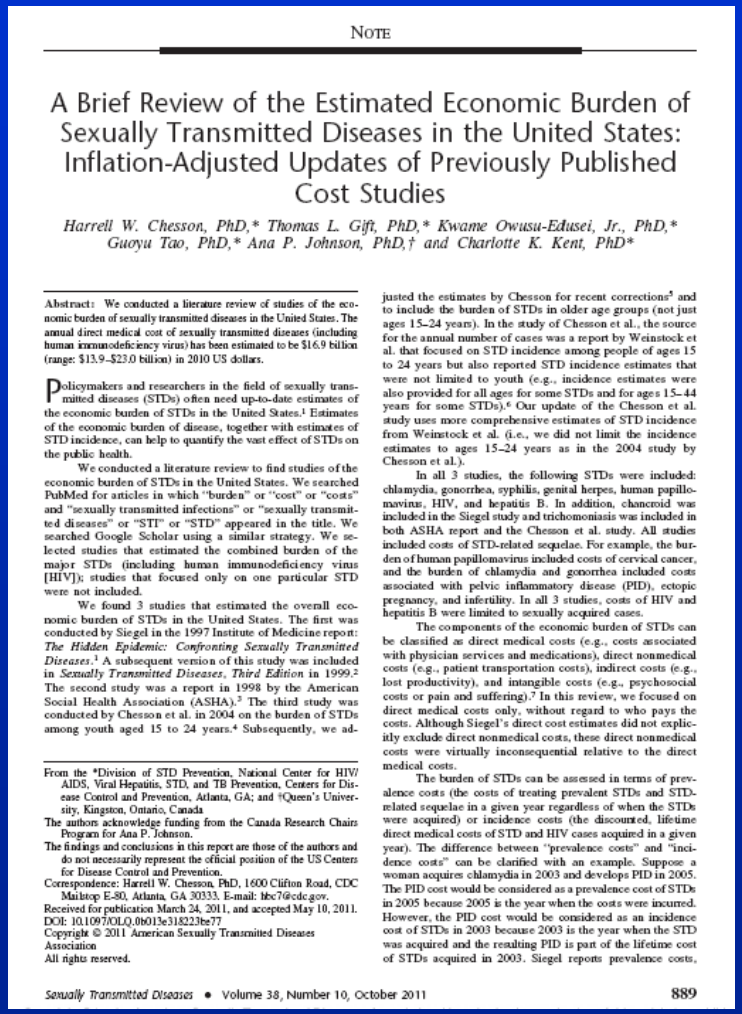
Methods

The National Prospective Monitoring System on the use, cost and outcome of HIV service provision in UK hospitals - HIV Health-economics Collaboration (NPMS-HHC) monitors prospectively the effectiveness, efficiency, equity and acceptability of

- "Only greater prevention efforts will reduce the number of people becoming infected with HIV."
- "A recent study from the US suggests that even if incidence is reduced drastically, the number of people newly infected with HIV will continue to increase."
- "While putting PLHIV on ART will reduce their infectivity and contribute to reducing the incidence of people newly infected with HIV, this in itself will not be sufficient to reduce incidence in a large number of settings."
- "Only comprehensive prevention strategies, responding directly to the epidemic dynamics operating in each country, will be able to reduce HIV incidence."

Sundhiya, M. et al. PLoS One 2010; 5: e15677.

Estimated economic burden of HIV and STIs in the United States in 2010



NOTE

A Brief Review of the Estimated Economic Burden of Sexually Transmitted Diseases in the United States: Inflation-Adjusted Updates of Previously Published Cost Studies

Harrell W. Chesson, PhD, Thomas L. Gift, PhD,* Kwame Owusu-Edusei, Jr., PhD,* Guoyu Tao, PhD,* Ana P. Johnson, PhD,† and Charlotte K. Kent, PhD**

Abstract: We conducted a literature review of studies of the economic burden of sexually transmitted diseases in the United States. The annual direct medical cost of sexually transmitted diseases (including human immunodeficiency virus) has been estimated to be $16.9 billion (range: $13.9–$23.0 billion) in 2010 US dollars.

Policymakers and researchers in the field of sexually transmitted diseases (STDs) often need up-to-date estimates of the economic burden of STDs in the United States.[1] Estimates of the economic burden of disease, together with estimates of STD incidence, can help to quantify the vast effect of STDs on the public health.

We conducted a literature review to find studies of the economic burden of STDs in the United States. We searched PubMed for articles in which "burden" or "cost" or "costs" and "sexually transmitted infections" or "sexually transmitted diseases" or "STI" or "STD" appeared in the title. We searched Google Scholar using a similar strategy. We selected studies that estimated the combined burden of the major STDs (including human immunodeficiency virus [HIV]); studies that focused only on one particular STD were not included.

We found 3 studies that estimated the overall economic burden of STDs in the United States. The first was conducted by Siegel in the 1997 Institute of Medicine report: *The Hidden Epidemic: Confronting Sexually Transmitted Diseases*.[1] A subsequent version of this study was included in *Sexually Transmitted Diseases, Third Edition* in 1999.[2] The second study was a report in 1998 by the American Social Health Association (ASHA).[3] The third study was conducted by Chesson et al. in 2004 on the burden of STDs among youth aged 15 to 24 years.[4] Subsequently, we adjusted the estimates by Chesson for recent corrections[5] and to include the burden of STDs in older age groups (not just ages 15–24 years). In the study of Chesson et al., the source for the annual number of cases was a report by Weinstock et al. that focused on STD incidence among people of ages 15 to 24 years but also reported STD incidence estimates that were not limited to youth (e.g., incidence estimates were also provided for all ages for some STDs and for ages 15–44 years for some STDs).[6] Our update of the Chesson et al. study uses more comprehensive estimates of STD incidence from Weinstock et al. (i.e., we did not limit the incidence estimates to ages 15–24 years as in the 2004 study by Chesson et al.).

In all 3 studies, the following STDs were included: chlamydia, gonorrhea, syphilis, genital herpes, human papillomavirus, HIV, and hepatitis B. In addition, chancroid was included in the Siegel study and trichomoniasis was included in both ASHA report and the Chesson et al. study. All studies included costs of STD-related sequelae. For example, the burden of human papillomavirus included costs of cervical cancer, and the burden of chlamydia and gonorrhea included costs associated with pelvic inflammatory disease (PID), ectopic pregnancy, and infertility. In all 3 studies, costs of HIV and hepatitis B were limited to sexually acquired cases.

The components of the economic burden of STDs can be classified as direct medical costs (e.g., costs associated with physician services and medications), direct nonmedical costs (e.g., patient transportation costs), indirect costs (e.g., lost productivity), and intangible costs (e.g., psychosocial costs or pain and suffering).[7] In this review, we focused on direct medical costs only, without regard to who pays the costs. Although Siegel's direct cost estimates did not explicitly exclude direct nonmedical costs, these direct nonmedical costs were virtually inconsequential relative to the direct medical costs.

The burden of STDs can be assessed in terms of prevalence costs (the costs of treating prevalent STDs and STD-related sequelae in a given year regardless of when the STDs were acquired) or incidence costs (the discounted, lifetime direct medical costs of STD and HIV cases acquired in a given year). The difference between "prevalence costs" and "incidence costs" can be clarified with an example. Suppose a woman acquires chlamydia in 2003 and develops PID in 2005. The PID cost would be considered as a prevalence cost of STDs in 2005 because 2005 is the year when the costs were incurred. However, the PID cost would be considered as an incidence cost of STDs in 2003 because 2003 is the year when the STD was acquired and the resulting PID is part of the lifetime cost of STDs acquired in 2003. Siegel reports prevalence costs,

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the US Centers for Disease Control and Prevention.

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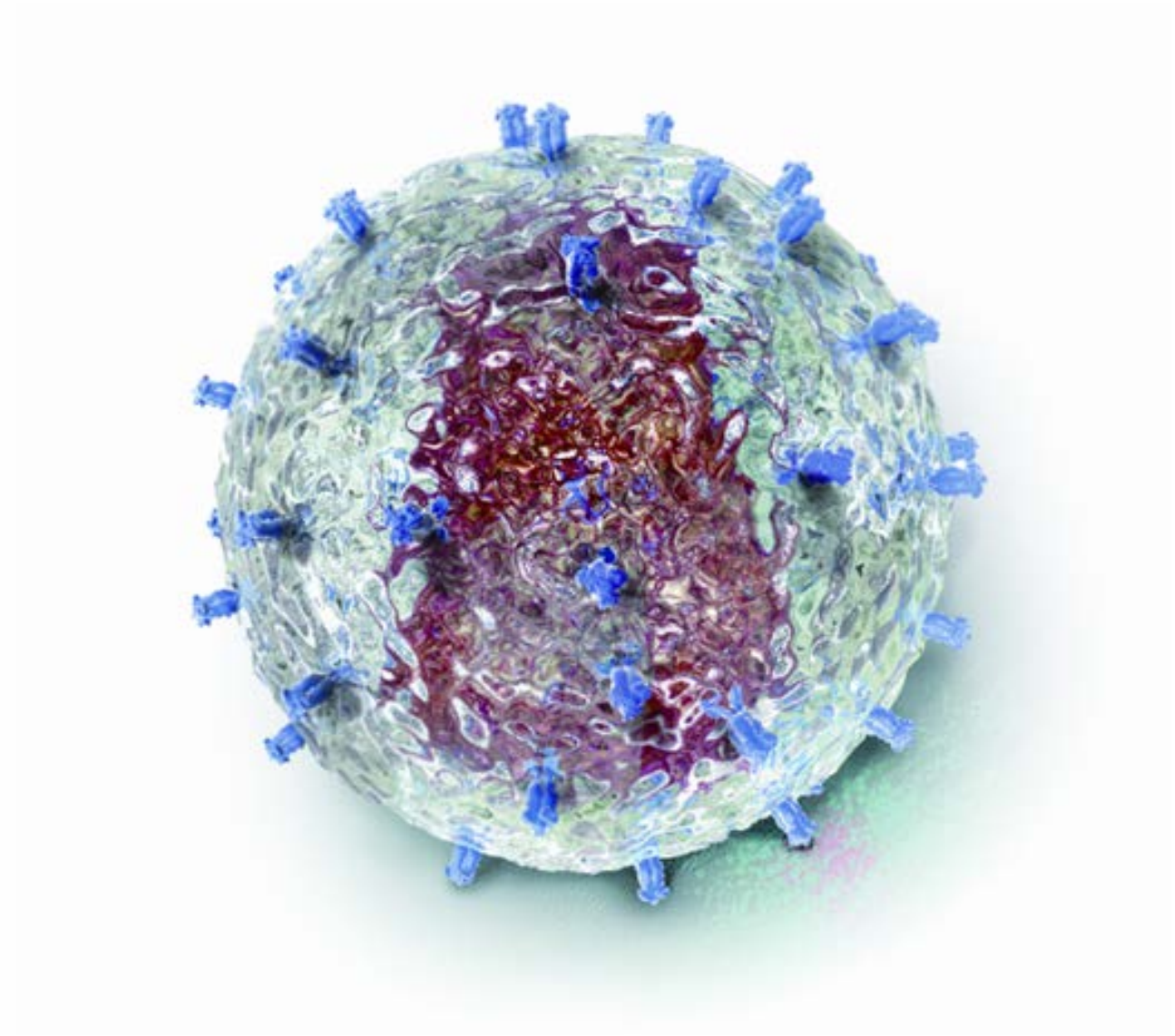
DOI: 10.1097/OLQ.0b013e31822be77

"In conclusion, the annual economic burden of all major STDs (including HIV) has been estimated to be $16.9 billion (range: $13.9 – $23.0 billion). These estimates are useful, but were obtained from studies published 7 to 14 years ago… and may not be fully representative of the current burden of STDs, even when adjusted for inflation. Updated estimates of the overall health and economic burden of STDs in the United States are needed."

Chesson, H.W. et al. Sex Transm Dis 2011; 38: 889-891.



Essential to remember that the biology of HIV acquisition and transmission is different in the:

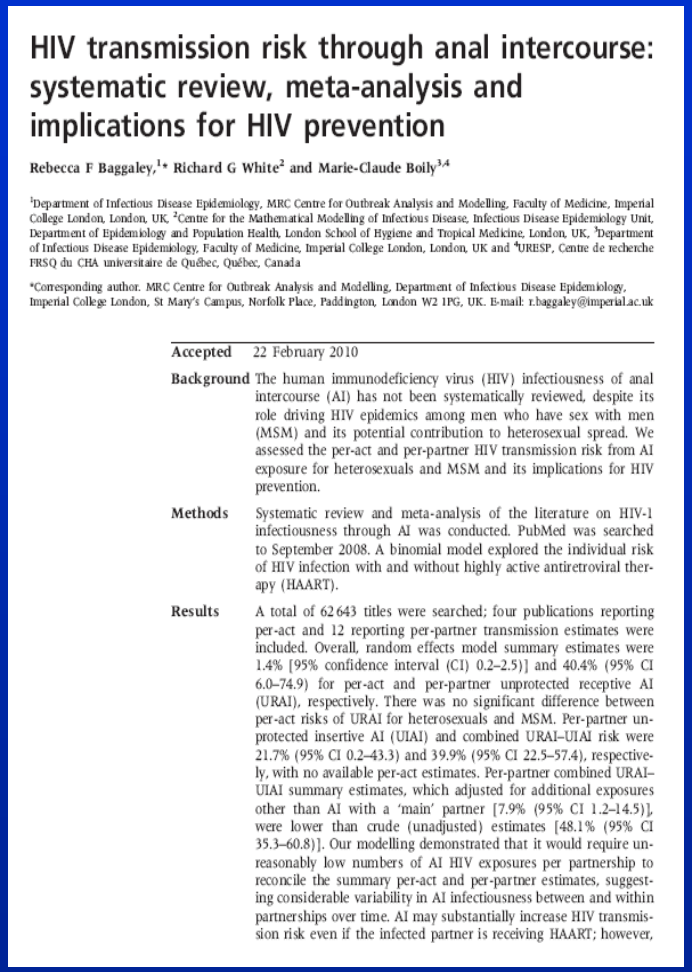
(a) Blood compartment

(b) Female genital tract

(c) Male genital tract

(d) Anorectal compartment

High HIV transmission risk through anal intercourse



HIV transmission risk through anal intercourse: systematic review, meta-analysis and implications for HIV prevention

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[1]Department of Infectious Disease Epidemiology, MRC Centre for Outbreak Analysis and Modelling, Faculty of Medicine, Imperial College London, London, UK, [2]Centre for the Mathematical Modelling of Infectious Disease, Infectious Disease Epidemiology Unit, Department of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK, [3]Department of Infectious Disease Epidemiology, Faculty of Medicine, Imperial College London, London, UK and [4]URESP, Centre de recherche FRSQ du CHA universitaire de Québec, Québec, Canada

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Accepted 22 February 2010

Background The human immunodeficiency virus (HIV) infectiousness of anal intercourse (AI) has not been systematically reviewed, despite its role driving HIV epidemics among men who have sex with men (MSM) and its potential contribution to heterosexual spread. We assessed the per-act and per-partner HIV transmission risk from AI exposure for heterosexuals and MSM and its implications for HIV prevention.

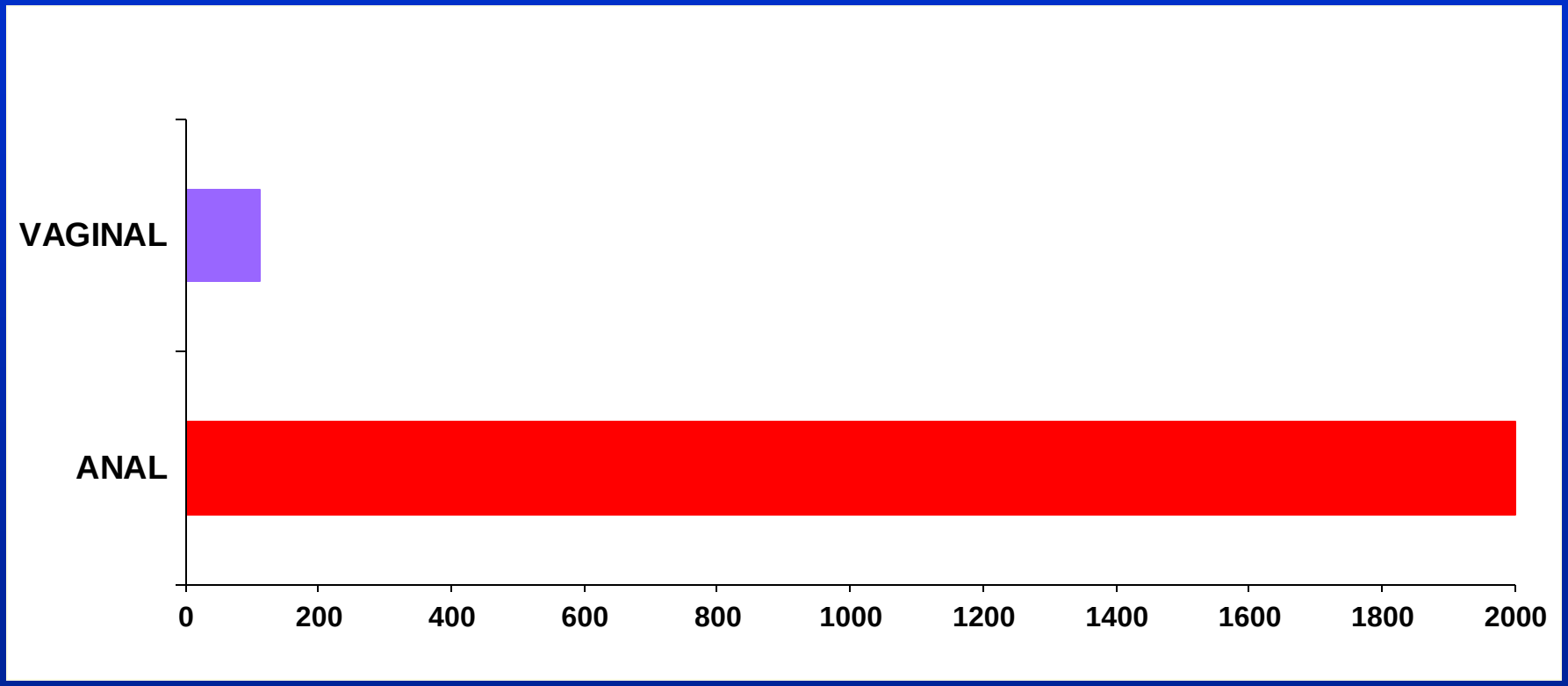
Methods Systematic review and meta-analysis of the literature on HIV-1 infectiousness through AI was conducted. PubMed was searched to September 2008. A binomial model explored the individual risk of HIV infection with and without highly active antiretroviral therapy (HAART).

Results A total of 62 643 titles were searched; four publications reporting per-act and 12 reporting per-partner transmission estimates were included. Overall, random effects model summary estimates were 1.4% [95% confidence interval (CI) 0.2–2.5)] and 40.4% (95% CI 6.0–74.9) for per-act and per-partner unprotected receptive AI (URAI), respectively. There was no significant difference between per-act risks of URAI for heterosexuals and MSM. Per-partner unprotected insertive AI (UIAI) and combined URAI–UIAI risk were 21.7% (95% CI 0.2–43.3) and 39.9% (95% CI 22.5–57.4), respectively, with no available per-act estimates. Per-partner combined URAI–UIAI summary estimates, which adjusted for additional exposures other than AI with a 'main' partner [7.9% (95% CI 1.2–14.5)], were lower than crude (unadjusted) estimates [48.1% (95% CI 35.3–60.8)]. Our modelling demonstrated that it would require unreasonably low numbers of AI HIV exposures per partnership to reconcile the summary per-act and per-partner estimates, suggesting considerable variability in AI infectiousness between and within partnerships over time. AI may substantially increase HIV transmission risk even if the infected partner is receiving HAART; however,

- HIV transmission risk through unprotected receptive anal intercourse is **18 times higher** than during unprotected receptive vaginal intercourse in developed countries in this major review.
- The absolute per act transmission risk for unprotected receptive anal intercourse (URAI) is 1.4% (95% CI 0.2 → 2.5).
- The same per act transmission risk for URAI (1.43%; 95% CI 0.48 → 2.85) was recently reported from the Australian HIM cohort study.
- The absolute per act transmission risk for unprotected receptive vaginal intercourse in developed countries is 0.08% (95% CI 0.06 → 0.11) in the review.
- Note that the per partner transmission risk for unprotected receptive anal intercourse is 40.4% (95% CI 6.0 → 74.9).

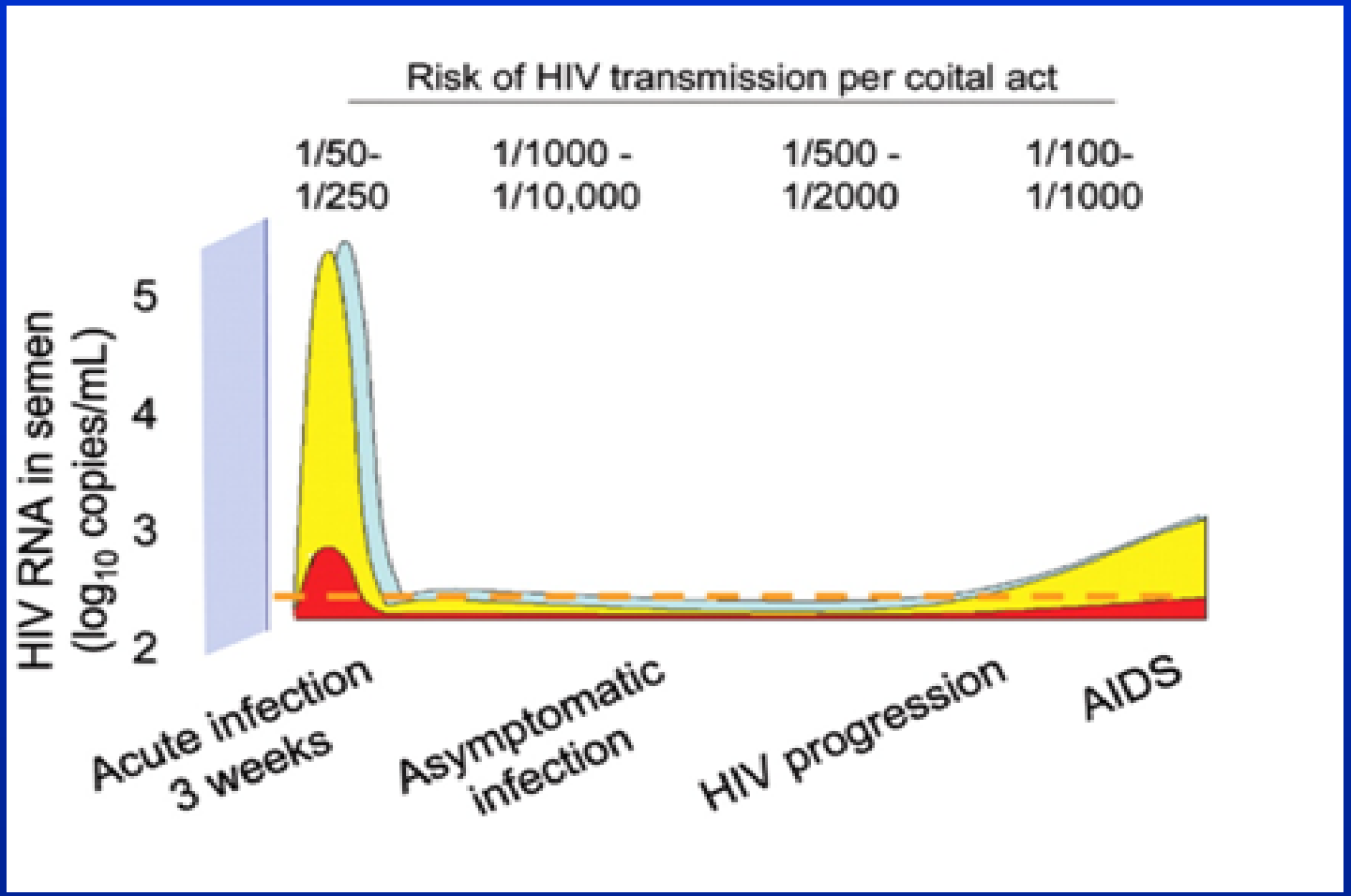
Baggaley, R. F. et al. Int J Epidemiol 2010; 39: 1048-63; Jin, F. et al. AIDS 2010; 24: 907-913.

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



Baggaley, White and Boily (2010); Boily et al (2009); Jin et al (2010).

Sharply increased HIV transmission risk in acute infection



Cohen, M .S. Pilcher , C.D. J Infect Dis 2005; 191: 1391-1393.

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

MAJOR ARTICLE

High Rates of Forward Transmission Events after Acute/Early HIV-1 Infection

Bluma G. Brenner,[1] Michel Roger,[2] Jean-Pierre Routy,[3] Daniela Moisi,[1] Michel Ntemgwa,[1] Claudine Matte,[2] Jean-Guy Baril,[4] Réjean Thomas,[5] Danielle Rouleau,[3] Julie Bruneau,[4] Roger Leblanc,[7] Mario Legault,[8] Cecile Tremblay,[3] Hugues Charest,[9] Mark A. Wainberg,[1] and the Quebec Primary HIV Infection Study Group[a]

[1]McGill AIDS Centre–Jewish General Hospital, [2]Centre Hospitalier de Université de Montréal (CHUM)–Hôpital Notre-Dame, [3]McGill University Health Centre, [4]Clinique Médicale du Quartier Latin, [5]Clinique Médicale l'Actuel, [6]CHUM–Hôpital St. Luc, [7]Clinique Médicale Goldberg, LeBlanc, & Rosengren, [8]Fonds de la Recherche en Santé du Québec–SIDA Network, [9]CHUM–Hôtel Dieu, and [10]Institut National de Santé Publique du Québec, Montreal, Canada

(See the editorial commentary by Pillay and Fisher, on pages 924–6.)

Background. A population-based phylogenetic approach was used to characterize human immunodeficiency virus (HIV)–transmission dynamics in Quebec.

Methods. HIV-1 *pol* sequences included primary HIV infections (PHIs; <6 months after seroconversion) from the Quebec PHI cohort (1998–2005; $n = 215$) and the provincial genotyping program (2001–2005; $n = 481$). Phylogenetic analysis determined sequence interrelationships among unique PHIs ($n = 593$) and infections from untreated ($n = 135$) and treated ($n = 660$) chronically infected (CI) potential transmitter populations (2001–2005). Clinical features, risk factors, and drug resistance for clustered and nonclustered transmission events were ascertained.

Results. Viruses from 49.4% (293/593) of PHIs cosegregated into 75 transmission chains with 2–17 transmissions/cluster. Half of the clusters included 2.7 ± 0.8 (mean ± SD) transmissions, whereas the remainder had 8.8 ± 3.5 transmissions. Maximum periods for onward transmission in clusters were 15.2 ± 9.5 months. Coclustering of untreated and treated CIs with PHIs were infrequent (6.2% and 4.8%, respectively). The ages, viremia, and risk factors were similar for clustered and nonclustered transmission events. Low prevalence of drug resistance in PHI supported amplified transmissions at early stages.

Conclusions. Early infection accounts for approximately half of onward transmissions in this urban North American study. Therapy at early stages of disease may prevent onward HIV transmission.

An understanding of HIV-transmission dynamics is important in the design of effective prevention and treatment interventions. A number of recent studies suggest that early stages of HIV infection may disproportionately contribute to viral transmission and spread of the epidemic [1–3]. Primary HIV infection (PHI) and early stages of infection are associated with high viral burden and viral set points in blood and semen, a major determinant of HIV transmission [1, 2,4–6]. The Rekai-Uganda surveillance study showed that 43.8% (10/23) of new transmissions occurred in discordant partners at 6–15 months subsequent to seroconversions of source partners [6].

In contrast, other groups have used viral load/epidemiological/behavioral data to contend that the role of PHIs in HIV transmission may be overestimated [7–9]. Many cofactors influence transmission, including access to antiretroviral therapy and medical care, high risk behaviors, sexually transmitted diseases, and coinfections [7–9]. The findings of the North Carolina program Screening and Tracing of Active Transmission

Received 6 September 2006; accepted 3 October 2006; electronically published 16 February 2007.

Potential conflicts of interest: none reported.

Presented in part: XIV International HIV Drug Resistance Workshop, Quebec City, Canada, 7–11 June 2005 (abstract 112).

Financial support: Canadian Institutes for Health Research (grant MT-14738 for resistance genotyping in the Quebec Primary HIV Infection [PHI] cohort study and for research on PHI; Réseau SIDA of the Fonds de la Recherche en Santé du Québec (funds to recruit patients into the Quebec PHI cohort study); Quebec Ministry of Health (funds to the provincial genotypic resistance testing program).

[a] Study group members are listed after the text.

Reprints or correspondence: Dr. Mark Wainberg, McGill AIDS Centre, 3755 Cote Ste. Catherine Rd., Montreal, Quebec, Canada H3W 1G4 (mark.wainberg@mcgill.ca).

The Journal of Infectious Diseases 2007; 195:951–9

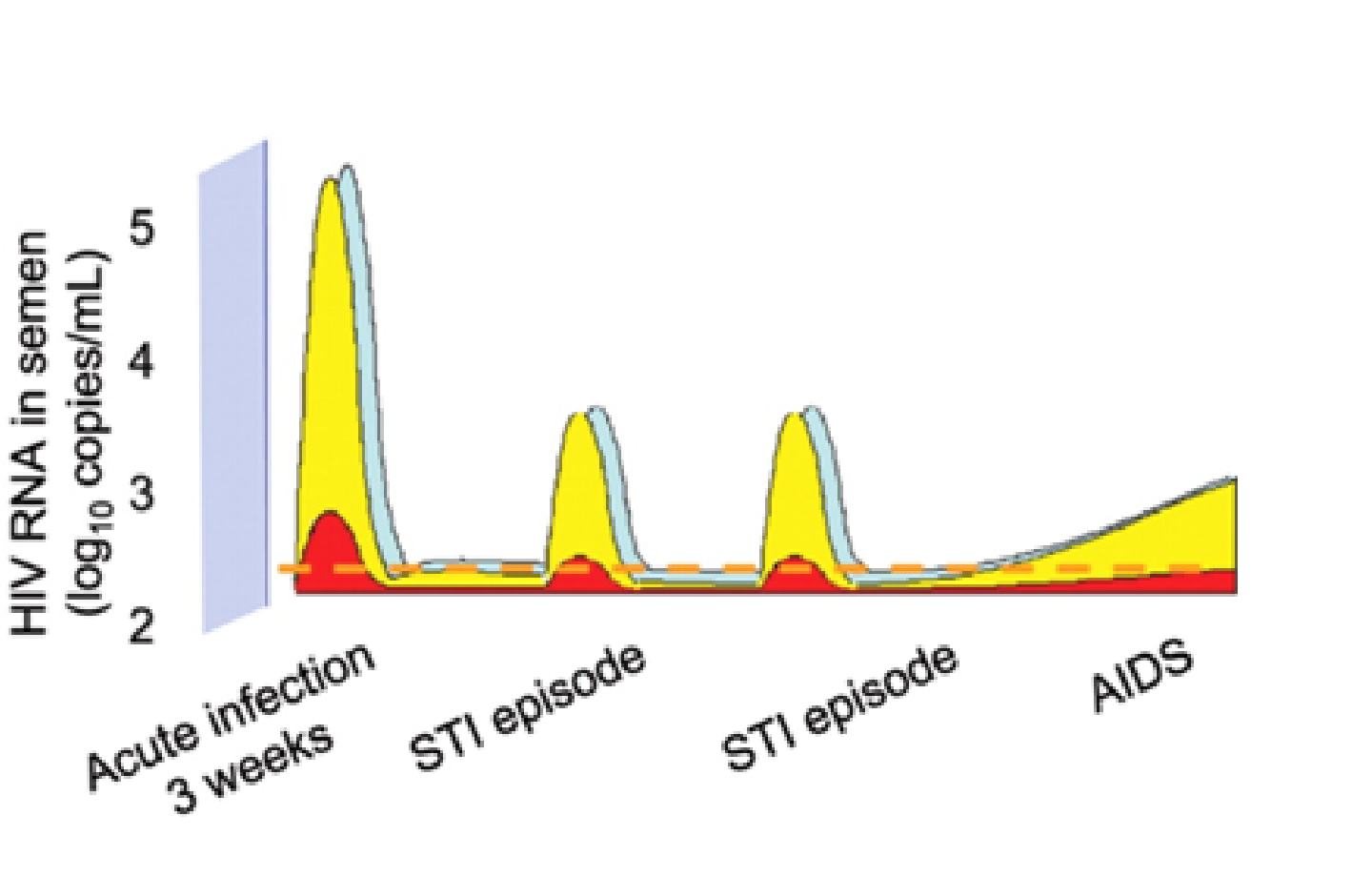
0022-1899/2007/19507-0007$15.00

DOI: 10.1086/512088

- 49% of all 'primary HIV infection' strains in Quebec form phylogenetic clusters, suggesting early infection may account for a major proportion of onward transmission.
- Less than 2% clustering is observed in the 'chronically infected' genotyped population in Quebec, mostly representing individuals receiving long-term antiretroviral therapy.
- So in this study, acute/early infection - less than 10% of the total sample - is responsible for nearly 50% of onward transmission events.

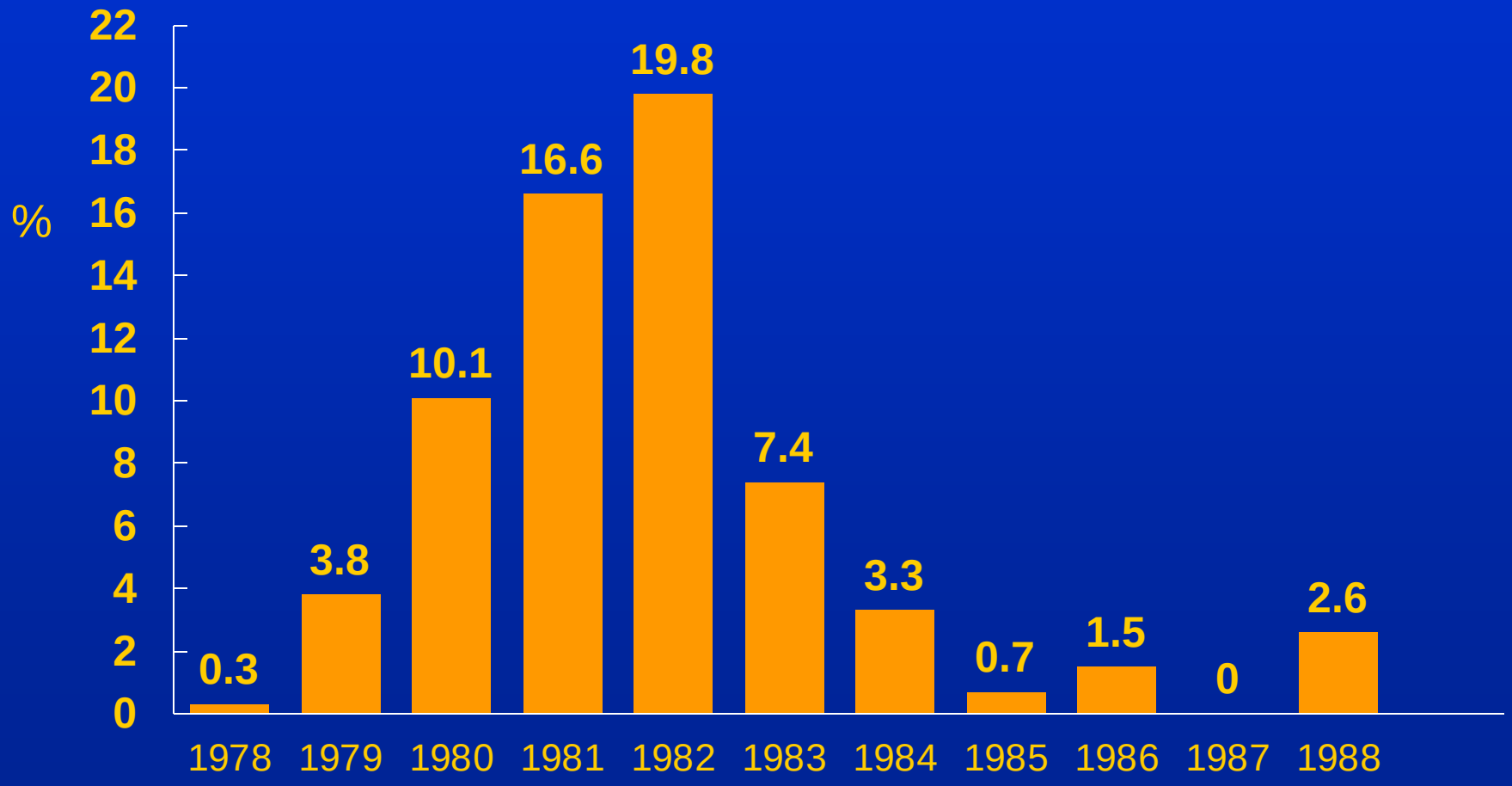
Brenner, B.G. et al. J Infect Dis 2007; 195: 951-959.

Increased HIV transmission risk with STIs and after AIDS diagnosis



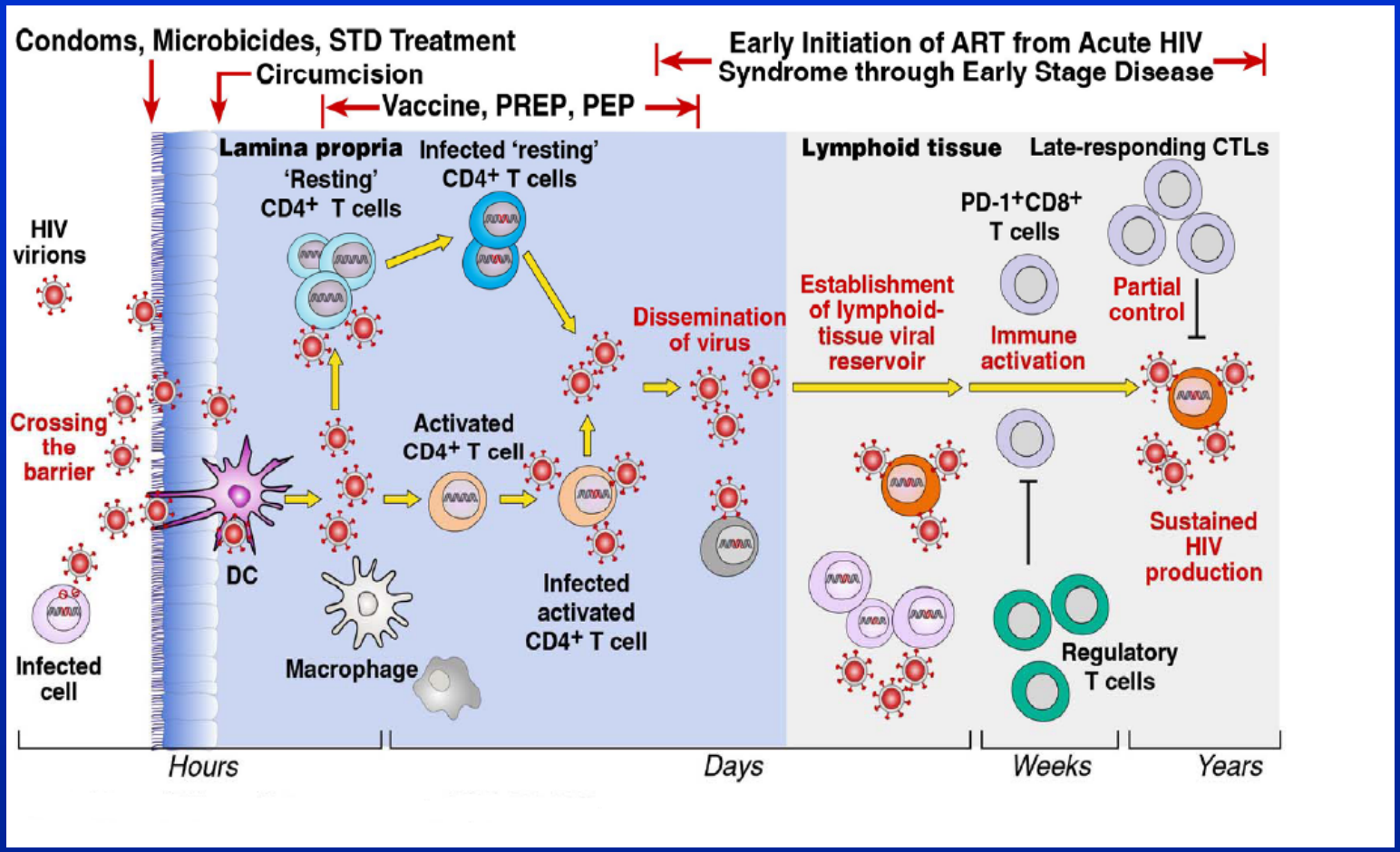
Cohen, M.S. Pilcher , C.D. J Infect Dis 2005; 191: 1391-1393.

Annual incidence of HIV infection among 320 Hepatitis B vaccine trial participants, San Francisco, 1978-1988



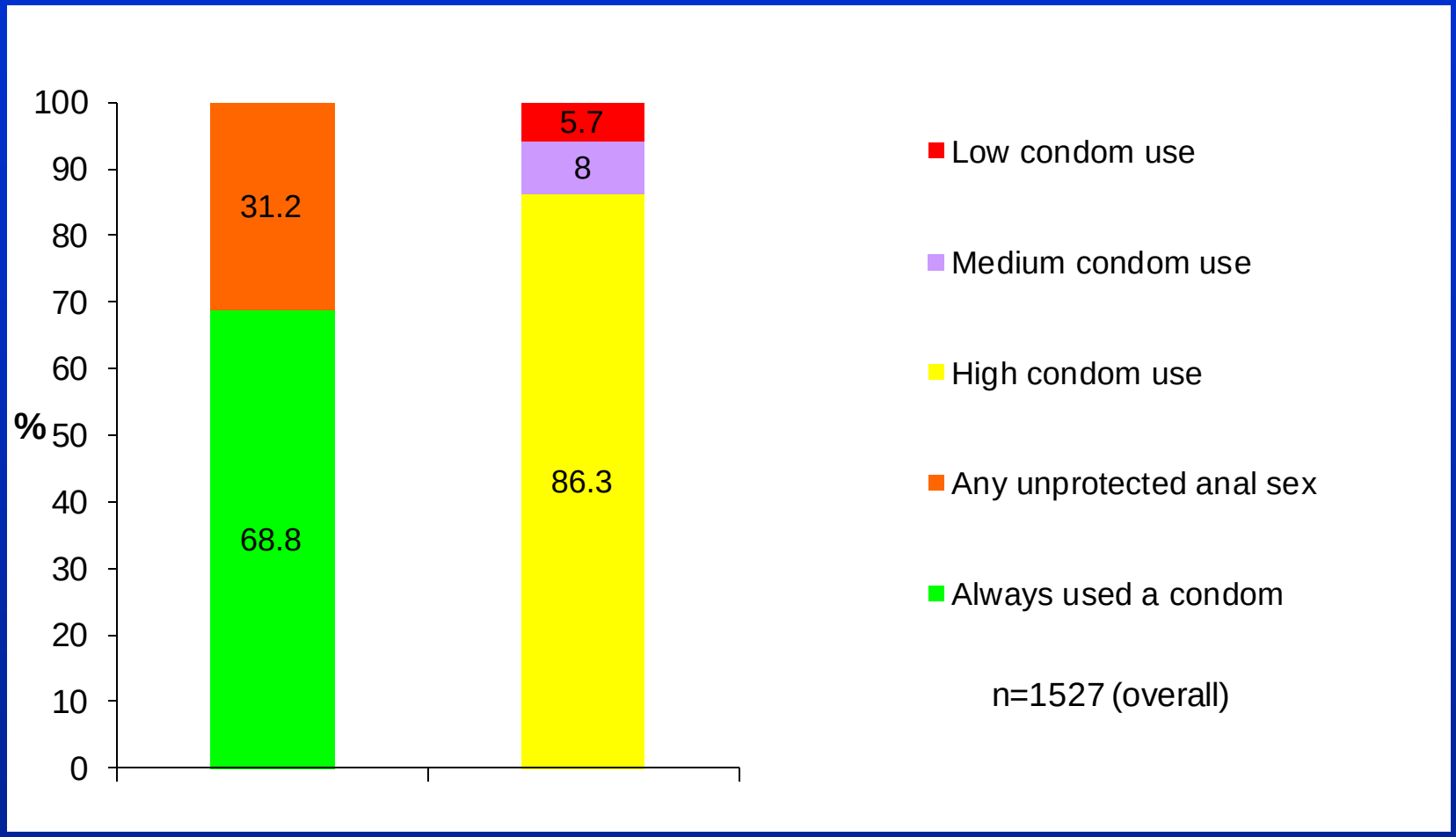
Hessol, NA. Lifson, AR. O'Malley, PM. et al. "Prevalence, incidence, and progression of Human Immunodeficiency Virus infection in homosexual and bisexual men in hepatitis B vaccine trials, 1978-1988." Am J Epidemiol 1989; 130: 1167-75.

Early events in HIV infection: Possibilities for intervention



Adapted from: Fauci, A.S. "New concepts in HIV/AIDS pathogenesis: Implications for interventions." Presentation: XVIII International AIDS Conference, 20 July 2010 and Haase, A.T. Nat Rev Immunol; 5: 783-92.

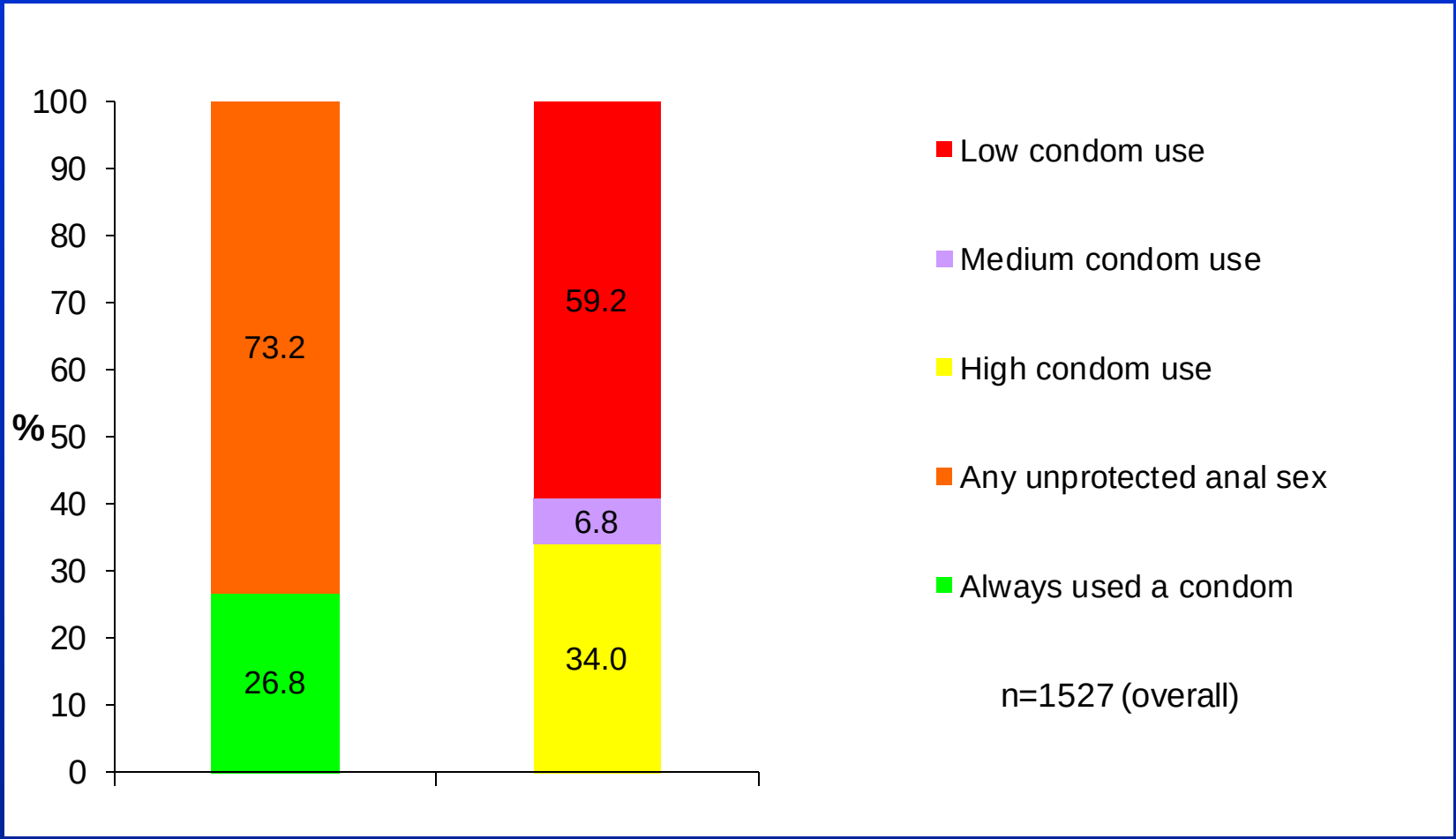
GAPSS 2008: Condom use for anal sex with casual partners in the last six months



Saxton, P. Dickson, N. and Hughes, T. "GAPSS 2008 : Findings from the Gay Auckland Periodic Sex Survey." Auckland: New Zealand AIDS Foundation 2010.

Saxton, P. et al. "How often do gay and bisexual men in New Zealand use condoms for anal sex with casual partners, and has this changed over time?" New Zealand Sexual Health Society Conference, 15-17 Oct 2009, Bay of Islands.

GAPSS 2008: Condom use for anal sex with current boyfriend in the last six months



Saxton, P. Dickson, N. and Hughes, T. "GAPSS 2008 : Findings from the Gay Auckland Periodic Sex Survey." Auckland: New Zealand AIDS Foundation 2010.

Saxton, P. et al. "How often do gay and bisexual men in New Zealand use condoms for anal sex with casual partners, and has this changed over time?" New Zealand Sexual Health Society Conference, 15-17 Oct 2009, Bay of Islands.

Condoms and HIV prevention: Position statement by UNAIDS, UNFPA and WHO, March 2009

"Condom use is a critical element in a comprehensive, effective and sustainable approach to HIV prevention and treatment. Prevention is the mainstay of the response to AIDS. Condoms are an integral and essential part of comprehensive prevention and care programmes, and their promotion must be accelerated."

"The male latex condom is the single, most efficient, available technology to reduce the sexual transmission of HIV and other sexually transmitted infections. The search for new preventive technologies such as HIV vaccines and microbicides continues to make progress, but condoms will remain the key preventive tool for many, many years to come."

UNAIDS, UNFPA, WHO 2009. Condoms and HIV prevention: Position statement, 19 March, 2009.

Condom use and early treatment for care: The role of HIV and STI testing

Accurate knowledge about the current HIV and STI status of one or both partners is not a prerequisite:

- Consistent condom use
- Regular HIV testing
- Regular STI testing

Accurate knowledge about the current HIV and STI status of one or both partners is required:

- Early HIV treatment
- Early STI treatment

Conclusion

(a) Maximise condom use for HIV and STI prevention in the MSM population.

(b) Ensure early HIV and STI treatment for care in the MSM population.

(c) Evaluate research that measures the individual-level *efficacy* of treatment to prevent the transmission of HIV in MSM.

(d) Await the development of a research programme that establishes the *effectiveness* of treatment to prevent the transmission of HIV at population level for MSM.

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