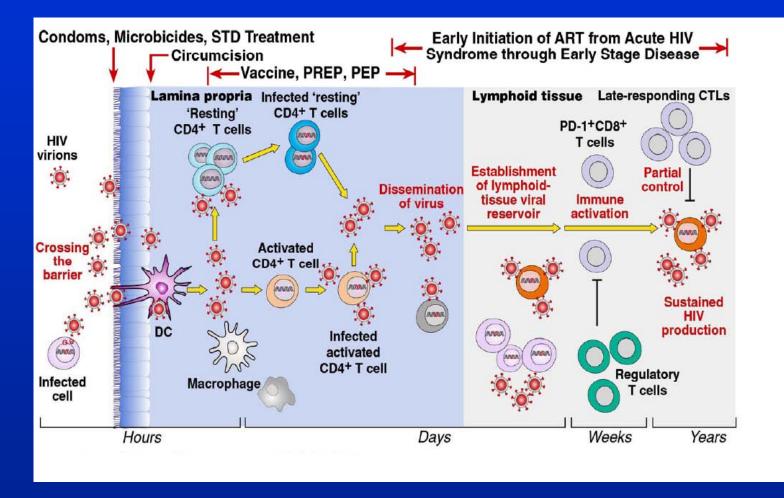
Avoiding a 'zero sum game' in HIV prevention for gay men

Tony Hughes Research Director New Zealand AIDS Foundation

HIV Treatments Update 2011, Pullman Hotel, Waterloo Quadrant, Auckland, 26th August 2011

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.

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

- 1. Blood compartment
- 2. Female genital tract
- 3. Male genital tract
- 4. Anorectal compartment

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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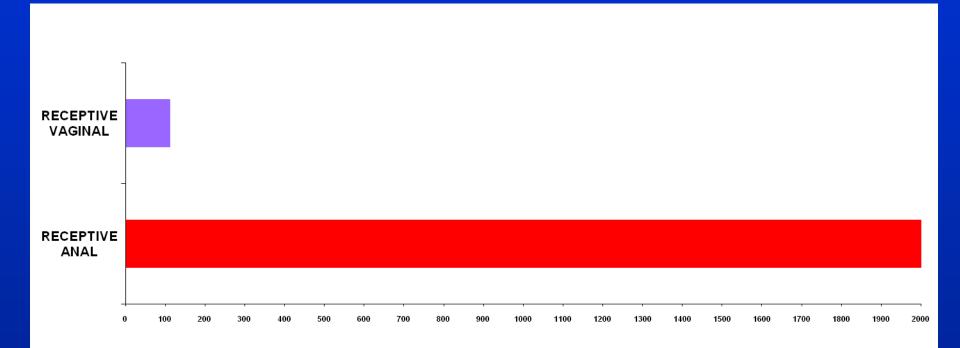
*Corresponding author. MRC Centre for Outbreak Analysis and Modelling, Department of Infectious Disease Epidemiology, Imperial College London, St Mary's Campus, Norfolk Place, Paddington, London W2 1PG, UK. E-mail: r.baggaley@imperial.ac.uk

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,

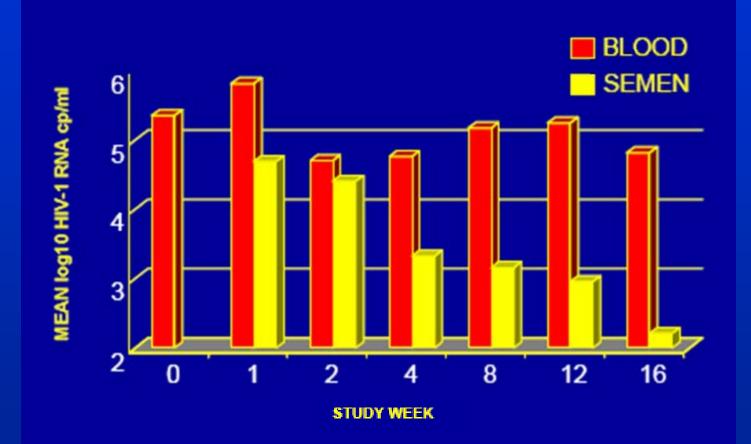
- HIV transmission risk through anal intercourse is
 18 times higher than during vaginal sex in this major review.
- The absolute per act transmission risk for unprotected receptive anal intercourse is 1.4% (95% Cl 0.2→ 2.5).
- This figure is the same as a recent Australian study which found a per act transmission risk for URAI of 1.43% (95% CI 0.48 → 2.85).
- Note that the per partner transmission risk for unprotected receptive anal intercourse is 40.4% (95% Cl 6.0→74.9).
- The absolute per act transmission risk for unprotected male to female vaginal intercourse in developed countries is 0.08% (95% CI 0.06 → 0.11).

Relative HIV risk for receptive anal and receptive vaginal sex in developed countries



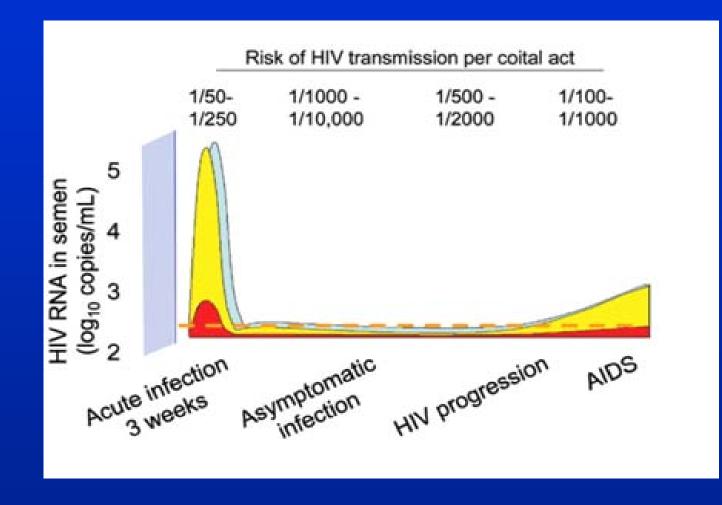
Baggaley, White and Boily (2010); Boily et al (2009); Jin et al (2010).

Viral loads in blood and semen during acute HIV infection (n=21/1441)



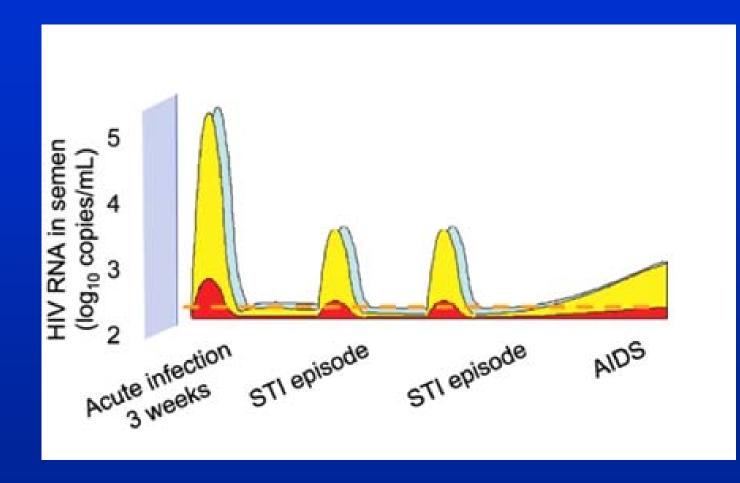
Cohen, M. 'Potential use of PrEP and trends in population transmission' Presented at IAS Industry Liaison Forum: Scientific and investment considerations for research on pre-exposure prophylaxis, February 2006, Denver USA. Graph adapted from Pilcher, C.D. et al. AIDS. 2007;21:1723-1730.

Sexual transmission of HIV



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

Acute HIV and STI episodes



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

Does 'undetectable' mean 'uninfectious'?

(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?

Sexual transmission of HIV according to viral load and antiretroviral therapy: systemic review and meta-analysis

Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis

Suzanna Attia^a, Matthias Egger^{a,b}, Monika Müller^a, Marcel Zwahlen^a and Nicola Low^{a,b}

Objectives: To synthesize the evidence on the risk of HIV transmission through unprotected sexual intercourse according to viral load and treatment with combination antiretroviral therapy (ART).

Design: Systematic review and meta-analysis.

Methods: We searched Medline, Embase and conference abstracts from 1996–2009. We included longitudinal studies of sendiscordant couples reporting on HW transmission according to plasma viral load or use of ART and used random-effects Poisson regression models to chatin summary transmission rates [with 95% confidence intervals, (CI)]. If there were no transmission events we estimated an upper 97.5% confidence limit.

Results: We identified 11 cohorts reporting on 5021 heterosexual couples and 461. HV-transmission events. The rate of transmission overall from ART-transide patients was 0.46 (9%) Cl 0.19–1.09) per 100 person-years, based on five events. The transmission rate from a seropositive patner with viral load below 400 copies/ml on ART, based on two studies, was zero with an upper 97.5% confidence limit of 1.27 per 100 personyears, and 0.16 (9%) Cl 0.02–1.13) per 100 person-years if not on ART, based on five studies and one event. There were instificient data to calculate rates according to the presence or absence of sexually transmitted infections, condom use, or vaginal or anal intercourse.

Conclusion: Studies of heterosexual discordant couples observed no transmission in patients treated with ART and with viral load below 400ccpies/ml, but data were compatible with one transmission pror 79 person-years. Further studies are needed to better define the risk of HIV transmission from patients on ART.

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AIDS 2009, 23:1397-1404

Keywords: highly active antiretroviral therapy, infectious, prevention of HIV infections, sexually transmitted diseases, transmission probability, viral load

See editorial comment on page 1431

Introduction

The efficacy of antiretroviral drugs in the prevention of mother-to-child transmission of HIV is well documented [1] and there may also be a role of antiretroviral therapy (ART) in the prevention of sexual transmission of HIV [2]. Any reduction in the capacity of HIV to replicate is likely to reduce the risk of HIV transmission, unless the effect is offset by behavioural risk compensation [2,3]. HIV-infected men treated with zidovudine monotherapy in latly were half as likely to transmit infection to their female partners than untreated men, after controlling for

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Tel: +41 31 631 35 01; e-mail: egger@ispm.unibe.ch Received: 1 February 2009; revised: 25 February 2009; accepted: 5 March 2009.

DOI:10.1097/QAD.0b013e32832b7dca

- The available studies found no episodes of HIV transmission in discordant heterosexual couples if the HIV-infected partner was treated with ART and had a viral load below 400 copies/ml.
- There was insufficient data to assess rates according to the presence of absence of sexually transmitted infections, use of condoms, direction of transmission, or practice of vaginal or anal sex.
- The comparison of overall rates in patients on ART and not on ART nevertheless indicate that heterosexual transmission was reduced by **92%** on ART.
- Of note, this review did not identify *any* study with data on ART and transmission risk in homosexual men.

Attia, S. et al. AIDS 2009; 23:1397-04.

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



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 The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Cohen at the University of North Carolina human immunodeficiency virus type 1 (HIV-1) in serodiscordant couples. at Chapel Hill, Institute for Global Health

METHODS

RESULTS

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.

and Infectious Diseases, Suite 2115, Bioinformatics Bidg., 130 Mason Farm Rd., CB 7030, Chapel Hill, NC 27599, or at mscohen@med.unc.edu. *Other members of the HIV Prevention Trials Network (HPTN) 052 Study Team

are listed in the Supplementary Appendix, available at NEJM.org. This article (10.1056/NEJMca1105243) was

published on July 18, 2011, at NEJM.org.

N Engl I Med 2011:365:493-505. Copyright @ 2011 M assachusetts Medical Society

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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 earlytherapy group (haz ard 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.)

N EN GLJ MED 365;6 NEJM.ORG AUGUST 11, 2011

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- 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/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.
- 39 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.
- 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.

The New England Journal of Medicine

Strategic limitations of HPTN 052

- Definitive 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.
- So in summary, the prevention effectiveness at the population level of earlier HIV treatment for MSM cannot be determined from this data alone.

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

The NEW ENGLAND IOURNAL of MEDICINE

ORIGINAL ARTICLI

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 The authors' affiliations are listed in the prevention of human immunodeficiency virus (HIV) acquisition.

and tenofovir disoproxil fumarate (FTC-TDF), or placebo once daily, All subjects re-

ceived HIV testing, risk-reduction counseling, condoms, and management of sexu-

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 en-

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

METHODS We randomly assigned 2499 HIV-seronegative men or transgender women who have

RESULTS

ally transmitted infections.

similar rates of serious adverse events (P=0.57).

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. sex with men to receive a combination of two oral antiretroviral drugs, emtricitabine

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 NEM.org.

rollment, and 100 became infected during follow-up (36 in the FTC-TDF group and N Engl J Med 2010. Copyright @ 2010 Massachusetts Medical Society 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%.

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.)

10.1056/NEIM031011205 NEIM.ORG

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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)

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Construction Dung Ahuse (NIDA) (2010-DA020366, LTE, Principal Investigator), Correspondence to: Sarit A. Golub, Phil. 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.cmy.edu). Copyright © 2010 by Lippincott Williams & Wilkins

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 antiretrovinal treatment¹⁻⁴ 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 humans⁵ 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 investigate today."

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

- 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)."

Four different strategic approaches to ART use in HIV positive populations



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

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

- (a) 'Seek and treat' strategy to increase treatment uptake in the population for those with low CD4+ levels.
- (b) 'Test and link' strategy to increase testing and ongoing linkage to clinical services.
- (c) 'Treat for care' strategy to begin treatment at the earliest stage that benefits patient care.
- (d) 'Test and treat' strategy to maximize testing and begin treatment immediately for public health benefit.

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

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

Rebecca F. Baggaley and Christophe Fraser

MRC Centre for Outbreak Analysis and Modelling, Decartment of Infectious Disease Epidemiology, Imperial College London, London, UK

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Current Opinion in HIV and AIDS 2010, 5269-276

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 © 2010 Woters Kluwer Health | Lippincott Williams & Wilkins 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

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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').

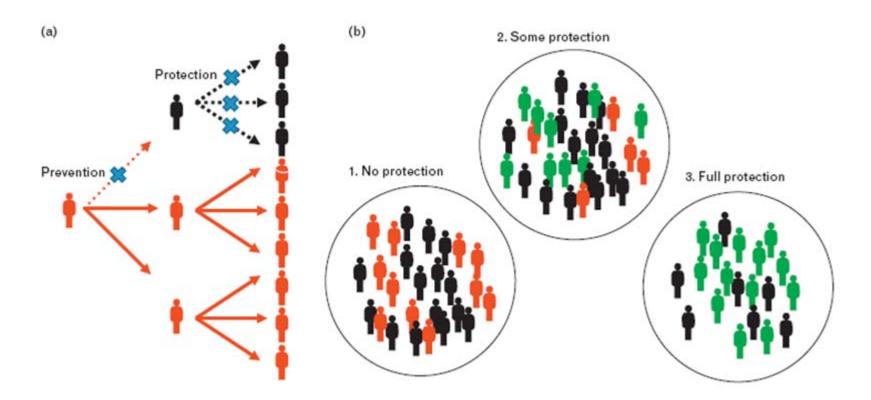
From efficacy to effectiveness

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

DOI:10.1097/COH.0b013e32833a51b2

- 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."

Demonstration of the impact of HIV prevention at the individual and population level



(a) HIV prevention method directly prevents one transmission event but indirectly prevents an additional three transmissions, which would have also taken place. (b) The population-level effect of prevention methods can be measured through cluster randomized trials or mathematical modelling analyses, which compare scenarios in which no protection is offered (1) to those wherein all those at risk of acquiring HIV infection are protected (3) or some degree of coverage in between (2).

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

Mark S. Clements, PhD,* Garrett Prestage, PhD,* Andrew Grulich, PhD,* Paul Van de Ven, PhD,† Susan Kippax, PhD,† Matthew G. Law, PhD*

Background: Previous mathematical models have indicated that any decrease in HIV incidence in homosexual men due to decreased infectiousness from antiretovinal readment (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 and intercourse with causal partners (UAIC) in homosexual mea 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 1955–2001 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 efficitive ARVs, with a slow increase during 1998–2001 due to increased levels of UARC when use of therapies was firstly stable. From 2001, a continued increase in UARC was predicted to lead to a fise in HIV incidence. A rise in UARC 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

(J Acquir Immune Defic Syndr 2004;35:401-406)

Received for publication June 4, 2003; accepted November 11, 2003. From *National Centre in HIV Epidemiology and Clinical Research and

From *National Centre in HIV Epidemiology and Clinical Research and †National Centre in HIV Social Research, The University of New South

Wales, Sydney, Australia. Conflict of interest: None.

Reprints: Matthew Law, National Centre in HIV Epidemiology and Clinical Research, The University of New South Wales, 376 Victoria Street, Durlinghurst, NSW 2010, Australia (e-mail: mlaw@nchecrunsw.edu.au). Copyright © 2004 by Lippinout Williams & Williams

/ Acquir Immune Defic Syndr • Volume 35, Number 4, April 1 2004

Previous mathematical models of HIV incidence in homosexual men have indicated that any decrease in HIV transmissions due to decreased indictiousness of men receiving antiretrovinal 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 and intercourse with casual pattners (UAIC) over the period 1996–2001.^{5,6} Among homosexually active men participating in periodic surveys, reported rates of UAIC increased in Sydhey from 14% in 1998 to 12% 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 reaciving treatments.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.^{5,6}

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^{3,0} 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/mm², 200 = CD4 \leq 500, CD4 < 200, AID8) 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

401

- 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."

Modelling of HIV incidence among MSM in Australia

incidence

HIV

incidence

22%

HIV

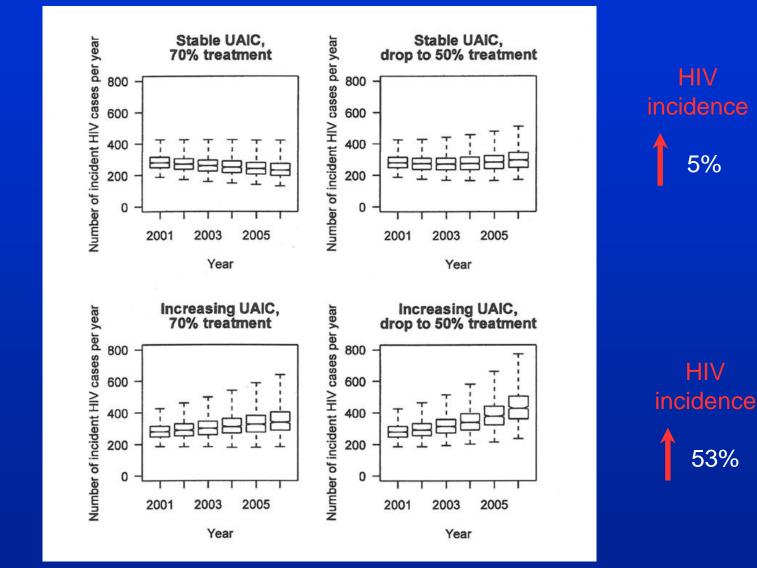


FIGURE 3. Modelled HIV incidence under different scenarios, 2001-2006. Clements et al. J Acq Imm Def Syn 2004; 35:401-06.

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

Fengyi Jin^{a,b}, James Jansson^a, Matthew Law^a, Garrett P. Prestage^a, Iryna Zablotska^c, John C.G. Imrie^c, Susan C. Kippax^c, John M. Kaldor^a, Andrew E. Grulich^a and David P. Wilson^a

> 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 ecceptive UAI was 1.43% [95% confidence interval (CI) 0.48–2.45] 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 0.0.20–0.24), and it was 0.65% (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.

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AIDS 2010, 24:907-913

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

Introduction

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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Received: 2 November 2009; revised: 17 December 2009; accepted

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

DOI:10.1097/QAD.0b013e3283372d90

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

- The per-contact probability of HIV transmission through unprotected anal intercourse in homosexual men in this study is similar to estimates reported from developed countries in the pre-HAART era.
- In Australia, homosexual men have very high rates of HIV testing, about 70% of HIV positive men are receiving HAART, and 75% of those on treatment have undetectable viral load.
- It is surprising that estimates of HIV transmission risk post-HAART were similar to those when few HIV positive men had an undetectable viral load.
- There are four potential explanations: Primary HIV infection may have a bigger role in population spread than expected; the proportion of undiagnosed HIV infection 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.

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

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

Daniela Bezemer^a, Frank de Wolf^{a,b}, Maarten C. Boerlijst^c, Ard van Sighem^a, T. Deirdre Hollingsworth^b, Maria Prins^{d,e}, Ronald B. Geskus^{d,f}, Luuk Gras^a, Roel A. Coutinho^{g,h} and Christophe Fraser^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 risk behaviour and resurgent epidemics have been widely reported posthighly 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 $\mathcal{R}(t)$, 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 $\mathcal{R}(t)$ to 1.44 in the latest period 2000–2004 (99%, 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. © 2008 Wohens Klaver Health [Lippicctt Williams & Wilkins

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."

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.

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

TRICK OR TREAT?

Antiretroviral therapy as HIV prevention EDITOR DEAN MURPHY "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...."

Others relate to social factors including rates of unprotected anal sex, sexual network structure, extent of behavioural disinhibition and risk compensation, rates of HIV testing, and community attitudes to HIV infection.

Susan Kippax, 2010.

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.

Examining the promise of HIV elimination by 'test and treat' in hyperendemic settings

Examining the promise of HIV elimination by 'test and treat' in hyperendemic settings

Peter J. Dodd, Geoff P. Garnett and Timothy B. Hallett

Background: It has been suggested that a new strategy for HIV prevention, 'Universal Test and Treat', whereby everyone is tested for HIV once a year and treated immediately with antiretroviral therapy (ART) if they are infected, could 'eliminate' the epidemic and reduce ART costs in the long term.

Methods: We investigated the impact of test-and-treat interventions under a variety of assumptions about the epidemic using a deterministic mathematical model.

Results: Our model shows that such an intervention can substantially reduce HIV transmission, but that impact depends crucially on the epidemiological context; in some situations, less agressive interventions achieve the same results, whereas in others, the proposed intervention reduces HIV by much less. It follows that testing every year and treating immediately is not necessarily the most cost-efficient strategy. We also show that a test-and-treat intervention that does not reach full implementation or coverage could, perversely, increase long-term ART costs.

Conclusion: Interventions that prevent new infections through ART scale-up may hold substantial promise. However, as plans move forward, careful consideration should be given to the nature of the epidemic and the potential for perverse outcomes. © 200 Wolkes Klaver Health Lipoincott Wilkins & Wilkins

AIDS 2010, 24:729-735

Keywords: antiretroviral therapy, modelling, prevention, test and treat, treatment

Introduction

The rate of new HIV infections has stabilized in recent years (2.7 million infections in 2007 [1]), and concomitantly, the global number of those infected on antiretroviral therapy (ART) has increased dramatically [2]. Despite this, the rate of new infections in developing countries still outpaces the rate at which individuals are started on treatment [2], and there is growing concern that this situation is unsustainable [3,4]. Incidence must be further reduced, but disappointingly, few HIV interventions have been shown to be effective in randomized controlled trials in developing countries: behaviour changes following counselling and testing are likely to have a minimal effect or even increase incidence [5,6]; two models of peer education for promoting reductions in risk behaviour have failed [7,8]; risk compensation and low adherence potentially contributed to no effect being found in triak to prevent HIV infection through

diaphragm use [9] and herpes treatment [10]; and, in the last year, another trial of herpes treatment showed no effect on the rate of HIV transmission from coinfected individuals [11]. These results bring the tally of trials showing no efficacy in reducing HIV incidence to more than 30 [12]. Male circumcition has been shown to reduce the risk of men acquiring infection [13–15], although it is understood that this will not be enough to eliminate HIV, even under the most optimistic conditions [16,17].

In contrast, scale-up of ART has substantially reduced mortality [2,17–19]. As the availability of treatment expanded, Montaner *et al.* [20] proposed using treatment as an intervention to prevent infection, and Granich *et al.* [21] recently used a mathematical model to evaluate that argument. The model suggested that in a high prevalence setting, with an incidence of two per 100 person-years at risk, an intervention that tested everyone annually and

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DOI:10.1097/QAD.0b013e32833433fe

- This model using heterosexual data incorporates recent estimates of transmission from acute infection, transmission rates on treatment and differences in sexual risk behaviour.
- The impact of 'test and treat' interventions depends crucially on epidemiological context, which is determined by properties of the sexual partner network such as heterogeneity, concurrency and mixing.
- "Although a high coverage implementation of 'test and treat' could lead to reductions in HIV incidence and ART use, failing to test frequently enough could just lead to a dramatic spiralling of treatment costs. In this scenario, the intervention does not interrupt transmission, so the pool of those developing treatment needs continues to grow."

Dodd, P.J. et al. AIDS 2010; 24:729-35.

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 as HIV 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 is now very uncommon in settings where widely reported scientific, public health HIV treatment is widely available. and community debate about the extent to For sexual transmission of HIV, the data which HIV treatment (through decreasing relating to reduction of HIV transmission blood and genital fluid HIV viral load) are less conclusive, but two recent highly may decrease the sexual transmission of controversial reports have energised the HIV. This current debate originated in field. First, a World Health Organization studies published a decade ago. These (WHO) research group reported their studies, in African heterosexual couples results of a mathematical model showing where the HIV-positive partner was that universal voluntary HIV testing not treated, demonstrate that there is a with immediate treatment of all those very strong relationship between blood diagnosed, a so-called 'test and treat' HIV viral load and risk of onwards HIV strategy, could substantially reduce severe transmission to the sexual partner. Based generalised heterosexual HIV epidemics,1 on a small number of couples, there were Second, a consensus statement released by no cases of HIV transmission when the the Swiss Federal Commission for HIV/ HIV-positive partner had an undetectable AIDS (the Swiss Statement, see Talkabout viral load. These data led some researchers 164) states that HIV-positive people on to speculate that the use of HIV therapy to effective HIV treatment with undetectable decrease blood viral load to undetectable blood viral load for six months or more may also markedly reduce onwards HIV who are free of other sexually transmitted transmission.

infections cannot transmit HIV through

The highest

quality studies

of viral load and

the risk of sexual

transmission

serodiscordant

couples because

such studies can

directly measure

exposure to and

transmission

of HIV

are in HIV

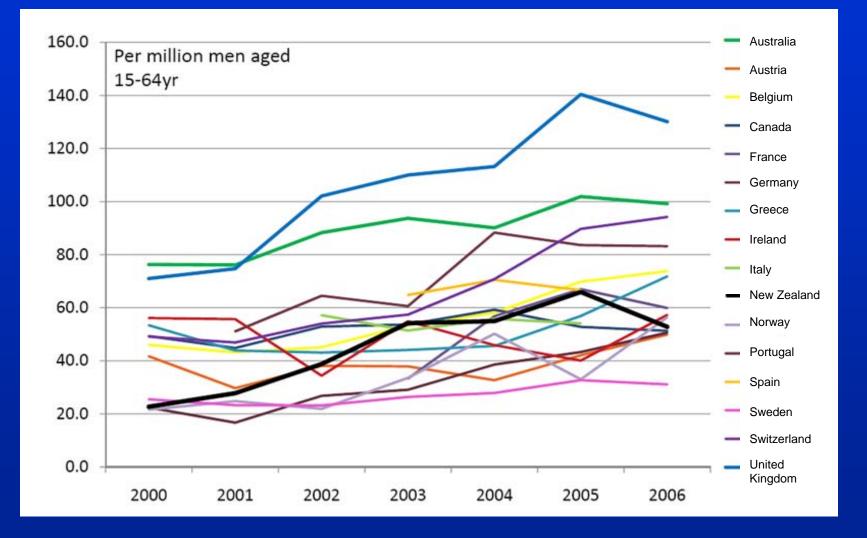
Other evidence in favour of using sexual contact. HIV treatment as prevention comes However, there is substantial concern from mother-to-child HIV transmission that these reports may overstate the case studies. Randomised controlled trials for HIV treatment as HIV prevention. have demonstrated that the use of HIV In response to the Swiss Statement, the therapies by pregnant women greatly joint United Nations Programme on HIV/ reduces the risk of HIV transmission to AIDS (UNAIDS) and national public her newborn baby. As a consequence, health authorities around the world and HIV transmission from mother to child in Australia emphasised that the effect of "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."

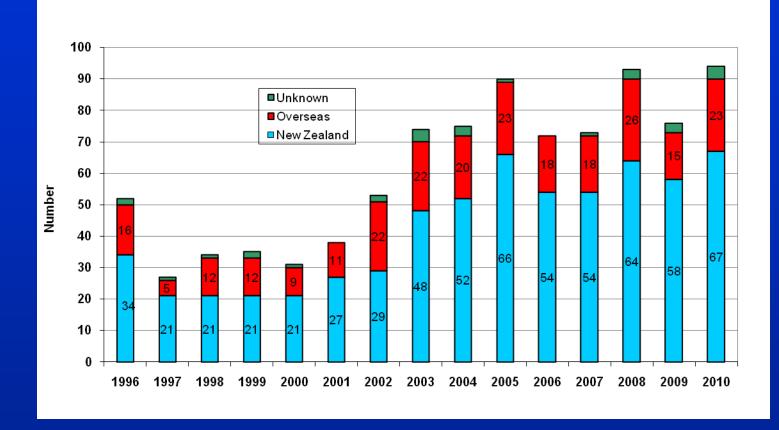
 "In Australia, as in most of the developed world, HIV transmission has recently increased markedly in homosexual men, despite the increasingly large majority of HIV-positive men on HIV therapy with undetectable viral load."

 "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."

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



Place of infection: Annual HIV diagnoses by antibody testing in homosexual/bisexual males in New Zealand,1996-2010

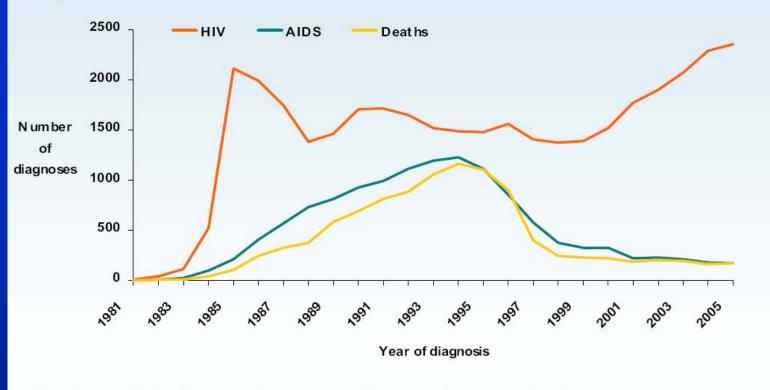


Data provided by AIDS Epidemiology Group, Department of Preventive and Social Medicine, University of Otago: Updated May 2011 Graph produced by Research, Analysis and Information Unit, New Zealand AIDS Foundation 2011.

Note (1): Includes both homosexual/bisexual and homosexual/bisexual/IDU.

Note (2): The most recent estimates (June and December 2010) indicate that 1400 – 1500 people are under treatment for HIV in New Zealand. On the basis that this represents 80% of all people alive with diagnosed HIV, the estimated total of those living with HIV in New Zealand in January 2011 is around 1800 (AIDS New Zealand, Issue 67, February 2011).

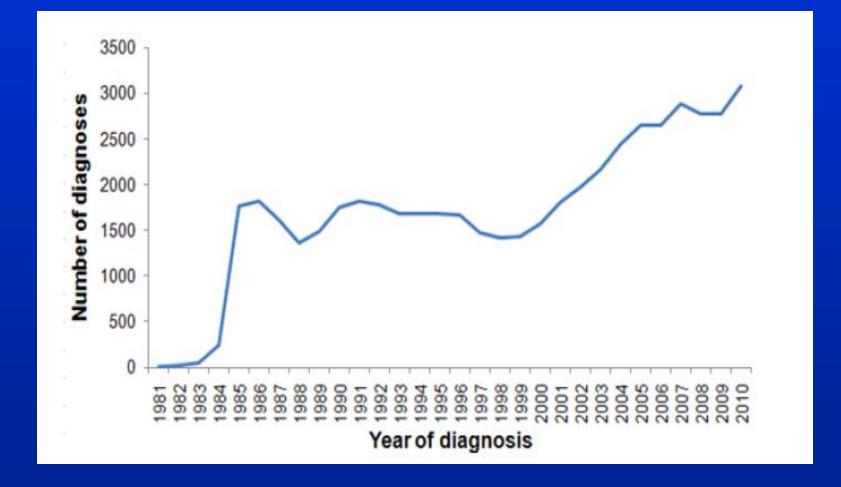
Annual HIV diagnoses and deaths for MSM, United Kingdom, 1981-2005



Numbers will rise for recent years as further reports are received Clinician reports of new HIV/AIDS diagnosis

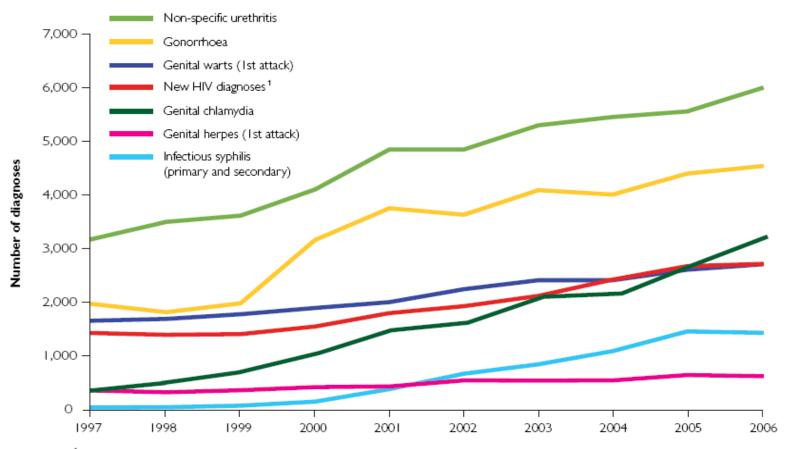
Hart,G. Epidemiology of HIV acquisition and transmission in MSM. Expert seminar on 'partnership patterns and HIV prevention amongst MSM' National AIDS Trust, June 2009.

Annual HIV diagnoses among MSM, 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.

Diagnoses of HIV and selected STI's among MSM, United Kingdom,1997-2006

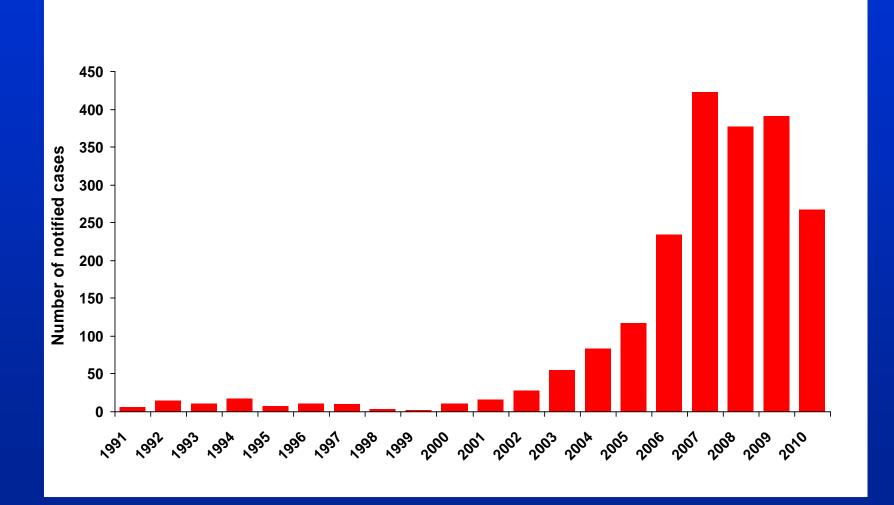


¹ Rates of new HIV diagnoses from 2003 onwards are adjusted for reporting delays

STI data from genitourinary medicine clinics and HIV/AIDS diagnoses

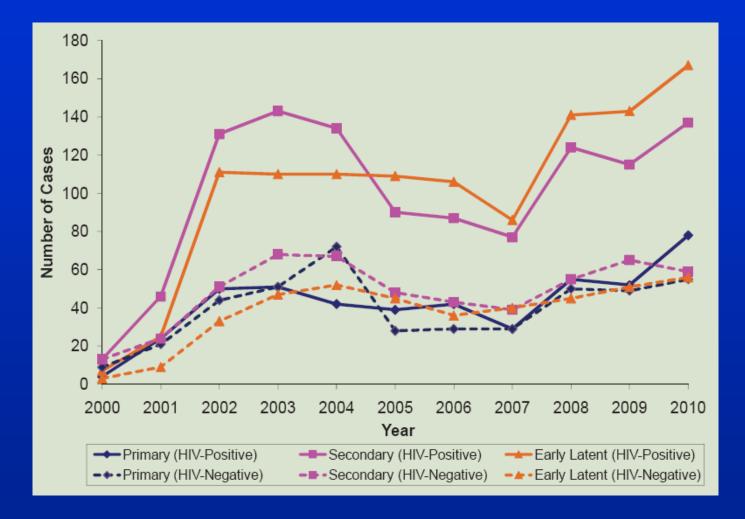
Health Protection Agency. Testing times, HIV and other sexually transmitted infections in the United Kingdom: 2007.

Annual notified cases of infectious syphilis, Victoria, Australia,1991-2010

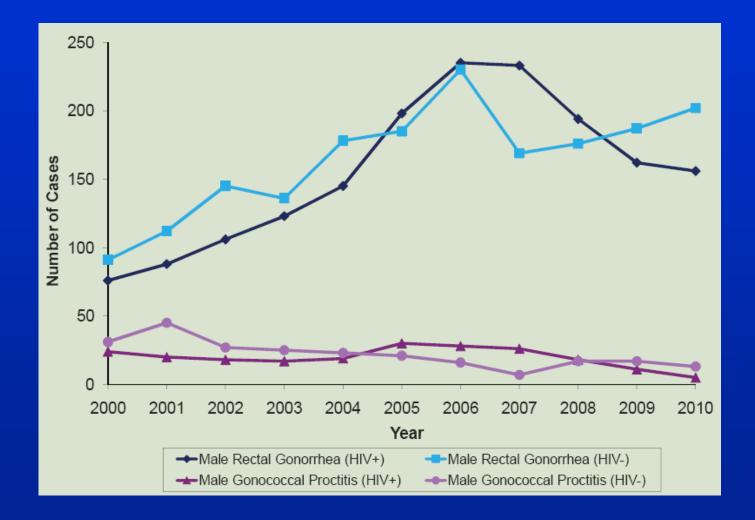


Source: Department of Health, Victoria. Victorian Infectious Disease Bulletin 2011; 14:(1) Fig 14.

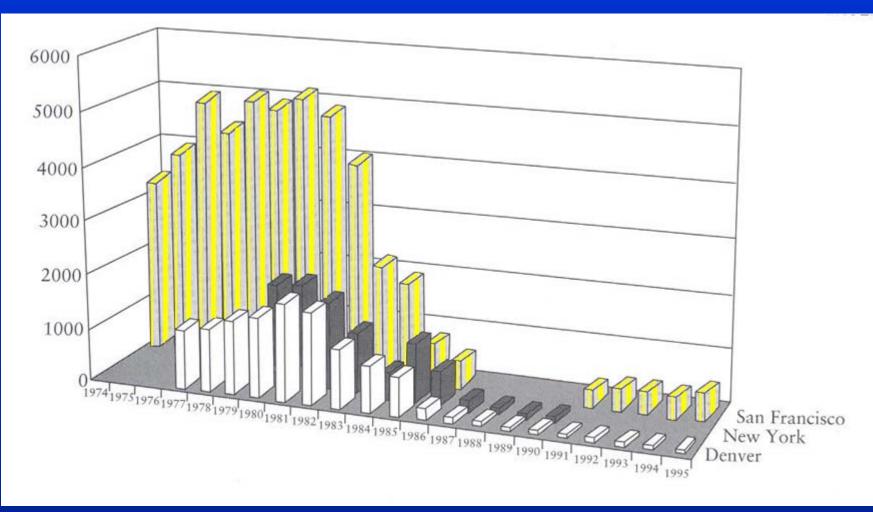
Early syphilis among MSM by HIV serostatus, 2000-2010, San Francisco



Rectal gonorrhoea among MSM by HIV serostatus, 2000-2010, San Francisco

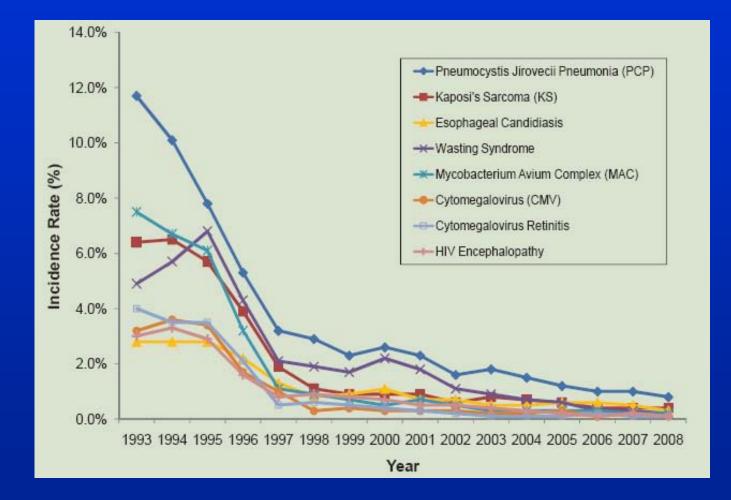


Annual rates of rectal gonorrhoea in men in three US cities, 1974-1995

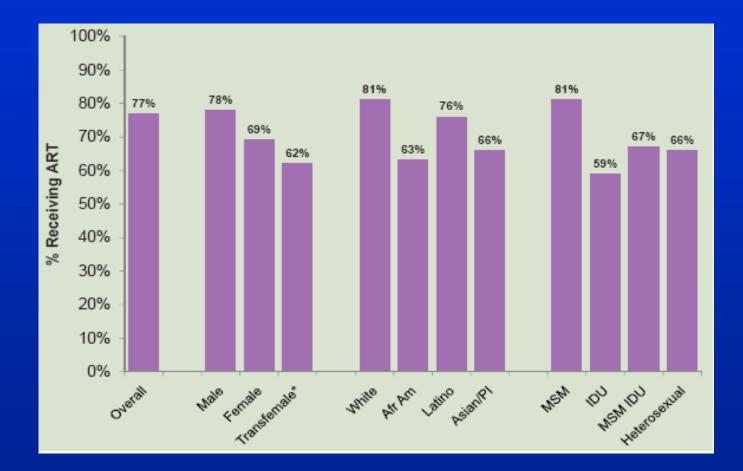


Doll, L.S. and Ostrow, D.G. in Holmes, K.K. et al, editors. Sexually transmitted diseases 1999 3rd ed. New York: McGraw-Hill; 1999. Fig 11-1:152.

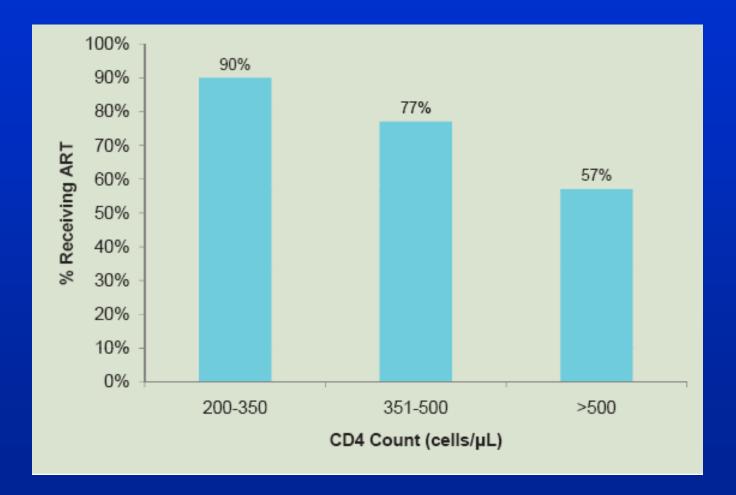
Incidence rate of opportunistic illnesses among adults and adolescents with AIDS, 1993-2008, San Francisco



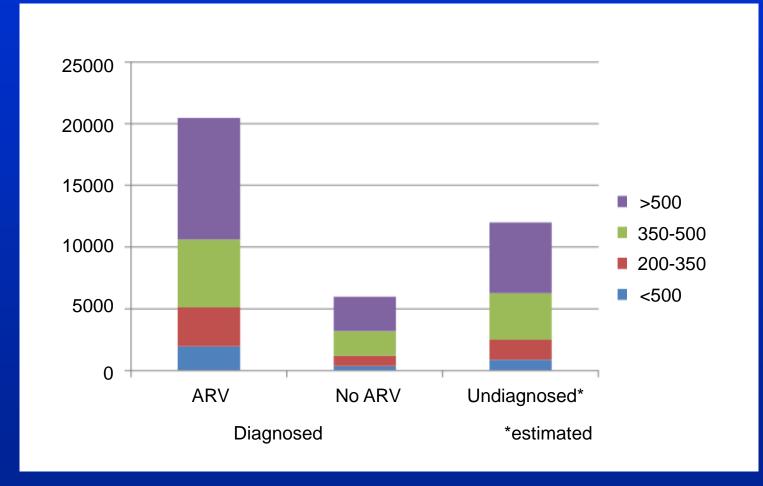
Estimate of antiretroviral therapy use in a sample of HIV (non-AIDS) cases through chart review, December 2010, San Francisco



Estimate of antiretroviral therapy use in a sample of HIV (non-AIDS) cases through chart review by CD4 level, December 2010, San Francisco

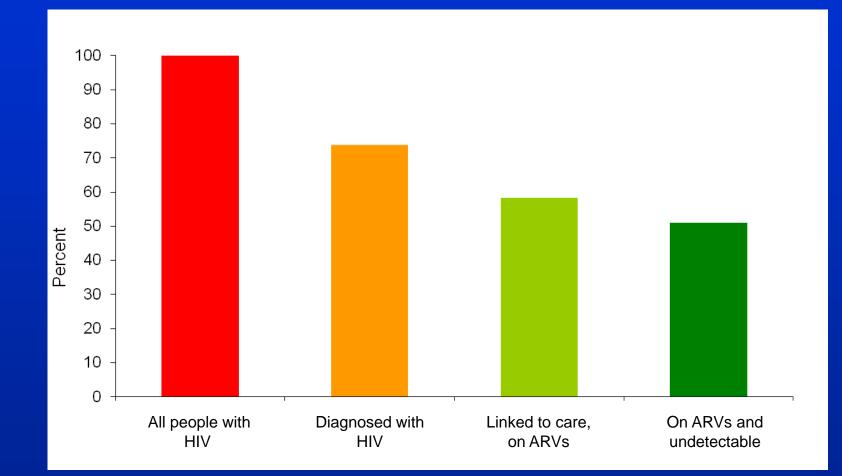


Number of HIV-infected MSM in the UK, by CD4 count, 2009



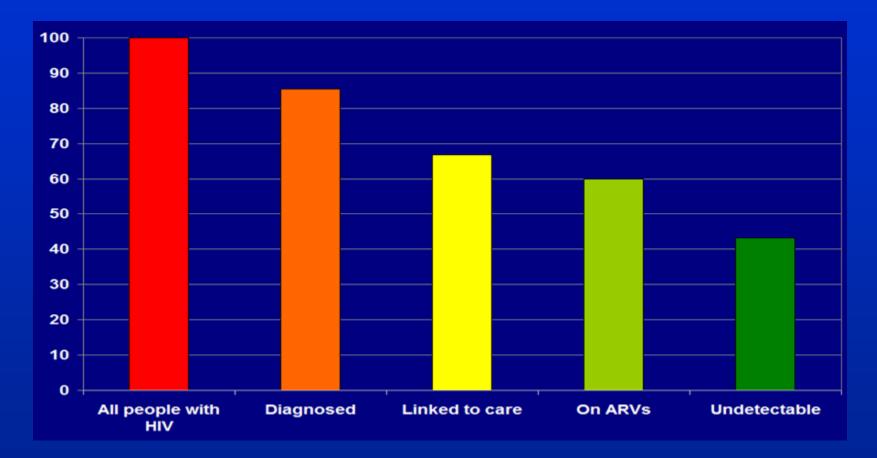
Delpech, V. Brown, A. The current efficacy of ARV in keeping viral loads down, the population perspective. Seminar on 'treatment as prevention'. National AIDS Trust, November 2010.

Treatment for care: HIV positive population in the United Kingdom, 2009



Data provided by Gus Cairns , www.aidsmap.com, from Health Protection Agency (UK) data sources: http://www.hpa.org.uk/hpr/archives/2011/news2211.htm http://www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1203064766492 http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1287145367237

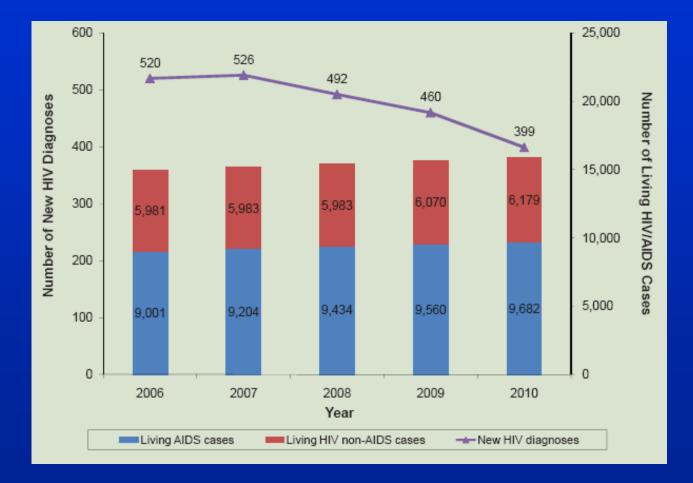
Treatment for care: HIV positive population in San Francisco, 2009



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.

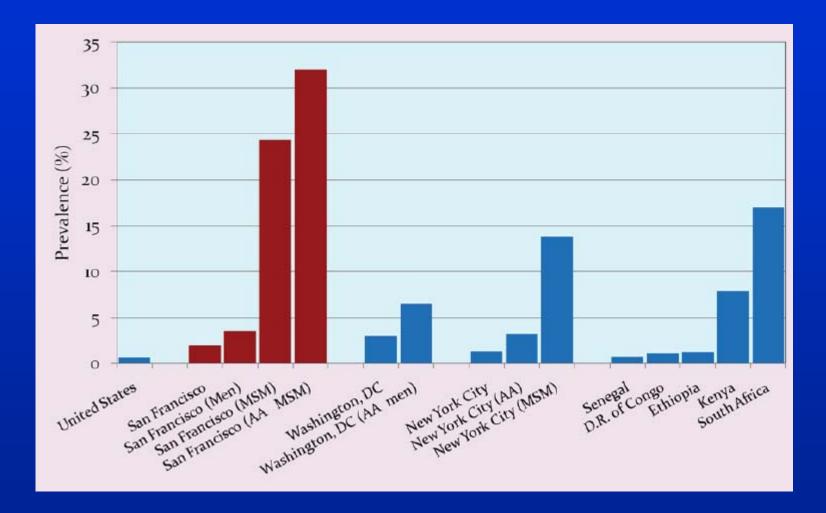
Cairns, G. Treatment as prevention: why? Expert seminar on 'treatment as prevention'. National AIDS Trust, November 2010.

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



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

HIV prevalence: MSM in San Francisco, 2007



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

HIV test status in sexual health clinic attenders in: 2005-2006

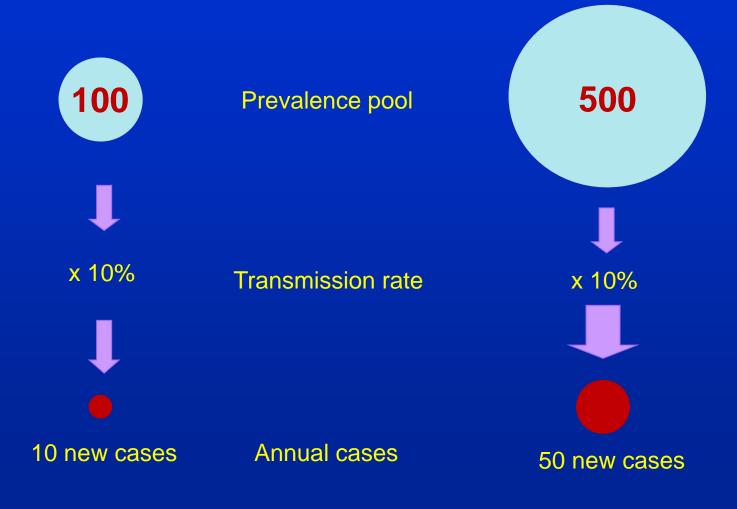
Group	% HIV +	% undiagnosed HIV +
Homosexual and bisexual men	4.41	2.01
Homosexual and bisexual women	0.00	0.00
Heterosexual men	0.12	0.06
Heterosexual women	0.14	0.04

Note: HIV prevalence in homosexual and bisexual men in sexual health clinics in Auckland is **6.07%**, outside Auckland is **2.07%**, and in New Zealand in total is **4.41%**.

AIDS Epidemiology Group. (2007). Unlinked anonymous study of HIV prevalence among attenders at sexual health clinics 2005/6. Report to the Ministry of Health. Dunedin: AIDS Epidemiology Group, University of Otago Medical School.

Prevalence drives incidence

Number of existing cases drives the number of new infections



Adapted from: Saxton, P. Second generation HIV surveillance among MSM in New Zealand. HIV Forum, 26th March 2009, Auckland.

The impact of the transmission dynamics of the HIV/AIDS epidemic on sexual behaviour: A new hypothesis to explain recent increases in risk taking-behaviour among men who have sex with men

Medical Hypotheses (2005) 65, 215–226

medical hypotheses

http://intl.elsevierhealth.com/journals/mehy

The impact of the transmission dynamics of the HIV/AIDS epidemic on sexual behaviour: A new hypothesis to explain recent increases in risk taking-behaviour among men who have sex with men

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Summary Increases in sexually transmitted infections and related high-risk behavious have been reported among men who have sex with men (MSM) in industrialised countries when effective antiretroviral therapy against HW infection has become widely available, in the mid-nineties. The reasons for these increases are not fully understood and often conflicting. Prevention fatigue, relapses to unsafe sex, as well as optimism toward the risk of developing ADS among people itving with HW are not unique to the era of antiretroviral therapy (ART). This has led researchers to highlight the need to investigate other potential reasons that could explain the increase in high-risk taking following the ART introduction. We put forward the hypothesis that the change in the transmission dynamics of the HIV/ADS epidemic before and after the introduction of ART has contributed to this change in high-risk behaviour.

It is suggested that a decline in sexual risk activities has occurred at the population-level following the initial spread of the HIV/AIDS epidemic because AIDS mortality and severe morbidity disproportionately depleted the pool of highrisk taking individuals. As a result, *non-volitional* changes may have occurred at the individual-level over time because the depletion of this pool of high-risk individuals made it more difficult for the remaining high-risk taking individuals to find partners to engage in risky sex with.

Following its introduction, ART has facilitated the differential replenishment of the pool of individuals willing to engage in high-risk taking behaviours because ART reduces AIDS mortality, and morbidity. Consequently, high-risk

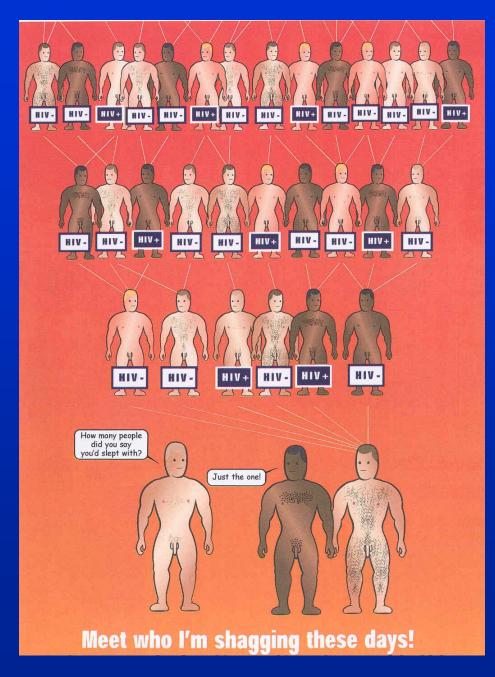
- "By reducing HIV related consequences, extending and favouring return to a more active sexual life... ART also enables the replenishment of the high-risk taking population by in-migrants or new sexually active recruits entering a given scene."
- These alterations in the proportion of high-risk taking individuals, which occur at the population-level, can be summarised as changes in sexual partner availability.

Boily, M. et al. Med Hypotheses 2005; 65:215-26.

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Exposed, Issue 9. Terrence Higgins Trust; June 2006.

Percentage of MSM reporting selected sexual behaviours and rate of male rectal gonorrhoea – San Francisco



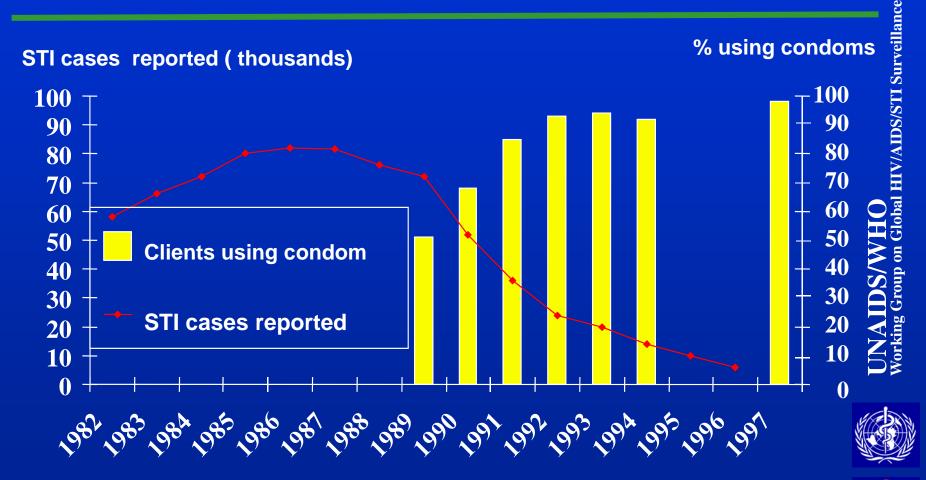
*Per 100,000 men aged ≥15 years.

[†]Condoms always used during anal sex during the previous 6 months. [§]Unprotected anal sex with two or more partners during the previous 6 months.



UNAIDS

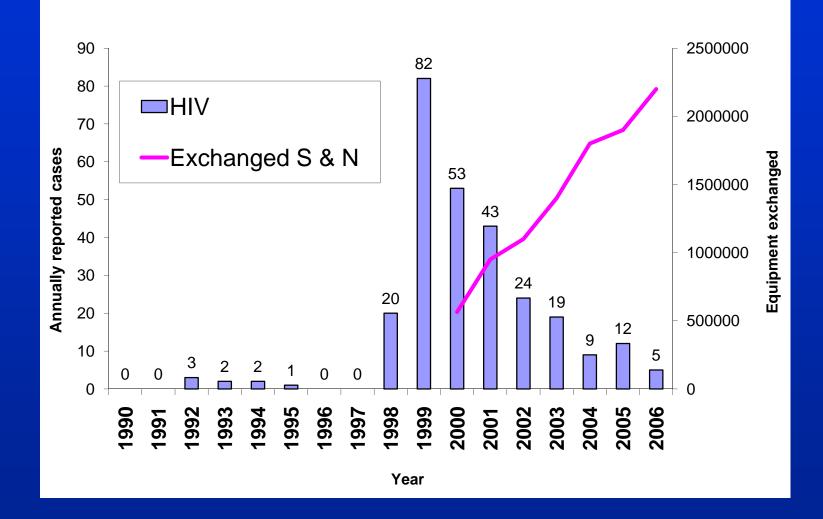
Condom use and reported STI cases - Thailand





Source: Sentinel Serosurveillance, Division of Epidemiology, Ministry of Public Health Thailand.

IDU associated HIV infection and needle/syringe exchange: Finland



Adapted from presentation: Salminen, M. Kansanterveyslaitos , KTL. HIV/AIDS epidemiology and prevention policy in Finland. National Public Health Institute

Condoms and HIV prevention: Position statement by UNAIDS, UNFPA and WHO, 19 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."

Conclusion

- (a) Maximise "condom use for prevention" in the MSM population.
- (b) Maximise "treatment for care" in the MSM population.
- (c) Continue research to establish the individual-level *efficacy* of treatment to prevent the transmission of HIV in MSM.
- (d) Develop a full research programme to determine the *effectiveness* of treatment to prevent the transmission of HIV at population level for MSM.

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