Treatment as Prevention debate

Marie Laga
Institute of Tropical Medicine
Antwerp, Belgium
TREATMENT IS PREVENTION

A scientific breakthrough in 2011 showed that HIV treatment not only saves lives, but reduces the risk by 96% of transmitting the disease.
Impact of increasing access to ART among MSM in Europe

PERSISTENT HIGH HIV INCIDENCE
Population-based HIV-1 incidence in France, 2003–08: a modelling analysis

Stéphane Le Vu, Yann Le Strat, Francis Barin, Josiane Pillonel, Françoise Cazein, Vanina Bousquet, Sylvie Brunet, Damien Thierry, Caroline Semaille, Laurence Meyer, Jean-Claude Desenclos

<table>
<thead>
<tr>
<th>New HIV-1 infections (95% CI)</th>
<th>Estimated population size</th>
<th>Incidence per 100 000 person-years (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heterosexual</td>
<td>3550 (3040–4050)</td>
<td>40 836 530</td>
</tr>
<tr>
<td>French women</td>
<td>810 (620–1000)</td>
<td>18 363 590</td>
</tr>
<tr>
<td>French men</td>
<td>1140 (830–1440)</td>
<td>18 848 440</td>
</tr>
<tr>
<td>Foreign women</td>
<td>940 (700–1180)</td>
<td>17 397 60</td>
</tr>
<tr>
<td>Foreign men</td>
<td>660 (460–870)</td>
<td>18 847 40</td>
</tr>
<tr>
<td>Men who have sex with men*</td>
<td>3320 (2830–3810)</td>
<td>329 950</td>
</tr>
<tr>
<td>Injecting drug users†</td>
<td>70 (0–190)</td>
<td>81 000</td>
</tr>
<tr>
<td>Overall</td>
<td>6940 (6200–7690)</td>
<td>41 247 480</td>
</tr>
</tbody>
</table>

Population (aged 18–69 years) size estimates at Jan 1, 2008 from Bajos and colleagues,⁹ Costes and colleagues,¹¹ and National Institute of Statistics and Economic Studies.¹² *All nationalities. †All nationalities, both sexes.

Table 2: Estimated new HIV-1 infections and incidence for France in 2008, by transmission group

**Interpretation** In France, HIV transmission disproportionately affects certain risk groups and seems to be out of control in the MSM population. Incidence should be tracked to monitor transmission dynamics in the various population risk groups and to help to target and assess prevention strategies.
A resurgent HIV-1 epidemic among men who have sex with men in the era of potent antiretroviral therapy

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

“The benefits of ART and early diagnosis, on individual infectivity reduction, have been offset by increases in risk behaviour “

AIDS 2008
The HIV epidemic among Men having Sex with Men in Belgium

Figuur 5bis: Evolutie van de HIV-diagnoses bij Belgen naar vermoedelijke overdrachtswijze, 1997-2010

Source WIV - HIV Surveillance report 2011
Increased HIV Incidence in Men Who Have Sex with Men Despite High Levels of ART-Induced Viral Suppression: Analysis of an Extensively Documented Epidemic

Andrew N. Phillips¹*, Valentina Cambiano¹, Fumiyo Nakagawa¹, Alison E. Brown², Fiona Lampe¹, Alison Rodger¹, Alec Miners³, Jonathan Elford⁴, Graham Hart¹, Anne M. Johnson¹, Jens Lundgren⁵, Valerie C. Delpech²

¹ Research Department of Infection & Population Health, UCL, London, United Kingdom, ² Health Protection Agency, London, United Kingdom, ³ London School of Hygiene and Tropical Medicine, London, United Kingdom, ⁴ City University, London, United Kingdom, ⁵ Copenhagen University Hospital/Rigshospitalet, and University of Copenhagen, Copenhagen, Denmark
HIV epidemic in MSM, UK

Despite high ARV coverage and retention in care.....
- Year on year increase in new diagnoses
- >3,000 in 2010, >25% are recently acquired (RITA)

**Impact of testing**

**HIV Testing**
- >85% in STI clinics
- 3.7 fold increase in testing from 16,000 in 2001 to 59,300 in 2010
- MSM accepting a test increased from 58% to over 90%
- In 2010, estimated 15 - 25% of all MSM aged 15-59 tested
Analysis of UK epidemic: Increased HIV incidence in MSM despite high levels of ART-induced viral suppression
Why has increased access to ART not resulted in HIV incidence declines?
HIV Treatment as Prevention: Natural Experiments Highlight Limits of Antiretroviral Treatment as HIV Prevention

David P. Wilson*

The Kirby Institute, Faculty of Medicine, University of New South Wales, Sydney, New South Wales, Australia
The sub-optimal Treatment Cascade

Series of steps required in order to reduce onward transmission from someone infected with HIV. If target is 90% for each step, 66% of HIV(+) people will be suppressed virus.

http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.1001231
Why is HIV transmission continuing in MSM?

Among 14,000 men who are infectious

- Treated: 5%
- Untreated >500: 16%
- Untreated 350-500: 12%
- Untreated <350: 5%
- Undiagnosed: 62%

Brown et al. HIV Med. 2013 HIV treatment as prevention among men who have sex with men in the UK: is transmission controlled by universal access to HIV treatment and care?
Increasing HIV prevalence as factor driving incidence

Estimated number of people living with HIV [prevalence] in Australia and per capita transmission rate [=average number of onward HIV infections resulting from each HIV(+) person] over time.

http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.1001231
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

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.

© 2010 Wolters Kluwer Health | Lippincott Williams & Wilkins

AIDS 2010, 24:907–913
ART and anal transmission?

- Rectal mucosa very fragile and high level of receptors
- Differential penetration of ARV
- Imperfect viral suppression in semen and rectum in presence of inflammation and other STI
Highly active antiretroviral therapy does not completely suppress HIV in semen of sexually active HIV-infected men who have sex with men

Joseph A. Politch\textsuperscript{a}, Kenneth H. Mayer\textsuperscript{b,d}, Seth L. Welles\textsuperscript{c}, William X. O’brien\textsuperscript{b}, Chong Xu\textsuperscript{a}, Frederick P. Bowman\textsuperscript{a} and Deborah J. Anderson\textsuperscript{a}

Results: Overall, HIV-1 was detected in 18/101 (18\%) blood and 30/101 (30\%) semen samples. Of 83 men with undetectable HIV in blood plasma, 25\% had HIV in semen with copy numbers ranging from 80 – 2,560. Multivariate analysis identified STI/urethritis (p = 0.003), TNF-\(\alpha\) (p = 0.0003), and unprotected insertive anal sex with an HIV-infected partner (p = 0.007) as independent predictors of seminal HIV detection.

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

© 2012 Wolters Kluwer Health | Lippincott Williams & Wilkins

AIDS 2012, 26:000–000
Increase in condomless anal sex?

• Some direct evidence (even if few prospective comparable data available)

• Increasing rates of STI as biologic markers

• Absolute number of HIV(+) MSM and sexual activity in HIV (+) men increases as a result of improved survival and life quality
“MSM are disproportionately affected by HIV and other STIs.”

“HIV reporting rates in MSM increased between 2004 and 2009 in the EU/EEA from 3.5 to 4.1 per 100,000 males.”

“Outbreaks of syphilis, LGV and HCV among MSM were reported by 13 countries.”

“Since 2003, the sharp increase in STIs seemed to have levelled off, and remained at a new high endemic level.”
Unsafe Sex and Increased Incidence of Hepatitis C Virus Infection among HIV-Infected Men Who Have Sex with Men: The Swiss HIV Cohort Study

Andri Rauch,1 Martin Rickenbach,2 Rainer Weber,3 Bernard Hirschel,4 Philip E. Tarr,5 Heiner C. Bucher,6 Pietro Vernazza,7 Enos Bernasconi,8 Annelies S. Zinkernagel,3 John Evison,1 and Hansjakob Furrer1, and the Swiss HIV Cohort Study*  

1Division of Infectious Diseases, University Hospital Berne, 2Data Center Swiss HIV Cohort Study, Lausanne, 3Division of Infectious Diseases, University Hospital Zurich, 4Division of Infectious Diseases, University Hospital Geneva, 5Division of Infectious Diseases, University Hospital Lausanne, 6Basel Institute for Clinical Epidemiology, University Hospital Basel, 7Division of Infectious Diseases, Kantonsspital St. Gallen, and 8Division of Infectious Diseases, Ospedale Civico Lugano, Switzerland
STIs in MSM, UK

- Experienced largest increase in new infections (all age groups) in 2011*
- Improved and increased testing
- Ongoing unsafe sexual behaviour – HIV transmission and STI outbreaks (e.g. LGV, Shigella)

* For cases in men where sexual orientation was recorded.
LGV: lymphogranuloma venereum
Condom use by serostatus among MSM – EMIS survey Belgian sample

% condom use and HIV concordancy last sex n=2912

- No anal intercourse with the last non-steady male partner
- Protected anal intercourse
- UAI with presumingly concordant partner
- UAI with partner of discordant/unknown HIV status

- Total
- Diagnosed positive
- Untested/Latest test negative
Ongoing HIV-1 transmission among men who have sex with men in Amsterdam: a 25-year prospective cohort study

Irálice A.V. Jansen\textsuperscript{a}, Ronald B. Geskus\textsuperscript{a,b}, Udi Davidovich\textsuperscript{a}, Suzanne Jurriaans\textsuperscript{c}, Roel A. Coutinho\textsuperscript{d,e}, Maria Prins\textsuperscript{a,e} and Ineke G. Stolte\textsuperscript{a}

Fig. 2. Percentage sexual risk behaviour in the preceding 6 months among MSM having anal sex in the Amsterdam Cohort Studies, 1984–2009. Distinction in UAI for steady and casual partners is available since 1991 onwards, as since then this distinction was made in the 6-monthly questionnaire.
Possible explanations for increased risk behaviour

**ART related:**
- Changing face of the epidemic: AIDS less visible and less deaths
- Young MSM (<20y) sexually active earlier, and never exposed to AIDS as a killer disease
- Condoms replaced by “negotiated safety” such as serosorting or viral load considerations

**Context:**
- Prevention fatigue: challenge of maintaining safe sex for extended period
- Internet as new way of recruiting partners
- “Gay communities” less organized and “community norms for safe sex” weakened
Does ART prevent HIV transmission among MSM?

Kathryn E. Muessig\textsuperscript{a}, M. Kumi Smith\textsuperscript{b}, Kimberly A. Powers\textsuperscript{a,b}, Ying-Ru Lo\textsuperscript{c}, David N. Burns\textsuperscript{d}, Andrew E. Grulich\textsuperscript{e}, Andrew N. Phillips\textsuperscript{f} and Myron S. Cohen\textsuperscript{a,b,g}

\textbf{Results:} Although ART treatment among MSM is likely to provide some preventive benefit, it is unknown whether it will reduce HIV infectiousness via anal intercourse to the same extent as via penile–vaginal intercourse. Additional research is needed on the pharmacokinetic properties of specific antiretroviral agents in the gastrointestinal tract. Estimates of risk behaviors and the incidence of HIV among MSM before and after the introduction and expansion of ART suggest that the population-level protective benefits of ART may be attenuated by a number of factors, most notably, continuing or increasing frequency of condomless anal intercourse and incidence of other sexually transmitted infections (STIs). Additional studies are needed on the impact of ART on HIV sexual risk behaviors and transmission among MSM outside of developed countries in North America, western Europe, and Australia.

\textbf{Conclusion:} The benefits of treatment as prevention for MSM are highly plausible, but not certain. In the face of these unknowns, treatment guidelines for earlier ART initiation should be considered within a combination prevention strategy that includes earlier diagnosis, expanded STI treatment, and structural and behavioral interventions.
Concerns with regard to very early Treatment (Cohen, Lancet 2013)

- **Acceptability** for the newly infected individual?
- Degree of reduction of early inflammation and health benefits?
- **Side effects** of long treatment?
- **Adherence** to treatment and transmission of resistant viruses?
- **Logistical challenges** (lack of VL measurements..) dealing with increasing numbers
- Prioritizing those with more advanced disease?
- **Behavioral disinhibition**
Conclusions: why TasP alone will not lead to 0 new infections among MSM

- Undiagnosed HIV and losses in treatment cascade
- Role of Acute infections in transmission?
- Imperfect viral suppression in semen and rectum
- Lower Condom use in favor of other approaches “negotiated safety”
- STI outbreaks and high endemic levels
- Increasing background HIV prevalence
Conclusion (Cont’d)

• Optimised Testing and linkage to care to reduce “community viral load” is a priority.

• Offering Early treatment should be promoted when possible and acceptable.

• Combination prevention, including condom promotion and other behavioral and structural approaches need to be reemphasized and strengthened, to make TasP work.
“Condoms, **when used** consistently and correctly, are still the most effective tool in preventing the sexual transmission of HIV and other STI.

As “negotiated safety” is not effective in settings of high partner exchange and low levels of trust, and viral suppression is imperfect in MSM, **condoms should be brought back to the centre of the prevention debate**!
Prevention is also Promoting Sexual Health
COMBINATION Prevention for maximum effect

- Biomedical tools & Interventions
- Structural changes & political
- HIV/STI Testing & Linkage to Care
- Community driven approaches & movements
- Individual & Small Group behavioral strategies

Adapted from Coates Lancet; 2008