Using Modeling to Set Programmatic Goals for HIV Prevention in MSM

Patrick S. Sullivan, DVM, PhD
Department of Epidemiology
April 10, 2018
HIV in men who have sex with men

Patrick S. Sullivan, Alan Hubbard-Bellinger, Thomas Catley, Simon M. Germaine, Ian McGowan, Eduardo Sambani, Adam Smith, Prabhu Sivan, Gomaphi Gove, Jorge Sanchez

Men who have sex with men (MSM) have been substantially affected by HIV epidemics worldwide. In MSM, we are re-emerging in many high-income countries and gaining greater recognition in many low-income and middle-income countries. Better HIV prevention strategies are urgently needed. Our review of HIV prevention strategies for MSM identified several important themes. At the beginning of the epidemic, stand-alone behavioral interventions mostly aimed to reduce unprotected and intermittent, which, although somewhat efficacious, did not reduce HIV transmission. Biomedical prevention strategies reduce the incidence of HIV infection. However, behavior and biomedical interactions with coordinated behavioral and structural strategies could optimise the effectiveness of prevention. Modelling suggests that, with sufficient coverage, available interventions are sufficient to arrest at least a quarter of new HIV infections in MSM in diverse countries. Scale-up of HIV prevention programmes for MSM is difficult because of homophobia and low willingness to access to HIV testing and care, and financial constraints.

### Introduction

Men who have sex with men (MSM) have always had a key role in the global HIV epidemics. HIV epidemics in MSM are re-emerging in high-income countries and have been noted in many low-income and middle-income countries. We review HIV prevention interventions for MSM, emphasizing the importance of the development and assessment of combination prevention package, and address challenges. The WHO used the highest standard of evidence (HASTE) system (which also includes data for implementation sciences) in its 2012 review of published work, whereas WHO used the grading of recommendations assessment, development and evaluation (GRADe) systems. We combine these reviews and our own comprehensive review of work and support a conceptual framework for packaging of interventions and modelling of the potential effect of scale-up of HIV prevention interventions for MSM.

### Search strategy and selection criteria

Between 1 Oct 2011, and 31 Mar 2012, we assessed HIV prevention interventions for MSM (published in English in PubMed, Embase, Scopus, ProQMD, Social Science Citation Index, Science Citation Index Expanded, Conference Proceedings Citation Index-Science, the Canadian Index to Nursing and Allied Health Literature, and focused on systematic reviews and meta-analyses (appendix). We also mentioned the results of meta-analyses of HIV prevention in MSM. We compiled 1725 unique citations and refined our results to identify 12 interventions with positive HIV prevention interventions tested in MSM. Further details of our search strategy and bibliographic for all included articles, systematic reviews, and meta-analyses are in the appendix.

### Key messages

- Governmental, academic, and community strategies have been implemented to reduce HIV epidemics in men who have sex with men (MSM). The prevention of HIV transmission in MSM is a high priority for public health agencies worldwide.
- The prevention of HIV transmission in MSM is a high priority for public health agencies worldwide. Various interventions have been considered, including behavioral, biomedical, and structural interventions.
- Behavioral interventions are often effective in reducing the incidence of HIV infection. However, they can be challenging to implement, especially in populations with high levels of homophobia and discrimination.
- Biomedical interventions, such as antiretroviral therapy (ART) and pre-exposure prophylaxis (PrEP), have been shown to be effective in reducing the incidence of HIV infection in MSM.
- Structural interventions, such as the implementation of policies that promote sexual rights and the reduction of stigma and discrimination, can also help to reduce the incidence of HIV infection in MSM.
- A combination of behavioral, biomedical, and structural interventions is necessary to effectively reduce the incidence of HIV infection in MSM.
Using HIV prevention technologies we have today, we could prevent a quarter of new infections among MSM in the next decade.

Existing Technologies + Smart Packaging + Political Will + Safe Places for Prevention = 25% reduction
Modeling of Prevention Impact

• Agent-based, stochastic model

• Kenya, USA, Peru, India

• Country-specific parameterization and calibration

• Three prevention approaches/packages:
  – PrEP
  – Treatment of positives
  – Increased condom use

• Outcome: Proportion of infections averted after 10 years
Estimated percent of new HIV infections among MSM prevented by three prevention approaches, four countries
Estimated percent of new HIV infections among MSM prevented by oral PrEP at varying levels of adherence, four countries

<table>
<thead>
<tr>
<th>Adherence</th>
<th>USA</th>
<th>Peru</th>
<th>Kenya</th>
<th>India</th>
</tr>
</thead>
<tbody>
<tr>
<td>50%</td>
<td>19%</td>
<td>23%</td>
<td>27%</td>
<td></td>
</tr>
<tr>
<td>75%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>90%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
HIV infections estimated to be averted by PrEP, reduction in UAI, and early ARV treatment in a stochastic simulation model of HIV transmissions among MSM in Africa
HIV infections estimated to be averted by PrEP, reduction in UAI, increased HIV testing, and early ARV treatment in a stochastic simulation model of HIV transmissions among MSM in Africa
Proportion of HIV infections among MSM averted by PrEP, by level of coverage, US, Peru, Kenya, India, and South Africa

Impact of HIV Pre-Exposure Prophylaxis among MSM in the United States
A Web-Based Modeling Tool for Public Health Practice

This software tool provides additional opportunities to explore the mathematical models of the paper:


This webtool provides tools to explore the simulation results from the main CDC guidelines modeling scenario (J2) that served as the basis of the main analysis results and sensitivity analyses.

To get started, enter a desired number of years in the simulation. One model alone or a two-model comparison set may be shown together based on different coverage and adherence parameters. The parameters are defined as follows:

- PrEP Coverage: the proportion of MSM indicated for PrEP under the CDC guidelines that initiate PrEP. The default value is 40% coverage.
- PrEP Adherence: the proportion of MSM who are highly adherent to PrEP, defined as taking ≥4 pills per week, which is associated with a 95% reduction in the per-act probability of infection. The default value is 60%, following adherence data from an open-label demonstration project.

After selecting the parameters set in each model, the model will automatically update the plots and summary data tables.

In addition to these model parameters, select a starting HIV prevalence that corresponds to the local value of interest and the number of years for the PrEP intervention simulation. Note that the model in the paper corresponds to a starting prevalence of 2% that corresponds to observed values in a cohort of Atlanta-area MSM. Bayesian calibration methods were used to arrive at the other starting prevalences by adjusting the frequency of anal intercourse within partnerships; since other factors may also contribute to variation in local HIV prevalence, this model assumption should be considered when evaluating the results.

We acknowledge support from the CDC/NCHSTP Epidemiological and Economic Modeling Agreement (SU38PS004648). The findings and conclusions used to build this tool are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention or the Department of Health and Human Services.

https://prism.shinyapps.io/cdc-prep-guidelines/
Observational Designs
• Implementation in clinic settings
• Less controlled setting
• Prospective cohorts

Stepped-wedge cluster RCT
• Immediate ARV initiation after HIV+ test
• 6 South African Communities
• Outcome: Time to viral suppression

RCT Design of self-testing
• Implementation by mailout of kits
• Usual care control arm
• Results: 5.5 vs 1.5 HIV tests per year for MSM

Hybrid Design
• Primary goal: Test implementation with alternative recruitment and support strategies
• Secondary: Linkage to appropriate followup care
Study Design

• Prospective HIV/STI incidence cohort study: 2010-2014
  • Sexually active black and white MSM in Atlanta
  • Ages 18 - 39

• Recruitment
  • MSM community venues, Facebook

• Procedures
  • Testing: HIV, Chlamydia, Gonorrhea, Syphilis
  • Behavioral questionnaire

• Enrollment
  • 803 men enrolled
  • 30% HIV-positive (BMSM: 44%, WMSM: 13%)
  • 562 HIV-negative MSM observed for 24 months
  • 79% retained in study at 24-months
## HIV Incidence

<table>
<thead>
<tr>
<th></th>
<th>Black MSM</th>
<th>White MSM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence rate</td>
<td>6.6% / year</td>
<td>1.7% / year</td>
</tr>
<tr>
<td>New HIV infections</td>
<td>24</td>
<td>8</td>
</tr>
<tr>
<td>% HIV-positive at end of study</td>
<td>11.3%</td>
<td>3.6%</td>
</tr>
<tr>
<td><strong>Age 18 – 24</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence rate</td>
<td>12.1% / year</td>
<td>1.0 % / year</td>
</tr>
<tr>
<td>New HIV infections</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td>% HIV-positive at end of study</td>
<td>16.6%</td>
<td>1.6%</td>
</tr>
<tr>
<td><strong>Age 25+</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence rate</td>
<td>3.5% / year</td>
<td>1.9% / year</td>
</tr>
<tr>
<td>New HIV infections</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>% HIV-positive at end of study</td>
<td>6.0%</td>
<td>4.5%</td>
</tr>
</tbody>
</table>
The PrEP Continuum

Applying a PrEP Continuum of Care for Men Who Have Sex With Men in Atlanta, Georgia

Colleen F. Kelley,1,2 Erin Kahle,2 Aaron Siegler,2 Travis Sanchez,2 Carlos del Rio,1,3 Patrick S. Sullivan,2 and Eli S. Rosenberg2

1Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine, 2Department of Epidemiology, and 3Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, Georgia

(See the Editorial Commentary by Mayer and Krakower on pages 598–600.)

Reductions in human immunodeficiency virus (HIV) incidence with pre-exposure prophylaxis (PrEP) for men who have sex with men (MSM) will require significant coverage of those at risk. We propose a simplified frame-
### Theoretical model of the PrEP care continuum, factors relevant to uptake, and areas for intervention.

**Factors Relevant to PrEP Uptake**

- Awareness/ willingness
  - Awareness of PrEP
  - Risk/benefit perceptions
  - Barriers to seeking PrEP
    - PrEP cost
    - PrEP side-effects
    - Perceived PrEP stigma

- Access to Healthcare
  - Individual
    - Has public or private health insurance
    - Regularly sees primary care doctor
    - Can afford medication
    - Transportation

- Likely to Receive Rx
  - Healthcare provider
    - Aware of PrEP
    - Willing to prescribe PrEP
    - SCREENs for risk and determines patient eligible
  - Patient
    - Adequately report behavior eligible for PrEP
    - PrEP not contraindicated

- Adherence and Efficacy
  - Side-effects/medication tolerance
  - Risk compensation
  - Dosing schedules
  - Long-term adherence and PrEP continuation

**Interventions to Enhance PrEP Uptake**

- Mass media campaigns
- Community mobilization
- Alternative PrEP formulations
- Community-based efforts to destigmatize PrEP

- Medication and/or co-payment waivers
- Free service provision
- Enhanced access
  - Centralized provision
  - Enhanced referral systems

- Provider education/training
- Electronic tools to assess sexual risk and indicate PrEP
- Automated systems to minimize provider burden

- Counseling
  - Medication adherence
  - Sexual risk reduction
- Home support systems to minimize patient testing burden
- Electronic adherence reminders/support

---

© The Author 2015. Published by Oxford University Press on behalf of the Infectious Diseases Society of America. All rights reserved. For Permissions, please e-mail: journals.permissions@oup.com.
Theoretical model of the PrEP care continuum, factors relevant to uptake, and areas for intervention.

Factors Relevant to PrEP Uptake

- Awareness of PrEP
- Risk/benefit perceptions
- Barriers to seeking PrEP
  - PrEP cost
  - PrEP side-effects
  - Perceived PrEP stigma

Access to Healthcare

- Individual
  - Has public or private health insurance
  - Regularly sees primary care doctor
  - Can afford medication
  - Transportation

- Healthcare provider
  - Aware of PrEP
  - Willing to prescribe PrEP
  - Screens for risk and determines patient eligible

- Patient
  - Adequately report behavior eligible for PrEP
  - PrEP not contraindicated

Likely to Receive Rx

Adherence and Efficacy

- Side-effects/medication tolerance
- Risk compensation
- Dosing schedules
- Long-term adherence and PrEP continuation

Interventions to Enhance PrEP Uptake

- Mass media campaigns
- Community mobilization
- Alternative PrEP formulations
- Community-based efforts to destigmatize PrEP

- Medication and/or co-payment waivers
- Free service provision

- Enhanced access
- Centralized provision
- Enhanced referral systems

- Provider education/training
- Electronic tools to assess sexual risk and indicate PrEP
- Automated systems to minimize provider burden

- Counseling
  - Medication adherence
  - Sexual risk reduction

- Home support systems to minimize patient testing burden
- Electronic adherence reminders/support


IR Outcomes:
- Sustainability
- Implementation
- Process
- Scalability
IR Outcomes:
- Implementation
- Process
- Scalability
IR Outcomes:
• Sustainability
• Implementation
• Speed
• Scalability

IR Outcomes:
- Barriers
- Implementation
- Process
- System effects

Source: Serota et al, Clinical Infect Dis, in press, 2018
Do Models work?

- Involve[men]t: cohort of HIV-negative Black, white MSM in Atlanta, 2010-2014
  - HIV incidence in Black MSM aged 18-29: 8.1/100 PY
- Lancet model prediction: 22%
- Emory CAMP/Jenness web tool prediction:
  - Instantaneous 50%: 34% reduction
  - Weighted coverage (30%): 24% reduction
- Ele[men]t: cohort of HIV-negative, Black MSM in Atlanta, 2016-present
  - 53% of men had attended PrEP initiation visit
  - HIV incidence in Black MSM aged 18-29: 6.2/100 PY
  - 23% reduction in incidence
Evaluation of Self-Testing Among Men who have sex with men Project (eSTAMP)

**GOAL**

To evaluate the public health benefits of providing free HIV Rapid Diagnostic Tests (RDTs) to internet recruited MSM.

**PRIMARY OUTCOMES**

- Frequency of HIV testing
- Diagnoses of HIV infection
- Differences in HIV sexual risk behaviors

PIs: Robin Macgowan (CDC) and Patrick Sullivan (Emory)
Study Flow

Randomized Control Trial (RCT)

Randomization

- Screened: n = 10,773
- Registered: n = 3,825
- Complete baseline: n = 2,665

Intervention n = 1,325
- 4 rapid tests after baseline, replenished after each survey
- Results reporting system

Control n = 1,340
- HIV testing information

Follow-up online surveys: 3, 6, 9, 12 months

Performance Assessment Kit (PAK)
HIV testing outcomes among MSM who completed ≥1 follow-up surveys, eSTAMP, 2015-2016

<table>
<thead>
<tr>
<th></th>
<th>Intervention</th>
<th>Control</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No HIV test reported</td>
<td>29/966 (3%)</td>
<td>343/958 (36%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Tested ≥ 3 times*</td>
<td>761/965 (79%)</td>
<td>214/958 (22%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Tested ≥ 3 times among never testers at enrollment</td>
<td>110/157 (70%)</td>
<td>10/136 (7%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>No. of tests, mean (SD)</td>
<td>5.5 (3.6)</td>
<td>1.5 (1.8)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>No. facility-based tests, mean (SD)</td>
<td>0.9 (1.5)</td>
<td>1.5 (1.8)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Facility-based HIV testing</td>
<td>395/966 (41%)</td>
<td>614/958 (64%)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

* Excludes missing data
Questions!!!!

• Who should distribute test kits?
• Are there better or worse online venues to recruit men to testing?
• How can we improve post-testing outcomes in terms of linkage to care?
• How often do kits need to be sent?
• How do we address needs for prevention counseling?
IR Outcomes:
- Sustainability
- Implementation
- Process
- Scalability
- Reach
- Costs
- Acceptability
Summary

• Modelling helps us to understand the targets for implementation
• Even if all models are wrong, the order of magnitude is likely right
• If you’re doing efficacy research or observational epidemiology from a public health perspective, you will come across important questions about implementation, and they can be answered systematically
• The methods used to answer questions about key IS questions range from familiar to exotic.
• You’re likely already doing some form of implementation science, formally or informally, with or without measured IR outcomes. If not, you probably have some great implementation questions that could be answered by IS, with friends (and hopefully IR outcomes).
Acknowledgements

• Eli Rosenberg
• Travis Sanchez
• Aaron Siegler
• David Serota
• Colleen Kelley
• Linda-Gail Bekker
• Nancy Phaswanamafuya
• Stefan Baral
• Sam Jenness
• Research Participants

Supported by

NIAID
NIMH
NICHD
NIDA
CDC
Emory CFAR
The MAC AIDS Fund
Gilead Sciences