IMPACT OF LESS STRINGENT DEFERRAL POLICIES FOR MEN HAVING SEX WITH MEN

PREDICTIONS VERSUS REALITY

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ISBT, London
June 26, 2015
Currently, the most common policy regarding the eligibility of men who had sex (MSM) with men: ‘Permanent deferral’

- e.g. in the US: *Sex with another man, even once, since 1977*
- Other countries with a permanent deferral: Germany, France, Sweden, Hong Kong, China, Egypt, etc.
  (See Benjamin et al., Vox sanguinis 2011)

But the international situation is changing…
Deferral policies for MSM: Inappropriate discrimination or justifiable safeguard?

- No restriction for MSM
- Temporary deferral only if multiple MSM partners, unprotected sex
- Temporary deferral only if unprotected sex with MSM partner
- Temporary deferral if multiple MSM partners, (unprotected sex or not)
- Temporary deferral if MSM behavior (regardless of number of partners; unprotected sex or not)
- Lifetime deferral (regardless of number of partners; unprotected sex or not)

What is the least restrictive deferral policy that could achieve optimal safety?
How can the impact of a less restrictive deferral policy be evaluated?

- Just implement the change and observe?
  Not very appealing from a risk management perspective

- Perform a ‘clinical trial’?
  Feasibility is a major issue

- Model the impact of the change?
  Let’s talk about that…
### Who tried what and when…

<table>
<thead>
<tr>
<th>First author</th>
<th>Reference</th>
<th>Year</th>
<th>What was modelled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dayton, A</td>
<td>BPAC meeting, FDA</td>
<td>2000</td>
<td>Change from permanent to 5-year deferral</td>
</tr>
<tr>
<td>Germain, M</td>
<td>Transfusion, vol. 43, p. 25</td>
<td>2003</td>
<td>Change from permanent to 1-year deferral</td>
</tr>
<tr>
<td>Soldan, K</td>
<td>Vox Sanguinis, vol. 84, p. 265</td>
<td>2003</td>
<td>Change from permanent to 1-year deferral, Change from permanent to no deferral</td>
</tr>
<tr>
<td>Anderson, SA</td>
<td>Transfusion, vol. 49, p. 1102</td>
<td>2009</td>
<td>Change from permanent to 5-year deferral, Change from permanent to 1-year deferral</td>
</tr>
<tr>
<td>Davison, KL</td>
<td>Vox Sanguinis, vol. 101, p. 291</td>
<td>2011</td>
<td>Change from permanent to 5-year deferral</td>
</tr>
<tr>
<td>Pillonel, J</td>
<td>Vox Sanguinis, vol. 102, p. 13</td>
<td>2012</td>
<td>Change from permanent to no deferral (if only one MSM partner in last 12 months)</td>
</tr>
<tr>
<td>Davison, KL</td>
<td>Vox Sanguinis, vol. 105, p. 85</td>
<td>2013</td>
<td>Change from permanent to 1-year deferral</td>
</tr>
<tr>
<td>Germain, M</td>
<td>Vox Sanguinis, Epub</td>
<td>2013</td>
<td>Change from permanent to 5-year deferral</td>
</tr>
</tbody>
</table>
Common features of most models:

- How many new donors would become eligible and donate under the revised policy?
- How many of these donors would be infected with HIV?
- How many of these infected units would end up being transfused? (because of errors, test failures, etc.)
- What is the uncertainty around these numbers? (sensitivity analysis, Monte Carlo simulation)
- **Note:** Generally, the impact is calculated for the first year post-implementation
MSM RISK MODELS; A SIMPLIFIED VISUAL REPRESENTATION

DONORS (RESTRICTIVE MSM DEFERRAL POLICY) 

RECIPIENTS

Transfusion Safety Features

Infected donation
MSM RISK MODELS; A SIMPLIFIED VISUAL REPRESENTATION

DONORS (LIBERAL MSM DEFERRAL POLICY)

- Infected donation
- Infected donation
- Infected donation

RECIPIENTS

Blood Products
Stem Cells
Human Tissues
The number of MSM who would become eligible and decide to donate in a given year ($N_{1y}$), under a five-year deferral policy, is given by the formula:

$$N_{1y} = \text{MSM}_{\text{tot}} \times P_{\text{elig}} \times P_{\text{don}},$$

where:

- $\text{MSM}_{\text{tot}}$ is the total number of MSM in the population
- $P_{\text{elig}}$ is the proportion of these MSM who would become eligible
- $P_{\text{don}}$ is the proportion of those eligible who would donate
The number of HIV-contaminated units that would be made available for transfusion in a given year ($U_{1y}$), as a result of this five-year deferral policy, is obtained as follows:

$$U_{1y} = N_{1y} \times P_{\text{hiv}} \times (P_{\text{falseneg}} + P_{\text{variant}} + P_{\text{window}} + P_{\text{tech}} + P_{\text{errinv}} + P_{\text{urgent}}),$$

where:

- $P_{\text{hiv}}$ is the proportion of newly eligible MSM donors who would be unknowingly seropositive, and...
**RISK MODEL; AN EXAMPLE**

\[ P_{\text{falseneg}} \] is the proportion of screening tests that give a false negative result (analytical sensitivity)

\[ P_{\text{variant}} \] is the proportion of donations contaminated with a variant strain of HIV undetectable by current screening tests

\[ P_{\text{window}} \] is the proportion of the donations made in the immunosilent phase of infection

\[ P_{\text{tech}} \] is the proportion of false-negative screening test results due to system errors (‘clinical’ sensitivity)

\[ P_{\text{errinv}} \] is the proportion of the units erroneously placed in inventory

\[ P_{\text{urgent}} \] is the proportion units that are released to inventory on an emergency basis, before being tested for communicable diseases
Some differences between models:

- Policy change being considered
  - One-year vs. permanent deferral
  - Five-year vs. permanent deferral
  - Single sexual partner vs. permanent deferral
  - No restriction

- Risk being evaluated: HIV only, other risks

- Effect of policy on overall compliance to screening questionnaire

- Manner in which risk is quantitatively reported
WHAT HAVE THE MODELS PREDICTED?

- Variable but very small additional risk to recipients

- Some examples:
  - Germain et al. (Vox sanguinis, 2013)
    Impact of a five-year deferral policy in Canada: One additional HIV contaminated unit every 6,500 years
  - Anderson et al. (Transfusion, 2009)
    Impact of a one-year deferral policy in the U.S.: One additional HIV contaminated unit every 5 years
Some countries have changed from a permanent to a temporary deferral, e.g. Australia, UK, Canada

What about the impact in terms of actual harm to recipients? (i.e. HIV transmission)
- The ‘predicted’ increase in risk is too small to be detectable, even on a large scale
CAN WE LOOK AT OTHER PREDICTIONS FROM THE MODELS?

DONORS (LIBERAL MSM DEFERRAL POLICY)

RECIPIENTS

Transfusion Safety Features

Infected donation

Infection donation
**Table 1** Estimation of additional human immunodeficiency virus (HIV)-infected donations that would be collected (probably during the first year) if active-MSM and MSM-past were accepted as blood donors

<table>
<thead>
<tr>
<th></th>
<th>London</th>
<th>Outside London</th>
<th>England and Wales</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male population 16–64 years old</td>
<td>2,637,895</td>
<td>14,834,197</td>
<td></td>
</tr>
<tr>
<td>Donor panel 16–64 years old</td>
<td>94,923</td>
<td>7,671,49</td>
<td></td>
</tr>
<tr>
<td>Percentage of male 16–64 population who are donors</td>
<td>3.6%</td>
<td>5.2%</td>
<td></td>
</tr>
<tr>
<td>Percentage and number of males who are active MSM (i.e. have had sex with men in the past 12 months)</td>
<td>3.6%</td>
<td>0.7%</td>
<td></td>
</tr>
<tr>
<td>Percentage and number of males who are MSM but who have not had sex in the past year (MSM-past)</td>
<td>4.8%</td>
<td>2.2%</td>
<td></td>
</tr>
<tr>
<td>Prevalence of undiagnosed HIV in active MSM</td>
<td>2.8%</td>
<td>0.5%</td>
<td></td>
</tr>
<tr>
<td>Prevalence of undiagnosed HIV in MSM-past</td>
<td>0.84%</td>
<td>0.07%</td>
<td></td>
</tr>
<tr>
<td>Prevalence of undiagnosed HIV in all MSM</td>
<td>1.67%</td>
<td>0.17%</td>
<td></td>
</tr>
<tr>
<td>Number of undiagnosed HIV-positive active MSM donors, if accepted</td>
<td>96</td>
<td>27</td>
<td>123</td>
</tr>
<tr>
<td>Number of undiagnosed HIV-positive MSM past donors, if accepted</td>
<td>39</td>
<td>11</td>
<td>50</td>
</tr>
</tbody>
</table>
CAN WE ‘VALIDATE’ THESE PREDICTIONS?

- **Yes**, by looking at those countries that went from a permanent to a temporary deferral:
  - Australia (2000) – One-year deferral
  - UK (2011) – One-year deferral
  - Canada (2013) – Five-year deferral

- Calculate the **predicted increase** in the number of HIV-positive male donors following the new deferral policy, according to various models

- Compare these predictions with the **observed increase** in the number HIV-positive male donors following the new deferral policy in these countries
OBSERVED VERSUS PREDICTED HIV-POSITIVE MALE DONORS FOLLOWING IMPLEMENTATION OF A TEMPORARY MSM DEFERRAL

- Annual HIV prevalence data for the countries that changed their deferral policy:
  - Australia (2000) - Seed et al. Transfusion 2010; 50:2722
  - UK (2011) – Katy Davison, personal communication
  - Canada (2013) – Sheila O’Brien, personal communication

- For a given model, apply the parameters to each of the three countries, taking into account the size of the adult male population;
- For each country, calculate the expected number of HIV-positive donors who would be added to the donor pool (first year post-change)

- Pool the data from the three countries
- Compare observed and predicted HIV prevalence in male donors after the policy change
### FOR EXAMPLE:
Predictions according to Soldan et al., 2003

<table>
<thead>
<tr>
<th>Parameter</th>
<th>U.K.</th>
<th>Australia</th>
<th>Canada</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult male population</td>
<td>17 472 092</td>
<td>7724348</td>
<td>12113000</td>
</tr>
<tr>
<td>Proportion of MSM among adult males</td>
<td>0,037</td>
<td>0,037</td>
<td>0,037</td>
</tr>
<tr>
<td>Number of MSM</td>
<td>651 446</td>
<td>288 002</td>
<td>451 633</td>
</tr>
<tr>
<td>Proportion of recently abstinent MSM</td>
<td>0,69</td>
<td>0,69</td>
<td>0,49</td>
</tr>
<tr>
<td>Number of newly eligible MSM</td>
<td>450 040</td>
<td>198 722</td>
<td>221 300</td>
</tr>
<tr>
<td>Proportion of newly eligible MSM who would donate</td>
<td>0,049</td>
<td>0,049</td>
<td>0,049</td>
</tr>
<tr>
<td>Number of newly eligible MSM who would donate</td>
<td>22 187</td>
<td>9 797</td>
<td>10 910</td>
</tr>
<tr>
<td>Proportion of newly eligible MSM who would be unknowingly infected</td>
<td>0,00225</td>
<td>0,00225</td>
<td>0,001125</td>
</tr>
<tr>
<td>Number of HIV-positive donors who would donate (during first year)</td>
<td>50</td>
<td>22</td>
<td>12</td>
</tr>
</tbody>
</table>

**TOTAL = 84**
OBSERVED VERSUS PREDICTED HIV PREVALENCE AMONG MALE DONORS FOLLOWING NEW MSM DEFERRAL POLICY (UK, CANADA, AUSTRALIA)

![Graph showing observed versus predicted HIV prevalence among male donors following new MSM deferral policy.](image)

- **OBSERVED (n=14)**
- **PREDICTED (n=96)** (Soldan et al., 2003)
- **PREDICTED (n=158)** (Germain et al., 2003 & 2013)
- **PREDICTED (n=30)** (Davison et al., 2011 & 2013)
- **PREDICTED (n=781)** (Anderson et al., 2009)

**Number of HIV-positive, male donors**

**YEAR RELATIVE TO NEW DEFERRAL POLICY**
TWO QUESTIONS:

1) Why the discrepancies between the different models?

2) Why the discrepancies between the models and the reality?
Sources of discrepancies between different model predictions:

Proportion of MSM among adult males

- Germain et al.
- Soldan et al.
- Anderson et al.
- Davison et al.

Proportion of unknowingly infected eligible MSM

- Germain et al.
- Soldan et al.
- Anderson et al.
- Davison et al.

Proportion of one-year abstinent MSM

- Germain et al.
- Soldan et al.
- Anderson et al.
- Davison et al.

Proportion who would donate

- Germain et al.
- Soldan et al.
- Anderson et al.
- Davison et al.

Applied only to males 16 to 44 years old
Why didn’t we observe the predicted increase in HIV prevalence?

Some parameters may have been greatly overestimated:

- Proportion of MSM in the population?
- Proportion of MSM who are abstinent?
- Proportion of newly eligible MSM who would be unknowingly infected?
- Proportion of newly eligible MSM who would donate (the first year, anyway)?

My guess
‘Only’ three countries considered
- It still represents a total population of 121 millions

No long term follow-up on all countries
- However, it seems unlikely that it would ‘flare up’ after a lag period
- No such trend observed in Australia (Seed et al., Transfusion 2010)

Larger-than-expected impact of increased compliance following the revised criteria?
- Possible, but no hard evidence; plus it would not explain the very wide gap between the predicted and the observed
Would that be true in other countries?

- It’s hard to argue that it would be very different elsewhere in the developed world.
- Some caution needs to be applied for countries with high HIV prevalence.

What about models that looked at ‘behavior-based’ deferrals (e.g. Pillonel et al. Vox sanguinis 2011)?

- No similar ‘natural experiment’ to validate the model.
- However, countries that use this approach seem to have higher rates of HIV among their donors (Italy, Spain).
Limitations / other considerations

- What about the accuracy of other parameters in those models (test error rates, quarantine release errors, etc.)?
  - A moot point, if there is no increase in the number of prevalent infections!

- What about other infections (HBV, HCV, HTLV, …)
  - It seems very unlikely that it would be a different story.
Models suggest that going from a permanent to a short term deferral for MSM poses very little (virtually undetectable) risk to recipients;

Based on observed HIV prevalence in countries that adopted a temporary deferral, it appears that most models greatly overestimated this (very small) risk;

Based on these considerations, a permanent deferral policy for MSM is hard to defend, at least from the perspective of HIV risk.
THANK YOU!

Questions?