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

PREDICTIONS VERSUS REALITY

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BACKGROUND

- Currently, the most common policy regarding the eligibility of men who had sex (MSM) with men :

  ‘Permanent deferral’

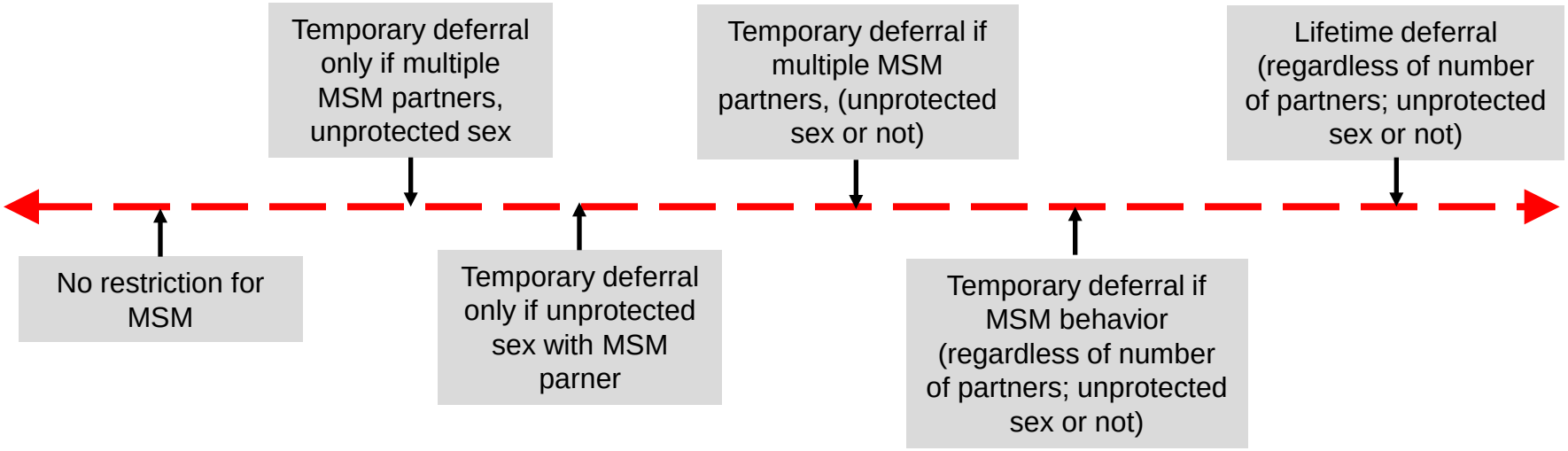
  - e.g. in the US: *Sex with another man, even once, since 1977*
  - Other countries with a permanent deferral: Germany, France, Sweden, Hong Kong, China, Egypt, etc.

    (See Benjamin et al., Vox sanguinis 2011)

- **But the international situation is changing…**

BACKGROUND

- Deferral policies for MSM: Inappropriate discrimination or justifiable safeguard?



- What is the least restrictive deferral policy that could achieve optimal safety?

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BACKGROUND

- 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…

MODELLING THE IMPACT OF MSM DEFERRAL STRATEGIES

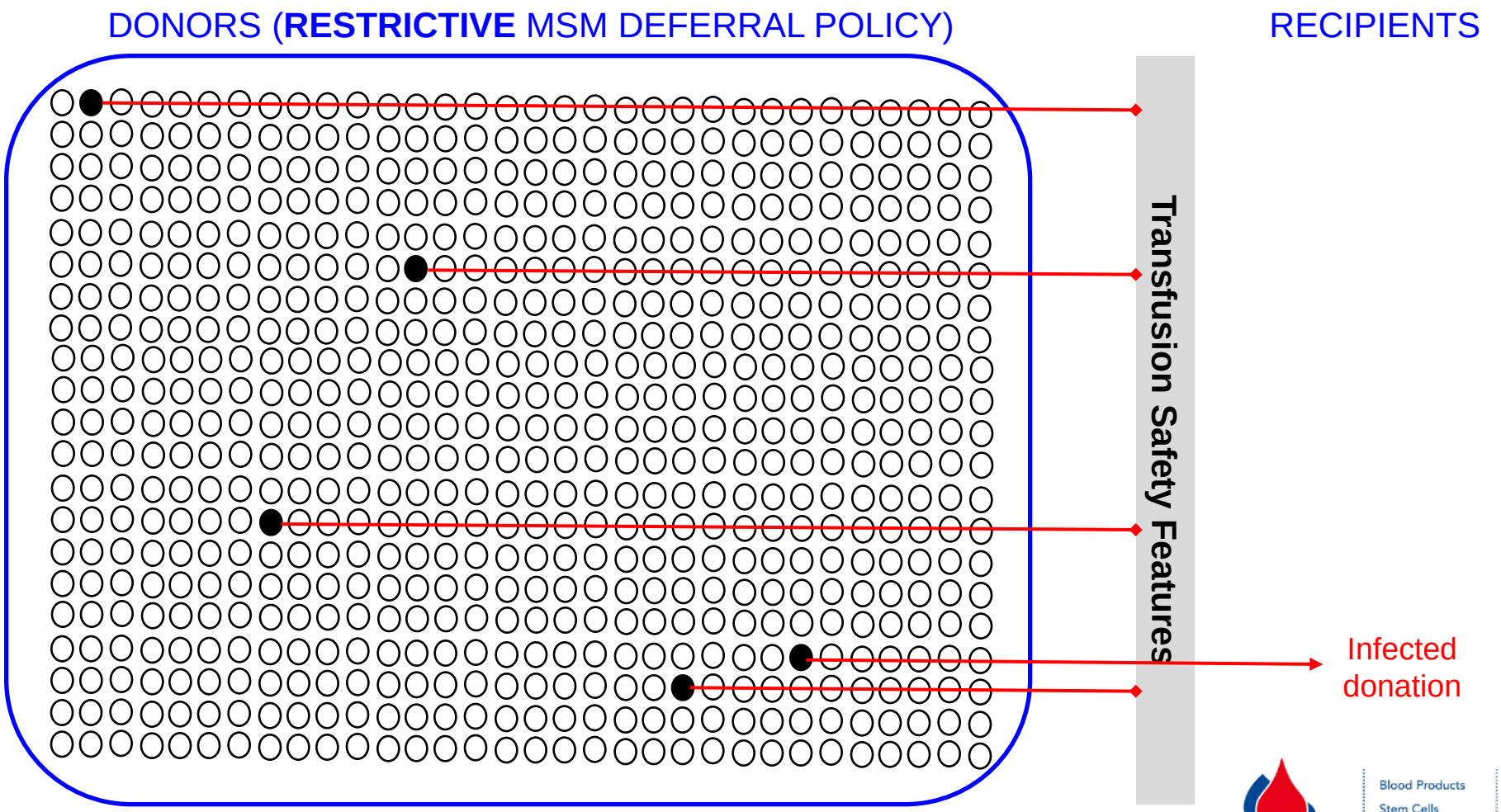
- Who tried what and when…

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

MODELLING THE IMPACT OF MSM DEFERRAL STRATEGIES

- 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



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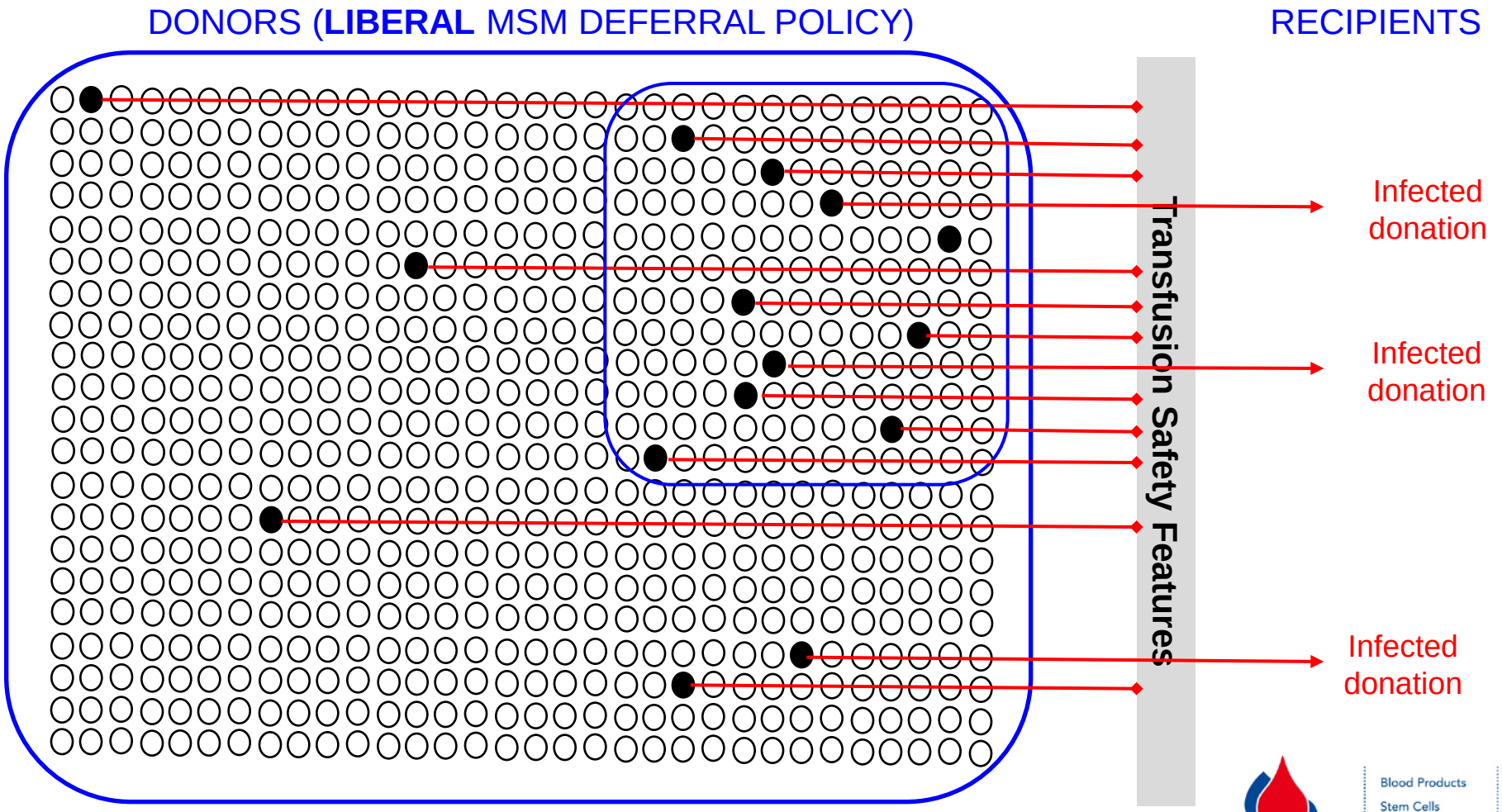

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RISK MODEL; AN EXAMPLE

- The number of MSM who would become eligible and decide to donate in a given year **(N1y)**, under a five-year deferral policy, is given by the formula:

  $\mathbf{N_{1y} = MSM_{tot} \times P_{elig} \times P_{don}}$, where:

  $\mathbf{MSM_{tot}}$ is the total number of MSM in the population

  $\mathbf{P_{elig}}$ is the proportion of these MSM who would become eligible

  $\mathbf{P_{don}}$ is the proportion of those eligible who would donate

RISK MODEL; AN EXAMPLE

- The number of HIV-contaminated units that would be made availble for transfusion in a given year **(U_{1y})**, as a result of this five-year deferral policy, is obtained as follows:

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

P_{hiv} is the proportion of newly eiligible MSM donors who would be unknowingly seropositive, and…

RISK MODEL; AN EXAMPLE

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

$P_{variant}$ is the proportion of donations contaminated with a variant strain of HIV undetectable by current screening tests

P_{window} is the proportion of the donations made in the immunosilent phase of infection

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

P_{errinv} is the proportion of the units erroneously

placed in inventory

P_{urgent} is the proportion units that are released to inventory on an emergency basis, before being tested for communicable diseases

MODELLING THE IMPACT OF MSM DEFERRAL STRATEGIES

- 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

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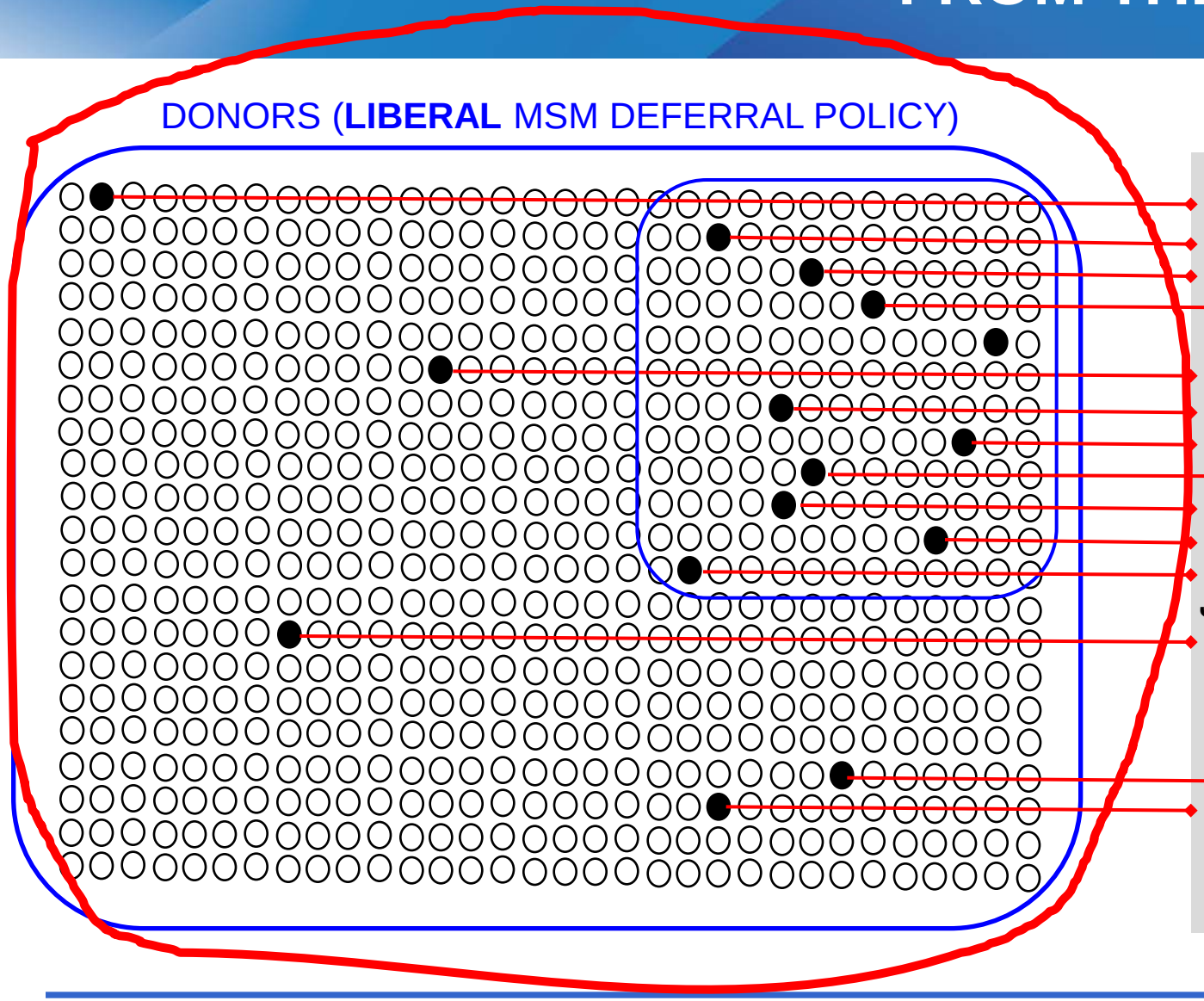
CAN WE VALIDATE THE MODELS BASED ON ACTUAL EXPERIENCE?

- 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?



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CAN WE LOOK AT OTHER PREDICTIONS FROM THE MODELS?

Soldan et al., Vox sanguinis 2003

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

	London	Outside London	England and Wales
Male population 16–64 years old	2 637 895	14 834 197	
Donor panel 16–64 years old	94 923	767 149	
Percentage of male 16–64 population who are donors	3·6%	5·2%	
Percentage and number of males who are active MSM (i.e. have had sex with men in the past 12 months)	3·6% 95 341	0·7% 106 065	
Percentage and number of males who are MSM but who have not had sex in the past year (MSM-past)	4·9% 128 880	2·2% 321 160	
Prevalence of undiagnosed HIV in active MSM	2·8%	0·5%	
Prevalence of undiagnosed HIV in MSM-past	0·84%	0·07%	
Prevalence of undiagnosed HIV in all MSM	1·67%	0·17%	
Number of undiagnosed HIV-positive active MSM donors, if accepted	96	27	123
Number of undiagnosed HIV-positive MSM past donors, if accepted	39	11	50

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

Observed

- 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

Predicted

- 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

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

TOTAL = 84

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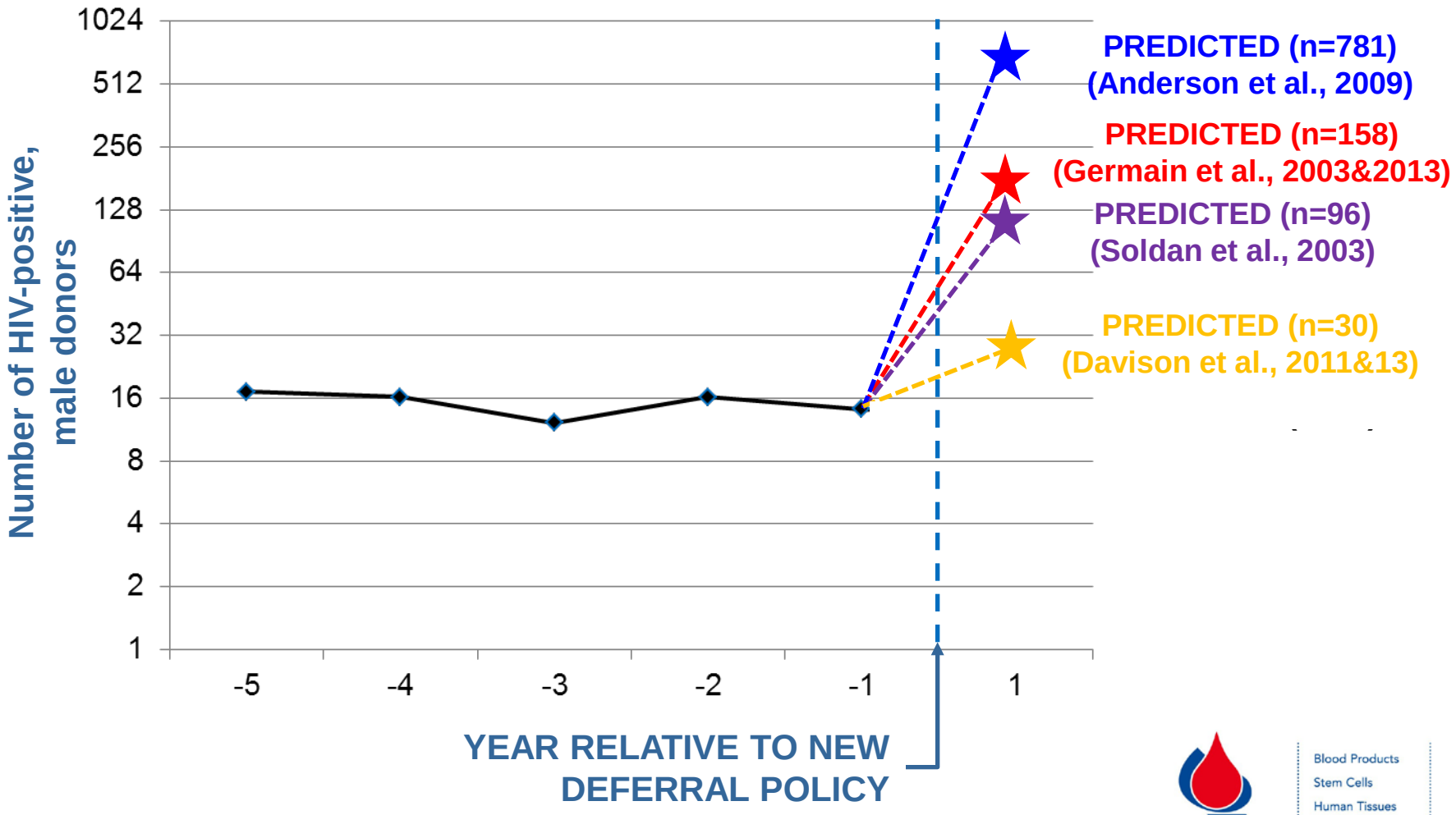
OBSERVED VERSUS **PREDICTED** HIV PREVALENCE AMONG MALE DONORS FOLLOWING NEW MSM DEFERRAL POLICY **(UK, CANADA, AUSTRALIA)**



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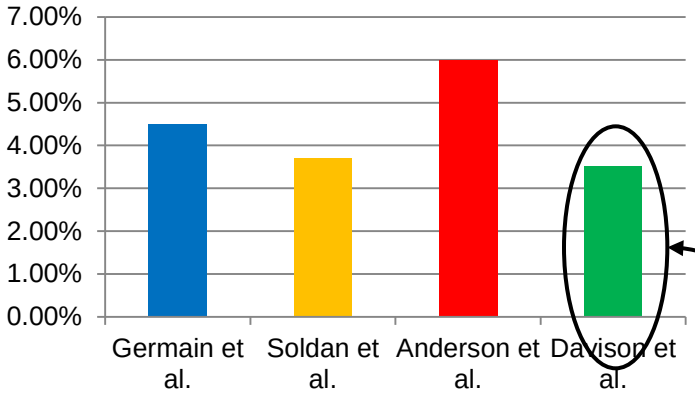
TWO QUESTIONS:

1) Why the discrepancies between the different models?

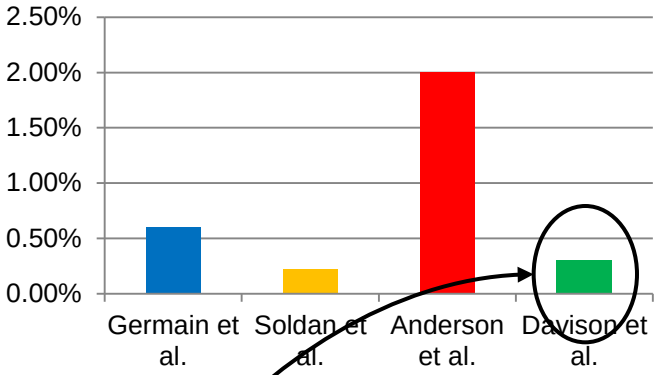
2) Why the discrepancies between the models and the reality?

Sources of discrepancies between different model predictions:

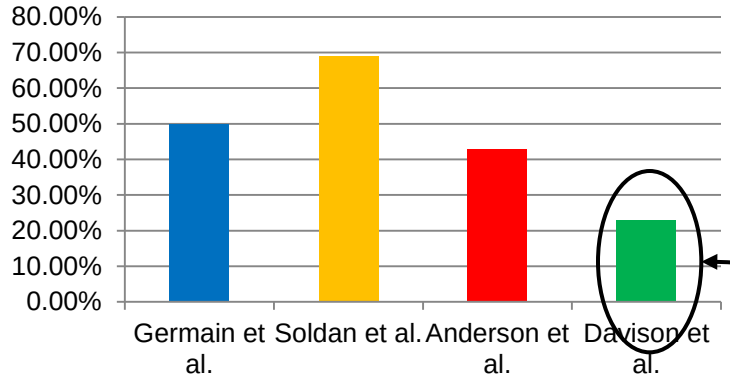
Proportion of MSM among adult males



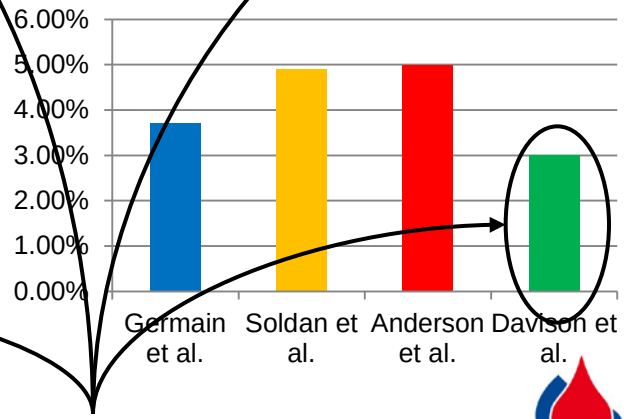
Proportion of unknowingly infected eligible MSM



Proportion of one-year abstinent MSM



Proportion who would donate



Applied only to males 16 to 44 years old

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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




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Limitations / other considerations

- '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

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Limitations / other considerations

- 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 need 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.

CONCLUSIONS

- 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?

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