Public Health England

Protecting and improving the nation's health

HÉMA-QUÉBEC

Blood Products
Stem Cells
Human Tissues

Australian Red Cross BLOOD SERVICE

NHS Blood and Transplant

The 'MSM Model'

Assessing HIV risk among MSM donors

Katy Davison - Public Health England, UK
Marc Germain and Yves Grégoire – Hema-Quebec, Canada
Clive Seed – Australian Red Cross Blood Service
On behalf of the ISBT TTID Working Party STRAP Sub Group

September 2016, ISBT Dubai

Katy.davison@phe.gov.uk

Background & rationale

Permanent deferral (est. 1980s) of men who have sex with men (MSM) to minimise TTI-HIV risk increasingly challenged

Some blood services relaxed to a time-based deferral

- Mathematical models developed to assess impact on HIV risk
- Approaches/assumptions differed; all predicted an increase, but of varying magnitude
- Post change validation suggests models overestimated risk (Germain *et al.* 2016)

Aim & methods

To develop an **'optimal model'** to quantitate the TTI-associated risk of reducing the duration of deferral for MSM

The ISBT working group (WG) undertook:

1. A review & assessment of current models to determine a basis for 'optimal model'
2. Developed & validated 'optimal model'
3. Identify limitations, assess applicability & create a FINAL model

Review and assessment process

1. Identify candidate models
2. Model review ‘template’ developed by WG

   Format, assumptions, inputs, equations, scope, limitations
3. Template for each candidate completed by two WG members
4. WG met to discuss whether any pre-existing model was ‘optimal’
5. Consensus was no – but that UK model (Davison et al) and Canadian model (Germain et al) could used as a basis for an ‘optimal model’

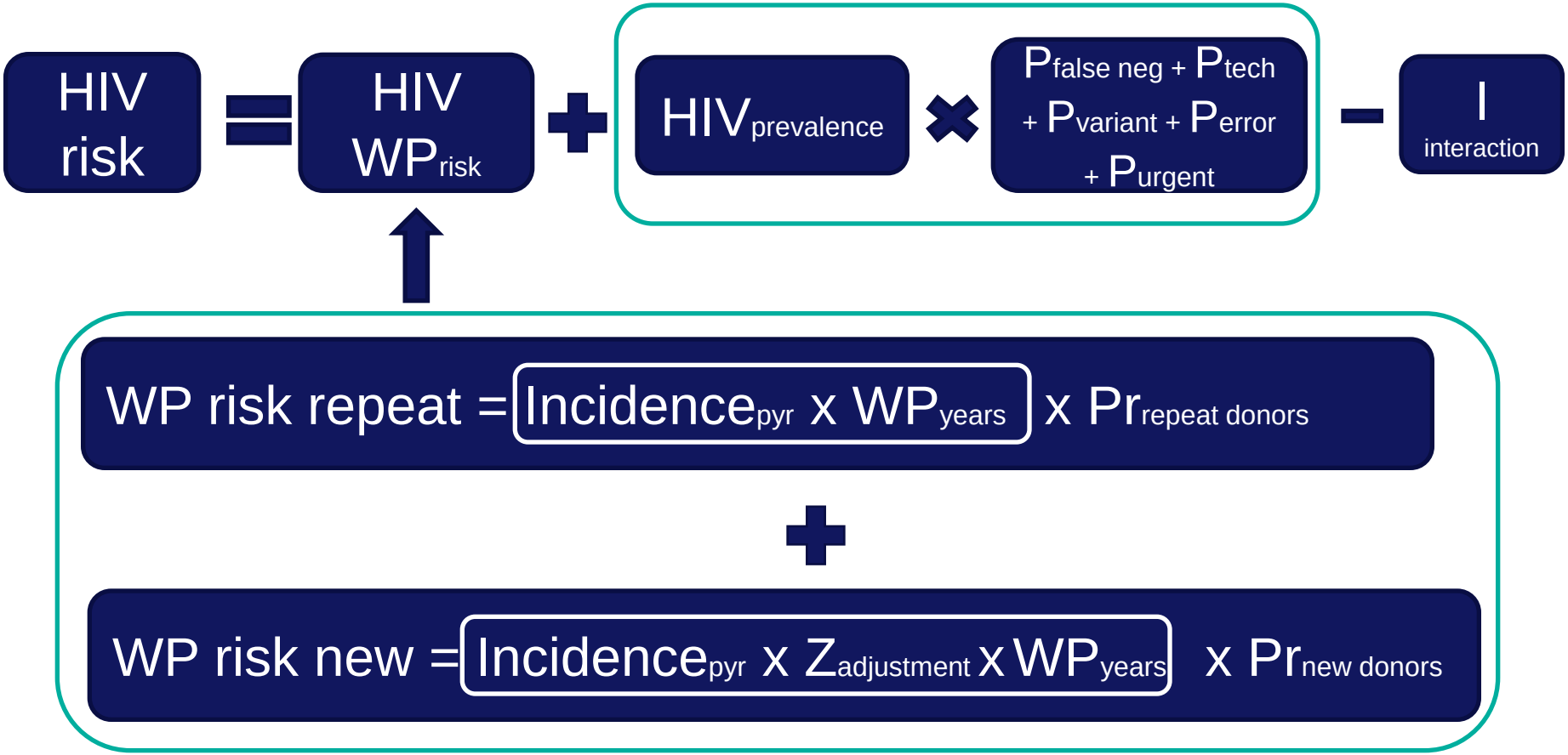
Candidate models reviewed (the long list)

	Year	MSM deferral	Summary	Optimal model (reason)?
Dayton (US) BPAC meeting, FDA	2000	5y		No
Germain (Canada) Transfusion, vol. 43, p. 25	2003	1y	HIV risk – false neg, error, variant, technical, urgency, WP. Simulation.	No (input parameters unpublished)
Soldan (UK) Vox Sang vol. 84, p. 265	2003	5y or no deferral	HIV risk new & repeat donors – WP, false neg & error. Compliance.	No (deferral period)
Anderson (US) Transfusion, vol. 49, p. 1102	2009	5y and 12m	HIV & HIV risk - false neg & QRE. Simulation.	No (only error/false negative risk)
Davison (UK) Vox Sang vol. 101, p. 291	2011	5y or no deferral	HIV risk new & repeat donors – WP, false neg & error. Compliance.	No (deferral period)
Edgren (Sweden) *Vox Sang* Vol. 103. 111	2012	6-months, with compliance @ 90%, 95% and 99%	HBV, HCV & HIV risk – WP. Compliance	No (only WP risk, accuracy of input data)
Pillonel (France) Vox Sang, vol. 102, p. 13	2012	>1 partner <12m	HIV risk – WP.	No (only WP risk, limitations of input data)
Davison (UK) Vox Sang vol. 105, p. 85	2013	1y	HIV risk new & repeat donors – WP, false neg & error. Compliance.	Yes
Germain (Canada) Vox Sang,vol.106, p. 372	2014	5y	HIV risk – false negative, error, variant, technical, urgency. Simulation.	Yes

The UK and Canada risk models

Variables in the model /other characteristics	UK	Canada
Newly eligible MSM - number	Yes	Yes
Newly eligible MSM - donor rate	Yes	Yes
Newly eligible MSM – number undiagnosed HIV	Yes	Yes
Risk due to prevalent HIV:		
HIV testing sensitivity	Yes	Yes
HIV testing error rate	Yes	Yes
HIV variant strain undetectable	No	Yes
Unit release error rate	No	Yes
Emergency release rate	No	Yes
Risk due to window period HIV (noncompliant MSM)	Yes	No
Sensitivity analysis	Yes	No
Calculation of **'baseline' risk** (risk difference)	Yes	No
Monte Carlo simulation	No	Yes

The risk calculation in the optimal model



Estimating HIV prevalence with MSM

$$\text{HIV prevalence} = \frac{\text{(HIV positive donations + } \mathbf{\text{expected extra MSM HIV}})}{\text{(tested donations + } \mathbf{\text{expected extra MSM}}}$$

Expected extra MSM = **No. males population** x **% MSM male population (MSMtot)** x **% MSM eligible (P_{elig})** x **Donor rate**

Expected extra MSM HIV = **Expected extra tested donation** x **Proportion of P_{elig} who would be unknowingly HIV seropositive**

Risk due prevalent HIV

Parameter values in the models

	Canada	UK	Optimal model	Distribution for simulation
MSM_{tot} : Proportion of male population MSM	4.5% (3.0 – 6.0%)	3.5%	3.5%	None
P_{elig} : Proportion of MSM eligible	22.5% (15 – 30%)	20%	20%	None
P_{don} : Proportion of **P_{elig}** donate	3.7%	3.4%	3.4%	None
P_{hiv} : Proportion **P_{elig}** HIV undiagnosed	**0.6% (0.2 – 1.0%)**	**0.334%**	**0.334%**	None
$P_{falseneg}$: HIV test sensitivity	**1:500,000 (1:1 million - 1:200,000)**	**1:2,000**	**1:2,000**	None
P_{tech} : HIV testing error rate	**1:100,000 (1:1 million - 1:35,500)**	**1:2,500**	**1:1,000,000**	None
$P_{variant}$: Proportion undetectable strain HIV	1:1,000,000 (1:10 million - 1:500,000)	*NA*	1:1,000,000 (1:10 million - 1:500,000)	*Triangular*
P_{errinv} : Proportion units in inventory erroneously	1:10,000,000 (1:100 million - 1:4 million)	*NA*	1:10,000,000 (1:100 million - 1:4 million)	*Triangular*
P_{urgent} : Prop of units released on an emergency basis < testing	1:500,000 (1:1 million - 1:250,000)	*NA*	1:500,000 (1:1 million - 1:250,000)	*Triangular*

Risk due to WP HIV - MSM non-compliance

Scenarios relating to compliance defined as follows:

Bi - Absolute compliance unchanged: Total number of non-compliant MSM donors remains the same under the temporary deferral policy, compared to the lifetime deferral, i.e. no added non-compliant MSM donors.

Bii - Relative compliance unchanged: Total number of non-compliant MSM donors increases under the temporary deferral policy, compared to lifetime deferral, in the same proportion that there is an increase in the number of prevalent HIV MSM donors

Biii - Perfect compliance: Total number of non-compliant MSM donors goes down to zero under the temporary deferral policy

Biv & Bv - Relative compliance increases or decreases: Defined as worse/better than base-case but not perfect

The simulation

Data parameters from UK model (2005-2007): relating to some relating to errors/failures – Canada (HIV variant, error and Purgent)

Distributions of parameters defined as far as possible: Most shown on previous slide, in addition:

WP (10 days :56% NAT, 44%Ab/Ag) - Normal

Z (new donors incidence adjustment) – Log normal.

Number HIV positive (prevalent and incident, MSM or otherwise) – Poisson.

Calculated number of expected MSM HIV positives (prevalent and incident) for scenarios Bi-Bv

Monte Carlo simulation (10,000 iterations) using SAS Enterprise Guide version 4.1 (SAS Institute, Cary, NC, USA): The mean value for HIV risk per million donations with 95% confidence intervals, for base-case and scenarios

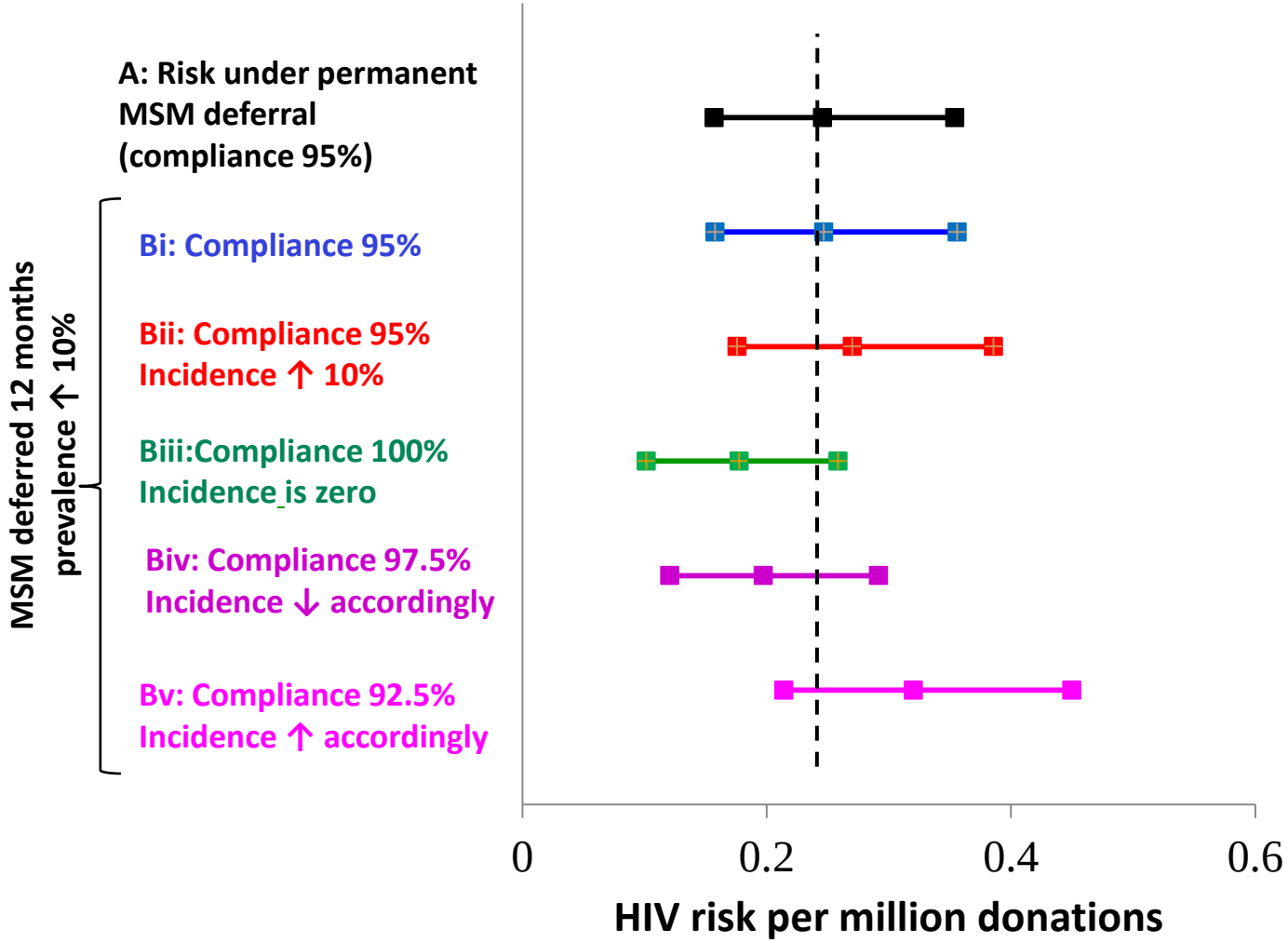
Results from the 'optimal model'

UK data (England and Wales 2005-2007)

	Prevalence	Incidence	Risk	% base-case	1 /million
A. Risk under permanent MSM deferral	1.28	0.91	0.246		4.07
MSM deferred 12m – scenarios:					
Bi. prevalence 10% higher, MSM compliance is 95%	1.41	0.91	0.247	100.4	4.05
Bii. prevalence and incidence 10% higher, MSM compliance is 95%	1.41	1.00	0.270	109.9	3.70
Biii. prevalence 10% higher, compliance 100%	1.41	0.63	0.178	72.2	5.63
Biv. prevalence 10% higher, compliance is 97.5%	1.41	0.72	0.197	80.3	5.07
Bv. prevalence 10% higher, compliance is 92.5%	1.41	1.19	0.320	130.2	3.12

Results from the 'optimal model'

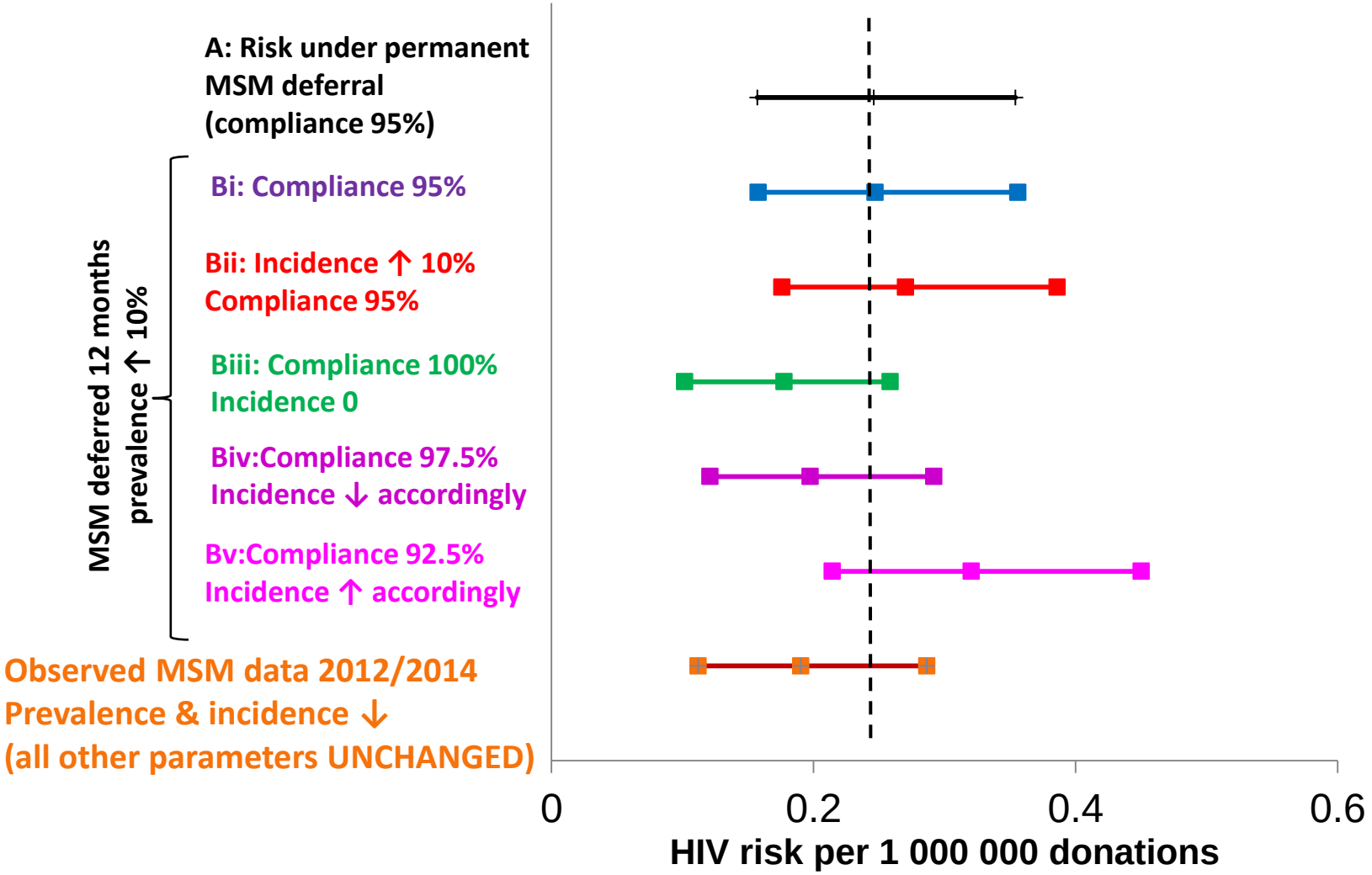
Mean and 95% CI



Validating the model

	'Optimal model'		UK model	
UK data (England and Wales 2005-2007)	**Point estimate (per million donations)**	**95% range (Monte Carlo)**	**Point estimate (per million donations)**	**95% range (Monte Carlo)**
A. Permanent deferral	**0.246**	**0.157-0.354**	**0.227**	**0.157-0.328**
MSM deferred 12m – scenarios:				
Bi. prevalence 10% higher, MSM compliance is 95%	**0.247**	**0.158-0.356**	**0.228**	**0.168-0.306**
Bii. prevalence and incidence 10% higher, MSM compliance is 95%	**0.270**	**0.176-0.386**	**0.249**	**0.186-0.323**
Biii. prevalence 10% higher, MSM compliance 100%	**0.178**	**0.102-0.259**	**0.161**	**0.112-0.228**

Validating the model with post change data



Conclusions

'Optimal' model defined: considers risk due to WP donations from non-compliant MSM and risk due to prevalent infections from errors/failures, also a measure of uncertainty (simulation)

Impact of MSM deferral on HIV risk remains small, albeit slightly greater than estimated in the original UK model: differences relate mostly to additional risk due to prevalent HIV arising from errors/failures (from Canadian model)

MSM compliance appears to be underestimated and could be revised: HIV risk estimates made using UK data post change suggest compliance exceeds 95%. This is supported by donor survey data (not shown)

The value over other models includes:

- Considers compliance
- Measure of uncertainty from simulation (95% CI)
- Adaptable to different populations (population specific data required)
- Relative differences in risk (bases-case v alternative scenarios)

Limitations & next steps

Assumptions about parameters

?MSM donate at same rate as other donors

?accuracy of estimate of undiagnosed HIV in MSM

?accuracy of estimate of MSM sex <12m

Often paucity of data in population of interest (potentially newly eligible donors) adds to uncertainty of outcome

Next steps : finalise the model (?), peer review publication, potentially broader application to other countries (pre-change)

Acknowledgements

Thanks to other members of the ISBT TTID WP SRAP Subgroup involved in this project (alphabetical): Mike Busch, Brian Custer, Sheila O'Brien, Josiane Pillonel, Whitney Steele