Discovery and continual monitoring of undisclosed antiretroviral therapy use in South African blood donors

Marion Vermeulen[1,2], Karin van den Berg [1,2,3], Wendy Sykes[1], Vernon Louw[3], Gary Maartens[3], Edward Murphy[4,5] for NHLBI Recipient Epidemiology and Donor Evaluation Study III (REDS-III)[1]

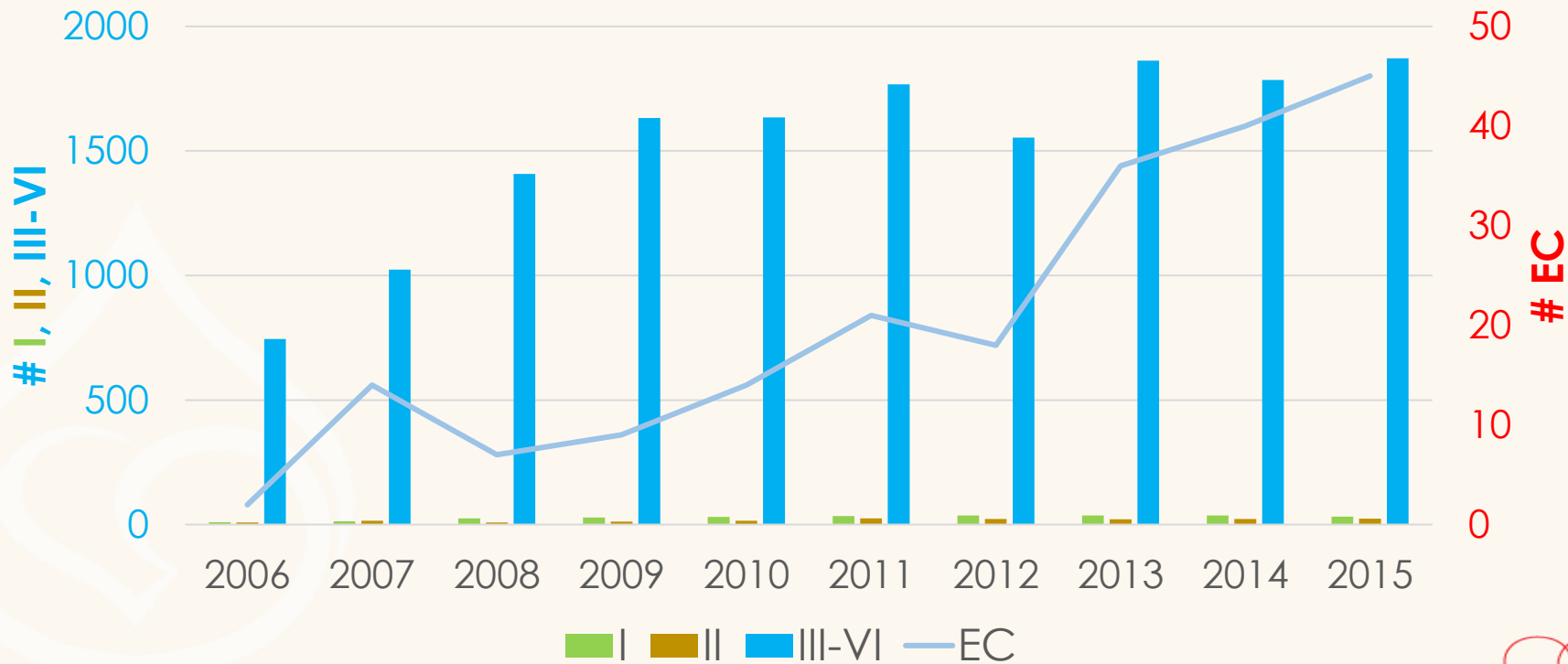1.   *SANBS, 2. UFS, 3. UCT, 4. UCSF, 5. Vitalant,*

- I have no conflicts of interest to report

- Present two different studies done at SANBS
  - Sykes, W *Journal of Infectious diseases* 2019
  - Van den Berg, K *Transfusion* submitted
- Ask some provocative questions

SANBS HIV+ donors according to year and Fiebig staging on index donation

- Loss of "Elite Control" by a MATHS participant

- Anecdotal evidence of Elite Controllers reporting ART and therefore "false EC" while recruiting and enrolling donors into the MATHS cohort study

- Apparent increase in EC over 1-2 years and during a winter incentive campaign

Loss of virologic control by an Elite controllers enrolled in MATHS*
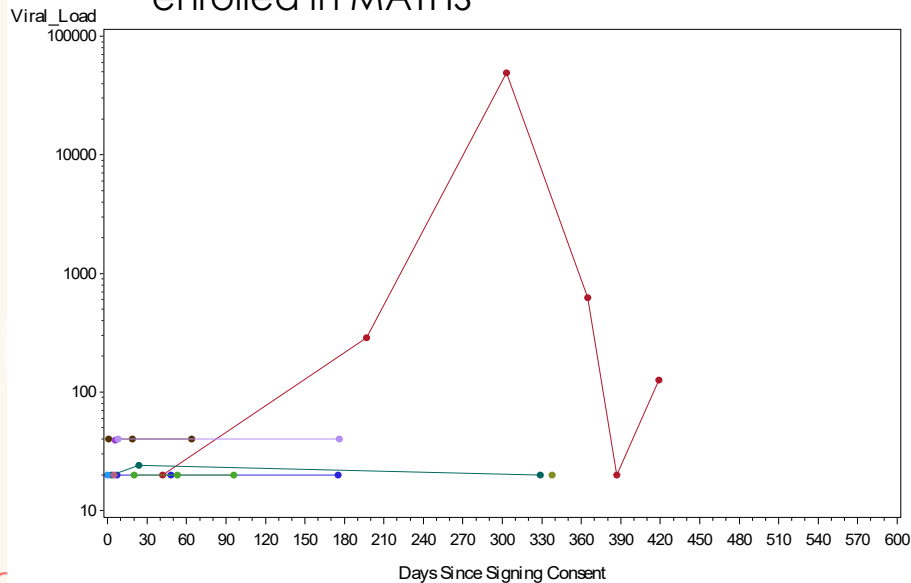
Antibody+, RNA- donations as a Proportion of all HIV positives
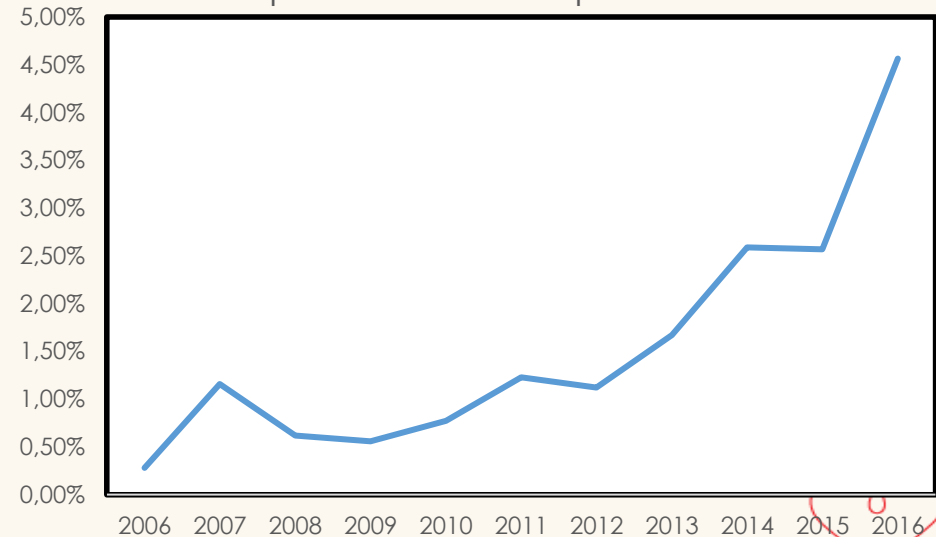
Aim

- To understand the extent of the false EC phenomenon and generate hypothesis for its genesis and prevention

- To determine the rate of false EC's more recently

- To determine the prevalence of undisclosed ART use in all HIV positive donors
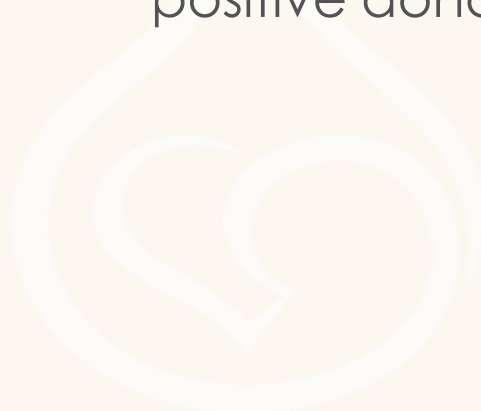
- All donations tested in parallel using Abbott Prism HIV antibody and Grifols Ultrio (Plus & Elite) ID-NAT assay
- 226 Potential EC identified between 2010 and 2015 tested for five ART drugs using qualitative liquid chromatography tandem mass spectrometry (sensitivity 0.02μg/mL)
  - Nevirapine, Efavirenz, Darunavir, Atazanavir, Lopinavir
- Test 2016 – 2019 EC for four ART drugs
  - Nevirapine, Efavirenz, Atazanavir, Lopinavir
- Test 1250 HIV RNA+, Antibody+ donors from 2017 for four ART drugs
- Compare the frequency of undisclosed ART use against blood drive characteristics, donor incentives and socio-demographic characteristics using bi variate and multivariable logistic regression

Donor Demographics	HIV Ab⁺/RNA⁻ Samples Sent for ART Testing, n	False Presumptive EC-Positive for ART Drugs, n (%)	OR	95% CI
Total	226	150 (66.4)		
Sex				
Male	51	38 (74.5)	1	—
Female	175	112 (64.0)	2.15	.97–5.10
Population group				
Non-Black[a]	14	1 (7.1)	1	—
Black	212	143 (67.5)	2.46	.72–8.53
Age, years				
<20	22	15 (68.2)	1	—
20–30	61	38 (62.3)	1.06	.33–3.26
31–40	91	66 (72.5)	1.78	.55–5.47
41–50	41	26 (63.4)	0.98	.26–3.54
>50	11	5 (45.5)	0.46	.08–2.43

No significant socio-demographics

Sykes, W *JID* 2019

Multivariable logistic regression of socio-demographic variables and year

Donor Demographics	HIV Ab+/RNA− Samples Sent for ART Testing, n	False Presumptive EC-Positive for ART Drugs, n (%)	OR	95% CI
Geographic area				
Eastern Cape	12	4 (33.3)	1	—
Egoli (Johannesburg)	42	29 (69.0)	0.20	.04–.90
Free State/North Cape	9	6 (66.7)	1.15	.20–7.73
KwaZulu Natal	52	38 (73.1)	1.22	.43–3.42
Mpumalanga	38	26 (68.4)	1.05	.36–3.08
Northern	43	29 (67.4)	0.94	.33–2.66
Vaal	30	18 (60.0)	0.73	.24–2.20
Donor incentives[b]				
No incentives offered	193	125 (64.8)	1	—
Incentives offered	33	25 (75.8)	1.03	.36–3.15
Clinic site				
Fixed site clinic	29	16 (55.2)	1	—
Mobile clinic	197	134 (68.0)	2.46	.98–6.22

| Donor Demographics	HIV Ab+/RNA− Samples Sent for ART Testing, n	False Presumptive EC-Positive for ART Drugs, n (%)	OR	95% CI
Year				
2010	13	5 (38.5)	1	—
2011	16	8 (50.0)	2.05	.41–10.92
2012	15	8 (53.3)	2.86	.53–16.6
2013	34	20 (58.8)	2.97	.71–13.3
2014	34	24 (70.6)	5.41	1.24–26.0
2015	47	34 (72.3)	7.16	1.55–36.3
2016	67	51 (76.1)	7.57	1.96–32.2

Type of clinic & year significant

Sykes, W *JID* 2019

The number of RNA-/Ab+ donors and treatment status

Sykes, W *JID* 2019
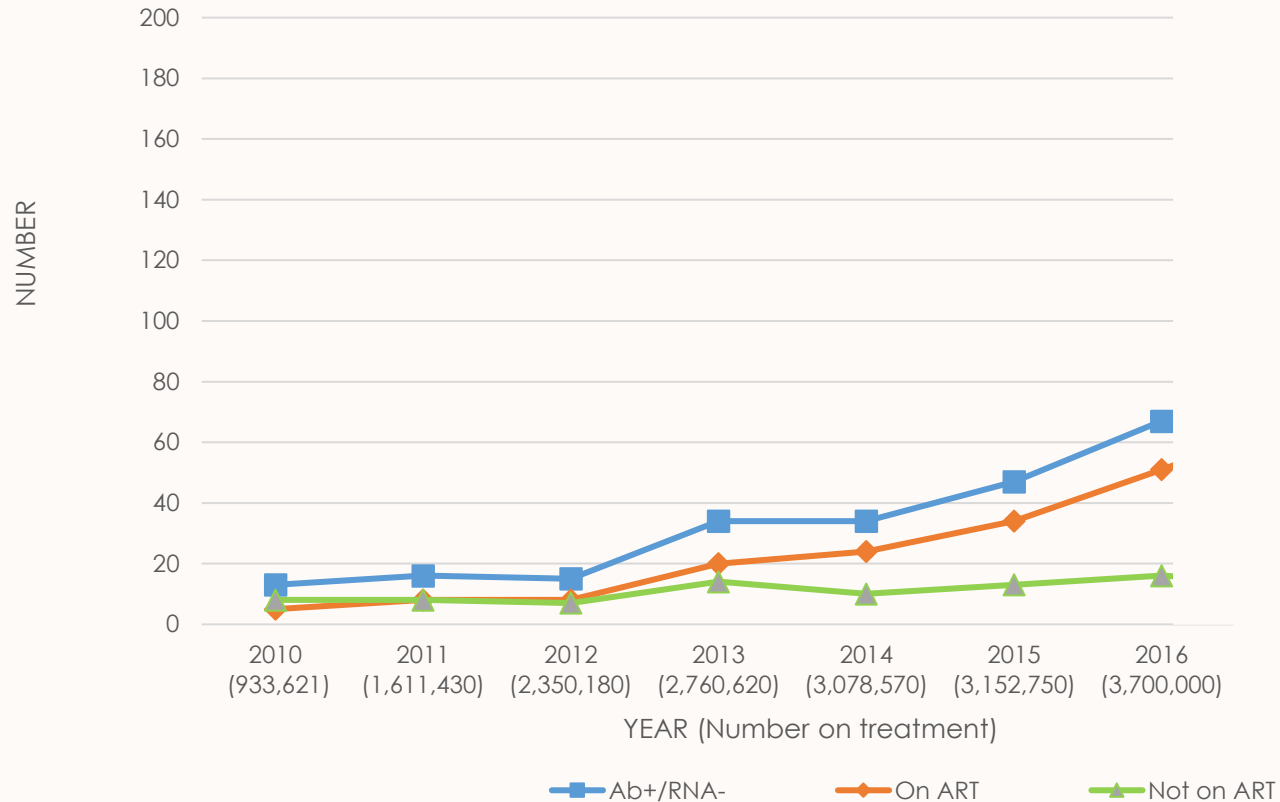
Participant ARV disclosure by HIV testing characterisitics-Year 2017

	ARV Positive		Total	P-Value
	N	%		
Total	122	9.8	1250	
Diagnostic category				<0.0001
RNA+/Ab-	0	0	62	
RNA-/Ab+	68	85.0	80	
RNA+/Ab+:	54	4.9	1108	
Recency category				<0.0001
Longstanding	74	9.2	806	
Recent	34	9.8	347	
Unknown	14	40.0	35	

94% tested positive for Efavirenz

Van den Berg, K; Submitted

Demographic characteristics of the 1250 HIV-positive donors by ARV status

	ARV Positive		Total	P-Value
	N	**%**		
Total	122	9.8	1250	
Gender				0.205
Female	94	10.4	902	
Male	28	8.1	348	
Ethnicity				0.505
Asian/Indian	1	9.1	11	
Black African	111	9.8	1132	
Coloured	5	14.3	35	
Unknown	4	12.1	33	
White	1	2.6	39	
Age Cat				**<0.0001**
<21	21	6.8	311	
21 - 30	35	6.8	514	
31 - 40	39	14.7	265	
>40	27	16.9	160	

	ARV Positive		Total	P-Value
	N	**%**		
Donor Type				**<0.0001**
First time	101	14.3	706	
Lapsed	13	4.9	263	
Repeat	8	2.9	281	
Clinic Type				**0.012**
Fixed	14	5.6	252	
Mobile	108	10.8	998	
Home Province				**0.010**
Eastern Cape	9	8.3	109	
Free State	11	10.5	105	
Gauteng	39	8.8	445	
KwaZulu Natal	35	14.7	234	
Limpopo	2	3.0	67	
Mpumalanga	25	11.3	221	
North West	0	0.0	58	
Northern Cape	1	9.1	11	

Multivariable model of factors associated with ARV use

Category	OR.	[95% Confidence Interval]	
Age Category			
<21	1		
21-30	1.5	0.8	2.7
31-40	**3.2**	**1.8**	**5.8**
>40	**3.7**	**2.0**	**7.0**
Donor Type			
Repeat	1		.
First time	**5.2**	**2.5**	**11.1**
Lapsed	1.5	0.6	3.7

Category	OR.	[95% Confidence Interval]	
Clinic Type			
Fixed	1		
Mobile	1.8	1.0	3.2
Geographic region			
Northern Rural*	**1**		
Eastern Cape	**4.6**	**1.2**	**18.0**
Free State	**6.4**	**1.7**	**24.3**
Gauteng	**4.1**	**1.2**	**13.7**
KwaZulu Natal	**9.1**	**2.7**	**30.7**
Mpumalanga	**5.5**	**1.6**	**18.8**

Donor presentations, deferrals, HIV status and sample avaialibility 2017

Donor presentations:
1,007,580

Non-high risk deferrals:
145,600 (14.4%)

Accepted for donation:
832,030 (82.6%)

High risk deferrals:
29,950 (3.0%)

High risk deferral breakdown:
Donor HIV+: 97 (0.3%)
ART use: 79 (0.3%)
Other high risk: 29,774 (99.4%)

Distinct donors tested
HIV positive:
1462 (0.18%)

No residual plasma:
212 (14.5%)

Tested for ARV:
1250 (85.5%)

ART +
122 (9.8%)

Van den Berg, K; Submitted
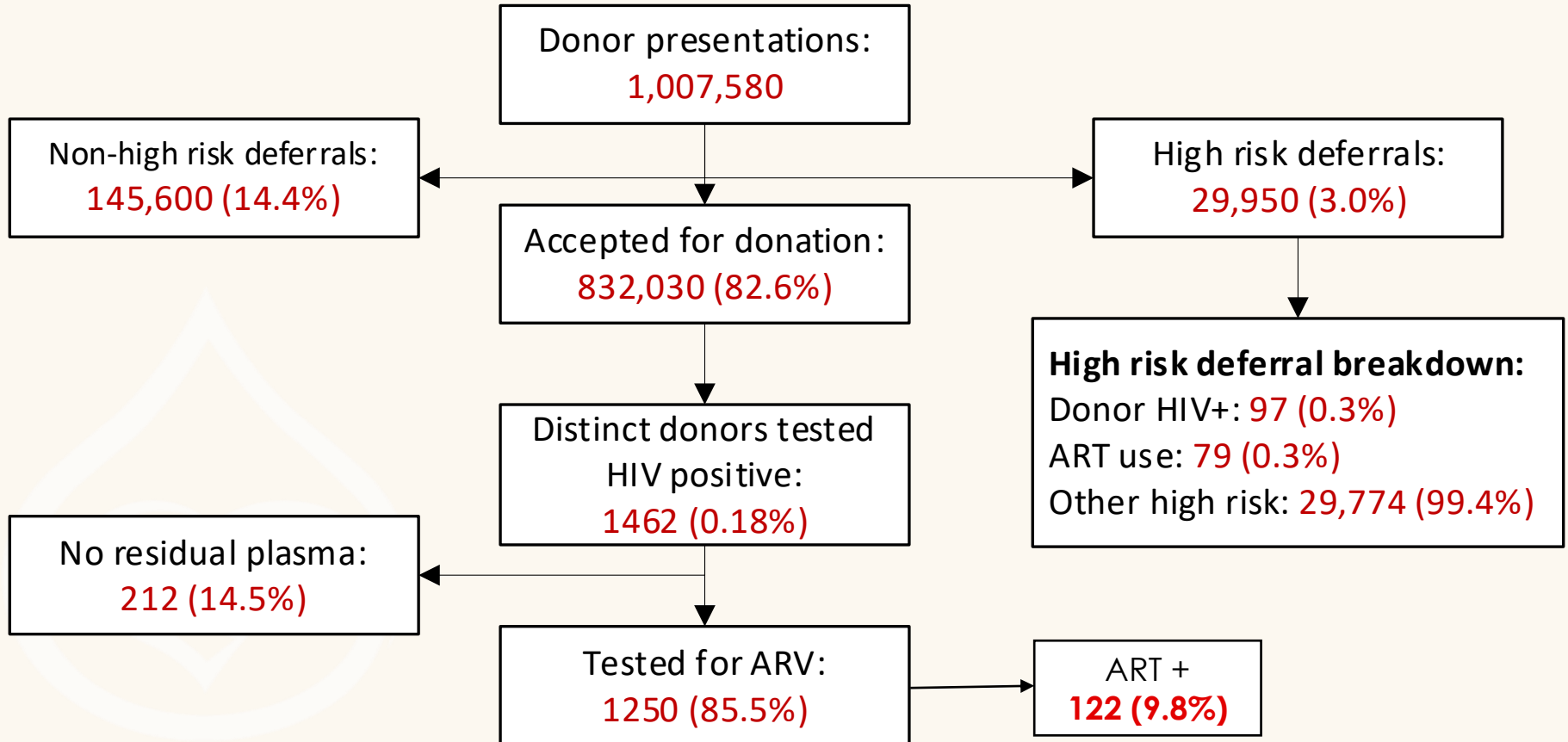
- 122/832,030 (0.015%) Knew they were HIV positive and were on treatment (non-disclosure)
- 176/1,007,580 (0.017%) marked that they were HIV positive on the questionnaire (disclosure)

$p=0.73$

Please Note: The following questions are of a sensitive nature. The term "sexual" includes oral, vaginal and anal sex with or without a condom.

Please **MARK** your answers

Staff Comments

Q10. Have you ever:

Q10.1. Tested positive for HIV?	YES	NO	
Q10.2. To the best of your knowledge had sexual contact with anyone who has tested HIV positive?	YES	NO	
Q10.3. Or do you now take anti-retroviral (ARV) medication, including pre- and post-exposure prophylaxis?	YES	NO	

Q11. In the past 3 months:

Q11.1. Have you started having sexual contact with a new partner?	YES	NO	
Q11.2. Have you had sexual contact with more than one partner?	YES	NO	
Q11.3. Have you had sexual contact with anyone who takes money, drugs or other favours for sex?	YES	NO	
Q11.4. Have you received money, drugs or other payment for sex?	YES	NO	
Q11.5. Were you sexually assaulted?	YES	NO	

The next slides are my own views and not those of SANBS

GUIDELINES
FOR THE PROVISION
OF PRE-EXPOSURE
PROPHYLAXIS (PrEP)
TO PERSONS AT
SUBSTANTIAL RISK
OF HIV INFECTION

Public health and rights-based approach: PrEP can enable and empower individuals to have an informed choice of HIV prevention options, using a public health approach. This includes confidentiality, access to non-discriminatory healthcare, privacy, choice, informed decision-making, and shared responsibility.

250,020 people on PrEP in SA

Specific populations considered to be at substantial risk of HIV infection include:
• Adolescent girls and young women
• Men who have sex with men
• People more than one sexual partner
• People who inject drugs
• People with a recent history of STI(s)
• People who recognise their own risk and request PrEP
• Serodiscordant couples if the HIV positive partner is not virally suppressed
• Sex workers

Risk

- SANBS state that PrEP deferral is not due to behavioural risk and is not an indirect discrimination
  - Deferral is due to the risk that the tests are ineffective
- PrEP can cause delayed seroconversion in breakthrough infections
- PrEP can result in lower VL's but little evidence to show it is below 10 copies/ml (95% LOD of ID-NAT)

Risk of a donor who is not on PrEP

$$Risk = pr\,(partner\;HIV\,+)\;x\;pr\,(donor\;WP)\;x\;pr\,(VL < LOD\;of\;NAT)\;x\;pr\,(VL\;inf)$$

Risk for a donor who is on PrEP

$$Risk = pr\,(partner\;HIV\,+)\;x\;pr\,(breakthrough\;inf)^{*}\;x\;pr\,(VL < LOD\;of\;NAT)\;x\;pr\,(VL\;inf)$$

- We should be careful that unconscious bias isn't driving risk decision making
- For non red cell products pathogen reduction is an option to remove the last remaining residual risk

*IPERGAY 14 vs 2 = 86% and the 2 returned all 60 pills ie non adherent

Conclusion

- High rate of non disclosure in South African HIV positive blood donors
- Equal number of people who do disclose their HIV status and ART drug use
- Probably a number of donors on PrEP who are not disclosing their PrEP use

- The risk of a young woman contracting HIV from her partner is 86% lower if she is on PrEP than if she was not

- With all other risks being equal isn't our young lady on PrEP a safer donor than the young lady who is not

Thank you