Introduction

- South Africa has the highest burden of HIV globally with 7.5 million people living with HIV

- The HIV prevalence in the general South African adult population is 19%

- The HIV incidence in the general population between 2012 and 2016 was approximately 10 – 12 per 1000 person years

- HIV incidence poses the largest risk to blood safety

Prevalence vs Incidence

- Prevalence
  - Reflects all the HIV positive donations detected divided by the population
  - Often used for total donor population rates but should actually only be used for first time donors
  - For example the HIV prevalence in first time donors at SANBS is 1% so 1 out of every hundred first time blood donors is HIV positive
  - Infections occurred at any point in the past and can be detected by most assays
  - Donor questionnaire not designed to detect prevalent infections as it only asks risk behavior for the past 3 months
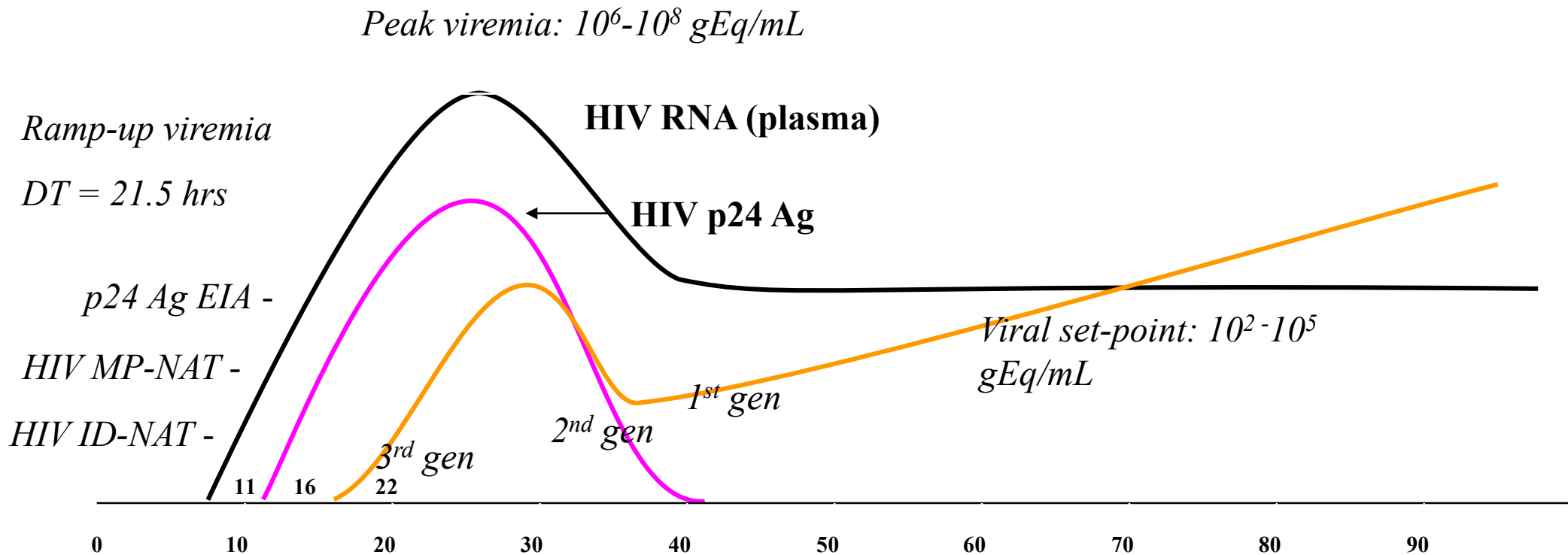
Prevalence vs Incidence

- Incidence
  - Reflects new infections and therefore is more relevant to window period and risk
  - Can be calculated for repeat donors as you know they had previous negative donations and can analyze rates of new infections divided by person-time
  - Can be estimated in first time donors by testing using more sensitive or less sensitive assays (e.g., NAT & Serology or Serology & LAg)
  - Incidence is required to estimate residual risk in repeat and first-time donors

HIV Viremia during early infection

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Peak viremia: 10^6-10^8 gEq/mL

HIV RNA (plasma)

Ramp-up viremia

DT = 21.5 hrs

HIV p24 Ag

p24 Ag EIA -

HIV MP-NAT -

Viral set-point: 10^2-10^5 gEq/mL

HIV ID-NAT -

1st gen

11 16

3rd gen

22

2nd gen

| 0 | 10 | 20 | 30 | 40 | 50 | 60 | 70 | 80 | 90 |

Slide adapted from M Busch

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Limitations of the Repeat donor method

$$Incidence = \frac{HIV + repeat\ donors}{Person-years} \times 1000$$
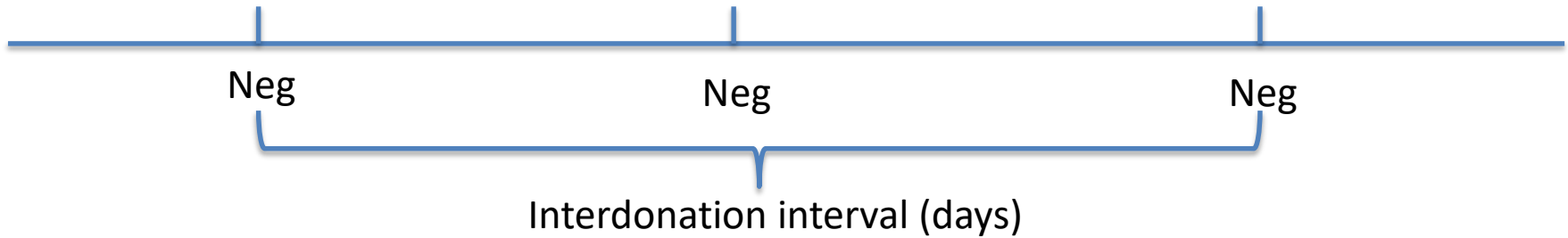
- Doesn't provide incidence for first time donors
- If your donor population doesn't have repeat donors or only a small number then the method does not add value
- Person-years is calculated as the sum of all the inter-donation intervals of the negative donors and the sum of half the inter-donation intervals for the HIV positive repeat donors; this requires a comprehensive database of donors/donations
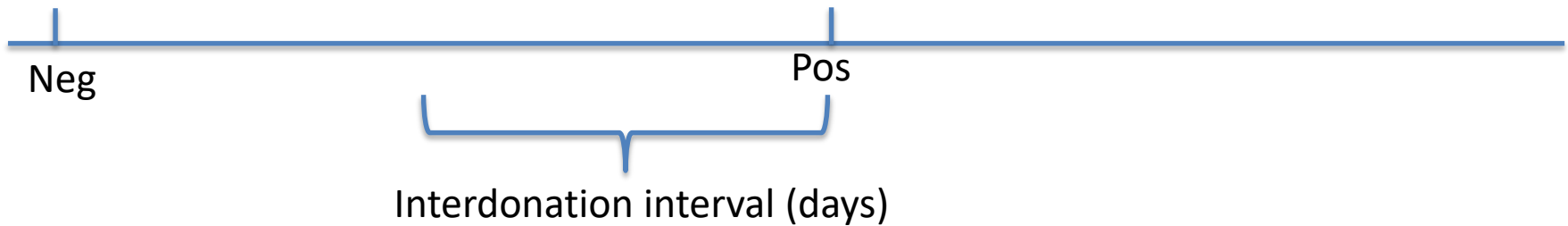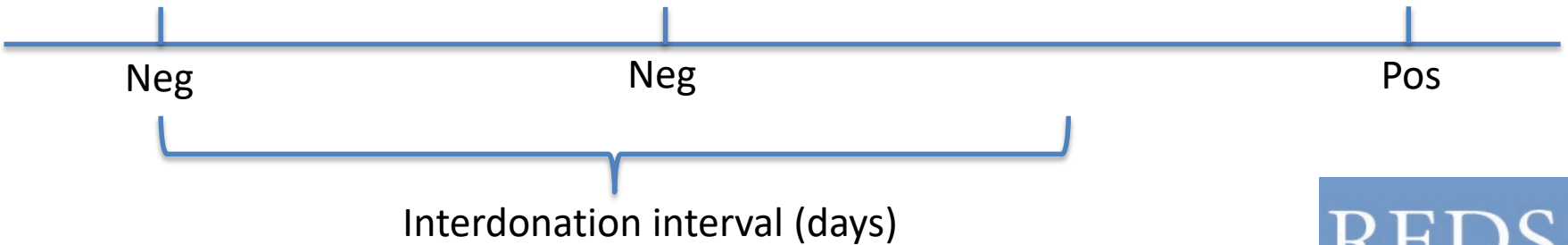
Person years classical method

Donor 1

Neg   Neg   Neg

Interdonation interval (days)

Donor 2

Neg   Pos

Interdonation interval (days)

Donor 3

Neg   Neg   Pos

Interdonation interval (days)
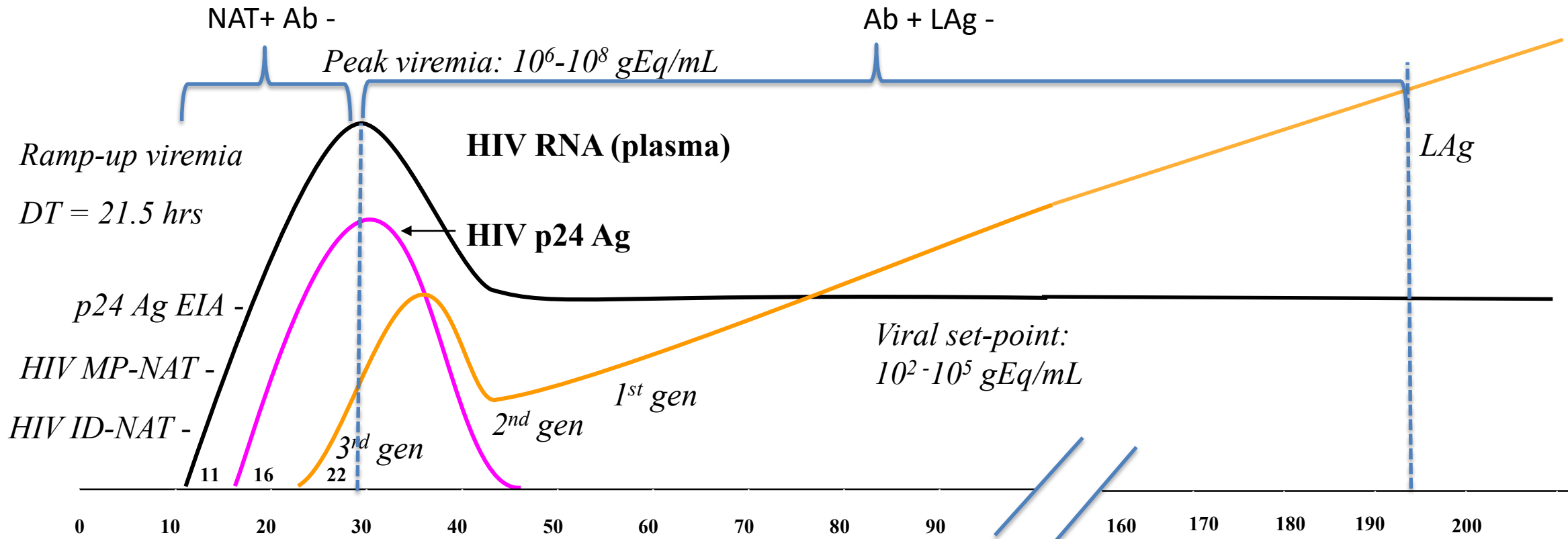
Limitations of the NAT yield method

- NAT yield method
  - Too few NAT yields to provide good confidence limits for most blood services
  - Small change in NAT yield provides a large change in incidence

HIV Viremia during early infection

SANBS

Anti-HIV antibodies have low avidity during the early phases

NAT+ Ab -

Ab + LAg -

Peak viremia: 10^6-10^8 gEq/mL

Ramp-up viremia

DT = 21.5 hrs

HIV RNA (plasma)

HIV p24 Ag

LAg

p24 Ag EIA -

HIV MP-NAT -

HIV ID-NAT -

Viral set-point: 10^2-10^5 gEq/mL

1st gen

2nd gen

3rd gen

11 16 22

0 10 20 30 40 50 60 70 80 90 160 170 180 190 200

Slide adapted from M Busch

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Limiting antigen avidity (LAg) assay

- Quantitative LAg avidity EIA for distinguishing between recent and long term HIV infections
- The principle of the test is based on the observation that following exposure to HIV-1, the immune system produces low avidity HIV-1 antibodies early in the infection, and as time progresses, the immune system matures and produces high avidity HIV-1 antibodies

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Methods

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- Plasma samples from HIV positive First time donors during 2012 to 2016 were tested on the LAg assay

- A Mean Duration of Recent Infection (MDRI) of 195 <u>(95% CI: 168-222)</u> days was used for clade C infections in SANBS donors at a normalized optical density (ODn)*

- Donations were classified into three groups, HIV Negative, recent HIV infection and long standing HIV infection

- Long standing HIV positives were classified as prevalent and not included in the analysis

*Grebe E, CROI 2018

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Methods

- HIV incidence = $\dfrac{\#\ of\ LAg\ recent\ infection\ donations}{\#\ donations\ x\ LAg\ MDRI/365}$ x *1000*

- Recent cases included NAT yields and HIV NAT+/Ab+/LAg recent

- Person years is derived from the LAg MDRI = 195 days
  - Each negative donation contributed the full MDRI of 195 days
  - Each LAg recent infection case contributed half the MDRI of 97.5 days

- Confidence limits for incidence estimates were derived from Poisson regression

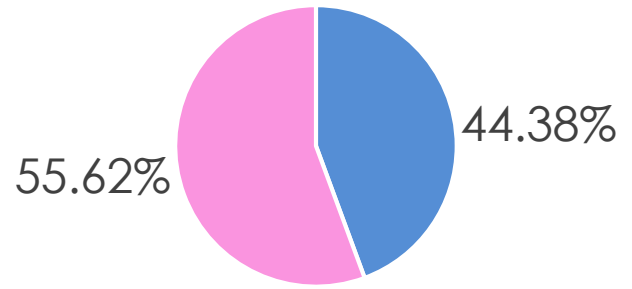# HIV Results of 513,334 First time donors (2012-2016)

- 5,540 (1.08%) tested HIV positive - Prevalence
- 879 (15.9%) classified as recent infection by LAg
- 4,538 classified as long standing; excluded from incidence analysis
- 123 had missing LAg results and an imputation was performed
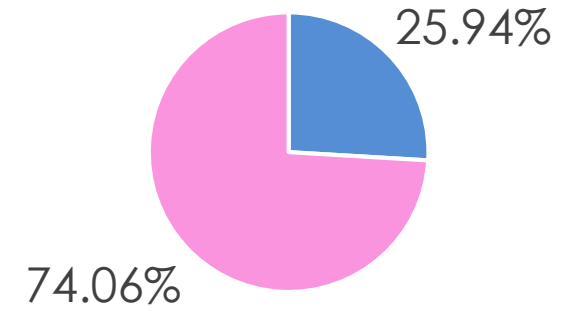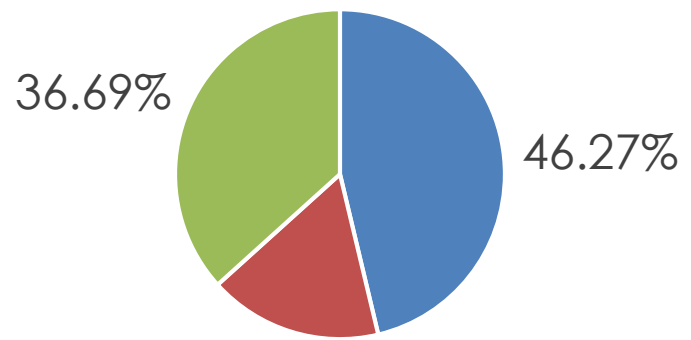
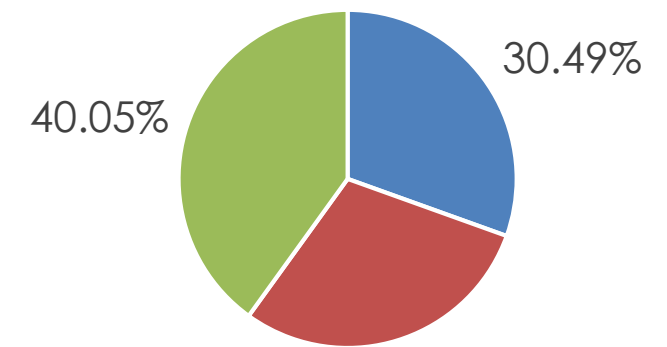# Frequency by Gender & Age

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HIV Negative

44.38% Male
55.62% Female

■ Male ■ Female

P<0.005

36.69%
46.27%
17.04%

■ 16-19 yrs ■ 20-25 yrs ■ 25+ yrs ■

HIV Recent

25.94%
74.06%
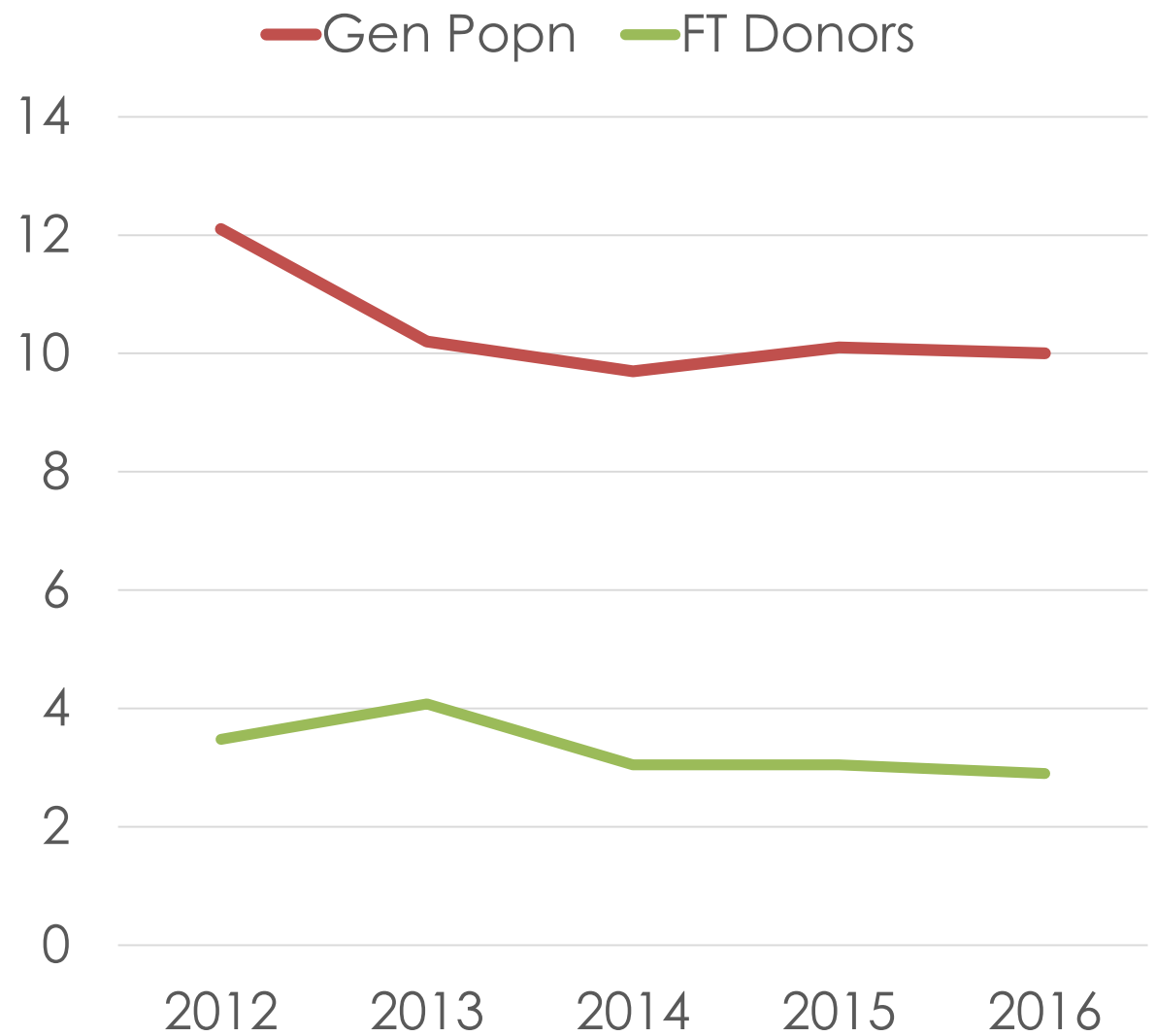
■ Male

30.49%
40.05%
29.47%

■ 16-19 yrs ■ 20-25 yrs ■ 25+ yrs ■

South African Incidence per 1000 (2012-2016)

Demographic	Incidence (Donors)
Overall	3.32 (3.11, 3.55)
Gender	
Female	4.43 (4.11, 4.78)
Male	1.94 (1.70, 2.20)
Age	
16-19	2.21 (1.96, 2.48)
20-25	5.71 (5.06, 6.44)
>25	3.62 (3.27, 4.02)
Race	
White	0.19 (0.12, 0.32)
Black	5.88 (5.50, 6.29)
Asian	0.12 (0.03, 0.48)
Coloured	1.38 (0.89, 2.13)
Unknown	1.27 (0.68, 2.36)

Legend: Gen Popn, FT Donors

An overall incidence of 3.32 (95% CI: 3.11- 3.55) per 1000 PY

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LP 2.61

MP 5.92

NW 1.42

GP 2.61

FS 4.29

KZN 4.42

NC 1.74

EC 2.98

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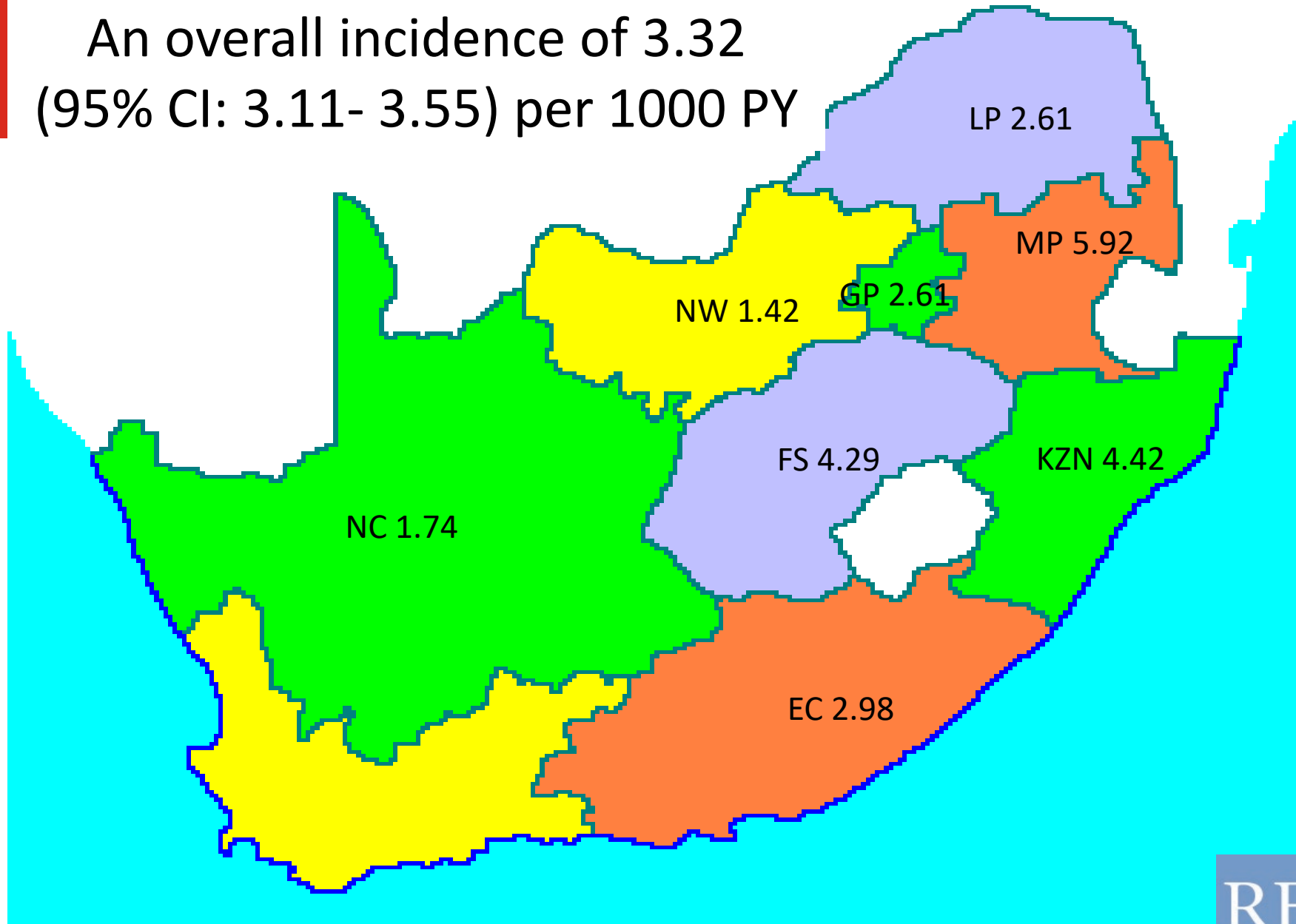
Discussion

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- Prevalence is 20 fold lower than the general population
- In South Africa HIV incidence in first time donors is 2 to 3 fold lower than in the general population. Incidence has remained steady over the last few years
- Incidence is twice as high in females vs males
- Highest incidence in Mpumalanga followed by Kwa Zulu Natal, and lowest incidence in North West province
- Possible over-estimation due to false recency due to donors on ART

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Discussion

- The use of antibody recency assays is an important new tool for countries that have large numbers of first time donors
- Future research will compare these results to those obtained using other incidence methods

Acknowledgments

SANBS

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THANK YOU