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## Background

- Cross-sectional incidence testing will be used for Population based HIV Impact Assessments in Kenya and Uganda countries where a significant portion of the population is infected with HIV-1 subtype D
- Incidence testing is being performed using the Limiting Antigen Avidity Assay (LAG-Avidity). Manufacturer's recommendation is to classify recent infections for those samples with a normalized optical density < 1.5 and a viral load (VL) > 1000 copies/mL
- Performance characteristics for this testing algorithm is characterized with a mean duration of recent infection (MDRI) and a false recent rate (FRR).
- Incidence is calculated  

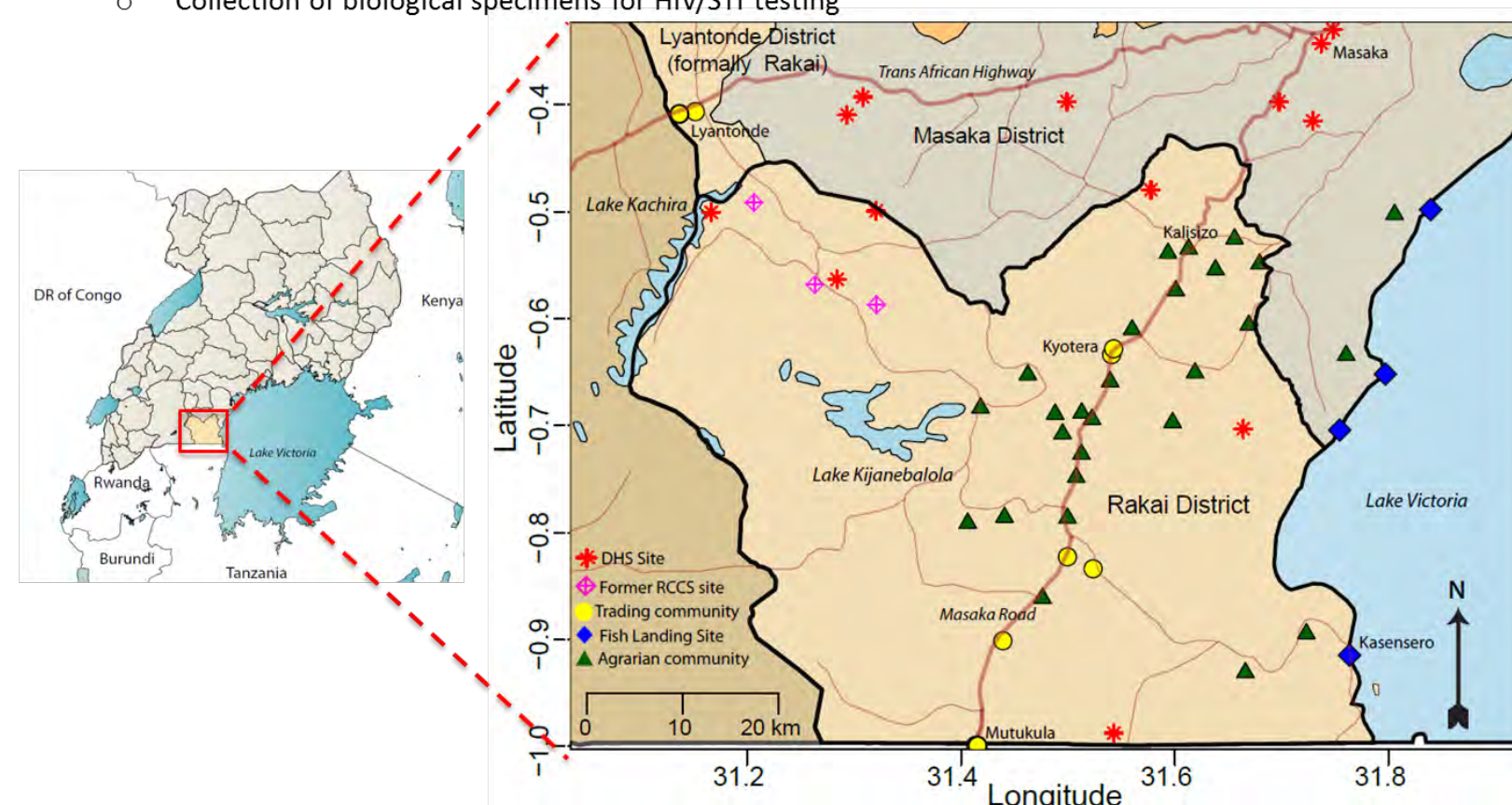
$$\frac{\# \text{ recent} - (\text{FRR} \times \text{total HIV+})}{\text{total HIV- in survey}} \times \frac{(365 \text{ days}) \times 100}{\text{MDRI}}$$
- Recommended
  - MDRI of 130 days
  - FRR 0%
- Previous studies have shown differential performance of the LAG-Avidity Assay for subtype A and D infected individuals
  - Subtype A (LAG+VL1000: MDRI = 143)
  - Subtype D (LAG+VL1000: MDRI = 217)
- gp41 sequence data (target of the LAG-Avidity assay) was used to determine the frequency of the different subtypes in the population
  - 45% subtype A
  - 55% subtype D
- We used a MDRI of 184 days - adjusted for the subtype A and D prevalence
  - $(143 \times 0.45) + (217 \times 0.55) = 184$

- We sought to evaluate the capacity of the LAG-Avidity + VL algorithm in an East African setting to:
  - Accurately estimate a point estimate of incidence
  - Accurately detect a decrease in incidence at the population
  - Determine if subtype specific MDRI was necessary to increase precision
  - Determine the impact of a survey specific FRR

## Methods

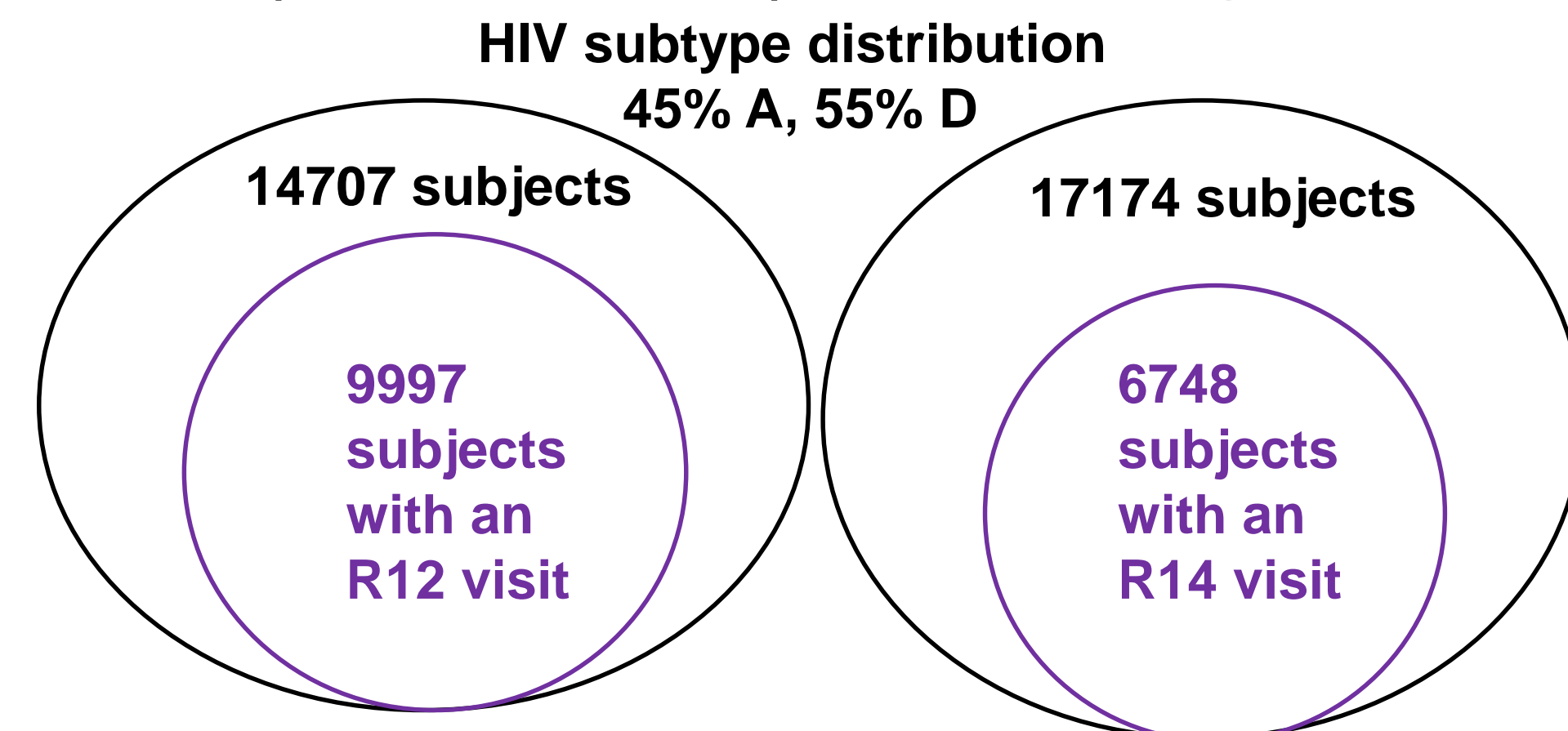
### Rakai Community Cohort Study (RCCS)

- Population-based HIV incidence cohort in 50 communities in Rakai District
- ~15,000 study participants in ~8000 households are surveyed on an annual basis.
- Ongoing since 1994 (17 survey rounds completed)
- Study includes census and individual interviews.
  - Household census (family relationships, migration data)
  - Sociodemographic and behavioral survey
  - Collection of biological specimens for HIV/STI testing

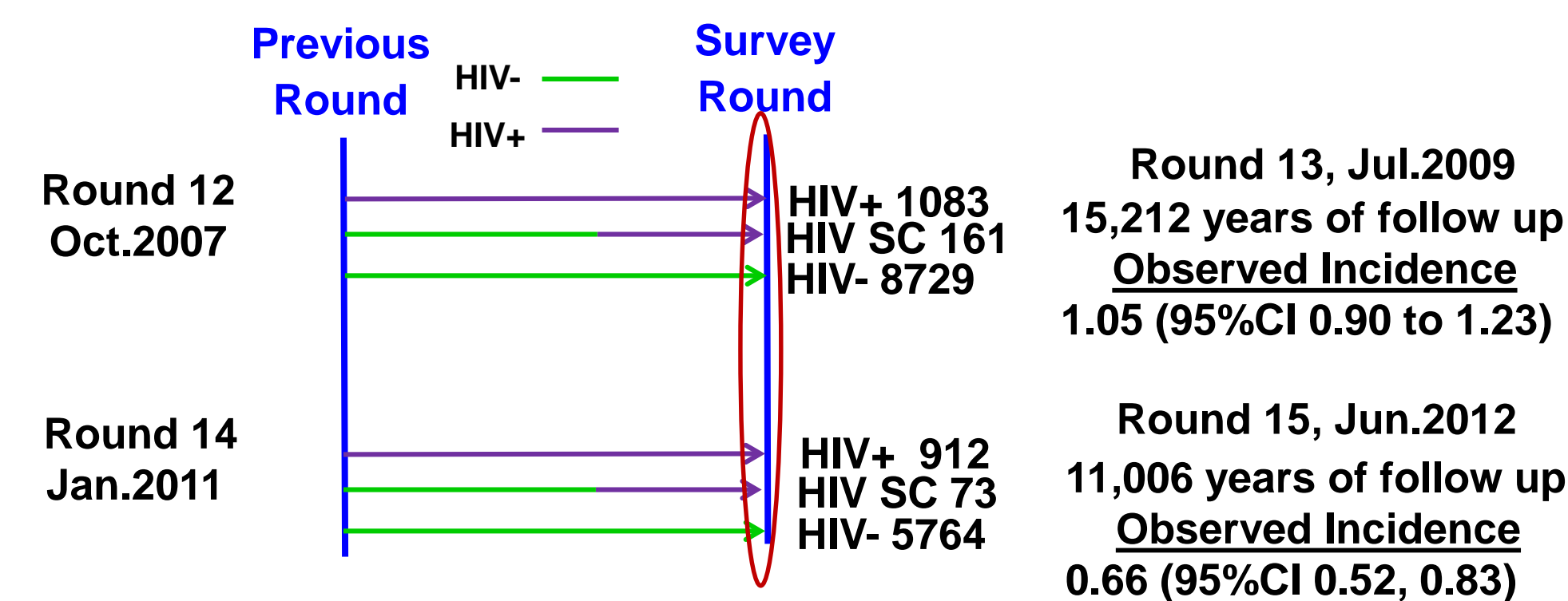


### RCCS Samples Tested and Comparisons Made

Round 13 Jul.2009 (Jun.2008-Dec.2009) Round 15 Jun.2012 (Aug.2011-May.2013)



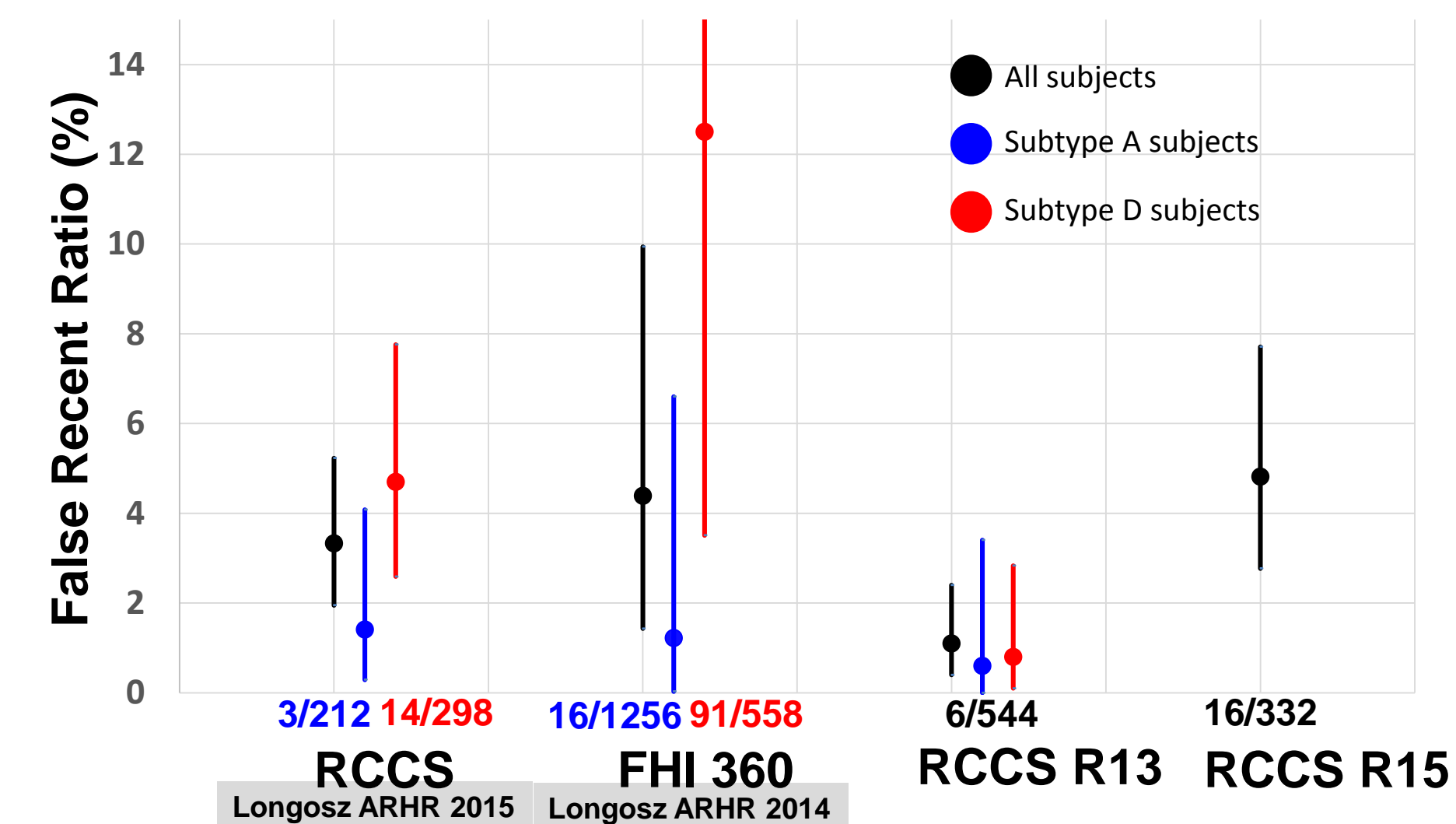
### Comparison of Cross-Sectional Incidence Testing to Observed Incidence



Compare the estimate using cross-sectional incidence testing to that observed longitudinally

## Results

### Ugandan FRR Estimates



### RCCS Point Estimates of Incidence

#### RCCS R13 2008-2009

8729 HIV-, 1244 HIV+  
358/1244 HIV+ on ART  
822/886 tested by LAg  
69 LAg < 1.5  
49 LAg < 1.5 + VL>1000

MDRI = 184 days (RSE 15%)  
FRR 1.1% (6/544)

Estimated Incidence:  
0.88% (95%CI 0.44, 1.33)

Observed Incidence:  
1.05% (95%CI 0.90, 1.23)

#### RCCS R15 2011-2013

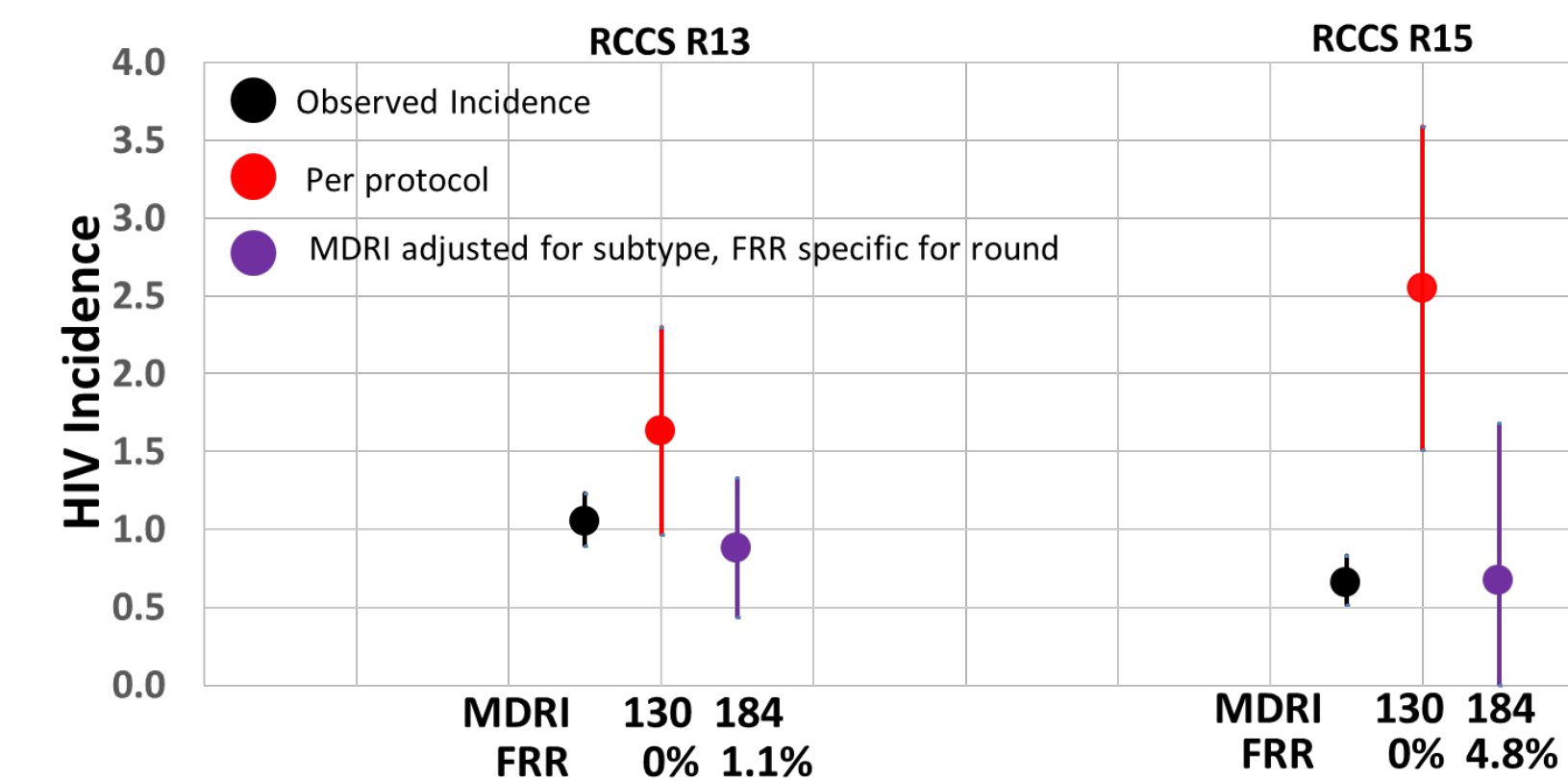
5764 HIV-, 985 HIV+  
423/985 HIV+ on ART  
500/562 tested by LAg  
84 LAg < 1.5  
56 LAg < 1.5 + VL>1000

MDRI = 184 days (RSE 15%)  
FRR 4.8% (16/332)

Estimated Incidence:  
0.67% (95%CI 0.00, 1.68)

Observed Incidence:  
0.66% (95%CI 0.52, 0.83)

### Impact of Inappropriate MDRI and FRR on Incidence Estimates



### Impact of MDRI and FRR assumptions on incidence estimates

Survey	MDRI	FRR	Incidence (95%CI)	Observed Incidence
2009 Survey Round	184	1.1	0.88% (0.44, 1.33)	1.05% (0.90, 1.23)
2009 Survey Round	184	4.8	0.00% (0.00, 0.54)	1.05% (0.90, 1.23)
2009 Survey Round	130	0.0	1.63% (0.97, 2.30)	1.05% (0.90, 1.23)
2012 Survey Round	184	1.1	1.88% (1.05, 2.70)	0.66 (0.52, 0.83)
2012 Survey Round	184	4.8	0.67% (0.00, 1.68)	0.66 (0.52, 0.83)
2012 Survey Round	130	0.0	2.55% (1.51, 3.59)	0.66 (0.52, 0.83)

Subtype adjusted MDRI 184 and survey round specific FRR

Subtype adjusted MDRI 184 and incorrect survey round specific FRR

Per protocol MDRI 130 and FRR 0%

## Conclusions

- Per protocol LAG-Avidity + Viral Load MDRI and FRR assumptions greatly overestimated HIV incidence
  - Nearly 4 fold excess incidence estimated in Round 15 survey
  - The change in incidence was opposite of observed
- Big assumptions made on which MDRI and FRR to use
- Using an MDRI proportional to the subtype distribution and a survey specific FRR, estimated incidence was close to observed incidence
- The FRR varied greatly by survey

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