



The Effects of MDRI Updates and Transition to a New Recency Assay on HIV Incidence Estimation in the United States

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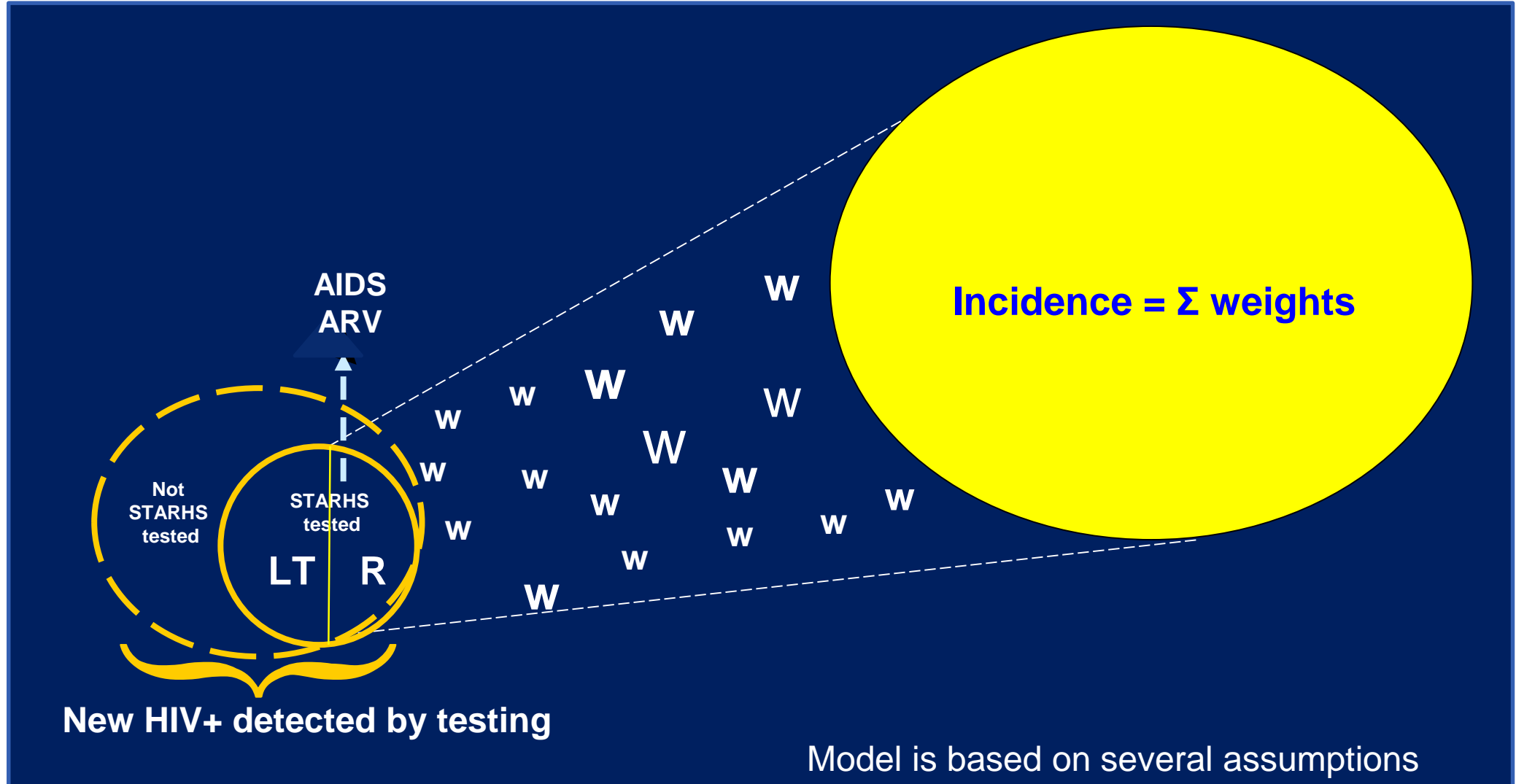
HIV Incidence Surveillance: A Component of the National HIV Surveillance System (NHSS)

- Primary source for monitoring HIV infection in the United States:
 - 50 states, the District of Columbia, and 6 U.S. dependent areas have regulatory authority and confidentiality protections to collect information on persons with HIV infection
- HIV incidence surveillance: 25 Jurisdictions
 - Monitor local, state, and national trends of new HIV infection
 - Provide a window into the HIV burden at an earlier stage of the disease

Background

- Data from the National HIV Surveillance System are used to estimate HIV incidence based on the stratified extrapolation approach
- HIV incidence estimation requires:
 - Demographic, risk, clinical and laboratory information
 - HIV testing history
 - Antiretroviral (ARV) use information
 - Recency results from the HIV diagnostic specimen
- NHSS transitioned from using the BED HIV-1 Incidence EIA (Sedia Corp., Calypte Corp.) to the avidity-based, modified Bio-Rad HIV-1/HIV-2 plus O EIA (Bio-Rad avidity) to determine recent infections

HIV Incidence Estimation using the Stratified Extrapolation Approach



Objective

- Determine the impact on trends in HIV incidence of changing from using the BED HIV-1 Incidence EIA (Sedia Corp., Calypte Corp.) (BED) to the avidity-based, modified Bio-Rad HIV-1/HIV-2 plus O EIA (Bio-Rad avidity) for HIV recency determination.
- Determine the impact of the updated BED mean duration of recent infection (MDRI) on HIV incidence estimates.

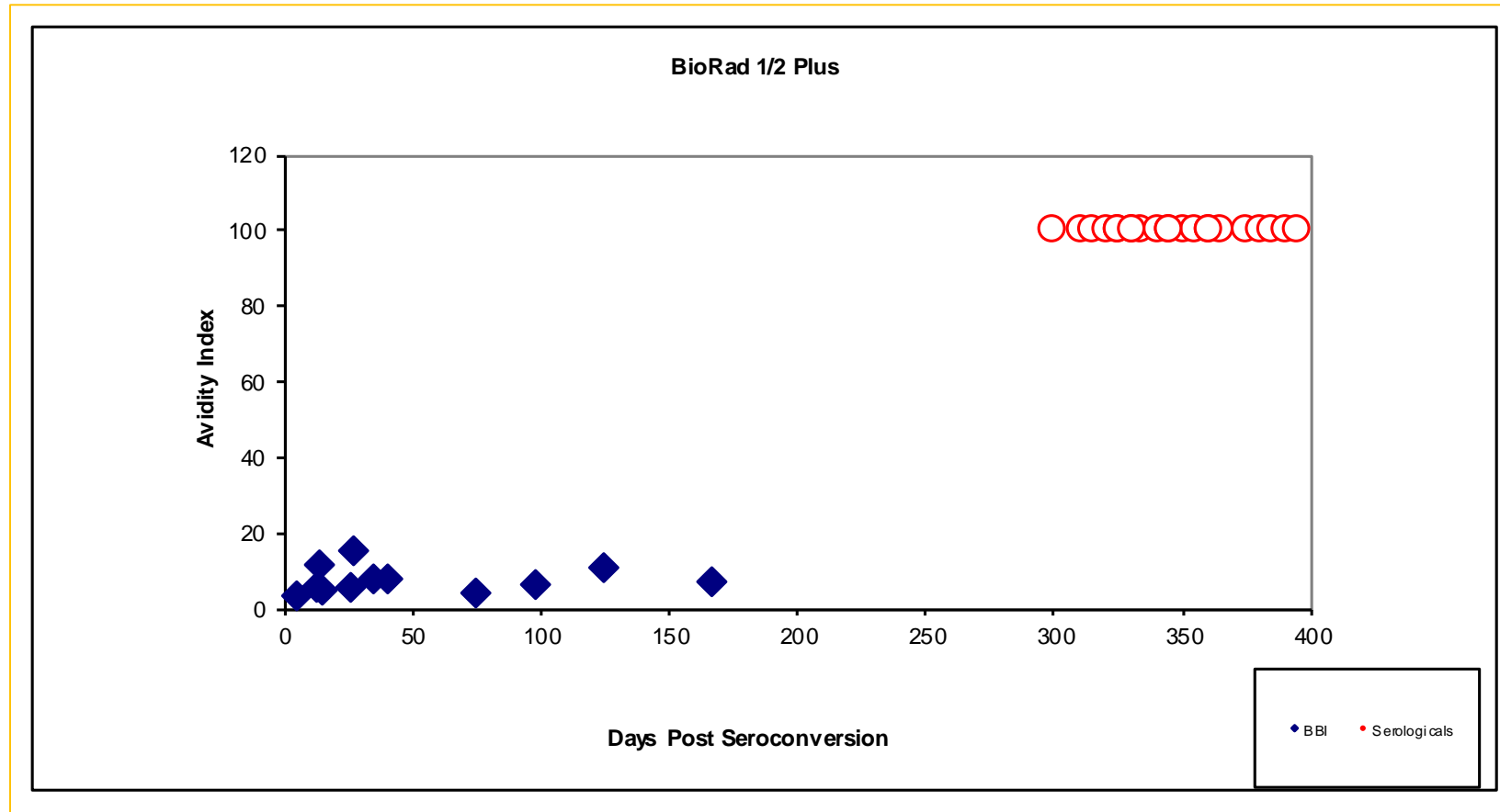
Bio-Rad Avidity

- Avidity
 - The combined strength of bond affinities in a complex or, more-simply, how tight the antibodies in a sample will bind
 - Low avidity antibody = recent infection, high avidity antibodies= long term infection
- False Recent Rate (FRR)
 - Number of samples known to be classified as false recent / total number of known long term samples
- Bio-Rad Avidity has low FRR with subtype B:
 - Less affected by viral suppression and late stage disease
 - ARV is challenging for the assay
 - Early therapy may affect antibody response

Mean Duration of Recent Infection (MDRI)

- An important parameter in calculating HIV incidence is the mean duration of recent infection (MDRI) of an assay, defined as the average time that a person with newly acquired HIV infection is classified by the assay as having recent infection
- Improved estimation methods that account for the wide variability in individual response to antibody maturation, and specifically the potential fluctuations surrounding the time a bioassay threshold is reached are important

Known Incident and Long Term



Methods

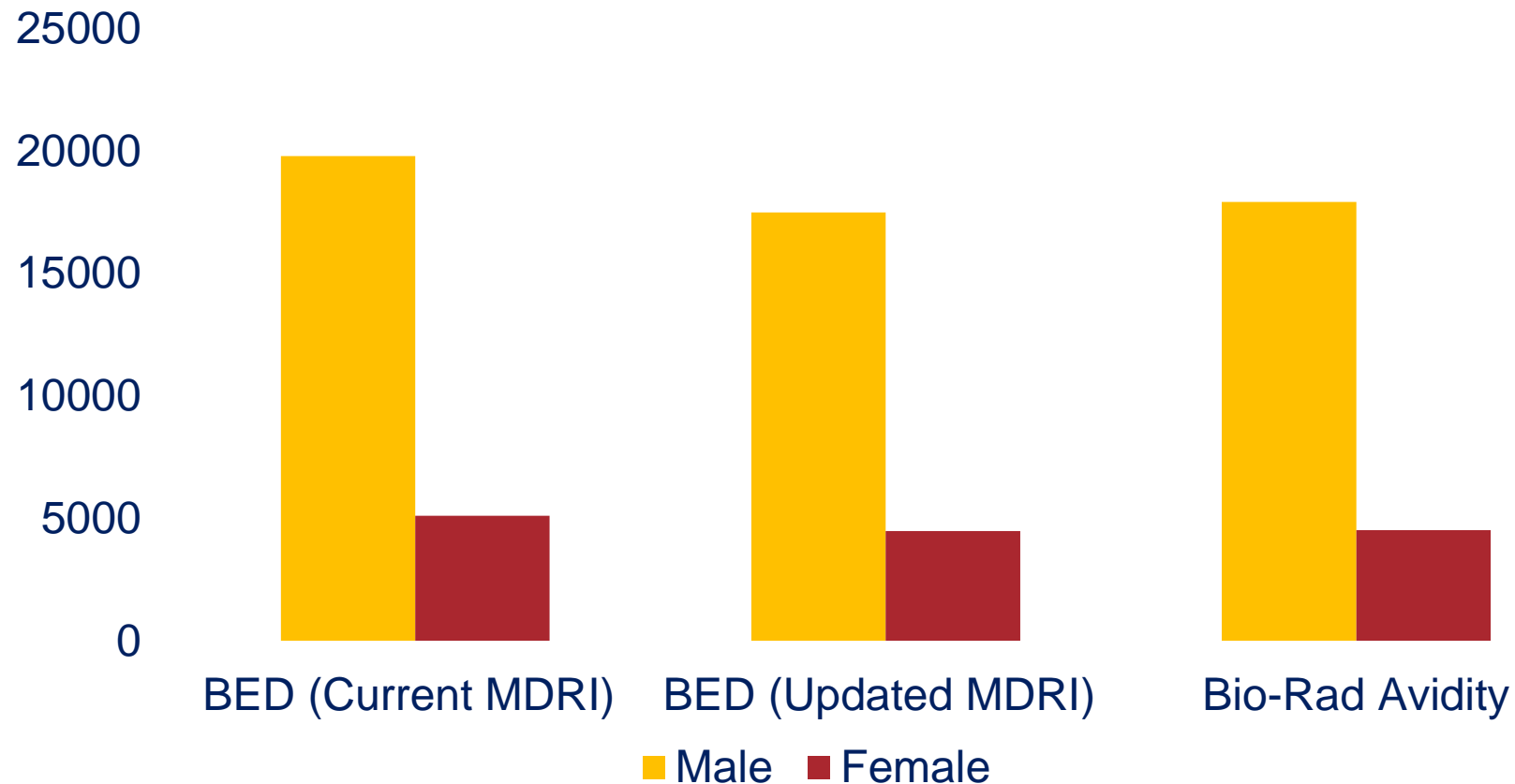
- Data from persons =>13 years with HIV diagnosed in 2010 and reported to the NHSS were used to estimate HIV incidence in selected surveillance areas using the stratified extrapolation approach
- MDRI for BED and Bio-Rad avidity were estimated using an improved estimation method (revised survival method) applied to longitudinal specimens from newly infected persons in the U.S. with subtype B
- Incidence estimates were calculated using BED (current MDRI=162 days and new MDRI=198 days) and Bio-Rad avidity (MDRI=239 days) at developer-recommended cutoffs for recent result (Bio-Rad avidity, index threshold=30; BED, normalized OD=0.8)
- Of the 12,893 specimens from persons with HIV diagnosed in 2010 with BED results, 5,423 (42%) were also tested with Bio-Rad avidity at the CDC DHAP laboratory
- Multiple imputation was used to account for missing data
- Simple z-score tests were used to compare incidence estimates

Estimated HIV Incidence in a Selected Number of Surveillance Jurisdictions using the Stratified Extrapolation Approach Based on BED or Bio-Rad Avidity, 2010

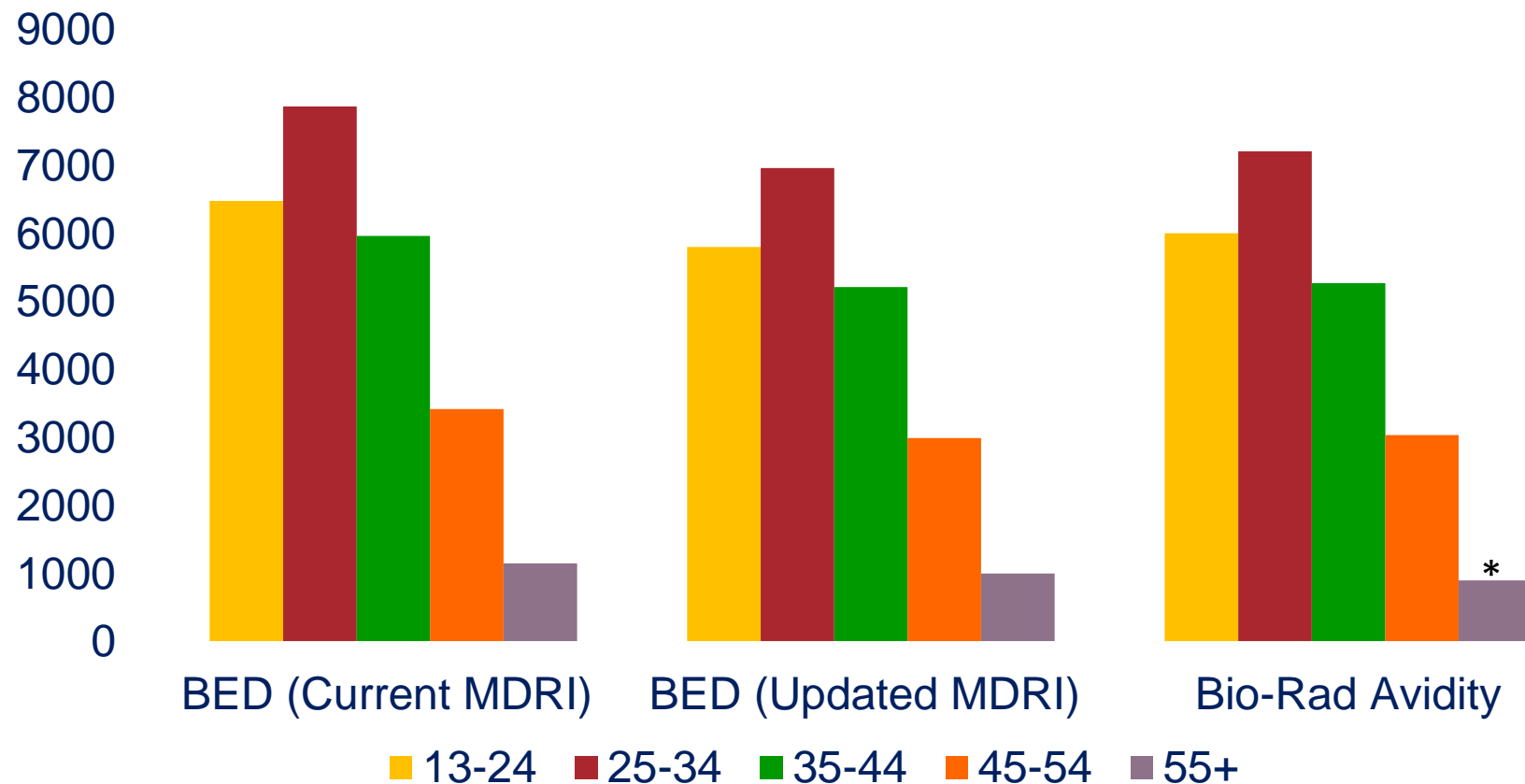
Assay	Cutoff BED ODn/ Bio-Rad Avidity Index	MDRI* (days)	Estimated HIV Incidence	95% Confidence Interval	p-value
BED (Updated MDRI)	0.8	198	21,999	18,889–25,109	Ref
BED (Current MDRI)	0.8	162	24,921	21,931–27,910	0.005
Bio-Rad Avidity	30	239	22,457	19,669–25,245	0.6

*Mean Duration of Recent Infection

Estimated HIV incidence in a selected number of surveillance areas using the stratified extrapolation approach based on BED and Bio-Rad avidity by sex

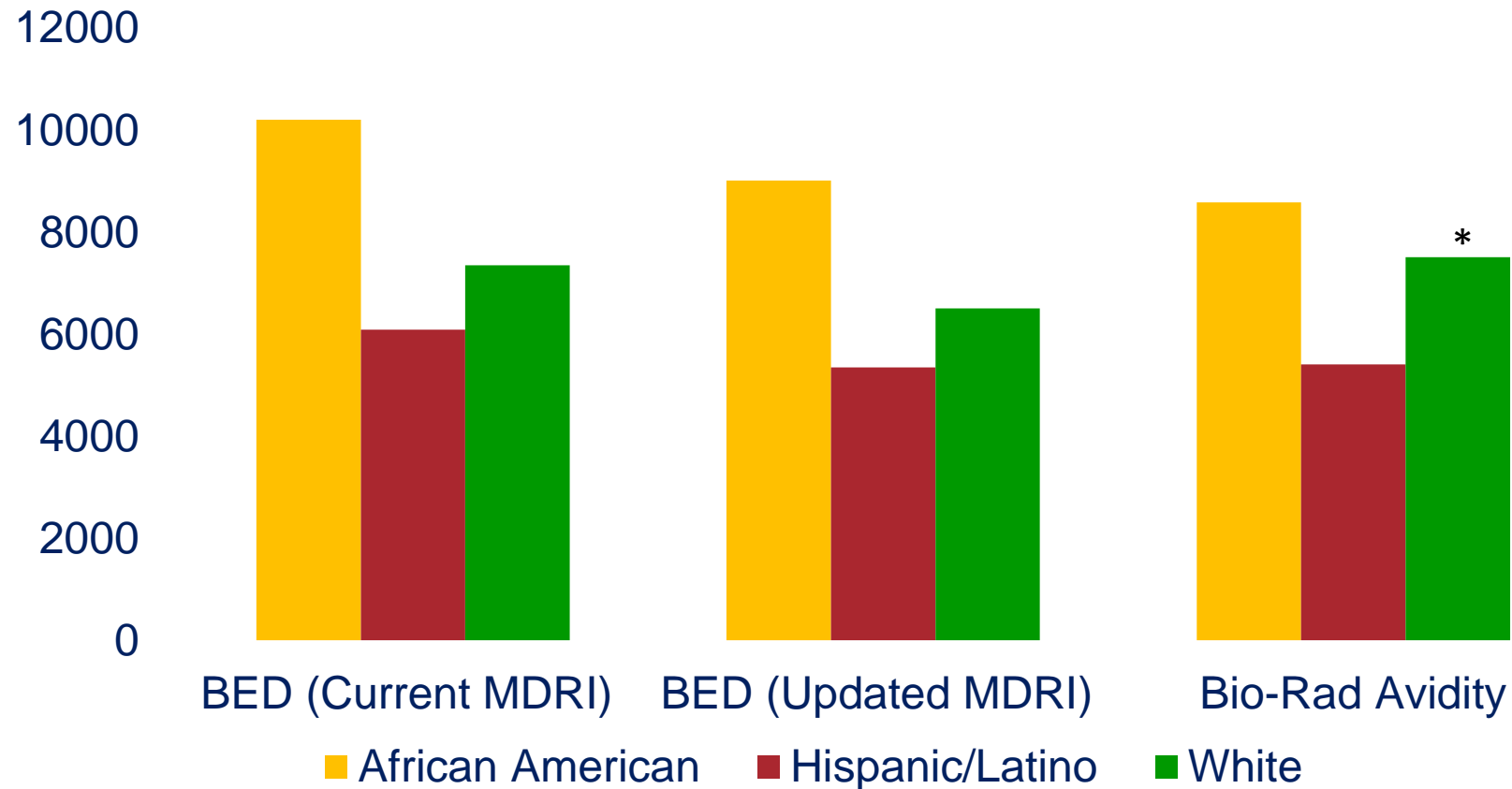


Estimated HIV Incidence in a Selected Number of Surveillance Jurisdictions using the Stratified Extrapolation Approach Based on BED or Bio-Rad Avidity, by Age, 2010



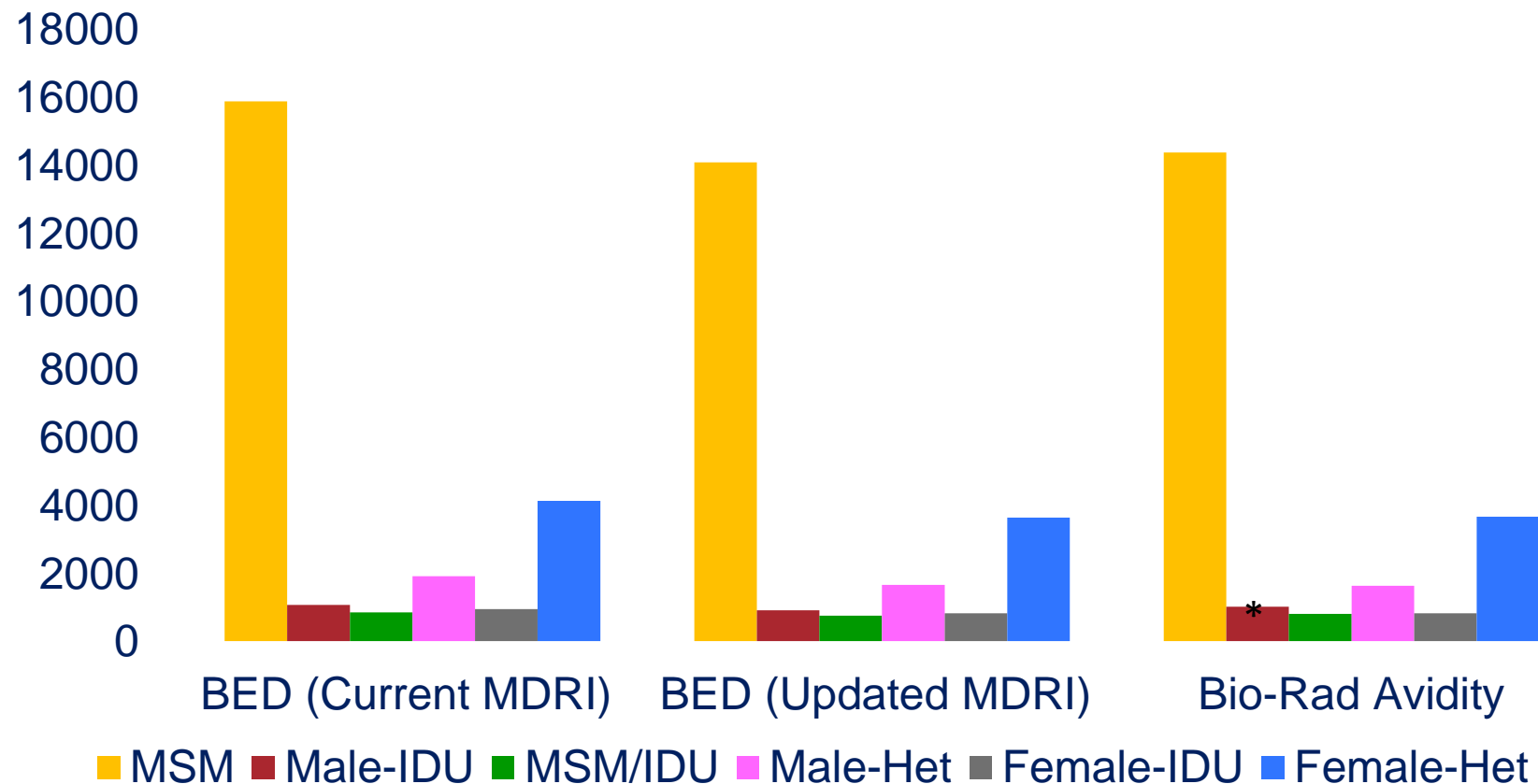
*Difference >5% compared to BED (Updated MDRI)

Estimated HIV Incidence in a Selected Number of Surveillance Jurisdictions using the Stratified Extrapolation Approach Based on BED or Bio-Rad Avidity, by Race/Ethnicity, 2010



*Difference >5% compared to BED (Updated MDRI)

Estimated HIV Incidence in a Selected Number of Surveillance Jurisdictions using the Stratified Extrapolation Approach Based on BED or Bio-Rad Avidity, by Transmission Category, 2010



*Difference >5% compared to BED (Updated MDRI)

Summary

- Estimates based on BED with MDRI=198 were significantly lower when compared to those derived using BED with MDRI=162.
- There was no significant difference between the overall estimate based on BED with MDRI=198 and Bio-Rad avidity
- However, Bio-Rad based estimates were higher than BED (MDRI=198) based estimates among whites and persons with infection attributed to injection drug use
- Further considerations, for the data, could be related to the convenience-based sample

Conclusions

- HIV incidence estimates depend on the accuracy of the MDRI and variations have an effect; a longer MDRI results in lower incidence estimates.
- A similar statistical approach was used to calculate MDRI estimates for BED and Bio-Rad avidity; the new BED MDRI was longer than previous estimates.
- HIV incidence estimates based on the new BED MDRI and the Bio-Rad avidity assay were comparable.

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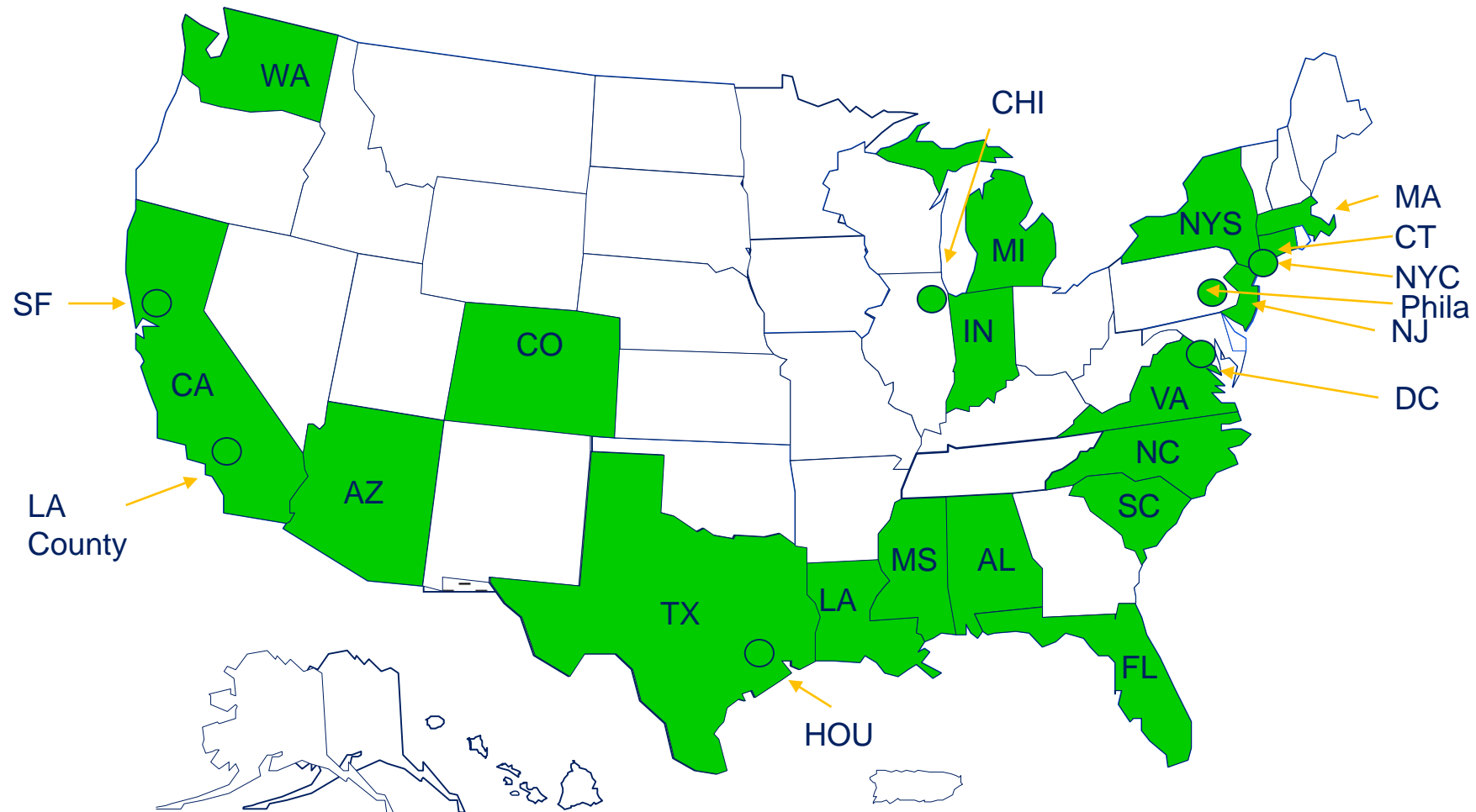
Questions

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



Jurisdictions conducting HIV Incidence Surveillance



Summary of Assumptions

- Conditional on the observed variables, missing data on testing history and BED results are missing at random
- Testing information, especially the date of last negative HIV test, is accurate
- The BED recency period distribution is well characterized
- Likelihood of HIV testing prior to AIDS diagnosis is constant
- All HIV infections will eventually be diagnosed either through testing or through death
- Ratio of HIV incidence to HIV diagnosis in BED-states is similar to the ratio in other states
- HIV incidence has been relatively stable in last two years
- Testing behavior has not changed over several