HIV Testing in the era of PrEP

Bernard M Branson MD

September 28, 2020

Argentinian HIV Clinical Forum - 2020

Background and Disclosure of Financial Relationships

- Dr. Branson previously served as Associate Director for Laboratory Diagnostics in CDC's Division of HIV/AIDS Prevention until October 2014.

- Dr. Branson currently serves as consultant to the Gilead Sciences FOCUS Program

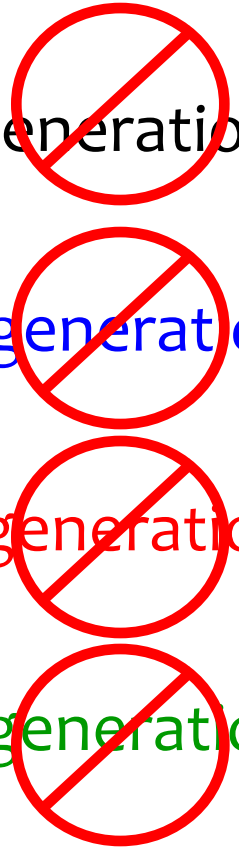
Use of Brand Names

- This presentation may refer to individual HIV tests by brand name for the purposes of identification and clarity.

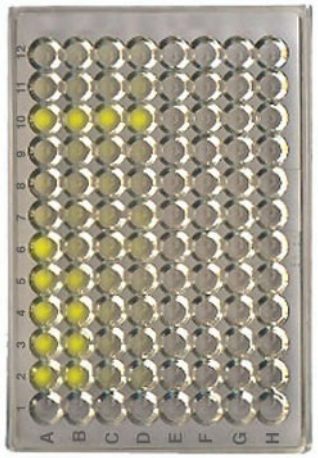
- No endorsement of any specific test is intended.

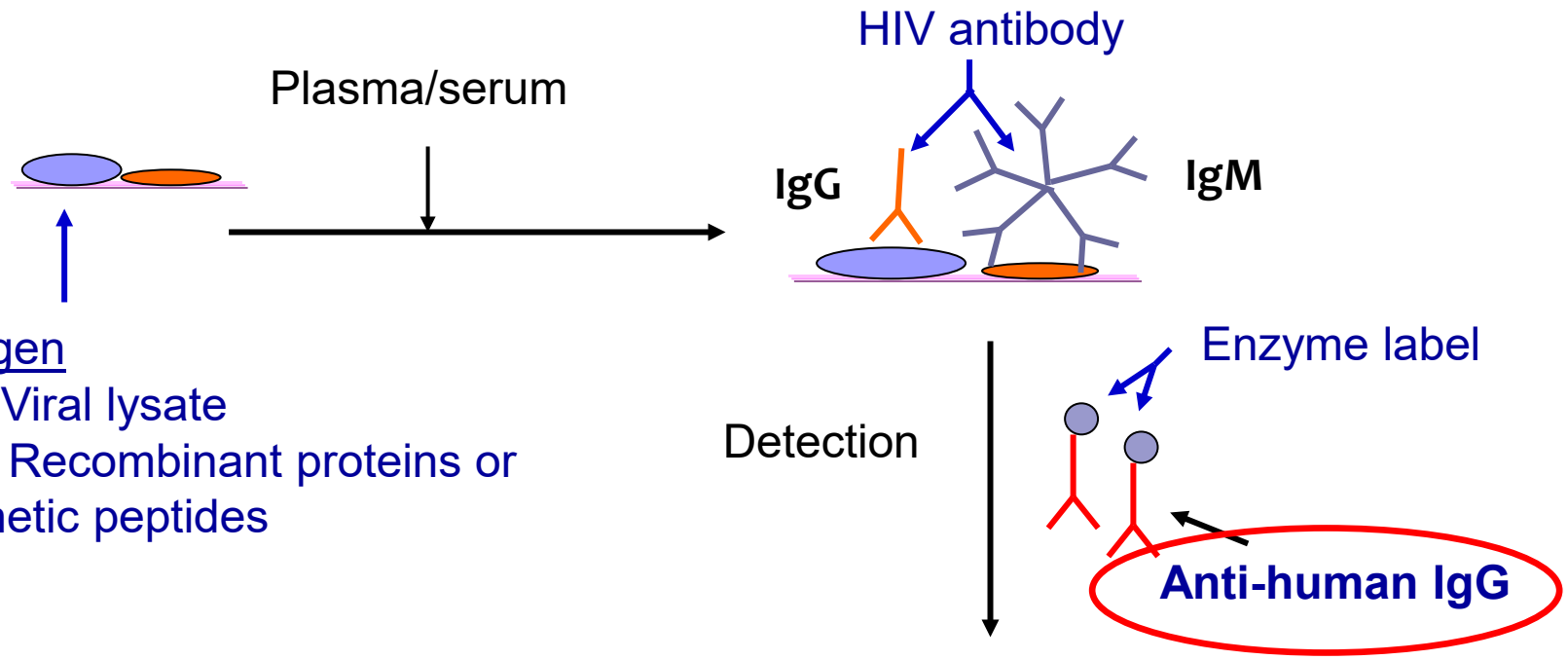
Evolution of HIV Tests

- 1st generation: whole viral lysate, detects IgG antibody
- 2nd generation: synthetic peptides, detects IgG antibody
- 3rd generation: synthetic peptides, detects IgM and IgG antibody
- 4th generation: detects IgM, IgG antibodies, p24 antigen

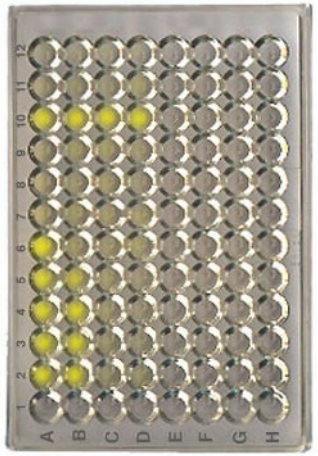


1st and 2nd Generation: Indirect EIA

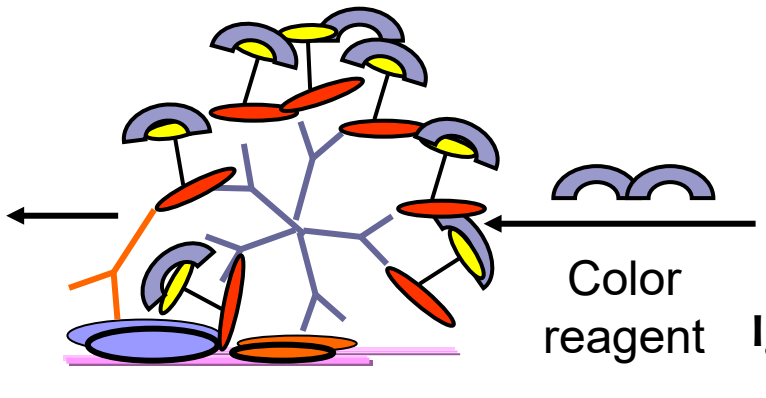




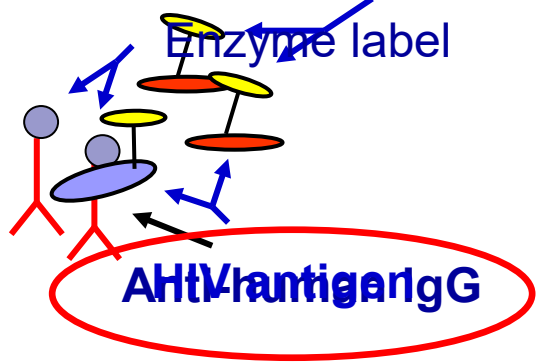
3rd Generation: Sandwich EIA



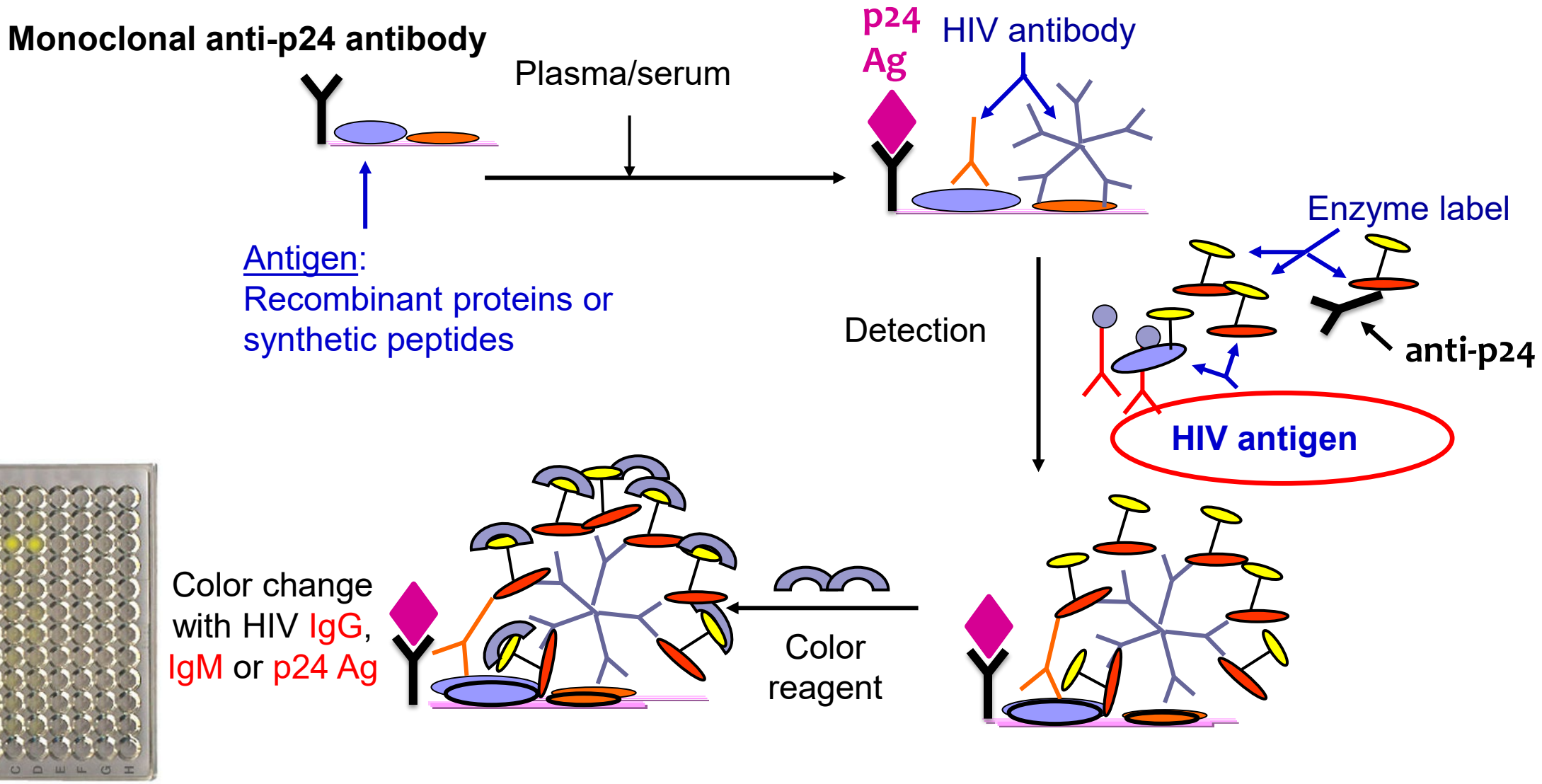
Color change with HIV IgG or IgM



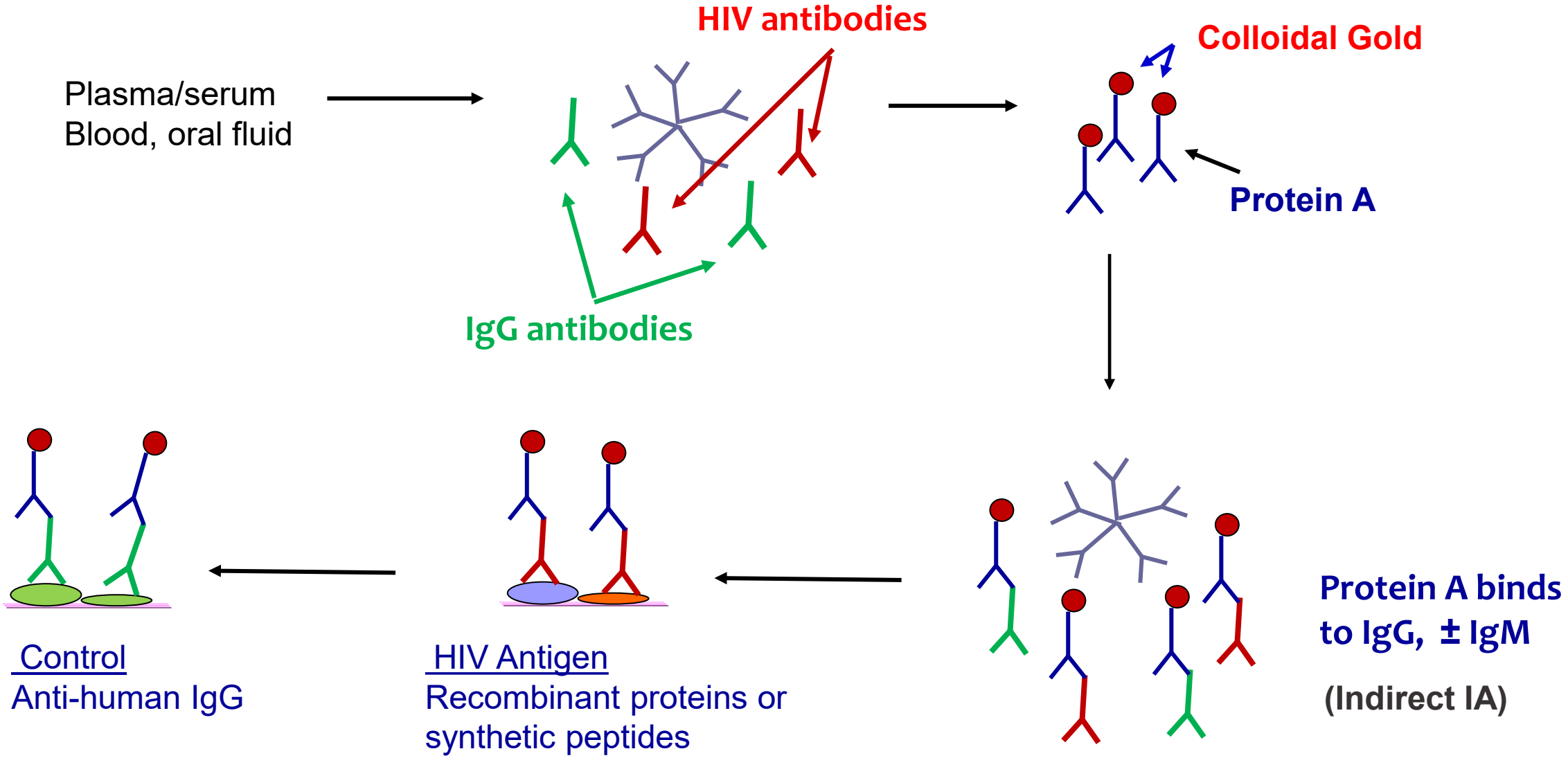
Detection



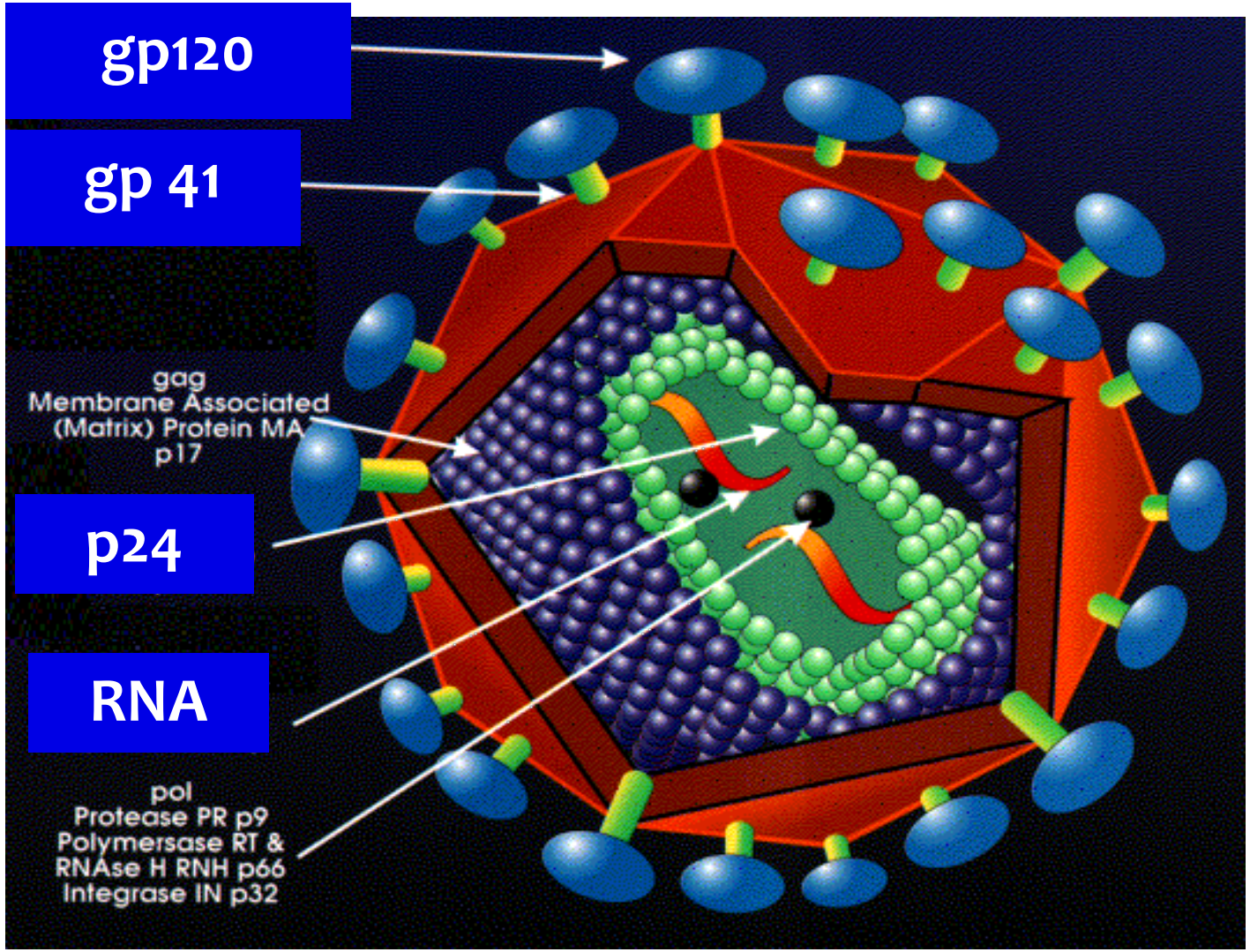
4th Generation: Sandwich EIA



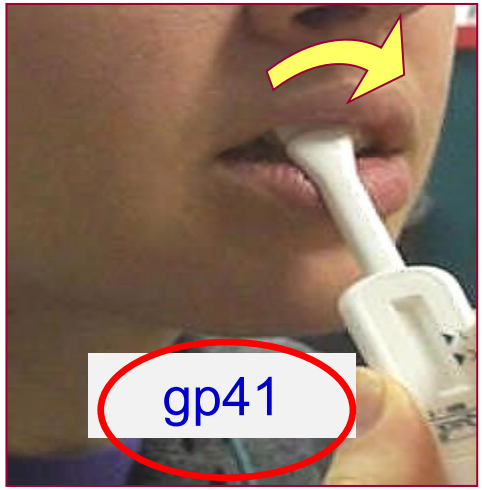
Rapid Tests: which generation?



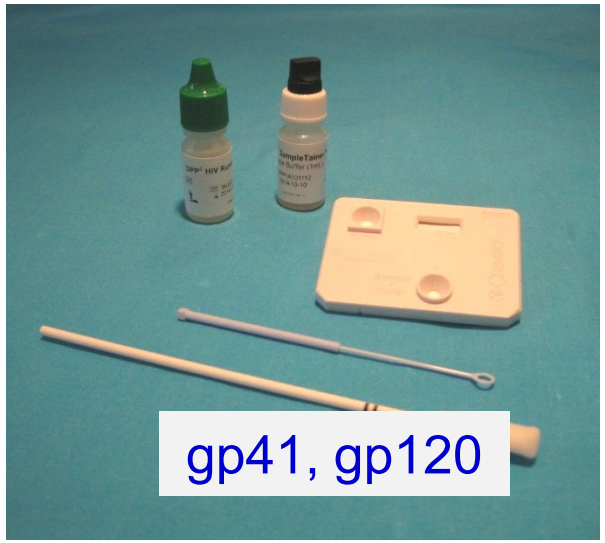
HIV-1: viral antigens and RNA



Which HIV antibodies do rapid tests detect?



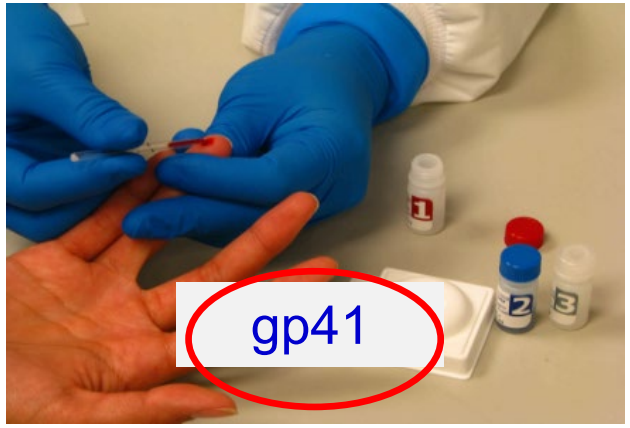
Oraquick Advance



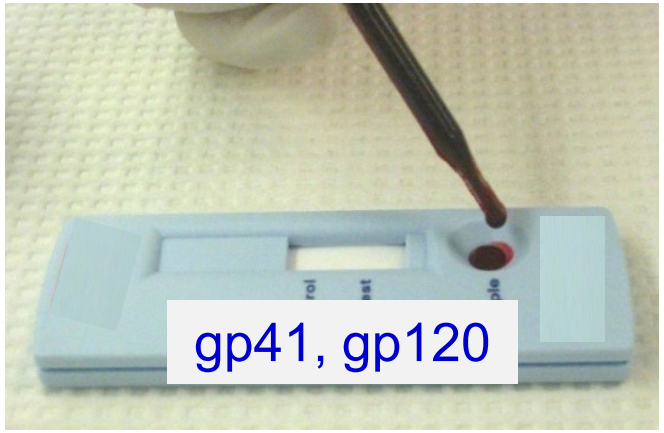
DPP HIV 1/2

Chembio Sure Check

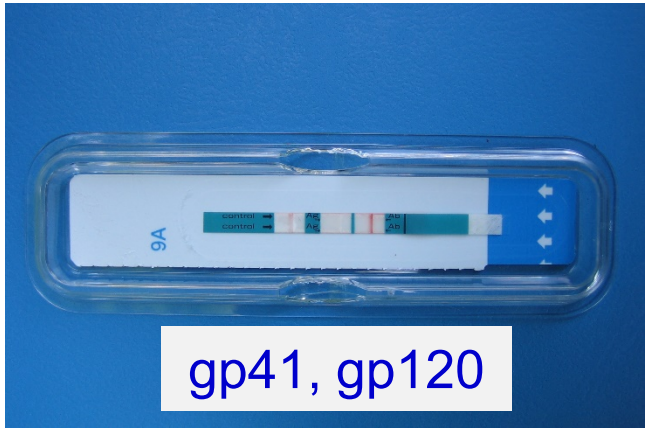
Chembio Stat Pak



INSTI HIV 1/2



Uni-Gold Recombigen



Determine Combo Ag/Ab

Which test is currently used most often to detect HIV infection?

A. CIA – Chemiluminescent Immunoassay

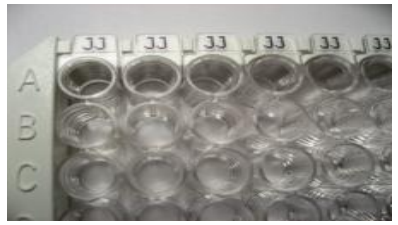
B. DIA – Defense Intelligence Agency

C. EIA – Enzyme Immunoassay

D. MFI – Multiplex Flow Immunoassay

E. None of the above

Abbott Architect Ag/Ab Combo
2010



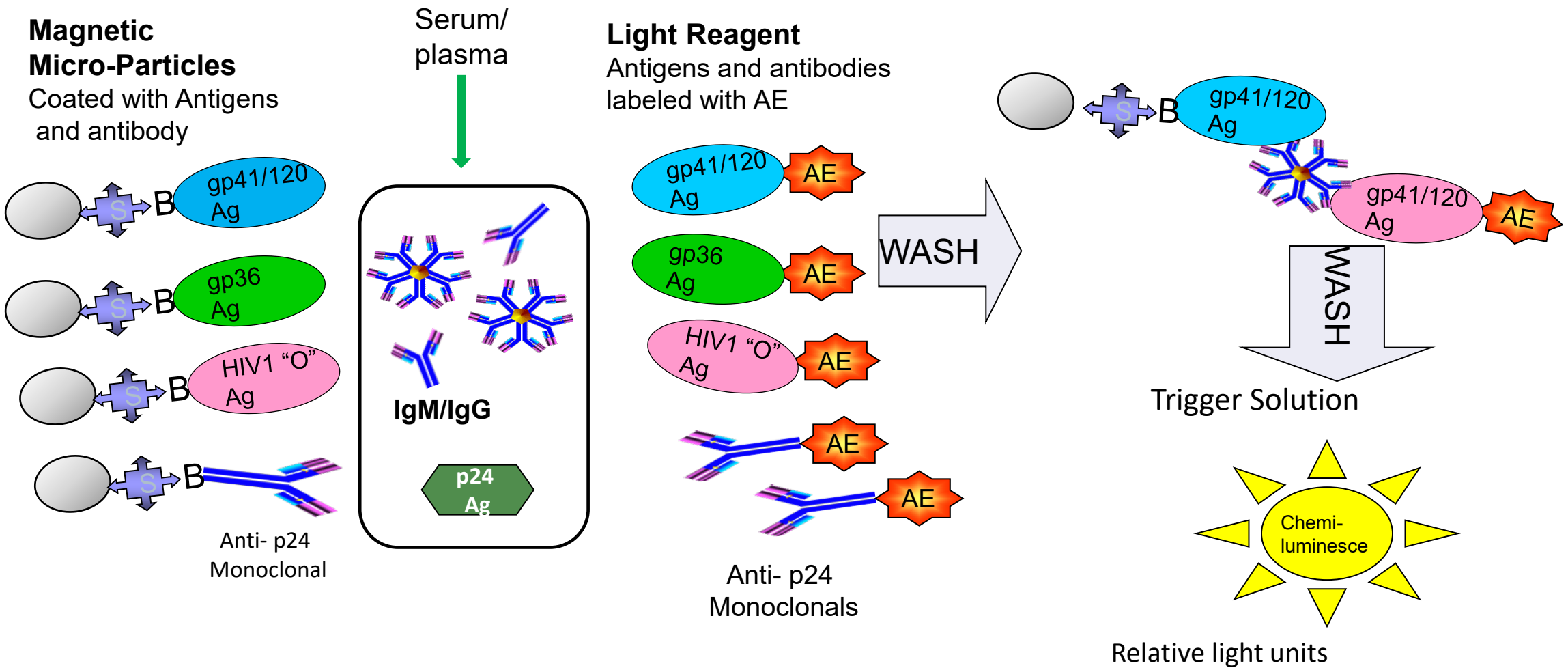
Bio-Rad Ag/Ab Combo EIA
2011

Siemens Advia Centaur® CHIV
2015

Elecsys HIV combi PT
July 2017

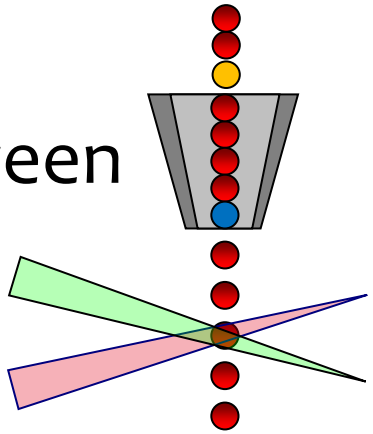
VITROS HIV combo
Dec 2017

Chemiluminescence Immunoassays



Multiplex Flow Immunoassay: Bioplex HIV Ag/Ab Combo

- Beads conjugated to HIV-1 Group M and O antigens, HIV-2 antigens, and p24 antibody



- Distinguishes between
  - p24 antigen
  - HIV-1 antibodies
  - HIV-2 antibodies
  - HCV
  - RPR and Treponemal syphilis

2015

"Fifth Generation"

New terminology

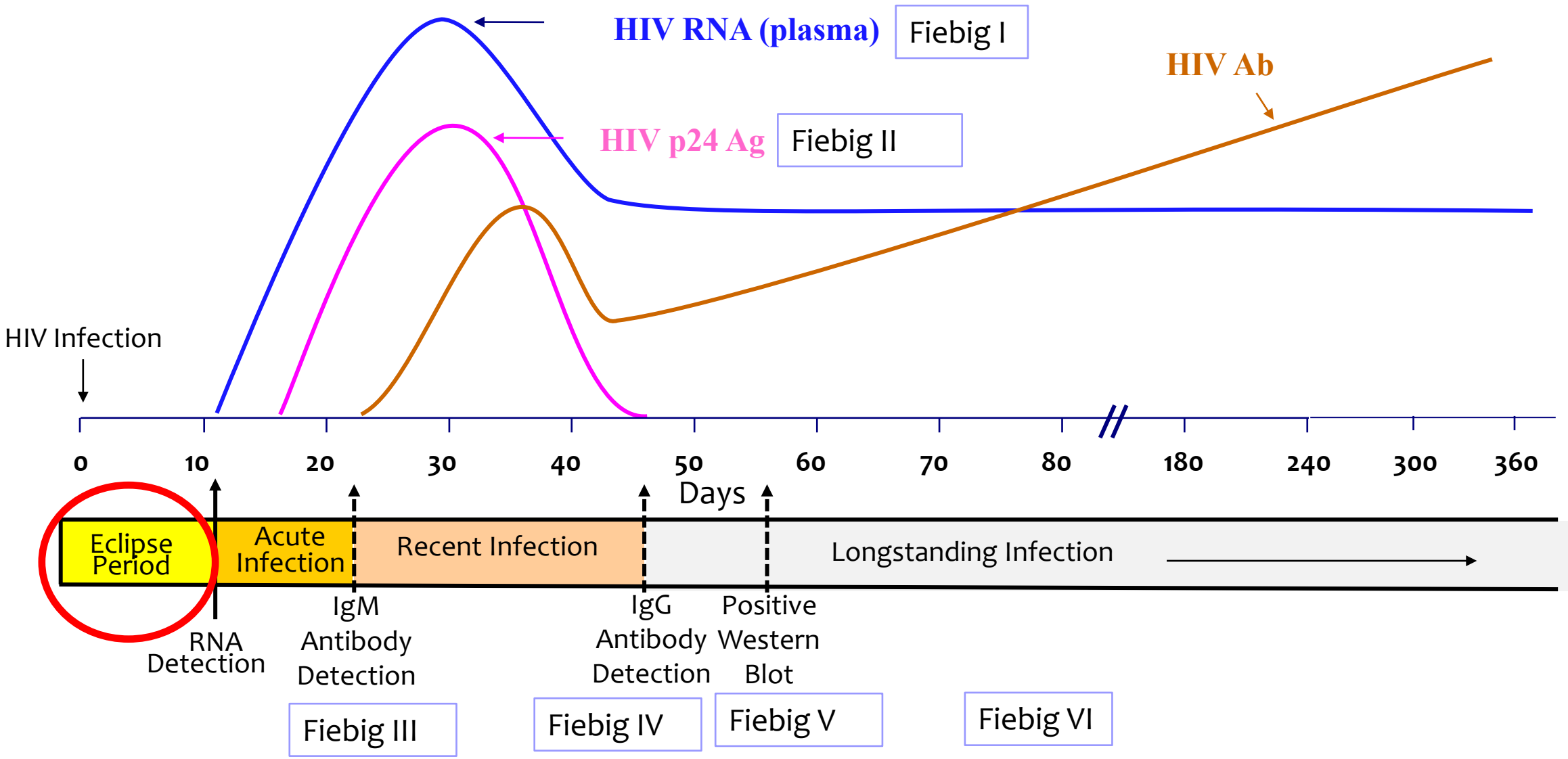
- Instrumented lab test
- Single-use rapid test

Antigens used by instruments to detect HIV-1

"3rd generation" instrumented antibody tests	
Bio-Rad GS HIV-1/2 Plus O	p24, gp160
Ortho Vitros Anti-HIV 1+2	p24, gp41, gp41/120
Siemens Advia Centaur HIV 1/O/2	p24, gp41/120
"4th generation" instrumented Ag/Ab combo tests	
Abbott Architect HIV Ag/Ab Combo	gp41
Bioplex 2200 HIV Ag-Ab	gp160
Bio-Rad GS HIV Combo Ag/Ab	gp41, gp160
Ortho Vitros combi	gp41, gp41/120
Siemens Advia	gp41/120
Roche Elecsys	gp41, RT

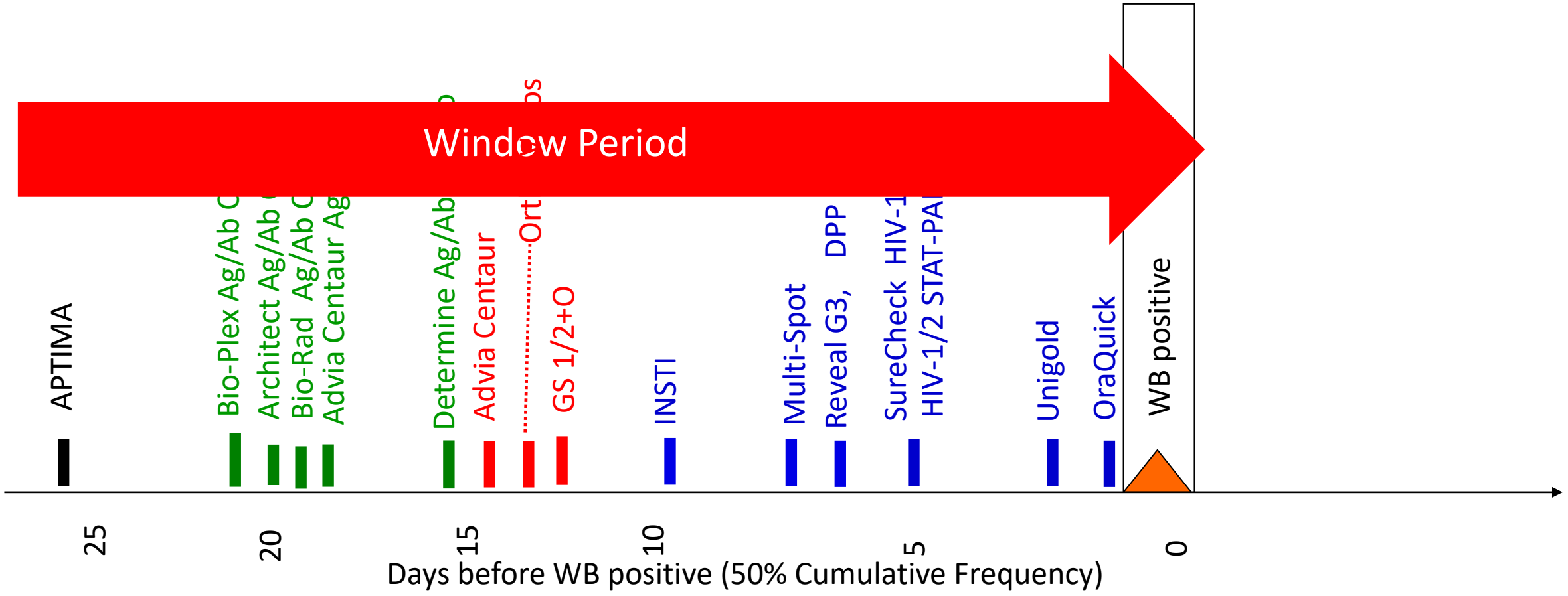
Just like single-use rapid tests

Timeline of Laboratory Markers



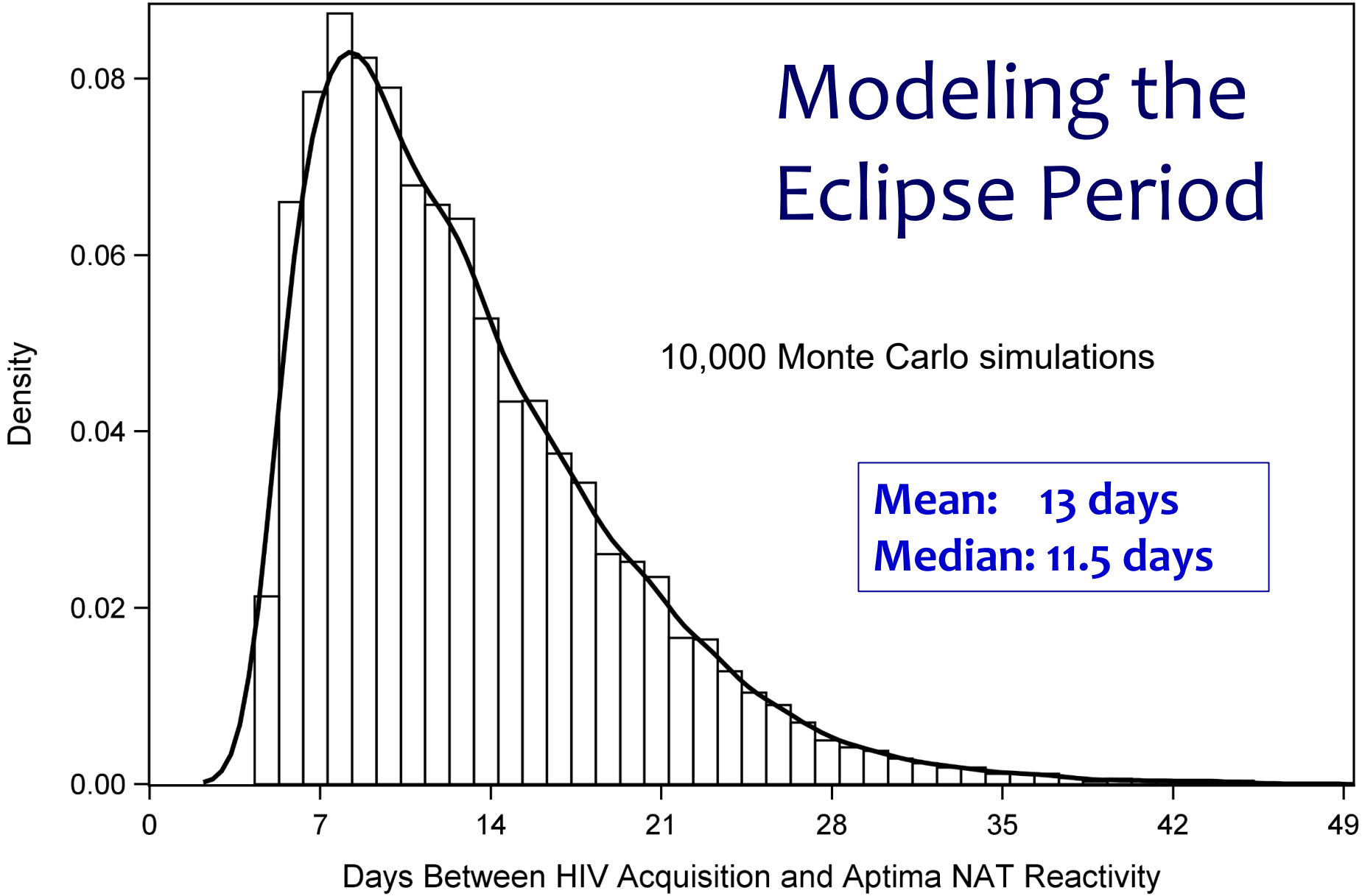
Sequence of Test Positivity Relative to WB (plasma)

166 specimens, 17 Seroconverters - 50 % Positive Cumulative Frequency



Delaney et al, Clin Inf Dis 2017

Modeling the Eclipse Period



10,000 Monte Carlo simulations

Mean: 13 days
Median: 11.5 days

Delaney et al, Clin Inf Dis 2017

Estimated Window Periods of Available HIV Tests - Plasma

When can I be sure?

Category (No. of Tests)	Median Days (Interquartile Range)	99th Percentile (Days)
Antibody/antigen instrumented (4)	17.8 (13.0, 23.6)	**44.3**
IgG/IgM-sensitive instgrumented (3)	23.1 (18.4, 28.8)	**49.5**
IgG-sensitive single-use rapid (6)	31.1 (26.2, 37.0)	**56.7**
IgG-sensitive supplemental (2)	33.4 (28.5, 39.2)	**58.2**
Western blot (viral lysate) (1)	**36.5 (31.0, 43.2)**	**64.8**

Delaney et al CID, 2017

ART is being initiated earlier and earlier, sometimes during Acute HIV Infection

The Effect of Same-Day Observed Initiation of Antiretroviral Therapy on HIV Viral Load and Treatment Outcomes in a US Public Health Setting

Christopher D. Pilcher, MD, Clarissa Ospina-Norvell, FN-P,* Aditi Dasgupta, BS,† Diane Jones, RN,* Wendy Hartogensis, PhD,* Sandra Torres, MSW,* Fabiola Calderon, MSW,* Erin Demicco, MPH,* Elvin Geng, MD,* Monica Gandhi, MD,* Diane V. Havlir, MD,* and Hiroyu Hatano, MD**

(*J Acquir Immune Defic Syndr* 2017;74:44–51)

RAPID COMMUNICATION

High Feasibility of Empiric HIV Treatment for Patients With Suspected Acute HIV in an Emergency Department

Kathleen R. Jacobson, MD, Sanjay Arora, MD, Kristin B. Walsh, MD, Meredith Lora, MD, Stephen Merjavy, MD, Shanna Livermore, MPH, and Michael Menchine, MD, MPH

(*J Acquir Immune Defic Syndr* 2016;72:242–245)

Clinical Infectious Diseases

MAJOR ARTICLE

HIV/AIDS

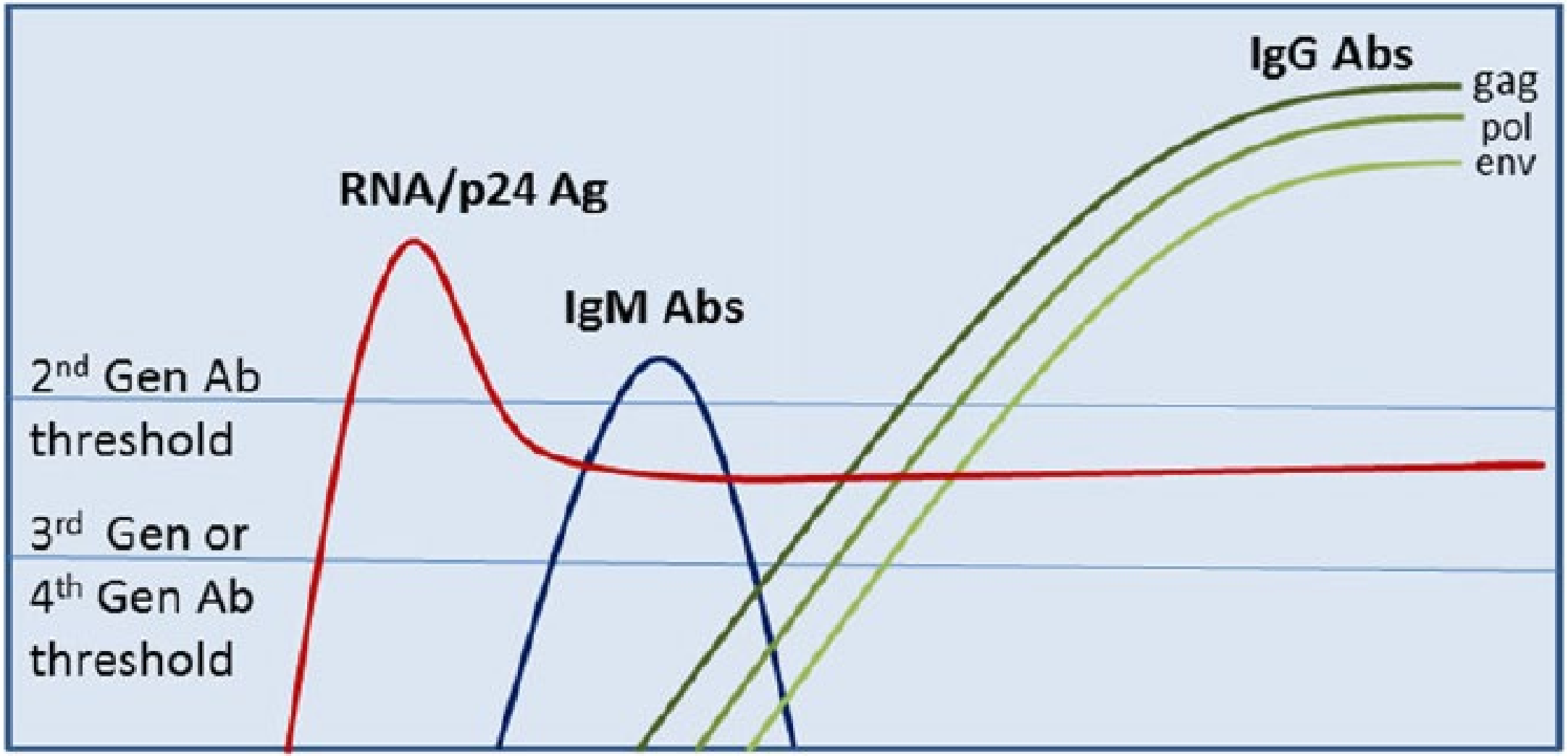
Initiation of Antiretroviral Therapy During Acute HIV-1 Infection Leads to a High Rate of Nonreactive HIV Serology

Mark S. de Souza,[1,2,3] Suteeraporn Pinyakorn,[4,5] Siriwat Akapirat,[6] Supanit Pattanachaiwit,[2] James L. K. Fletcher,[1] Nitiya Chomchey,[1] Eugene D. Kroon,[1,2] Sasiwimol Ubolyam,[7] Nelson L. Michael,[5,8] Merlin L. Robb,[4,5] Praphan Phanuphak,[1,2] Jerome H. Kim,[9] Nittaya Phanuphak,[1,2] and Jintanat Ananworanich[1,4,5], for the RV254/SEARCH010 Study Group

Clinical Infectious Diseases® 2016;63(4):555–61

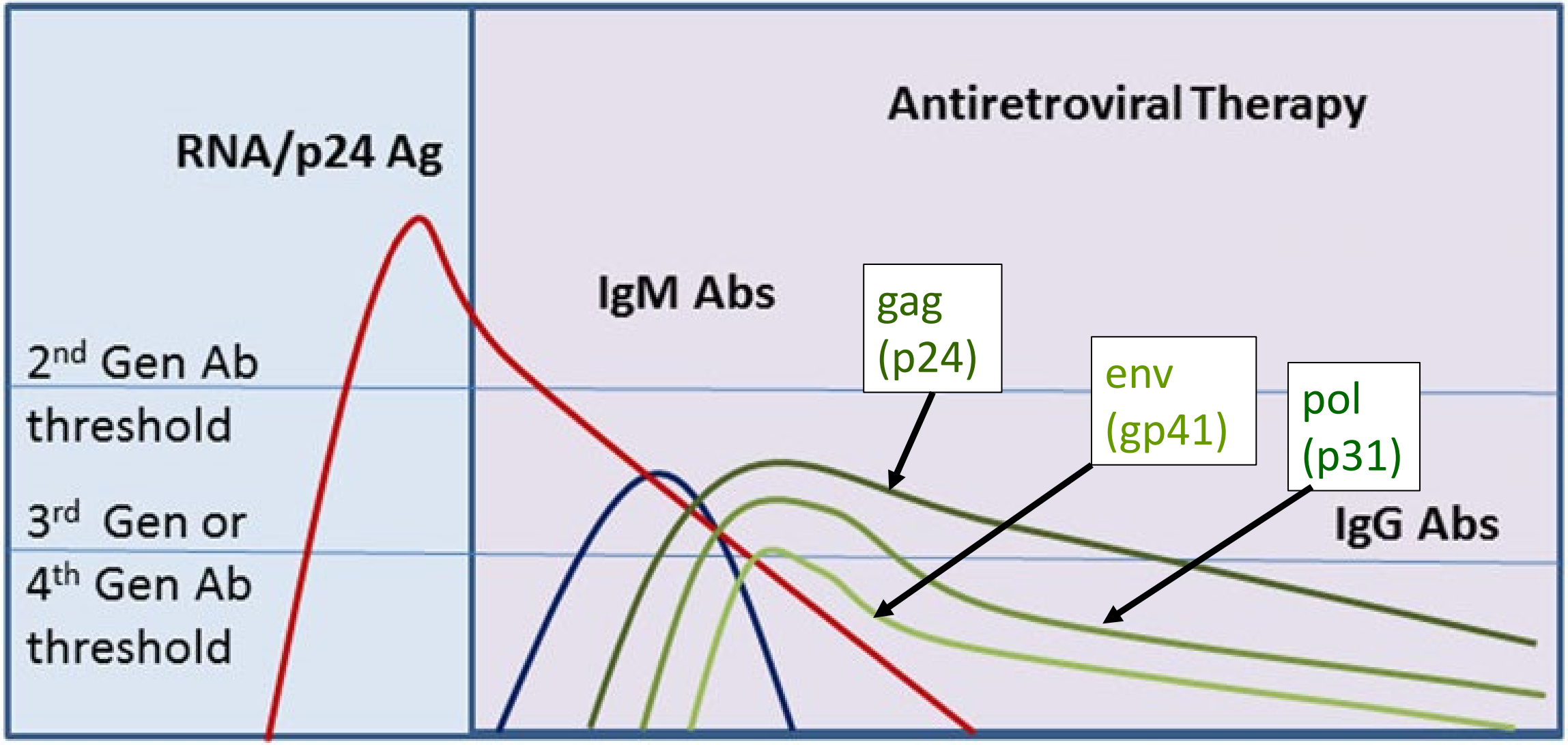
- 234 patients enrolled in AHI study Bangkok, Thailand
  - 41 Fiebig I (NAT+ / Ag- / IgM-, IgG-, WB-)
  - 72 Fiebig II (NAT+/ Ag+/ IgM-, IgG-, WB-)
  - 92 Fiebig III (NAT+/ Ag+/ IgM+, IgG-, WB-)
  - 19 Fiebig IV (NAT+/ Ag+/ IgM+, IgG-, WB ind)
  - 10 Fiebig V (NAT+/ Ag+, IgM+, IgG+, WB+ without p31)

Antibody Response to HIV (without treatment)



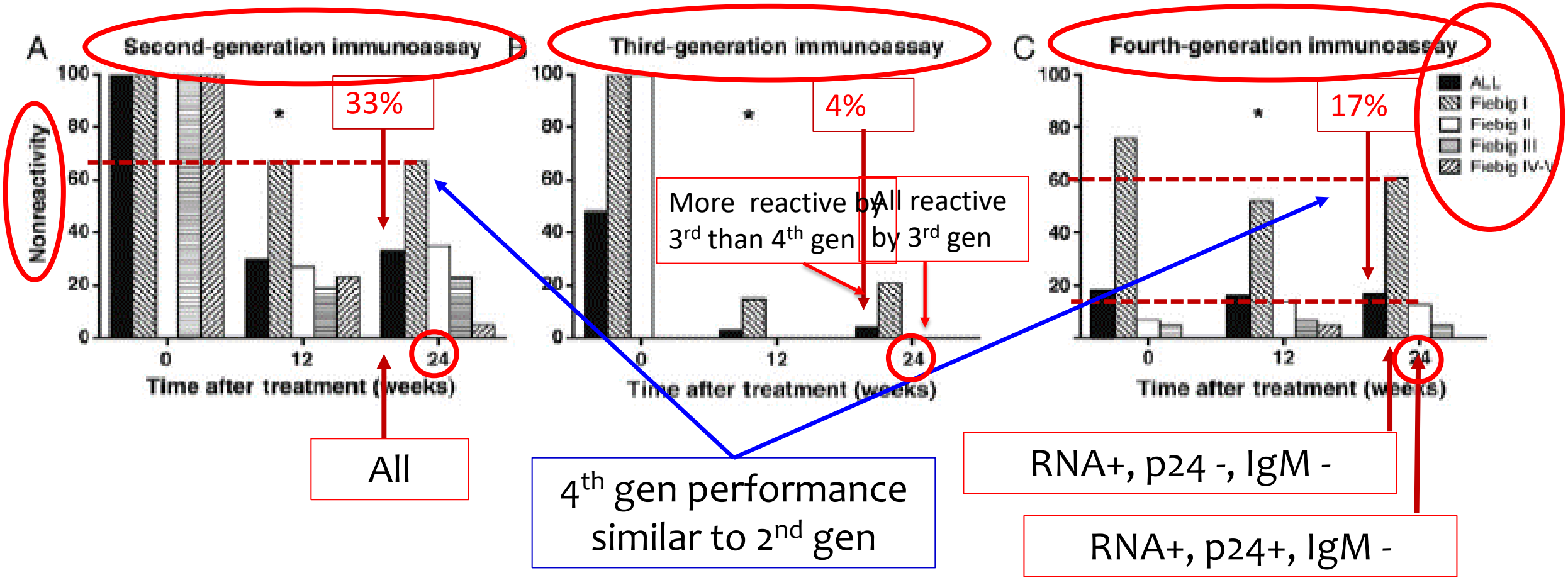
- Keating et al CID, 2016

Effect of ART during Acute HIV



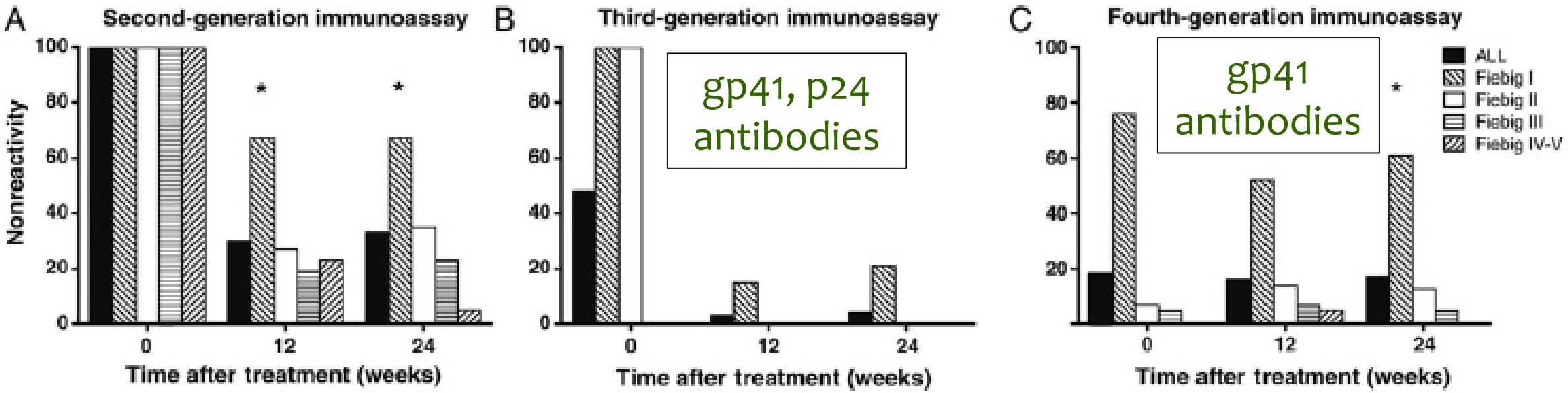
- Keating et al CID, 2016

Initiation of ART During Acute HIV Infection Leads to a High Rate of Nonreactive HIV Serology

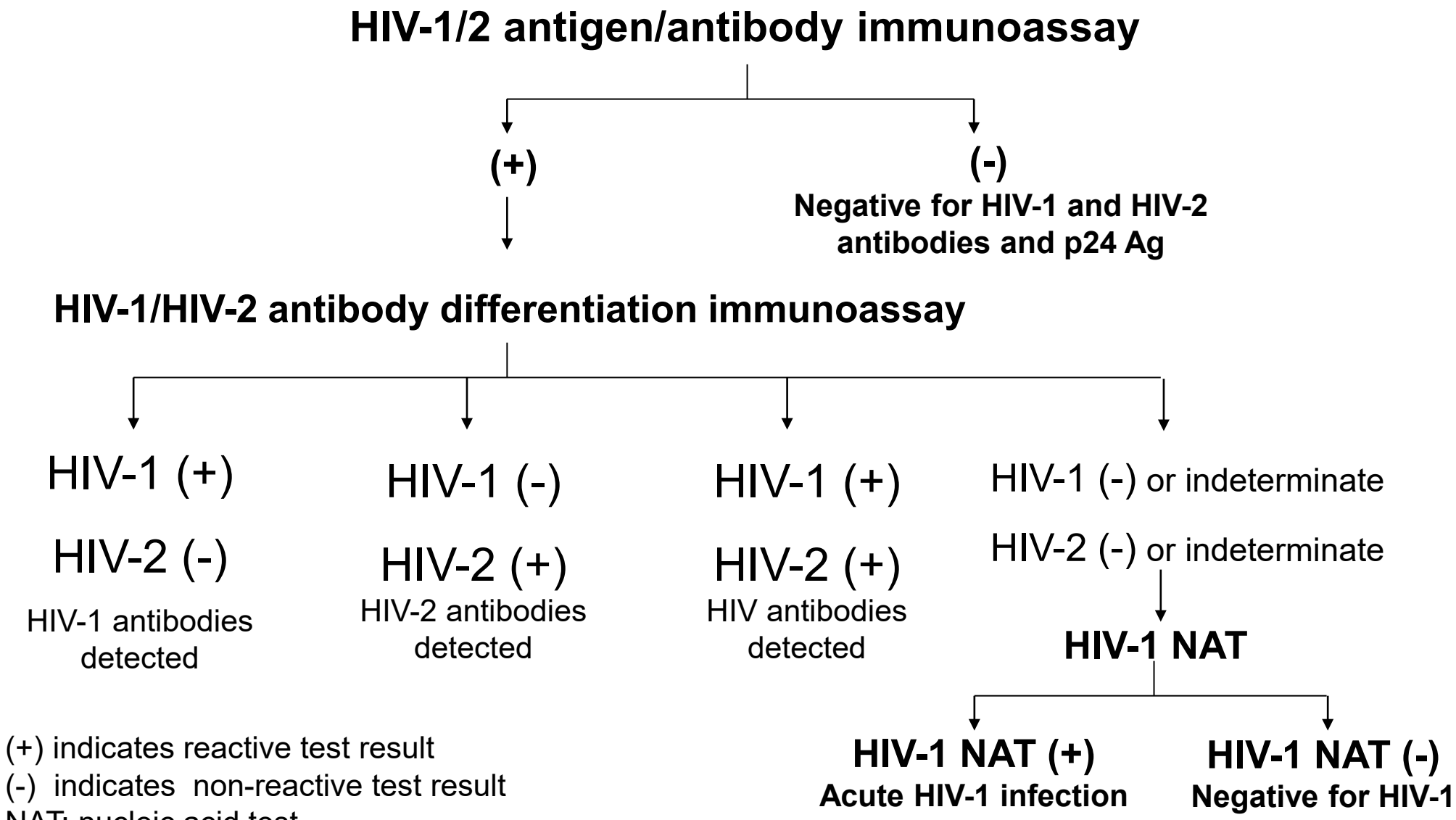


De Souza et al CID, 2016

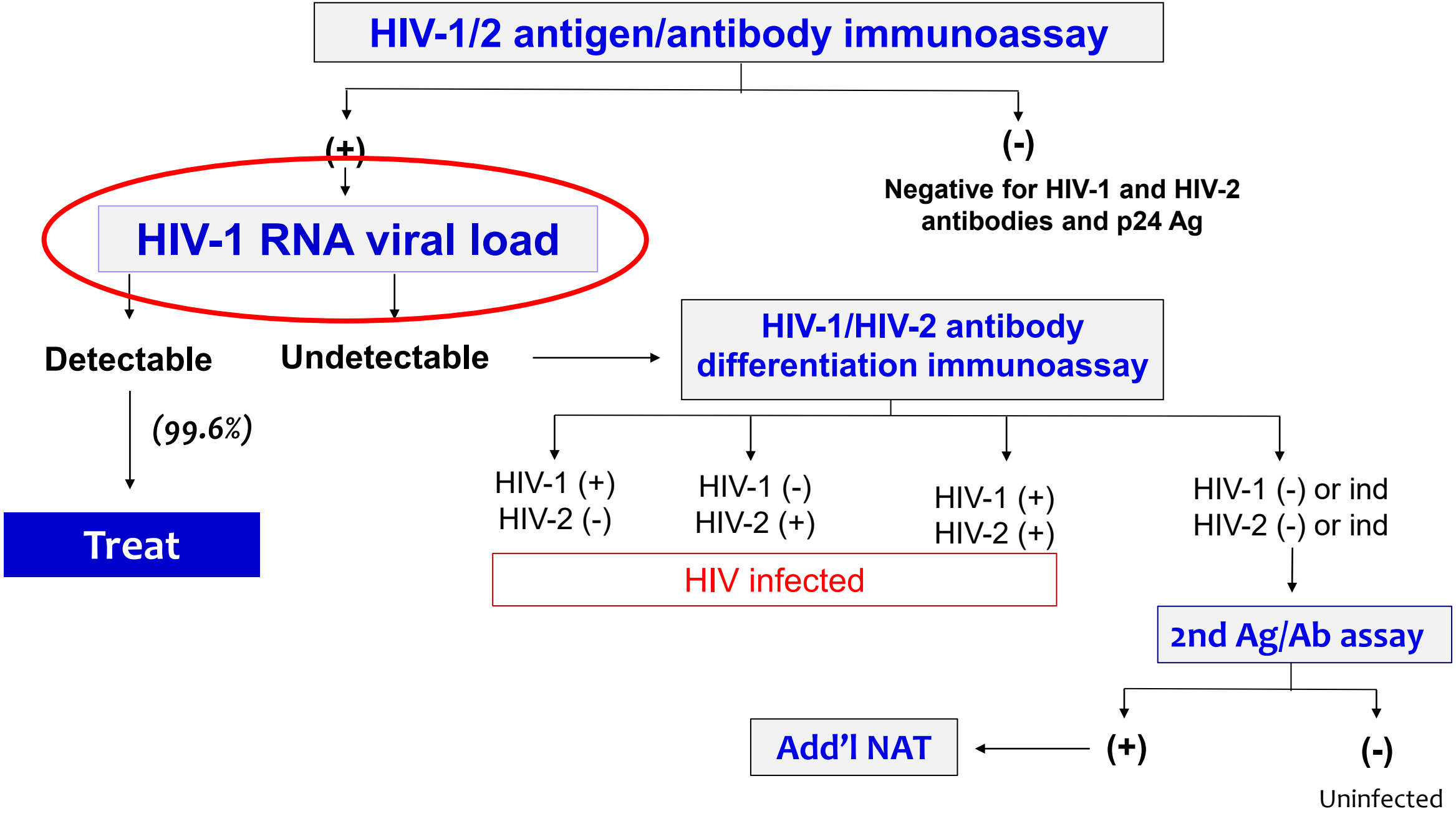
Antigens in 3rd gen and 4th gen antibody assays differ




On the Horizon…



(+) indicates reactive test result
(-) indicates non-reactive test result
NAT: nucleic acid test


HIV-1/2 antigen/antibody immunoassay
(+)
(-)
Negative for HIV-1 and HIV-2 antibodies and p24 Ag
HIV-1 RNA viral load
Detectable
Undetectable
(99.6%)
Treat
HIV-1/HIV-2 antibody differentiation immunoassay
HIV-1 (+) HIV-2 (-)
HIV-1 (-) HIV-2 (+)
HIV-1 (+) HIV-2 (+)
HIV infected
HIV-1 (-) or ind HIV-2 (-) or ind
2nd Ag/Ab assay
Add'l NAT
(+)
(-)
Uninfected

“Point-of-Care” Nucleic Acid Tests

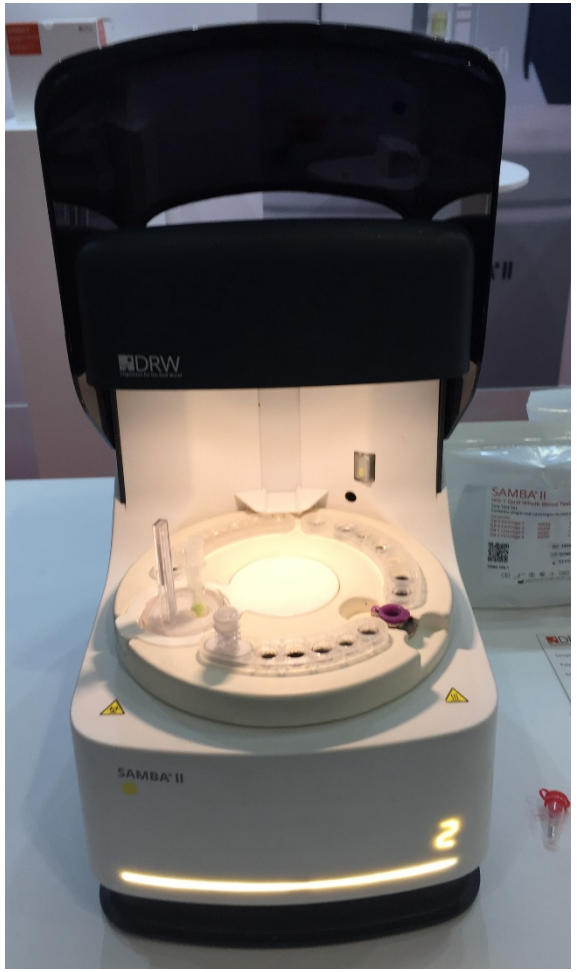
GeneXpert

- Xpert HIV-1 viral load
  - 1 ml plasma
  - Results in 90 minutes
  - LOD 32 copies/mL
  - CE-marked December 2014

Not yet available in U.S.

“Point-of-Care” Nucleic Acid Tests

m-PIMA



SAMBA II

Summary

- HIV tests differ in subtle ways that affect their performance in different circumstances
- RNA & viral load will play an increasingly important role in HIV diagnosis
- Early treatment (and PrEP) can lead to non-reactive serology and undetectable RNA
  - New techniques (such as whole blood total nucleic acid) are needed.