

Evaluation of newly approved HIV Antigen-Antibody tests individually and when used in the CDC/APHL HIV diagnostic algorithm

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The views expressed in this presentation are those of the authors and do not necessarily represent those of the Centers for Disease Control and Prevention

Background

- Since the publication of the updated laboratory algorithm in June 2014 several new HIV tests have been approved by the FDA

“New” Tests included in this evaluation



Abbott Architect HIV Ag/Ab Combo



Bio-Rad GS HIV Combo Ag/Ab EIA



ADVIA Centaur
HIV Ag/Ab Combo (CHIV)



Determine HIV-1/2 Ag/Ab Combo

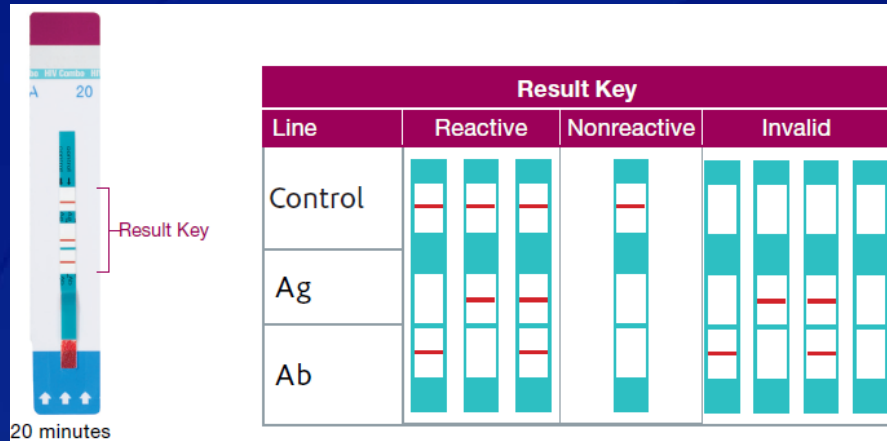


BioPlex®2200 HIV Ag-Ab



Genius™ HIV 1/2 Supplemental Assay

Tests included in this evaluation that create questions for the 2014 algorithm



Determine HIV-1/2 Ag/Ab Combo



BioPlex®2200 HIV Ag-Ab

These two tests give a separate report for Ag reactivity

Tests included in this evaluation that create questions for the 2014 algorithm

Image

Interpretation

Interpretation type: Automatic

Band analysis:

| # | Name | Result | Expected | Compare |
|---|-------|---------|----------|---------|
| 1 | gp36 | Present | Present | ✓ |
| 2 | gp140 | Present | Present | ✓ |
| 3 | p31 | Present | Present | ✓ |
| 4 | gp160 | Present | Present | ✓ |
| 5 | p24 | Present | Present | ✓ |
| 6 | gp41 | Present | Present | ✓ |
| 7 | CTRL | Present | Present | ✓ |

Geenius™ HIV 1/2 Supplemental Assay

Geenius yields a lot more results to consider

| HIV- | HIV Indeterminate | | HIV Positive | |
|-----------------|-------------------|-----------------------------|--------------|--------|
| HIV Negative | HIV-1 Ind | HIV Positive, Untypeable | HIV-2+ | HIV-1+ |

Tests included in this evaluation that create questions for the 2014 algorithm

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| HIV Negative | HIV Ind | HIV-2 Ind | HIV-1 Ind | HIV Positive, Untypeable | HIV-2 Positive with HIV-1 cross-reactivity | HIV-2+ | HIV-1+ |

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| | | | | | | |
|-------------------------|---------------------------------|--------------|--------------|-----------------------------|--|---------------|
| HIV- HIV Negative | HIV Indeterminate HIV Ind | HIV-2 Ind | HIV-1 Ind | HIV Positive, Untypeable | HIV Positive HIV-2 Positive with HIV-1 cross-reactivity | HIV-2+ HIV-1+ |
|-------------------------|---------------------------------|--------------|--------------|-----------------------------|--|---------------|

Tests included in this evaluation that create questions for the 2014 algorithm

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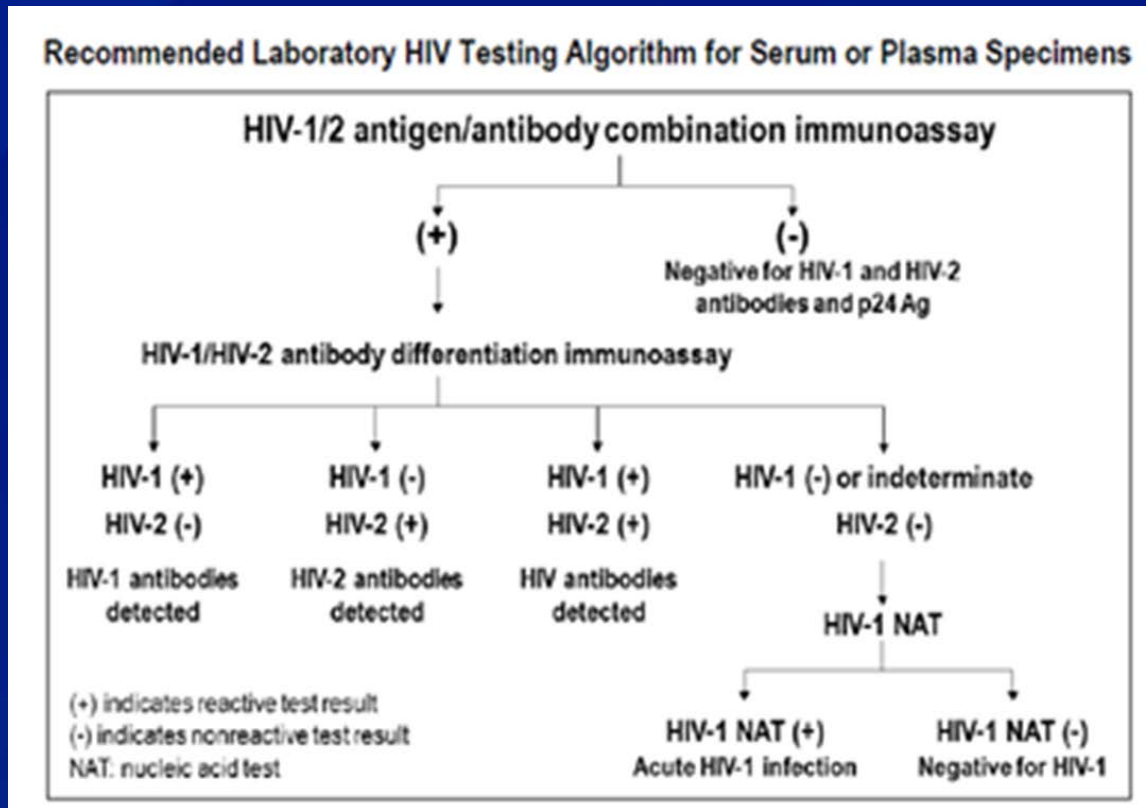
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Objectives

- ❑ Evaluate the performance of the newest HIV tests
 - Individually
 - In the algorithm recommended for Laboratory testing for the Diagnosis of HIV Infection



Description of specimens included in this evaluation



Current Study

- > 6000 specimens were collected from mostly MSM attending STD clinics in Los Angeles, CA from 2003-2005
- Tested with 6 rapid tests, (including Multispot) BioRad 1/2/O (3rd gen), WB and Aptima
- In 2010-2011, tested with Vitros HIV-1/2/0, Siemens Advia HIV-1/2/0, Abbott 3a77 (all 3rd Gen) and Abbott Ag/AB Combo (4th gen)
- 644 EIA/WB Positive
- 15 WB neg/IND, Aptima positive (Acute)
- 988 WB and Aptima negative;
 - 211 False-positive on at least one test

Analysis

□ Individual tests

■ Sensitivity

- Acute infection specimens (n=15 WB neg/IND, APTIMA Pos)
- Treated known HIV-positive specimens (n=370)
- Untreated positive (newly and previously identified, n=274)

■ Specificity

- 988 HIV WB and APTIMA negative specimens

Analysis

❑ Algorithm performance

- Specimens with reactive results on each screening test followed through the algorithm with both Multispot (MS) and Geenius
- If MS or Geenius negative or indeterminate, APTIMA result is the gold standard
- The N for these analyses changes depending on the screening test used, and availability of MS results:
 - 165 Western blot and APTIMA Negative with a false-reactive result on ANY laboratory screening test
 - 42 on a 4th gen screening test
 - 659 total HIV+ specimens (including 15 acutes)
 - 333 with results for both Geenius and MS

Summary of screening test performance

| Test | Sensitivity for Acute infection | Sensitivity for Treated infection | Sensitivity for Untreated infection | Specificity |
|-----------------------|---------------------------------|-----------------------------------|-------------------------------------|------------------------|
| Abbott Architect | 53% (27-79) | 100.0% (99.0-100) | 100.0% (98.7-100) | 98.3% (97.3-99.0) |
| BioRad AG/ AB Combo | 60% (32-84) | 100.0% (99.0-100) | 100.0% (98.7-100) | 98.9% (98.0 – 99.4) |
| BioPlex | 60% (32-84) | 100.0% (99.0-100) | 100.0% (98.7-100) | 98.6% (97.6 – 99.2) |
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Adjusted Specificity 99.3%

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- All (n=14) BioPlex false-reactive specimens were reactive for HIV-1 AB only; of 10 Determine false-positives 1 was AG-only, 2 were AG/AB

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- ❑ All (n=14) BioPlex false-reactive specimens were reactive for HIV-1 AB only; of 10 Determine false-positives 1 was AG-only, 2 were AG/AB
 - ❑ None of the 1700+ specimens tested on Bioplex were reactive for HIV-2

Sensitivity for acute infection was similar for 4th gens, and all were better than 3rd gen

- 11 specimens had results on all 3rd and 4th Gen tests

| ID | Abbott 3a77 | Vitros | Advia | BioRad 3rd | APTIM A | Roche VL 1.5 | Abbott 4th | Stem -ens 4th | Det AG | Det AB | Bio-Rad 4th | BioPl ex HIV1 | BioPle x Ag | Biople x HIV-2 |
|----|-------------|--------|-------|------------|---------|--------------|------------|---------------|---------------------|---------------------|-------------|---------------|-------------|----------------|
| 1 | N | N | N | N | P | missing | 0.18 | 0.17 | Ag Neg | Ab Neg | 0.21 | 0.03 | 0.05 | 0.03 |
| 2 | N | N | N | N | P | missing | 0.07 | 0.07 | Ag Neg | Ab Neg | 0.17 | 0.05 | 0.07 | 0.04 |
| 3 | N | N | N | N | P | 2,140 | 0.18 | 0.28 | Ag Neg | Ab Neg | 0.26 | 0.05 | 0.46 | 0.05 |
| 4 | N | N | N | N | P | missing | 0.41 | 0 | Ag Neg | Ab Neg | 0.22 | 0.08 | 0.06 | 0.07 |
| 5 | N | 11.30 | 3.54 | P | P | 1e6 | 97.37 | 12 | Ag Pos | Ab neg | 13.36 | 0.22 | 40.79 | 0.06 |
| 6 | 0.22 | 4.42 | 2.09 | P | P | 1e6 | 65.10 | 12 | Ag Pos ^w | Ab pos ^w | 13.21 | 67.42 | 84.60 | 0.06 |
| 7 | 2.98 | 12.70 | 8.33 | P | P | 482,592 | 18.32 | 12 | Ag Pos ^w | Ab pos ^w | 11.35 | 7.36 | 39.06 | 0.06 |
| 8 | 1.54 | 5.16 | 1.85 | P | P | missing | 96.48 | 12 | Ag Pos | Ab Neg | 13.21 | 3.74 | 200 | 0.12 |
| 9 | N | N | N | N | P | 222,929 | 201.57 | 12 | Ag Pos | Ab Neg | 13.21 | 0.16 | 200 | 0.17 |
| 10 | N | N | N | N | P | 165,996 | 7.00 | 3.19 | Ag Neg | Ab Neg | 3.26 | 0.12 | 14.89 | 0.06 |
| 11 | N | N | N | N | P | 294 | 5.37 | 1.83 | Ag Neg | Ab Neg | 1.646 | 0.05 | 13.79 | 0.05 |

Sensitivity for acute infection was similar for 4th gens, and all were better than 3rd gen

- 4 of these specimens were negative on all tests

| ID | Abbott 3a77 | Vitros | Advia | BioRad 3rd | APTIMA | Roche VL 1.5 | Abbott 4th | Siemens 4th | Det AG | Det AB | Bio-Rad 4th | BioPlex HIV1 | BioPlex Ag | Bioplex HIV-2 |
|----|-------------|--------|-------|------------|--------|--------------|------------|-------------|-----------|-----------|-------------|--------------|------------|---------------|
| 1 | N | N | N | N | P | missing | 0.18 | 0.17 | Ag Neg | Ab Neg | 0.21 | 0.03 | 0.05 | 0.03 |
| 2 | N | N | N | N | P | missing | 0.07 | 0.07 | Ag Neg | Ab Neg | 0.17 | 0.05 | 0.07 | 0.04 |
| 3 | N | N | N | N | P | 2,140 | 0.18 | 0.28 | Ag Neg | Ab Neg | 0.26 | 0.05 | 0.46 | 0.05 |
| 4 | N | N | N | N | P | missing | 0.41 | 0 | Ag Neg | Ab Neg | 0.22 | 0.08 | 0.06 | 0.07 |

Sensitivity for acute infection was similar for 4th gens, and all were better than 3rd gen

- 4 were weakly antibody positive and picked up by almost all tests

| ID | Abbott 3a77 | Vitros | Advia | BioRad 3rd | APTIMA | Roche VL 1.5 | Abbott 4th | Siemens 4th | Det AG | Det AB | Bio-Rad 4th | BioPlex x HIV1 | BioPlex Ag | Bioplex HIV-2 |
|----|-------------|--------|-------|------------|--------|--------------|------------|-------------|---------------------|---------------------|-------------|----------------|------------|---------------|
| 5 | N | 11.30 | 3.54 | P | P | 1e6 | 97.37 | 12 | Ag Pos | Ab neg | 13.3 6 | 0.22 | 40.79 | 0.06 |
| 6 | 0.22 | 4.42 | 2.09 | P | P | 1e6 | 65.10 | 12 | Ag Pos ^w | Ab pos ^w | 13.2 1 | 67.4 2 | 84.60 | 0.06 |
| 7 | 2.98 | 12.70 | 8.33 | P | P | 482,592 | 18.32 | 12 | Ag Pos ^w | Ab pos ^w | 11.3 5 | 7.36 | 39.06 | 0.06 |
| 8 | 1.54 | 5.16 | 1.85 | P | P | missing | 96.48 | 12 | Ag Pos | Ab Neg | 13.2 1 | 3.74 | 200 | 0.12 |

Sensitivity for acute infection was similar for 4th gens, and all were better than 3rd gen

- 3 were only detected by the 4th gen tests
 - Determine missed 2 of these

| ID | Abbott 3a77 | Vitros | Advia | BioRad 3rd | APTIMA | Roche VL 1.5 | Abbott 4th | Siemens 4th | Det AG | Det AB | BioRad 4th | BioPlex HIV1 | BioPlex Ag | Bioplex HIV-2 |
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| 11 | N | N | N | N | P | 294 | 5.37 | 1.83 | Ag Neg | Ab Neg | 1.646 | 0.05 | 13.79 | 0.05 |

Geenius HIV-1/HIV-2 Differentiation Assay- Sensitivity Overall

- ❑ Geenius was HIV-negative on 14 of 15 Acute infection specimens
 - 1 specimen was HIV-2 Indeterminate
- ❑ Of 643 HIV Western blot positive specimens
 - 642 were HIV-1 positive
 - 2 were HIV+ untypeable
 - Both were positive for both HIV-1 and HIV-2 using MS but HIV-1 only at 1:10 dilution
 - 9 other specimens that had required the dilution protocol with MS were HIV-1 only positive on Geenius
 - 1 specimen was HIV-1 indeterminate (HIV-1+ using MS)

Geenius HIV-1/HIV-2 Differentiation Assay- Specificity Overall

- ❑ 165 Aptima negative specimens were reactive on at least one laboratory screening test
 - This includes specimens that were not repeatedly reactive
 - 149 were HIV-negative
 - 2 of these had some reactivity (only 1 spot) on MS
 - 2 were HIV-1 Indeterminate
 - 1 MSnegative, 1 MSHIV-1 IND (1 spot)
 - 13 were initially HIV-2 indeterminate
 - 2 were still HIV-2 indeterminate on repeat
 - 1 was HIV-1 positive
 - This specimen had been single-well reactive on Abbott 3a77 and Bio-Rad HIV-1/2/0, but not repeatedly reactive, therefore
- ❑ There were no false-positive algorithm results

Geenius HIV-1/HIV-2 Differentiation Assay- Specificity – After 4th Gen Screening

- ❑ 42 Aptima negative specimens were reactive on at least one 4th gen screening test and had results for both MS and Geenius
 - 37 were HIV negative
 - 1 of these had some reactivity (only 1 spot) on MS
 - 1 was HIV-1 Indeterminate
 - 4 were initially HIV-2 indeterminate
 - 1 was still HIV-2 indeterminate on repeat

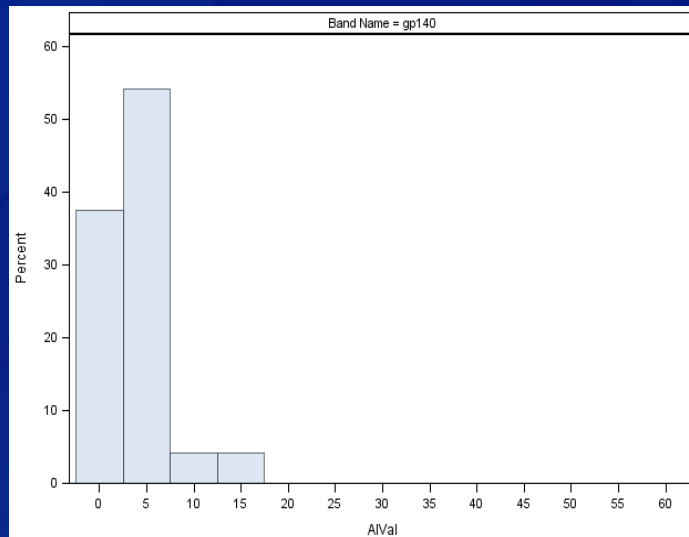
- ❑ There were no false-positive algorithm results

Geenius HIV-1/HIV-2 Differentiation Assay-Specificity – After 4th Gen Screening

- ❑ 42 Aptima negative specimens were reactive on at least one 4th gen screening test and had results for both MS and Geenius
 - 37 were HIV negative
 - 1 of these had some reactivity on MS
 - 1 was HIV-1 Indeterminate
 - 4 were initially HIV-2 indeterminate
 - 1 was still HIV-2 indeterminate on repeat
 - ❑ There were no false-positive algorithm results
-
- These would go on to HIV-1 NAT in the current algorithm
- Should these also go on to an HIV-1 NAT??

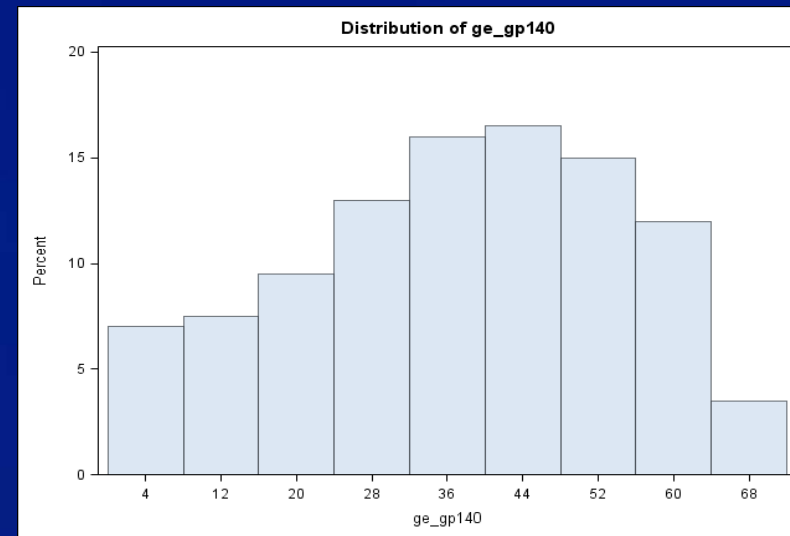
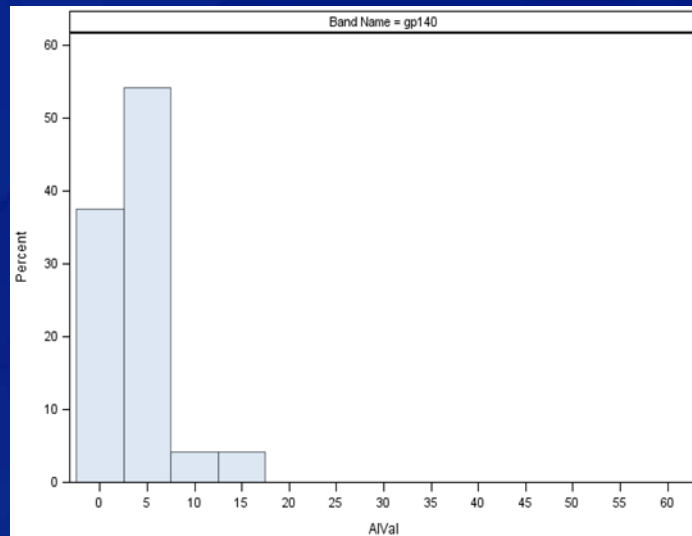
HIV-2 Indeterminate?

- ❑ All HIV-2 Indeterminate specimens (14 initially) showed reactivity only to the gp140 band
- ❑ All of these were weakly reactive for gp140
 - But this did include 1 early HIV-1 infection



HIV-2 Indeterminate?

- ❑ All HIV-2 Indeterminate specimens showed reactivity only to the gp140 band
- ❑ All of these were weakly reactive for gp140
- ❑ Most gp140 reactivity for true HIV-2 specimens was much stronger



Comparison between Geenius and MS

| Test | TP | FN | Sensitivity | TN | FP | Specificity |
|-----------|-----|----|------------------|----|----|------------------|
| Geenius | 328 | 5 | 98.5 (96.5-99.5) | 40 | 2 | 95.2 (83.8-99.4) |
| Multispot | 327 | 6 | 98.2 (96.1-99.3) | 40 | 2 | 95.2 (83.8-99.4) |

- Geenius and MS seem to have equivalent performance as the second test in a multi-test algorithm

Comparison between Geenius and MS

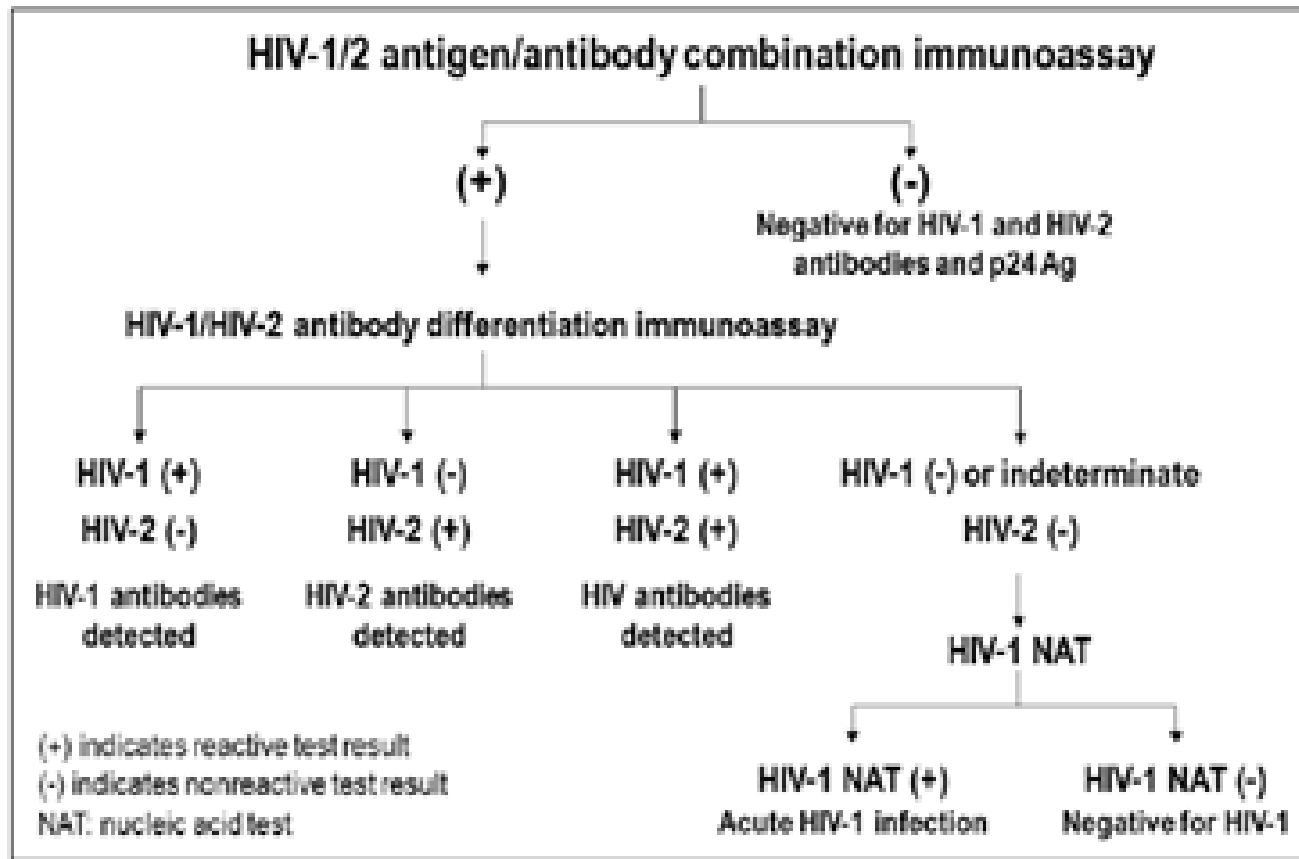
| Test | TP | FN | Sensitivity | TN ^a | FP | Specificity |
|-----------|-----|----|------------------|-----------------|----|------------------|
| Geenius | 328 | 5 | 98.5 (96.5-99.5) | 31 | 0 | 100 (90.8-100) |
| Multispot | 327 | 6 | 98.2 (96.1-99.3) | 30 | 1 | 96.8 (83.8-99.9) |
| Oraquick | 327 | 6 | 98.2 (96.1-99.3) | 31 | 0 | 100 (90.8-100) |
| Reveal G2 | 327 | 6 | 98.2 (96.1-99.3) | 31 | 0 | 100 (90.8-100) |
| Surecheck | 327 | 6 | 98.2 (96.1-99.3) | 31 | 0 | 100 (90.8-100) |
| StatPak | 326 | 7 | 97.9 (95.7-99.2) | 31 | 0 | 100 (90.8-100) |
| Unigold | 325 | 8 | 97.6 (95.3-99.0) | 31 | 0 | 100 (90.8-100) |

- ❑ But, so do all the other rapid tests

^a Only 31/42 4th gen false-reactive specimens had results for all rapid tests (all 11 missing StatPak results)

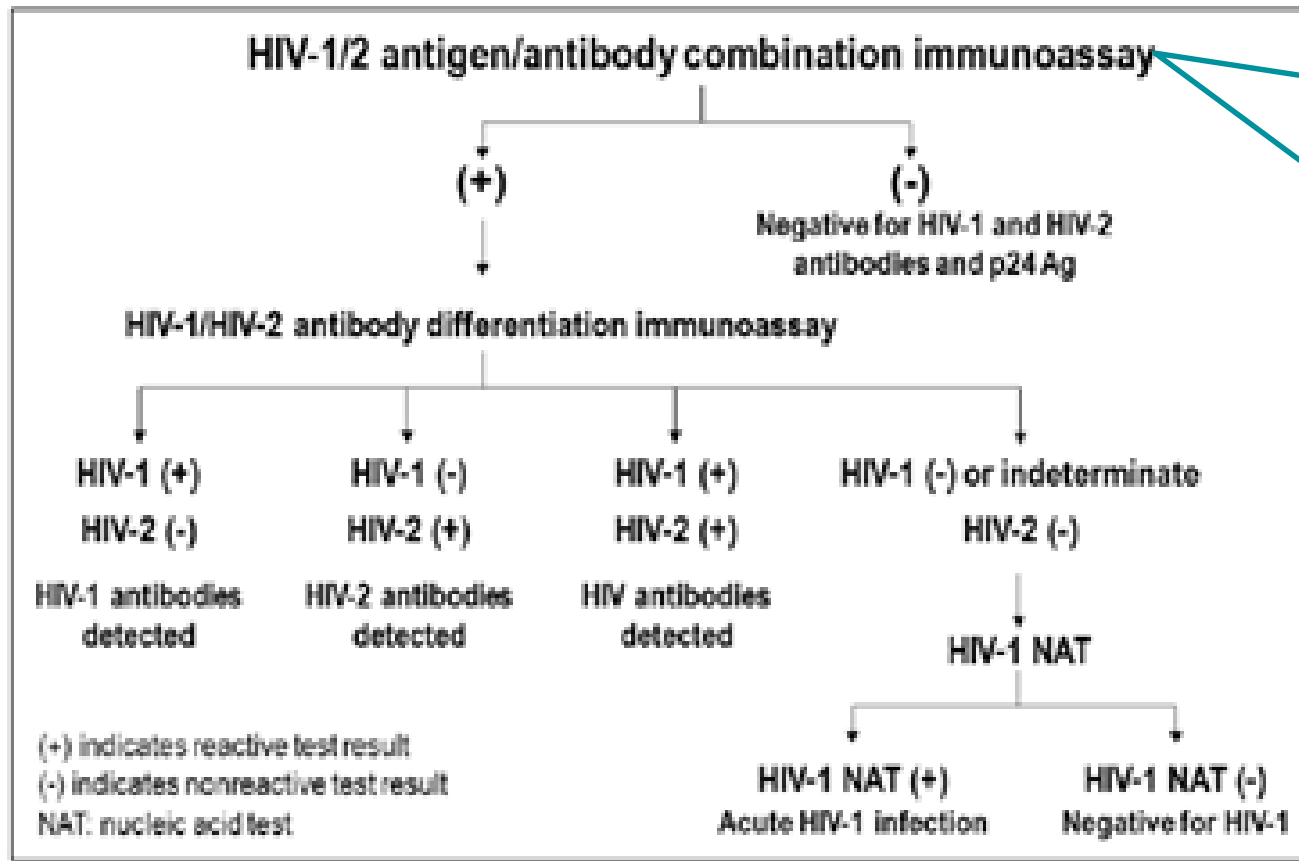
Implications for the Algorithm

Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens



Implications for the Algorithm

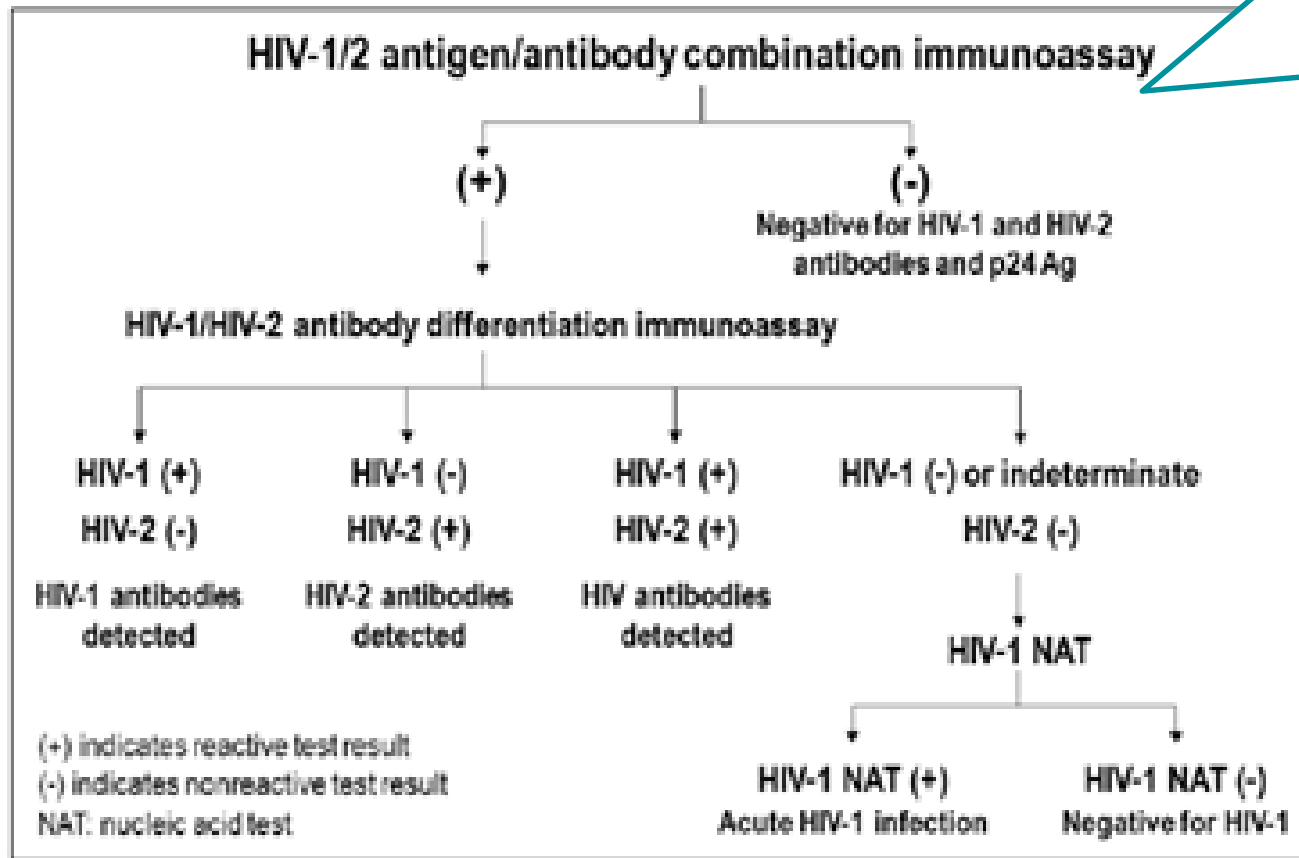
Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens



All of the lab-based Combos perform similarly for both established and acute infections

Implications for the Algorithm

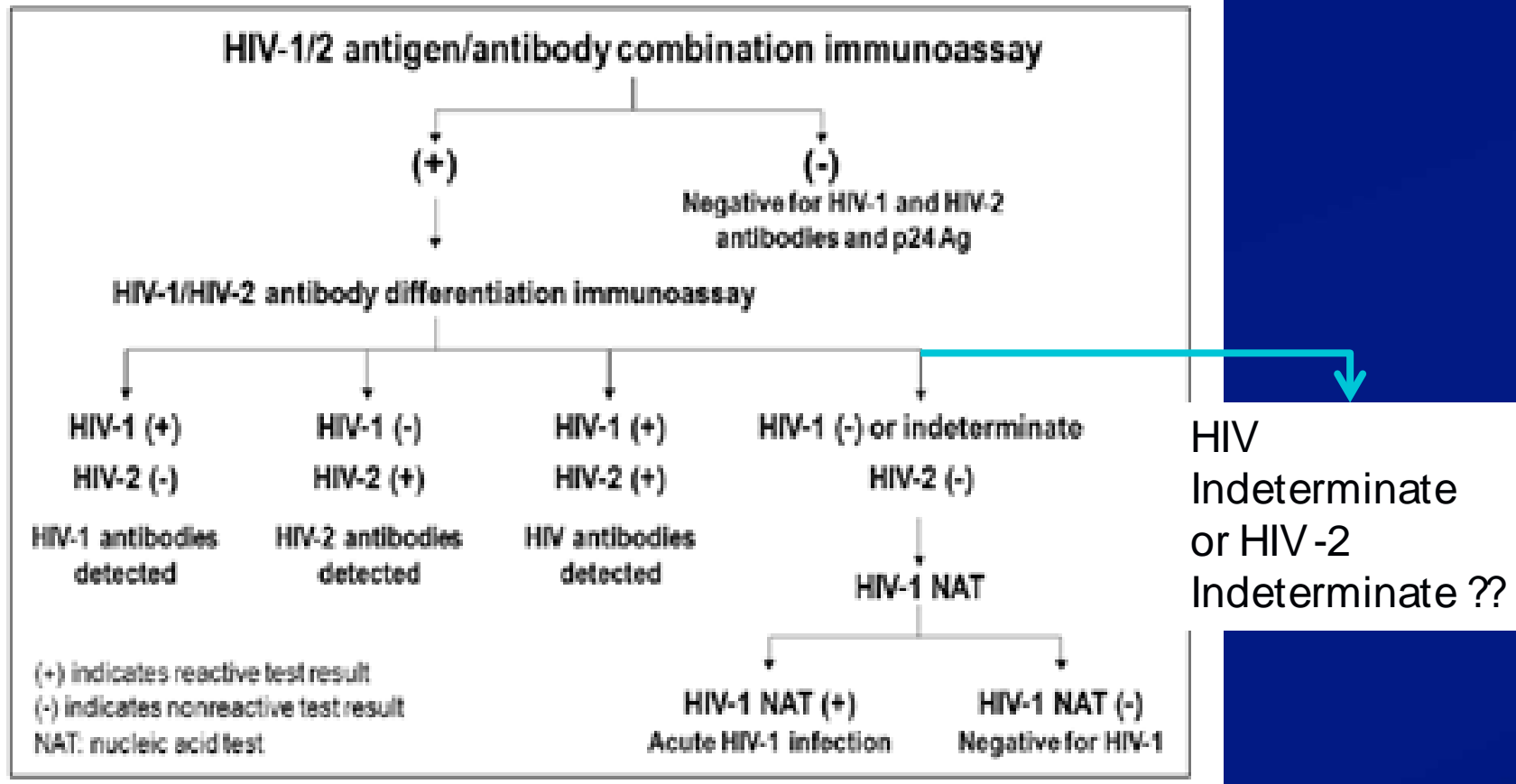
Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimen



While Determine may not be as sensitive as the lab-based Combo tests, it did pick up specimens missed by some AB only lab tests

Implications for the Algorithm

Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens



Thank You

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