HARVARD MEDICAL SCHOOL

The Clinical and Cost Implications of Using HIV RNA Instead of Antibody Testing to Confirm Reactive HIV Screening Tests in the United States

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March 29, 2022

Grant support: National Institutes of Health (K01HL123349, K08HD094638, R37DA015612, R01AI042006)
and the Jerome and Celia Reich HIV Scholar Award (EPH)

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MEDICAL PRACTICE EVALUATION CENTER

I have no relevant financial disclosures

Diagnosing HIV in the US

- Prompt diagnosis of HIV is crucial
  - Faster linkage to care can lead to earlier initiation of antiretroviral therapy (ART)
  - Early ART improves outcomes for persons with HIV and reduces the potential for new transmissions
- False positive HIV tests can induce stress
  - Goal is to reduce time to reassurance

Current Standard of Care (SOC)

HIV Diagnosis

1. Screen: 4th generation HIV p24 antigen + antibody (Ag/Ab)
2. If reactive, antibody differentiation assay (AbDiff)
3. If AbDiff is (-) or indeterminate: *qualitative* RNA (QL-RNA)

HIV Treatment

1. Baseline *quantitative* RNA (QT-RNA) on plasma specimen
2. ART initiation
3. Perform serial QT-RNA to monitor virologic response

HIV RNA Now Approved for Diagnosis

- FDA approved QT-RNA for diagnosis in Nov 2020
  - Plasma specimen:
    - Quantitative results are FDA-approved to be reported as a value
  - Serum specimen:
    - Quantitative results are FDA-approved to be reported as “detectable” or “undetectable”

Objective

To use simulation modeling to compare the clinical and cost implications of an HIV diagnostic algorithm with QT-RNA as the 2nd test, instead of AbDiff

Model Overview

- Diagnostic algorithms

1. Standard of Care (Ag/Ab -> AbDiff -> QL-RNA)
2. RNAplasma (Ag/Ab -> QT-RNA -> AbDiff)

Model Population

- All specimens tested for HIV
  - No HIV infection
  - With HIV infection
    - Chronic HIV-1
    - Acute HIV-1
    - Elite control of HIV-1
    - HIV-2

Model Outcomes

1. Time-based outcomes
   - Time to action
     - When clinicians initiate ART for people diagnosed with HIV or complete the diagnostic algorithm for specimen without HIV
   - Time to reassurance
     - When clinicians can inform a person with a false positive Ag/Ab of a negative RNA test (low likelihood of HIV diagnosis)
2. Visits for specimen collection (i.e., blood draws)
3. Testing cost

HIV Prevalence

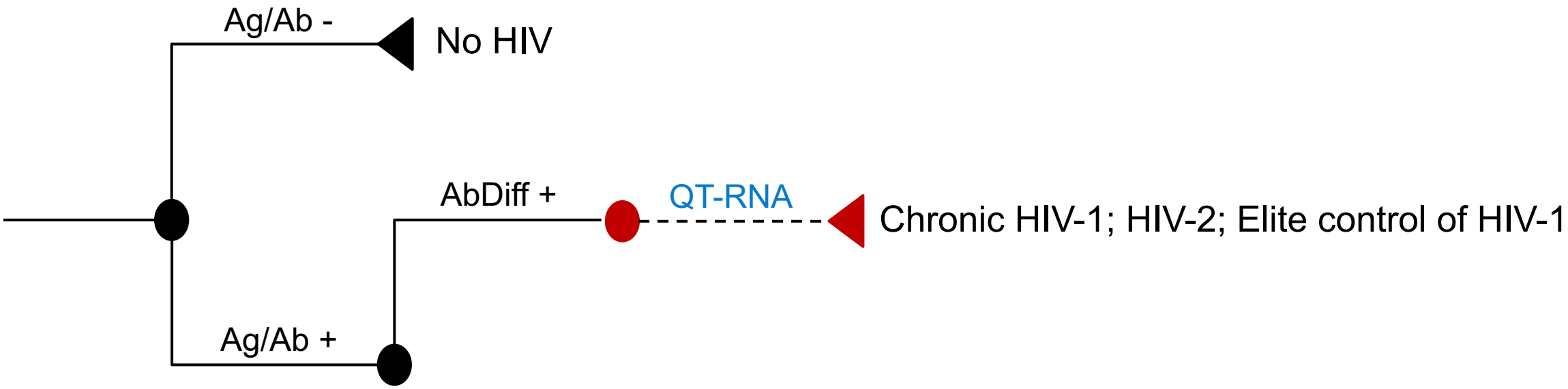
- We populated the model with data from three large US laboratory systems
  - Low: **0.25%** (75/30,000) (Personal Communication)
  - Moderate: **0.51%** (64,713/12,761,155) (Quest Diagnostics)
  - High: **1.98% (**973/49,181) (Personal Communication)

- We examined the algorithms in each setting

Additional Model Input Parameters

- Performance characteristics: from published package inserts
- Turnaround time (specimen collection -> result reported)
  - Reflex: performed on same specimen as a prior assay
    - AbDiff 12 hours, RNA 24 hours
  - Return: requires visit for specimen collection
    - Add 60h to reflex test time
- Cost: from CMS Laboratory Fee Schedule
  - AbDiff $13.71, QL-RNA $35.09, QT-RNA $85.10

SOC

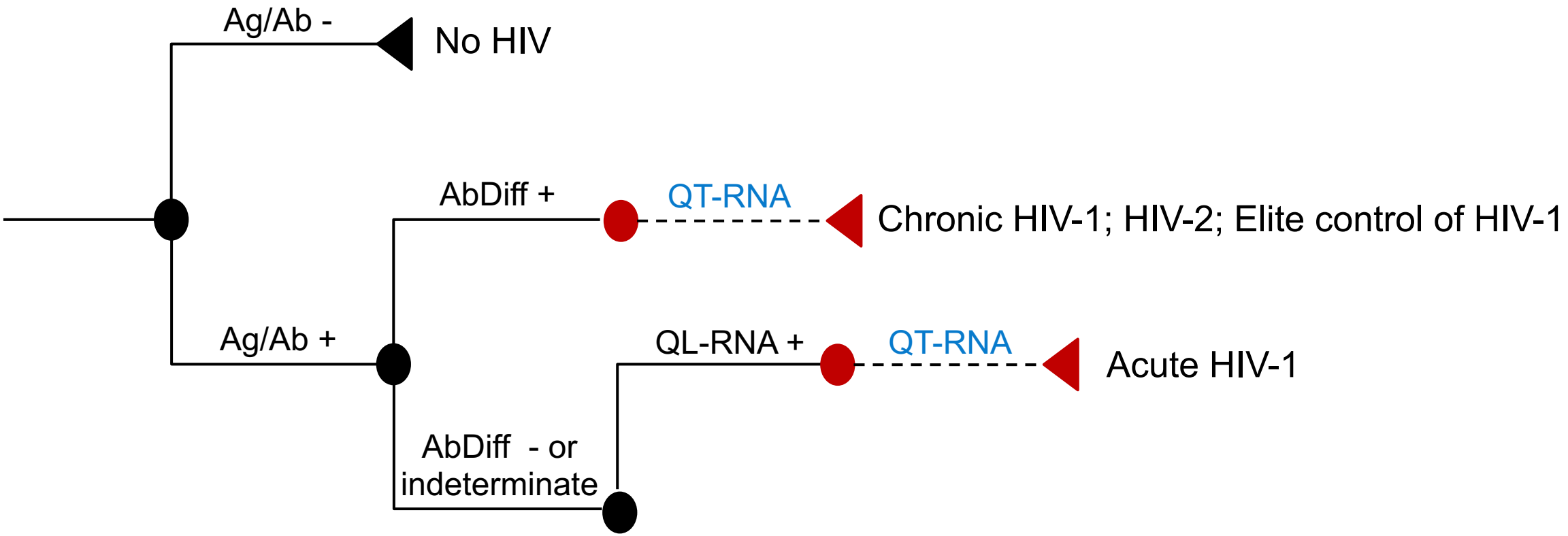


Key
Serum specimen – black
Plasma specimen – blue

Diagnosed without HIV -- black
Diagnosed with HIV -- red

———— dx algorithm
- - - - - - - tx algorithm

SOC



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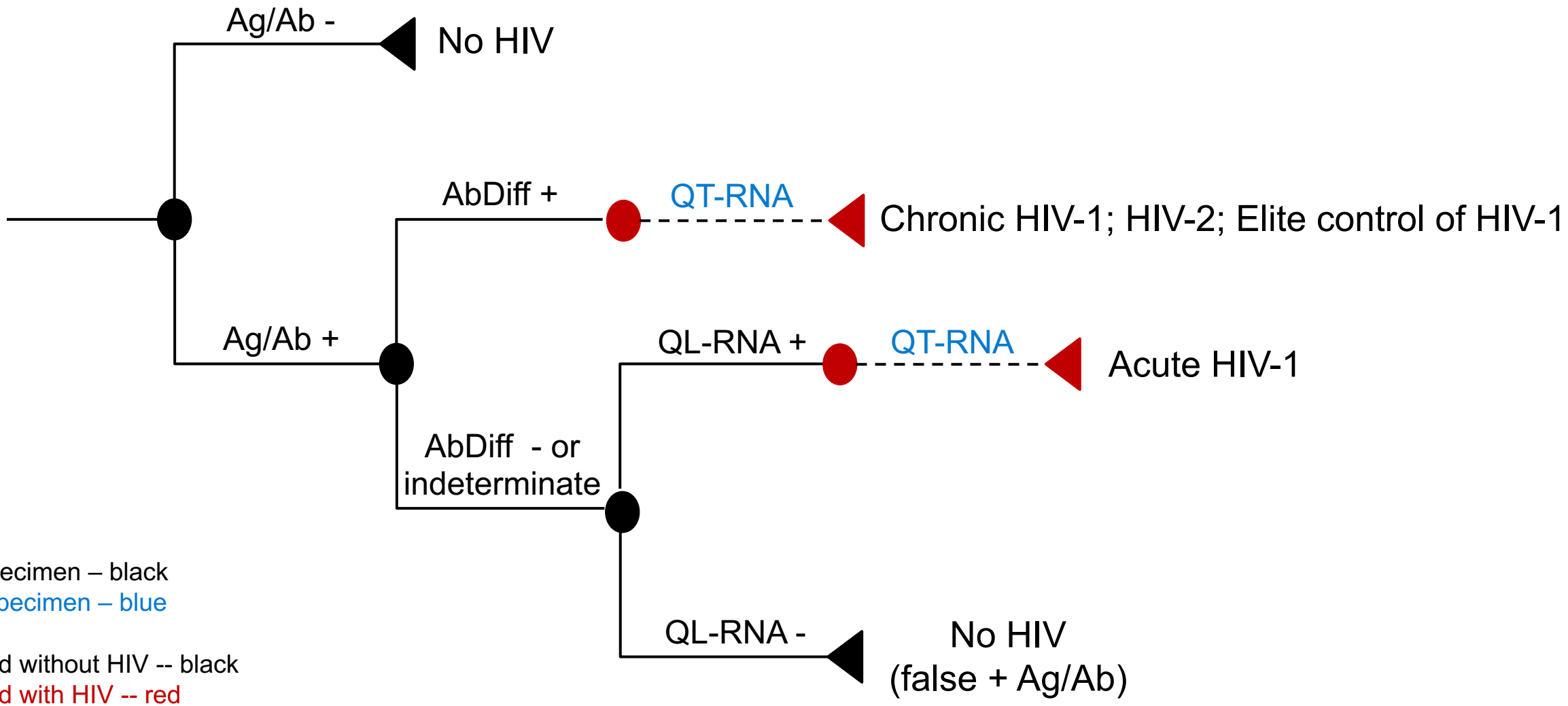

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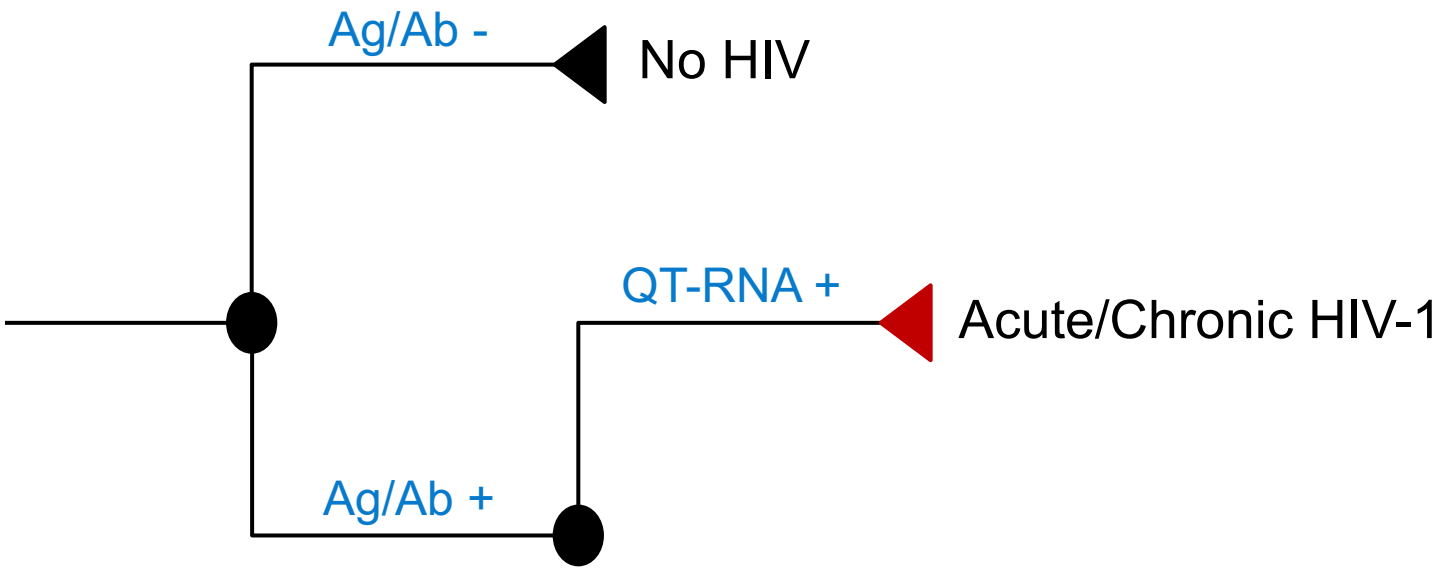
RNAplasma



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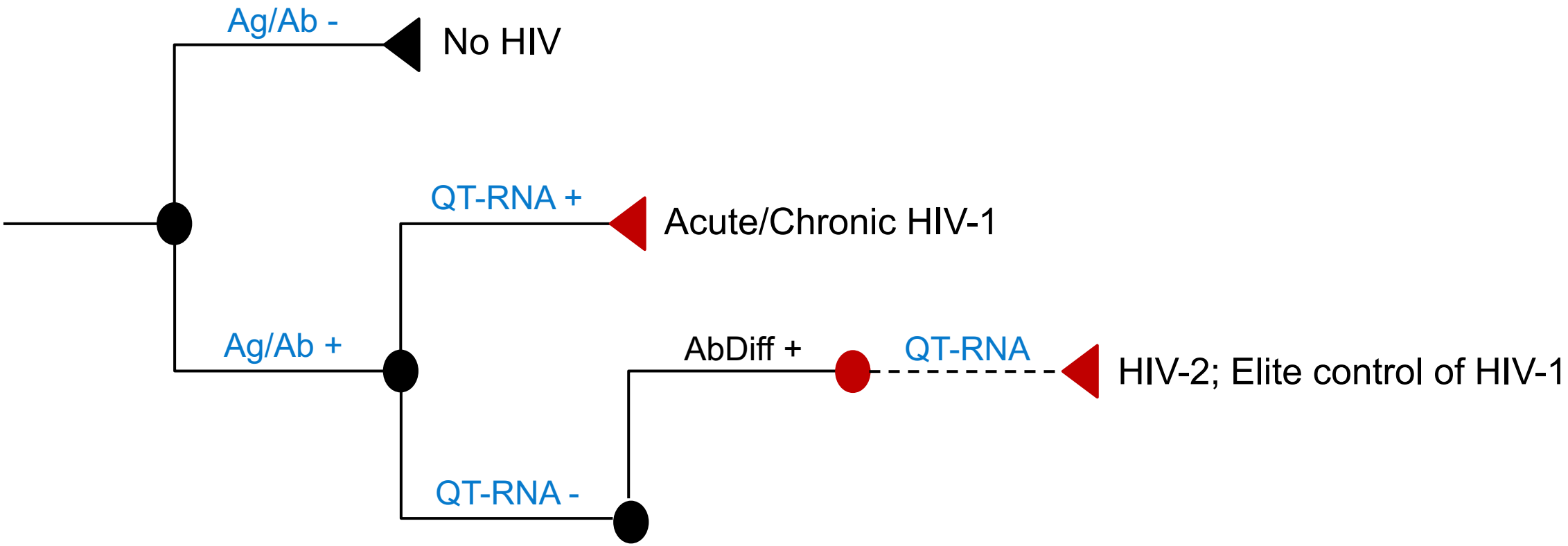

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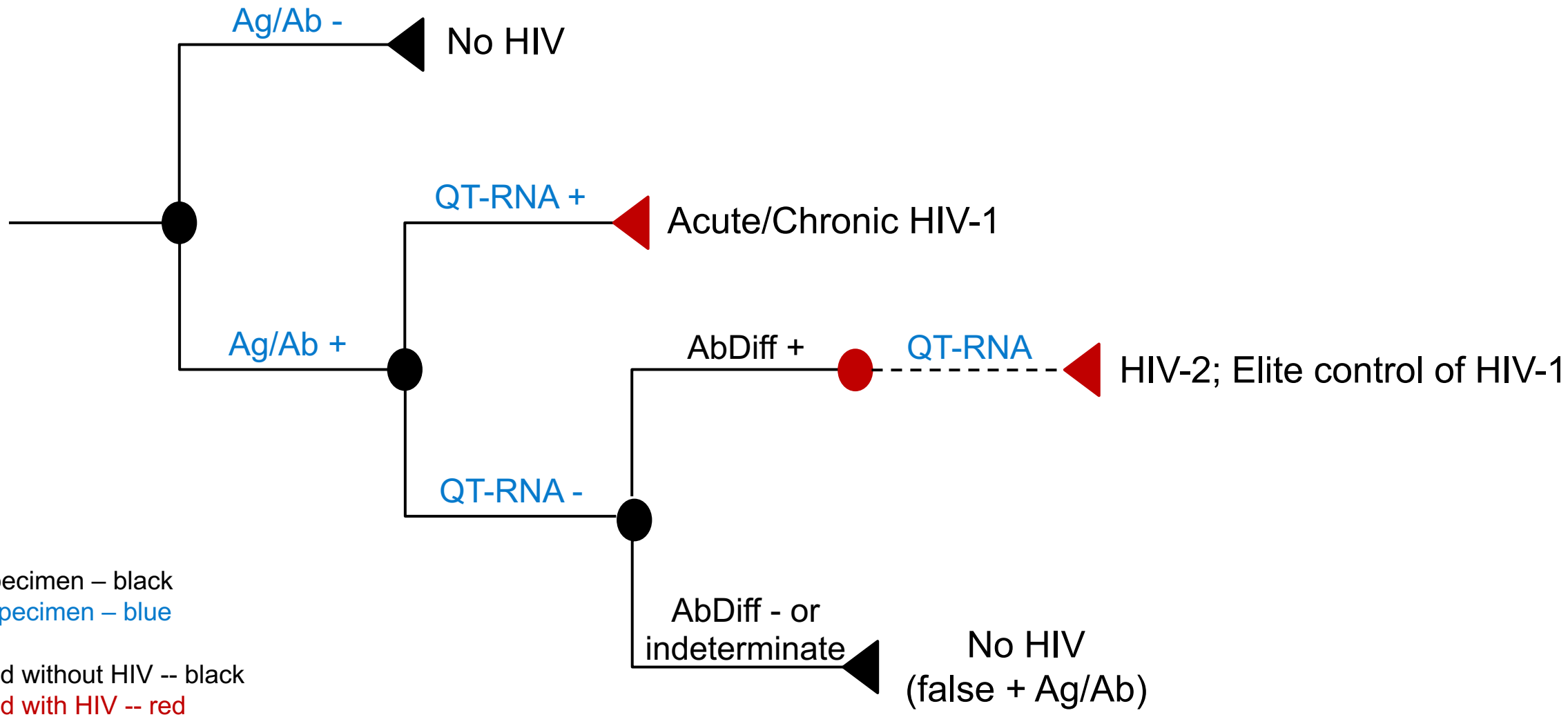

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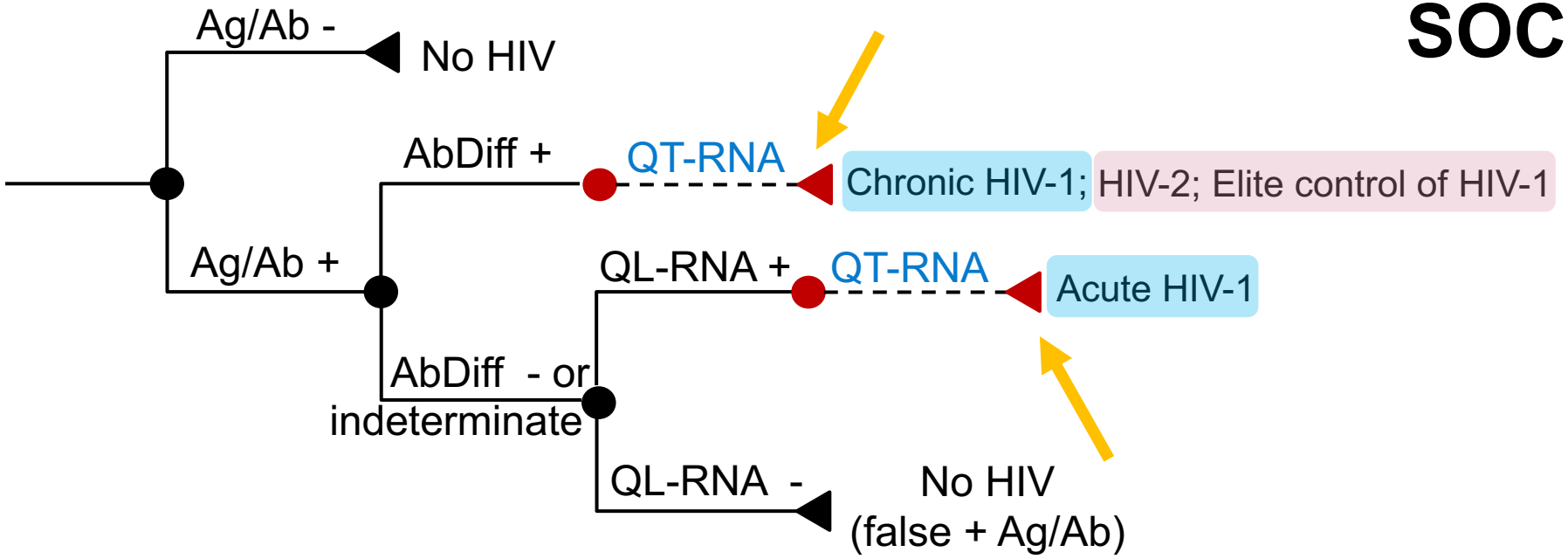

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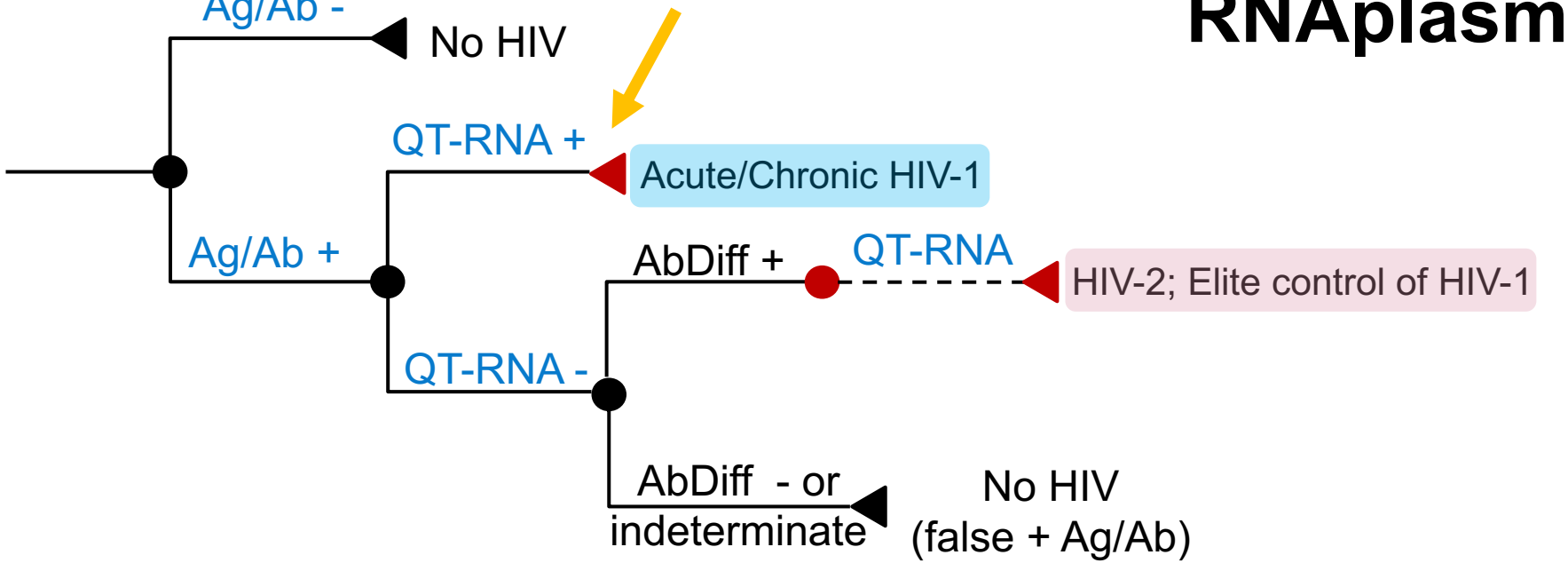


Base Case Results: Time to Action

- RNAplasma would reduce time to action compared with SOC for persons with HIV

RNAplasma:	60 hours
SOC:	112 hours

Base Case Results: Time to Reassurance

- RNAplasma would reduce time to reassurance compared with SOC for persons with a false positive Ag/Ab

RNAplasma:	60 hours
SOC:	132 hours

Base Case Results: Visits for Specimen Collection

- RNAplasma would reduce visits for specimen collection before ART initiation compared with SOC for persons with HIV

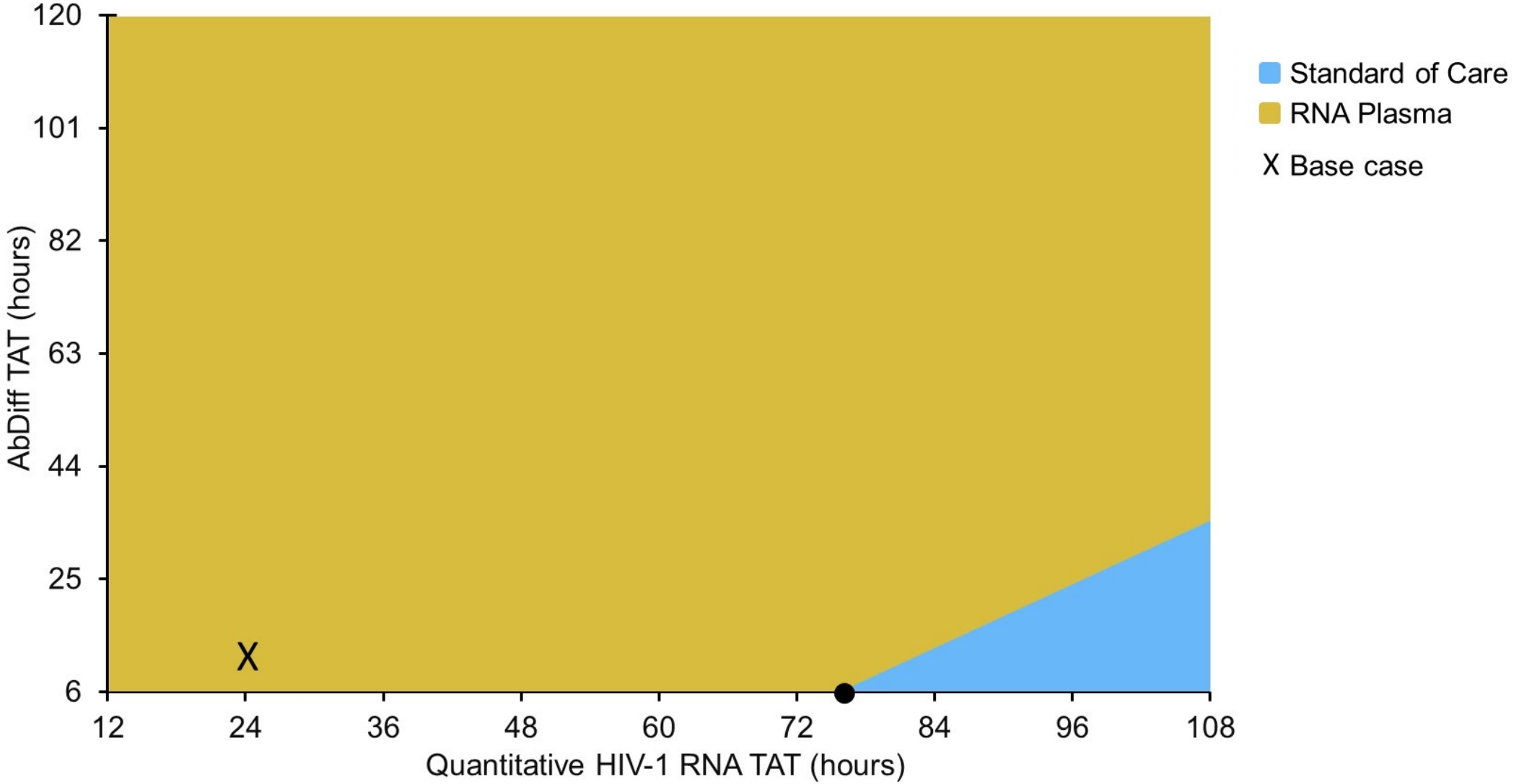
RNAplasma:	1.01 visits/person
SOC:	2.05 visits/person

Base Case Results: Testing Cost

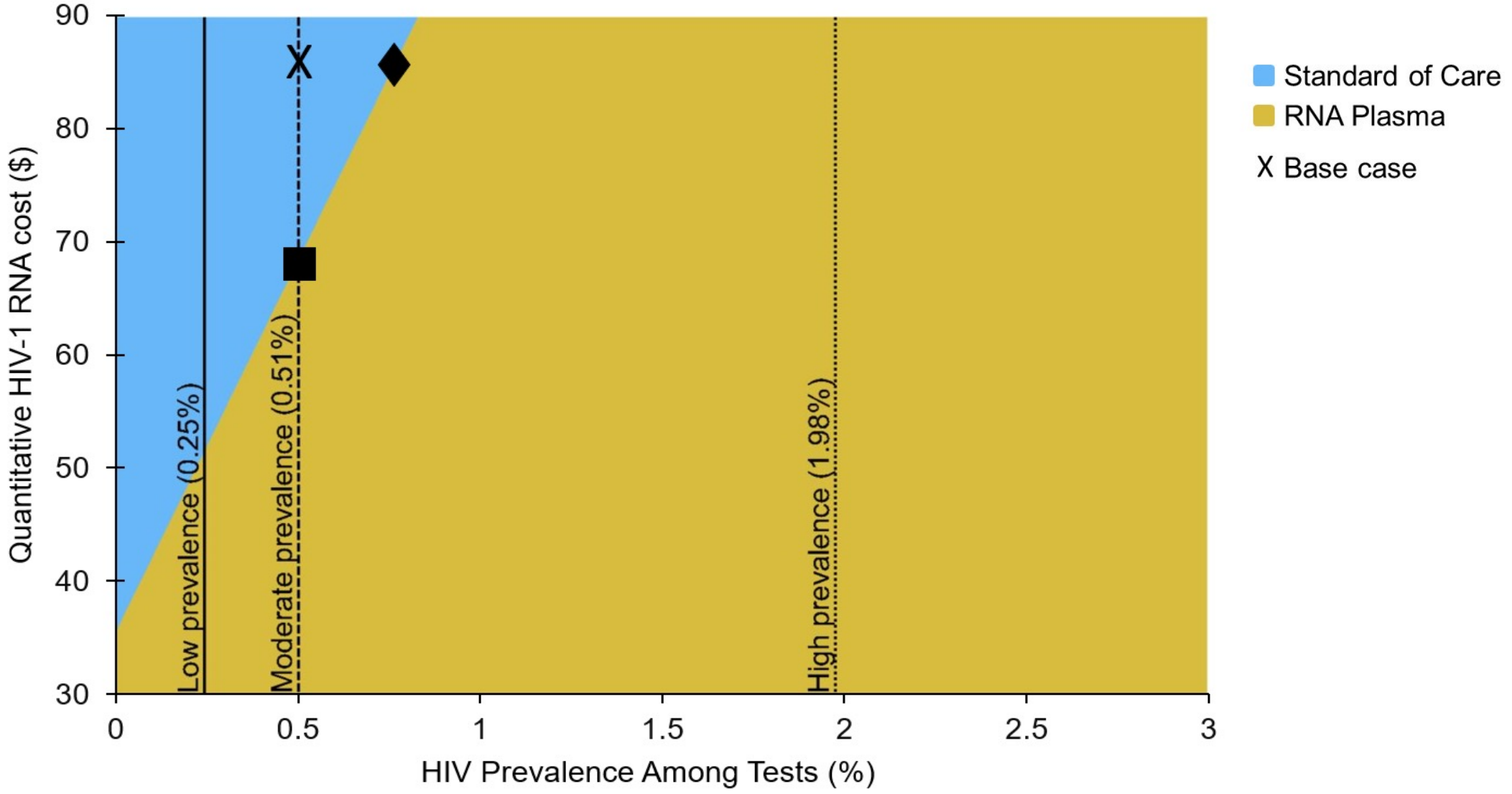
- RNAplasma and SOC would result in similar costs for all tested

RNAplasma:	$24.74
SOC:	$24.70

2-Way Sensitivity Analysis
Time to Action



2-Way Sensitivity Analysis
Testing Cost



Limitations

- Obtained turnaround time and cost estimates from the published literature and expert opinion
  - Examined a wide range of estimates with sensitivity analyses

- Did not explicitly simulate laboratories with low testing volumes
  - Examined the implications of long turnaround times to account for off-site testing but not changes to test costs with limited use

- Did not explicitly examine specimens from persons on PrEP or ART

Accessibility of QT-RNA testing

- Some laboratories may not have access to QT-RNA that is also approved for diagnosis, which affects:
  - On-site vs send-out testing decisions by laboratories
  - Specimen handling and shipping requirements are more stringent for RNAplasma than for the SOC algorithm

Conclusions

- RNAplasma algorithm (QT-RNA after Ag/Ab) would:
  - Reduce time to action and visits for persons with HIV
  - Reduce time to reassurance for persons with false + Ag/Ab
  - Reduce costs of the testing algorithm at lower QT-RNA costs or higher HIV prevalence

- Laboratory-specific needs must be considered
  - Serum vs plasma specimen collection
  - Performing assays on-site or sending to reference lab
  - Labor and reagent costs and test turnaround times

Acknowledgements

- Medical Practice Evaluation Center at MGH
- Quest Diagnostics
- Dr. Berry Bennett, Florida Bureau of Public Health Laboratories
- Dr. Joseph Yao, Mayo Medical Laboratories
- My co-authors

Grant support: National Institutes of Health (K01HL123349 (EPH), K08HD094638 (AMN), R37DA015612, R01AI042006), and the Jerome and Celia Reich HIV Scholar Award (EPH)

Supplemental Slides

HIV RNA on Serum Specimen

- How would our results be affected if QT-RNA was performed on serum specimens instead of plasma?
  - QT-RNA is not FDA-approved to report quantified results from serum
  - Clinicians use the quantified value (viral load) to follow response to ART
  - Without quantified results, a RNAserum algorithm would never be preferred as long as viral load is needed prior to ART initiation
  - If laboratories report RNA values (not FDA-approved) from serum specimens, then a RNAserum strategy would be equivalent to RNAplasma in our outcomes tested