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Laboratory Testing and Result Reporting
of Antibody to Hepatitis C Virus

MMWR

Recommendations and Reports

February 7, 2003 / 52(RR03);1-16

Guidelines for Laboratory Testing and Result Reporting of Antibody to Hepatitis C Virus

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Anti-HCV Testing

- Testing for anti-HCV antibodies is performed for:
  - Clinical diagnosis of patients with liver disease
  - Screening asymptomatic persons to identify HCV infected individuals
  - Management of occupational and perinatal exposures
  - Public health surveillance

Anti-HCV Screening Assays

- FDA-licensed anti-HCV screening test kits comprise 3 immunoassays
  - Abbott HCV v. 2.0 EIA
  - ORTHO HCV v. 3.0 ELISA
  - ORTHO VITROS CIA

HCV Supplemental Tests

- FDA-cleared serologic tests
  - Verification of anti-HCV status
    - Chiron RIBA HCV v. 3.0 SIA
- FDA-cleared nucleic acid tests
  - Active versus resolved infection
    - Roche AMPLICOR HCV Test v. 2.0 (RT-PCR)
    - Roche COBAS AMPLICOR HCV Test v. 2.0 (RT-PCR)
    - Bayer VERSANT HCV Qualitative Assay (TMA)
    - Bayer VERSANT HCV Quantitative Assay (bDNA)

Confirmation of Positive Anti-HCV Screening Tests

- Specificity of screening tests $\geq$ 99%
- Specificity of 99% does not provide desired PPV in low prevalence populations (<10%)
  - Average false positive rate for screening tests is 35% (range 15 to 60%)
- Verification of anti-HCV status minimizes unnecessary medical visits and psychological harm for persons with false positive screening test results

The Problem

- Many laboratories do not perform reflexive supplemental testing for positive anti-HCV screening tests
  - Lack of established guidelines for such testing
  - Lack of understanding by health-care professionals regarding performance characteristics and interpretation of screening and supplemental test results
  - High cost of supplemental tests

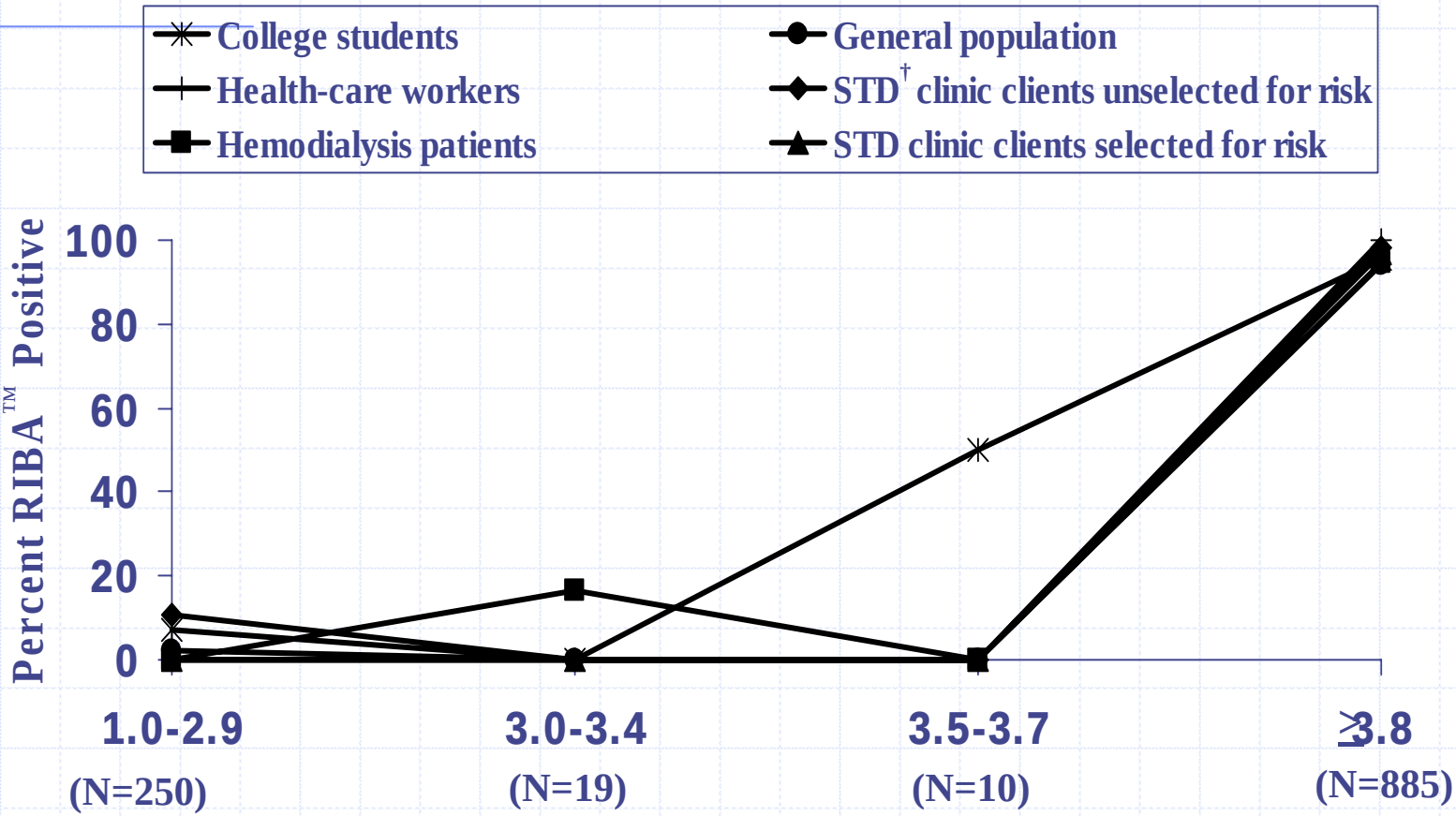
Anti-HCV Testing Practices, 2002

Testing Practices	PH Labs	VAMC Labs
Tests offered	n=43	n=67
Screening test	65%	100%
RIBA	38%	21%
Qualitative NAT	29%	75%
Quantitative NAT	13%	98%
Supplemental testing performed	n=29	n=67
All screening test positive results	35%	22%
Low-positive screening test results	10%	3%
Only by physician request	17%	75%
None offered	38%	0%
Type of supplemental test performed	n=13	n=16
RIBA only	31%	31%
NAT only	15%	63%
NAT->RIBA, if NAT negative	39%	6%
RIBA->NAT, if RIBA-positive	15%	0%

The Process

- Review of available knowledge
- Establish working group comprised of representatives from FDA, public health, hospital, and independent laboratories, and medical laboratory professional organizations (e.g. ASCP, CAP, AACC)
- Consultation with other stake holders
- Establish consensus guidelines through two meetings and draft document review

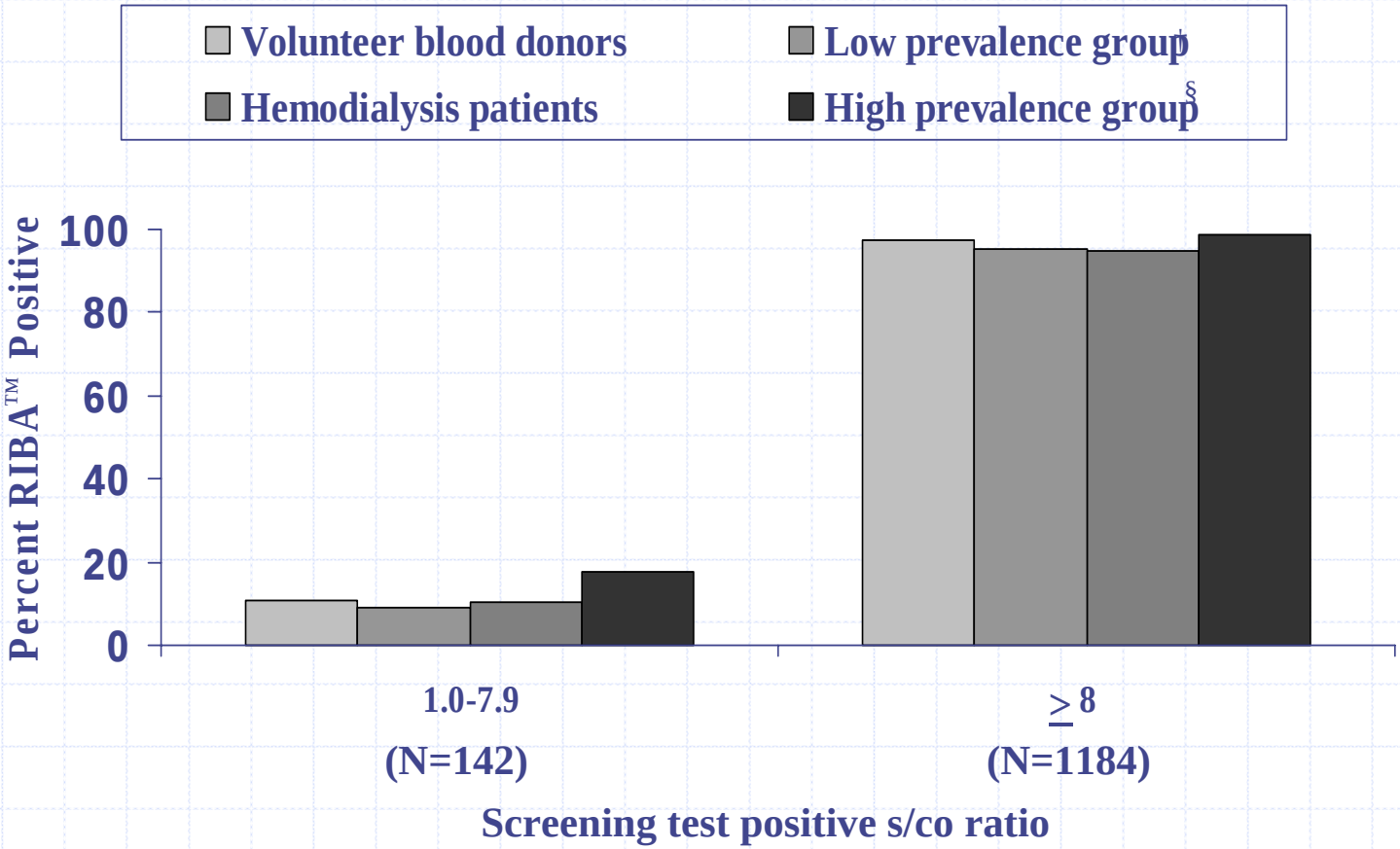
Proportion of antibody to hepatitis C virus enzyme immunoassay* screening-test-positive results that tested RIBA 3.0 positive by average s/co ratios and group tested



* HCV EIA 2.0 or HCV Version 3.0 ELISA

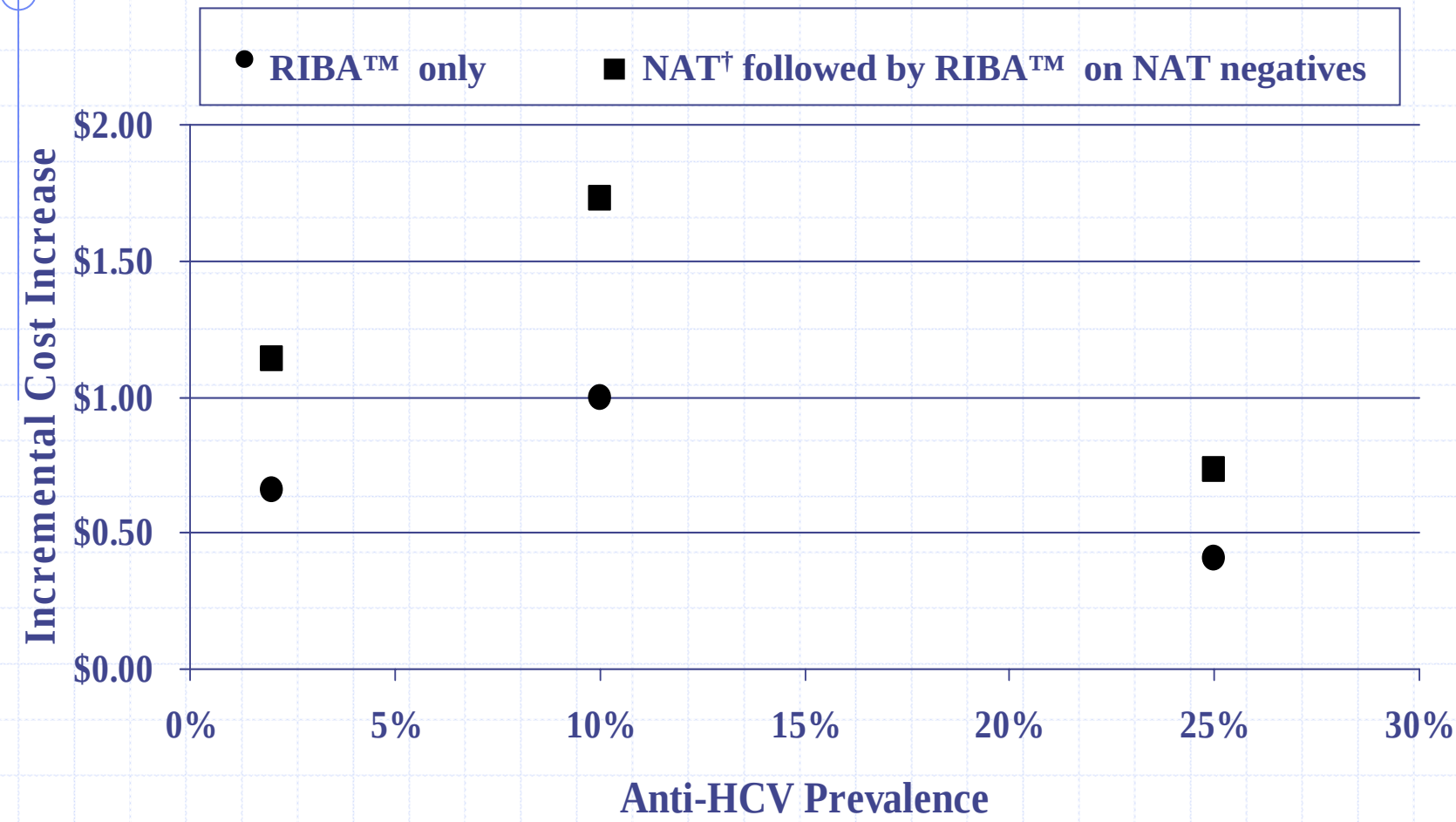
† Sexually transmitted diseases

Proportion of antibody to hepatitis C virus CIA* screening-test-positive results that tested RIBA 3.0 positive by s/co ratios and group tested



* *Vitros*® Anti-HCV
† College students, general population, health-care workers
§ Hospital-based patients

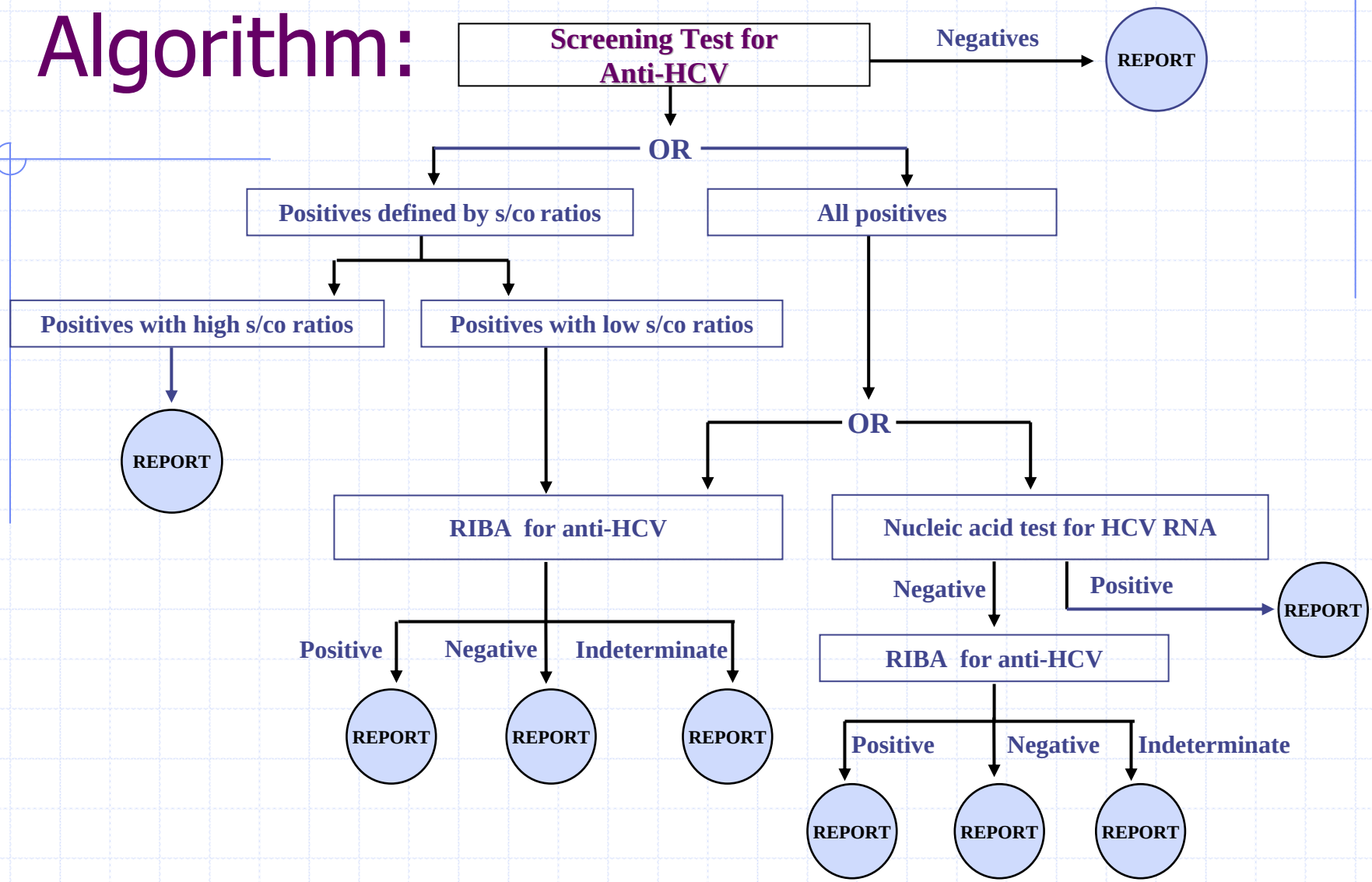
Estimated increased cost per sample for reflex supplemental testing of anti-HCV screening-test-positive results with low* average s/co ratios compared to performing only the screening test in populations with different anti-HCV prevalences



* <3.8 by HCV EIA 2.0 or HCV Version 3.0 ELISA

† Nucleic acid test

Algorithm:

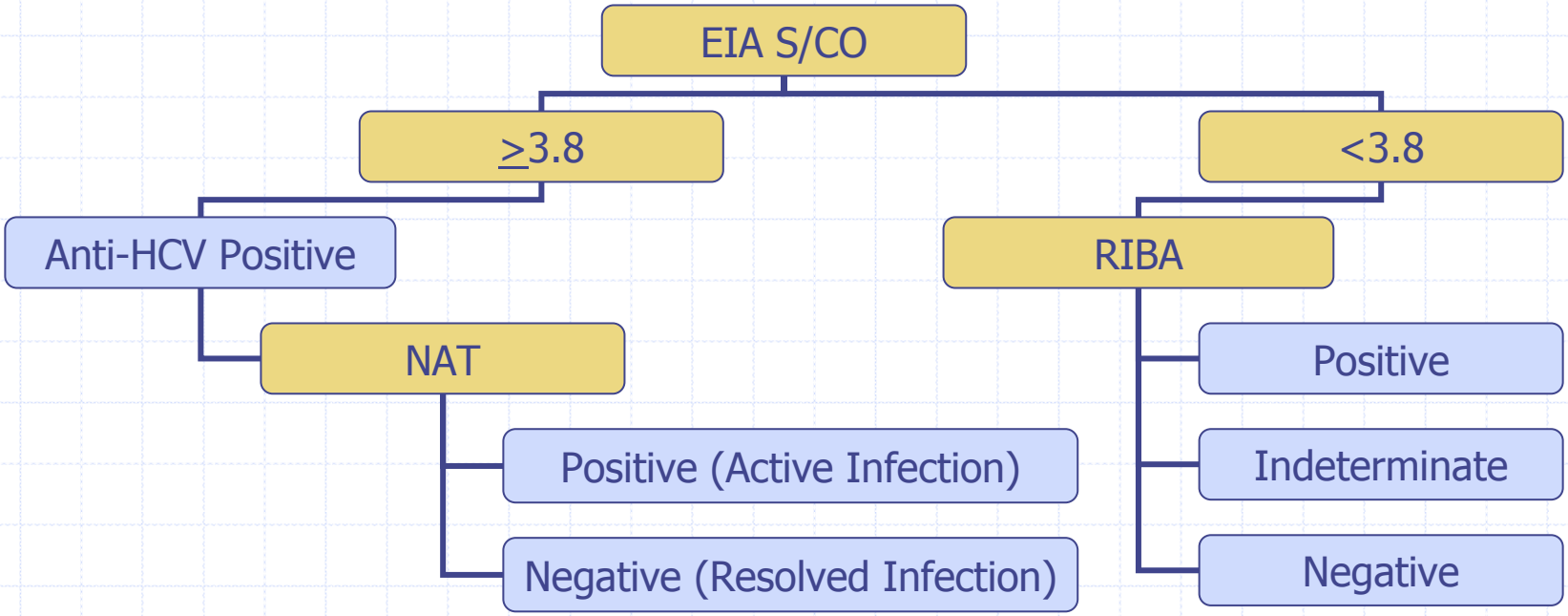

Screening Test for Anti-HCV
Negatives
REPORT
OR
Positives defined by s/co ratios
All positives
Positives with high s/co ratios
Positives with low s/co ratios
REPORT
OR
RIBA for anti-HCV
Nucleic acid test for HCV RNA
Positive
Negative
Indeterminate
REPORT
REPORT
REPORT
Negative
Positive
REPORT
RIBA for anti-HCV
Positive
Negative
Indeterminate
REPORT
REPORT
REPORT

EML Correlation of Positive HCV EIA S/CO Ratios and RIBA Results (1,034 tested)

EIA 2.0	RIBA 3.0			
S/CO	Positive	Indeterminate	Negative	Totals
≥3.8	64	0	1	65
<3.8	3	5	2	10
Totals	67	5	3	75

- 7.5% anti-HCV seroprevalence
- 13.3% samples with s/co <3.8
- 98.5% samples with s/co ≥3.8 were RIBA positive
- 30% samples with s/co <3.8 were RIBA positive

EML Anti-HCV Reflex Testing Algorithm



Anti-HCV Result Reporting

- High positive (s/co ratio ≥3.8)

"This sample is strongly positive for antibody to HCV. Greater than 98% of strongly positive samples are also positive in the supplemental RIBA. A qualitative HCV RNA (PCR) has been ordered to distinguish active from resolved infection."

Anti-HCV Result Reporting

- Low positive (s/co ratio <3.8)

"This sample is weakly positive for antibody to HCV and has been sent for supplemental testing by a recombinant immunoblot assay. A qualitative HCV RNA test (PCR) is recommended for all confirmed antibody positive samples to distinguish active from resolved infections, but must be ordered separately."

Impact on Cost of Confirmation

Test	Location	EML cost	EML charge	CPT	GA MR
RIBA	ARUP	$125	$156	86804	$22
NAT	EML	$29	$165	87521	$27

Impact on Cost of Confirmation

No. anti-HCV tests performed annually	5,000
Cost of reflex testing of all anti-HCV positives by RIBA (n=375)	$46,875
Cost of reflex testing of high positives by NAT (n=325) and low positives by RIBA (n=50)	$15,773
Annual cost avoidance	$31,102

Acceptance of Guidelines by Laboratory Community

- Follow-up survey of state public health laboratories
  - 89% were aware of guidelines
  - 55% changed testing policy after reviewing guidelines
    - % of labs performing supplemental testing increased by 30%
    - A few labs chose to report s/co ratios but without supplemental testing
  - 39% of labs that did not change testing practices were already performing supplemental testing

Impact of Anti-HCV Testing Guidelines

- Facilitate and improve reflex supplemental testing algorithm
- Improve accuracy of results
- Better utilization of medical resources
- Better public health surveillance