Importance of Evidence Based Medicine in POCT
<table>
<thead>
<tr>
<th></th>
<th>Agenda</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Influenza</td>
</tr>
<tr>
<td>2</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>3</td>
<td><strong>C. difficile</strong></td>
</tr>
<tr>
<td>4</td>
<td>HIV</td>
</tr>
</tbody>
</table>
1970: William Stewart, the Surgeon General of the United States declared the U.S. was “ready to close the book on infectious disease as a major health threat”; modern antibiotics, vaccination, and sanitation methods had done the job.

1995: Infectious disease had again become the third leading cause of death, and its incidence is still growing!
Advantages of Rapid Testing for Infectious Diseases

Faster directed therapy to reduce:

- antibiotic resistance
- hospital length-of-stay

Reduced length-of-stay in Emergency Department

Timely application of appropriate infection control procedures

Less adverse consequences

Teachable moment
Inpatient Settings

One in every three patients will receive two or more antibiotics in the course of their hospital stay.

Of the patients receiving antibiotics, three out of every four will receive unnecessary or redundant therapy, resulting in excessive use of antibiotics.

CDC – Get Smart Campaign
Outpatient Settings

Each year, tens of millions of antibiotics are prescribed unnecessarily for upper viral respiratory infections.

Antibiotic use in primary care is associated with antibiotic resistance at the individual patient level.

The presence of antibiotic-resistant bacteria is greatest during the month following a patient’s antibiotics use and may persist for up to 1 year.

CDC – Get Smart Campaign
AMR: If We Don’t Take Action Now

Deaths attributable to AMR every year compared to other major causes of death

- AMR now: 700,000 (low estimate)
- AMR in 2050: 10 million
- Tetanus: 60,000
- Road traffic accidents: 1.2 million
- Measles: 130,000
- Diarrhoeal disease: 1.4 million
- Cholera: 100,000-120,000
- Diabetes: 1.5 million
- Cancer: 8.2 million

Deaths attributable to AMR every year by 2050

- Europe: 390,000
- North America: 317,000
- Latin America: 392,000
- Africa: 4,150,000
- Asia: 4,730,000
- Oceania: 22,000

Mortality per 10,000 population

- 5
- 6
- 7
- 8
- 9
- 10
- >

number of deaths
The Challenge with Respiratory Patients

- Influenza?
- Common cold?
- Pneumonia?
What are the issues of respiratory disease?

The symptoms of respiratory diseases are vague

- Pneumonia symptoms
  - Cough
  - Fever
  - Chills
  - Difficulty breathing
- Influenza
  - Cough
  - Fever
  - Chills
  - Malaise

Treatment is different

- Bacteria
  - Broad spectrum antibiotic
  - Narrow spectrum antibiotic
- Influenza
  - Antiviral
  - Treat symptoms only

Complications of mistreatment

- Mistreatment of bacterial etiology
  - May increase morbidity/mortality
  - May have longer hospital stay
  - May get *C. difficile*
- Mistreatment of influenza
  - May have increased resistance and *C. difficile*
  - Antiviral may reduce symptoms
Knowing now matters™ in Influenza testing
Spread of Influenza

Flu is spread person-to-person through coughing or sneezing.

• Quick incubation of around 2 days

Hands can spread influenza if the person then touches their nose.

Healthy adults can infect others one day BEFORE symptoms develop and up to 5-7 days after.
Aren’t you supposed to build immunity to influenza?

The problem with influenza, like the common cold, is that there are many different strains.

That is also why the performance of rapid tests are different every year!
Influenza Sample Collection

Appropriate specimens

- Nasal wash/aspirate, nasopharyngeal swab, or nasal swab
- Throat swabs have dramatically reduced sensitivity

Samples should be collected within first 24 to 48 hours of symptoms since that is when viral titers are highest and antiviral therapy is effective

Testing can be done immediately with rapid test or sample placed in transport media

- Infectivity is maintained up to 5 days when stored @ 4-8°C
- If the sample cannot be evaluated in this time period, the sample should be frozen @ -70°C.
Influenza Testing with Rapid Direct Antigen Tests

**PROS**
- Economical
- CLIA-waived
- High specificity so no confirmatory testing for positive results
- Easy to batch

**CON**
Variable sensitivity so negatives should be backed up by molecular or culture testing
Results – Flu Negative

- MD unaware, n = 92
- MD aware, n = 97

Bar chart showing:
- CBC: 7 (MD unaware) vs 13 (MD aware)
- Blood Culture: 6 (MD unaware) vs 12 (MD aware)
- Urine Dipstick: 7 (MD unaware) vs 7 (MD aware)
- Urinalysis: 8 (MD unaware) vs 10 (MD aware)
- Urine culture: 5 (MD unaware) vs 12 (MD aware)
- CSF studies/culture: 2 (MD unaware) vs 3 (MD aware)
- Chest X-ray: 23 (MD unaware) vs 22 (MD aware)
- Antibiotics: 27 (MD unaware) vs 27 (MD aware)
- Antivirals: 2 (MD unaware) vs 0 (MD aware)

Results – Flu Positive

- MD unaware, n =106
- MD aware, n=96

<table>
<thead>
<tr>
<th>Test</th>
<th>MD unaware</th>
<th>MD aware</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBC</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Blood Culture</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Urine Dipstick</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Urinalysis</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Urine culture</td>
<td>12</td>
<td>14</td>
</tr>
<tr>
<td>CSF studies/culture</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>Chest X-ray *</td>
<td>26</td>
<td>26</td>
</tr>
<tr>
<td>Antibiotics *</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Antivirals</td>
<td>18</td>
<td>7</td>
</tr>
</tbody>
</table>

* - p ≤ 0.001

Key Operational Metrics

**FLU POSITIVE**

<table>
<thead>
<tr>
<th>Lab/Rad Charges*</th>
<th>Time to Discharge (min)*</th>
<th>MD unaware, n =106</th>
<th>MD aware, n=96</th>
</tr>
</thead>
<tbody>
<tr>
<td>$92.37</td>
<td>49</td>
<td>$15.65</td>
<td>25</td>
</tr>
</tbody>
</table>

**FLU NEGATIVE**

<table>
<thead>
<tr>
<th>Lab/Rad Charges</th>
<th>Time to Discharge (min)</th>
<th>MD unaware, n =92</th>
<th>MD aware, n=97</th>
</tr>
</thead>
<tbody>
<tr>
<td>$93.07</td>
<td>42</td>
<td>$68.91</td>
<td>45</td>
</tr>
</tbody>
</table>

* p ≤ 0.001

Why molecular?
The power of sample amplification

Conventional non-molecular methods can have suboptimal limits of detection.
Samples with low viral or bacterial load could result in a false negative.

With molecular, even a few hundred infectious particles can be amplified billions of times!
Amplification increases likelihood of detection, and may compensate for suboptimal sample collection.
Knowledge of a Positive Test Has Been Shown to:

- Limit unnecessary antibiotic use
- Limit unnecessary diagnostic procedures
- Increase the appropriate use of antivirals
How many people have had RSV in their lives?
Almost ALL people in this room had RSV by the age of 2!
What is RSV?¹

RSV is a single-stranded RNA virus of the family paramyxoviridae, which includes common respiratory viruses such as those causing measles and mumps.

RSV is divided into 2 subtypes: A and B. More severe clinical illnesses involve subtype A strains, which tend to predominate in most outbreaks.
RSV—A significant global pathogen

The **single most important cause of severe respiratory illness** in infants/young children

RSV disease burden is estimated at **64M cases and 160,000 deaths** every year.

RSV is **the most frequent cause of hospitalization** of infants and young children in industrialized countries.

RSV believed to represent a **similar burden to Flu** in >64yrs

RSV-related illness represents a **significant healthcare burden** in the US
US Burden of RSV

In the US, the **hospitalization rate is three times higher** than that from influenza in children <5 years old.

Over **2 million children 5 years old and younger** receive care for RSV infection in US each year (Extrapolated data):
- 57,500 require hospitalization
- 518,000 receive care in the ED
- Over 1.5 million children are treated each year in practices.

RSV-associated costs based on US Medicaid databases for full-term infants:
- $11,000 for each RSV hospitalization
- >$3,000 for RSV-related outpatient visit

Total US Healthcare believed to be **~$2.6bN per year** for RSV associated infections.
Prevalence / Incidence

RSV accounts for 1 in every 13 visits to pediatrician³

177,000 hospitalizations & 14,000 deaths per year in over 65⁶

126,000 infants hospitalized every year with RSV⁷
  20% are premature infants

Most common cause of pneumonia in < 1 year old

By age 3, virtually every child has had RSV!
  Infects 50% infants in first year of life

400 children each year⁷ under the age of 1 die due to RSV
RSV around the Country

Source: http://www.cdc.gov/rsv/research/us-surveillance.html
How is RSV spread

People infected with RSV are usually contagious for 3 to 8 days. However, in the young and elderly with weakened immune systems, RSV can be contagious for up to 4 weeks. RSV can be spread by:

- Infected person coughs or sneezes into the air, creating virus-containing droplets that can linger briefly in the air.
- Direct and indirect contact with nasal or oral secretions from infected people and then rub their eyes or nose.
- RSV can survive on hard surfaces such as tables and crib rails for many hours. However, RSV typically lives on soft surfaces such as tissues and hands for shorter amounts of time.
RSV is Contagious!⁹

- RSV is one of the most contagious human pathogens
- Comparable to measles virus.
- In prospective studies, the natural introduction of RSV into a day-care setting resulted in infection of more than 90% of infants and children
- Children pass RSV onto adults and vice versa
- RSV is readily introduced and spreads with ease in hospitals, nursing homes, families, and other close-contact settings
RSV Symptoms

RSV disease includes a wide array of symptoms, including:

<table>
<thead>
<tr>
<th>Rhinitis</th>
<th>Croup</th>
<th>Pneumonia</th>
<th>Bronchiolitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammation of mucous membranes inside the nose</td>
<td>Inflammation of larynx &amp; trachea causing breathing problems</td>
<td>Inflammation of the lungs</td>
<td>Inflammation of the bronchioles</td>
</tr>
</tbody>
</table>

However, these symptoms are not specific and can be linked to other respiratory illnesses therefore making rapid and accurate diagnosis of RSV essential for the treatment and management of patients.

It may also cause other diseases like otitis media (ear aches) that RSV tests aren’t currently meant to test for.
Knowing now matters™ in Pneumonia
Current Number of Pneumonia Cases (US)

37 million ambulatory care visits per year for acute respiratory infections (physician and ER visits combined)

Community-Acquired Pneumonia (CAP)
- Each year millions cases of CAP result in ~10 million
- physician visits & 500,000 hospitalizations in the US
- Average mortality is 10-25% in hospitalized patients with CAP

Healthcare Associated Pneumonia
- Standard definition: onset of symptoms occurs approx 3 days after admission
- 250,000 - 350,000 cases of nosocomial pneumonia per year
- 25 - 50% mortality rate
Directed, rather than broad spectrum therapy has significant advantages and can:

- **Lead to more effective antibiotics for the pathogen**
- **Reduce morbidity/mortality and hospital length of stay**
- **Reduce antibiotic resistant micro-organisms**
Etiological Agents

Newborns (0 to 30 days)

• Group B *Streptococcus, Lysteria monocytogenes*, or Gram negative rods are common
• RSV in premature babies

Infants and toddlers

• 90% of lower respiratory tract infections are viral with the most common being RSV, Influenza A&B, and parainfluenza. Bacterial infections are rare, but could be *S. pneumoniae*, Hib, or *S. aureus*. 
Etiological Agents

Outpatient

- *S. pneumoniae*, *H. influenzae*, *M. pneumoniae*, *C. pneumoniae*, and respiratory viruses

Inpatient (non-ICU)

- With the above agents, add *L. pneumophila*

Inpatient (ICU)

- *S. pneumoniae*, *S. aureus*, *L. pneumophila*, Gram-negative bacteria, and *H. influenzae*
The Future of Pneumococcal Pneumonia

Between 2004 and 2040, the US population is expected to increase 38%.

Pneumococcal pneumonia cases may increase 96%:
- Roughly 400,000 cases to 790,000.

Absent intervention, the cost of pneumococcal pneumonia will increase $2.5 billion annually.
Table 5. Clinical indications for more extensive diagnostic testing.

<table>
<thead>
<tr>
<th>Indication</th>
<th>Blood culture</th>
<th>Sputum culture</th>
<th>Legionella UAT</th>
<th>Pneumococcal UAT</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensive care unit admission</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X^a</td>
</tr>
<tr>
<td>Failure of outpatient antibiotic therapy</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Cavitary infiltrates</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukopenia</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Active alcohol abuse</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Chronic severe liver disease</td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Severe obstructive/structural lung disease</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Asplenia (anatomic or functional)</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recent travel (within past 2 weeks)</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td>X^c</td>
</tr>
<tr>
<td>Positive Legionella UAT result</td>
<td>X^d</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive pneumococcal UAT result</td>
<td>X</td>
<td>X</td>
<td></td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X^a</td>
</tr>
</tbody>
</table>

**NOTE.** NA, not applicable; UAT, urinary antigen test.

- **a** Endotracheal aspirate if intubated, possibly bronchoscopy or nonbronchoscopic bronchoalveolar lavage.
- **b** Fungal and tuberculosis cultures.
- **c** See table 8 for details.
- **d** Special media for *Legionella*.
- **Star** Thoracentesis and pleural fluid cultures.
Decreasing total cost of a community-acquired pneumonia (CAP) admission may best be achieved with improving processes and treatments.

In 2009 dollars, eliminating a day during the course of a CAP admission is potentially worth $2,273 to $2,373 per patient.

In this study, “1-day reduced” is the result of efficiencies or improved outcomes throughout the hospitalization.

Using *Legionella* and *S. pneumoniae* as part of the pathway for community-acquired pneumonia led to...

- Fewer adverse drug reactions
- No reduction in hospital readmission, case fatality, or patient satisfaction
Clinical Usefulness of *S. pneumoniae* Urinary Antigen Test

The study evaluated 474 episodes of community-acquired pneumonia

- *Streptococcus pneumoniae* was the causative pathogen in 171 cases (36.1%).
- It was detected exclusively by urinary antigen test in 75 cases (43.8%).

Resulting in...

- Narrowing the broad spectrum to IV penicillin or ampicillin or switch to oral amoxicillin.
- removing macrolide in patients empirically treated with β-lactam and macrolide combination or partial reduction of broad spectrum.
CDC Reported cases of legionellosis per 100,000 population, by year — United States, 2000–2014

http://www.cdc.gov/mmwr/volumes/65/wr/mm6522e1.htm?s_cid=mm6522e1_e#
CDC Reported cases of legionellosis per 100,000 population, by year — United States, 2000–2014

Legionellosis cases are increasing in the US and the mortality is “substantial.”

- Cases have risen dramatically over a 14 year period
- Seeing about a 10% mortality
- 4% were outbreak associated

Significant gaps in water treatment could be seen in many outbreaks

- Especially if low levels of chlorine or other disinfectants along with warmer temperatures
Knowing now matters™
in *Clostridium difficile*
Pathogenesis of CDAD

*Clostridium difficile* is spread via the fecal-oral route. The organism is ingested either as the vegetative form or as hardy spores, which can survive for long periods in the environment and can traverse the acidic stomach.

In the small intestine, spores germinate into the vegetative form.

In the large intestine, *C. difficile*-associated disease can arise if the normal flora has been disrupted by antibiotic therapy.

*C difficile* reproduces in the intestinal crypts, releasing toxins A and B, causing severe inflammation. Mucous and cellular debris are expelled, leading to the formation of pseudomembranes.

Toxin A attracts neutrophils and monocytes, and toxin B degrades the colonic epithelial cells, both leading to colitis, pseudomembrane formation, and watery diarrhea.
Antibiotic-Associated Diarrhea: Life’s a Beach with *C. difficile*
Clinical Manifestations of CDAD

Asymptomatic Colonisation

No Symptoms

Diarrheal illness

• Diarrhea- Mild to severe (explosive)
• Abdominal Pain
• Fever

PMC Toxic megacolon

Increasing disease severity
What are the issues with *Clostridium difficile*?

Diarrhea is a common symptom of gastrointestinal diseases

Many patients are carriers of *C. difficile*

- Don’t need treatment but may be misdiagnosed and mistakenly treated

Overuse of antibiotics can trigger *C. difficile* infections by wiping out the natural gut flora

There is no single answer that identifies both carriers and patients with active disease

- Toxin tests won’t detect carriers
- Molecular tests can’t differentiate carriers from active infections
Consequences of Not Distinguishing Between a C. difficile Carrier and True Disease

May be pulling patient off of most effective antibiotic for the initial infection.

Treatment for C. difficile will deplete the normal gut microflora, potentially making the person more susceptible to getting a C. difficile infection.

Higher reportable C. difficile rates

Unnecessary isolation
Sample Collection & Testing

No need to collect from asymptomatic people

- Babies can have high carriage rates
- Usually 3 loose stools within 24 hour period
- Don’t use assays for test of cure

Molecular or GDH Antigen as first step

- Toxin testing not considered sensitive enough for first step
- Molecular usually targets the gene for toxin
- GDH is present in toxigenic and non toxigenic strains
Johns Hopkins – Adherence to C. difficile IDSA/SHEA Guidelines

Retrospective data showed adherence of only 65.7% to guidelines

- Test only loose specimens
- Repeat testing for 7 days is discouraged
- PCR positive with no diarrhea – don’t treat

43% of pre-intervention patients were taking a laxative within 48 hours of test
Table 3. Sensitivity and Specificity of individual assays and algorithms compared with cell cytotoxin assay – Training dataset (n = 6761)

<table>
<thead>
<tr>
<th></th>
<th>Single assays-Manufacturers’ cut-offs</th>
<th>Two stage assays-Manufacturers’ cut-offs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GDH EIA</td>
<td>NAAT</td>
</tr>
<tr>
<td>Sensitivity %</td>
<td>95.9</td>
<td>96.9</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(93.4-97.6)</td>
<td>(94.7-98.4)</td>
</tr>
<tr>
<td>Specificity %</td>
<td>92.1</td>
<td>94.9</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(91.4-92.8)</td>
<td>(94.3-95.4)</td>
</tr>
<tr>
<td>PPV%</td>
<td>42.7</td>
<td>54.0</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(39.4-46.1)</td>
<td>(50.2-57.7)</td>
</tr>
<tr>
<td>NPV%</td>
<td>99.7</td>
<td>99.8</td>
</tr>
<tr>
<td>(95% CI)</td>
<td>(99.5-99.8)</td>
<td>(99.6-99.9)</td>
</tr>
</tbody>
</table>

GDH EIA (or NAAT) positive, toxin EIA (or cytoxin) positive:
CDI is likely to be present
→ for mandatory reporting to HPA

or

GDH EIA (or NAAT) positive, toxin EIA negative:
*C. difficile* could be present i.e. potential
*C. difficile* excretor
→ not for mandatory reporting
  (but may have transmission potential and be suitable for local reporting)

or

GDH EIA (or NAAT) negative:
*C. difficile* or CDI is very unlikely to be present
→ not for mandatory reporting
  but may have transmission potential (other pathogens)

Refer to the following local policies:
- Remember the SIGHT list
- *Clostridium difficile* Policy
- *Clostridium difficile* Treatment Guideline
- Source Isolation Policy
- Source Isolation Cleaning Policy

Consider other causes of diarrhoea
Consider continuation of single room isolation and other measures to reduce risk of CDI

Consider other causes of diarrhoea; if not infective may consider ending single room isolation
IDSA/SHEA Guidelines

From the guidelines:

Are there pre-agreed institutional criteria for patient stool submission?

- **NO**
  
  **Best performing method:**
  
  Use a stool toxin test as part of a multistep algorithm *rather than a NAAT alone* for all specimens received in the clinical laboratory

- **YES**
  
  **Most sensitive method:**
  
  Use a *multistep algorithm or NAAT alone* for testing rather than a toxin test alone

McDonald et al. *Clin Infect Dis* 2018; cix1085, https://doi.org/10.1093/cid/cix1085
Knowing now matters™ in HIV testing
Summary of the Recommendations

- Routine screening in all healthcare settings with undiagnosed prevalence ≥0.1% for patients aged 13 to 64 years
- Repeat testing should be performed at least annually for those determined to be high-risk
- Routine screening for all pregnant women
- Screening should be voluntary using opt-out consent
ACEP 2014 Policy Statement

Early diagnosis and treatment of HIV
- Prolongs life
- Reduces transmission
- Is a cost-effective public health intervention

Candidates for HIV screening
- All from 15-65 years old
- High risk adolescents and elderly
- All pregnant women with unknown HIV status

ED HIV screening programs are best when
- Local prevalence of HIV is ≥ 0.1%
- Procedures are practical and feasible
- Integrated with resources of the healthcare system (linkage to care)
Is Rapid Testing in the ED Feasible?

**PROS**

- High-risk populations use the ED as their sole source for medical care
- Seroprevalence is relatively high (> 0.1% per CDC guidance) and this affords an outstanding opportunity to determine risk and to test for HIV
- Rapid tests are quick and accurate
- Growing experience and body of literature demonstrating clinical and cost effectiveness

**CONS**

- Perceptions regarding ED-based prevention efforts vary
- Program implementation will vary depending on resources and site
- Limited comparative data
- Funding
Reduction of high-risk behavior\(^1\)

Reduces the risk of forward transmission:
Individuals with acute HIV infection are 43 times more contagious than chronically infected HIV patients\(^2\)

Allows individuals with HIV to seek treatment earlier which:\(^3,4,5\)

- Will improve their health
- Reduces the risk of premature death
- Reduces their viral load, reducing the risk of forward transmission

\(^4\)CDC. MMWR 2011;60(47):1618–23.
CDC/APHL HIV Diagnostic Algorithm

1. **HIV-1/2 antigen/antibody combination immunoassay**
   - (+) **Negative for HIV-1 and HIV-2 antibodies and p24 Ag**
   - (-) **HIV-1/HIV-2 antibody differentiation immunoassay**

2. **HIV-1/HIV-2 antibody differentiation immunoassay**
   - HIV-1 (+) **HIV-2 (-)**
     - **HIV-1 antibodies detected**
     - **Initiate Care**
   - HIV-1 (-) **HIV-2 (+)**
     - **HIV-2 antibodies detected**
   - HIV-1 (+) **HIV-2 (+)**
     - **HIV antibodies detected**
   - HIV-1 (-) or indeterminate **HIV-2 (-)**
     - **HIV-1 NAT**
     - **HIV-1 NAT (+)**
       - **Acute HIV-1 infection**
     - **HIV-1 NAT (-)**
       - **Negative for HIV-1**

---

*Note: (+) indicates reactive test result, (-) indicates nonreactive test result. NAT: nucleic acid test.*
Advantages of the new CDC HIV Diagnostic algorithm

- More Accurate Diagnosis of acute/early HIV-1 infection
- Equally accurate laboratory diagnosis of established HIV-1 infection
- More accurate laboratory diagnosis of HIV-2 infection
- Fewer indeterminate results
- Faster turnaround time for most test results
<table>
<thead>
<tr>
<th>Test</th>
<th>Number of Identified Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Architect Combo</td>
<td>29</td>
</tr>
<tr>
<td>Determine Combo</td>
<td>25</td>
</tr>
<tr>
<td>Genetic Systems</td>
<td>19</td>
</tr>
<tr>
<td>Multisport</td>
<td>11</td>
</tr>
<tr>
<td>Clearview Complete</td>
<td>8</td>
</tr>
<tr>
<td>Unigold Rec</td>
<td>8</td>
</tr>
<tr>
<td>Clearview Stat-Pak</td>
<td>7</td>
</tr>
<tr>
<td>Oraquick Advance</td>
<td>7</td>
</tr>
</tbody>
</table>

CDC Study: Early HIV screening

Number of identified cases (out of 33)
Performance of Tests Compared to Western Blot

AVERAGE DAYS BEFORE POSITIVE WESTERN BLOT

NAT

4th gen IA

3rd gen IA

Conventional antibody only rapid tests
Questions?