ABBOTT RAPID DIAGNOSTICS

Point of Care Technology – Why Knowing Now Matters in the ED

Ellis Jacobs, Ph.D., DABCC, FACB
Director, Scientific Affairs, Abbott Rapid Diagnostics
Adjunct Associate Professor of Pathology, Mount Sinai School of Medicine

ASCLS 2017 Northwest Medical Laboratory Symposium
Newport News, VA

20 | Apr | 2018

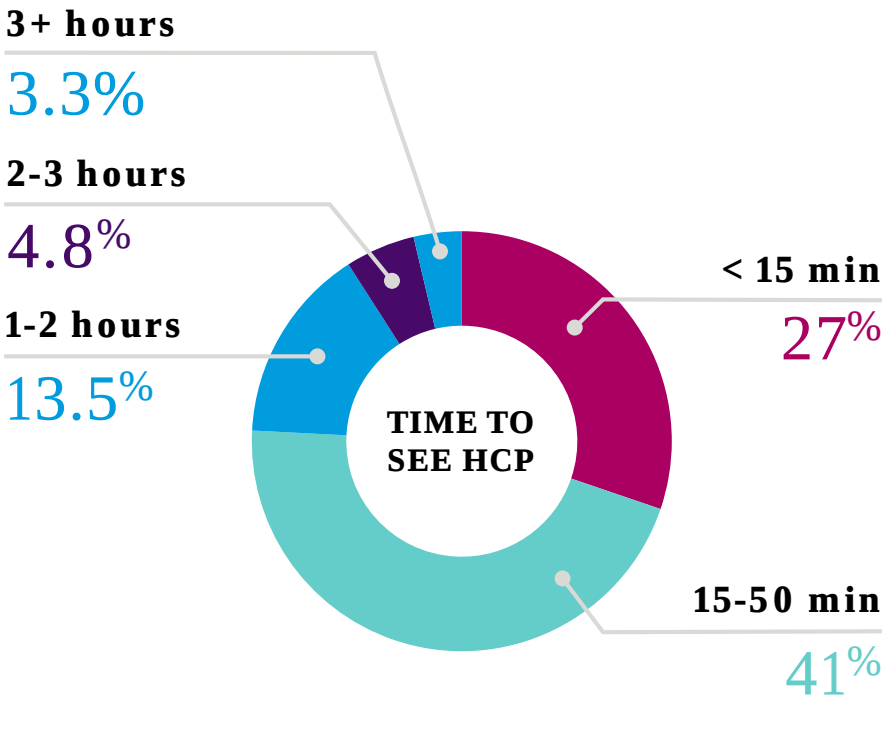
Agenda

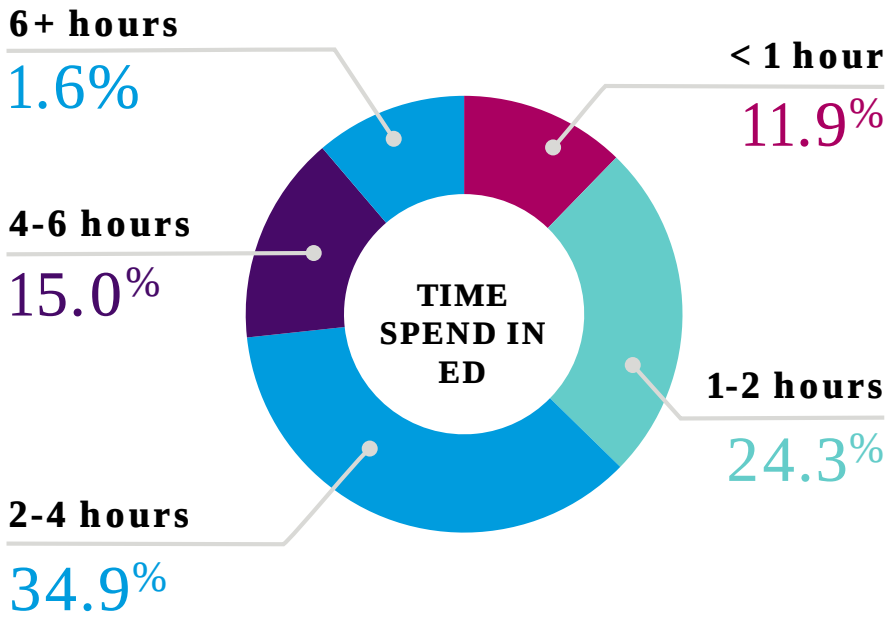
1. Emergency Department Facts and Figures
2. Why knowing now matters for Chest Pain
3. Why knowing now matters for Sepsis
4. Why knowing now matters for Infectious Disease

There are data in this presentation that are taken from individual published studies. They are individual evaluations and are not meant to replace or represent product claims which are found in the package inserts.

ED Stats: 2011

>136 MM ED visits = 44.5 visits/100 persons/year





http://www.cdc.gov/nchs/data/ahcd/nhamcs_emergency/2011_ed_web_tables.pdf

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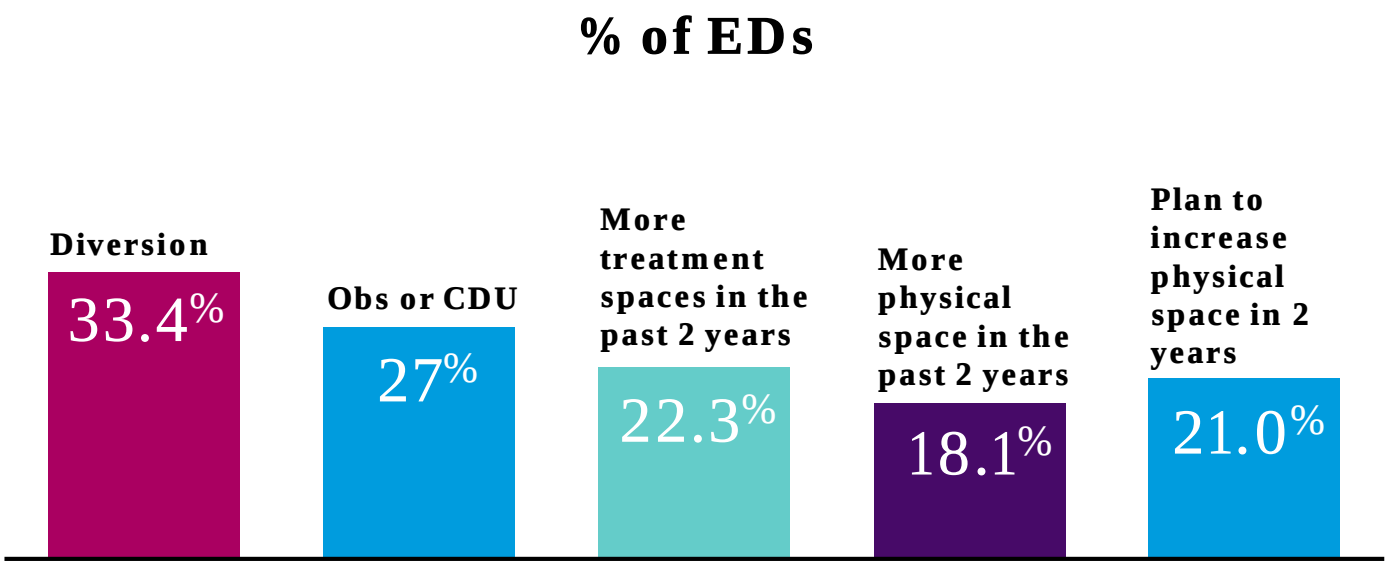


http://www.cdc.gov/nchs/data/ahcd/nhamcs_emergency/2011_ed_web_tables.pdf

ED: 2015

Approximately **three-quarters** of emergency room (ER) physicians **have seen increases** in patient visits since January 2014.

In addition to a national shortage of primary care doctors, experts cite a **lack of physicians willing to accept Medicaid patients** as contributing factors to increased ER usage.

7 in 10

survey respondents to a ACEP survey say **their emergency departments are not ready** for continuing, and potentially significant, increases in volume.

[1]USA Today 5/4/2015 http://www.usatoday.com/story/news/nation/2015/05/04/emergency-room-visits-rise-under-affordable-care-act/26625571/

Delay in the ED Leads to Poor Outcomes

71%-79%

higher likelihood of death
when ED length of stay
is greater than 6 hours[1]

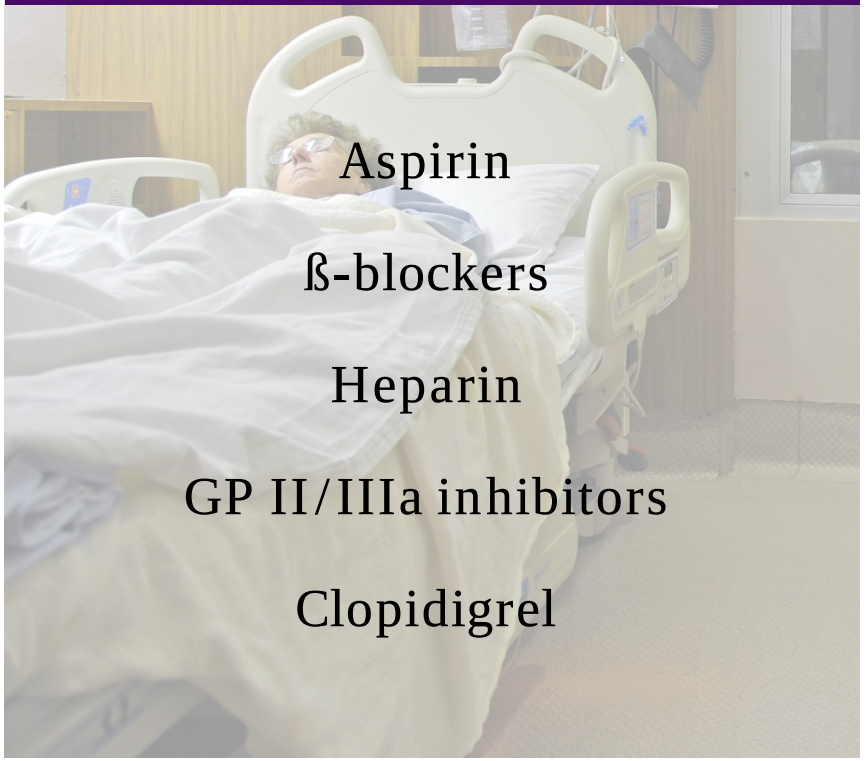
20% increase

in risk of death for every hour
an ED patient waits[2]

10% increase

In risk of death for a one hour increase
in overall length of ED stay[2]

Long ED stay leads to worse adherence to ACC/AHA guideline care for NSTEMI patients[3]

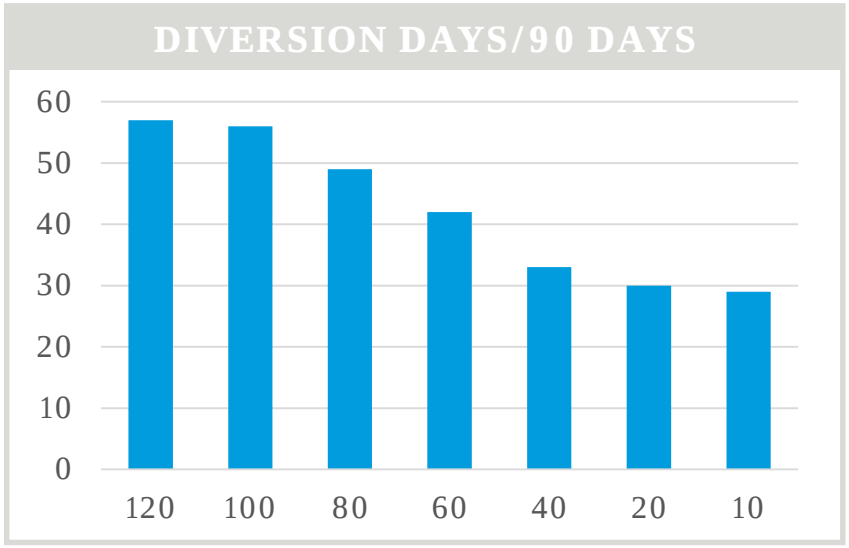


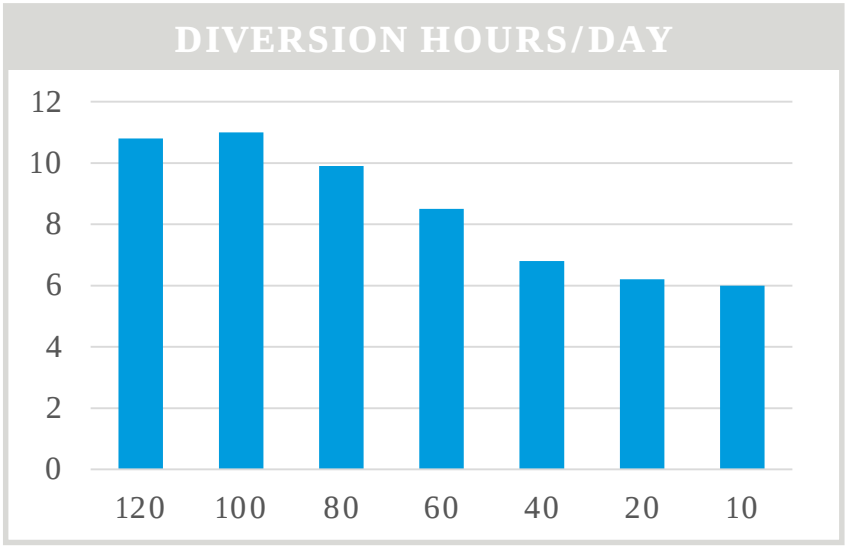
1.BMJ (2011) 342: d2983

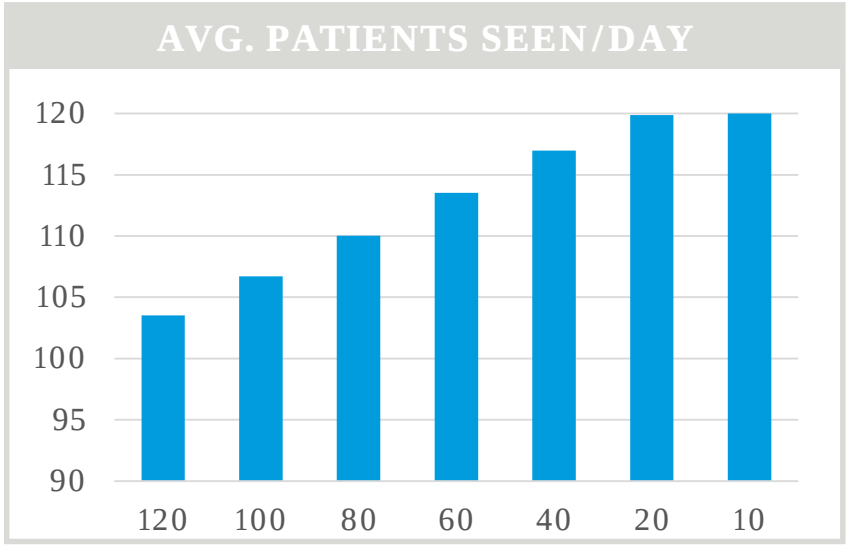
2 MJA (2006) 182: 208-212

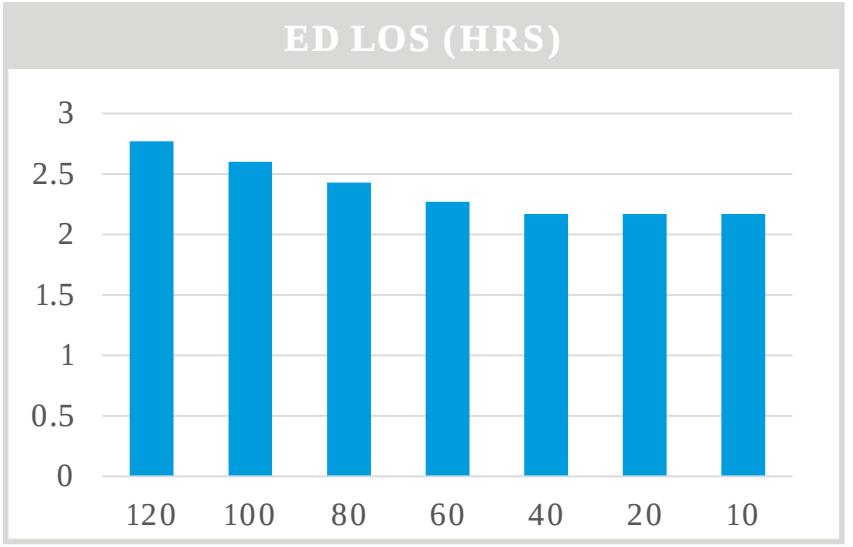
3 Ann Emerg Med. (2007); 50; 489-96

Theoretical TAT Impact on ED Operations





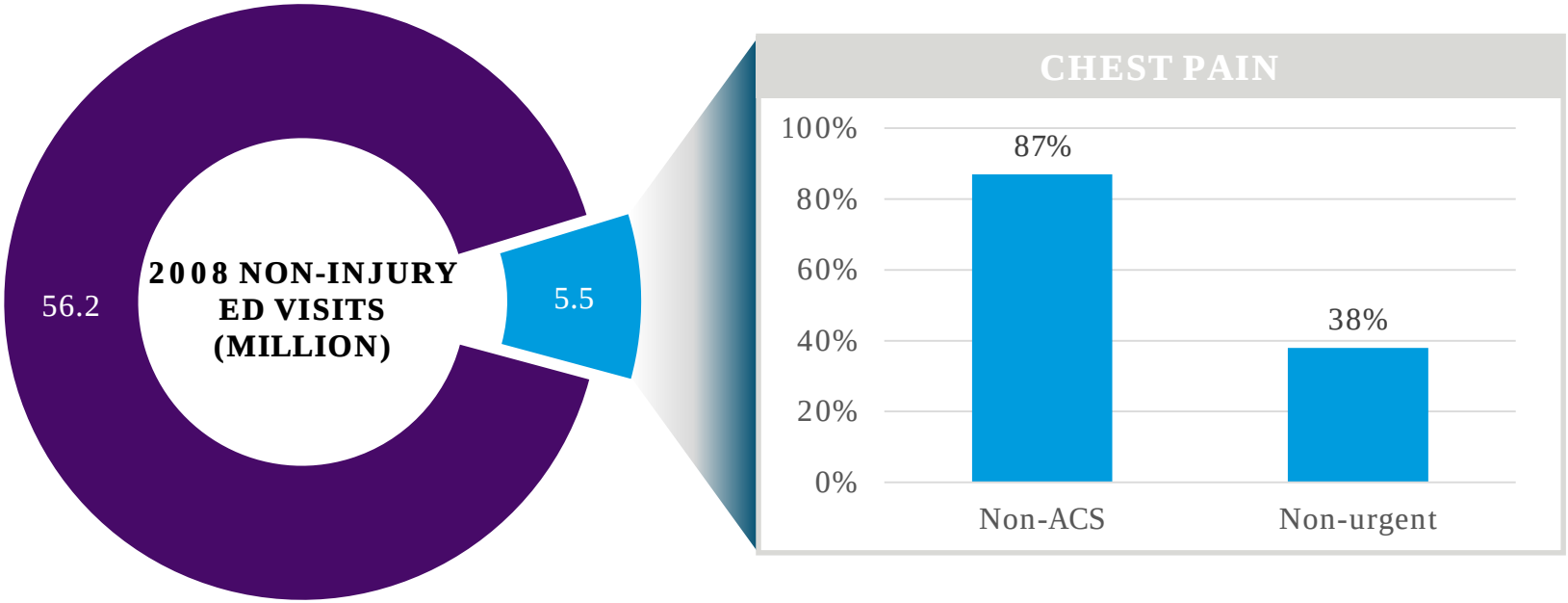




Storrow, AB *et, al,* Acad. Em Med (2008) 15:1130-1135

Why knowing now matters in the ED - Chest Pain

Challenges in Chest Pain Triage



For patients 45+ years old, non-specific chest pain is the most common ED presentation resulting in discharge

CDC NCHS Data Brief, No 43, September 2010
Weiss, AJ *et al* HCUP Statistical Brief #174, June 2014

Chest Pain Could Be....

Heart	Gastro-intestinal	Lung	Muscle/ Bone	Other
Heart attack	Acid reflux (heartburn)	Pneumonia	Bruised or broken ribs	Shingles
Angina	Swallowing problems related to disorders of the esophagus	Viral bronchitis	Sore muscles from exertion or chronic pain syndromes	Panic attack
Pericarditis	Gallstones or inflammation of the gallbladder or pancreas	Pneumothorax	Compression fracture, causing pressure on a nerve	
Myocarditis				
Cardiomyopathy				
Aortic dissection				

NSTEMIs Are Not Just Chest Pain

COMMONLY:

- Chest pain or discomfort
- Upper body discomfort
- Shortness of breath

BUT CONSIDER….

- Pain and discomfort could be mild, and could come and go over hours
- Diabetics may have no, or very mild, symptoms
- Cold sweat
- Nausea and vomiting
- Light-headedness or sudden dizziness

WOMEN:

- Feeling unusually tired for no reason, sometimes for days
- Pain in the back, shoulders, and jaw

Some NSTEMIs have no symptoms at all

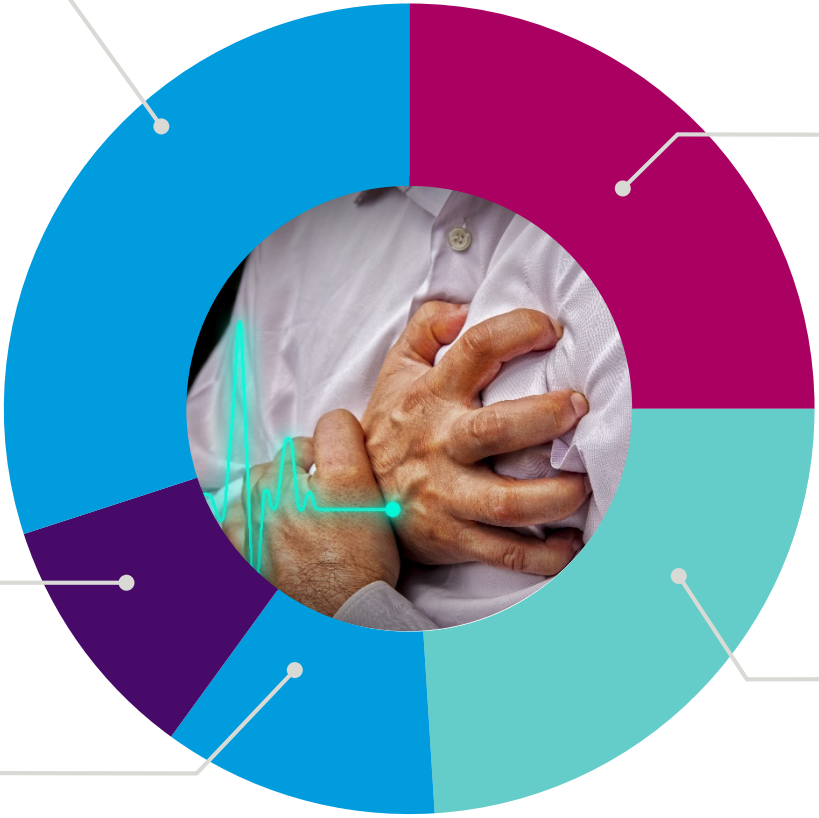
Chest Pain Patients Get to the ED Quickly

>10 hours

30%

< 2 hours

25%



6-10 hours

10%

2-3 hours

24%

4-6 hours

11%

McCord *et. al*. Circulation (2001) 104:1483-1488

OBSERVATION

DISCHARGE

ADMIT

CATH LAB

Universal Definition of MI

(Joint ESC/ACCF/AHA/WHF Task Force)

MI is:	Myocardial necrosis in a clinical setting consistent with myocardial ischemia

Rise and/or fall of cardiac biomarkers (preferably troponin) with at least one value above the 99th percentile with at least one of the following:

- Symptoms of ischemia
- New or presumed new significant ST-segment changes or new left bundle branch block
- Development of pathological Q waves in the ECG
- Imaging evidence: loss of myocardium or wall motion abnormality
- ID of intracoronary thrombus by angiography or autopsy

Cardiac death with symptoms of ischemia

PCI patients: Cardiac marker elevations of 5 x 99th percentile or rise of 20%

Stent thrombosis identified by angiography or autopsy

CABG patients: Cardiac marker elevations of 10 x 99th percentile

Thygesen. *et al* JACC (2012) 60:1581-1598

Important to Remember

A positive Tn is no longer an MI

A positive Tn means cardiac damage

- It could be an MI
- It could be something else…

Non-ACS/HF Tn Elevations

Cardiac and Vascular

- Acute aortic dissection
- Cerebrovascular accident
  - Ischemic stroke
  - Intracerebral hemorrhage
  - Subarachnoid hemorrhage

Respiratory

- Acute PE, ARDS

Muscular Damage

Cardiac Inflammation

- Endocarditis, Myocarditis, Pericarditis

Infectious

- Sepsis, Viral illness, Kawasaki disease. Apical ballooning syndrome. Thrombotic thrombocytopenic purpura, Rhabdomyolysis, Birth complications in infants (low birth weight, preterm)

Acute Complications of Inherited Disorders

- Neurofibromatosis, Duchenne muscular dystrophy, Klippel-Feil syndrome

Environmental Exposure

- Carbon monoxide, Hydrogen sulfide, Colchicine

Chronic Disease

- ESRD, Cardiac infiltrative disorders (Amyloidosis, Sarcoidosis, Hemochromatosis), Scleroderma, Hypertension, Diabetes, Hyperthyroidism

Iatrogenic Disease

- Invasive procedures (Heart transplant, Congenital defect repair, Lung resection, ERCP, RFCA)
- Noninvasive procedures (Cardioversion, Lithotripsy)
- Pharmacological sources (Chemotherapy, Other medications)

Myocardial Injury

- Blunt chest injury, Endurance athletes, Envenomation (Snake, Jellyfish, Spider, Centipede, Scorpion)

How to Best Use TnI Results

99th Percentile Value: Apparently healthy population, results are typically close to zero

AMI Cutoff: Value that determines if a patient is experiencing an AMI based on WHO criteria

Normal Range for the Assay

ANY value above the 99th percentile is abnormal and is now defined as an MI ***if accompanied with signs and symptoms of ischemia.***

AMI per WHO criteria

Serial draws are recommended to detect temporal rise and fall of troponin-I levels characteristic of MI, and should be used in conjunction with other information such as other cardiac markers, ECG, clinical symptoms, etc.

Compiled from multiple guidelines from ACC, AHA, ESC, and WHO

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The American College of Emergency Physicians (ACEP) Guidelines for Non-ST Elevation Chest Pain Patients

All patients

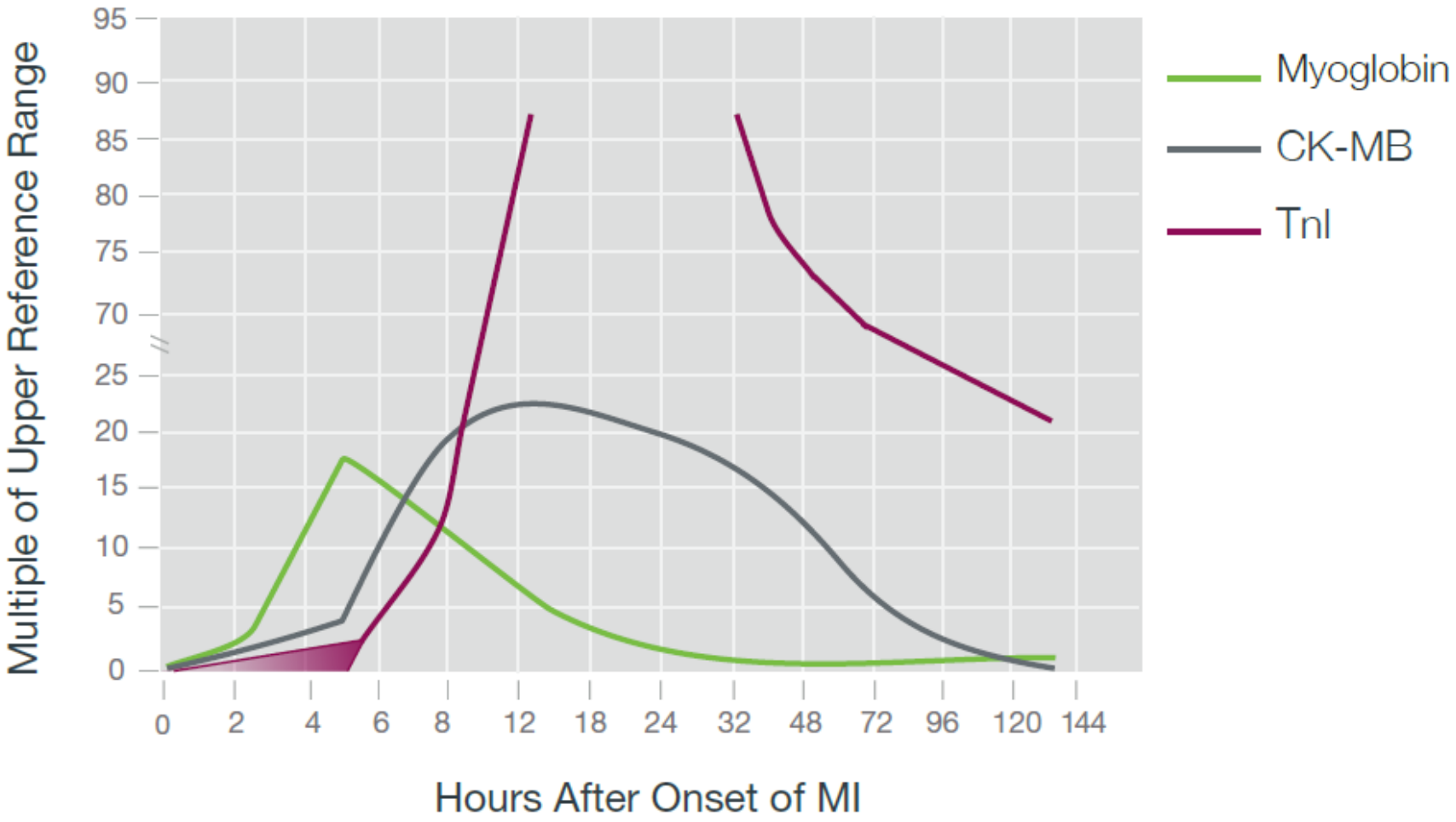
- No rule-in recommendation.
- For rule-out:
  A single negative CK-MB mass, Troponin I or Troponin T measured 8-12 hours after symptom onset.

Early presenters
(<6-8 hours after symptom onset)

- A negative myoglobin in conjunction with a negative CK-MB mass, or negative Troponin when measured at baseline and 90 minutes.
- A negative 2-hour delta CK-MB mass in conjunction with a negative 2-hour delta Troponin.

Fesmire *et al.* Ann Emerg Med (2006) 48:270-301

How to Best Use TnI Results



FOR DISCUSSION PURPOSES ONLY. *The temporal release patterns of modern troponin assays have not been conclusively established in the literature. Individual patients may exhibit unique cardiac marker profiles.*

Rapid Disposition Algorithm and Strategy

Data from three Dallas-area hospitals:

Medical Center of Arlington
~ one hour intervals

Plaza Medical Center
~ two-hour intervals

Medical City Dallas
~ three hour intervals

If any of the three criteria below were met, the patient was considered positive for an MI:

1. A TnI ≥ 0.4 ng/mL on any draw
2. A doubling of myoglobin between sequential draws with any detectable TnI by the last draw
3. A doubling of myoglobin between sequential draws with a 50% or greater increase in CK-MB without detectable TnI on any of the draws

Testing performed on the Alere Triage platform.

Straface , AL *et al* Am. J. Clin. Path. (2008) 129:788-795

	SINGLE DRAW		SERIAL DRAWS	
	0.05 ng/mL	0.4 ng/mL	0.05 ng/mL	0.4 ng/mL
Sensitivity (%)	79.7	57.4	97.3	68.2
Specificity (%)	96.1	99.8	95.0	99.8
Accuracy (%)	95.6	98.6	95.1	98.9
PPV (%)	37.2	87.6	36.4	89.4
NPV (%)	99.4	98.8	99.9	99.1

Straface , AL *et al* Am. J. Clin. Path. (2008) 129:788-795

Clinical Value of Rapid Disposition Algorithm

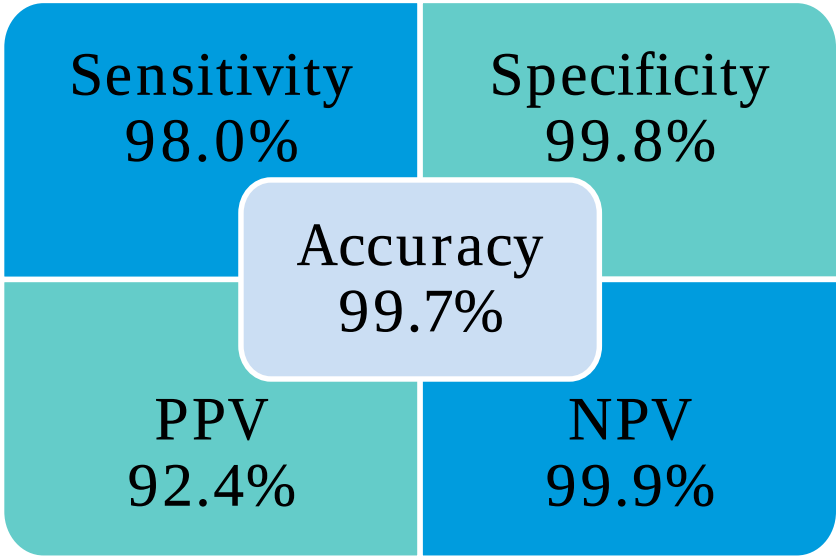
5,241
patients

30,087
test results generated

1.9
draws per patient

5.7
test results per patient

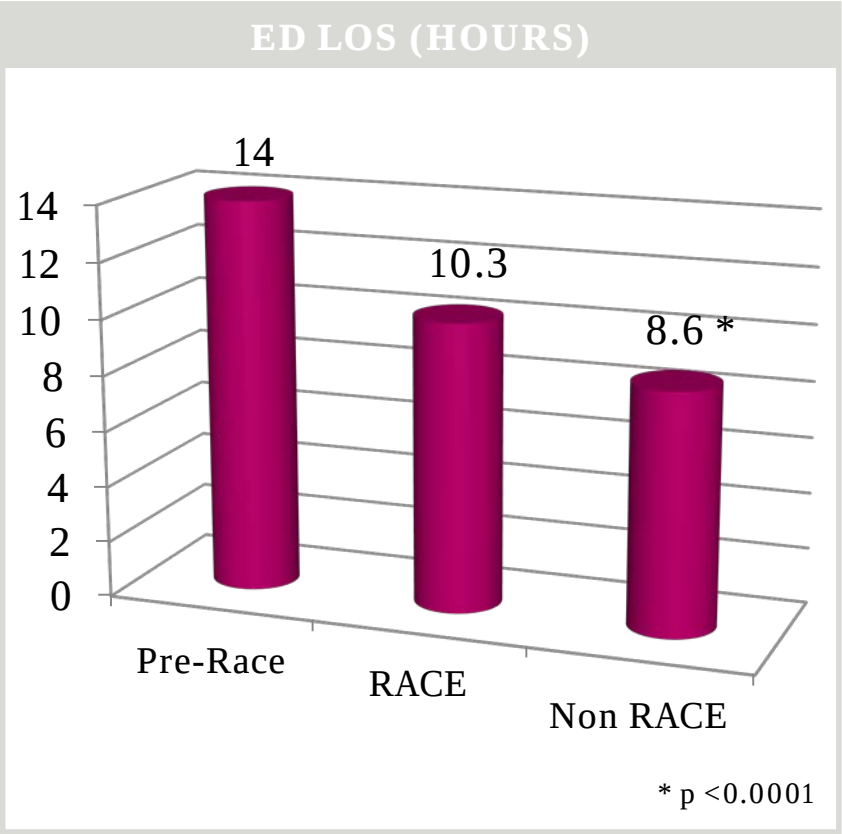
Non-diseased vs. Diseased diagnosis

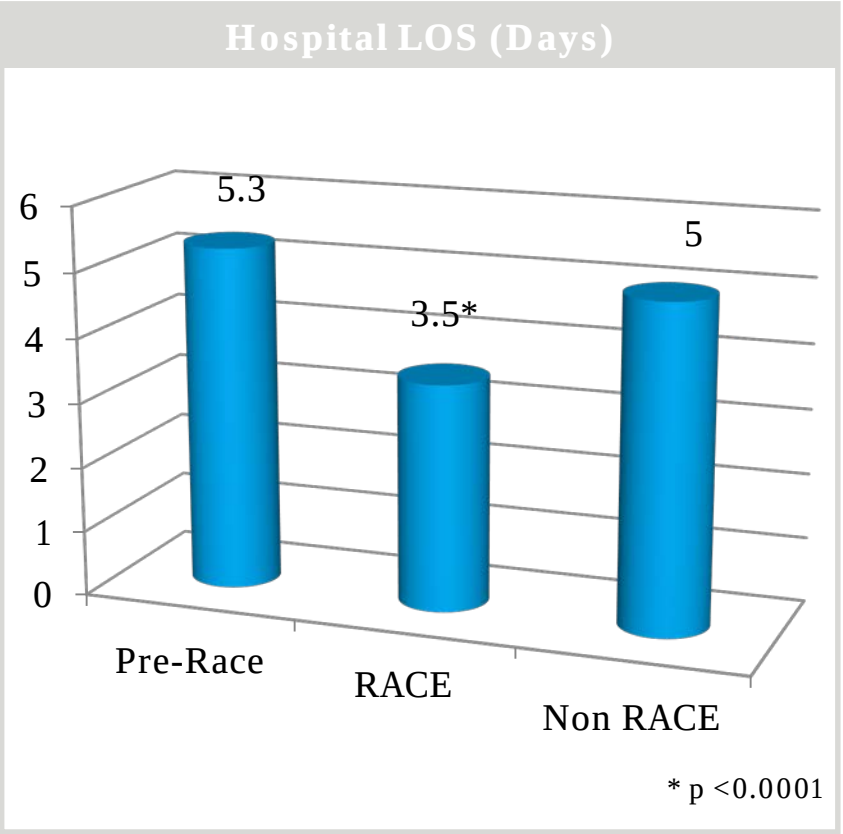


Panel Results		+	–	Total
	+	145	12	157
	–	3	5041	5044
	Total	148	5053	5201

Straface , AL *et al* Am. J. Clin. Path. (2008) 129:788-795

Improving Patient Flow in Acute Coronary Syndromes in the Face of Hospital Crowding



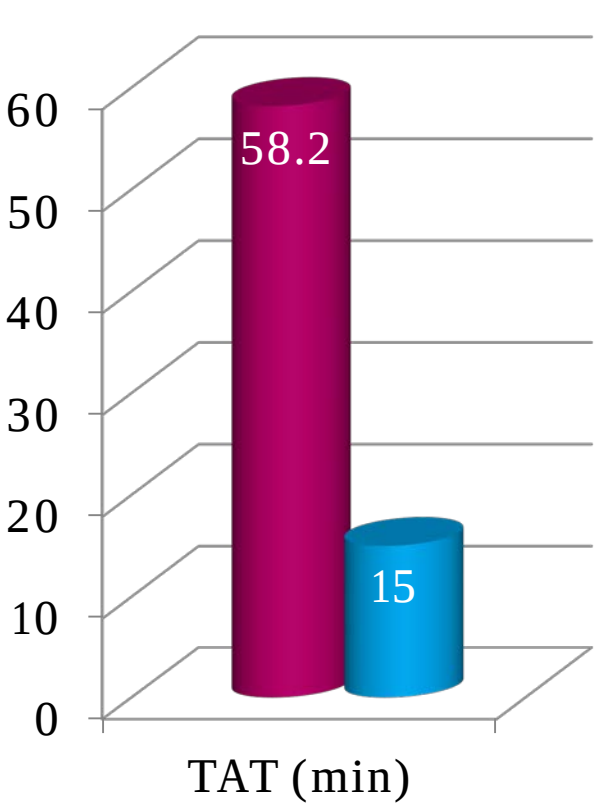


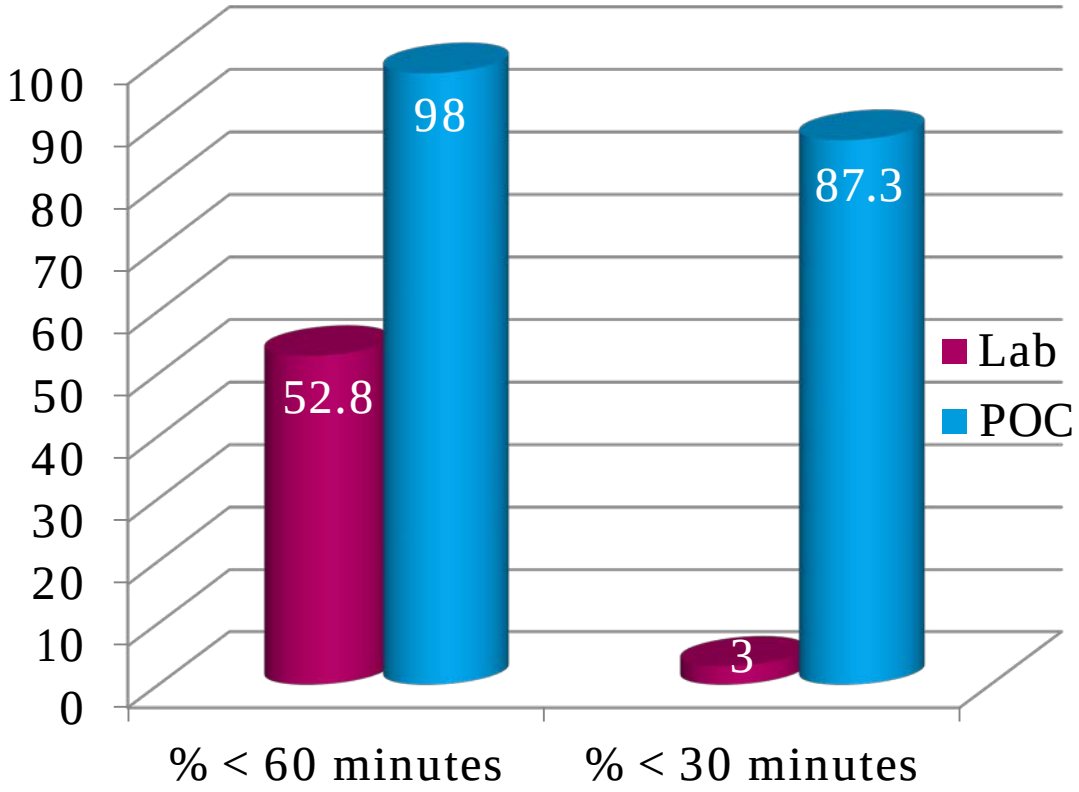
In the post-implementation period there was:

- 20% reduction in hospital LOS.
- 33% reduction in ED LOS
- 62% decrease (5% vs. 1.9%) in 30-day mortality

Birkhahn, RH, *et al*, J Em Med, (2012), 43:356–365

POCT Alone is Not Enough





Ryan, R.J. *et al*. Ann Em Med (2009), 53:321-328

Impact on ED Operations

	Admitted	Discharged
Disposition	↓ –7.8 minutes	↓ –20.4 minutes
Departure	↓ –9 minutes	↓ –7.2 minutes

Ryan, R.J. *et al*. Ann Em Med (2009), 53:321-328

Why knowing now matters in the ED - Sepsis

Definition of Sepsis

Systemic, deleterious host response to infection

- Presence (probable or documented) of infection together with systemic manifestations of infection which may include:

Fever
>38.3°C

or

Core temp
<36°C

HR >90/min or more than 2SD above normal for age

Altered Mental Status
and/or

Tachypnea

WBC count
>12,000/mm3 or
<4,000/mm3
or >10% immature forms

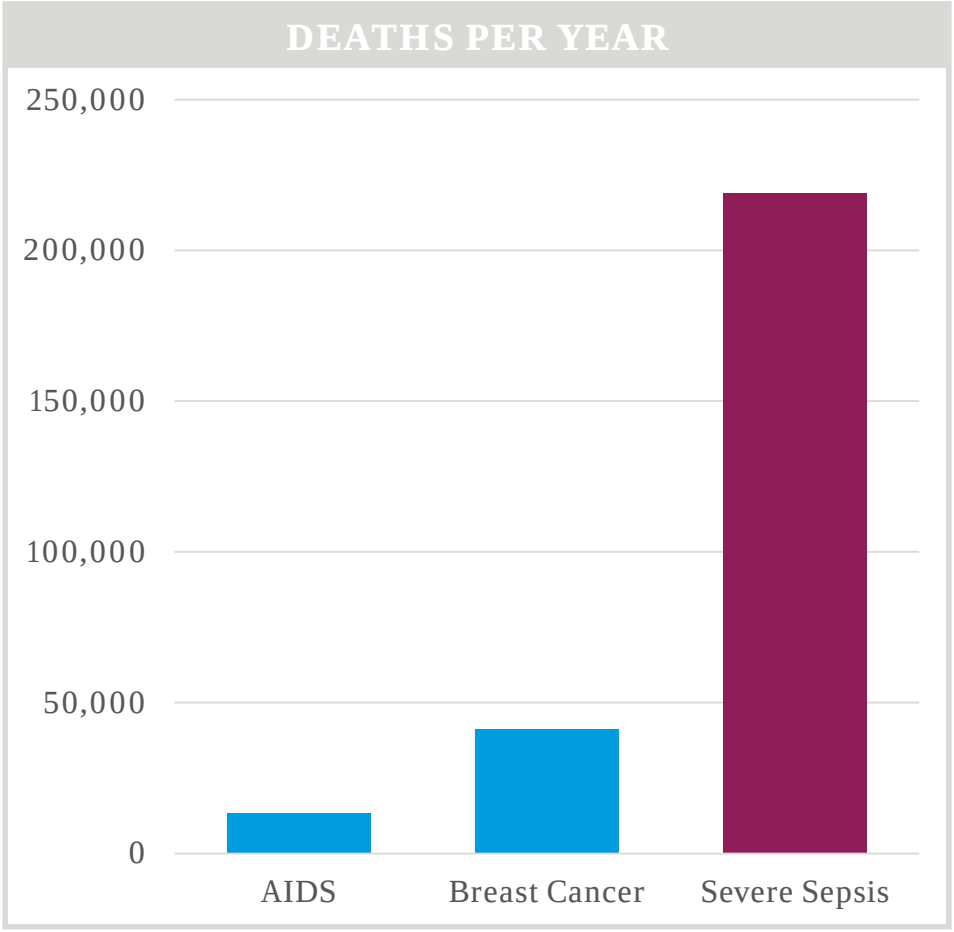
Hyperlactatemia
> 1mmol/L

Plasma Procalcitonin
more than 2SD above normal

Dellinger RP, *et al*. Crit Care Med. 2013;41:580-637.

Mortality Rates

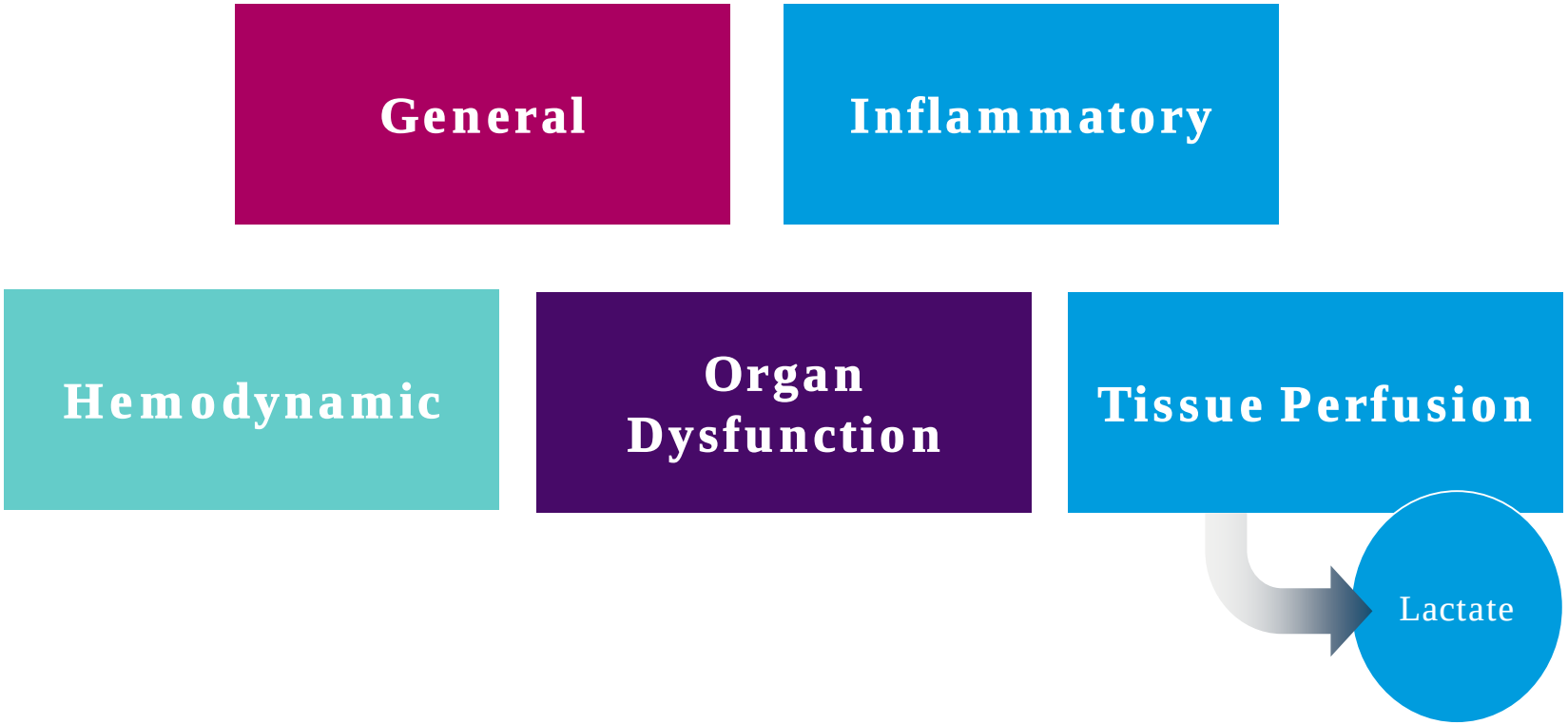
- Sepsis remains the leading cause of death in critically ill patients in the United States.
- Each year 750,000 people will develop sepsis.
- Leading non-cardiac cause of death in ICUs
- Mortality rates between 28-38%



NIH HIV AIDS Statistics, 2001.
Breast Cancer Figures 2005-2006
Angus DC, Linde-Zwirble WT, Lidicker J et al. Crit Care Med. (2001) 29:1303-10.

Diagnostic Criteria for Sepsis

Infection, documented or suspected, and some of the following:



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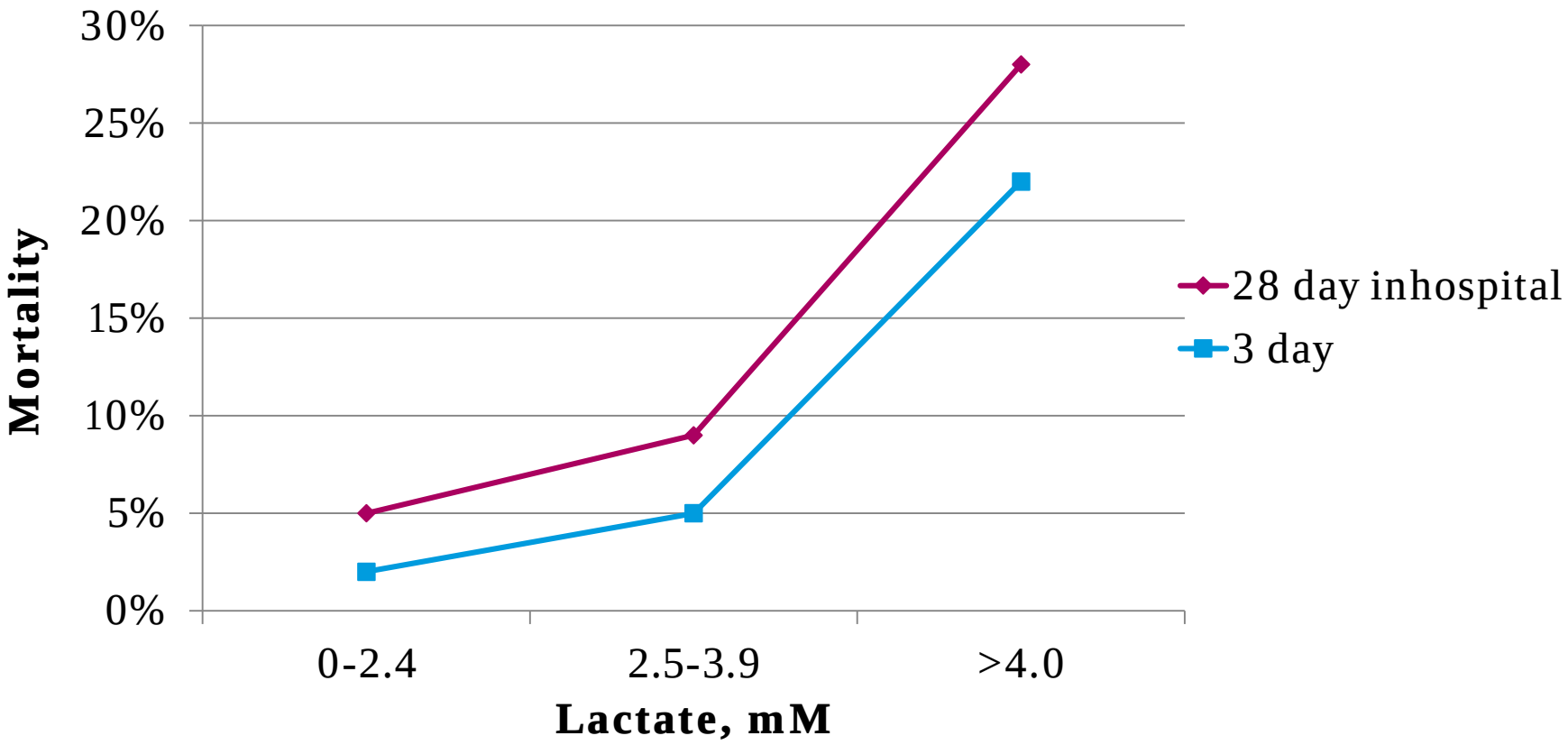
Lactate Predicts Mortality



Rooney and Schilling. Critical Care (2014) 18:692–399

Initial Resuscitation and Infection Issues - The Overall Goal

Protocolized resuscitation of patients with sepsis-induced hypoperfusion

- Hypotension after initial fluid challenge or
- Lactate > 4 mmol/L

6-hour goals

- CVP 8-12 mm Hg
- MAP > 65 mm Hg
- Urine output >0.5 mL* kg*hr
- $ScvO_2$ 70% or SvO_2 65%

Normalize an elevated lactate

Dellinger RP, *et al*. Crit Care Med. (2013) 41:580-637

Improve Patient Outcomes

Lactate clearance is associated with improved patient outcome.

Lactate measurement is associated with increased risk of death independent of other aspects of sepsis bundle guidelines.

Point-of-care measurements of lactate are faster than central laboratories.

- May be beneficial for serial measurements.

Nguyen HB, Rivers EP, Knoblich BP *et al*. Crit Care Med. (2004) 32:1637-42.
Afessa B, Keegan MT, Schramm GE *et al*. Crit Care Med. (2011) 15(Suppl 1): P286.
Boldt J, Kumle B, Suttner S *et al.* Acta Anaesthesiol Scand. *(*2001) 45:194–9.

Implementation of the Surviving Sepsis Protocols

15,775 patients at 252 participating Surviving Sepsis sites[1]

Unadjusted **hospital mortality decreased** from 37% to 30.8% over a 2-year period

[1]Intensive Care Med (2010) 36:222-231.

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33-month study period at Mayo-MN[2]

Bundle compliance rose from 12.7% to 52.7%

Mortality declined from 30.3% to 22%

[1]Intensive Care Med (2010) 36:222-231.
[2]. Crit Care Med (2011) 39:252-258,

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Medical City Plano (TX) evaluation[3]

Mortality in the non-bundle group: 61.1%

Mortality in the bundle group: 20%

[1]Intensive Care Med (2010) 36:222-231.
[2]. Crit Care Med (2011) 39:252-258,
[3]. Ann Pharmacother (2010) 44:1733-1738

Rapid Lactates for Septic Patients: CMS Core Measure

SEP-1: Early Management Bundle, Severe Sepsis/Septic Shock Specifications Manual for National Hospital Inpatient Quality Measures

Discharges 10-01-15 (4Q15) through 06-30-16 (2Q16) SEP-3

Severe Sepsis

Within 3 hours of presentation time, patient must have:

- Lactate drawn
- Blood cultures drawn
- Broad-spectrum antibiotics administered
- Within 6 hours of presentation time:
- Repeat lactate must be drawn if the initial lactate was >2.0 mmol/L

Septic Shock

Within 3 hours of presentation time, patient must have:

- Resuscitation with 30ml/kg of crystalloid fluid for hypotension or lactate ≥4 mmol /liter
- Within 6 hours of presentation time (and only if hypotension persists after fluid administration):
  - Vasopressors
  - Reassessment of volume status and tissue perfusion must be documented in the medical record

INITIATED ON OCTOBER 1, 2015

Point-of-Care Analyte Benefits

A 2010 study published in the Journal of Emergency Medicine found that point-of-care testing provided a reliable and feasible way to measure serum lactate at the bedside.[1]

Point-of-care lactate is useful in the diagnosis of sepsis at the bedside

- Recommended for institutions where clinical decisions are limited by lack of laboratory infrastructure or reliability.[2]

[1]Shapiro NI, Fisher C, Donnino M *et al.* J Emerg Med. (2010) 39:89-94.
[2]Moore CC, Jacob ST, Pinkerton R *et al*. Clin Infect Dis. (2008) 46:215-22.

Turnaround Time

- Serum lactate must be available with rapid turnaround time (within minutes) to effectively treat severely septic patients.
- An arterial blood gas analyzer located in the clinical laboratories usually accomplishes this.
- Hospitals should invest in adequate equipment in to meet present standards of care for septic patients.

http://www.survivingsepsis.org/SiteCollectionDocuments/SSC-Implementation-Guide.pdf

Don’t Forget Creatinine

Prior to any imaging procedure that requires the use of a contrast dye, an measurement of creatinine levels is required to confirm kidney function.

POC creatinine can play a key role in these diagnostic pathways.

Why knowing now matters in the ED - Infectious Diseases

Advantages of Rapid Testing for Infectious Diseases

Better directed therapy to reduce

- antibiotic resistant
- hospital length-of-stay

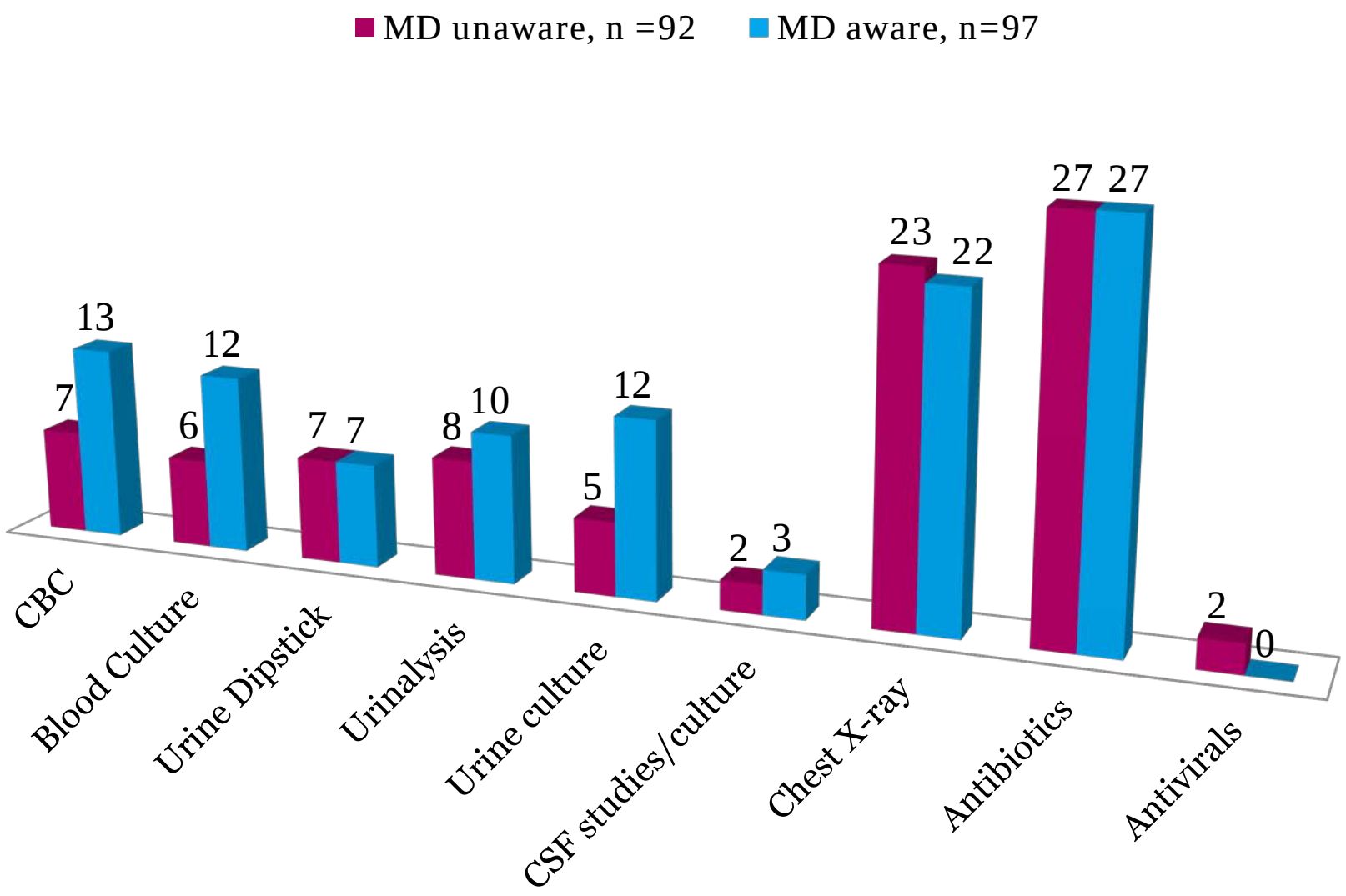
Less adverse consequences

Reduced length-of-stay in emergency department

Timely application of appropriate Infection control procedures

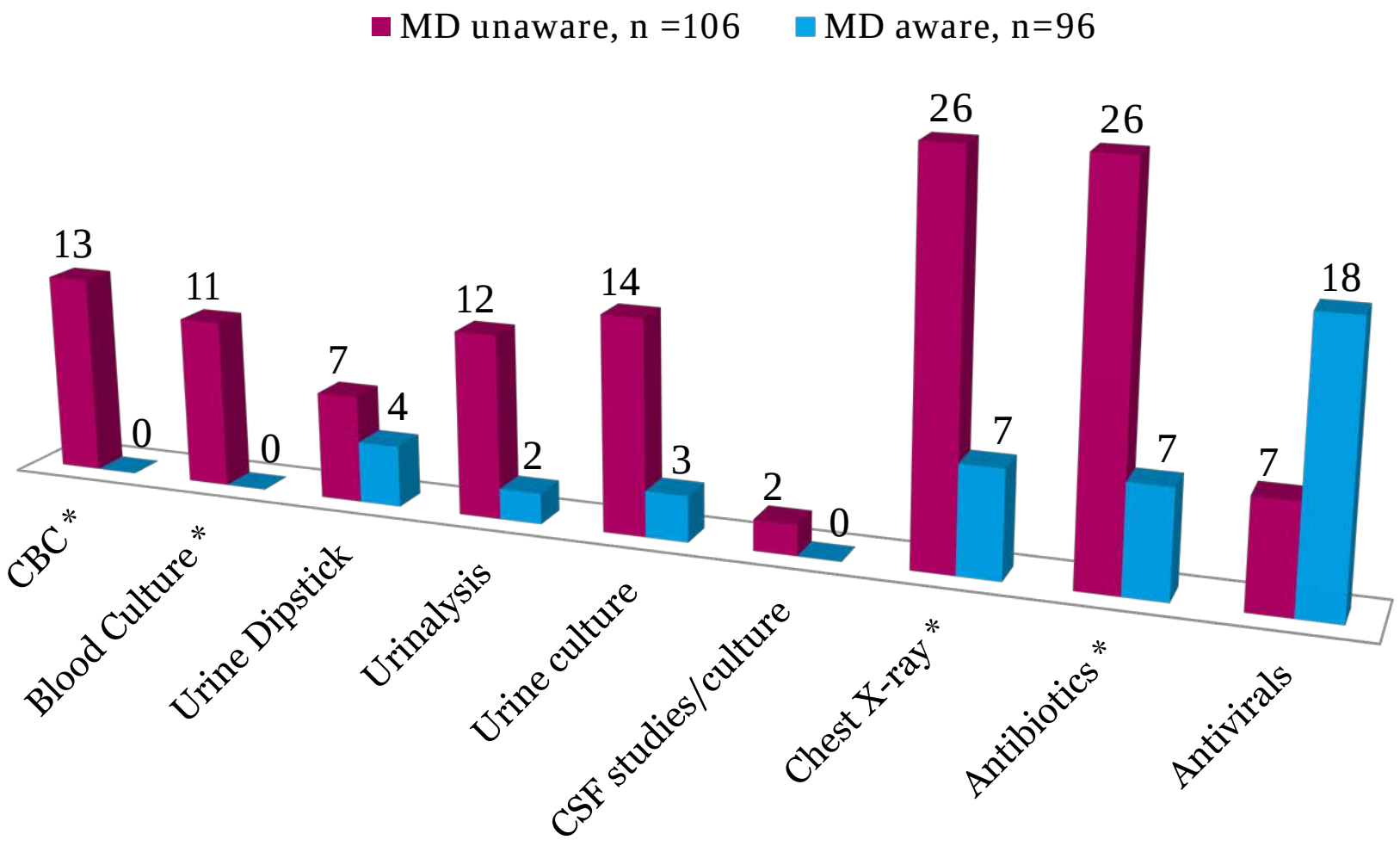
Teachable moment

Results – Flu Negative



Bonner, *et al,* Pediatrics (2003) 112:363-367

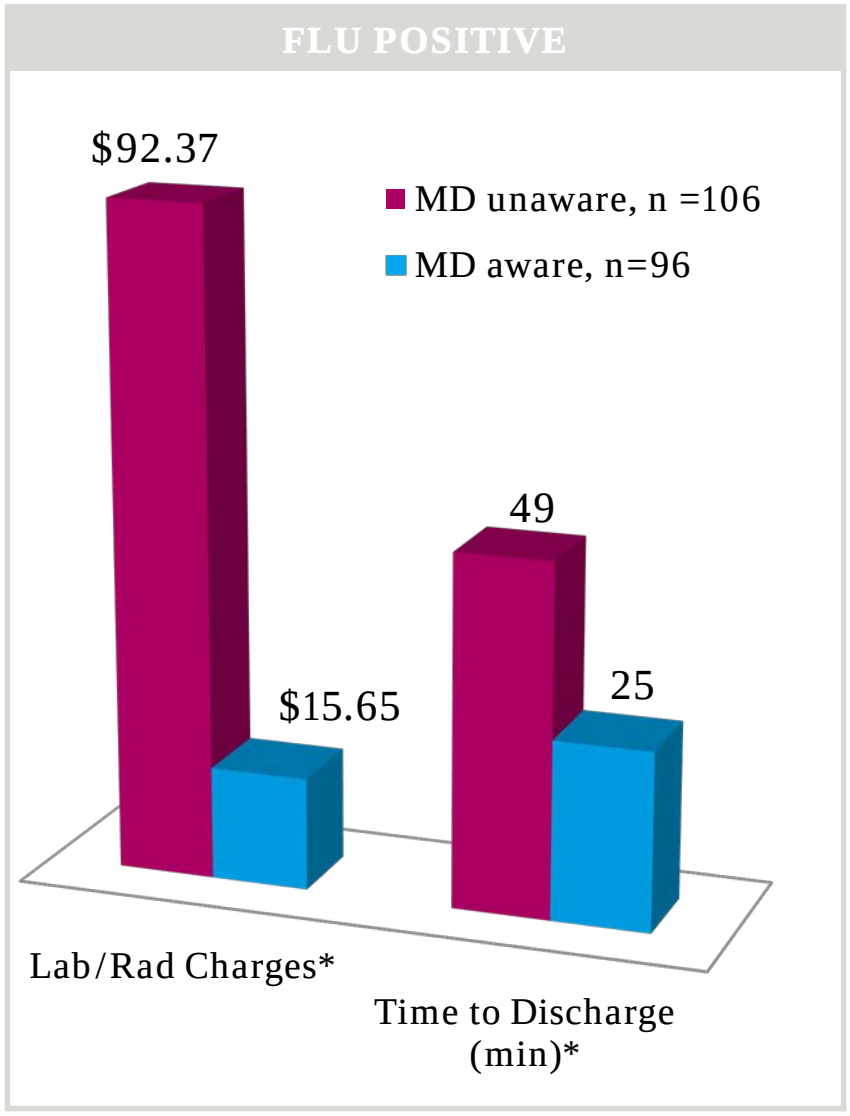
Results – Flu Positive

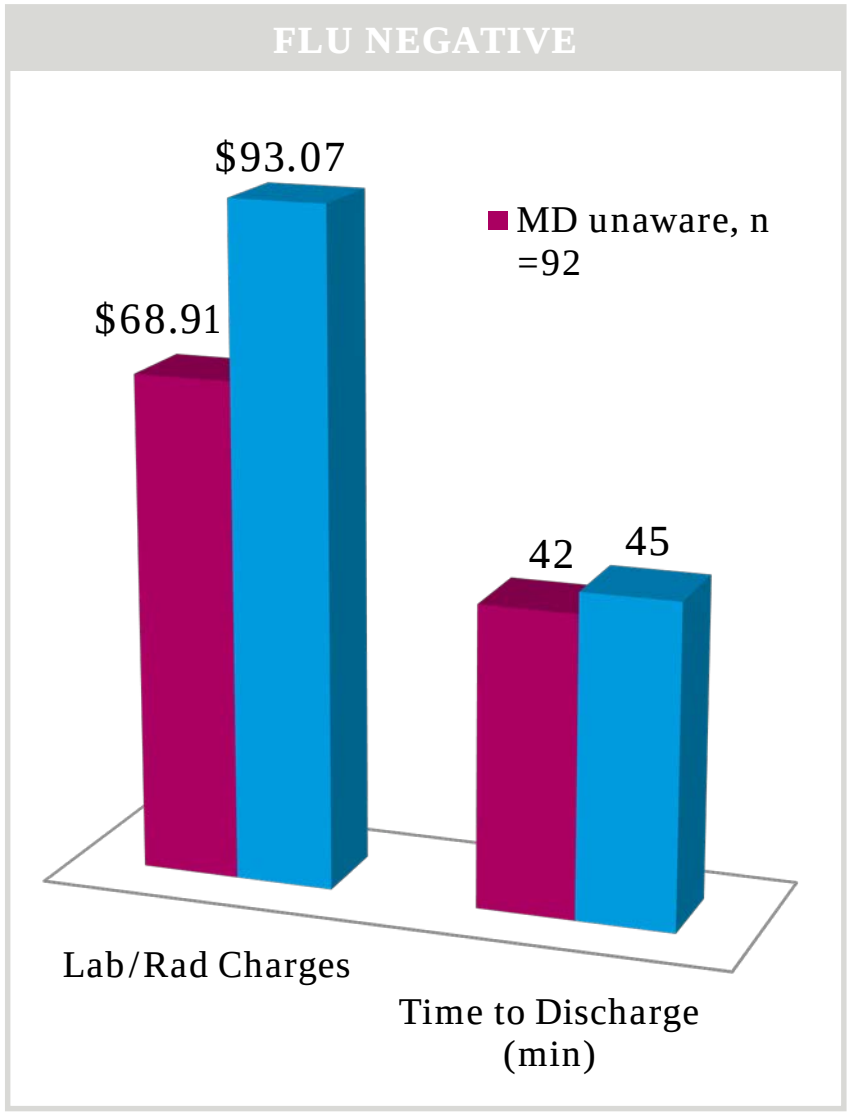


* - p ≤ 0.001

Bonner, *et al,* Pediatrics (2003) 112:363-367

Key Operational Metrics





* $p \leq 0.001$

Bonner, et al, Pediatrics (2003) 112:363-367

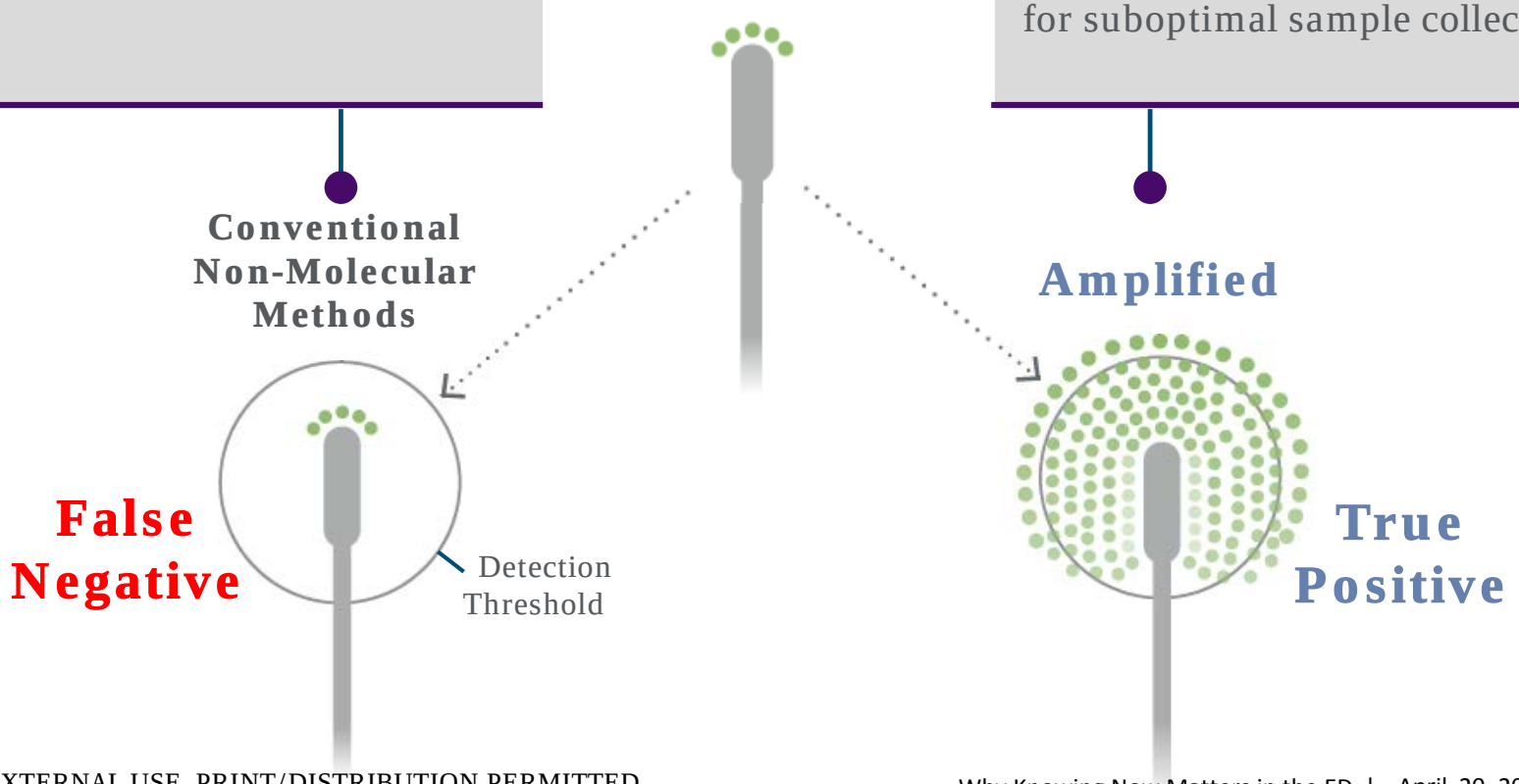
Why molecular?
The power of sample amplification

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.



Flu Clinical Trial Results: vs PCR

Alere™ i Influenza A & B against RT-PCR for Influenza A

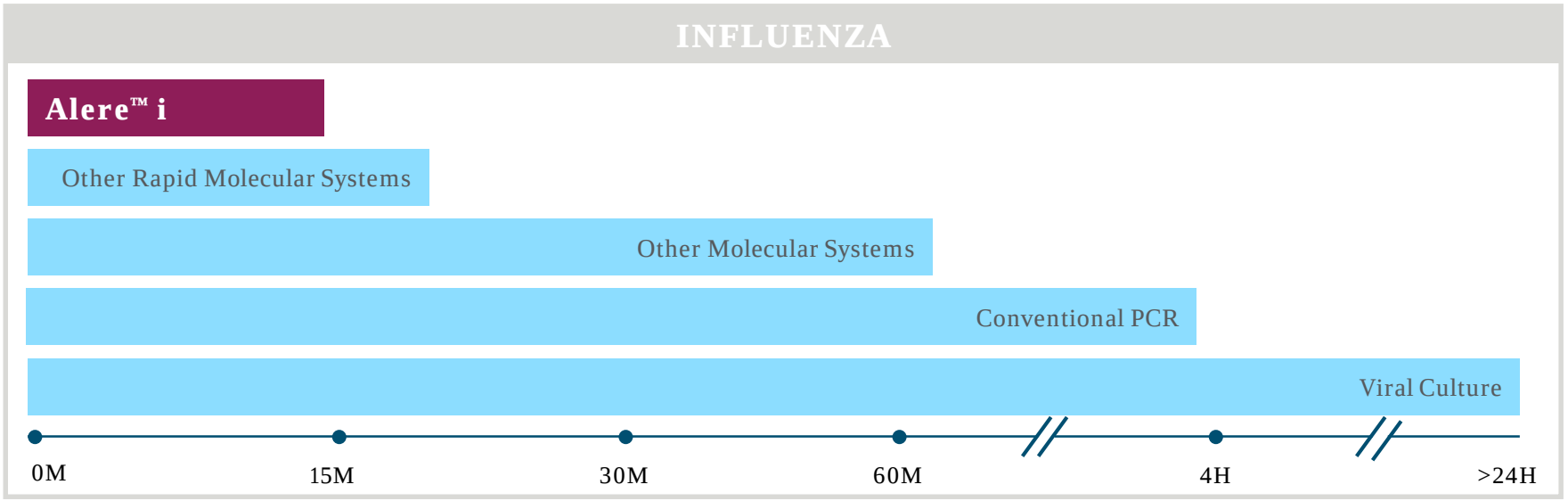
Alere™ i Influenza A & B – Flu A	RT-PCR		
	Positive	Negative	Total
Positive	147	11	158
Negative	8	464	472
Total	155	475	630
Positive Percent Agreement: 147/155	**94.8%**	(95%CI: 90.1%–97.4%)	
Negative Percent Agreement: 464/475	**97.7%**	(95%CI: 95.9%–98.7%)	

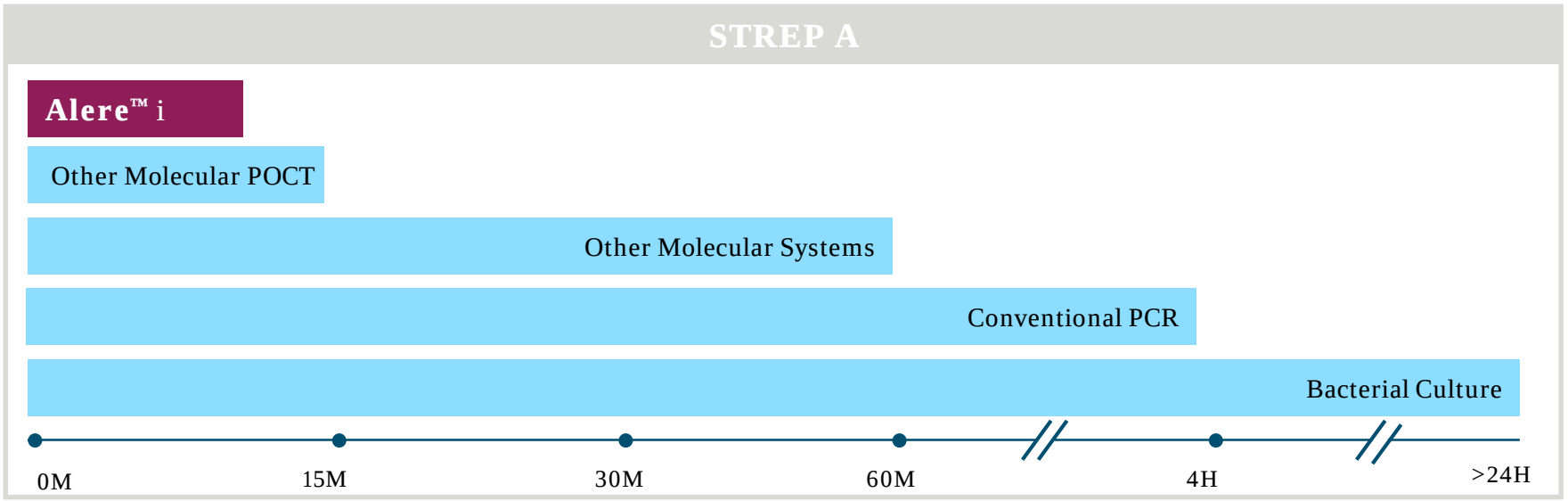
Alere™ i Influenza A & B against RT-PCR for Influenza B

Alere™ i Influenza A & B – Flu B	RT-PCR		
	Positive	Negative	Total
Positive	123	3	126
Negative	2	500	502
Total	125	503	628
Positive Percent Agreement: 123/125	**98.4%**	(95%CI: 94.4%–99.6%)	
Negative Percent Agreement: 500/503	**99.4%**	(95%CI: 98.3%–99.8%)	

Alere™ i Influenza A & B package insert

Every Minute Counts at the Point of Care





Why Test?

Knowledge of a Positive Test Has Been Shown to:

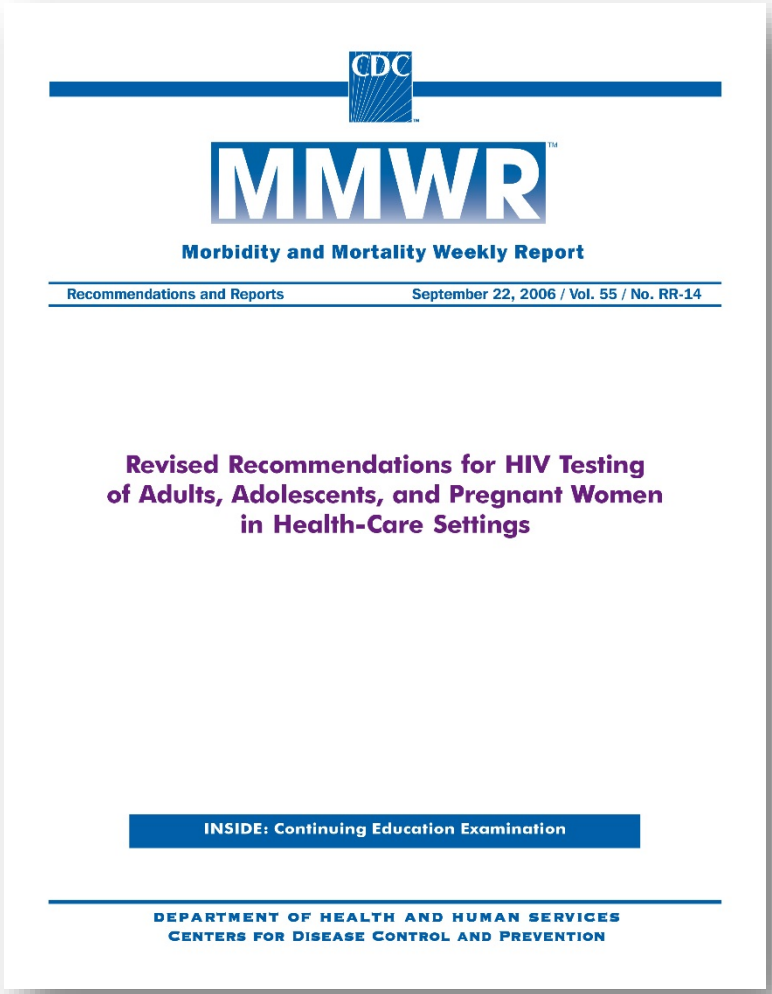
Limit unnecessary antibiotic use

Limit unnecessary diagnostic procedures

Increase the appropriate use of antivirals

Alere™ i is *significantly faster* than other molecular methods and more accurate than conventional rapid testing giving you the *confidence* to make effective *patient management decisions sooner.*

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**

Centers for Disease Control and Prevention. MMWR 2006;55(No. RR-14)

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)

Ann Emerg Med. (2014) 64:563

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

Benefits of Early Diagnosis of HIV Infection

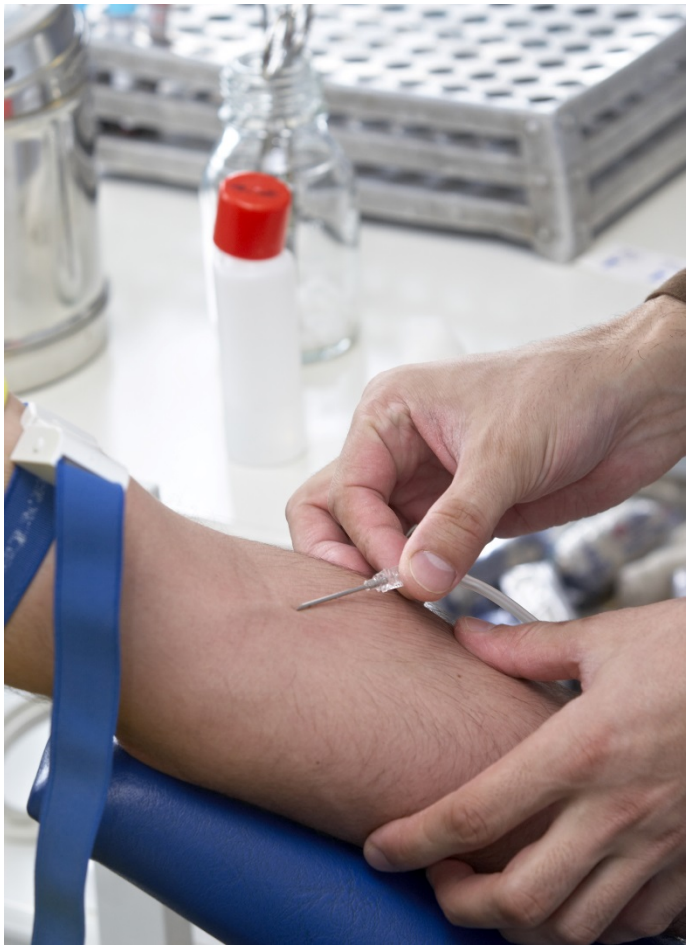
Reduction of high-risk behavior[1]

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



[1]Marks G, *et al.* JAIDS (2005) 39:446-453

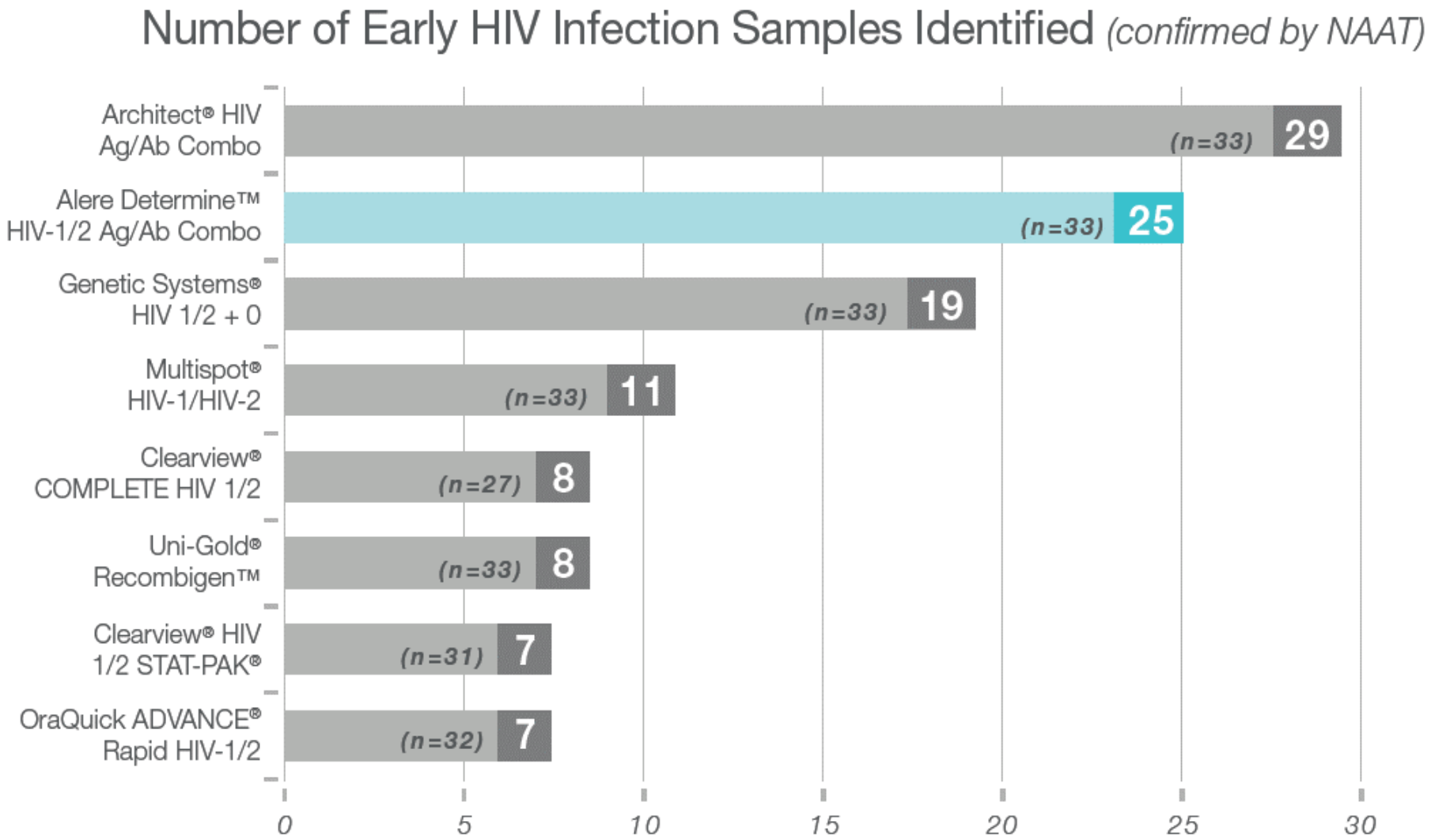
[2]Pinkerton, S.D. AIDS Behav. (2008 September) 12: 677–684. doi:10.1007/s10461-007-9329-1.

[3]Moyer VA, *et al.* Ann Intern Med. (2013) 159:51-60.

[4]CDC. MMWR (2011) ;60(47):1618–23.

[5]Starting antiretroviral treatment early improves outcomes for HIV infected individuals. http://www.nih.gov/news/health/may2015/niaid-27.htm

Performance of Alere Determine™ HIV-1/2 Ag/Ab Combo



Patel *et al* J. Clin Virol (2012) 54: 42-47

Is POCT in the ED Cost Effective?

Is POCT Cost Effective?

Review article covering the value of POCT for:

ACS	VTE	Sepsis	Stroke

> *With respect to the numerous manual steps to be performed in transferring a blood sample to the central laboratory and to retrieve the results consecutively, the total costs of POCT devices tend not to exceed those of central analysis.*

POC staff do need to learn how to operate the POCT, but expediting patient flow might reduce the strain on this staff.

> *When used effectively and in the appropriate context, POCT has been shown to reduce delays to treatment initiation in the critically ill, improve outcomes, increase timely patient discharge rates, and decrease total length of stay. Elevated costs of POCT per analysis seem to be outweighed by the total gain of expedited patient flow in the appropriate setting.*

Rooney and Schilling, *Critical Care* (2014), 18:692-699

Questions?

ellis.jacobs@alere.com

Abbott