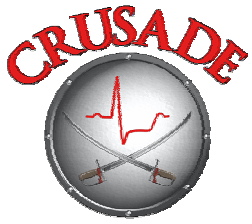


Is there a need for speed?

Robert H. Christenson, Ph.D., DABCC, FACB
Professor of Pathology
Professor of Medical and Research Technology
University of Maryland School of Medicine

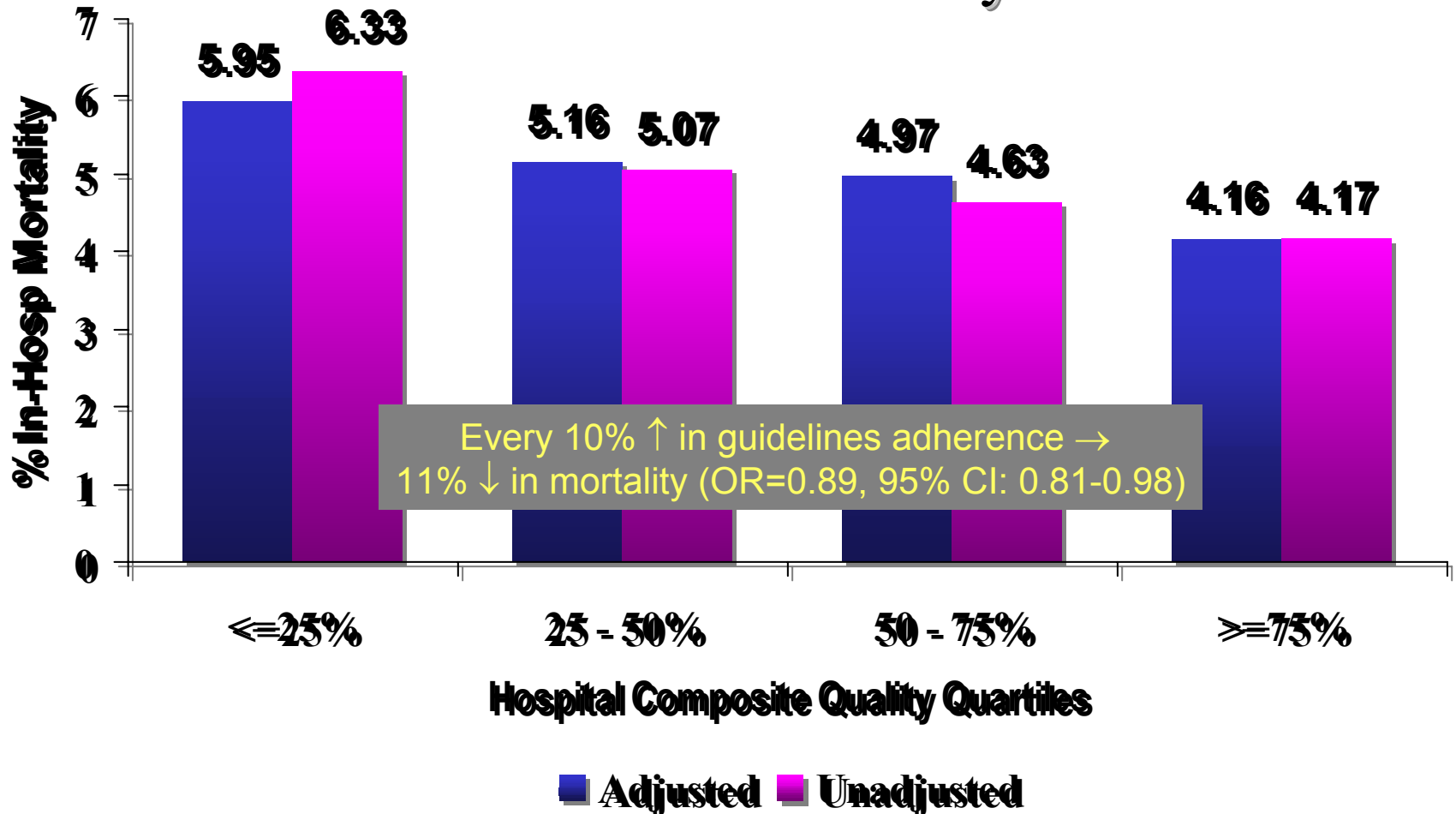
NACB Cardiac Markers POC Subcommittee

- Robert H. Christenson, Ph.D., Chair
- Show-Hong Duh, Ph.D.
- Alan B. Storrow, M.D.
- Howard J. Kirchick, Ph.D.
- Gregory W. Shipp, M.D.



Adherence to Guidelines Is Important!

Link Between Overall Guidelines Adherence and Mortality



National Academy of Clinical
Biochemistry-*Laboratory Medicine*
Practice Guidelines



Biomarkers of Acute
Coronary Syndrome and
Heart Failure

ACC/AHA Recommendation Classes

I	IIa	IIb	III
X			
	X		
		X	
			X

Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective.

Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment. **Weight of evidence/opinion is in favor of usefulness/efficacy.**

Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment. **Usefulness/efficacy is less well established by evidence/opinion.**

Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective and in some cases may be harmful.

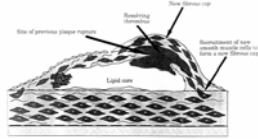
Weighing the Evidence

- Weight of evidence grades
 - A = Data from many large, randomized trials
 - B = Data from fewer, smaller randomized trials, careful analyses of nonrandomized studies, observational registries
 - C = Expert consensus

Overview

AGE →

Fatty streaks →



→ **Plaque Accumulation**

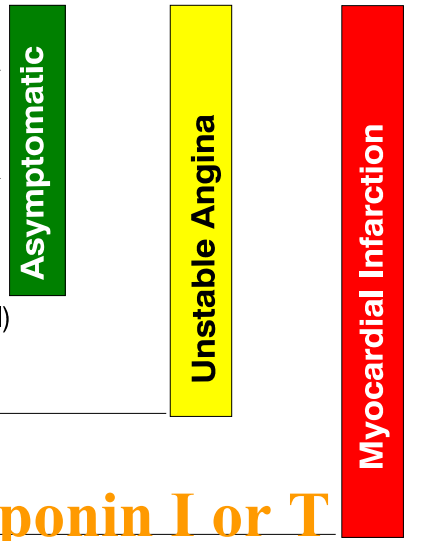
Acute Coronary Syndromes

Heart Failure

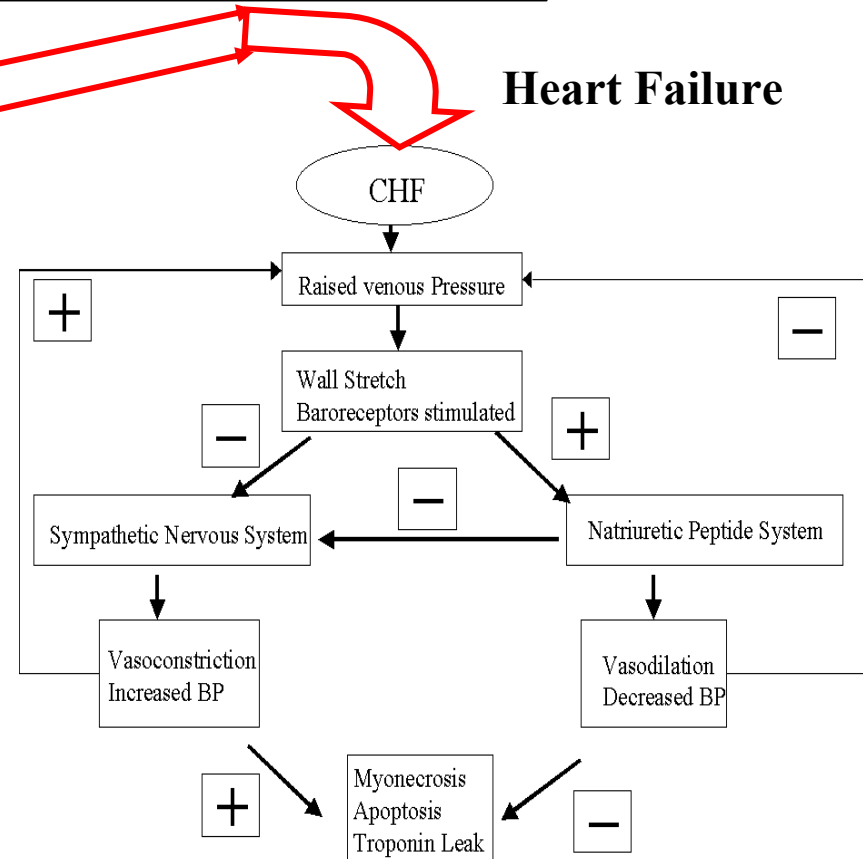
Pathophysiology



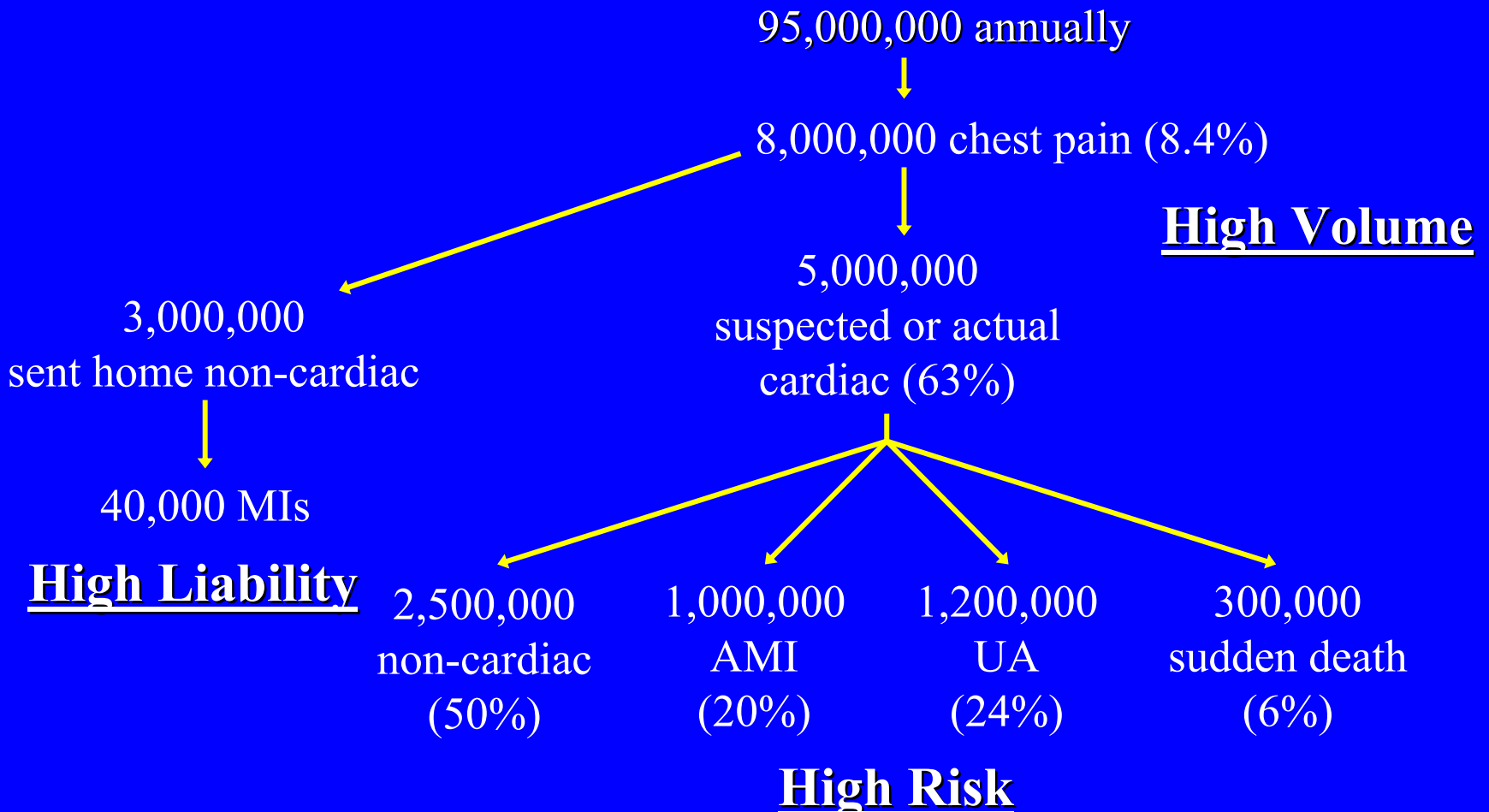
- Plaque Rupture**
- ↓ amyloid A protein
C-reactive protein
- Intracoronary Thrombosis**
- ↓ soluble fibrin
P-selectin
- Reduced Blood Flow**
- ↓ perfusion imaging (MIBI)
angiography
- Myocardial Ischemia**
- ↓ electrocardiogram
echo / MIBI with gating
- Myocardial Necrosis**
- ↓ markers of necrosis



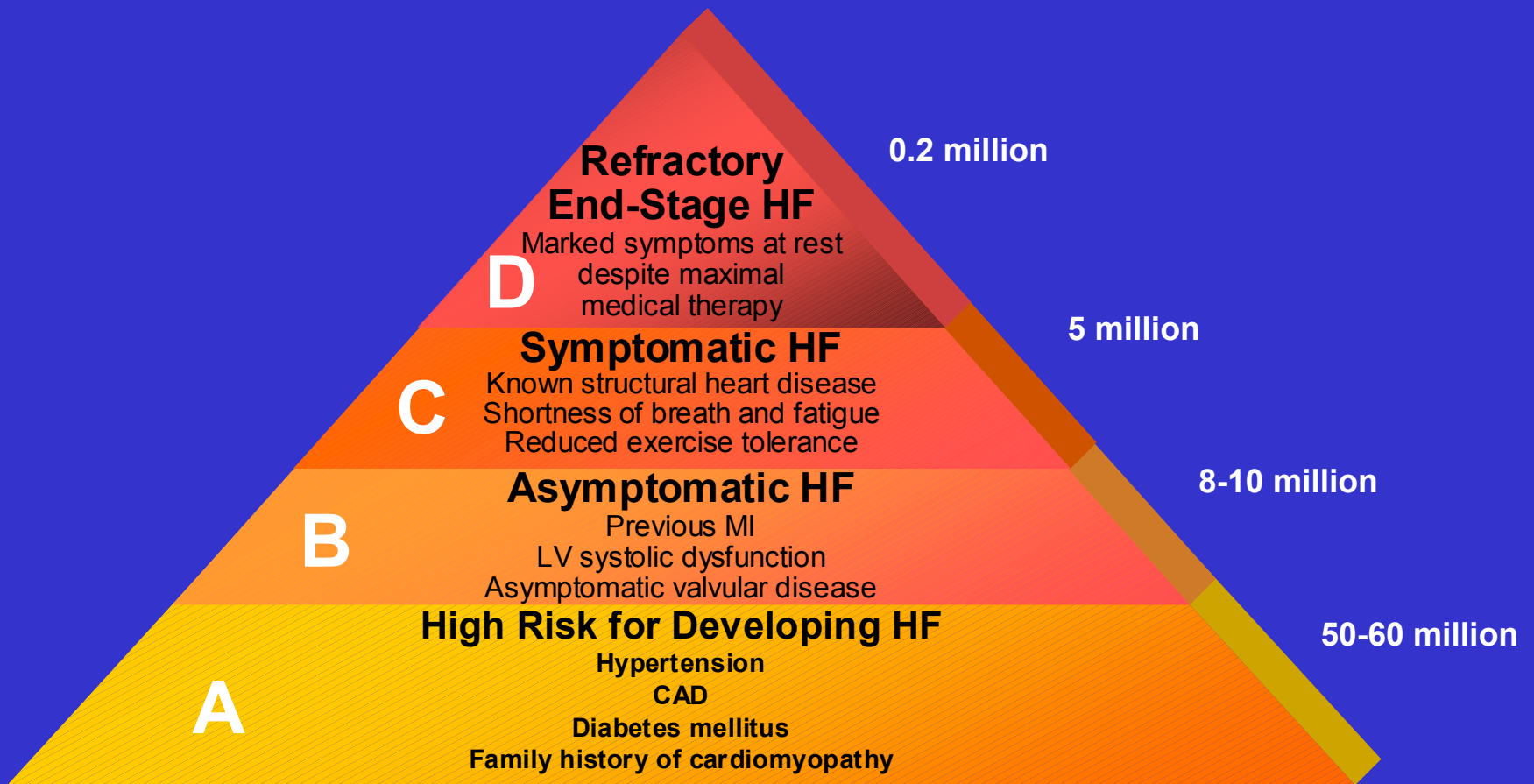
Troponin I or T
Clinical Diagnosis



ED Visits - United States



Scope of the Heart Failure Problem



Heart Failure is Huge Healthcare Issue

- Most common discharge Dx in patients > 65 years
- 400,000 - 700,000 new cases yearly
- 10% of individuals over 65 years
- 4.7 million patients
- 50% of patients are symptomatic
- 11 million office visits each year
- 3.5 million hospitalizations
- 250,000 deaths
- Cost exceeds 56 billion dollars



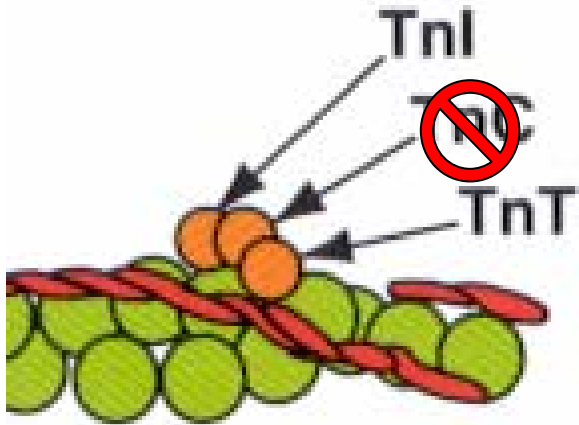
Troponin
CK-MB
Myoglobin



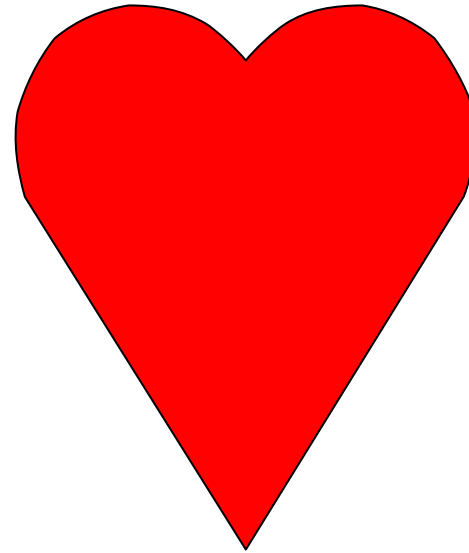
Natriuretic
Peptides

When troponin is increased think heart

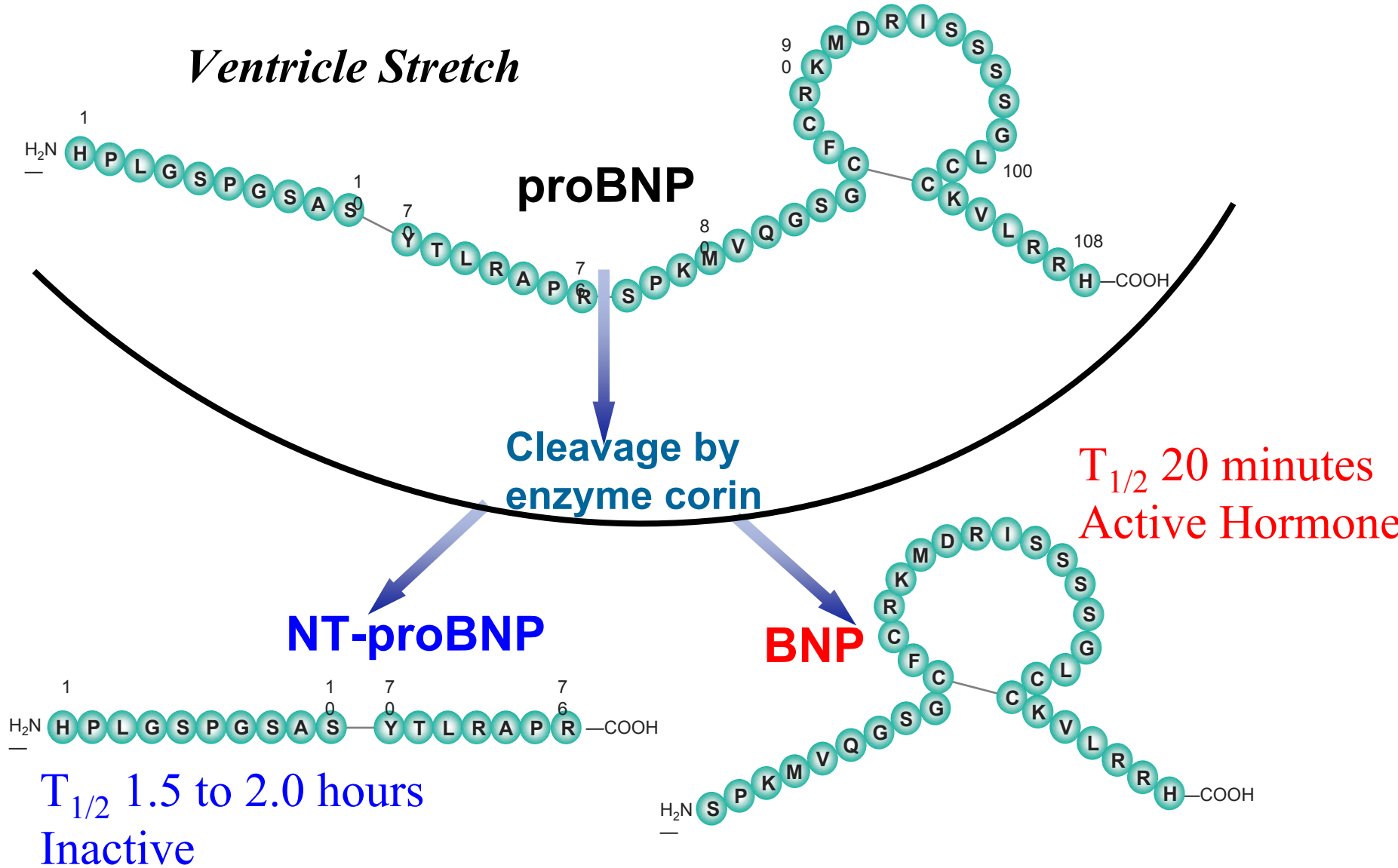
Cardiac isoforms in blood



=



BNP and NTproBNP Release



Recommendation 1: The clinical and analytical performance criteria for Point of Care measurements of cardiac biomarkers of acute coronary syndromes and heart failure must be equivalent to criteria for biomarker measurement in the central laboratory.

Strength/consensus of recommendation: Class I

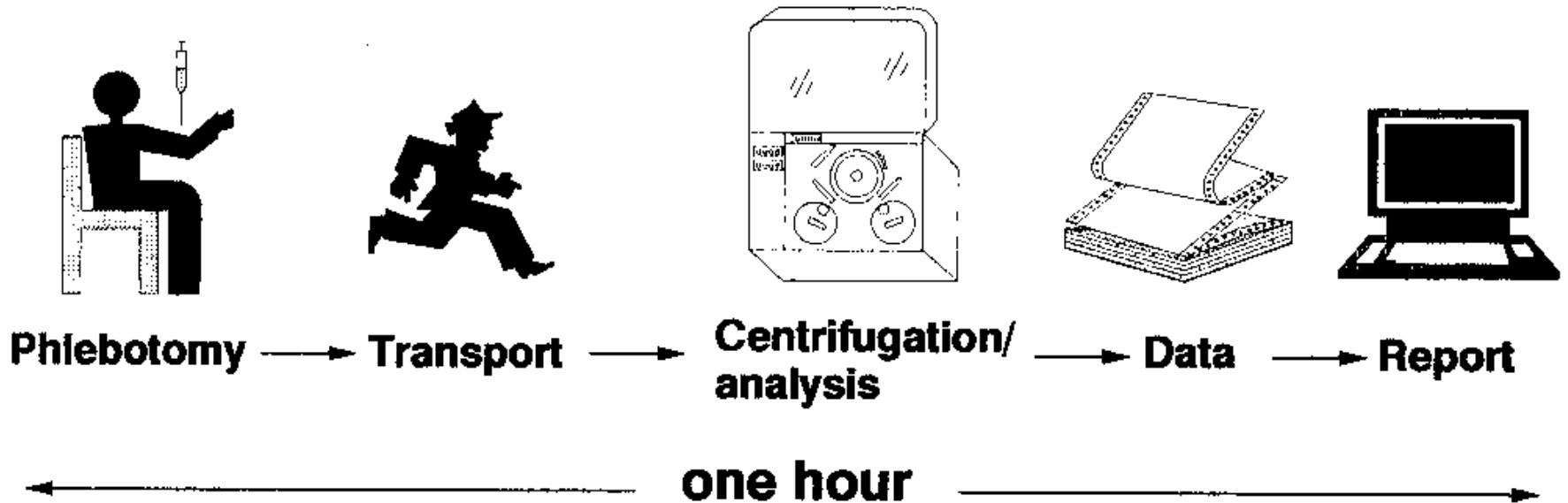
Grade of Evidence: C

Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective.

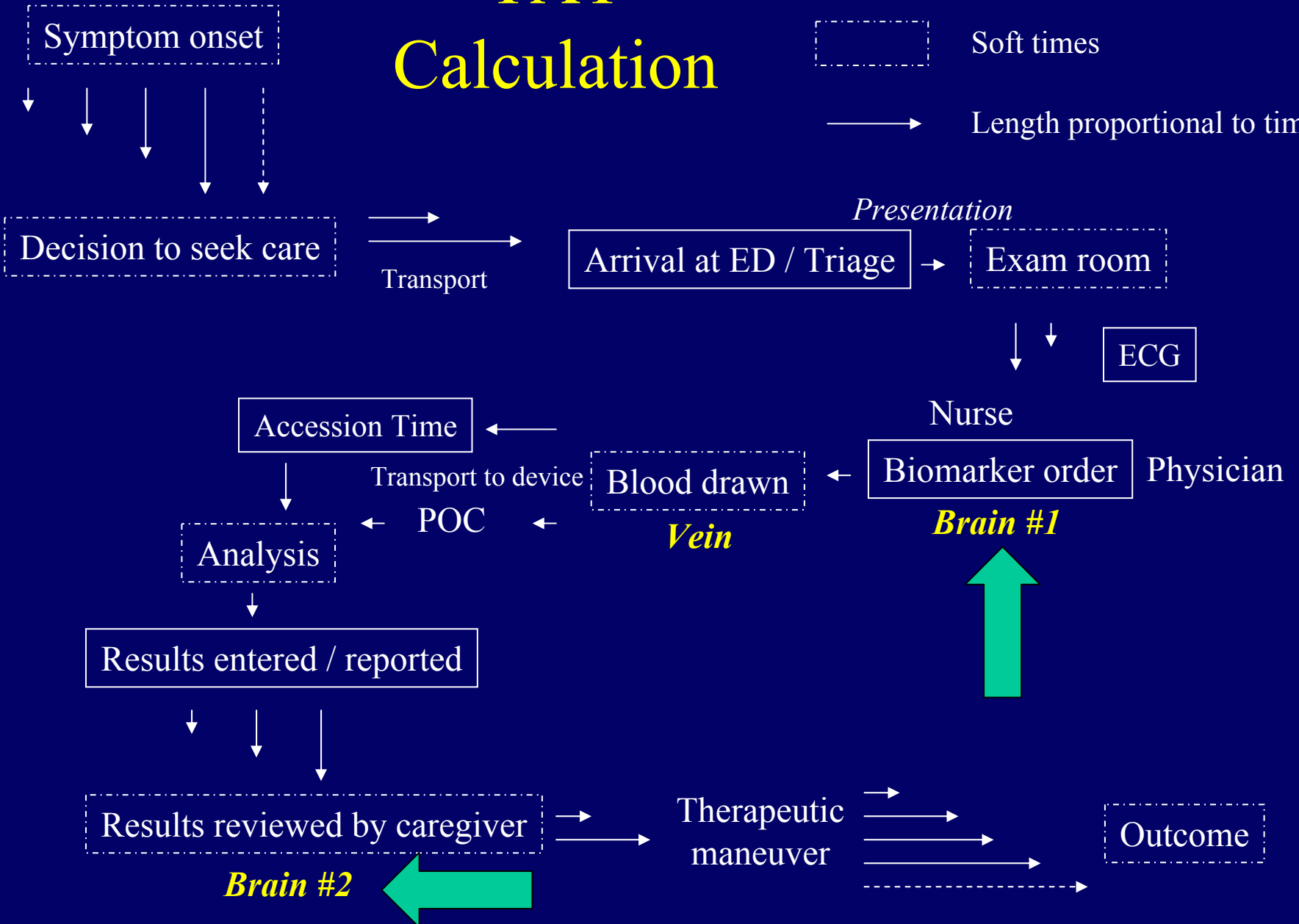
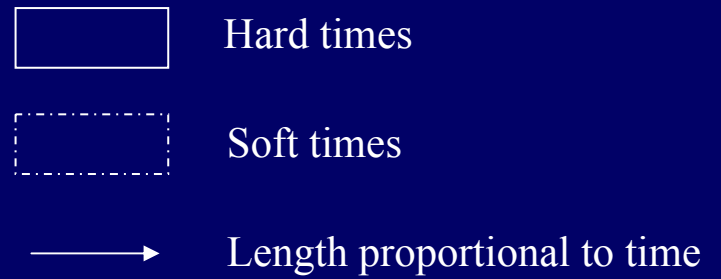
Expert Consensus

Biomarkers Turnaround Time

National Academy of Clinical Biochemistry "Arm to Report" Program



TAT Calculation



ACC/AHA Guidelines for UA/NSTEMI: Importance of a Panel of Markers

Biochemical Markers required for diagnosis of NSTEMI

- “When the central lab is used, results should be available within 60 minutes, preferably within 30 minutes...”
- ...POC Systems...have the advantage of reducing delays in transportation and processing...and can reduce delays at all hours...
- “Portable devices... That allow simultaneous, rapid measurement of myoglobin, CK-MB, and troponin at the bedside are likely to be useful in the assessment of patients with ACS”

How are we doing, with
Vein-to-Brain
Turnaround (TAT)
Times?

Biomarkers Turnaround Time

Arch Pathol Lab Med 2004;128:158-164

- Determine normative rates of TAT and examine hospital and lab practices associated with faster TATs
- 159 hospitals participating in CAP Q-probes
- Disconnected impression of reasonable vein-to-brain times
 - 82% of Laboratorians, order to report time 60 minutes
 - 75% of ED physicians, vein to brain time 45 minutes
- 7020 troponin and 4368 CK-MB measurements

Biomarkers Turnaround Time

Arch Pathol Lab Med 2004;128:158-164

Cardiac markers performed in institution

Troponin	99.3%
CK-MB	92.1%

Biomarkers ordered on ED presentation with signs and symptoms of ACS

Troponin	98.7%
CK-MB	83.0%

Cardiac marker testing most commonly performed

Main Laboratory	92.8%
ED or Satellite	7.2%

Results of cardiac marker testing performed in lab are reported by

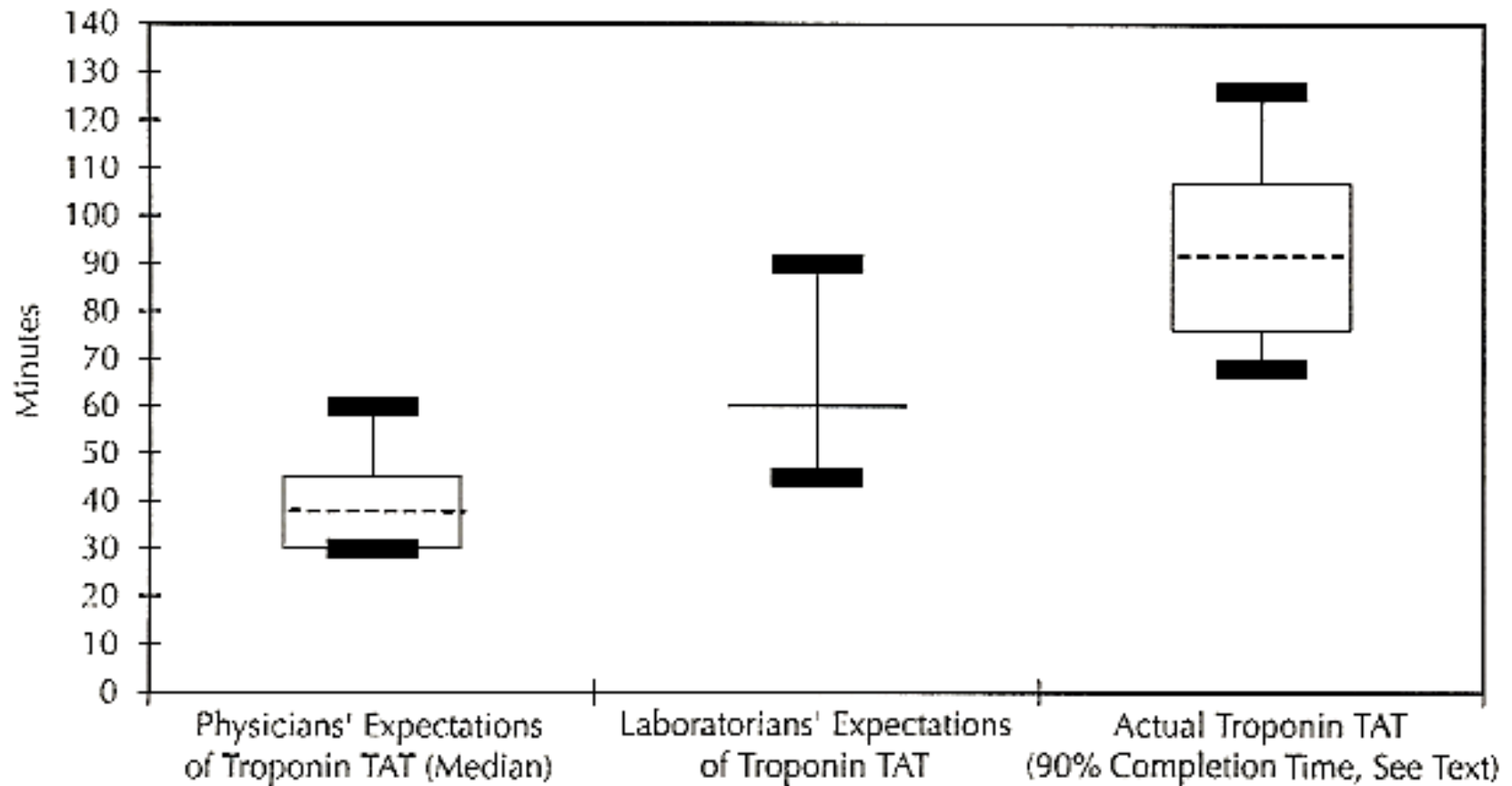
Telephone	1.4%
Computer	98.6%

Specimen most commonly collected for biomarker testing is

Fingerstick	0.6%
Serum	25.7%
Plasma	73.7%

Biomarkers Turnaround Time

Arch Pathol Lab Med 2004;128:158-164



Biomarkers Turnaround Time

Arch Pathol Lab Med 2004;128:158-164

- TAT expectations of clinicians exceed those lab personnel producing the results.
- Actual TAT meet expectations of neither the lab nor the clinical groups
- Improving TAT performance will require that clinicians and laboratorians work together to develop standards that meet the needs of the medical staff and that are achievable by laboratory personnel.

Impact of a POC Satellite Lab in the ED

Arch Pathol Lab Med 2003;127:456-460.

- Physician satisfaction
 - Test TAT
 - Testing Accuracy
- Turnaround time difference
- ED Length of stay before and after implementation of a satellite lab

In-lab TAT for Markers

Test	Turnaround Time Before POCT, min	Turnaround Time During POCT, min	Change in Turnaround Time After Initiation of POCT, min†
Urinalysis	40 (n = 37)	4 (n = 106)	-36 (90%)
Pregnancy testing	78 (n = 44)	5 (n = 54)	-73 (94%)
Glucose	10 (n = 128)	6 (n = 28)	-4 (60%)
Cardiac markers	110 (n = 62)	17 (n = 128)	-93 (84.5%)
Mean	59.5	8	-51.5 (86.6%)

ED Length of Stay

Test	ED Length of Stay Before POCT, min	ED Length of Stay During POCT, min	Change in ED Length of Stay After Initiation of POCT†
Urinalysis	395 (n = 37)	358 (n = 106)	37 (P = .25)
Pregnancy testing	386 (n = 44)	346 (n = 54)	40 (P = .22)
Glucose	380 (n = 128)	404 (n = 56)	-24 (P = none; see text)
Cardiac markers	386 (n = 62)	338 (n = 128)	47 (P = .06)
Mean‡	389	347	41 (P = .006)

Clinician Satisfaction

Test	Before POCT (15 RNs, 36 MDs)	During POCT Program (13 RNs, 17 MDs)	Difference (During - Before)
Urinalysis	1.8	4.5	2.7
Pregnancy testing	1.5	4.4	2.9
Glucose	2.4	4.3	1.9
Cardiac markers	2.1	4.0	1.9
Mean	1.95	4.3	2.35 (P < .001)

Satisfaction with Accuracy

Test	Before POCT (15 RNs, 36 MDs)	During POCT (13 RNs, 17 MDs)	Difference (During -- Before)
Urinalysis	4.0	4.6	0.6
Pregnancy testing	4.4	4.9	0.5
Glucose	4.3	4.9	0.6
Cardiac markers	4.3	3.7	-0.6
Mean	4.25	4.53	0.28

Arch Pathol Lab Med 2003;127:456-460.

Arch Pathol Lab Med 2003;127:456-460.

Conclusion: The POCT satellite laboratory decreased test TAT and decreased ED LOS. There was excellent satisfaction with test accuracy and TAT.

Use of BNP in the Evaluation and Management of Acute Dyspnea

N Engl J Med 2004;350:647-54

- Prospective, randomized, controlled study
- 452 patients
 - 225 strategy including measurement of BNP
 - 227 assessed in standard way
- Primary endpoints
 - Time to discharge
 - Total cost of treatment

Endpoints

N Engl J Med 2004;350:647-54

Endpoint	BNP Group n=225	Control Group n=227	P Value
Time to Rx			0.003
Median	63 min	90 min	
25 th -75 th	16-153	20-205	
Time to D/C			0.001
Median	8.0 days	11.0 days	
25 th -75 th	1.0-16.0	5.0-18.0	
Hospitalization	169 (75%)	193(85%)	0.008
Total Rx Cost			0.006
Median	\$5,410	\$7,264	
25 th -75 th	\$4516-6304	\$6301-8227	
30-d Mortality	22(10%)	28(12%)	0.45
30-d Readmission	26(12%)	23 (10%)	0.63
In-hospital death	13 (6%)	21 (9%)	0.21

Use of BNP in the Evaluation and Management of Acute Dyspnea

N Engl J Med 2004;350:647-54

“...BNP in the emergency department improved the evaluation and treatment of patients with acute dyspnea and thereby reduced the time to discharge and total cost of treatment.”

POCT & CLT Compared

P O Collinson et al. Ann Clin Biochem (in press)

- Comparison of point of care testing (POCT) with central laboratory testing (CLT).
- 263 consecutive admissions with chest pain and suspected acute coronary syndrome
- Randomised to measurement of cardiac troponin T by POCT or CLT only
- Diagnostic accuracy, CLT as “Gold standard”, result TAT, mortality and length of stay in all patients, and those with a protocol driven early discharge policy.

POCT & CLT Compared

P O Collinson et al. Ann Clin Biochem (in press)

- Median diagnosis: ($p < 0.0001$)
 - 17.8 h (CI 16.3-21.1) for CLT
 - 14.7 h (CI 13.3-15.8) for POCT
- Median TAT ($p < 0.0001$)
 - POCT was 20 min; (range 20-38)
 - CLT was 79 min; (range 25-1018)
- MACE ($p = \text{NS}$)
 - combined endpoints of death, MI, readmission with unstable angina or need for urgent revascularisation

POCT & CLT Compared

P O Collinson et al. Ann Clin Biochem (in press)

	Randomisation		CLT vs POCT
	CLT	POCT	
All patients			
CCU stay (h)	48.4 (46-52.8) 8.5-202.0	52.2 (45.8-57.5) 4.5-373.2	ns
Non CCU stay (h)	162.3 (137.8 – 196.5) 0-1700.0	136.0 (115.0-163.25) 0-1093.5	ns
Hospital stay (h)	218.0 (192.6-258.8) 14.3-1808.8	202.3 (166.9-240.8) 4.5-1219.0	ns
Rapid rule-out group			
CCU stay (h)	39.4 (25.0-52.8) 9.5-164.0	53.0 (43.0-68.3) 10.3-146.5	ns
Non CCU stay (h)	145.3 (63.0-210.8) 0-914.0	79.5 (61.5-134.0) 0-260.7	P < 0.05
Hospital stay (h)	209.3 (158.0-265.8) 18.5-927.7	149.9 (108.0-165.5) 30.0-354.3	P < 0.05

POCT & CLT Compared

P O Collinson et al. Ann Clin Biochem (in press)

A protocol based management with rapid diagnosis using point of care testing significantly reduces length of stay in low risk patients admitted with suspected acute coronary syndromes.

Recommendation 2: The laboratory should perform cardiac marker testing with a turnaround time (TAT) of 1 hour, optimally 30 minutes, or less. The TAT is defined as the time from clinician order to caregiver awareness.

Strength/consensus of recommendation: IIa

Grade of Evidence: C

Recommendation 3: Institutions that cannot consistently deliver cardiac marker turnaround times of approximately 1 hour should consider implementation of point-of-care (POC) testing devices.

Strength/consensus of recommendation: **Class IIb**

Strength of Evidence: **C**

Recommendation 4: Laboratory personnel must be involved in the selection of devices, the training of individuals to perform the analysis, the maintenance of POC equipment, the verification of the proficiency of operators on a regular basis, and the compliance of documentation with requirements by regulatory agencies.

Strength/consensus of recommendation: Class I

Strength of Evidence: C

Recommendation 5: While it is recognized that qualitative systems do provide useful information, it is recommended that POC systems provide quantitative results.

Strength/consensus of recommendation: Class IIa

Strength of Evidence: C

Questions? Issues?



Discussion

Recommendation 1: The clinical and analytical performance criteria for Point of Care measurements of cardiac biomarkers of acute coronary syndromes and heart failure must be equivalent to criteria for biomarker measurement in the central laboratory. **Class I, C**

Recommendation 2: The laboratory should perform cardiac marker testing with a turnaround time (TAT) of 1 hour, optimally 30 minutes, or less. The TAT is defined as the time from clinician order to caregiver awareness. **Class IIa, C**

Recommendation 3: Institutions that cannot consistently deliver cardiac marker turnaround times of approximately 1 hour should consider implementation of point-of-care (POC) testing devices. **Class IIb, C**

Recommendation 4: Laboratory personnel must be involved in the selection of devices, the training of individuals to perform the analysis, the maintenance of POC equipment, the verification of the proficiency of operators on a regular basis, and the compliance of documentation with requirements by regulatory agencies. **Class I, C**

Recommendation 5: While it is recognized that qualitative systems do provide useful information, it is recommended that POC systems provide quantitative results. **Class IIa, C**