Advances in the Management of STEMI

Timothy A Mixon MD FACC FSCAI

Interventional Cardiology
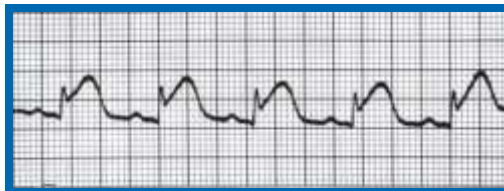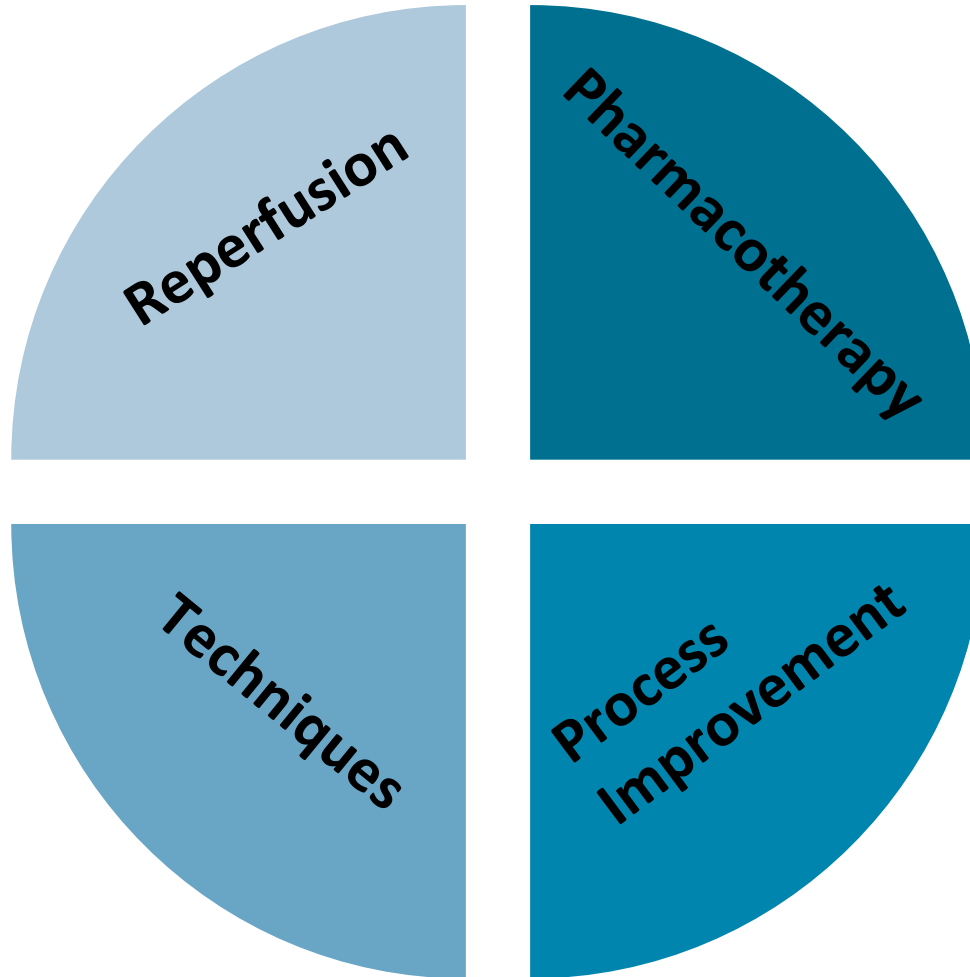
Baylor Scott & White, Temple, TX

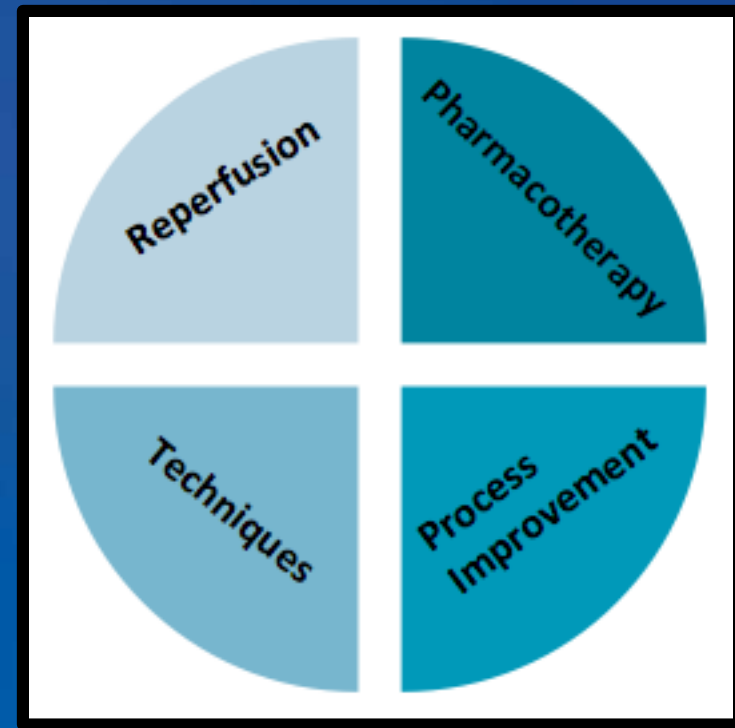Associate Professor of Medicine, Texas A&M COM

#stemitexas

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STEMI Care

REPERFUSION

Time is muscle…

- Circumflex occlusion of variable length (40 min, 3 hrs, 6 hrs, or permanent) in open-chest dogs
- Subsequent histologic examination to determine extend and distribution of infarct
- Infarct location began in endocardium, spread in a wave-front toward epicardium
- Infarction involved
  - (% of ischemic bed at rest):
    – 28% at 40 min
    – 70% at 3 hr
    – 72% at 6 hr
    – 79% with permanent occlusion
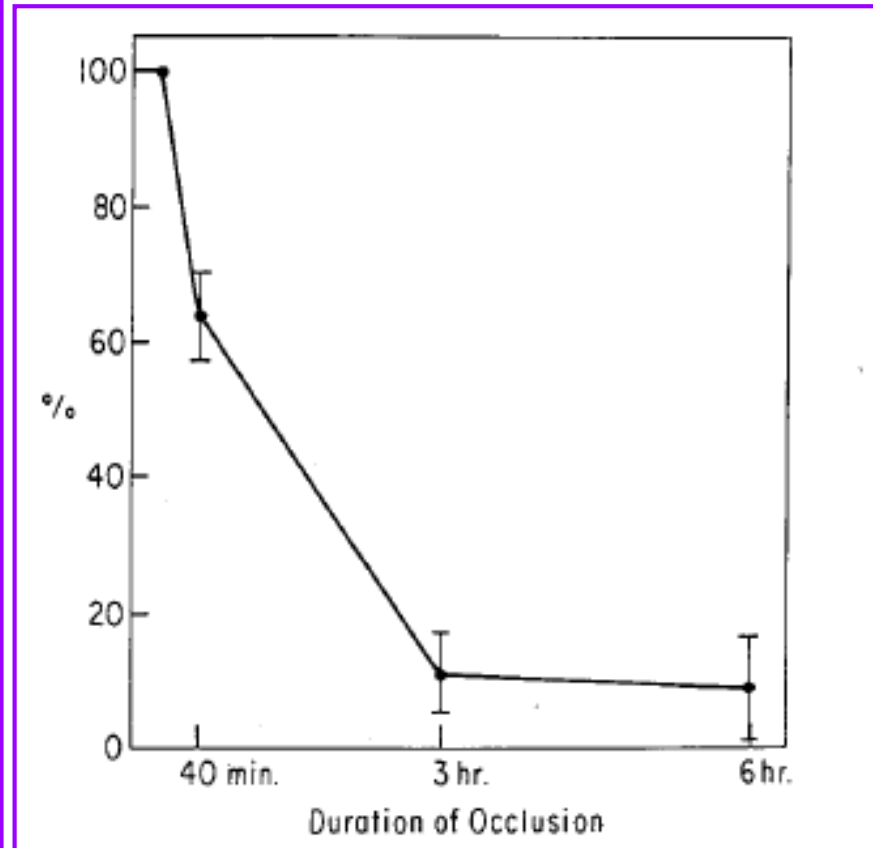
Reimer and Jennings, Lab Invest, 1979.

Background: Fibrinolytic
Early Reperfusion Therapy

Figure 4: **Absolute 35-day mortality reduction versus treatment delay**
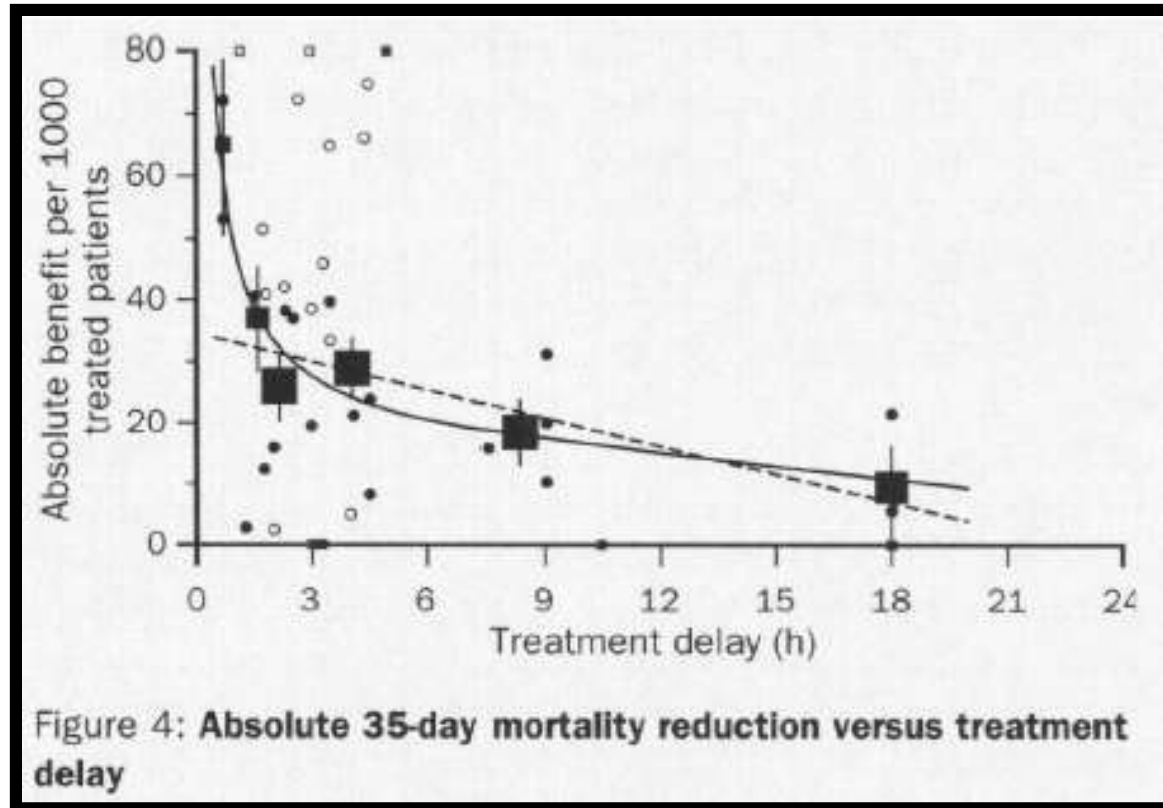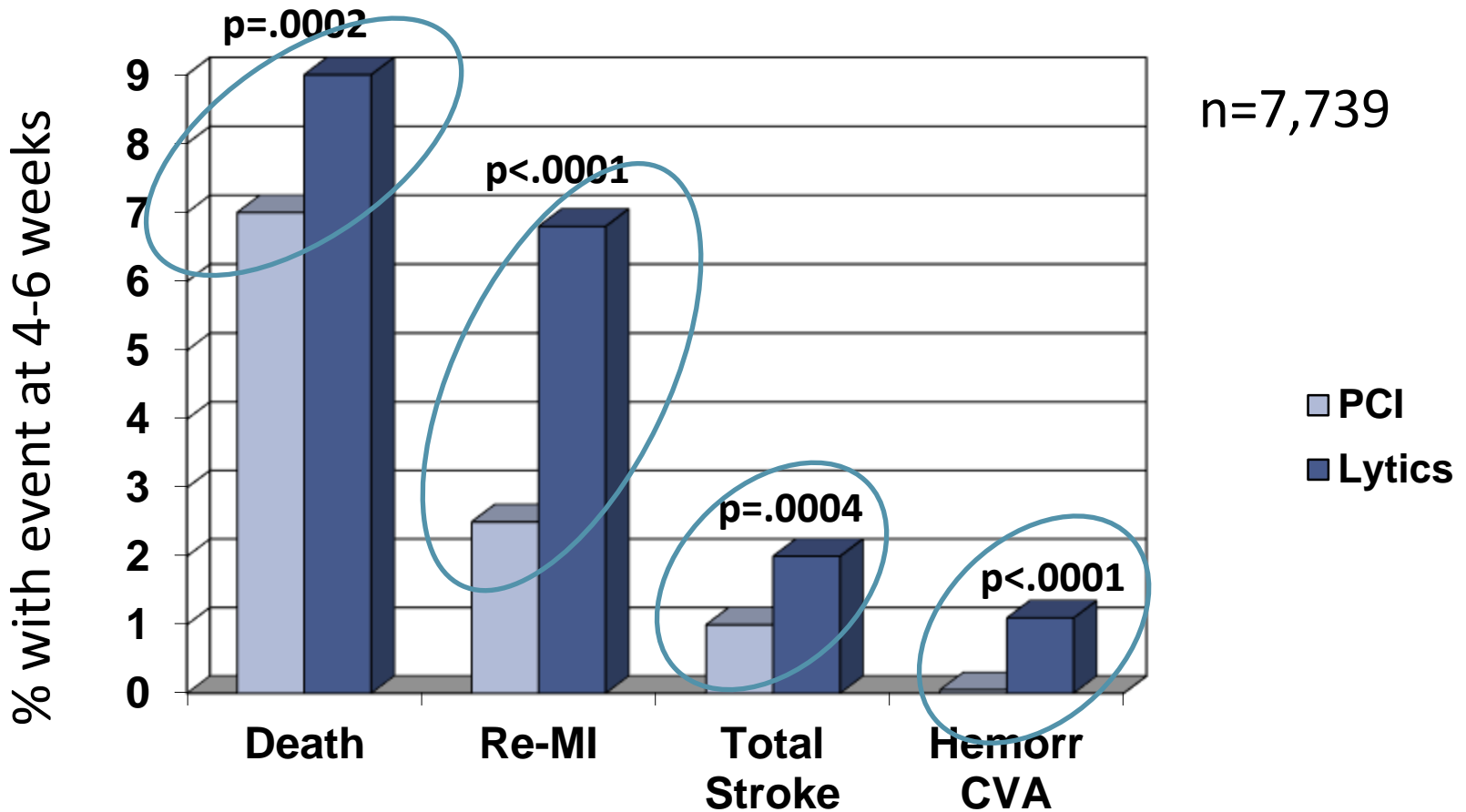
- Strong, nonlinear relationship between *time to therapy* and *mortality*
- Benefit most pronounced early; modest benefit at 6-12 hrs

Boersma & Maas. Lancet 1996

Primary PCI
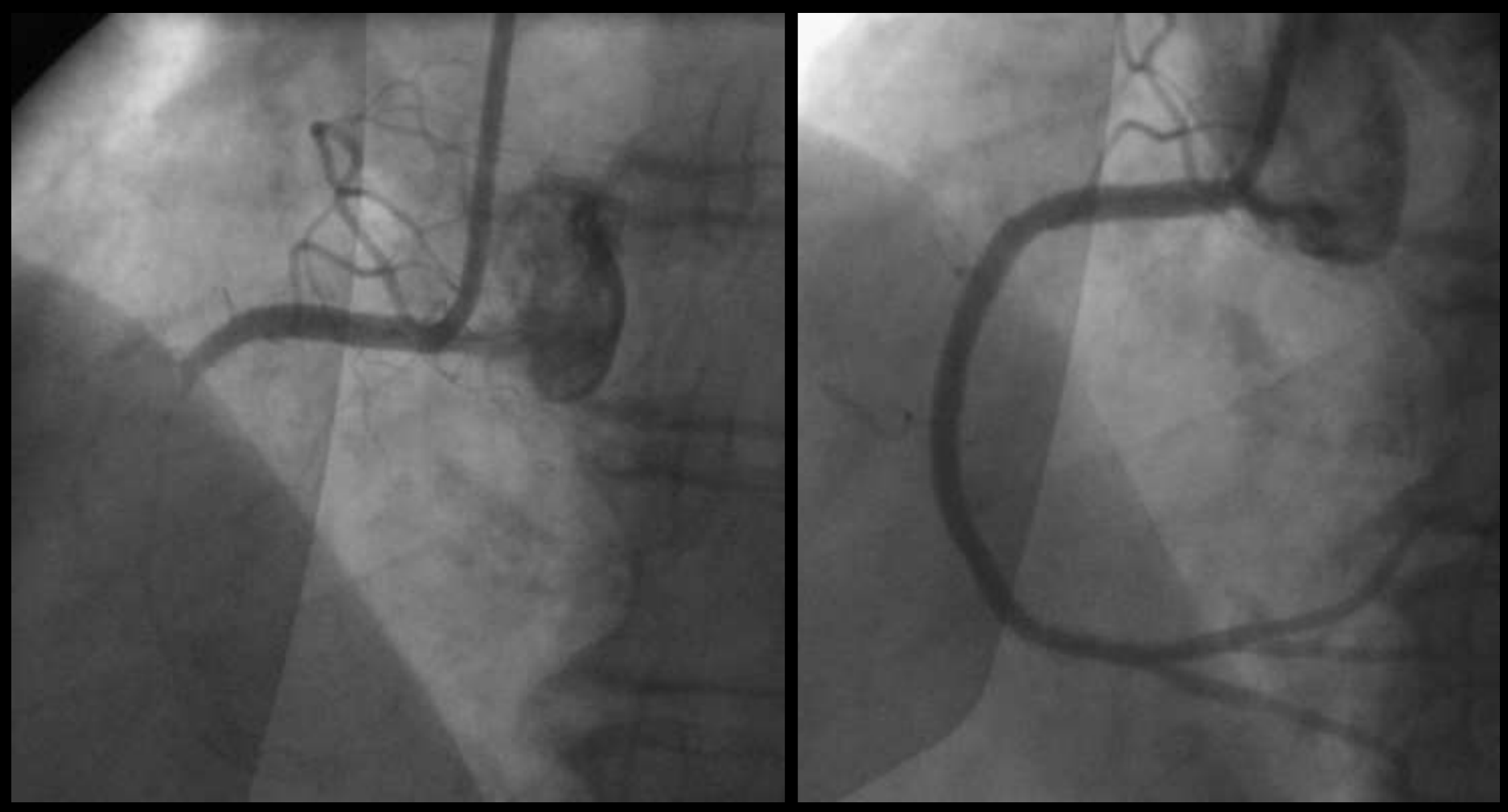
Meta-analysis of 23 Randomized Trials of Fibrinolytics vs. Primary PCI

n=7,739

Keeley et al. Lancet 2003; 361:13-20
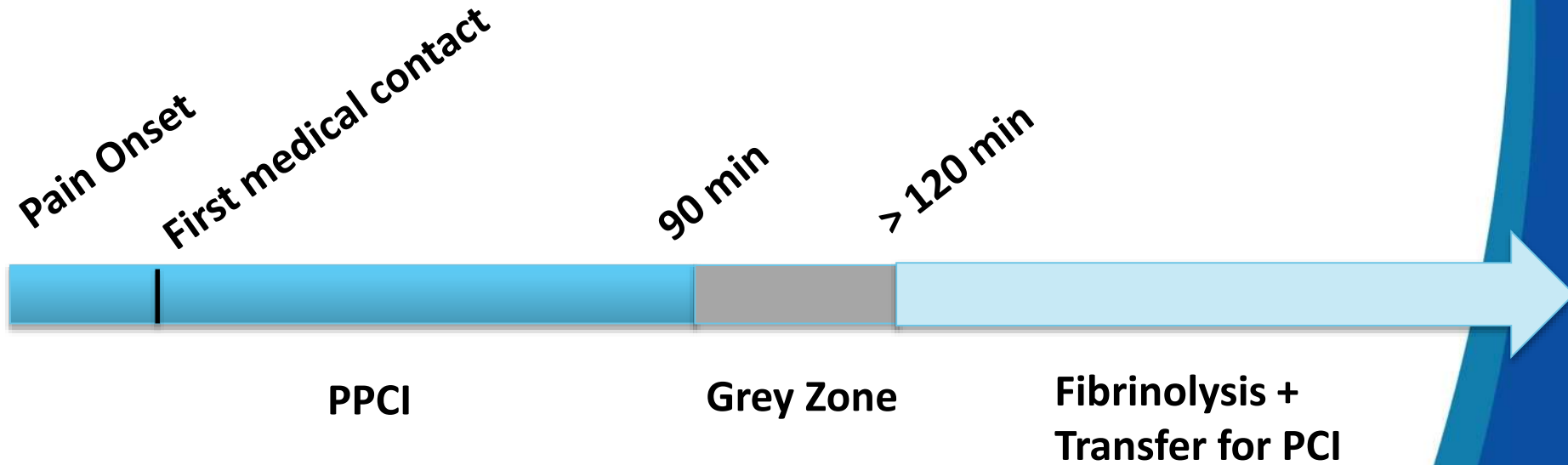
STREAM Trial

Compared PPCI vs. fibrinolytic therapy (with rescue PCI as needed) in patients *at least* 1 hour away from a PPCI center

Relevant Time Periods (minutes)

Both Groups

| Symptom-to-FMC | 62 |
| FMC-to-random | 30 |

Lytic

| FMC-to-drug | 40 |

PPCI

| FMC-to-balloon | 117 |
| Δ Time | 77 |
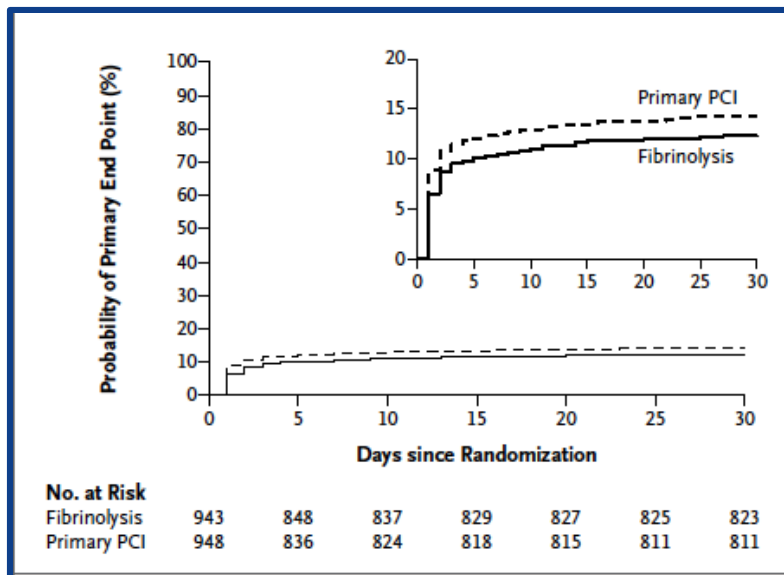
Equal rate of composite end point
No difference in total mortality
Non-significant trend toward less HF/shock with lytics (numbers small)

STREAM Trial

Positive or negative trial?

CARESS-in-AMI: Results

Legend: ■ Immediate PCI ■ Conserv/Rescue

4.4% vs 10.7%

p=ns

p=ns

0.3% vs 4.0%

12
10
8
6
4
2
0

Primary End — Death — Re-MI — Refract Ischem

"CARESS was designed to address optimum treatment when primary PCI is not readily available"
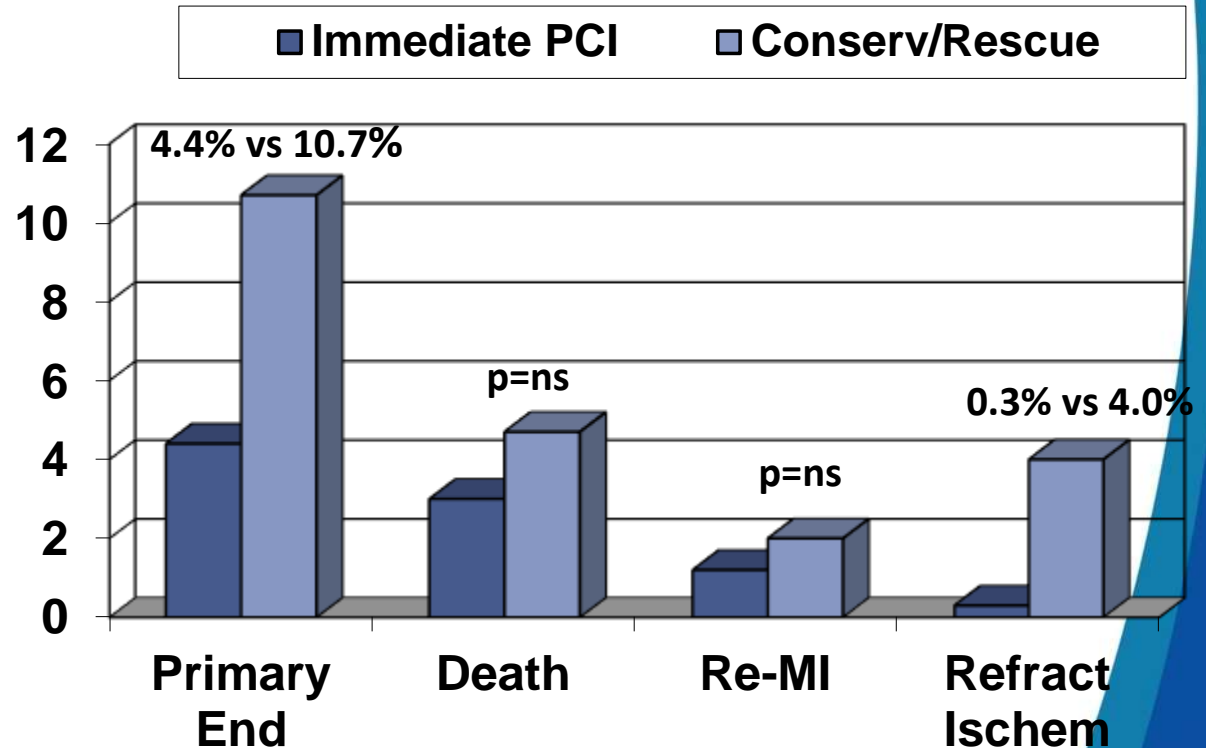
Conclusion: "...a strategy of immediate transfer for PCI after a combination of half-dose fibrinolytic plus abciximab is better than continuing standard management at the same centre"

Summary:
Transfer-AMI and Caress-in-AMI

1. Routine strategy of urgent transfer appears warranted

2. Among "routine therapy", urgent cath required in ~ 33%

3. Results show:
   - Fewer acute ischemic events
   - Trend toward lower re-infarction
   - No difference in mortality
   - Nonsignificant trend toward increased bleeding

Conclusions: Reperfusion Therapy

1. Occlusion leads to permanent myocardial damage
   - Beginning at 20 minutes
   - Significant damage by 90-120 minutes
2. Early fibrinolytic therapy promotes coronary reperfusion and reduces mortality from STEMI
3. PPCI, if performed in a timely manner, is superior to fibrinolytic therapy
4. Time to treatment > 120 min: consider lytics
5. Fibrinolytic therapy should be used if emergent, *timely PCI not possible*
   - Early transfer to a PCI-capable hospital for:
     - Rescue PCI or early systematic PCI
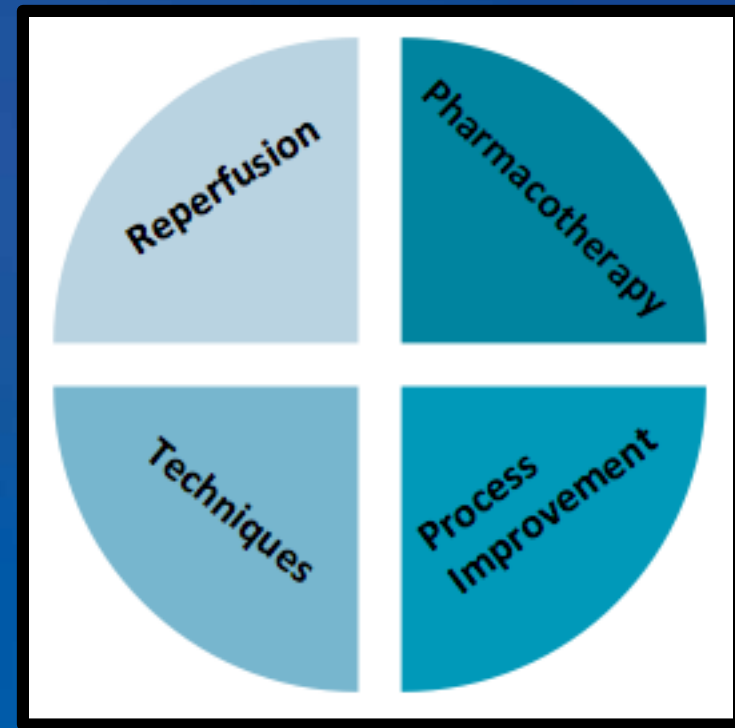
PHARMACOTHERAPY

Novel P2Y12 Receptor Antagonist

Clopidogrel

Moderate platelet inhibition

Slow onset of action

Complex bioactivation

Genetic variants impact efficacy

Drug-drug interactions

Prasugrel & Ticagrelor

High level platelet inhibition

Rapid onset of action

Simpler/rapid bioactivation

No known genetic impact

No known drug-drug interactions

Novel P2Y12 Receptor Antagonist

Results: RRR   ARR
 – Composite endpoint: 16-19%   2%
 – Reduction in MI: 16-24%   2%
 – Difference in stroke: no difference
 – Stent thrombosis: 25-52%   1%

Mortality: RRR   p value
 – Ticagrelor: 21%   p=.001
 – Prasugrel: 11%   p=.31

Triton TIMI 38 N Eng J Med 2007; 357:2001f
PLATO N Eng J Med 2009; 361: 1045f

ACCOAST & ATLANTIC Trials

What is the utility of pre-loading novel P2Y12 blockers?

> ACCOAST: prasugrel in ACS bound for CL
>
> ATLANTIC: ticagrelor in STEMI

ACCOAST / ACS

- No benefit in overall cohort (n=4,033)
- Increased bleeding ($\approx$ 3x) with pre-treatment
- ACCOAST PCI: similar results for both ischemic and bleeding

ATLANTIC / STEMI

- Failed to meet primary endpoint (pre-reperfusion endpoints)
- Lowered acute stent thrombosis by $\approx$ 1%

Montalescot N Eng J Med 2013; 369:999-1010
Montalescot J Am Coll Cardiol 2014; 64: 2563-71
Montalescot N Eng J Med 2014; 371: 1016-1027

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UFH vs. Bivalirudin

Reduced ischemic complications

UFH + IIb/IIIa superior to UFH alone

*1990s
EPIC, EPILOG, EPISTENT*

More potent P2Y12 antagonist?
⬇ bleeding due to radial?
Inadequate bivalirudin dosing?
Single center, underpowered?

?

Bivalirudin superior to UFH + IIb/IIIa

*2008 Horizons AMI
2013 EuroMax*

? UFH alone superior to Bivalirudin ?

2014 HEAT PPCI

Equal ischemic complications + lower bleeding = mortality benefit

Reduced ischemic complications
Equal bleeding

Bivalirudin vs. UFH

- Both remain Class I
- Both are measurable/verifiable
- Current dosing (? + radial approach) reduces bleeding
- Provisional IIb/IIIa antagonist ($\approx$ 10-15%)
- Early (? in lab) prasugrel or ticagrelor
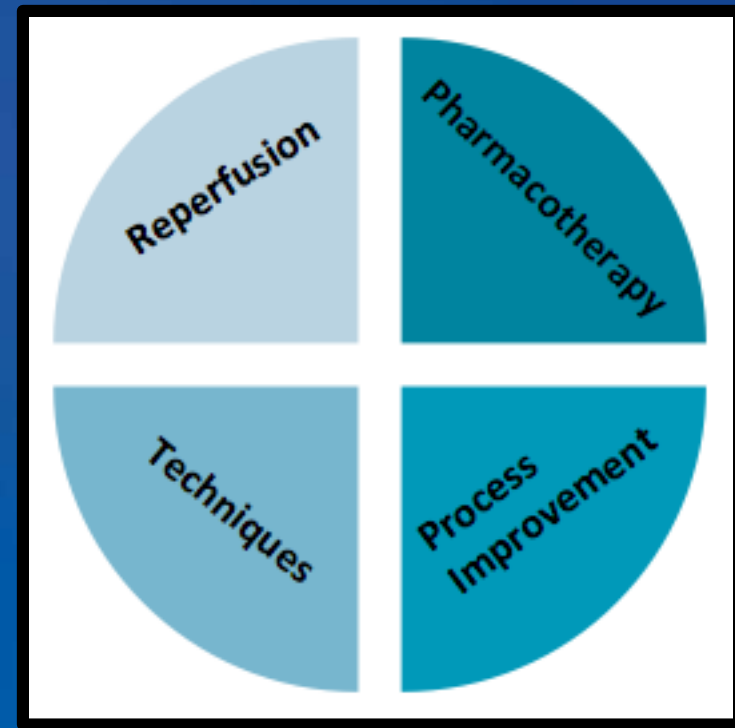- Corroborative, multicenter, blinded trial data needed

The S&W STEMI Cocktail

Pre-Cath Lab

1. Aspirin 162-325 mg, chew and swallow ASAP
2. UFH 60 U/kg IV (max 4,000 U): no drip

In Cath Lab

3. Bivalirudin (+/- post PCI dosing)
4. Oral anti-platelet agent
   High bleeding risk: clopidogrel 600 mg po
   Normal bleeding risk: prasugrel or ticagrelor
5. Bailout IIb/IIIa antagonist prn

Procedural Technique and Adjunctive Therapy

Adjunctive Cardioprotective Therapies

- Metabolic manipulation
  - Trimetazidine, magnesium, GIK, exenatide
- Inflammation
  - Pexelizumab, others
- Kinases signaling pathways
  - Delcasertib, carperitide, epoetin
- Pre- post- remote- conditioning,
- Aqueous hyperoxygenation
- Hypothermia
- Distal EPD
- Adenosine

Investigations still underway:
Remote ischemic conditioning
Hypothermia
Aqueous hyper-oxygenemia

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Aspiration Thrombectomy

Promise & Benefit

1. Clears the vessel

2. Clarifies underlying disease

3. Small studies suggest:
   - Improved ST resolution,
   - Improved microvascular obstruction
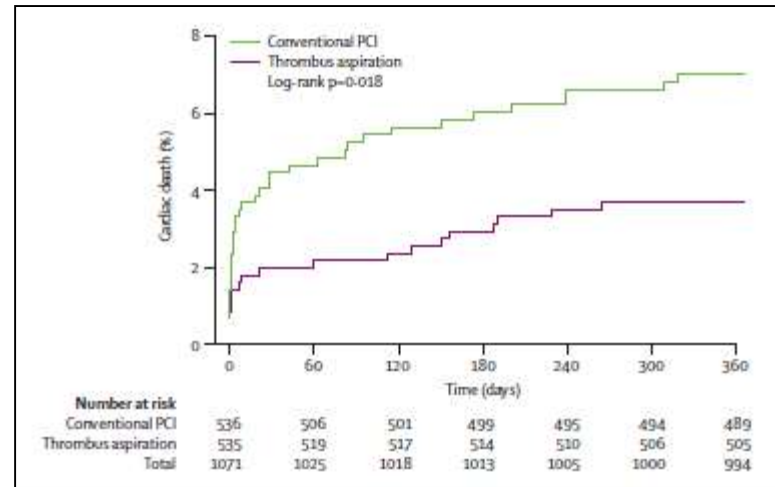   - Lower re-MI / re-hospitalization
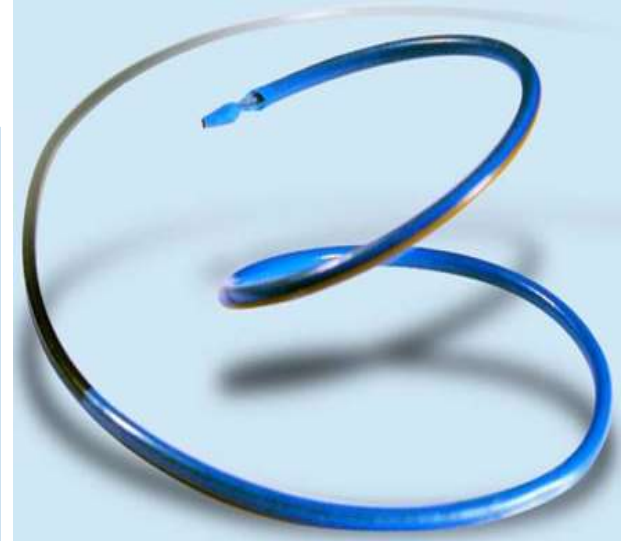
Getting our hopes up…

TAPAS Trial

Cardiac death @ 1 yr

    3.6% vs. 6.7% (HR 1.93)

Death or MI @ 1 yr

    5.6% vs. 9.9% (HR 1.81)

Top: CV mortality
Below: CV mortality and MI

Table 7. Recommendation for Thrombus Aspiration During PCI for STEMI

2009 Joint STEMI/PCI Focused Update Recommendation	Comments
Class IIa	
1. Aspiration thrombectomy is reasonable for patients undergoing primary PCI (17,18,102). (*Level of Evidence: B*)	New recommendation

2009 Focused Update PCI/STEMI
& 2013 STEMI Guidelines
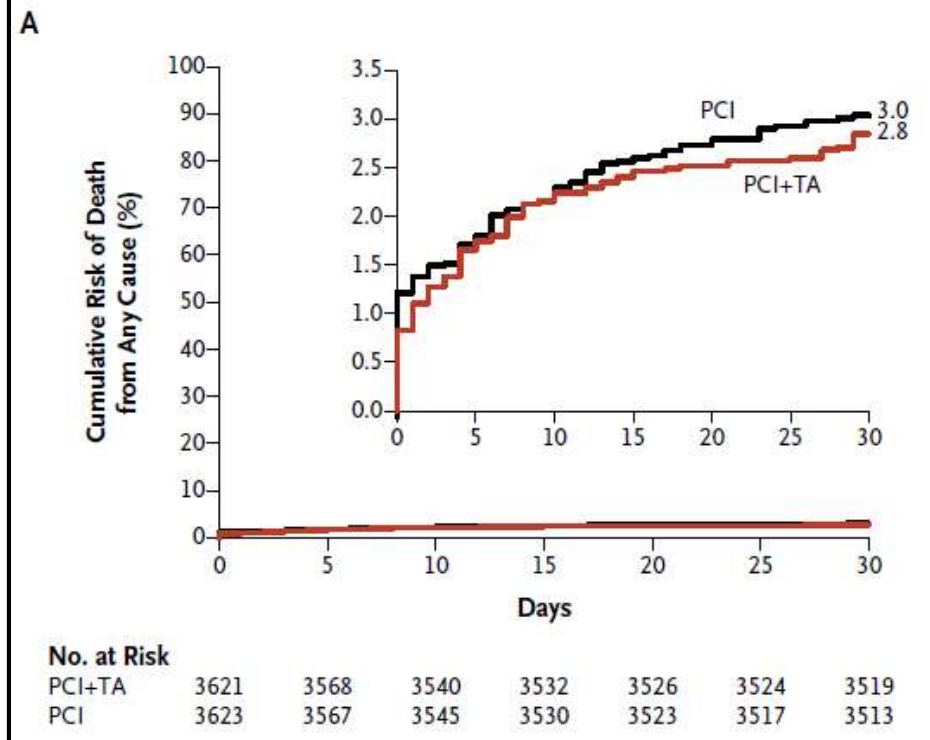
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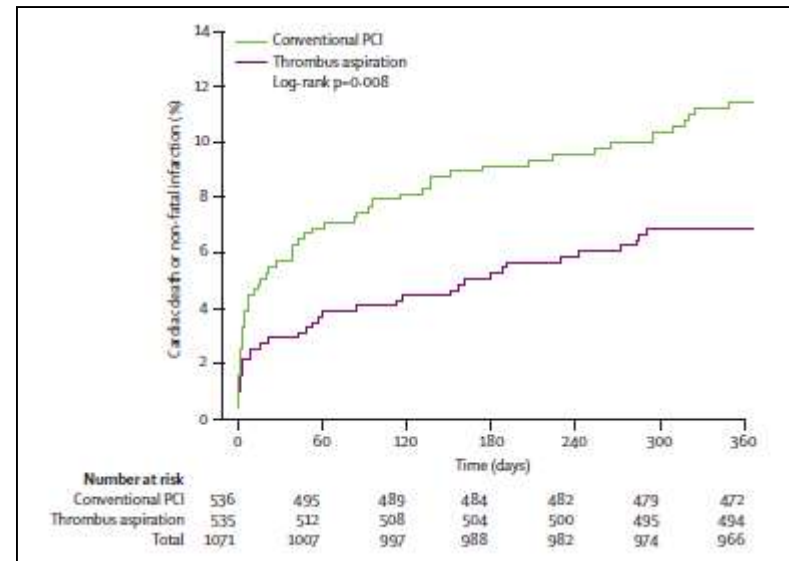
(Taste) Trial

- **No difference in all cause mortality**
- **Nonsignificant trends toward reduction in stent thrombosis & rehospitalization due to MI**

No STEMI/PCI Guidelines since publication
Likely to be downgraded to Class IIb

Large, confirmatory TOTAL Trial enrolling, n=10,700, powered for mortality

A

Cumulative Risk of Death from Any Cause (%)

No. at Risk							
PCI+TA	3621	3568	3540	3532	3526	3524	3519
PCI	3623	3567	3545	3530	3523	3517	3513

Frobert et al. *N Engl J Med* 2013
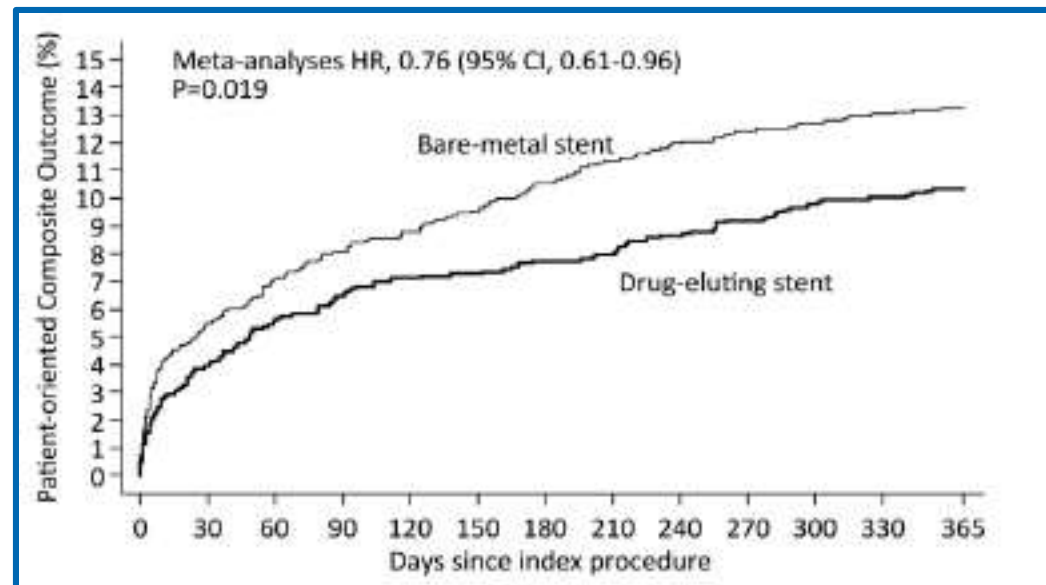
Summary of Aspiration Thrombectomy

- Currently Class IIa recommendation

- Largest trial to date: No mortality benefit

- Reasonable to utilize when heavy thrombus burden present, to facilitate successful procedure

- Current trials: Routine use vs. no use, rather than…
  - Selective use or
  - Only in setting of large thrombus

Stent Selection

Meta-analysis of EXAMINATION & COMFORTABLE

* {
- 8% reduction in death (ns)
- 42% reduction in any reinfarction (p=0.05)
- 33% reduction in any revascularization (p=.005)
- 68% reduction in TLR (p<.001)
- 50-65% reduction in stent thrombosis (depending on definition used)

34% relative reduction in *patient oriented composite outcomes

Meta-analyses HR, 0.76 (95% CI, 0.61-0.96)
P=0.019

Bare-metal stent

Drug-eluting stent

Patient-oriented Composite Outcome (%)

Days since index procedure

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Multivessel PCI during STEMI ?

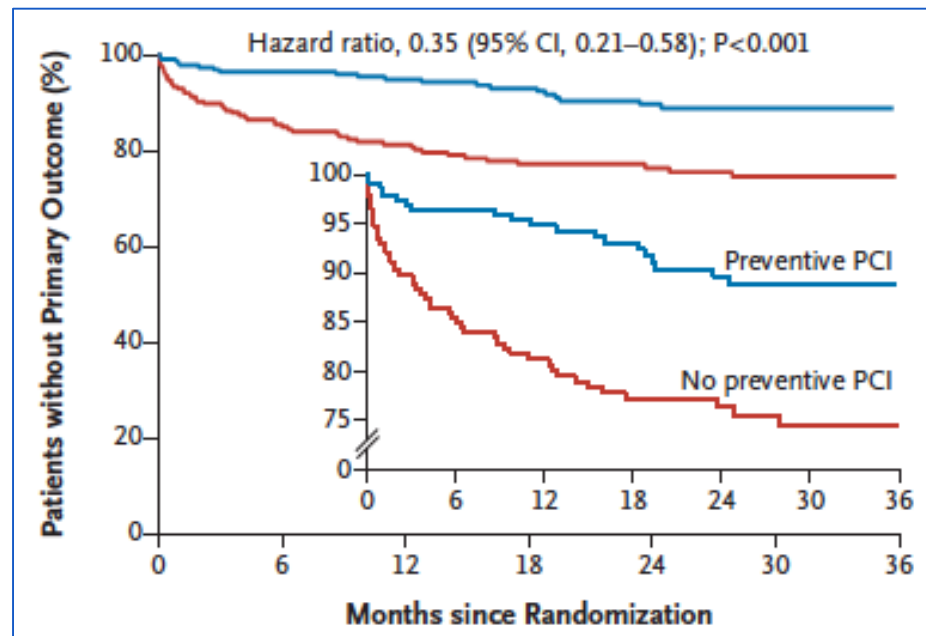Background: PCI of a nonculprit lesion considered Class III

PCI in 2015:
- ⇧ consistency,
- ⇧ predictability,
- Better pharmaceuticals
  - Less thrombosis, embolization, vessel closure

PRAMI and CvLPRIT

Treatment of non-culprit lesions resulted in:

- – Lower recurrent MI
- – Lower recurrent angina
- – Lower repeat revascularization
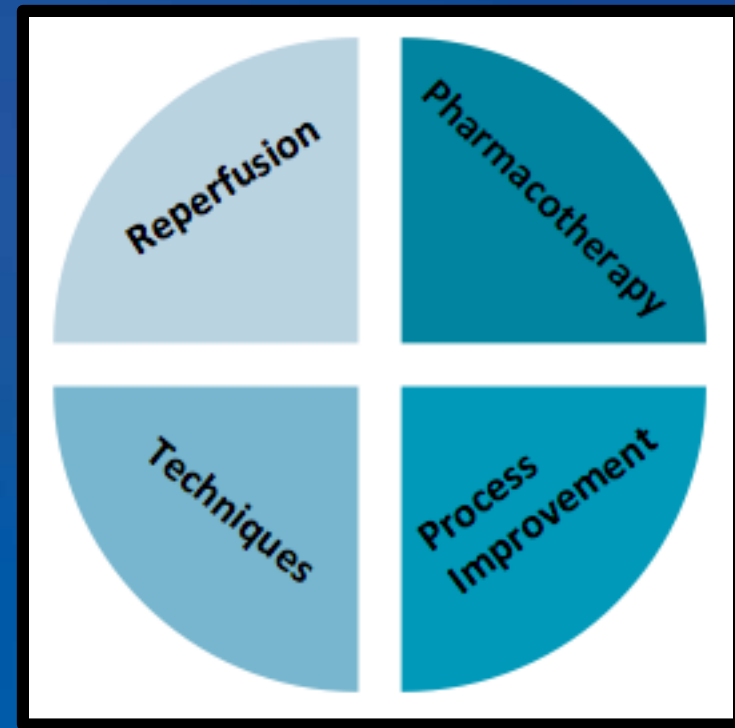
Freedom from death, MI, recurrent angina

32

PRAMI and CvLPRIT

Critiques

- Small, underpowered trials
- Examined *same setting* MV PCI vs culprit only PCI
  - Not *early staged* MV PCI

✓ Unlikely to Δ class III recommendation (? IIb)
✓ Await large COMPLETE trial (2018), n=4,000 comparing early staged PCI vs. medical therapy

Process Improvement

Translational Science / Systems Applications

"Humanity's greatest advances are not in its discoveries – but in *how those discoveries are applied*…"

Bill Gates
Commencement speech
Harvard University, 2007

"Major advances in health care occur not from results of randomized clinical trials or real-world registries, but from the *application of those results to complex healthcare systems*, which requires the successful interaction of healthcare workers and their patients.

Tim Henry MD
Circulation 2012; 126(2): 189-195

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What is a STEMI system of care?

Definition: An "integrated group of entities within a region coordinating…services"

System includes:

1. EMS providers (PH personnel)

2. Referral/non PCI hospitals

3. PPCI hospitals

Jacobs et al. Circulation 2007; 116: 217-30.

What is a STEMI system of care?

Goal: Optimizes *patient outcomes* via *collaboration*

Strategies:
- Assist each entity in *applying* scientific discoveries
- Promoting efficient and effective *collaboration*
  - Especially *communication* and *inter-hospital transfer*
- Data collection and sharing
- Ongoing feedback and quality improvement

STEMI Systems—Ideal Practices
STEMI Receiving Centers
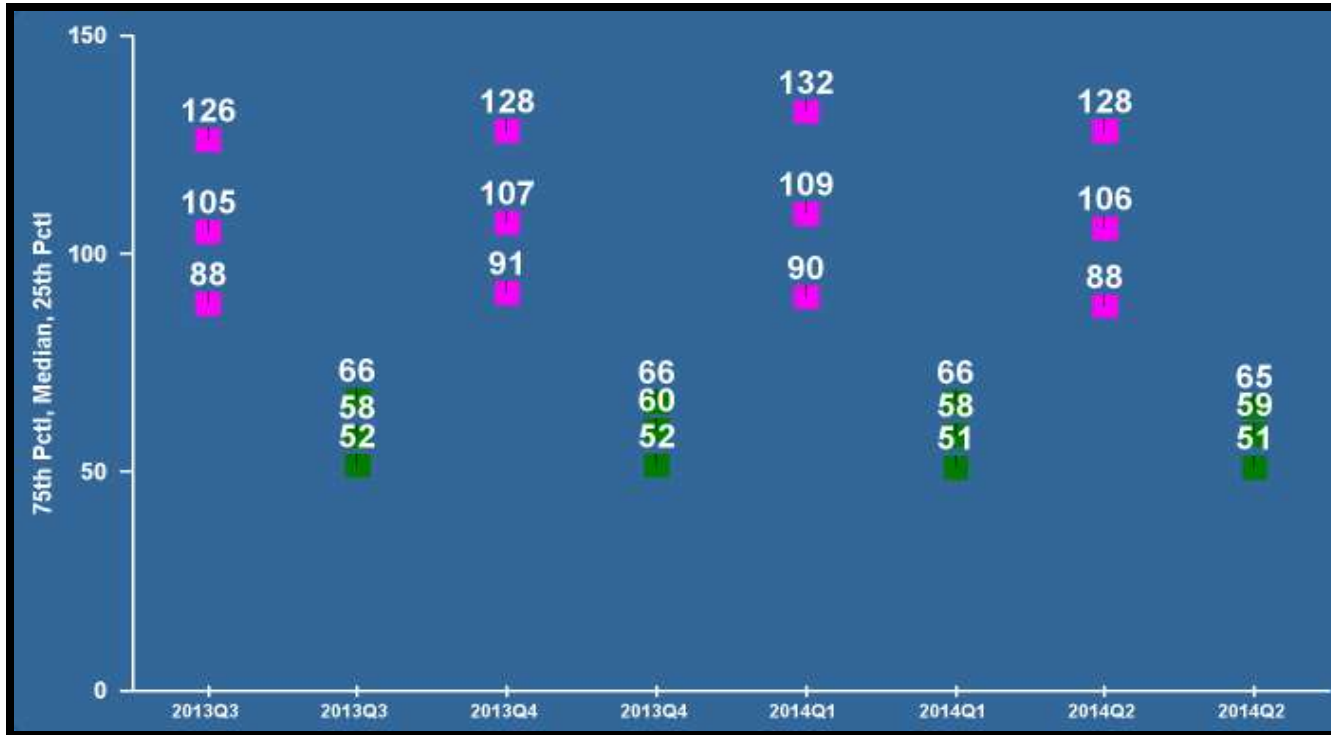
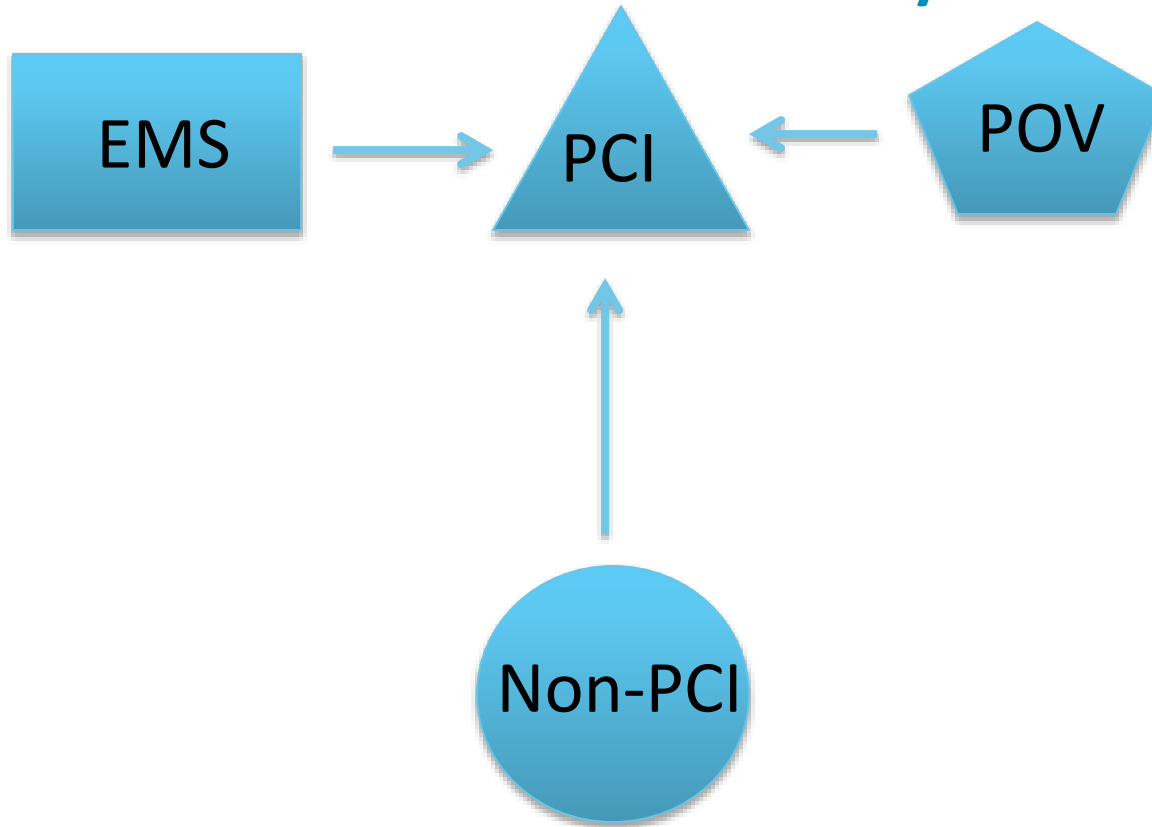ACTION Registry-GWTG DATA:

July 01, 2013 - June 30, 2014

	Non-transfers	**Transfers**
% D2B < 90 min	95%	32%

Portals of Entry

STEMI Systems—Ideal Practices
ED Principles of Rapid, Safe, and Effective STEMI Care—**Non PCI Hospital**
Door-In-Door-Out (DIDO)Time

- D2b times in US have improved…dramatically
- 40-60% of patients presenting to non-PCI…not benefitting
- Main factor of FMC2b < 90 for transfer patient…DIDO

Glickman et al. Circ Cardiovasc Qual 2011; 4: 382-8.

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STEMI Systems—Ideal Practices
ED Principles of Rapid, Safe, and Effective STEMI Care—**Non PCI Hospital**

What we know:

1. DIDO Times

- ✓ 10% of transfer have DIDO < 30 min
- ✓ 31% had DIDO > 90 min
- ✓ Median DIDO time ≈ 60 min

2. DIDO time < 30 min → ↑chance of FMC2b < 90

- 60% vs. 13% achieved d2b goal
- 85 min vs. 127 min

3. Outcome: In-hospital mortality, stratified by DIDO time

- 2.7% vs. 5.9%
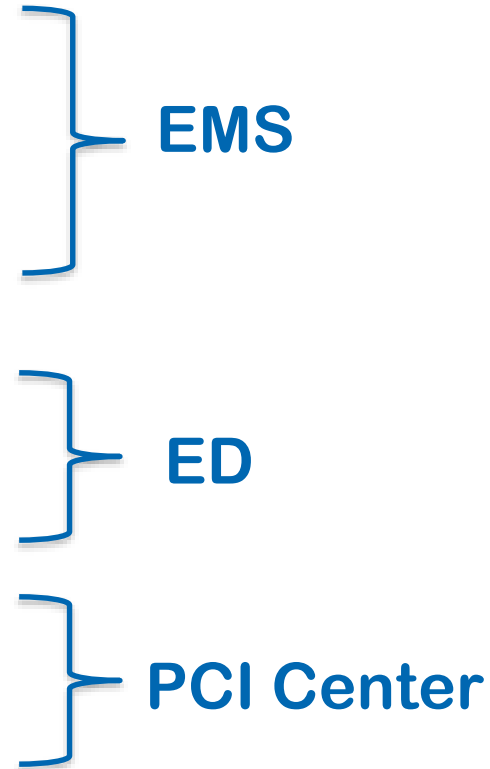
Glickman et al. Circ Cardiovasc Qual 2011; 4: 382-8.

STEMI Systems—Ideal Practices
ED Principles of Rapid, Safe, and Effective STEMI Care—**Non PCI Hospital**

Factors Associated with Reduced DIDO

1. Equipment for 12 lead ECG
2. EMS program to read ECG
3. Local ambulance < 50 miles
4. Keep patient on stretcher

   EMS

5. ECGs within 10 min
6. Single call to activate CL

   ED

7. STEMI team/leadership
8. Specified reperfusion plan

   PCI Center

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Glickman et al. Circ Cardiovasc Qual 2011; 4: 382-8.

STEMI Systems—Ideal Practices
ED Principles of Rapid, Safe, and Effective STEMI Care—**Non PCI Hospital**

Door-in-door-out: time, process

1. Pre-established plans of transfers
   - Relationship with STEMI center(s)
   - Transport options with contingency plan
   - Division of labor
   - Mock drills
2. Medical protocols
   - Standardized
   - Simple
3. ED empowerment to activate CL
   - Processes in parallel

Portals of Entry
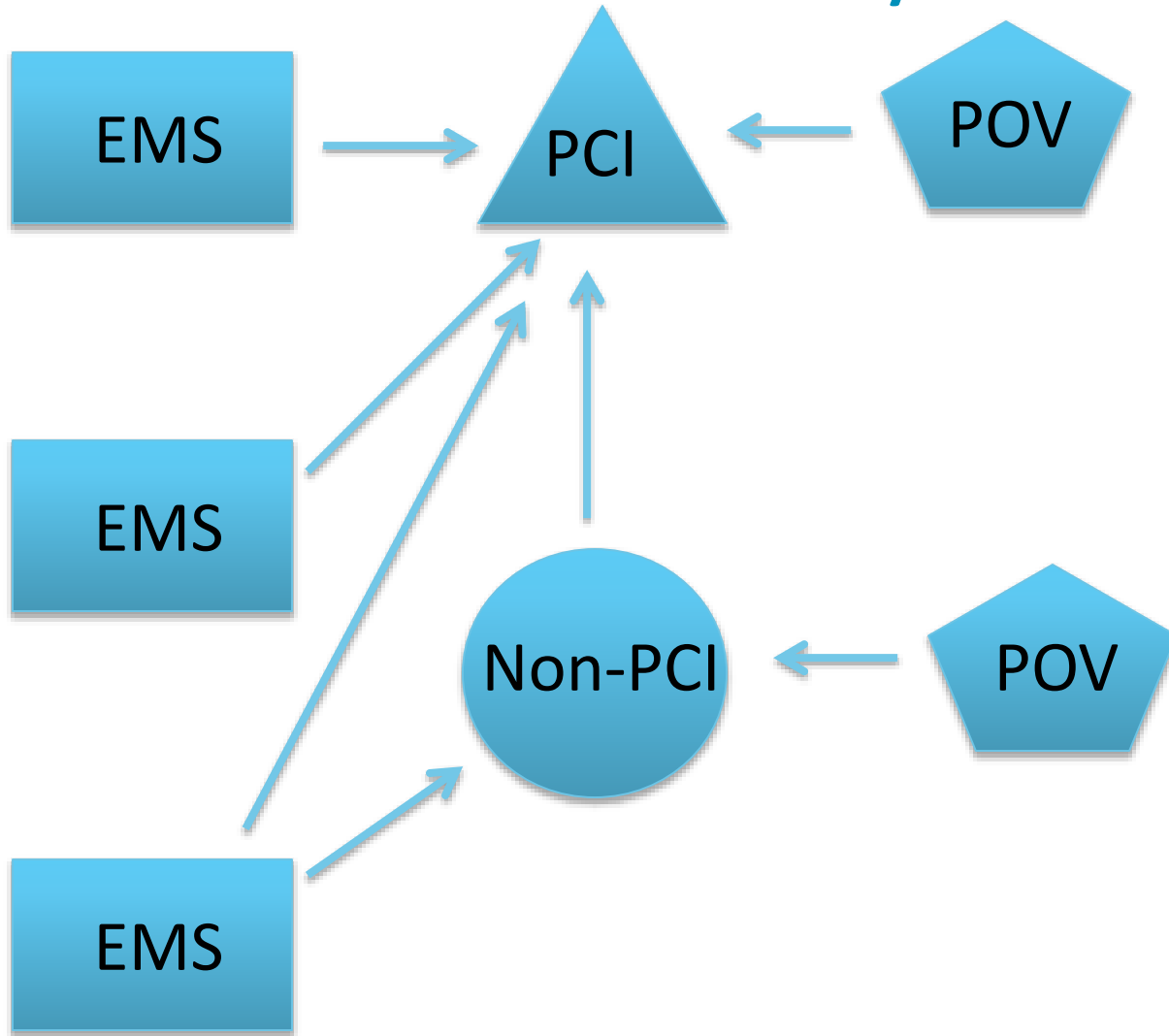
Driving Times and Distances to Hospitals With Percutaneous Coronary Intervention in the United States
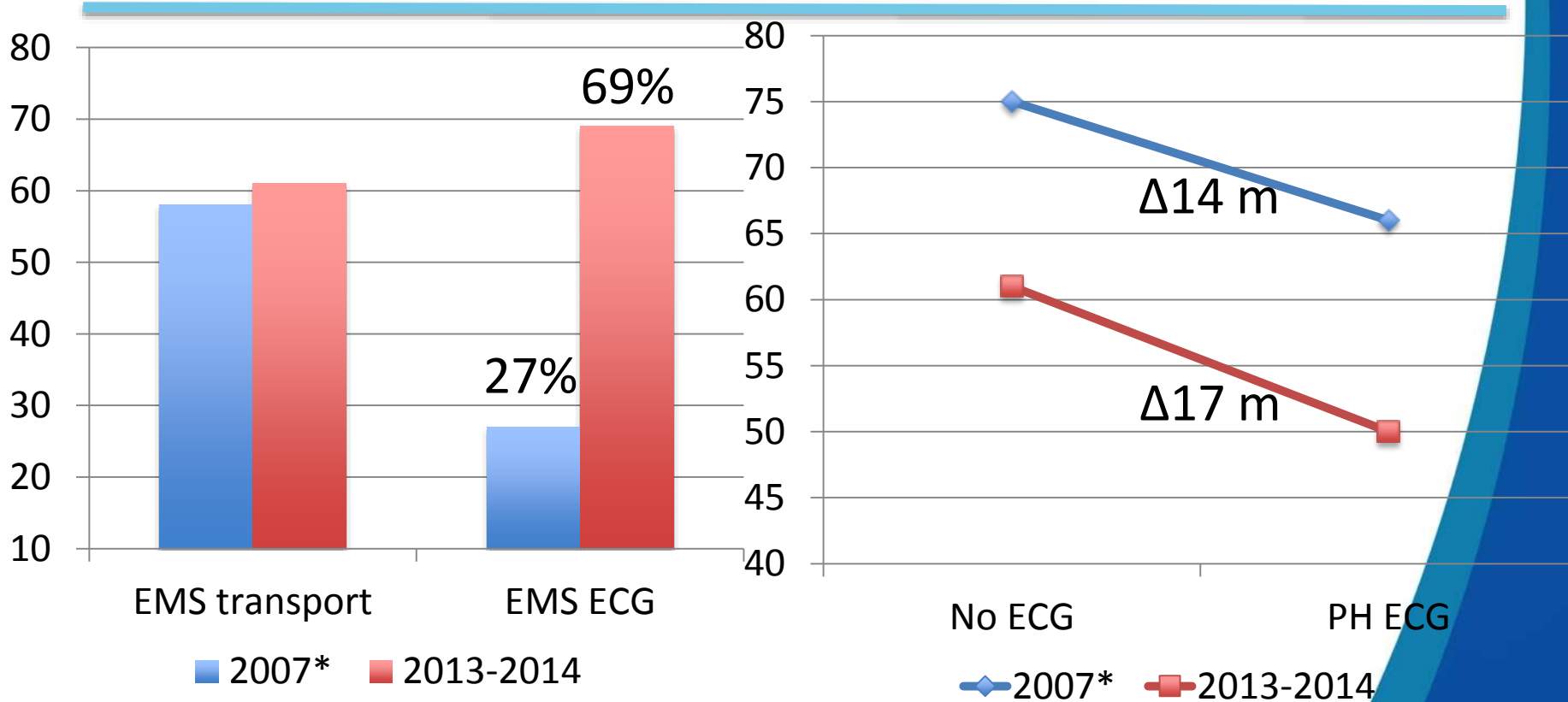**Implications for Prehospital Triage of Patients With ST-Elevation Myocardial Infarction**

Brahmajee K. Nallamothu, MD, MPH; Eric R. Bates, MD; Yongfei Wang, MS;
Elizabeth H. Bradley, PhD; Harlan M. Krumholz, MD, SM

- 25% of US hospitals have 24/7 PCI capability
- 42% present to PCI center
- Remaining 58%…
  - 75% could *bypass & transfer* to PCI hospitals < 30 minutes
  - 80% of US population within 60 min *transfer* of PCI center

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STEMI Systems—Ideal Practices
EMS Care
Utilization of PH ECG

69%

27%

EMS transport   EMS ECG

■ 2007*   ■ 2013-2014

Δ14 m

Δ17 m

No ECG   PH ECG

◆ 2007*   ■ 2013-2014

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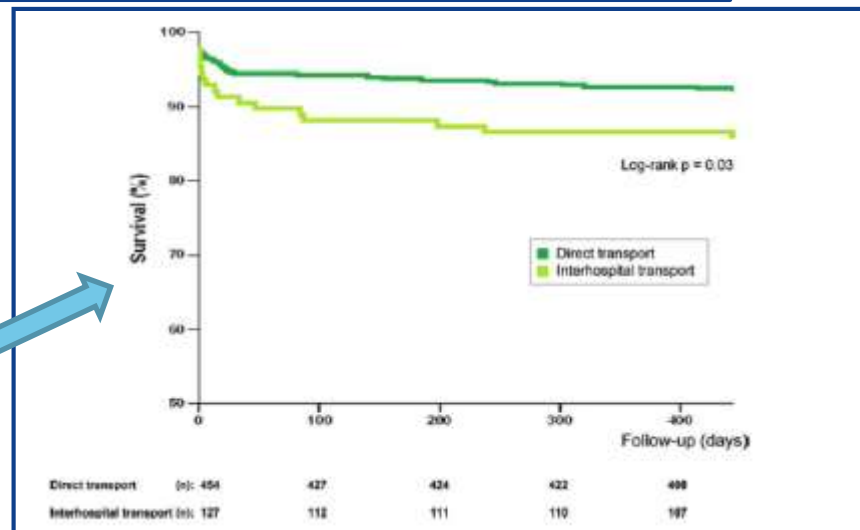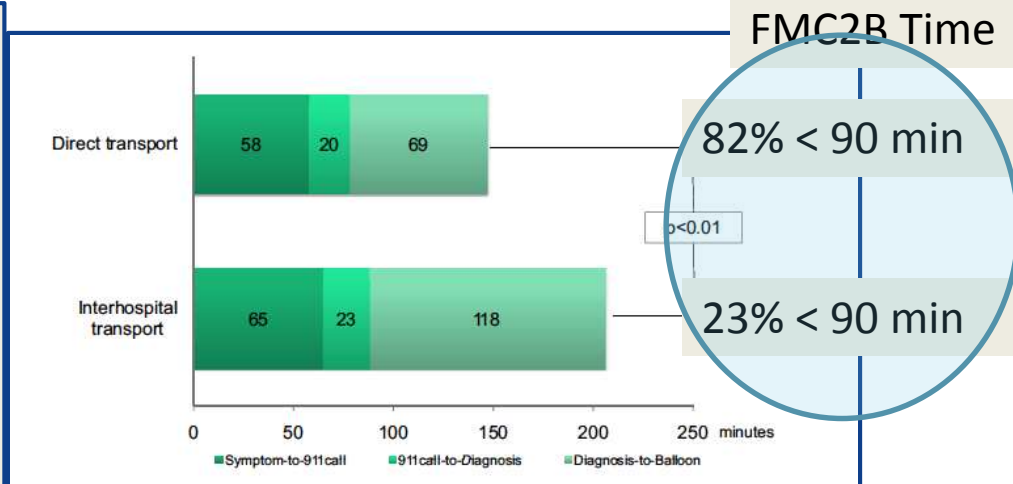* Diercks et al. J Am Coll Cardiol 2009; 53: 161-6

EMS Diversion to STEMI Center

- n= 581 over 3 yrs, one SRC

- Excludes patients diagnosed at referring hospital

- After PH diagnosis
  - Direct transfer to SRC: 78%
  - Transfer from referring: 22%

- Death during transport: Zero!

- VF: 14%

FMC2B Time

82% < 90 min

23% < 90 min

Symptoms to balloon time:

149 min vs. 219 min (Δ70 min)

1 yr mortality: 7% vs. 13%

Dieker HJ, et al. JACC CV Interv. 2010

STEMI Systems—Ideal Practices
EMS Care

- 12 lead ECG
  - Protocols for use
  - Early, frequent, and rapid application
- Pre-hospital cath lab activation
- Transport & Diversion Protocols
- Initiation of standardized medical therapy
  - Less = more
  - No drips!
  - "Grab and go"

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STEMI Systems—Ideal Practices
# **EMS Care**

Prehospital ECG

Benefits

- – Earlier recognition/diagnosis in the field
- – Leads to earlier treatment (via lytics or PCI)
- – *Smarter* triage in the field
  - • Bypass non PCI hospital to SRC
  - • Rendevous arrangement with air transport
- – Improved outcomes:
  - • Reduce short term mortality
  - • Long term survival

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TEXAS

STEMI Systems of Care Conclusions & Call to Action:

1. STEMI systems of care now a societal expectation
   - Concerted effort to optimize care for the most patients

2. Concept of Rx times must include ***all entities*** of the team

3. PCI centers must take the lead
   - Accountability (public reporting soon)
   - Leadership teams, funding, DATA! (Get in ACTION-GTWG)

4. Transfer patients
   - Prehospital triage with *diversion protocols*
   - Streamline care in non-PCI hospitals (Measure DIDO time)
   - Fibrinolytics if FMC2b > 120 min

5. EMS cooperation & collaboration
   - Leadership, metrics, data

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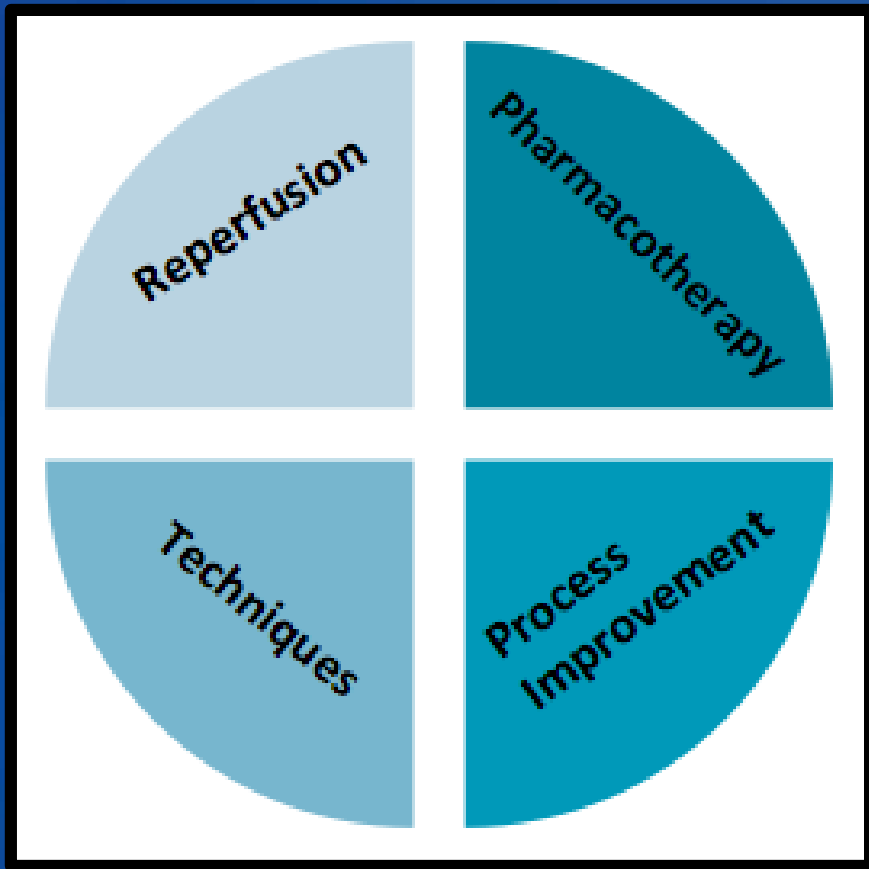
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