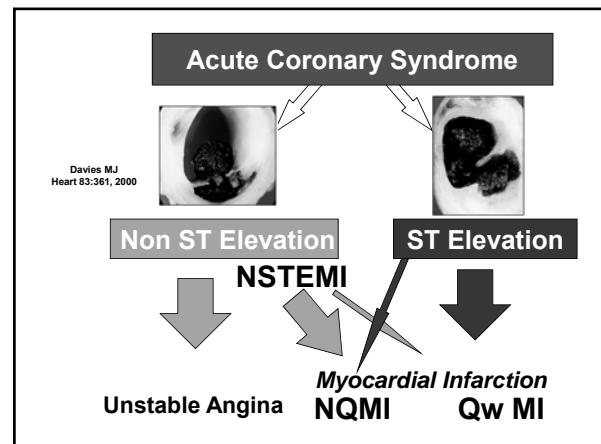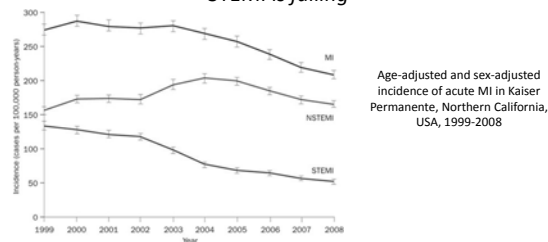## Pathophysiology of Acute Coronary Syndromes and Potential Pharmacologic Interventions

4. Downstream from thrombus myocardial ischemia/necrosis (Beta-blockers, Nitrates etc)

3. Activation of clotting cascade - Thrombin (Heparin/LMWH/Bivalirudin)

2. Platelet adhesion/ activation/aggregation (ASA, clopidogrel IIb/IIIa inhibitors)

1. Plaque rupture, Cholesterol content, Inflammation (hs-CRP) (Statins, ACEI)

Acute Coronary Syndrome

Davies MJ
Heart 83:361, 2000

Non ST Elevation

NSTEMI

ST Elevation

Myocardial Infarction

Unstable Angina   NQMI   Qw MI

Epidemiology of ACS

With changes in definition and improvements in therapy, proportion of NSTEMI is *rising* while that of STEMI is *falling*

Age-adjusted and sex-adjusted incidence of acute MI in Kaiser Permanente, Northern California, USA, 1999-2008

Yeh RW, et al, *N Engl J Med.* 2010.

---

10 Steps to Managing Non-ST Elevation ACS

1. Make an initial diagnosis
2. Give aspirin
3. Control symptoms
4. Manage rate pressure product
5. Perform initial risk stratification
6. Decide if <u>and when</u> the patient should undergo cath
7. Determine which $P2Y_{12}$ inhibitor to use, when to start it, and how long to continue
8. Select between UFH and enoxaparin
9. Initiate secondary prevention medications
10. Cardiac Rehab

---

10 Steps to Managing Non-ST Elevation ACS

1. Make an initial diagnosis
2. Give aspirin
3. Control symptoms
4. Manage rate pressure product
5. Perform initial risk stratification
6. Decide if <u>and when</u> the patient should undergo cath
7. Determine which $P2Y_{12}$ inhibitor to use, when to start it, and how long to continue
8. Select between UFH and enoxaparin
9. Initiate secondary prevention medications
10. Cardiac Rehab

2014 ACC/AHA NSTEACS Guidelines

Risk Assessment Dependent on Contingent Probabilities
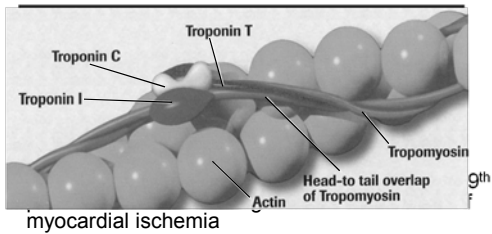
Diagnosis

- **Likelihood of obstructive CAD as cause of symptoms**
  - Dominated by acute findings
    - Examination
    - Symptoms
    - Markers
  - Traditional risk factors are of limited utility
- **Does this patient have symptoms due to acute ischemia from obstructive CAD?**

Prognosis

- **Risk of bad outcome**
  - Dominated by acute findings
    - Older age very important
    - Hemodynamic abnormalities critical
    - ECG, markers
- **What is the likelihood of death, MI, heart failure?**

Amsterdam EA. 2014 AHA/ACC guideline for the management of patients with non–ST-elevation acute coronary syndromes. J Am Coll Cardiol 2014;64:e139–228.
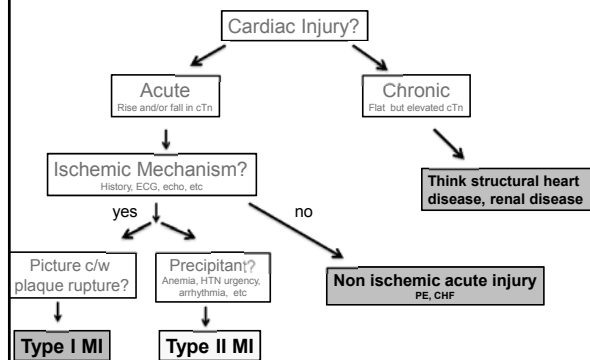
Diagnostic Criteria for MI

Troponin T
Troponin C
Troponin I
Tropomyosin
Head-to tail overlap of Tropomyosin
Actin

myocardial ischemia
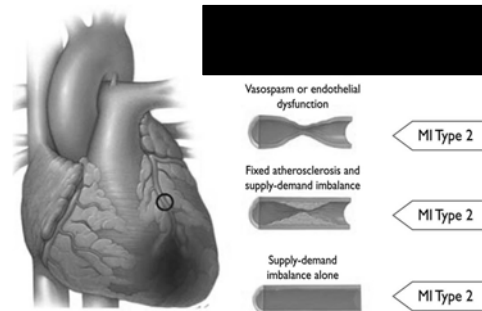
Circulation. 2012 Aug 24. Epub

Non-ACS ↑ of Cardiac Troponins in Hospitalized Patients

- Pulmonary embolism
- Congestive Heart Failure
- Sepsis
- Renal Failure
- Chronic CAD
- LVH

What is an MI in 2016?

Cardiac Injury?

Acute — Rise and/or fall in cTn
Chronic — Flat but elevated cTn

Ischemic Mechanism? — History, ECG, echo, etc

yes / no

Think structural heart disease, renal disease

Picture c/w plaque rupture?
Precipitant? — Anemia, HTN urgency, arrhythmia, etc
Non ischemic acute injury — PE, CHF

Type I MI   Type II MI

Differentiating Type 1 vs. Type 2

Vasospasm or endothelial dysfunction — MI Type 2
Fixed atherosclerosis and supply-demand imbalance — MI Type 2
Supply-demand imbalance alone — MI Type 2

Thygesen et al. EHJ 2012; 33: 2551-2567.

Initial Chest Pain Evaluation

Symptoms Suggestive of ACS

Possible ACS   Definite ACS

(–) ECG; Normal biomarkers

No ST ↑   ST ↑

Observe; repeat ECG, markers at 4-8 hrs

ST-T Δ's, chest pain, ↑ markers

Use MI Guidelines

No recurrent pain; (–) follow-up studies
Recurrent pain; (+) follow-up studies

Stress test; √ LV function if ischemia   (+) test

(–) test: outpt follow-up

Admit, Use Acute Ischemia Pathway
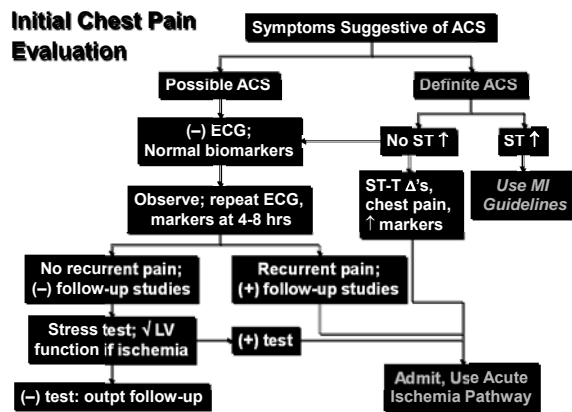
Diagnostic Options in Chest Pain Patient

- ETT
- Perfusion imaging
  - Staged stress/rest
- Stress/Dobutamine echo
- CTA

Summary of RCTs of Cardiac CTA in ED
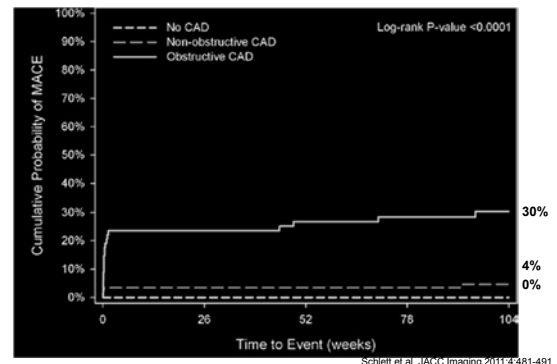
Study	Sites	TIMI score	No.	LOS (h)	30-day MACE (%)	Cost ($)
CT-STAT	16	0-4	699	2.9 vs. 6.3*	0.8 vs. 0.4	2137 vs. 3458*
ACRIN-PA	5	0-2	1370	18 vs. 24.8*	1 vs. 1	N/A
ROMICAT II	9	Low/Int Risk	985	23.2 vs. 30.8*	0.4 vs. 1.2	2101 vs. 2566* (ED) 4026 vs. 3874 (Total)

*P<0.05

Prognostic Value of Normal CCTA

Schlett et al. JACC Imaging 2011;4:481-491

The 10 Steps

1. Make an initial diagnosis
2. Give aspirin
3. Control symptoms
4. Manage rate pressure product
5. Perform initial risk stratification
6. Decide if _and when_ you are going to cath the patient
7. Determine which P2Y$_{12}$ inhibitor to use, when to start it, and how long to continue
8. Select between UFH and enoxaparin
9. Initiate secondary prevention medications
10. Cardiac Rehab

Antiplatelet Therapy for ACS

I IIaIIb III
A

Non–enteric-coated, chewable aspirin (162 mg to 325 mg) should be given to all patients with NSTE-ACS without contraindications as soon as possible after presentation

I IIaIIb III
B

It is reasonable to use 81 mg of aspirin per day in preference to higher maintenance doses after primary PCI.

Distribution of Aspirin Dosing at Discharge

- <0.01%
- 36%
- 61%
- 3%
- ■ 81 mg (78,729)
- 162 mg (7,351)
- ■ 325 mg (134,615)
- ■ other (504)
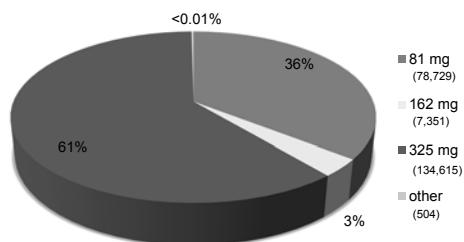
Hall L, Das S. AHA 2012

The 10 Steps

1. Make an initial diagnosis
2. Give aspirin
3. Control symptoms
4. Manage rate pressure product
5. Perform initial risk stratification
6. Decide if _and when_ you are going to cath the patient
7. Determine which P2Y$_{12}$ inhibitor to use, when to start it, and how long to continue
8. Select between UFH and enoxaparin
9. Initiate secondary prevention medications
10. Cardiac Rehab

Anti-Ischemic Therapy

[I IIa IIb III / C] Patients with UA/NSTEMI with ongoing ischemic discomfort should receive sublingual NTG (0.4 mg) every 5 min for a total of 3 doses, after which assessment should be made about the need for intravenous NTG, if not contraindicated.

[I IIa IIb III / B] Intravenous NTG is indicated in the first 48 h after UA/NSTEMI for treatment of persistent ischemia, heart failure (HF), or hypertension.

Amsterdam EA. 2014 AHA/ACC guideline for the management of patients with non–ST-elevation acute coronary syndromes. J Am Coll Cardiol 2014;64:e139–228.

Beta Blockers

- **β-blocker therapy**
  - **Initiate oral therapy within first 24 h unless HF, low-output state, increased risk for cardiogenic shock, or relative contraindications (I, A)**
  - **IV therapy may be harmful with contraindications to beta blockade, signs of HF or low-output state, or other risk factors for cardiogenic shock (III, A)**

Amsterdam EA. 2014 AHA/ACC guideline for the management of patients with non–ST-elevation acute coronary syndromes. J Am Coll Cardiol 2014;64:e139–228.

ACE/ARB

[I IIa IIb III / A] An ACE inhibitor should be administered orally within the first 24 h to NSTEACS patients with pulmonary congestion or LV ejection fraction (LVEF) ≤ 40%, in the absence of hypotension (SBP < 100 mm Hg or < 30 mm Hg below baseline) or known contraindications.

[I IIa IIb III / A] An angiotensin receptor blocker should be administered to UA/NSTEMI patients who are intolerant of ACE inhibitors and have either clinical or radiological signs of HF or LVEF ≤ 40%.

Aldosterone Antagonists

[I IIa IIb III / A] Long-term aldosterone antagonist if:
- no significant renal dysfunction (eGFR> 30 ml/min) or hyperkalemia (potassium ≤ 5 mEq/L)
- therapeutic doses of an ACE inhibitor
- LVEF ≤ 40%
- either symptomatic HF or diabetes mellitus

The 10 Steps

1. Make an initial diagnosis
2. Control symptoms
3. Manage rate pressure product
4. Perform initial risk stratification
5. Decide if _and when_ you are going to cath the patient
6. Determine whether clopidogrel should be loaded.
7. Decide if the patient should receive a GP IIb/IIIa inhibitor
8. Select between UFH and enoxaparin
9. Initiate secondary prevention medications
10. Cardiac Rehab

Balancing risk of ischemia vs risk of bleeding
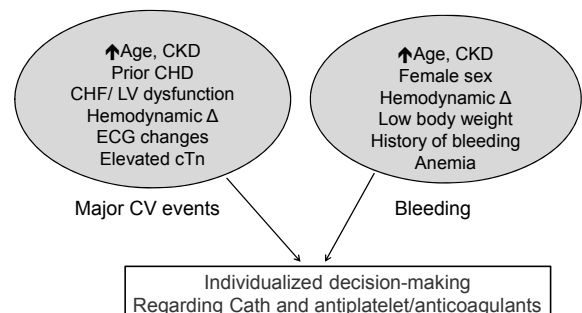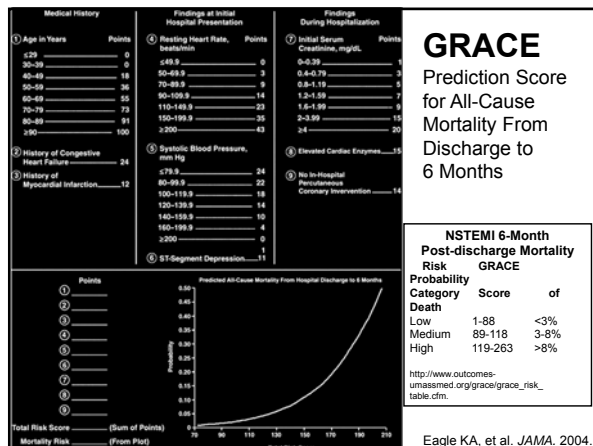
↑Age, CKD
Prior CHD
CHF/ LV dysfunction
Hemodynamic Δ
ECG changes
Elevated cTn

Major CV events

↑Age, CKD
Female sex
Hemodynamic Δ
Low body weight
History of bleeding
Anemia

Bleeding

Individualized decision-making
Regarding Cath and antiplatelet/anticoagulants

GRACE

Prediction Score for All-Cause Mortality From Discharge to 6 Months

NSTEMI 6-Month Post-discharge Mortality

Risk Category	GRACE Score	Probability of Death
Low	1-88	<3%
Medium	89-118	3-8%
High	119-263	>8%

http://www.outcomes-umassmed.org/grace/grace_risk_table.cfm

Eagle KA, et al. *JAMA*. 2004.

The 10 Steps

1. Make an initial diagnosis
2. Give aspirin (more complicated than it seems)!
3. Control symptoms
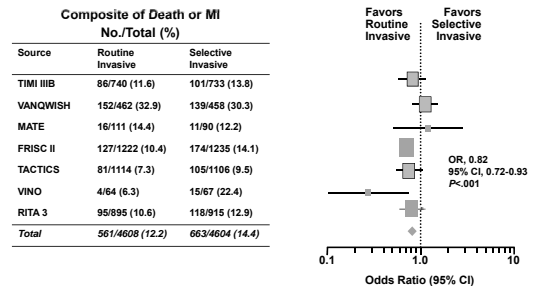4. Manage rate pressure product
5. Perform initial risk stratification
6. Decide if *and when* the patient should undergo cath
7. Determine which P2Y12 inhibitor to use, when to start it, and how long to continue
8. Select between UFH and enoxaparin
9. Initiate secondary prevention medications
10. Cardiac Rehab

Early Invasive versus Early Conservative Management of ACS

- **Early Conservative Strategy (*Ischemia-guided, selective invasive*)**
  - Angiography reserved for:
    - Angina at rest or with minimal activity
    - Dynamic ST changes on resting ECG
    - Positive exercise test
  - Above should occur on aggressive medical tx
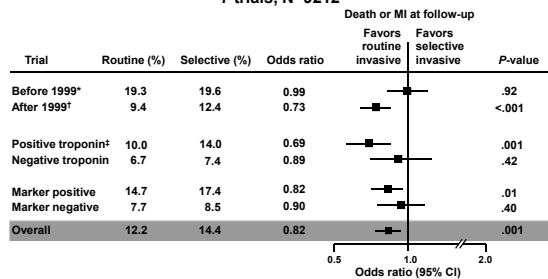- **Early Invasive Strategy**
  - Routine angiography

Routine vs Selective Invasive Strategies in ACS

Composite of *Death* or MI No./Total (%)		
Source	**Routine Invasive**	**Selective Invasive**
TIMI IIIB	86/740 (11.6)	101/733 (13.8)
VANQWISH	152/462 (32.9)	139/458 (30.3)
MATE	16/111 (14.4)	11/90 (12.2)
FRISC II	127/1222 (10.4)	174/1235 (14.1)
TACTICS	81/1114 (7.3)	105/1106 (9.5)
VINO	4/64 (6.3)	15/67 (22.4)
RITA 3	95/895 (10.6)	118/915 (12.9)
Total	*561/4608 (12.2)*	*663/4604 (14.4)*

OR, 0.82 95% CI, 0.72-0.93 P<.001

Mehta S, et al. *JAMA*. 2005;293;2908-2917.

Invasive Management of UA/NSTEMI Meta-analysis: Subgroups

7 trials, N=9212

Trial	Routine (%)	Selective (%)	Odds ratio	P-value
Before 1999*	19.3	19.6	0.99	.92
After 1999†	9.4	12.4	0.73	<.001
Positive troponin‡	10.0	14.0	0.69	.001
Negative troponin	6.7	7.4	0.89	.42
Marker positive	14.7	17.4	0.82	.01
Marker negative	7.7	8.5	0.90	.40
Overall	12.2	14.4	0.82	.001

*TIMI 3B, VANQWISH, MATE; †FRISC II, TACTICS, VINO, RITA 3; ‡Data by troponin status available only in FRISC II, TACTICS, RITA 3. UA, unstable angina.
Mehta SR, et al. *JAMA*. 2005;293:2908-2917.

Who to Refer for Early Invasive Therapy? ACC/AHA Guidelines

- **Highest risk patients with:**
  - ECG changes, known CAD, positive biomarkers
  - CHF, VT, hypotension during initial presentation
- **Intermediate risk patients:**
  - Diabetics, elderly
  - Multiple risk factors
- **Conservative approach most appropriate for lowest risk patients**

When to cath?

- **As soon as possible!**
- **In most circumstances, not a medical emergency**
- **On the otherhand, there is no benefit to "cooling off" the patient prior to cath**

DETERMINE WHETHER THE PATIENT IS AN APPROPRIATE DES CANDIDATE

The 10 Steps

1. Make an initial diagnosis
2. Give aspirin (more complicated than it seems)!
3. Control symptoms
4. Manage rate pressure product
5. Perform initial risk stratification
6. Decide if _and when_ you are going to cath the patient
7. Determine which $P2Y_{12}$ inhibitor to use, when to start it, and how long to continue
8. Select between UFH and enoxaparin
9. Initiate secondary prevention medications
10. Cardiac Rehab

$P2Y_{12}$ Inhibitor Basic Pharmacology

	Clopidogrel	Prasugrel	Ticagrelor
Class	Thienopyridine	Thienopyridine	Triazolopyrimidine
Reversibility	Irreversible	Irreversible	Reversible
Activation	Prodrug, limited by metabolism	Prodrug, not limited by metabolism	Active drug
Onset of Effect^	2-4 hours	30 minutes	30 minutes
Duration of Effect	3-10 days	5-10 days	3-4 days
Withdrawal before major surgery	5 days	7 days	5 days

^ 50% inhibition of platelet aggregation

Hamm CW, et al. Eur Heart J. 2011.

CURE Trial: Primary Composite Endpoint*
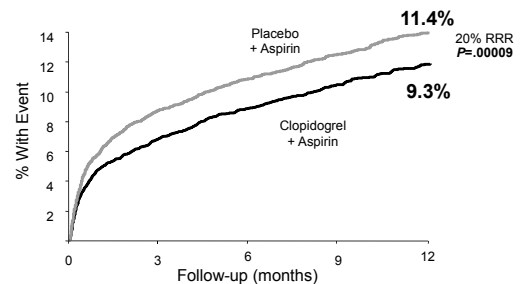
*= MI/Stroke/CV Death, patients with NSTE-ACS; clopidogrel vs. placebo

Yusuf S, et al. *N Engl J Med.* 2001.

CURE: Primary Outcome by Type of Intervention

Fox KAA, et al. *Circulation.* 2004;110:1202-1208.

Primary Endpoint CV Death, MI, Stroke

TRITON TIMI-38

Wiviott S. NEJM 2007;357:2001-15

Bleeding Events
Safety Cohort
(N=13,457)

TRÎTON TIMI·38

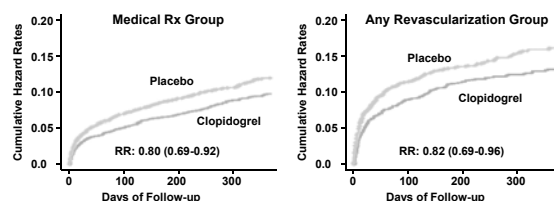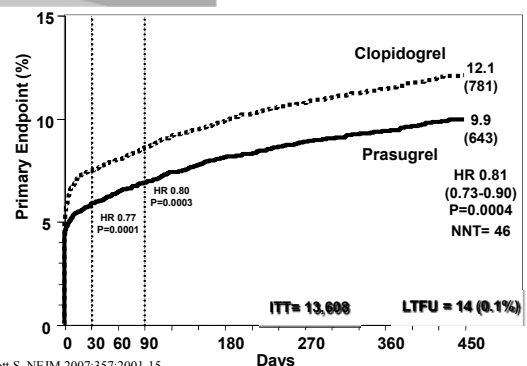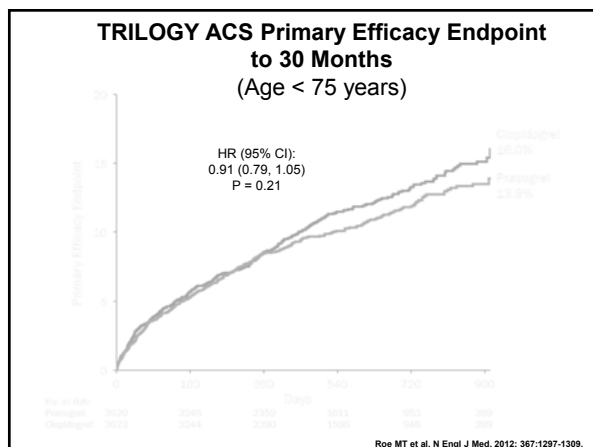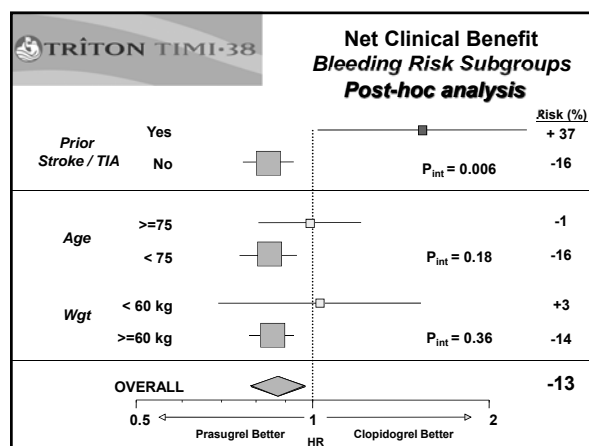| ARD 0.6% HR 1.32 P=0.03 NNH=167 | ARD 0.5% HR 1.52 P=0.01 | ARD 0.2% P=0.23 | ARD 0.3% P=0.002 | ARD 0% P=0.74 |

Net Clinical Benefit
Bleeding Risk Subgroups
Post-hoc analysis

TRÎTON TIMI·38

			Risk (%)
Prior Stroke / TIA	Yes		+ 37
	No	P_{int} = 0.006	-16
Age	>=75		-1
	< 75	P_{int} = 0.18	-16
Wgt	< 60 kg		+3
	>=60 kg	P_{int} = 0.36	-14
OVERALL			-13

0.5 — Prasugrel Better — 1 — HR — Clopidogrel Better — 2

TRILOGY ACS Primary Efficacy Endpoint to 30 Months
(Age < 75 years)

HR (95% CI):
0.91 (0.79, 1.05)
P = 0.21

Clopidogrel
Prasugrel

Roe MT et al. N Engl J Med. 2012; 367:1297-1309.

Conclusion

Prasugrel a reasonable option for <u>invasively managed</u> ACS patients, but

1. Expensive
2. Longer half life, so wait longer for surgical procedures
3. More bleeding
4. Avoid in prior stroke/TIA
5. Caution in elderly, low body weight (use lower dose)

Primary Outcome (composite of CV death, MI or stroke)

Clopidogrel 11.7
Ticagrelor 9.8

HR 0.84 (95% CI 0.77–0.92), p=0.0003

Wallentin NEJM 2009;361:1045-57
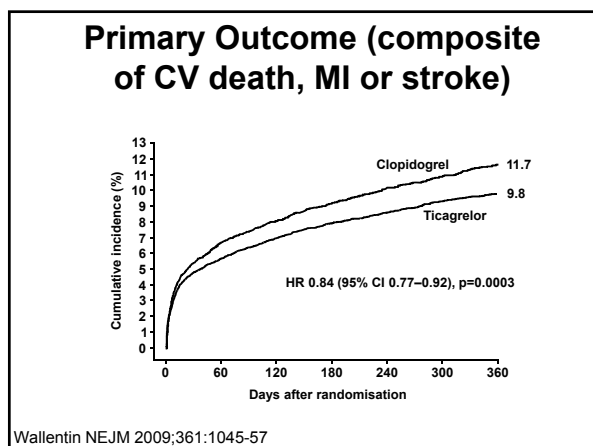
PLATO: Major efficacy endpoints

	Ticagrelor (n=9,333)	Clopidogrel (n=9,291)	HR for (95% CI)	p value†
Primary objective, n (%)				
CV death + MI + stroke	864 (9.8)	1,014 (11.7)	0.84 (0.77–0.92)	<0.001
Secondary objectives, n (%)				
Myocardial infarction	504 (5.8)	593 (6.9)	0.84 (0.75–0.95)	0.005
CV death	**353 (4.0)**	**442 (5.1)**	**0.79 (0.69–0.91)**	**0.001**
Stroke	125 (1.5)	106 (1.3)	1.17 (0.91–1.52)	0.22
Stent thrombosis, n (%)				
Definite	71 (1.3)	106 (1.9)	0.67 (0.50–0.91)	0.009
Total death	**399 (4.5)**	**506 (5.9)**	**0.78 (0.69–0.89)**	**<0.001**

Wallentin NEJM 2009;361:1045-57

Non-CABG and CABG-related major bleeding

K-M estimated rate (% per year)

Legend: Ticagrelor, Clopidogrel

- Non-CABG PLATO major bleeding: 4.5 / 3.8, p=0.026
- Non-CABG TIMI major bleeding: 2.8 / 2.2, p=0.025
- CABG PLATO major bleeding: 7.4 / 7.9, NS
- CABG TIMI major bleeding: 5.3 / 5.8, NS
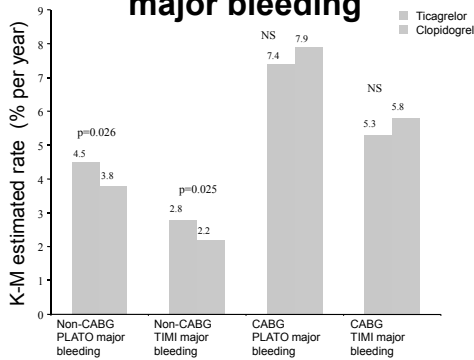
Wallentin NEJM 2009;361:1045-57

PLATO: Medical Therapy Subgroup

Non-invasive / Invasive
Ticagrelor, Clopidogrel

All-cause Mortality (%) vs Days after Randomization

8.2% / 6.1% HR 0.75 P=.01
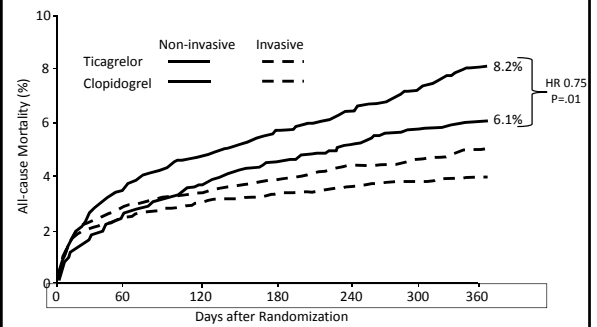
James SK, et al. BMJ. 2011.

Other Findings

All patients	Ticagrelor (n=9,235)	Clopidogrel (n=9,186)	p value[*]
Dyspnea, %			
Any	13.8	7.8	<0.001
With discontinuation of study treatment	0.9	0.1	<0.001
7 day Holter Results			
Ventricular pauses ≥3 seconds, %	5.8	3.6	0.01
Ventricular pauses ≥5 seconds, %	2.0	1.2	0.10

Wallentin NEJM 2009;361:1045-57

Conclusion

Ticagrelor attractive option for both invasively and conservatively managed ACS patients.

1. **Mortality benefit unique, but has not yet been validated**
2. **Expensive**
3. **More bleeding**
4. **Functional half-life similar to clopidogrel**
5. **Requires low dose (81 mg) ASA**

Post-Discharge Antiplatelet Therapy

How Long and How Strong?

Dual Antiplatelet Therapy (DAPT) Study: Design

Randomization*

Study Drug Treatment Ends

12-Month Observational Period: Open-Label Thienopyridine + Aspirin Required

Thienopyridine* + Aspirin

Placebo + Aspirin

3-Month Observational Period: Off Thienopyridine, On Aspirin

Time in months after index stent procedure

0 — 12 — 30 — 33
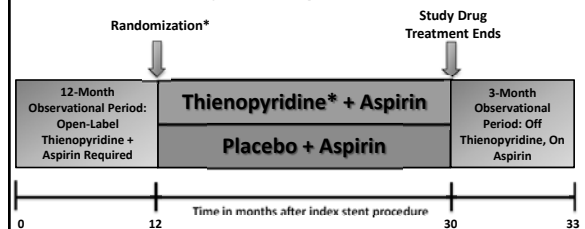
Enrolled: Subjects treated with FDA-approved DES or BMS. Subjects on oral anticoagulant therapy or with life expectancy < 3 years excluded.

Randomized: Free from MI, stroke, repeat revascularization, and moderate or severe bleeding, and adherent with thienopyridine (80% to 120% of doses taken and no interruption > 14 days).

*Clopidogrel or prasugrel

Mauri, Kereiakes et al AHJ 2010; 160(6): 1035-1041

DAPT Study – Co-Primary Effectiveness End Points and Components: 12-30 Months

Cumulative Incidence (%)

Endpoint	Thienopyridine	Placebo	P-value
ST (Definite/Probable)	0.4%	1.4%	<0.001
Definite ST	0.3%	1.2%	<0.001
Probable ST	0.1%	0.1%	0.55
MACCE	4.3%	5.9%	<0.001
Death	2.0%	1.5%	0.052
MI	2.1%	4.1%	<0.001
Ischemic stroke	0.5%	0.7%	0.16
Hemorrhagic stroke	0.3%	0.2%	0.68

Thienopyridine (N=5020) Placebo (N=4941)

Mauri L, et al. *N Engl J Med.* 2014.

DAPT Study – Primary Safety End Point (Moderate or Severe Bleeding): 12-30 Months

Cumulative Incidence (%)

	Thienopyridine	Placebo	P-value
Moderate or Severe	2.5%	1.6%	0.001
Moderate	1.7%	1.0%	0.004
Severe	0.8%	0.6%	0.15
BARC Type 2	3.1%	1.5%	<0.001
BARC Type 3	2.6%	1.5%	<0.001
BARC Type 5	0.1%	0.1%	0.38

Thienopyridine (N=4710) Placebo (N=4649)

Mauri L, et al. *N Engl J Med.* 2014.

DAPT: Treatment Effects in Patients who underwent PCI for ACS

Continued Thienopyridine
Placebo

Endpoint	Continued Thienopyridine	Placebo	
MACE	3.9%	6.8%	HR 0.56 (0.42-0.76) P<.001
ST	0.5%	1.9%	HR 0.27 (0.13-0.57) P<.001
Cardiac Death	0.6%	0.9%	
MI	2.2%	5.2%	
Non-CV Death	0.6%	0.5%	

Yeh R, et al. *J Am Coll Cardiol.* 2015.

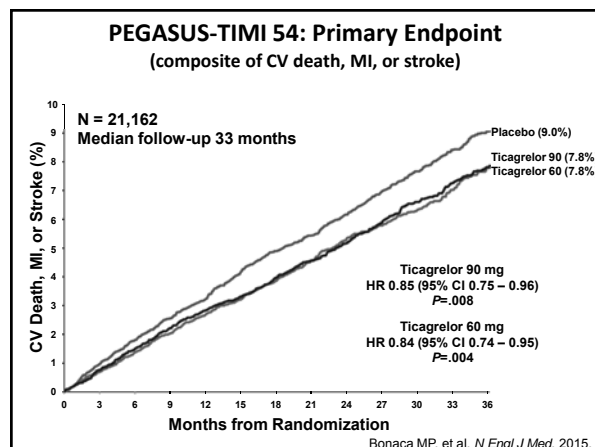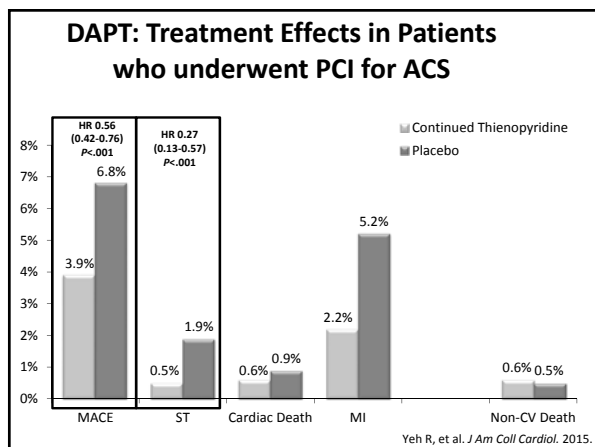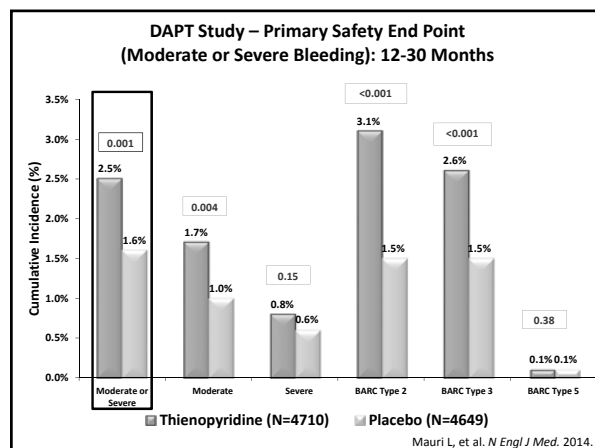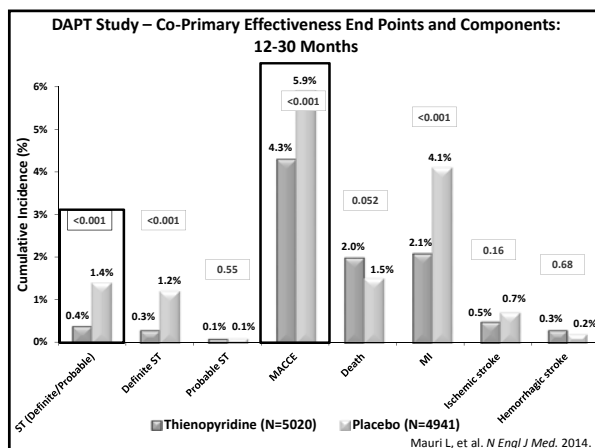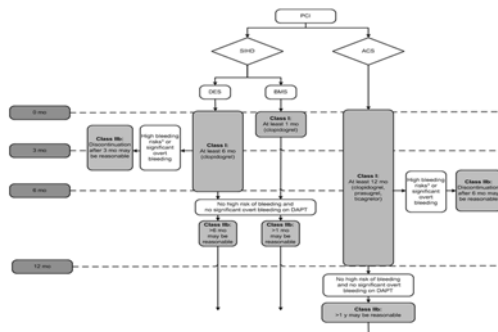## PEGASUS-TIMI 54: Primary Endpoint
(composite of CV death, MI, or stroke)

N = 21,162
Median follow-up 33 months

CV Death, MI, or Stroke (%)

Placebo (9.0%)
Ticagrelor 90 (7.8%)
Ticagrelor 60 (7.8%)

Ticagrelor 90 mg
HR 0.85 (95% CI 0.75 – 0.96)
P=.008

Ticagrelor 60 mg
HR 0.84 (95% CI 0.74 – 0.95)
P=.004

Months from Randomization

Bonaca MP, et al. *N Engl J Med.* 2015.

Reduction in MACE with Ticagrelor by Time from P2Y$_{12}$ Inhibitor Withdrawal

Time from P2Y$_{12}$ Inhibitor withdrawal to randomization

Group	HR (95% CI)	P-value
≤30 days N=7,181	0.70 (0.57 – 0.87)	
	0.75 (0.61 – 0.92)	
	0.73 (0.61 – 0.87) 27% RRR	<.001
>30 days to 1 year N=6,501	0.90 (0.72 – 1.12)	
	0.82 (0.65 – 1.02)	
	0.86 (0.71 – 1.04) 14% RRR	.11
>1 year N=5,079	0.96 (0.73 – 1.26)	
	1.06 (0.81 – 1.38)	
	1.01 (0.80 – 1.27) Ø RRR	.96

P-interaction 0.0097

Ticagrelor Better 1.0 Placebo Better

Ticagrelor 90 mg
Ticagrelor 60 mg
Pooled

Bonaca MP. *ESC* 2015

Continued Thienopyridine vs. Placebo High vs. Low DAPT Score

Risk Difference (Continued Thienopyridine – Placebo), 12-30M

Myocardial Infarction or Stent Thrombosis P<0.001
-0.66% / -3.02%

GUSTO Moderate or Severe Bleed P=0.02
1.55% / 0.37%

DAPT Score < 2
DAPT Score ≥ 2

Variable	Points
Patient Characteristic	
Age	
≥ 75	-2
65 - <75	-1
< 65	0
Diabetes Mellitus	1
Current Cigarette Smoker	1
Prior PCI or Prior MI	1
CHF or LVEF < 30%	2
Index Procedure Characteristic	
MI at Presentation	1
Vein Graft PCI	2
Stent Diameter < 3mm	1

Yeh R. JAMA 2016;315:1735-49

Slide 1

Treatment Algorithm for Duration of P2Y$_{12}$ Inhibitor Therapy in Patients Treated With PCI
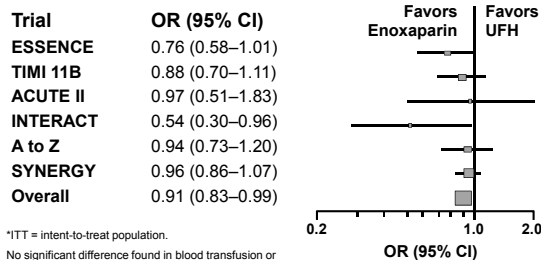

Levine GN et al. Circulation 2016 Mar 29 (epub ahead of print)

Slide 2

The 10 Steps

1. **Make an initial diagnosis**
2. **Give aspirin (more complicated than it seems)!**
3. **Control symptoms**
4. **Manage rate pressure product**
5. **Perform initial risk stratification**
6. **Decide if and when you are going to cath the patient**
7. **Determine which oral P2Y$_{12}$ inhibitor to use and when to start it**
8. **Select between UFH and enoxaparin**
9. **Initiate secondary prevention medications**
10. **Cardiac Rehab**

Slide 3

Enoxaparin vs Unfractionated Heparin in UA/NSTEMI: A Systematic Overview (N=21,946)
Death or MI at 30 Days (ITT*)

Trial	OR (95% CI)
ESSENCE	0.76 (0.58–1.01)
TIMI 11B	0.88 (0.70–1.11)
ACUTE II	0.97 (0.51–1.83)
INTERACT	0.54 (0.30–0.96)
A to Z	0.94 (0.73–1.20)
SYNERGY	0.96 (0.86–1.07)
Overall	0.91 (0.83–0.99)

Favors Enoxaparin — Favors UFH

OR (95% CI): 0.2 — 1.0 — 2.0

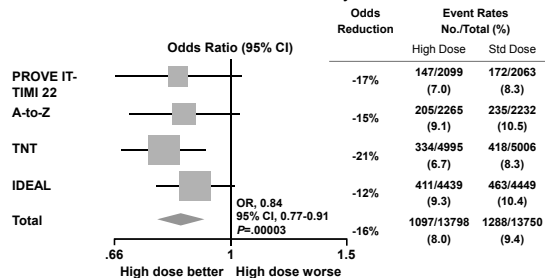*ITT = intent-to-treat population.

No significant difference found in blood transfusion or major bleeding at 7 days after randomization in overall safety population or in population of patients receiving no prerandomization antithrombin therapy.

Adapted with permission from Petersen JL, et al. *JAMA*. 2004;292:89-96.

Slide 4

The 10 Steps

1. **Make an initial diagnosis**
2. **Give aspirin (more complicated than it seems)!**
3. **Control symptoms**
4. **Manage rate pressure product**
5. **Perform initial risk stratification**
6. **Decide if and when you are going to cath the patient**
7. **Determine which oral P2Y$_{12}$ inhibitor to use and when to start it**
8. **Select between UFH and enoxaparin**
9. **Initiate secondary prevention medications**
10. **Cardiac Rehab**

Slide 5

CV Outcomes Trials Comparing Intensive vs Moderate Statin Therapy
Reduction in Risk of Coronary Death or MI

	Odds Ratio (95% CI)	Odds Reduction	Event Rates No./Total (%) High Dose	Std Dose
PROVE IT-TIMI 22		-17%	147/2099 (7.0)	172/2063 (8.3)
A-to-Z		-15%	205/2265 (9.1)	235/2232 (10.5)
TNT		-21%	334/4995 (6.7)	418/5006 (8.3)
IDEAL		-12%	411/4439 (9.3)	463/4449 (10.4)
Total	OR, 0.84 95% CI, 0.77-0.91 P=.00003	-16%	1097/13798 (8.0)	1288/13750 (9.4)

.66 — 1 — 1.5
High dose better   High dose worse

Adapted with permission from Cannon CP, et al. *J Am Coll Cardiol.* 2006;48:438-445.

Slide 6

The 10 Steps

1. Make an initial diagnosis
2. Control symptoms
3. Manage rate pressure product
4. Perform initial risk stratification
5. Decide if and when you are going to cath the patient
6. Determine when to load clopidogrel.
7. Decide if the patient should receive a GP IIb/IIIa inhibitor
8. Select between UFH and enoxaparin
9. Initiate secondary prevention medications
10. Cardiac Rehab