Overtreatment in Cardiology in 2018! What is Reasonable?

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Presenter Disclosure Information

David R. Holmes, Jr., M.D.

**"Overtreatment in Cardiology in 2018!
What is Reasonable?"**

The following relationships exist related to this presentation:

None

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Overtreatment in 2018

- Treatment that does not need to be done
- Treatment that should not be done
- Treatment that is dependent on operator experience

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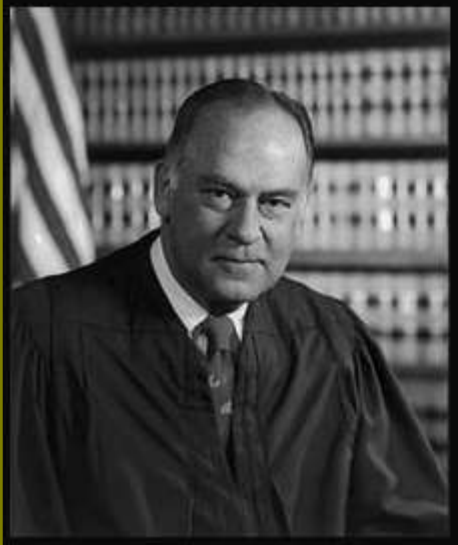

I shall not today attempt further to define the kinds of material but I know it when I see it.

(Potter Stewart)

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Overtreatment in 2018
What are the Causes of the Issues

- Who/what defines over treatment
- Changing guidelines
  - What used to be is no longer
- Science overtakes practice
- New data
- Better recognition and understanding of the issues

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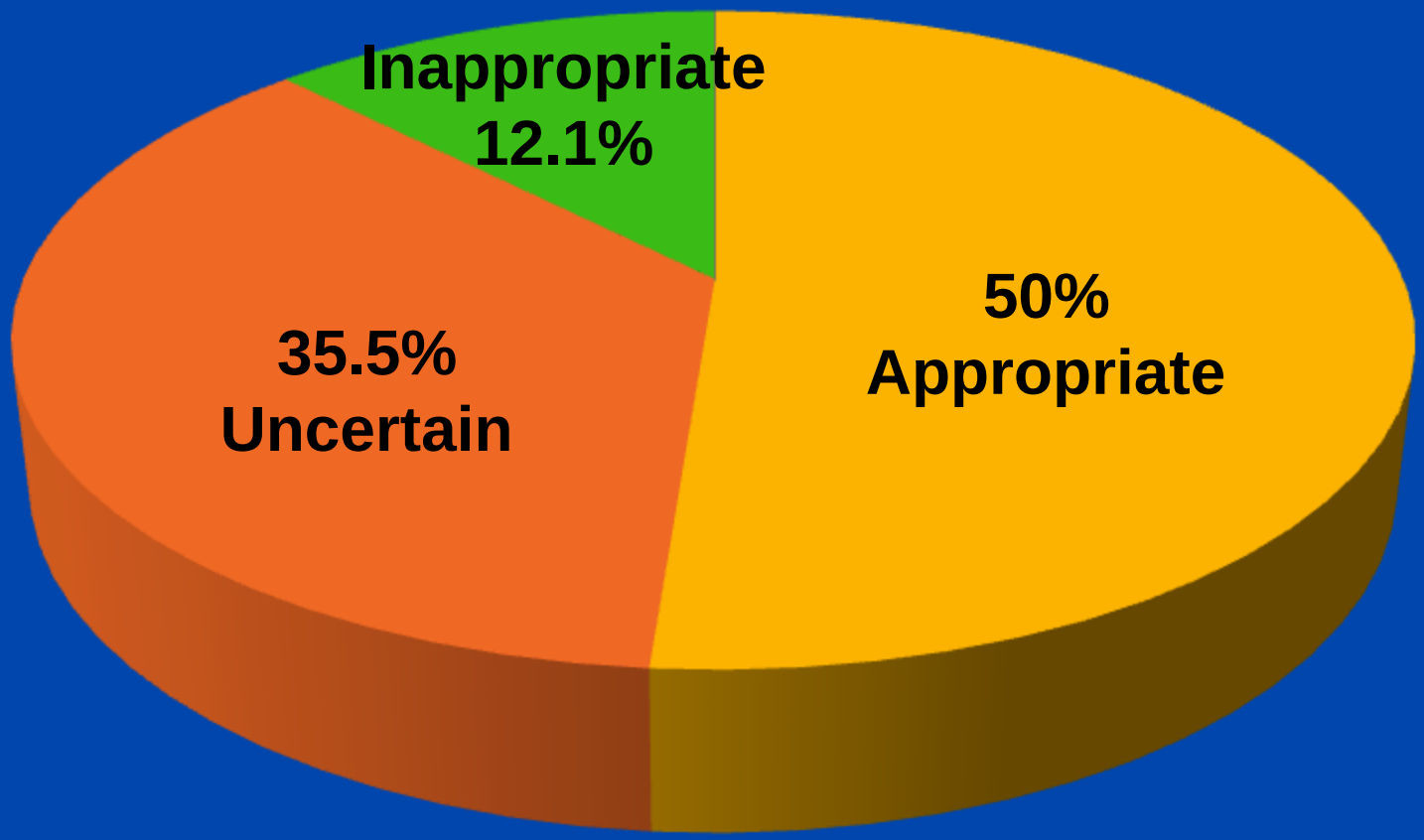
Appropriateness
203,531



Bradley et al: Circ Cardiovasc Qual Outomes 4:290-297, 2012

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Appropriateness
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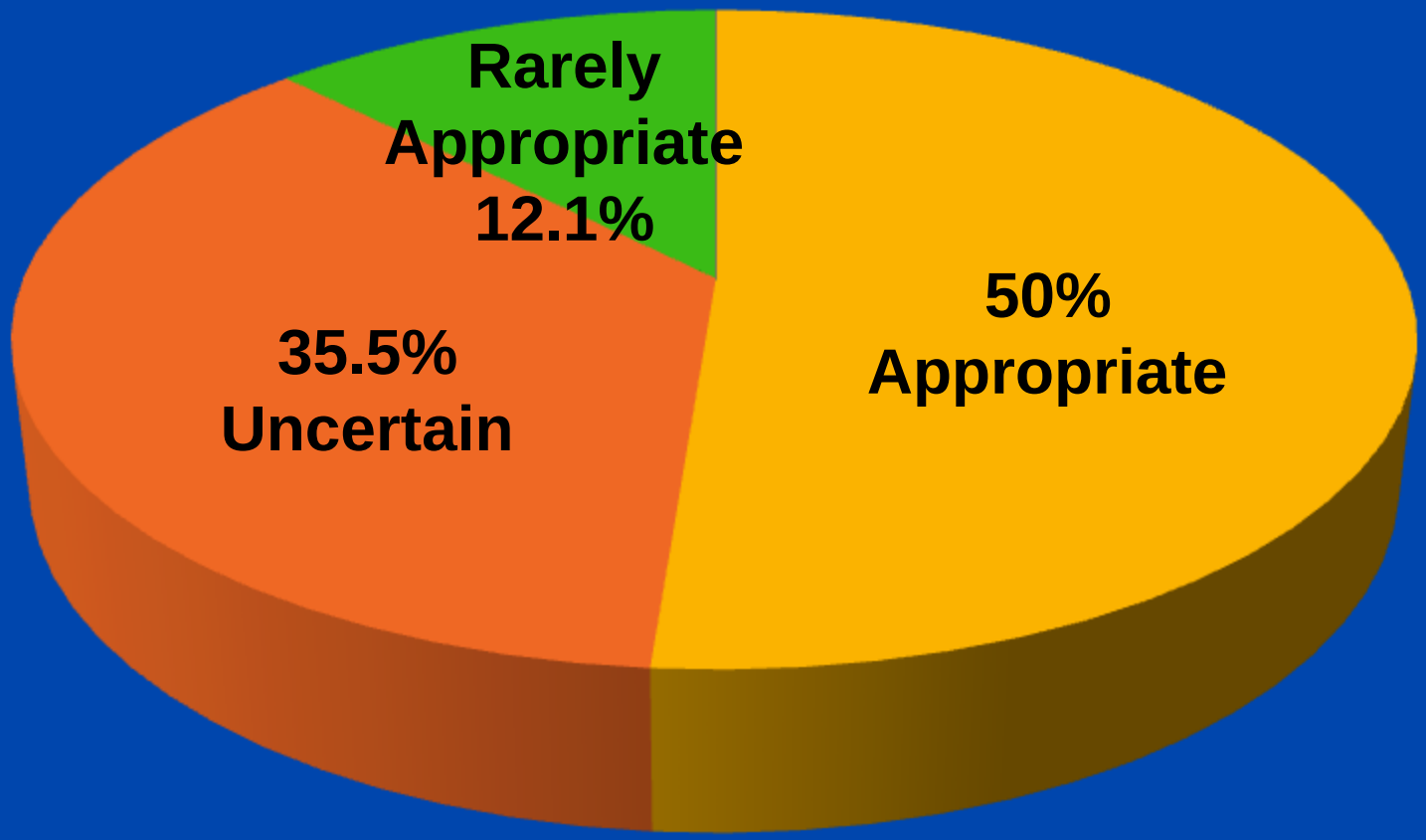

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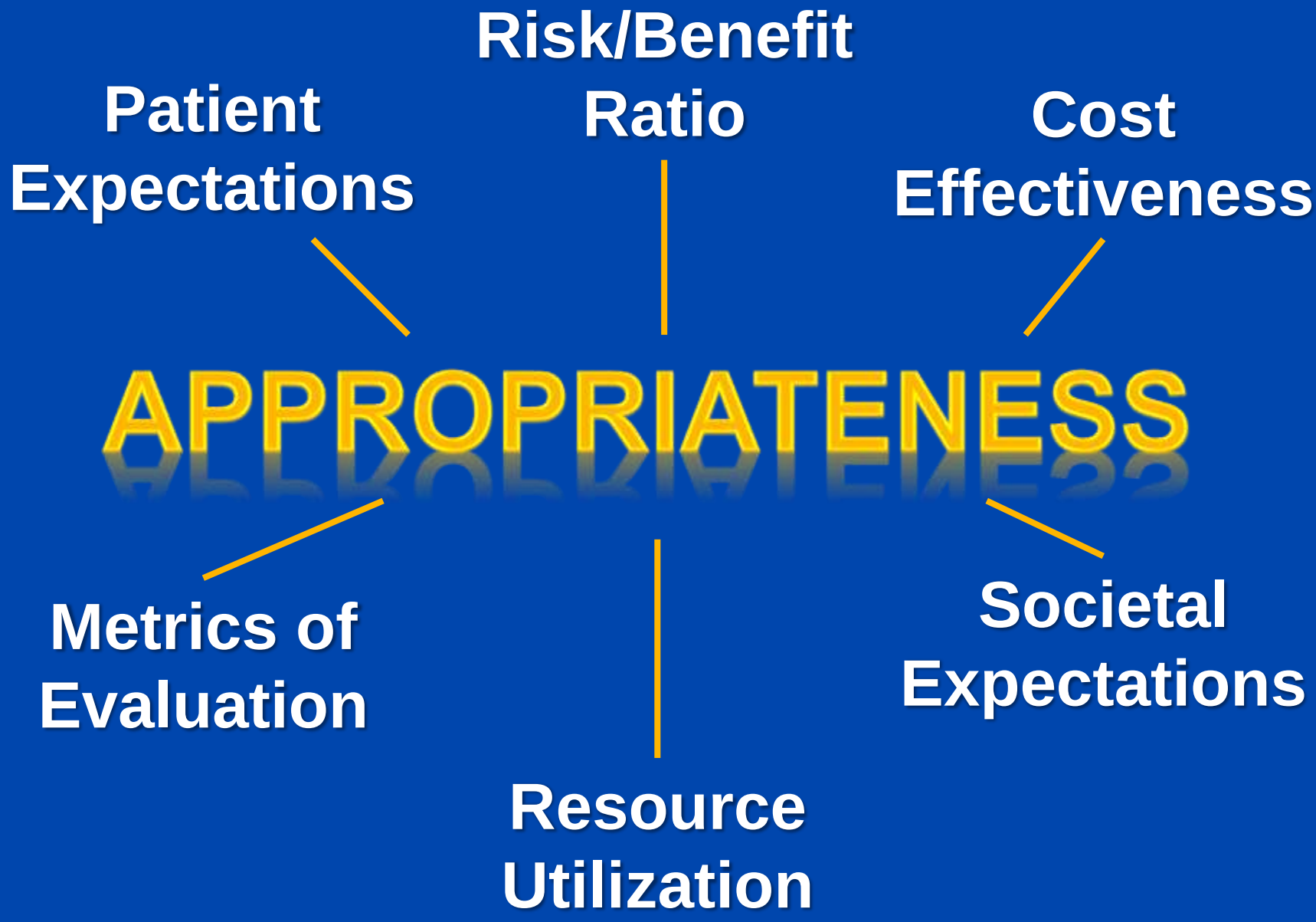
Risk/Benefit Ratio
Patient Expectations
Cost Effectiveness
APPROPRIATENESS
Metrics of Evaluation
Societal Expectations
Resource Utilization

Dr. Oz – Stents Unnecessary?

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Overtreatment in 2018

- Thrombus aspiration during acute MI
- Triple antiplatelet therapy
- Treatment of nonculprit lesions during AMI
- Biovascular absorbable scaffolds
- Emergency department activation

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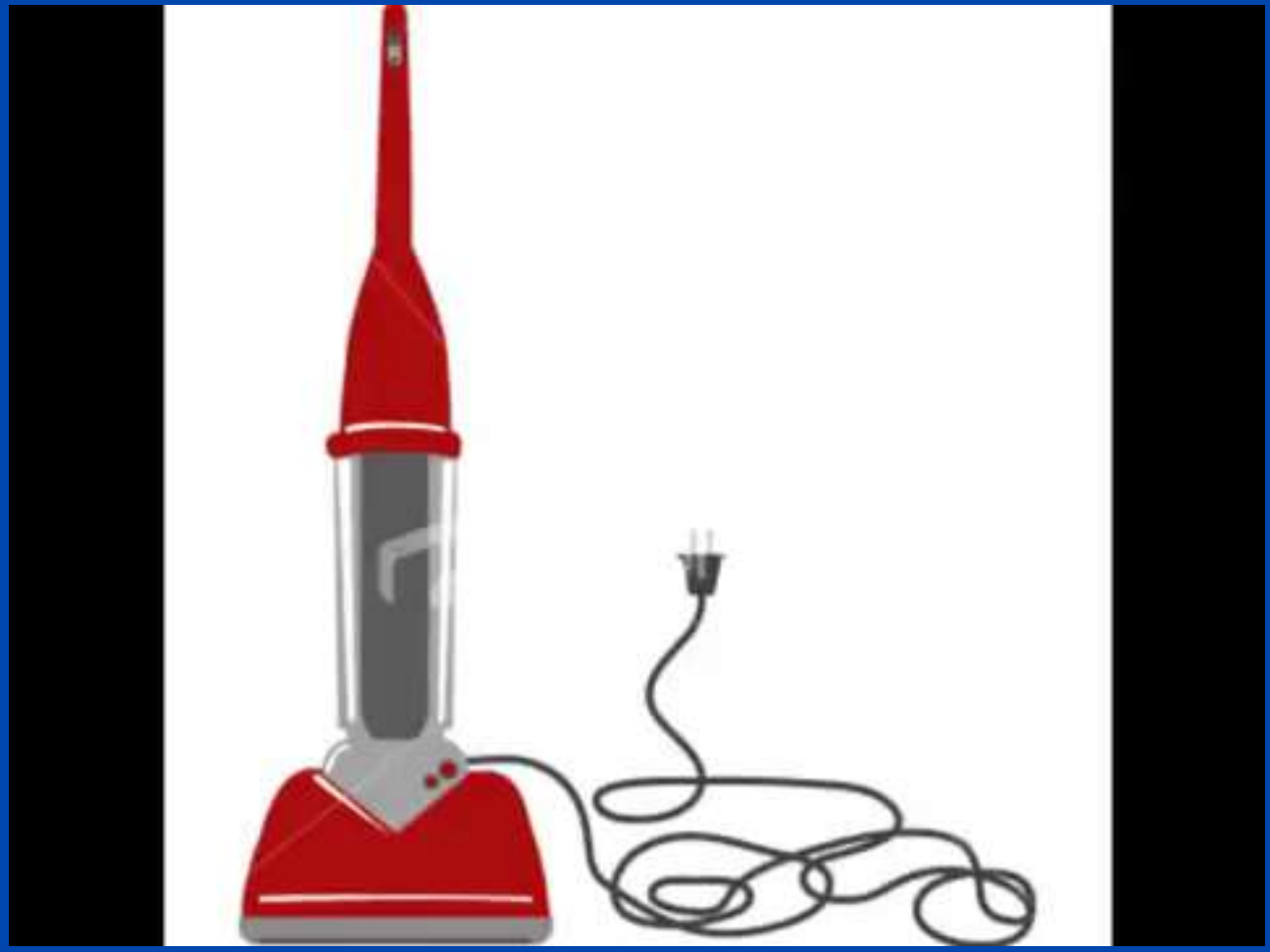
Vacuum Cleaner



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Thrombectomy Trialists Collaboration Individual Level Meta-analysis

- Three eligible RCT's of thrombus aspiration
- TAPAS
- TASTE
- Total
- 19,047 patients
- 18,306 underwent PCI

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Thrombectomy Trialists Collaboration Findings at 30 Days

- Cardiovascular death
- TA: 2.4%
- PCI: 2.9%
- HR 0.84, 95% CI 0.70-1.01, p= 0.06
- Stroke/TIA
- TA: 0.8%
- PCI: 0.5%
- OR 1.43, 95% CI 0.98-2.10, p=0.06

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Thrombus Aspiration in ST-Segment–Elevation Myocardial Infarction

An Individual Patient Meta-Analysis: Thrombectomy Trialists Collaboration

BACKGROUND: Thrombus aspiration during percutaneous coronary intervention (PCI) for the treatment of ST-segment–elevation myocardial infarction (STEMI) has been widely used; however, recent trials have questioned its value and safety. In this meta-analysis, we, the trial investigators, aimed to pool the individual patient data from these trials to determine the benefits and risks of thrombus aspiration during PCI in patients with ST-segment–elevation myocardial infarction.

METHODS: Included were large (n≥1000), randomized, controlled trials comparing manual thrombectomy and PCI alone in patients with ST-segment–elevation myocardial infarction. Individual patient data were provided by the leadership of each trial. The prespecified primary efficacy outcome was cardiovascular mortality within 30 days, and the primary safety outcome was

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Stefan James, MD, PhD
Vladimir Džavík, MD
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Karim D. Mahmoud, MD, PhD
Felix Zijlstra, MD, PhD
Salim Yusuf, MBBS, DPhil
Goran K. Olivecrona, MD, PhD
Henrik Renlund, PhD

CONCLUSIONS: Routine thrombus aspiration during PCI for ST-segment–elevation myocardial infarction did not improve clinical outcomes. In the high thrombus burden group, the trends toward reduced cardiovascular death and increased stroke or transient ischemic attack provide a rationale for future trials of improved thrombus aspiration technologies in this high-risk subgroup.

CONCLUSIONS: Routine thrombus aspiration during PCI for ST-segment–elevation myocardial infarction did not improve clinical outcomes. In the high thrombus burden group, the trends toward reduced cardiovascular death and increased stroke or transient ischemic attack provide a rationale for future trials of improved thrombus aspiration technologies in this high-risk subgroup.

CLINICAL TRIAL REGISTRATION: URLs: http://www.ClinicalTrials.gov http://www.crd.york.ac.uk/prospero/. Unique identifiers: NCT02552407 and CRD42015025936.

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Sources of Funding, see page 151

Key Words: meta-analysis [publication type] ■ myocardial infarction ■ thrombectomy

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Thrombectomy for AMI
How do we integrate the data?

- Routine thrombectomy although intuitively obvious has not been proven beneficial and should not be routine
- In selected patients with high thrombus burden eg large RCA with long occlusion, or VG occlusion, it can be considered when performed carefully
- More data are needed in selected high risk patient groups.

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Overtreatment in 2018

- Thrombus aspiration during acute MI
- Triple antiplatelet therapy
- Treatment of nonculprit lesions during AMI
- Biovascular absorbable scaffolds
- Emergency department activation

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Background

- Atrial fibrillation most common cardiac arrhythmia
  - Increases risk of cardioembolic events 5x
- Coronary artery disease co-exists in 20-30% of patients with AF
  - 5-7% of these patients undergo PCI
- DAPT is more protective than ASA for prevention of cardioembolic events in AF patients
- AF patients undergoing PCI may potentially benefit from OAC
- Bleeding an issue

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AFib and PCI: Spectrum of Options for Antithrombotic Regimens

- ASA alone
- Warfarin alone

- ASA + clopidogrel
- ASA + prasugrel
- ASA + ticagrelor

- ASA+ Warfarin

- ASA + clopid. + warfarin
- ASA + Pras + warfarin
- ASA + Ticag + warfarin

- Clopidogrel + warfarin
- Pras + warfarin
- Ticag + warfarin

- NOAC (novel anticoagulant) alone

- ASA+ NOAC

- ASA + clopid +NOAC (low dose)
- ASA + clopid + NOAC (high dose)
- ASA + Pras + NOAC
- ASA + Ticag + NOAC

- Clopidogrel + NOAC
- Pras + NOAC
- Ticag + NOAC

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“You can’t keep everyone happy, you’re not wine!”

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WOEST

- Open label, multicenter, RCT
  - 2009-2011
- 573 patients receiving oral anticoagulants and undergoing PCI
  - Randomization to clopidogrel alone
  - Clopidogrel + ASA
- Primary endpoint
  - Any bleeding during 1 year
- Composite
  - Death, MI, stroke, TVR, ST

Dewilde et al: Lancet 381:1107-15, 2013

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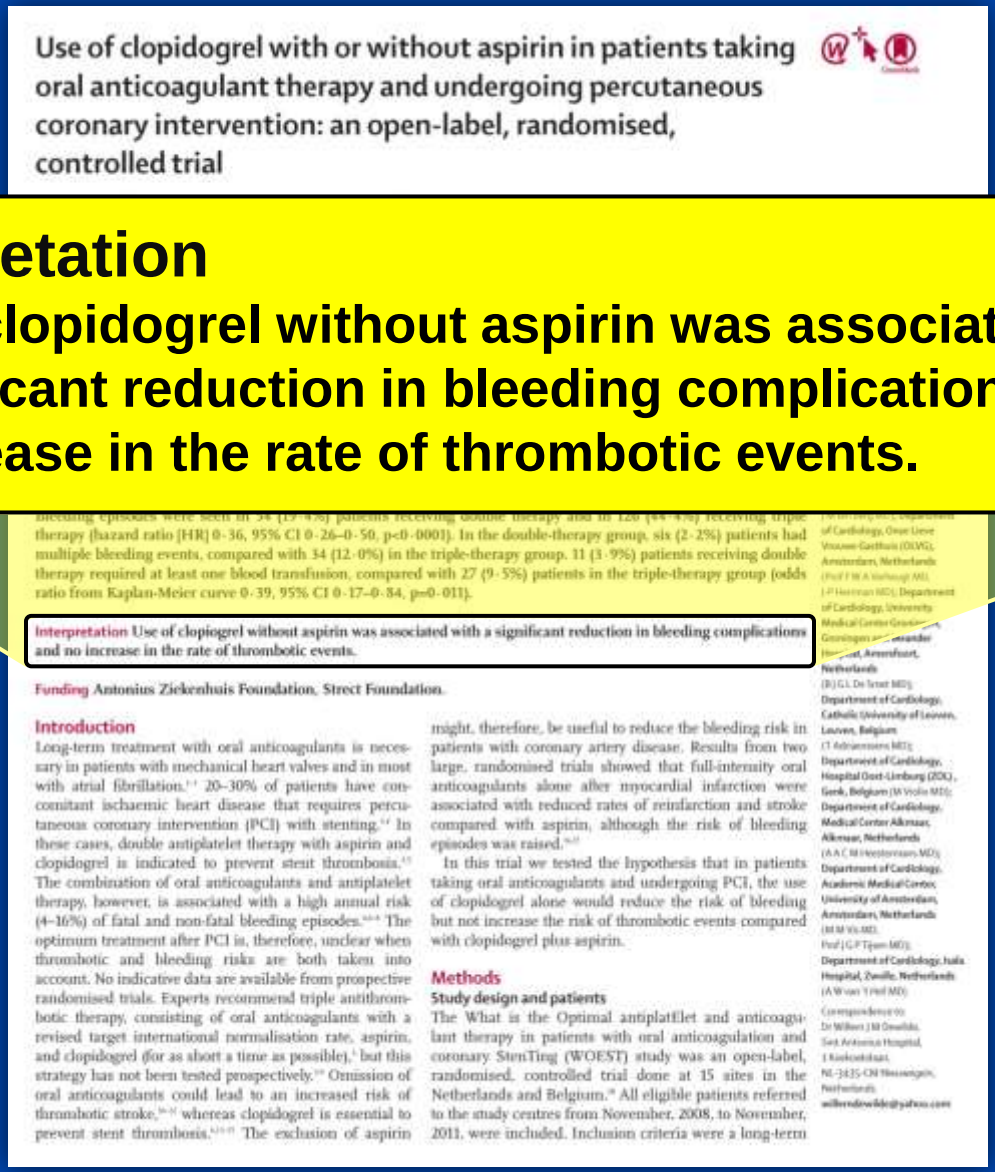

Use of clopidogrel with or without aspirin in patients taking oral anticoagulant therapy and undergoing percutaneous coronary intervention: an open-label, randomised, controlled trial

Interpretation

Use of clopidogrel without aspirin was associated with a significant reduction in bleeding complications and no increase in the rate of thrombotic events.

therapy (hazard ratio [HR] 0·36, 95% CI 0·26–0·50, p<0·0001). In the double-therapy group, six (2·2%) patients had multiple bleeding events, compared with 34 (12·0%) in the triple-therapy group. 11 (3·9%) patients receiving double therapy required at least one blood transfusion, compared with 27 (9·5%) patients in the triple-therapy group (odds ratio from Kaplan-Meier curve 0·39, 95% CI 0·17–0·84, p=0·011).

Interpretation Use of clopiogrel without aspirin was associated with a significant reduction in bleeding complications and no increase in the rate of thrombotic events.

Funding Antonius Ziekenhuis Foundation, Strect Foundation.

Introduction

Long-term treatment with oral anticoagulants is necessary in patients with mechanical heart valves and in most with atrial fibrillation.[1,2] 20–30% of patients have concomitant ischaemic heart disease that requires percutaneous coronary intervention (PCI) with stenting.[3,4] In these cases, double antiplatelet therapy with aspirin and clopidogrel is indicated to prevent stent thrombosis.[5,7] The combination of oral anticoagulants and antiplatelet therapy, however, is associated with a high annual risk (4–16%) of fatal and non-fatal bleeding episodes.[8,9] The optimum treatment after PCI is, therefore, unclear when thrombotic and bleeding risks are both taken into account. No indicative data are available from prospective randomised trials. Experts recommend triple antithrombotic therapy, consisting of oral anticoagulants with a revised target international normalisation rate, aspirin, and clopidogrel (for as short a time as possible),[5] but this strategy has not been tested prospectively.[10] Omission of oral anticoagulants could lead to an increased risk of thromboticstroke,[11,12] whereas clopidogrel is essential to prevent stent thrombosis.[4,5,13] The exclusion of aspirin might, therefore, be useful to reduce the bleeding risk in patients with coronary artery disease. Results from two large, randomised trials showed that full-intensity oral anticoagulants alone after myocardial infarction were associated with reduced rates of reinfarction and stroke compared with aspirin, although the risk of bleeding episodes was raised.[14,15]

In this trial we tested the hypothesis that in patients taking oral anticoagulants and undergoing PCI, the use of clopidogrel alone would reduce the risk of bleeding but not increase the risk of thrombotic events compared with clopidogrel plus aspirin.

Methods

Study design and patients

The What is the Optimal antiplatElet and anticoagulant therapy in patients with oral anticoagulation and coronary StenTing (WOEST) study was an open-label, randomised, controlled trial done at 15 sites in the Netherlands and Belgium.[16] All eligible patients referred to the study centres from November, 2008, to November, 2011, were included. Inclusion criteria were a long-term

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Dewilde et al: Lancet 381:1107-15, 2013

Dual or Single Antiplatelet Therapy + AC

- "At first sight these outcomes suggest a resounding success for antiplatelet therapy without ASA. Yet practice should not be changed on the basis of this study alone."
- Major bleeding not decreased
- More aggressive AP regimen than in guidelines
  - Most patients received AP regimen for >6 mos
- Radial access in only 25-27%
- Underpowered

Fox, Lancet 381:1080-81, 2013

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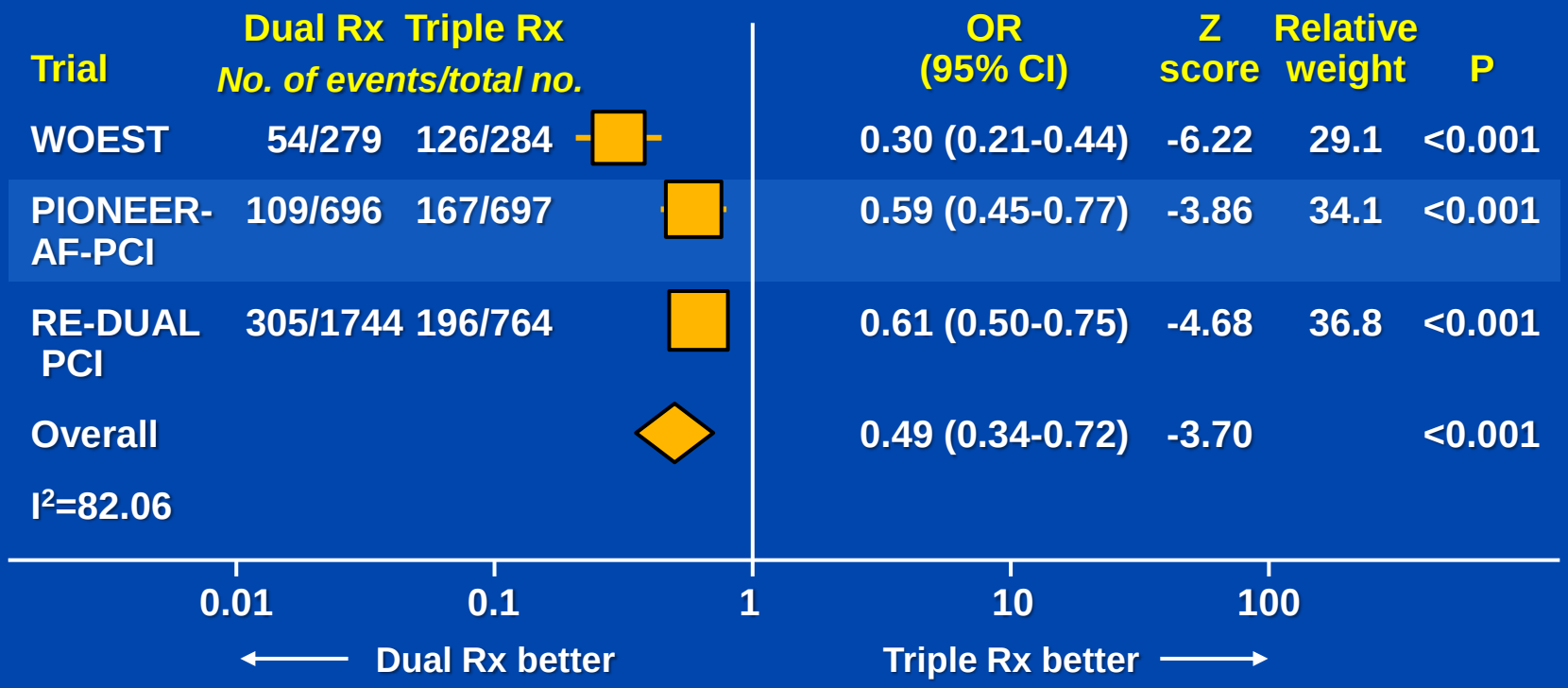
Triple Therapy for AF After PCI

Safety: Major and Minor Bleeding Events



Piccini and Schuyler: NEJM 377:1580, 2017

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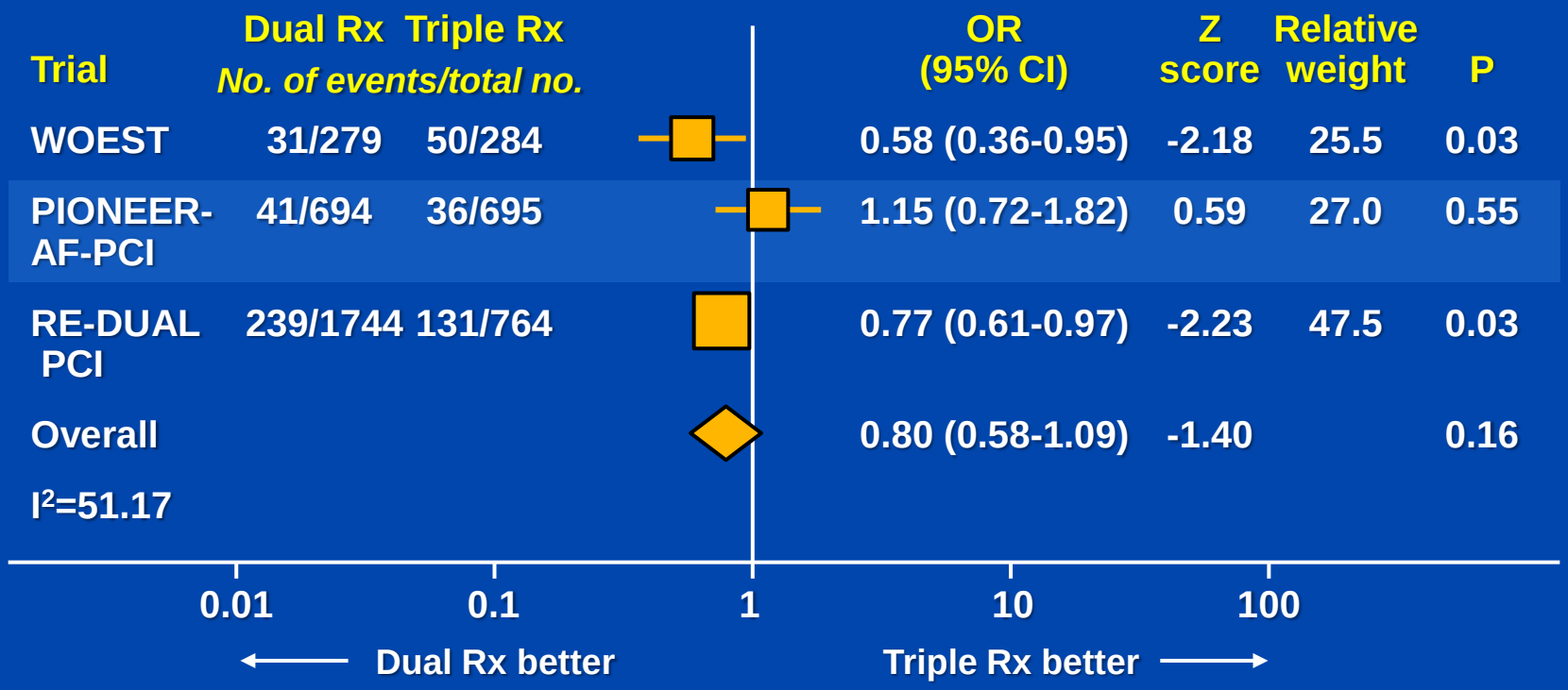
Triple Therapy for AF After PCI

Efficacy: Major Adverse Cardiovascular Events



Piccini and Schuyler: NEJM 377:1580, 2017

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Triple Therapy for AF After PCI

- No single trial has been adequately powered to completely rule out an increase in ischemic events with dual therapy versus triple therapy. However, the consistency across these three major trials and the significantly lower risk of bleeding with dual therapy make it hard to argue that triple therapy should be used routinely. The aggregate evidence suggests that the net clinical benefit of dual therapy should give cardiologists confidence to drop aspirin when they are using a contemporary PCI strategy with drug-eluting stents. Moving forward, the key questions will be: What combination of drugs should be included in dual therapy, and how will we test this strategy?

Piccini and Schuyler: NEJM 377:1580, 2017

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Overtreatment in 2018

- Thrombus aspiration during acute MI
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PCI, STEMI & Cardiogenic Shock

- Multicenter RCT
  - 706 patients with cardiogenic shock
  - BP <90 mm/Hg for >30 min on catecholamines to maintain BP ≥90
  - Clinical pulmonary congestion
  - Impaired organ perfusion
- Randomization
  - Culprit lesion PCI
  - Multivessel PCI
- Primary endpoint
  - All-cause death, severe renal failure
  - RRT <30 days

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Thiele et al: NEJM; 377:2419-32, 2017

PCI, STEMI & Cardiogenic Shock
Clinical Outcomes at 30 Days

Outcome	Culprit-Lesion Only PCI Group (n=344)	Multivessel PCI Group (n=341)	RR (95% CI)	P
	No./total no. (%)			
Primary endpoint: death from any cause or renal-replacement therapy	158/344 (45.9)	189/341 (55.4)	0.83 (0.71-0.96)	0.01
Death from any cause	149/344 (43.3)	176/341 (51.6)	0.84 (0.72-0.98)	0.03
Renal-replacement therapy	40/344 (11.6)	56/341 (16.4)	0.71 (0.49-1.03)	0.07
Indication for renal-replacement Rx				
Hyperkalemia	7/40 (17.5)	9/56 (16.1)		
Metabolic acidosis	18/40 (45.0)	20/56 (35.7)		
Uremia	13/40 (32.5)	20/56 (35.7)		
Volume overload	12/40 (30.0)	17/56 (30.4)		
Other cause	6/40 (15.0)	4/56 (7.1)		
Recurrent MI	4/344 (1.2)	3/341 (0.9)	1.32 (0.30-5.86)	1.00
Rehospitalization for CHF	1/344 (0.3)	1/342 (0.3)	0.99 (0.10-9.50)	0.99
Death, recur MI, or rehosp for CHF	151/344 (43.9)	179/342 (52.3)	0.84 (0.72-0.98)	0.03

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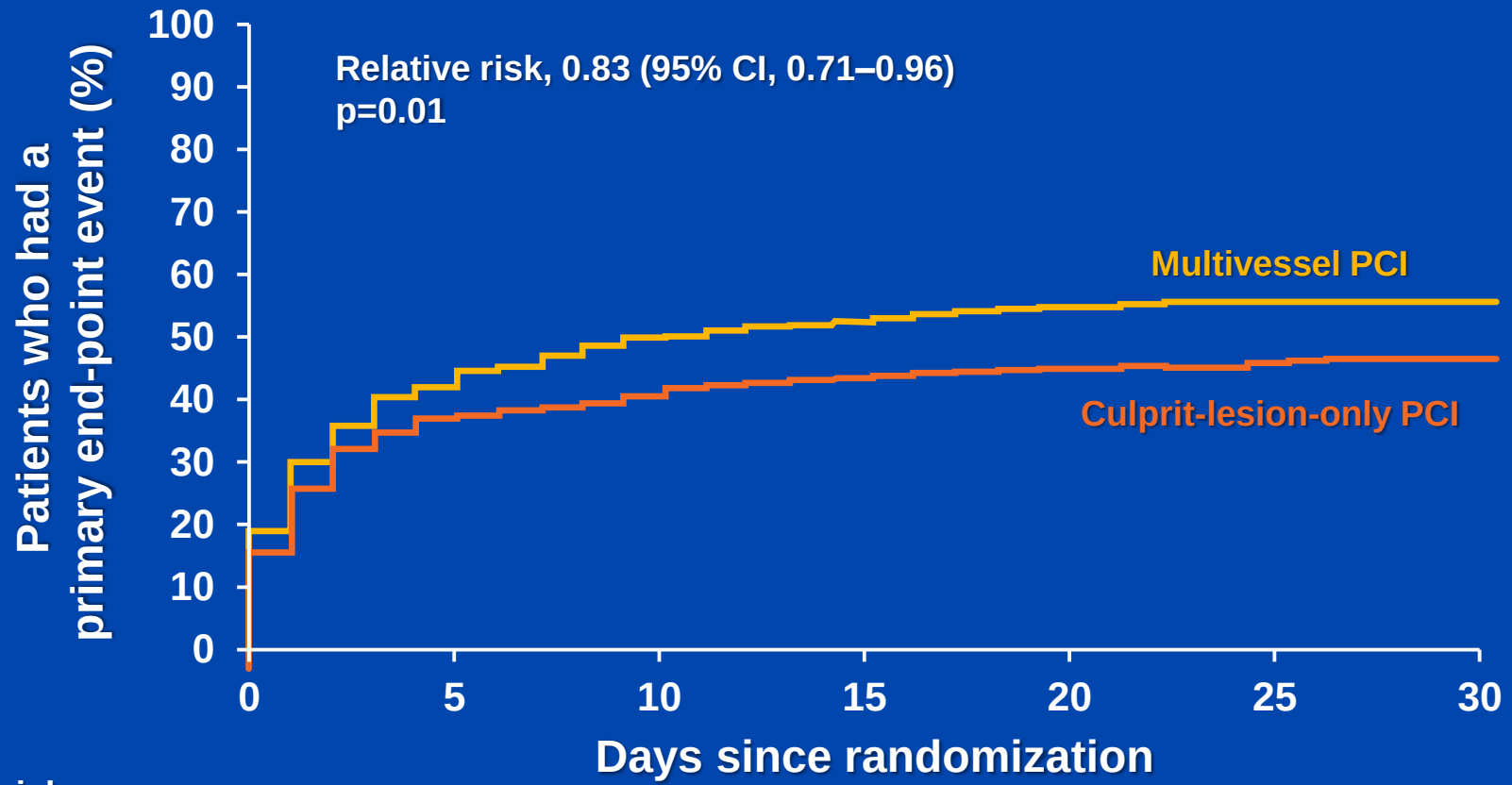
Thiele et al: NEJM; 377:2419-32, 2017

PCI, STEMI & Cardiogenic Shock
Composite Primary End Point



No. at risk

Multivessel PCI	341	199	172	162	156	153	152
Culprit-lesion-only PCI	344	219	207	198	192	189	184

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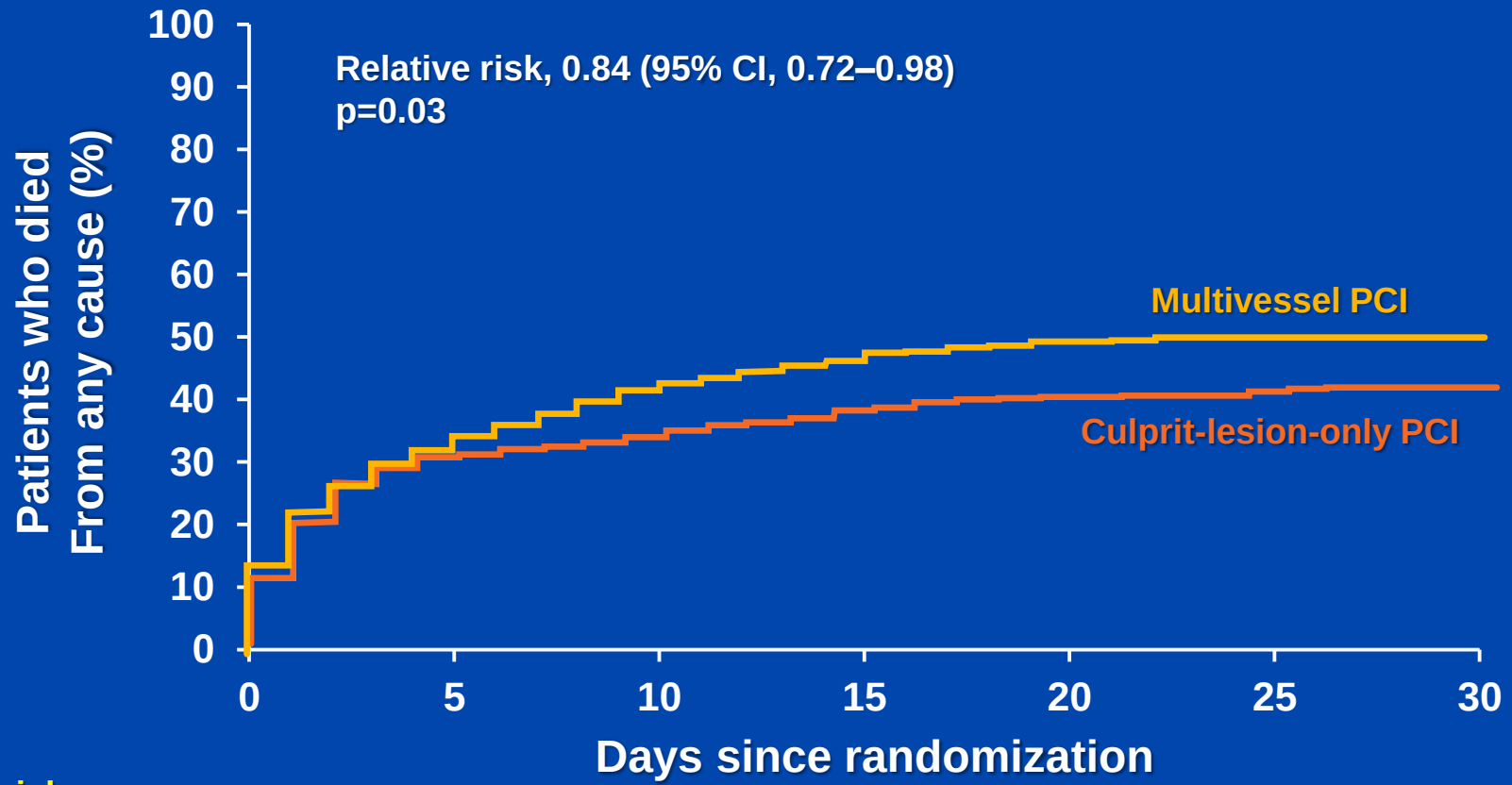
Thiele et al: NEJM; 377:2419-32, 2017

PCI, STEMI & Cardiogenic Shock

Death from Any Cause



No. at risk

Multivessel PCI	341	299	197	179	170	166	165
Culprit-lesion-only PCI	344	237	226	211	203	198	193

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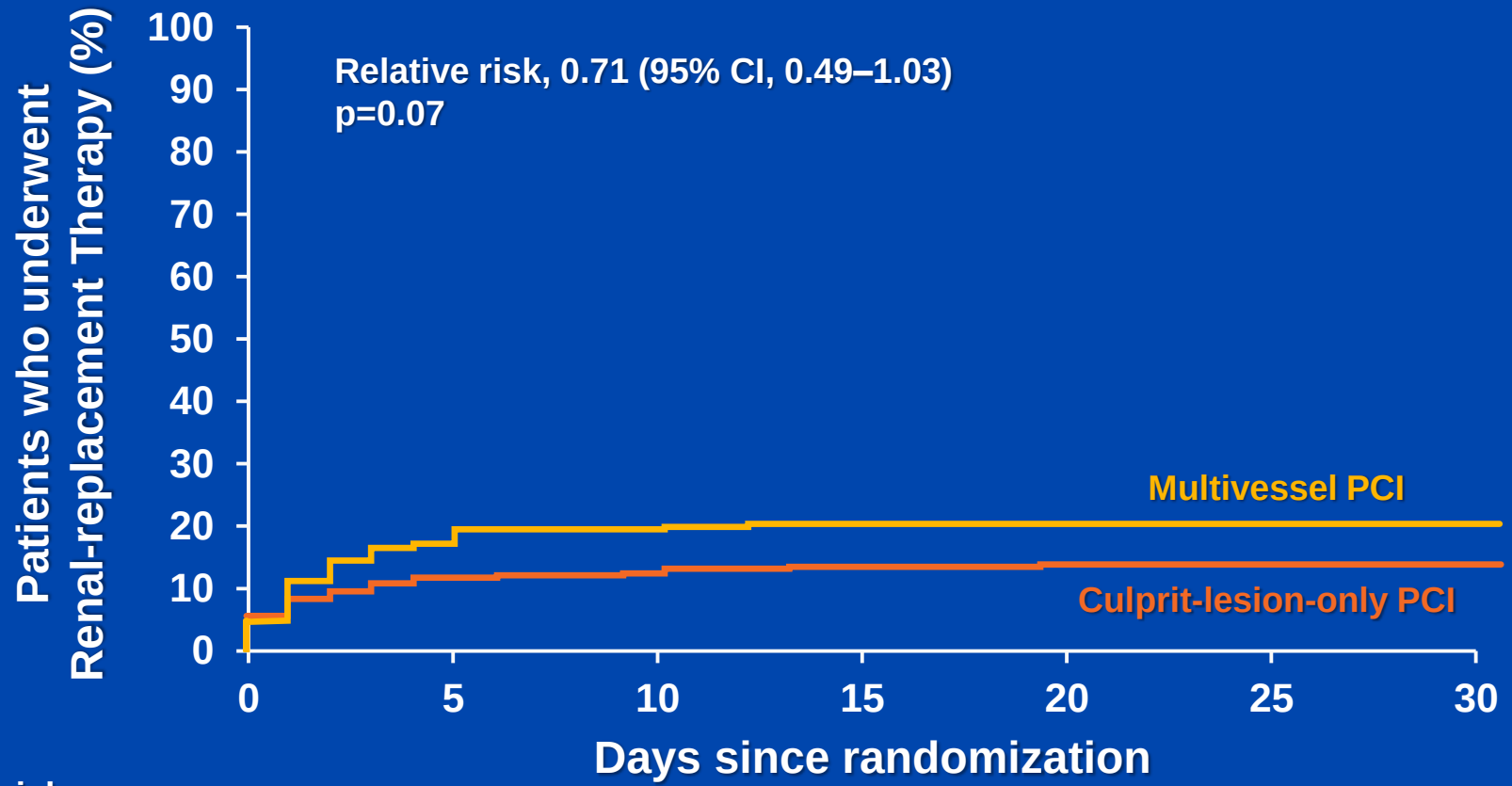
Thiele et al: NEJM; 377:2419-32, 2017

PCI, STEMI & Cardiogenic Shock
Renal-Replacement Therapy



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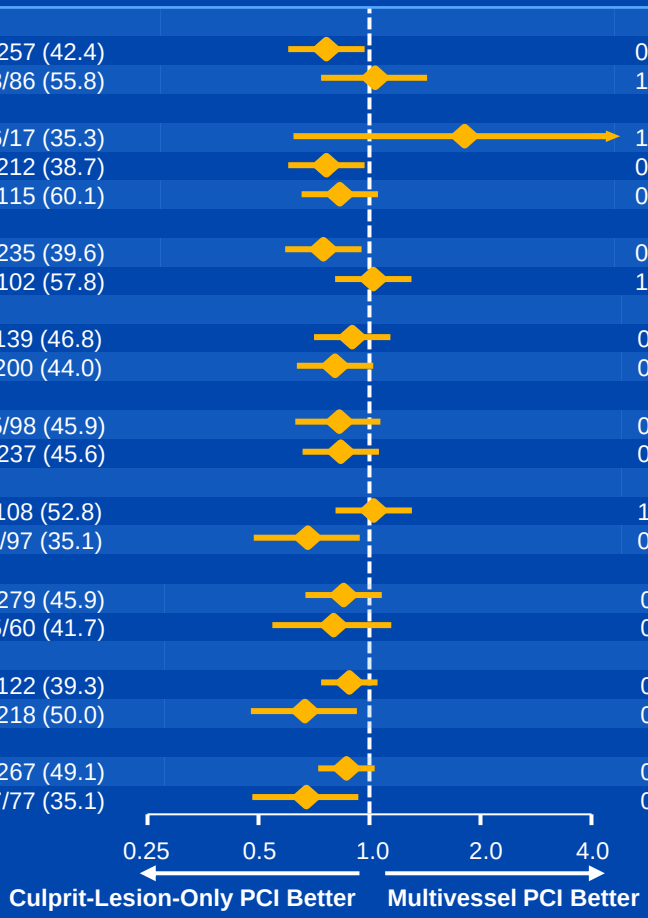
Thiele et al: NEJM; 377:2419-32, 2017

PCI, STEMI & Cardiogenic Shock

Primary End Point at 30 Days

Subgroup	Primary End-Point Event: Multivessel PCI (No. of Patients with Event/Total No. (%))	Primary End-Point Event: Culprit-Lesion-Only PCI (No. of Patients with Event/Total No. (%))	Relative Risk (95% CI)	P Value for Interaction
Sex				0.11
Male	148/266 (55.6)	109/257 (42.4)	0.76 (0.64–0.91)	
Female	41/75 (54.7)	48/86 (55.8)	1.02 (0.77–1.35)	
Age				0.24
<50 yr	3/16 (18.8)	6/17 (35.3)	1.88 (0.56–6.29)	
50–75 yr	114/226 (50.4)	82/212 (38.7)	0.77 (0.62–0.95)	
>75 yr	72/99 (72.7)	70/115 (60.1)	0.84 (0.69–1.01)	
Diabetes				0.08
No	116/218 (53.2)	93/235 (39.6)	0.74 (0.61–0.91)	
Yes	66/116 (56.9)	59/102 (57.8)	1.02 (0.81–1.28)	
Hypertension				0.47
No	68/129 (52.7)	65/139 (46.8)	0.89 (0.70–1.13)	
Yes	114/205 (55.6)	88/200 (44.0)	0.79 (0.65–0.97)	
Type of Infarction				0.96
NSTEMI	54/97 (55.7)	45/98 (45.9)	0.82 (0.62–1.09)	
STEMI	128/233 (54.9)	108/237 (45.6)	0.83 (0.69–0.99)	
Location of STEMI				0.07
Anterior	59/113 (52.2)	57/108 (52.8)	1.01 (0.79–1.30)	
Nonanterior	48/92 (52.2)	34/97 (35.1)	0.67 (0.48–0.94)	
Previous Infarction				0.83
No	154/281 (54.8)	128/279 (45.9)	0.84 (0.71–0.99)	
Yes	28/53 (52.8)	25/60 (41.7)	0.79 (0.53–1.17)	
Affected Vessels (no.)				0.56
2	64/124 (51.6)	48/122 (39.3)	0.76 (0.58–1.01)	
3	124/215 (57.7)	109/218 (50.0)	0.87 (0.73–1.03)	
Chronic Total Occlusion				0.26
No	146/259 (56.4)	131/267 (49.1)	0.87 (0.74–1.02)	
Yes	43/82 (52.4)	27/77 (35.1)	0.67 (0.46–0.97)	



Thiele et al: NEJM; 377:2419-32, 2017

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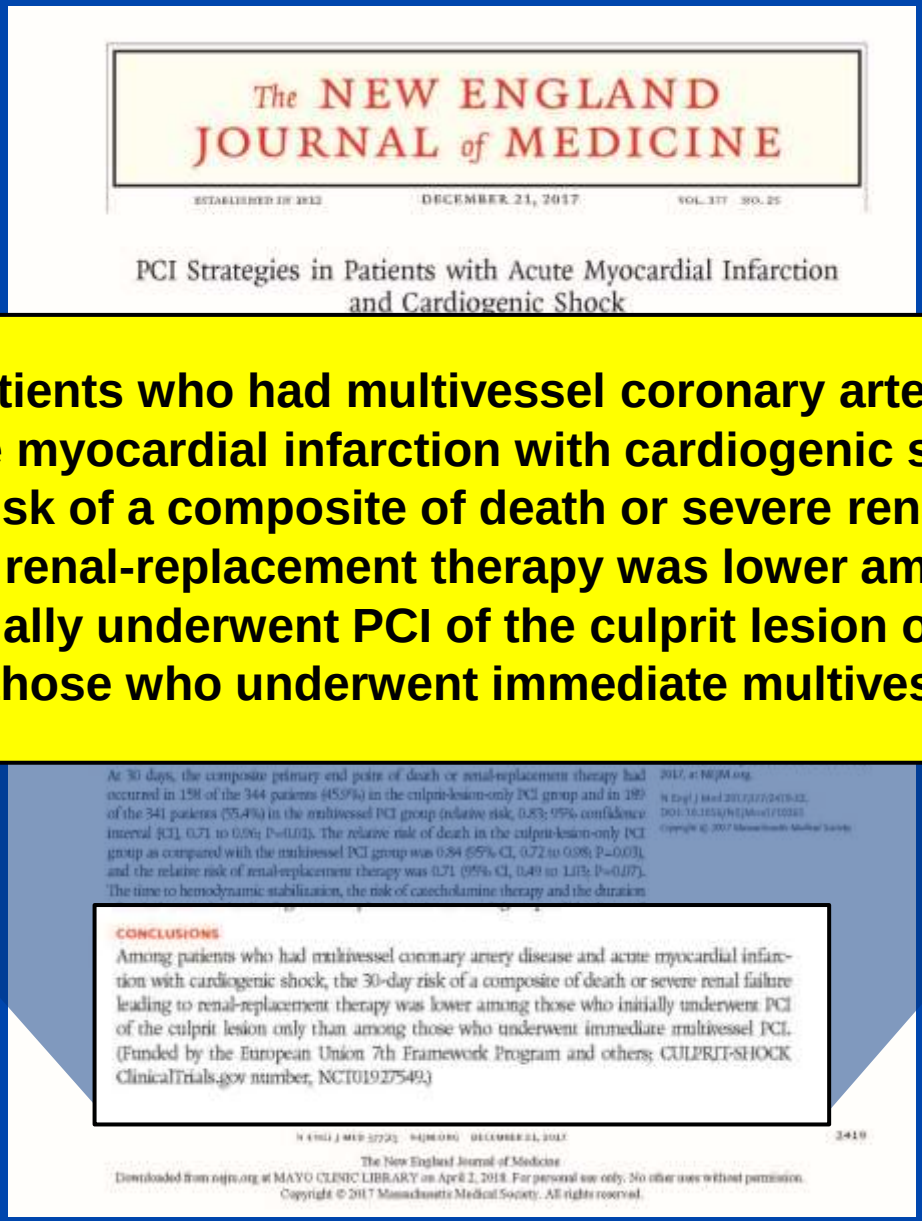
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 21, 2017 VOL. 377 NO. 25

PCI Strategies in Patients with Acute Myocardial Infarction and Cardiogenic Shock

At 30 days, the composite primary end point of death or renal-replacement therapy had occurred in 158 of the 344 patients (45.9%) in the culprit-lesion-only PCI group and in 189 of the 341 patients (55.4%) in the multivessel PCI group (relative risk, 0.83; 95% confidence interval [CI], 0.71 to 0.96; P=0.01). The relative risk of death in the culprit-lesion-only PCI group as compared with the multivessel PCI group was 0.84 (95% CI, 0.72 to 0.98; P=0.03), and the relative risk of renal-replacement therapy was 0.71 (95% CI, 0.49 to 1.03; P=0.07). The time to hemodynamic stabilization, the risk of catecholamine therapy and the duration

2017 at NEJM.org.

N Engl J Med 2017;377:2419-32.
DOI: 10.1056/NEJMoa1710261

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CONCLUSIONS

Among patients who had multivessel coronary artery disease and acute myocardial infarction with cardiogenic shock, the 30-day risk of a composite of death or severe renal failure leading to renal-replacement therapy was lower among those who initially underwent PCI of the culprit lesion only than among those who underwent immediate multivessel PCI. (Funded by the European Union 7th Framework Program and others; CULPRIT-SHOCK ClinicalTrials.gov number, NCT01927549.)

N ENGL J MED 377;25 NEJM.ORG DECEMBER 21, 2017 2419

The New England Journal of Medicine

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Thiele et al: NEJM; 377:2419-32, 2017

Overtreatment in 2018

- Thrombus aspiration during acute MI
- Triple antiplatelet therapy
- Treatment of nonculprit lesions during AMI
- Biovascular absorbable scaffolds
- Emergency department activation

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The Japanese eat very little fat and suffer fewer heart attacks than do the Americans

The Mexicans eat a lot of fat and suffer fewer heart attacks than do the Americans

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The Chinese drink very little red wine and suffer fewer heart attacks than do the Americans

The Italians drink a lot of red wine and suffer fewer heart attacks than do the Americans

The Germans drink a lot of beer and eat lots of sausages and suffer fewer heart attacks than do the Americans

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CONCLUSION

Eat and drink what you like.
Speaking English is
apparently what kills you.

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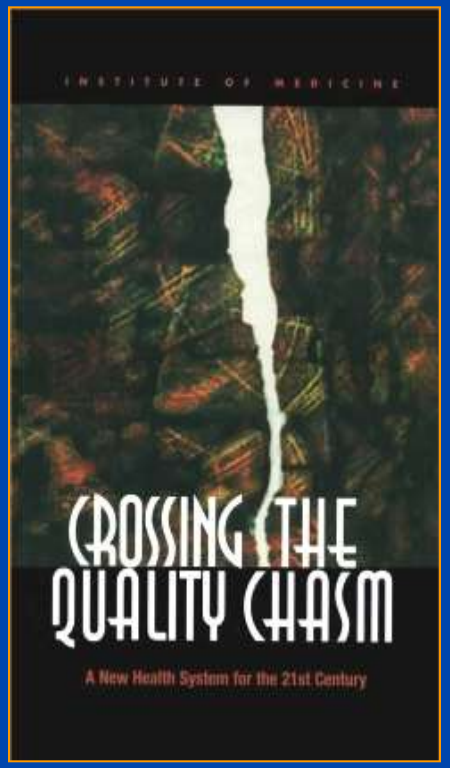
Institute of Medicine
Priorities for ~~America~~ the World



Appropriate

- Safe, timely, equitable, efficient, evidence-based and patient-centered

Care should

- Be customized to patients' needs and values
- Have the patient be the source of control
- Enable knowledge to be shared freely

Institute of Medicine, Crossing the Quality Chasm: A New Health System for the Twenty-first Century

Adams, K & Corrigan, JM. Priority Areas for National Action: Transforming Health Care Quality, IOM 2003

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