Welcome

Presented by
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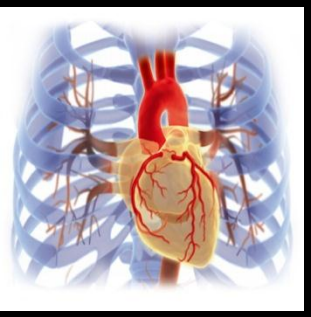
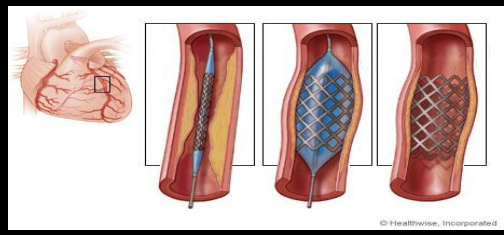
Associate Professor
Internal Medicine
DMCH



ACUTE CORONARY SYNDROMES

TREATED WITH ***PCI***



Clopidogrel as a part of Dual Antiplatelet therapy

FOR HOW LONG?

Death is inevitable but

Premature death is not.

- Sir Richard Doll

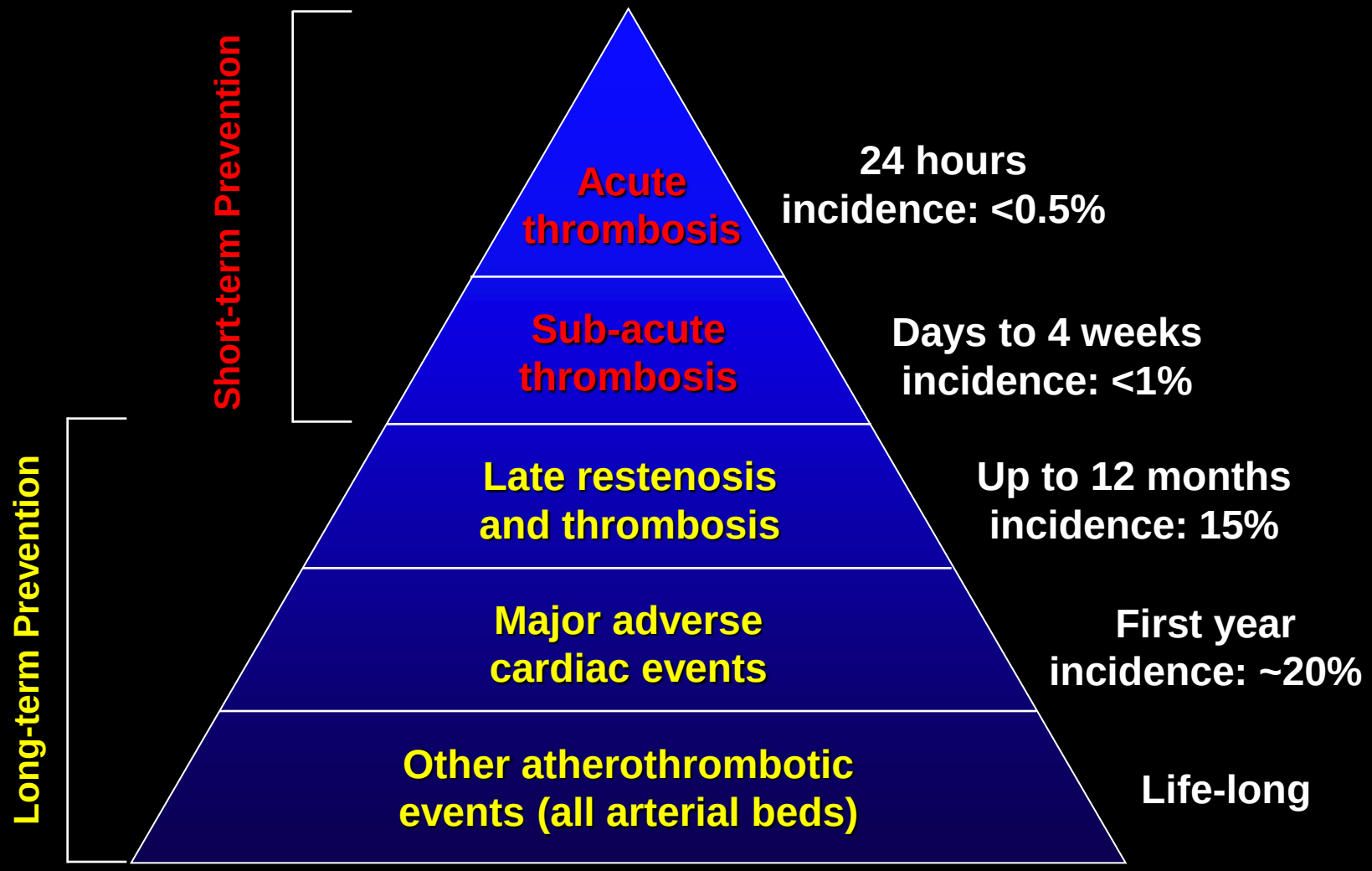
ASPIRIN

DEMAND
BAYER
ASPIRIN
DOES NOT AFFECT THE HEART

Preamble

The scope of management

Secondary and long-term prevention



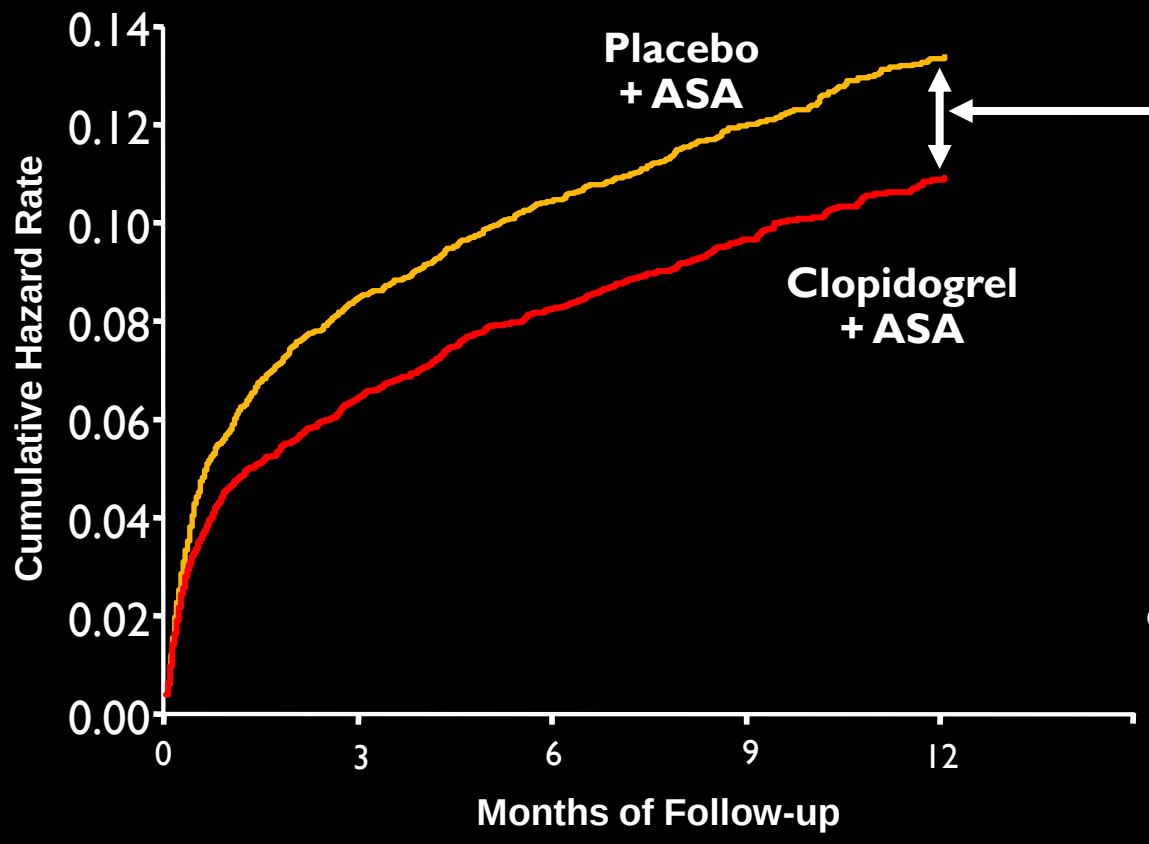
Road Map of Presentation

- What is the evidence supporting dual antiplatelet therapy for 12 months or more?
- Is there any risk of late thrombosis with drug-eluting stents?
- What may happen if dual antiplatelet therapy is discontinued?
- What do the guidelines recommend in patients with acute coronary syndromes or coronary stents?

Dual Anti platelet Therapy

- Dual anti-platelet therapy with aspirin and clopidogrel has been shown to be effective in reducing the risk of acute/sub acute stent thrombosis.
- Different Guidelines now recommend extending dual anti-platelet therapy to at least 12 months after implantation of DES, and even longer in patients at high risk of stent thrombosis

CURE – risk of MI, stroke or cardiovascular death (N=12,562)



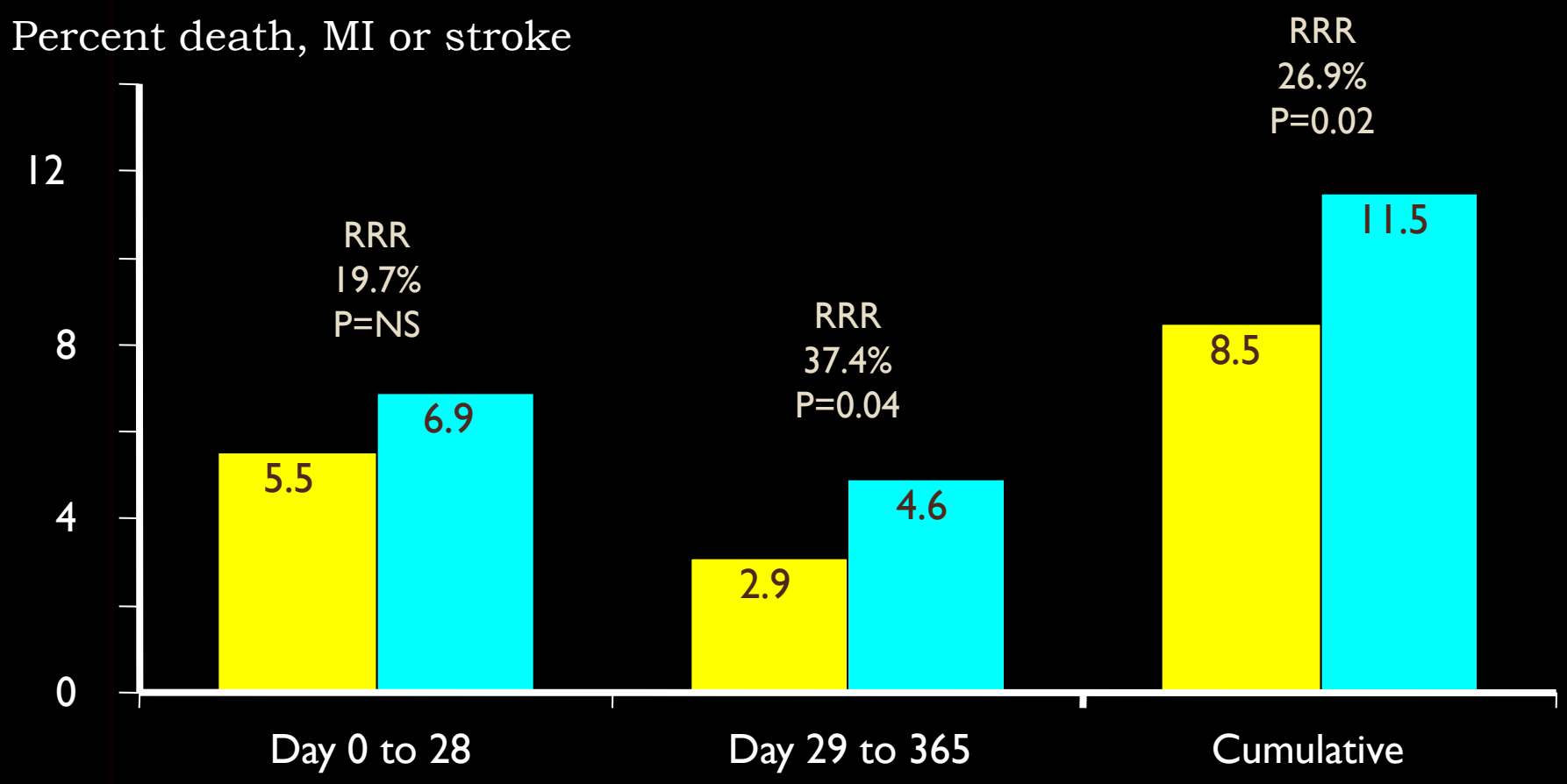
20%
Relative
Risk Reduction
P=0.00009

Study subjects had ACS
(UA/non–ST-elevation MI)

The primary outcome occurred in 9.3% of patients in the clopidogrel + ASA group and 11.4% in the placebo + ASA group

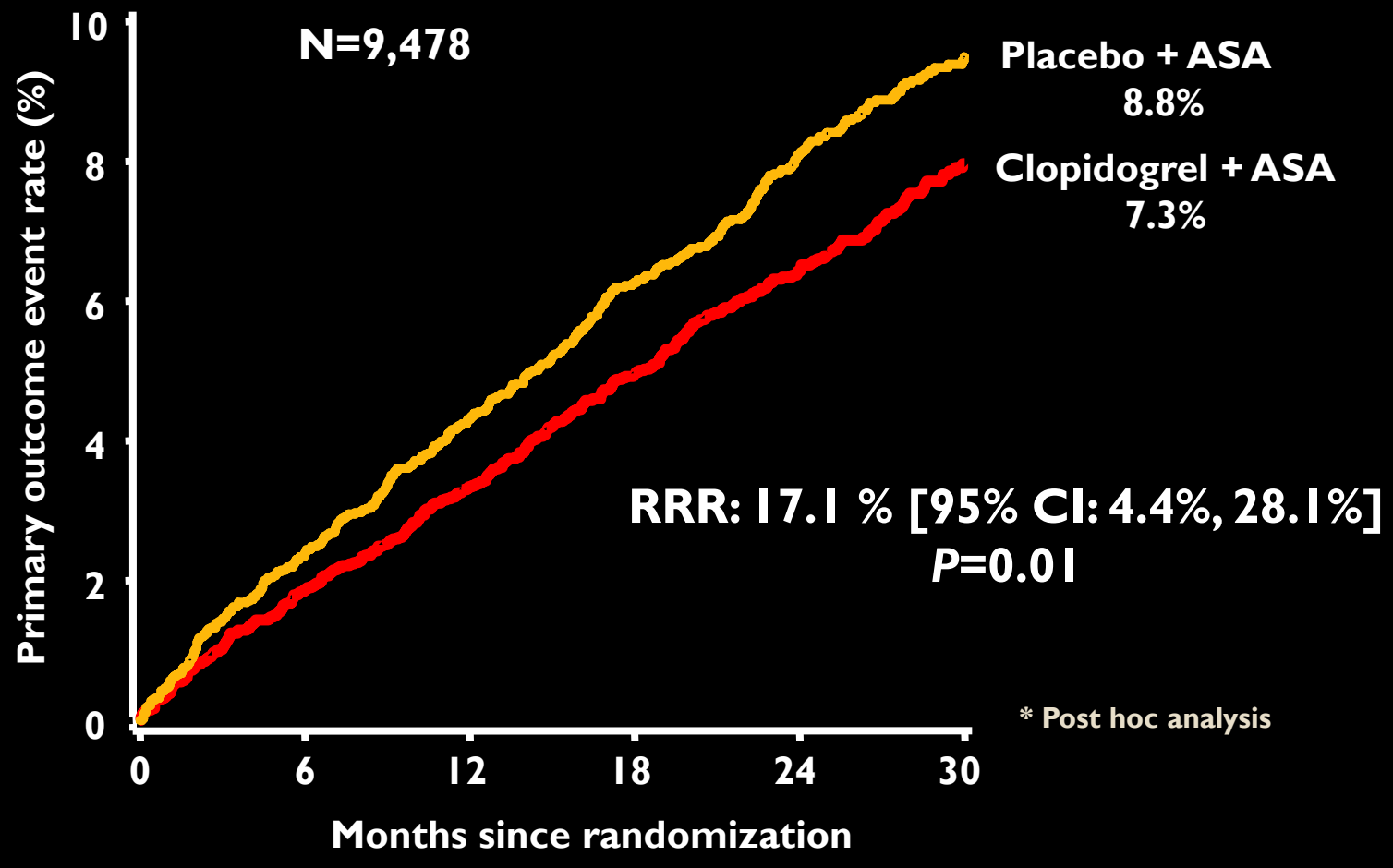
CURE Trial Investigators. N Engl J Med. 2001;345:494-502.

CREDO - 1 year Primary Outcome



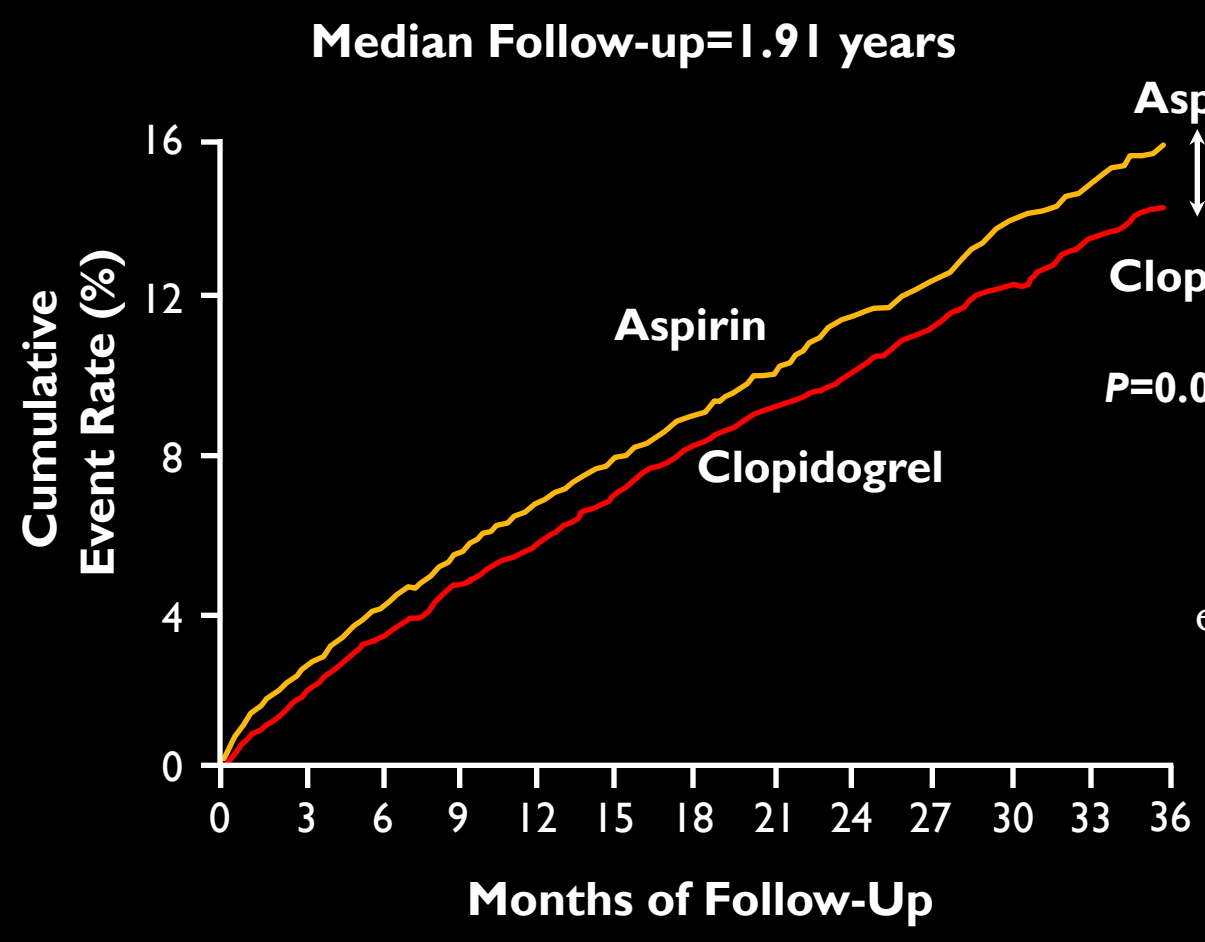
Adapted from Steinhubl SR, et al. JAMA. 2002;288:2411-2420.

CHARISMA primary end point (MI/stroke/CV death) in pts with previous MI, stroke or PAD*



Bhatt DL, et al. J Am Coll Cardiol 2007;49:1982–8

CAPRIE - efficacy of clopidogrel in MI, ischemic stroke, or vascular death (N=19,185)



8.7%*
Overall Relative Risk Reduction

Study subjects had either recent MI, recent ischemic stroke, or established peripheral arterial disease.

- ITT analysis.

CAPRIE Steering Committee. Lancet. 1996;348:1329-1339.

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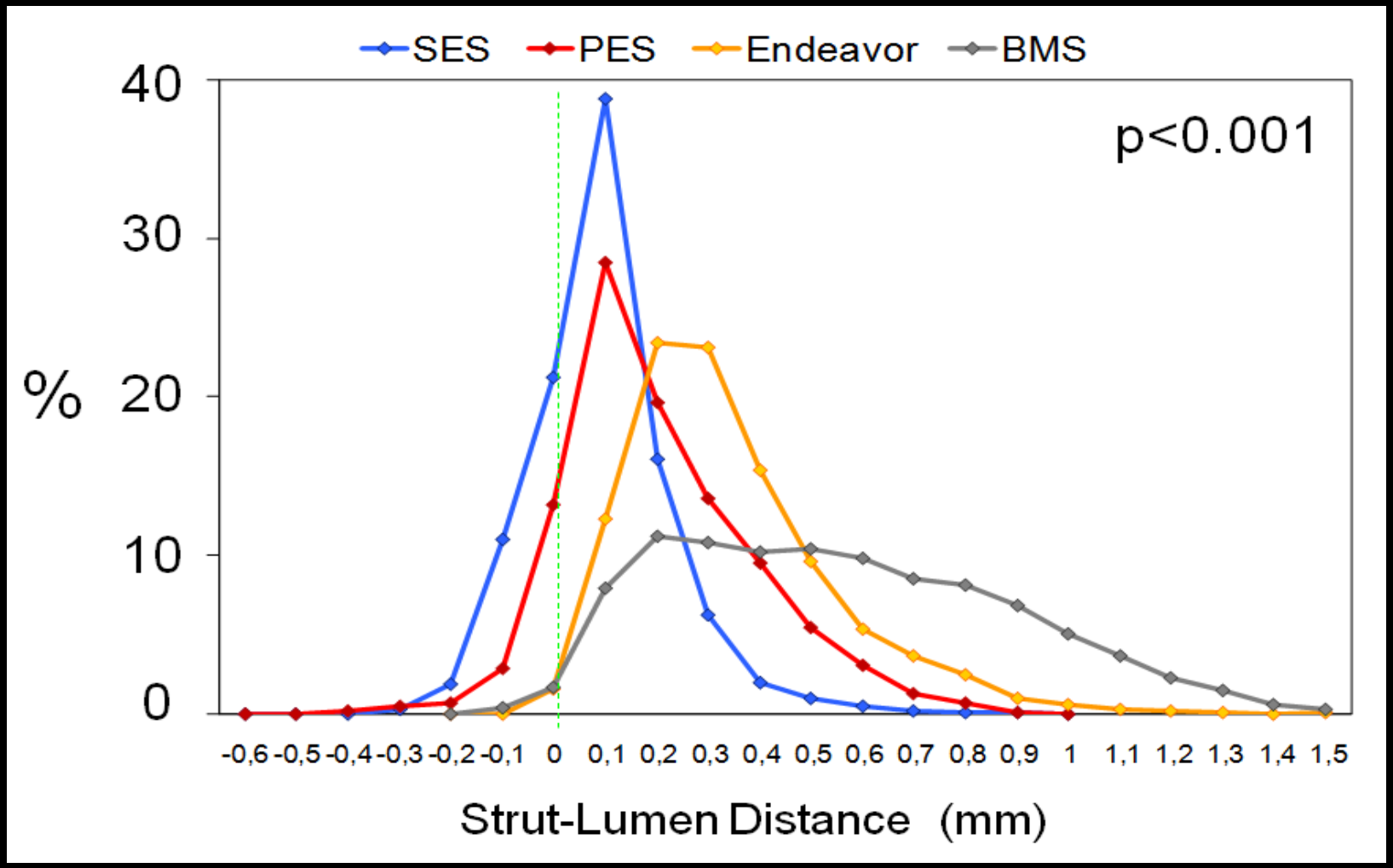
Risk of Late Stent Thrombosis!!!

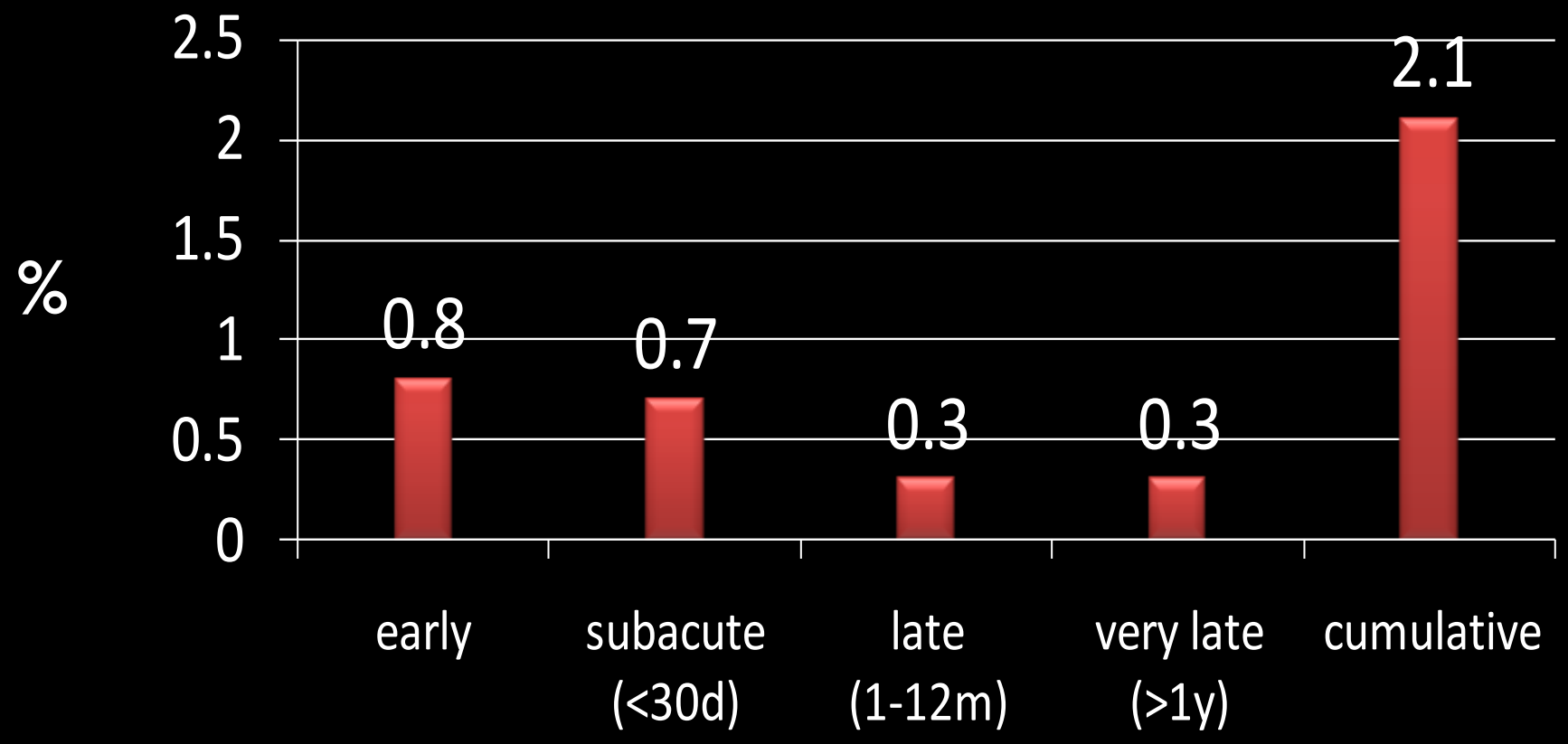
- DES markedly reduces the need for revascularization compared with bare-metal stenting, but appears to be associated with an increased risk of late stent thrombosis
- Neointimal hyperplasia is the dominant mechanism underlying in-stent restenosis.
- DES have been associated with an increased risk of stent thrombosis more than 6 months after implantation

Delayed endothelialization in DES: 6-month optical coherence tomography



Guagliumi G et al. TCT 2009

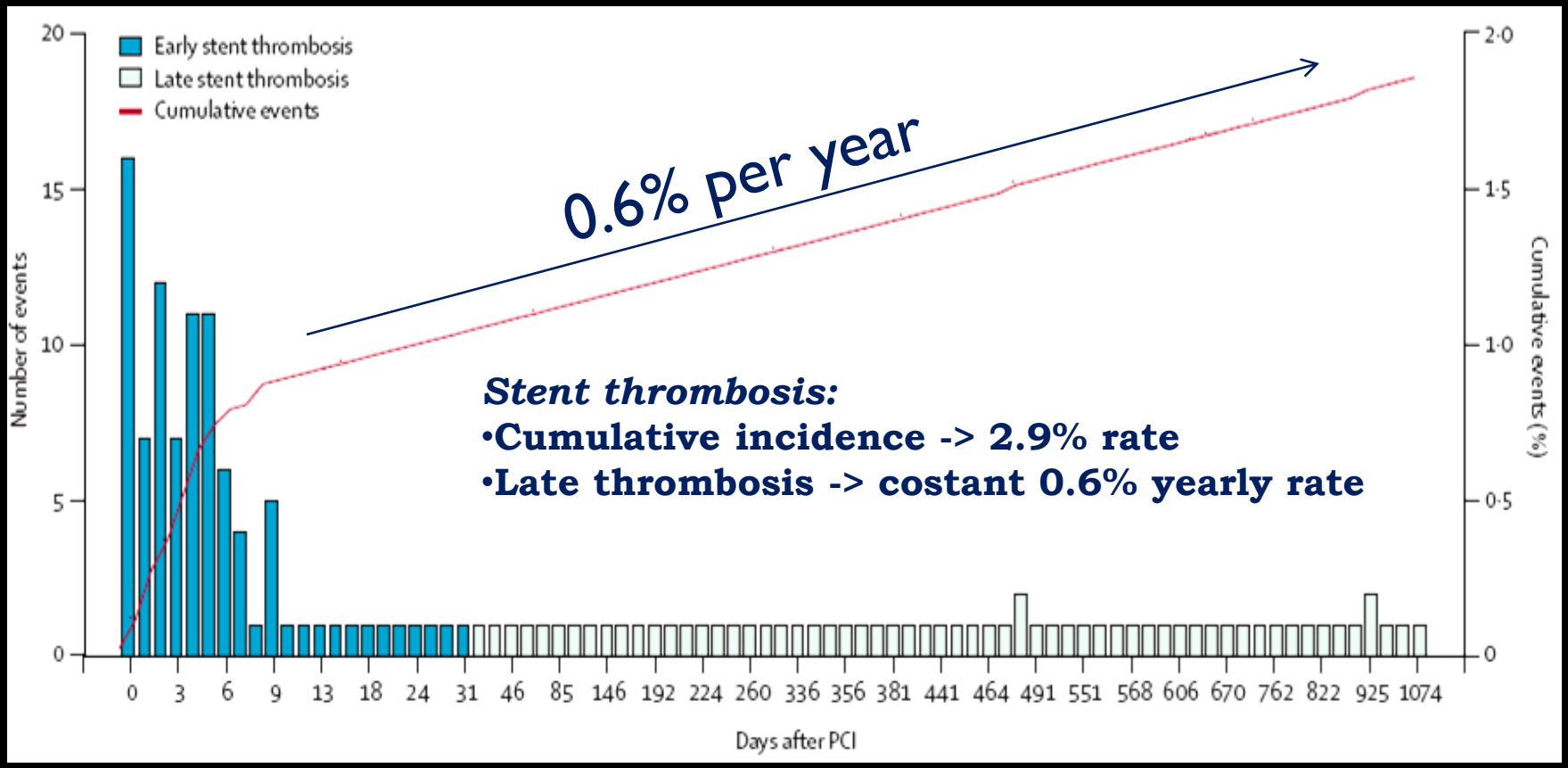
Dutch registry – incidence of stent thrombosis from 21,009 patients



van Werkum JW et al. JACC 2009;53:1399-409

Rotterdam-Bern registry – long-term incidence of DES thrombosis

8146 patients treated with DES (sirolimus or paclitaxel-eluting stents) followed for a mean of 1.7 years (up to 3)



Daemen J et al. Lancet 2007;369:667–78

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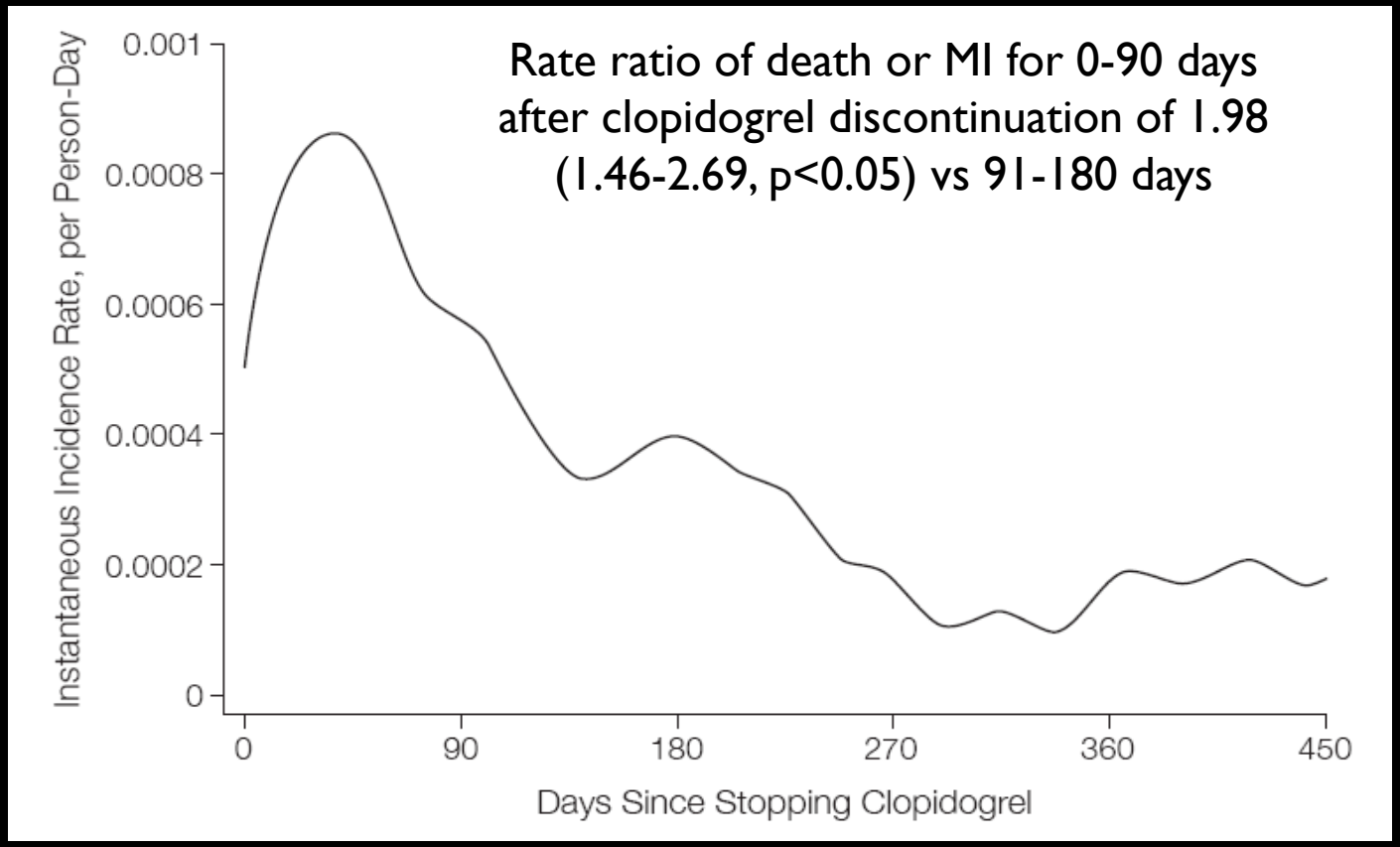
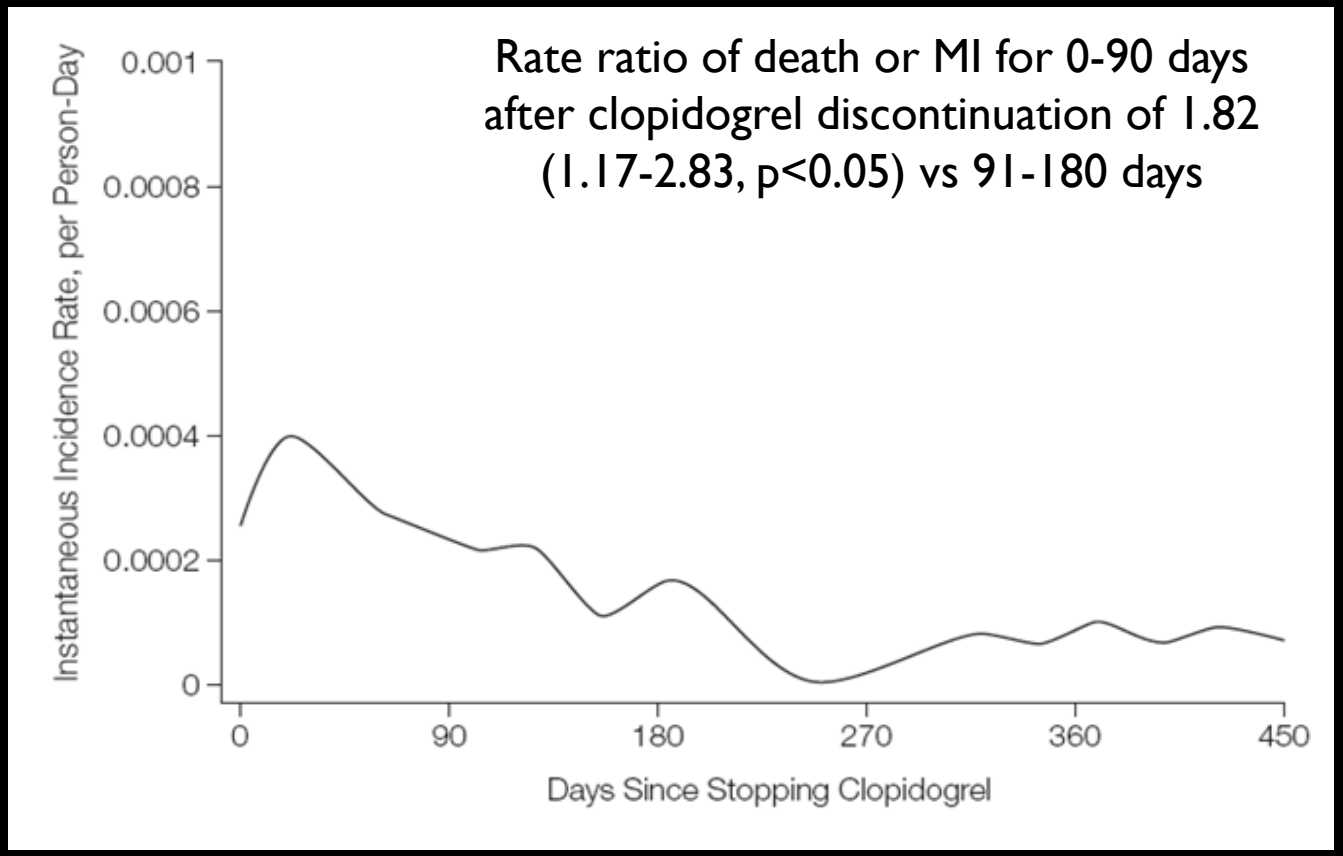
Risk of adverse events after discontinuation of clopidogrel: Medically treated patients with ACS



Ho PM et al. JAMA 2008;299:532-9

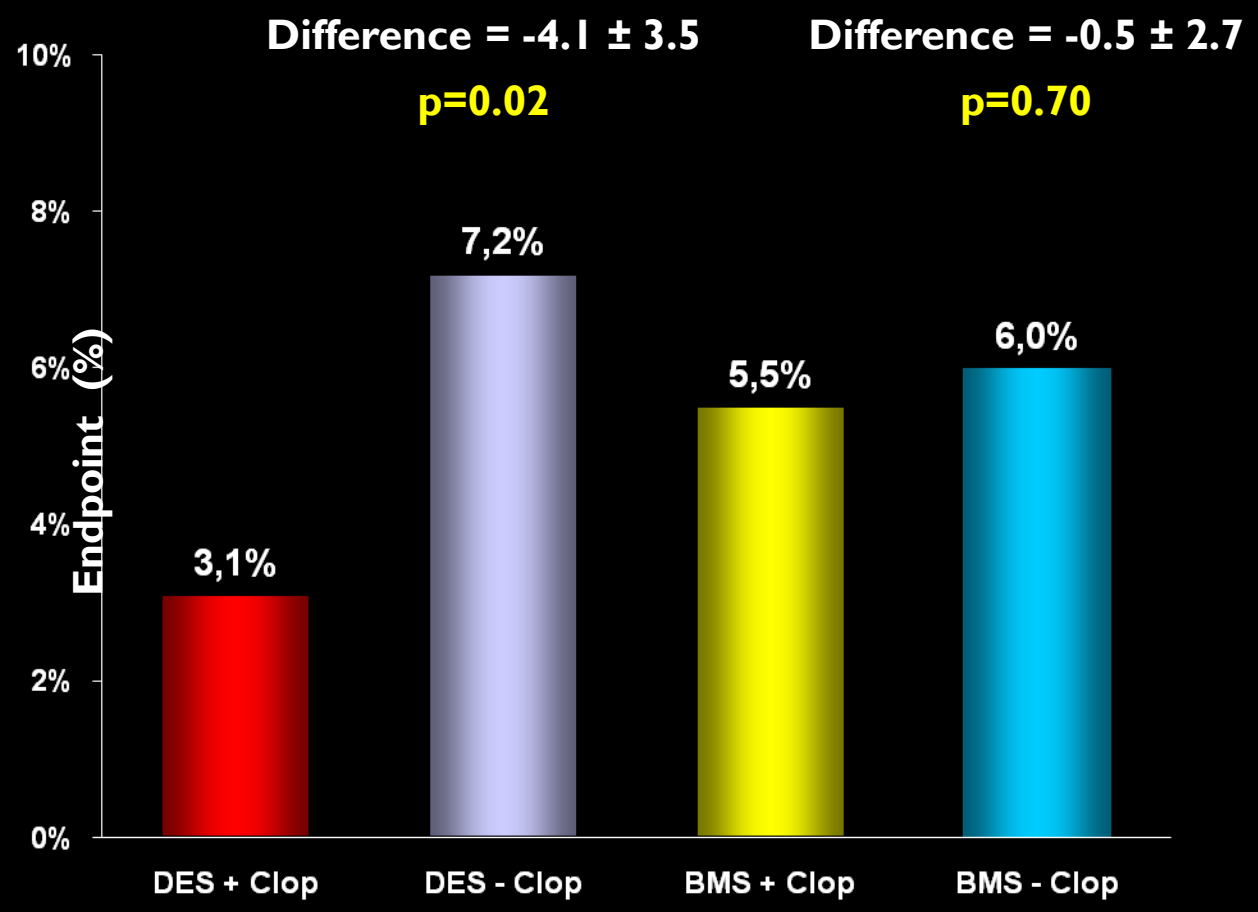
Risk of adverse events after discontinuation of clopidogrel: PCI treated patients with ACS



Ho PM et al. JAMA 2008;299:532-9

Duke Registry – clopidogrel and long-term outcomes after DES implantation

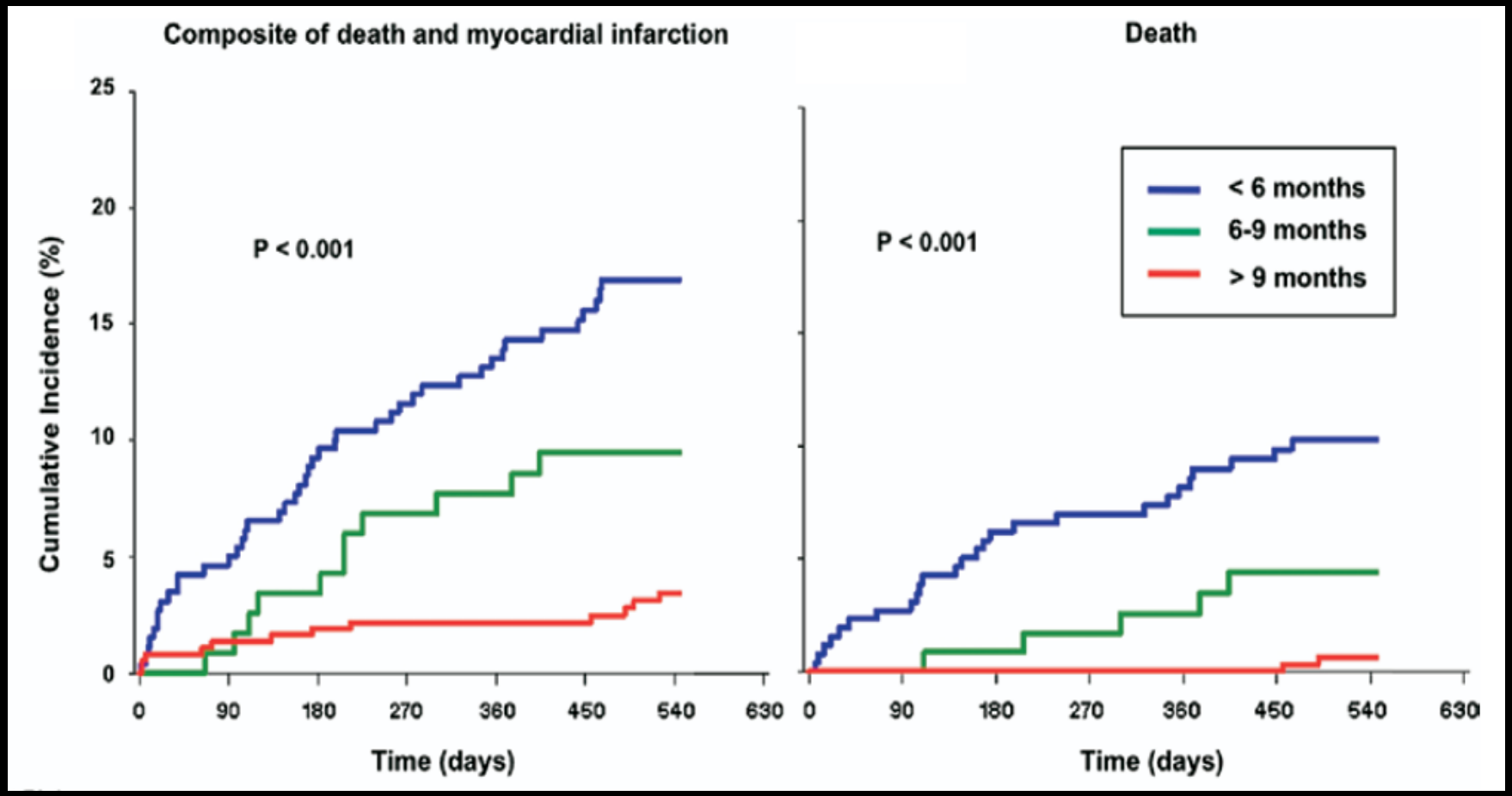
Adjusted rates of death or MI starting at 6 months



Eisenstein EL et al. JAMA 2007;297:159–68

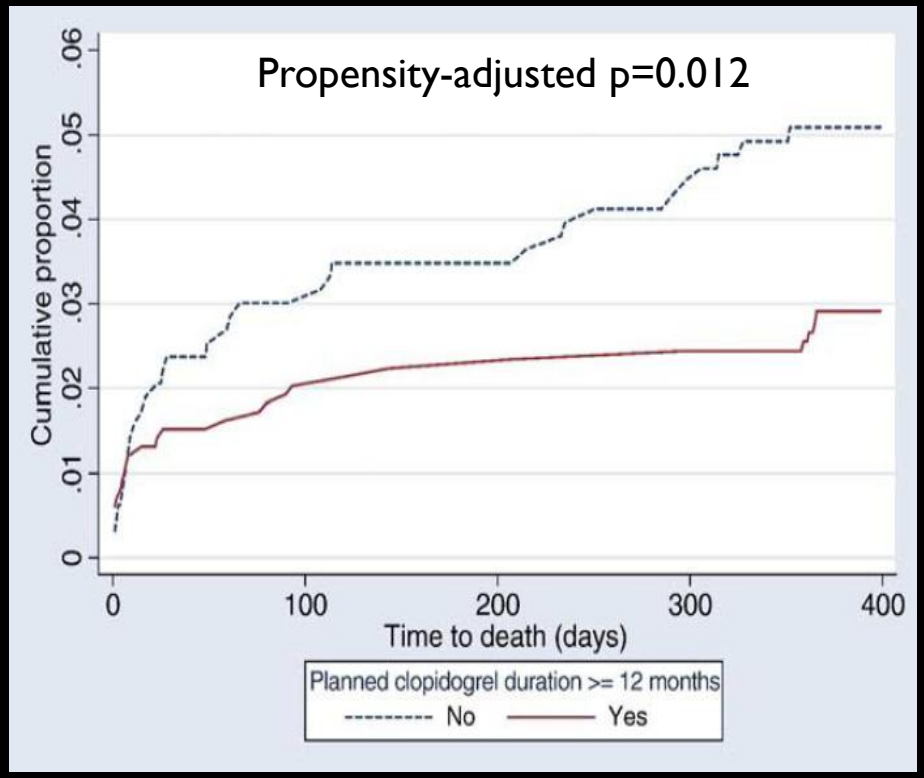
- **Adjusted outcomes were analyzed at 24 months**
- **Patients in the DES with clopidogrel group had significantly lower rates of death or MI than did patients in the DES without clopidogrel group**
- **Among BMS patients, there were no differences in death or MI**

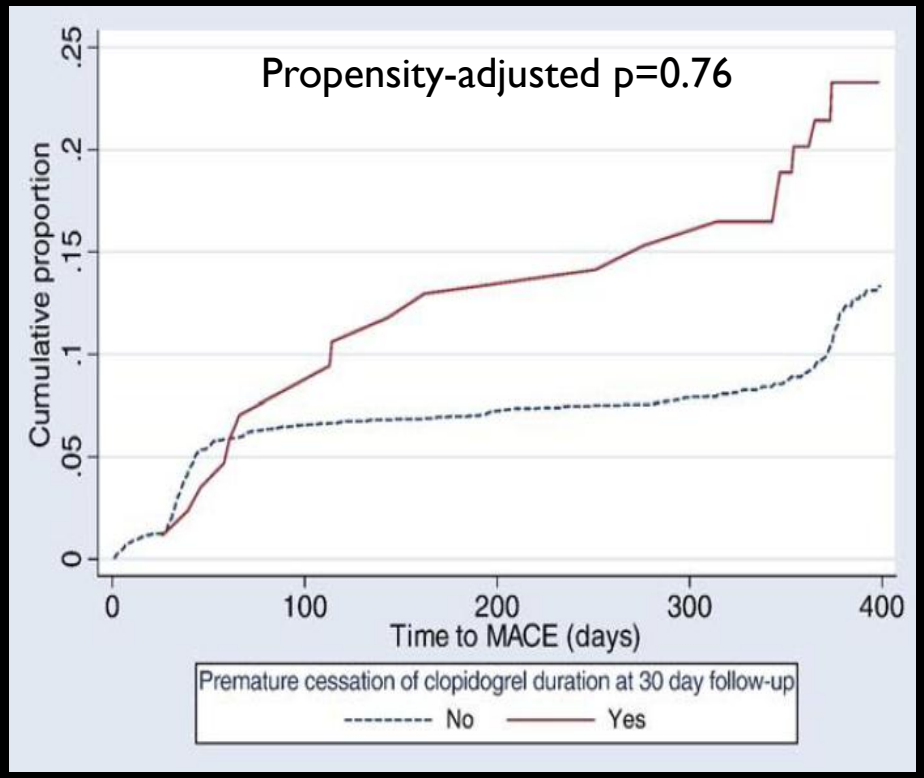
Impact of duration of clopidogrel after PCI with stents in diabetics



Brar SS et al. JACC 2008;51:2220-7

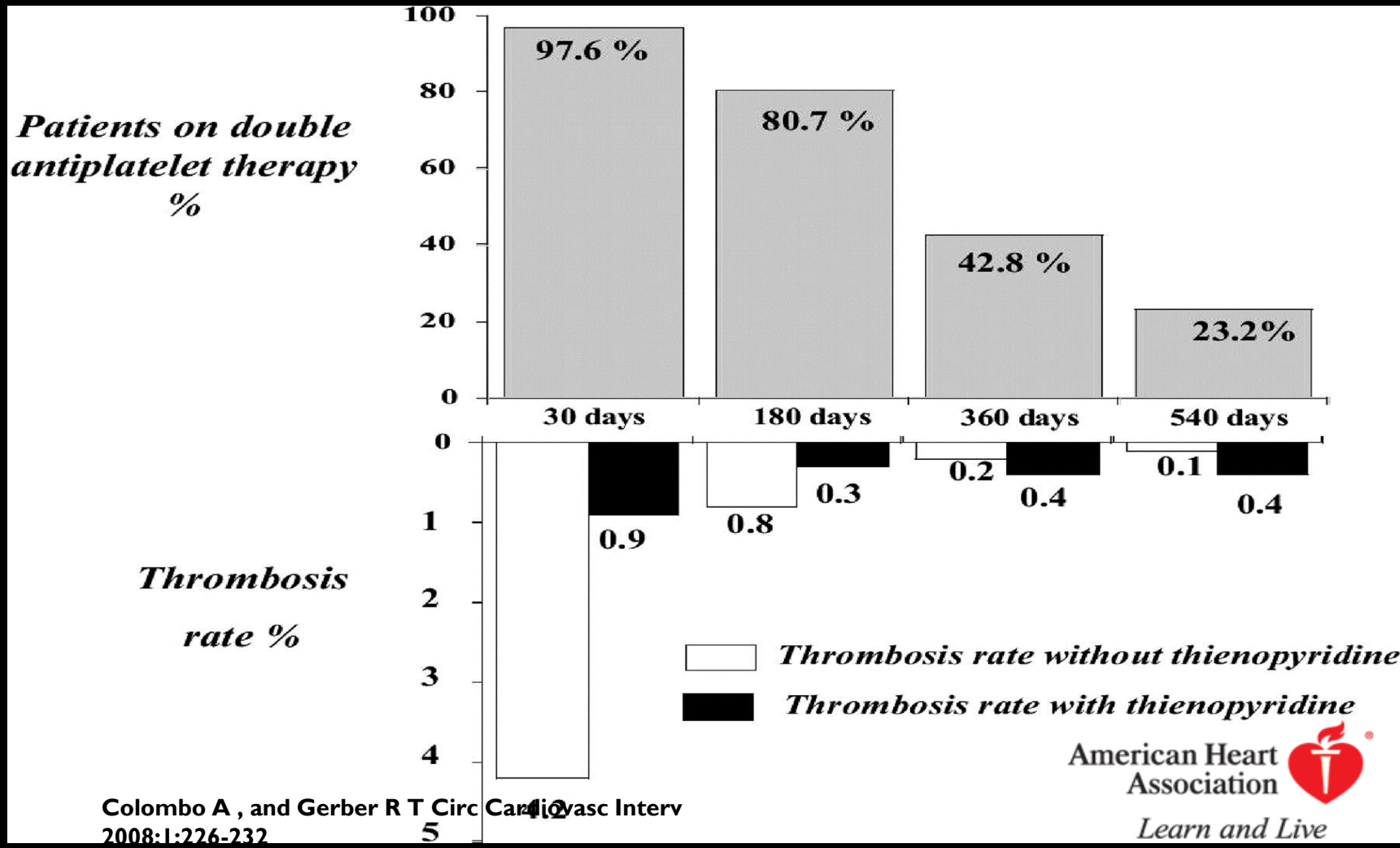
Planned duration of clopidogrel after DES implantation: the Melbourne registry





Butler MJ et al. AHJ 2009;157:899-907

Figure 2. Percentages of patients on DAT. Upper bars represent proportion of patients taking DAT, and the lower bar chart illustrates the specific antiplatelet therapy (with or without thienopyridines) in patients sustaining stent thrombosis at different ti...



Colombo A , and Gerber R T Circ Cardiovasc Interv 2008;1:226-232

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ESC NSTE-ACS guidelines 2007 update

Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes

The Task Force for the Diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndromes of the European Society of Cardiology

Online publish-ahead-of-print 14 June 2007

Authors/Task Force Members, Jean-Pierre Bassand* (Chair) *(France), Christian W. Hamm* (Co-Chair) (Germany), Diego Ardissino (Italy), Eric Boersma (The Netherlands), Andrzej Budaj (Poland), Francisco Fernández-Avilés (Spain), Keith A.A. Fox (UK), David Hasdai (Israel), E. Magnus Ohman (USA), Lars Wallentin (Sweden), William Wijns (Belgium)*

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Bassand J-P et al. Eur Heart J 2007;28:1598–1660.

NSTE-ACS – recommendations for oral antiplatelet drugs (2007)

- Aspirin is recommended for all patients presenting with NSTE-ACS without contraindication at an initial loading dose of 160 - 325mg (non-enteric) (I-A), and at a maintenance dose of 75 to 100mg long-term (I-A)
- For all patients immediate 300mg loading dose of clopidogrel is recommended, followed by 75mg clopidogrel daily (I-A).
- Clopidogrel should be maintained for 12 months unless there is an excessive risk of bleeding (I-A)
- For all patients with contraindication to aspirin, clopidogrel should be given instead (I-B)

Bassand J-P et al. Eur Heart J 2007;28:1598–1660.

ESC PCI 2005 guidelines

Publish-Ahead-of-Print published March 15, 2005

European Heart Journal
doi:10.1093/eurheartj/ehi138

EUROPEAN SOCIETY OF CARDIOLOGY®

ESC Guidelines

Guidelines for Percutaneous Coronary Interventions

The Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology

Authors/Task Force Members: Sigmund Silber, Chairperson* (Germany), Per Albertsson (Sweden), Francisco F. Avilés (Spain), Paolo G. Camici (UK), Antonio Colombo (Italy), Christian Hamm (Germany), Erik Jørgensen (Denmark), Jean Marco (France), Jan-Erik Nordrehaug (Norway), Witold Ruzyllo (Poland), Philip Urban (Switzerland), Gregg W. Stone (USA), William Wijns (Belgium)

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Silber S et al. Eur Heart J 2005;26:804-47.

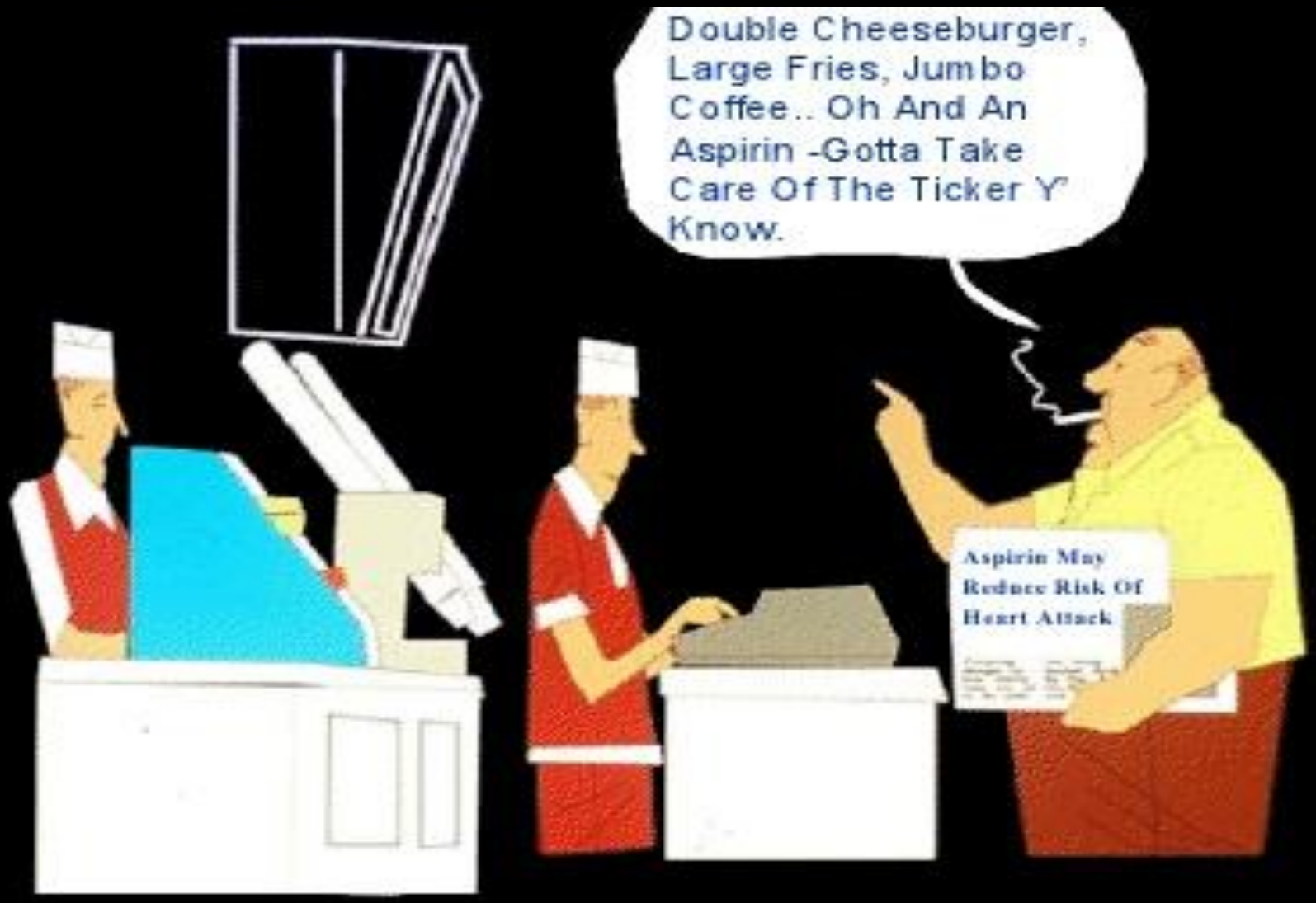
PCI – recommendations for oral antiplatelet drugs (2005)

- Aspirin is recommended for all patients undergoing PCI (I-A)
- For all stable patients clopidogrel is recommended after bare-metal stents for 1 month (I-A), drug-eluting stents for 6–12 months and brachytherapy for 12 months (I-C)
- For patients with NSTE-ACS clopidogrel is recommended for 9–12 months (I-B)

PCI - recommendations for oral anti-platelet drugs

- The current minimum recommended duration of dual antiplatelet therapy is 3 months with Sacrolimus eluting Stents and 6 months with Paclitaxel-eluting stents, but it is better to continue 12 months.
- The ideal duration of clopidogrel treatment after PCI for STEMI is unknown, but is influenced by the type of stent placed and the patient's risk for bleeding

High Risk Patients


Double Cheeseburger, Large Fries, Jumbo Coffee.. Oh And An Aspirin -Gotta Take Care Of The Ticker Y' Know.
Aspirin May Reduce Risk Of Heart Attack

French Fries

20 years ago

210 calories
2.4 ounces

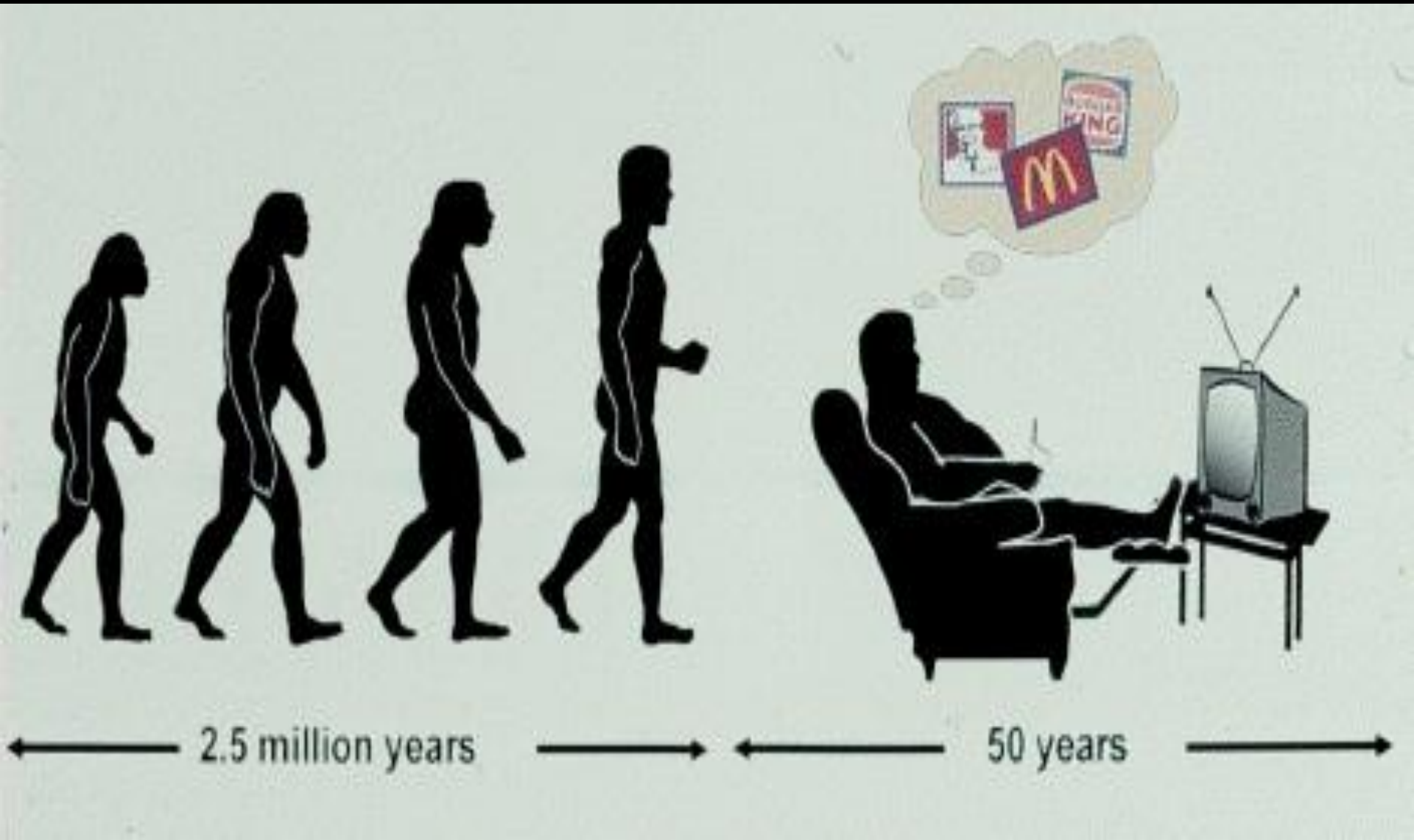
Today

610 calories
6.9 ounces

Calorie difference: 400 Calories

How to burn* 400 calories:
Walk 2 hour 20 minutes

*Based on 130-pound person.


2.5 million years
50 years

Walking the Dog

High Risk Conditions Requiring Clopidogrel Therapy beyond one year

- Multiple overlapping stents
- Multi vessel stents
- Stents in coronary artery bypass grafts
- Stents at the site of vessel bifurcations

The decision to continue Clopidogrel is dependent on the risk benefit ratio.

International up dates

2009 Focused Updates: ACC/AHA Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction (Updating the 2004 Guideline and 2007 Focused Update) and ACC/AHA/SCAI Guidelines on Percutaneous Coronary Intervention (Updating the 2005 Guideline and 2007 Focused Update)

A Report of the American College of Cardiology Foundation/
American Heart Association Task Force on Practice Guidelines

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Steven R. Bailey, MD, FACC, FSCAI; Eric R. Bates, MD, FACC, FAHA;
James C. Blankenship, MD, FACC, FSCAI; Donald E. Casey, Jr, MD, MPH, MBA;
Lee A. Green, MD, MPH; Judith S. Hochman, MD, FACC, FAHA;
Alice K. Jacobs, MD, FACC, FAHA, FSCAI; Harlan M. Krumholz, MD, SM, FACC, FAHA;

International updates – US PCI guidelines (2009)

- For all patients receiving a DES, clopidogrel 75 mg daily should be given for ≥12 months if patients are not at high risk of bleeding (I-B)
- For those receiving a BMS, clopidogrel should be given for ≥1 month and ideally up to 12 months (unless the patient is at increased risk of bleeding; then it should be given for ≥2 weeks) (I-B)
- Continuation of clopidogrel therapy beyond 1 year may be considered in patients undergoing DES placement (IIb-C)

Take home messages

Take home messages

- The benefit of dual antiplatelet therapy for 12 months following ACS is well established.
- Most recent data and guidelines support dual antiplatelet therapy for 12 months in subjects treated with DES without high bleeding risk.
- Patients at high thombotic but low bleeding risks may benefit from dual antiplatelet therapy beyond 12 months.
- In any case, compliance should be recommended and verified, to avoid early and/or unsupervised discontinuation

Take medicine every day; but before you swallow it, take it out for a five mile walk

Clinical practice

Unfortunately, most patients prefer to prescriptions of pills to the prescriptions of harmful lifestyles

Thank you