GLI ECCESSI DELLA CARDIOLOGIA INTERVENTISTICA

Simposio: La medicalizzazione eccessiva può portare un danno al paziente o ad un utilizzo improprio delle risorse. Less is more?
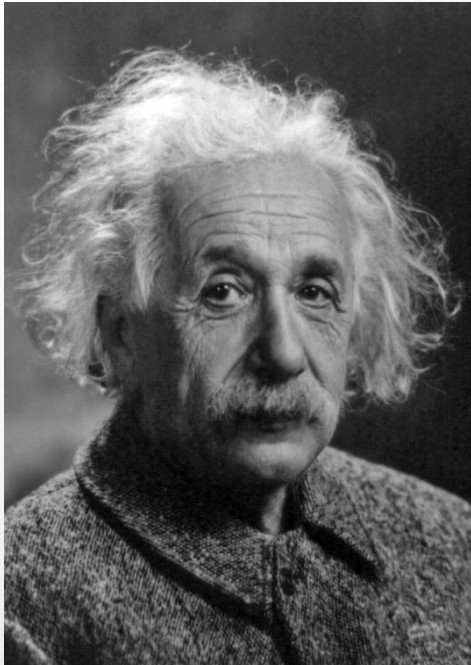
Milano, 5-7 maggio 2014

Bruno Passaretti

responsabile reparto di Cardiologia Riabilitativa
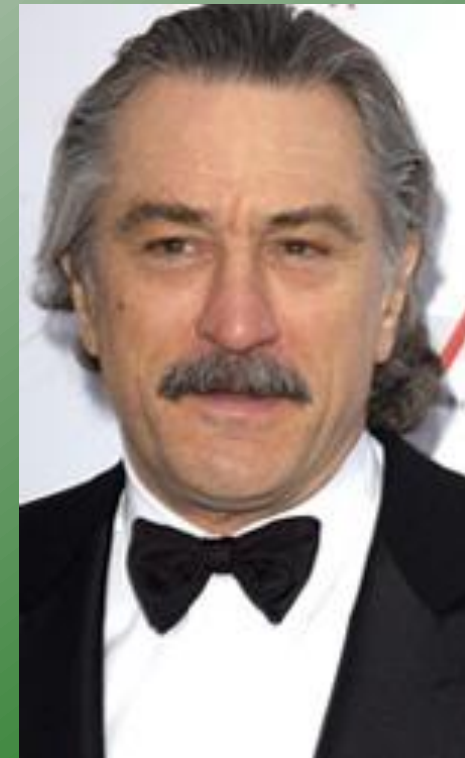e Unità Operativa di Riabilitazione
Humanitas Gavazzeni, Bergamo

nessun conflitto di interesse (e ci mancherebbe pure…)
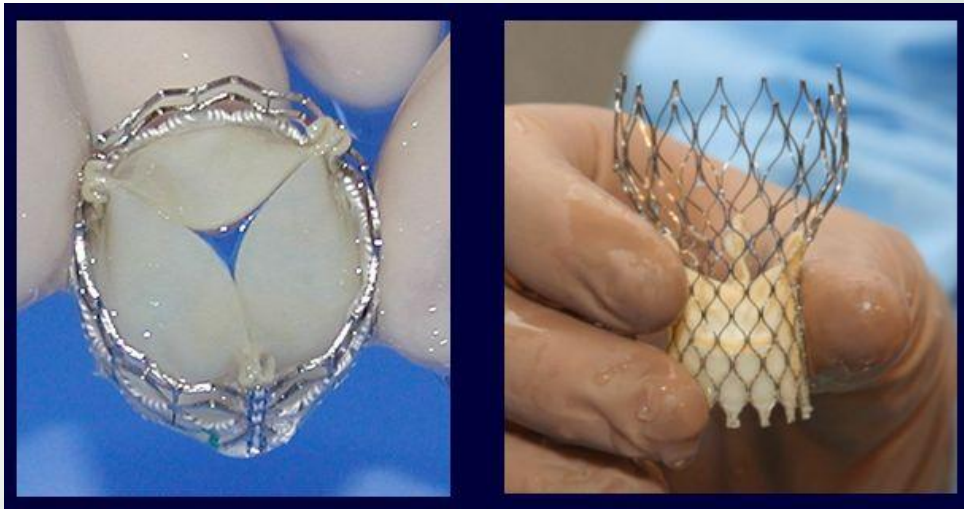
VII CONGRESSO DI **ECOCARDIOCHIRURGIA**

"non è la tecnologia ad essere giusta o sbagliata, è l'uso che se ne fa"
(A. Einstein?, o alla peggio io)

"ci sono tre modi di fare le cose qui: il modo giusto, il modo sbagliato e il modo in cui le faccio io"
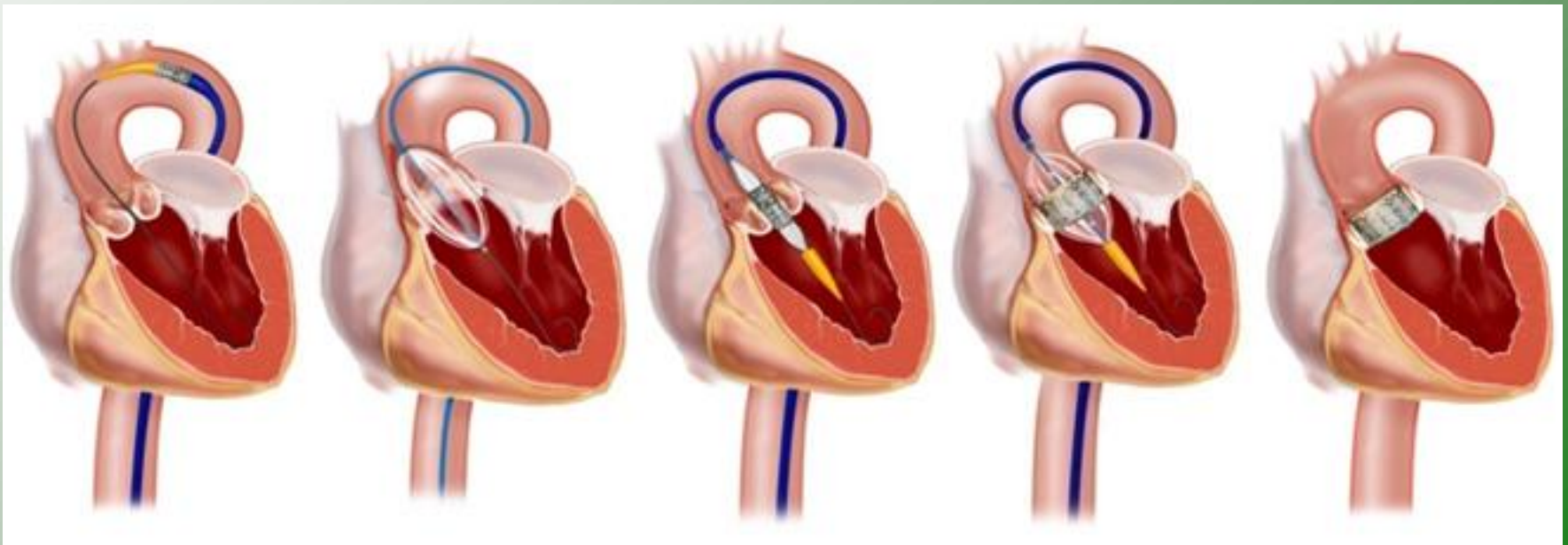(R. De Niro, Casinò)

TAVI

…la TAVI…

Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D.,
Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D.,
Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D.,
Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela S. Douglas, M.D.,
John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D.,
and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators*

	High risk patients*			Inoperable patients		
	TAVI	AVR	P value	TAVI	Control	P value
No of patients	348	351		179	179	
1 year all cause mortality (% (No of events))§	24.2 (84)	26.8 (89)	0.44	30.7 (55)	50.7 (89)	<0.001
1 year stroke rate (% (No of events))¶	8.3 (27)	4.3 (13)	0.04	10.6 (19)	4.5 (8)	0.04

TAVI= transcatheter aortic valve implantation, AVR=surgical aortic valve replacement.

*Hazard ratio with TAVI in high risk patients: 0.93 (95% CI 0.71 to 1.22; P=0.62)

†Hazard ratio with TAVI in inoperable patients (pivotal trial): 0.55 (95% CI 0.40 to 0.74; P<0.001);

‡No P value or hazard ratio was published for the continued access study.

§ Kaplan-Meier estimates.

¶ Includes any stroke and transient ischaemic attack; stroke rate in continued access study includes "major stroke" only.

Heart Valve Disease

Aortic Stenosis in the Elderly

Disease Prevalence and Number of Candidates for Transcatheter Aortic Valve Replacement: A Meta-Analysis and Modeling Study

This systematic review and meta-analysis of population-based studies found that the prevalence of AS and severe AS among the elderly is 12.4%, and 3.4%, respectively. The overall burden of disease due to severe AS in the general elderly population is substantial. Our model showed that under the current indications approximately 290,000 elderly patients at high or prohibitive surgical risk could potentially be treated with TAVR in Europe and North America, and that each year there are approximately 27,000 new TAVR candidates. These estimates have considerable clinical, economic, and social implications.

Heart Valve Disease

Aortic Stenosis in the Elderly

Annual number of new TAVR candidates

Country	Candidates (95%CI)
Austria	263 (115-152)
Belgium	402 (172-232)
Czech Republic	316 (136-581)
Denmark	179 (78-325)
Finland	192 (82-349)
France	2,265 (990-4,160)
Germany	3,952 (1,684-7,227)
Greece	529 (226-954)
Italy	2,679 (1,145-4,958)
Ireland	110 (46-203)
Luxembourg	15 (6-27)
Norway	131 (55-24)
Poland	1,220 (512-2,226)
Portugal	463 (197-844)
Spain	1,737 (728-3,155)
Sweden	318 (133-582)
Switzerland	270 (115-495)
The Netherlands	526 (224-965)
The United Kingdom	2,217 (896-3,904)
Total 19 European countries	**17,712 (7,590-32,691)***
The United States	8,205 (3,470-15,139)
Canada	970 (408-1,777)
Total North America	**9,189 (3,898-16,682)***

Heart Valve Disease

Aortic Stenosis in the Elderly

Disease Prevalence and Number of Candidates for Transcatheter Aortic Valve Replacement: A Meta-Analysis and Modeling Study

The number TAVR candidates. Nearly 40.5% of all patients with symptomatic severe AS did not undergo SAVR (Fig. 4B). Possible explanations for the lower than expected rates of SAVR include excessive operative risk, advanced age, comorbidities, and patient preference (21,22). TAVR is a safe, effective, and less invasive treatment strategy for a highly selected proportion of the patients who do not undergo SAVR (23), represented by the 40.3% of patients who underwent TAVR (Fig. 4C). The treatment decisions reflect heart team discussions, in which (interventional) cardiologists and cardiac surgeons combine risk models with additional factors such as frailty, porcelain aorta, and vessel tortuosity (24).

The estimated large number of TAVR candidates has clinical, economic, and social implications. If the index admission costs (US $72,000) of the PARTNER (Placement of Aortic Transcatheter Valves) trial are applied (25), treating all TAVR candidates would represent a budget impact of $13.7 billion in the European countries and $7.2 in North America. At a price of $30,000, the total device turnover would be approximately $8.7 billion.

Despite budgetary concerns, current clinical trials are evaluating TAVR for patients at intermediate surgical risk (NCT01314313 and NCT01586910) (9,29). If TAVR proves to be noninferior to SAVR in this population, we estimate that a further 145,000 patients would become TAVR eligible. Indeed, there is some evidence that suggests that TAVR is already being performed in these intermediate-risk patients (18,30). Thus, our estimates of the impact of positive outcomes in the ongoing trials are likely to be conservative. In the future, TAVR may even compete with SAVR in patients at low surgical risk (30,31), a group that comprises 730,000 severe AS patients in the European countries and North America combined.

BMJ

ANALYSIS

Transcatheter aortic valve implantation (TAVI): risky and costly

Many of the 40 000 transcatheter procedures so far carried out cannot be justified on medical or cost effectiveness grounds. **Hans Van Brabandt**, **Mattias Neyt**, and **Frank Hulstaert** examine why practice has gone beyond the evidence

Hans Van Brabandt *researcher*[1][2], Mattias Neyt *researcher*[1], Frank Hulstaert *researcher*[1]

[1]KCE, Belgian Health Care Knowledge Centre, Administratief Centrum Kruidtuin, Kruidtuinlaan 55, 1000 Brussels, Belgium; [2]CEBAM, Belgian Centre for Evidence-Based Medicine and Branch of the Dutch Cochrane Centre, Leuven, Belgium

BMJ   **ANALYSIS**

Transcatheter aortic valve implantation (TAVI): risky and costly

solid. But a health technology assessment we carried out, commissioned by the Belgian government, concluded that the Belgian health authorities should pay for TAVI in only a minority of patients (10%) of those currently considered for treatment—those who are deemed inoperable for technical reasons such as a series of previous operations or irradiation of the chest wall.[8] The United Kingdom's National Institute for

BMJ   **ANALYSIS**

BMJ 2012;345:e4710 doi: 10.1136/bmj.e4710 (Published 31 July 2012)

Transcatheter aortic valve implantation (TAVI): risky and costly

Based on current evidence, and considering efficient use of limited resources, it is difficult to see how healthcare payers can justify reimbursing TAVI for patients suitable for surgery, given that the risk of stroke is twice as high after TAVI. In addition, TAVI is much more expensive, on average about €20 000 more per patient in our analysis of Belgian data. Based on observational data, the costs during the initial hospital admission, inclusive of an Edwards Sapien valve of €18 000, are on average €43 600 for TAVI versus €23 700 for surgical valve replacement. The average cost of transapical TAVI is higher than for the transfemoral approach (€49 800 *v* €40 900).[26]

BMJ

ANALYSIS

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adequate. The Sapien valve was approved on the basis of a trial called PARTNER (Placement of Aortic Transcatheter Valve). We reviewed the conduct and results of the trial through papers published in peer reviewed journals, proceedings from congresses, press releases, and direct contacts with the manufacturer, the FDA, the *New England Journal of Medicine* (*NEJM*) (where it was published), and the principal investigators.

Our rigorous analysis of all the available data, in combination with a study of real world TAVI practice in Europe, led us to conclude that the arguments supporting the widespread use of TAVI do not stand up to scrutiny. In addition, the PARTNER trial seems to have important problems, the most relevant being publication bias and lack of data transparency, unbalanced patient characteristics, and incompletely declared conflicts of interest.

BMJ

BMJ 2012;345:e4710 doi: 10.1136/bmj.[...]

**Transcatheter a[...]
and costly**

Taken together, these results suggest that TAVI can be justified for inoperable patients on clinical grounds, though cost effectiveness calculations are more equivocal. But even this conclusion is thrown into doubt by a follow-up study authorised by the FDA, in which 41 inoperable patients were randomised to TAVI and 49 to standard therapy. This study remains unpublished, and our attempts to gain access to further details have been rebuffed by the FDA and the study sponsor. But the data presented at an FDA meeting on 20 July 2011 showed that the TAVI patients fared worse than those given standard therapy (one year mortality 34.3% v 21.6%).[15]

Table 1| One year mortality and stroke rate in [...]

	High risk patients*			Pivotal trial†			Continued access study‡	
	TAVI	**AVR**	**P value**	**TAVI**	**Control**	**P value**	**TAVI**	**Control**
No of patients	348	351		179	179		41	49
1 year all cause mortality (% (No of events))§	24.2 (84)	26.8 (89)	0.44	30.7 (55)	50.7 (89)	<0.001	34.3 (13)	21.6 (10)
1 year stroke rate (% (No of events))¶	8.3 (27)	4.3 (13)	0.04	10.6 (19)	4.5 (8)	0.04	2.4 (1)	0 (0)

TAVI= transcatheter aortic valve implantation, AVR=surgical aortic valve replacement.

*Hazard ratio with TAVI in high risk patients: 0.93 (95% CI 0.71 to 1.22; P=0.62)

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§ Kaplan-Meier estimates.

¶ Includes any stroke and transient ischaemic attack; stroke rate in continued access study includes "major stroke" only.

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ANALYSIS

Transcatheter aortic valve implantation (TAVI): risky and costly

We have repeatedly sought access to further details of this follow-on trial, carried out under FDA auspices as a formally approved "continued access study," the purpose of which is to enable sponsors of clinical investigations to continue to enrol patients while a market application is being sought. The FDA responded that any further data analysis of a premarket application is proprietary information and that it was up to the sponsor to release it, if so inclined. But our requests to the sponsor (Edwards) and the principal investigator went unanswered. In our view, this behaviour is both ethically and scientifically unacceptable and should be legally regulated in future. Study sponsors should be obliged to make the results of a negative trial public so that policy makers can reach rational and balanced decisions.

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BMJ 2012;345:e4710 doi: 10.1136/bmj.e4710 (Published 31 July 2012)

Transcatheter aortic valve implantation (TAVI): risky and costly

Given our failure to make progress with the FDA or the sponsor, we approached the *NEJM* which had published the PARTNER trial. We put our objections to the *NEJM*, which passed them on to the investigators. Their response convinced the *NEJM* editors that "while each of the points we raised deserved a thoughtful review, they did not, either individually or together, fundamentally place the findings of the PARTNER trial in serious doubt." Asked what the responses of the investigators had been, *NEJM* responded that it had not requested permission from them to pass them on, since they were intended for its own confidential evaluation. We were recommended to request this information directly from the study sponsor, which we did, to no avail.

BMJ

ANALYSIS

BMJ 2012;345:e4710 doi: 10.1136/bmj.e4710 (Published 31 July 2012)

Transcatheter aortic valve implantation (TAVI): risky and costly

Our concerns about the PARTNER trial go further than this, however. Published data on the inoperable patients, who had the most convincing results, show that the treatment and control groups are unbalanced in a way that would favour TAVI. The control group contained more patients with comorbidities, more who had had a previous heart attack, and more who were classified as frail than the TAVI group. There were fewer patients with an extensively calcified aorta. All these differences could have arisen from a flawed randomisation or by chance; but since they favour TAVI, an analysis that adjusted for prognosis at baseline would have produced a more realistic estimate of the effect size.

BMJ — ANALYSIS

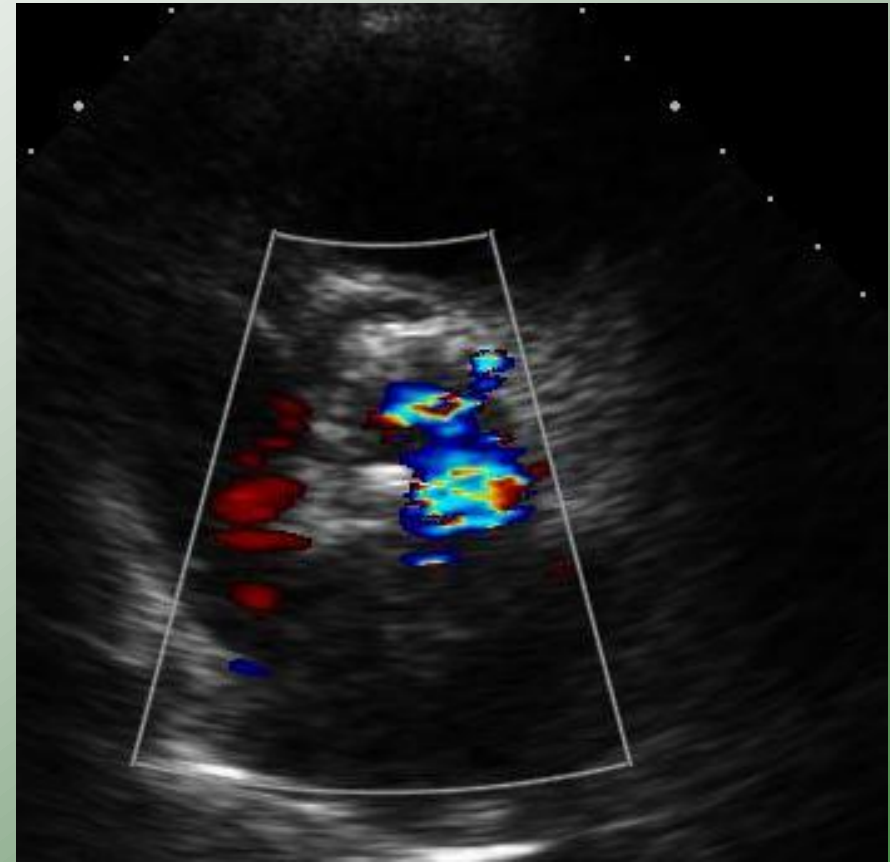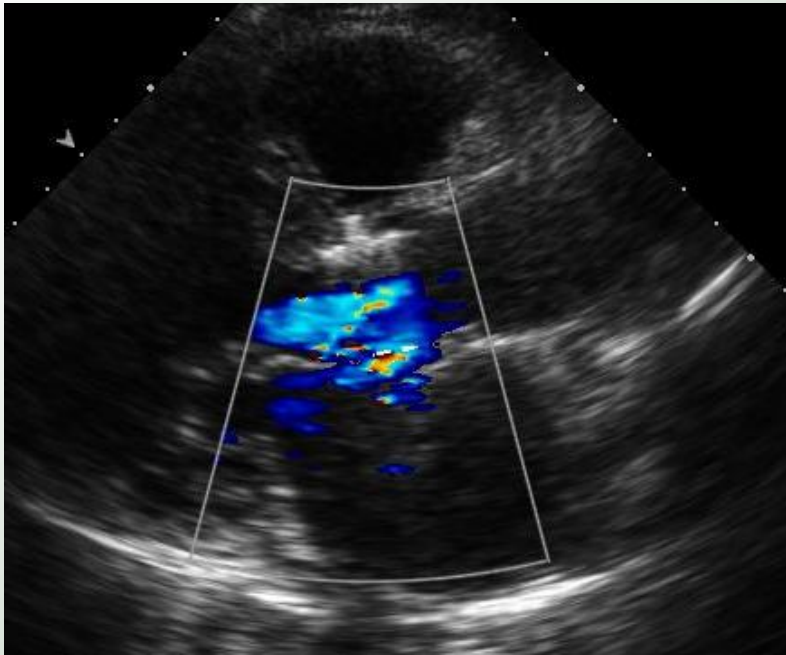## Transcatheter aortic valve implantation (TAVI): risky and costly

Disclosure of interests

Martin Leon, the principal investigator of the PARTNER trial, has substantial financial interests that we do not believe were fully disclosed. As the original developer of the Sapien valve, he is reported to have received $6.9m from Edwards Lifesciences when it bought the company he founded, Percutaneous Valve Technologies, for $125m in 2004.[18] The *NEJM* paper article acknowledges under Leon's conflicts of interest "2004—payment for equity holdings as company was sold to Edwards Lifesciences." But it does not mention that he was to receive three further payments on the achievement of three milestones: successful treatment of 50 patients, regulatory approval in Europe, and limited approval in the US.[18] In an interview with *Businessweek*, Leon said that he had donated his milestone payments to a Manhattan school.[18]
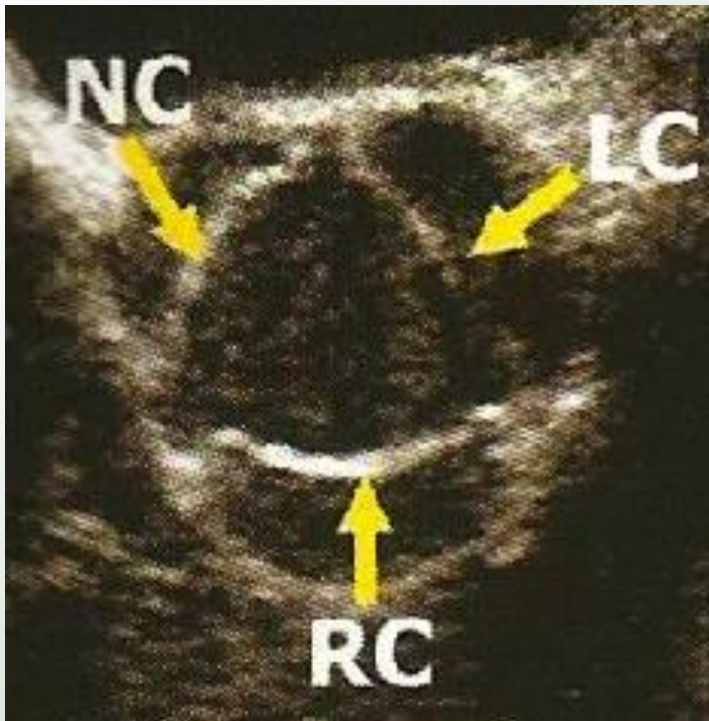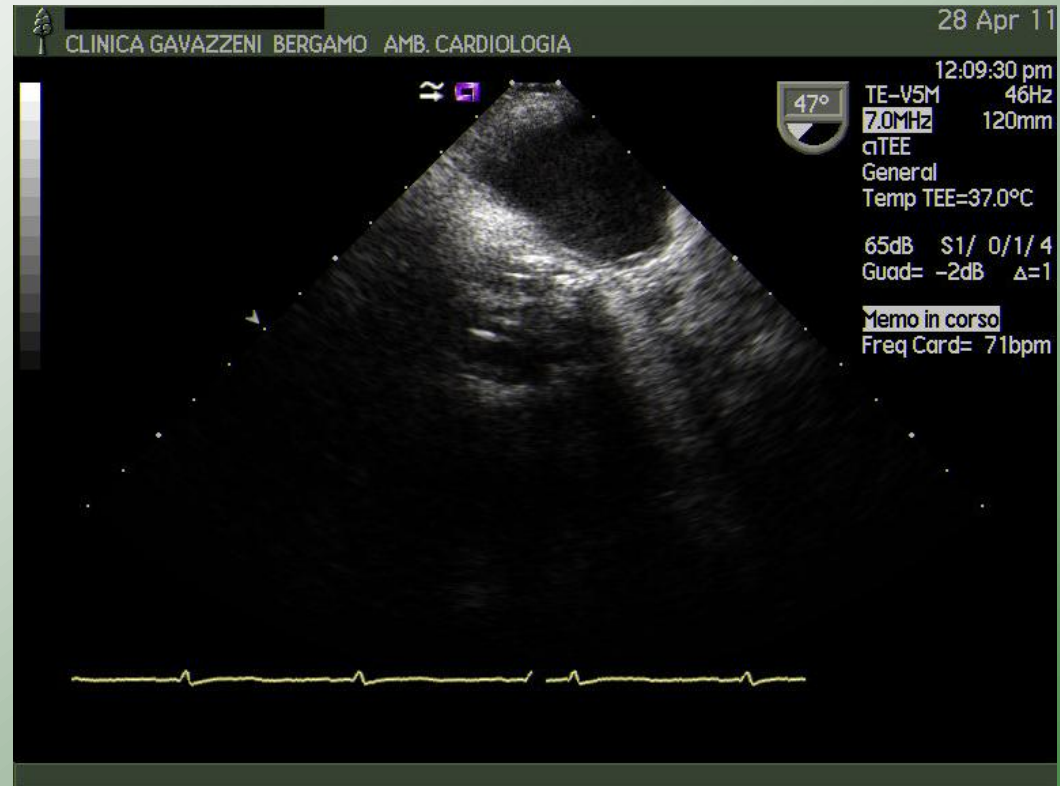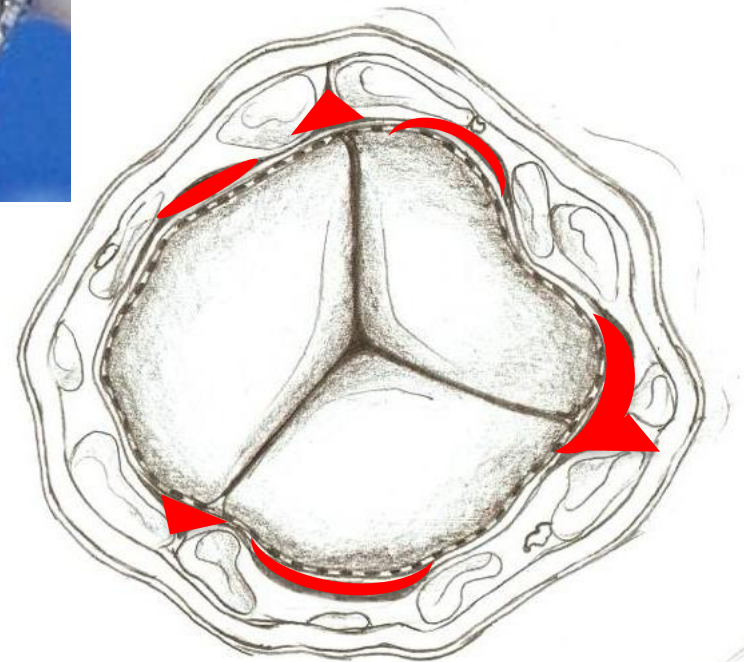
Transcatheter aortic valve replacement - Evidence and Indications update
An article from the e-journal of the ESC Council for Cardiology Practice

The 2-year follow-up data of patients in the PARTNER trial cohort A supported the use of TAVI as an alternative to surgery in high-risk patients with a comparable 2-year mortality rate (33.9% vs. 35.0%; P=0.78). The early increase in the risk of stroke with TAVI was attenuated over time (7.7% vs. 4.9%; P=0.17). In this analysis, mild to severe peri-prosthetic aortic regurgitation following TAVI was more frequent after TAVI and associated with a more than two times increased 2-year mortality risk. Surprisingly, also mild peri-prosthetic aortic regurgitation had a negative impact on survival after TAVI.
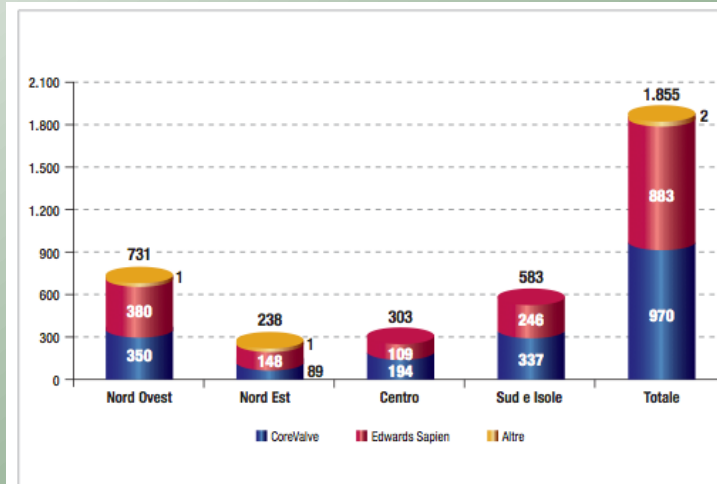
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Canada	970 (408-1,777)
Total North America	**9,189 (3,898-16,682)***

Protesi aortiche per via percutanea (TAVI)

Nel 2011 sono state impiantate **1.855** protesi aortiche per via percutanea, di cui:
970 CoreValve Medtronic (52,3% del totale)
883 Edwards Sapien (47,6% del totale)
2 altre (0,1% del totale)

Log-EuroSCORE

Patients undergoing TAVI procedure (N = 1544)

Pazients reporting difficult thoracic approach, porcelain aorta or severe frailty score are excluded
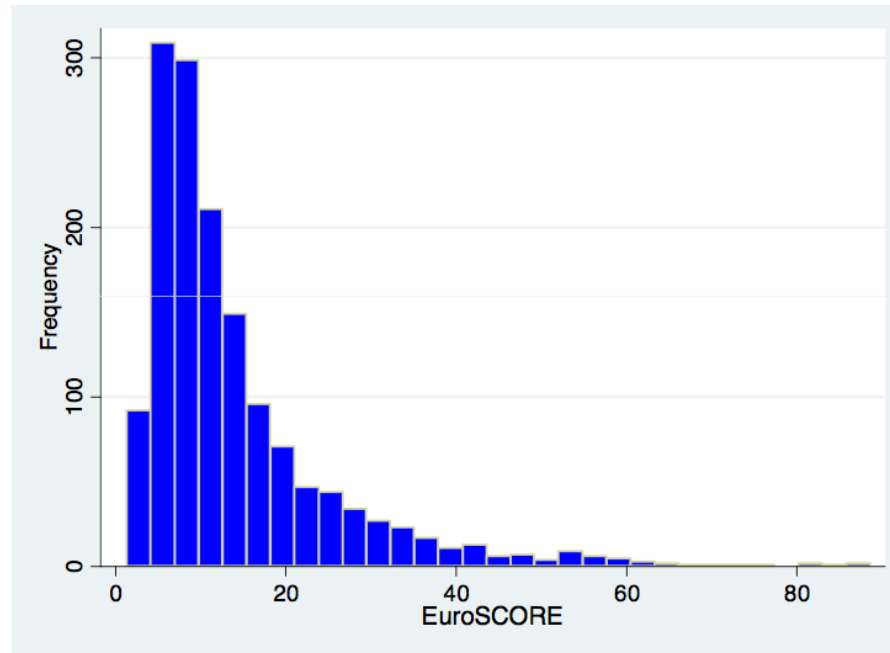
Log - EuroSCORE :	Mean=	14.1 $\pm$ 11.8
	Median=	10.3
	75° percentile =	16.9

…il PFO…
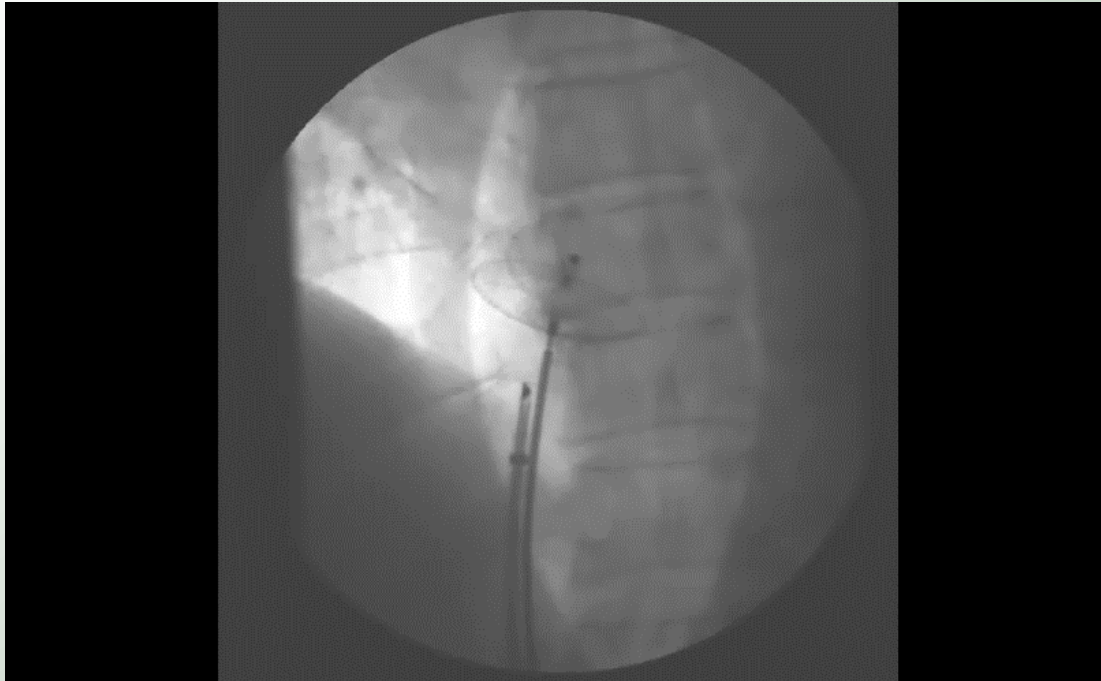
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Closure or Medical Therapy for Cryptogenic Stroke with Patent Foramen Ovale

Anthony J. Furlan, M.D.,
Laura Mauri, M.D., Ha
Robert Felberg, M.D.,
Michael Lan
and Lawrence Wechs

The **NEW ENGLAND**
JOURNAL *of* **MEDICINE**

Percutaneous Closure of Patent Foramen Ovale in Cryptogenic Embolism

Bernhard Meier, M.D., Bindu Kalesan, Ph.D., Heinrich P.
David Hildick-Smith, M.D., Dariusz Dudek, M.D., Greth
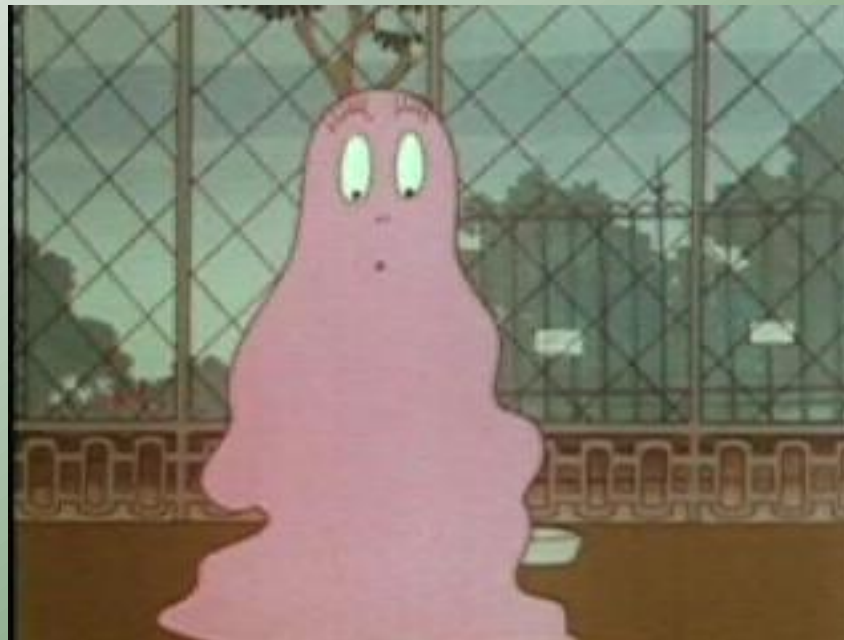Gerhard Schuler, M.D., Antony S. Walton, M.D., Andreas
and Peter Jüni, M.D., for the PC Tr

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Closure of Patent Foramen Ovale versus Medical Therapy after Cryptogenic Stroke

John D. Carroll, M.D., Jeffrey L. Saver, M.D., David E. Thaler, M.D., Ph.D.,
Richard W. Smalling, M.D., Ph.D., Scott Berry, Ph.D., Lee A. MacDonald, M.D.,
David S. Marks, M.D., and David L. Tirschwell, M.D.,
for the RESPECT Investigators*
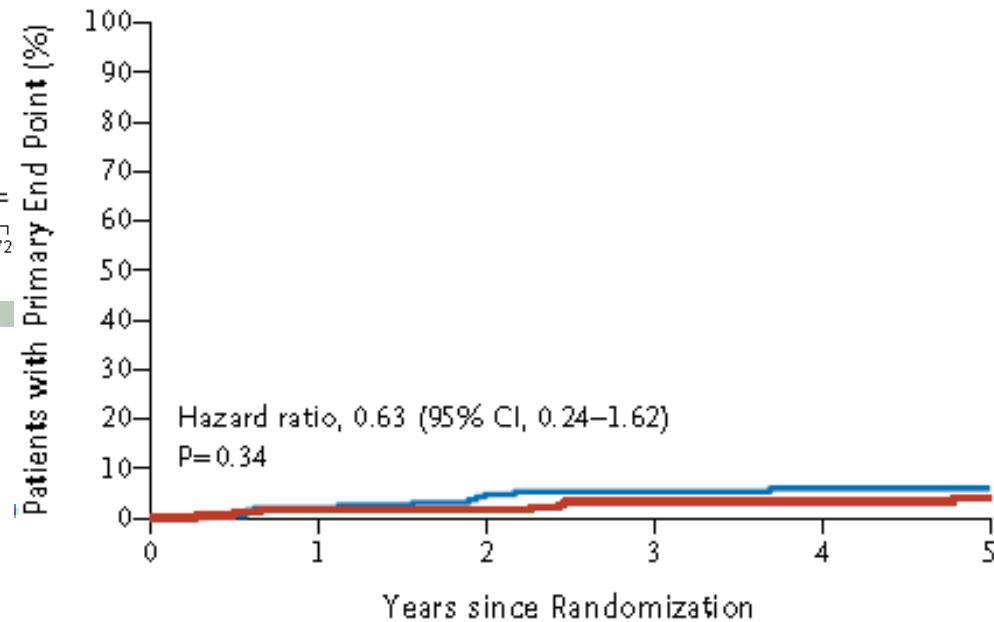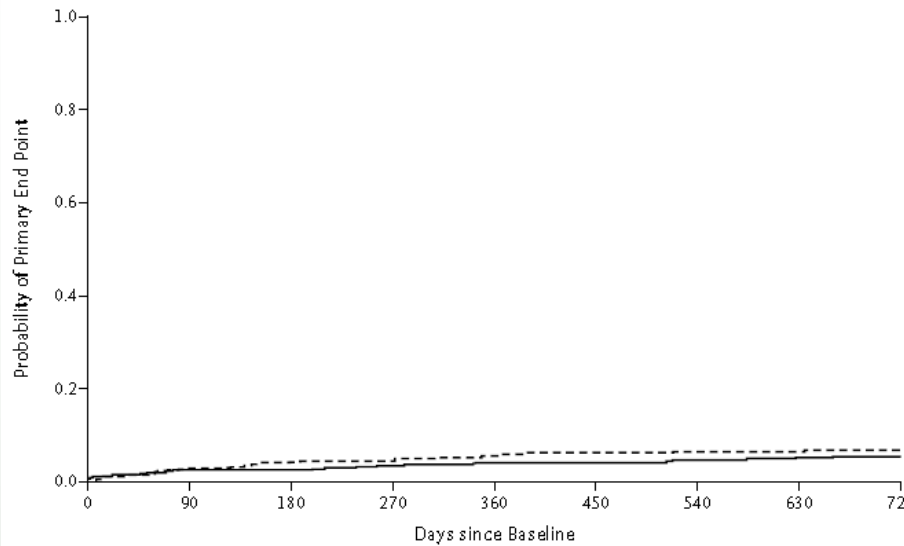
A Intention-to-Treat Cohort
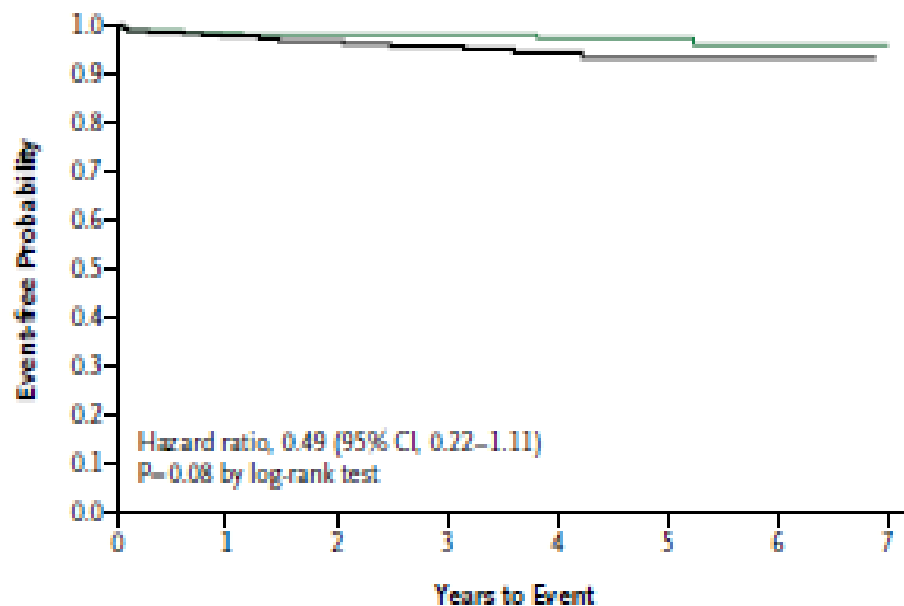
Hazard ratio, 0.49 (95% CI, 0.22–1.11)
P=0.08 by log-rank test

Hazard ratio, 0.63 (95% CI, 0.24–1.62)
P=0.34

Percutaneous closure of patent foramen ovale for cryptogenic stroke: A meta-analysis of randomized controlled trials ☆,☆☆

Joey S.W. Kwong, Yat-Yin Lam, Cheuk-Man Yu *   *International Journal of Cardiology 168 (2013) 4132–4138*

Institute of Vascular Medicine, Li Ka Shing Institute of Health Sciences, S.H. Ho Cardiovascular Disease and Stroke Centre, Heart Education And Research Training (HEART) Centre and Division of Cardiology, Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong Special Administrative Region
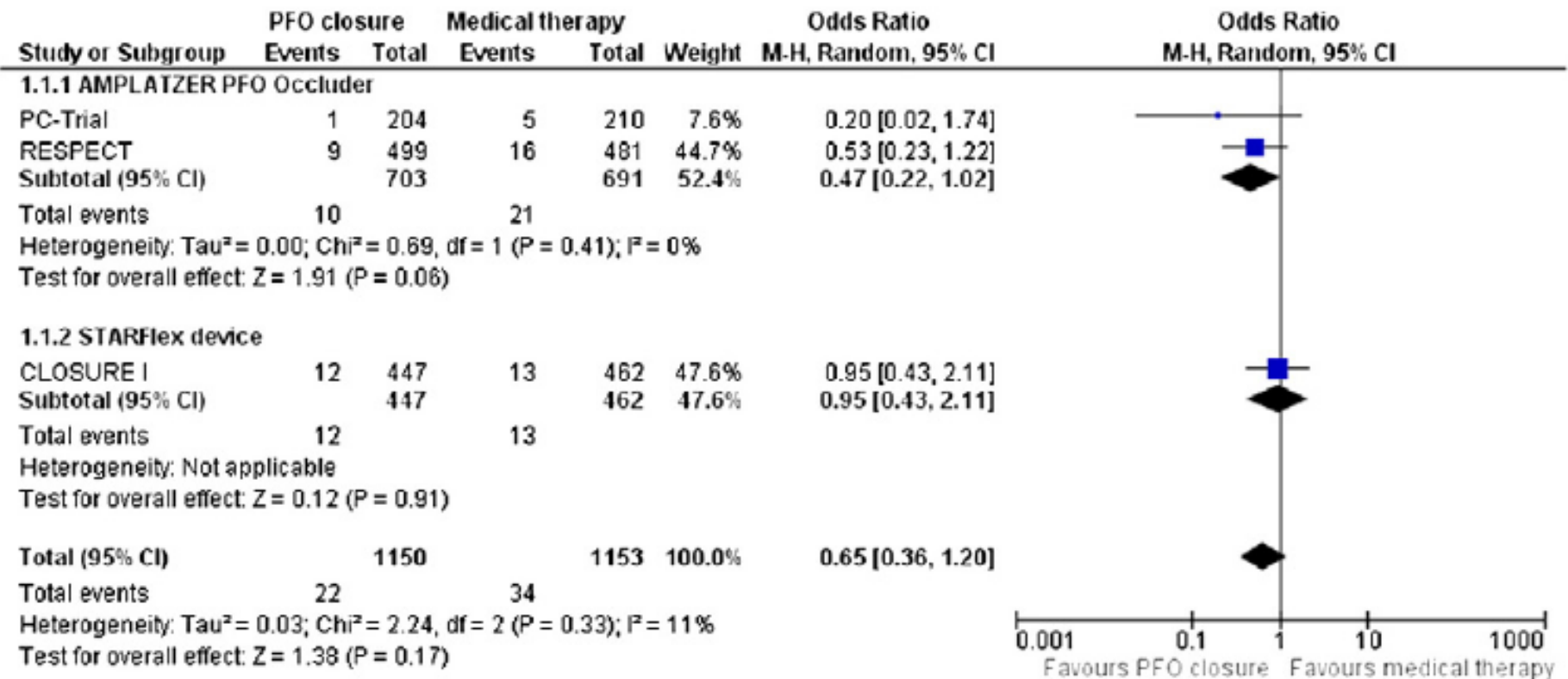
Fig. 3. Forest plot of stroke.

Percutaneous closure of patent foramen ovale for cryptogenic stroke: A meta-analysis of randomized controlled trials ☆,☆☆

Joey S.W. Kwong, Yat-Yin Lam, Cheuk-Man Yu *

Institute of Vascular Medicine, Li Ka Shing Institute of Health Sciences, S.H. Ho Cardiovascular Disease and Stroke Centre, Heart Education And Research Training (HEART) Centre and Division of Cardiology, Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong Special Administrative Region
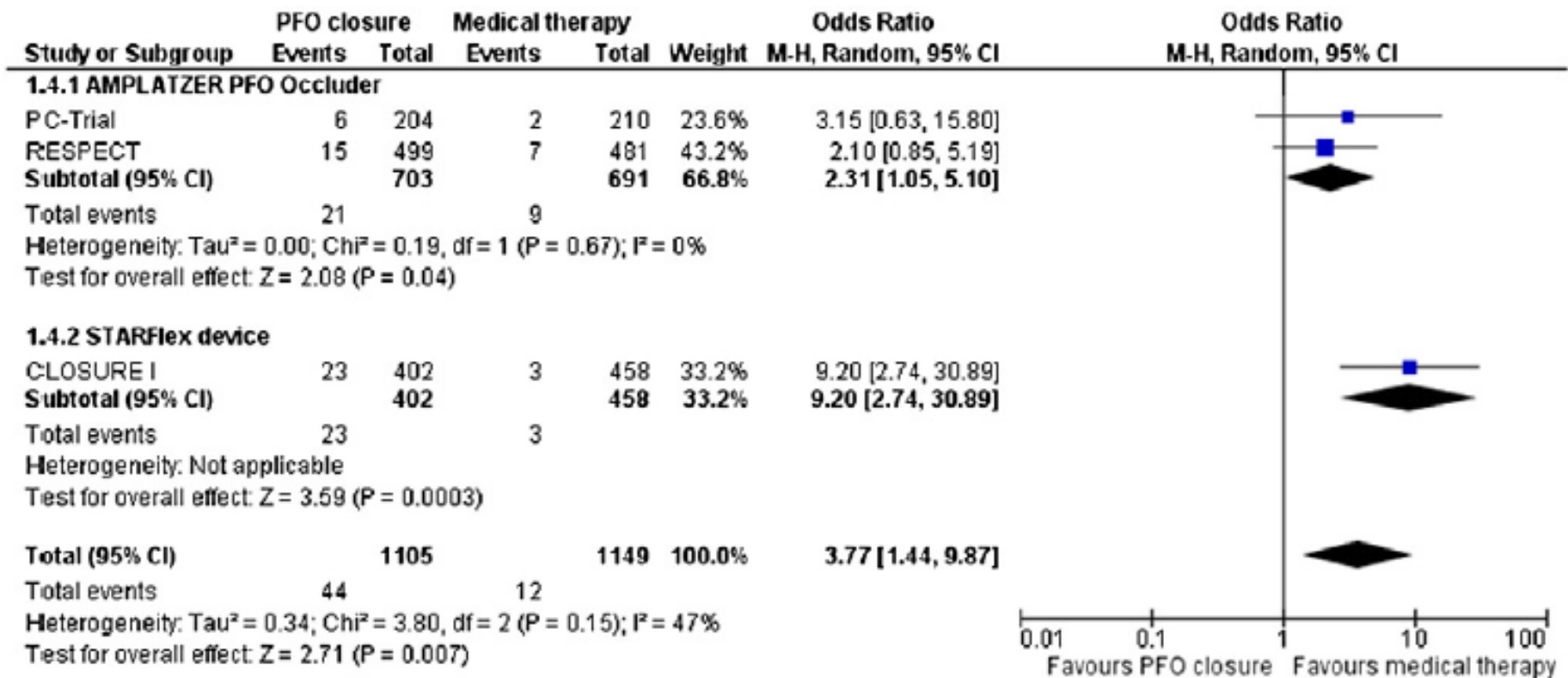
Fig. 4. Forest plot of new-onset AF.

The bad news for NMT Medical began in earnest in June of 2010, when the company received news that its septal repair implant, a device to treat structural heart disease, failed to meet its target endpoint.

Just weeks after announcing it did not have enough cash to file required federal documents, NMT Medical Inc. reports it is liquidating its business and selling assets to pay off creditors and has let go any employees left.

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2010   Mag   Giu   Lug

CONCLUSIONS

In patients with cryptogenic stroke or TIA who had a patent foramen ovale, closure with a device did not offer a greater benefit than medical therapy alone for the prevention of recurrent stroke or TIA. (Funded by NMT Medical; ClinicalTrials.gov number, NCT00201461.)

Low cerebrovascular event rate in subjects with patent foramen ovale and different clinical presentations
Results from a prospective non randomized study on a population including patients with and without patent foramen ovale closure

Pompilio Faggiano [a,*,1], Silvia Frattini [a,1], Piergiuseppe Piovesana [b], Roberto Lorusso [c], Ermanna Chiari [a], Francesco Scolari [d], Alessandro Padovani [e], Livio Dei Cas [a]

The main result of this study, performed on a large population of subjects with PFO, during a mean follow-up of more than four years, indicates a low rate of new cerebrovascular events (fatal and non fatal stroke, TIAs), that is 12 in 446 pts (2.7%), corresponding to a stroke and TIA annual incidence of ~0.2% and ~0.4% respectively. Incidence of cerebrovascular events resulted roughly similar in pts with closed PFO (group 1) and in pts with not closed PFO (group 2). Survival free from cerebrovascular events was higher in group 2 pts (PFO not closed) at Kaplan–Meyer analysis.
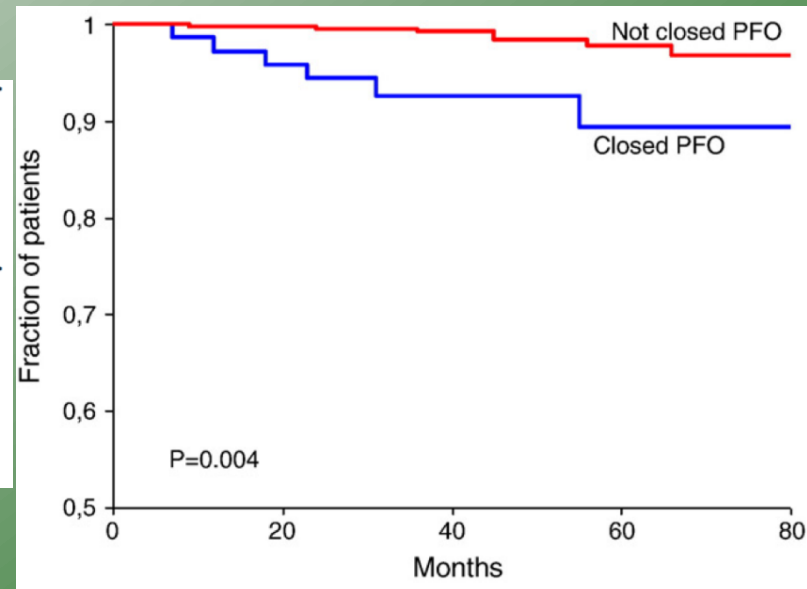
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Percutaneous Closure of Patent Foramen Ovale in Cryptogenic Embolism

Subgroup	PFO Closure	Medical Therapy	Hazard Ratio (95% CI)	P Value for Interaction
	no. of patients/total no. (%)			
Overall	7/204 (3.4)	11/210 (5.2)	0.63 (0.24–1.62)	
Age				0.10
<45 yr	1/91 (1.1)	6/97 (6.2)	0.16 (0.02–1.31)	
≥45 yr	6/113 (5.3)	5/113 (4.4)	1.22 (0.37–3.99)	
Atrial septal aneurysm				0.09
Yes	4/47 (8.5)	2/51 (3.9)	2.09 (0.38–11.4)	
No	3/157 (1.9)	9/159 (5.7)	0.32 (0.09–1.18)	
Cardiovascular index event				0.78
Stroke	5/165 (3.0)	8/163 (4.9)	0.58 (0.19–1.76)	
Transient ischemic attack or pulmonary embolism	2/39 (5.1)	3/47 (6.4)	0.78 (0.13–4.66)	
>1 Previous cardiovascular event				0.22
Yes	2/76 (2.6)	6/79 (7.6)	0.28 (0.06–1.41)	
No	5/128 (3.9)	5/131 (3.8)	0.99 (0.29–3.45)	

Closure Better   Medical Therapy Better

0.03 0.10 0.25 0.50 1.00 2.00 5.00 10.00

Closure of Patent Foramen Ovale versus Medical Therapy after Cryptogenic Stroke

Figure 2. Analysis of the Primary End-Point According to Subgroup, in the Intention-to-Treat Cohort.

… la PCI nella card. ischemica stabile …
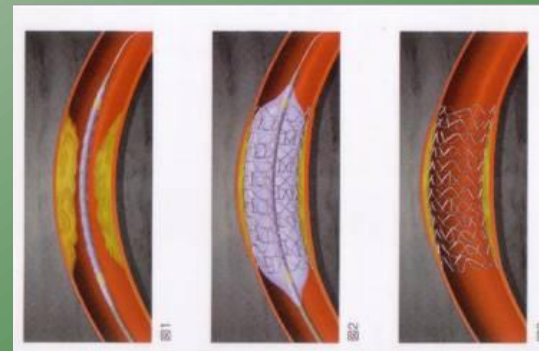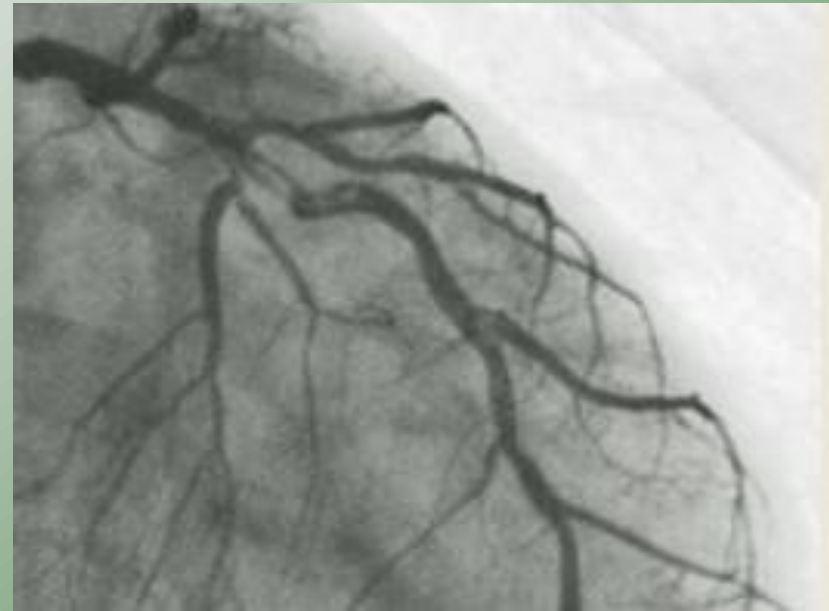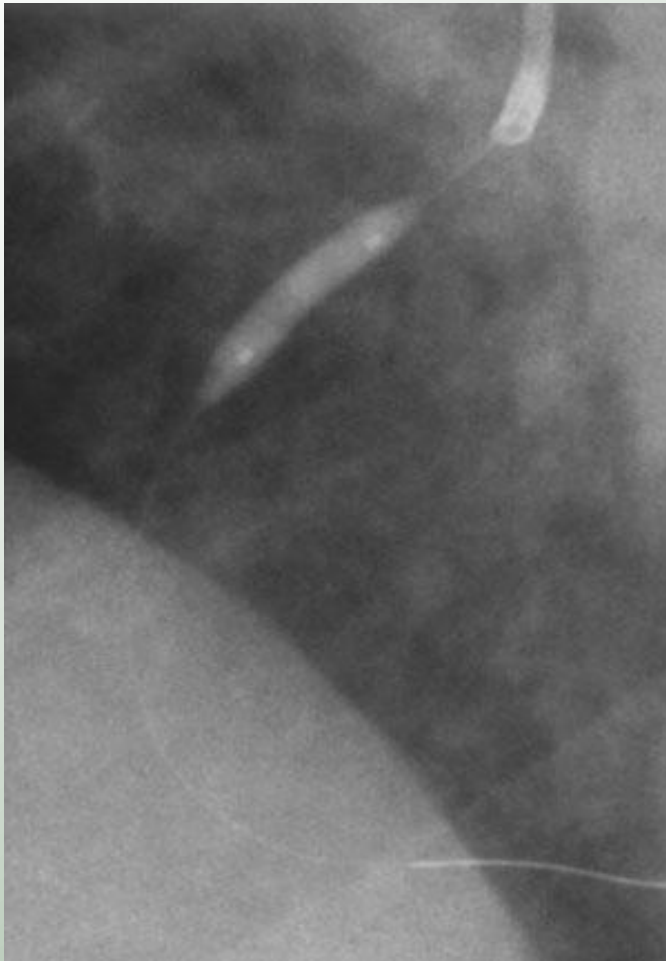
Economic analysis of treatments reducing coronary heart disease mortality in England and Wales, 2000–2010

D. FIDAN[1]*, B. UNAL[1,2], J. CRITCHLEY[3] and S. CAPEWELL[1]

[1]From the Division of Public Health, University of Liverpool, [2]Department of Public Health, Dokuz Eylul University School of Medicine, 35340 Izmir, Turkey, [3]International Health Research Group, Liverpool School of Tropical Medicine, Liverpool, UK

Discussion: The cost-effectiveness ratios for standard CHD treatments varied by over 100-fold. Large amounts of NHS funding are being spent on relatively less cost-effective interventions, such as statins for primary prevention, angioplasty and CABG surgery. This merits debate.

Overtesting and Overtreating

The Year in Medicine 2013: News That Made a Difference
Deborah Flapan; Tanya Priber
December 10, 2013   01 of 17

2013 YEAR IN MEDICINE

THE BIGGEST MEDICAL NEWS OF THE YEAR

A total of 17 medical societies released a list of almost 90 common but often unnecessary tests and procedures, many of them ordered for asymptomatic patients. Twelve of the guidelines issued as part of the "Choosing Wisely" campaign caution physicians that asymptomatic patients probably do not need a given treatment. Two examples are stress echocardiograms, which are not recommended for asymptomatic patients who meet "low-risk" scoring criteria for coronary disease, and computed tomography, which should not be used to evaluate children's minor head injuries. Separately, a national summit involving a wide range of medical groups, as well as hospital organizations, and government agencies, issued a policy paper detailing strategies for dealing with 5 overused treatments that can harm patient safety and quality: antibiotics for the common cold, blood transfusions, ear tubes for children, early-scheduled births, and cardiac stents.

(…non stiamo parlando di IMA o angina instabile…)

L'angioplastica nei pazienti con sindrome coronarica acuta riduce l'incidenza di morte/infarto miocardico

Negli USA eseguite > 1.000.000 PCI nel 2006

≈85% PCI vengono eseguite su pazienti con cardiopatia ischemica stabile

In questi pz la PCI ha ≤ 1% complicanze gravi (morte – IMA - BPAC) e ≥ 95% successo

QUINDI???

SCIENCE OF MEDICINE

Patients Overestimate the Potential Benefits of Elective Percutaneous Coronary Intervention

by John H. Lee, MD, Kenny Chuu, MD, John Spertus, MD, David J. Cohen, MD, James A. Grantham, MD, Fengming Tang, MS & James H. O'Keefe, MD

Figure 1
Patient perceived benefits of elective PCI.
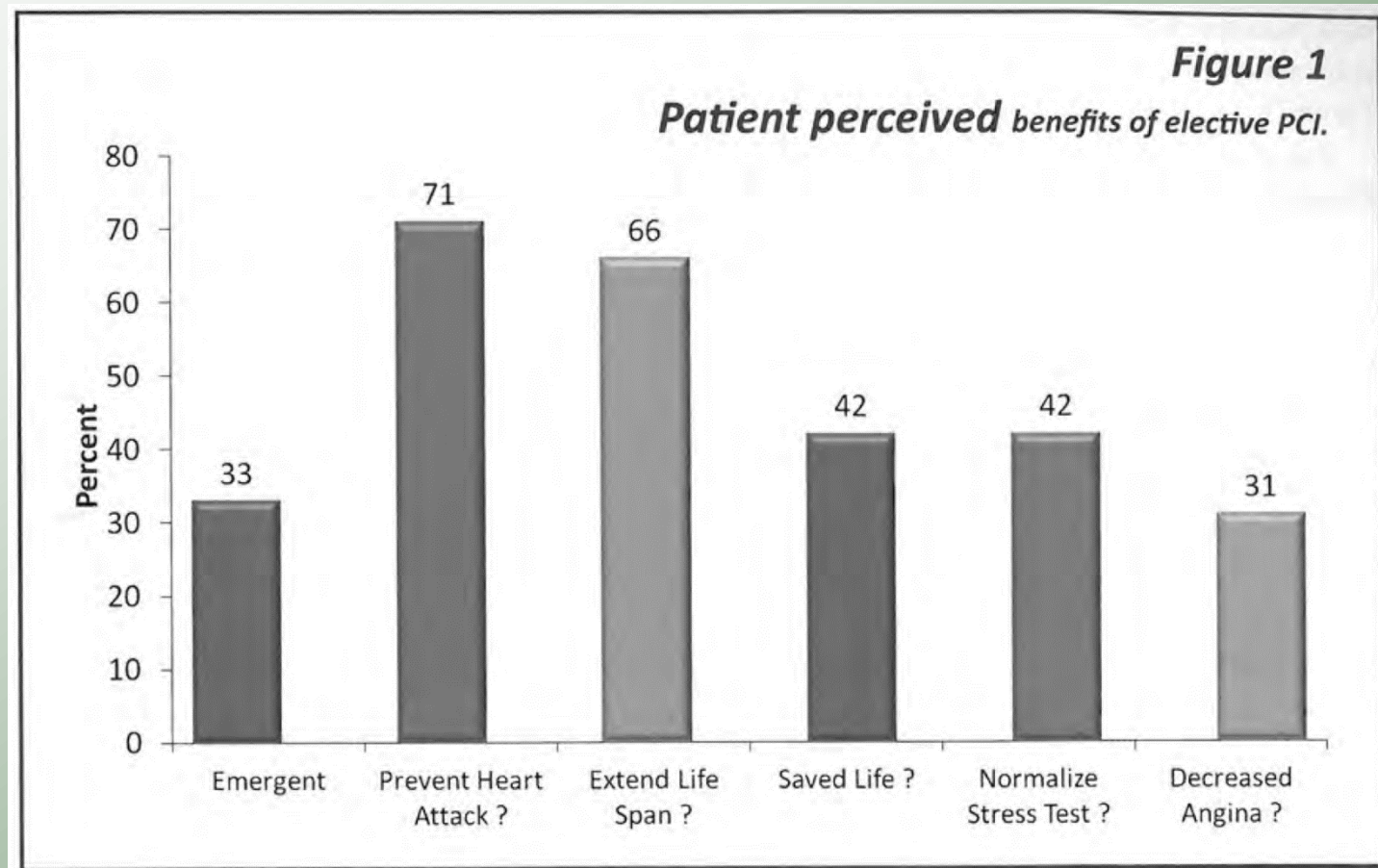
BMJ

Percutaneous transluminal coronary angioplasty versus medical treatment for non-acute coronary heart disease: meta-analysis of randomised controlled trials

Heiner C Bucher, Peter Hengstler, Christian Schindler and Gordon H Guyatt

Study	
	Folland 1997[13]
Parisi 1992[17]	RITA-2 1997[14]
Sievers 1993[16]	
MASS 1995[18]	AVERT 1999[15]

End point	Risk ratio (95% CI)
Angina*	0.70 (0.50 to 0.98)
Fatal and non-fatal myocardial infarction	1.42 (0.90 to 2.25)
Death	1.32 (0.65 to 2.70)
PTCA*	1.29 (0.71 to 3.36)
CABG	1.59 (1.09 to 2.32)

*Test of heterogeneity P<0.001

0.4 0.6 0.8 1 2 3

Favours PTCA   *Favours medical treatment*
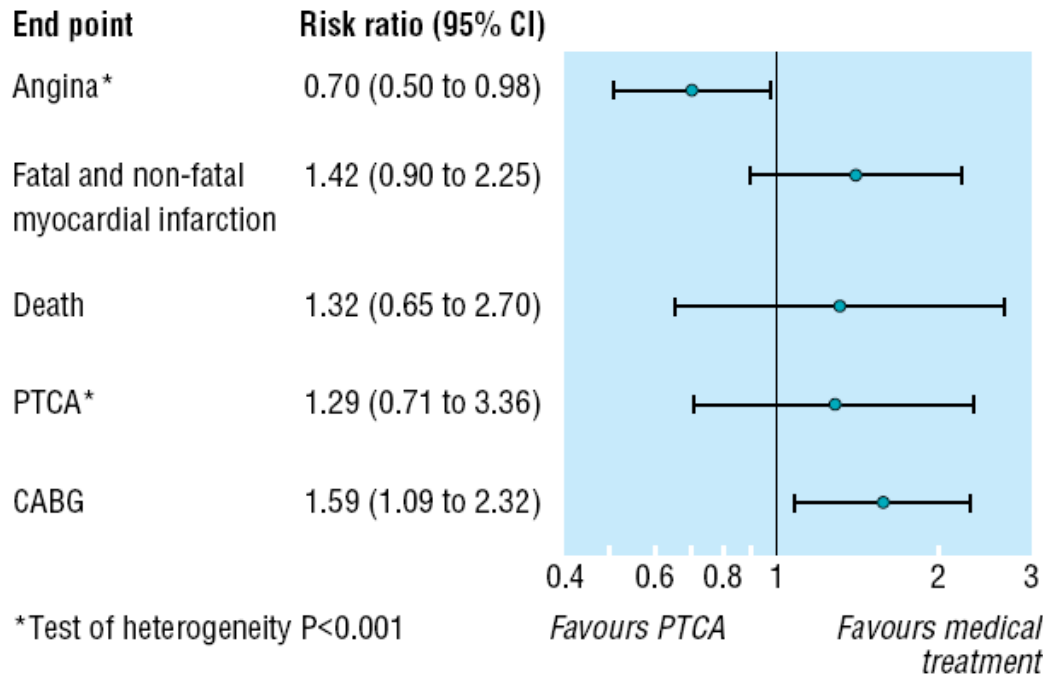
What this study adds

In non-acute coronary disease percutaneous transluminal coronary angioplasty may result in greater relief from angina than medical treatment, though the magnitude of effect varies considerably

The procedure may lead to an increase in coronary bypass grafting compared with medical treatment and is unlikely to reduce non-fatal myocardial infarction, death, or repeated angioplasty

The procedure should be use only in patients with non-acute coronary in whom angina cannot be controlled by medical treatment, though coronary artery bypass grafting is an alternative

…sì va beh, ma allora non c'erano gli stent…

Circulation

Percutaneous Coronary Intervention Versus Conservative Therapy in Nonacute Coronary Artery Disease
A Meta-Analysis

Demosthenes G. Katritsis, MD, PhD; John P.A. Ioannidis, MD

Background—Percutaneous coronary intervention (PCI) has been shown to improve symptoms compared with conservative medical treatment in patients with stable coronary artery disease (CAD); however, there is limited evidence on the effect of PCI on the risk of death, myocardial infarction, and subsequent revascularization. Therefore, we performed a meta-analysis of 11 randomized trials comparing PCI to conservative treatment in patients with stable CAD.

Methods and Results—A total of 2950 patients were included in the meta-analysis (1476 received PCI, and 1474 received conservative treatment). There was no significant difference between the 2 treatment strategies with regard to mortality, cardiac death or myocardial infarction, nonfatal myocardial infarction, CABG, or PCI during follow-up. By random effects, the risk ratios (95% CIs) for the PCI versus conservative treatment arms were 0.94 (0.72 to 1.24), 1.17 (0.88 to 1.57), 1.28 (0.94 to 1.75), 1.03 (0.80 to 1.33), and 1.23 (0.80 to 1.90) for these 5 outcomes, respectively. A possible survival benefit was seen for PCI only in trials of patients who had a relatively recent myocardial infarction (risk ratio 0.40, 95% CI 0.17 to 0.95). Except for PCI during follow-up, there was no significant between-study heterogeneity for any outcome.

Conclusions—In patients with chronic stable CAD, in the absence of a recent myocardial infarction, PCI does not offer any benefit in terms of death, myocardial infarction, or the need for subsequent revascularization compared with conservative medical treatment. (*Circulation.* 2005;111:2906-2912.)

A. Death
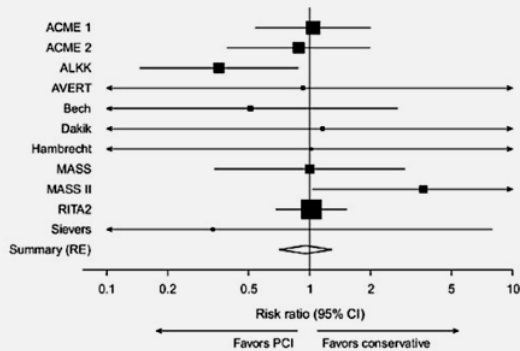
B. Cardiac death or myocardial infarction
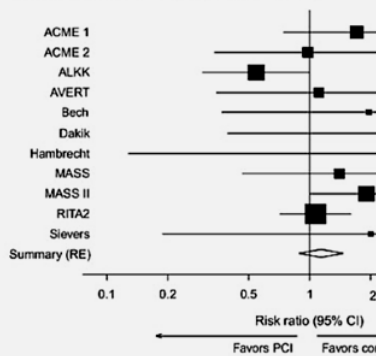
D. Coronary artery bypass grafting
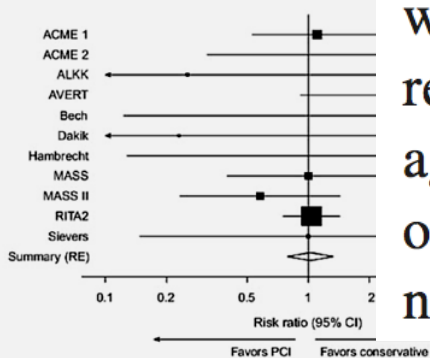
TABLE 3. Summary Risk Ratios for Major Outcomes with PCI vs Conservative Medical Treatment

Outcome	RE Risk Ratio (95% CI)	P	Q (I²)	FE Risk Ratio (95% CI)	P
Death	0.94 (0.72–1.24)	0.68	10.05 (0%)	0.95 (0.72–1.23)	0.68
Cardiac death or MI	1.17 (0.88–1.57)	0.28	11.3 (13%)	1.16 (0.91–1.48)	0.24
Nonfatal MI	1.28 (0.94–1.75)	0.12	4.93 (0%)	1.32 (0.97–1.79)	0.077
CABG	1.03 (0.80–1.33)	0.82	9.16 (0%)	1.04 (0.81–1.34)	0.76
PCI	1.23 (0.80–1.90)	0.34	38.4 (74%)	0.91 (0.77–1.07)	0.25

RE indicates random effects; FE, fixed effects.

Acknowledging these caveats, we conclude that for patients with chronic CAD and good left ventricular function, PCI does not confer any clear benefit in terms of long-term hard clinical outcomes compared with conservative medical treatment. At the same time, the early fear of an increased need for revascularization after PCI probably also is not warranted. PCI may be indicated in special circumstances, eg, relatively early after MI. By comparing the benefits, if any, against cost considerations, we believe that many percutaneous interventions that currently are performed in patients with nonacute CAD probably are not justified.

…eh già, ma non esistevano ancora gli stent medicati…

Percutaneous coronary interventions for non-acute coronary artery disease: a quantitative 20-year synopsis and a network meta-analysis

Thomas A Trikalinos, Alawi A Alsheikh-Ali, Athina Tatsioni, Brahmajee K Nallamothu, David M Kent

Findings 61 eligible trials (25 388 patients) investigated four of six possible comparisons between the four interventions; no trials directly compared DES with medical therapy or PTCA. In all direct or indirect comparisons, succeeding advancements in percutaneous coronary intervention did not produce detectable improvements in deaths or myocardial infarction. The risk ratio (RR) for indirect comparisons between DES and medical therapy was 0·96 (95% CI 0·60–1·52) for death and 1·15 (0·73–1·82) for myocardial infarction. By contrast, we recorded sequential significant reductions in target lesion or vessel revascularisation with BMS compared with PTCA (RR 0·68 [0–60·0·77]) and with DES compared with BMS (0·44 [0·35–0·56]). The RR for the indirect comparison between DES and PTCA for target lesion or vessel revascularisation was 0·30 (0·17–0·51).

Interpretation Sequential innovations in the catheter-based treatment of non-acute coronary artery disease showed no evidence of an effect on death or myocardial infarction when compared with medical therapy. These results lend support to present recommendations to optimise medical therapy as an initial management strategy in patients with this disease.
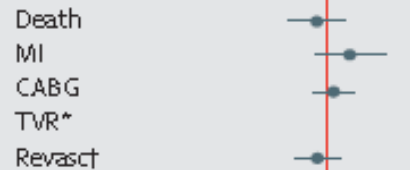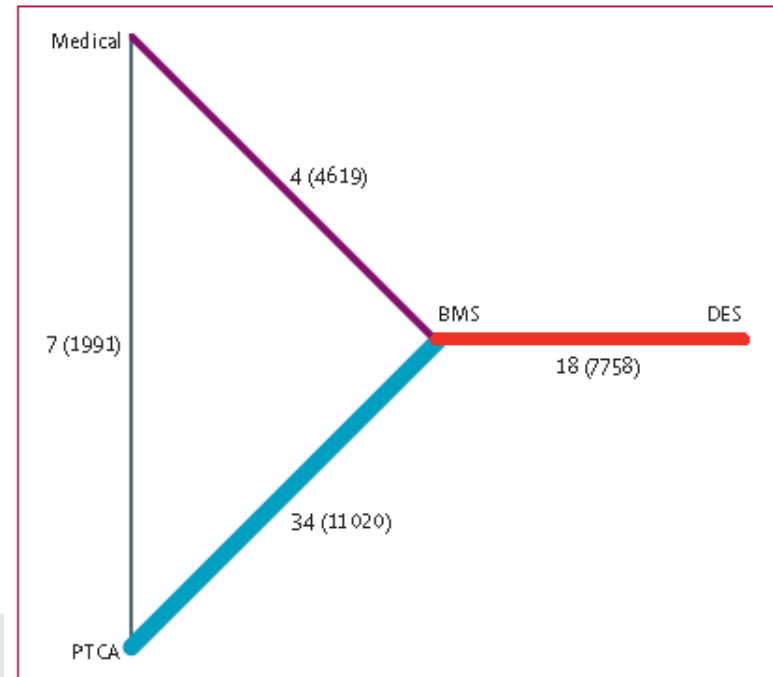
Percutaneous Coronary Intervention Versus Optimal Medical Therapy in Stable Coronary Artery Disease
A Systematic Review and Meta-Analysis of Randomized Clinical Trials

Seema Pursnani, MD, MPH; Frederick Korley, MD; Ravindra Gopaul, MBA, MPH;
Pushkar Kanade, MBBS, MPH; Newry Chandra, MBBS, MPH; Richard E. Shaw, PhD, MA;
Sripal Bangalore, MD, MHA

Conclusions—In this most rigorous and comprehensive analysis in patients with stable coronary artery disease, PCI, as compared with OMT, did not reduce the risk of mortality, cardiovascular death, nonfatal myocardial infarction, or revascularization. PCI, however, provided a greater angina relief compared with OMT alone, larger studies with sufficient power are required to prove this conclusively. **(*Circ Cardiovasc Interv.* 2012;5:476-490.)**

Percutaneous Coronary Intervention Versus Optimal Medical Therapy in Stable Coronary Artery Disease
A Systematic Review and Meta-Analysis of Randomized Clinical Trials

Percutaneous Coronary Intervention Versus Optimal Medical Therapy in Stable Coronary Artery Disease
A Systematic Review and Meta-Analysis of Randomized Clinical Trials

revascularization

Study or Subgroup	PCI Events	Total	OMT Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Overall Analysis						
ACME-1 (3yrs) 1992	44	105	46	107	8.1%	0.97 [0.71, 1.33]
ACME-2 (5yrs) 1997	41	51	35	50	8.9%	1.15 [0.92, 1.44]
ALKK (1yr) 2003	9	149	24	151	4.4%	0.38 [0.18, 0.79]
AVERT (1.5yrs) 1999	29	177	20	164	6.0%	1.34 [0.79, 2.28]
BARI 2D (5yrs) 2009	213	798	315	807	9.5%	0.68 [0.59, 0.79]
COURAGE (5yrs) 2007	228	1149	348	1138	9.5%	0.65 [0.56, 0.75]
DEFER (5yrs) 2001	18	90	15	91	5.2%	1.21 [0.65, 2.26]
JSAP (3.3yrs) 2008	41	188	70	191	7.9%	0.60 [0.43, 0.83]
MASS-1 (5yrs) 1995	56	72	12	72	6.0%	4.67 [2.74, 7.94]
MASS-2 (5yrs) 2004	66	205	59	203	8.3%	1.11 [0.83, 1.48]
RITA-2 (2.7yrs) 1997	235	504	223	514	9.6%	1.07 [0.94, 1.23]
RITA-2 (7yrs) 1997	137	504	182	514	9.2%	0.77 [0.64, 0.92]
SWISS-2 (10.2yrs) 2007	26	96	46	105	7.3%	0.62 [0.42, 0.92]
Total (95% CI)		4088		4107	100.0%	0.93 [0.76, 1.14]
Total events	1143		1395			

Heterogeneity: Tau² = 0.11; Chi² = 101.10, df = 12 (P < 0.00001); I² = 88%
Test for overall effect: Z = 0.72 (P = 0.47)

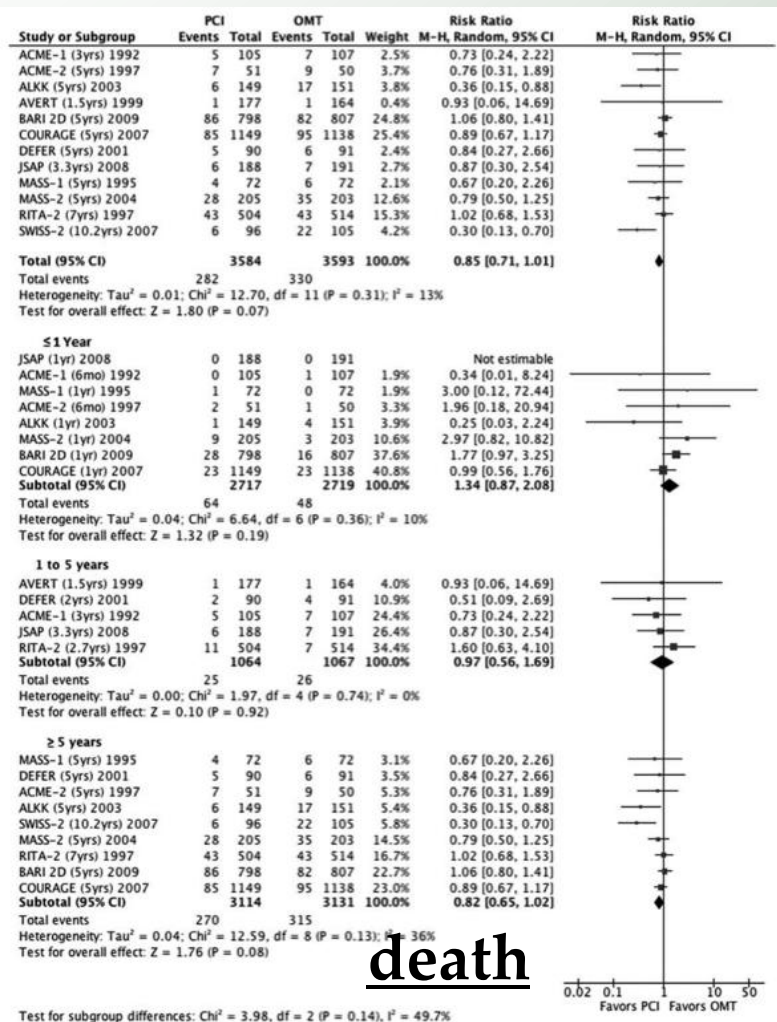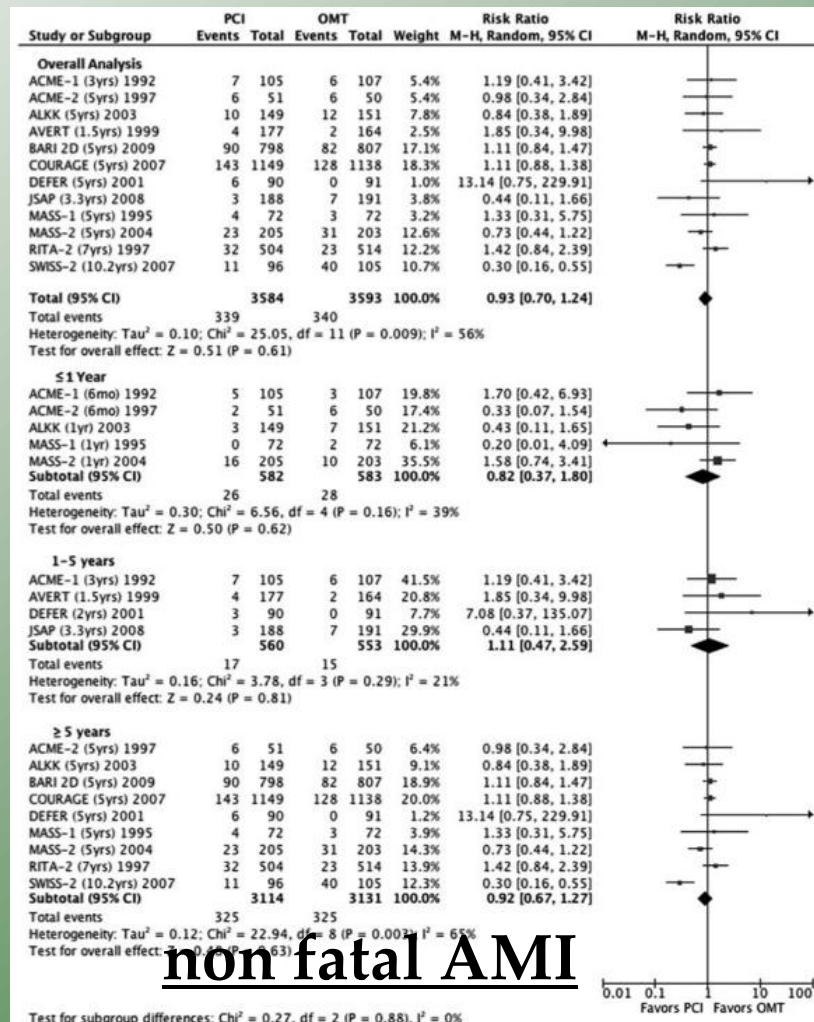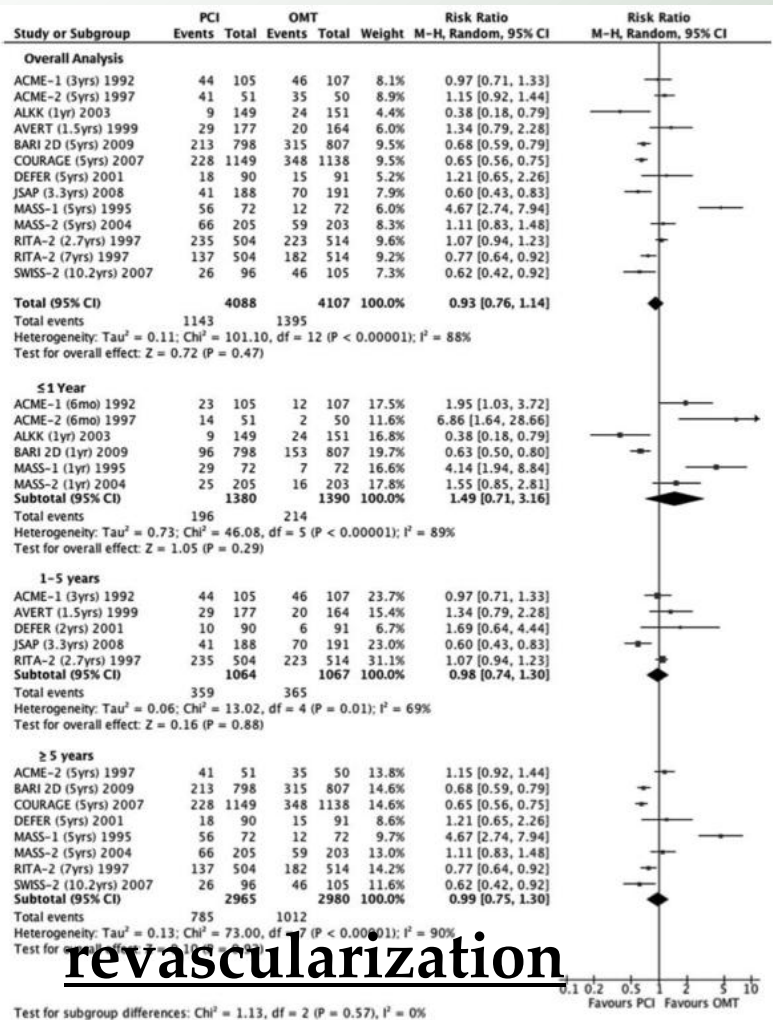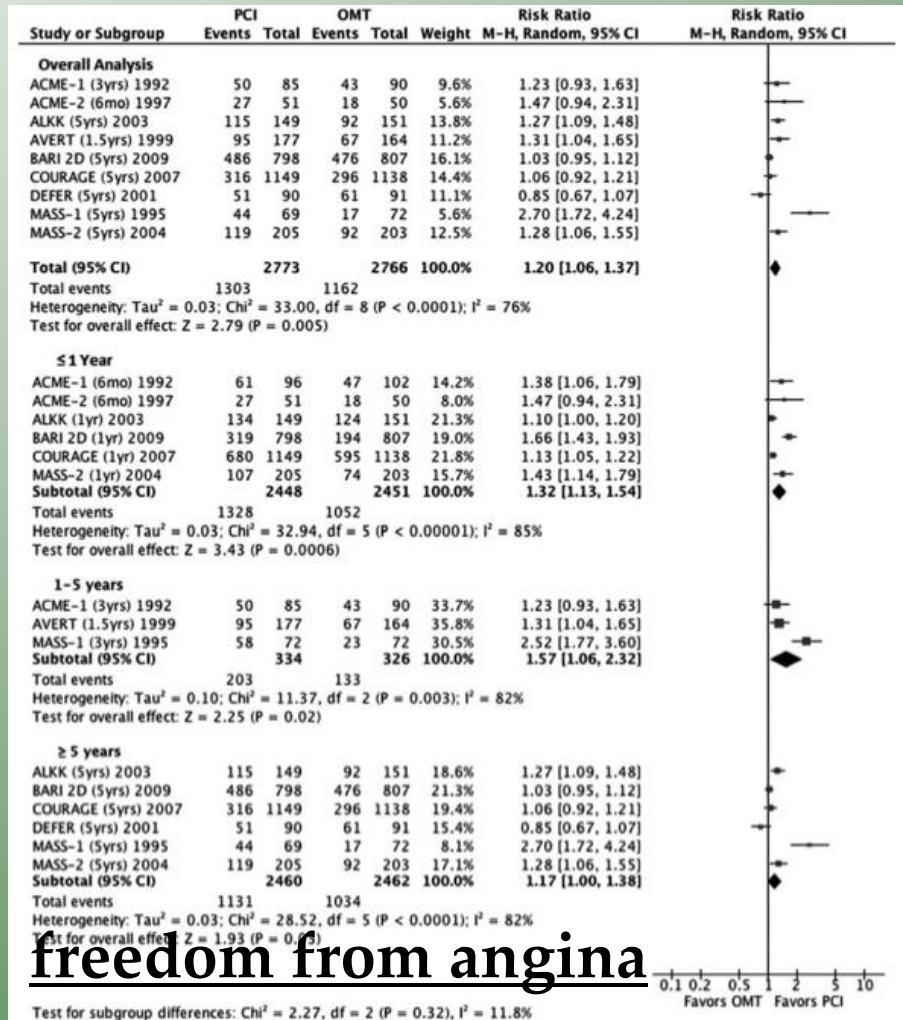| **≤1 Year**						
ACME-1 (6mo) 1992	23	105	12	107	17.5%	1.95 [1.03, 3.72]
ACME-2 (6mo) 1997	14	51	2	50	11.6%	6.86 [1.64, 28.66]
ALKK (1yr) 2003	9	149	24	151	16.8%	0.38 [0.18, 0.79]
BARI 2D (1yr) 2009	96	798	153	807	19.7%	0.63 [0.50, 0.80]
MASS-1 (1yr) 1995	29	72	7	72	16.6%	4.14 [1.94, 8.84]
MASS-2 (1yr) 2004	25	205	16	203	17.8%	1.55 [0.85, 2.81]
Subtotal (95% CI)		1380		1390	100.0%	1.49 [0.71, 3.16]
Total events	196		214			

Heterogeneity: Tau² = 0.73; Chi² = 46.08, df = 5 (P < 0.00001); I² = 89%
Test for overall effect: Z = 1.05 (P = 0.29)

1-5 years						
ACME-1 (3yrs) 1992	44	105	46	107	23.7%	0.97 [0.71, 1.33]
AVERT (1.5yrs) 1999	29	177	20	164	15.4%	1.34 [0.79, 2.28]
DEFER (2yrs) 2001	10	90	6	91	6.7%	1.69 [0.64, 4.44]
JSAP (3.3yrs) 2008	41	188	70	191	23.0%	0.60 [0.43, 0.83]
RITA-2 (2.7yrs) 1997	235	504	223	514	31.1%	1.07 [0.94, 1.23]
Subtotal (95% CI)		1064		1067	100.0%	0.98 [0.74, 1.30]
Total events	359		365			

Heterogeneity: Tau² = 0.06; Chi² = 13.02, df = 4 (P = 0.01); I² = 69%
Test for overall effect: Z = 0.16 (P = 0.88)

≥5 years						
ACME-2 (5yrs) 1997	41	51	35	50	13.8%	1.15 [0.92, 1.44]
BARI 2D (5yrs) 2009	213	798	315	807	14.6%	0.68 [0.59, 0.79]
COURAGE (5yrs) 2007	228	1149	348	1138	14.6%	0.65 [0.56, 0.75]
DEFER (5yrs) 2001	18	90	15	91	8.6%	1.21 [0.65, 2.26]
MASS-1 (5yrs) 1995	56	72	12	72	9.7%	4.67 [2.74, 7.94]
MASS-2 (5yrs) 2004	66	205	59	203	13.0%	1.11 [0.83, 1.48]
RITA-2 (7yrs) 1997	137	504	182	514	14.2%	0.77 [0.64, 0.92]
SWISS-2 (10.2yrs) 2007	26	96	46	105	11.6%	0.62 [0.42, 0.92]
Subtotal (95% CI)		2965		2980	100.0%	0.99 [0.75, 1.30]
Total events	785		1012			

Heterogeneity: Tau² = 0.13; Chi² = 73.00, df = 7 (P < 0.00001); I² = 90%

Test for subgroup differences: Chi² = 1.13, df = 2 (P = 0.57), I² = 0%

Favours PCI Favours OMT (0.1 0.2 0.5 1 2 5 10)

freedom from angina

Study or Subgroup	PCI Events	Total	OMT Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Overall Analysis						
ACME-1 (3yrs) 1992	50	85	43	90	9.6%	1.23 [0.93, 1.63]
ACME-2 (6mo) 1997	27	51	18	50	5.6%	1.47 [0.94, 2.31]
ALKK (5yrs) 2003	115	149	92	151	13.8%	1.27 [1.09, 1.48]
AVERT (1.5yrs) 1999	95	177	67	164	11.2%	1.31 [1.04, 1.65]
BARI 2D (5yrs) 2009	486	798	476	807	16.1%	1.03 [0.95, 1.12]
COURAGE (5yrs) 2007	316	1149	296	1138	14.4%	1.06 [0.92, 1.21]
DEFER (5yrs) 2001	51	90	61	91	11.1%	0.85 [0.67, 1.07]
MASS-1 (5yrs) 1995	44	69	17	72	5.6%	2.70 [1.72, 4.24]
MASS-2 (5yrs) 2004	119	205	92	203	12.5%	1.28 [1.06, 1.55]
Total (95% CI)		2773		2766	100.0%	1.20 [1.06, 1.37]
Total events	1303		1162			

Heterogeneity: Tau² = 0.03; Chi² = 33.00, df = 8 (P < 0.0001); I² = 76%
Test for overall effect: Z = 2.79 (P = 0.005)

≤1 Year						
ACME-1 (6mo) 1992	61	96	47	102	14.2%	1.38 [1.06, 1.79]
ACME-2 (6mo) 1997	27	51	18	50	8.0%	1.47 [0.94, 2.31]
ALKK (1yr) 2003	134	149	124	151	21.3%	1.10 [1.00, 1.20]
BARI 2D (1yr) 2009	319	798	194	807	19.0%	1.66 [1.43, 1.93]
COURAGE (1yr) 2007	680	1149	595	1138	21.8%	1.13 [1.05, 1.22]
MASS-2 (1yr) 2004	107	205	74	203	15.7%	1.43 [1.14, 1.79]
Subtotal (95% CI)		2448		2451	100.0%	1.32 [1.13, 1.54]
Total events	1328		1052			

Heterogeneity: Tau² = 0.03; Chi² = 32.94, df = 5 (P < 0.00001); I² = 85%
Test for overall effect: Z = 3.43 (P = 0.0006)

1-5 years						
ACME-1 (3yrs) 1992	50	85	43	90	33.7%	1.23 [0.93, 1.63]
AVERT (1.5yrs) 1999	95	177	67	164	35.8%	1.31 [1.04, 1.65]
MASS-1 (3yrs) 1995	58	72	23	72	30.5%	2.52 [1.77, 3.60]
Subtotal (95% CI)		334		326	100.0%	1.57 [1.06, 2.32]
Total events	203		133			

Heterogeneity: Tau² = 0.10; Chi² = 11.37, df = 2 (P = 0.003); I² = 82%
Test for overall effect: Z = 2.25 (P = 0.02)

≥5 years						
ALKK (5yrs) 2003	115	149	92	151	18.6%	1.27 [1.09, 1.48]
BARI 2D (5yrs) 2009	486	798	476	807	21.3%	1.03 [0.95, 1.12]
COURAGE (5yrs) 2007	316	1149	296	1138	19.4%	1.06 [0.92, 1.21]
DEFER (5yrs) 2001	51	90	61	91	15.4%	0.85 [0.67, 1.07]
MASS-1 (5yrs) 1995	44	69	17	72	8.1%	2.70 [1.72, 4.24]
MASS-2 (5yrs) 2004	119	205	92	203	17.1%	1.28 [1.06, 1.55]
Subtotal (95% CI)		2460		2462	100.0%	1.17 [1.00, 1.38]
Total events	1131		1034			

Heterogeneity: Tau² = 0.03; Chi² = 28.52, df = 5 (P < 0.0001); I² = 82%
Test for overall effect: Z = 1.93 (P = 0.05)

Test for subgroup differences: Chi² = 2.27, df = 2 (P = 0.32), I² = 11.8%

Favours OMT Favours PCI (0.1 0.2 0.5 1 2 5 10)

LESS IS MORE

Initial Coronary Stent Implantation With Medical Therapy vs Medical Therapy Alone for Stable Coronary Artery Disease

Meta-analysis of Randomized Controlled Trials

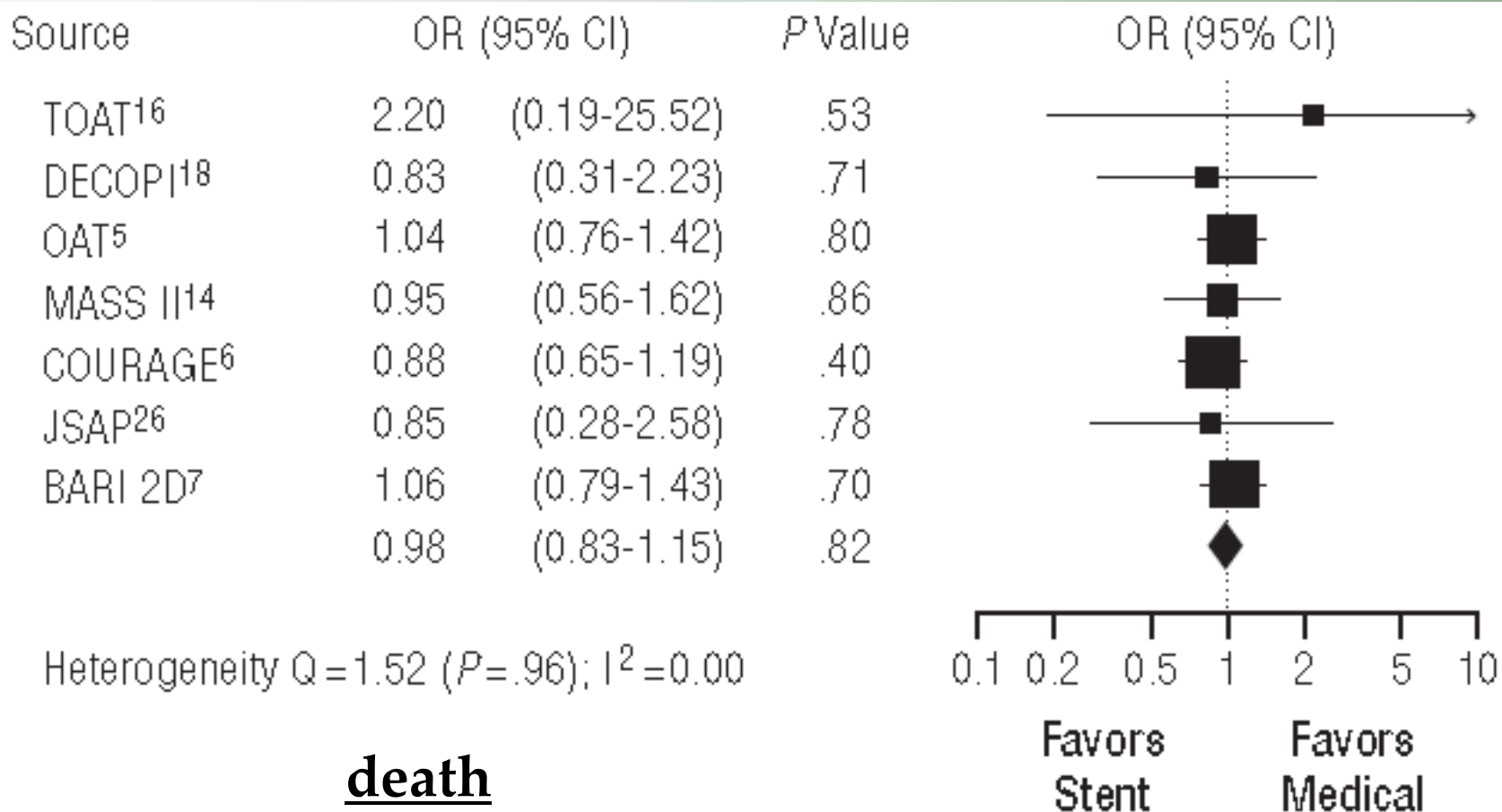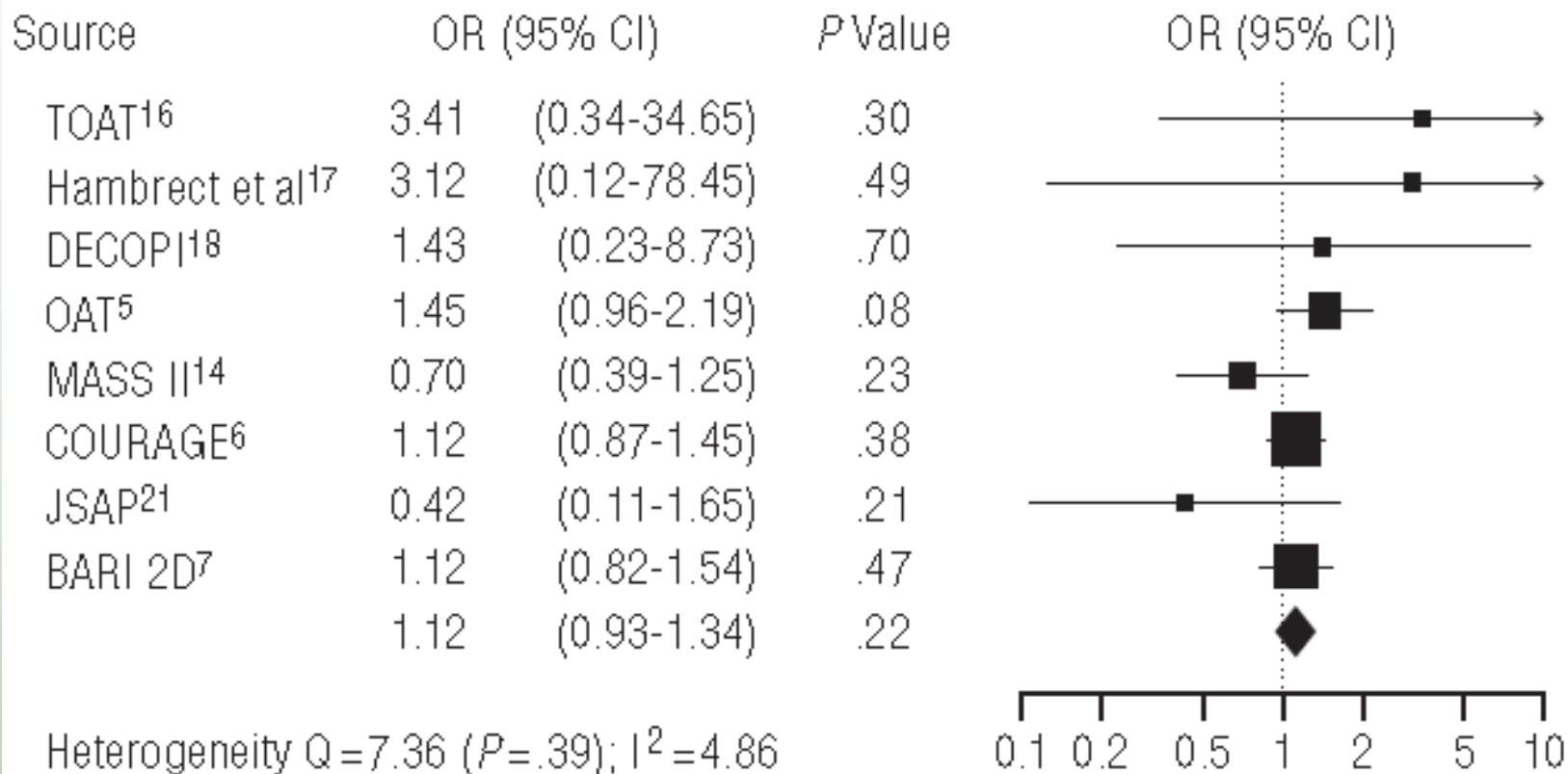Kathleen Stergiopoulos, MD, PhD; David L. Brown, MD

Conclusion: Initial stent implantation for stable CAD shows no evidence of benefit compared with initial medical therapy for prevention of death, nonfatal MI, unplanned revascularization, or angina.

Arch Intern Med. 2012;172(4):312-319

Initial Coronary Stent Implantation With Medical Therapy vs Medical Therapy Alone for Stable Coronary Artery Disease

Arch Intern Med. 2012;172(4):312-319

Source	OR (95% CI)		P Value	OR (95% CI)
TOAT[16]	2.20	(0.19-25.52)	.53	
DECOPI[18]	0.83	(0.31-2.23)	.71	
OAT[5]	1.04	(0.76-1.42)	.80	
MASS II[14]	0.95	(0.56-1.62)	.86	
COURAGE[6]	0.88	(0.65-1.19)	.40	
JSAP[26]	0.85	(0.28-2.58)	.78	
BARI 2D[7]	1.06	(0.79-1.43)	.70	
	0.98	(0.83-1.15)	.82	

Heterogeneity Q = 1.52 (P = .96); I^2 = 0.00

0.1 0.2 0.5 1 2 5 10

Favors Stent — Favors Medical

death

Initial Coronary Stent Implantation With Medical Therapy vs Medical Therapy Alone for Stable Coronary Artery Disease

Arch Intern Med. 2012;172(4):312-319

Source	OR	(95% CI)	P Value
TOAT[16]	3.41	(0.34-34.65)	.30
Hambrect et al[17]	3.12	(0.12-78.45)	.49
DECOPI[18]	1.43	(0.23-8.73)	.70
OAT[5]	1.45	(0.96-2.19)	.08
MASS II[14]	0.70	(0.39-1.25)	.23
COURAGE[6]	1.12	(0.87-1.45)	.38
JSAP[21]	0.42	(0.11-1.65)	.21
BARI 2D[7]	1.12	(0.82-1.54)	.47
	1.12	(0.93-1.34)	.22

Heterogeneity Q =7.36 (P=.39); I^2 =4.86

OR (95% CI)

0.1 0.2 0.5 1 2 5 10

Favors Stent   Favors Medical

non fatal AMI

Initial Coronary Stent Implantation With Medical Therapy vs Medical Therapy Alone for Stable Coronary Artery Disease *Arch Intern Med. 2012;172(4):312-319*

Source	OR (95% CI)		P Value
TOAT[16]	0.69	(0.11-4.42)	.69
Hambrect et al[17]	8.14	(0.96-68.81)	.05
DECOPI[18]	0.66	(0.26-1.72)	.40
OAT[5]	1.20	(0.68-2.13)	.53
MASS II[14]	0.60	(0.40-0.89)	.01
COURAGE[6]	0.91	(0.67-1.24)	.56
JSAP[21]	0.46	(0.29-0.72)	<.001
BARI 2D[7]	0.92	(0.75-1.12)	.39
	0.79	(0.60-1.05)	.10

Heterogeneity Q=16.8 (*P*=.02); I^2=58.2

Favors Stent — Favors Medical

persistent angina at F.U.
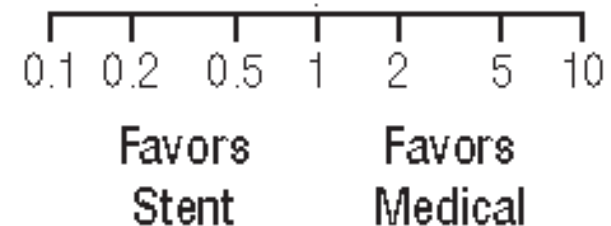
Use of Drug-Eluting Stents as a Function of Predicted Benefit

Clinical and Economic Implications of Current Practice

Amit P. Amin, MD, MSc; John A. Spertus, MD, MPH; David J. Cohen, MD, MSc; Adnan Chhatriwalla, MD;
Kevin F. Kennedy, MS; Katherine Vilain, MS; Adam C. Salisbury, MD, MSc; Lakshmi Venkitachalam, PhD;
Sue Min Lai, PhD; Laura Mauri, MD; Sharon-Lise T. Normand, PhD; John S. Rumsfeld, MD, PhD;
John C. Messenger, MD; Robert W. Yeh, MD, MSc

Conclusions: Use of DES in the United States varies widely among physicians, with only a modest correlation to patients' risk of restenosis. Less DES use among patients with low risk of restenosis has the potential for significant cost savings for the US health care system while minimally increasing restenosis events.

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

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2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease: Executive Summary: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons

Table 7. Revascularization to Improve Symptoms With Significant Anatomic (≥50% Left Main or ≥70% Non-Left Main CAD) or Physiological (FFR ≤0.80) Coronary Artery Stenoses

Clinical Setting	COR	LOE
≥1 significant stenoses amenable to revascularization and unacceptable angina despite GDMT	1—CABG	A
	1—PCI	
≥1 significant stenoses and unacceptable angina in whom GDMT cannot be implemented because of medication contraindications, adverse effects, or patient preferences	IIa—CABG	C
	IIa—PCI	C
Previous CABG with ≥1 significant stenoses associated with ischemia and unacceptable angina despite GDMT	IIa—PCI	C

Annals of Internal Medicine

ARTICLE
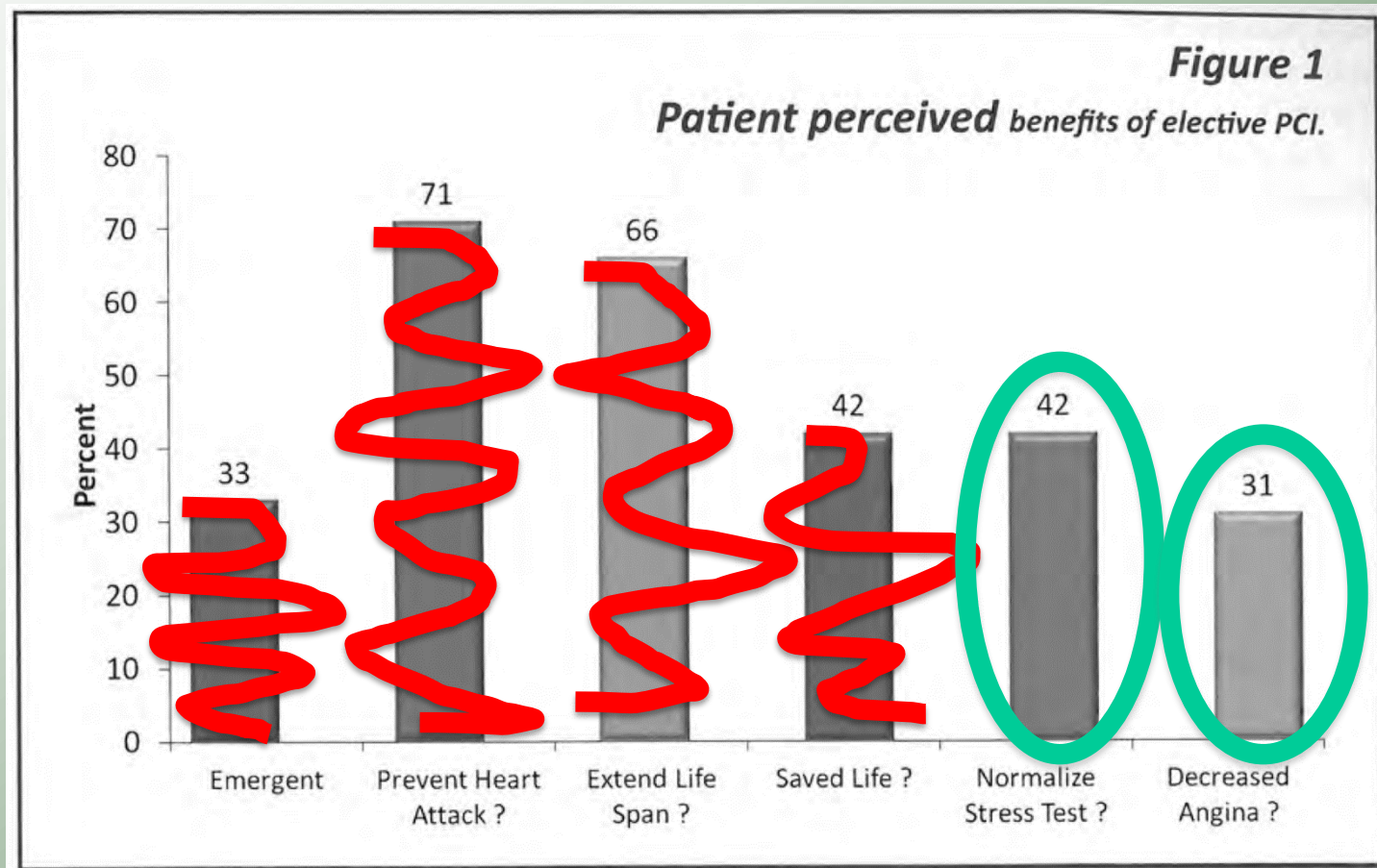
Patients' and Cardiologists' Perceptions of the Benefits of Percutaneous Coronary Intervention for Stable Coronary Disease

Michael B. Rothberg, MD, MPH; Senthil K. Sivalingam, MD; Javed Ashraf, MD, MPH; Paul Visintainer, PhD; John Joelson, MD; Reva Kleppel, MSW, MPH; Neelima Vallurupalli, MD; and Marc J. Schweiger, MD
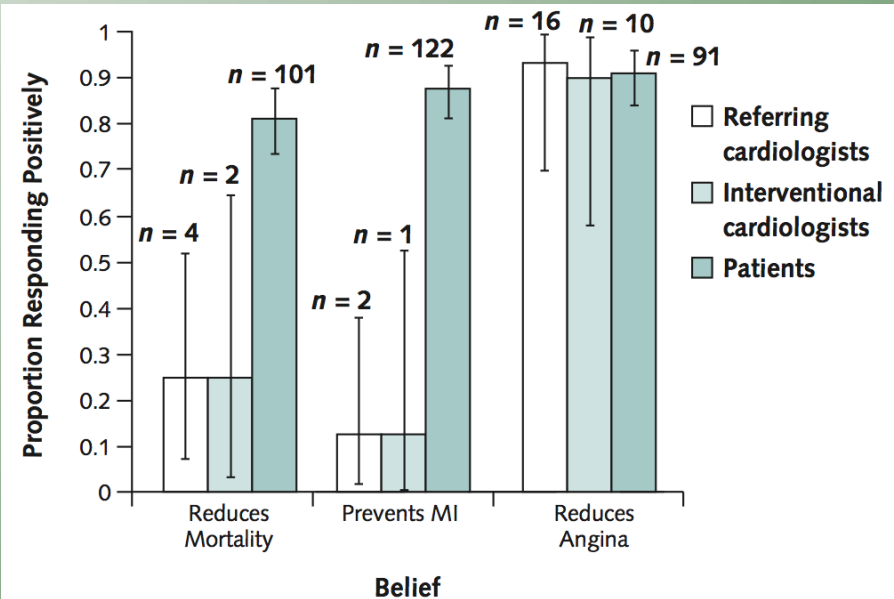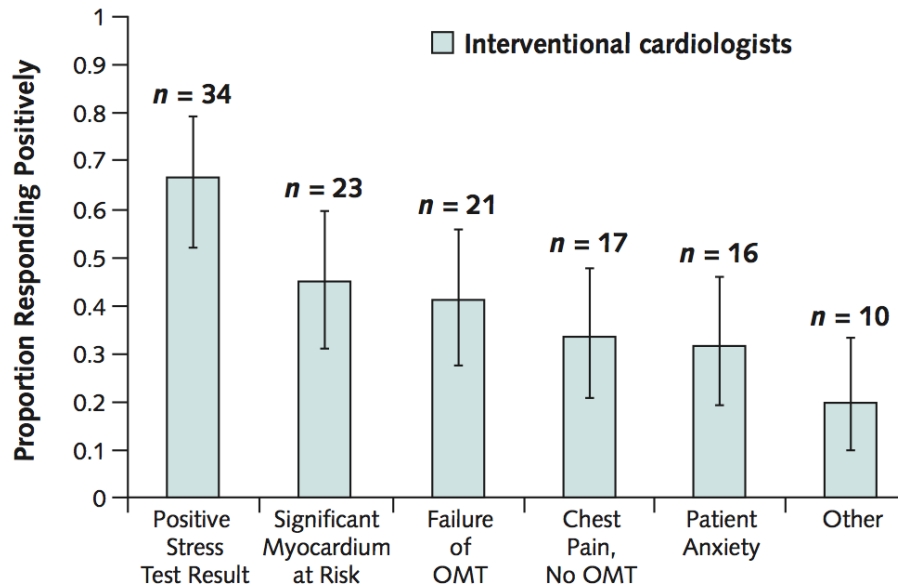
After publication of COURAGE, many cardiologists no longer believe that PCI will prevent MI in stable coronary disease but continue to perform elective PCI for other reasons, most often after an abnormal stress test result. In contrast, most patients undergoing the procedure still believe that PCI will prevent infarction or death. Further efforts should be directed toward improving communication of medical evidence to help patients make informed decisions about this common procedure.

"Sweeping, honest and brave... You will finish this arresting book reluctantly, with a new appreciation of what American medicine could be."
—HARRIET A .WASHINGTON, author of Deadly Monopolies: The Shocking Corporate Takeover of Life Itself and the Consequences for Your Health and Our Medical Future

HOW WE DO HARM

A DOCTOR BREAKS RANKS

ABOUT BEING SICK

IN AMERICA

OTIS WEBB BRAWLEY, M.D.

with Paul Goldberg

"distingui:
- quello che sai
- quello che non sai
- e quello che credi
e spiega bene al paziente la differenza"

Predicting prognosis in stable angina—results from the Euro heart survey of stable angina: prospective observational study

Caroline A Daly, Bianca De Stavola, Jose L Lopez Sendon, Luigi Tavazzi, Eric Boersma, Felicity Clemens, Nicholas Danchin, Francois Delahaye, Anselm Gitt, Desmond Julian, David Mulcahy, Witold Ruzyllo, Kristian Thygesen, Freek Verheugt, Kim M Fox, on behalf of the Euro Heart Survey Investigators

Table 3 Major clinical events occurring during follow-up in the overall population and in patients with confirmed coronary disease

End point	Stable angina (n=3031)		Stable angina with confirmed CAD (n=994)	
	No of events	Event rate (95% CI) per 100 patient years	No of events	Event rate (95% CI) per 100 patient years
Death*	50	1.5 (1.1 to 1.9)	19	1.8 (1.1 to 2.8)
Non-cardiovascular death	14 (28%)		2 (11%)	
Non-fatal myocardial infarction	48	1.4 (1.1 to 1.9)	34	3.2 (2.3 to 4.4)
Death and non-fatal myocardial infarction	93	2.3 (1.9 to 2.8)	50	3.9 (2.9 to 5.1)
Cerebrovascular event	34	1.1 (0.8 to 1.5)	15	1.6 (1.0 to 2.6)
Heart failure	49	1.5 (1.1 to 2.0)	20	2.1 (1.3 to 3.2)
Unstable angina	164	5.2 (4.4 to 6.0)	114	12.1 (10.1 to 14.6)
All cardiovascular events†	328	10.3 (9.3 to 11.5)	207	21.9 (19.1 to 25.2)

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

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Percutaneous Coronary Angioplasty Compared With Exercise Training in Patients With Stable Coronary Artery Disease
A Randomized Trial

Rainer Hambrecht, MD; Claudia Walther, MD; Sven Möbius-Winkler, MD; Stephan Gielen, MD; Axel Linke, MD; Katrin Conradi, MD; Sandra Erbs, MD; Regine Kluge, MD; Kai Kendziorra, MD; Osama Sabri, MD; Peter Sick, MD; Gerhard Schuler, MD

Background—Regular exercise in patients with stable coronary artery disease has been shown to improve myocardial perfusion and to retard disease progression. We therefore conducted a randomized study to compare the effects of exercise training versus standard percutaneous coronary intervention (PCI) with stenting on clinical symptoms, angina-free exercise capacity, myocardial perfusion, cost-effectiveness, and frequency of a combined clinical end point (death of cardiac cause, stroke, CABG, angioplasty, acute myocardial infarction, and worsening angina with objective evidence resulting in hospitalization).

Methods and Results—A total of 101 male patients aged ≤ 70 years were recruited after routine coronary angiography and randomized to 12 months of exercise training (20 minutes of bicycle ergometry per day) or to PCI. Cost efficiency was calculated as the average expense (in US dollars) needed to improve the Canadian Cardiovascular Society class by 1 class. Exercise training was associated with a higher event-free survival (88% versus 70% in the PCI group, $P=0.023$) and increased maximal oxygen uptake ($+16\%$, from 22.7 ± 0.7 to 26.2 ± 0.8 mL O_2/kg, $P<0.001$ versus baseline, $P<0.001$ versus PCI group after 12 months). To gain 1 Canadian Cardiovascular Society class, $6956 was spent in the PCI group versus $3429 in the training group ($P<0.001$).

Conclusions—Compared with PCI, a 12-month program of regular physical exercise in selected patients with stable coronary artery disease resulted in superior event-free survival and exercise capacity at lower costs, notably owing to reduced rehospitalizations and repeat revascularizations. (*Circulation.* 2004;109:1371-1378.)
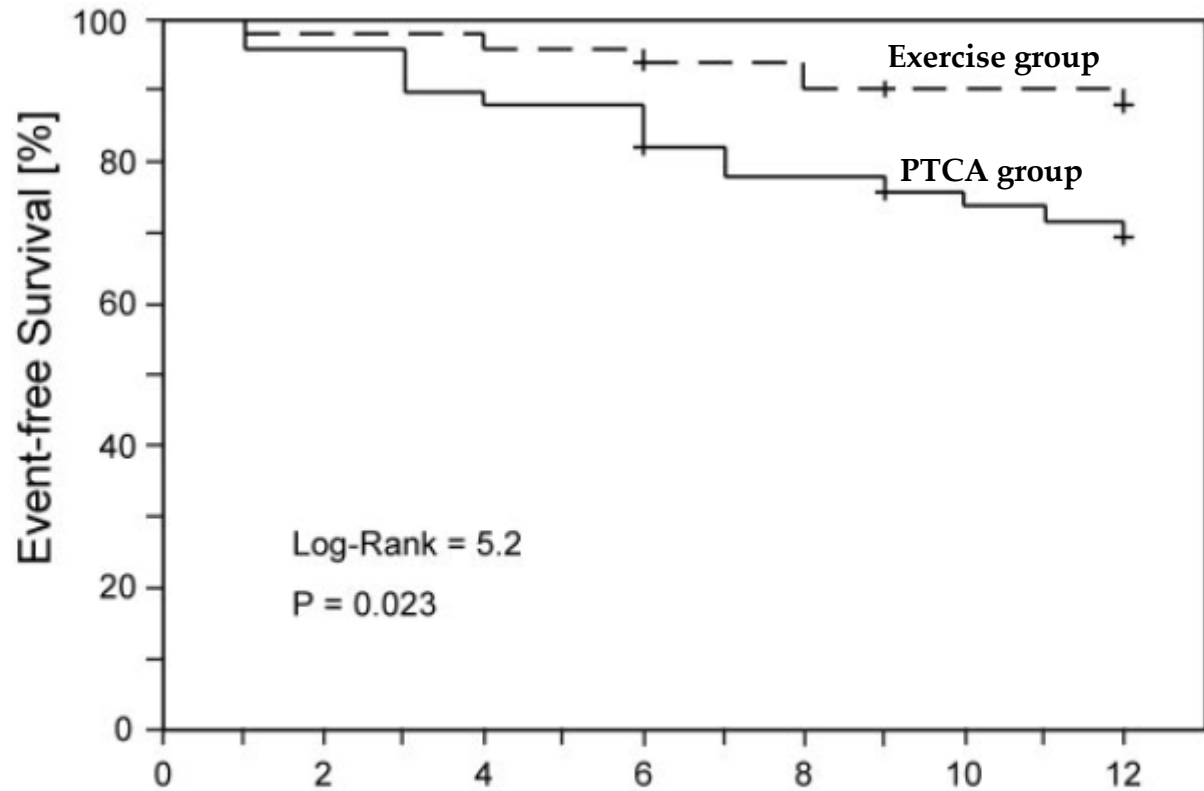
Hambrecht R et al. Circulation 2004; 109: 1371-8

AGGRESSIVE LIPID-LOWERING THERAPY COMPARED WITH ANGIOPLASTY IN STABLE CORONARY ARTERY DISEASE

BERTRAM PITT, M.D., DAVID WATERS, M.D., WILLIAM VIRGIL BROWN, M.D., AD J. VAN BOVEN, M.D., PH.D., LEONARD SCHWARTZ, M.D., LAWRENCE M. TITLE, M.D., DANIEL EISENBERG, M.D., LINDA SHURZINSKE, M.S., AND LISA S. MCCORMICK, PHARM.D., FOR THE ATORVASTATIN VERSUS REVASCULARIZATION TREATMENT INVESTIGATORS*

Conclusions In low-risk patients with stable coronary artery disease, aggressive lipid-lowering therapy is at least as effective as angioplasty and usual care in reducing the incidence of ischemic events. (N Engl J Med 1999;341:70-6.)
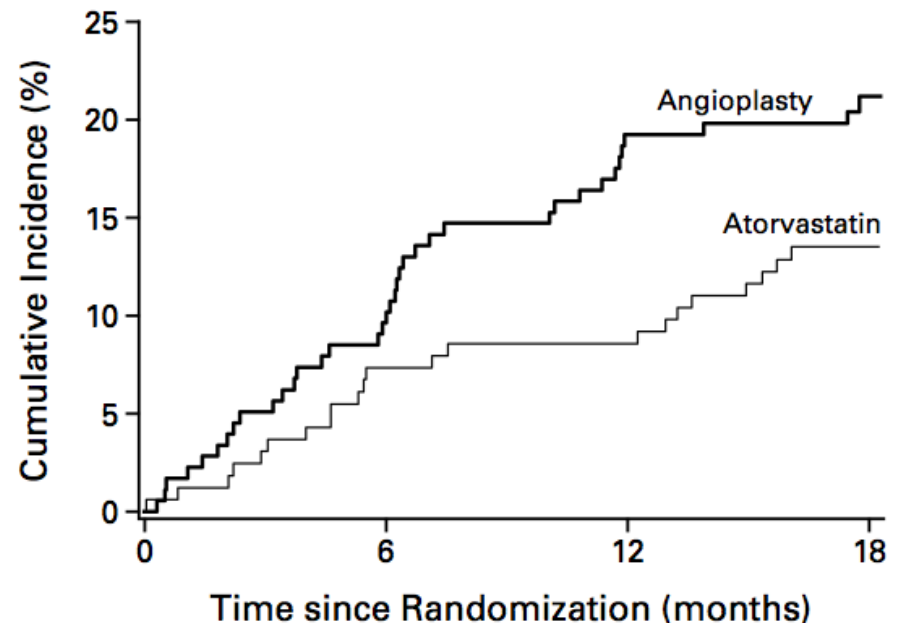
Figure 2. Cumulative Incidence of First Ischemic Events.

The time to an ischemic event was significantly longer in the atorvastatin group (P=0.03), and the risk reduction was 36 percent (95 percent confidence interval, 5 to 67 percent).

AGGRESSIVE LIPID-LOWERING THERAPY COMPARED WITH ANGIOPLASTY IN STABLE CORONARY ARTERY DISEASE

BERTRAM PITT, M.D., DAVID WATERS, M.D., WILLIAM VIRGIL BROWN, M.D., AD J. VAN BOVEN, M.D., PH.D., LEONARD SCHWARTZ, M.D., LAWRENCE M. TITLE, M.D., DANIEL EISENBERG, M.D., LINDA SHURZINSKE, M.S., AND LISA S. McCORMICK, PHARM.D., FOR THE ATORVASTATIN VERSUS REVASCULARIZATION TREATMENT INVESTIGATORS*

Hotline Editorial

Is a mechanical or a metabolic approach superior in the treatment of coronary disease? Results of the Atorvastatin Versus Revascularization (AVERT) Trial

evidence supporting aggressive cholesterol lowering in such patients is incontrovertible. As cardiologists, our attitude should be a lot more 'metabolic' and a lot less 'mechanical'.

D. WATERS
*Cardiology Division,
San Francisco General Hospital,
San Francisco, California, U.S.A.*

Figure 2. Kaplan–Meier Survival Curves.

In Panel A, the estimated 4.6-year rate of the composite primary outcome of death from any cause and nonfatal myocardial infarction was 19.0% in the PCI group and 18.5% in the medical-therapy group. In Panel B, the estimated 4.6-year rate of death from any cause was 7.6% in the PCI group and 8.3% in the medical-therapy group. In Panel C, the estimated 4.6-year rate of hospitalization for acute coronary syndrome (ACS) was 12.4% in the PCI group and 11.8% in the medical-therapy group. In Panel D, the estimated 4.6-year rate of acute myocardial infarction was 13.2% in the PCI group and 12.3% in the medical-therapy group.

Ma cosa vuol dire OMT?

1)terapia antiaggregante con ASA o clopidogrel (entrambi per il gruppo PCI)

2)metoprololo, amlodipina e ISMN + lisinopril o losartan come prevenzione secondaria

3)simvastatina da sola o con ezetimibe + (eventualmente) niacina e/o fibrati, in modo da ridurre l'LDL da 60 a 85 mg/dl, aumentare l'HDL sopra i 40 mg/dl e ridurre i trigliceridi sotto i 150 mg/dl

4)esercizio fisico, dieta, cessazione del fumo

Follow-up a 5 anni:

70% dei soggetti con LDL < 85 mg/dl

65% con pressione sistolica < 130 mmHg

94% con pressione diastolica < 85 mmHg

45% dei diabetici con emoglobina glicata ≤ 7 %

elevata aderenza a dieta, esercizio fisico regolare e abolizione del fumo

Comparative-Effectiveness of Revascularization Versus Routine Medical Therapy for Stable Ischemic Heart Disease: A Population-Based Study.

Wijeysundera HC; Bennell MC; Qiu F; Ko DT; Tu JV; Wijeysundera DN; Austin PC,
Journal Of General Internal Medicine [J Gen Intern Med]

Background: Randomized studies have shown optimal medical therapy to be as efficacious as revascularization in stable ischemic heart disease (IHD). It is not known if these efficacy results are reflected by real-world effectiveness. Objective: To evaluate the comparative effectiveness of routine medical therapy versus revascularization with percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) in stable IHD.

We identified 39,131 stable IHD patients, of whom 15,139 were treated medically, and 23,992 were revascularized (PCI = 15,604; CABG = 8,388). Mean follow-up was 2.5 years. Revascularization was associated with fewer deaths, MIs (HR 0.78; 95 and repeat PCI/CABG (HR 0.59; 95 % CI 0.50-0.70; than medical therapy. In the propensity-matched analysis of 12,362 well-matched pairs of revascularized and medical therapy patients, fewer deaths (8.6 % vs 12.7 %=), Mis (11.7 % vs 14.4%) and repeat PCI/CABG (17.4 % vs 24.1 %) occurred in revascularized patients, over the 4.1 years of follow-up. The revascularization patients had higher uptake of clopidogrel, β-blockers and statins in the 1-year post-angiogram.

Conclusions: Stable IHD patients treated with revascularization had improved risk-adjusted outcomes in clinical practice, potentially due to under-treatment of medical therapy patients.

Long-term compliance with beta-blockers, angiotensin-converting enzyme inhibitors, and statins after acute myocardial infarction

Gunnar H. Gislason[1,2]*, Jeppe N. Rasmussen[2], Steen Z. Abildstrøm[2,3], Niels Gadsbøll[4], Pernille Buch[1,2], Jens Friberg[1], Søren Rasmussen[2], Lars Køber[5], Steen Stender[6], Mette Madsen[2], and Christian Torp-Pedersen[1]
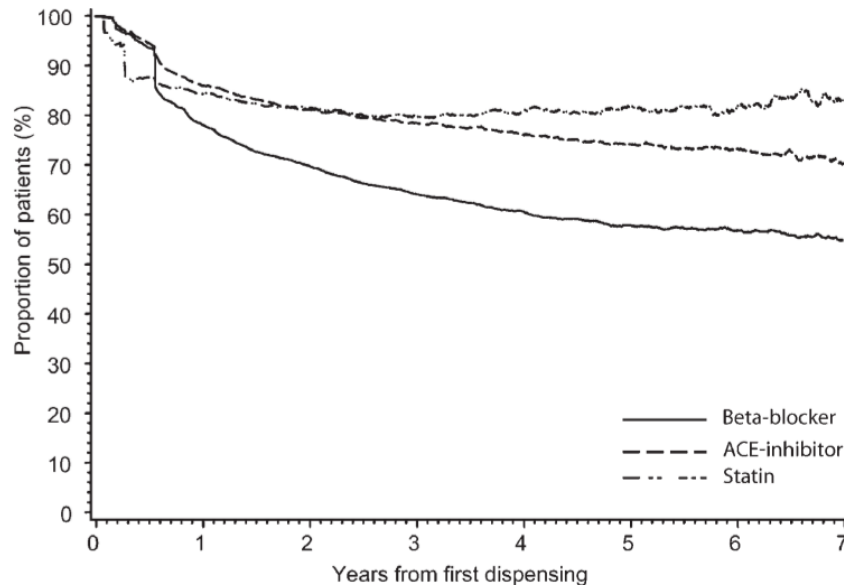
Number of patients under observation (alive)

Beta-blockers	32 259	25 253	19 275	14 478	10 684	7 275	4 449	2 038
ACE-inhibitors	16 068	11 778	8 695	6 469	4 752	3 238	1 973	943
Statins	16 433	13 493	9 566	6 651	4 260	2 500	1 360	503

Figure 2 Persistence with therapy in patients who claimed at least one prescription early after AMI. Each point represents number of patients with available medication divided by the number of patients alive at that time.

β-Blocker use following myocardial infarction: Low prevalence of evidence-based dosing

Jeffrey J. Goldberger, MD,[a] Robert O. Bonow, MD,[a] Michael Cuffe, MD,[b] Alan Dyer, PhD,[a] Yves Rosenberg, MD,[c] Robert O'Rourke, MD,[d] Prediman K. Shah, MD,[e] and Sidney C. Smith, Jr, MD[f] for the PACE-MI Investigators
Chicago, IL; Durham and Chapel Hill, NC; Bethesda, MD; San Antonio, TX; and Los Angeles, CA

Conclusions Underdosing of β-blockers is highly prevalent among patients post-MI. This represents an important opportunity in quality improvement for the care of patients who have suffered an MI. (Am Heart J 2010;160:435-442.e1.)
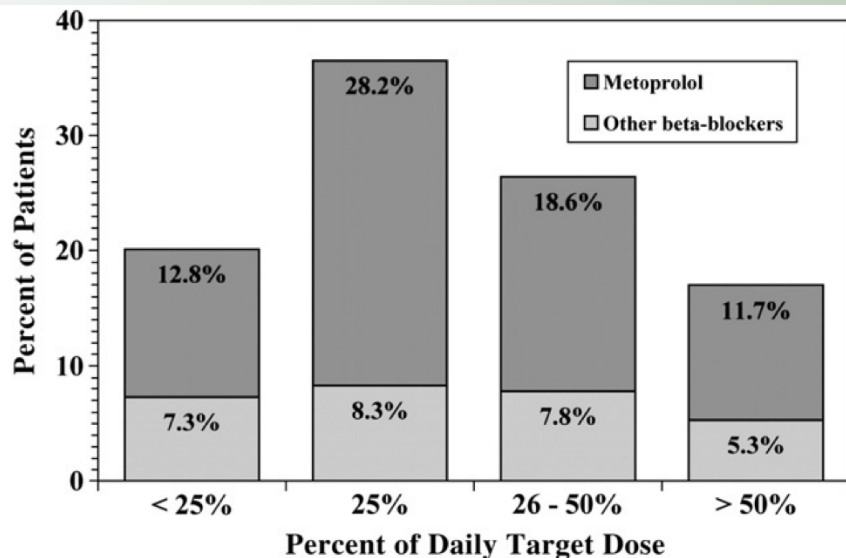
The graph shows the percentage of patients taking various doses of β-blockers at discharge. Doses are shown as the proportion or percentage of daily target dose: <25%, n = 347; 25%, n = 629; 26% to 50%, n = 454; >50%, n = 293. Each bar is subdivided to indicate metoprolol dosing and dosing of other β-blockers.
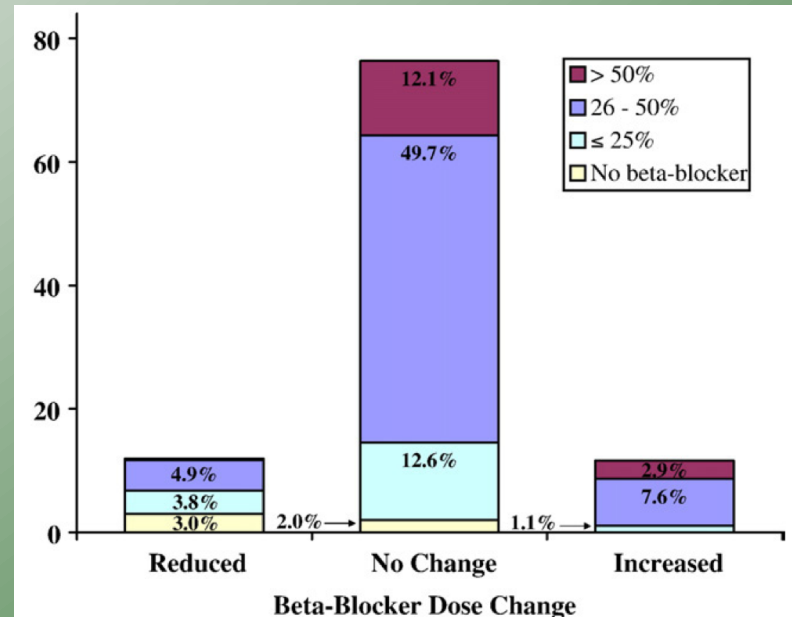
The graph shows the distribution of β-blocker dosing (shown as percentage of daily target dose; see legend) at 3 weeks stratified by whether the dose was reduced (n = 171), remained the same (n = 1095), or increased (n = 167) since hospital discharge.

INVITED COMMENTARY

Mounting Evidence for Lack of PCI Benefit in Stable Ischemic Heart Disease

What More Will It Take to Turn the Tide of Treatment?

Informed Strategies for Treating Coronary Disease

More than 1 million stents are implanted annually in the United States to treat coronary disease, in the continuing hope that they are more effective than medical therapy in preventing heart attacks and prolonging life, despite abundant evidence to the contrary. Despite the highly publicized COURAGE findings, fewer than half of Americans with stable CAD who undergo stent placement have received medical therapy first. This latest meta-analysis, looking at recent PCI trials, again finds no benefit of PCI compared with medical therapy. Increasing use of American College of Cardiology Appropriate Use Criteria and realigning incentives for evidence-based approach will help improve quality of care. A "PCI first" strategy for patients with stable CAD gets a *Less Is More* designation because there is no known benefit and there are definite harms.

Rita F. Redberg, MD, MSc
Editor

BMJ

Editor's Choice

How to avoid unnecessary interventions

BMJ 2009; 339 doi: http://dx.doi.org/10.1136/bmj.b3304 (Published 13 August 2009)
Cite this as: BMJ 2009;339:b3304

Fiona Godlee, editor

"Avoiding unnecessary intervention makes sense for patients because almost all treatments and tests have the potential to do harm. It also makes sense for health care, especially in times of financial constraint"

UNNECESSARY INTERVENTIONS

If less is more, how much is zero?

If we need less medicine,[1] how much less? Given the accumulating evidence that revascularisation may not add anything to patients' changing their lifestyle, how much angioplasty or coronary artery bypass grafting should be performed? The peer reviewed evidence overwhelmingly suggests that in most stable cases the answer is none.

Why has primary health care failed? Why has Health for All by 2000 been lost to oblivion? Why is prevention a far cry? Why has caring for

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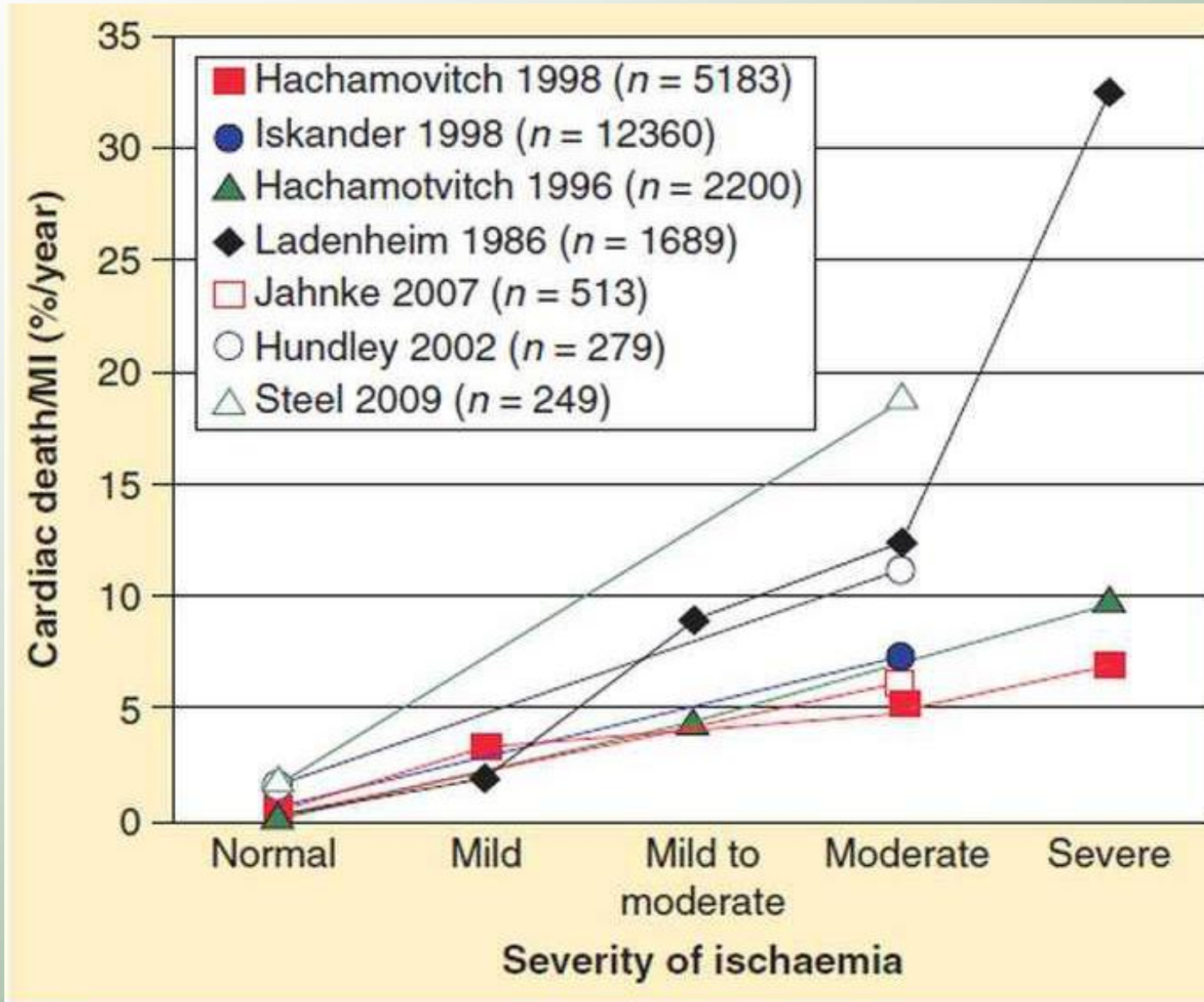
American Heart Association®

Optimal Medical Therapy With or Without Percutaneous Coronary Intervention to Reduce Ischemic Burden: Results From the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) Trial Nuclear Substudy

Leslee J. Shaw, Daniel S. Berman, David J. Maron, G. B. John Mancini, Sean W. Hayes, Pamela M. Hartigan, William S. Weintraub, Robert A. O'Rourke, Marcin Dada, John A. Spertus, Bernard R. Chaitman, John Friedman, Piotr Slomka, Gary V. Heller, Guido Germano, Gilbert Gosselin, Peter Berger, William J. Kostuk, Ronald G. Schwartz, Merill Knudtson, Emir Veledar, Eric R. Bates, Benjamin McCallister, Koon K. Teo and William E. Boden

Conclusions—In COURAGE patients who underwent serial MPS, adding PCI to OMT resulted in greater reduction in ischemia compared with OMT alone. Our findings suggest a treatment target of $\geq 5\%$ ischemia reduction with OMT with or without coronary revascularization. (*Circulation.* 2008;117:1283-1291.)

Optimal Medical Therapy With or Without Percutaneous Coronary Intervention to Reduce Ischemic Burden: Results From the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) Trial Nuclear Substudy
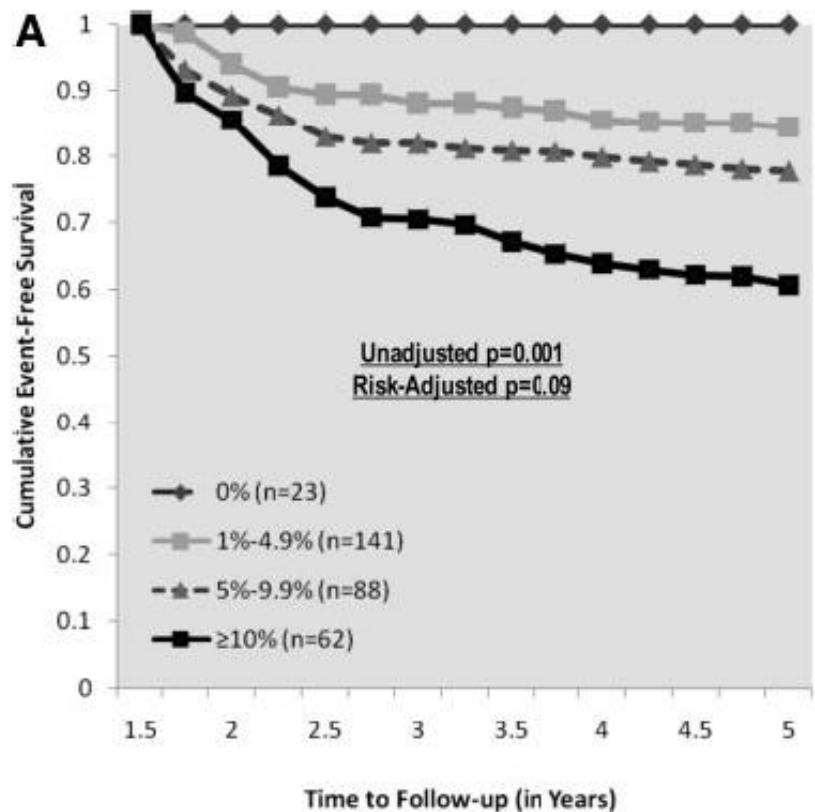
Conclusions

From this substudy of selected COURAGE patients who underwent serial MPS imaging, adding PCI to OMT resulted in greater reduction in inducible ischemia compared with OMT alone, and the benefit was greatest among patients with more severe baseline ischemia. Our exploratory analysis of clinical outcomes revealed that, regardless of treatment assignment, the magnitude of residual ischemia on follow-up MPS was proportional to the risk for death or MI, and a $\geq 5\%$ reduction in ischemia was associated with a significant reduction in risk. These observations should inform the design of future randomized controlled trials to test the utility of reducing myocardial ischemia to $\leq 5\%$ in patients with moderate to severe pretreatment ischemia to optimize prognosis.

Frequency of Stress Testing to Document Ischemia Prior to Elective Percutaneous Coronary Intervention

Grace A. Lin, MD, MAS

R. Adams Dudley, MD, MBA

F. L. Lucas, PhD

David J. Malenka, MD

Eric Vittinghoff, PhD

Rita F. Redberg, MD, MSc

Conclusion The majority of Medicare patients with stable coronary artery disease do not have documentation of ischemia by noninvasive testing prior to elective PCI.

Frequency of Stress Testing to Document Ischemia Prior to Elective Percutaneous Coronary Intervention

Grace A. Lin, MD, MAS
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Conclusion The majority of Medicare patients with stable coronary artery disease do not have documentation of ischemia by noninvasive testing prior to elective PCI.

Figure 3. Factors Predicting Receipt of Stress Test Prior to Elective Percutaneous Coronary Intervention (PCI)
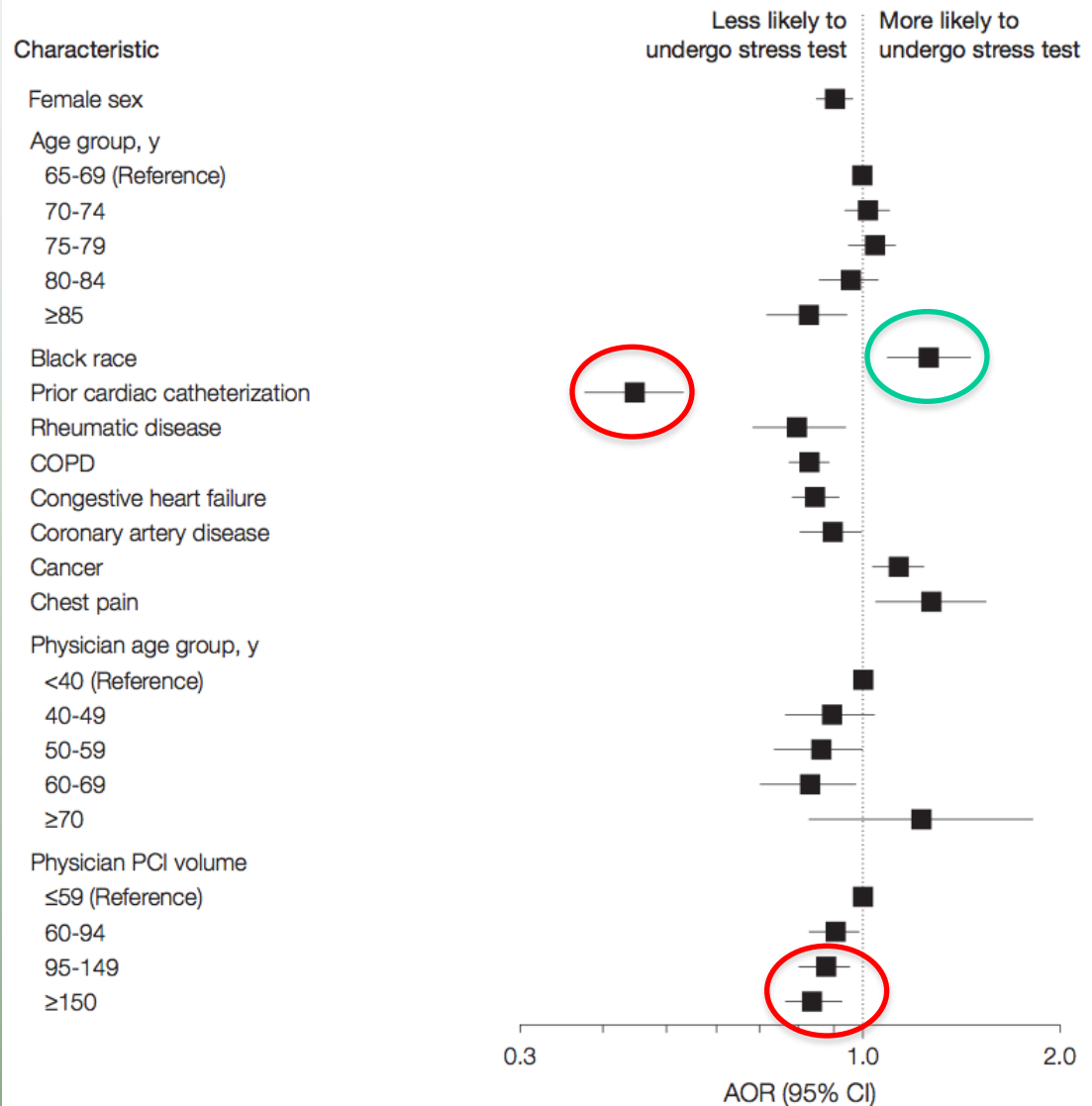
Appropriateness of Percutaneous Coronary Intervention
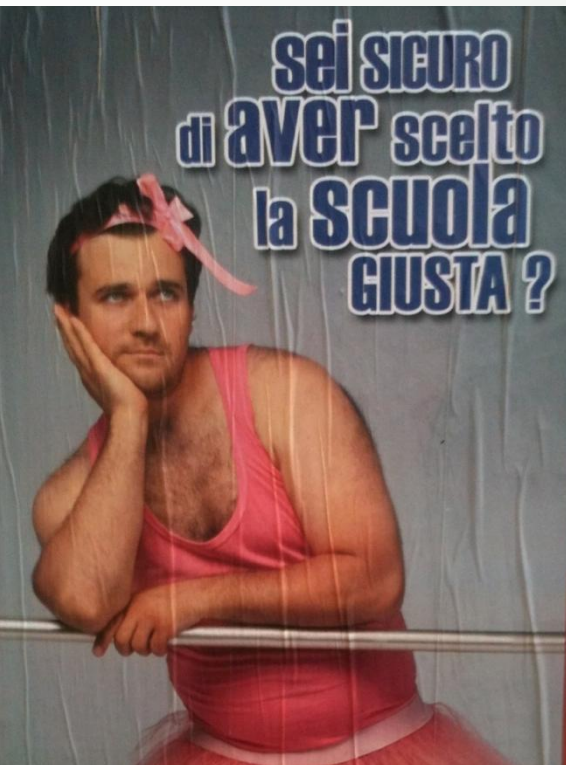
Paul S. Chan, MD, MSc

Conclusions In this large contemporary US cohort, nearly all acute PCIs were classified as appropriate. For nonacute indications, however, 12% were classified as inappropriate, with substantial variation across hospitals.

JAMA. 2011;306(1):53-61   www.jama.com
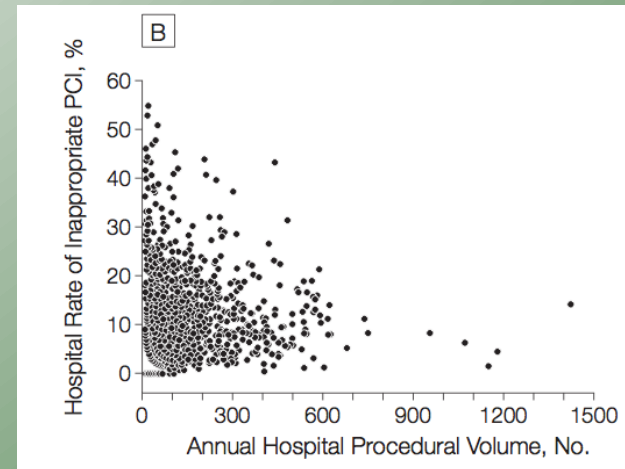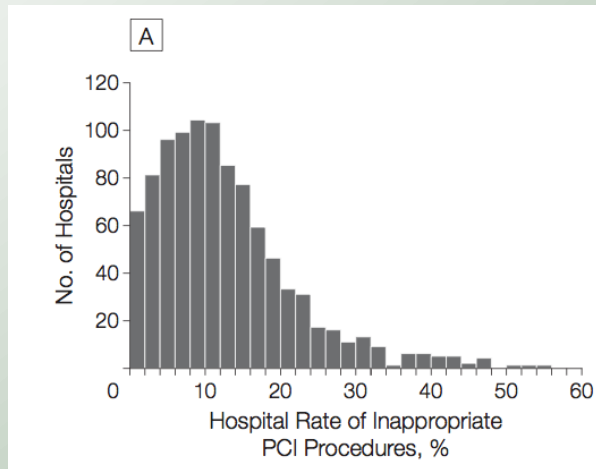
For nonacute indications, 72 911 PCIs (50.4%) were classified as appropriate, 54 988 (38.0%) as uncertain, and 16 838 (11.6%) as inappropriate. The majority of inappropriate PCIs for nonacute indications were performed in patients with no angina (53.8%), low-risk ischemia on noninvasive stress testing (71.6%), or suboptimal (≤1 medication) antianginal therapy (95.8%).