

Management of Stable CAD: Primary & Secondary Prevention

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Outline

A. Management of CAD

- Definition
- Medical therapy
- Indication for & type of revascularisation
- Tests and Interventions (refer to other lectures)

B. Primary and Secondary Prevention

- Definitions & Rationale
- Estimation of CAD Risks
- Other Risk Markers
- Risk Factor Interventions

Management of Stable Coronary Artery Disease

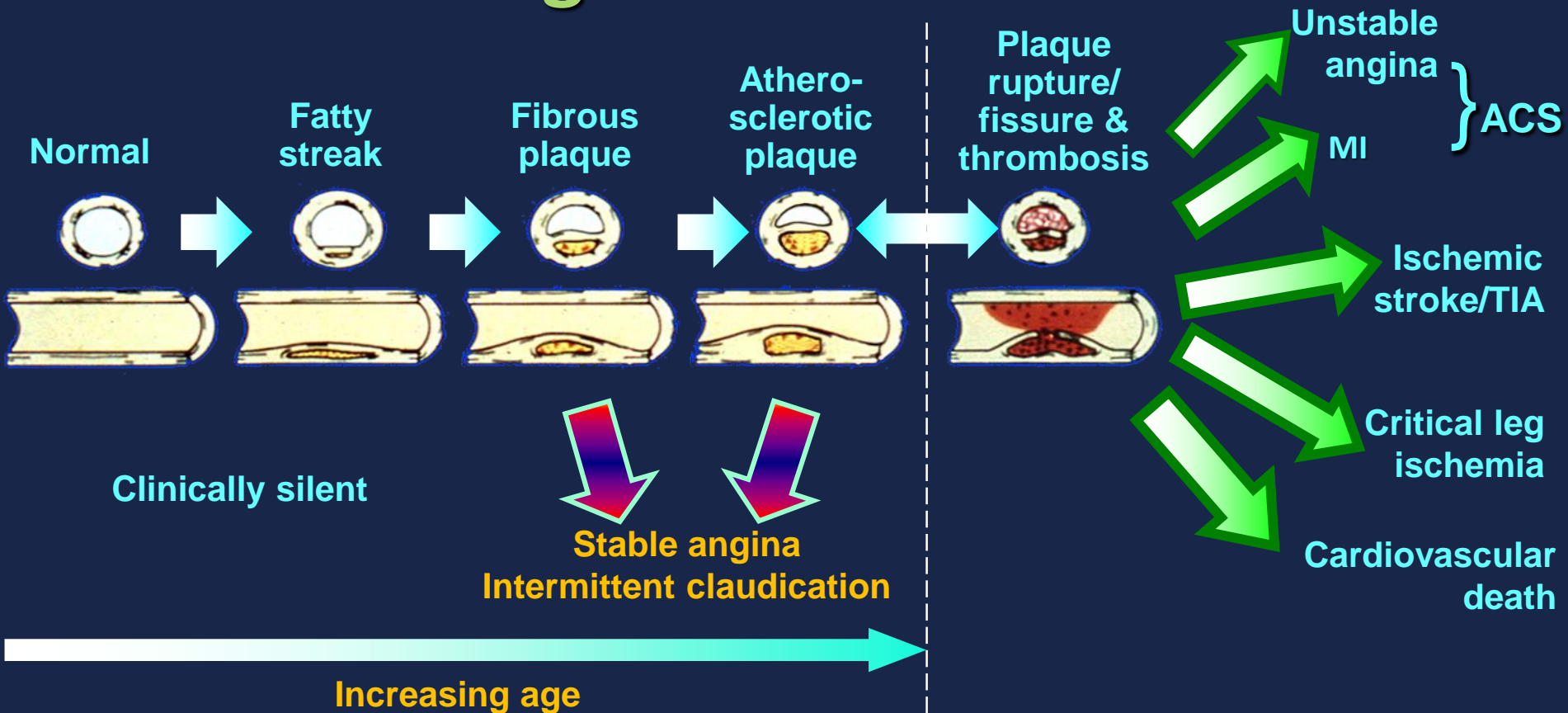
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References

- **2013 ESC Guidelines on Stable CAD. EHJ 2013**
- **2014 ACC Focused update on Stable IHD. JACC 2014**
- **2017 ACC/AATS/AHA Appropriate criteria for revascularisation in stable CAD**

Atherothrombosis: a Generalized and Progressive Process



ACS, acute coronary syndrome; TIA, transient ischemic attack

Angina Pectoris: ESC Guideline Definition

1. Typical substernal discomfort, <30mins
2. Provoked by exercise or stress
3. Relieved by rest or sublingual nitrate in 5 minutes

Typical angina	All 3
Probable angina	2/3
Atypical chest pain	0 or 1/3

Characteristic of Tests to Diagnose CAD

ESC Guideline 2013. Montalescot F et al. EHJ 2013;34:2949-3003

	Diagnosis of CAD	
	Sensitivity (%)	Specificity (%)
Functional tests		
Exercise ECG	45 – 50	85 – 90
Exercise stress echocardiography	80 – 85	80 – 88
Exercise stress SPECT	73 – 92	63 – 87
Dobutamine stress echocardiography	79 – 83	82 – 86
Dobutamine stress MRI	79 – 88	81 – 91
Vasodilator stress echocardiography	72 – 79	92 – 95
Vasodilator stress SPECT	90 – 91	75 – 84
Vasodilator stress MRI	67 – 94	61 – 85
Vasodilator stress PET	81 – 97	74 -91
Anatomical Tests		
Coronary CTA	95 – 99	64 – 83
Coronary Angiogram	100	100

Pre-test Probabilities of CAD in Chest Pain and Diagnostic Tests

white or red=no further CAD dx test; blue=exercise test; pink=NI-functional tests

	Typical angina		Atypical angina		Non-anginal pain	
Age	Men	Women	Men	Women	Men	Women
30-39	59	28	29	10	18	5
40-49	69	37	38	14	25	8
50-59	77	47	49	20	34	12
60-69	84	58	59	28	44	17
70-79	89	68	69	37	54	24
>80	93	76	78	47	65	32

Evaluation of Stable CAD

Diagnosis:

- Pre-test probability: low (<15%), high (>85%); midrange (15-65% EST, 65-85% NI-imaging)
- Seek alternative explanation if negative

Risk stratification:

- Low risk (CV death < 1%/yr, e.g. no ischaemia, normal or plaques only in CTA)
- Intermediate (1-3%, e.g. ischaemia 1-10% LV area, CTA lesions in between)
- High (>3%, e.g. CTA sig 3VD, LM, pLAD, ischaemic area >10%, ≥ 3 ischaemic areas)

'ABCDE' in Management of CAD

- **A = Aspirin and ACEI/ARB**
- **B= Betablocker and blood pressure**
- **C= Cigarette smoking and cholesterol control**
- **D= Diet and Diabetes**
- **E = Education and Exercise**

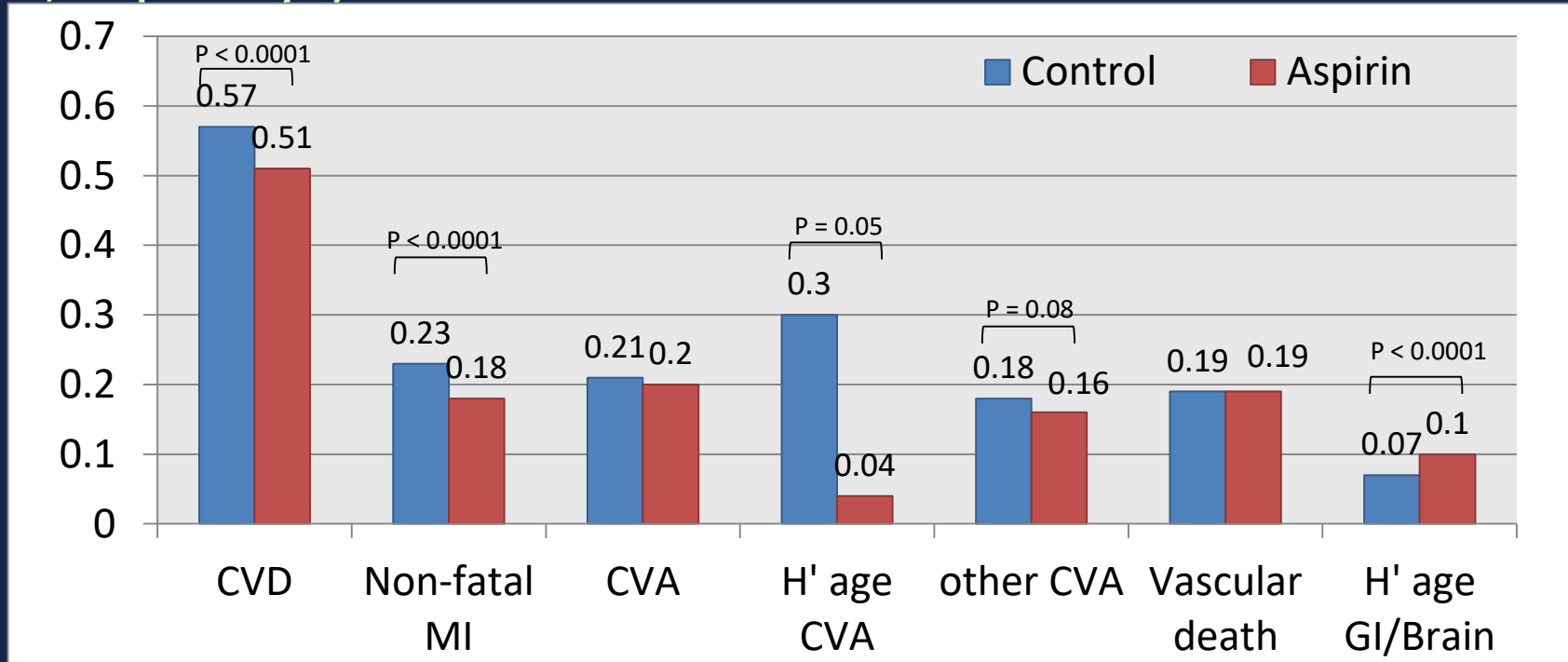
Angina: Medical therapy

- Improve Outcome (↓ CV events):
antiplatelet, lipid modulating agents (statins),
ACEI/ARB, BB (\pm)
- Symptoms (and ischaemia): BB, nitrate,
calcium channel blockers, ivabradine,
trimetazidine, ranolazine, allopurinol

Aspirin in Primary & Secondary Prevention Trials

Antithrombotic Trialist. Lancet 2009;373;1849-1860

6 primary prevention (660,000 person- yrs) and 16 secondary prevention trials (43,000 person- yrs)



Conclusion: Aspirin reduces CVD by decreasing non-fatal MI, but increase haemorrhage without change in vascular death. In secondary prevention, a more significant reduction of serious vascular events occurred.

Are Antiplatelet Agents Different ?

Clopidogrel Vs ASA (CAPRIE Trial)

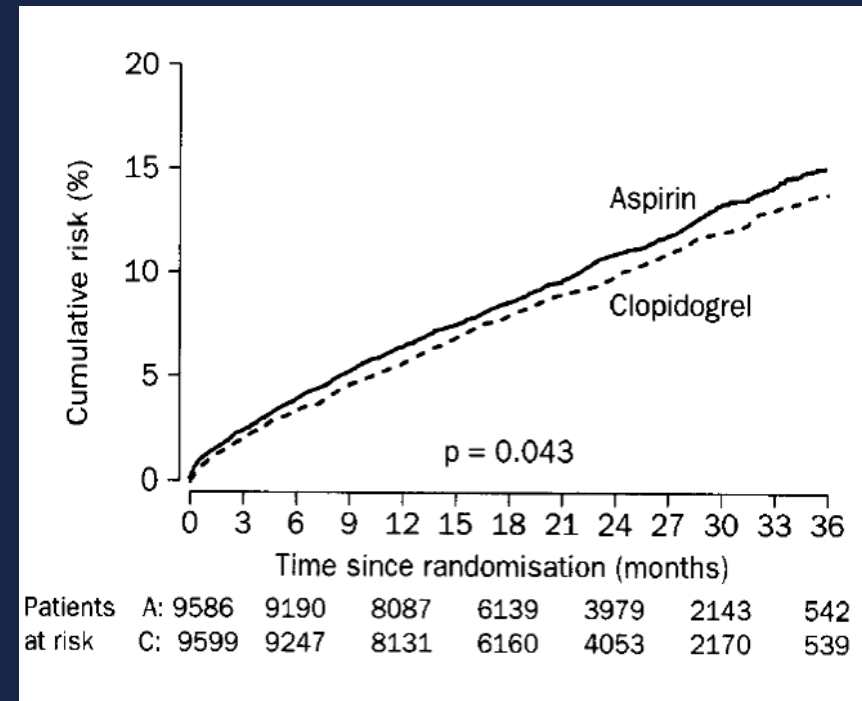
Gent M et al. Lancet 1996;348:1329-39


Background: Indirect comparison of trials showed no significant difference between ASA and other antiplatelet therapy

Methods: 19185 pts with history of MI, CVA or PVD received either clopidogrel or ASA for 3 years

Conclusion: Clopidogrel reduces major vascular events by 8.7% (0.3-16.5%) but the differences are small and are mainly seen in pts with PVD. Clopidogrel has a lower risk of severe GIB (0.49 vs 0.71%)

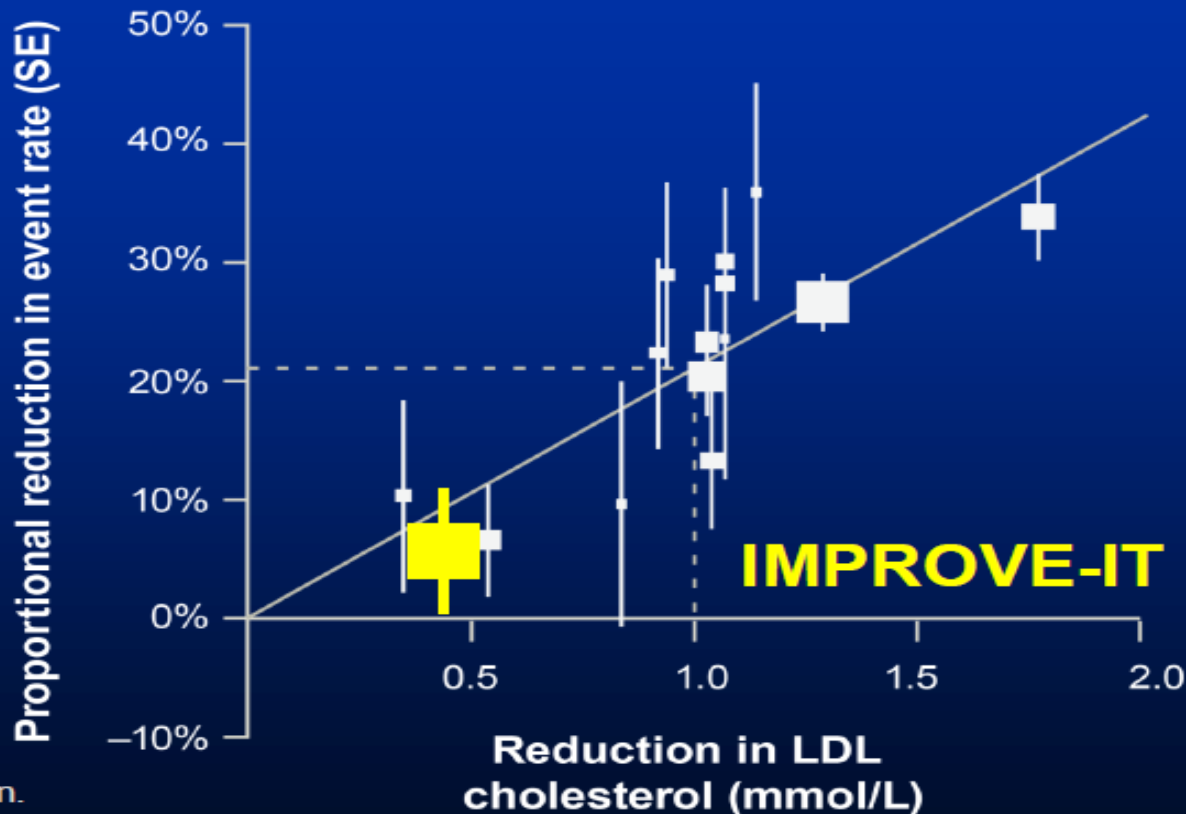
Results:



A red carpet event with a sign asking 'Are Statins Dangerous ??'. The sign is white with a black border and is mounted on a red background. The text is written in a black, cursive font. The sign is surrounded by a string of warm white lights. The background is a wood-paneled wall. In the foreground, there is a red carpet and a red velvet rope held up by two gold stanchions.

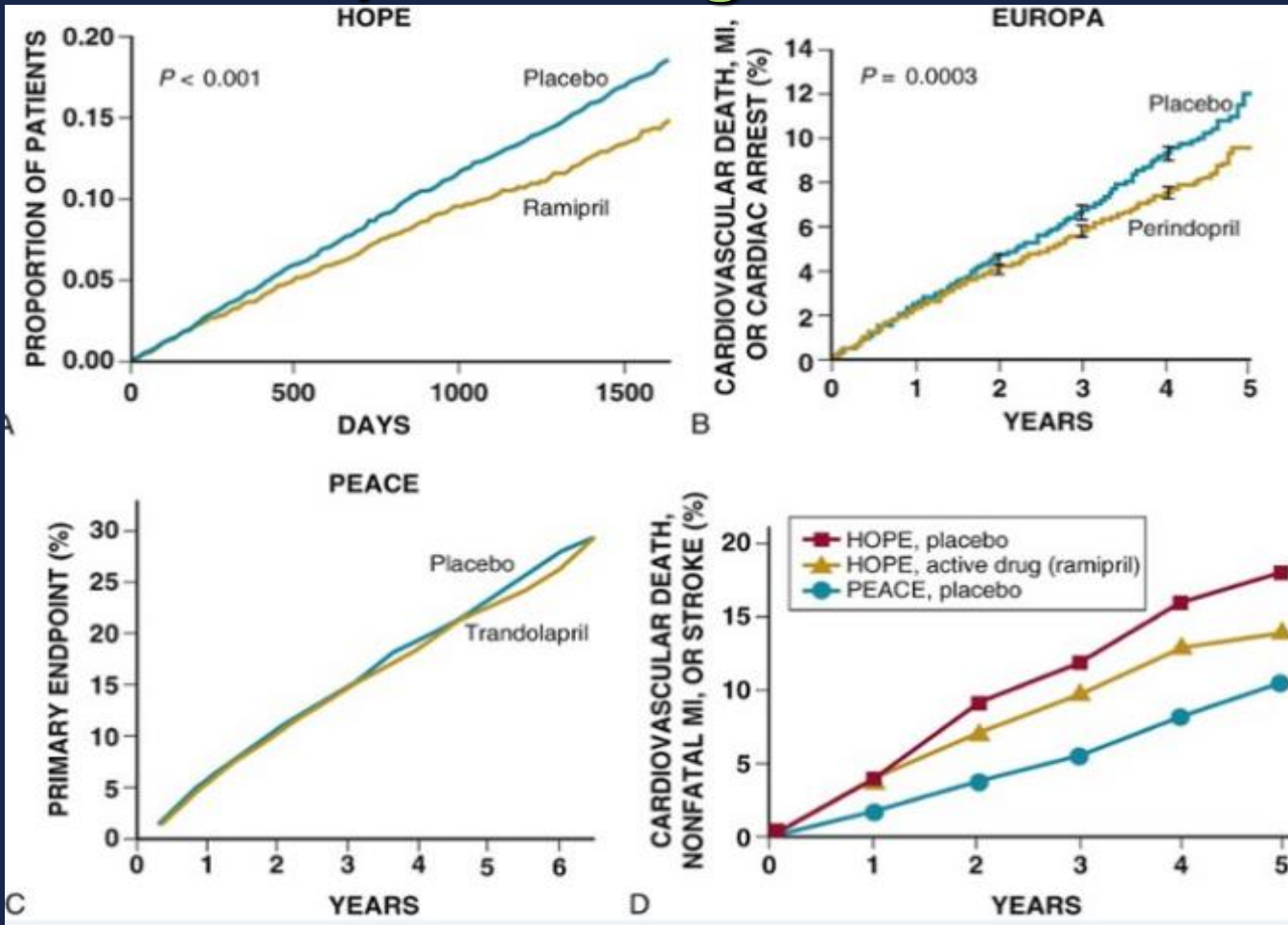
*Are Statins
Dangerous
??*

IMPROVE-IT vs. CTT: Ezetimibe vs. Statin Benefit



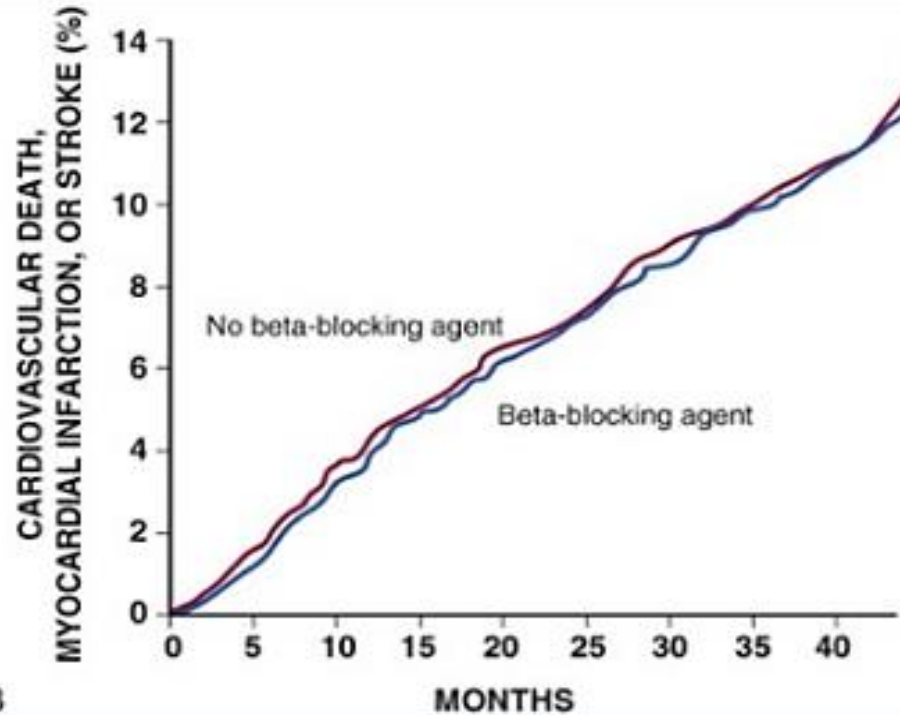
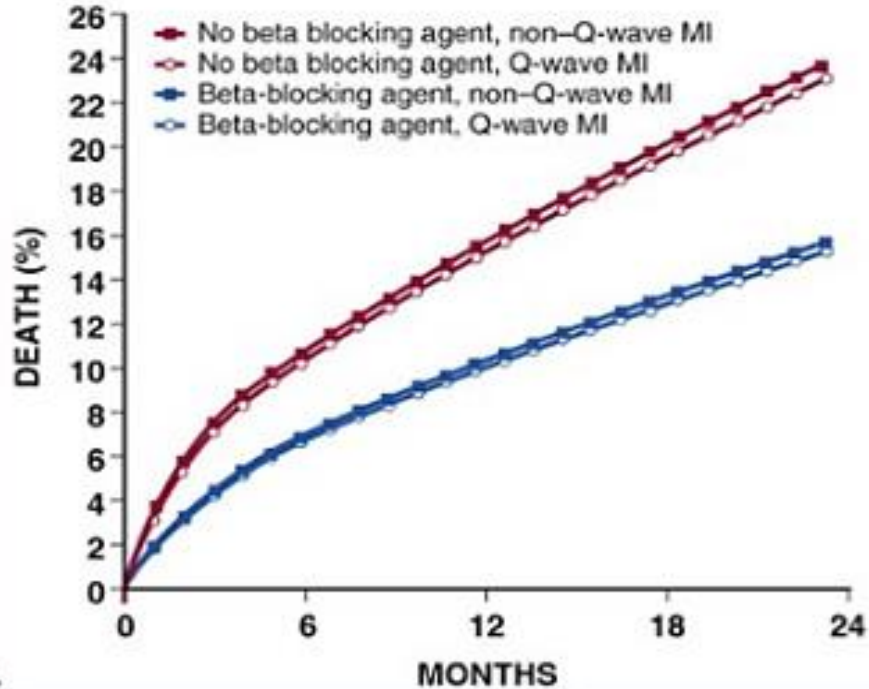
CTT Collaboration.
Lancet 2005; 366:1267-78;
Lancet 2010;376:1670-81.

ACEI/ARB in High Risk CAD



Mann, Zipes, Libby, Bonow. Braunwald's HEART DISEASE. A Textbook of Cardiovascular Medicine. (10th Edition)

BB in Different CAD Subsets



Newer Anti-ischaemic Agents: second line agents ESC 2013

Ivabradine:

7.5 mg bd: ↓ CV events in pts with stable angina with resting HR \geq 70 bpm (IIa, B)

Nicorandil:

Stimulates ATP sensitive K channel.

↓ CV events by 14% (IONA study, Lancet 2002) (IIa, B)

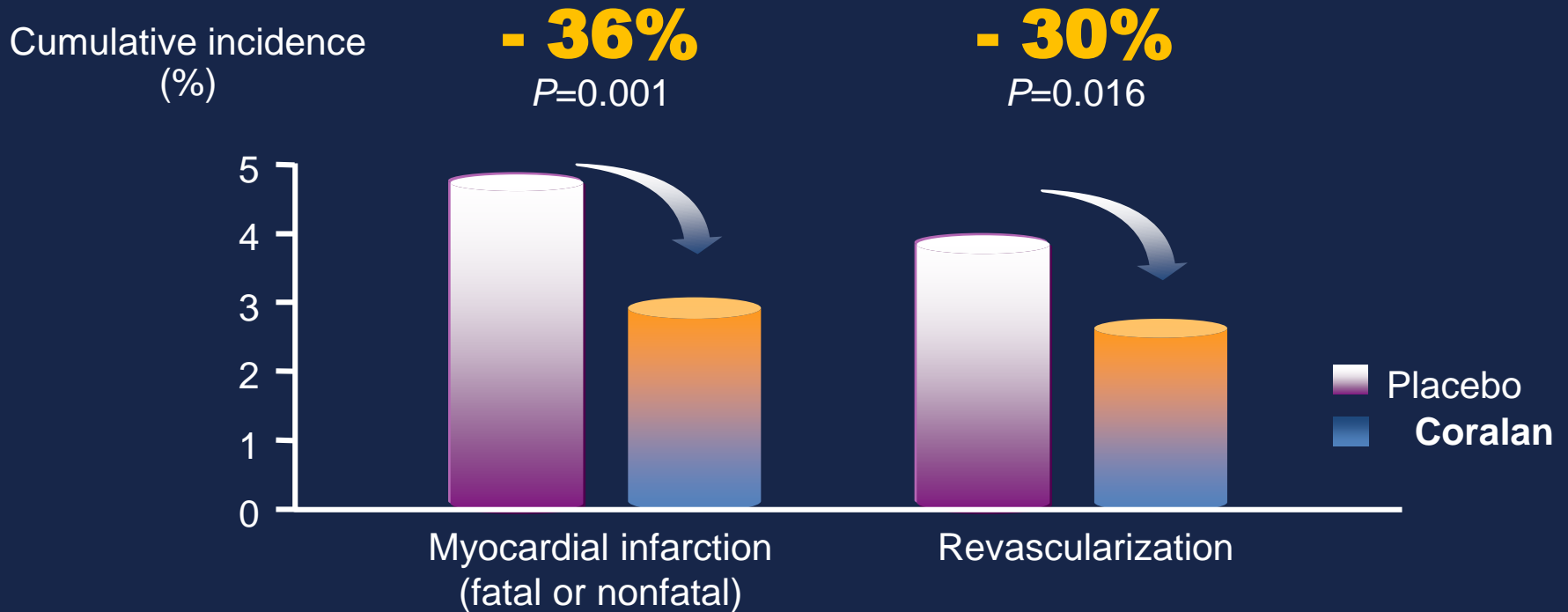
Trimetazidine:

Anti-ischaemic metabolic modulator and improves exertional ischaemia, improves HBA1c. No large outcome studies.

Ranolazine:

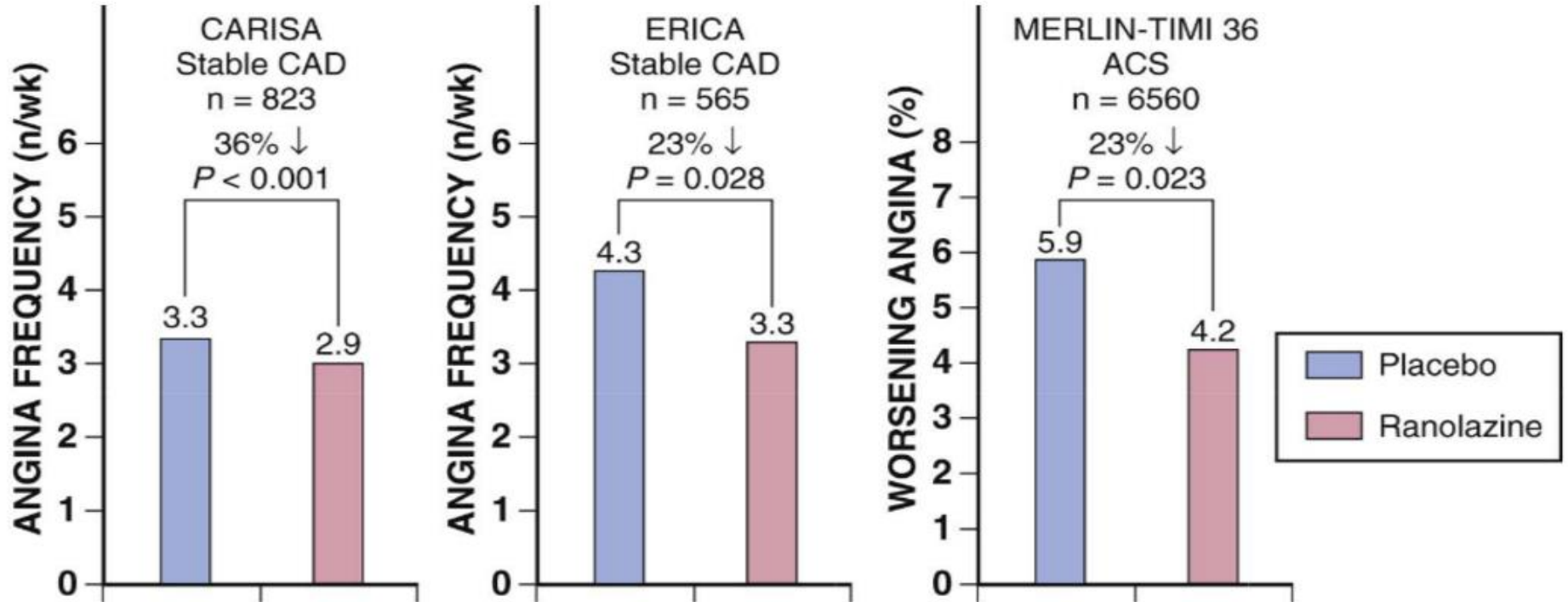
Selective late Na current inhibitor with anti-ischaemic and metabolic properties (IIa, B)

Ibravadin (Coralan) reduces myocardial infarction and revascularization



in patients with heart rate ≥ 70 bpm

Ranolazine



ACC/AHA/ESC Classes

Class	Wordings	Benefit/Risk	Meaning
I	Indicated	$B \ggg R$	Generally applied
IIa	Reasonable	$B \gg R$	Controversial but evidence favourable
IIb	May be considered	$B \geq R$	Evidence less well established
III	Not indicated	$B < R$	Consensus against

Usual Practice: I & IIa only

ACC/AHA/ESC Level of Evidence

Level of Evidence	Meaning
A	Multiple RCTs
B	1 RCT or non-randomized studies
C	Consensus or standard of care

Stable CAD: Medical therapy to Prevent MI/death (I and IIa)

Antiplatelet

1. Aspirin (I)
2. Clopidogrel (I) if aspirin contraindicated

Betablockers

1. LV dysfunction (I)
2. After ACS (I)

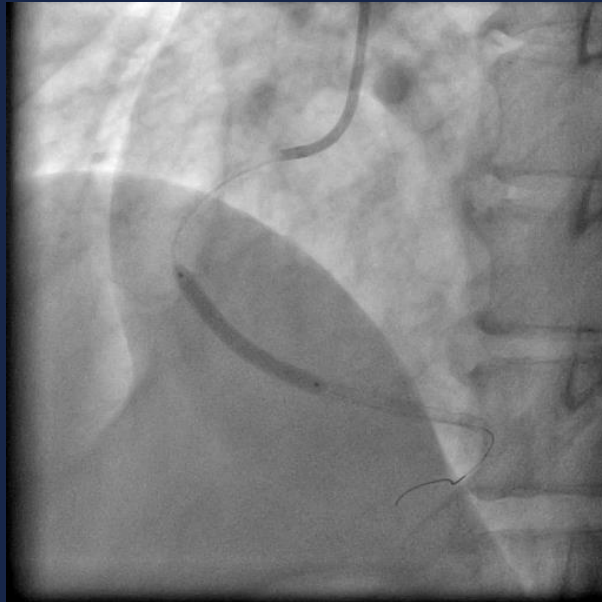
ACEI/ARB

1. If concomitant DM, LVEF \leq 40%, CKD (I)
2. ARB useful if ACEI contraindicated (I)
3. CAD with other vascular diseases (IIa)

Lipid Lowering

1. Life style change, diet (I)
2. statin (I)

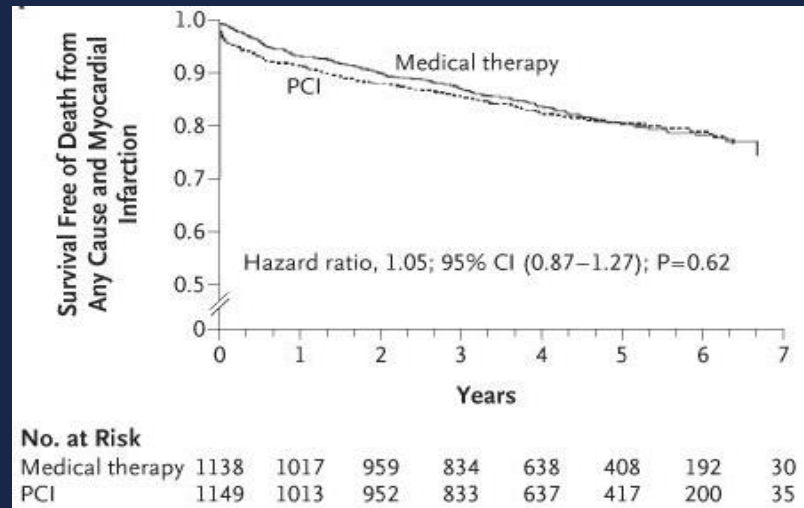
Percutaneous coronary Intervention (PCI)



Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) Trial. Boden WE. NEJM 2007

Pts & Methods :

2287 pts with stable angina and significant coronary artery disease (but excluding 'high risk' categories) received OMT vs PTCA



Conclusion :

OMT (including LDL ~1.8, HDL ~1, and ABCDE) is a reasonable initial option

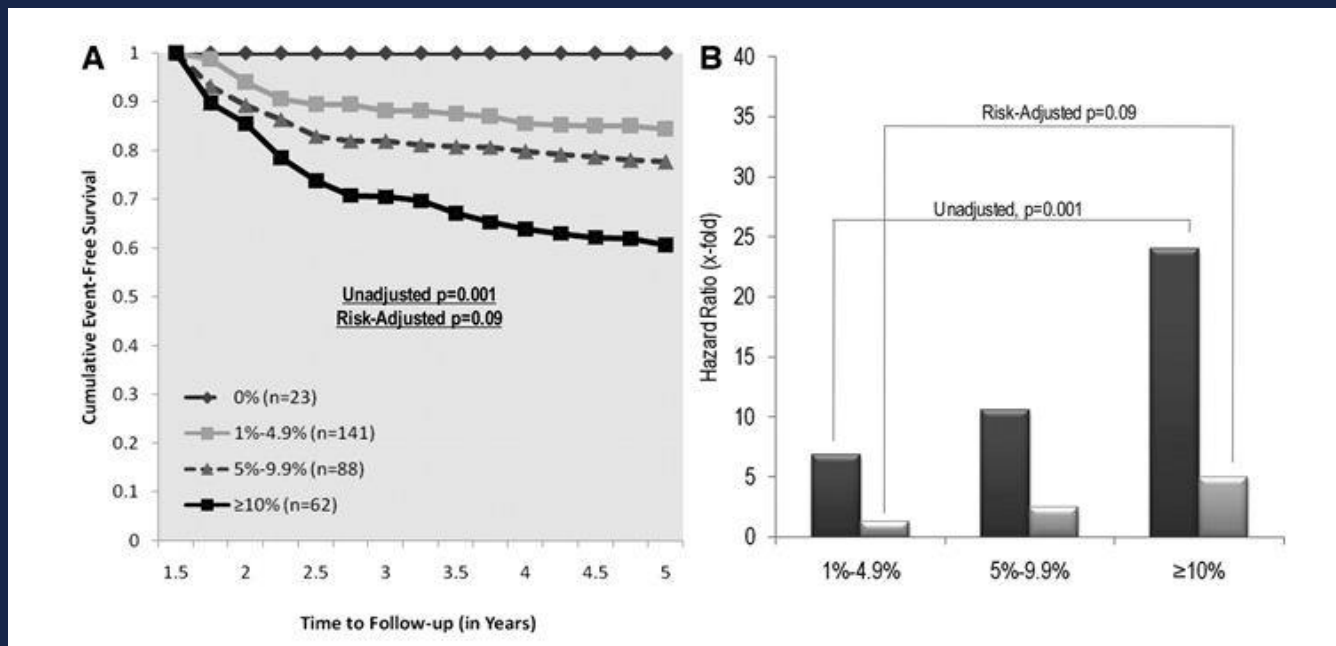
Perspective :

High residual events, bare metal stents, 32% cross over to PTCA/CABG

Clinical Outcomes Utilizing Revascularisation and Aggressive Drug Evaluation (COURAGE) Nuclear Substudy

Shaw LJ et al, Circ 2008; 117:1283-91

Pts & Methods: NR studies suggest ischaemia driven revascularization improve outcome. A subgroup of COURAGE prospective randomized study compared OMT vs OMT + PCI



Conclusion: OMT + PCI significantly reduced ischaemia (-2.7% vs -0.5% with OMT alone) and is associated with improved clinical outcome

PCI in Stable Angina (ORBITA) (1)

Al-Lamee R et al. Lancet 2018;391:31-40

Background: ↓Angina is the 1° goal of PCI in stable angina, but there is no RCT

Pts & Methods: **O**bjective **R**andomised **B**linded **I**nvestigation with Optimal Medical **T**herapy or **A**ngioplasty study randomised 230 pts in the UK with ≥ 70% stenosis of a single artery. Pts underwent ETT, dobutamine stress and symptom assessment. All underwent CC + FFR only (placebo) or CC + FFR + stenting (PCI group) and followed up 6 weeks.

Lesions:	Area stenosis	84.4 ± 10.2%
	FFR	0.69 ± 0.16
	Instantaneous wave-free ratio	0.76 ± 0.22

PCI in Stable Angina (ORBITA) (2)

Al-Lamee R et al. Lancet 2018;391:31-40

Endpoints:

1° Increase exercise time 16.6s (NS)

2° Increase complete freedom of angina (49.5 vs 31.5%, P<0.05)

2° Reduced objective ischaemia

Conclusion:

In patients with stable angina on OMT, PCI did not increase exercise time by more than a placebo procedure

Comments:

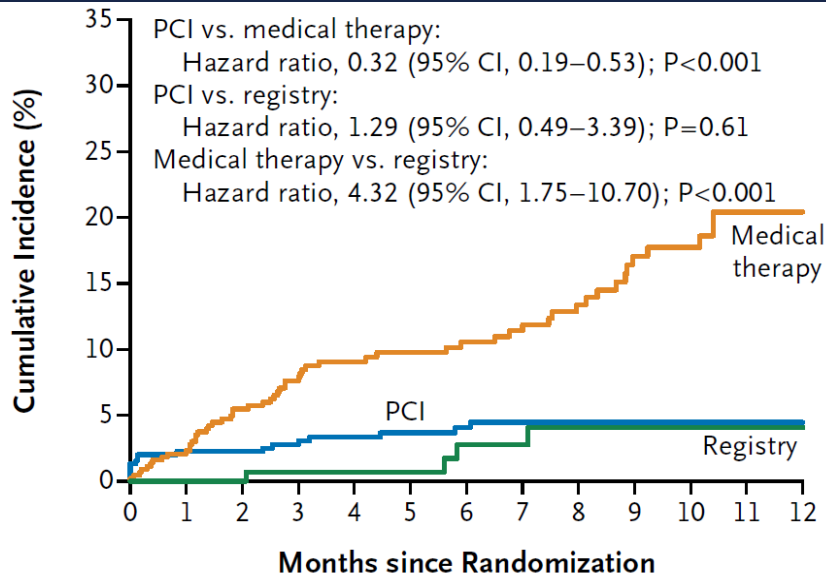
(1) Small study and short follow up for events

(2) Only for SVD and pt with normal LVEF

(3) Importance of “sham” procedure

Fractional Flow Reserve – Guided PCI vs Medical Therapy in Stable CAD (FAME-2)

De Bruyne B et al. *N Engl J Med.* 2012 ;367:991-1001



No. at Risk	0	1	2	3	4	5	6	7	8	9	10	11	12
Medical therapy	441	414	370	322	283	253	220	192	162	127	100	70	37
PCI	447	414	388	351	308	277	243	212	175	155	117	92	53
Registry	166	156	145	133	117	106	93	74	64	52	41	25	13

Pts & Background:

Preferred initial treatment for stable CAD is OMT. Functional assessment using FFR may be superior to anatomical guidance. In 1220 pts, FFR guided PCI was either performed if $FFR < 0.8$ or continued with OMT in random order. $FFR > 0.8$ were continued on OMT.

Conclusion:

1. FFR guided PCI in functional ischaemic pts is superior to OMT if $FFR < 0.8$
2. OMT is superior to PCI if FFR is negative for ischaemia

PCI vs CABG : The SYNTAX study

NEJM 2009; 360 : 961-972

Pts & Background :

1800 pts with severe CAD (3VD, LMS) were randomised to PCI (Taxus stent) vs CABG for 12 months

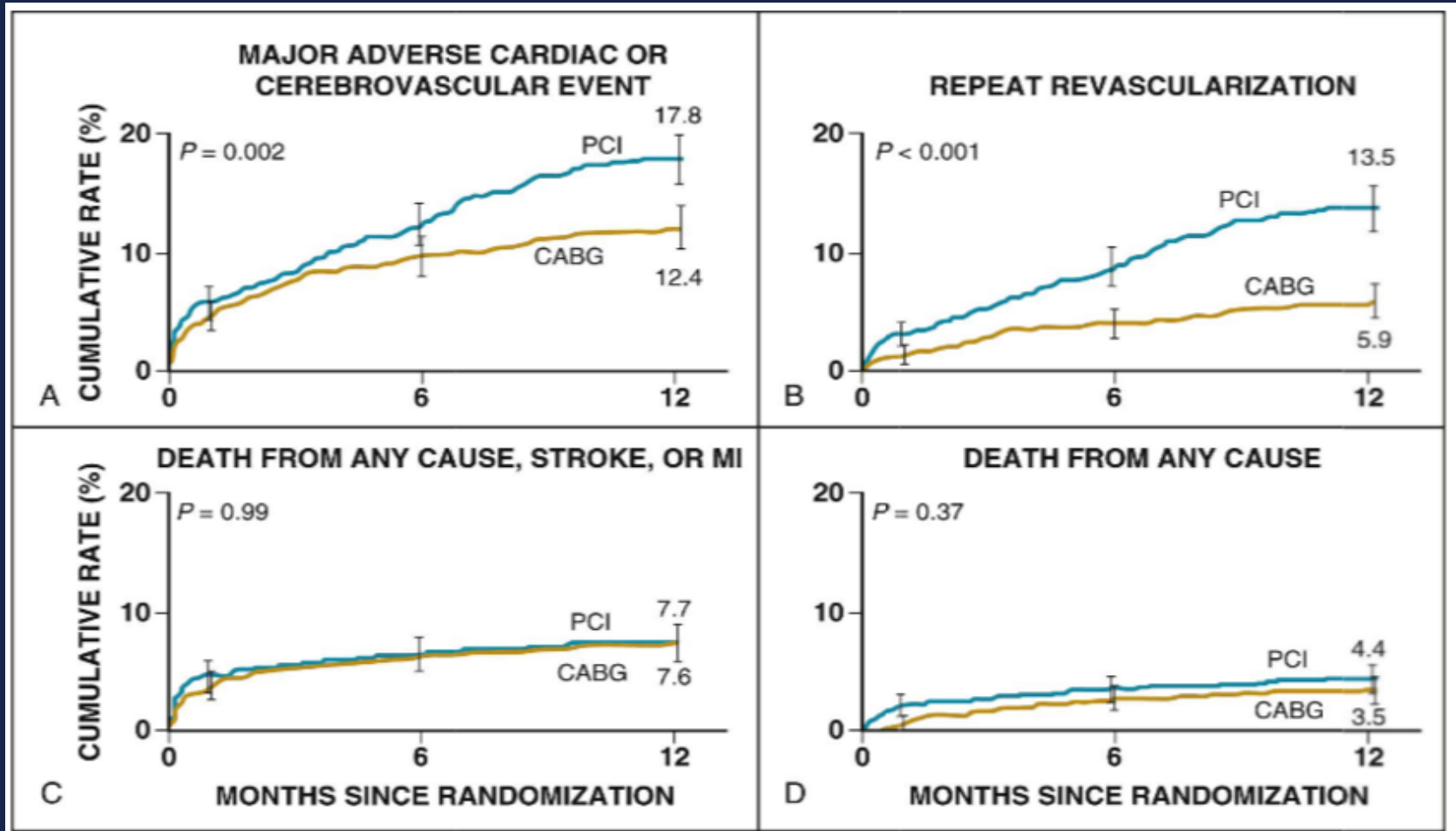
Results :

	PCI	CABG	P
MACE+CVA	17.8%	12.4%	=0.002
Repeat procedure	13.5%	5.9%	P<0.001
Death/MI/CVA	7.7%	7.6%	NS
CVA	0.6%	2.2%	P=0.003

Conclusion :

Short term study suggests CABG may be superior to PCI in severe CAD, at the risk of increase in strokes

PCI vs CABG



Mann, Zipes, Libby, Bonow. Braunwald's HEART DISEASE. A Textbook of Cardiovascular Medicine. (10th Edition)

HKCCCCT Module 1

Hong Kong, 8 Jul, 2018

Coronary Angiography in stable Angina: Indications

Remains the “gold-standard” to diagnose CAD ($\geq 50\%$ stenosis)

Class I

1. Severe stable angina (or high risk profile): Mortality/yr $> 3\%$ [IC]
2. Mild or no symptom + positive non-invasive test [IC]

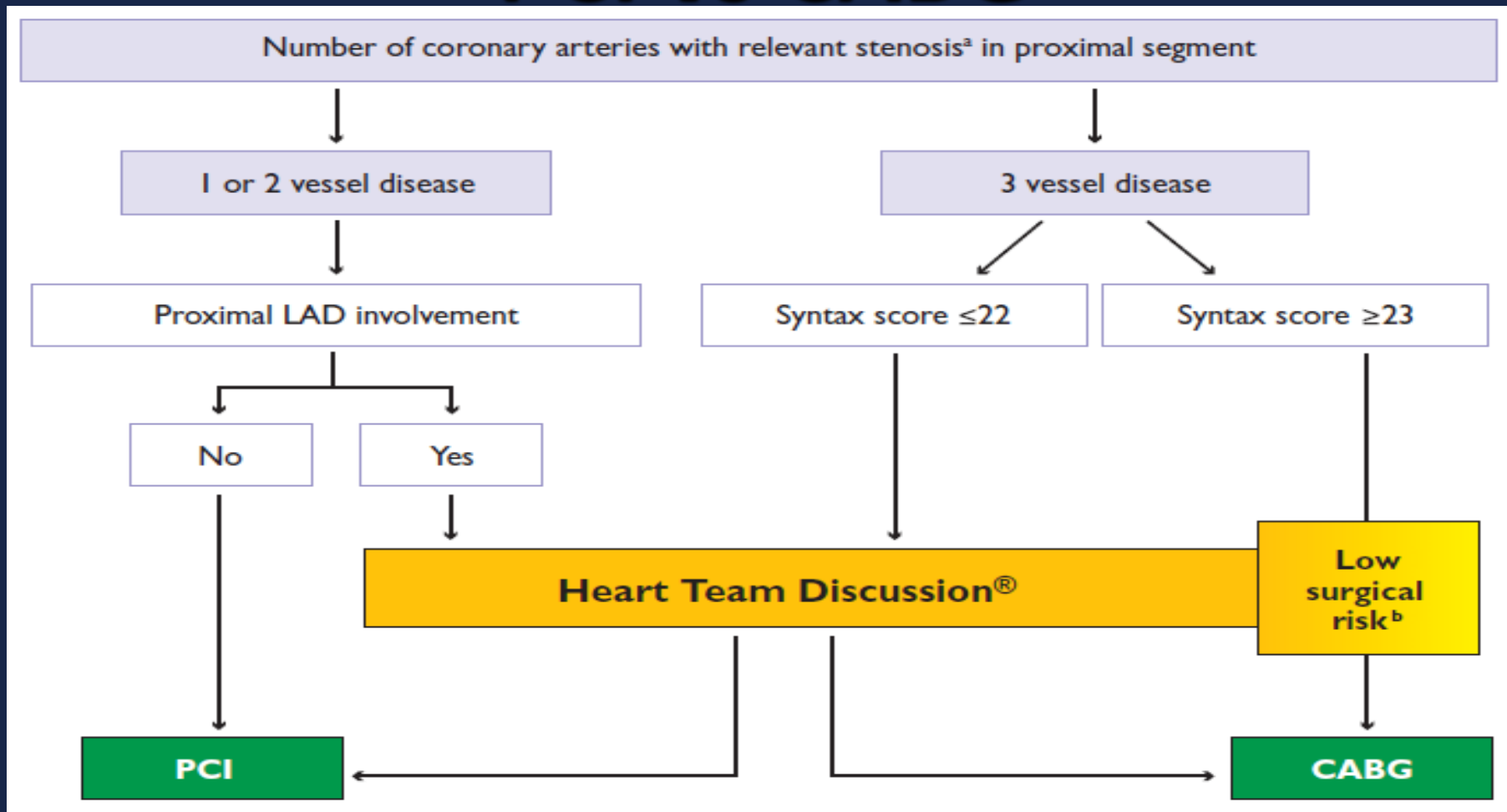
Class IIa

1. Inconclusive (or unable to perform) non-invasive test
2. Calcific CTA finding with possible overestimate of stenosis (alternative to additional functional testing)

Indications For Revascularisation

Indication ^a	To improve prognosis:		To improve symptoms persistent on OMT:		Ref. ^f
	Class ^d	Level ^e	Class ^d	Level ^e	
A Heart Team approach to revascularization is recommended in patients with unprotected left main, 2–3 vessel disease, diabetes or comorbidities.	I	C	I	C	172, 426–428
Left main >50% diameter stenosis ^b .	I	A	I	A	172
Any proximal LAD >50% diameter stenosis ^b .	I	A	I	A	172
2–3 vessel disease with impaired LV function / CHF.	I	B	IIa	B	172
Single remaining vessel (>50% diameter stenosis ^b).	I	C	I	A	172
Proven large area of ischaemia (>10% LV ^c)	I	B	I	B	172
Any significant stenosis with limiting symptoms or symptoms non responsive/intolerant to OMT.	NA	NA	I	A	172
Dyspnoea/cardiac heart failure with >10% ischaemia/viability ^c supplied by stenosis >50%.	IIb	B ^{429, 430}	IIa	B	172
No limiting symptoms with OMT in vessel other than left main or proximal LAD or single remaining vessel or vessel subtending area of ischaemia <10% of myocardium or with FFR ≥0.80.	III	A	III	C	23, 25, 172, 400

PCI vs CABG



Considerations of Deferring PCI

- Medications intolerance or non-compliance
- Effect on life style: occupation, exercise etc
- Development of CTO
- Medico-legal consideration

