21st TCTAP 2016

Future Role of CABG for LM and MVD

David P Taggart

Professor of Cardiovascular Surgery, University of Oxford



Conflicts of Interest:

(i) Clinical: Cardiac Surgeon

(ii) Academic: ESC/EACTS Guideline Writer; Chair Surgical Cttee EXCEL trial)

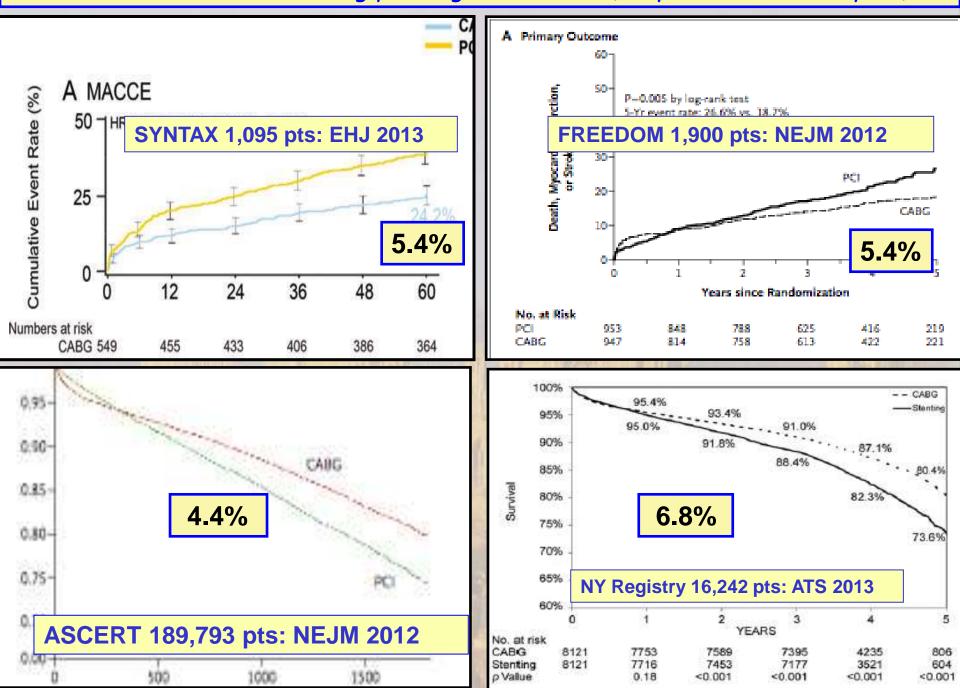
(ii) Commercial: Consultant to VGS, Medistim, Somahlution (Research Funding, Speaking Fees, Share Options in VGS)

Future Role of CABG for LM and MVD:

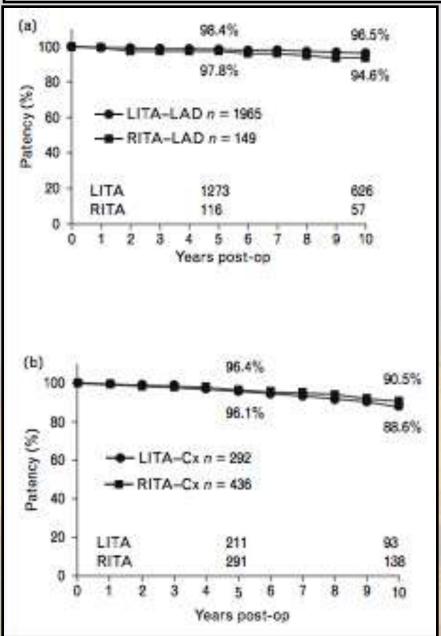
'Must Knows'

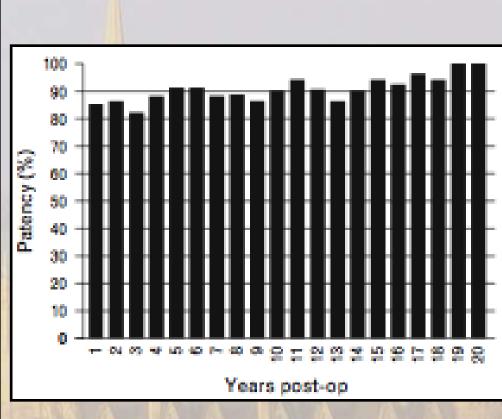
- 1 Are study patients 'typical' (? Parallel registry: SYNTAX, EXCEL)
- 2 Duration of Follow-Up (must be > 5 years)
- 3 Guideline Based Medical Therapy (always worse with CABG)
- 4 Patients with Diabetes, Poor Ventricles
- 5 Pathophysiological difference between PCI and CABG
- 6 CABG vs PCI in MVD + LM (Guidelines)

CABG Survival vs PCI increasingly diverges with time (< 5 yr is 'interim' analyses)



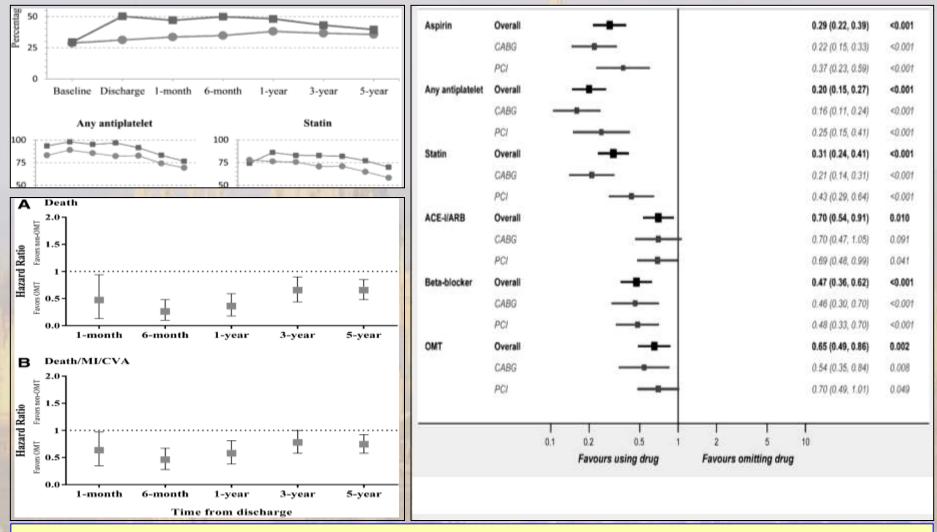
Patency of BIMA to 20 years [Tatoulis, Buxton et al Curr Op Cardiol 2011]





Optimal Medical Therapy Improves Clinical Outcomes in Patients Undergoing Revascularization With Percutaneous Coronary Intervention or Coronary Artery Bypass Grafting Insights From the Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery (SYNTAX) Trial at the 5-Year Follow-Up CIRC 2015

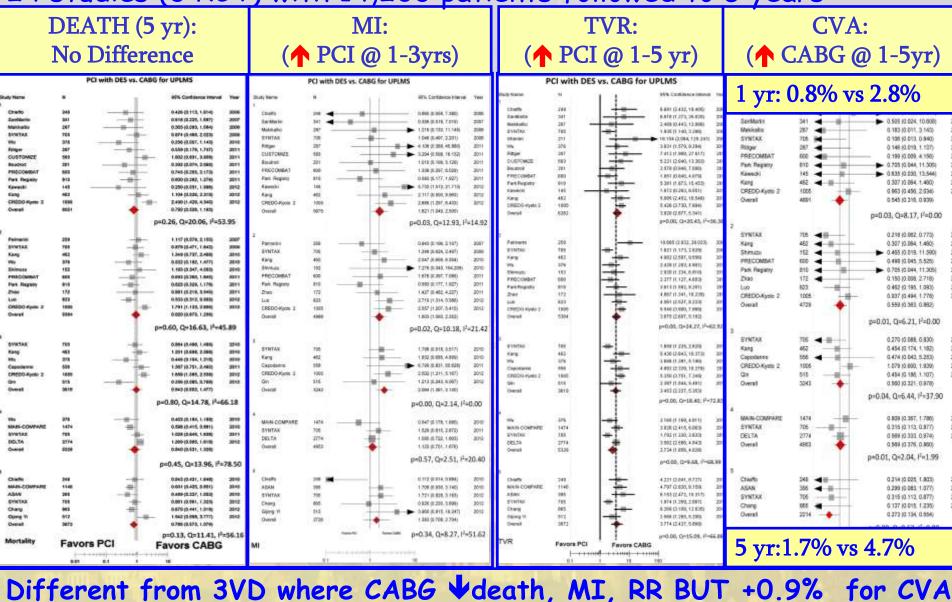
Javaid Iqbal, MRCP, PhD*; Yao-Jun Zhang, MD*; David R. Holmes, MD;



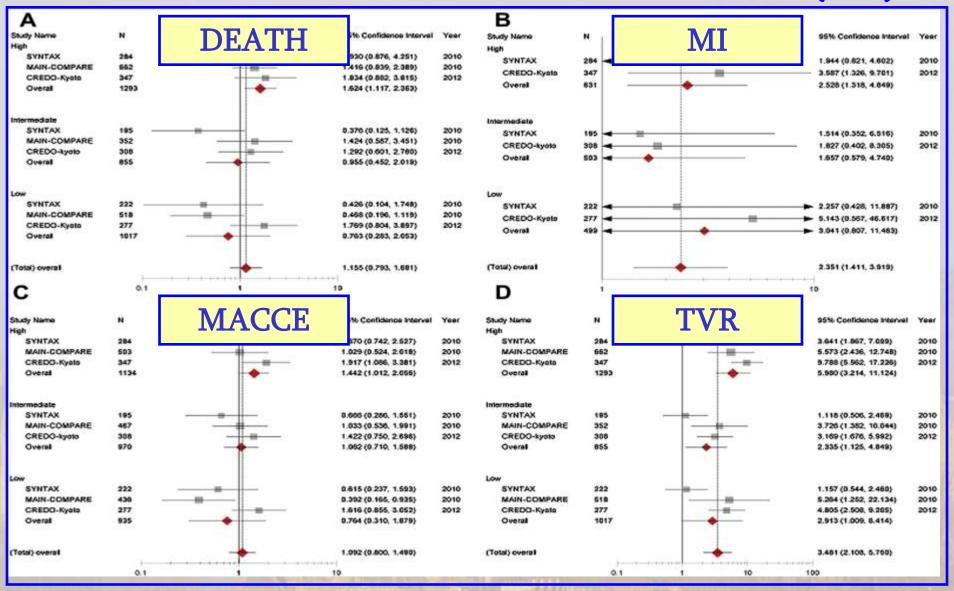
Substantially inferior OMT in CABG group: \uparrow mortality and MACCE

A Meta-Analysis of Drug-Eluting Stents Versus Coronary Artery Bypass Grafting

24 studies (3 RCT) with 14,203 patients followed to 5 years



LM: CABG BEST ONLY FOR HIGH TERCILES (>32)



In LM @ SYNTAX <32 (ie less proximal CAD)? Excess competitive flow 2 completed trials of LM: NOBLE and EXCEL will report TCT 2016

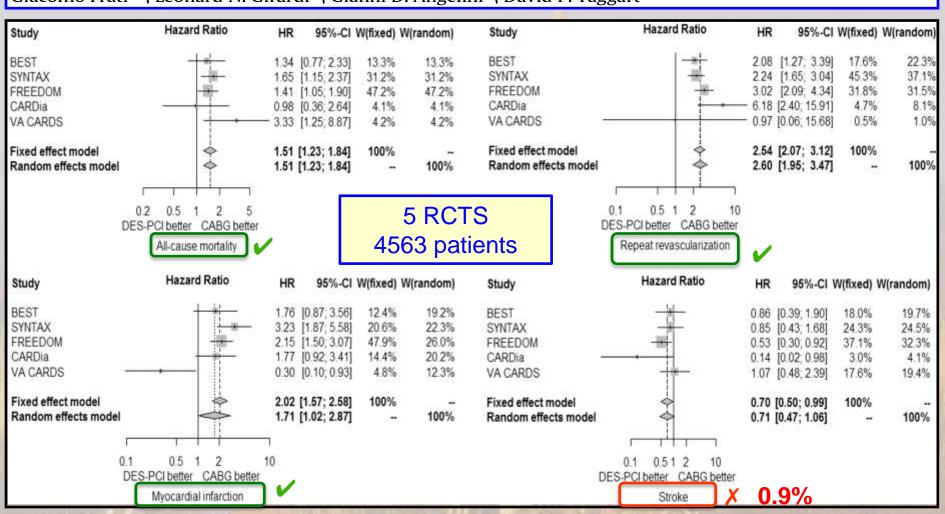
Coronary surgery is superior to drug eluting stents in multivessel disease.

CrossMark

Systematic review and meta-analysis of contemporary randomized controlled trials

[IJC 2016]

Umberto Benedetto ^{a,*,1}, Mario Gaudino ^{b,1}, Colin Ng ^a, Giuseppe Biondi-Zoccai ^{c,d}, Fabrizio D'Ascenzo ^e, Giacomo Frati ^{c,f}, Leonard N. Girardi ^b, Gianni D. Angelini ^a, David P. Taggart ^g

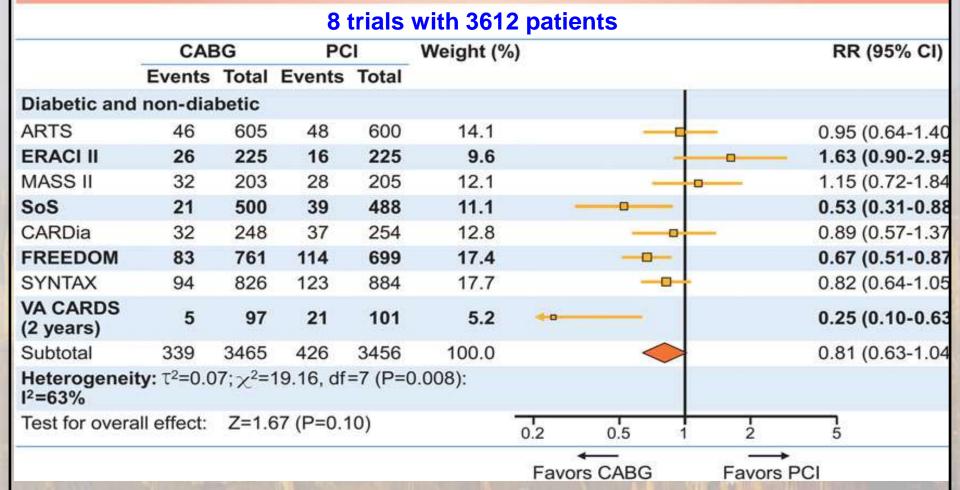


All RCTs and Propensity Matched studies show superior survival with CABG over PCI that continues to increase past 5 years with diverging survival curves

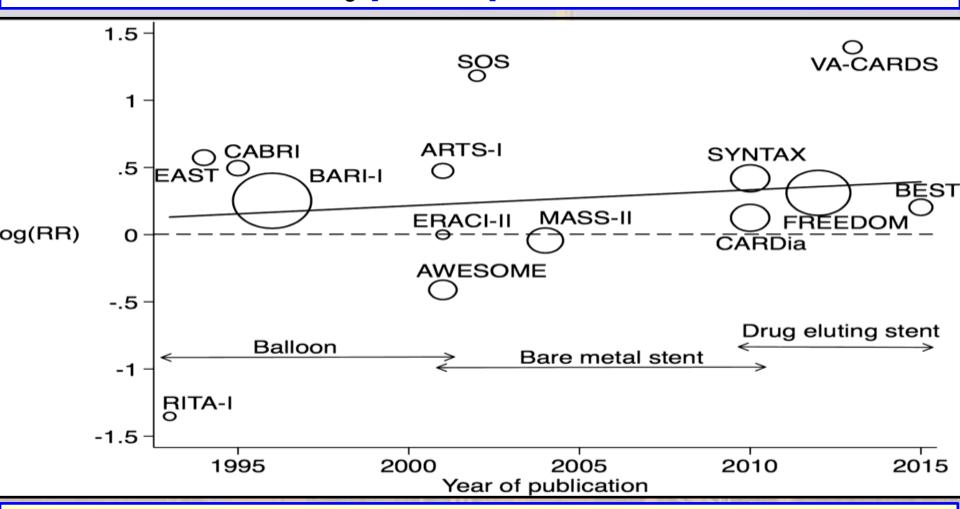
Comparison of coronary artery bypass surgery and percutaneous coronary intervention in patients with diabetes: a meta-analysis of randomised controlled trials

Verma S et al: [LANCET DIABETES and ENDOCRINOLOGY 2013]

CABG & PCI in Diabetes All-Cause Mortality at 5-Year Follow-up



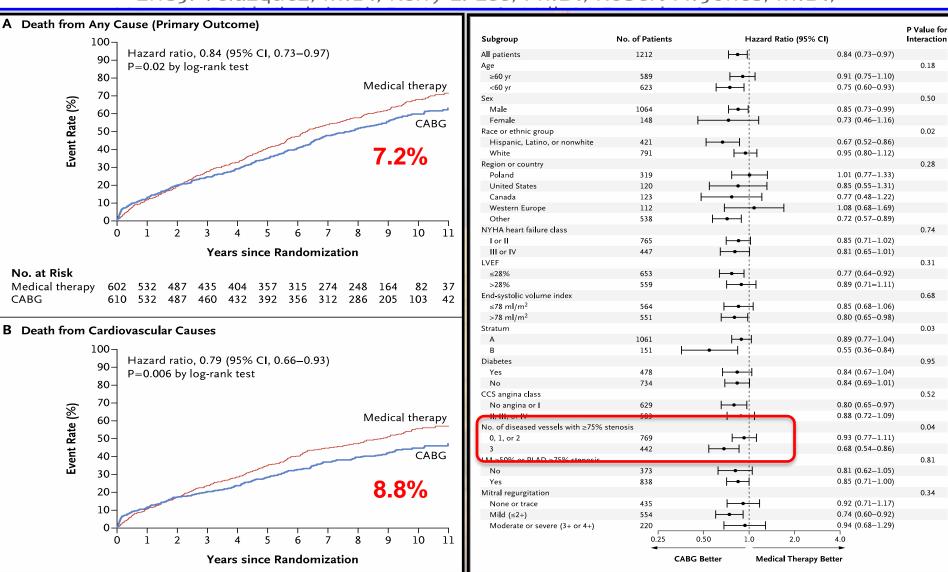
Has the difference in mortality between percutaneous coronary intervention and coronary artery bypass grafting in people with heart disease and diabetes changed over the years? A systematic review and meta-regression Peter Herbison, Cheuk-Kit Wong [BMJ 2015]



In DM even with 3rd generation stents CABG still has strong survival advantage

Coronary-Artery Bypass Surgery in Patients with Ischemic Cardiomyopathy

Eric J. Velazquez, M.D., Kerry L. Lee, Ph.D., Robert H. Jones, M.D.,



THE 3 REASONS CABG HAS SUCH A SURVIVAL BENEFIT OVER PCI

1. Anatomically, atheroma is mainly located in the proximal coronary arteries Placing bypass grafts to the <u>MID CORONARY VESSEL</u> has <u>TWO</u> effects

(i) Complexity of proximal 'CULPRIT' lesion is irrelevant

(ii) over the long term offers prophylaxis against **FUTURE** 'culprit' lesions

In contrast, PCI only treats <u>'SUITABLE'</u> localised proximal 'culprit' lesions but has **NO PROPHYLACTIC BENEFIT** against new disease

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THE NEW ENGLAND JOURNAL OF MEDICINE

Aug. 25, 1988

IMA elutes NO into coronary circulation reducing risk of further disease
DIFFERENCE BETWEEN ENDOTHELIUM-DEPENDENT RELAXATION IN ARTERIAL AND IN
VENOUS CORONARY BYPASS GRAFTS

THOMAS F. LÜSCHER, M.D., DENNIS DIEDERICH, M.D., ROBERT SIEBENMANN, M.D., KURT LEHMANN, M.D.,

Drug-Eluting Stent and Coronary Thrombosis Biological Mechanisms and Clinical Implications [CIRC 2007]

Thomas F. Lüscher, MD; Jan Steffel, MD; Franz R. Eberli, MD; Michael Joner, MD; impairs re-endothelialization, downstream endothelial function and creates pro-thrombotic milieu

- 3. PCI means incomplete revascularization (Hannan Circ 2006)
- Of 22,000 PCI 69% had incomplete revascularization
- >2 vessels (+/- CTO) HR for mortality 1.4 (95% CI = 1.1-1.7)
- Residual SYNTAX score > 8 increases mortality and MACCE (Farooq, Serruys CIRC 2013)

PCI will 'never' match the results of CABG for LM/MVD (POBA; BMS; DES)





2014 ESC/EACTS Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

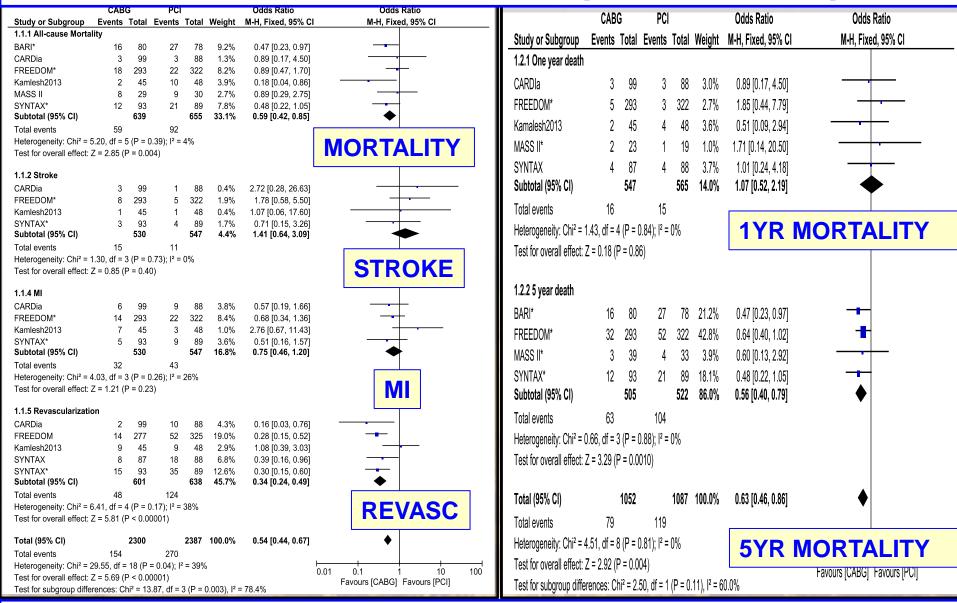
Recommendations according to extent of CAD	CA	ABG	PCI		
Complex CAD should be discussed by Heart Team IC	Class ^a	Level ^b	Class ^a	Level ^b	
One or two-vessel disease without proximal LAD stenosis.	IIb	С	- 1	С	
One-vessel disease with proximal LAD stenosis.	1	A	-	A	
Two-vessel disease with proximal LAD stenosis.	I	В	- 1	С	
Left main disease with a SYNTAX score ≤ 22.	1	В	1	В	
Left main disease with a SYNTAX score 23–32.	1	В	lla	В	
Left main disease with a SYNTAX score >32. 66%	I	В	Ш	В	
Three-vessel disease with a SYNTAX score ≤ 22.	1	Α	- 1	В	
Three-vessel disease with a SYNTAX score 23–32.	ı	A	III	В	
Three-vessel disease with a SYNTAX score >32.	I	A	Ш	В	

CABG superior even although most grafts are veins and despite inferior OMT

State of the Art in Coronary Artery Revascularization: Evidence Basis in 2016 for

- 1 CABG Best in 79% MVD + 66% LM (Guidelines)
- 2 CABG benefits greater in Diabetes and Poor Ventricles
- 3 Importance of Duration of Follow-Up (>5years)
- 4 Importance of Guideline Based Medical Therapy in CABG
- 5 Fundamental pathophysiological difference PCI vs CABG

Coronary artery bypass surgery compared with percutaneous coronary interventions in patients with insulin-treated type 2 diabetes mellitus a systematic review and meta-analysis of 6 randomized controlled trials. PK Bundhun, ZJ Wu, MH Chen [Cardiovasc Diabet 2016]



CABG decreases mortality and repeat revasc (> at 5 yrs); NS for MI and stroke

Effectiveness of Percutaneous Coronary Intervention With Drug-Eluting Stents Compared With Bypass Surgery in Diabetics With Multivessel Coronary Disease: Comprehensive Systematic Review and Meta-analysis of Randomized Clinical Data 2013

Abdul Hakeem, MD; Nadish Garg, MD; Sabha Bhatti, MD; Naveen Rajpurohit, MD; Zubair Ahmed, MD; Barry F. Uretsky, MD

(A)	PCI		CABG			Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
FREEDOM trial	114	953	83	947	37.7%	1.36 [1.04, 1.78]	2012	
SYNTAX TRIAL	44	231	26	221	25.9%	1.62 [1.03, 2.54]	2012	
CARDIA Study	37	254	32	248	26.4%	1.13 [0.73, 1.75]	2013	
VA CARDS	21	101	5	97	9.9%		2013	
Total (95% CI)		1539		1513	100.0%	1.51 [1.09, 2.10]		ne ·
Total events	216		146			- 120 DO DO	X	11.0
Heterogeneity: Tau ² =	0.06; Chi2	= 6.28	df = 3 (P	= 0.10)); 12 = 529	DEATH	m,	0,1 1 10 100
							•	Favors PCI Favors CABG
(B)	PCI		CAB	G		rease w		Favors PCI Favors CABG Risk Ratio
(B) Study or Subgroup	PCI Events	Total		G Total	Weigh	ocrease W	Year	Risk Ratio M-H, Random, 95% CI
		Total	Events	Total	Weip	increase w increase w 	Year 2012	Risk Ratio M-H, Random, 95% CI
Study or Subgroup	Events	Total	Events	Total	Weigh	1.51 [1.09, 2.10] DEATH M rease W 1.51 [1.09, 2.10]	Year 2012 2012	Risk Ratio M-H, Random, 95% CI
SYNTAX TRIAL	Events 28	Total	Events	Total	weigh	ncrease w 1,05 [1.10, 3.87] 1.40 [0.99, 1.97] 2.11 [0.76, 5.86]	Year 2012 2012 2013	Risk Ratio M-H, Random, 95% CI
Study or Subgroup SYNTAX TRIAL FREEDOM trial	Events 28 73	Total	Events	Total	gery	1.57 [1.17, 2.09]		Risk Ratio M-H, Random, 95% CI
Study or Subgroup SYNTAX TRIAL FREEDOM trial VA CARDS	Events 28 73	231 953 101 1285	13 52	Total	weight 9ery 100.0%	1.40 [0.99, 1.97] 2.11 [0.76, 5.86]		Risk Ratio M-H, Random, 95% CI

	Berrei		CABG			Risk Ratio		Risk Ratio		
	events	Total	Events	Total	Weight	M-H, Random, 95% CF	Year	M-H, Rando	om, 95% CI	
Study o	75	231	28	221	25.5%	2.56 [1.73, 3.80]	2012			
FREE	117	953	42	947	26.1%	2.77 [1.97, 3.89]	2012	\$ I	-	
CARDL	57	254	23	248	24.6%	2.42 [1.54, 3.80]	2013	į l	-	
VA CARDS	19	101	29	97	23.8%	0.63 [0.38, 1.04]	2013	2.5 .5.		
Total (95% CI)		1539		1513	100.0%	1.85 [1.00, 3.40]		1	•	
Total events	268		122			DEVACC				
Heterogeneity: Tau*	= 0.34; Chi*	= 25.6	9, df = 3/	(P < 0.0	J001); I* =	88% REVASC		0.01 0.1 1	10 100	
Test for overall effect	t: Z = 1.97 (P = 0.0	(5)	**********					Favors CABG	