Managing multi-vessel disease detected at P-PCI for STEMI:

The **C**omplete **v**ersus **L**esion-only **PR**imary PCI **T**rial **(CvLPRIT)**

Anthony H Gershlick

University Hospitals of Leicester

United Kingdom

On behalf of the CvLPRIT Investigators

Jamal Nasir Khan, Damian J Kelly, John P. Greenwood, Thiagarajah Sasikaran, Nick Curzen ,Daniel J Blackman, Miles Dalby, Kathryn L Fairbrother ,Winston Banya, Duolao Wang, Marcus Flather, Simon L Hetherington, Andrew D Kelion , Suneel Talwar, Mark Gunning, Roger Hall , Howard Swanton ,Gerry P McCann

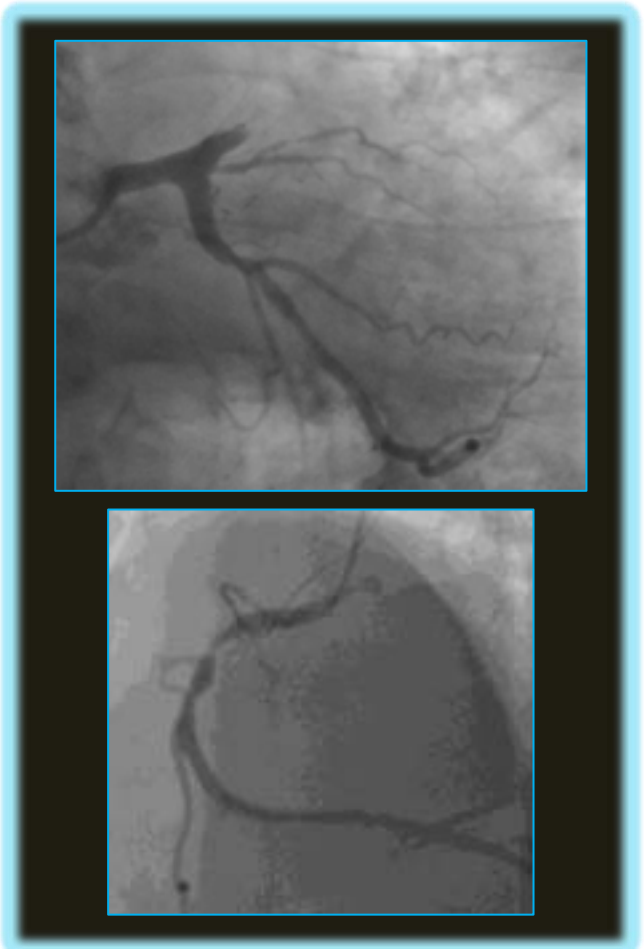
British Heart Foundation

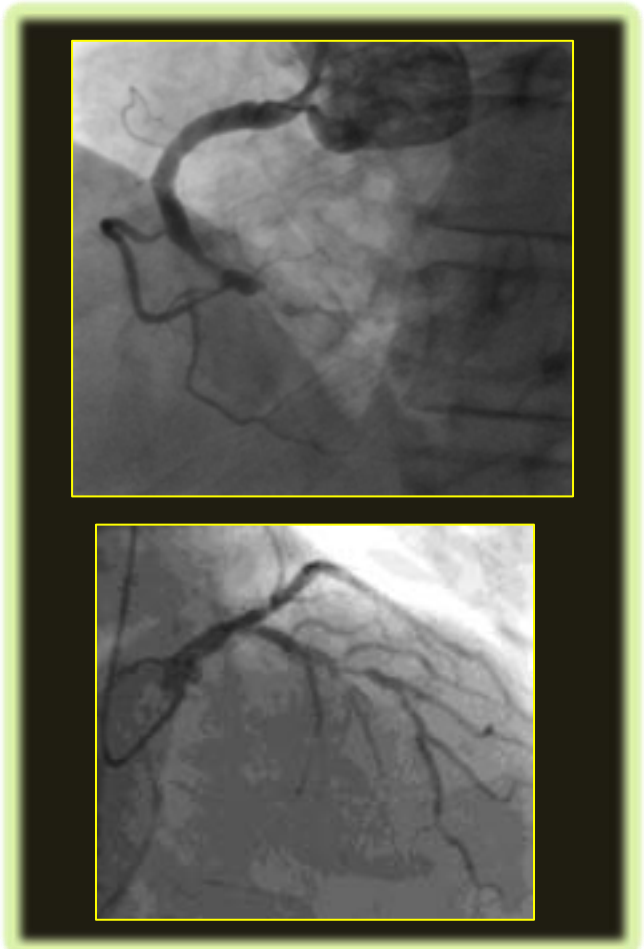
NHS National Institute for Health Research

Multi-vessel Disease in the setting of Primary-PCI seen in 30-40% patients

Muller DW, et al Multivessel coronary artery disease: a key predictor of short-term prognosis after reperfusion therapy for acute myocardial infarction. Thrombolysis and Angioplasty in Myocardial Infarction (TAMI) Study Group. Am Heart J 1991;121:1042-9

Toma M,, et al. Non-culprit coronary artery percutaneous coronary intervention during acute ST-segment elevation myocardial infarction: insights from the APEX-AMI trial. European Heart Journal 2010;31:1701-7





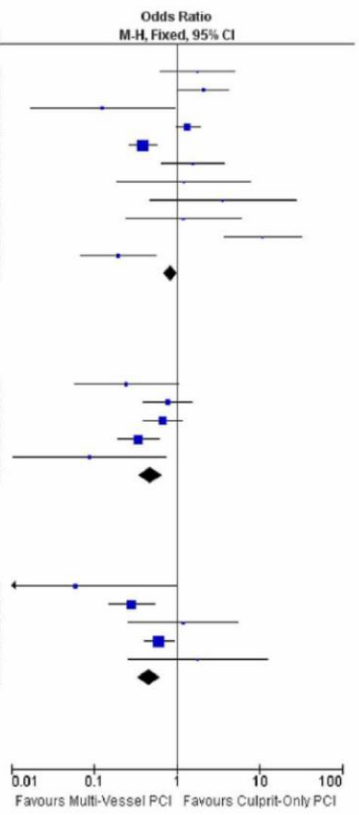
Complete vs culprit-only revascularization for patients with multivessel disease undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction: A systematic review and meta-analysis

Am Heart J 2014;167:1-14.e2

Kevin R. Bainey, MD, MSC,[a] Shamir R. Mehta, MD, MSC,[b] Tony Lai, MBBS,[b] and Robert C. Welsh, MD[a] *Alberta, and Ontario, Canada*

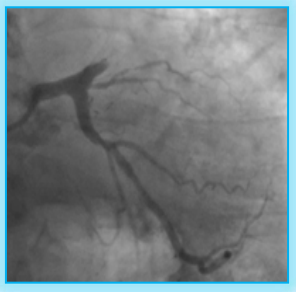
Figure 5

Study or Subgroup	Multi-Vessel PCI Events	Total	Culprit-Only PCI Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
1.21.1 Index Catheterization						
Corpus 2004	5	26	42	354	2.0%	1.77 [0.63, 4.94]
Dziewierz 2010	11	70	57	707	3.8%	2.13 [1.06, 4.27]
Esteves-Loureiro 2010	1	59	25	208	4.8%	0.13 [0.02, 0.95]
Hannan 2010	59	503	116	1300	25.2%	1.36 [0.97, 1.89]
Hudzik 2009	32	457	265	1642	47.3%	0.39 [0.27, 0.57]
Jin 2007	7	215	19	901	3.1%	1.56 [0.65, 3.77]
Khattab 2008	2	25	3	45	0.9%	1.22 [0.19, 7.82]
Mohamad 2009	2	7	3	30	0.4%	3.60 [0.47, 27.35]
Qarawani 2008	9	95	2	25	1.3%	1.20 [0.24, 5.96]
Roe 2001	17	25	10	61	0.8%	10.84 [3.68, 31.90]
Seo 2009	4	82	45	217	10.4%	0.20 [0.07, 0.56]
Subtotal (95% CI)		**1564**		**5490**	**100.0%**	**0.85 [0.70, 1.03]**
Total events	149		587			
Heterogeneity: Chi² = 68.36, df = 10 (*P* < .00001); I² = 85%						
Test for overall effect: Z = 1.66 (*P* = .10)						
1.21.2 Staged - In Hospital						
Barringhaus2010	2	252	30	956	9.8%	0.25 [0.06, 1.04]
Corpus 2004	12	126	42	354	15.7%	0.78 [0.40, 1.54]
Hannan 2010	16	259	116	1300	28.5%	0.67 [0.39, 1.15]
Kalarus 2007	14	193	112	605	39.6%	0.34 [0.19, 0.62]
Rigattieri 2008	1	64	7	46	6.3%	0.09 [0.01, 0.75]
Subtotal (95% CI)		**894**		**3261**	**100.0%**	**0.48 [0.35, 0.67]**
Total events	45		307			
Heterogeneity: Chi² = 7.97, df = 4 (*P* = .09); I² = 50%						
Test for overall effect: Z = 4.41 (*P* < .0001)						
1.21.3 Staged - Elective Outpatient						
Barringhaus2010	0	252	30	956	10.0%	0.06 [0.00, 0.99]
Chen 2010	13	210	66	351	36.3%	0.28 [0.15, 0.53]
Han 2008	3	93	4	148	2.3%	1.20 [0.26, 5.49]
Hannan 2010	30	538	116	1300	50.2%	0.60 [0.40, 0.91]
Mohamad 2009	2	12	3	30	1.1%	1.80 [0.26, 12.41]
Subtotal (95% CI)		**1105**		**2785**	**100.0%**	**0.46 [0.33, 0.64]**
Total events	48		219			
Heterogeneity: Chi² = 9.38, df = 4 (*P* = .05); I² = 57%						
Test for overall effect: Z = 4.70 (*P* < .00001)						
Test for subgroup differences: Chi² = 14.69, df = 2 (*P* = .0006), I² = 86.4%						



Forest plot of long-term mortality stratified by timing of multivessel PCI.

- Trend towards improved long term survival when done during index P-PCI but studies heterogeneous
- Survival benefit when staged



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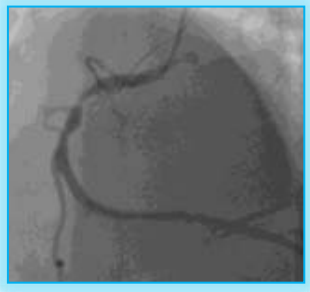


Management of MVD seen during P-PCI remains controversial

- Retrospective registry data and meta-analyses suggest outcomes improved by treating Non Infarct related lesions

- But several questions remain unanswered

? How to judge significance , when to treat etc

- One question :

  If a clinician is presented with angiographically significant stenoses in N-IRA should these be treated on that admission ?

  Retrospective registry data suggest **not** but

PRAMI : reduction of 65 % MACE with total revascularisation **at time P-PCI**

** Wald DS, **PRAMI** Investigators. N Engl J Med. 2013 369 :1115-23.*

- **CvLPRIT** initiated at similar time –circa 2008 - both asked similar trial questions but distinctive differences

ISRCTN 70913605

CvLPRIT

UK open-label randomised study
comparing

treatment of IRA only
with
complete revascularisation at index admission

randomisation was stratified for
- site of infarct (anterior/non-anterior)
- symptom onset to balloon time (< or >3 hours)

included CMR and nuclear sub-studies

: The primary endpoint was MACE :
composite of total mortality, recurrent MI, heart failure and ischaemia-driven revascularisation at 12 months

Inclusion criteria

Suspected or proven acute myocardial infarction; Significant ST elevation or left bundle branch block (LBBB) on ECG (in cases of LBBB, angiographic confirmation of IRA occlusion is required)

< 12 hrs of symptom onset

Scheduled for Primary PCI for clinical reasons

Provision of verbal assent followed by written informed consent

Multi-vessel coronary artery disease at angiography defined as:

Infarct related artery (IRA) plus at least one non-infarct related epicardial artery (N-IRA) with at least one lesion deemed angiographically significant (>70% diameter stenosis in one plane or > 50% in 2 planes).

The N-IRA should be **a major (>2mm) epicardial** coronary artery or **branch (>2mm)** and be suitable for stent implantation.

Exclusion criteria

Any exclusion criteria for PPCI

< 18 years age

Clear indication for, or contraindication to, multi vessel PPCI according to operator judgement

Previous Q wave myocardial infarction

Patients with prior CABG

Cardiogenic Shock

VSD or moderate/severe mitral regurgitation

Chronic kidney disease (Cr>200µmol/l or eGFR<30ml/min/1.73m^2)

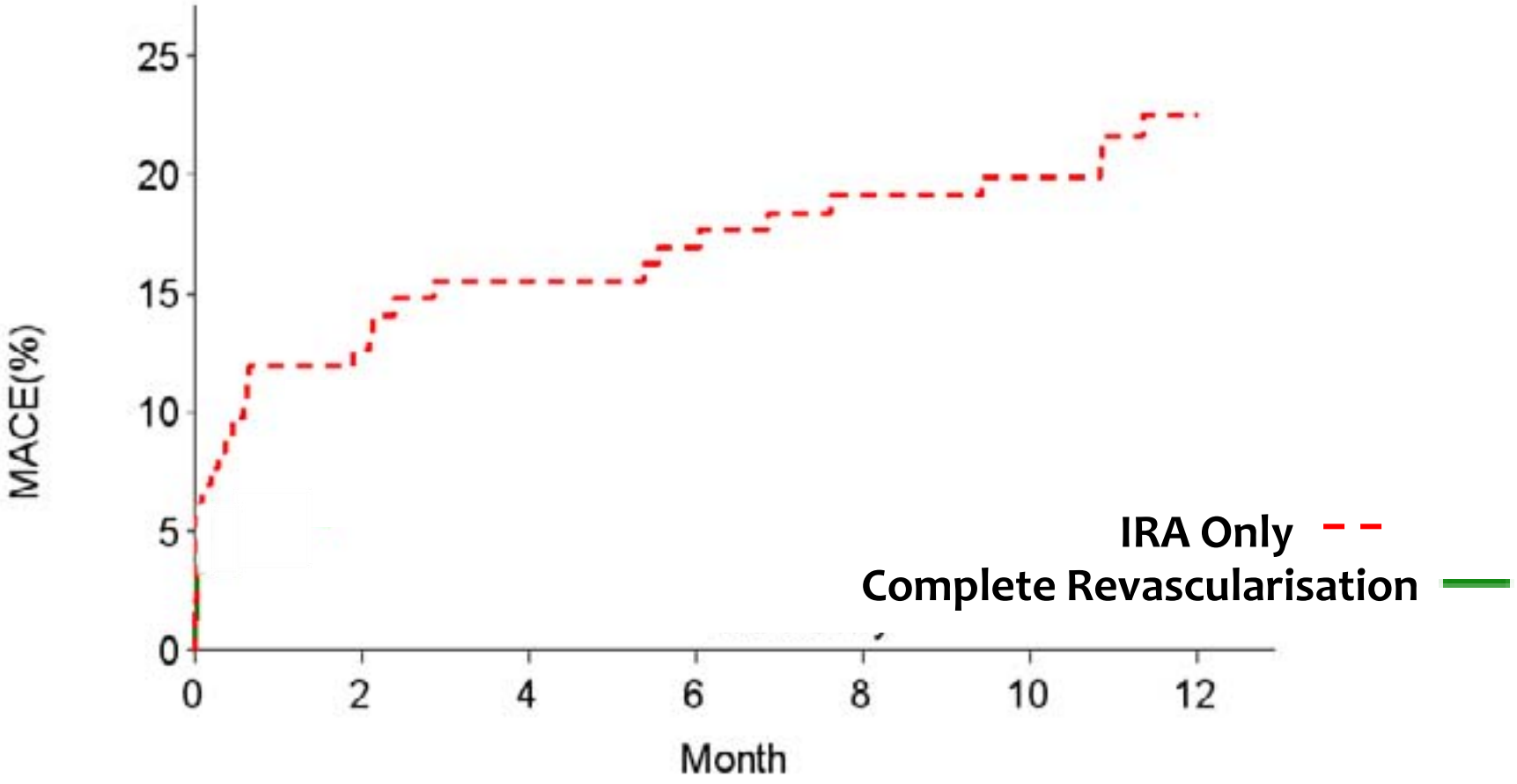
Suspected or confirmed thrombosis of a previously stented artery

Where the only significant N-IRA lesion is a chronic total occlusion

RESULTS

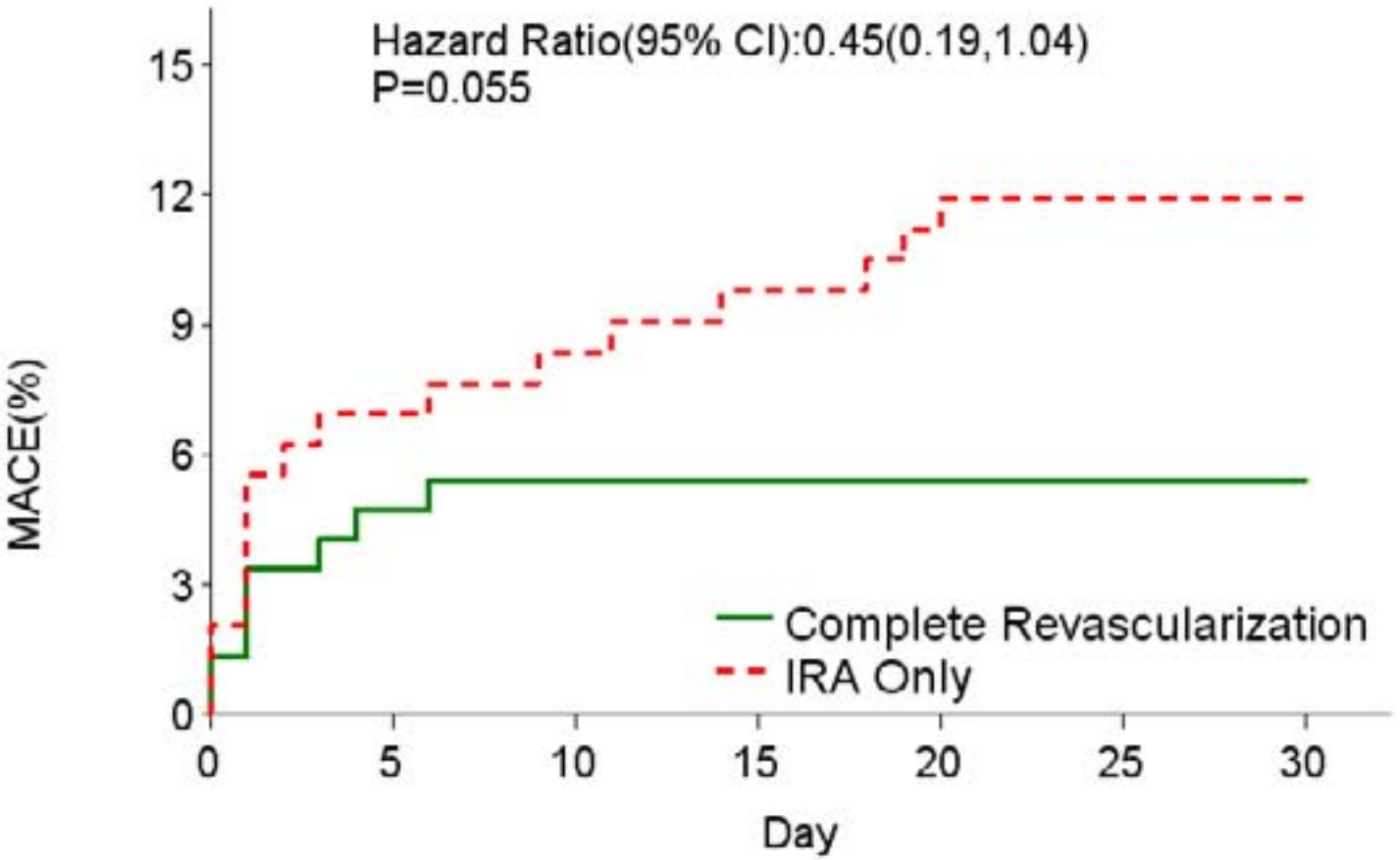
Results 1: Percent MACE at 12 months

The primary endpoint composite of total mortality, recurrent MI, heart failure and ischaemia-driven revascularisation at 12 months



Variable	IRA only (N=146)	Complete Revascularisation (N=150)	HR (95% CI)	P value
Time to First Event				
MACE N= (%)	31 (21.2)	15 (10.0)	0.45 (0.24, 0.84)	0.009
Components N=(%)				
All-cause mortality	6 (4.1)	2 (1.3)	0.32 (0.06, 1.60)	0.14
Recurrent MI	4 (2.7)	2 (1.3)	0.48 (0.09, 2.62)	0.39
Heart failure	9 (6.2)	4 (2.7)	0.43 (0.13, 1.39)	0.14
Repeat Revascularisation	12 (8.2)	7 (4.7)	0.55 (0.22, 1.39)	0.2

MACE to 30 days



Number at risk:						
Complete:150	136	133	133	133	133	133
IRA Only:146	131	128	126	124	123	123

Summary and Conclusions

CvLPRIT demonstrated 55% reduction in MACE in those patients presenting for P-PCI when Non-IRA artery is also treated on index admission

With no adverse safety signal

Hard events (death, MI, HF) similarly reduced (5 v 13%) compared to repeat revascularisation (4.7% v 8.2%)

- Indicates in-hospital treatment of the N-IRA seen during P-PCI results in improved clinical outcomes
- Suggests this strategy may be need to be considered by future STEMI Guideline Committees

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Independent Chair
H Swanton
Independent members
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G. Thompson (Lay member)
D.Hetmanski (UHL Trial Sponsor)

Data Safety and Monitoring Board:
R. Hall (Chair)
T. Gilbert
M. Roughton

Clinical Trials and Evaluation Unit
(Imperial College)
T. Sasikaran Winston Banya
Senior CTEU Advisor
M. Flather
(University East Anglia)

Statisticians:
Winston Banya
Duolao Wang
(Liverpool School of Tropical Medicine)

Coordinating Centre (Royal Brompton):
T.Sasikaran,
M. Yanez-Lopez,
W. Aslam,
D. Babalis,
E. Matesanz,
E. Zbrzeska,
N. Lago,
J. Booth,
F. Nugara,

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Thank you for your attention

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Reserve slide 1

Variable	IRA only	Multi-vessel PCI IRA plus N-IRA	HR (95% CI)	P
MACE	28/138 (20.3)	9/136 (6.6)	0.31 (0.15, 0.65)	0.0011
All-cause mortality	5/138 (3.6)	1/136 (0.7)	0.20 (0.02, 1.73)	0.106
Recurrent MI	4/138 (2.9)	2/136 (1.5)	0.50 (0.09, 2.74)	0.418
Heart failure	7/138 (5.1)	3/136 (2.2)	0.43 (0.11, 1.66)	0.207
Repeat Revasc	12/138 (8.7)	3/136 (2.2)	0.24 (0.07, 0.85)	0.016
CV mortality	3/138 (2.2)	1/136 (0.7)	0.33 (0.03, 3.22)	0.343
Stroke	2/138 (1.4)	1/136 (0.7)	0.50 (0.04, 5.47)	0.559
Major Bleed	6/138 (4.3)	3/136 (2.2)	0.50 (0.12, 1.99)	0.314

Clinical Outcomes (Primary Endpoint) at 12 months (Per Protocol Population)
(Mace – Death, MI, HF, Revascularisation)

Reserve slide 2

ITT Population				
Variable	IRA only	Multi-vessel PCI IRA plus N-IRA	HR (95% CI)	P
All-cause mortality or Recurrent MI	14/146 (9.6)	6/150 (4.0)	0.41 (0.16, 1.07)	0.060

Clinical Outcomes at 12 months: (Death or Recurrent MI)

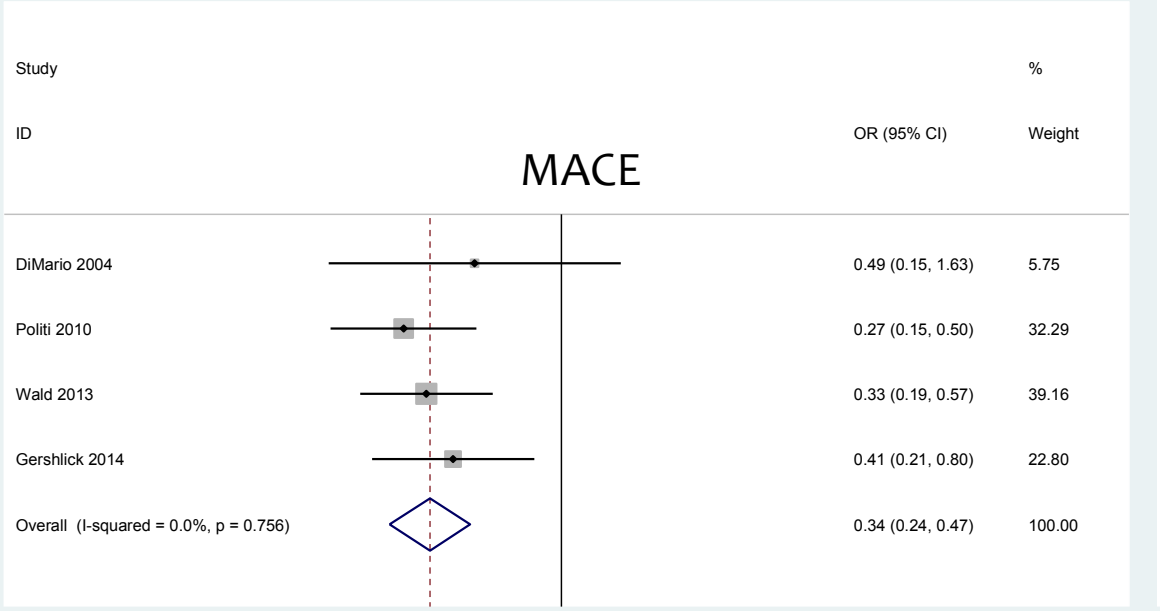
Reserve slide 3

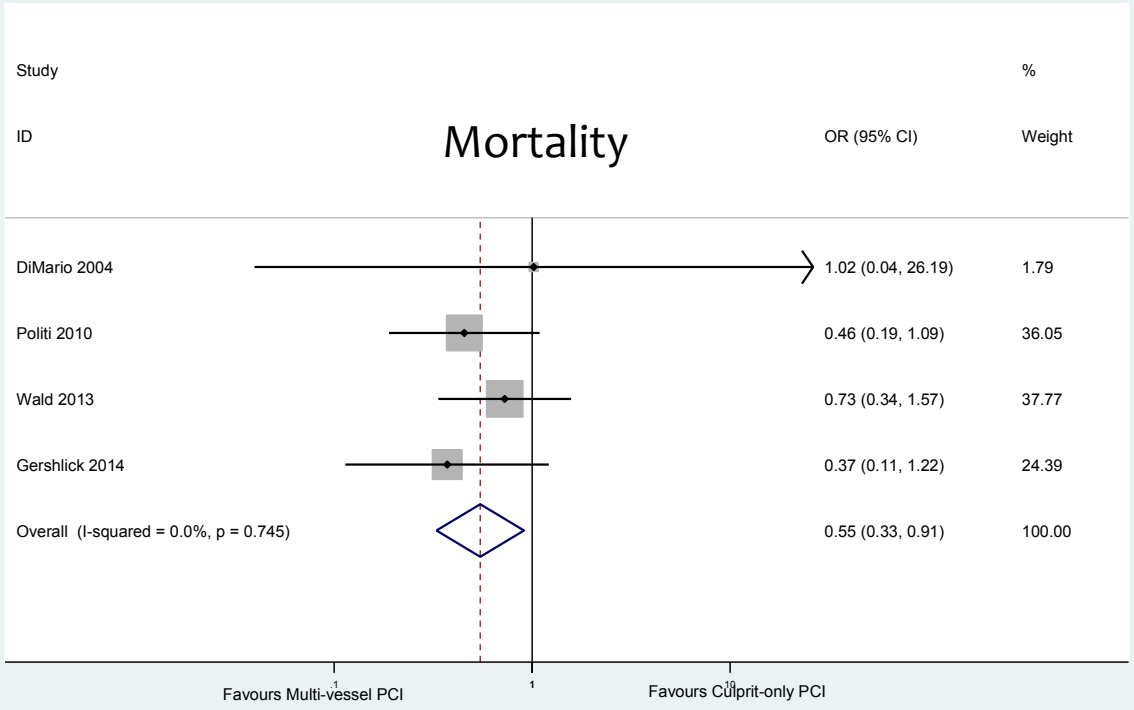
Excluding crossovers, N-IRA PCI was undertaken at the same sitting as the P-PCI in 89/150 (59 %) of patients while 41/150 (27%) were undertaken as a staged procedure, at a median time 1.5 days post-admission

Variable	IRA only	Multi-vessel PCI at same sitting as IRA	HR (95% CI)	P
MACE	28/138 (20.3)	7/89 (7.9)	0.39 (0.10, 0.55)	0.012

Variable	IRA only	Multi-vessel PCI staged prior to discharge	HR (95% CI)	P
MACE	28/138 (20.3)	8/41 (19.5)	0.96 (0.80, 1.22)	0.913

Clinical outcomes at 12 months: Immediate or delayed (staged IP) N-IRA PCI


Study
ID
MACE
OR (95% CI)
%
Weight
DiMario 2004
0.49 (0.15, 1.63)
5.75
Politi 2010
0.27 (0.15, 0.50)
32.29
Wald 2013
0.33 (0.19, 0.57)
39.16
Gershlick 2014
0.41 (0.21, 0.80)
22.80
Overall (I-squared = 0.0%, p = 0.756)
0.34 (0.24, 0.47)
100.00


Study
ID
Mortality
OR (95% CI)
%
Weight
DiMario 2004
1.02 (0.04, 26.19)
1.79
Politi 2010
0.46 (0.19, 1.09)
36.05
Wald 2013
0.73 (0.34, 1.57)
37.77
Gershlick 2014
0.37 (0.11, 1.22)
24.39
Overall (I-squared = 0.0%, p = 0.745)
0.55 (0.33, 0.91)
100.00
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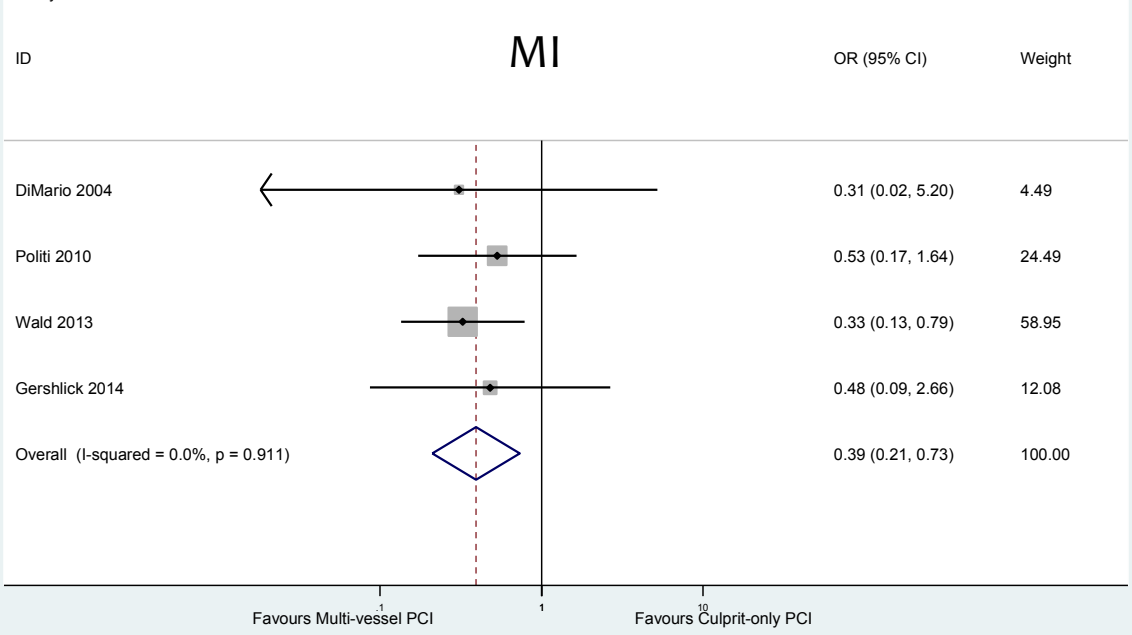
Favours Multi-vessel PCI
Favours Culprit-only PCI


MI
ID
OR (95% CI)
Weight
DiMario 2004
0.31 (0.02, 5.20)
4.49
Politi 2010
0.53 (0.17, 1.64)
24.49
Wald 2013
0.33 (0.13, 0.79)
58.95
Gershlick 2014
0.48 (0.09, 2.66)
12.08
Overall (I-squared = 0.0%, p = 0.911)
0.39 (0.21, 0.73)
100.00
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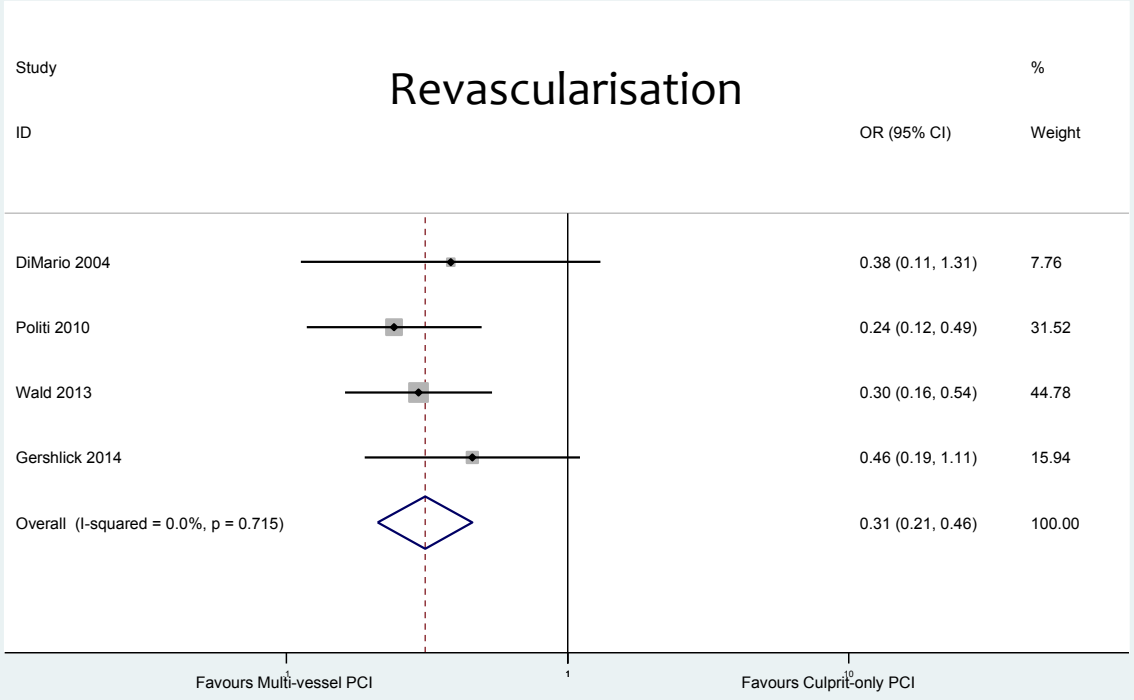
Favours Multi-vessel PCI
Favours Culprit-only PCI


Study
Revascularisation
%
ID
OR (95% CI)
Weight
DiMario 2004
0.38 (0.11, 1.31)
7.76
Politi 2010
0.24 (0.12, 0.49)
31.52
Wald 2013
0.30 (0.16, 0.54)
44.78
Gershlick 2014
0.46 (0.19, 1.11)
15.94
Overall (I-squared = 0.0%, p = 0.715)
0.31 (0.21, 0.46)
100.00
.1
1
10
Favours Multi-vessel PCI
Favours Culprit-only PCI