Percutaneous Coronary Intervention as Revascularisation Strategy in Advanced Chronic Kidney Disease

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Stages of Chronic Kidney Disease

Stage	Description	GFR (mL/min/1.73 m²)
1	Kidney damage with normal or GFR	≥ 90
2	Kidney damage with mild GFR	89-60
3A	Mild to moderate GFR	59-45
3B	Moderate GFR	45-30
4	Severe GFR	30-15
5	Kidney failure	< 15 or dialysis

CKD, chronic kidney disease; GFR, glomerular filtration rate.

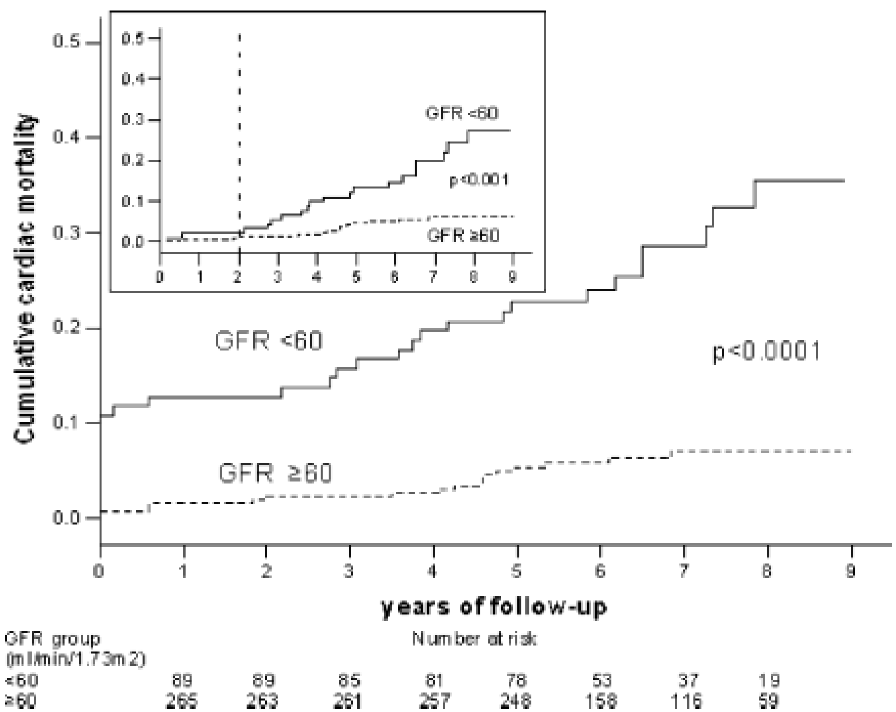
CKD (stages 2–5)

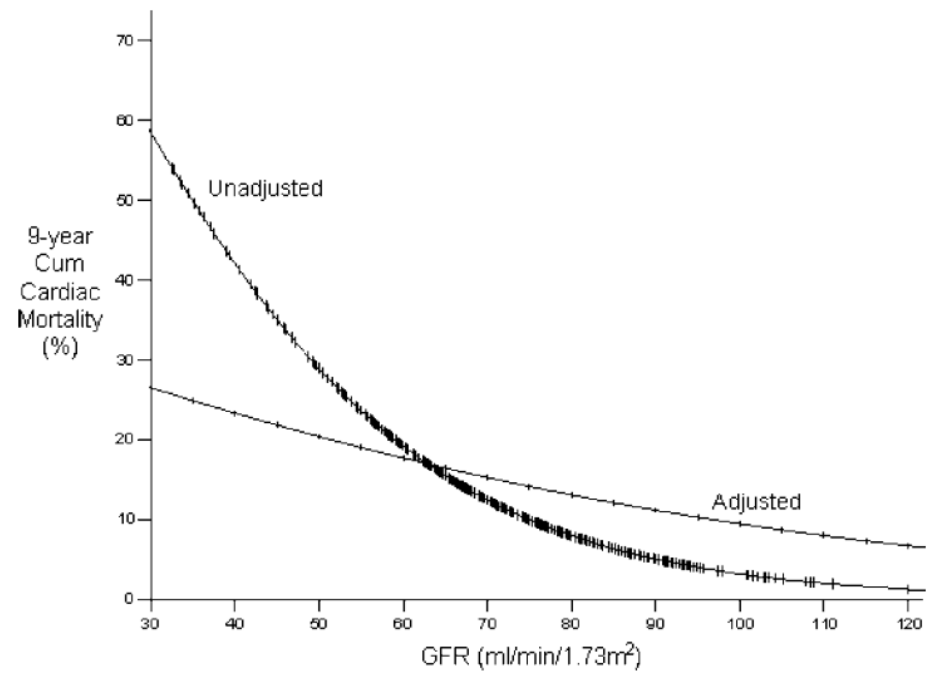
ESRF (stage 5)

Renal Association (www.renal.org). Accessed Feb 2019

Worse Outcomes After PCI in CKD patients

Correlation with eGFR level

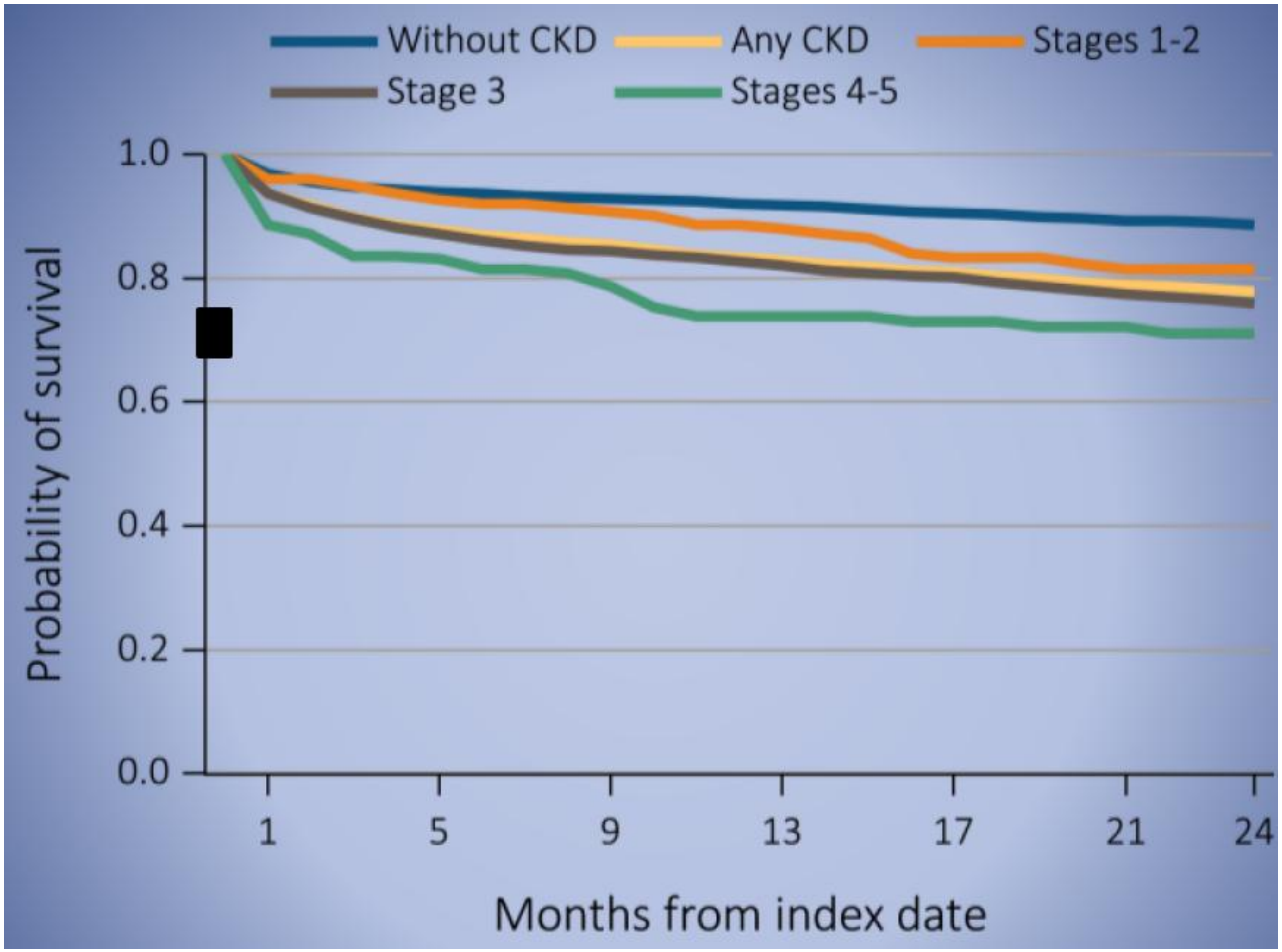




Papafaklis M et al. *Cather Cardiovasc Intv* 2007; 69:189-97

Worse Outcomes After CABG in CKD patients

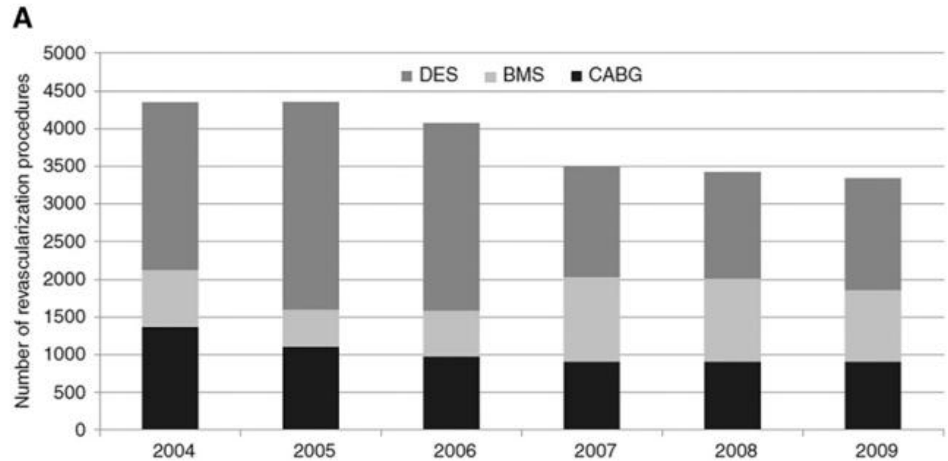
Association with CKD Stage



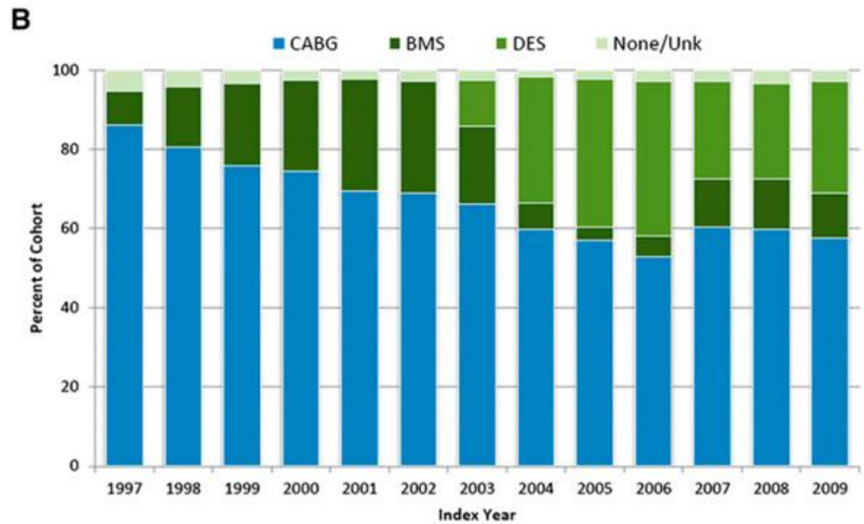
US Medicare. 2016 Annual Data Report

Trends in Coronary Revascularization in End-Stage Renal Failure

Trends in Coronary Revascularization



Trends in Multivessel Revascularization



Chang T et al. *J Am Soc Nephrol* 2012; 23:2042-49

PCI as an Option of Revascularization in Advanced CKD patients

Is there any difference between PCI and CABG in Mortality and Adverse Events in the short and long term ?

Is there any difference between PCI and CABG in Acute Kidney Injury?

Advanced CKD Under-Represented in Contemporary Revascularization vs. Medicine SIHD trials

- BARI-2D: Subjects with creatinine >2 mg/dl excluded

- COURAGE: Only 16 patients with GFR <30 ml/min

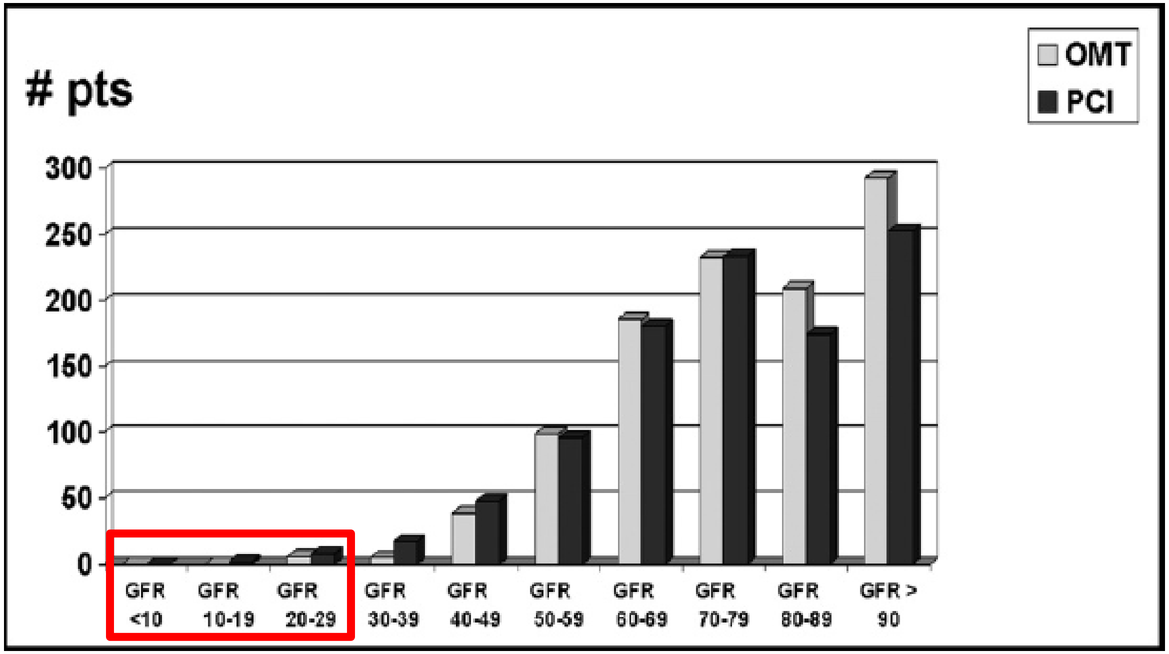


Figure 1. Distribution of GFR by treatment group.

Sedlis et al. *Am J Cardiol* 2009;104:1647–1653

CKD is Under Represented in RCTs for CABG vs PCI

Study	Sample Size	Diabetes % (CABG)/(PCI)	CKD% (CABG)/(PCI)
ARTS (2005)	1,174	16/19	Not reported ("Severe" renal failure was exclusion)
MASS II (2007)	408	29/23	Not reported
SOS (2008)	988	15/14	Not reported
CARDIA (2010)	490	100/100	4.0/5.5
SYNTAX (2011)	1,095	35/36	7.3/4.1 (data not reported in primary study)
FREEDOM (2012)	1,900	100/100	6.7% (overall) Severe CKD and ESRF excluded

Prasad A. *TCT* 2017

Randomized Controlled Trials of Revascularization Strategy in Patients with CKD and Multivessel CAD

0

- Forces us to
  - Infer outcomes from general studies on PCI vs CABG
  - Use diabetes as a surrogate (conflate / extrapolate results)
  - Look at non-randomized data

Prasad A. *TCT* 2018

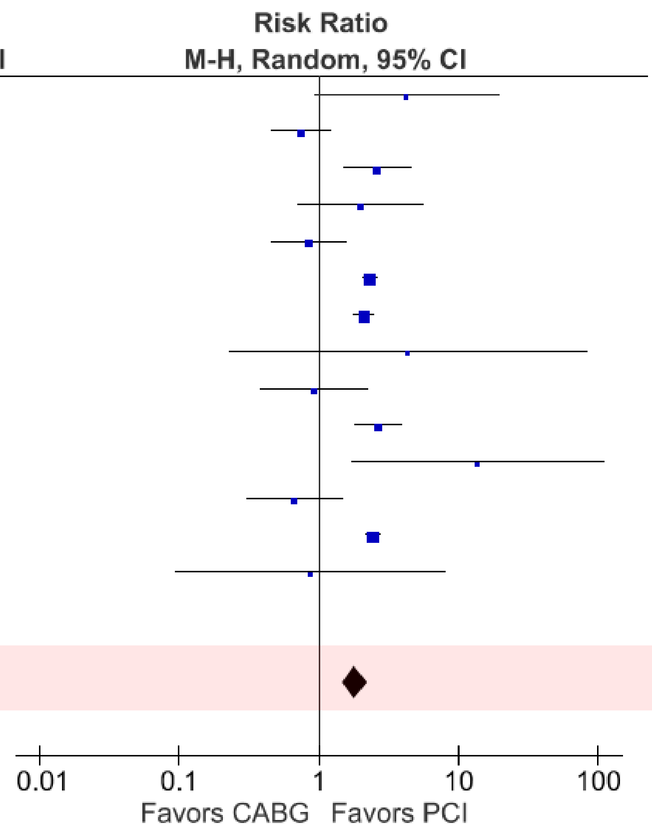
Meta-analysis of 58 studies
≈55000 CKD patients with Revascularization

PCI advantage over CABG for Short-term Mortality

Study or Subgroup	CABG Events	CABG Total	PCI Events	PCI Total	Weight	Risk Ratio M-H, Random, 95% CI
Agirbasli 2000	9	130	2	122	1.8%	4.22 [0.93, 19.16]
Chan 2015	28	893	38	893	9.1%	0.74 [0.46, 1.19]
Charytan 2006	23	130	22	322	8.0%	2.59 [1.50, 4.48]
CREDO-Kyoto 2014	7	130	7	258	3.4%	1.98 [0.71, 5.54]
Eisenstein 2009	18	469	21	462	7.0%	0.84 [0.46, 1.56]
Herzog 1999	930	7419	371	6887	16.3%	2.33 [2.07, 2.61]
Herzog 2002	572	6668	175	4280	15.5%	2.10 [1.78, 2.47]
Ivens 2001	3	65	0	40	0.5%	4.35 [0.23, 82.05]
Khoso 2014	8	74	10	85	4.4%	0.92 [0.38, 2.21]
MIDAS 2012	45	536	52	1649	10.9%	2.66 [1.81, 3.92]
Ohmoto 1999	7	47	1	92	1.0%	13.70 [1.74, 108.11]
Oyama 2013	6	35	31	120	5.1%	0.66 [0.30, 1.46]
Shroff 2013	507	6178	573	16855	16.3%	2.41 [2.15, 2.71]
Sunagawa 2010	1	29	3	75	0.9%	0.86 [0.09, 7.95]
Terazawa 2012	0	67	0	58		Not estimable
Total (95% CI)		**22870**		**32198**	**100.0%**	**1.81 [1.47, 2.24]**
Total events	2164		1306			

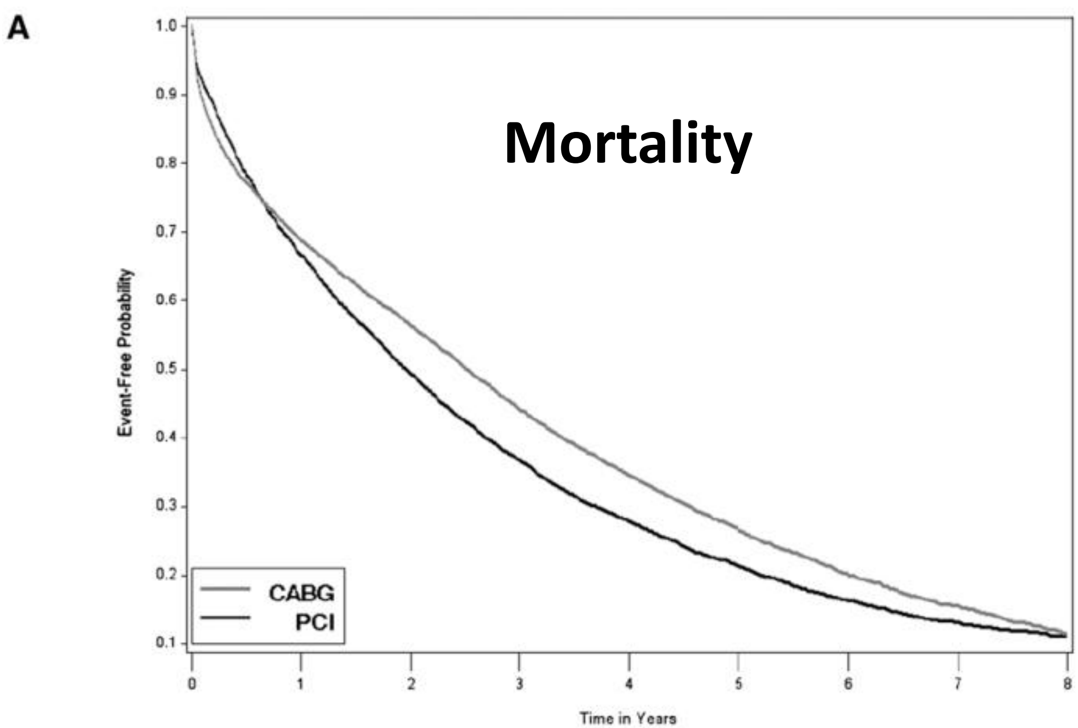
Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 51.57$, df = 13 ($P < 0.00001$); $I^2 = 75\%$

Test for overall effect: $Z = 5.51$ ($P < 0.00001$)



Volodarskiy A et al. *Am J Med* 2016; 129:1288-98

US Renal Data System (USRDS)
PCI or CABG between 1997-2009 for MVD in Patients on Dialysis (N=21,981)



	6 months	1 year	2 years	5 years	Overall
HR CABG vs. PCI (95% CI)	1.08 (1.01-1.16)	0.96 (0.90-1.02)	0.86 (0.82-0.90)	0.90 (0.86-0.93)	0.88 (0.85- 0.92)

LIMITATIONS

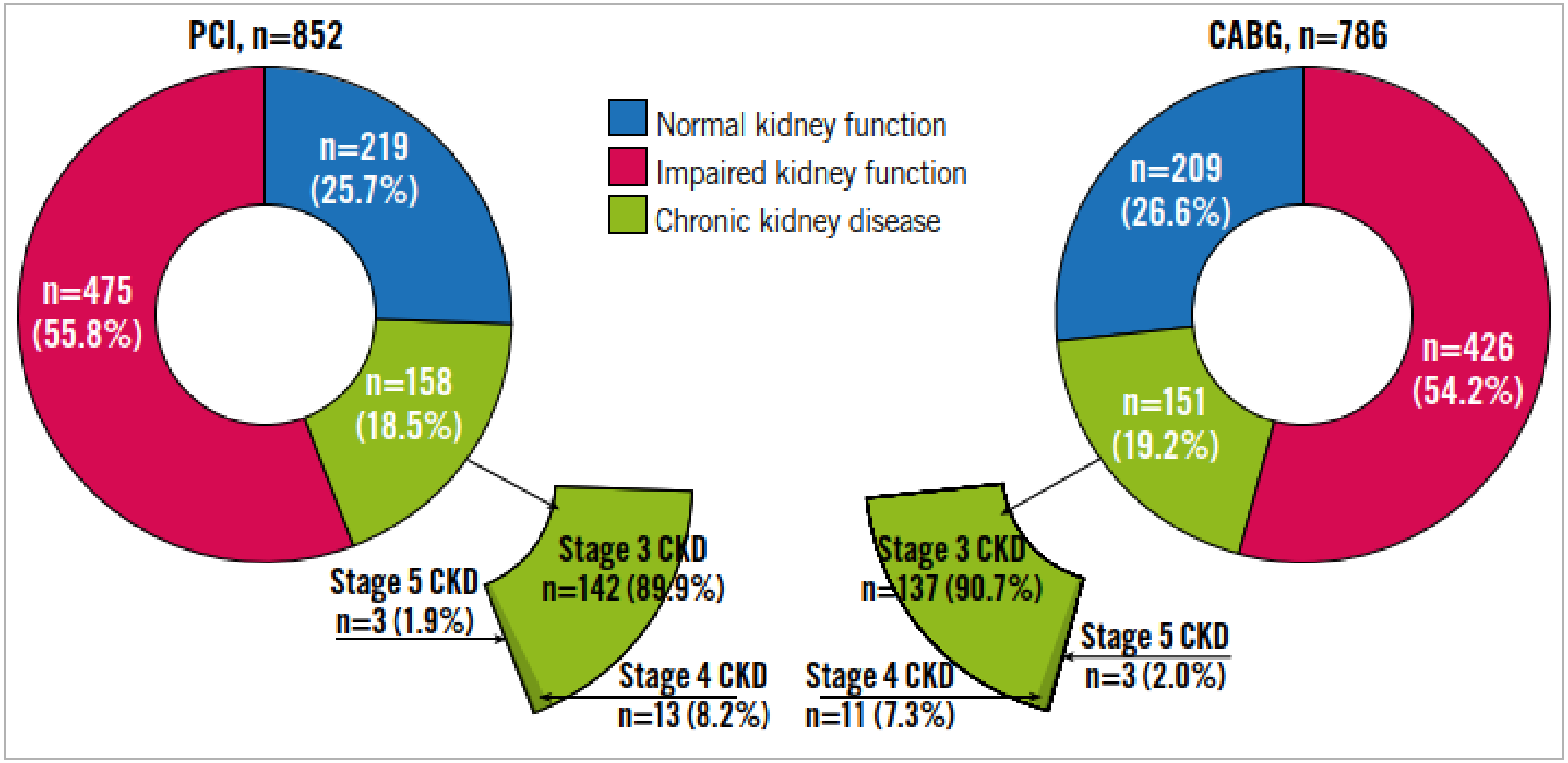
- Observational study without randomization
- Medicare claims data and ICD-9 used for comorbid conditions
- No details of coronary anatomy
- No information on medication
- BMS and 1st generation DES in PCI

Chang T et al. *J Am Soc Nephrol* 2012; 23:2042-49

SYNTAX substudy - CKD: 5-year outcomes

1st generation DES (Taxus)

309 patients with CKD

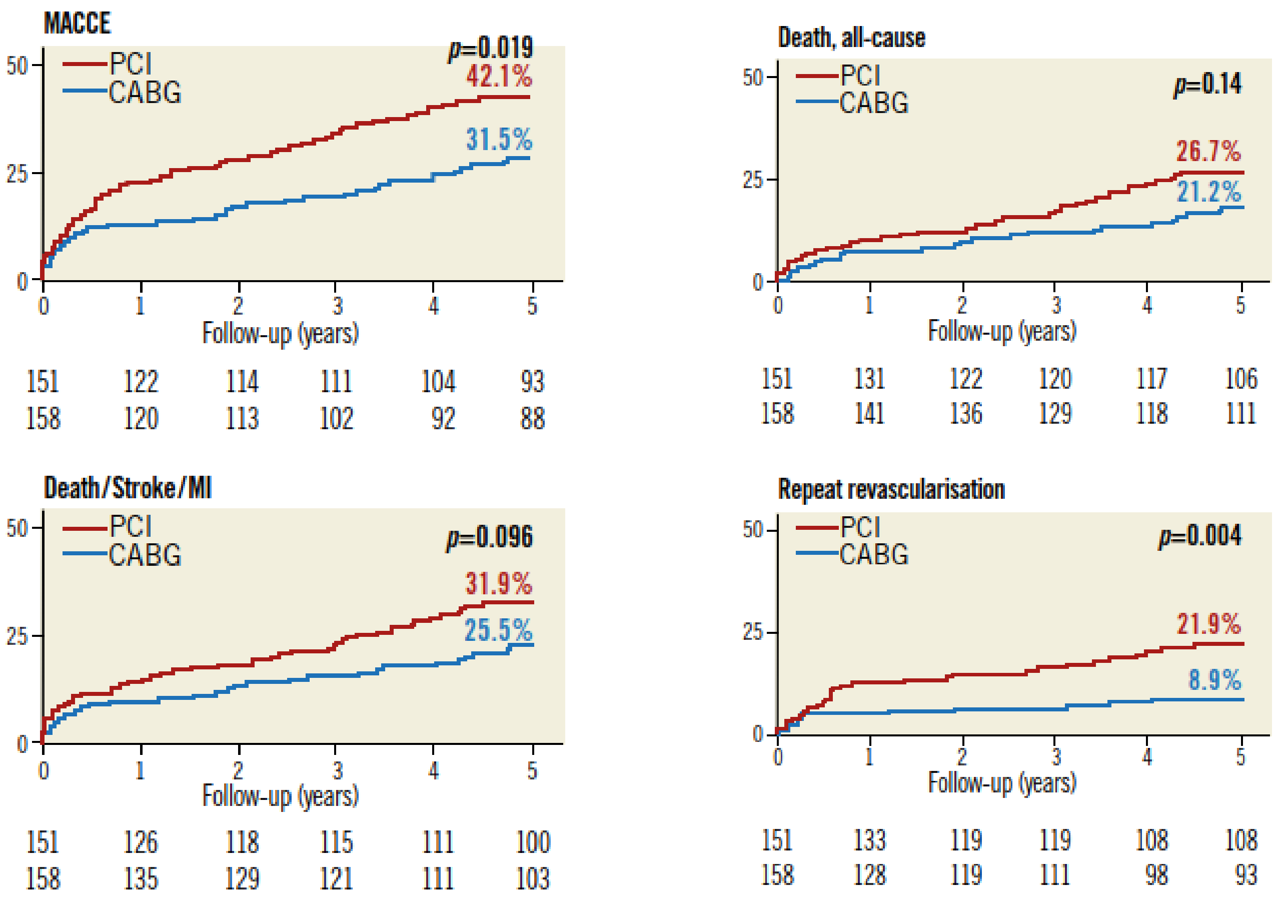


Milojevic M et al. *EuroIntervention* 2018; 14:102-111

SYNTAX substudy - CKD: 5-year outcomes

1st generation DES (Taxus)

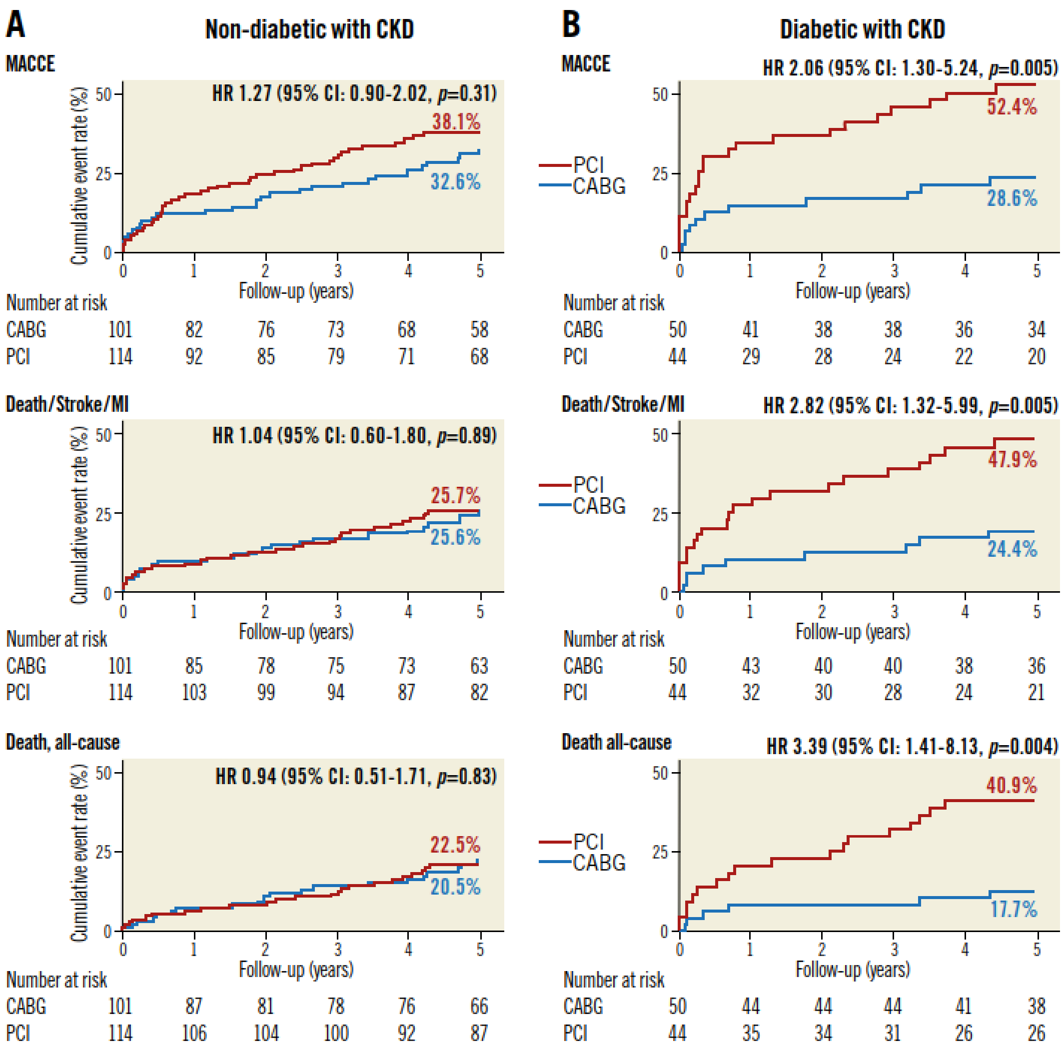
Comparable outcomes for Death/Stroke/MI
Difference in MACCE driven by Repeat Revascularization



Milojevic M et al. *EuroIntervention* 2018; 14:102-111

SYNTAX substudy - CKD: 5-year outcomes

1st generation DES (Taxus)



Negative impact of CKD stronger in PCI compared to CABG especially in **Diabetic patients**

Milojevic M et al. *EuroIntervention* 2018; 14:102-111

Syntax Score II

Creatinine clearance showed weak interaction effects in influencing long-term (4-year) mortality predictions with CABG and PCI

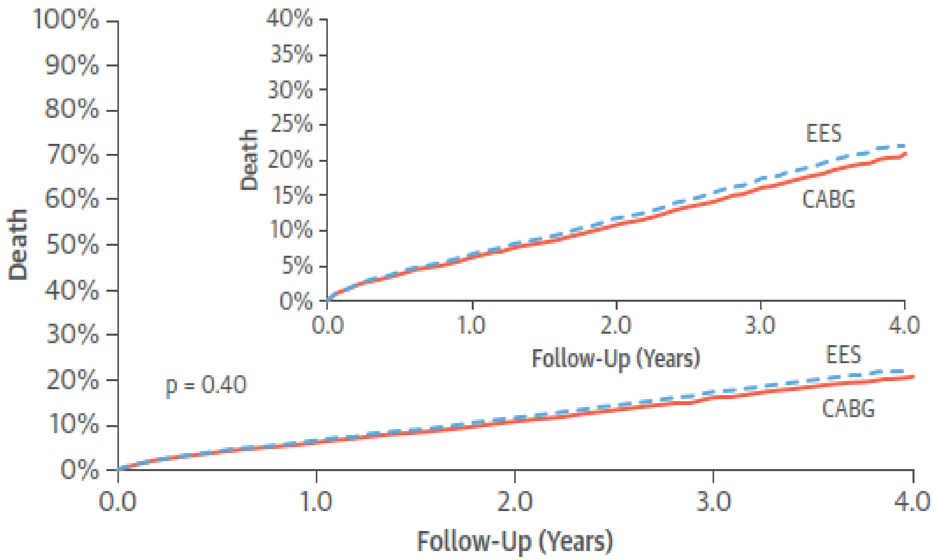
	Multivariable adjusted HR (95% CI)		Interaction effect (HR_{PCI}/HR_{CABG}); HR (95% CI; p value)
	CABG 4-year mortality	PCI 4-year mortality	
Development population , SYNTAX trial (n=1800)			
Anatomical SYNTAX score (per 10 point increase)	0·97 (0·79–1·18)	1·27 (1·08–1·50)	1·32 (1·01–1·71; p=0·039)
Age (per 10 year increase)	1·88 (1·34–2·64)	1·29 (0·97–1·71)	0·69 (0·44–1·07; p=0·095)
Creatinine clearance† (per 10 mL/min increase)	0·91 (0·77–1·07)	0·82 (0·72–0·93)	0·89 (0·73–1·10; p=0·30)
LVEF (per 10% increase)	0·84 (0·61–1·16)	0·56 (0·43–0·73)	0·67 (0·44–1·00; p=0·053)
Peripheral vascular disease*	2·79 (1·66–4·71)	2·79 (1·72–4·53)	1·00 (0·49–2·04; p=1·00)
ULMCA disease	1·47 (0·93–2·34)	0·82 (0·54–1·23)	0·56 (0·30–1·03; p=0·062)
Women	0·59 (0·32–1·10)	1·70 (1·11–2·60)	2·87 (1·35–6·07; p=0·0059)
COPD	2·84 (1·64–4·90)	1·35 (0·74–2·47)	0·48 (0·21–1·08; p=0·074)
External validation population, DELTA registry (n=2891)			
Anatomical SYNTAX score (per 10 point increase)	1·12 (0·95–1·32)	1·32 (1·20–1·46)	1·18 (0·98–1·42; p=0·083)
Age (per 10 year increase)	1·46 (1·15–1·85)	1·34 (1·19–1·52)	0·92 (0·70–1·21; p=0·56)
Creatinine clearance (per 10 mL/min increase)	0·91 (0·78–1·06)	0·93 (0·86–1·00)	1·02 (0·86–1·21; p=0·82)
LVEF (per 10% increase)	0·59 (0·47–0·75)	0·57 (0·50–0·65)	0·96 (0·72–1·27; p=0·75)
Peripheral vascular disease	1·37 (0·68–2·79)	1·77 (1·01–3·09)	1·29 (0·51–3·22; p=0·59)
Women	0·52 (0·31–0·87)	1·09 (0·82–1·46)	2·09 (1·16–3·76; p=0·014)
COPD	3·63 (1·31–10·04)	1·97 (0·88–4·42)	0·54 (0·20–1·47; p=0·23)

Farooq V et al. *Lancet* 2013; 381:639-50

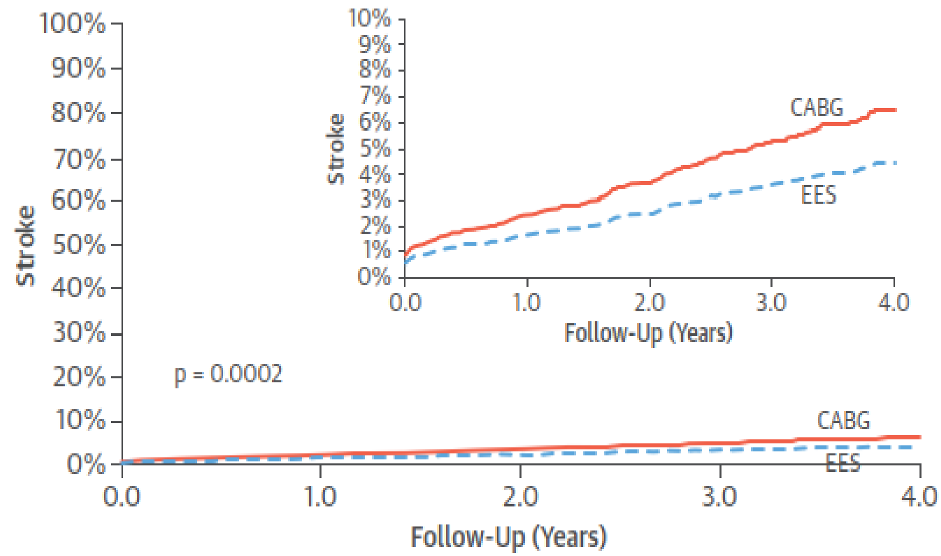
Revascularization in Patients With Multivessel Coronary Artery Disease and Chronic Kidney Disease

Everolimus-Eluting Stents Versus Coronary Artery Bypass Graft Surgery

5920 patients
eGFR<60ml/min & MVD
Propensity-matched Analysis



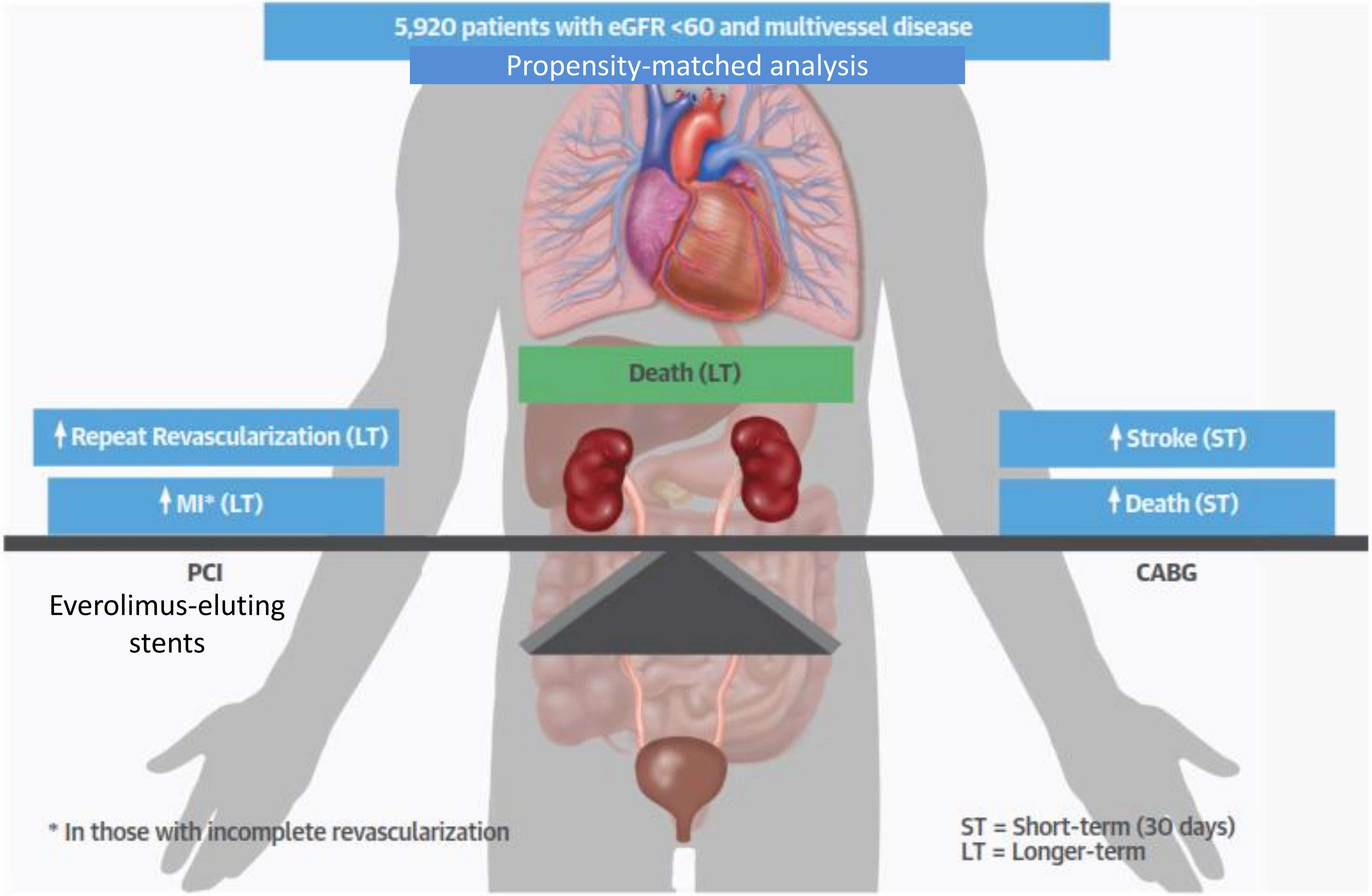
No. at Risk	0.0	1.0	2.0	3.0	4.0
EES	2,960	2,775	1,865	986	274
CABG	2,960	2,770	2,093	1,396	679



No. at Risk	0.0	1.0	2.0	3.0	4.0
EES	2,960	2,741	1,832	961	265
CABG	2,960	2,709	2,033	1,341	650

Bangalore S et al. *JACC* 2015; 66:1209-20

PCI (EES) vs CABG for MVD in CKD



Bangalore S et al. *JACC* 2015; 66:1209-20

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 73, NO. 4, 2019

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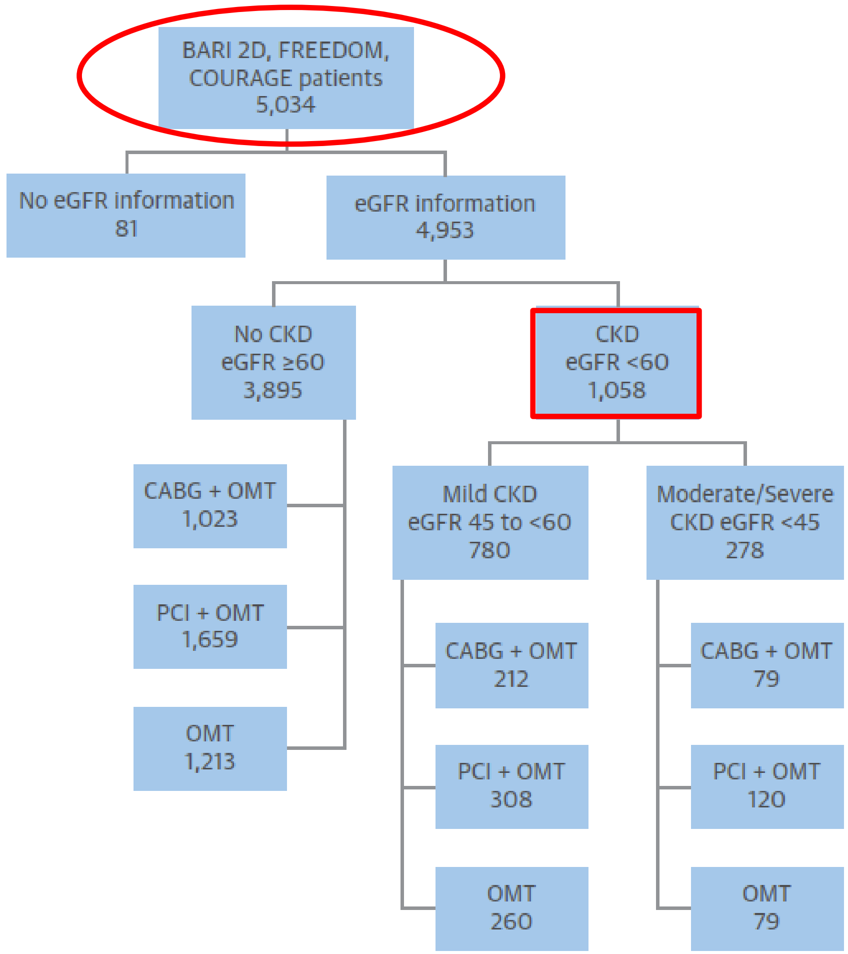
Impact of Chronic Kidney Disease on Outcomes of Myocardial Revascularization in Patients With Diabetes



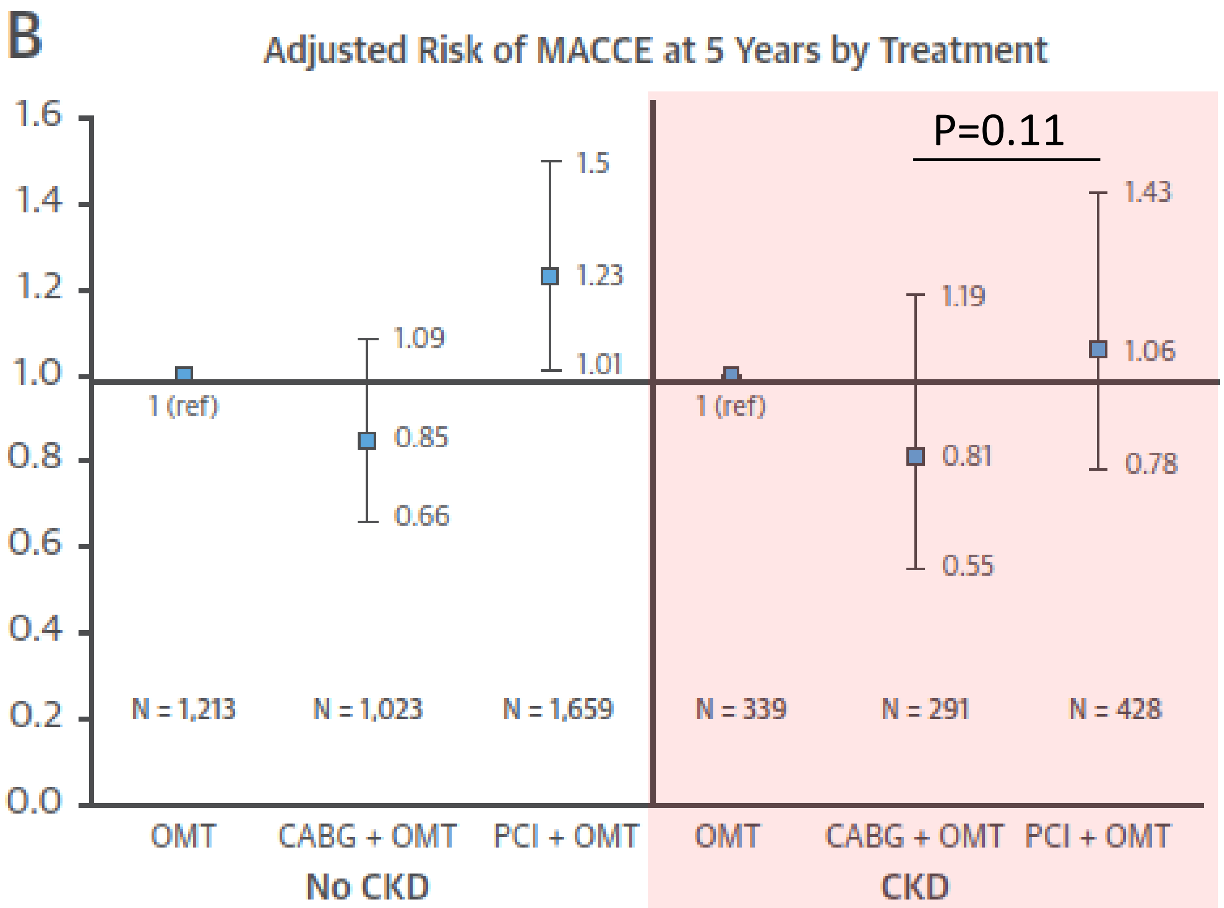
Limitations

- Older alongside newer generation of stents
- No data on cause of death
- Relatively small subgroup of severe CKD

Farkouh M et al. *JACC* 2019; 73:400-11

Pooled analysis in Diabetic Patients with Stable Coronary Artery Disease

MACCE



No significant differences in MACCE between CABG and PCI for patients with DM and CKD on optimal medical therapy

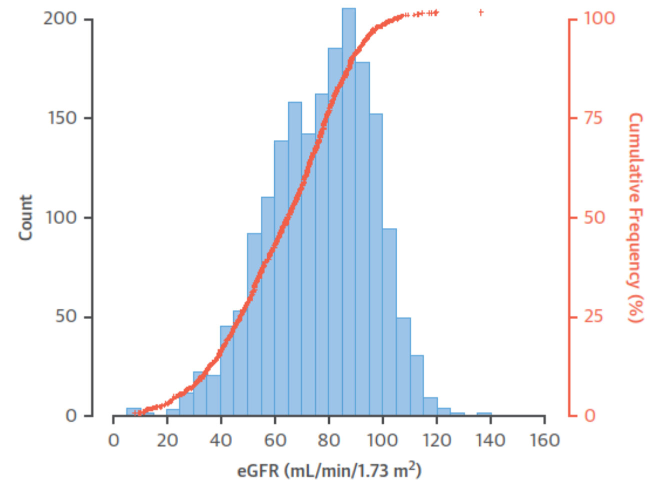
Farkouh M et al. *JACC* 2019; 73:400-11

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 72, NO. 7, 2018

Left Main Revascularization With PCI or CABG in Patients With Chronic Kidney Disease

EXCEL Trial

- Significant LM disease
- Syntax Score ≤32
- Everolimus-eluting stents used during PCI



Distribution of eGFR in EXCEL Trial

30-day Events

	Chronic Kidney Disease (n = 361)			
	PCI (n = 177)	CABG (n = 184)	Hazard Ratio (95% CI)	p Value
Major adverse events, any	10.9 (19)	29.8 (54)	0.36 (0.23-0.59)	<0.0001
Death	1.1 (2)	1.7 (3)	0.69 (0.12-4.08)	1.00
Myocardial infarction	4.0 (7)	6.6 (12)	0.60 (0.24-1.50)	0.27
Stroke	1.1 (2)	1.7 (3)	0.69 (0.12-4.08)	1.00
Transfusion of ≥2 U blood	6.3 (11)	24.3 (44)	0.26 (0.14-0.48)	<0.0001
TIMI major or minor bleeding	3.4 (6)	12.2 (22)	0.28 (0.12-0.68)	0.002
Major arrhythmia	2.3 (4)	19.9 (36)	0.11 (0.04-0.32)	<0.0001
Unplanned coronary revascularization for ischemia	1.1 (2)	2.2 (4)	0.52 (0.10-2.79)	0.69
Any unplanned surgery or therapeutic radiological procedure	0.6 (1)	8.3 (15)	0.07 (0.01-0.52)	0.0004
Acute renal failure*	2.3 (4)	7.7 (14)	0.30 (0.10-0.88)	0.02

Giustino G et al. *JACC* 2018; 72:754-65

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 72, NO. 7, 2018

Left Main Revascularization With PCI or CABG in Patients With Chronic Kidney Disease

EXCEL Trial

Acute Renal Failure at 30 Days was significantly increased in the CABG group

TABLE 6 **Acute Renal Failure at 30 Days in Patients With or Without CKD Undergoing PCI Versus CABG**

	Chronic Kidney Disease (n = 361)			No Chronic Kidney Disease (n = 1,508)			
	PCI (n = 177)	CABG (n = 184)	Hazard Ratio (95% CI)	PCI (n = 757)	CABG (n = 751)	Hazard Ratio (95% CI)	$p_{interaction}$
Acute renal failure*	2.3 (4)	7.6 (14)	0.28 (0.09-0.87)	0.3 (2)	1.3 (10)	0.20 (0.04-0.90)	0.71
New requirement for dialysis	1.1 (2)	5.4 (10)	0.20 (0.04-0.92)	0.1 (1)	0.5 (4)	0.25 (0.03-2.22)	0.87
Hemodialysis	0.6 (1)	2.7 (5)	0.20 (0.02-1.76)	0.1 (1)†	0.4 (3)	0.33 (0.03-3.18)	0.76
CVVH	0.6 (1)	2.7 (5)	0.20 (0.02-1.76)	0.1 (1)†	0.1 (1)	0.99 (0.06-15.89)	0.38

Values are % (n) unless otherwise indicated. *Defined as the rise in serum creatinine >5 mg/dl or a new requirement for dialysis. †One patient in the no chronic kidney disease group had both CVVH and hemodialysis.

CVVH = continuous venovenous hemofiltration; other abbreviations as in Table 4.

Giustino G et al. *JACC* 2018; 72:754-65

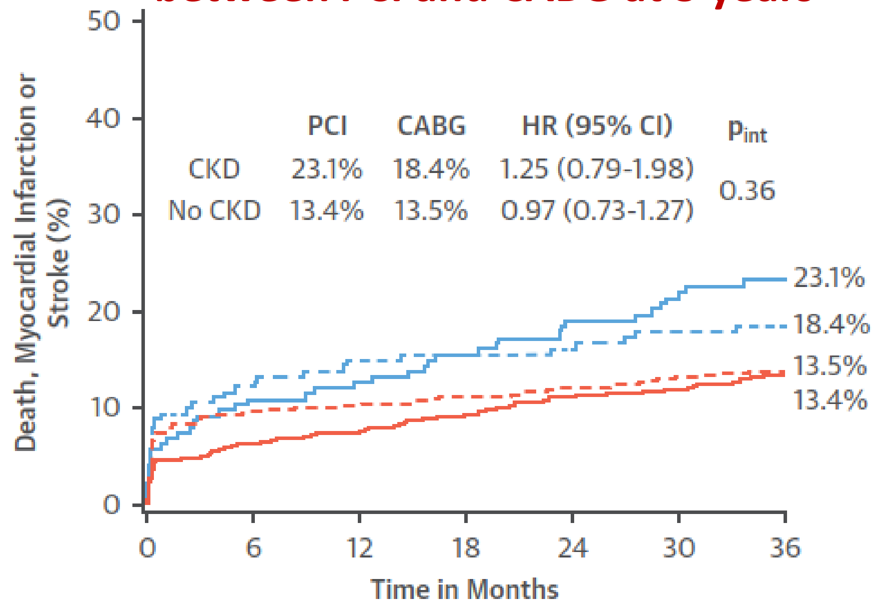
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 72, NO. 7, 2018

Left Main Revascularization With PCI or CABG in Patients With Chronic Kidney Disease

EXCEL Trial

MACE up to 3 years

No significant difference between PCI and CABG at 3 years

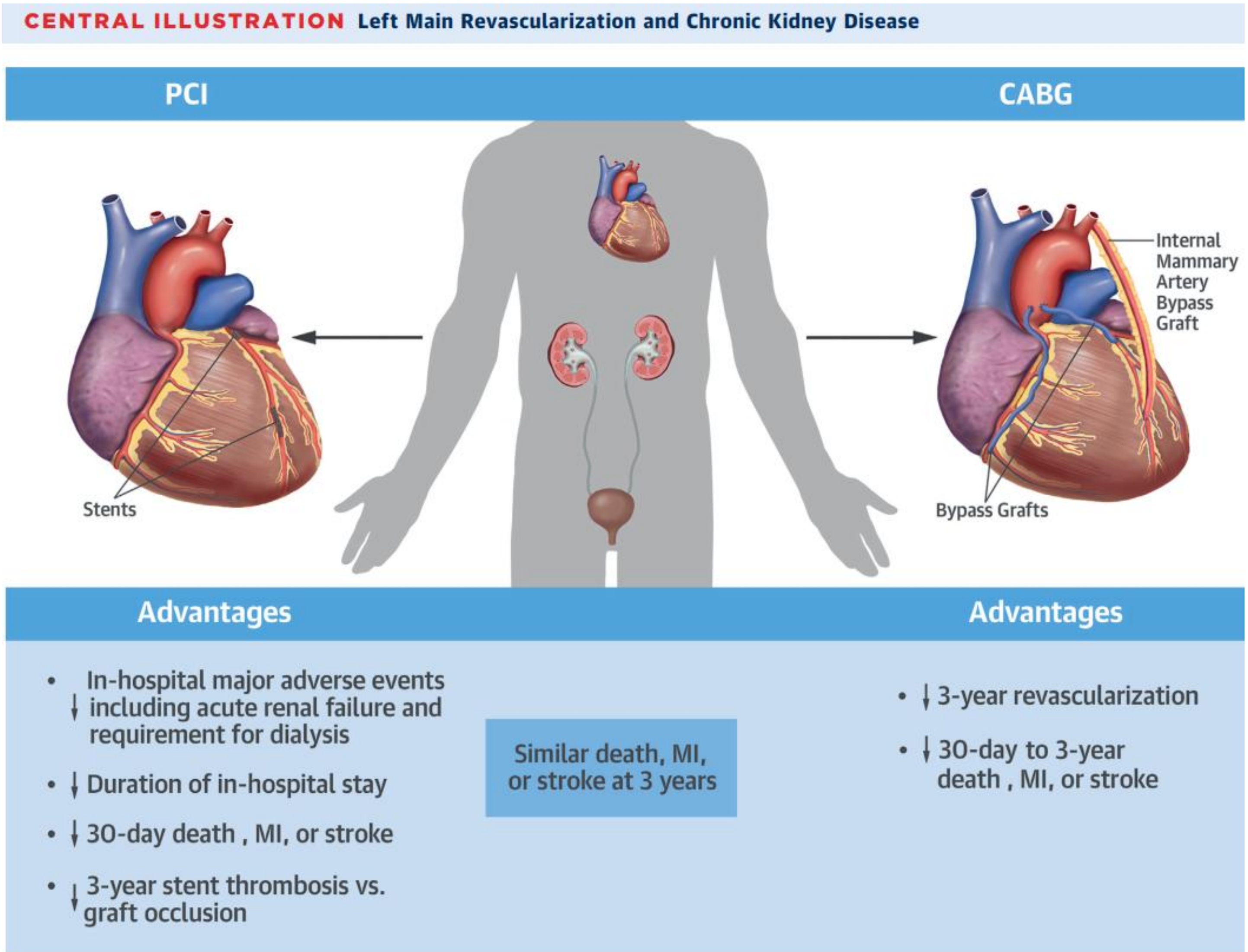


Number at risk:

	0	6	12	24	36
CKD-PCI	177	155	151	138	121
CKD-CABG	184	158	151	146	128
No CKD-PCI	757	708	694	657	580
No CKD-CABG	751	667	658	635	561

Giustino G et al. *JACC* 2018; 72:754-65

PCI and CABG: Both "acceptable" strategies



Giustino G et al. *JACC* 2018; 72:754-65

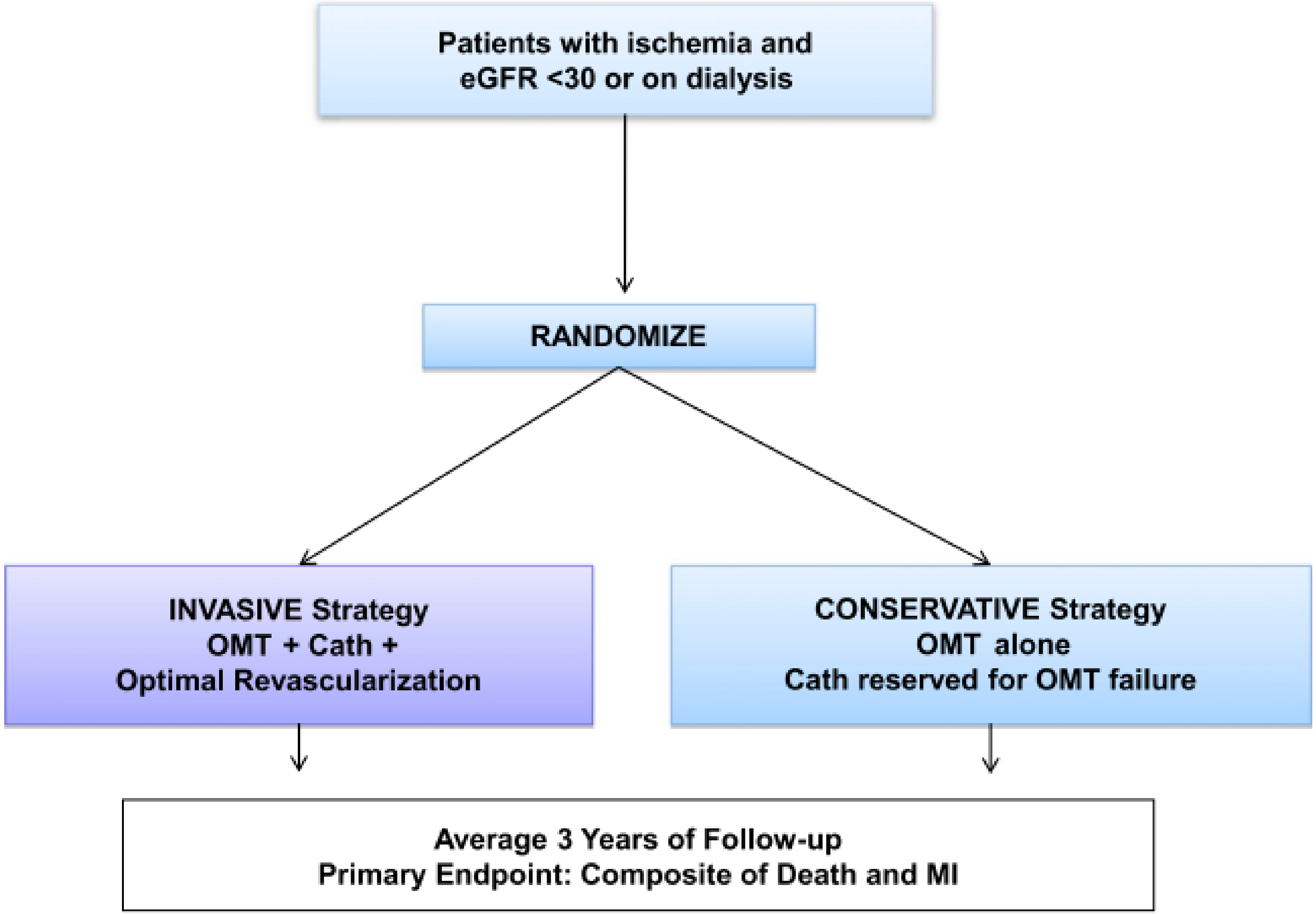
Summary

- Clinical outcomes in CKD are worse after either PCI or CABG
- Under-representation of CKD patients in large RCTs
- Short-term adverse events are less after PCI vs CABG
  - Acute kidney injury is favorable after PCI compared to CABG
- Long-term mortality (or combined with MI/Stroke) is comparable between PCI and CABG in recent studies (*with a numerical trend favoring CABG*)

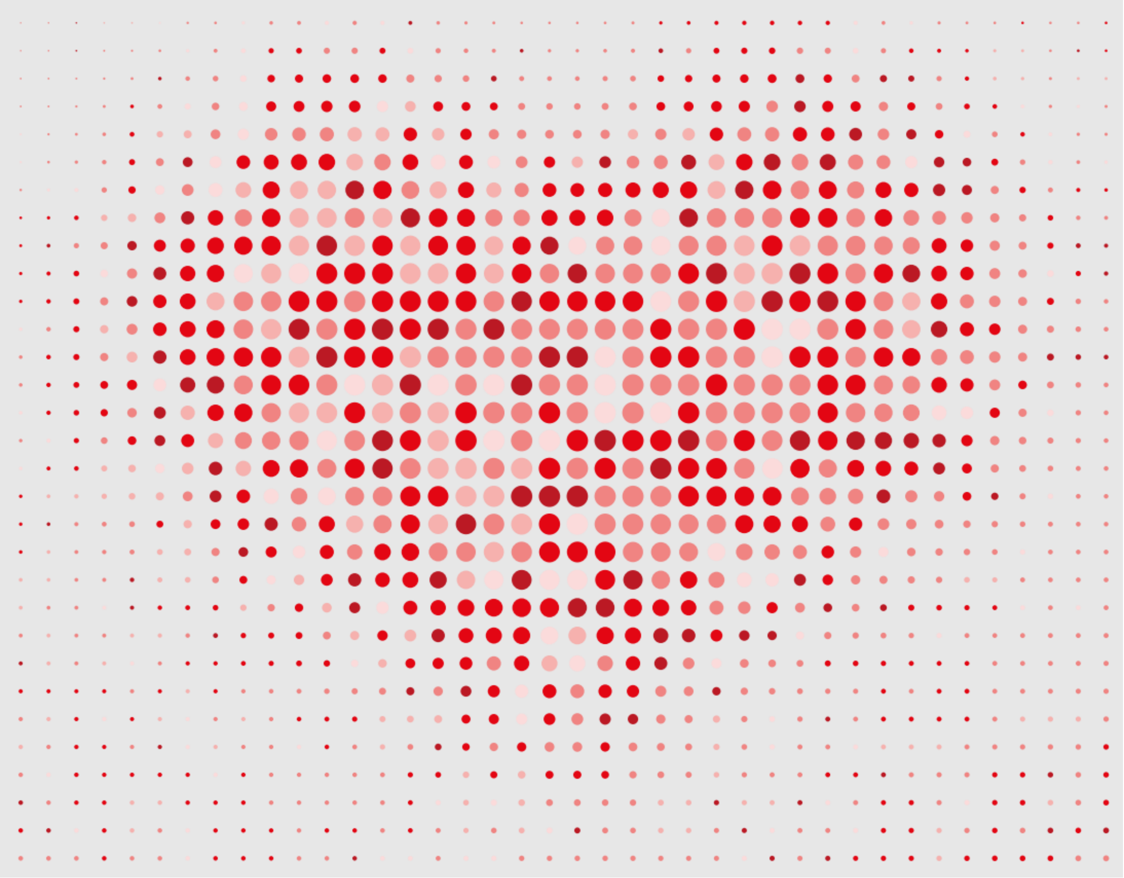
PCI seems to be a reasonable and acceptable option in CKD patients

BUT, currently there are no randomized data of which revascularization strategy is better in CKD patients

ISCHEMIA-CKD Randomized Trial



ISCHEMIA-CKD will be the <u>largest treatment strategy trial</u> in advanced CKD patients with stable ischemic heart disease



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