Final Results from the ACCF-STS Database Collaboration on the Comparative Effectiveness of Revascularization Strategies (ASCERT)

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Conflicts of Interest

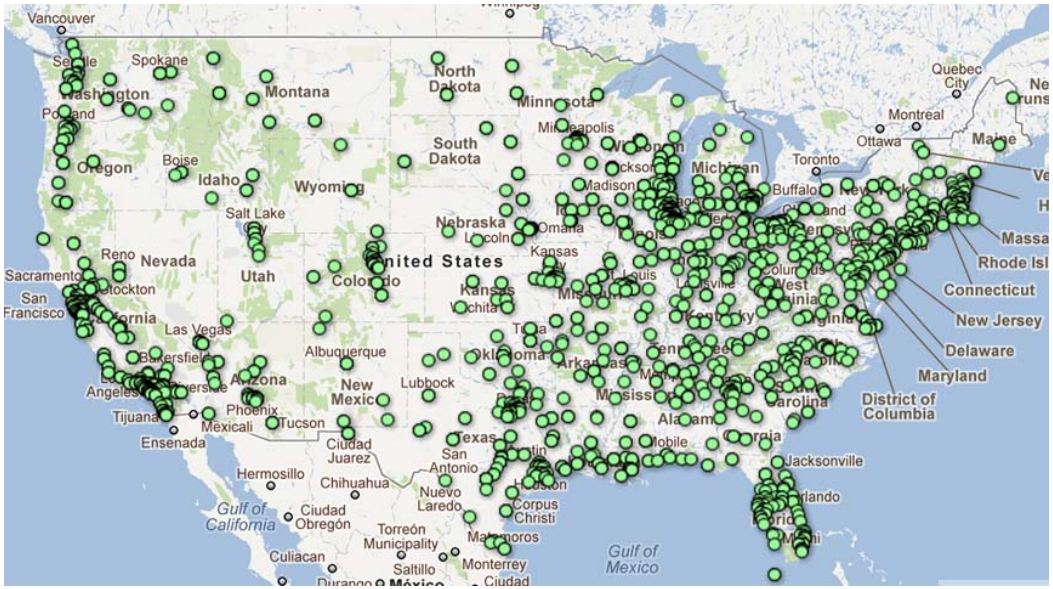
- Dr. Dangas reports receiving consulting fees from Abbott Vascular, Astra Zeneca, Eli Lilly, Johnson & Johnson, and Ogilvy, receiving grant support from Bristol-Myers Squibb, Eli Lilly, Daichi-Sankyo, Medicines Co., and Sanofi-Aventis, lecture fees from Abbott Vascular, AstraZeneca, Boston Scientific, Bracco, Bristol-Myers Squibb, Guerbet, Eli Lilly, Johnson & Johnson, the Medicines Co., and Sanofi-Aventis, royalties from Wiley and Informa, and travel support from the Cardiovascular Research Foundation
- Dr. Edwards, being an employee of the Society of Thoracic Surgeons
- Dr. Mayer, receiving honorarium and travel support from CHMC Cardiovascular Surgical Foundation
- Dr. Messenger, receiving grant support from the Medtronic Corporation
- Dr. Popma, receiving consulting fees from Abbott Vascular, Boston Scientific, and Covidien, and grant support from Abbott Vascular, Abiomed, Boston Scientific, Cordis, and Medtronic

Source of Funding

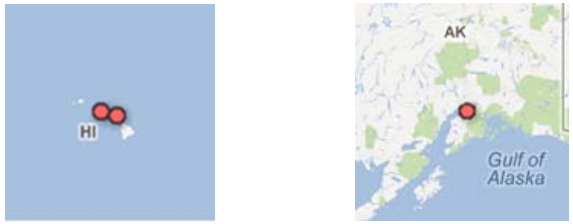
- *Award Number RC2HL101489 from the National Heart, Lung, and Blood Institute*

Data from 644 Sites

NCDR Sites



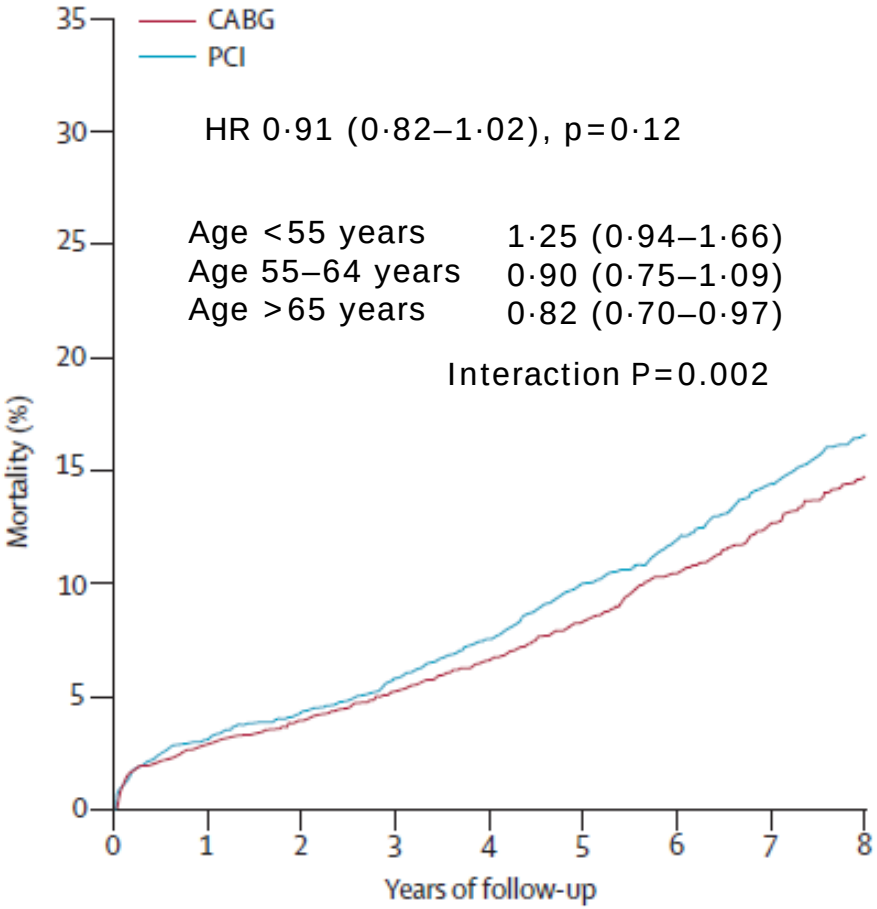
STS Sites

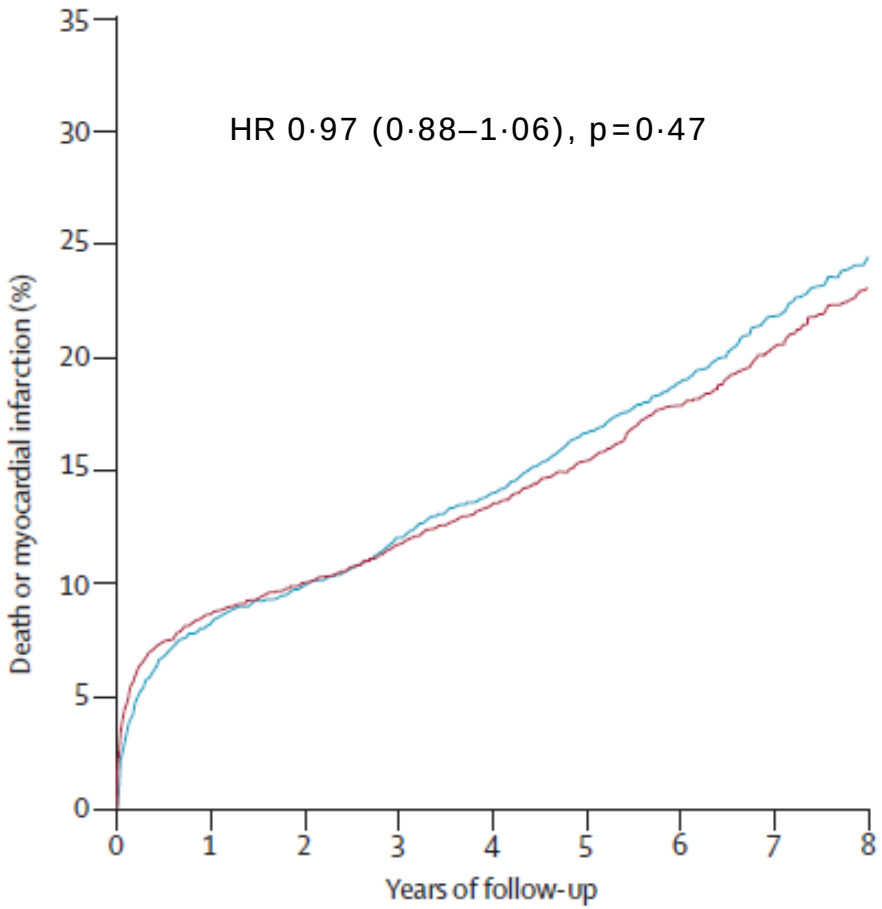


Purpose

- To compare long-term mortality of coronary artery bypass surgery and percutaneous coronary intervention

Meta-Analysis of 10 Trials, 7812 Patients

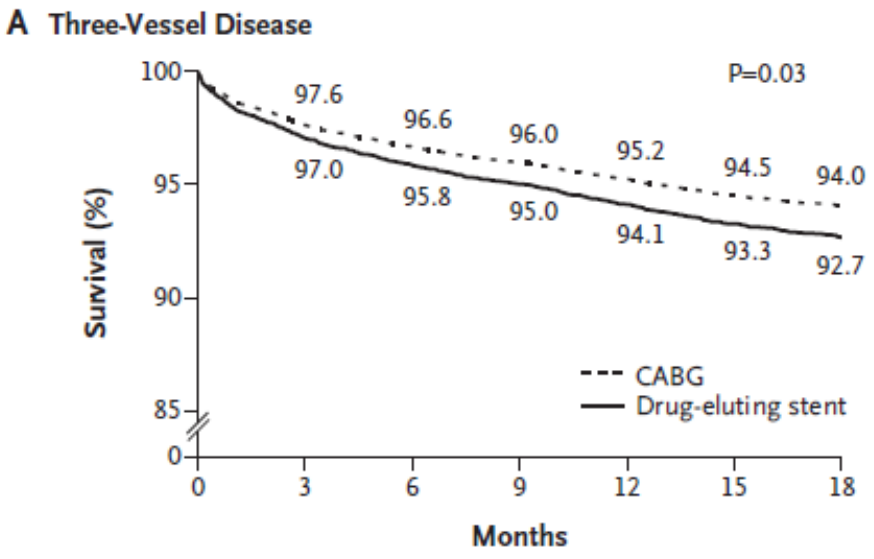


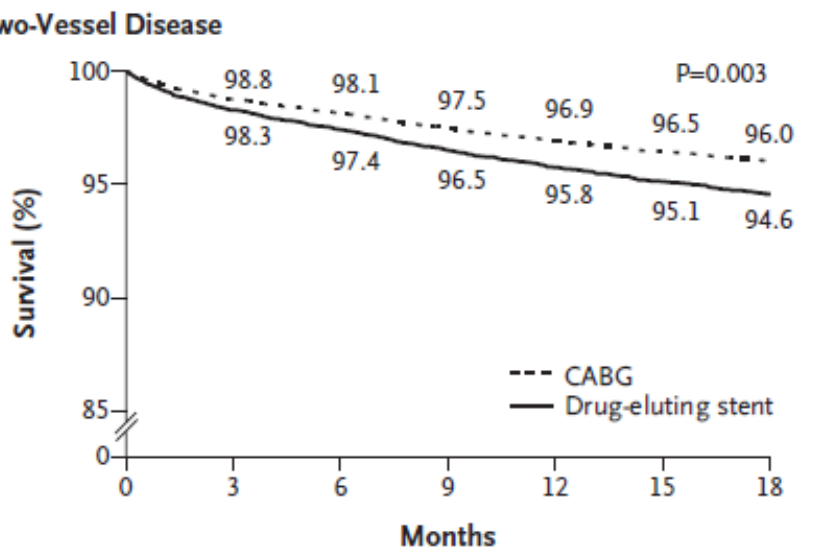


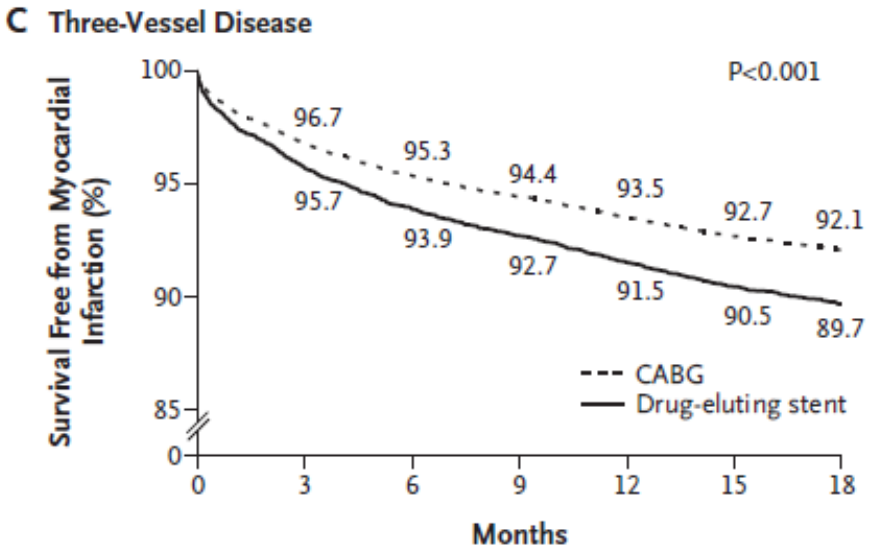
Hlatky et al, Lancet 2009; 373: 1190–97

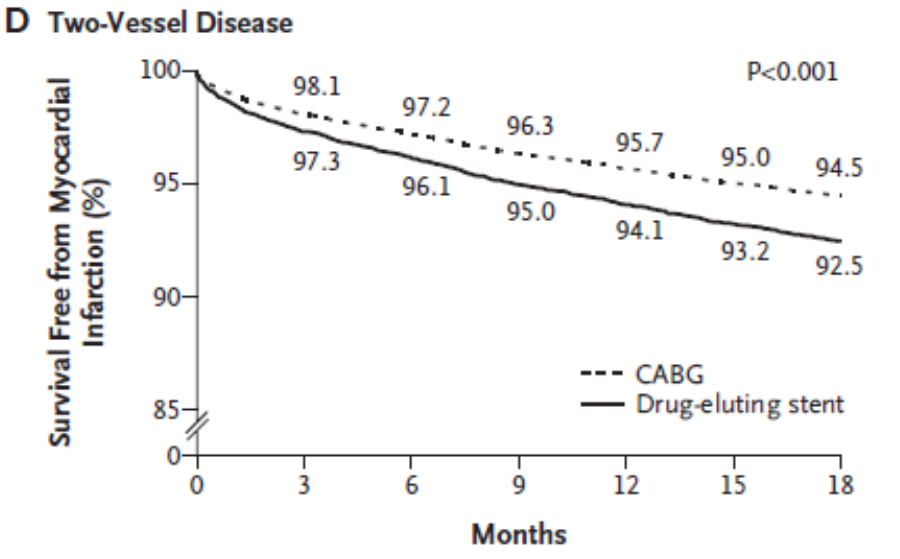
NY State Database

Observational Study,17,400 Patients









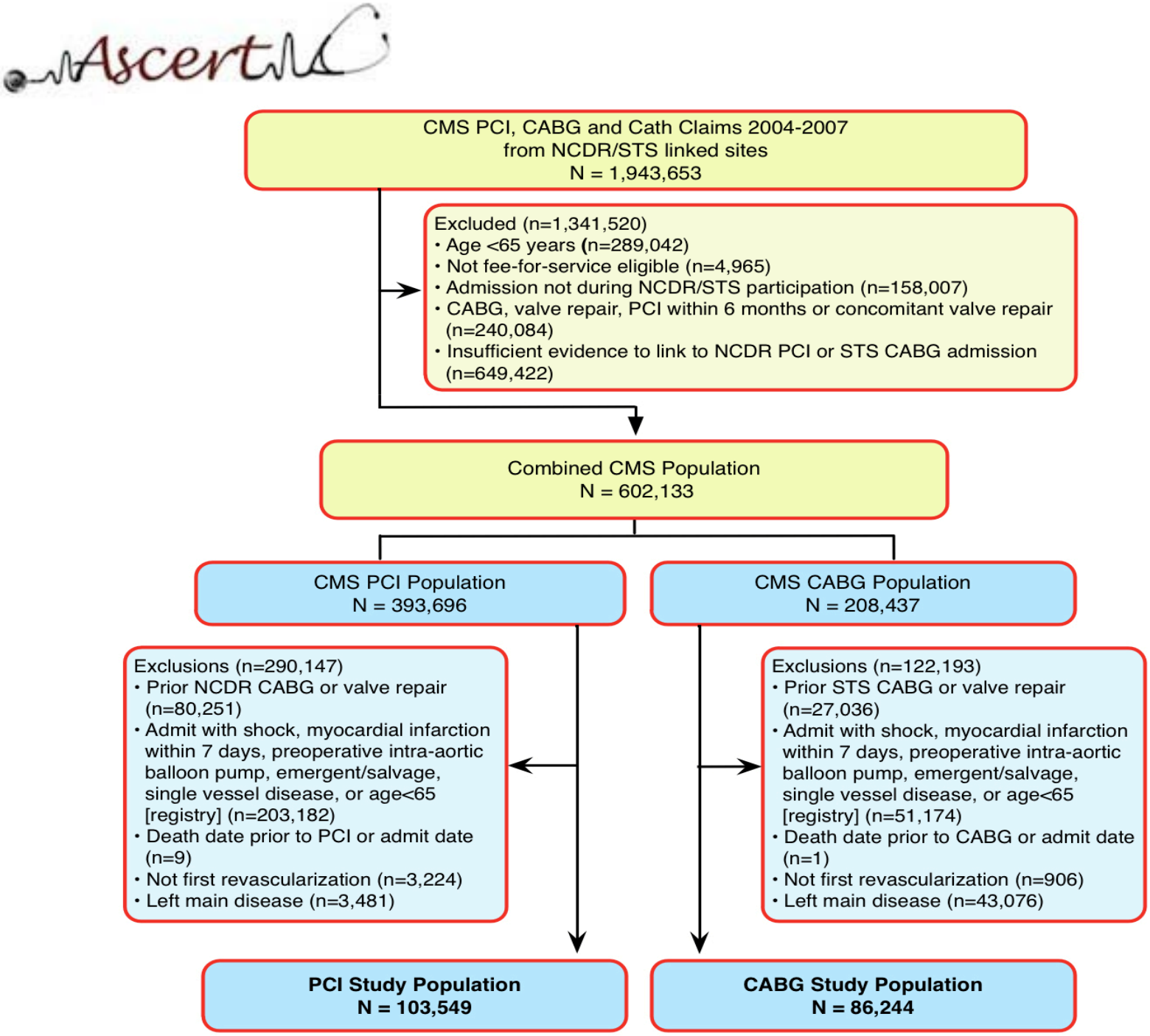
Hannan et al, N Engl J Med 2008;358:331-41.

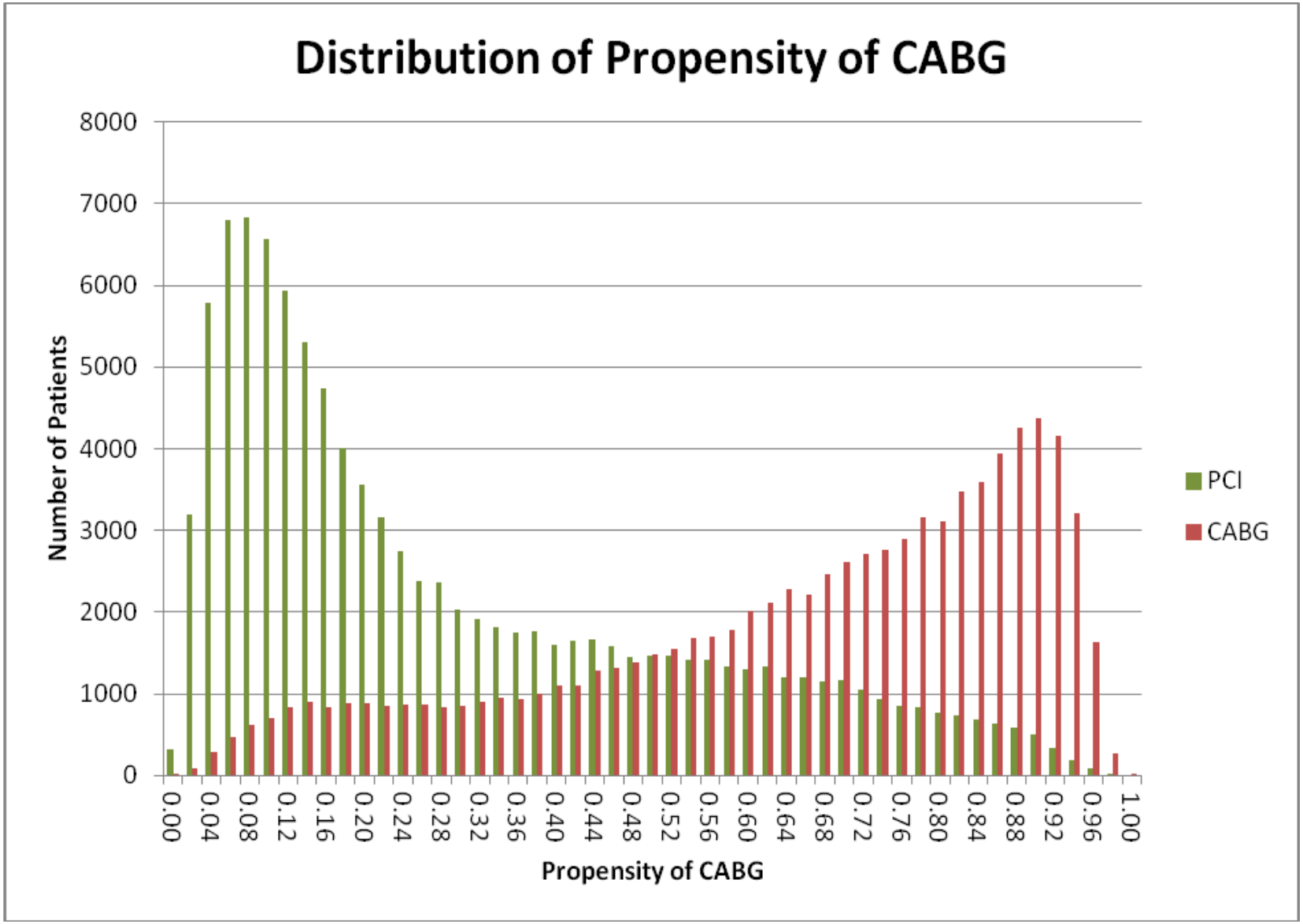
Statistical Methods

- Patients from NCDR CathPCI and STS Registries from 2004-2007, followed until end 2008
- Each linked to CMS 100% denominator file linked by probabilistic matching, using admit date, discharge date, race, sex, age
- Propensity for CABG determined for all patients by logistic regression
- Patients differences brought into balance by inverse probability weighting, allowing comparisons of groups
- Sensitivity analysis with propensity matched, Cox model and double robust methods
- Sensitivity analysis for possible unmeasured confounders by the method of Lin et al

Sources of Data

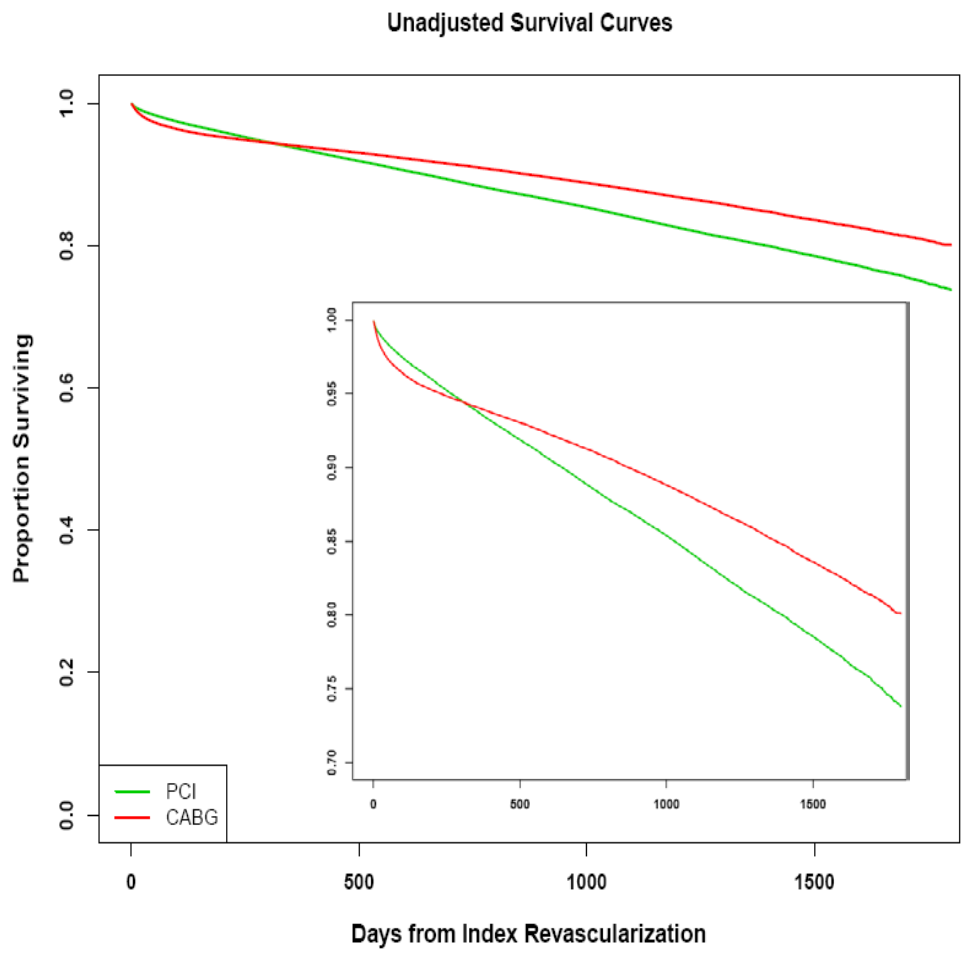
- PCI: NCDR CathPCI Registry
- CABG: STS Registry
- Long term followup: CMS 100% denominator file

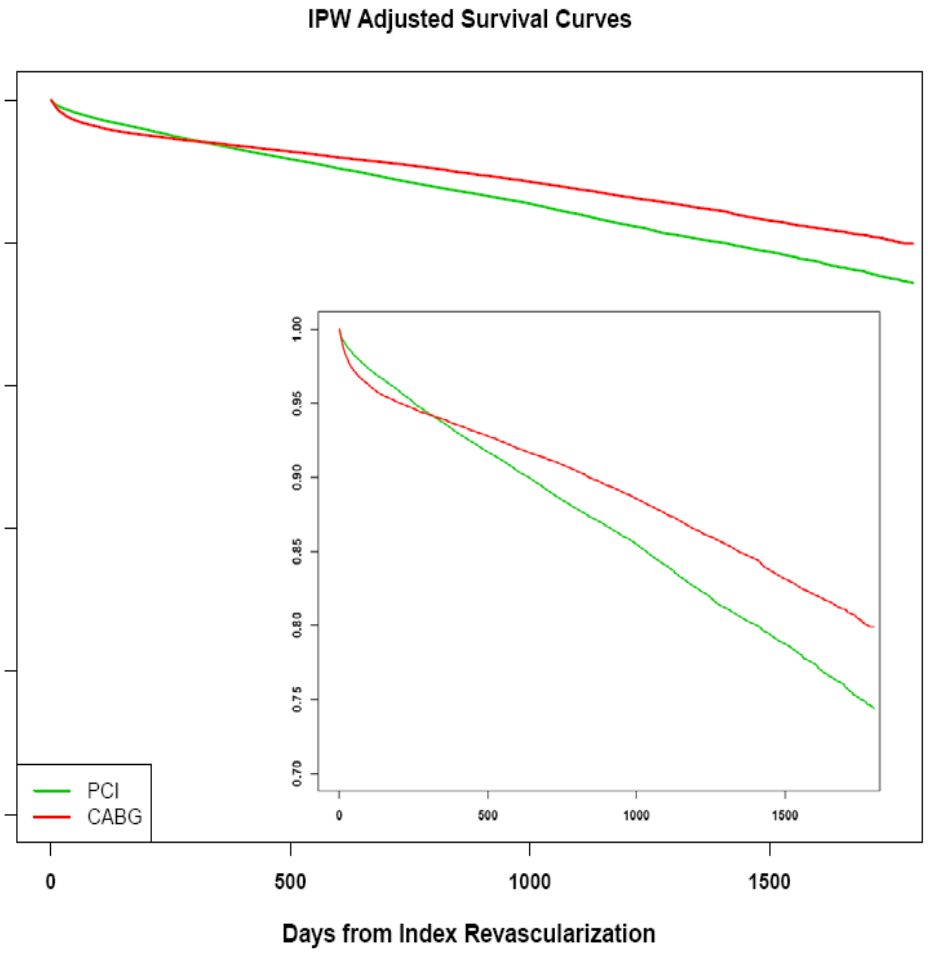

CMS PCI, CABG and Cath Claims 2004-2007
from NCDR/STS linked sites
N = 1,943,653
Excluded (n=1,341,520)
• Age <65 years (n=289,042)
• Not fee-for-service eligible (n=4,965)
• Admission not during NCDR/STS participation (n=158,007)
• CABG, valve repair, PCI within 6 months or concomitant valve repair (n=240,084)
• Insufficient evidence to link to NCDR PCI or STS CABG admission (n=649,422)
Combined CMS Population
N = 602,133
CMS PCI Population
N = 393,696
CMS CABG Population
N = 208,437
Exclusions (n=290,147)
• Prior NCDR CABG or valve repair (n=80,251)
• Admit with shock, myocardial infarction within 7 days, preoperative intra-aortic balloon pump, emergent/salvage, single vessel disease, or age<65 [registry] (n=203,182)
• Death date prior to PCI or admit date (n=9)
• Not first revascularization (n=3,224)
• Left main disease (n=3,481)
Exclusions (n=122,193)
• Prior STS CABG or valve repair (n=27,036)
• Admit with shock, myocardial infarction within 7 days, preoperative intra-aortic balloon pump, emergent/salvage, single vessel disease, or age<65 [registry] (n=51,174)
• Death date prior to CABG or admit date (n=1)
• Not first revascularization (n=906)
• Left main disease (n=43,076)
PCI Study Population
N = 103,549
CABG Study Population
N = 86,244


Distribution of Propensity of CABG
Number of Patients
8000
7000
6000
5000
4000
3000
2000
1000
0
0.00
0.04
0.08
0.12
0.16
0.20
0.24
0.28
0.32
0.36
0.40
0.44
0.48
0.52
0.56
0.60
0.64
0.68
0.72
0.76
0.80
0.84
0.88
0.92
0.96
1.00
Propensity of CABG
PCI
CABG

Baseline Data

	Unadjusted			IPW Adjusted		
	CABG (n=86,244)	PCI (n=103,549)	P Value	CABG (n=86,244)	PCI (n=103,549)	P Value
Age	73.1 ± 5.6	74.7 ± 6.5	<0.0001	74.0 ± 9.2	74.0 ± 8.3	0.49
Male	68.6	57.8	<0.0001	62.3	62.8	0.17
History of CHF	11.5	10.2	<0.0001	11.2	10.8	0.067
History of MI	25.3	24.6	0.0001	24.5	24.7	0.51
Diabetes	38.6	34.4	<0.0001	35.8	35.8	0.97
Insulin Requiring	10.2	9.8	0.0069	9.7	9.9	0.35
Hypertension	84.8	83.4	<0.0001	83.9	83.8	0.58
Renal Failure	6.1	6.2	0.57	6.1	6.1	0.80
CKD	20.7	18.9	<0.0001	19.4	19.6	0.50
CVD	17.6	15.8	<0.0001	16.6	16.6	0.86
PAD	17.9	15.3	<0.0001	16.4	16.4	0.97
BMI	28.7 ± 5.8	28.7 ± 5.9	0.78	28.8 ± 8.6	28.7 ± 7.9	0.97
Former Smoker	44.0	42.5	<0.0001	43.0	43.3	0.45
Current Smoker	12.9	11.6	<0.0001	11.9	12.0	0.74
No Angina	21.8	30.8	<0.0001	26.4	26.8	0.23
Stable Angina	49.6	22.6	<0.0001	34.6	34.9	0.46
Unstable Angina	28.6	46.6	<0.0001	39.0	38.3	0.066
Ejection Fraction	52.9± 12.2	55.5 ± 11.4	<0.0001	54.4 ± 17.6	54.4 ± 16.2	0.58
3 Vessel Disease	80.3	32.1	<0.0001	53.2	53.8	0.043
Status Urgent	68.6	57.8	<0.0001	62.3	62.8	0.17

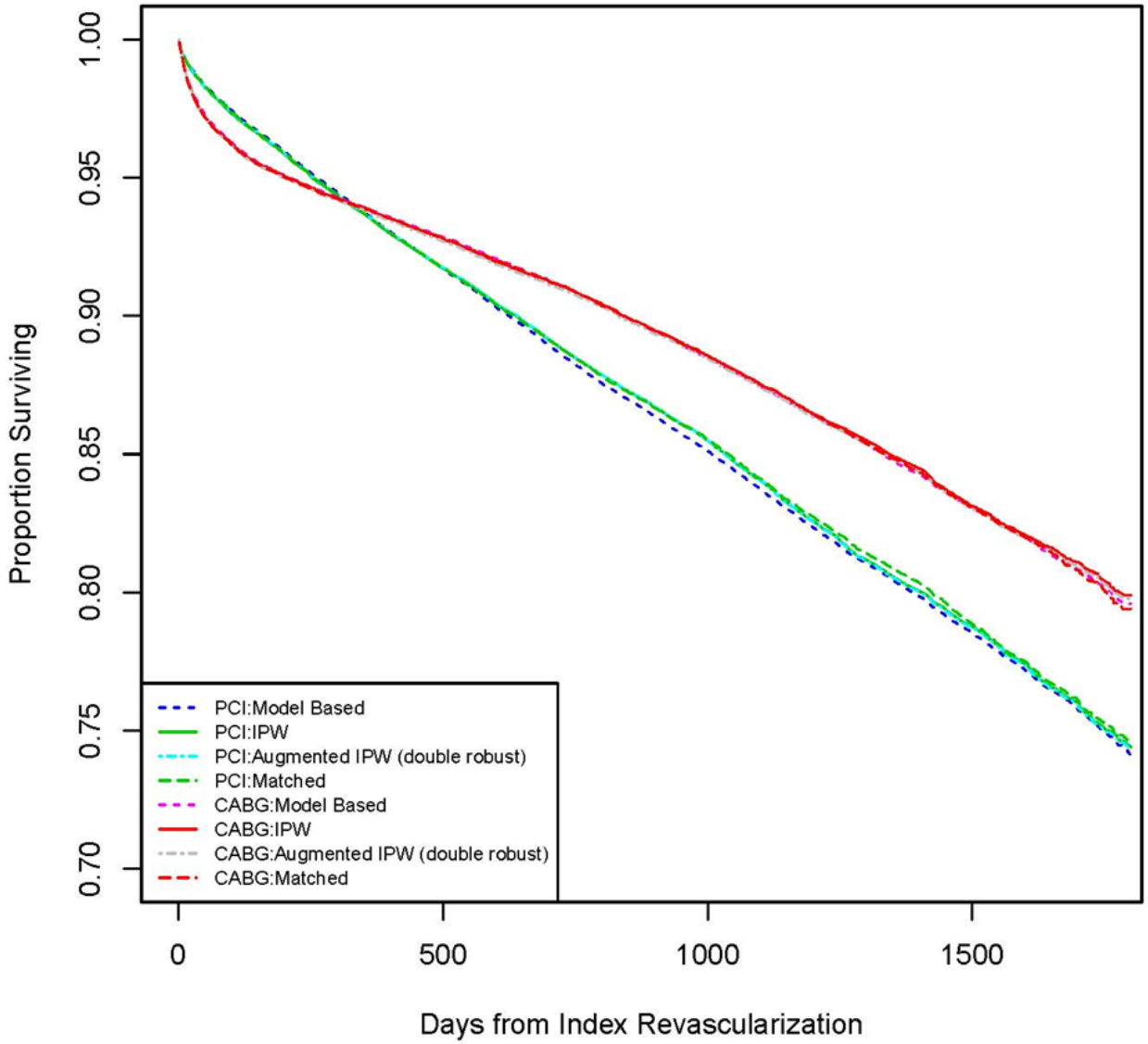


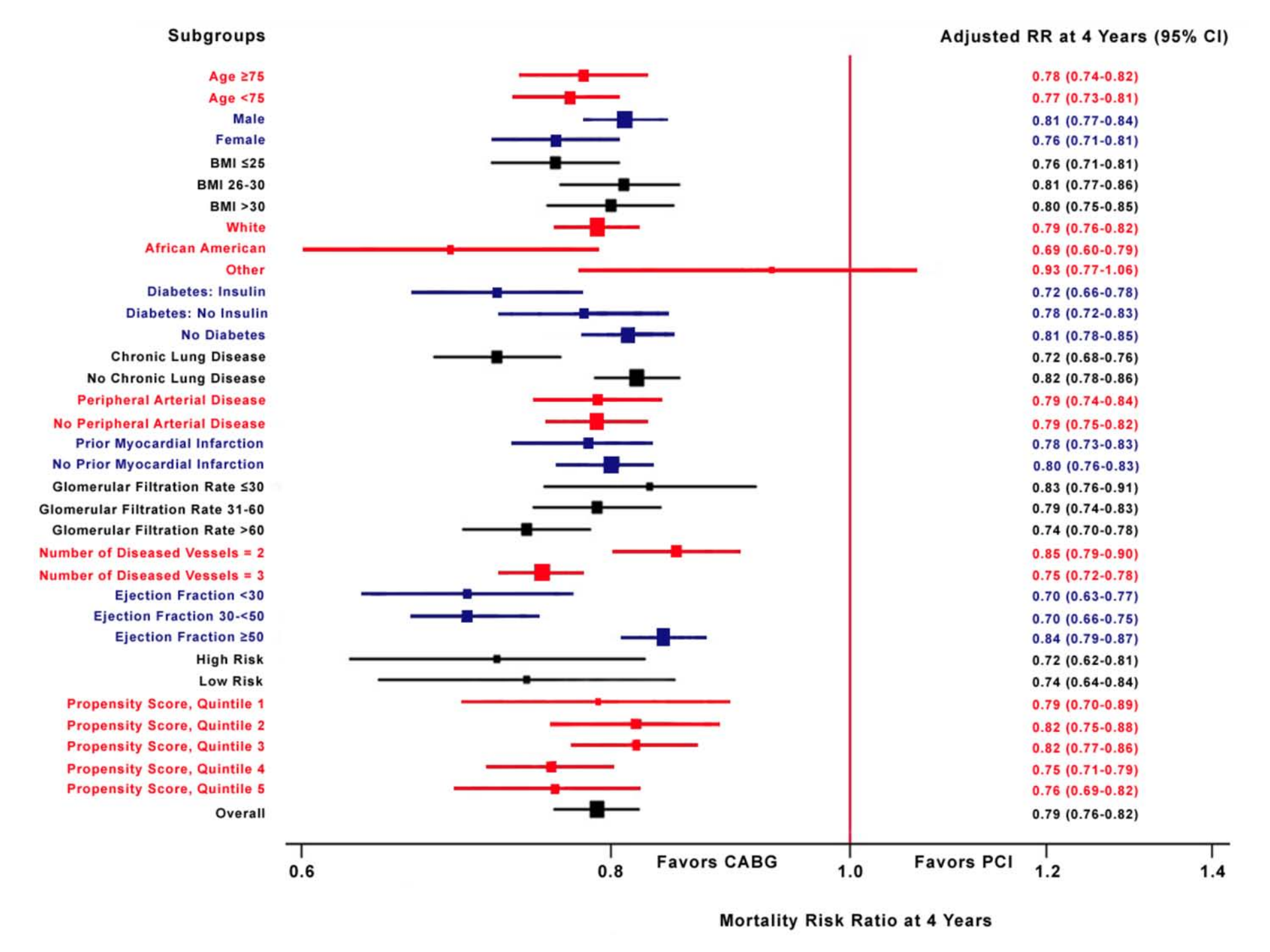


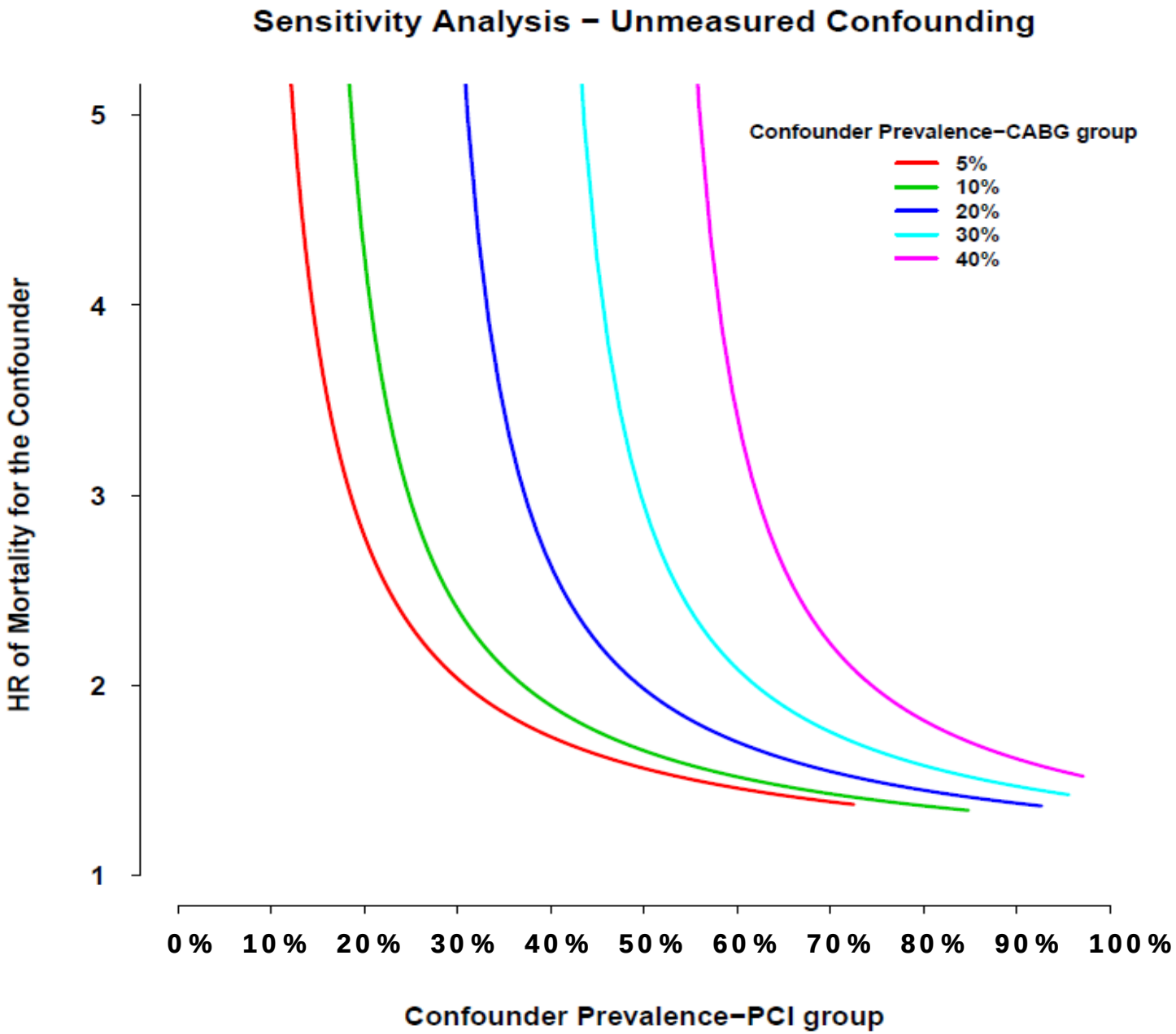
	30-Day	1-Year	2-Year	3-Year	4-Year	30-Day	1-Year	2-Year	3-Year	4-Year
CABG mortality	2.07% (1.98-2.17)	6.00% (5.58-6.17)	8.76% (8.56-8.94	12.1% (11.9-12.4)	16.0% (15.7-16.3)	2.25% (2.09-2.41)	6.24% (5.97-6.50)	8.98% (8.68-9.29)	12.4% (12.0-12.8)	16.4% (15.9-16.9)
PCI mortality	1.21% (1.14-1.27)	6.36% (6.22-6.51)	11.2% (11.0-11.4)	16.0% 15.7-16.2)	20.9% (20.6-21.3)	1.31% (1.21-1.41)	6.55% (6.35-6.76)	11.3% (11.0-11.6)	15.9% (15.6-16.3)	20.8% (20.4-21.2)
Relative Risk	1.72 (1.58-1.84)	0.94 (0.91-0.97)	0.78 (0.76-0.80)	0.76 (0.74-0.78)	0.76 (0.75-0.78)	1.72 (1.52-1.89)	0.95 (0.90-1.00)	0.79 (0.76-0.83)	0.78 (0.75-0.81)	0.79 (0.76-0.82)

Baseline Data

	Unadjusted			Propensity Matched Groups		
	CABG (n=86,244)	PCI (n=103,549)	P Value	CABG (n=43,084)	PCI (n=43,084)	P Value
Age	73.1 ± 5.6	74.7 ± 6.5	<0.0001	73.8 ± 5.9	73.8 ± 6.0	0.62
Male	68.6	57.8	<0.0001	63.7	63.5	0.68
History of CHF	11.5	10.2	<0.0001	10.8	11.0	0.30
History of MI	25.3	24.6	0.0001	24.1	24.2	0.88
Any Diabetes	38.6	34.4	<0.0001	36.6	36.4	0.73
Insulin Requiring	10.2	9.8	0.0069	10.0	10.1	0.73
Hypertension	84.8	83.4	<0.0001	83.9	84.0	0.39
Renal Failure	6.1	6.2	0.57	3.8	3.8	0.92
CLD	20.7	18.9	<0.0001	19.8	19.8	0.99
CVD	17.6	15.8	<0.0001	16.7	16.7	0.94
PAD	17.9	15.3	<0.0001	16.4	16.6	0.45
BMI	28.7 ± 5.8	28.7 ± 5.9	0.78	28.8 ± 5.8	28.8 ± 5.8	0.77
Former Smoker	44.0	42.5	<0.0001	43.1	43.4	0.56
Current Smoker	12.9	11.6	<0.0001	12.3	12.1	0.56
No Angina	21.8	30.8	<0.0001	27.7	27.7	0.89
Stable Angina	49.6	22.6	<0.0001	33.9	34.0	0.89
Unstable Angina	28.6	46.6	<0.0001	38.4	38.3	0.89
Ejection Fraction	52.9± 12.2	55.5 ± 11.4	<0.0001	54.2 ± 11.6	54.3 ± 11.9	<0.0001
3 Vessel Disease	80.3	32.1	<0.0001	62.6	62.7	0.88
Status Urgent	34.7	36.0	<0.0001	35.6	35.5	0.82


Comparison of Risk Adjusted Survival Methods
Proportion Surviving
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0
500
1000
1500
Days from Index Revascularization
PCI:Model Based
PCI:IPW
PCI:Augmented IPW (double robust)
PCI:Matched
CABG:Model Based
CABG:IPW
CABG:Augmented IPW (double robust)
CABG:Matched


Subgroups
Adjusted RR at 4 Years (95% CI)
Age ≥75
0.78 (0.74-0.82)
Age <75
0.77 (0.73-0.81)
Male
0.81 (0.77-0.84)
Female
0.76 (0.71-0.81)
BMI ≤25
0.76 (0.71-0.81)
BMI 26-30
0.81 (0.77-0.86)
BMI >30
0.80 (0.75-0.85)
White
0.79 (0.76-0.82)
African American
0.69 (0.60-0.79)
Other
0.93 (0.77-1.06)
Diabetes: Insulin
0.72 (0.66-0.78)
Diabetes: No Insulin
0.78 (0.72-0.83)
No Diabetes
0.81 (0.78-0.85)
Chronic Lung Disease
0.72 (0.68-0.76)
No Chronic Lung Disease
0.82 (0.78-0.86)
Peripheral Arterial Disease
0.79 (0.74-0.84)
No Peripheral Arterial Disease
0.79 (0.75-0.82)
Prior Myocardial Infarction
0.78 (0.73-0.83)
No Prior Myocardial Infarction
0.80 (0.76-0.83)
Glomerular Filtration Rate ≤30
0.83 (0.76-0.91)
Glomerular Filtration Rate 31-60
0.79 (0.74-0.83)
Glomerular Filtration Rate >60
0.74 (0.70-0.78)
Number of Diseased Vessels = 2
0.85 (0.79-0.90)
Number of Diseased Vessels = 3
0.75 (0.72-0.78)
Ejection Fraction <30
0.70 (0.63-0.77)
Ejection Fraction 30-<50
0.70 (0.66-0.75)
Ejection Fraction ≥50
0.84 (0.79-0.87)
High Risk
0.72 (0.62-0.81)
Low Risk
0.74 (0.64-0.84)
Propensity Score, Quintile 1
0.79 (0.70-0.89)
Propensity Score, Quintile 2
0.82 (0.75-0.88)
Propensity Score, Quintile 3
0.82 (0.77-0.86)
Propensity Score, Quintile 4
0.75 (0.71-0.79)
Propensity Score, Quintile 5
0.76 (0.69-0.82)
Overall
0.79 (0.76-0.82)
0.6
0.8
Favors CABG
1.0
Favors PCI
1.2
1.4
Mortality Risk Ratio at 4 Years


Sensitivity Analysis – Unmeasured Confounding
Confounder Prevalence–CABG group
5%
10%
20%
30%
40%
HR of Mortality for the Confounder
5
4
3
2
1
0 %
10 %
20 %
30 %
40 %
50 %
60 %
70 %
80 %
90 %
100 %
Confounder Prevalence–PCI group

Limitations

- All observational studies have possible treatment selection bias
- This can be approached, but not fully resolved, by careful database design, statistical analysis and sensitivity analysis
- Several variables were not available (e.g. frailty) or of limited quality (e.g. angiographic details) in the ASCERT data
- There was missing data for several variables (e.g. GFR and EF)
- ASCERT outcomes are limited to patients age 65 and older
- This presentation concerns mortality only (composite endpoints, angiographic analyses, economic analysis will follow)

Comparative Effectiveness Research
Implications of ASCERT

- Observational studies can provide real-world outcomes with greater generalizability than randomized trials
- Linking robust clinical databases with administrative database capitalizes on the advantages of both
- This allows for very large studies with power to examine subgroups
- Administrative databases can also supplement clinical databases with resource use/cost data
- There are also limitations to observational studies
- For comparative effectiveness to reach is potential, randomized trials and observational studies will both have critical roles to play

Conclusions

- Survival was similar in the two arms at 1 years
- Survival was higher in the CABG than PCI arm at 4 years
- The results were largely consistent across subgroups
- This is largely consistent with both clinical trial and observational studies
- Causal inference requires considering the totality of the data, of which ASCERT is a critical part
- ASCERT offers critical experience in comparative effectiveness research using observational data

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Comparative Effectiveness of Revascularization Strategies

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