Who Should Not Undergo TAVR?
Insights from Recent Trials and Registries

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Disclosures

Grant Support/Drugs

- Daiichi-Sankyo

Grant Support/Devices

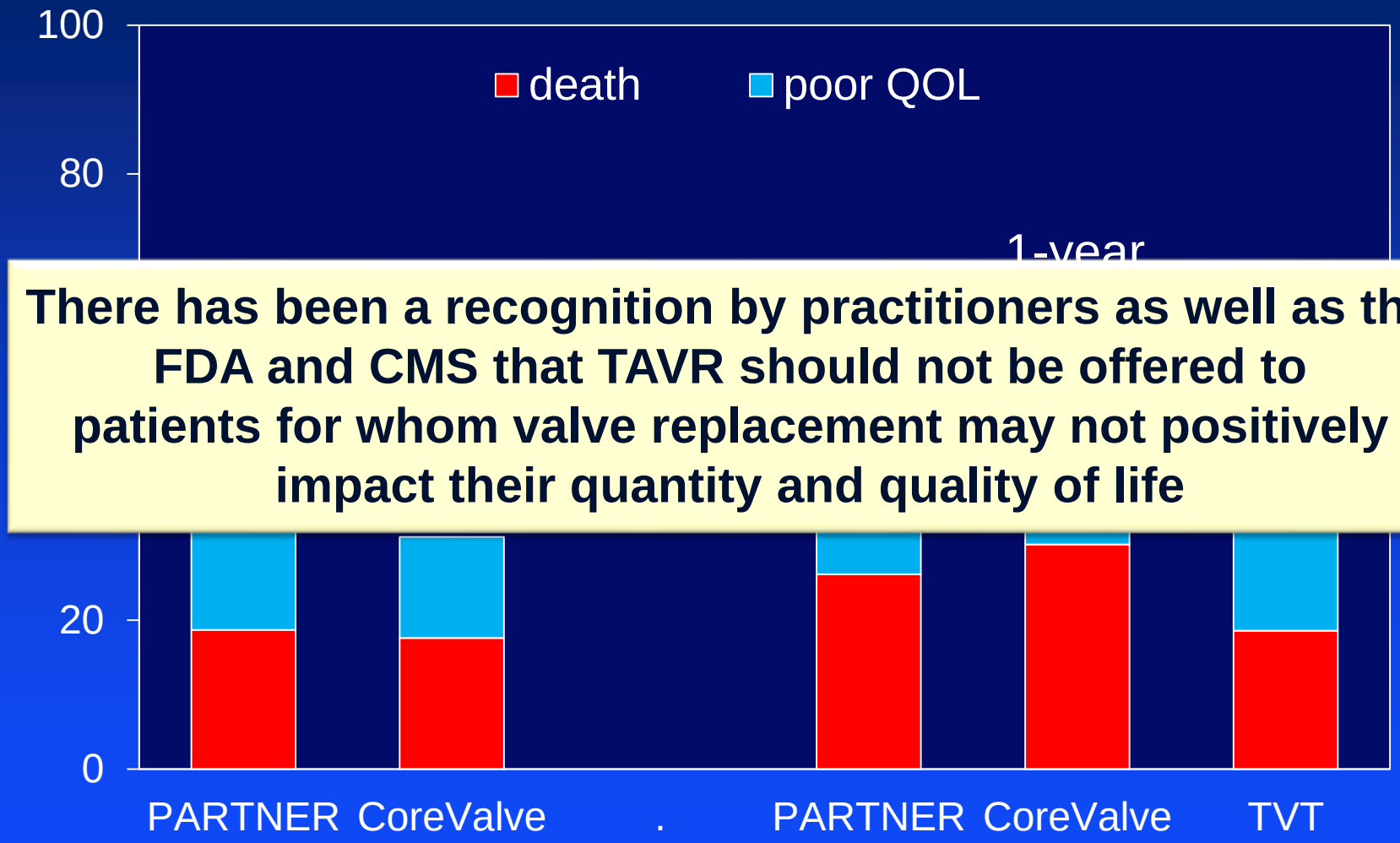
- Edwards Lifesciences - Abbott Vascular
- Medtronic - Boston Scientific
- CSI - Corvia
- V-Wave Medical - Svelte

Consulting/Advisory Boards

- Medtronic - Edwards Lifesciences
- Janssen Pharmaceuticals - Heartflow

DJC: 8/19

Outcomes After TAVR



There has been a recognition by practitioners as well as the FDA and CMS that TAVR should not be offered to patients for whom valve replacement may not positively impact their quantity and quality of life

Arnold et al. Circ Cardiovasc Qual Outcomes 2013.

Arnold et al. Circulation 2014

Arnold et al. JACC Cardiovasc Interv 2015

When should a procedure not be performed?

Perspective	General Principle	Application
Patient	A procedure should not be performed when the expected benefits do not outweigh the potential harm	Shared Decision Making Appropriate Use Criteria

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Patient	A procedure should not be performed when the expected benefits do not outweigh the potential harm	Shared Decision Making Appropriate Use Criteria
Society	A procedure should not be performed when its expected costs (including induced costs) could provide greater benefit in an alternative use	Guidelines Coverage and Reimbursement Policy

When is TAVR Futile?

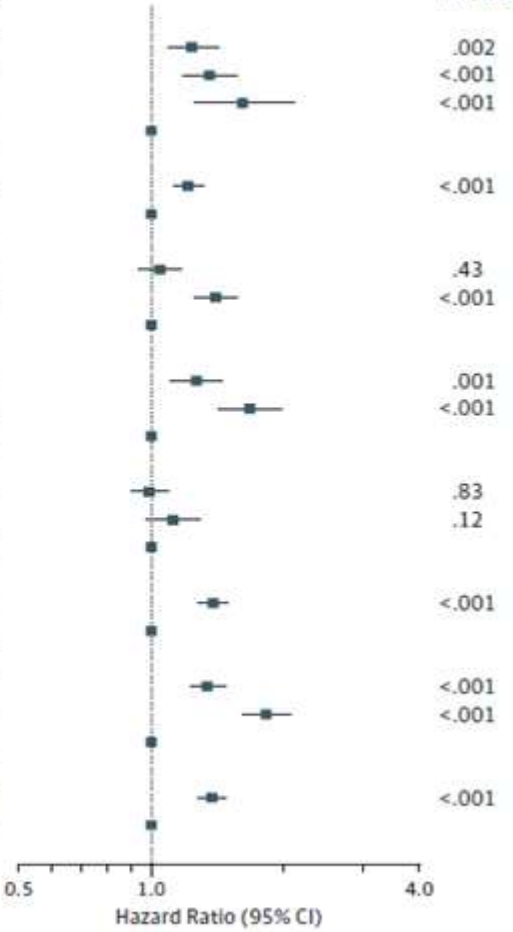
<u>Key Insight #1</u>

No single risk factor is sufficient to identify "futility"

Impact of Baseline Factors on 1-Year Mortality

Figure 2. Multivariate Risk-Adjusted Outcome of Mortality

	Mortality		Hazard Ratio	*P* Value
	No./Total	% (95% CI)	(95% CI)	
Age, y				
75-84	934/4652	23.8 (22.4-25.2)	1.23 (1.08-1.41)	.002
85-94	1203/5726	24.5 (23.2-25.7)	1.35 (1.18-1.55)	<.001
≥95	72/258	31.4 (25.3-37.7)	1.61 (1.24-2.09)	<.001
<75	241/1546	18.9 (16.8-21.2)	1 [Reference]	
Sex				
Male	1273/5848	25.8 (24.6-27.1)	1.21 (1.12-1.31)	<.001
Female	1176/6316	21.7 (20.6-22.8)	1 [Reference]	
COPD				
Moderate	376/1709	25.9 (23.6-28.3)	1.04 (0.94-1.17)	.43
Severe	457/1640	33.1 (30.5-35.7)	1.39 (1.25-1.55)	<.001
None/mild	1597/8694	21.6 (20.6-22.5)	1 [Reference]	
Renal function				
Creatinine ≥2 mg/dL without dialysis	221/798	31.5 (28.0-35.1)	1.26 (1.10-1.44)	.001
Dialysis	163/474	41.0 (35.9-46.0)	1.66 (1.41-1.95)	<.001
Creatinine <2 mg/dL without dialysis	2056/10861	22.3 (21.4-23.2)	1 [Reference]	
LVEF, %				
30-45	476/2177	25.7 (23.7-27.8)	0.99 (0.90-1.09)	.83
<30	215/836	30.4 (26.9-34.0)	1.11 (0.97-1.28)	.12
>45	1689/8803	22.6 (21.6-23.6)	1 [Reference]	
Access site				
Other	1200/5256	26.6 (25.2-27.9)	1.37 (1.27-1.48)	<.001
Transfemoral	1211/6807	21.2 (20.1-22.3)	1 [Reference]	
STS PROM score, %				
8-15	868/3748	27.1 (25.5-28.7)	1.33 (1.21-1.46)	<.001
>15	503/1444	39.5 (36.7-42.2)	1.82 (1.60-2.06)	<.001
<8	1078/6988	18.6 (17.5-19.6)	1 [Reference]	
Preoperative atrial fibrillation				
Yes	1252/5086	29.0 (27.6-30.4)	1.37 (1.27-1.48)	<.001
No	1193/7058	19.9 (18.9-21.0)	1 [Reference]	



COPD indicates chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; STS-PROM, Society of Thoracic Surgeons Predicted Risk of Mortality.

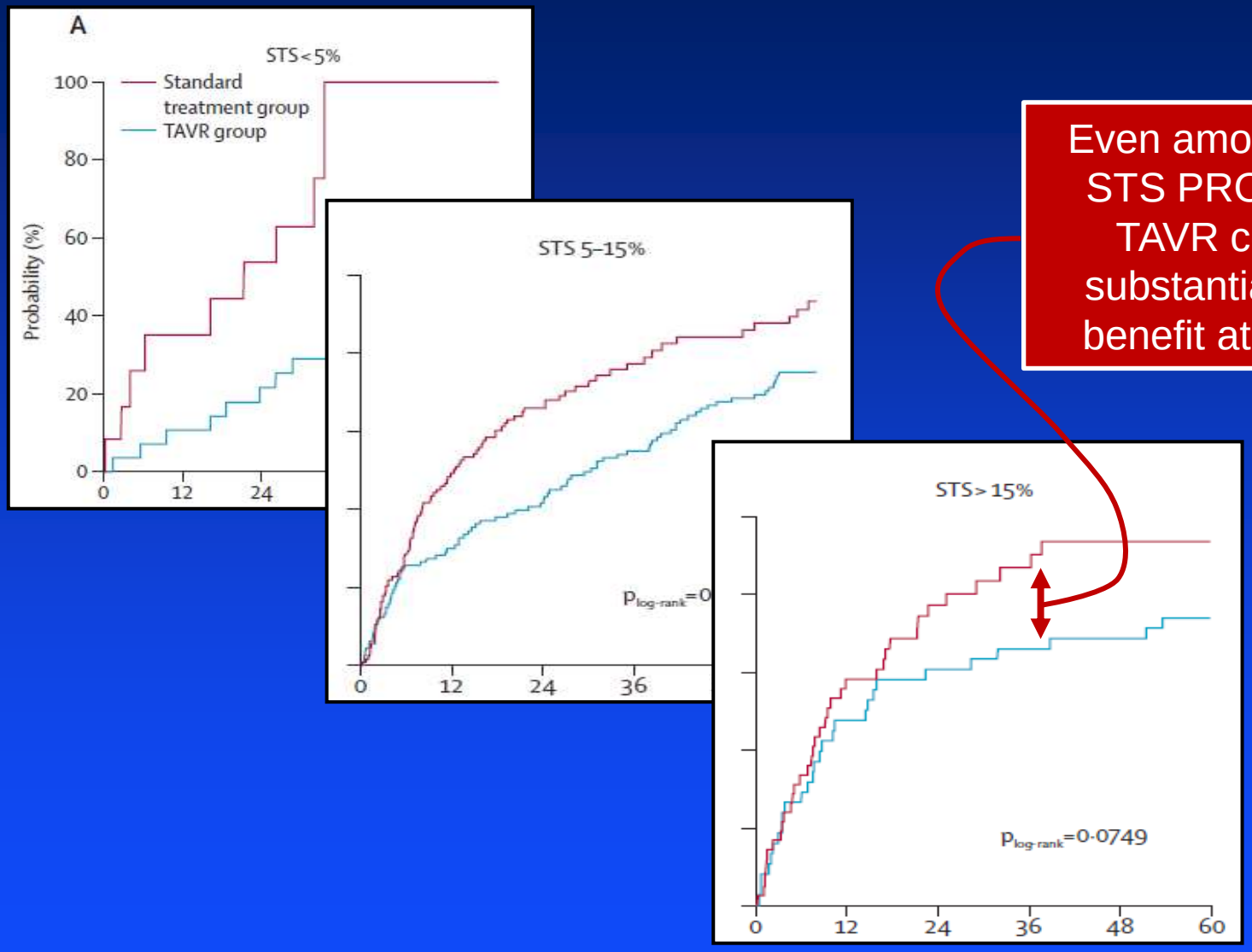
Holmes DR, et al. JAMA 2015;1019-28

When is TAVR Futile?

<u>Key Insight #2</u>

Combinations of risk factors improve prediction, but still may not be sufficient

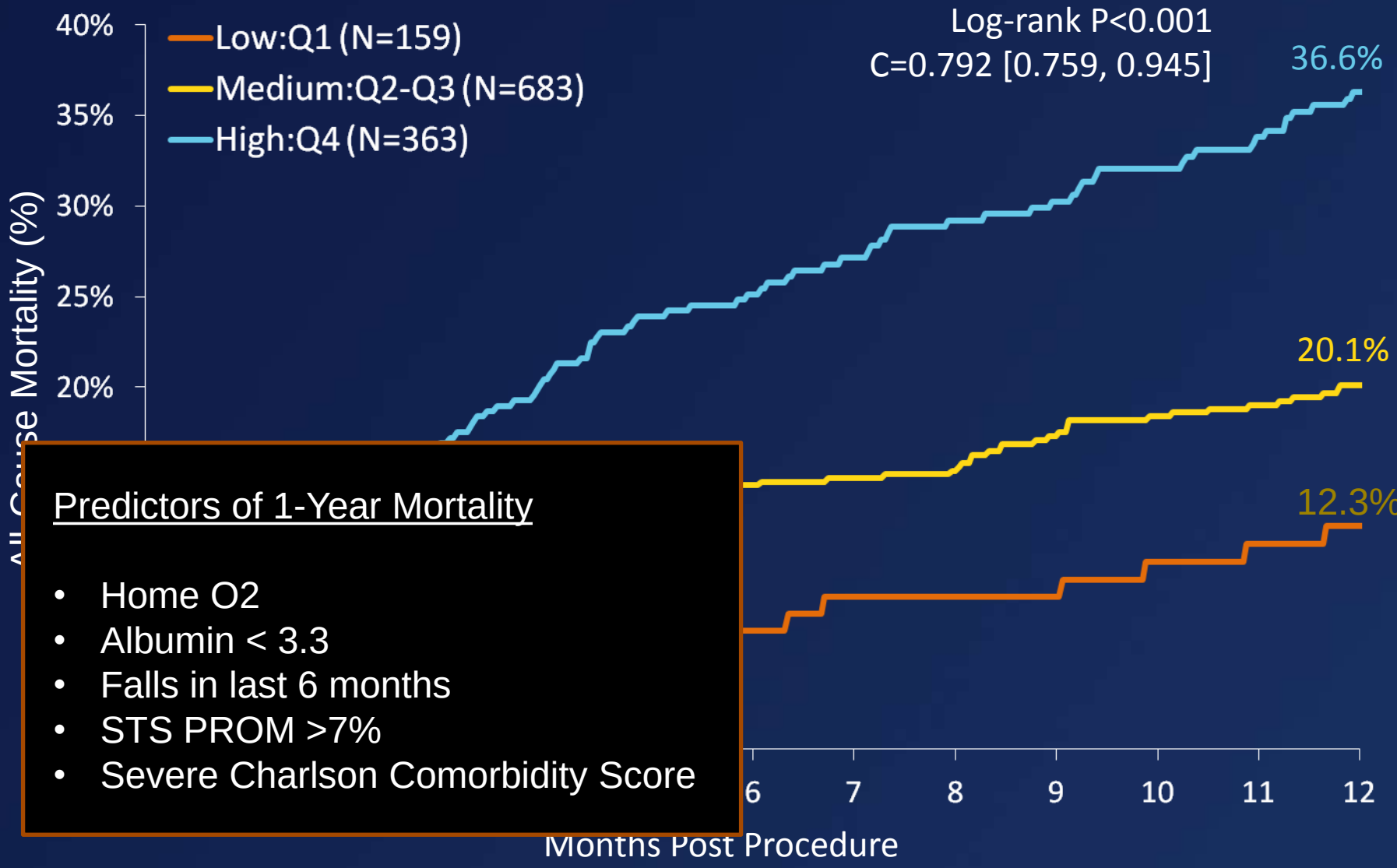
Identifying Futility in TAVR: STS PROM



Even among pts with STS PROM >15%, TAVR confers a substantial survival benefit at 3-5 years

Kapadia SR, et al. Lancet 2015

1-Year Mortality by Risk Level

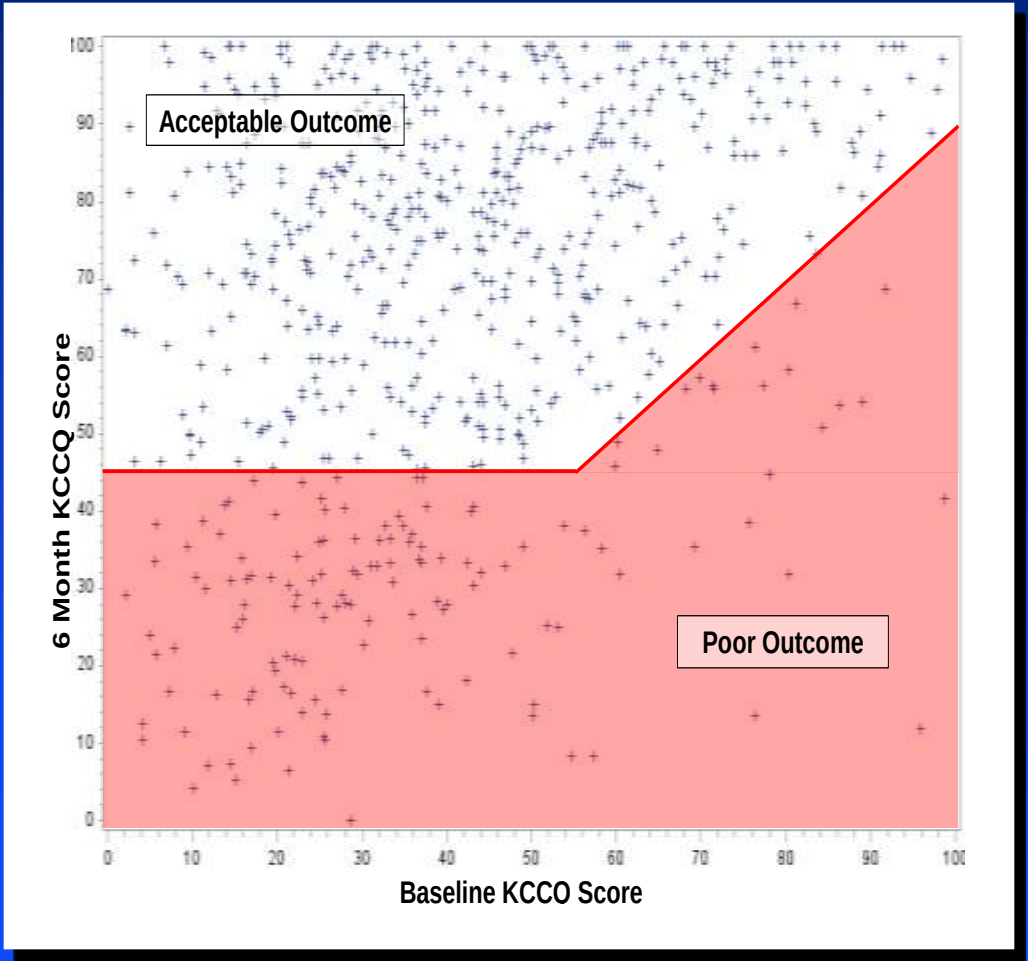


Predictors of 1-Year Mortality

- Home O2
- Albumin < 3.3
- Falls in last 6 months
- STS PROM >7%
- Severe Charlson Comorbidity Score

Validation cohort

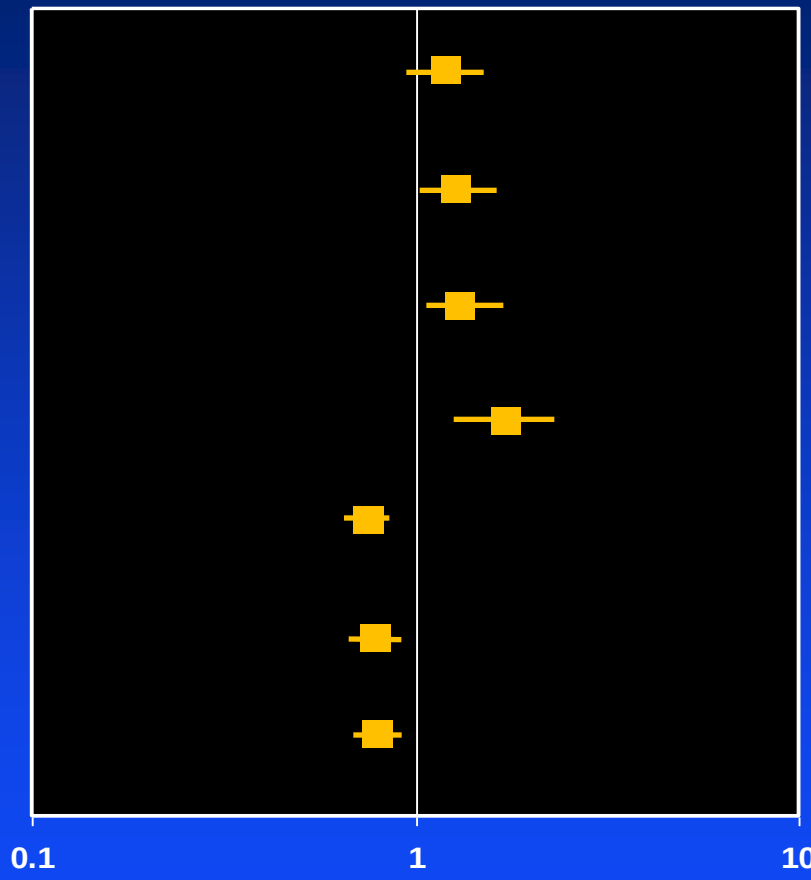
Poor Outcome: Conceptual Framework



- For patients at high risk of surgical AVR, a poor outcome should include both a mortality and a QOL component
- Conceptual analysis of PARTNER trial data suggest that a reasonable definition might be:
  - *Death within 6 months*
  - *Persistent KCCQ-OS <45*
  - *KCCQ-OS decrease of > 10 points vs. baseline*

Arnold SV, et al. Circ CV Qual Outcome 2013

Predictors of Poor Outcome

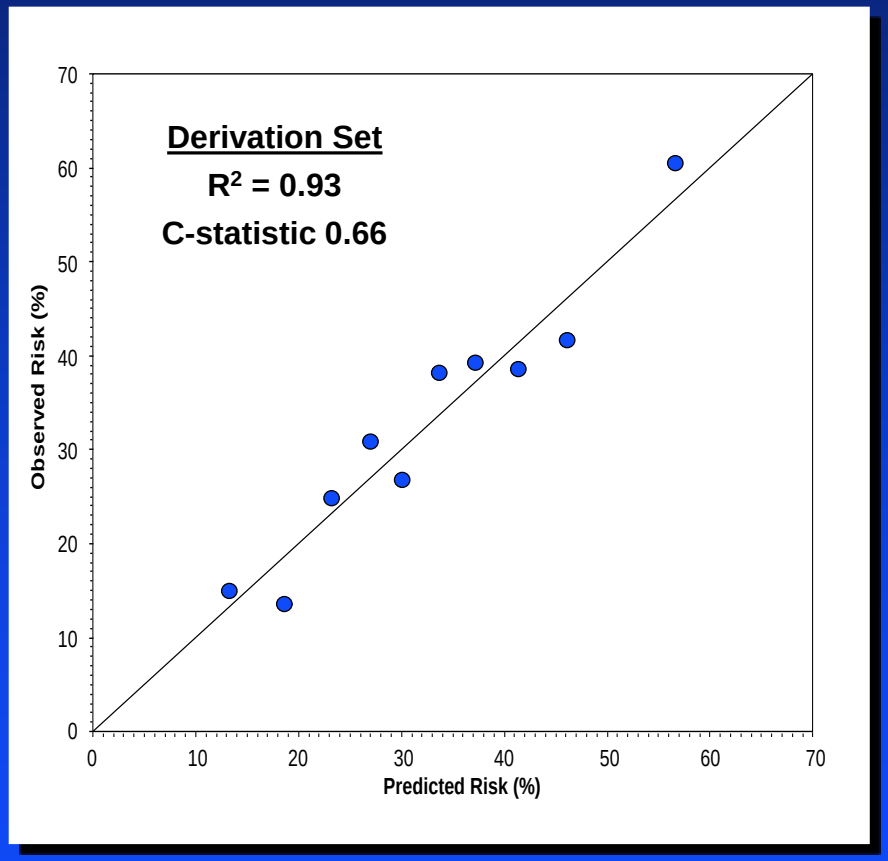


	Adjusted P-Value
Male Sex	0.097
Major Arrhythmia (AF)	0.036
Serum Creatinine	0.028
O2 dependent	0.002
Mean AoV gradient	<0.001
MMS Exam Score	0.036
6 Minute Walk Dist	<0.001

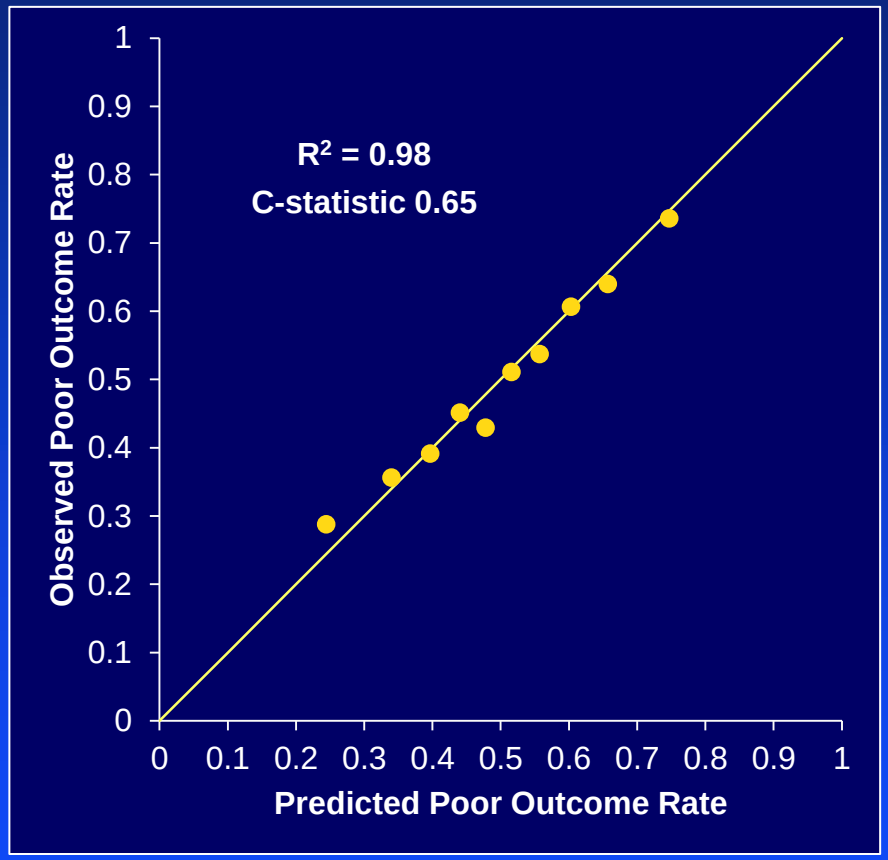
* Poor Outcome: (1) Death within 6 months; (2) KCCQ-OS < 45; or KCCQ-OS decrease more than 10 points vs. baseline

Model Calibration and Validation

Calibration (PARTNER data)



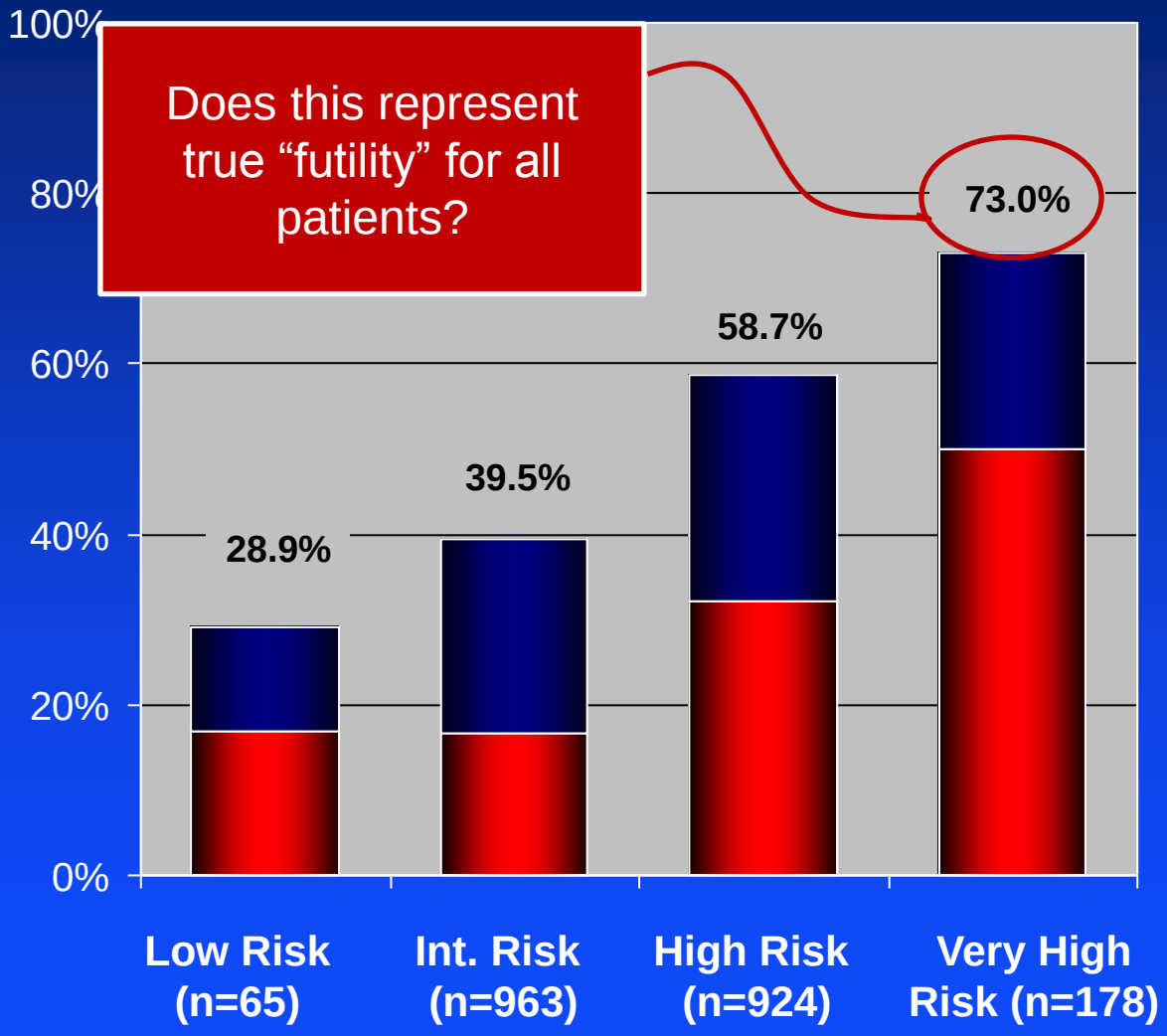
Validation (CoreValve data)



Arnold SV, et al. Circulation. 2014;129:2682-2690

Arnold SV, et al. JACC 2016;1868-77

Predictive Utility (1 year outcomes)



1 Year Model

- Expanded definition of poor outcome (death, KCCQ <60, KCCQ ↓ 10 points)
- Able to prospectively identify ~8% of patients with >70% likelihood of death or poor QOL at 1 yr

Poor Outcome Risk Model: Examples

	Patient 1
KCCQ-12 score	65 points (NYHA II)
Mean aortic valve gradient	50 mmHg
Home oxygen	No
Creatinine	1.0 mg/dL
Atrial fibrillation/flutter	No
Diabetes mellitus	No
Risk of Poor Outcome	**27%**

Arnold SV TCT 2017.

Poor Outcome Risk Model: Examples

	Patient 1	Patient 2
KCCQ-12 score	65 points (NYHA II)	50 points (NYHA III)
Mean aortic valve gradient	50 mmHg	40 mmHg
Home oxygen	No	NO
Creatinine	1.0 mg/dL	1.3 mg/dL
Atrial fibrillation/flutter	No	Yes
Diabetes mellitus	No	No
Risk of Poor Outcome	**27%**	**42%**

Arnold SV TCT 2017.

Poor Outcome Risk Model: Examples

	Patient 1	Patient 2	Patient 3
KCCQ-12 score	65 points (NYHA II)	50 points (NYHA III)	25 points (NYHA IV)
Mean aortic valve gradient	50 mmHg	40 mmHg	30 mmHg
Home oxygen	No	NO	Yes
Creatinine	1.0 mg/dL	1.3 mg/dL	2.5 mg/dL
Atrial fibrillation/flutter	No	Yes	Yes
Diabetes mellitus	No	No	No
Risk of Poor Outcome*	**27%**	**42%**	**71%**

Arnold SV TCT 2017.

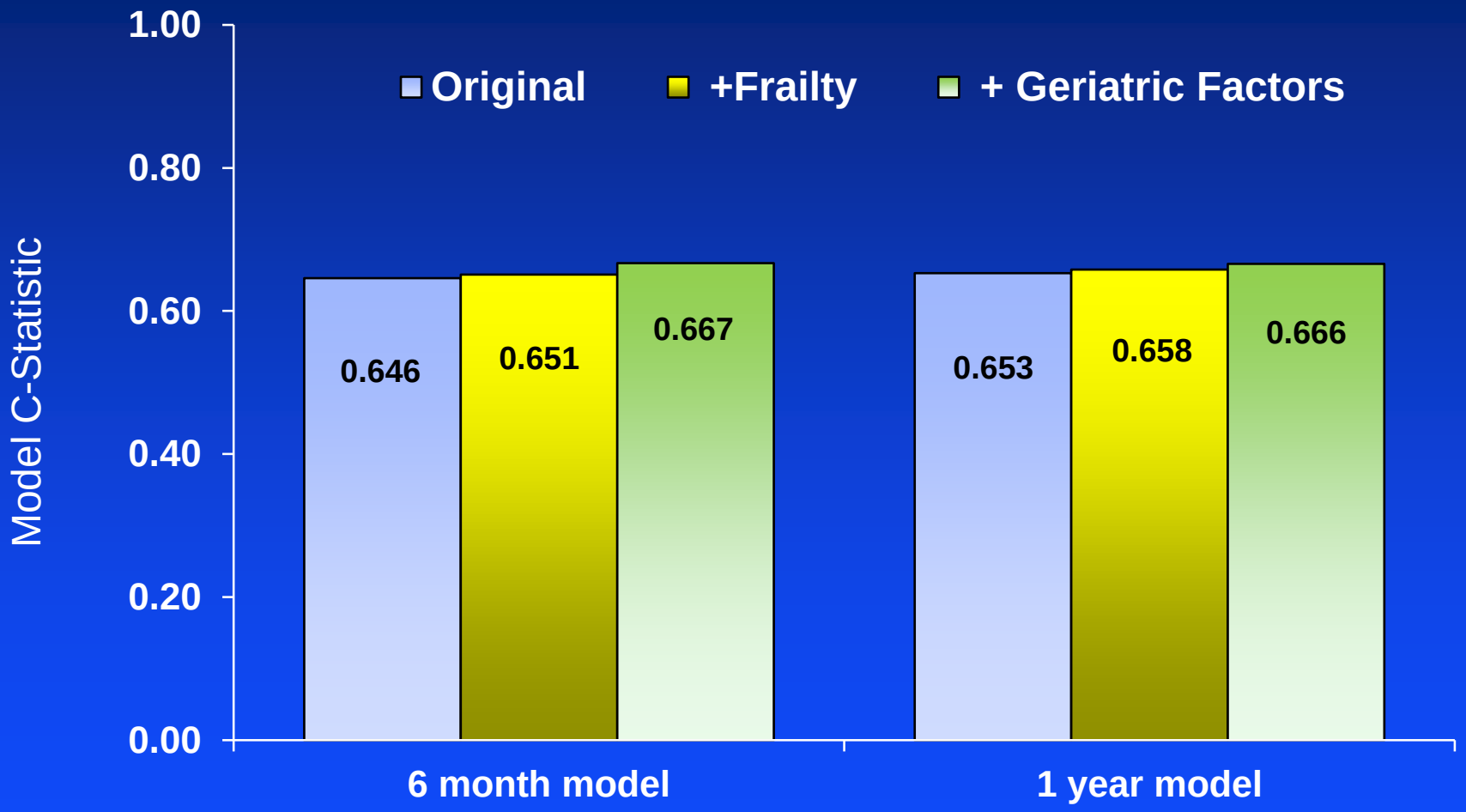
How much does frailty add to prediction?

Risk Factor	Adjusted OR for Poor Outcome	
	6 Month	1 Year
+ Frailty	1.33 (1.11-1.59)	1.42 (1.18-1.69)
+ Geriatric Components		
Disability (per ADL)	1.25 (1.16-1.35)	1.19 (1.09-1.30)
Weight Loss	1.52 (1.17-1.96)	1.61 (1.21-2.14)
Exhaustion	1.33 (1.10-1.60)	1.35 (1.12-1.63)

*P<0.003 for all factors

Arnold SV, et al. JACC 2016;1868-77

How much does frailty add to discrimination?



Arnold SV, et al. JACC 2016;1868-77

Summary

- For most patients who are currently considered for TAVR, QOL outcomes are at least as important as improved survival
- Although no single risk factor is predictive of TAVR outcomes, validated risk scores can be developed that provide reasonable discrimination of long-term outcomes that integrate both survival and QOL
- Since currently available models provide only moderate discrimination (c-statistic ~0.65), it may not be possible to identify patients for whom TAVR is expected to be truly “futile”

Future Directions

- Extension of risk models to other populations (e.g., intermediate risk, all-comers)
- Exploration of contribution of additional risk factors (e.g., biomarkers, myocardial performance/fibrosis)
- Are these the right endpoints for our patients?
- How best to provide this information and to whom (patient, provider, both)?