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Developments In TAVR

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Healthcare for what's next.

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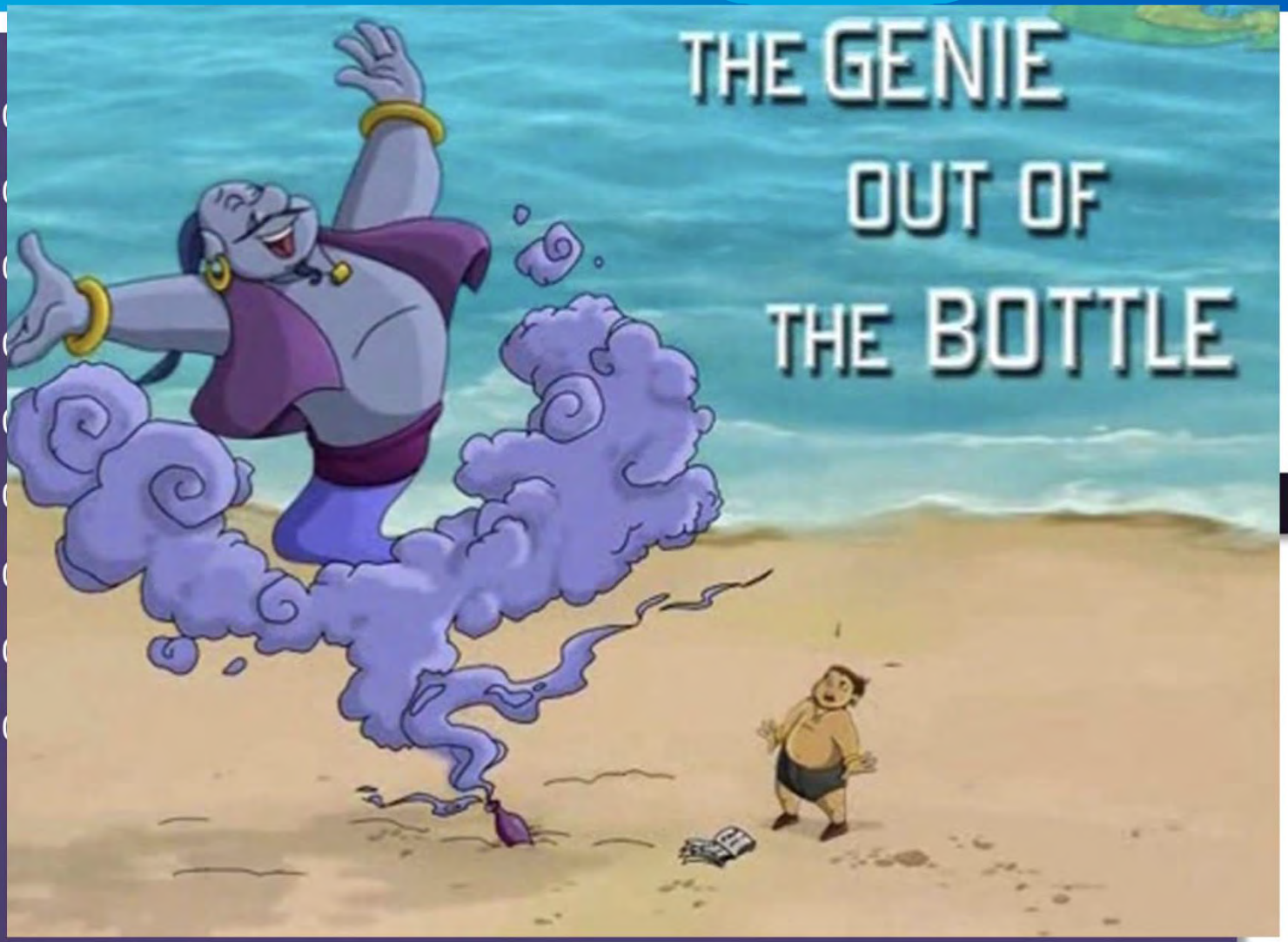
NO DISCLOSURES

Healthcare for what's ❯ next.

Introduction

- Transcatheter aortic valve replacement (TAVR) first performed in 2002 by Cribier. First prototype designed by Cribier and his start up Percutaneous Valve Technologies.
- Evolution of TAVR technology for the last 15 years has been unprecedented.
- Randomized trials have demonstrated that TAVR versus SAVR
- Lower Stroke
- Lower Mortality
- Lower rates of Atrial Fibrillation
- Quicker recovery, no scars
- Better hemodynamics

Aortic Valve Replacement



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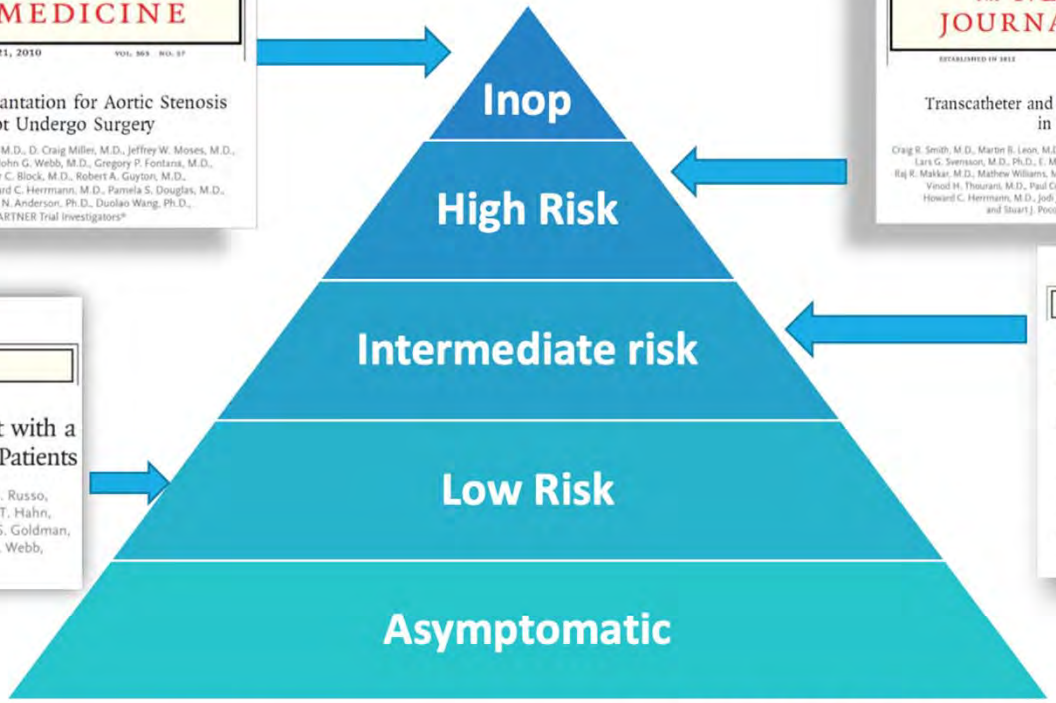
Balloon-expandable Valve

Risk Trends in Transcatheter Aortic Valve Therapy



N Engl J Med. 2010;363(17):1597-607.

N Engl J Med. 2011;364(23):2187-98.
N Engl J Med 2016; 374:1609-1620

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Presented at the American College of Cardiology, Sunday, March 17, 2019

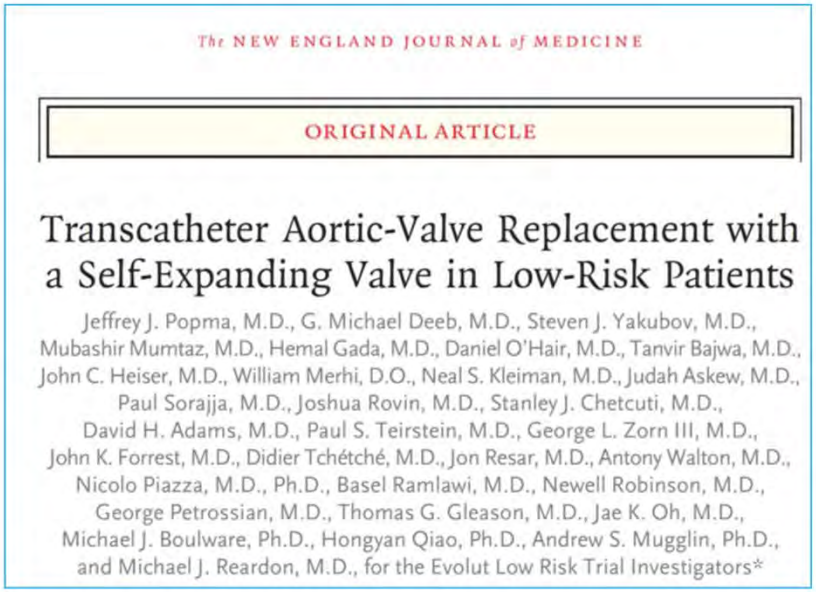
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients

M.J. Mack, M.B. Leon, V.H. Thourani, R. Makkar, S.K. Kodali, M. Russo, S.R. Kapadia, S.C. Malaisrie, D.J. Cohen, P. Pibarot, J. Leipsic, R.T. Hahn, P. Blanke, M.R. Williams, J.M. McCabe, D.L. Brown, V. Babaliaros, S. Goldman, W.Y. Szeto, P. Genereux, A. Pershad, S.J. Pocock, M.C. Alu, J.G. Webb, and C.R. Smith, for the PARTNER 3 Investigators*

Mack MJ, Leon MB, Thourani VH, et al. Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients. March 16, 2019,DOI: 10.1056/NEJMoa1814052



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients

Jeffrey J. Popma, M.D., G. Michael Deeb, M.D., Steven J. Yakubov, M.D., Mubashir Mumtaz, M.D., Hemal Gada, M.D., Daniel O'Hair, M.D., Tanvir Bajwa, M.D., John C. Heiser, M.D., William Merhi, D.O., Neal S. Kleiman, M.D., Judah Askew, M.D., Paul Sorajja, M.D., Joshua Rovin, M.D., Stanley J. Chetcuti, M.D., David H. Adams, M.D., Paul S. Teirstein, M.D., George L. Zorn III, M.D., John K. Forrest, M.D., Didier Tchétché, M.D., Jon Resar, M.D., Antony Walton, M.D., Nicolo Piazza, M.D., Ph.D., Basel Ramlawi, M.D., Newell Robinson, M.D., George Petrossian, M.D., Thomas G. Gleason, M.D., Jae K. Oh, M.D., Michael J. Boulware, Ph.D., Hongyan Qiao, Ph.D., Andrew S. Mugglin, Ph.D., and Michael J. Reardon, M.D., for the Evolut Low Risk Trial Investigators*

Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients. March 16, 2019 DOI: 10.1056/NEJMoa1816885

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THE PARTNER 3 TRIAL

PARTNER 3 Clinical Sites

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Endpoints

Primary Endpoint

- **Non-hierarchical composite of all-cause mortality, all strokes, or CV re-hospitalization at 1 year**
  - Primary analysis was non-inferiority, followed by superiority
  - Analysis cohort was the 'as-treated' (AT) population, defined as all randomized patients in whom the procedure was initiated.
  - Multiple sensitivity analyses performed

Study Endpoints

Evolut Low Risk Trial

Primary Safety and Effectiveness Endpoint
All-cause mortality or disabling stroke at 2 years

Hierarchical Powered Secondary Endpoints

Noninferiority
- Mean gradient at 1 year
- EOA at 1 year
- Change in NYHA class from baseline to 1 year
- Change in KCCQ score from baseline to 1 year

Superiority
- Mean gradient at 1 year
- EOA at 1 year
- Change in KCCQ score from baseline to 30 days

Other Secondary Endpoints
- 30-day safety composite of
  - All-cause mortality
  - Disabling stroke
  - Life-threatening bleeding
  - Major vascular complications
  - Stage 2 or 3 acute kidney injury
- New pacemaker implantation at 30 days
- Heart failure rehospitalizations at 1 year
- Aortic-valve reintervention at 1 year
- Moderate/severe AR at 1 year
- All stroke at 1 year
- Life-threatening bleeding at 1 year

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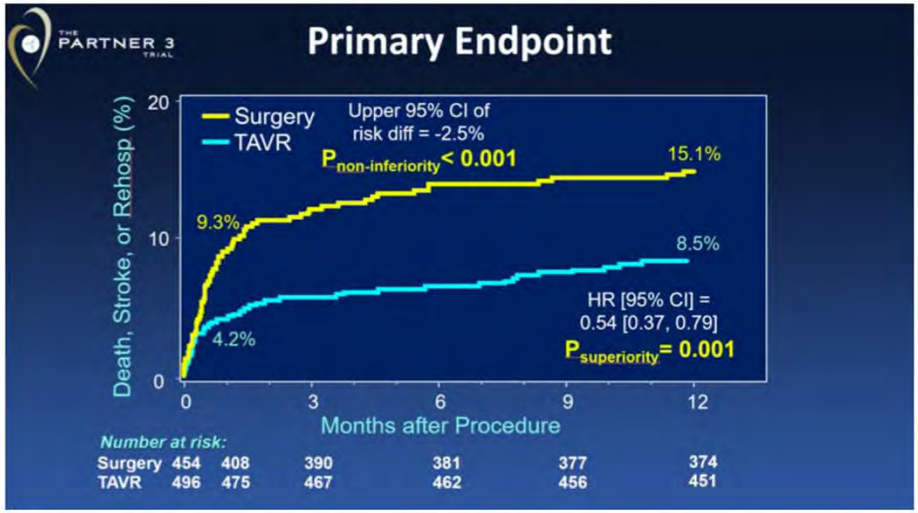
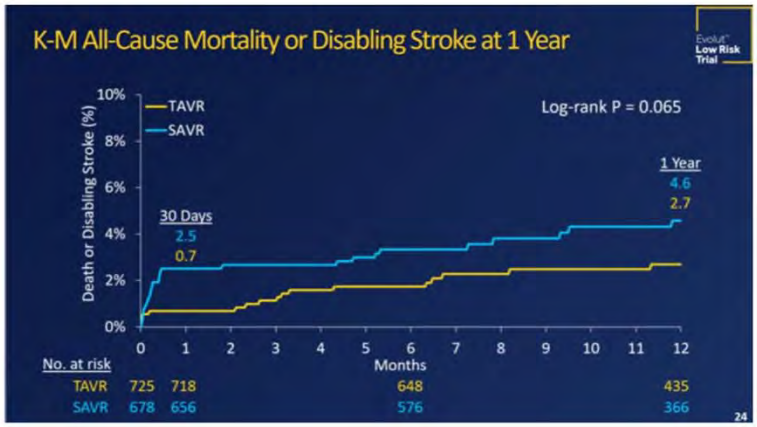
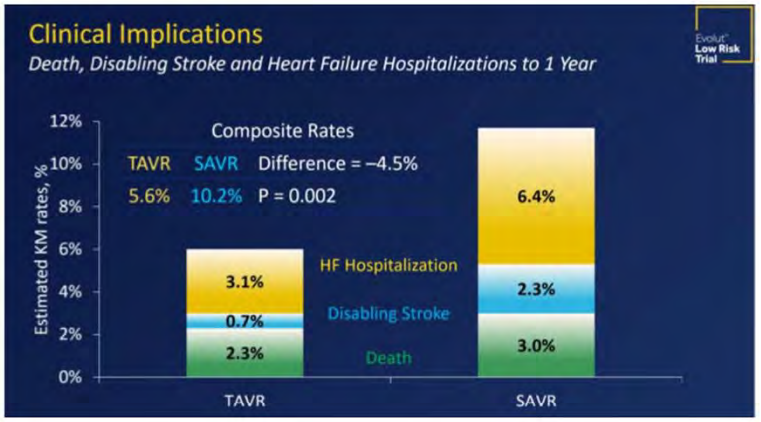
Primary Endpoint







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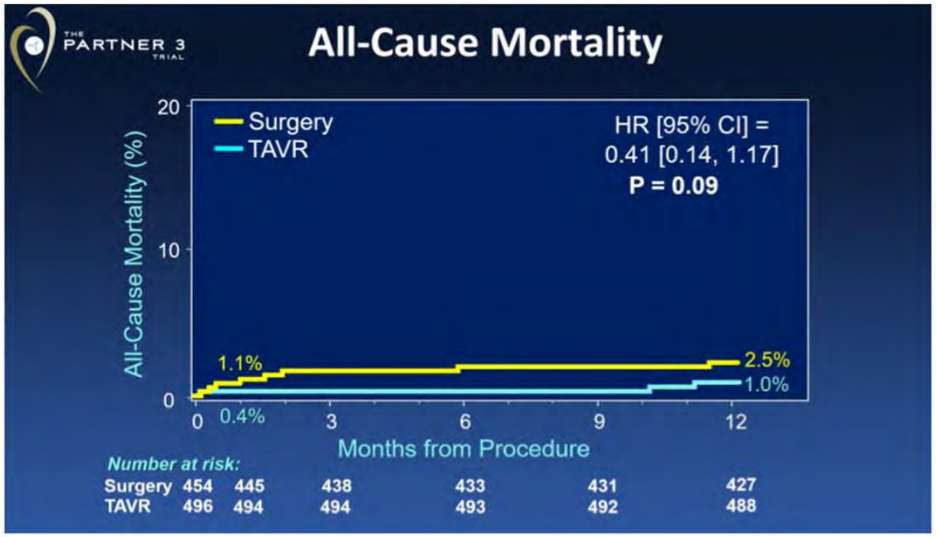
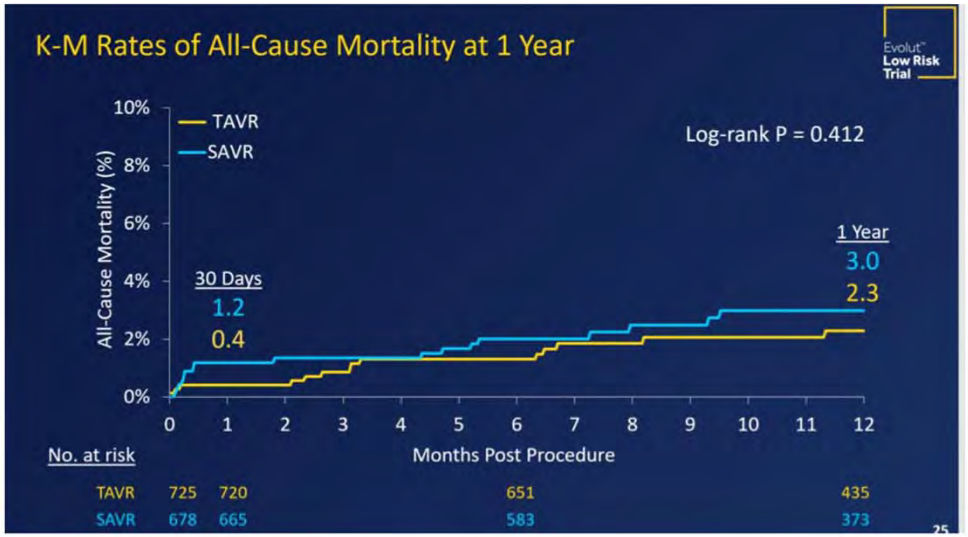
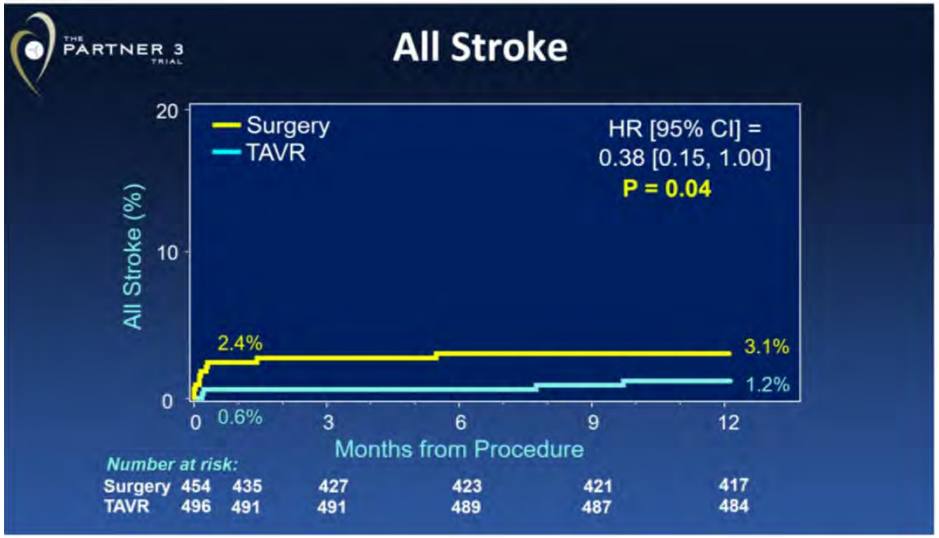
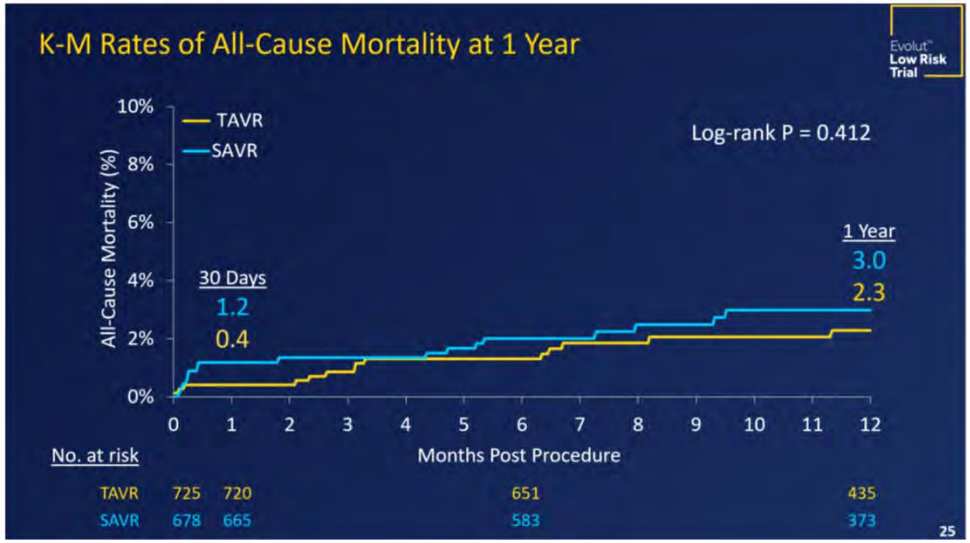
All-Cause Mortality





Stroke


THE PARTNER 3 TRIAL
All Stroke
Surgery
TAVR
HR [95% CI] = 0.38 [0.15, 1.00]
P = 0.04
All Stroke (%)
20
10
0
2.4%
0.6%
3.1%
1.2%
0
3
6
9
12
Months from Procedure
Number at risk:
Surgery 454 435 427 423 421 417
TAVR 496 491 491 489 487 484


K-M Rates of All-Cause Mortality at 1 Year
Evolut Low Risk Trial
TAVR
SAVR
Log-rank P = 0.412
All-Cause Mortality (%)
10%
8%
6%
4%
2%
0%
30 Days
1.2
0.4
1 Year
3.0
2.3
0 1 2 3 4 5 6 7 8 9 10 11 12
Months Post Procedure
No. at risk
TAVR 725 720 651 435
SAVR 678 665 583 373
25

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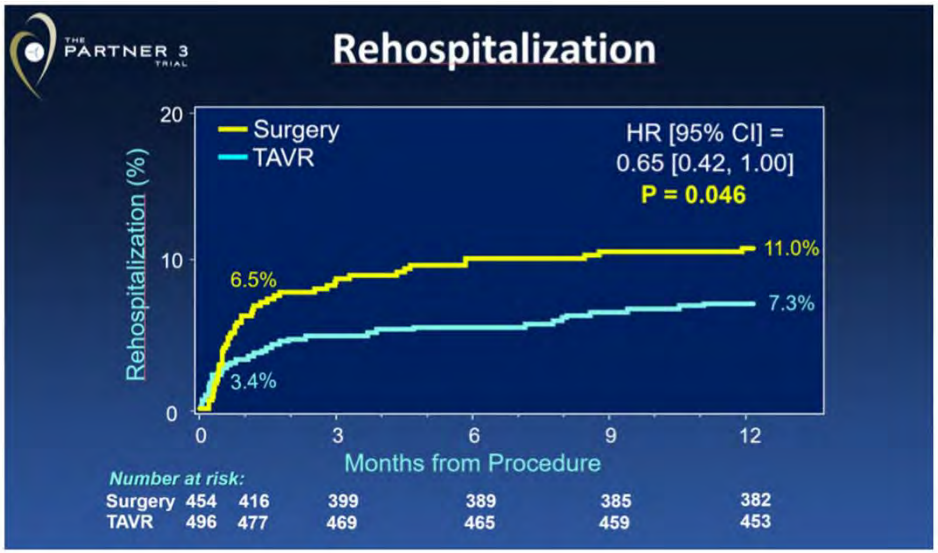
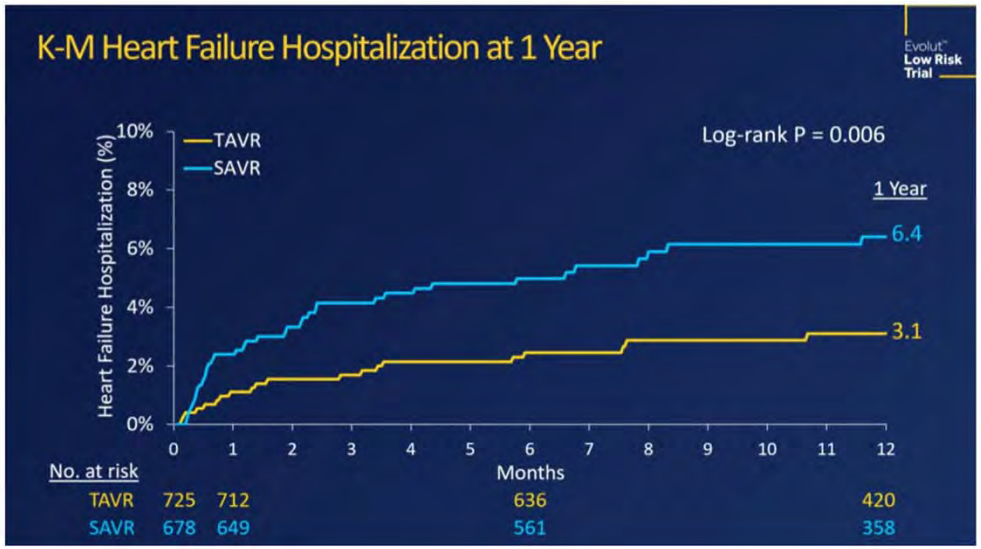
Rehospitalization





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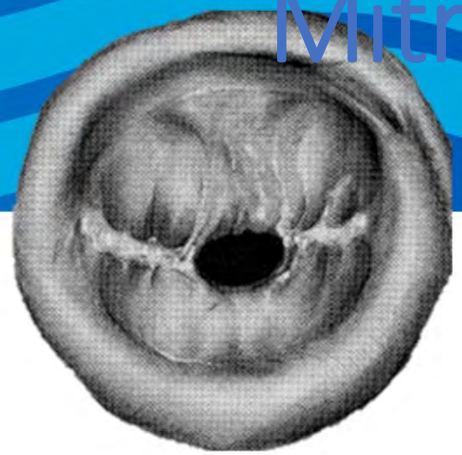
Conclusions

- TAVR in low surgical risk using the Sapien 3 Valve:
  - Significantly reduces the rate of death, stroke, or re-hospitalization at 1 year by 46%
  - Secondary endpoints (adjusted) showed that TAVR reduced new-onset atrial fibrillation, index hospitalization days, and measure of poor treatment outcome (death or low KCCQ score at 30 days)
  - Other secondary endpoint analysis showed reduced bleeding after TAVR and no difference in the need for new permanent pacemaker placement, major vascular complications, coronary obstruction, and moderate to severe perivalvular leak
  - Some secondary endpoints favored surgery, including reduced LBBB, reduced mild PVR, and lower aortic gradients

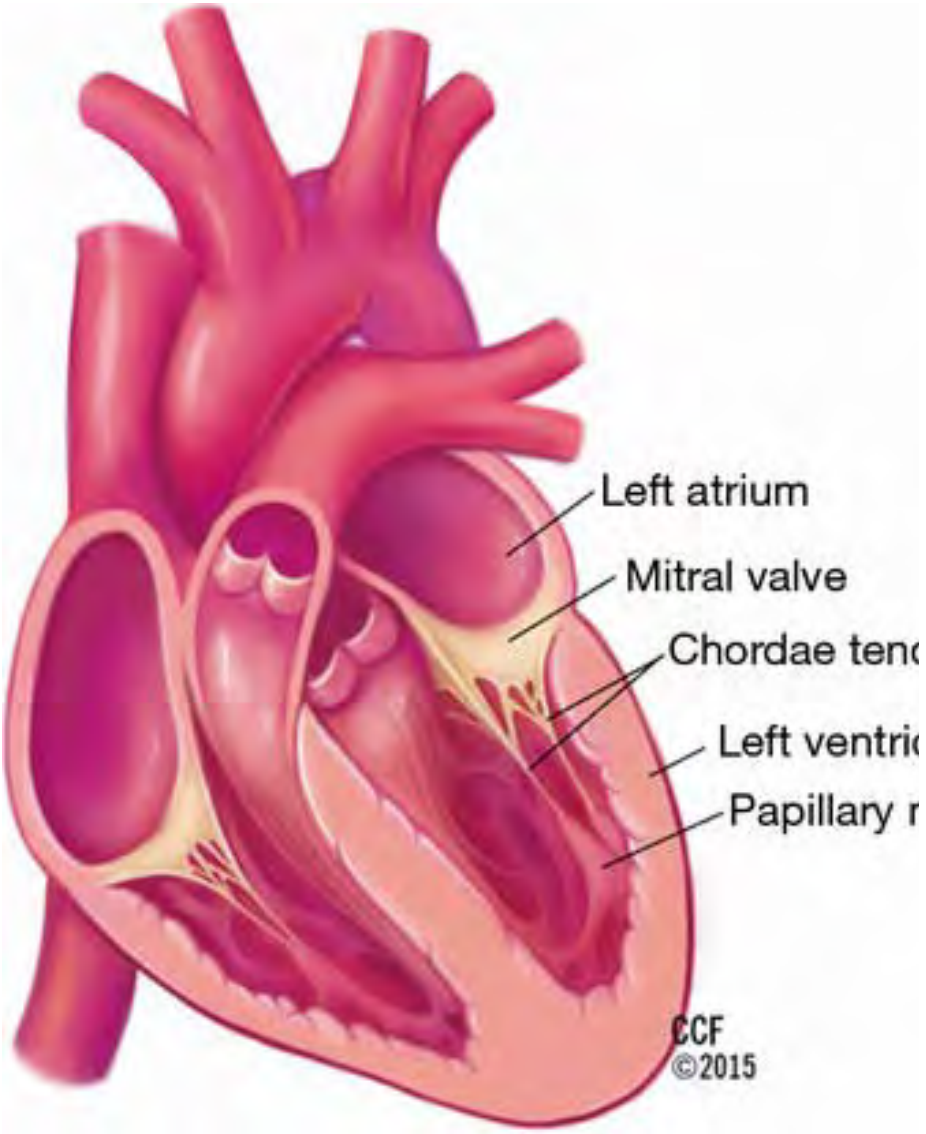
Mitra

- 1902
  - Concept of mitral commisurotomy proposed
  - Brunton
- 1920
  - 1st successful Surgical Mitral Commissurotomy
- 1950 -60
  - Transatrial and Transventricular Closed MV commissurotomy
- 1982
  - Inoue
  - Percutaneous Transvenous MV Commissurotomy (PTMC)
- 1994
  - PMBV Clinically approved in US
- 2014
  - FDA approval for Mitral Clip in High Risk Degenerative MR
- 2019
  - FDA approval for Mitral Clip in Functional MR



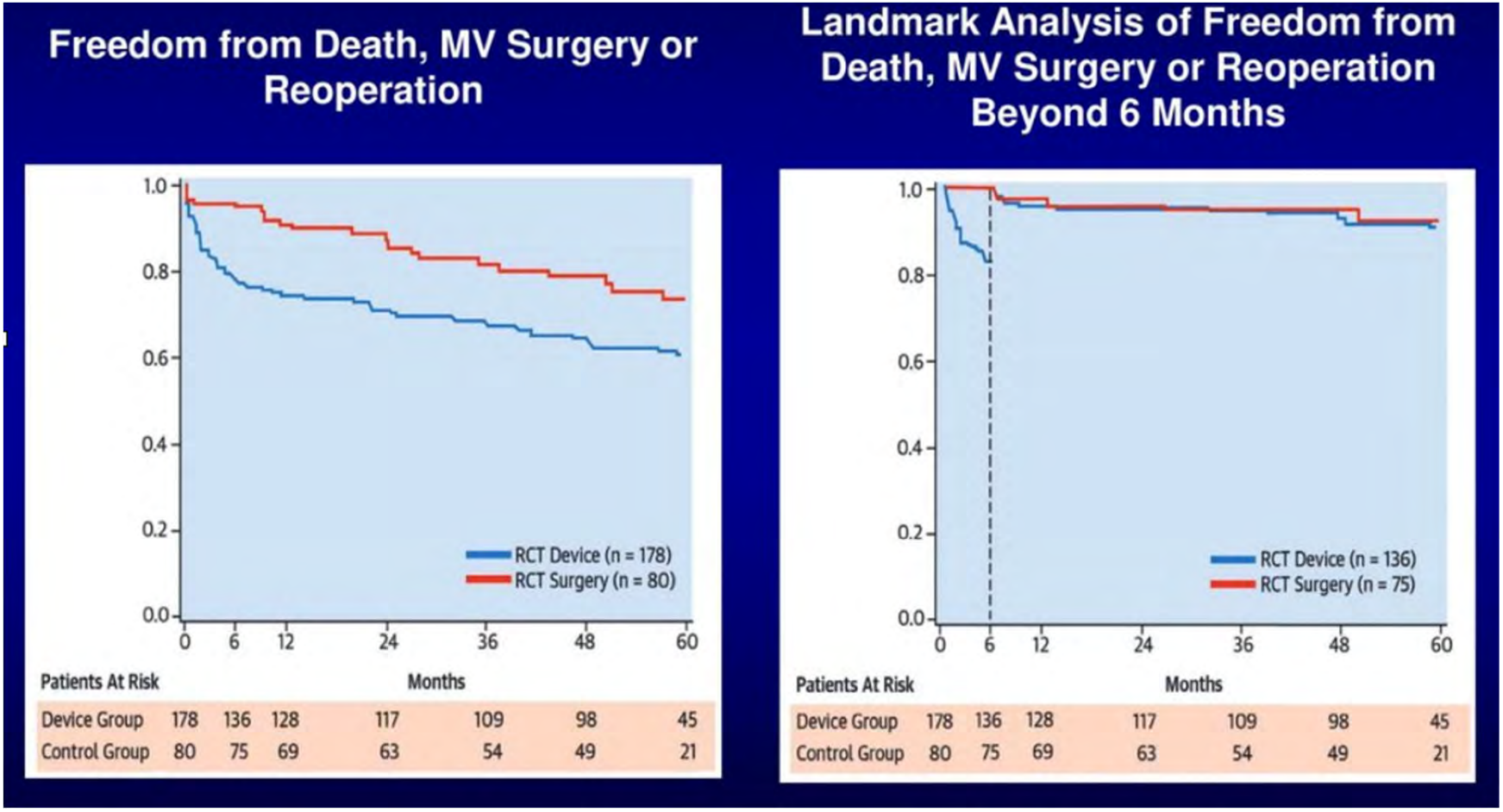
6 Anatomical Parts of the Mitral Valve

- Leaflets
- Annulus
- Chordae
- Papillary Muscles
- Left Ventricle
- Left Atrium



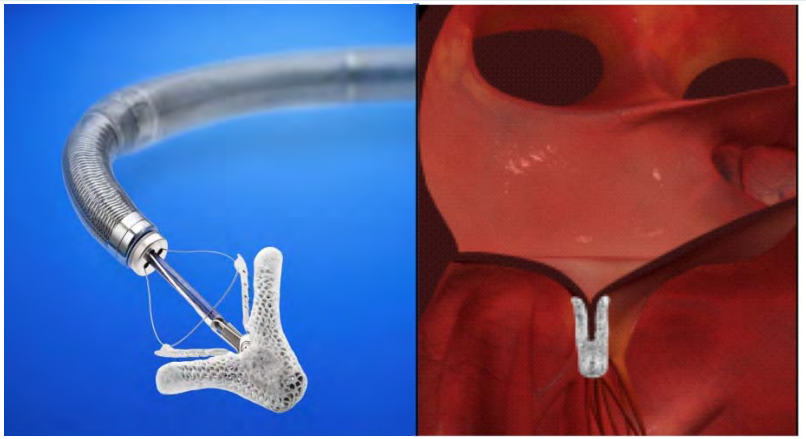
Intervention Mechanism		Abandoned	In Development and/or Approved
Mitral Repair	Leaflet Repair	Mobius Edwards	MitraClip (Degenerative & Functional)
			PASCAL
	Indirect Annuloplasty	Monarch Edwards	MitraFlex
		PMTA Viacor	Arto-MVRx
	Direct Annuloplasty	ReCor (US)	Cardioband
			Millipede
			MitraSpan TASRA
			Micardia Encor
			Mitral Bridge
			QuantumCor (RF)
	Chordal Repair		Harpoon
			Valtech Vchordal
			MISTRAL
			Mitralis
	Enhanced Coaptation	Myocor Coapsys	MitraSpacer
			Middle Peak
			MitrAssisst
	LV Remodeling	Acorn	Accucinch
		Myocor	BACE Mardil
Mitral Replacement	Replacement		**Sapien 3**
			Cephea
			Tiara

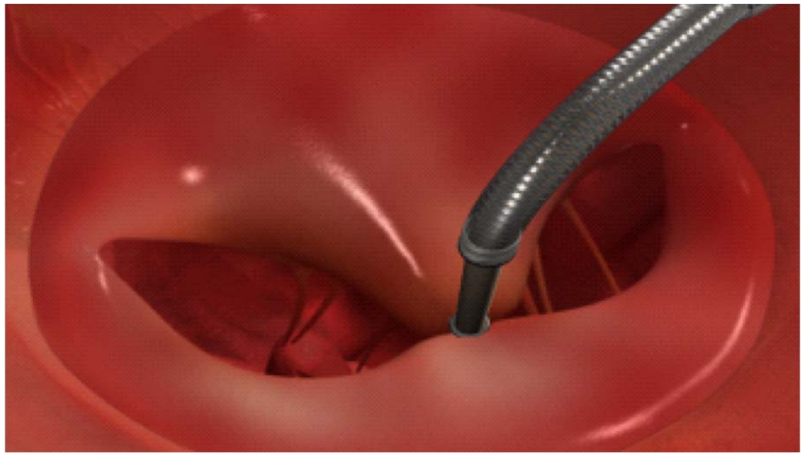
EVEREST II TRIAL: 5 year Clinical Outcomes Clip vs. Surgery



COAPT

A Randomized Trial of Transcatheter Mitral Valve Leaflet Approximation in Patients with Heart Failure and Secondary Mitral Regurgitation

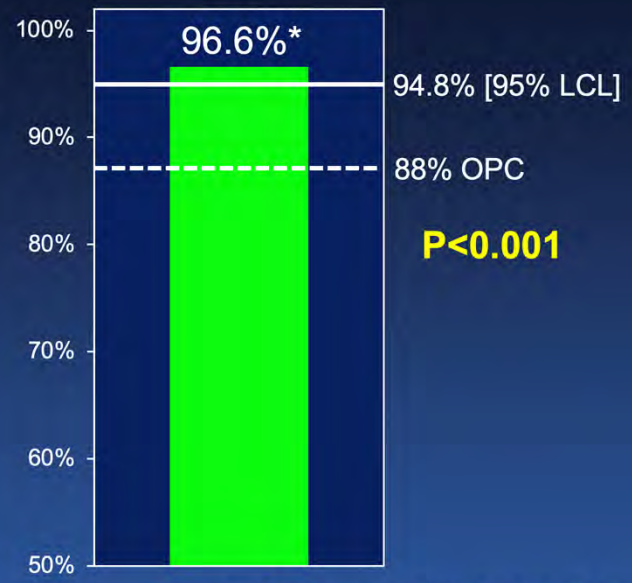




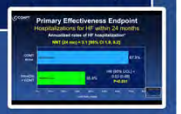
COAPT TRIAL

Primary Safety Endpoint

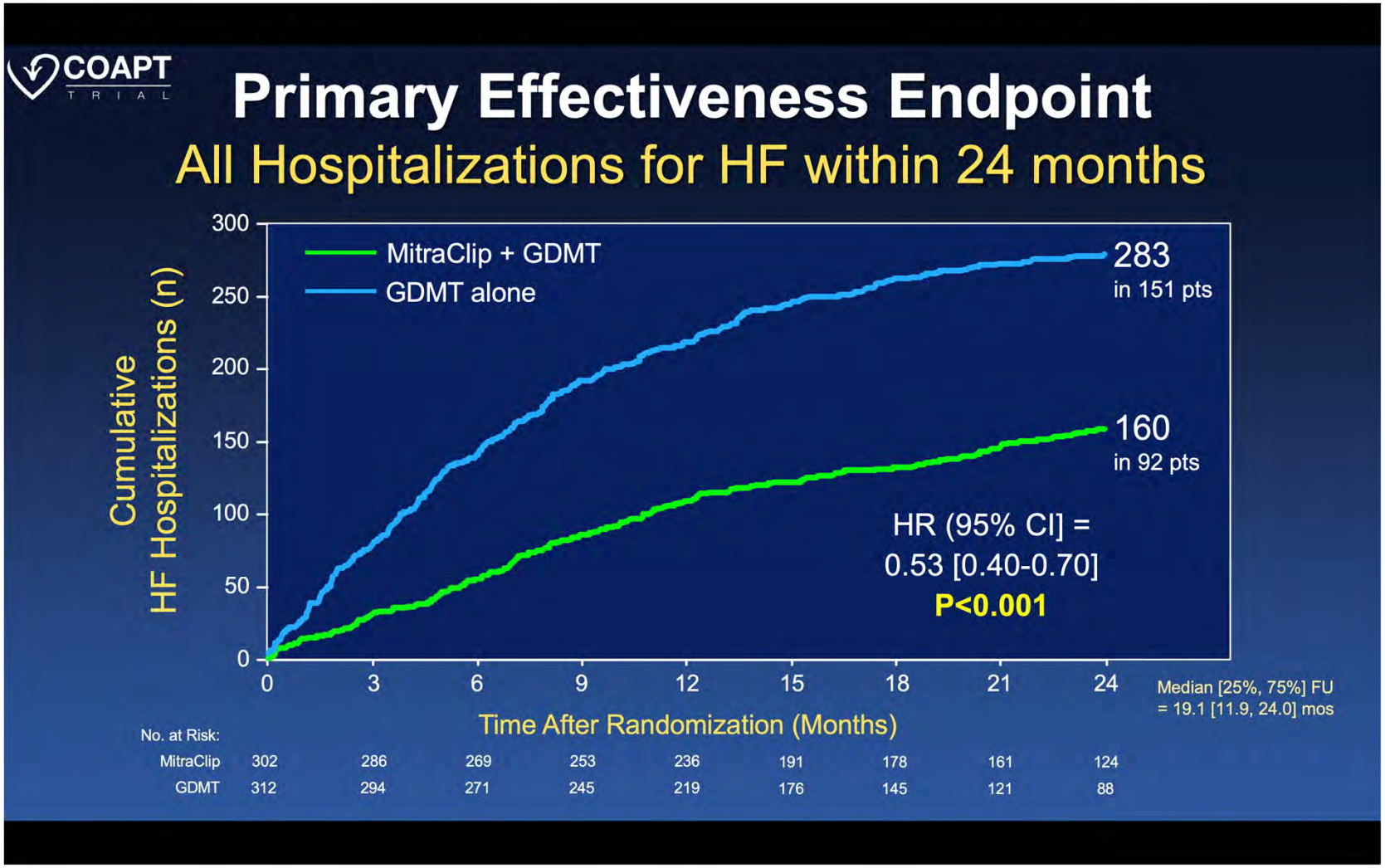
Freedom from Device-related Complications within 12 months

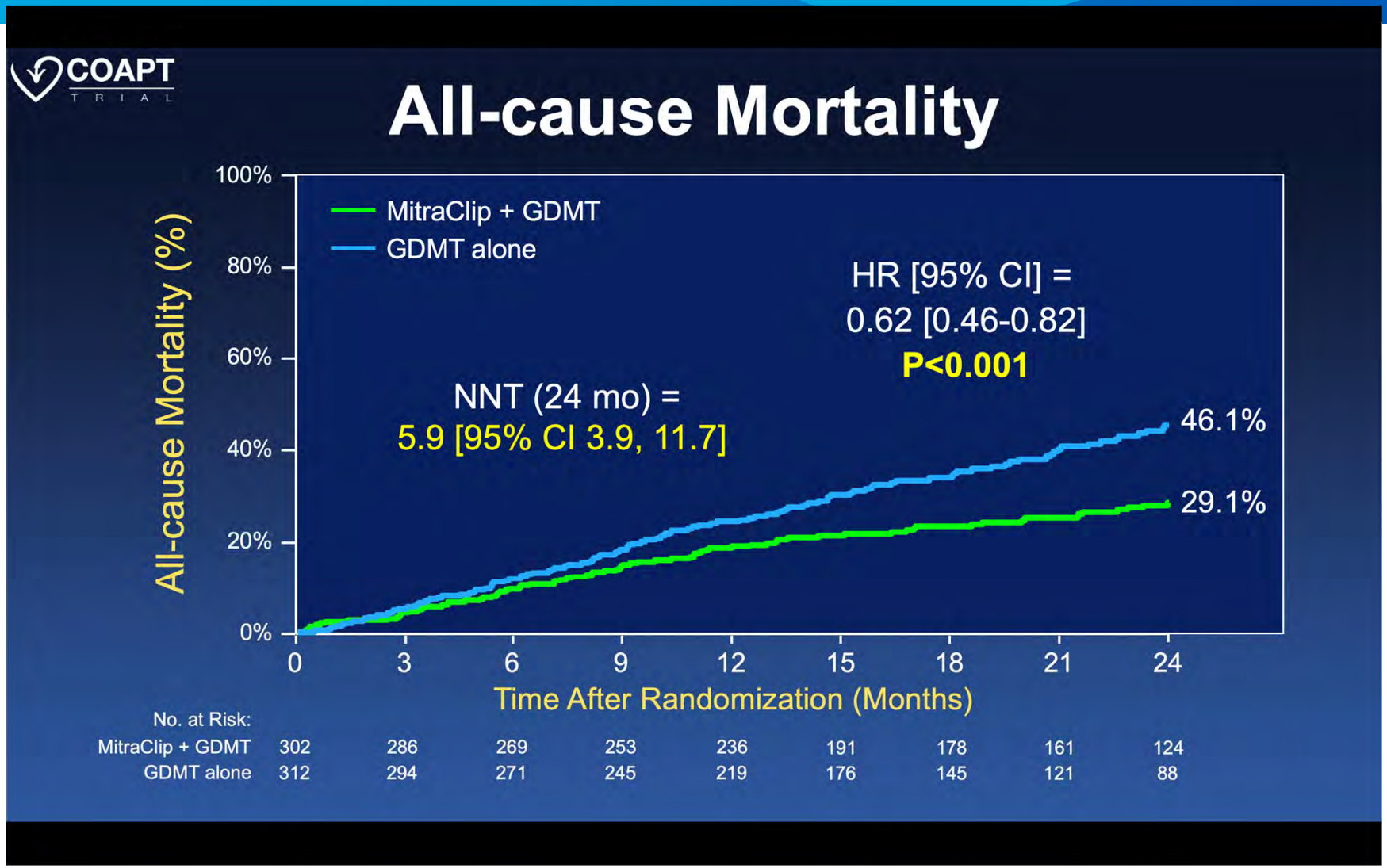


MitraClip procedure attempted	N=293
Device-related complications	9 (3.4%)
- Single leaflet device attachment	2 (0.7%)
- Device embolization	1 (0.3%)
- Endocarditis requiring surgery	0 (0.0%)
- Mitral stenosis requiring surgery	0 (0.0%)
- Left ventricular assist device implant	3 (1.2%)
- Heart transplant	2 (0.8%)
- Any device-related complication requiring non-elective CV surgery	1 (0.3%)



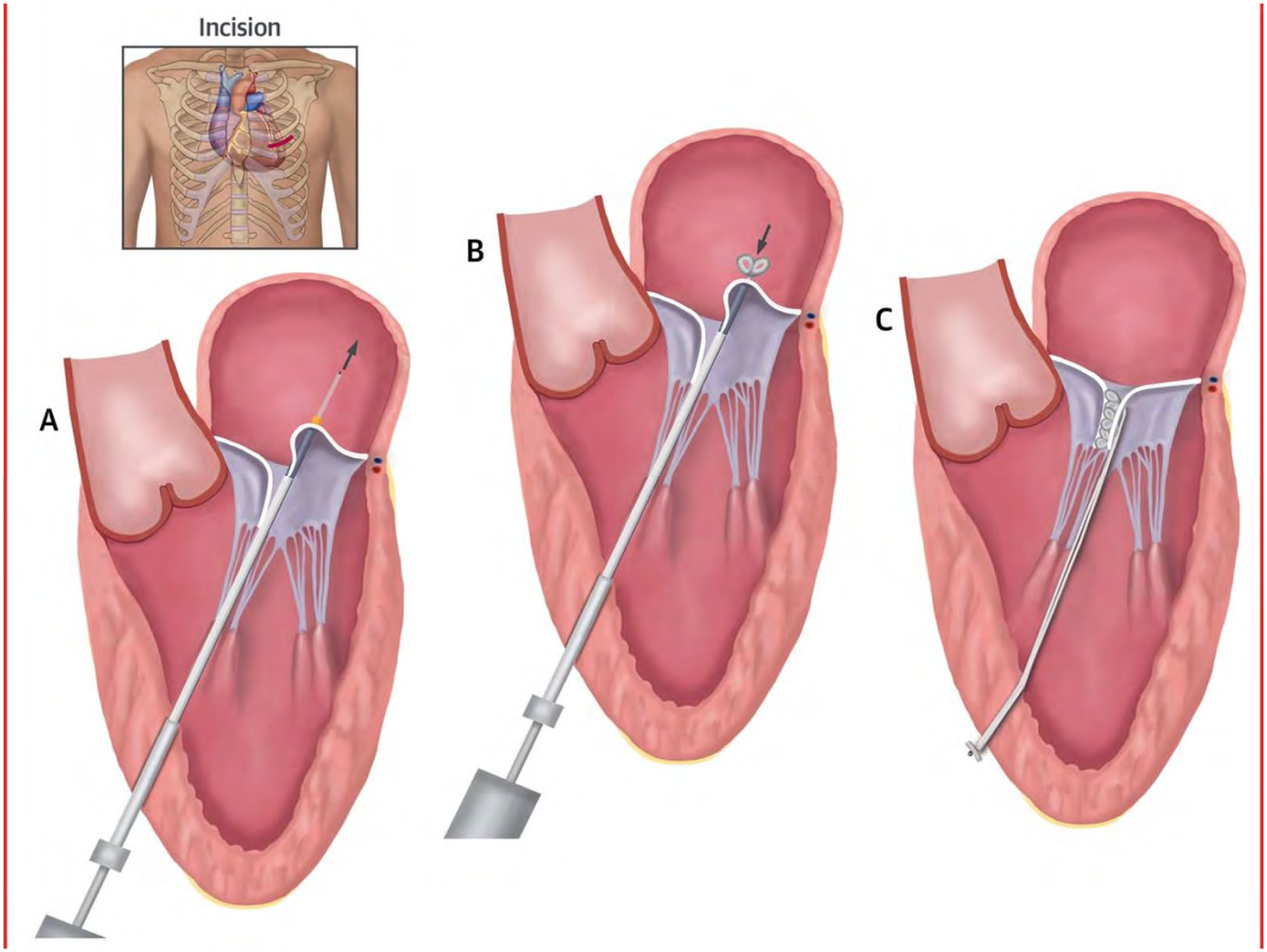
*KM estimate; **Calculated from Z test with Greenwood's method of estimated variance against a pre-specified objective performance goal of 88%


COAPT
TRIAL
Primary Effectiveness Endpoint
All Hospitalizations for HF within 24 months
Cumulative HF Hospitalizations (n)
300
250
200
150
100
50
0
MitraClip + GDMT
GDMT alone
283
in 151 pts
160
in 92 pts
HR (95% CI] =
0.53 [0.40-0.70]
P<0.001
0
3
6
9
12
15
18
21
24
Time After Randomization (Months)
Median [25%, 75%] FU
= 19.1 [11.9, 24.0] mos
No. at Risk:
MitraClip 302 286 269 253 236 191 178 161 124
GDMT 312 294 271 245 219 176 145 121 88

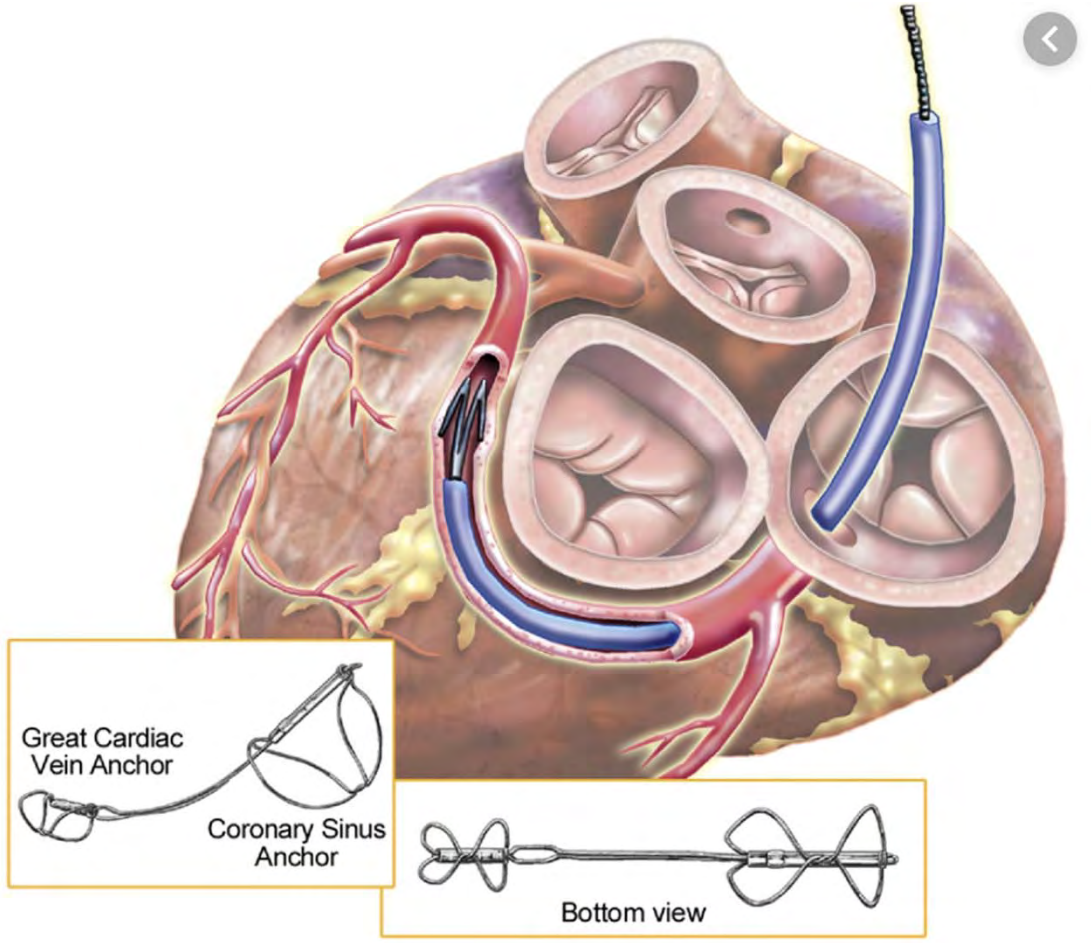

COAPT
TRIAL
All-cause Mortality
All-cause Mortality (%)
100%
80%
60%
40%
20%
0%
MitraClip + GDMT
GDMT alone
HR [95% CI] =
0.62 [0.46-0.82]
P<0.001
NNT (24 mo) =
5.9 [95% CI 3.9, 11.7]
46.1%
29.1%
0
3
6
9
12
15
18
21
24
Time After Randomization (Months)
No. at Risk:
MitraClip + GDMT 302 286 269 253 236 191 178 161 124
GDMT alone 312 294 271 245 219 176 145 121 88

Chordal repair

Harpoon



Indirect Annuloplasty



Direct Annuloplasty

Mitral Valve Replacement

Braile Biomedica

Braile Biomedica

CardiAQ 1st G

CardiAQ Edwards

Cephea

Direct Flow Medical

Twelve Medtronic

M-Valve

Edwards Fortis

HighLife

Navigate

Neovasc Tiara

PermaValve MID

Sinomed

Tendyne Abbott

SATURN TMVR

Valtech CardioValve

Caisson

Others: MitraHeal, Mitrassist, Mitraltech, Mehr Medical, Mitracath, Mitralix MAESTRO, Nakostech, St. George ATLAS, Transcatheter Technologies Tresillo

Sapien M-3