Mitra clip
Clinical Outcomes for functional and degenerative mitral regurgitation

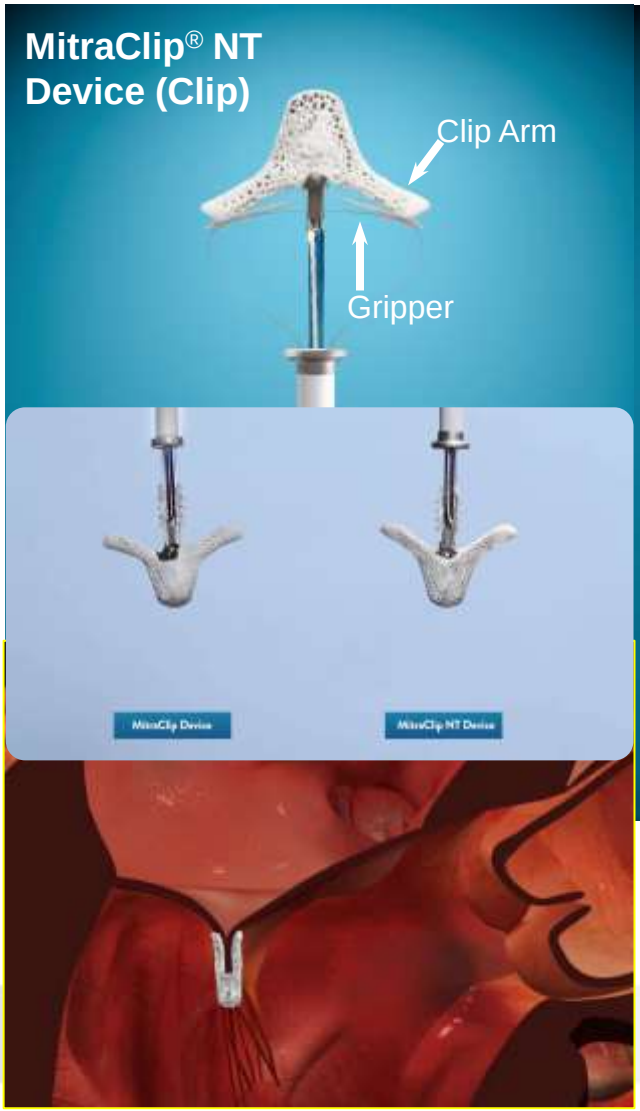
Professor Darren Walters

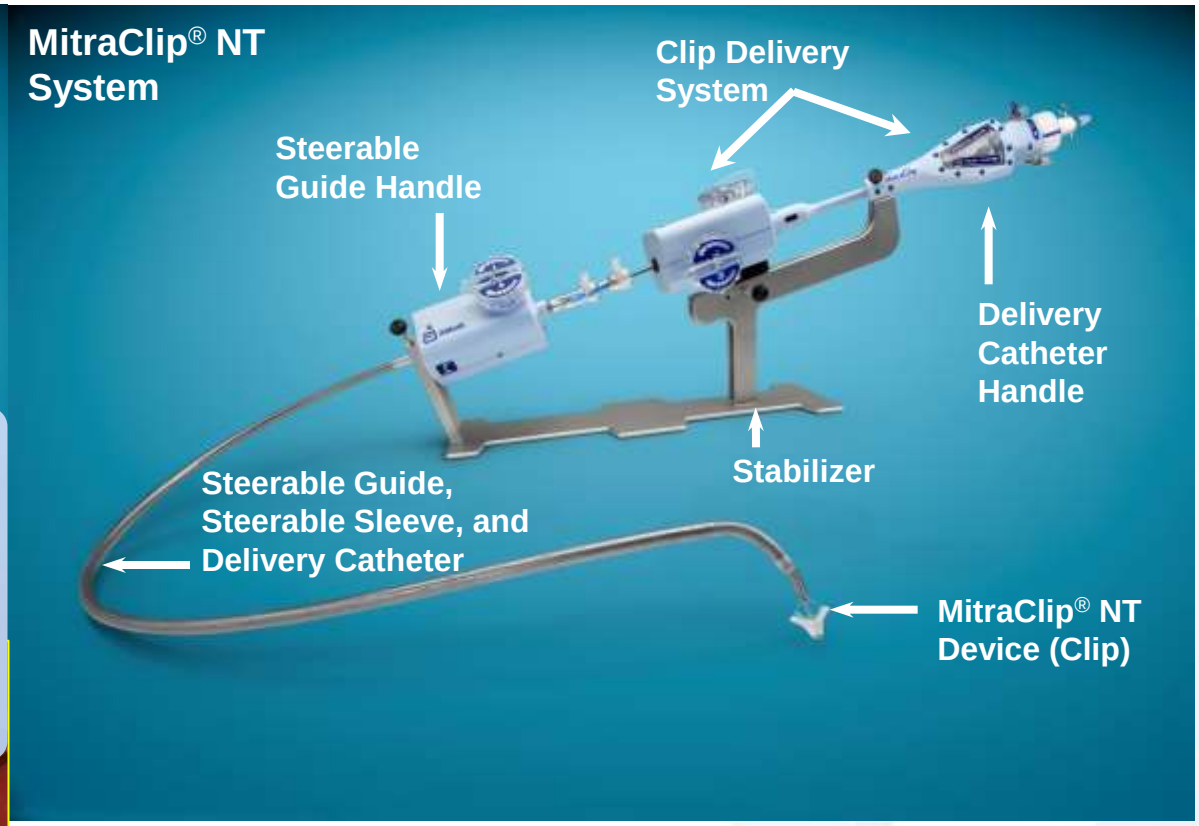
University of Queensland

Heart Lung Institute

The Prince Charles Hospital

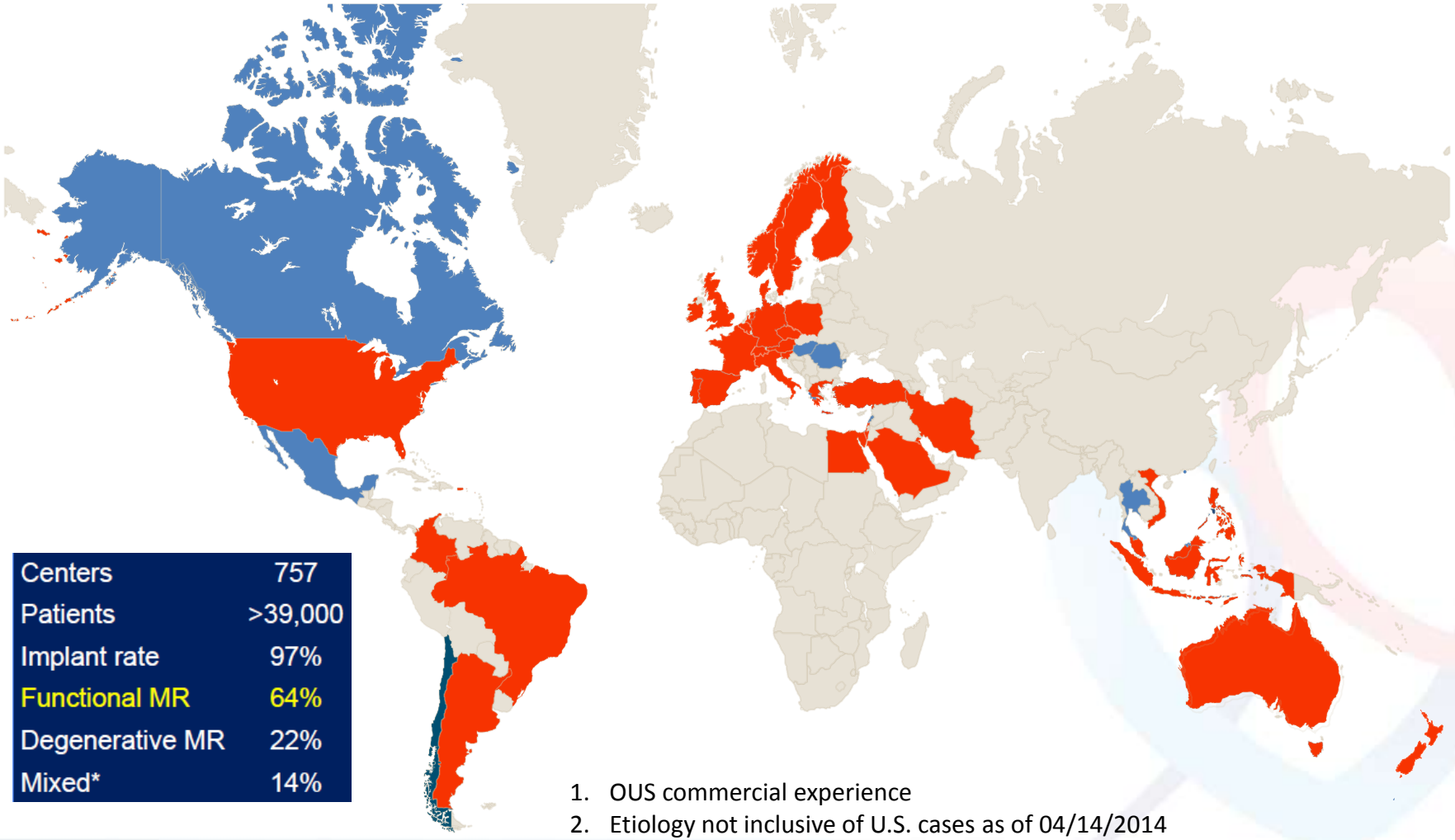
The Mitraclip® NT System





- Complex
- Minor iteration
- Number of technical pitfalls-independant grasping/predictability alignment/multi-clips

Mitra Clip Therapy
Global Use through October 2016



Centers	757
Patients	>39,000
Implant rate	97%
Functional MR	64%
Degenerative MR	22%
Mixed*	14%

1. OUS commercial experience
2. Etiology not inclusive of U.S. cases as of 04/14/2014
3. First-time procedures only. Includes commercial pts, ACCESS I and II

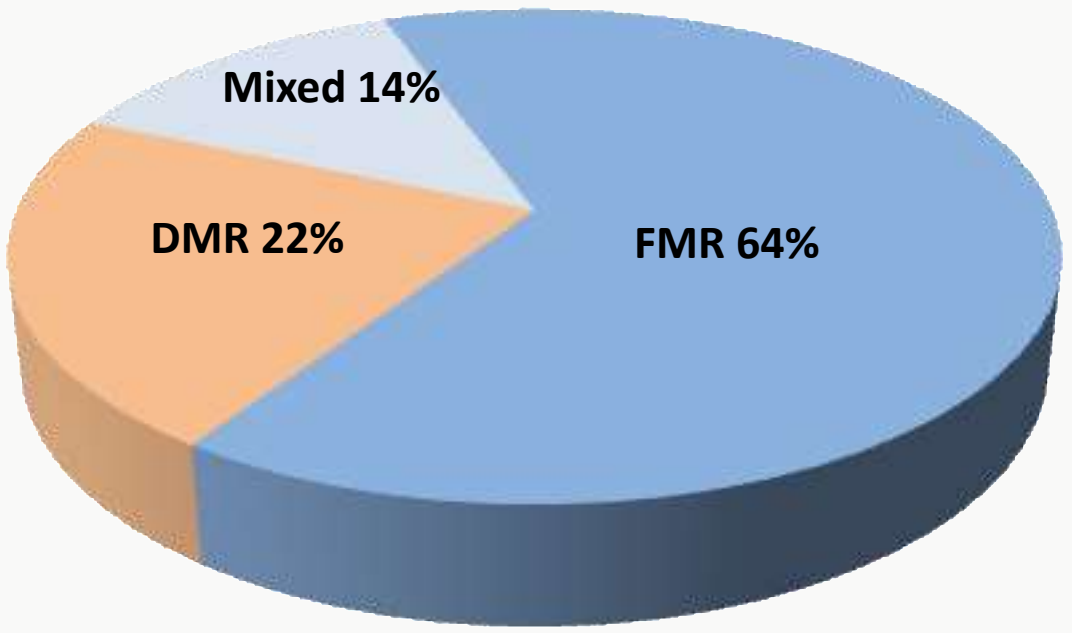
innovation and collaboration

Data source: Abbott Vascular

Mitra Clip Worldwide Experience

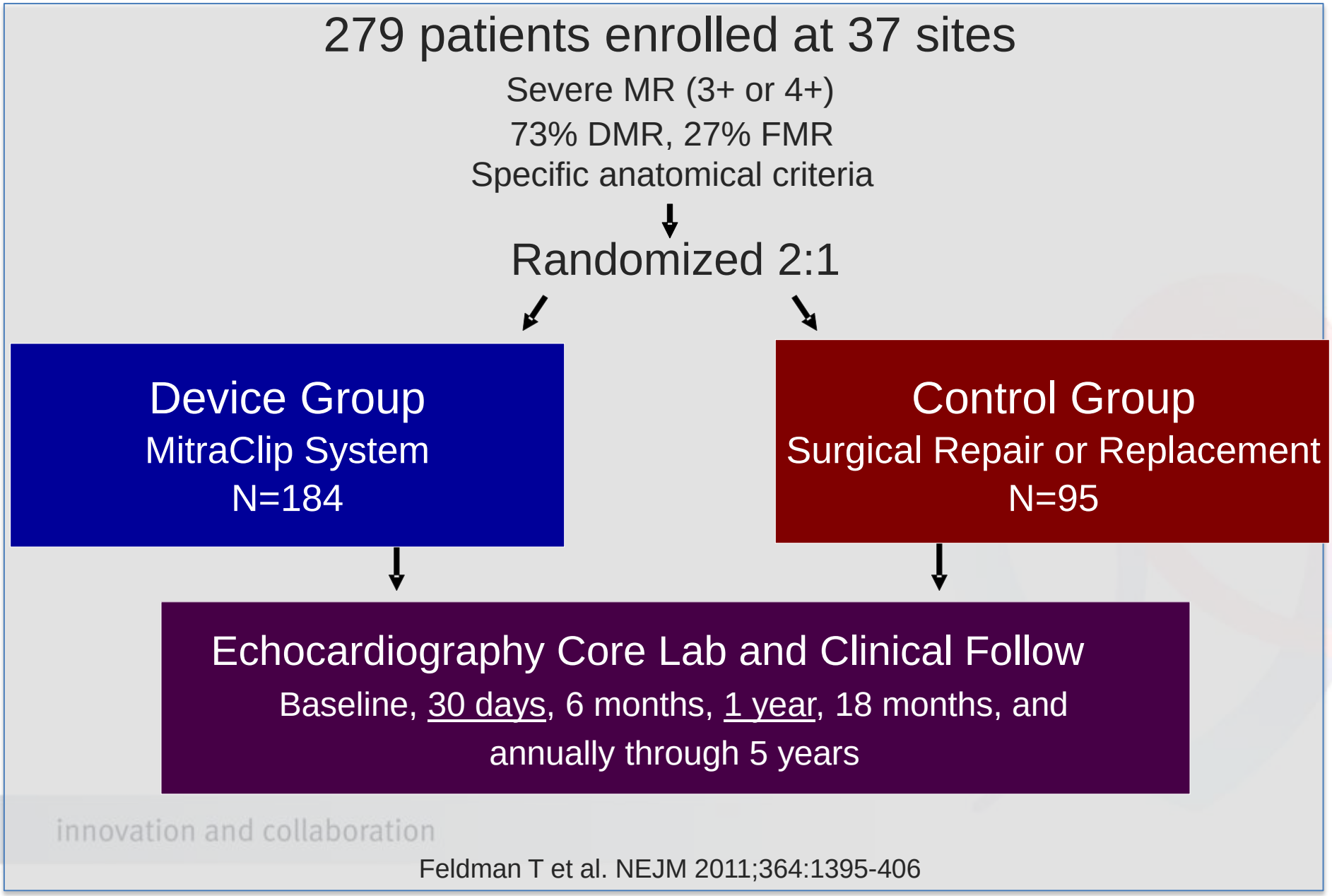
>48,000 Patients

Implant Rate: 97%



Data as of April 2017. Source: Abbott Vascular

EVEREST II Randomized Clinical Trial



Feldman T et al. NEJM 2011;364:1395-406

Randomized Comparison of Percutaneous Repair and Surgery for Mitral Regurgitation

5-Year Results of EVEREST II

Ted Feldman, MD,* Saibal Kar, MD,† Sammy Elmariah, MD, MPH,†§ Steven C. Smart, MD,* Alfredo Trento, MD,‖ Robert J. Siegel, MD,† Patricia Apruzzese, MS,§ Peter Fail, MD,¶ Michael J. Rinaldi, MD,# Richard W. Smalling, MD, PhD,** James B. Hermiller, MD,†† David Heimansohn, MD,‡‡ William A. Gray, MD,§§ Paul A. Grayburn, MD,‖‖ Michael J. Mack, MD,¶¶ D. Scott Lim, MD,## Gorav Ailawadi, MD,*** Howard C. Herrmann, MD,††† Michael A. Acker, MD,‡‡‡ Frank E. Silvestry, MD,††† Elyse Foster, MD,§§§ Andrew Wang, MD,‖‖‖ Donald D. Glower, MD,¶¶¶ Laura Mauri, MD,§### for the EVEREST II Investigators

ABSTRACT

BACKGROUND In the second Endovascular Valve Edge-to-Edge Repair Study trial, treatment of mitral regurgitation (MR) with a novel percutaneous device showed superior safety compared with surgery, but less effective reduction in MR at 1 year.

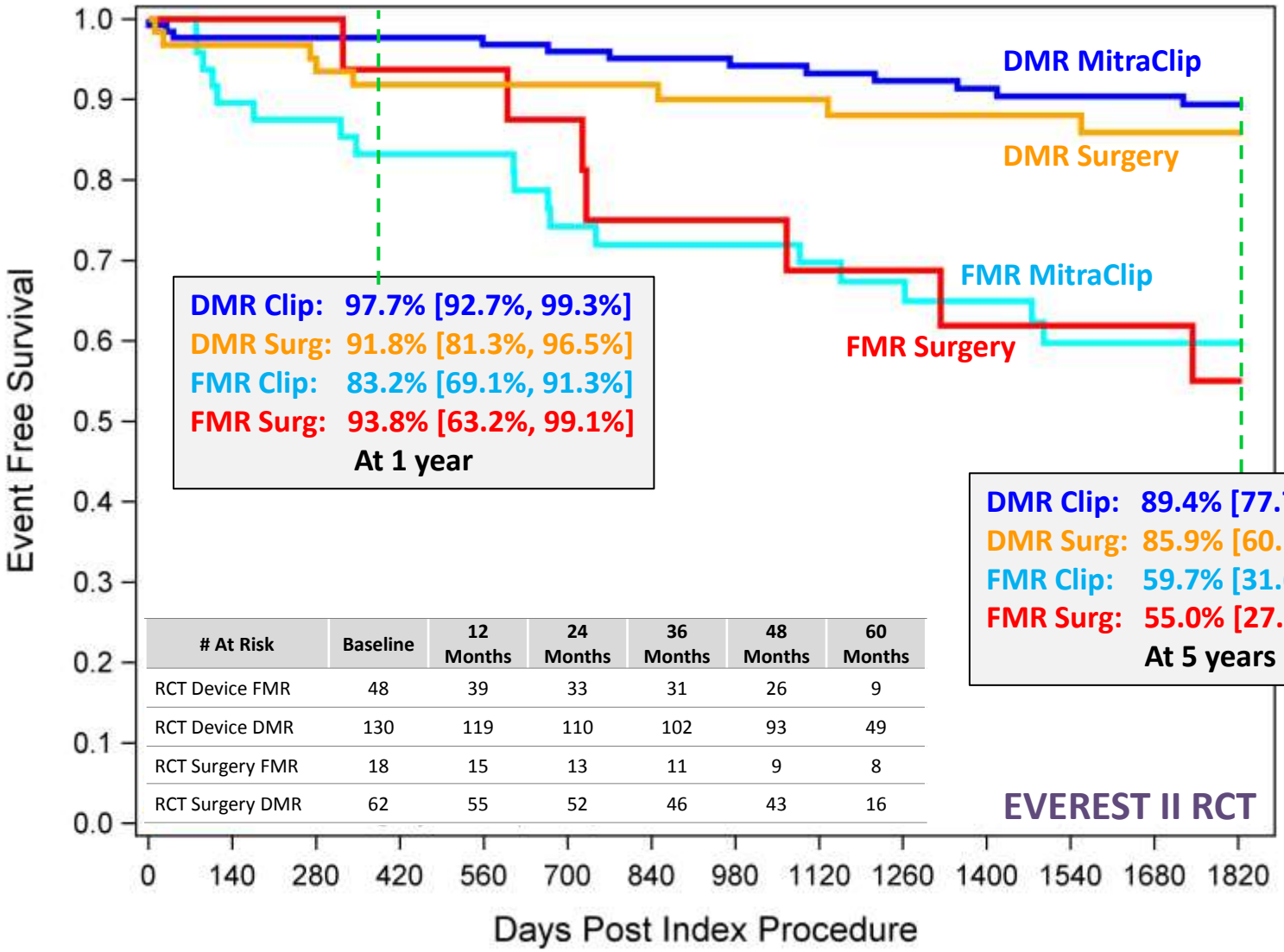
OBJECTIVES This study sought to evaluate the final 5-year clinical outcomes and durability of percutaneous mitral valve (MV) repair with the MitraClip device compared with conventional MV surgery.

METHODS Patients with grade 3+ or 4+ MR were randomly assigned to percutaneous repair with the device or conventional MV surgery in a 2:1 ratio (178:80). Patients prospectively consented to 5 years of follow-up.

RESULTS At 5 years, the rate of the composite endpoint of freedom from death, surgery, or 3+ or 4+ MR in the as-treated population was 44.2% versus 64.3% in the percutaneous repair and surgical groups, respectively ($p = 0.01$). The difference was driven by increased rates of 3+ to 4+ MR (12.3% vs. 1.8%; $p = 0.02$) and surgery (27.9% vs. 8.9%; $p = 0.003$) with percutaneous repair. After percutaneous repair, 78% of surgeries occurred within the first 6 months. Beyond 6 months, rates of surgery and moderate-to-severe MR were comparable between groups. Five-year mortality rates were 20.8% and 26.8% ($p = 0.4$) for percutaneous repair and surgery, respectively. In multivariable analysis, treatment strategy was not associated with survival.

CONCLUSIONS Patients treated with percutaneous repair more commonly required surgery for residual MR during the first year after treatment, but between 1- and 5-year follow-up, comparably low rates of surgery for MV dysfunction with either percutaneous or surgical therapy endorse the durability of MR reduction with both repair techniques. (EVEREST II Pivotal Study High Risk Registry; NCT00209274). (J Am Coll Cardiol 2015;66:2844-54) © 2015 by the American College of Cardiology Foundation.

Freedom From Mortality & Reintervention



# At Risk	Baseline	12 Months	24 Months	36 Months	48 Months	60 Months
RCT Device FMR	48	39	33	31	26	9
RCT Device DMR	130	119	110	102	93	49
RCT Surgery FMR	18	15	13	11	9	8
RCT Surgery DMR	62	55	52	46	43	16

Kaplan-Meier estimate

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Percutaneous Mitral Valve Repair for Mitral Regurgitation in High-Risk Patients

Results of the EVEREST II Study

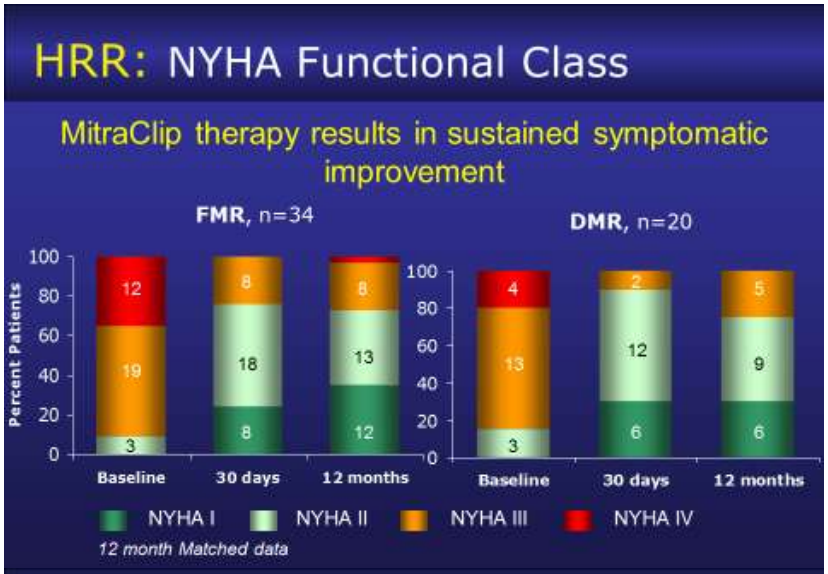
Donald
Ramon
Michae

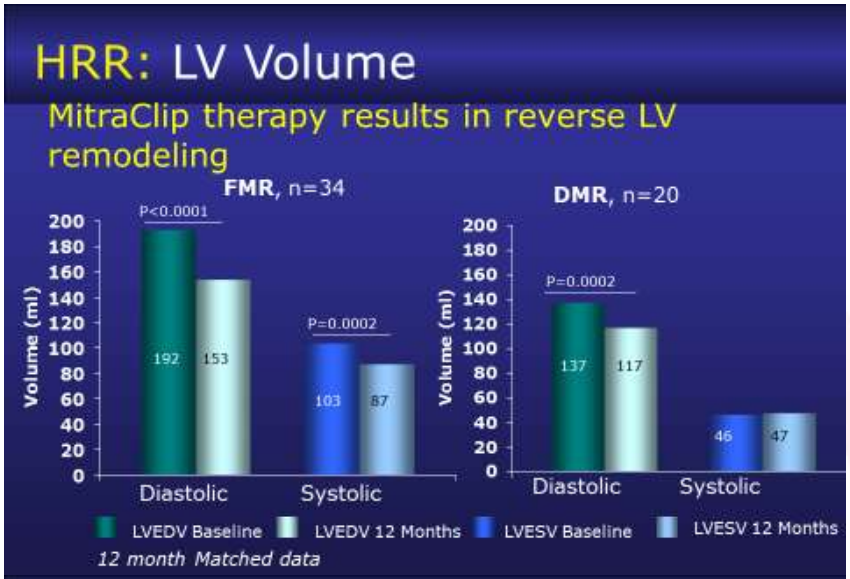
RESULTS In the studies, 327 of 351 patients completed 12 months of follow-up. Patients were elderly (76 ± 11 years of age), with 70% having functional MR and 60% having prior cardiac surgery. The mitral valve device reduced MR to ≤2+ in 86% of patients at discharge ($n = 325$; $p < 0.0001$). Major adverse events at 30 days included death in 4.8%, myocardial infarction in 1.1%, and stroke in 2.6%. At 12 months, MR was ≤2+ in 84% of patients ($n = 225$; $p < 0.0001$). From baseline to 12 months, left ventricular (LV) end-diastolic volume improved from 161 ± 56 ml to 143 ± 53 ml ($n = 203$; $p < 0.0001$) and LV end-systolic volume improved from 87 ± 47 ml to 79 ± 44 ml ($n = 202$; $p < 0.0001$). New York Heart Association functional class improved from 82% in class III/IV at baseline to 83% in class I/II at 12 months ($n = 234$; $p < 0.0001$). The 36-item Short Form Health Survey physical and mental quality-of-life scores improved from baseline to 12 months ($n = 191$; $p < 0.0001$). Annual hospitalization rate for heart failure fell from 0.79% pre-procedure

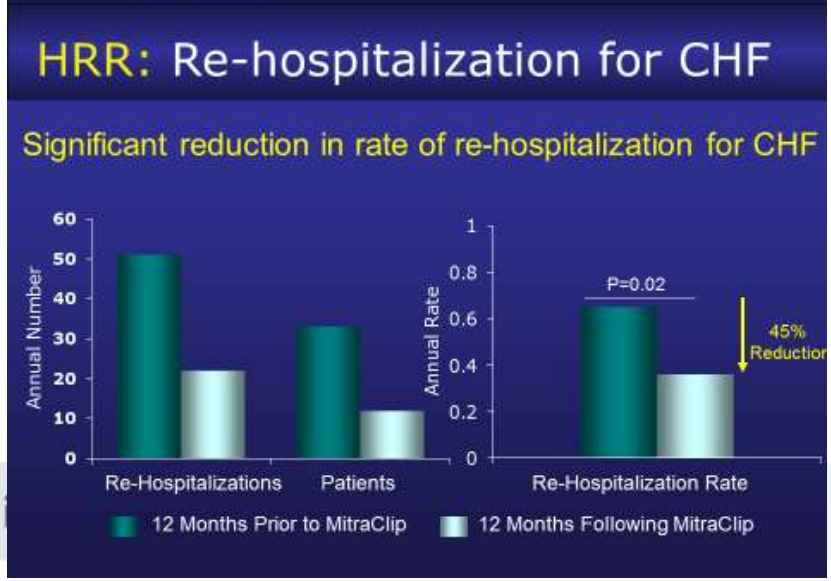
The percutaneous mitral valve device significantly reduced MR, improved clinical symptoms, and decreased LV dimensions at 12 months in this high-surgical-risk cohort.

J Am Coll Cardiol 2014;64:172–81

Everest High Risk registry







Improved Functional Status and Quality of Life in Prohibitive Surgical Risk Patients With Degenerative Mitral Regurgitation After Transcatheter Mitral Valve Repair

D. Scott Lim, MD,* Matthew R. Reynolds, MD, MSc,†‡ Ted Feldman, MD,§ Saibal Kar, MD,‖
Howa
Paul G

METHODS A prohibitive-risk DMR cohort was identified by a multidisciplinary heart team that retrospectively evaluated high-risk DMR patients enrolled in the EVEREST (Endovascular Valve Edge-to-Edge Repair Study) II studies.

RESULTS A total of 141 high-risk DMR patients were consecutively enrolled; 127 of these patients were retrospectively identified as meeting the definition of *prohibitive risk* and had 1-year follow-up (median: 1.47 years) available. Patients were elderly (mean age: 82.4 years), severely symptomatic (87% New York Heart Association class III/IV), and at prohibitive surgical risk (STS score: 13.2 ± 7.3%). TMVR (MitraClip) was successfully performed in 95.3%; hospital stay was 2.9 ± 3.1 days. Major adverse events at 30 days included death in 6.3%, myocardial infarction in 0.8%, and stroke in 2.4%. Through 1 year, there were a total of 30 deaths (23.6%), with no survival difference between patients discharged with MR ≤1+ or MR 2+. At 1 year, the majority of surviving patients (82.9%) remained MR ≤2+ at 1 year, and 86.9% were in New York Heart Association functional class I or II. Left ventricular

including decreases in rehospitalization, functional improvements, and favorable ventricular remodeling, at 1 year.
(Real World Expanded Multi-center Study of the MitraClip System [REALISM]; NCT01931956)

TMVR in prohibitive surgical risk patients is associated with safety and good clinical outcomes, including decreases in rehospitalization, functional improvements, and favorable ventricular remodeling, at 1 year.

innovation and collaboration

J Am Coll Cardiol 2014;64:182–92

Mitra clip role
USA view

- Severely symptomatic patients (NYHA class III-IV)
- with chronic severe **primary MR** (stage D)
- favorable anatomy for the repair procedure
- a reasonable life expectancy
- prohibitive surgical risk because of severe comorbidities
- remain severely symptomatic despite optimal GDMT for HF

COR	LOE
IIb	B

JACC (2014) 63,(22), e57–185

STS/ACC TVT Registry
Clinical Outcomes at 1-year ACC 2017

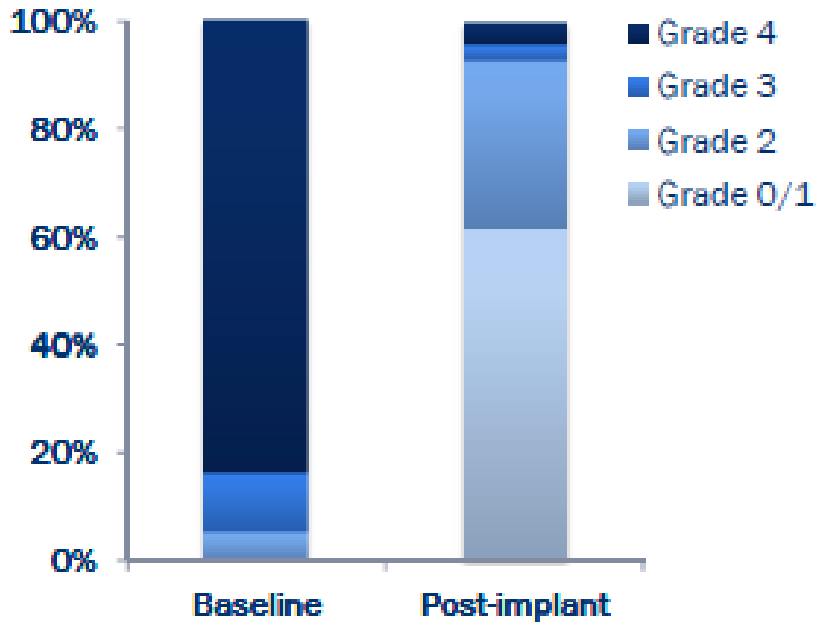
Paul Sorajja, MD, Sreekanth Vemulapalli MD, Ted Feldman, MD, Michael Mack, MD, David R. Holmes, Jr. MD, Amanda Stebbins, MS, Saibal Kar, MD, Vinod Thourani, MD, and Gorav Ailawadi, MD

- Patient characteristics, procedural, and in-hospital events sourced from TVT registry (n=2,952)
- 30-day and 1-year events from linked CMS claims data (n=1,867 or 63%)
- Examined death, MV surgery, and re-hospitalization for heart failure

Patients

- Median age……82 yrs (74, 86 yrs)
- Male gender……55.8%
- NYHA III or IV……85.0%
- Grade 3 or 4 MR……93.0%
- Degenerative MR only……85.9%
- Functional MR only……8.6%
- DMR and FMR……8.9%
- Frailty……50.3%
- STS-PROM (MV repair)…… 6.1% (3.7%, 9.9%)
- STS-PROM (MV replacement)……9.2% (6.0%, 14.1%)

Lessons From the TVT Registry ACC 2017: Acute Procedural Results



Acute procedural success 92.8%

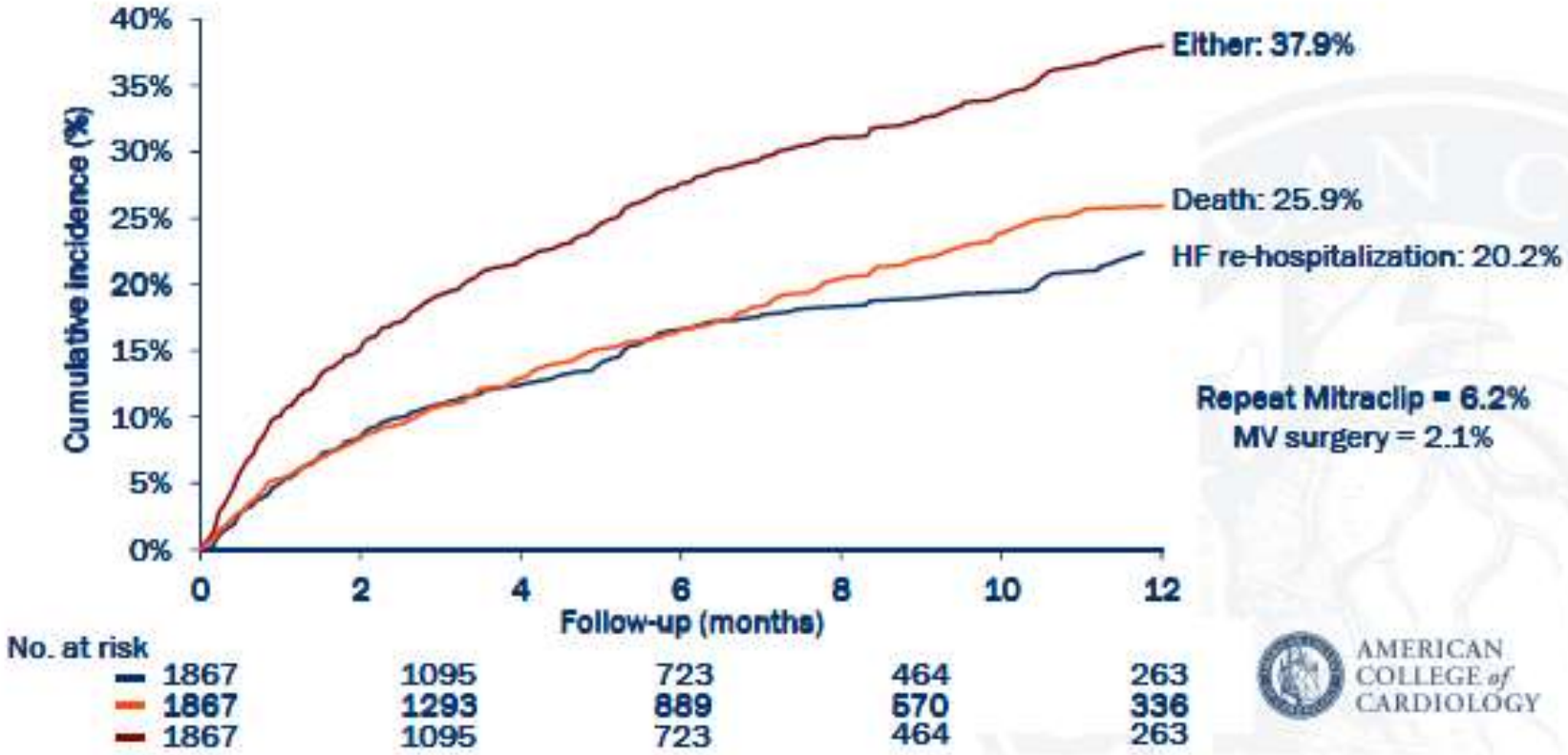
SLDA 1.5%

Hospital mortality 2.7%

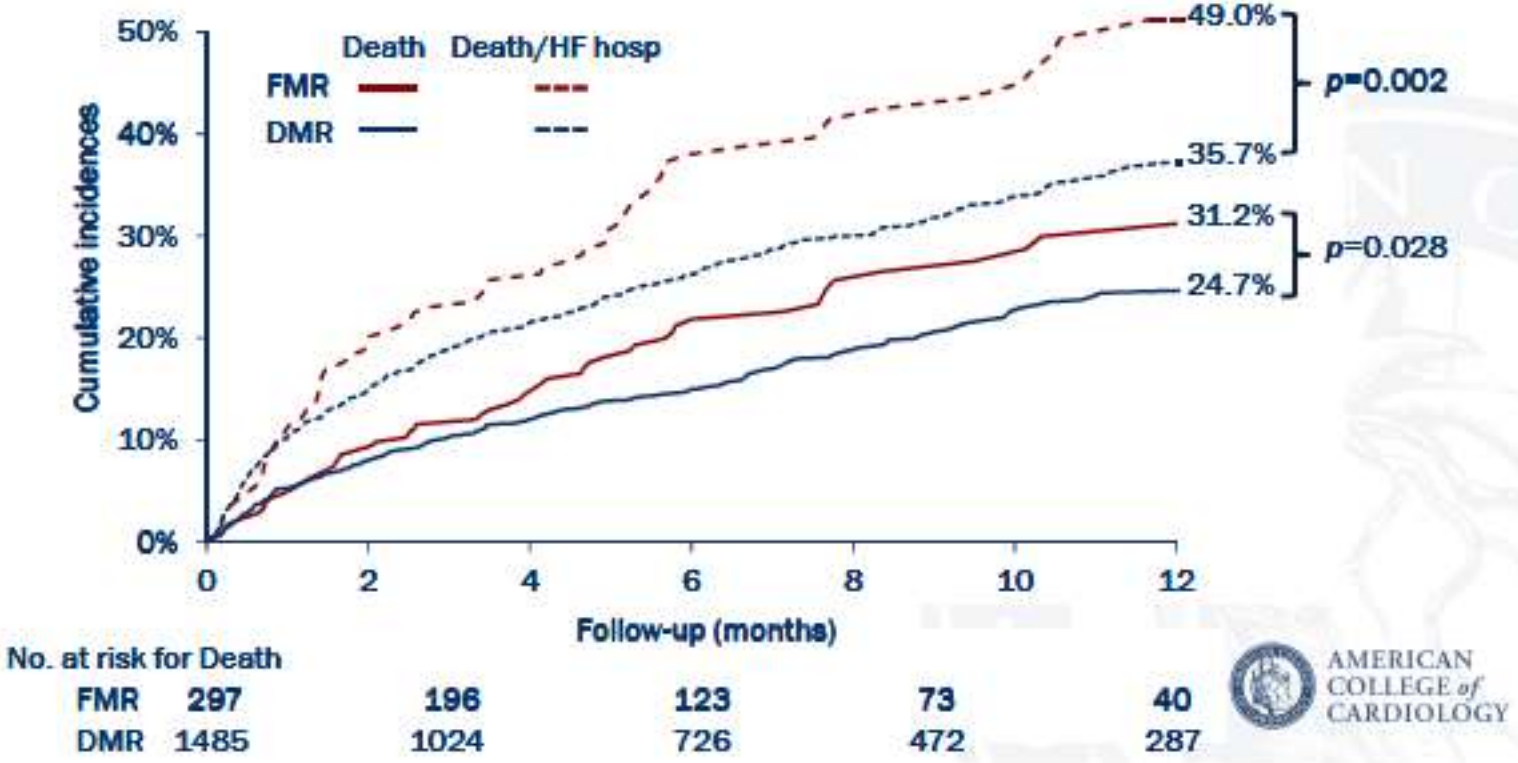
D/C home 85.9%

LOS (median) 2 days (1, 5)

Lessons From the TVT Registry : One-Year Outcomes

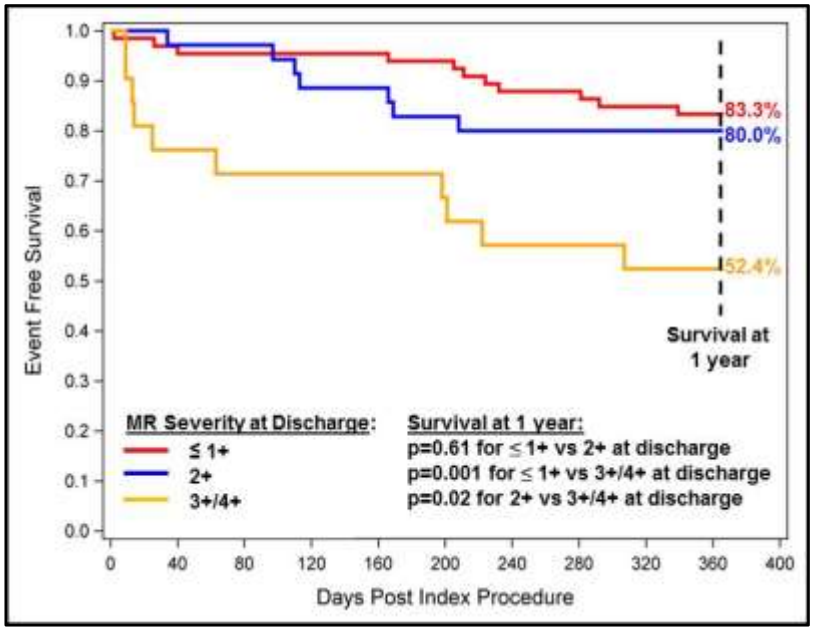


Lessons From the TVT Registry : Outcomes: FMR vs DMR



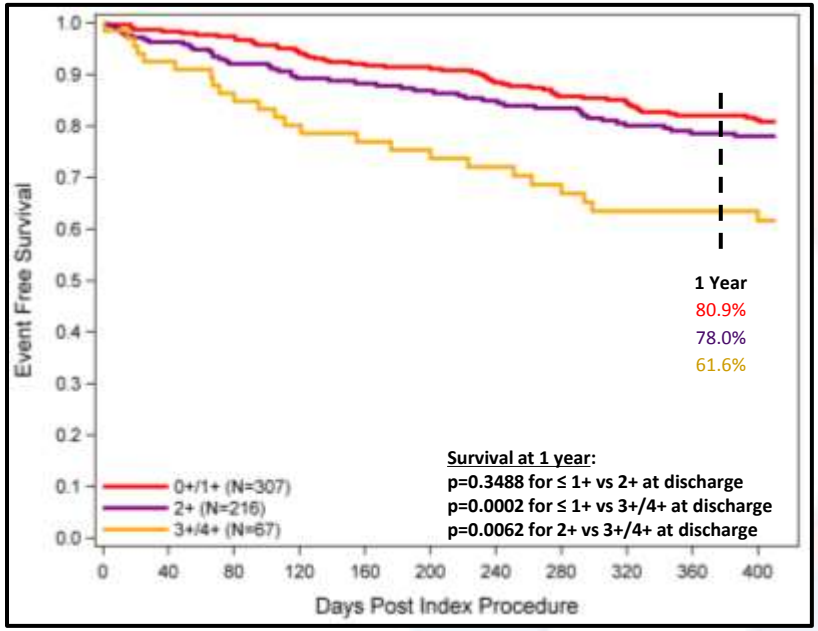
Lessons From the TVT Registry : Survival by MR at Discharge

Prohibitive Risk DMR (n=127)



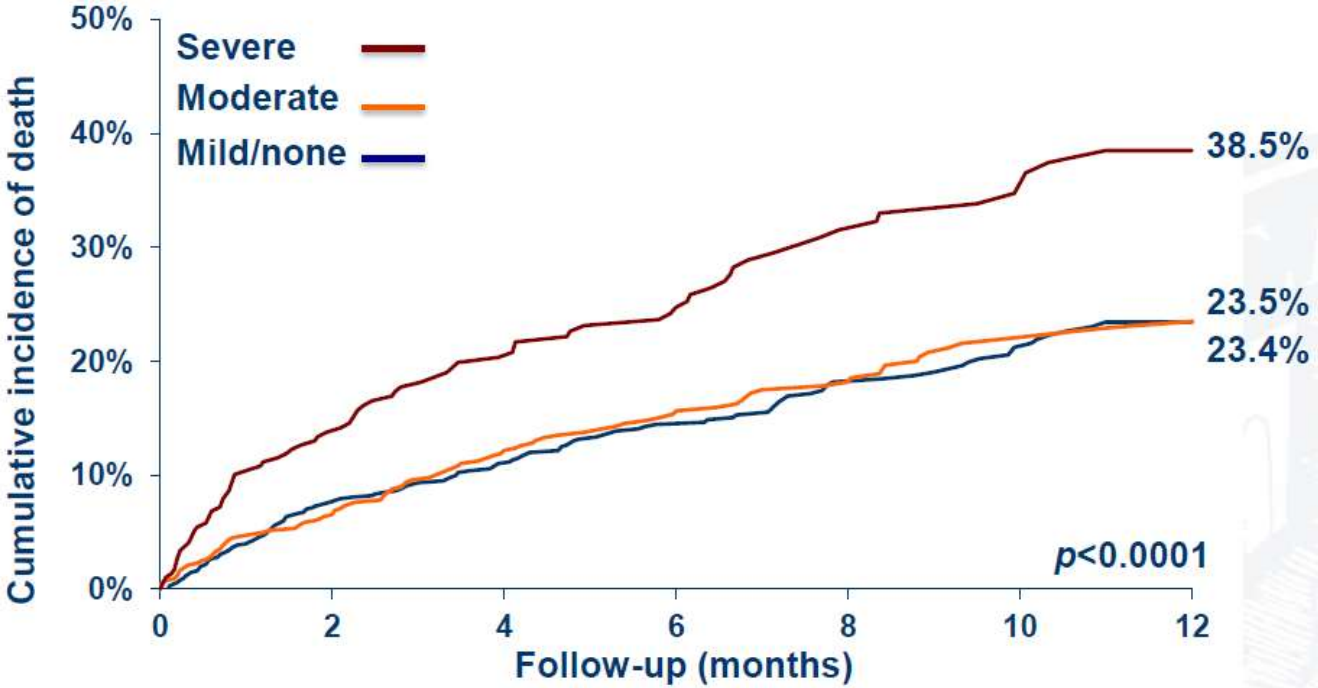
Lim DS, et al, JACC 2014

High and Low Risk FMR (n=619)



Ailiwadi G, et al, submitted 2017

Lessons From the TVT Registry : Survival by TR at Discharge



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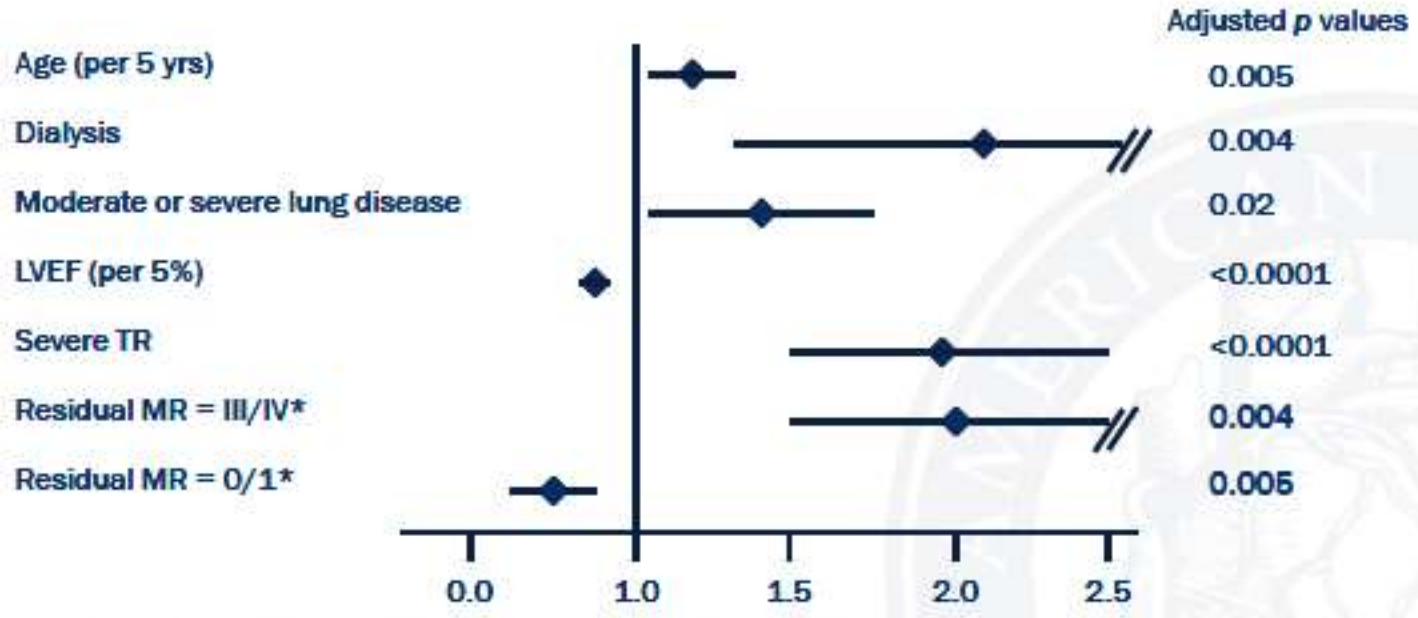
Lessons From the TVT Registry : Multivariate Predictors of Outcome



STS/ACC TVT Registry

The Society of Thoracic Surgeons

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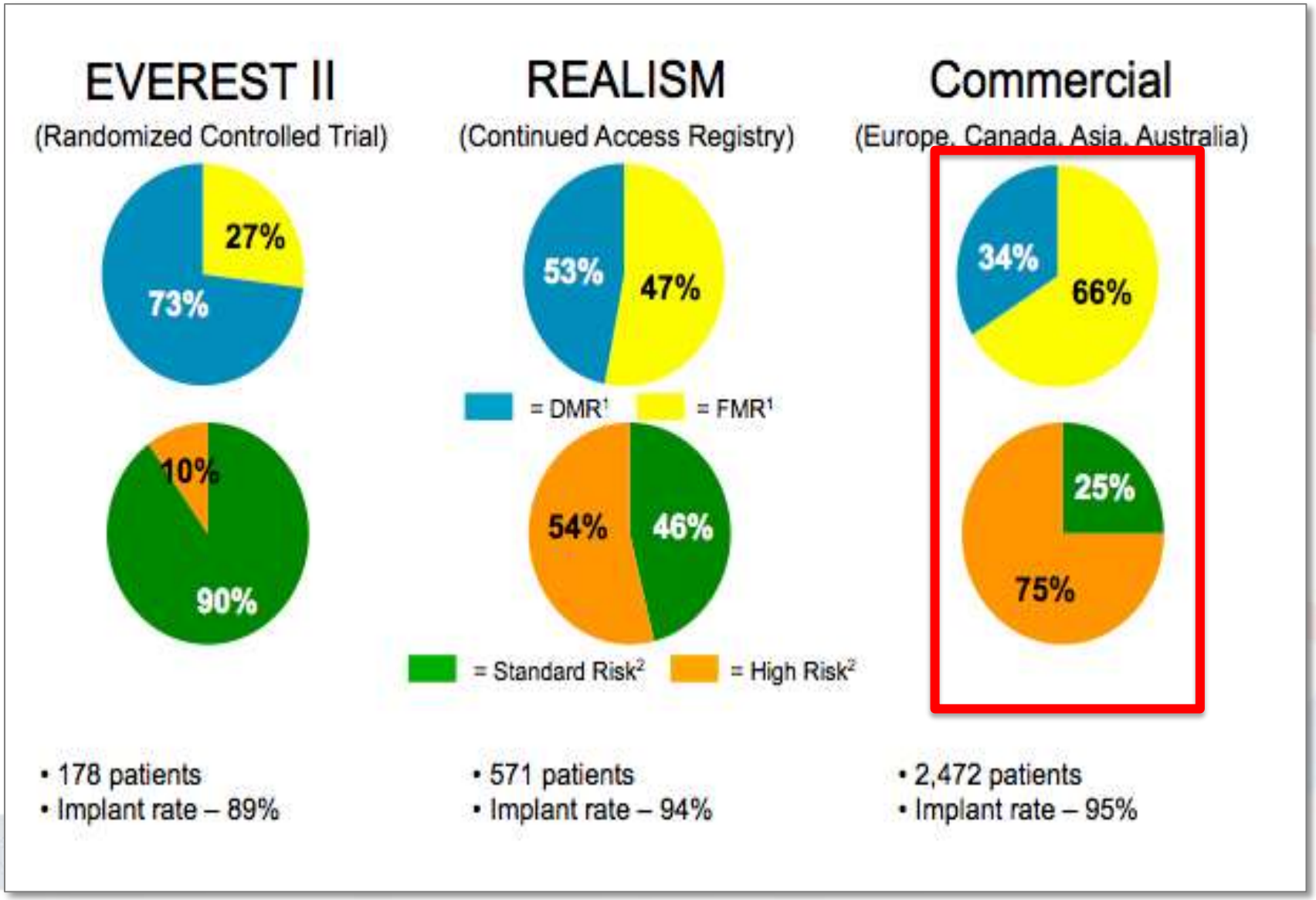
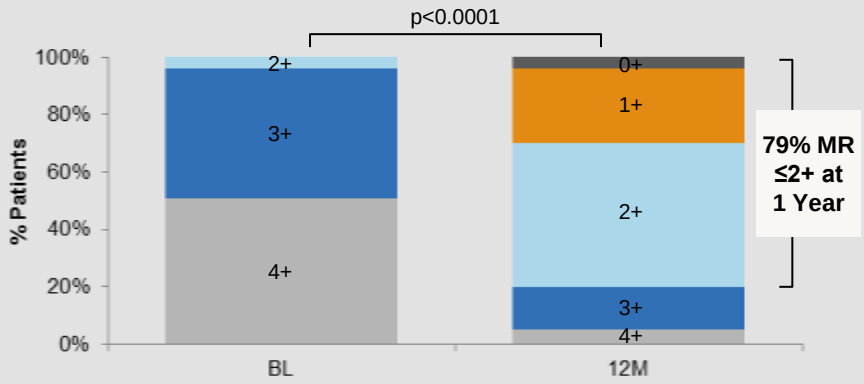
Changing demographics



ACCESS EU - Real-World Clinical Experience

Mitral Regurgitation Grade Reduction

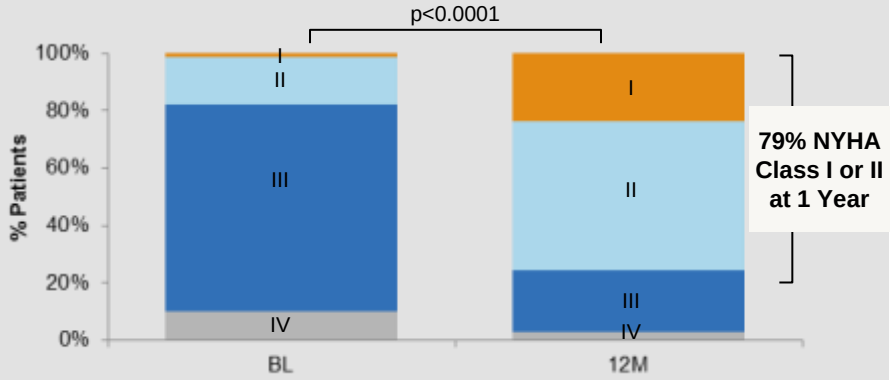


As assessed by sites (N=327, matched)

Demonstrated safety with low adverse event rates

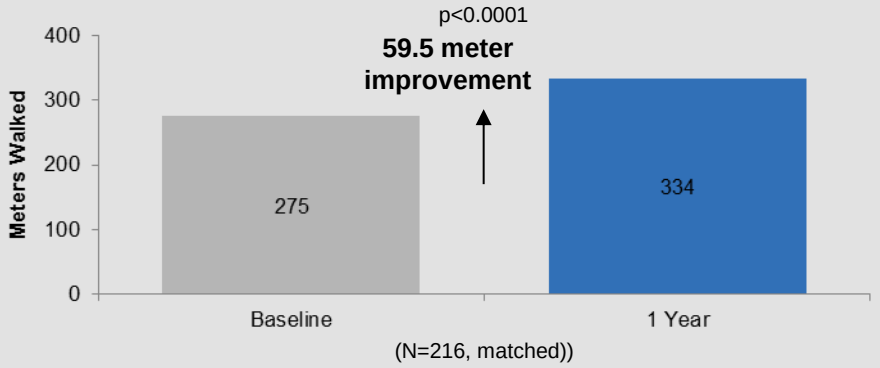
Description of Event	Site Reported Safety Events at 30 Days
Death	19 (3.4)
Stroke	4 (0.7)
Myocardial Infarction	4 (0.7)
Renal Failure	27 (4.8)
Respiratory Failure	4 (0.7)
Need for Resuscitation	10 (1.8)
Cardiac Tamponade	6 (1.1)
Bleeding Complications	22 (3.9)

Significant NYHA Functional Class Improvements



(N=343, matched)

Functional Improvement in 6-Minute Walk Test

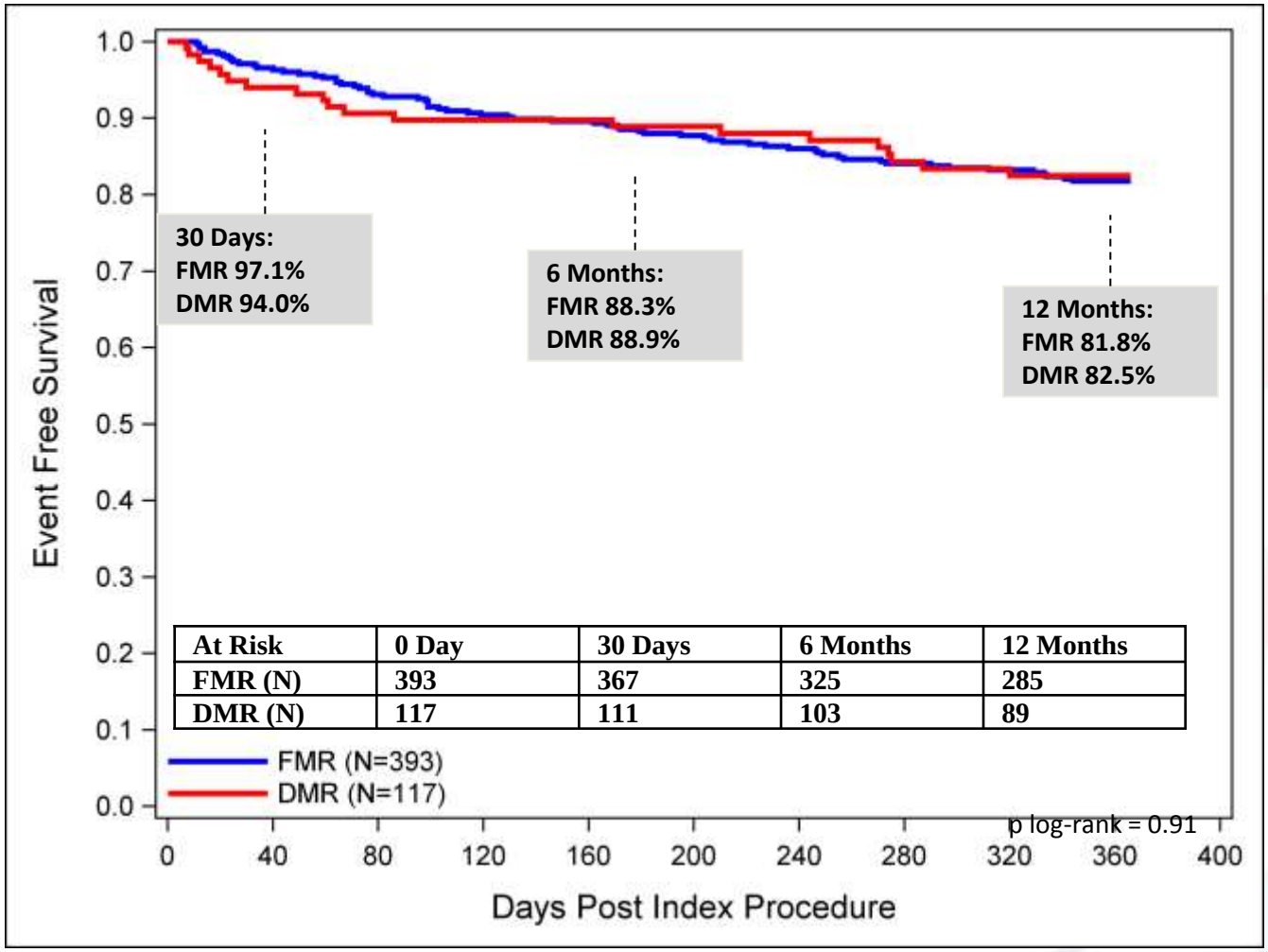


(N=216, matched))

Data presented as mean ±95% confidence intervals (44.5, 74.6)

Maisano F. et. al. Percutaneous Mitral Valve Interventions in the Real World: Early and One Year Results From the ACCESS-EU, a Prospective, Multicenter, Non-Randomized Post-Approval Study of the MitraClip® Therapy in Europe.. J Am Coll Cardiol. 2013

ACCESS EU
Kaplan-Meier Freedom from Death

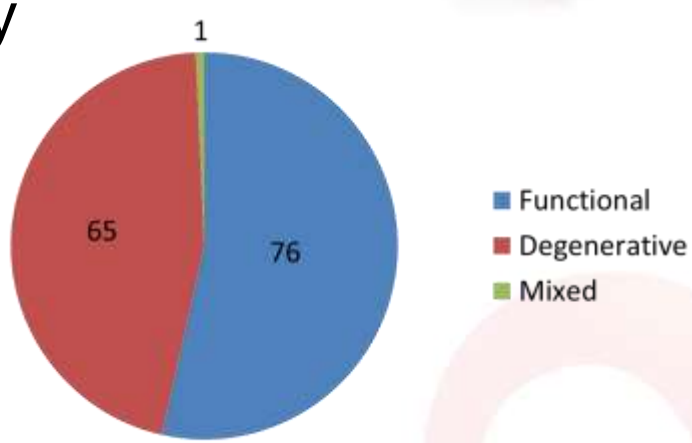


At Risk	0 Day	30 Days	6 Months	12 Months
FMR (N)	393	367	325	285
DMR (N)	117	111	103	89

RS von Bardeleben TCT 2013 data courtesy: H Reichenspurner, F Maisano, W Schillinger

MARS Registry

- Asia-Pacific MitraClip Registry
- Retrospective registry
- 8 sites in 5 countries
- Feb 2011- Feb 2016



EuroIntervention 2014; 9-online publish-ahead-of-print January 2014
Percutaneous mitral valve repair with the MitraClip: early results from the MitraClip Asia-Pacific Registry (MARS) Yeo KK, Yap J, Yamen E, Muda N, Tay E, Walters DL, Santoso T, Liu X, Jansz P, Yip J, Zambahari R, Passage J, Koh TH, Wang J, Scalia G, Kuntjoro I, Soesanto AM, Muller D.

International Registry / Trial Data

after Grayburn

Study	N	Age (yrs)	DMR (%)	MR ≤ 2	Hosp Mortality (%)
EVEREST I	51	71	79	74	0.9
EVEREST II RCT	279	67	73	77	1.1
REALISM FMR	619	73	0	86	3.6
Sentinel	628	74	28	95	2.9
ACCESS EU	567	74	23	91	-
TRAMI	1064	75	29	95	2.9
MitraSwiss	100	77	38	85	4.0
FRANCE	62	73	23	88	3.3
GRASP-IT	117	72	24	100	-
MARS (Asia)	163	73	46	94	4.2
STS/TVT Registry*	1867	82	86	93	2.7
Summary	5517	75	DMR USA FMR EU	85-90	2.7-4.0%

* Presented at ACC 2017

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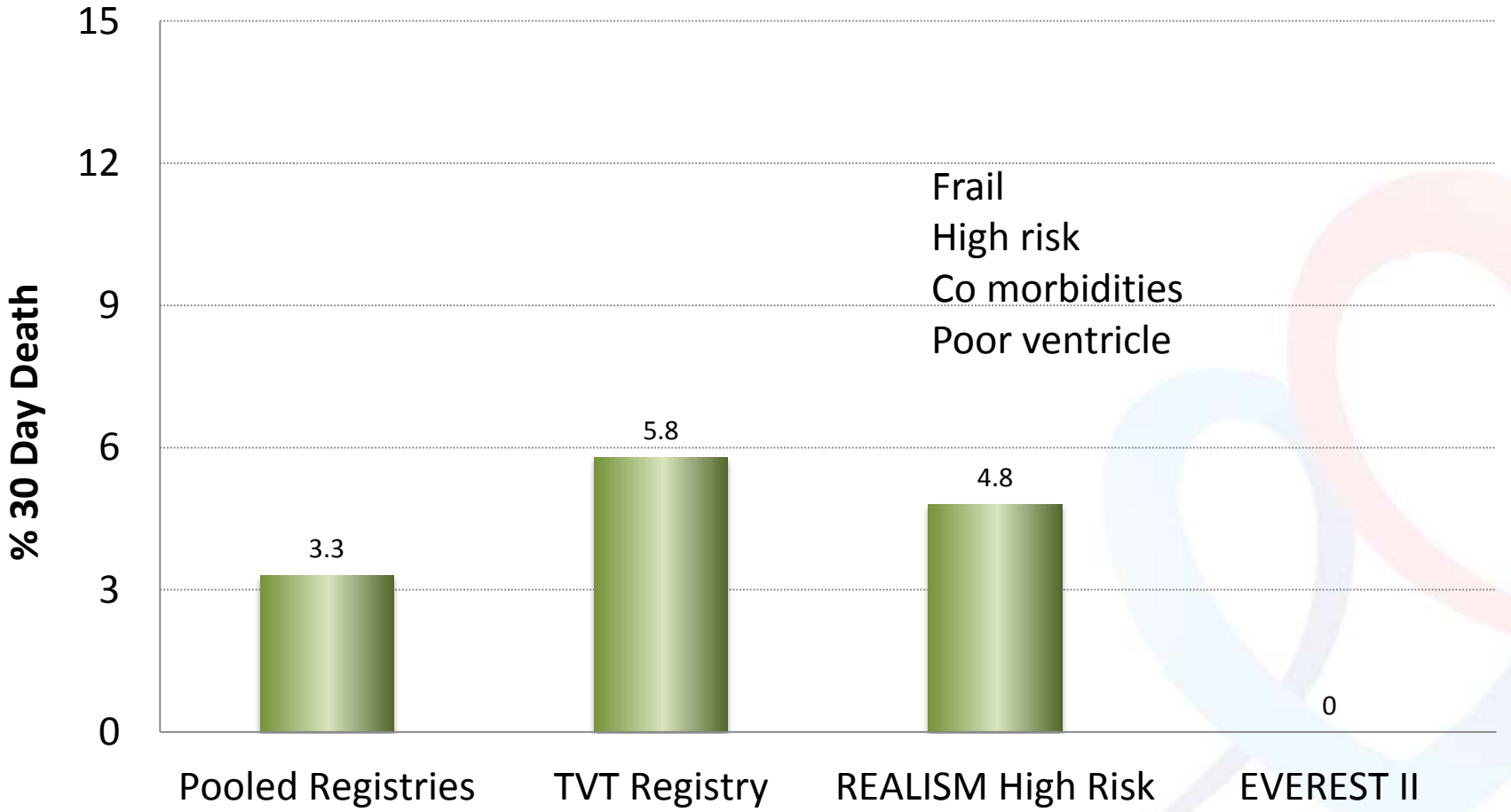
STS/TVT Registry*	1867	82	86	93	2.7
Summary	5517	75	DMR USA FMR EU	85-90	2.7-4.0%

* Presented at ACC 2017

MitraClip
30 Day Mortality



Current Approach to Surgical & Interventional Therapy for Mitral Regurgitation

	Degenerative	Evidence base
Low Surgical Risk	Surgical Mitral Repair	Everest RCT Registry
High Surgical Risk	Commercial MitraClip	Everest RCT Registry

Current Approach to Surgical & Interventional Therapy for Mitral Regurgitation

	Functional	Evidence base
Low Surgical Risk	??? Surgery X Commercial MitraClip Cardioband Carillion	Surgical Outcomes poor Everest RCT unconvincing Registry/New tech Awaiting RCTs
High Surgical Risk	??? Commercial MitraClip Cardioband Carillion	Registry/New tech Propensity Matched Awaiting RCTs

Clinical Outcomes Assessment of the MitraClip Percutaneous Therapy for High Surgical Risk

COAPT TRIAL

>610 patients enrolled at >85 US sites

Significant FMR ≥3+ core lab; EF<50%; CHF hospitalization or BNP>300

High risk for mitral valve surgery- Local Heart Team

Specific valve anatomic criteria

Randomize 1:1

MitraClip

Control group Standard of care

Safety: Composite death, stroke, worsening renal function, LVAD implant, heart transplant at 12 months

Effectiveness: Recurrent heart failure hospitalizations

Protocol conditionally approved by FDA July 26, 2012

MitraClip RCTs in Functional MR

- 5 trials randomizing ~1641 patients with heart failure and secondary (functional) MR to MitraClip vs. GDMT or MV Surgery
  - As of June 10th, 2016, 736 patients
    - have been randomized:

- COAPT – 430/555 (77%)
- MITRA-FR – 201/288 (70%)
- RESHAPE-HF-2 – 76/380 (20%)
- MATTERHORN – 29/210 (14%)
- EVOLVE-HF – 0/168 (0%)

Transcatheter MV Repair: Device Landscape 2017

Edge-to-edge
- MitraClip***
- MitraFlex

Coronary sinus annuloplasty
- Cardiac Dimensions Carillon**
- Cerclage annuloplasty

Direct annuloplasty and basal ventriculoplasty
- Mitralign TAMR**
- Valtech Cardioband**
- GDS Accucinch*
- Millipede IRIS*
- MVRx ARTO*
- Mardil BACE*
- Mitraspan*
- Valcare Amend*
- Micardia enCor
- Cardiac Implants RDS
- QuantumCor (RF)

MV replacement
- Edwards CardiAQ*
- Edwards Fortis*
- Neovasc Tiara*
- Abbott Tendyne*
- Medtronic Intrepid*
- HighLife*
- MValve*
- Cephea
- NCSI NaviGate
- St. Jude
- Micro Interventional
- Valtech CardioValve
- ValveXchange
- MitrAssist
- Braile Quattuor
- Caison
- Direct Flow
- Sinomed Accufit

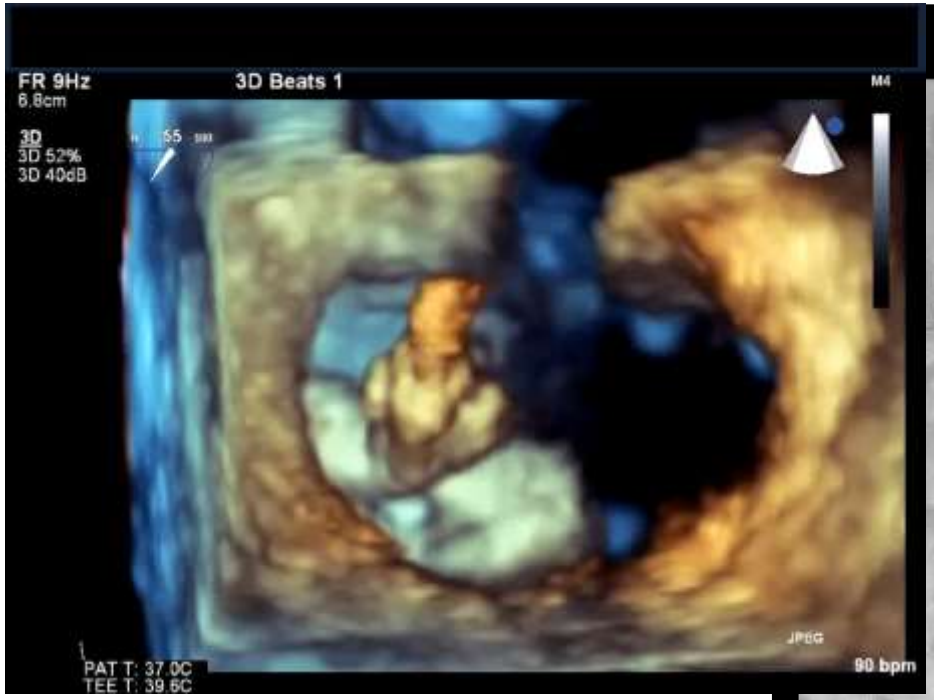
MV replacement (cont)
- MitralHeal
- HT Consultant Saturn
- Lutter valve
- Transcatheter Technologies Tresillo
- Venus
- Verso
- Transmural Systems

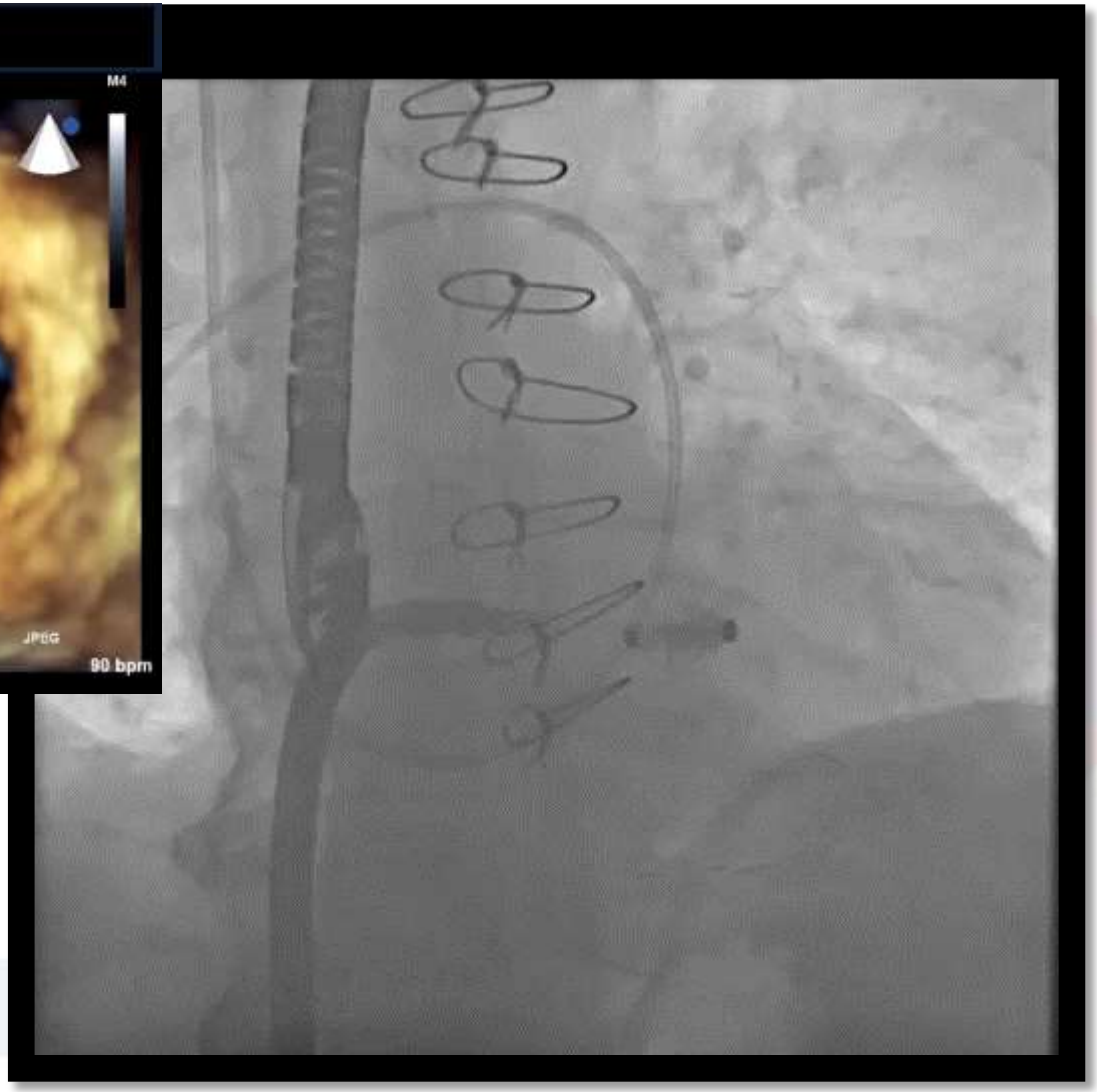
Other approaches
- NeoChord DS 1000**
- Harpoon neochords*
- Babic chords*
- Middle Peak Medical*
- St. Jude leaflet plication*
- Cardiosolutions Mitra-Spacer*
- Valtech Vchordal
- Mitralix

*In patients *CE mark *FDA approved

From G Stone

Transcatheter Mitral Valve Repair System Clasp #1





Implant System
First patient –First in Man
Prince Charles Brisbane

Conclusion

- Significant global uptake of Mitraclip with regional variation in application
- from high risk/elderly patients with DMR to all comers with FMR in patients with significant CCF
- A morbid cohort
  - 30-day mortality 2.7-4.0%
  - significant rates of rehospitalization and death to one year
  - high risk nature of patients
  - poor outcomes with 3 or 4+ residual MR/significant TR
- Great potential use in FMR
  - Stronger evidence base for FMR much anticipated from COAPT & other RCTs
- Future directions
  - Improved procedural success rates 85-90 % to 98%
  - Better predictors of success in given patient
  - New devices knocking at the door