2019 euro PCR

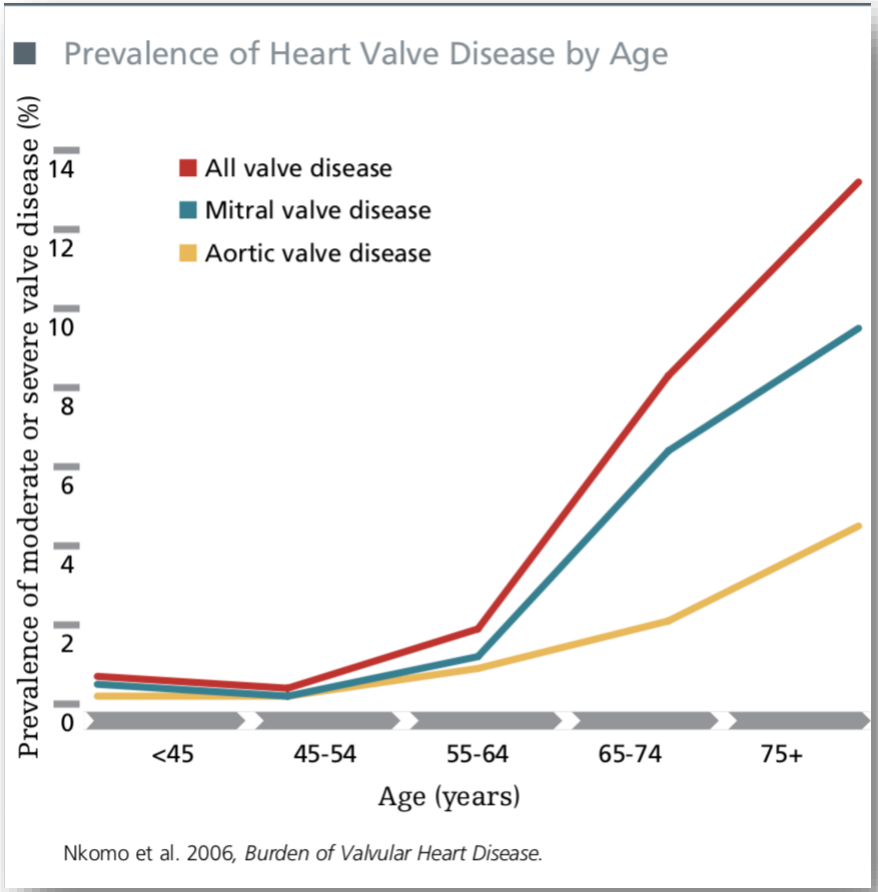
PERCUTANEOUS EDGE-TO-EDGE REPAIR IN PATIENTS WITH HEART FAILURE AND SECONDARY MITRAL REGURGITATION

PCR/EAPCI STATEMENT

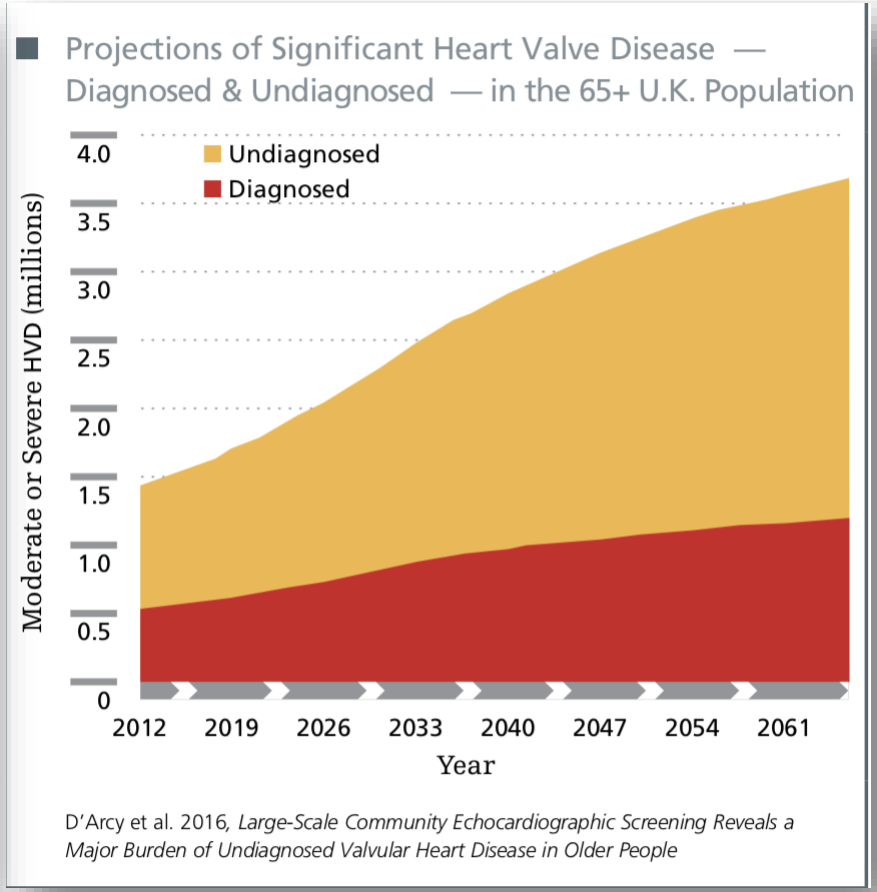
Bernard Prendergast

St Thomas' Hospital, London, UK

MR is common…

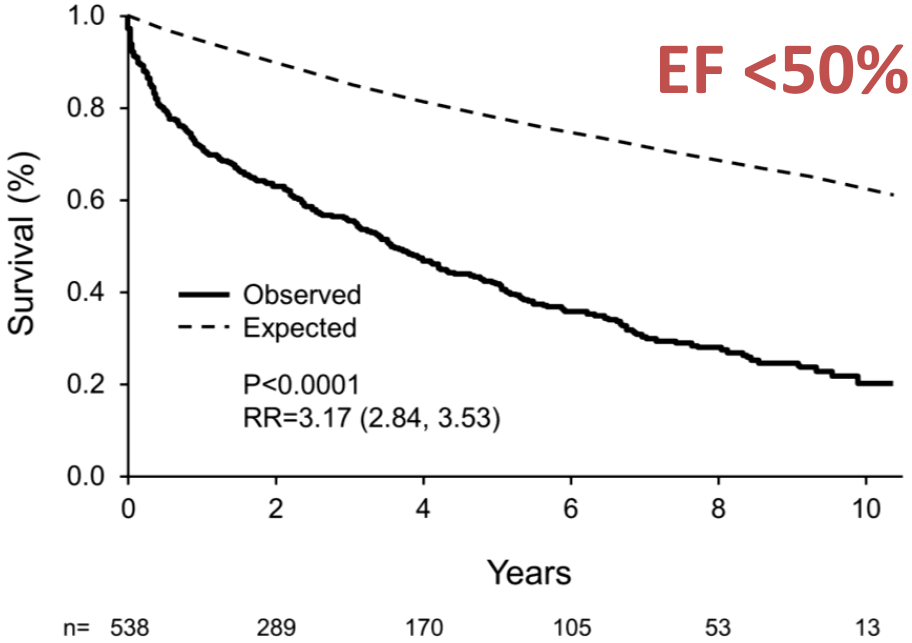


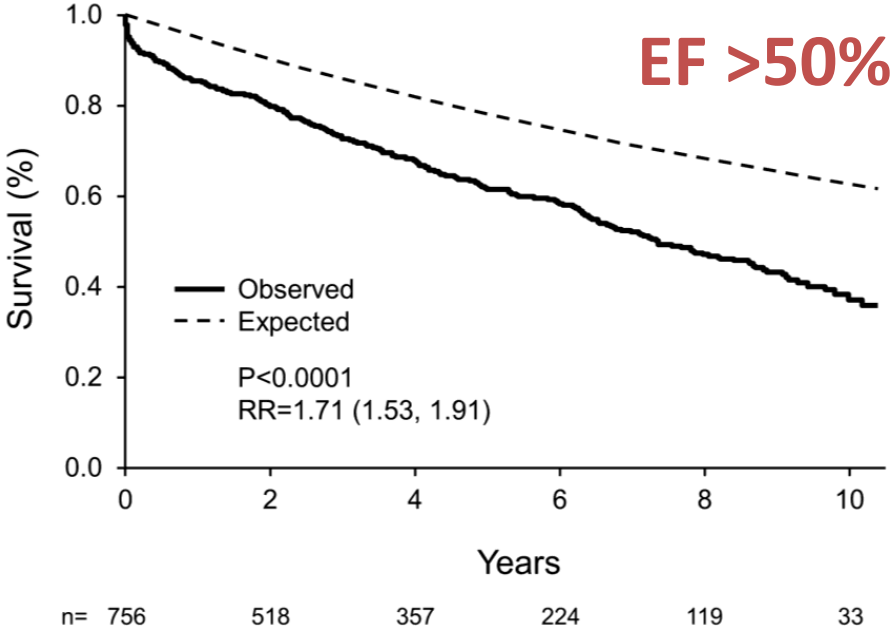
Nkomo et al. 2006, *Burden of Valvular Heart Disease.*



D'Arcy et al. 2016, *Large-Scale Community Echocardiographic Screening Reveals a Major Burden of Undiagnosed Valvular Heart Disease in Older People*

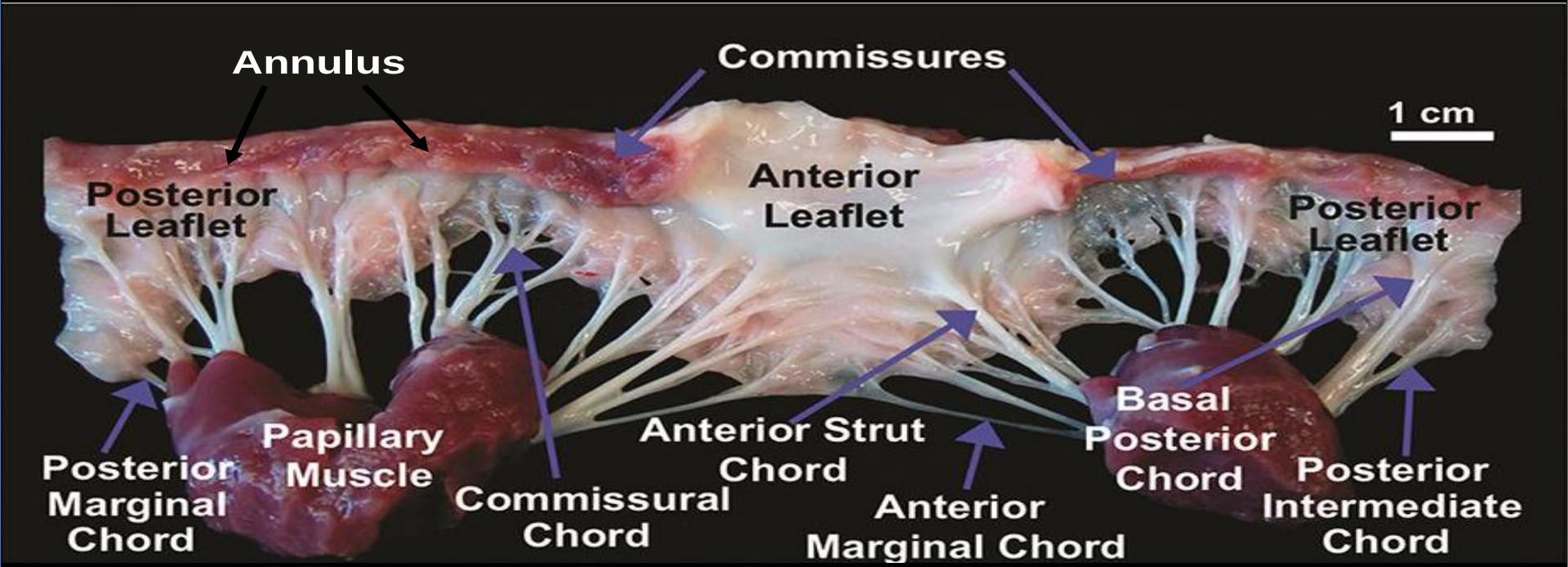
MR is dangerous…





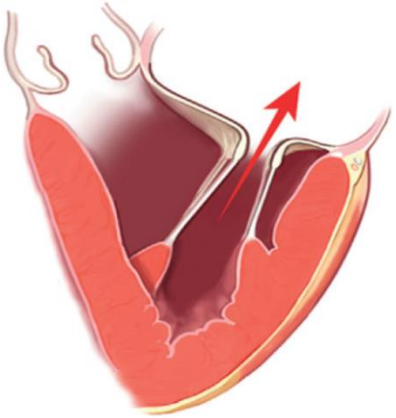
Dziadzko V *et al*. Lancet 2018;391:960-969.

THE MITRAL VALVE IS COMPLEX



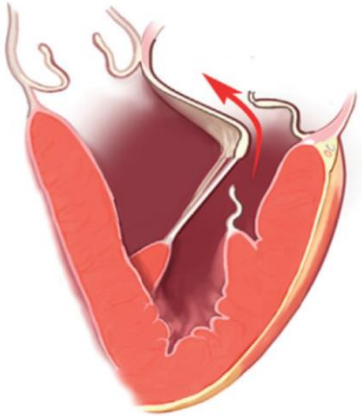
CARPENTIER CLASSIFICATION

PRIMARY MR



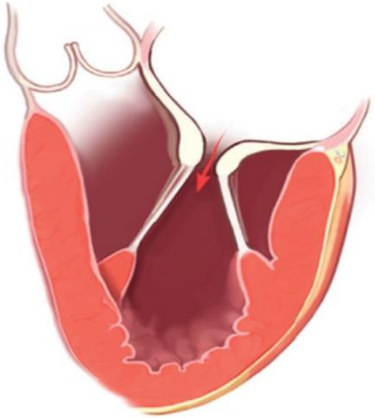
Type I
Normal leaflet motion

LEAFLET PERFORATION ANNULAR DILATION



Type II
Increased leaflet motion

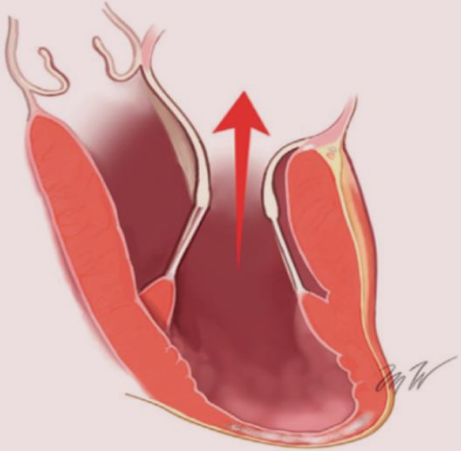
CORDAL ELONGATION OR RUPTURE



Type IIIa
Restricted leaflet motion
(systole and diastole)

RHEUMATIC DISEASE

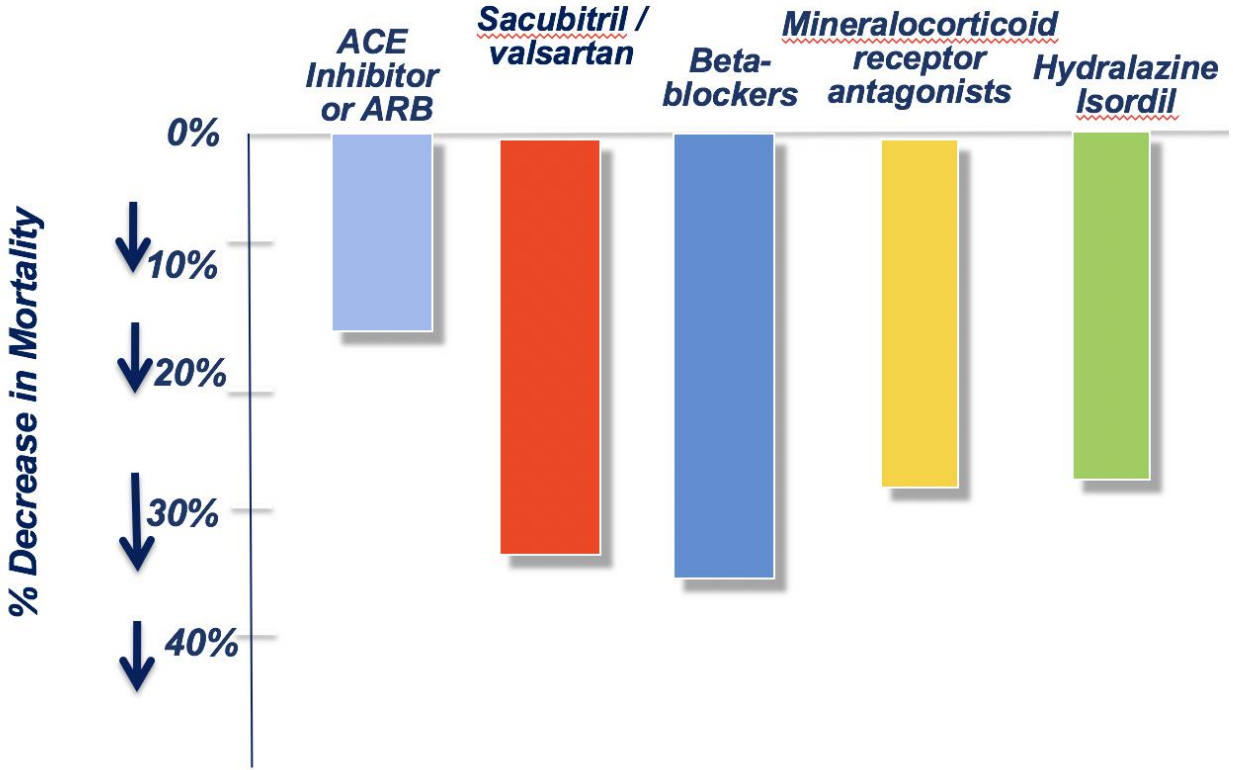
SECONDARY MR



Type IIIb
Restricted leaflet motion
(systole)

ISCHEMIC OR NONISCHEMIC LV REMODELING

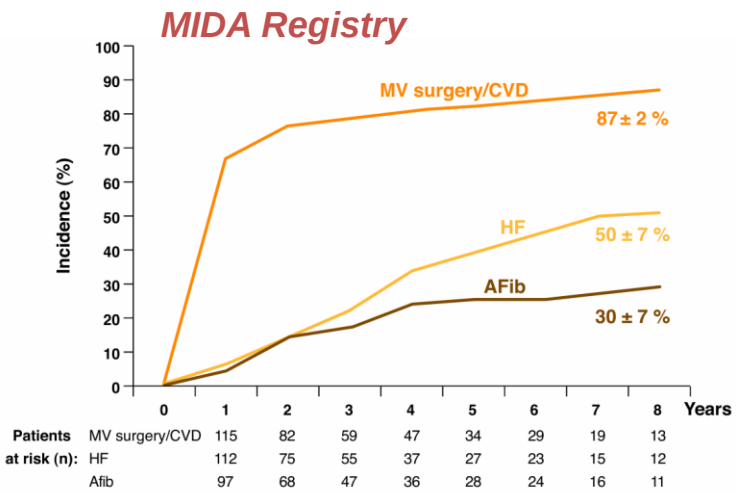
Medical Therapy: An Impressive Evidence Base



Medical Therapy: A Limited Impact

Primary MR

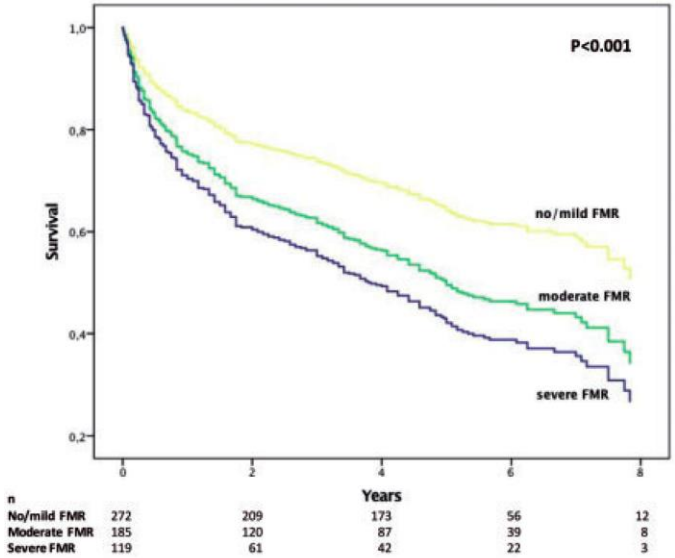
Grigioni et al. *JACC CV Imaging* 2008;1:133-41



Pts with nonsurgical management with severe MR due to flail leaflet (N =394)

Secondary MR

Goliasch G et al. *EHJ* 2018;39:39-46



576 pts with HFrEF; 47% died during median 5-year FU; severe FMR in 21%, mod FMR in 32%

Cardiac Resynchronisation Therapy

- CRT reduces FMR in patients with QRS prolongation
  - Improved global LV function
  - Reduced LV remodeling
  - Reduced papillary muscle dyssynchrony
  - Improved leaflet alignment
- Modest reduction only (EROA seldom <0.2)
- Reduced MR (majority assumed to be functional) following CRT implantation in pivotal CHF studies
- No prospective RCTs in the setting of severe MR

Cleland JG *et al*. CARE-HF trial. *N Engl J Med* 2005;352:1539-49.

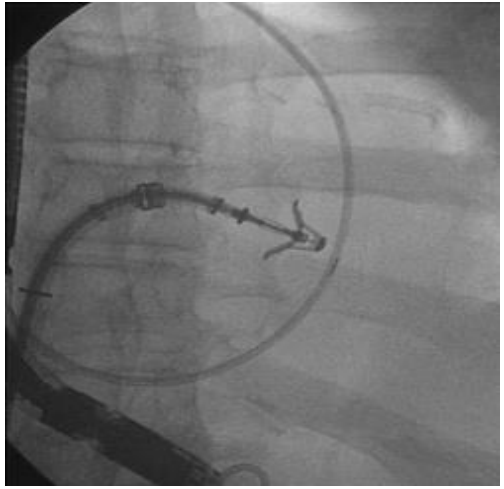
St John Sutton MG *et al*. MIRACLE trial. *Circulation* 2003;107:1985-90.

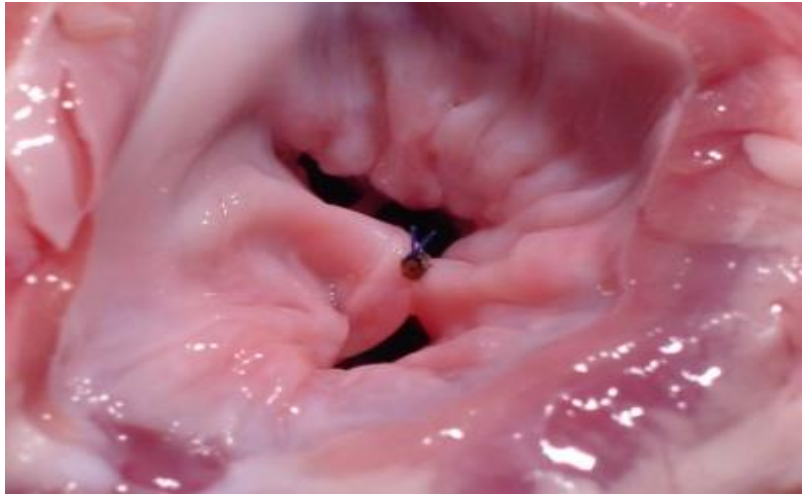
Mitral Valve Surgery

- Limited evidence
- Current ESC/EACTS guidelines
  - Severe SMR + LVEF >30% in patients undergoing CABG (IC)
  - Severe SMR + LVEF <30% with viability and revascularization options (IIa C)
  - Severe SMR + LVEF >30% but not suitable for revascularization (IIb C)
- Surgery for isolated SMR seldom performed
- Patients with severe SMR and advanced HF may be candidates for transplant or VAD implantation
  - Destination therapy
  - Bridge to transplantation

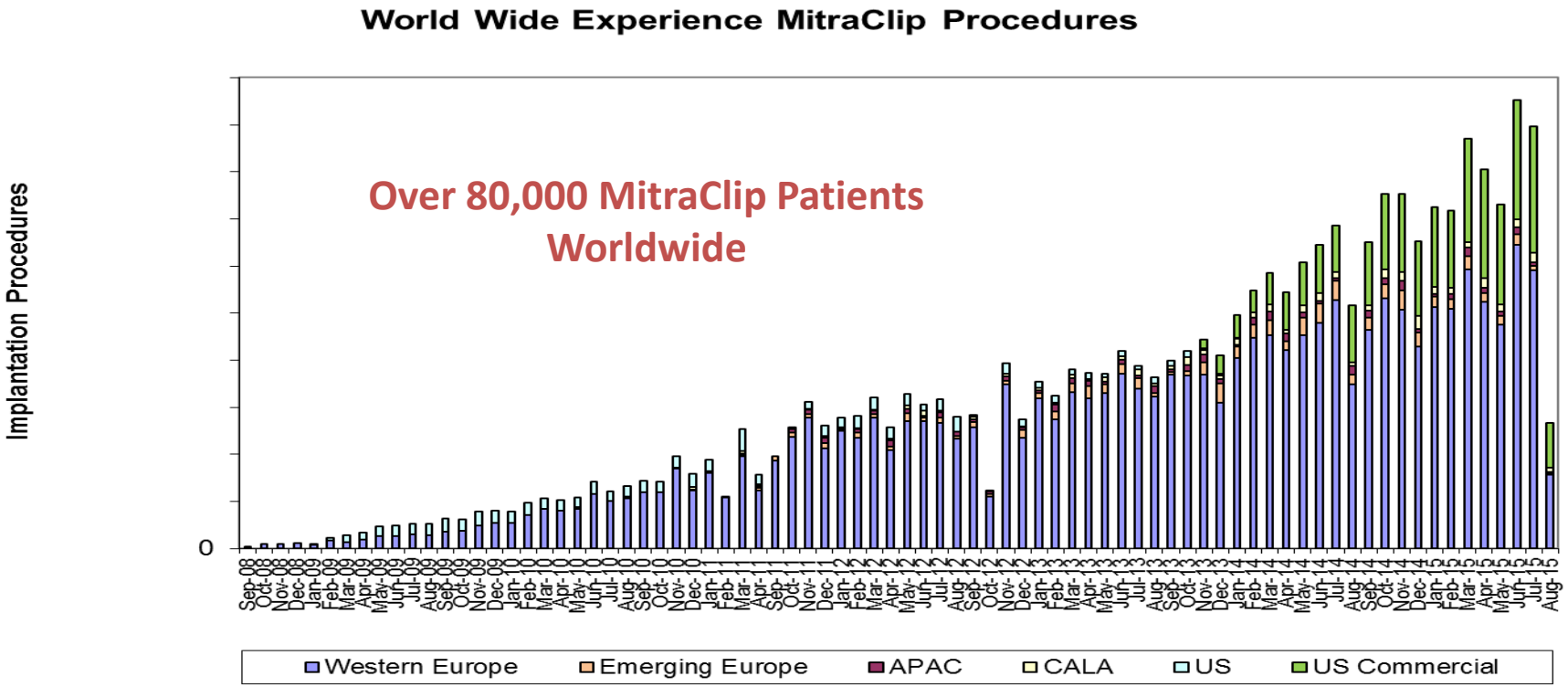
Wu AH *et al*. *J Am Coll Cardiol* 2005;45:381-7.

Acker MA *et al*. *N Engl J Med* 2014;370:23-32.



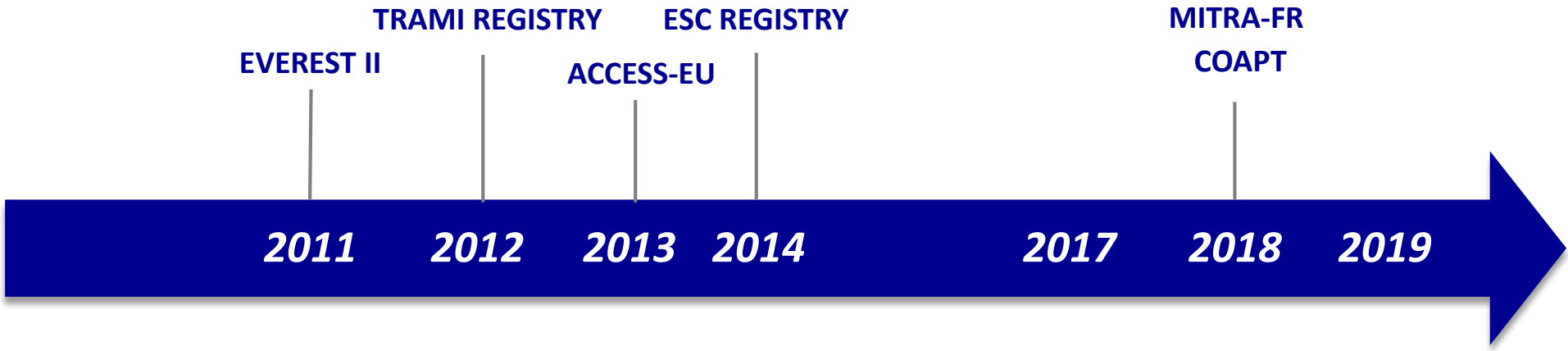


Global MitraClip Experience



MIND THE GAP
020 7222 1234
020 7918 3015
www.tfl.gov.uk
UNDERGROUND

Evidence and Guidelines



ESC European Society of Cardiology

EACTS European Association For Cardio-Thoracic Surgery

Extreme risk	IIb	C
High risk	IIb	C

Extreme risk	IIb	C
High risk	IIb	C

Waiting for...

American Heart Association.

AMERICAN COLLEGE of CARDIOLOGY

Prohibitive risk*	IIb	B

Prohibitive risk*	IIb	B

Waiting for...

*Primary MR only; not approved for secondary MR

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter Mitral-Valve Repair in Patients with Heart Failure

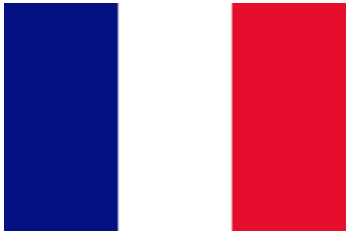
G.W. Stone, J.A. Lindenfeld, W.T. Abraham, S. Kar, D.S. Lim, J.M. Mishell, B. Whisenant, P.A. Grayburn, M. Rinaldi, S.R. Kapadia, V. Rajagopal, I.J. Sarembock, A. Brieke, S.O. Marx, D.J. Cohen, N.J. Weissman, and M.J. Mack, for the COAPT Investigators*

ORIGINAL ARTICLE

Percutaneous Repair or Medical Treatment for Secondary Mitral Regurgitation

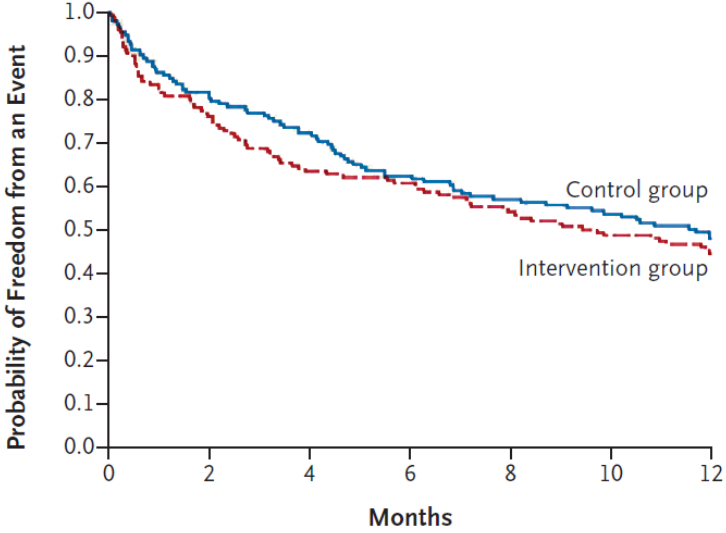
J.-F. Obadia, D. Messika-Zeitoun, G. Leurent, B. Iung, G. Bonnet, N. Piriou, T. Lefèvre, C. Piot, F. Rouleau, D. Carrié, M. Nejjari, P. Ohlmann, F. Leclercq, C. Saint Etienne, E. Teiger, L. Leroux, N. Karam, N. Michel, M. Gilard, E. Donal, J.-N. Trochu, B. Cormier, X. Armoiry, F. Boutitie, D. Maucort-Boulch, C. Barnel, G. Samson, P. Guerin, A. Vahanian, and N. Mewton, for the MITRA-FR Investigators*

Two RCT's in NEJM in the same month with vastly different results!



MITRA-FR: PRIMARY ENDPOINT AND SUBGROUP ANALYSIS

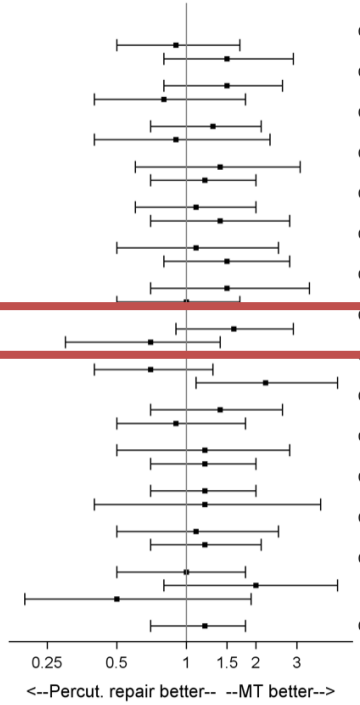
Obadia JF *et al*. N Engl J Med 2018;379:2297-2306.



No. at Risk

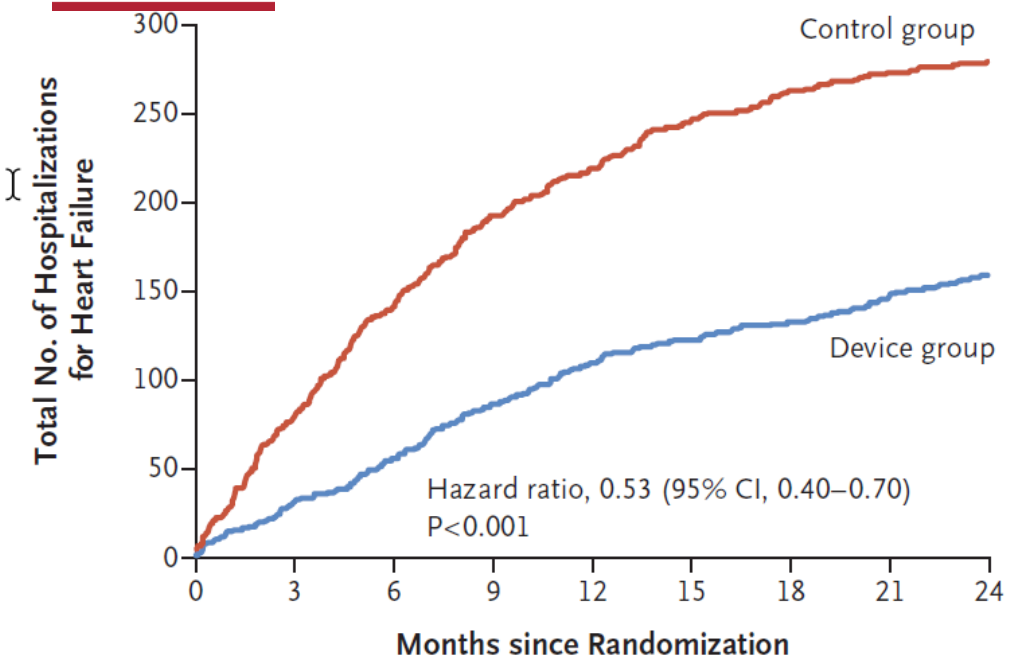
Control group	152	123	109	94	86	80	73
Intervention group	151	114	95	91	81	73	67

Subgroup	Percut. repair Events/N (%)		Medical treatment Events/N (%)		OR (95% CI)	P Value*
CENTRE SIZE						0.27
N <= 15 Randomized patients	33/73	(45.2)	35/73	(47.9)	0.90 (0.50, 1.70)	
N > 15 Randomized patients	50/77	(64.9)	43/78	(55.1)	1.50 (0.80, 2.90)	
AGE						0.20
<= 75 Yr	52/100	(52.0)	39/93	(41.9)	1.50 (0.80, 2.60)	
> 75 Yr	31/50	(62.0)	39/58	(67.2)	0.80 (0.40, 1.80)	
GENDER						0.55
Male	67/120	(55.8)	53/106	(50.0)	1.30 (0.70, 2.10)	
Female	16/30	(53.3)	25/45	(55.6)	0.90 (0.40, 2.30)	
NYHA						0.73
Class II	26/56	(46.4)	17/44	(38.6)	1.40 (0.60, 3.10)	
Class III/IV	57/94	(60.6)	61/107	(57.0)	1.20 (0.70, 2.00)	
ISCHEMIC CARDIOMYOPATHY						0.63
Yes	49/94	(52.1)	42/84	(50.0)	1.10 (0.60, 2.00)	
No	34/56	(60.7)	35/66	(53.0)	1.40 (0.70, 2.80)	
PULMONARY ARTERY PRESSURE						0.58
< 50 mmHg	23/53	(43.4)	18/44	(40.9)	1.10 (0.50, 2.50)	
≥ 50 mmHg	49/73	(67.1)	51/88	(58.0)	1.50 (0.80, 2.80)	
ATRIAL FIBRILLATION						0.37
Yes	30/49	(61.2)	24/47	(51.1)	1.50 (0.70, 3.40)	
No	46/91	(50.5)	51/99	(51.5)	1.00 (0.50, 1.70)	
PREVIOUS HOSPIT FOR CHF						0.06
< 2	53/95	(55.8)	38/87	(43.7)	1.60 (0.90, 2.90)	
≥ 2	30/55	(54.5)	40/62	(64.5)	0.70 (0.30, 1.40)	
CREATININE						0.17
< 1 5 mg/dl	31/75	(41.3)	43/85	(50.6)	0.70 (0.40, 1.30)	
≥ 1 5 mg/dl	51/72	(70.8)	34/65	(52.3)	2.20 (1.10, 4.50)	
HEMOGLOBINE						0.59
< Median	43/75	(57.3)	33/65	(50.8)	1.40 (0.70, 2.60)	
≥ Median	38/72	(52.8)	42/80	(52.5)	0.90 (0.50, 1.80)	
LVEF						0.99
< 30%	21/35	(60.0)	27/48	(56.3)	1.20 (0.50, 2.80)	
≥ 30%	62/115	(53.9)	51/102	(50.0)	1.20 (0.70, 2.00)	
TRICUSPID REGURGITATION						0.93
Mild	60/110	(54.5)	60/118	(50.8)	1.20 (0.70, 2.00)	
Moderate/Severe	19/29	(65.5)	14/23	(60.9)	1.20 (0.40, 3.80)	
LV TELEDIASTOLIC DIAMETER						0.84
< 65 mm	21/43	(48.8)	21/45	(46.7)	1.10 (0.50, 2.50)	
≥ 65 mm	62/107	(57.9)	56/105	(53.3)	1.20 (0.70, 2.10)	
MITRAL REGURGITANT ORIFICE						0.85
< 30 mm2	37/77	(48.1)	39/80	(48.8)	1.00 (0.50, 1.80)	
30-40 mm2	28/44	(63.6)	24/51	(47.1)	2.00 (0.80, 4.50)	
> 40 mm2	18/29	(62.1)	15/20	(75.0)	0.50 (0.20, 1.90)	
OVERALL	83/150	(55.3)	78/151	(51.7)	1.20 (0.70, 1.80)	0.53



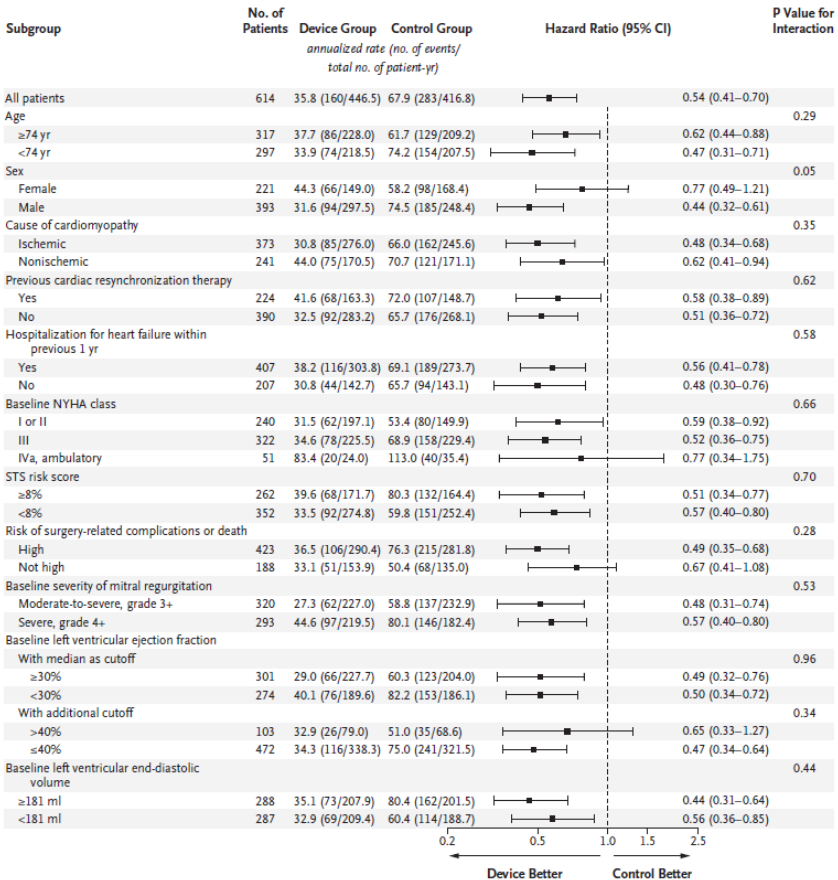
COAPT: PRIMARY ENDPOINT AND SUBGROUP ANALYSIS

Stone GW *et al*. N Engl J Med 2018;379:2307-2318.



No. at Risk

Control group	312	294	271	245	219	176	145	121	88
Device group	302	286	269	253	236	191	178	161	124



Subgroup	No. of Patients	Device Group	Control Group	Hazard Ratio (95% CI)	P Value for Interaction
		annualized rate (no. of events/ total no. of patient-yr)			
All patients	614	35.8 (160/446.5)	67.9 (283/416.8)	0.54 (0.41–0.70)	
Age					0.29
≥74 yr	317	37.7 (86/228.0)	61.7 (129/209.2)	0.62 (0.44–0.88)	
<74 yr	297	33.9 (74/218.5)	74.2 (154/207.5)	0.47 (0.31–0.71)	
Sex					0.05
Female	221	44.3 (66/149.0)	58.2 (98/168.4)	0.77 (0.49–1.21)	
Male	393	31.6 (94/297.5)	74.5 (185/248.4)	0.44 (0.32–0.61)	
Cause of cardiomyopathy					0.35
Ischemic	373	30.8 (85/276.0)	66.0 (162/245.6)	0.48 (0.34–0.68)	
Nonischemic	241	44.0 (75/170.5)	70.7 (121/171.1)	0.62 (0.41–0.94)	
Previous cardiac resynchronization therapy					0.62
Yes	224	41.6 (68/163.3)	72.0 (107/148.7)	0.58 (0.38–0.89)	
No	390	32.5 (92/283.2)	65.7 (176/268.1)	0.51 (0.36–0.72)	
Hospitalization for heart failure within previous 1 yr					0.58
Yes	407	38.2 (116/303.8)	69.1 (189/273.7)	0.56 (0.41–0.78)	
No	207	30.8 (44/142.7)	65.7 (94/143.1)	0.48 (0.30–0.76)	
Baseline NYHA class					0.66
I or II	240	31.5 (62/197.1)	53.4 (80/149.9)	0.59 (0.38–0.92)	
III	322	34.6 (78/225.5)	68.9 (158/229.4)	0.52 (0.36–0.75)	
IVa, ambulatory	51	83.4 (20/24.0)	113.0 (40/35.4)	0.77 (0.34–1.75)	
STS risk score					0.70
≥8%	262	39.6 (68/171.7)	80.3 (132/164.4)	0.51 (0.34–0.77)	
<8%	352	33.5 (92/274.8)	59.8 (151/252.4)	0.57 (0.40–0.80)	
Risk of surgery-related complications or death					0.28
High	423	36.5 (106/290.4)	76.3 (215/281.8)	0.49 (0.35–0.68)	
Not high	188	33.1 (51/153.9)	50.4 (68/135.0)	0.67 (0.41–1.08)	
Baseline severity of mitral regurgitation					0.53
Moderate-to-severe, grade 3+	320	27.3 (62/227.0)	58.8 (137/232.9)	0.48 (0.31–0.74)	
Severe, grade 4+	293	44.6 (97/219.5)	80.1 (146/182.4)	0.57 (0.40–0.80)	
Baseline left ventricular ejection fraction					
With median as cutoff					0.96
≥30%	301	29.0 (66/227.7)	60.3 (123/204.0)	0.49 (0.32–0.76)	
<30%	274	40.1 (76/189.6)	82.2 (153/186.1)	0.50 (0.34–0.72)	
With additional cutoff					0.34
>40%	103	32.9 (26/79.0)	51.0 (35/68.6)	0.65 (0.33–1.27)	
≤40%	472	34.3 (116/338.3)	75.0 (241/321.5)	0.47 (0.34–0.64)	
Baseline left ventricular end-diastolic volume					0.44
≥181 ml	288	35.1 (73/207.9)	80.4 (162/201.5)	0.44 (0.31–0.64)	
<181 ml	287	32.9 (69/209.4)	60.4 (114/188.7)	0.56 (0.36–0.85)	

MITRA-FR and COAPT: Key Differences

	MITRA-FR (n=304)	COAPT (n=614)
Severe MR entry criteria	Severe FMR by EU guidelines: EROA >20 mm^2 or RV >30 mL/beat	Severe FMR by US guidelines: EROA >30 mm^2 or RV >45 mL/beat
EROA (mean ± SD)	31 ± 10 mm^2	41 ± 15 mm^2
LVEDV (mean ± SD)	135 ± 35 mL/m^2	101 ± 34 mL/m^2
GDMT at baseline and FU	Receiving HF meds at baseline – allowed variable adjustment in each group during follow-up per "real-world" practice	CEC confirmed pts were failing maximally-tolerated GDMT at baseline – few major changes during follow-up
Acute results: No clip / ≥3+ MR	9% / 9%	5% / 5%
Procedural complications*	14.6%	8.5%
12-mo MitraClip ≥3+ MR	17%	5%

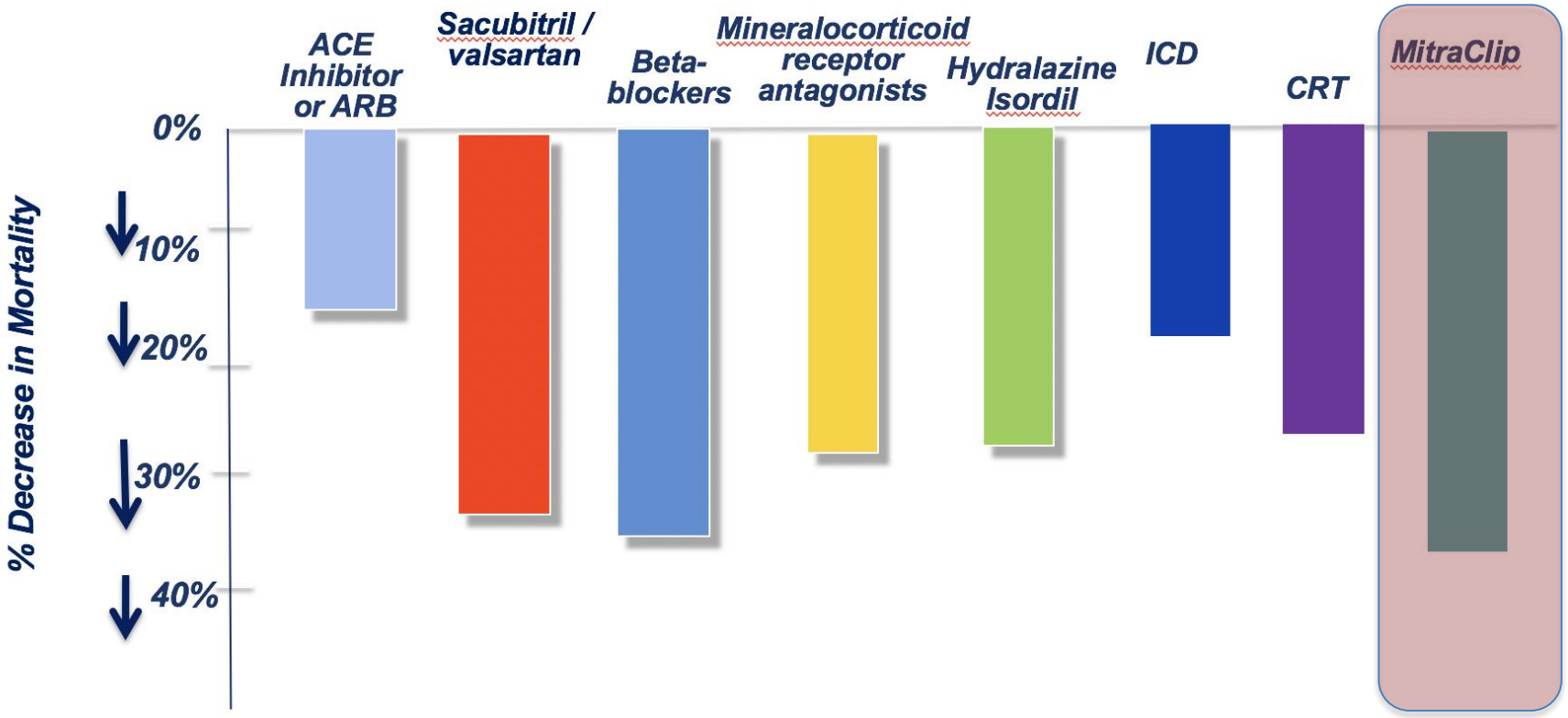
MORE MR
SMALLER LV

OPTIMAL
MEDICATION

BETTER
TECHNIQUE

Stone GW. TCT presentation. September 2018.
Praz F, Prendergast B *et al*. Eur Heart J 2018.

FMR Therapy: An Impressive Evidence Base



US POPULATION PROJECTIONS

CHF POPULATION

6 million

ELIGIBLE FOR MITRACLIP (COAPT criteria)

250,000

Stone GW. CIT presentation March 2019.

PCR CARDIOPOLL: Monday May 20 @0700hrs

Cardio Poll Results: Functional mitral regurgitation repair – how did your practice change after the results of COAPT and MitraFr?

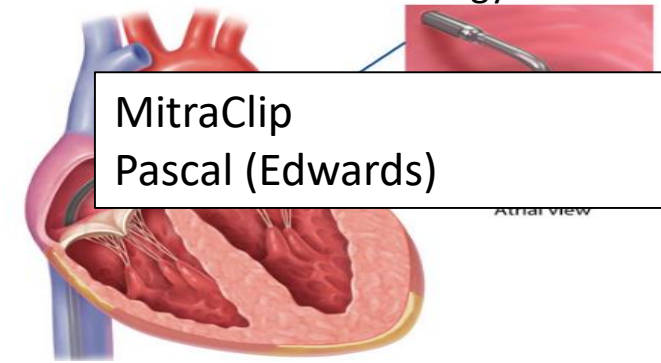
Thank you for voting!

How did your practice change after the results of COAPT and MitraFr?

Choices	Percentage	Count
Increase in FMR indications	*53.04%*	61
No change	*35.65%*	41
Decrease in FMR indications	*11.30%*	13
	Total	**115**

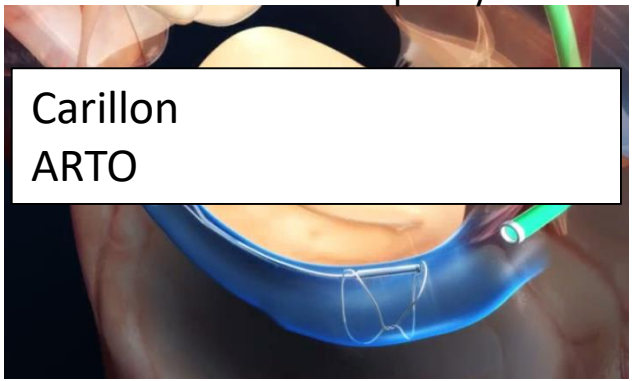
Alternative Transcatheter Techniques Under Investigation

Leaflet Technology



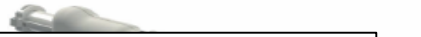
MitraClip
Pascal (Edwards)

Indirect Annuloplasty



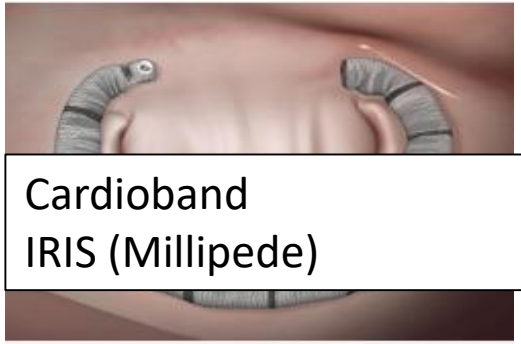
Carillon
ARTO

Chordal Repair



Neochord
Harpoon

Direct Annuloplasty



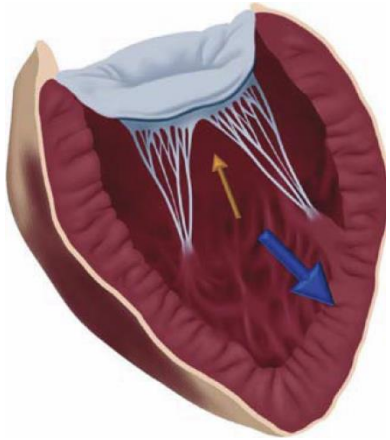
Cardioband
IRIS (Millipede)

Mitral Valve Replacement

Tendyne (Abbott)
CardiaQ (Edwards)
Intrepid (Medtronic)
Tiara (Neovasc)

FMR: UNANSWERED QUESTIONS

The Need, Mode and Timing of Intervention



Myocardial Injury

↓

Ventricular Remodelling

↓

Mitral Apparatus Remodeling

↓

Mitral Valve Dysfunction

Further Studies

Need (other populations, COAPT, MATTERHORN)

Mode (annuloplasty, combined techniques, repair vs replacement)

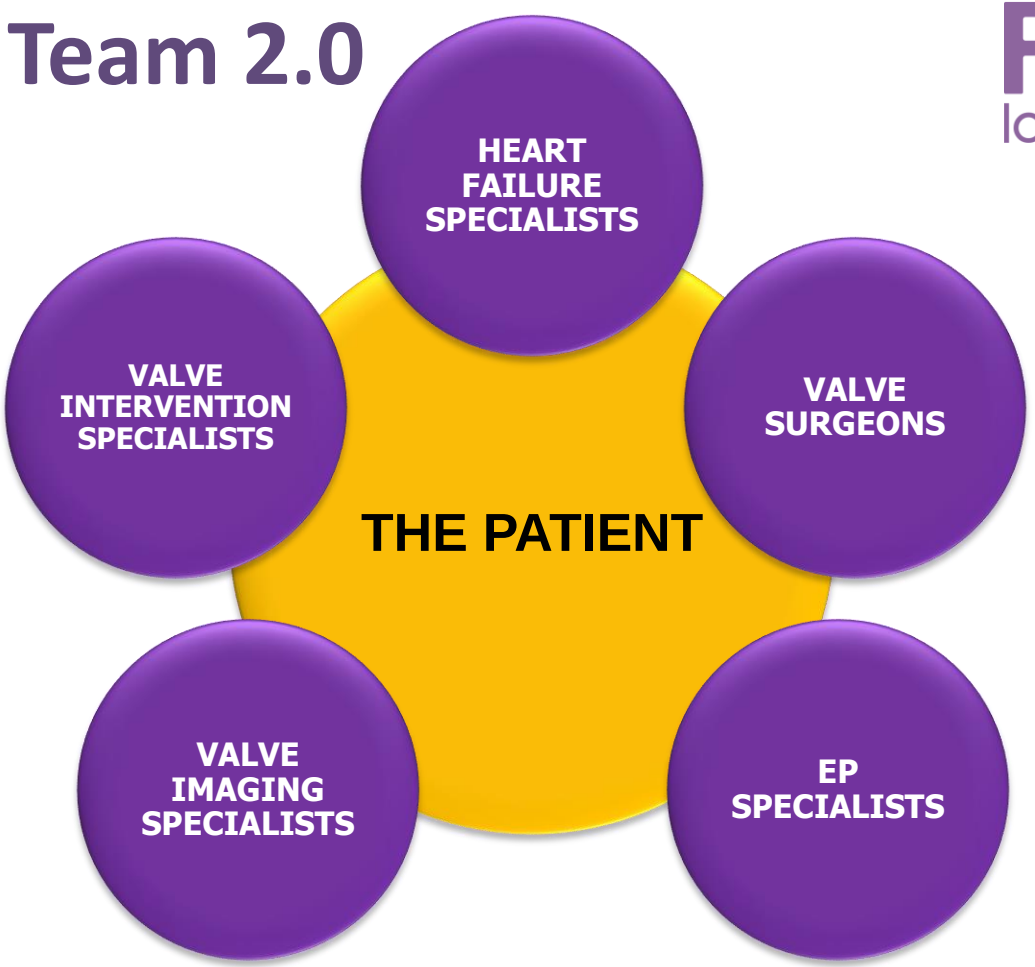
Timing (severity and type of cardiomyopathy)

Heart Failure & Reduced EF
No MR

Endstage CHF
Severe FMR

Praz F, Prendergast B *et al*. Eur Heart J 2018.

The Heart Team 2.0



SUMMARY AND CONCLUSIONS (I)

- SMR is a common consequence of LV remodelling and associated with adverse prognosis.
- Patients with symptomatic HF and moderate/severe MR should be referred early to a multidisciplinary Heart Team.
- The Heart Team should evaluate and optimise medical therapy and consider the roles of device therapy, transcatheter mitral intervention and surgery.
- Transcatheter edge-to-edge repair is appropriate in carefully selected patients who remain symptomatic despite optimal medical therapy (including CRT):
  - Severe SMR (EROA ≥30 mm^2, regurgitant volume ≥45 ml or regurgitant fraction ≥50%)
  - Suitable valve morphology (assessed by comprehensive echocardiography)
  - LV end-systolic dimension <70mm
  - Absence of significant right ventricular dysfunction, TR and pulmonary hypertension

SUMMARY AND CONCLUSIONS (II)

- The role of other transcatheter treatment options remains under investigation.
- Surgical treatment of SMR may be considered in patients with CAD undergoing surgical revascularisation.
- Circulatory support devices and cardiac transplantation may be an alternative in patients with extreme LV and/or RV failure.
- Futile interventions should be avoided in patients with short life expectancy – specialist palliative care is more appropriate.

Management of Patients with Heart Failure and Functional Mitral Regurgitation

A Joint Position Statement

EAPCI European Association of Percutaneous Cardiovascular Interventions

EHRA European Heart Rhythm Association

EACVI European Association of Cardiovascular Imaging

HFA Heart Failure Association

Ruschitzka F, Prendergast B *et al*. Under review.

2019 euro PCR