

Gender Based Disparities in TAVR Utilization

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Disclosures

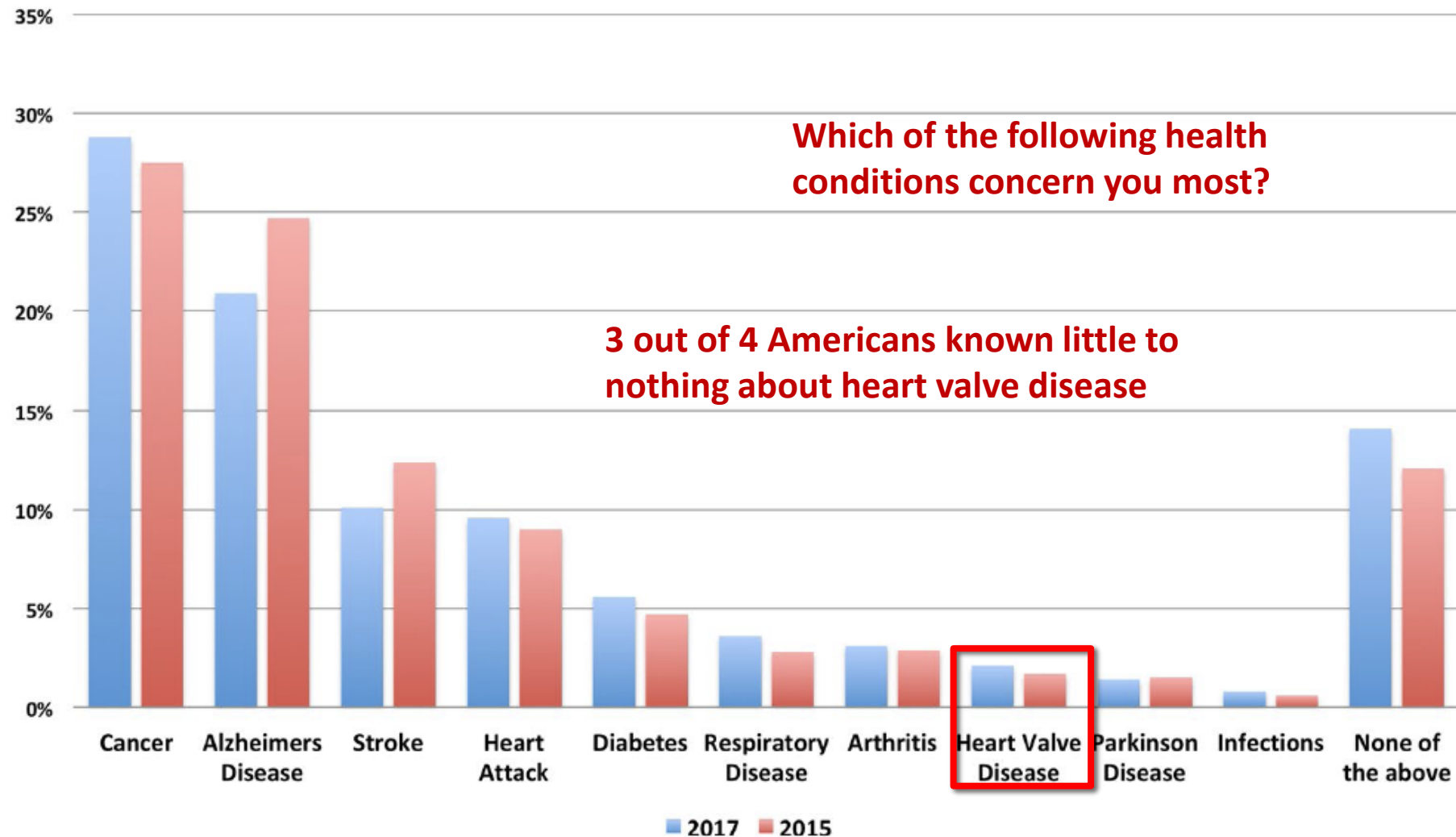
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<u>Presenter</u>	<u>Disclosure</u>
Dan Inder S Sraow, MD	None

Heart Valve Awareness in General Population

n=12,820 people 60 years of older at 11 European countries



Aortic Stenosis Gender Differences

- Valvular Heart Disease affects as many as **11 million** in the United States
 - With a **prevalence of 12.4%** among elderly patients, aortic stenosis is considered the most common form
- Valvular heart disease occurs with equal frequency in men and women
- Historically, rheumatic heart disease was the predominant cause of valvular heart disease, whereas today, **the primary etiology of valvular heart disease** in industrialized countries is **degenerative**.

Differences in Imaging Findings Among Women Presenting for TAVR

Aorta and aortic root

Smaller aortic annulus and LVOT diameters resulting in smaller transcatheter heart valve (THV) sizes

**Less aortic valve calcium but more fibrosis*

Higher transaortic gradients (at presentation for TAVR)

Higher pulmonary pressures (at presentation for TAVR)

More women in PLFLG severe AS subgroup (similar prognosis to high gradient severe AS post-TAVR)

Fewer women in low-EF, low-gradient severe AS subgroup (poorer survival than PLFLG or high-gradient severe AS post-TAVR)

Lower coronary heights and smaller sinus of Valsalva diameters

Left ventricle

Better LV ejection fraction (at presentation for TAVR)

Less myocardial fibrosis

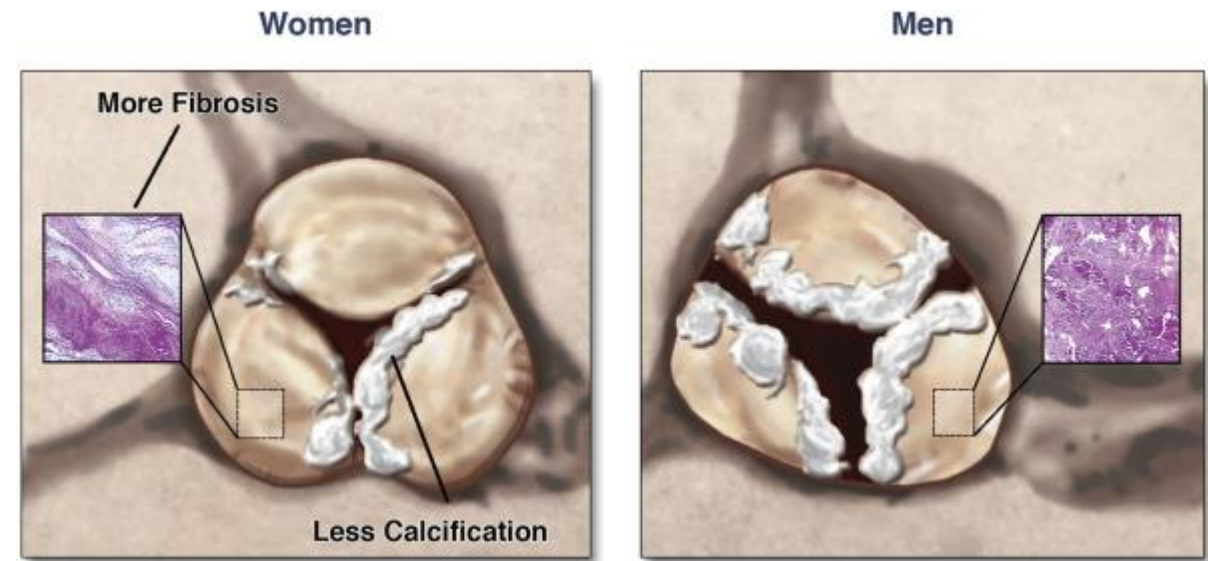
More pronounced concentric LV remodeling

Peripheral vascular

Less peripheral arterial disease and calcification but smaller iliofemoral luminal diameters

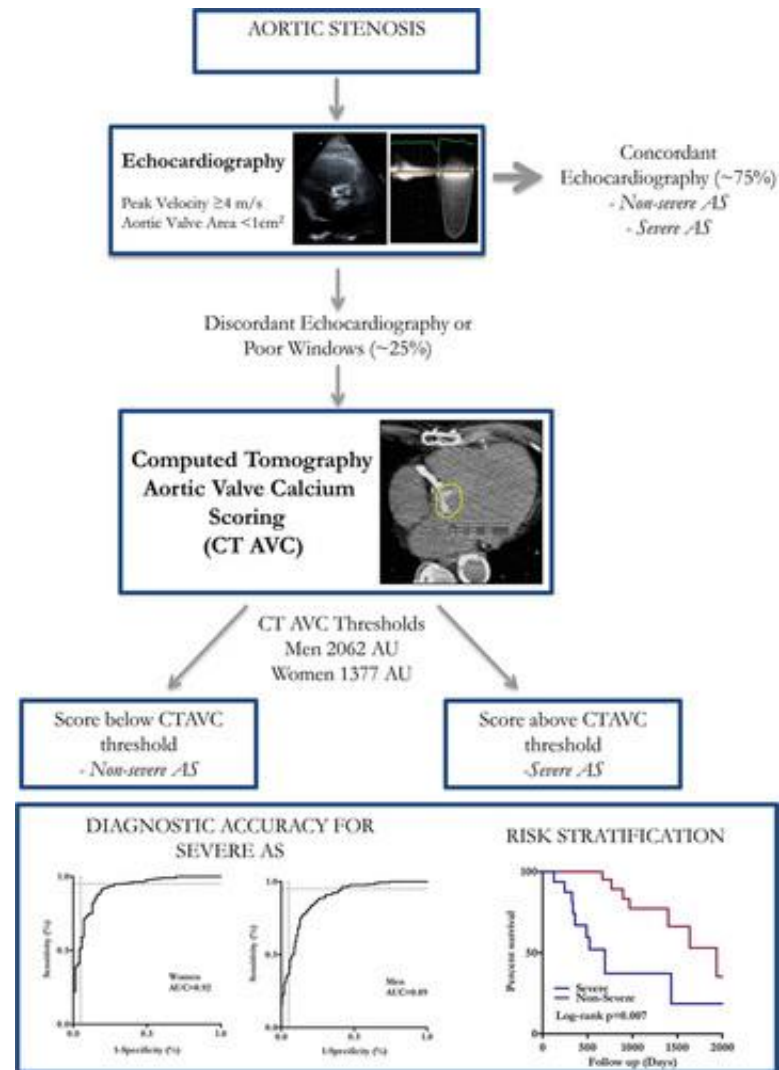
- The calcium load in the aortic valve has been shown to correlate with AS hemodynamic severity.
- There is a higher burden of fibrosis observed in women compared to men on histopathological evaluation of surgically resected aortic valve tissue (less calcification).
- Sex-specific AVC score cutoffs have been formalized (total AVC 2,065 in men and 1,275 in women) predictive of survival in AS patients independent of clinical and echocardiographic factors

Differences in Aortic Valve Calcification



1 Naoum C, et al. Clinical Outcomes in Women Undergoing TAVR. JACC: Cardiovascular Imaging. Nov 4 2016 (9): 483-493.

2 Clavel MA, et al. Impact of aortic valve calcification, as measured by MDCT, on survival in patients with aortic stenosis: results of an international registry study. J Am Coll Cardiol 2014;64:1202-13



Baseline Clinical Profile in Women

- **Overall preoperative risk stratification scores are lower in women presenting for TAVR compared with men. They demonstrate:**
 - Lower burden of overall cardiovascular risk factors including dialysis
 - Lower rates of previous cerebrovascular accident and peripheral vascular disease
 - Better systolic function at presentation

Does this mean better Clinical Outcomes Following TAVR?

Aortic Stenosis Gender Differences

- Female patients are older
In Sweden (1989-2009):¹
Males 54.7% vs 45.3%
If <75 years of age >60% men,
If >75 years >50% women
- Female patients have higher surgical risk profile²

1.- Maftrinson, et al. Circulation 2015;131:988-994.

2.- Thourani et al. Ann Thorac Surg 2015;99:55-61.

Studies of Transcatheter Aortic Valve Replacement in Women

Reference	Study Design	Site	No. of Patients	Women (%)	Follow-Up Duration
Buchanan GL, et al. ² (2011)	Observational	Single center (Italy)	305	47.5	30 d
Stangl V, et al. ³ (2012)	Observational	Single center (Germany)	100	58	90 d
Hayashida K, et al. ⁴ (2012)	Observational	Single center (France)	260	50.4	217 d
Humphries KH, et al. ⁵ (2012)	Observational	Dual centers (Canada)	641	51.3	302 d; survival est. 2 yr
Williams M, et al. ⁶ (2014)	Retrospective analysis of RCT	Multicenter	699	42.9	2 yr
Chandrasekhar J, et al. ⁷ (2016)	Observational	Multicenter registry	11,808	49.9	1 yr

est. = estimate; RCT = randomized controlled trial

Buchanan GL, Chieffo A, Montorfano M, Maisano F, Latib A, Godino C, et al. The role of sex on VARC outcomes following transcatheter aortic valve implantation with both Edwards SAPIEN™ and Medtronic CoreValve ReValving System® devices: the Milan registry. *EuroIntervention* 2011; 7 5: 556– 63.

Female Patients in TAVR Trials

	TAVR	SAVR or comparator
PARTNER I Extreme risk ¹	54.2%	53.1% Med Rx
PARTNER I High Risk ²	42.2%	43.3% SAVR
PARTNER IIA Intermediate risk ³	45.8%	45.2% SAVR
CoreValve Extreme risk ⁴	52.1%	
SURTAVI Intermediate Risk ⁵	42.2%	45% SAVR
REPRISE High or Extreme Risk ⁵	50.1% Lotus	52.1% CoreValve
NOTION low risk ⁷	46.2%	47.4% SAVR

¹ Leon et al, NEJM 2010

² Smith et al, NEJM 2011

³ Leon et al, NEJM 2016

⁴ Popma et al, JACC 2014

⁵ Reardon NEJM 2017

⁶ Feldman et al, JAMA 2017

⁷ Sondergaard et al, TVT 2018

More female patients in extreme high risk trials

TAVR Outcomes in Intermediate-High Risk Female Patients

Female vs. Male

	%	Age	STS PROM	Bleeding	Vascular complications	30-Day Mortality	1-year Mortality
TVT 2011-2014 ¹ n=23,652	49.9%	82.2 vs 81.6 p<0.0001	9% vs 8% p<0.0001	8 vs 5.9% p= 0.06	8.27 vs 4.39% p<0.0001	In-hosp 5.6 vs 4.28% p=0.29	21.3 vs 24.5% p<0.001
PARTNER I ² n=2,559	47.7%	84.9 vs 84.1	11.9 vs 11.1%	10.5 vs 7.7% p=0.012	17.3 vs 10% p < 0.001	6.48 vs 5.9% p=0.52	19 vs 25.9% p<0.001
US CoreValve Trials ³ n=3,687	46.3%	84 vs 82.7 p <0.01	9.6 vs 8.3% p <0.01	29.7 vs 21.7% p <0.01	9.7% vs 4.9% p <0.01	5.8 vs 5.9% p= 0.87	21.3 vs 24.1% p=0.08
REPRISE III ⁴ n=874	50%	83.2 vs 82.3 p= 0.07	7.9 vs 5.7% p <0.01	20 vs 15% p=0.05	8.2 vs 4.7% p=0.04	3.2 vs 2.8% p=0.69	12.1 vs 11.9 p=0.98
WIN-TAVI ⁵ n=1,010	100%	82.5	8.3% (±7.4)	7.7%	7.7%	3.4%	NA

¹ Chandrasekhar et al, JACC 2016

² Kodali et al, Ann Intern Med 2016

³ Forrest et al, Am J Cardiol 2016

⁴ Guerrero et al, EuroPCR 2018

⁵ Chieffo et al, JACC Interv 2016

The Women Paradox:

Higher risk profile, more bleeding and vascular complications...
Equal or lower mortality than men

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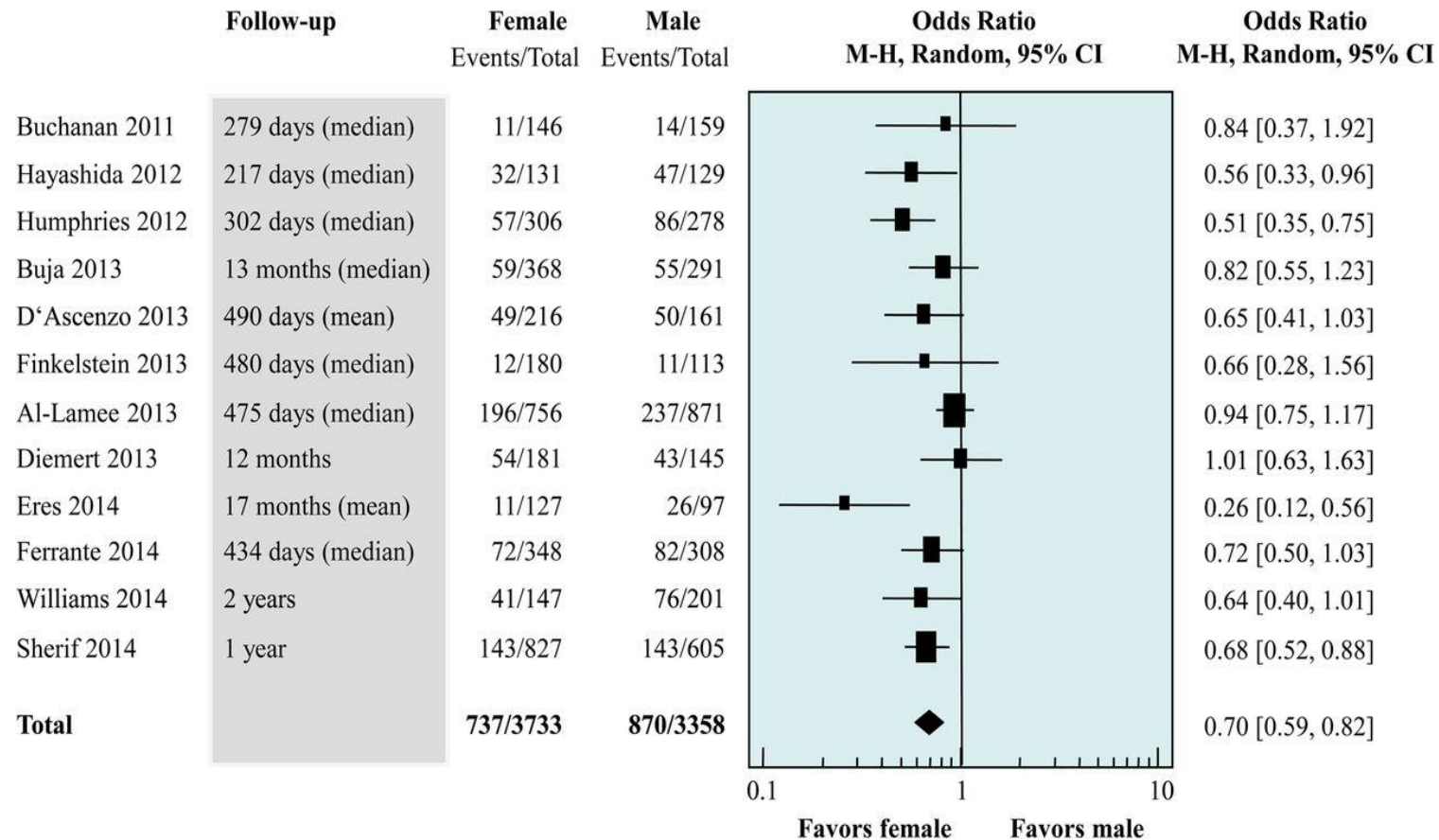
⁵ Chieffo et al, JACC Interv 2016

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Gender differences in TAVI outcome. Meta-analysis of published trials with the end point total mortality ...



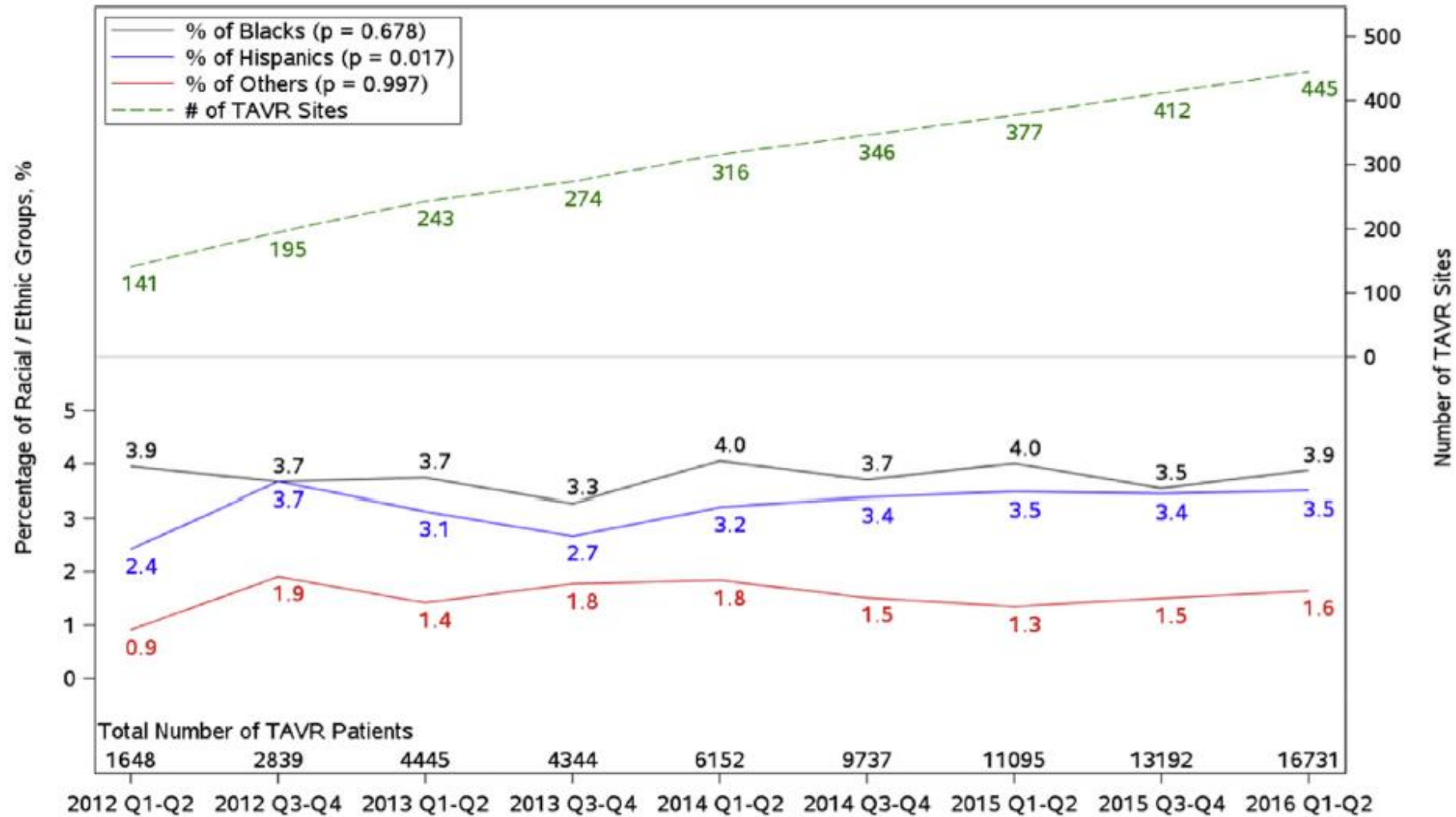
If female patients have higher surgical risk + and better outcomes with TAVR = TAVR for all women with symptomatic AS

Is this what happens in real practice?

TVT Registry

70,221 patients treated between 2011 and 2016 (47.7% female)

91.3% white (47% F), 3.8% black (60.7% F), 3.4% Hispanic (51.7% F) and 1.5% Asian/Native American (48.3%)

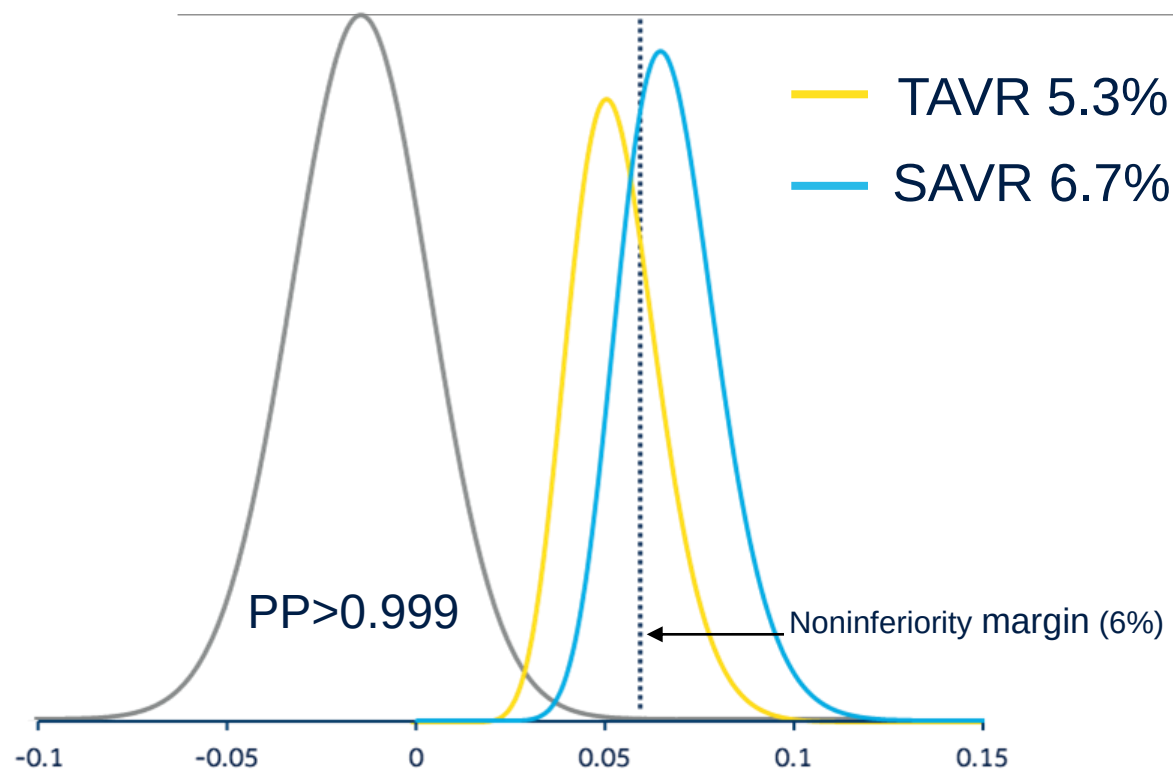


Strategies to decrease burden of AS in women

- Increase awareness in general population
- Modify risk factors to decrease incidence and/or delay onset
- Early treatment to decrease morbidity and mortality
- Treat women with TAVR instead of SAVR
- If women tend to have lower risk profiles, treat patients with severe, symptomatic aortic stenosis, independent of surgical risk
- Novel Techniques to reduce complications (i.e. vascular)

Evolut Low Risk Trial – Primary Endpoint
ALL-CAUSE MORTALITY OR DISABLING STROKE AT 2 YEARS

Bayesian analysis



TAVR – SAVR difference = -1.4% (95% BCI; -4.9, 2.1)

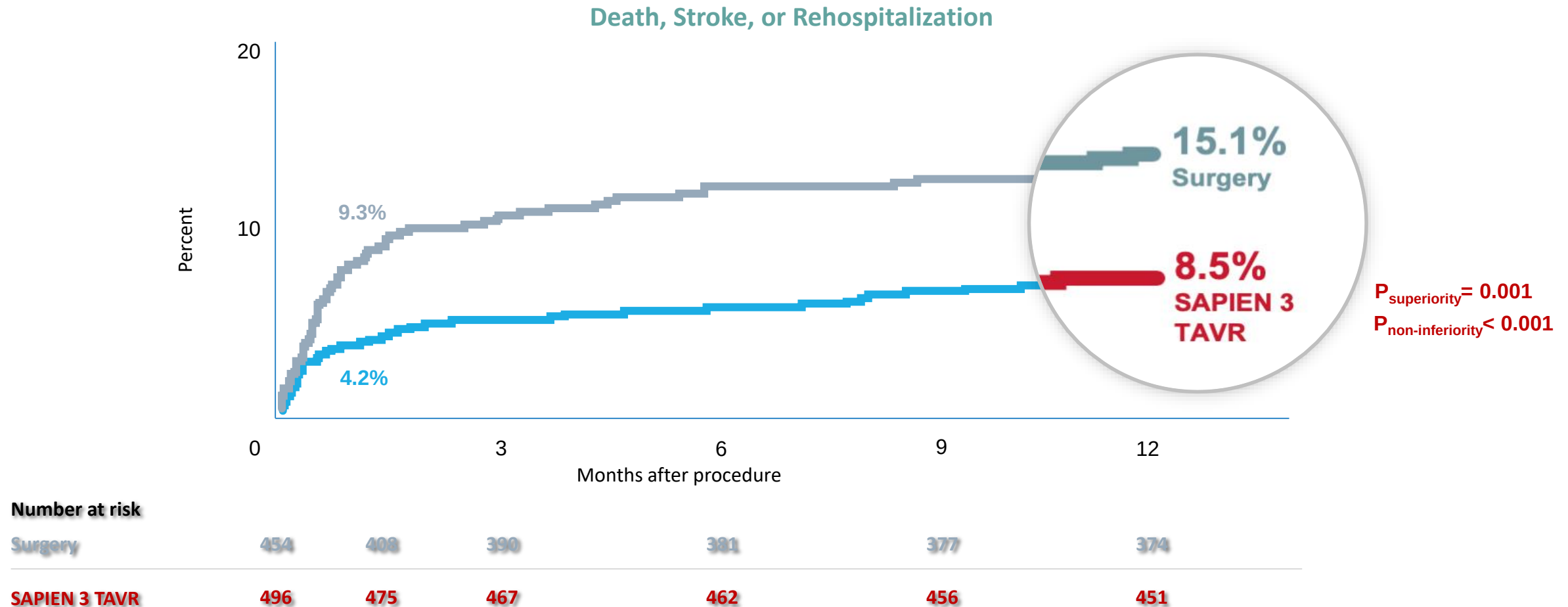
Primary Endpoint Met
TAVR is noninferior to SAVR

Posterior probability of noninferiority
>0.999

- Prespecified criteria for success was a posterior probability of >0.972 to maintain $\alpha < 0.05$

BCI = Bayesian credible interval

SAPIEN 3 TAVR proven superior to surgery in low-risk patients



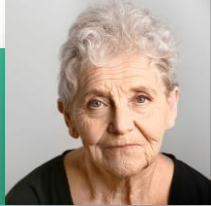
TAVR is FDA-Approved for use in patients with severe, symptomatic calcific aortic stenosis (AS), *independent of surgical risk*

1% death or
disabling stroke
at 1 year*

Partner III and EVOLUT

*Compared to 2.9% death or disability stroke at 1 year for surgery (P=0.03). The PARTNER 3 Trial, SAPIEN 3 TAVR proven superior to surgery on the primary endpoint (all-cause death, all stroke, and rehospitalization) and multiple pre-specified secondary endpoints.

Seek a TAVR evaluation for severe, symptomatic AS patients, *independent of surgical risk*

	Susan Low Surgical Risk 	David Intermediate 	Patricia High Surgical Risk 
AS Disease Progression	Severe AS, symptoms include decreased exercise tolerance	Severe AS, symptoms include fatigue, dyspnea upon exertion	Severe AS, symptoms include reduced mobility and inability to walk short distances
Age/Gender	73 -year old female	81-year old male	88-year old female
NYHA Class	II	III	III
Frailty Indicators	0	Passed 3 out of 4 with exception of grip test	Failed 4/4
Surgical Risk Score	2%	6%	10%
Comorbidities	None	Diabetes, High Blood Pressure, Previous PCI . No other comorbidities.	Oxygen-dependent chronic obstructive pulmonary disease, hypertension, and previous pacemaker implantation due to sick sinus syndrome
QoL Expectations	Retired nurse who enjoys frequent travel, working out and bike rides. She looks forward to an extended life expectancy due to her age and active lifestyle.	Semi-retired executive for an insurance company. Enjoys walking trails around his home and playing with his grandkids.	Retired teacher and requires assistance in daily life activities.
	✓ TAVR Patient	✓ TAVR Patient	✓ TAVR Patient

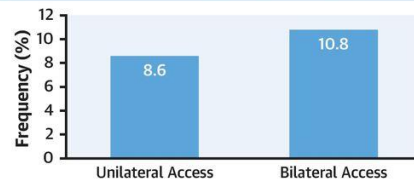
How many more of your patients would you now consider for TAVR?

Single-Side Vascular Access.

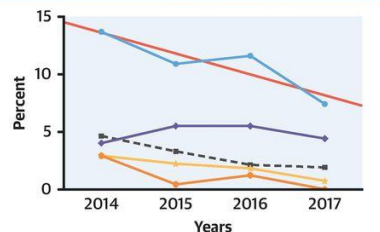
Novel Approach to Decrease Complications?

CENTRAL ILLUSTRATION: Trend and Type of Access-Site Vascular Complications With Comparison of Unilateral and Bilateral Transcatheter Aortic Valve Replacement Patients

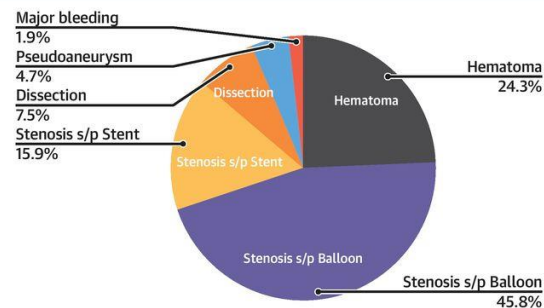
Comparison of Unilateral vs Bilateral Access (PSM Matched)



Trends of Vascular Complications Over the Study Duration



Percent of Individual Vascular Complications



Key findings:
-Overall decrease in the vascular access site complications from 2014 to 2017
-Unilateral access TAVR provides similar safety and efficacy to bilateral TAVR

Khubber, S. et al. J Am Coll Cardiol Interv. 2019;12(21):2210-20.

- TAVR can be made more user friendly by placing both arterial sheaths on the same side of the body
- About 30% of the complications following TAVR are shown to be due to the contralateral access site
- A gradual decline in access site–related vascular complications was observed, from 13.7% in 2014 to 7.4% in 2017.
 - After propensity-score matching, peripheral vascular complications were similar between bilateral access and unilateral access (10.8% vs. 8.6%) ($p = 0.543$).
- Preferred for women?
 - 58% offered single-site access were men

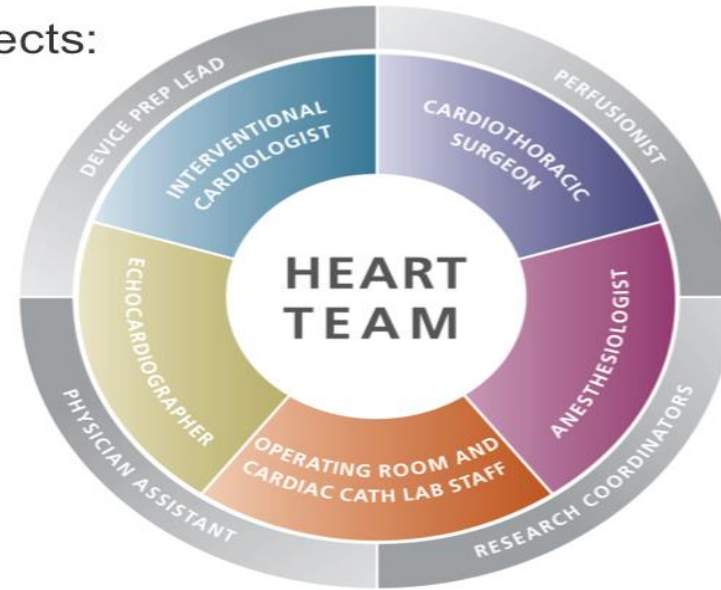
Strategies to decrease burden of AS in women (continued)

Barriers

- Access to health care
- Referral bias
- Collaborate with Women's Heart Health Programs?

Patient-Focused Multidisciplinary Heart Team Approach

- Multidisciplinary in all aspects:
 - Patient selection
 - Procedure planning
 - Patient treatment
 - Post-operative care



Dignity Health East Valley Heart Valve Team

Dan Inder S Sraow, MD, FACC, FSCAI (Director, Structural Heart Health)

Kevin Brady, MD (Co-Chief CT Surgery)

Kenneth Ashton, MD (Co-Chief CT Surgery)

Roger Bies (MDCT, Non-invasive Imaging)

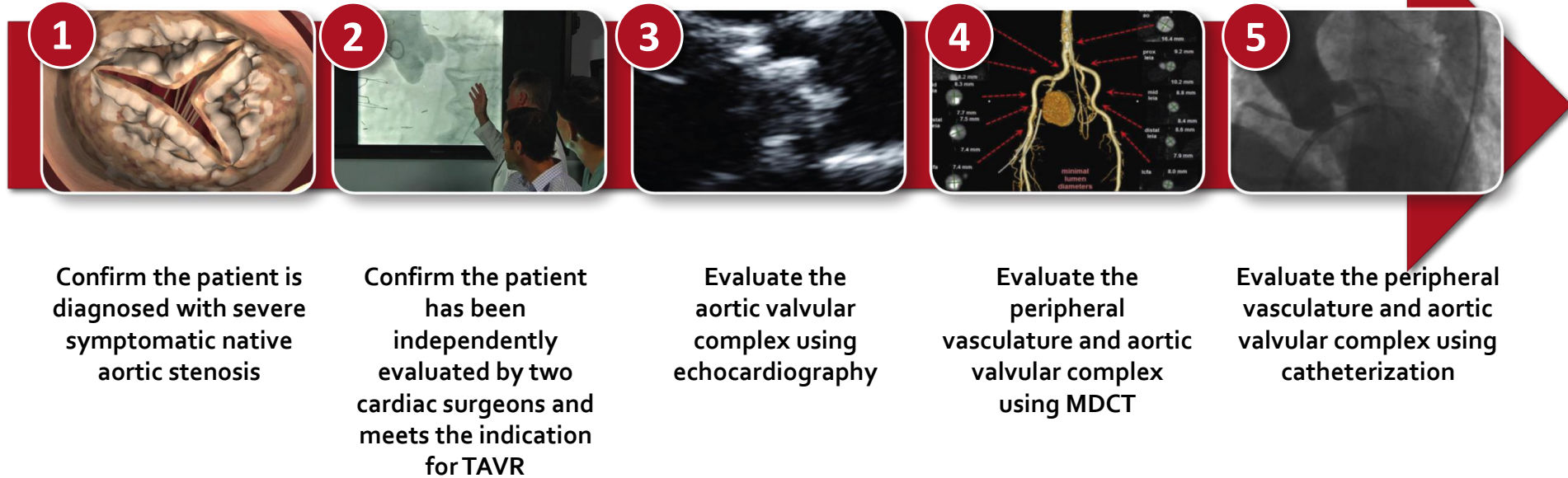
Linda Baker (Coordinator)

Peggy Banyai (Coordinator)

Melody Valles (Quality)

Rachel M Bond, MD, FACC
(Director, Women's Heart Health)

Following Patient Referral, the TAVR Team will Perform Further Evaluation



Note: Evaluation using CT is typically not done unless the Heart Team confirms that patient is a candidate for TAVR

Aortic Stenosis in Women Summary

- Incidence similar to men but clinical presentation at a later age
- Higher surgical risk than men
- Lower risk profile in TAVR compared with men (comorbidities)
- Higher rates of bleeding and vascular complications
- Similar or better clinical outcomes after TAVR compared with men

Thank You!

