Brigham and Women's Hospital
Founding Member, Mass General Brigham

Updates in Valvular Disease

Yee-Ping Sun, MD FACC
Director, Structural Heart Disease Imaging Program
Director, CV Medicine Fellowship Program
Cardiovascular Division
Brigham and Women's Hospital
Assistant Professor of Medicine
Harvard Medical School

Yee-Ping Sun, MD FACC

- Medical School: Harvard Medical School
- Medicine Residency: Brigham and Women's Hospital
- Cardiovascular Fellowship: Columbia University Medical Center
- Advanced Echocardiography Fellowship: Columbia University Medical Center
- Director, Structural Heart Disease Imaging Program
- Director, CV Medicine Fellowship Program
- Clinical focus: Valvular Heart Disease, 3D Echocardiography,
- Research focus:
  - Transcatheter Valve Therapies
  - Endocarditis

Disclosures

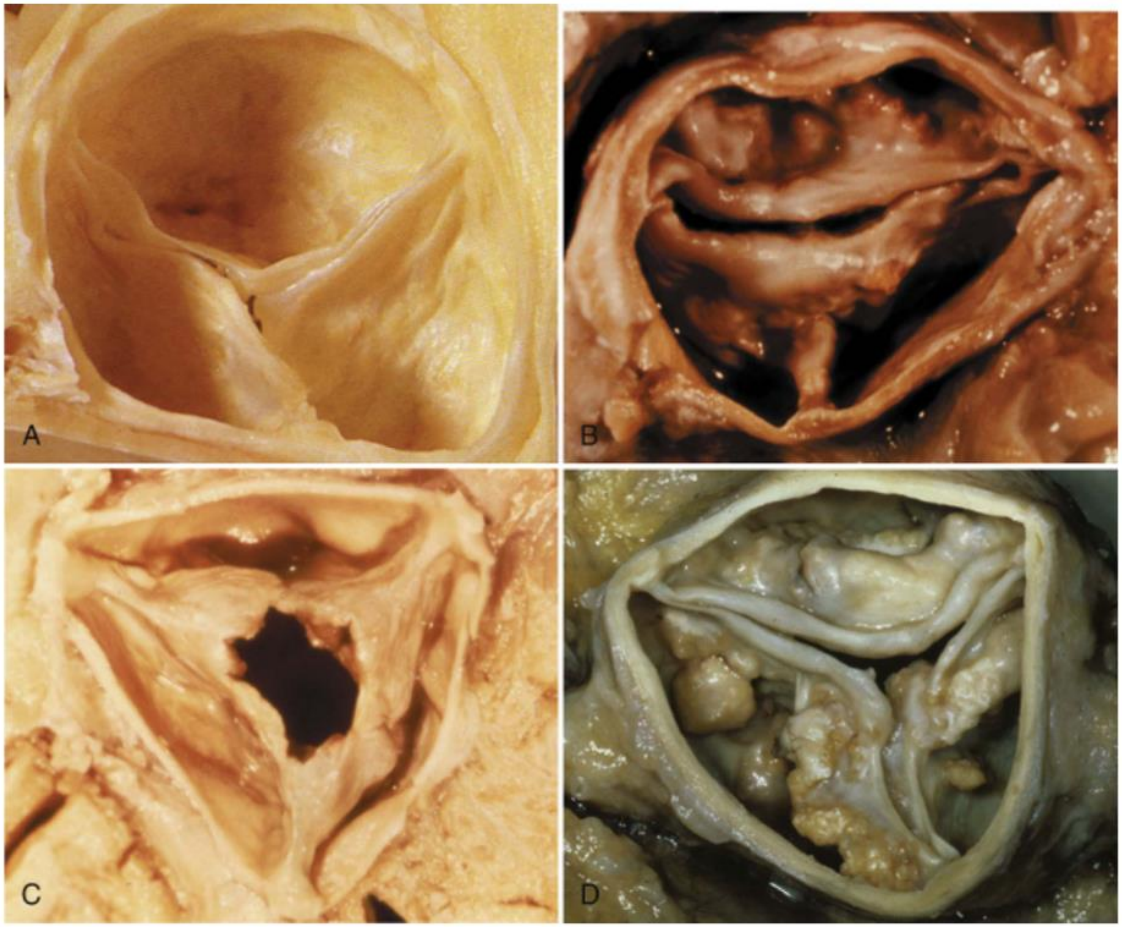
- None

Learning Objectives

- Understand the current role of transcatheter therapies in the management of valvular disease
- Appropriately utilize antithrombotic therapies in patients with valvular heart disease
- Identify appropriate utilization of antibiotic prophylaxis in the prevention of infectious endocarditis

Aortic Stenosis Etiology

Normal



Bicuspid

Rheumatic

Fibrocalcific

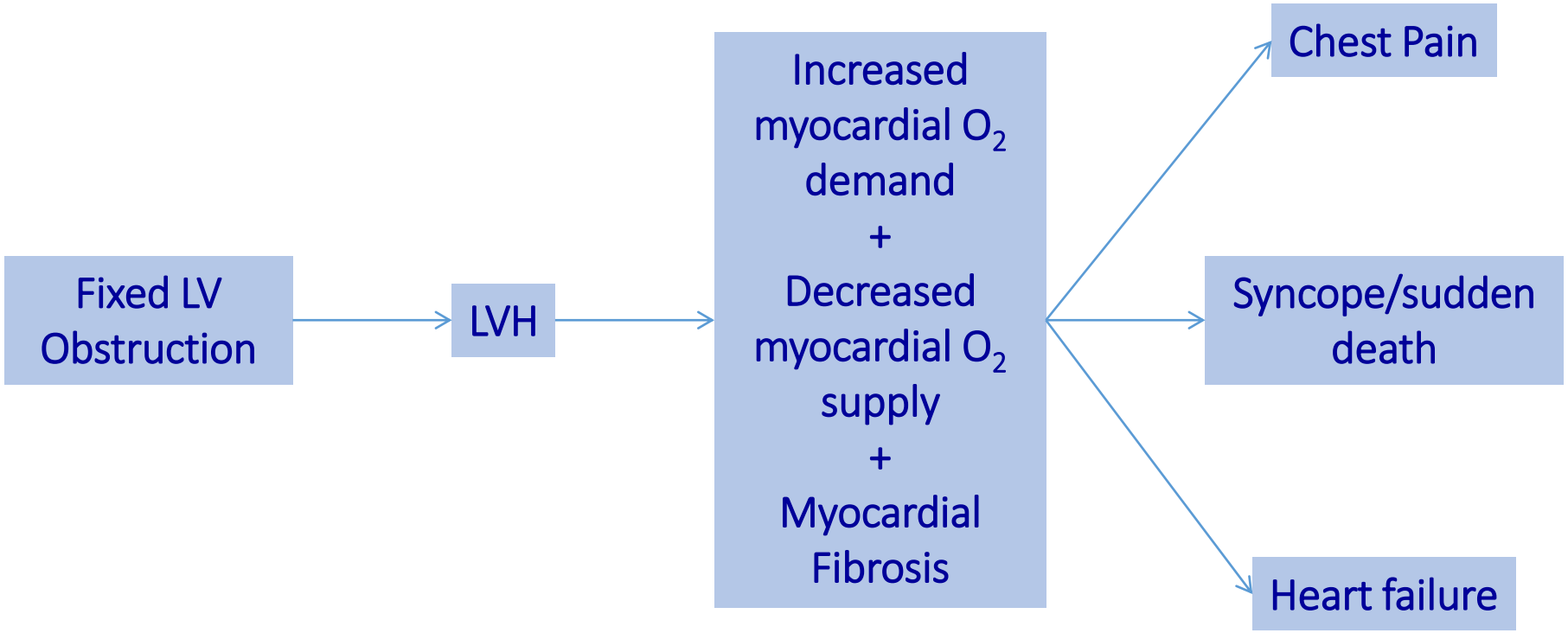
Otto and Bonow. Braunwald's Heart Disease.

Aortic Stenosis Etiology

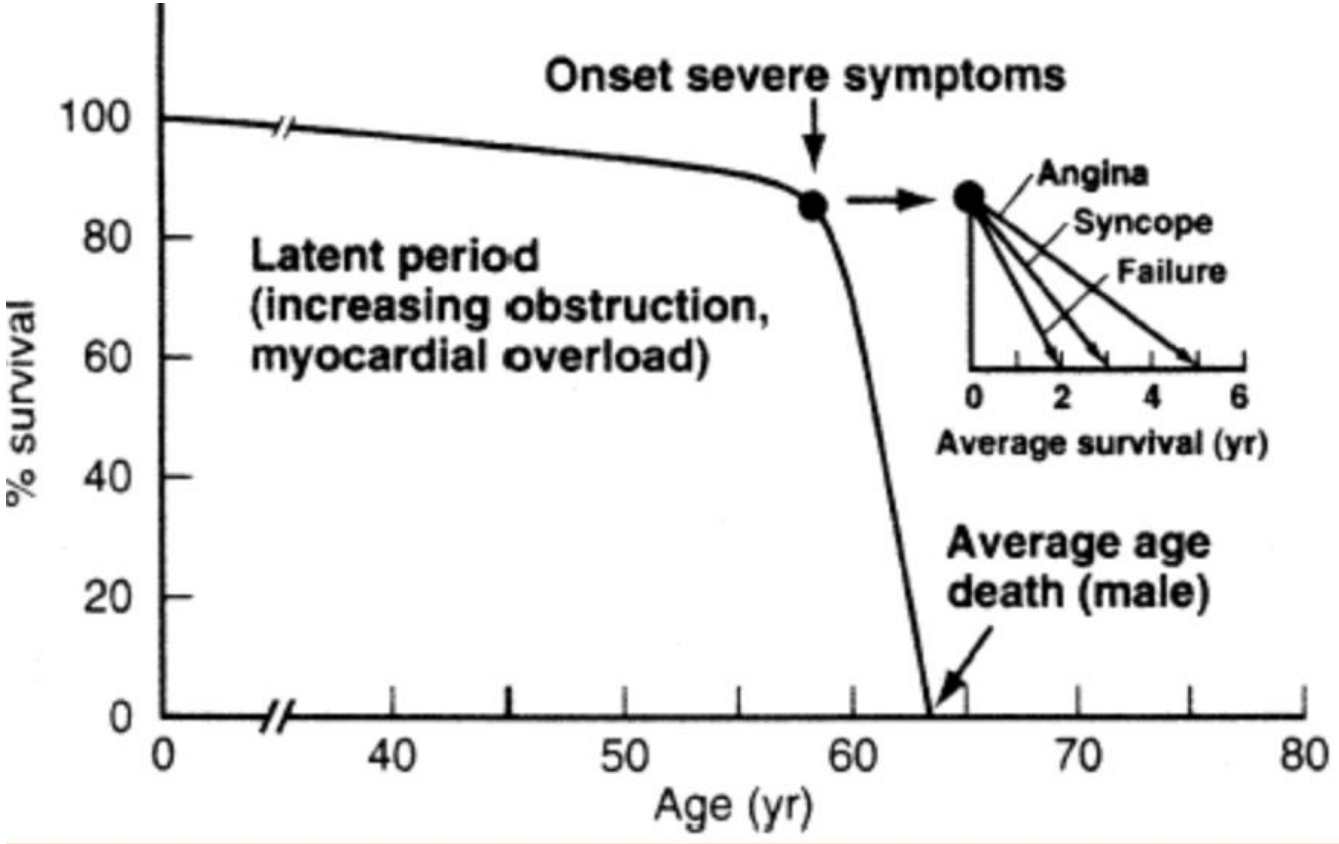
- Age predictive of etiology
  - < 50, nearly all have bicuspid (or unicuspid)
  - 50-70: 2/3 with bicuspid
  - >70: 60% with fibrocalcific AS
- Onset of AS ~10 years earlier in bicuspid v tricuspid AV
- Premature tricuspid AS mainly seen in calcium disorders (ESRD, hyperparathyroidism), inflammatory disorder, elevated LP(a)

Otto and Bonow. Braunwald's Heart Disease.

Pathophysiology of Aortic Stenosis



Prognosis of AS



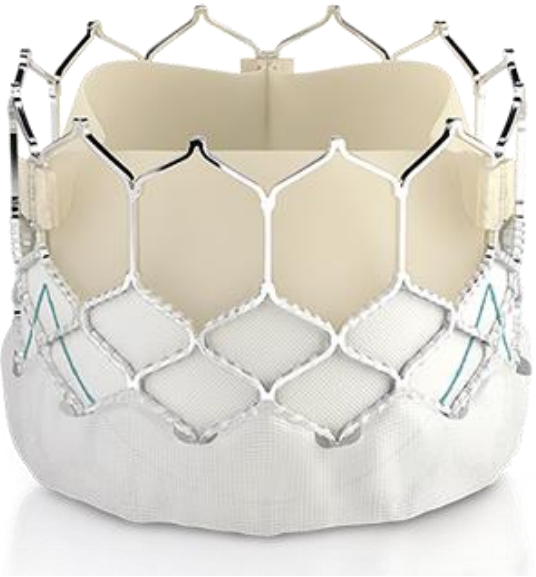
Ross and Braunwald. Circulation 1968.

Indications for AVR

- Symptomatic severe AS: angina, heart failure or dyspnea attributable to aortic stenosis
- Asymptomatic severe AS AND:
  - Abnormal LV function
  - Abnormal ETT (poor functional capacity, hypotensive BP response)
  - Very severe (peak velocity > 5 m/s) AND low surgical risk
- Moderate or worse AS undergoing other cardiac surgery

Baumgartner et al. EHJ 2018.
Otto et al. JACC 2021.

TAVI/TAVR



TAVI – Procedural Basics

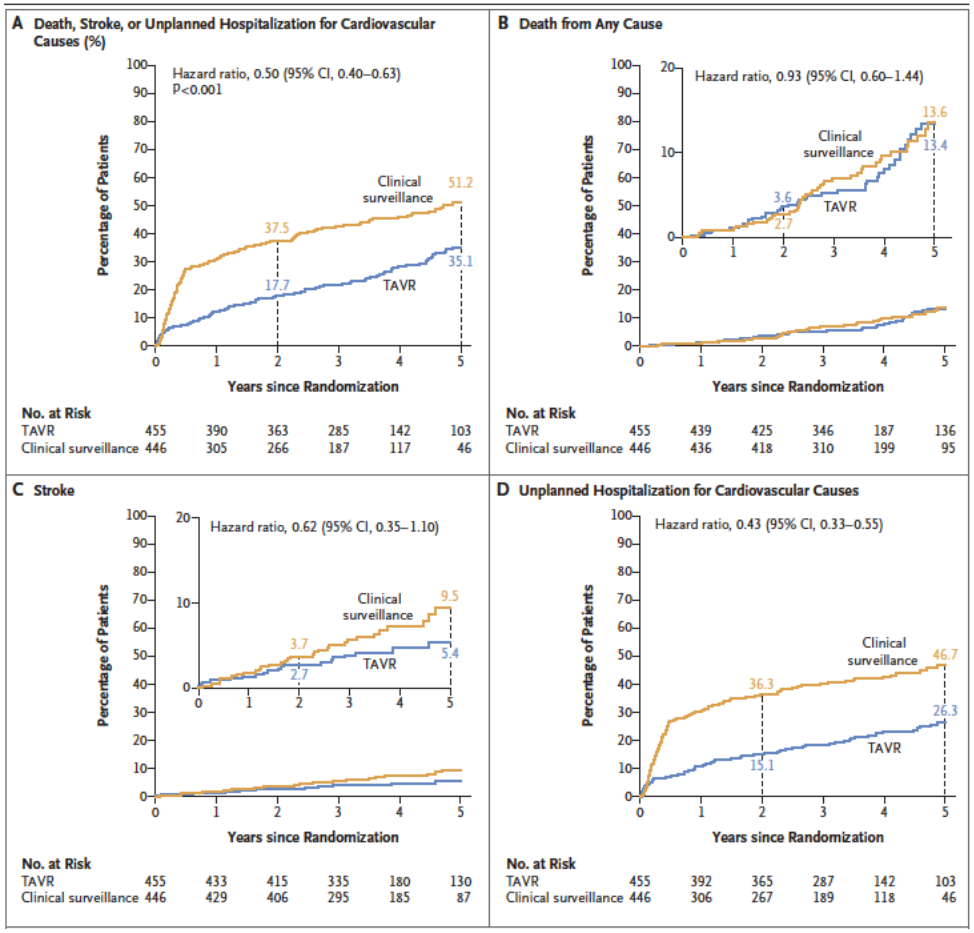
- FDA approved across all surgical risk groups
- Transfemoral access preferable, alternative access (trans-carotid, transcaval)
- Mainly done under conscious sedation, ambulating within hours after procedure
- Majority discharged next day, moving towards same day discharge

TAVR for Asymptomatic Severe AS

- EARLY TAVR Trial
- Inclusion: Asymptomatic aortic stenosis (confirmed with normal stress testing with severe AS (peak velocity > 4 m/s or mean gradient > 40 AND AVA < 1 cm2)
- ~900 patients randomized to active surveillance versus TAVR
- Primary endpoint: combination of death, stroke or unplanned hospitalization for cardiovascular cause

Genereaux et al. NEJM 2024.

TAVR Reduced Primary Outcome



but driven all by need for unplanned hospitalization…

Genereaux et al. NEJM 2024.

TAVR for Asymptomatic AS - Takehomes

- 87% of patients of active surveillance required TAVR within 3 years
- Benefit driven by prevention of urgent hospitalization for TAVR
- Asymptomatic TAVR is reasonable if patient interested in just getting done but not clear that we are preventing something bad by doing upfront TAVR
- In contrast to SAVR in low surgical risk → clear mortality benefit!

Genereaux et al. NEJM 2024.

TAVI versus SAVR

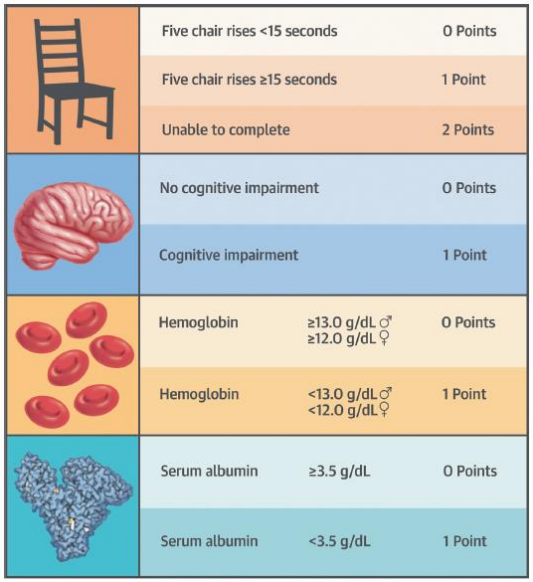
- Lower up-front procedural risk
- Stroke risk similar (2-4%)
- Higher risk for pacemaker (7-10%)
- Comparable short and medium (5 years) outcomes, longer-term durability unknown

TAVI is NOT for everyone!

- Poor vascular access
- Concomitant coronary or valvular disease
- Anatomic considerations
  - Risk of coronary obstruction
  - Risk of paravalvular leak (bicuspid?)
  - Risk of annular rupture (bicuspid?)
- Very young patient and concerns on long-term durability

Beware of TAVR/TAVI in Frail Patients!

- TAVR/TAVI only if > 1+ year life expectancy
- Frailty associated with poor outcomes with TAVR/TAVI



Five chair rises <15 seconds		0 Points
Five chair rises ≥15 seconds		1 Point
Unable to complete		2 Points
No cognitive impairment		0 Points
Cognitive impairment		1 Point
Hemoglobin	≥13.0 g/dL ♂ ≥12.0 g/dL ♀	0 Points
Hemoglobin	<13.0 g/dL ♂ <12.0 g/dL ♀	1 Point
Serum albumin	≥3.5 g/dL	0 Points
Serum albumin	<3.5 g/dL	1 Point

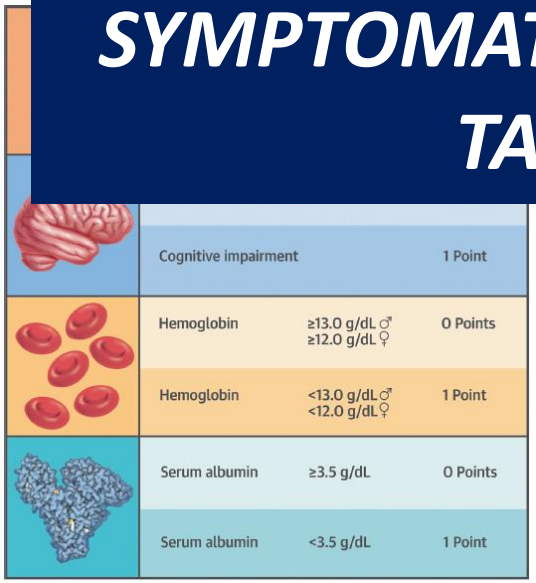
EFT Score	1-Year Mortality TAVR	SAVR
0-1	6%	3%
2	15%	7%
3	28%	16%
4	30%	38%
5	65%	50%

Afilalo et al. JACC 2017.

Beware of TAVR/TAVI in Frail Patients!

- TAVR/TAVI only if > 1+ year life expectancy
- Frailty associated with poor outcomes with TAVR/

NOT ALL PATIENTS WITH SEVERE SYMPTOMATIC AS SHOULD GET TAVI/TAVR!



Cognitive impairment		1 Point	
Hemoglobin	≥13.0 g/dL ♂ ≥12.0 g/dL ♀	0 Points	
Hemoglobin	<13.0 g/dL ♂ <12.0 g/dL ♀	1 Point	
Serum albumin	≥3.5 g/dL	0 Points	
Serum albumin	<3.5 g/dL	1 Point	

0-1	6%	3%
2	15%	7%
3	28%	16%
4	30%	38%
5	65%	50%

Afilalo et al. JACC 2017.

Post TAVI/TAVR Management Pearls

- Aspirin or clopidogrel monotherapy sufficient
- If already on DOAC/warfarin, no need for additional anti-platelet therapy
- Beware of post-procedure heart block
  - Timing unpredictable
  - Risk factors: pre-existing or new LBBB/RBBB, pre-procedural increase in PQ interval, anatomic features
- TTE at 1 month, 1 year and then annually – risk of subclinical leaflet thrombosis high ~ 15%

Question 1

A 70 year old man with a history of an On-X double tilting disc mechanical AVR for bicuspid aortic stenosis presents to your office to transition care after recently moving to the area. He has not yet established cardiovascular care. He feels great and has no symptoms. He is on warfarin but in his move, has stopped checking his INR and he was discharged from his prior anticoagulation clinic and instructed to establish care in his new locale. He has no history of stroke or embolic events. Transthoracic echocardiogram showed normal biventricular function and normal functioning AVR. What is the next best step in management of his mechanical AVR? He weighs 55 kg and his creatinine is 1.7.

A. Dose adjusted warfarin for INR goal 2.5-3.5 with aspirin
B. Dose adjusted warfarin for INR goal 2-3 without aspirin
C. Dose adjusted warfarin for INR goal 1.5-2 without aspirin
D. Apixaban 5 mg twice daily
E. Apixaban 2.5 mg twice daily

Question 1

A 70 year old man with a history of an On-X double tilting disc mechanical AVR for bicuspid aortic stenosis presents to your office to transition care after recently moving to the area. He has not yet established cardiovascular care. He feels great and has no symptoms. He is on warfarin but in his move, has stopped checking his INR and he was discharged from his prior anticoagulation clinic and instructed to establish care in his new locale. He has no history of stroke or embolic events. Transthoracic echocardiogram showed normal biventricular function and normal functioning AVR. What is the next best step in management of his mechanical AVR? He weighs 55 kg and his creatinine is 1.7.

A. Dose adjusted warfarin for INR goal 2.5-3.5 with aspirin

B. Dose adjusted warfarin for INR goal 2-3 without aspirin

C. Dose adjusted warfarin for INR goal 1.5-2 without aspirin

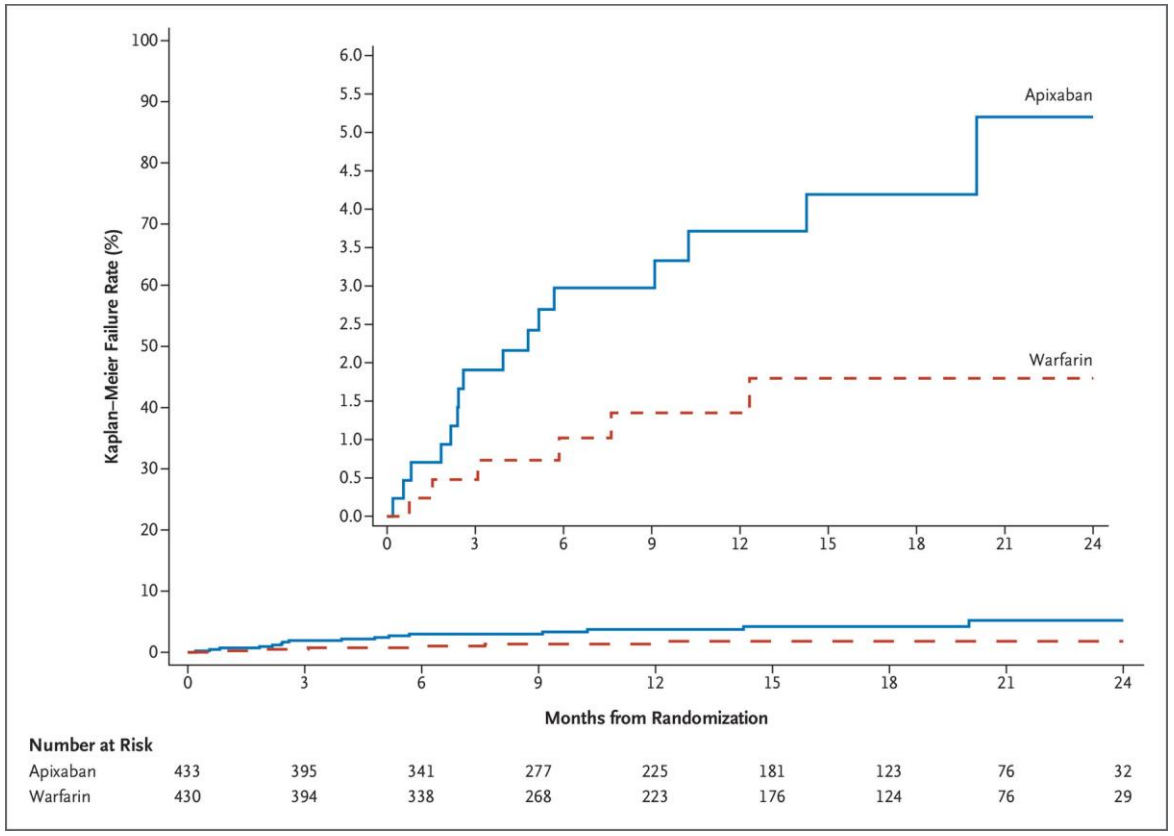
D. Apixaban 5 mg twice daily

E. Apixaban 2.5 mg twice daily

Prosthetic Valve Anticoagulation

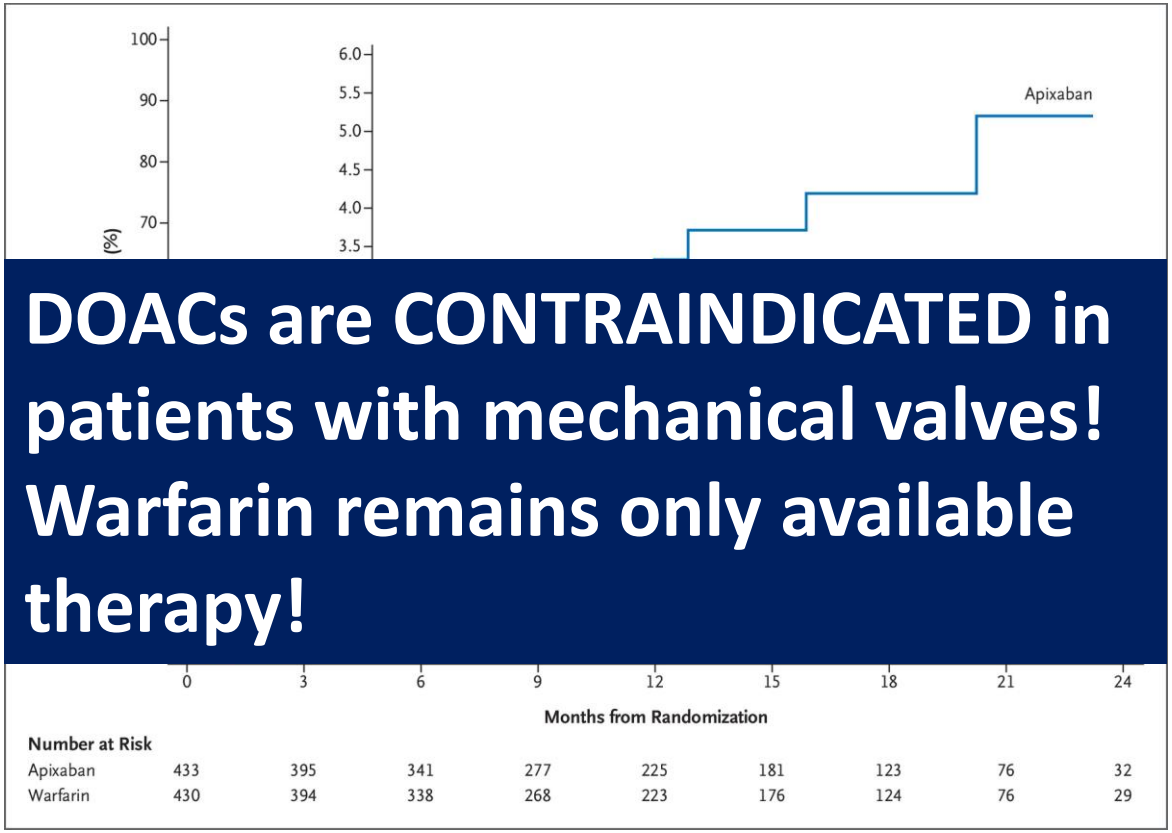
- Warfarin typically preferred first 3-6 months after bio AVR/MVR though DOACs often utilized
- DOACs appropriate in patients with SAVR/TAVI and alternative indication for anticoagulation, after first 3-6 months
- DOACs appropriate in patients with bioprosthetic MVR and alternative indication for anticoagulation after first 3-6 months UNLESS initial indication for bioprosthetic MVR was mitral stenosis → warfarin
- INR Goals:
  - Mechanical MVR: 2.5-3.5
  - Mechanical AVR: 2-3 UNLESS LV Dysfunction, AF and/or stroke → 2.5-3.5

Anticoagulation in Mechanical Valves



Wang et al. NEJM Evid. 2023.

Anticoagulation in Mechanical Valves



DOACs are CONTRAINDICATED in patients with mechanical valves! Warfarin remains only available therapy!

Wang et al. NEJM Evid. 2023.

What about Mitral Regurgitation?

Patient A

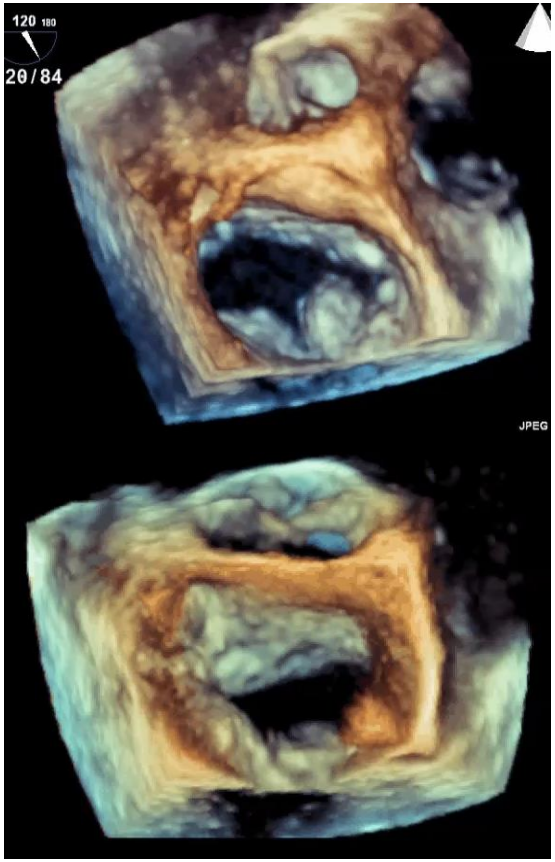
50F with history of MV prolapse has known severe MR. She is asymptomatic and runs 30 miles weekly. She is seen by cardiology and is referred for surgical mitral valve repair.

Patient B

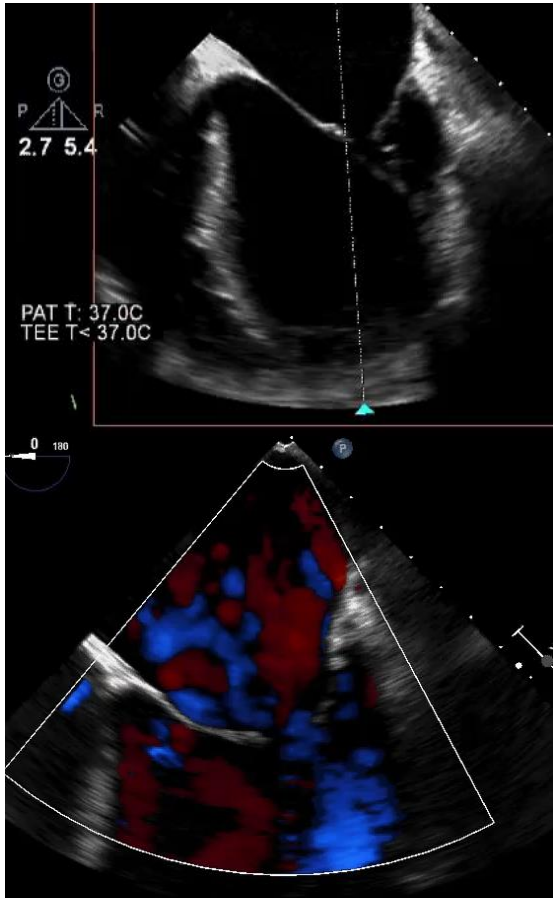
60M has a history of RCA STEMI with mild LV dysfunction presents with heart failure. He is markedly hypertensive on evaluation and is on metoprolol only. After diuresis, he is found to have severe MR. Medical therapy is recommended and MV intervention is deferred.

Why the difference in management?

Etiology of MR is Key!



Primary – Valve Problem!



Secondary – Ventricular/Atrial Problem!

Etiology of MR is Key!

Primary MR
Flail/Prolapse
Rheumatic
Calcific
Endocarditis

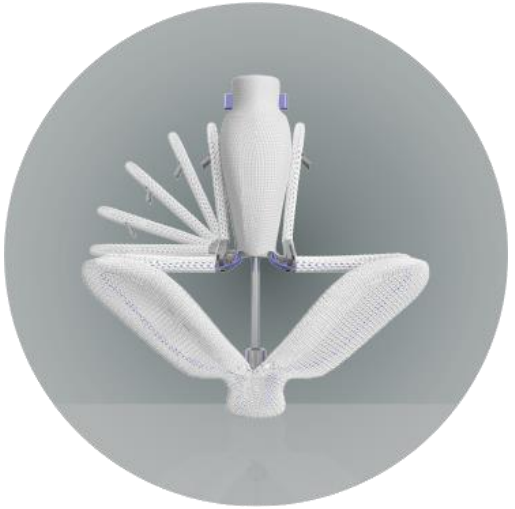
→ ***Fix the Valve First!***

Secondary MR
Severe LV dysfunction
Long-standing AFib

→ ***Treat the LV/AF first, then consider the valve!***

Transcatheter Edge-to-Edge Repair (TEER)

- Femoral venous access
- Access LA via transseptal puncture
- Requires GA, 2-4 hours
- Majority discharged next day
- Very safe procedure (risks MUCH lower than TAVI)
- TEE guided – no contrast required



Primary MR

- Surgery remains only FDA approved therapy for low or moderate surgical risk patients with severe primary MR
- TEER can be considered if high or prohibitive surgical risk
- Equipoise has not been demonstrated between TEER and surgery
- TEER probably less efficacious than surgery for primary MR

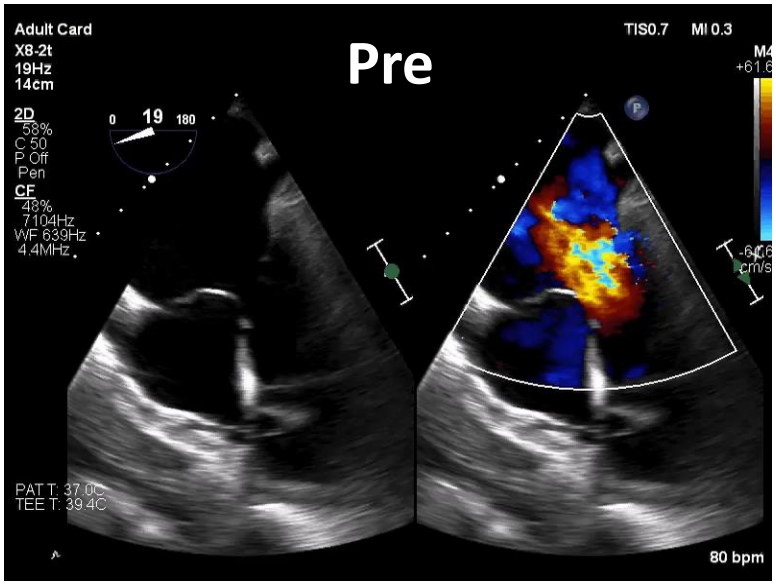
Baumgartner et al. EHJ 2018.
Otto et al. JACC 2021.

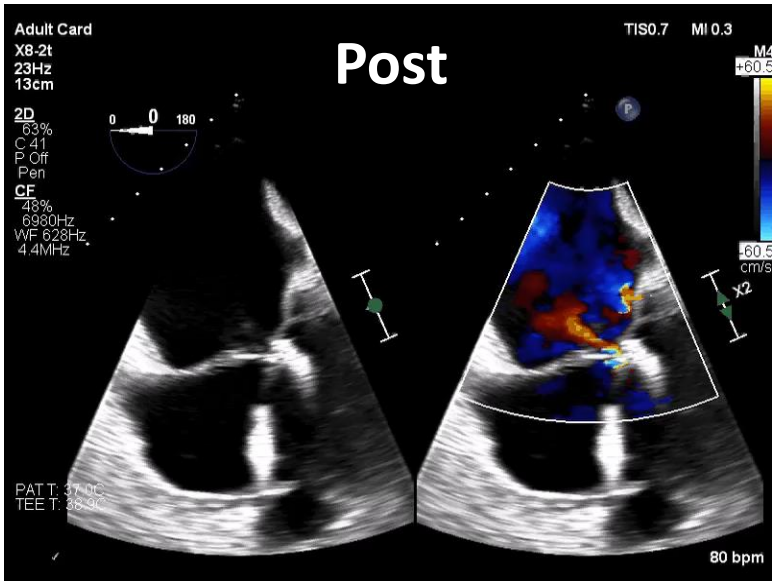
Secondary MR – consider TEER

- COAPT:
  - HFrEF on GDMT
  - Randomized TEER v medical therapy
  - TEER associated with 50% mortality reduction!
- TEER FDA approved for treatment in patients with HFrEF who are optimally medically managed
- ONLY consider if optimally medically managed – we require evaluation by HF specialist!

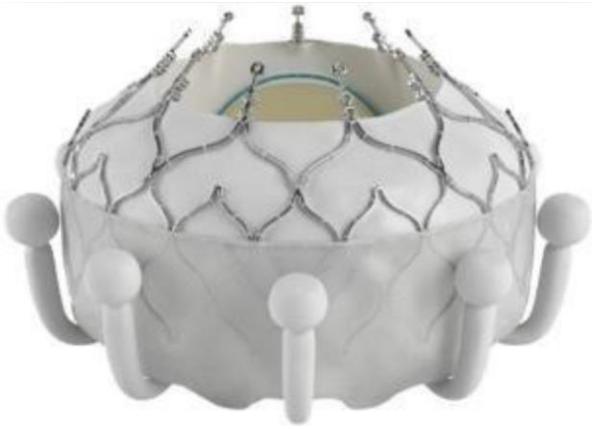
Baumgartner et al. EHJ 2018.
Otto et al. JACC 2021.

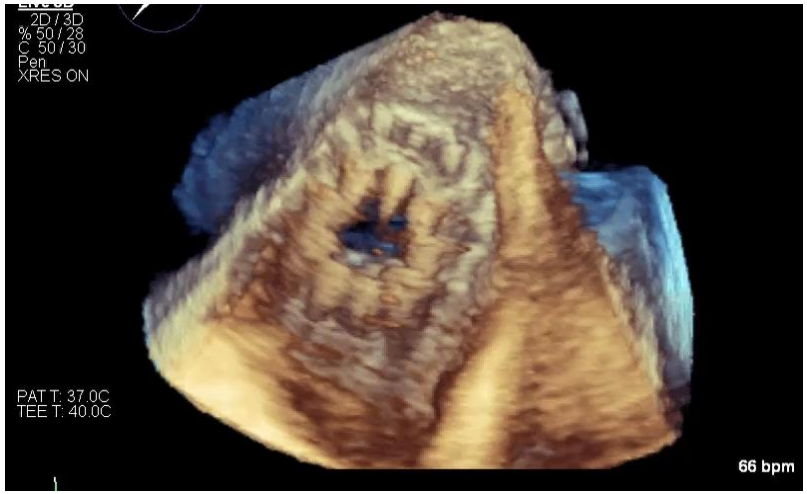
Transcatheter Therapies for TR

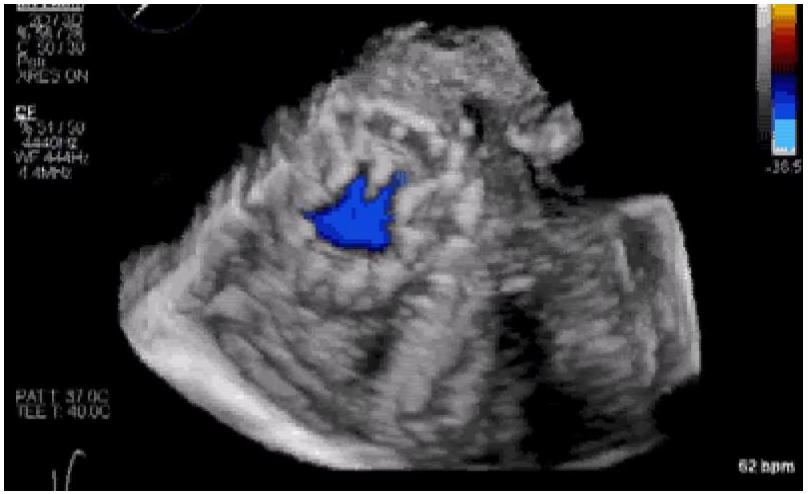




Transcatheter Therapies for TR







Transcatheter Therapies for TR

- tTEER and TTVR FDA approved
- Both associated with symptomatic improvement but NOT hard endpoints (mortality, HF hospitalization)
- tTEER probably safer than TTVR
- TTVR probably more effective (both with TR reduction and symptomatic improvement)
- Both require GA and are TEE-guided but device selection complex

Question 2

A 60-year-old woman with a history of severe mitral regurgitation status post mitral valve repair 15 years ago calls your office with regards to an upcoming deep dental cleaning. She is feeling great and has recently moved to the area and has yet to establish cardiovascular care. She asks about the need for antibiotic prophylaxis prior to her dental visit. She has a documented hive allergy to penicillin and ceftriaxone. Which of the following is the best recommendation?

A. No indication for antibiotic prophylaxis as there is no prosthetic material
B. Clindamycin 600 mg 30-60 minutes prior to the dental visit
C. Azithromycin 500 mg 30-60 minutes prior to the dental visit
D. Cephalexin 2 g 30-60 minutes prior to the dental visit

Question 2

A 60 year old woman with a history of severe mitral regurgitation status post mitral valve repair 15 years ago calls your office with regards to an upcoming deep dental cleaning. She is feeling great and has recently moved to the area and has yet to establish cardiovascular care. She asks about the need for antibiotic prophylaxis prior to her dental visit. She has a documented hive allergy to penicillin and ceftriaxone. Which of the following is the best recommendation?

A. No indication for antibiotic prophylaxis as there is no prosthetic material

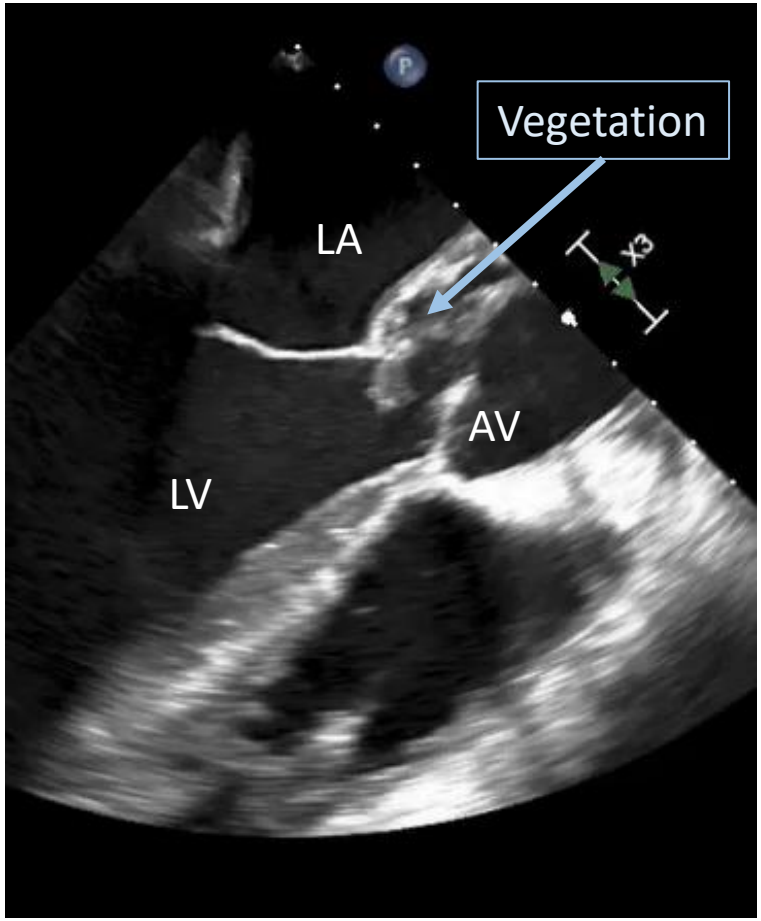
B. Clindamycin 600 mg 30-60 minutes prior to the dental visit

C. Azithromycin 500 mg 30-60 minutes prior to the dental visit

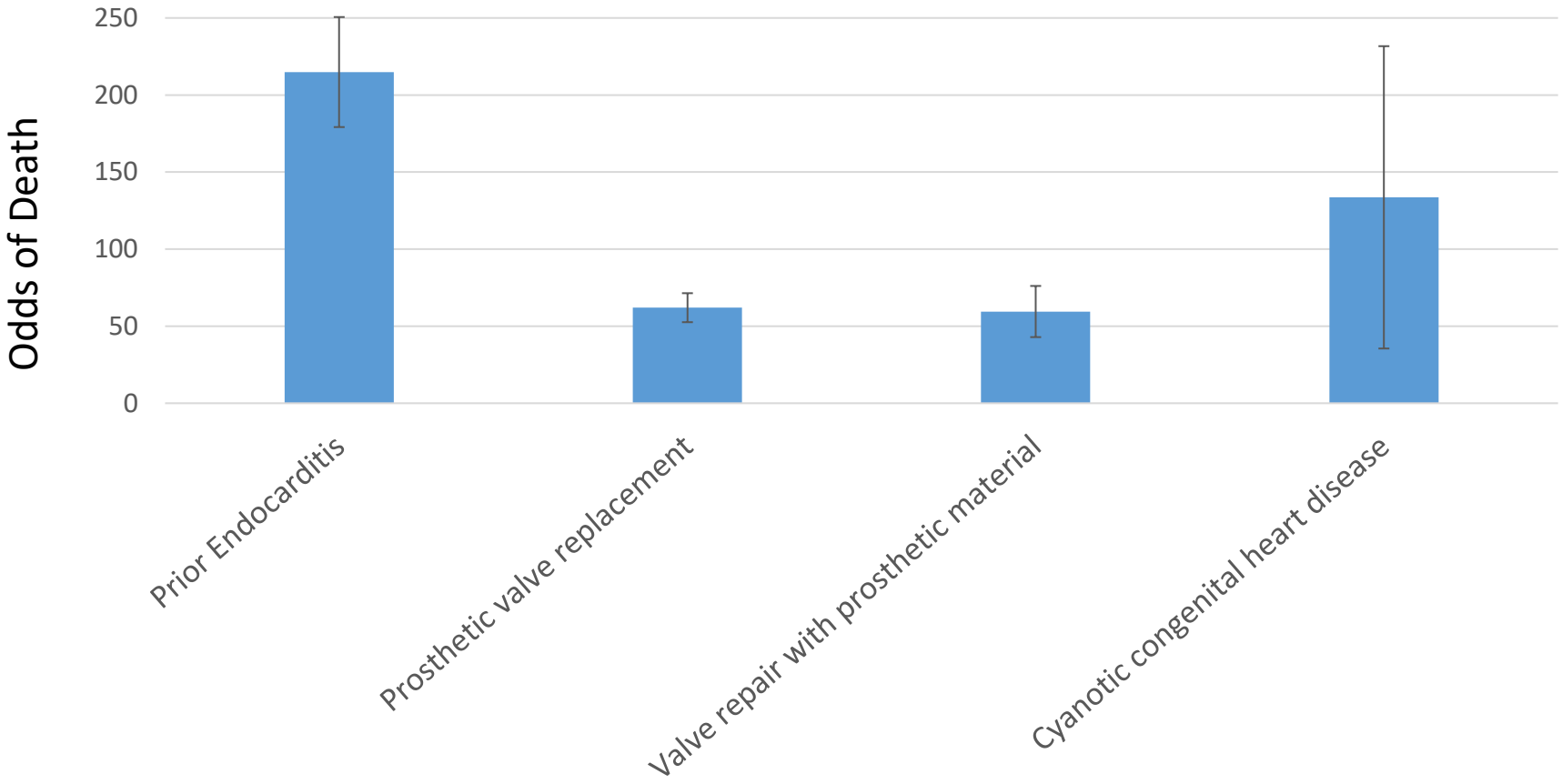
D. Cephalexin 2 g 30-60 minutes prior to the dental visit

Endocarditis – why the oral focus?

- Relatively rare – 1.5-11.6 cases per 100000 person-years
- Despite advances in therapy, in-hospital mortality ~ 20%
- Oral flora accounts for 30% of causes (Strep and enterococcus)

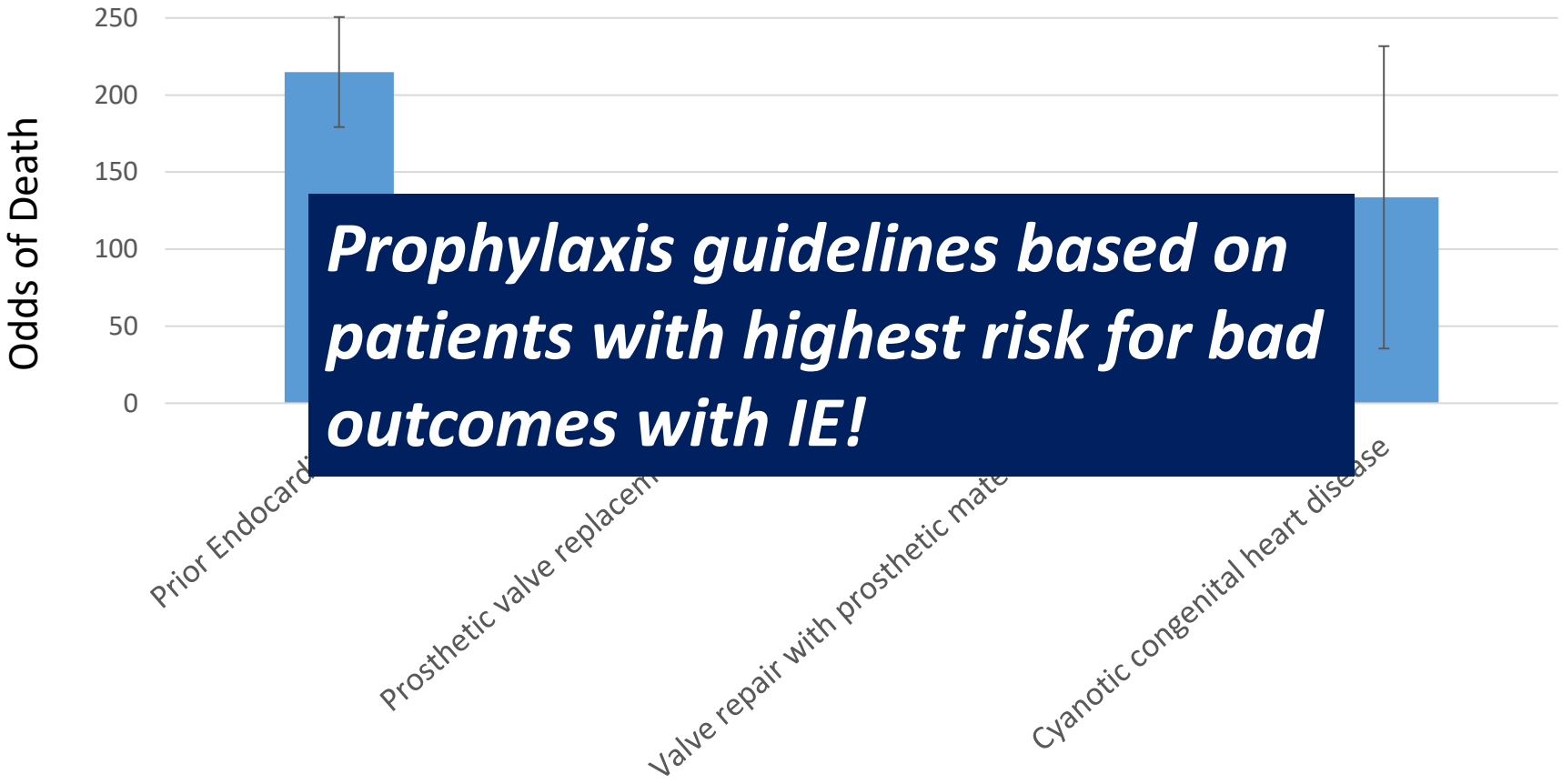


High-Risk Conditions



Adapted from Thornhill et al. EHJ 2018.

High-Risk Conditions

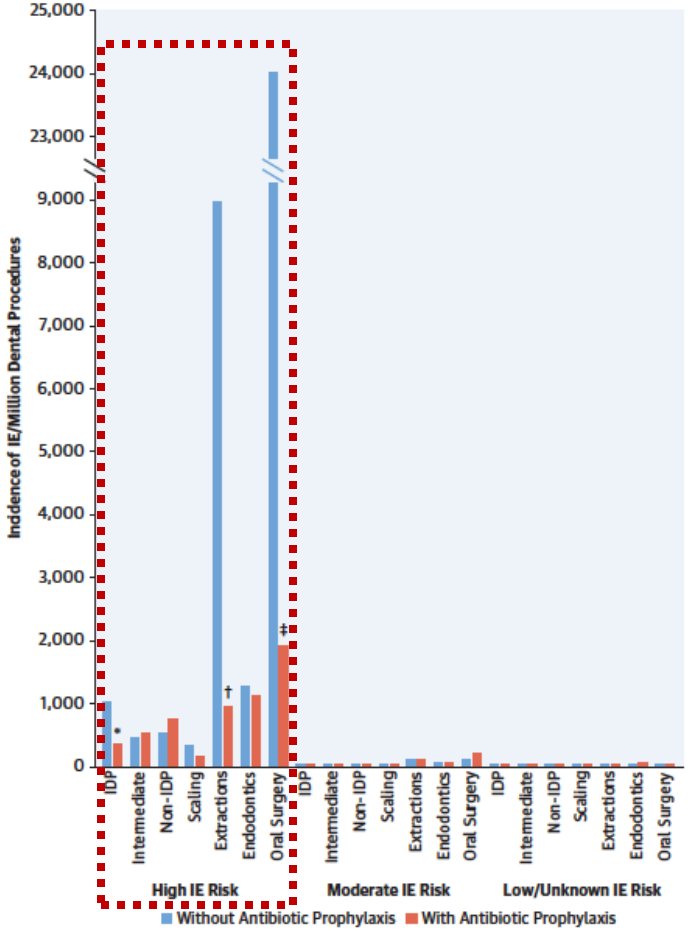


Prophylaxis guidelines based on patients with highest risk for bad outcomes with IE!

Adapted from Thornhill et al. EHJ 2018.

Antibiotic Prophylaxis Associated with Reduction in Risk of IE

- Case cross-over design, patient compared to self (3800 patients)
- Abx prophylaxis associated with 50% reduction in IE in high-risk group
- Only 30% of high-risk patients received Abx!



Thornhill et al. JACC 2022.

Guidelines for ABX Prophylaxis

History of IE
Prosthetic cardiac valve or prosthetic material for valve repair
Congenital heart disease • Unrepaired cyanotic congenital heart disease • Completely repaired congenital heart defects with prosthetic material/device w/in 6 months of correction • Repaired defects with residual defects
Cardiac transplantation patients with valvulopathy

Wilson et al. Circulation 2021.

Who does NOT require ABX prophylaxis?

Moderate Risk Patients
Mitral valve prolapse
Bicuspid aortic valve disease
Rheumatic heart disease
Hypertrophic cardiomyopathy
Implantable cardiac devices
Coronary stents

Wilson et al. Circulation 2021.

Recommended prophylaxis regimens

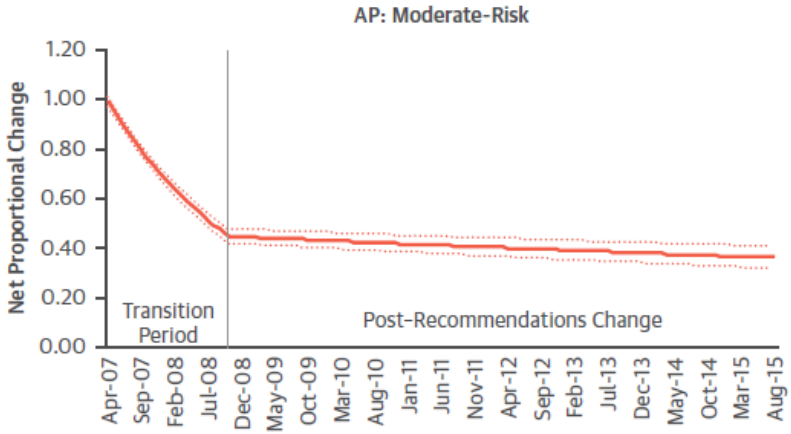
1st line	Amoxicillin 2 g
Penicillin-allergic	Cephalexin 2 g
	Azithromycin 500 mg
	Clarithromycin 500 mg
	Doxycycline 100 mg
IV or IM	Ampicillin (2 g), Cefazolin (1 g), Ceftriaxone (1 g)

Clindamycin NO LONGER recommended

Should be taken 30-60 minutes before procedure

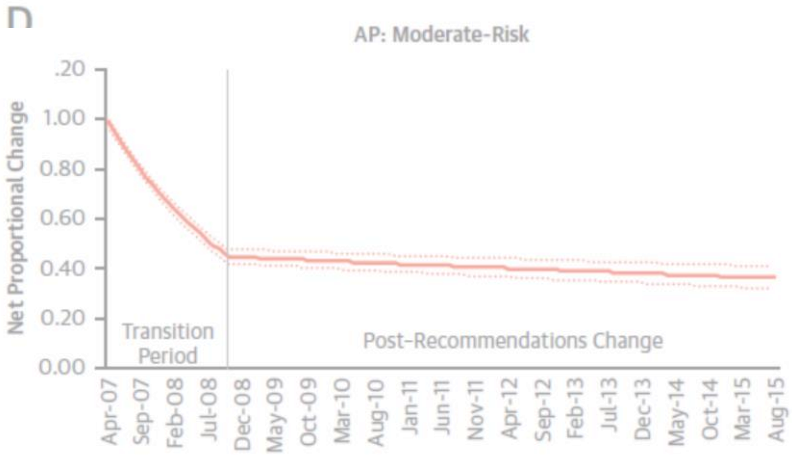
Wilson et al. Circulation 2021.

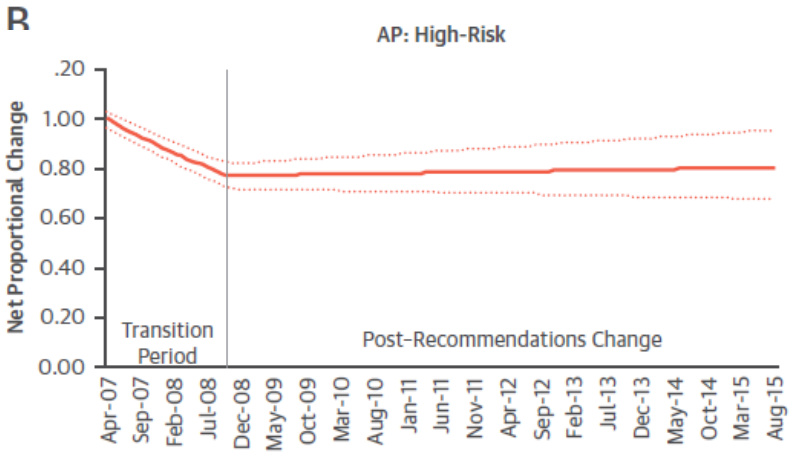
Trends in ABX Prophylaxis



Thornhill et al. JACC 2018.

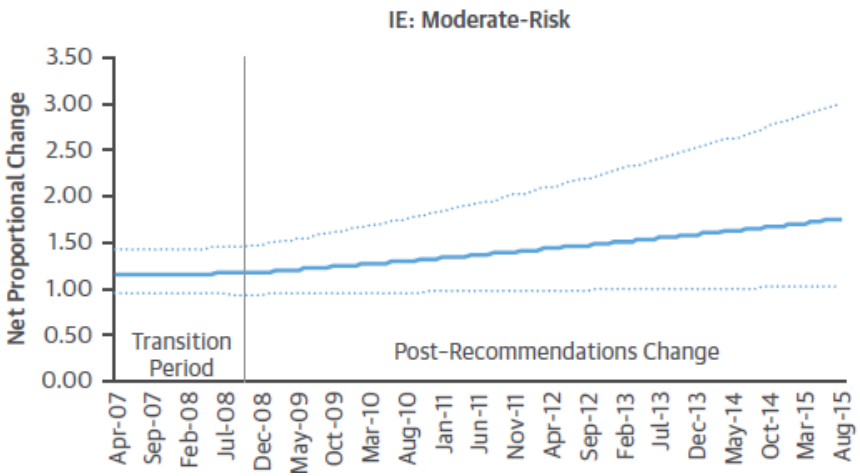
Trends in ABX Prophylaxis

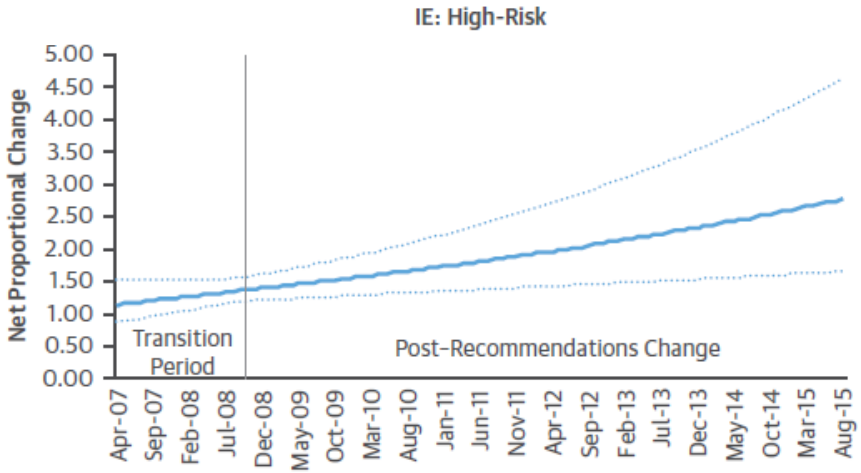




Thornhill et al. JACC 2018.

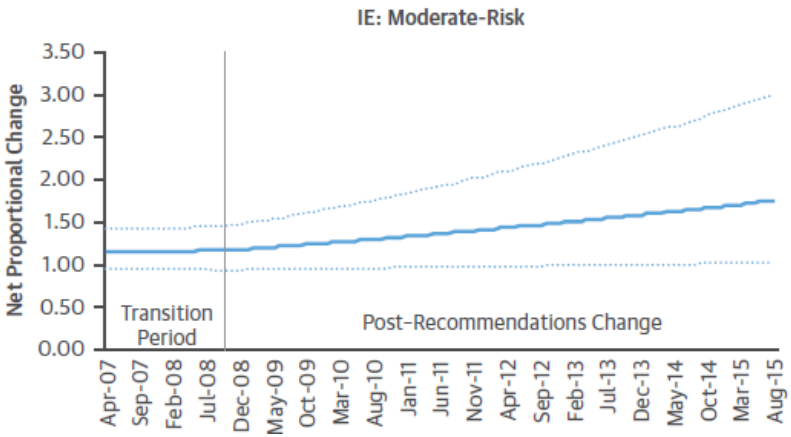
Trends in ABX Prophylaxis

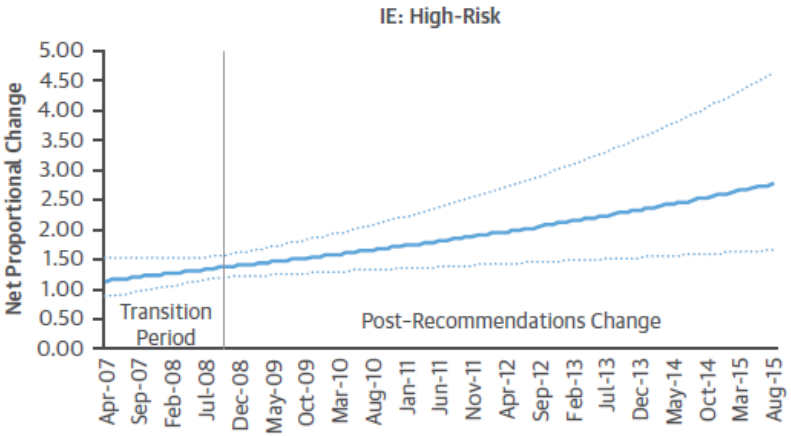




Thornhill et al. JACC 2018.

Trends in ABX Prophylaxis





Increase in IE ***may*** be related to a decrease in prophylaxis in high risk groups!
Ensure that high risk patients receive prophylaxis!

Thornhill et al. JACC 2018.

Take-Home Points

- TAVI is a reasonable options for patients with severe symptomatic aortic stenosis across all risk spectrums **THOUGH** there remain some patients for whom the risks outweigh the benefits
- Secondary MR will improve for the majority of patients with aggressive medical therapy that may obviate the need for TEER, however in those with persistent severe severe secondary MR ***despite*** maximal medical therapy, TEER can be considered
- Transcatheter intervention can be considered for high-risk patients with symptomatic severe secondary TR ***despite*** maximal medical therapy
- DOACs can be used in patients with bioprosthetic valves after the initial 3-6 month post-op period UNLESS the primary indication was mitral stenosis, in whom warfarin is preferred
- Antibiotic prophylaxis is indicated ***only*** in patients with high-risk conditions
- Amoxicillin and cephalexin remain 1st/2nd line therapy for IE prophylaxis, but azithromycin is next option

References

Baumgartner H et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J 2017; 38: 273-2791

Otto C et al. 2020 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease. J Am Coll Cardiol. 2021; 77(4):e25-e197.

Thornhill M. et al. *Quantifying infective endocarditis risk in patients with predisposing cardiac conditions. Eur Heart J 2017; 39: 586-595.*

Thornhill M et al. Antibiotic Prophylaxis and Incidence of Endocarditis Before and After the 2007 AHA Recommendations. J Am Coll Cardiol. 2018; 72(20): 2443 – 2454.

Thornhill M et al. Antibiotic Prophylaxis Against Infective Endocarditis Before Invasive Dental Procedures. J Am Coll Cardiol. 2022; 80(11):1029-1041.

Wang TY et al. Apixaban or Warfarin in Patients with an On-X Mechanical Aortic Valve. N Engl J Med Evid 2023;2(7).

Wilson WR et al. Prevention of Viridans Group Streptococcal Infective Endocarditis: A Scientific Statement From the American Heart Association. Circulation. 2021; 143:e963-E978.