



From Throat Ache to Heartache A Tale of Rheumatic Fever Through Time and Across Continents

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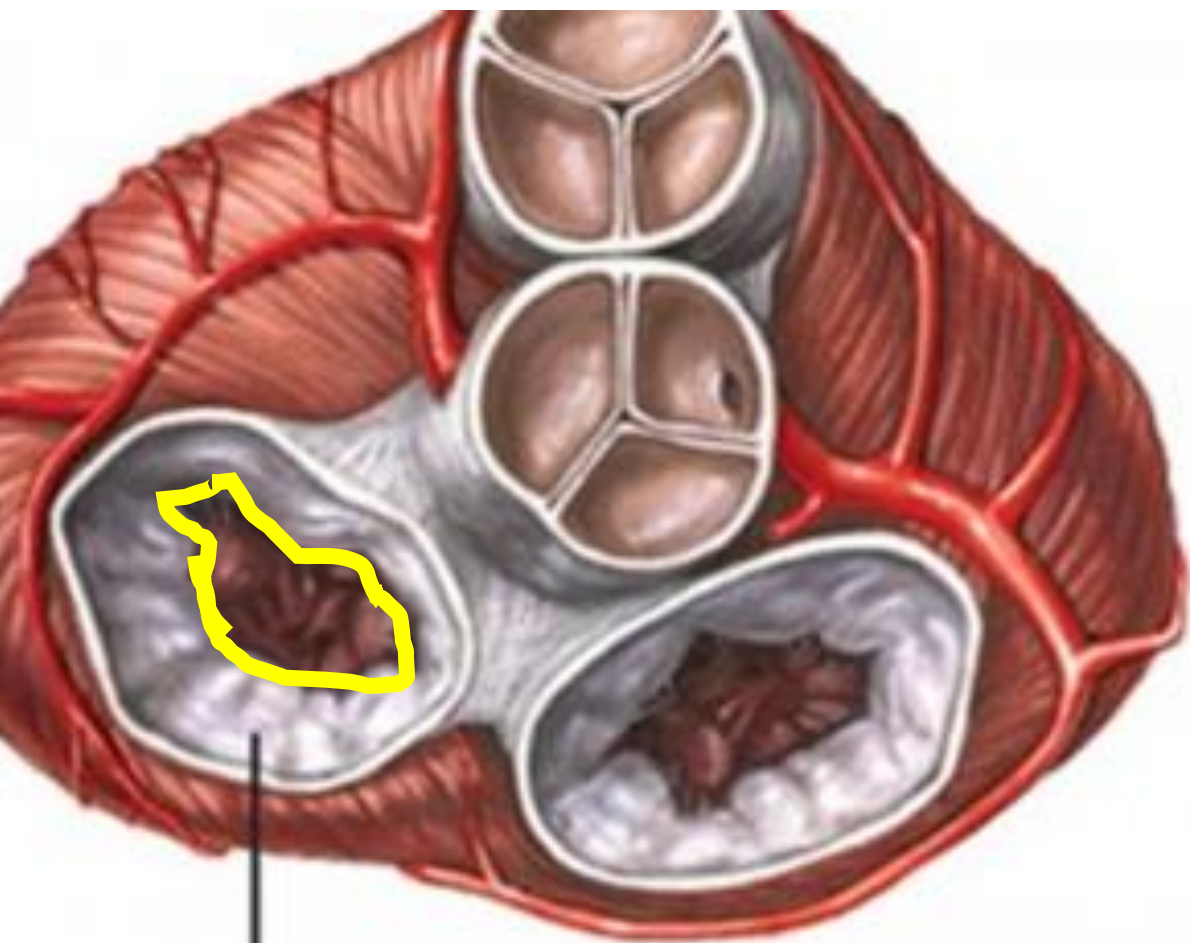


A Real Story (“Case History”)

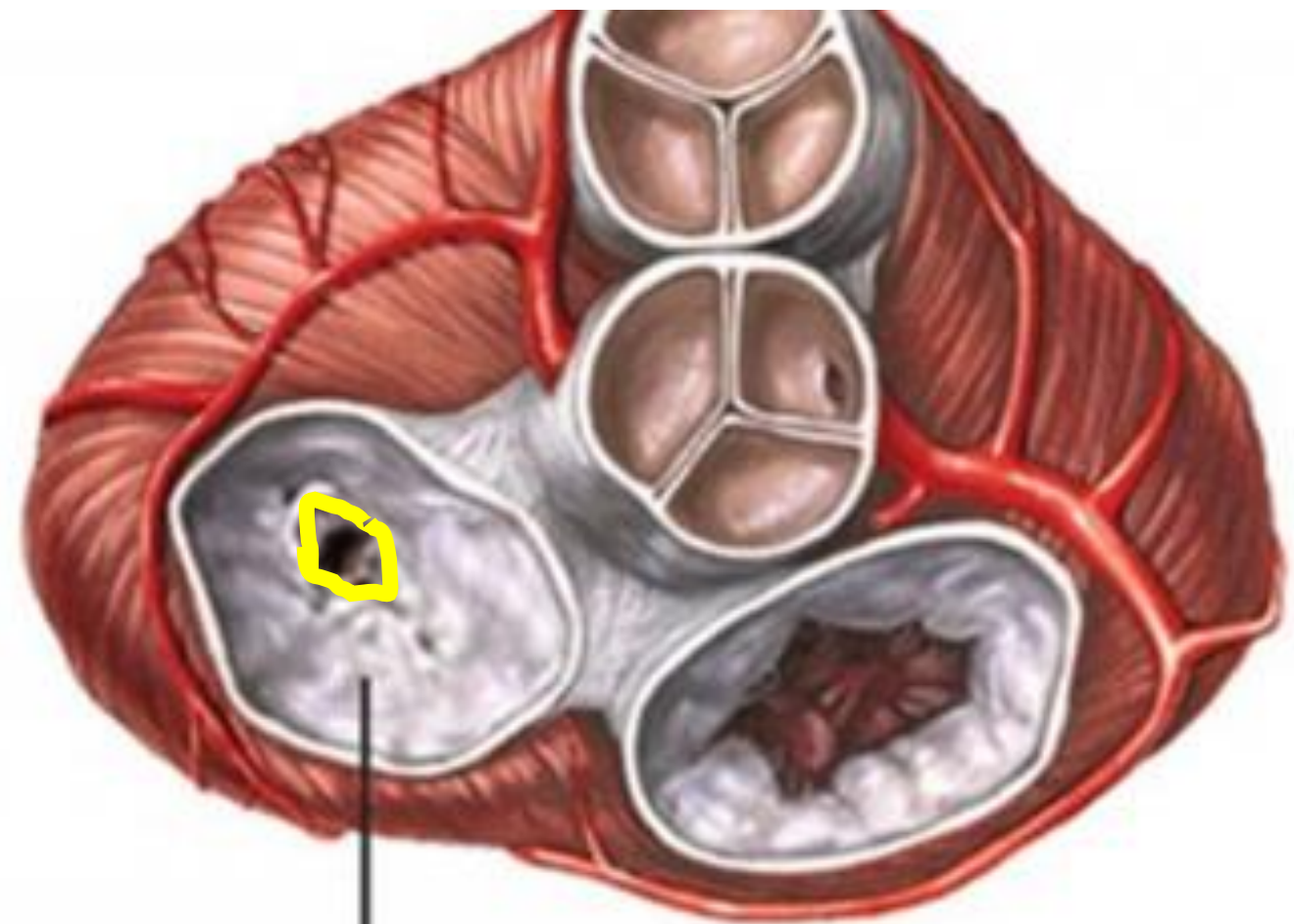
- A 36 year old woman, originally from India, presents during pregnancy because she is severely short of breath. She is evaluated and is found to have a scarred and narrowed heart valve (“mitral”).
- The reason that she is so short of breath is that the narrowed mitral heart valve prevents blood in the lungs from exiting properly; additionally, her circulation has expanded to provide blood to both mother and fetus as is typical in pregnancy.
- The medical question is how to deal with this problem so that she can continue her pregnancy and we end up with a healthy mother and healthy baby after delivery.

Plan for This Afternoon's Talk

- Review the relationship between a bacterial infection of the pharynx (“strep throat”) and subsequent heart damage
- Outline how the incidence and prevalence of the disease differs around the world and how (and why) it has changed over time
- Discuss the treatment options for damaged heart valves, and how the entire problem can be (but often isn't) prevented
- Present our research findings that now form the foundation for treatment of this condition
- Along the way, touch on various cultural and socioeconomic issues that we encountered in our numerous trips to south-central India



Normal mitral valve



Rheumatic mitral valve (with stenosis)



Where a Sore Throat Becomes a Death Sentence

Once a year, doctors travel to Rwanda to perform lifesaving surgery on people with damaged heart valves — a disease caused by untreated strep throat.

By [Denise Grady](#) Sept. 16, 2018

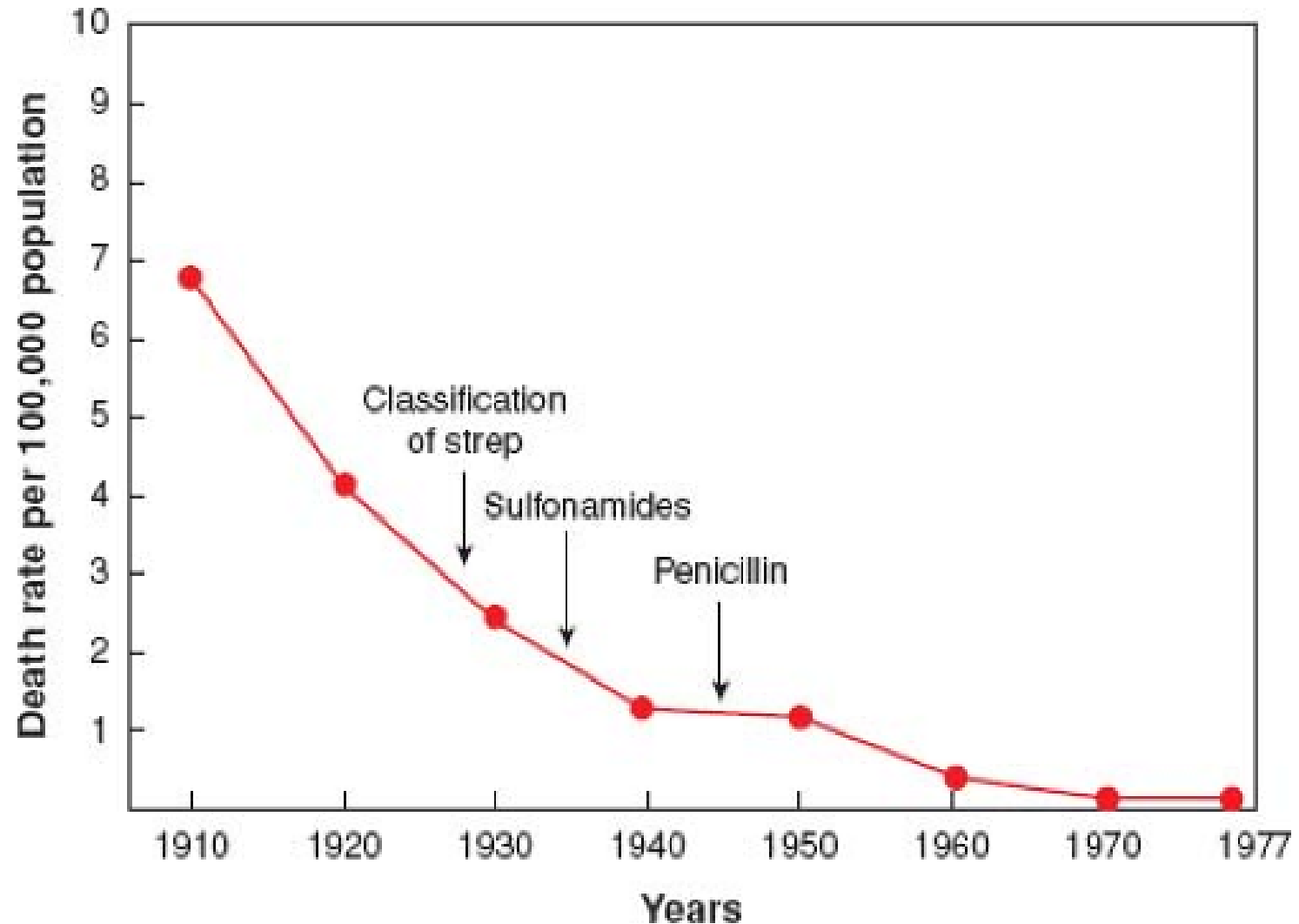
Changing Prevalence of Rheumatic Heart Disease (Mitral Stenosis)



Comparative Incidence of Rheumatic Heart Disease in Various Countries

Delhi (1951-55)	Mexico ⁴⁵ (1942)	Philippines ³⁷ (1953)	New England ⁴⁴ (1928)	New England ⁴ (1951)
2360	2400	4304
39.1%	41.0%	47.1%	39.5%	23.5%

Changing Impact of Rheumatic Disease



Source: Gordis L. The virtual disappearance of rheumatic fever in the United States: lessons in the rise and fall of disease. T. Duckett Jones memorial lecture. *Circulation*. 1985;72:1155–1162

What Accounts for the Changing Prevalence of Rheumatic Heart Disease?

- Prevalence of rheumatic fever started to decline **before** the introduction of antibiotics
 - Less crowding
 - Improved living conditions
 - Improved socio-economic status
- These improvements, along with antibiotics for strep sore throat, have largely (not completely) eliminated rheumatic fever in developed countries

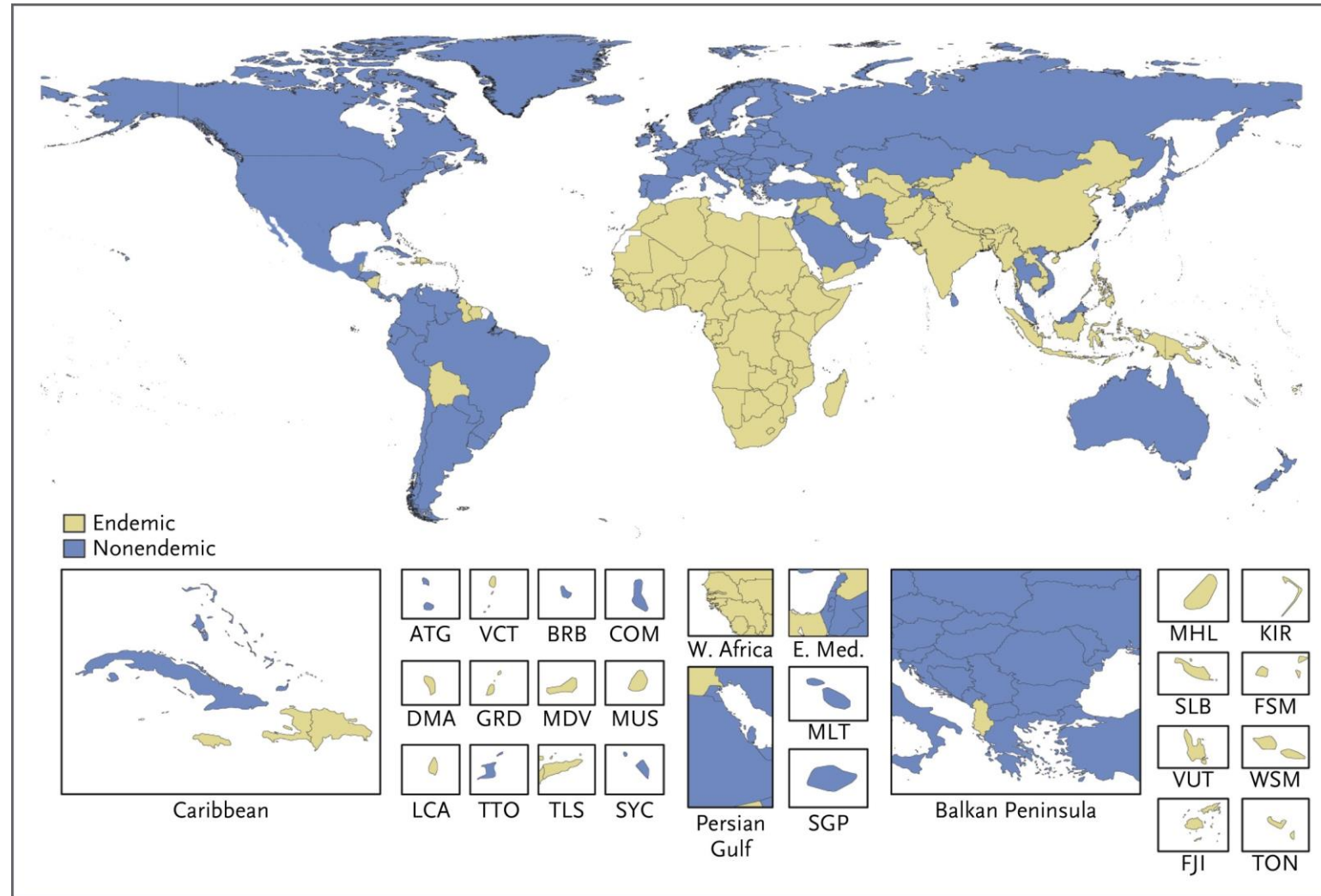
Burden of Rheumatic Heart Disease

- Remains common (even endemic) in many developing countries around the world, especially those in sub-tropical locations
- In the US, rheumatic fever/rheumatic heart disease is having a re-appearance:
 - Immigration
 - Military barracks (young people clustered together)
 - Inner city

Worldwide Trends in Rheumatic Heart Disease from 1990 to 2015

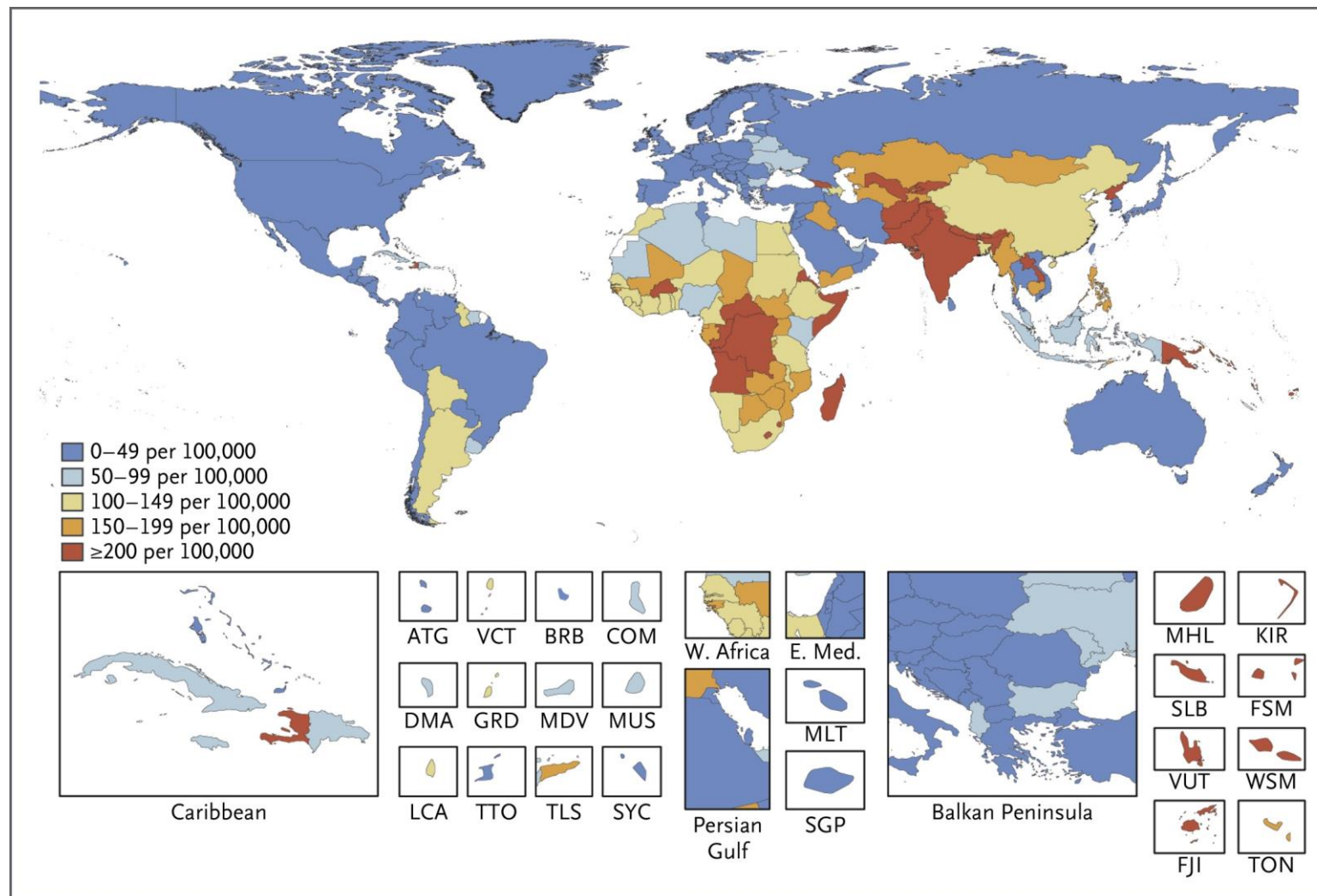
- This report estimated the global disease prevalence of and mortality due to rheumatic heart disease over a 25-year period (from 1990 until 2015).
- Mortality decreased by nearly 50%
- But still there were nearly 320,000 deaths worldwide in 2015
- There were over 30 million cases of rheumatic heart disease in 2015!
→ The health-related burden of rheumatic heart disease declined worldwide, but high rates of disease persist in some of the poorest regions in the world (like Oceania, South Asia, and central sub-Saharan Africa).

Classification of Countries as Having an Endemic or Nonendemic Pattern of Rheumatic Heart Disease



Source: Watkins DA et al: **Global, Regional, and National Burden of Rheumatic Heart Disease, 1990–2015**
 N Engl J Med 2017; 377:713-722. DOI: 10.1056/NEJMoa1603693

Age-Standardized Disability-Adjusted Life-Years Due to Rheumatic Heart Disease per 100,000 Population, 2015



Source: Watkins DA et al: **Global, Regional, and National Burden of Rheumatic Heart Disease, 1990–2015**
 N Engl J Med 2017; 377:713-722. DOI: 10.1056/NEJMoa1603693

Deaths and Research Funding for Various Infectious Diseases

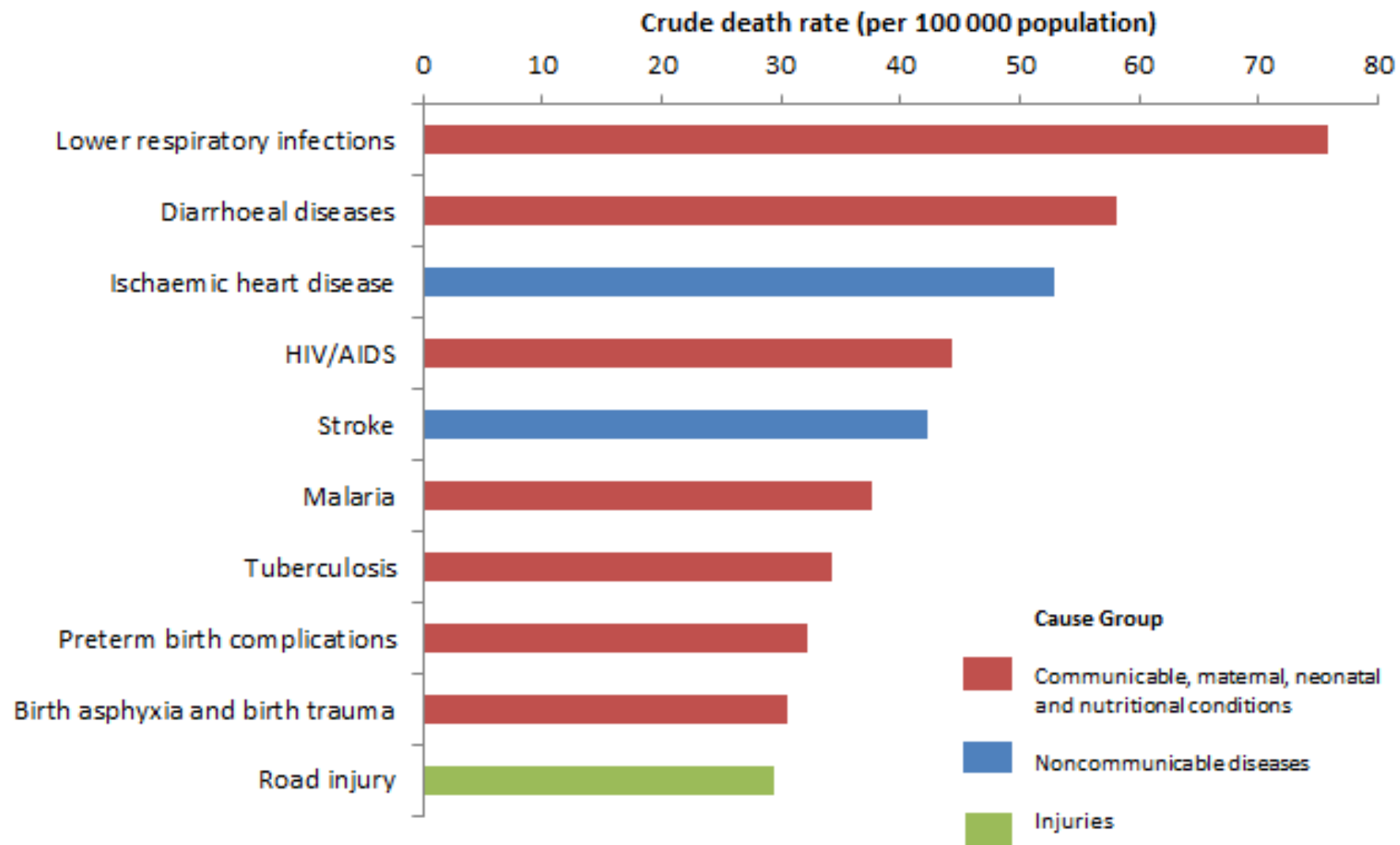
Table 1. Deaths from and Research and Development Funding for Rheumatic Fever and Other Global Infectious Diseases.

Disease	2013 Deaths*	2013 Funding in U.S. Dollars†
HIV–AIDS	1,341,000	1,091,000,000
Tuberculosis	1,290,300	559,000,000
Malaria	854,600	533,000,000
Rheumatic fever	275,100	900,000

* Data are from the GBD 2013 Mortality and Causes of Death Collaborators.⁶

† Data are from Chapman et al.⁷

Top 10 causes of deaths in low-income countries in 2016



Source: Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2016. Geneva, World Health Organization; 2018.
World Bank list of economies (June 2017). Washington, DC: The World Bank Group; 2017 (<https://datahelpdesk.worldbank.org/knowledgebase/articles/906319-world-bank-country-and-lending-groups>).

X8-2t
27Hz
8.0cm

3D Brats 1



3D Zoom
2D / 3D
% 51 / 51
C 50 / 30
Gen



M4



PAT T: 37.0C
TEE T: 39.0C

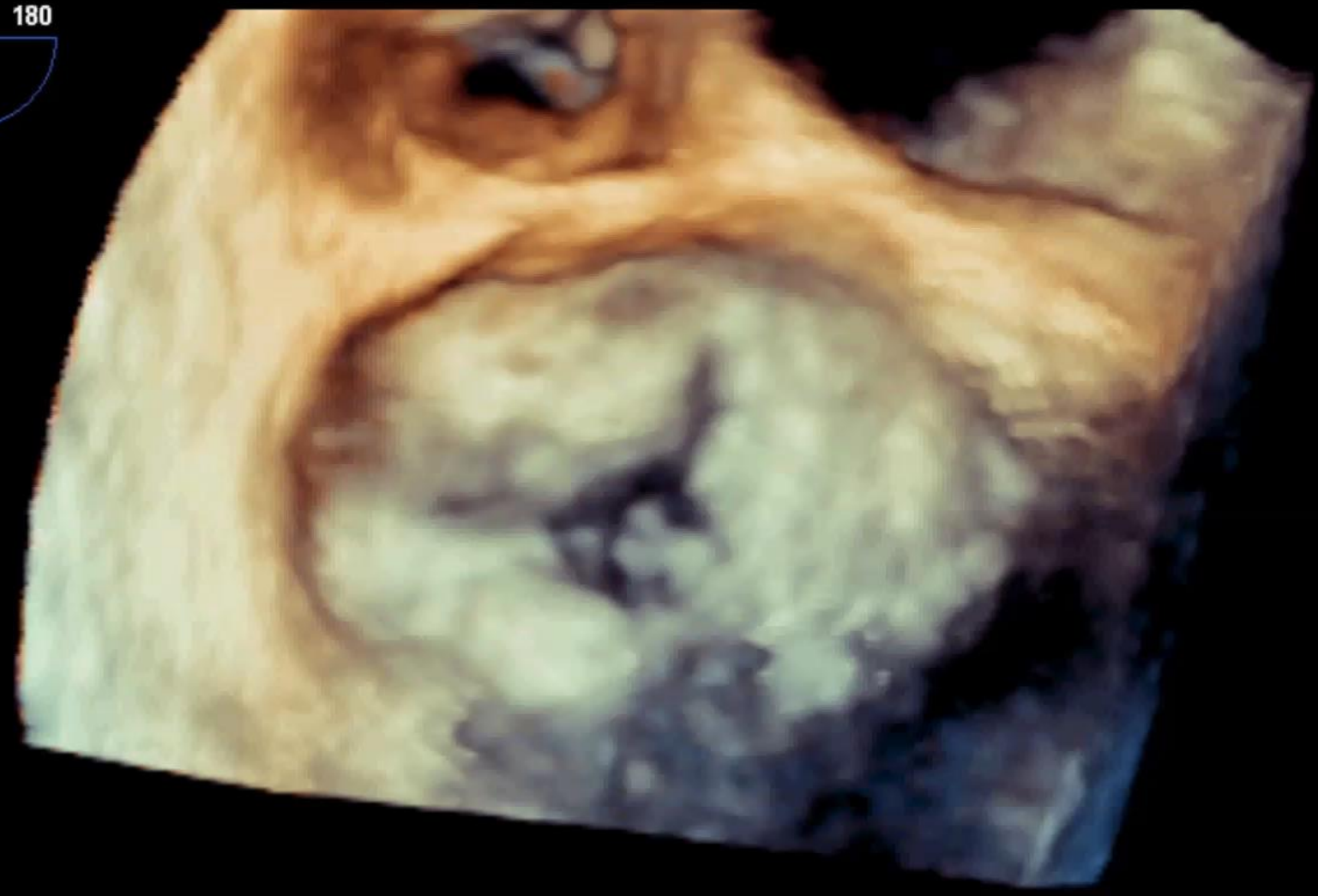
71 bpm

X8.2L
19Hz
7.6cm

3D Zoom
2D / 3D
% 40 / 50
C 50 / 30
HGen



M4



PAT T: 37.0C
TEE T: 40.1C



105 bpm

X8-2t
27Hz
8.0cm

3D Brats 1



3D Zoom
2D / 3D
% 51 / 51
C 50 / 30
Gen



M4



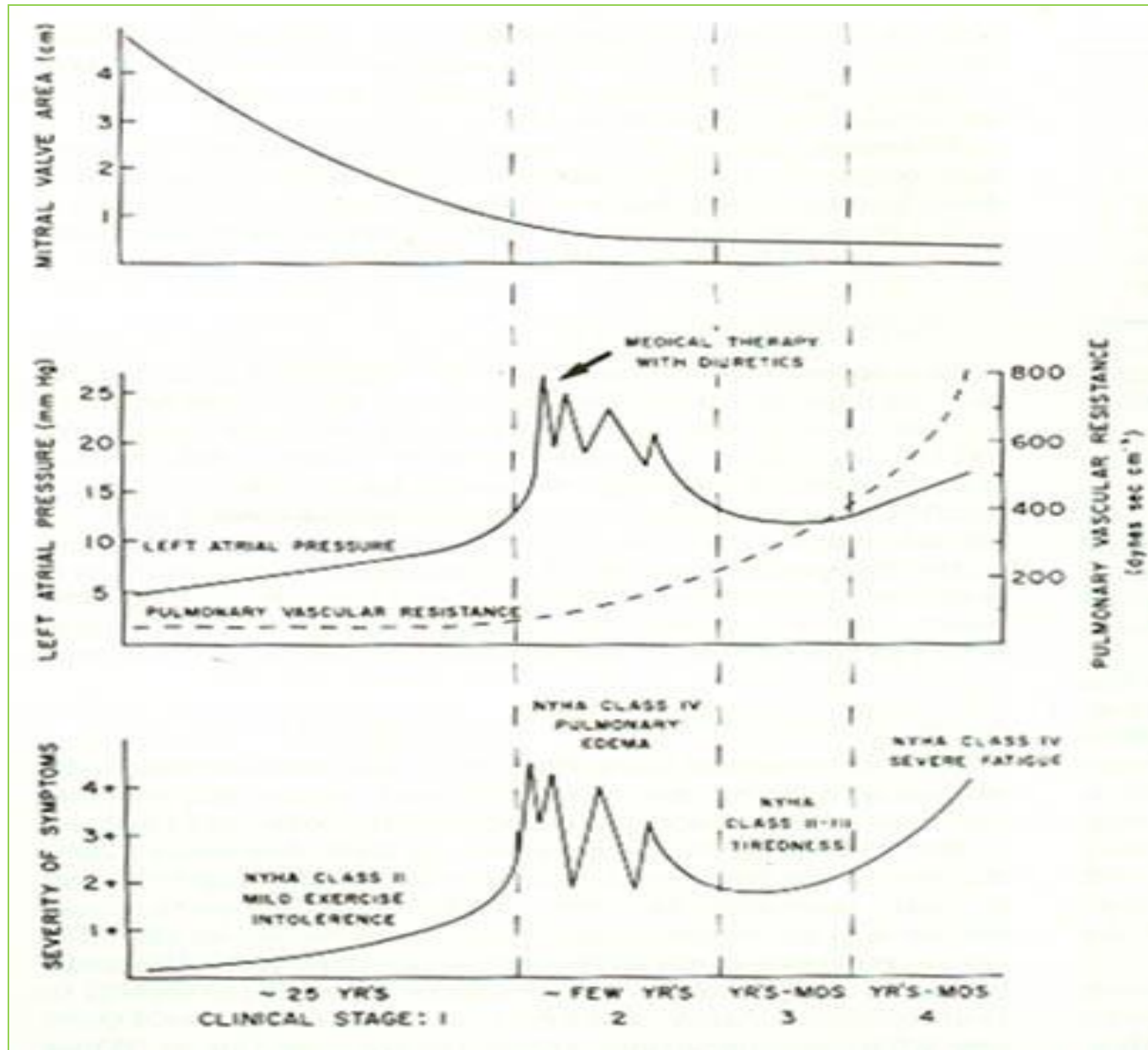
PAT T: 37.0C
TEE T: 39.0C

71 bpm

Progression of Valve Narrowing (Mitral Stenosis)

- Rate of progression of valve disease is slow and variable
- Related to recurrent episodes of acute rheumatic fever
 - Can be retarded or prevented by *continuous and ongoing* antibiotic suppression
- There typically is a several decade lag (~ 25 years) between the first episode of acute rheumatic fever and subsequent valve damage
- Like our case, a patient often first presents with symptomatic valve damage in their 30s or 40s

Natural History of Mitral Stenosis

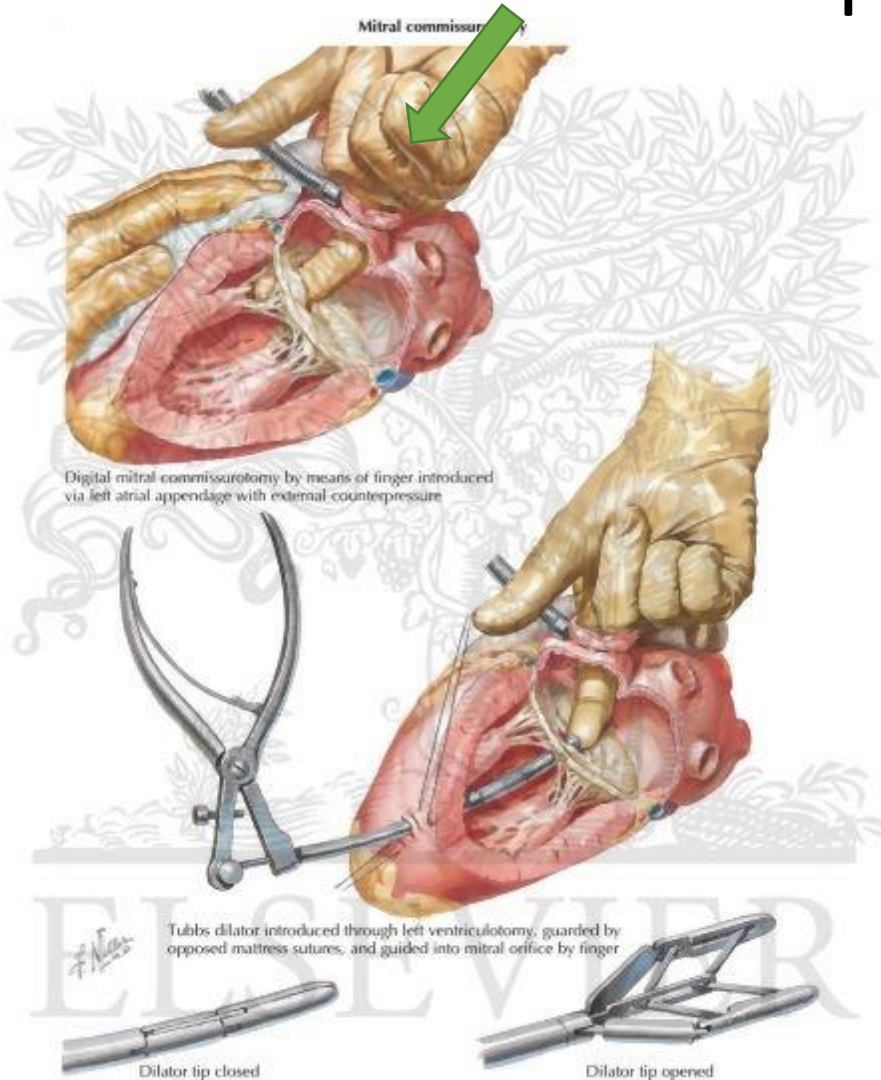


Medical Management of Mitral Stenosis

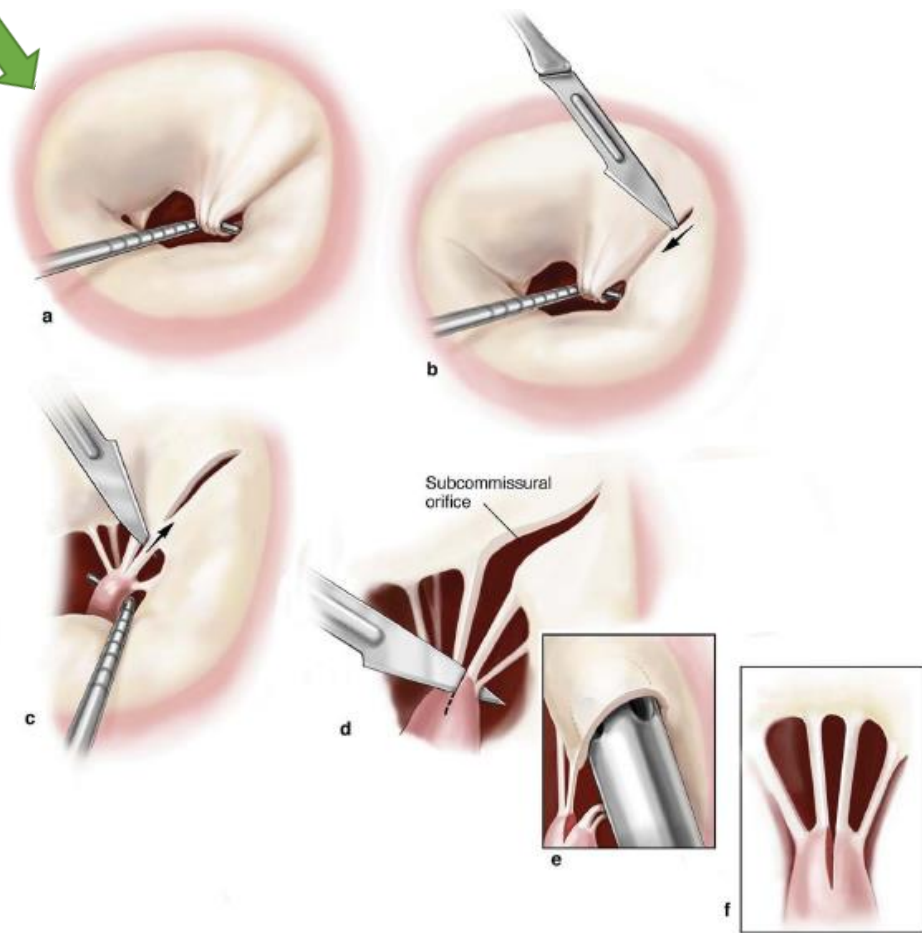
- Fluid pills
- Control of heart rate if fast
- Conversion of irregular rhythm to normal (regular) rhythm
- Thinning of the blood to prevent blood clots
- Prevention of recurrent strep infections/repeat rheumatic fever episodes by chronic administration of antibiotics

Surgical Management of Mitral Stenosis

Closed and Open Commissurotomy



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Surgical Management of Mitral Stenosis

Mitral Valve Replacement



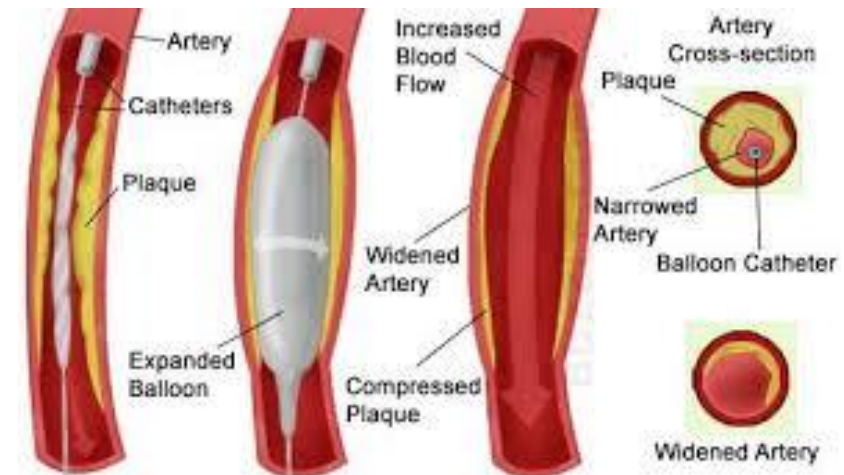
Mechanical and Tissue Mitral Valves

Surgical Management of Mitral Stenosis

- Closed mitral commissurotomy performed primarily in developing countries
- Open mitral commissurotomy has an operative mortality of $< 1\%$ but involves open heart surgery
- Mitral valve replacement (MVR) has an operative mortality of 2 - 7% and is not routinely available in low-income countries

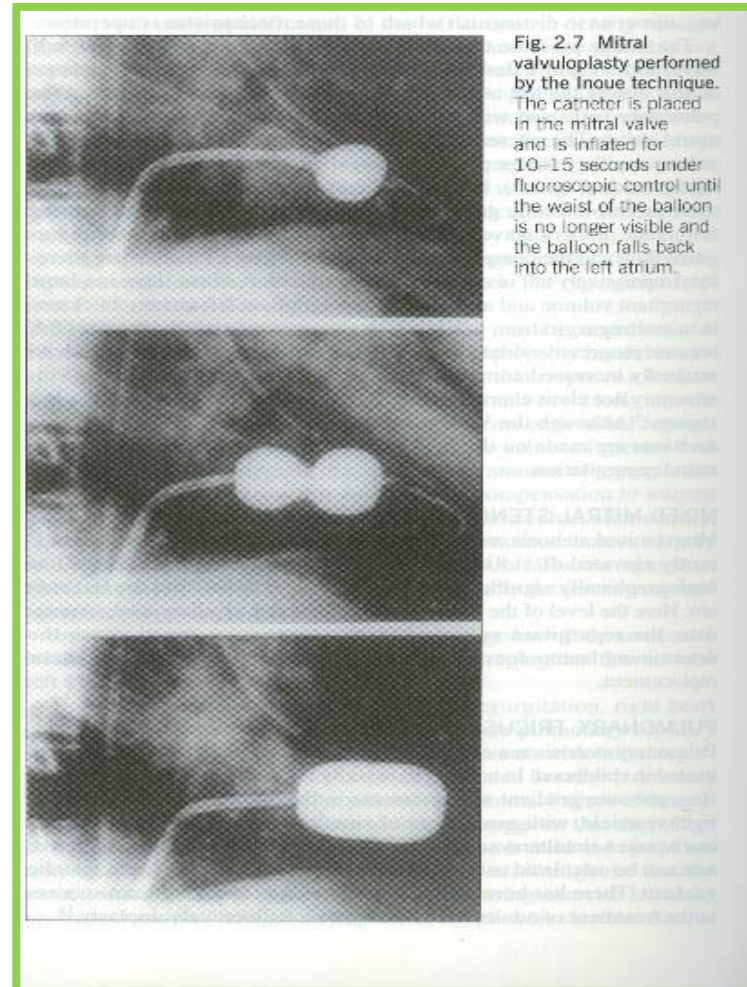
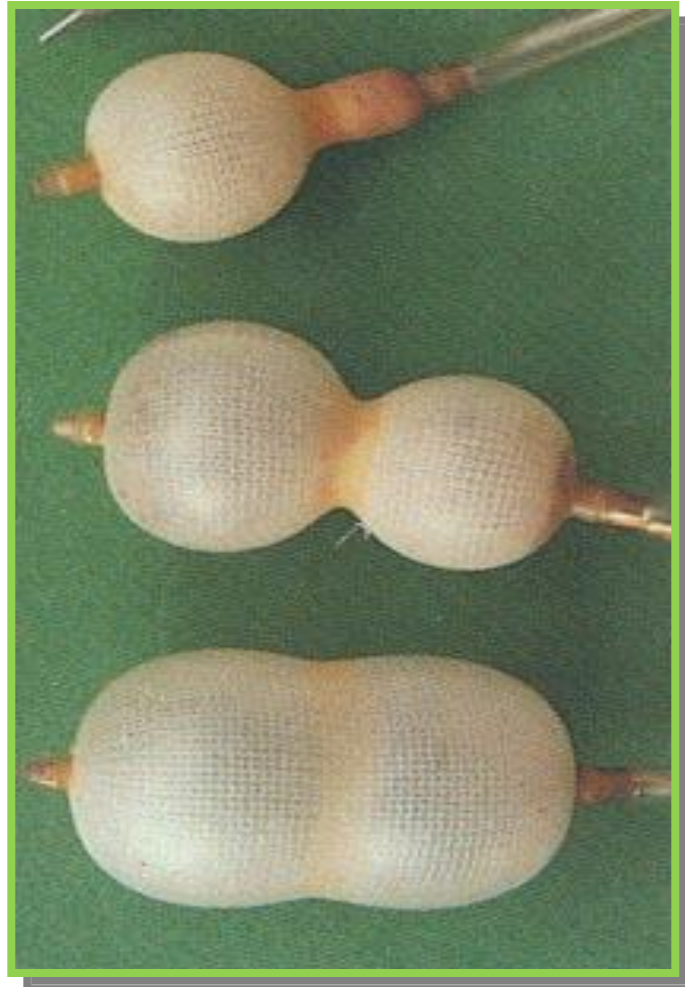
Use of Balloons to Treat Heart Disease

- First use of a balloon to open a coronary artery (“angioplasty”) was on Sept. 14, 1977, some 41 years ago.
 - The first patient is still going strong more than four decades later (although he has undergone two subsequent angioplasty/stent procedures)



- Only a few years after the first coronary angioplasty, a much larger balloon was developed with the thought that it could be used to open up narrowed heart valves.

Percutaneous Balloon Mitral Valvuloplasty (PBMV)



From Crawford MH and DiMarco JP: Cardiology 2001

Percutaneous Balloon (PBMV) vs. Surgical Commisurotomy

Randomized Trials with 10 year
follow-up

Hyderabad, India



Investigators

Hyderabad

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Introduction

- We randomized 100 patients with severe symptomatic mitral stenosis into two prospective studies comparing percutaneous balloon mitral valvuloplasty (PBMV) with surgical closed or open mitral commissurotomy
- We have 10 year follow-up data on the combined series

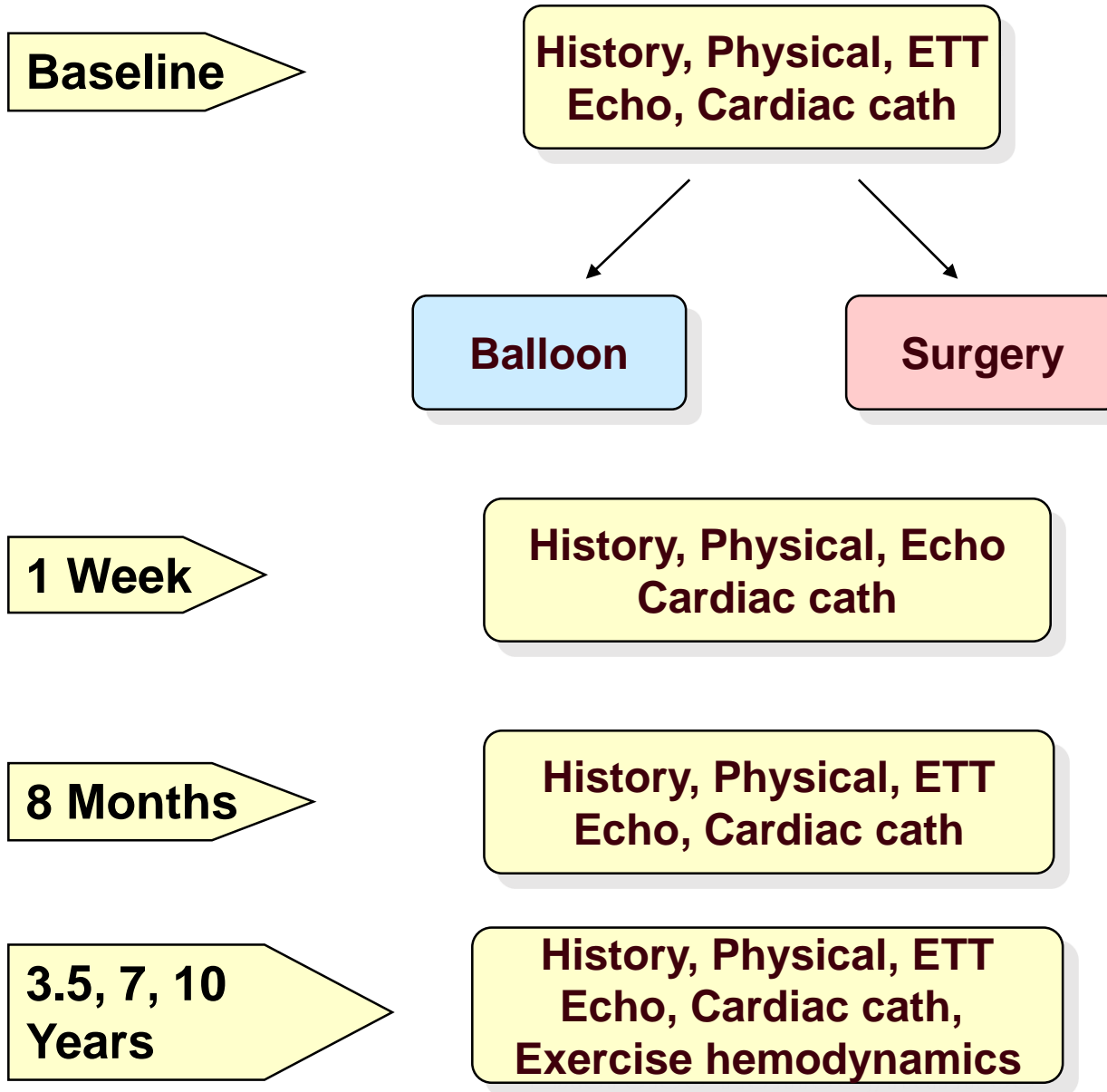
Study Challenges

- Language (Hindi, Telugu, English)
- Culture
- Shared understanding of concept of randomized trial
- How do you obtain informed consent from patients when you don't speak the language or understand the culture?
- How do you ensure that the reported data are accurate and reliable?

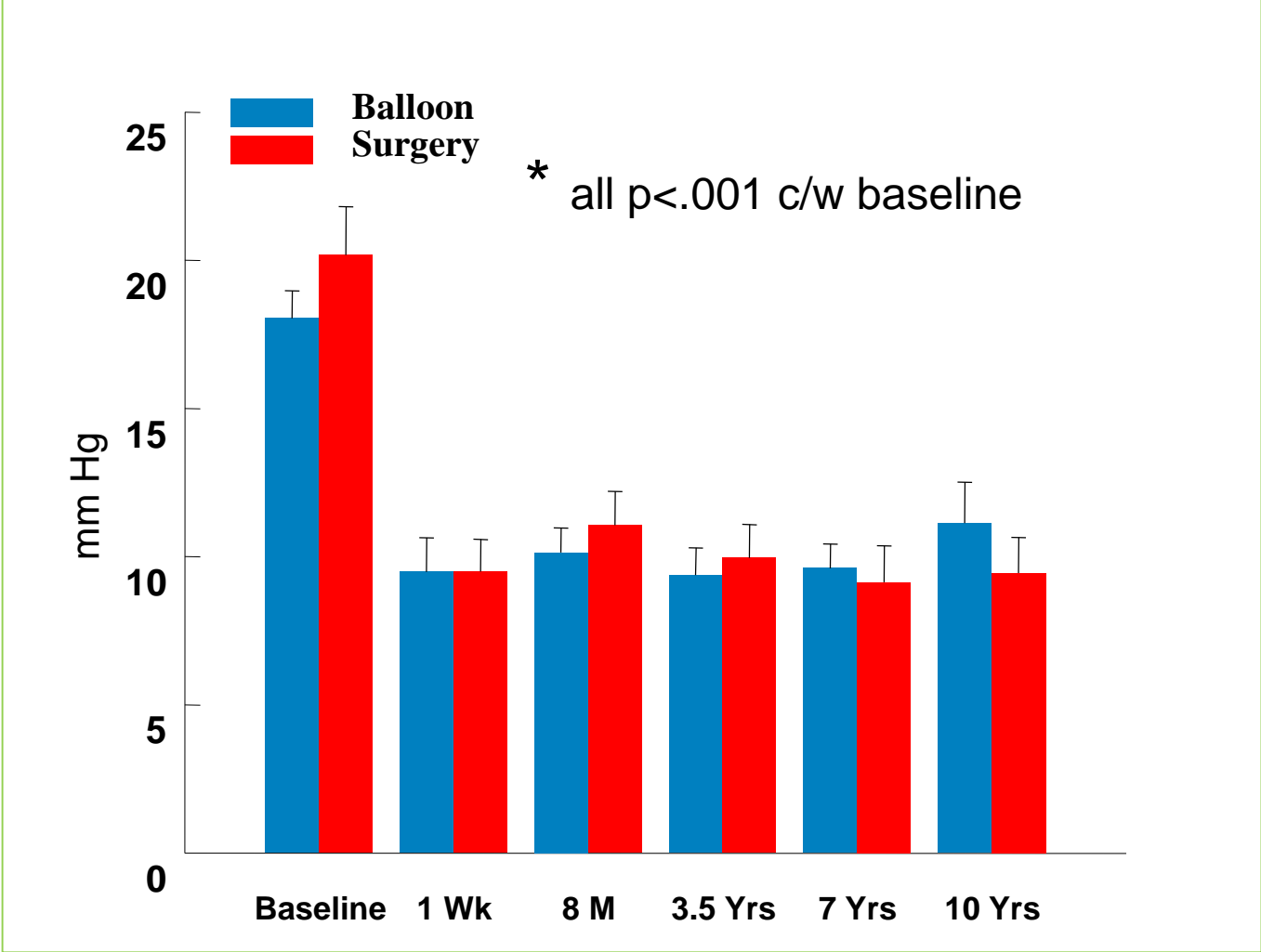
Study Challenges

- How do you get complete follow-up during a ten year study, especially when most of the patients are indigent and have to travel often long distances (typically by public bus) to get to the hospital where the study is being conducted?

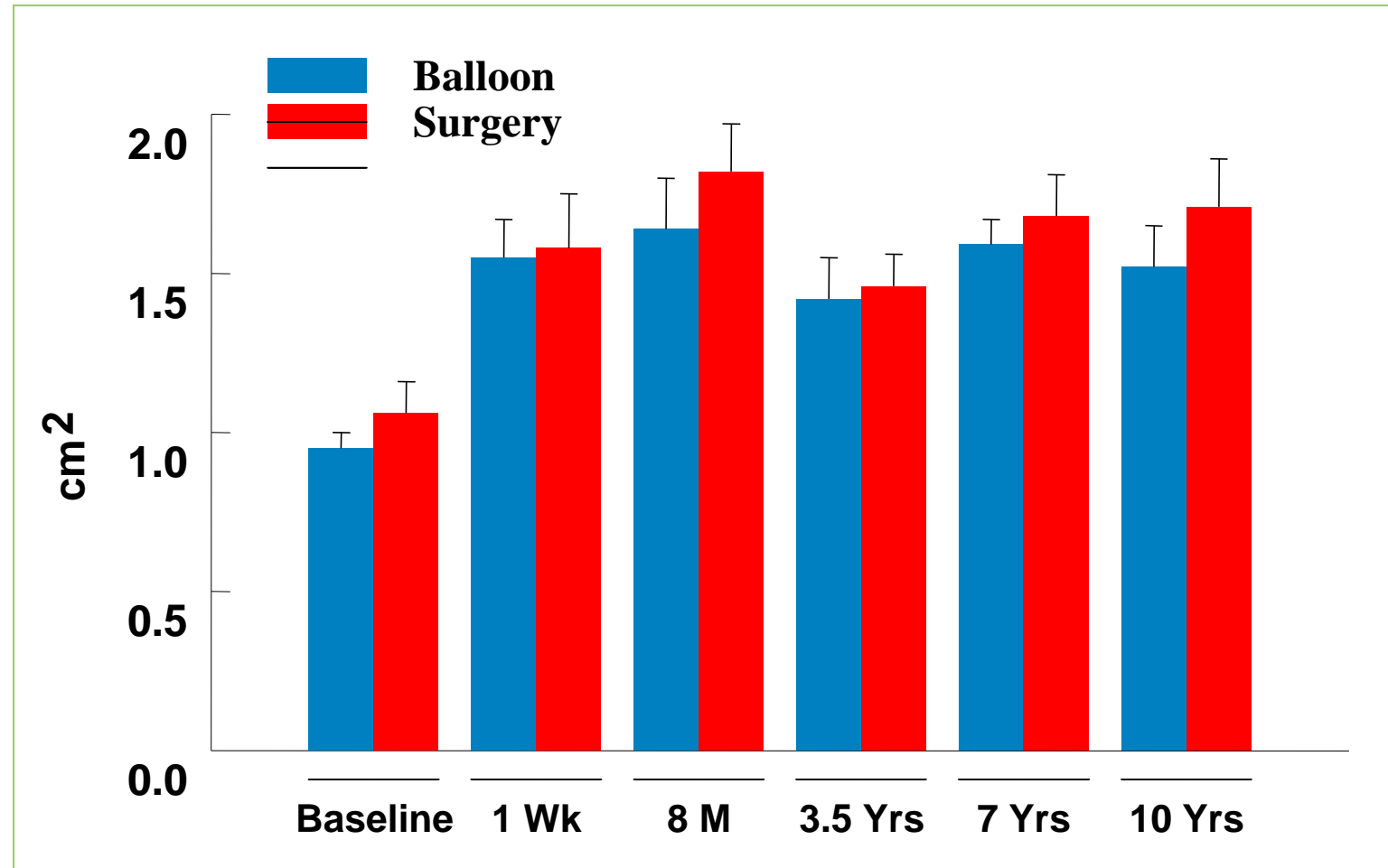
Study Design



Pressure Difference Across the Mitral Valve



Mitral Valve Orifice Area (Size of the Open Valve)



* all $p < .001$ c/w baseline except 3.5 yr Surgery = $p < .02$

Re-Narrowing ("Re-stenosis") of the Valve at 10 Years

Balloon

Surgery

**MVA < 1.5 cm² and
> 50% loss of gain**

6 (30%)

9 (45%)

Clinical restenosis

5 (25%)

6 (30%)

Complications (through 10 years)

Balloon

Surgery

Cardiovascular death	1	0
Stroke	0	0
Heart Attack	0	0
Moderate valve leaking	1	4
Severe valve leaking	2 (1 MVR)	1
Irregular heart rhythm	2	2

Other Advantages of Balloon (PBMV) Intervention



- Patient comfort
- Avoidance of chest incision
- Shorter hospitalization

Summary

- There were no significant differences in outcomes or post-procedure mitral valve size through 10 year follow-up in patients randomized to balloon or surgery.
- Re-narrowing of the valve (“re-stenosis”) is common by 10 years regardless of intervention, especially if objective criteria are used.
- In patients with favorable mitral valve anatomy, percutaneous balloon mitral valvuloplasty has efficacy and safety equal to closed or open surgical commissurotomy.

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PERCUTANEOUS BALLOON VALVULOPLASTY COMPARED WITH OPEN SURGICAL COMMISSUROTOMY FOR MITRAL STENOSIS

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SHAILENDER SINGH, M.D., D. PRASADA RAO, M.S., M.CH., P.V. SATYANARAYANA, M.S., M.CH.,
AND ZOLTAN G. TURI, M.D.



2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

J Am Coll Cardiol. 2014;63(22):e57-e185. doi:10.1016/j.jacc.2014.02.536

Class I (= This is the preferred management strategy)

Percutaneous mitral balloon commissurotomy is recommended for symptomatic patients with severe MS (mitral valve area ≤ 1.5 cm², stage D) and favorable valve morphology in the absence of left atrial thrombus or moderate to severe MR.

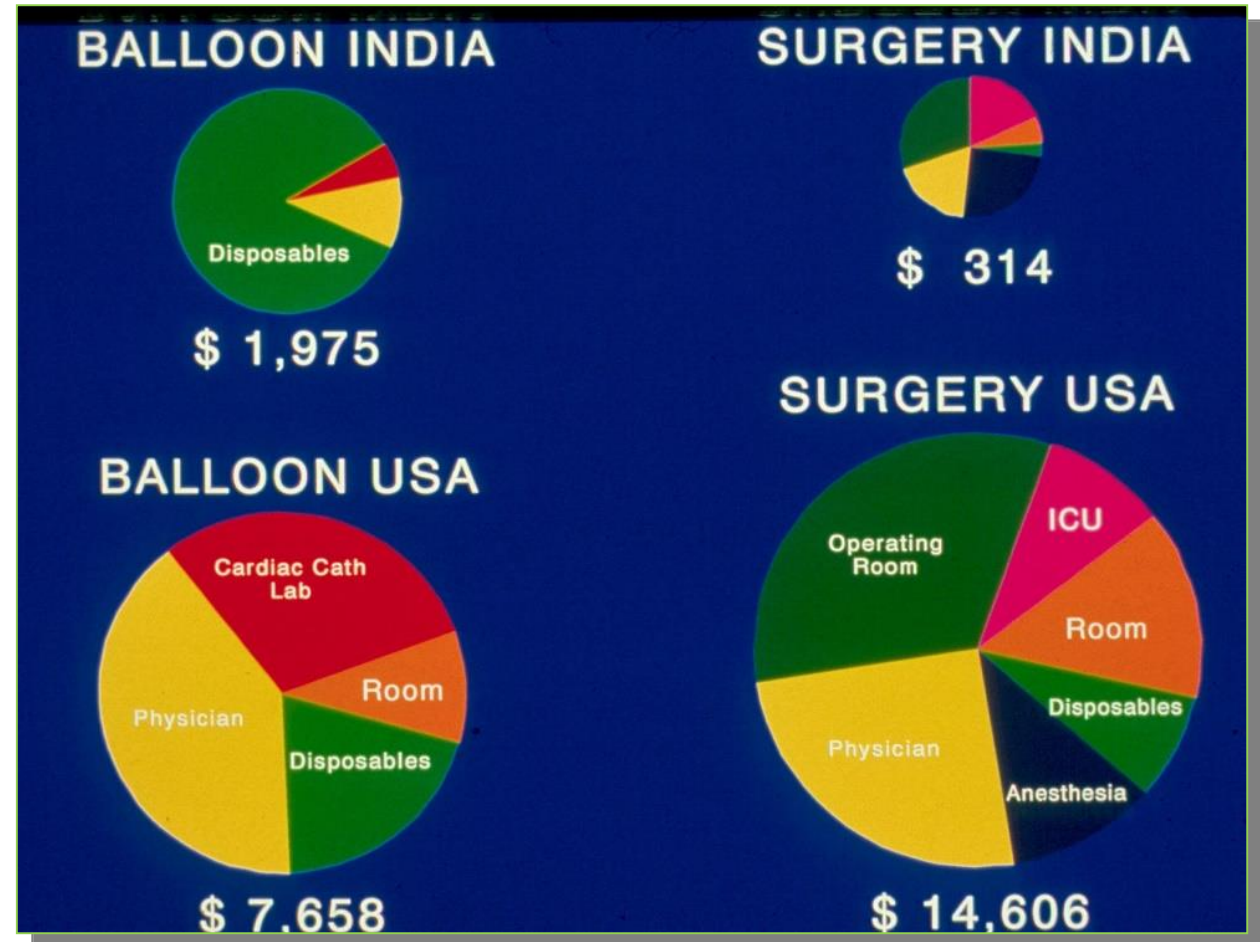
(Level of Evidence: A = Rigorous randomized trials support the recommendation)

Management Issues in Mitral Stenosis

- A 36 year old female, originally from India, presents during pregnancy with severe dyspnea and is found to have moderately severe MS.

- How should she be managed?
 - Medical management with diuretics and beta blockers
 - Closed mitral commissurotomy
 - Open mitral commissurotomy
 - Mitral valve replacement
 - Balloon valvuloplasty

Other Considerations



U.S. Health Care Expenditures 2018

(Estimated by CMS)

\$3.68 TRILLION

18.2% of GDP

\$11,193 per person

SOURCES: Centers for Medicare & Medicaid Services, Office of the Actuary; U.S. Department of Commerce, Bureau of Economic Analysis; and U.S. Bureau of the Census

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A high-angle, wide shot of a modern, multi-level office building interior. The space is characterized by large glass windows, white walls, and grey carpeting. In the upper level, a group of five people in business attire are gathered near a glass railing, engaged in conversation. A woman in a teal top is walking across the upper level. A staircase with a glass railing leads up from the upper level. In the lower level, a group of people is sitting around a white table, and others are walking. The overall atmosphere is professional and active.

Questions?