

# Session II: Lessons Learned from Successes & Failures in Other Fields

Committee on Research Priorities for Preventing & Treating ADRD

NATIONAL  
ACADEMIES

Sciences  
Engineering  
Medicine

*Hope, Hype, Humility, & the Future*

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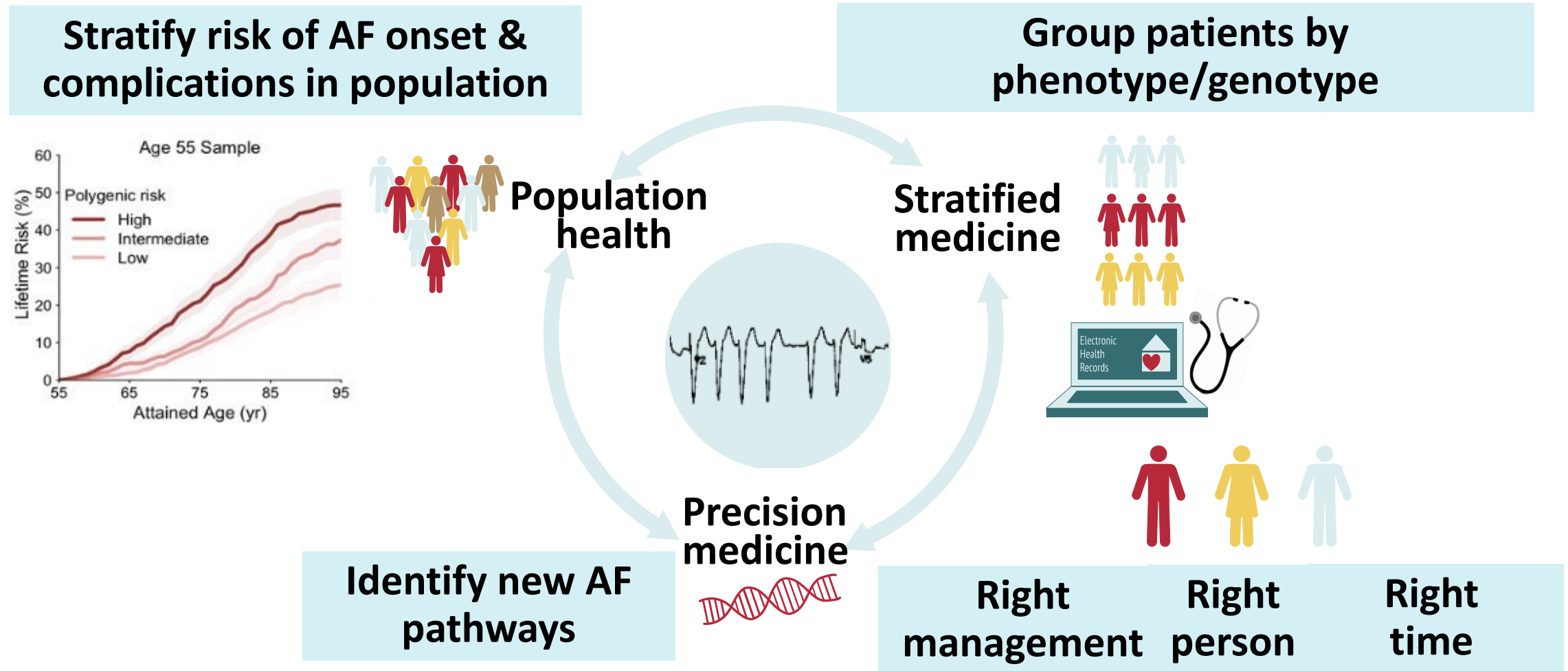
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NHLBI & Boston University's Framingham Heart Study

**January 16, 2024**

# Disclosures - Genetics Grants & NHLBI Workshops

- **AF Genetics**      R01HL092577; AHA AF 18SFRN34110082
- **NHLBI**
  - Co-Chair AF Prevention of AF Workshop**
    - Prevention of AF. *Circulation*. 2009;119:606
  - Co-Chair, AF Research Working Group**
    - Screening. *Circulation*. 2021;143:372
    - Secondary Prevention. *JAHA*. 2021;10:e021566
    - AF Social Determinants. *JAMA Cardiol*. 2023;8:182

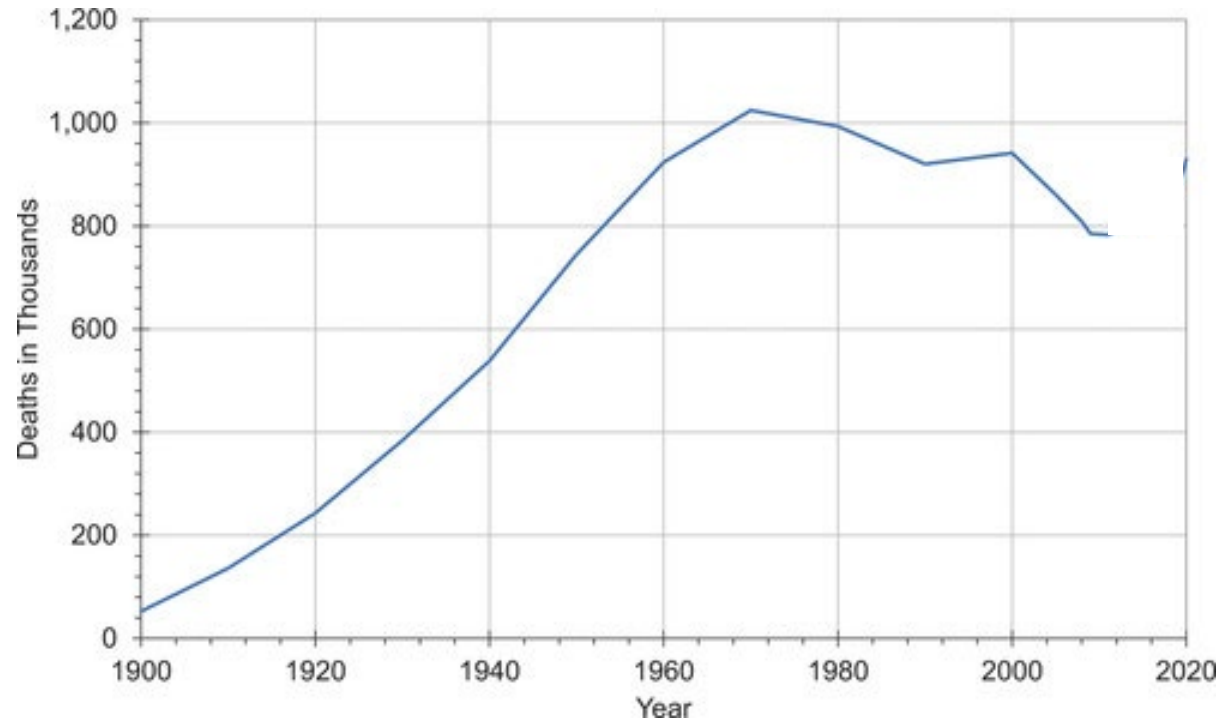
# Advancing AF Precision Medicine Project Overview



Hope

Benjamin MPI AF Genetics Grants R01HL092577; AHA AF 18SFRN34110082

# Decline in Mortality



Deaths attributable to CVD, US, 1900 to 2020

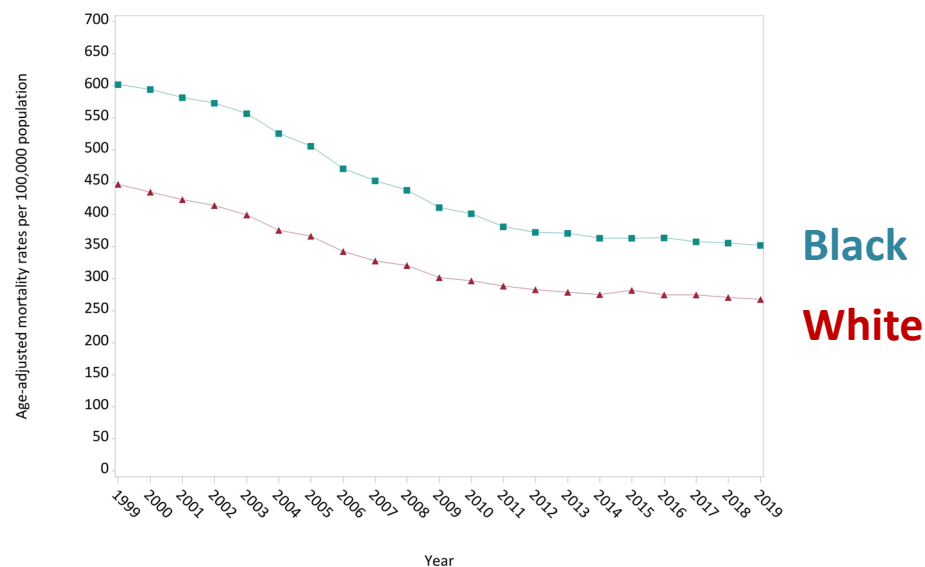


## CHD Mortality

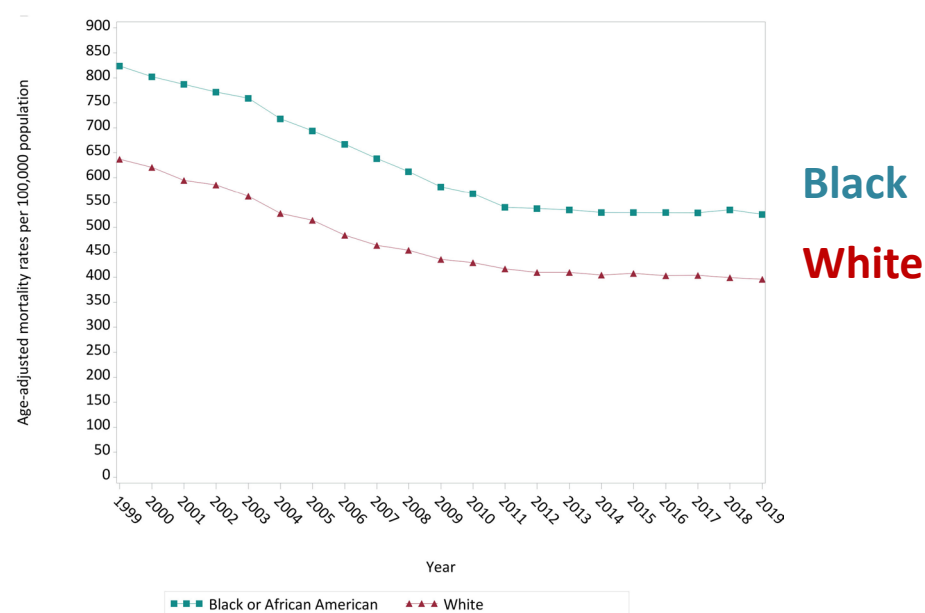
- 47% evidence-based medical & surgical Rx
- 44% reductions in major risk factors

# CDC WONDER US Decline in CHD Mortality 1999-2019

## Women



## Men





*Study Shows Promise for Expensive Cholesterol Drugs, but They Are Still Hard to Obtain*

# Hope & Hype: PCSK9 Inhibitors An End to Heart Disease? Not Quite

Share full article



Mahendra Mahabir, 41, started applying for a PCSK9 inhibitor last June. Mr. Mahabir finally got approved on Monday. Peter W. Cross for The New York Times

By [Gina Kolata](#)

Nov. 15, 2016

Share full article



Over about two years of study, researchers found that Repatha, when added to statin therapy, further reduced the risk of heart attack or stroke by about 15 percent. Robert Dawson/Amgen, via Associated Press

By [Harlan M. Krumholz](#)

March 20, 2017

These Cholesterol-Reducers May Save Lives. So Why Aren't Heart Patients Getting Them?

Powerful PCSK9 inhibitors were supposed to revolutionize care for cardiac patients. But insurers and other payers balked at sky-high prices.

Share full article



Heart condition that killed her grandfather, lower left, at age 30. Her mother, lower right, had heart disease. Peter W. Cross for The New York Times



By [Gina Kolata](#)

Oct. 2, 2018

Hope  
& Hype

# Cautionary Tale for Dementia Drugs?

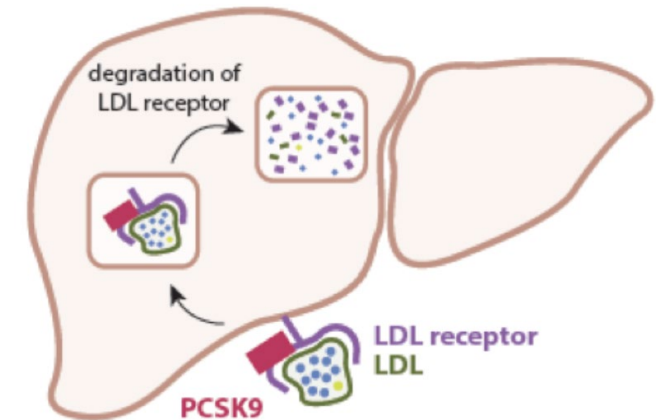
PCSK9inhibitors, monoclonal AB to Rx resistant hypercholesterolemia  
Gap elegant precision discovery → utility @ practice, patient, & population level

## Barriers

- Cost
- Complexity of use
- Marginal value

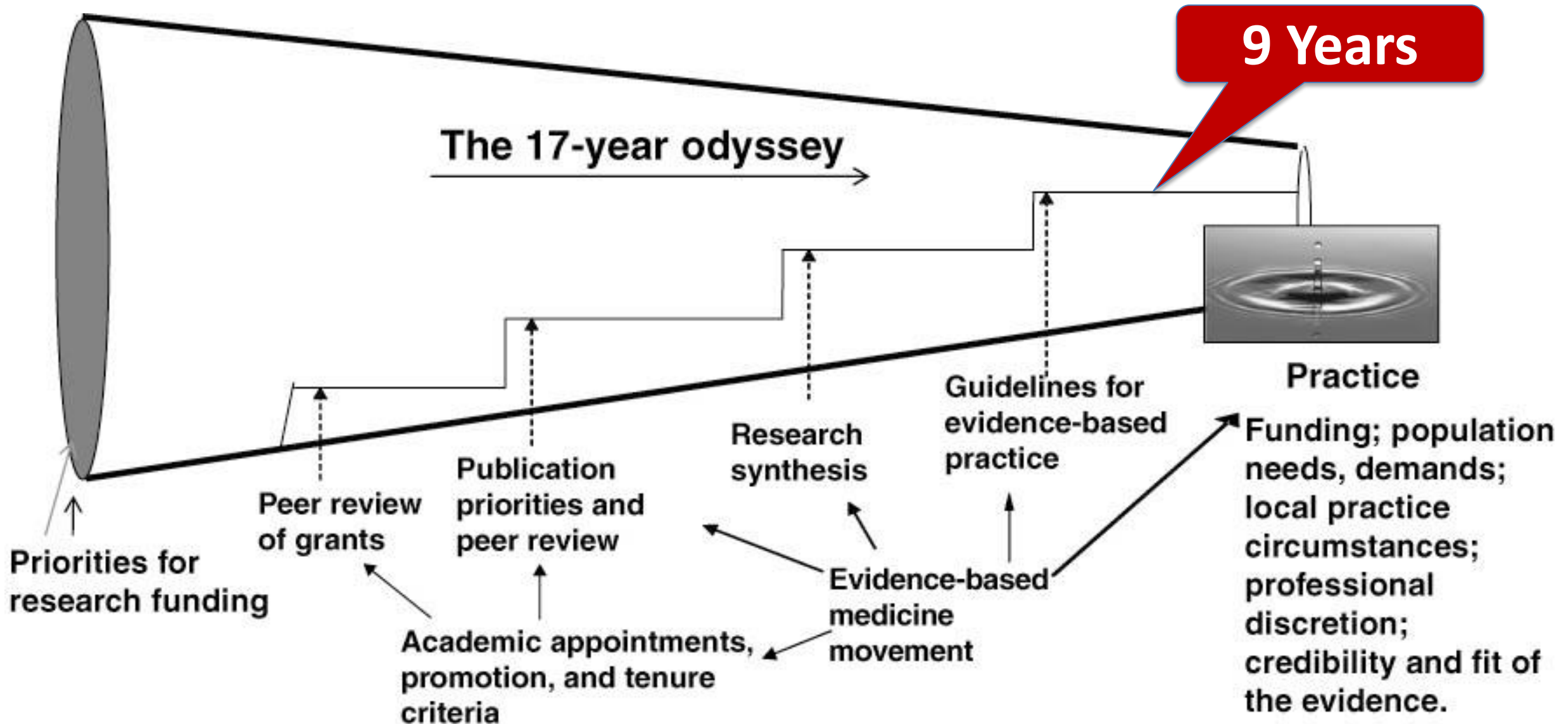
## Unintended consequences

- ↑ health inequities: race, ethnicity, age, rurality, health literacy, SES, etc.
- Displace efficacious medications such as anticoagulants
- Off target effects



PCSK9 binding to the LDL receptor:  
• LDL receptor is degraded  
• less LDL can be removed from blood

# Is 17 Years Unrealistically Optimistic?

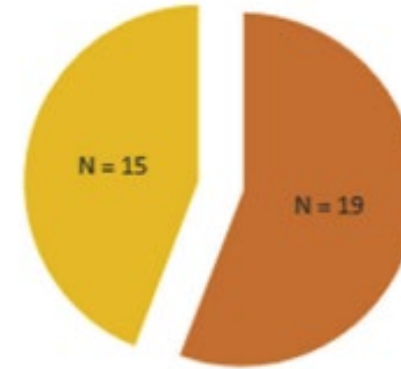


**Humility**

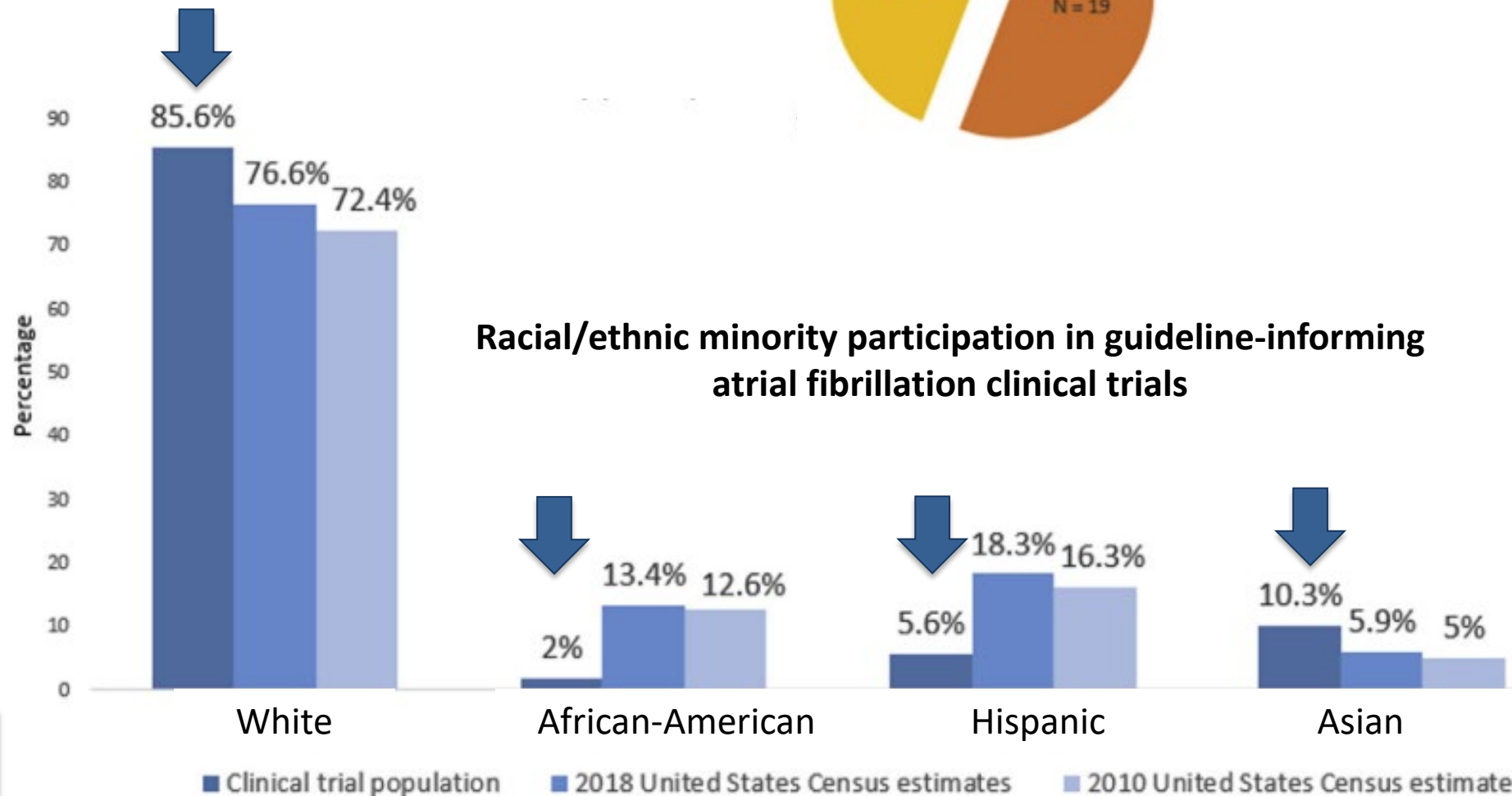


# Under-Reporting & Under-Representation AF Clinical Trials

Under-reporting of participant racial/ethnic data in  
guideline-informing AF clinical trials

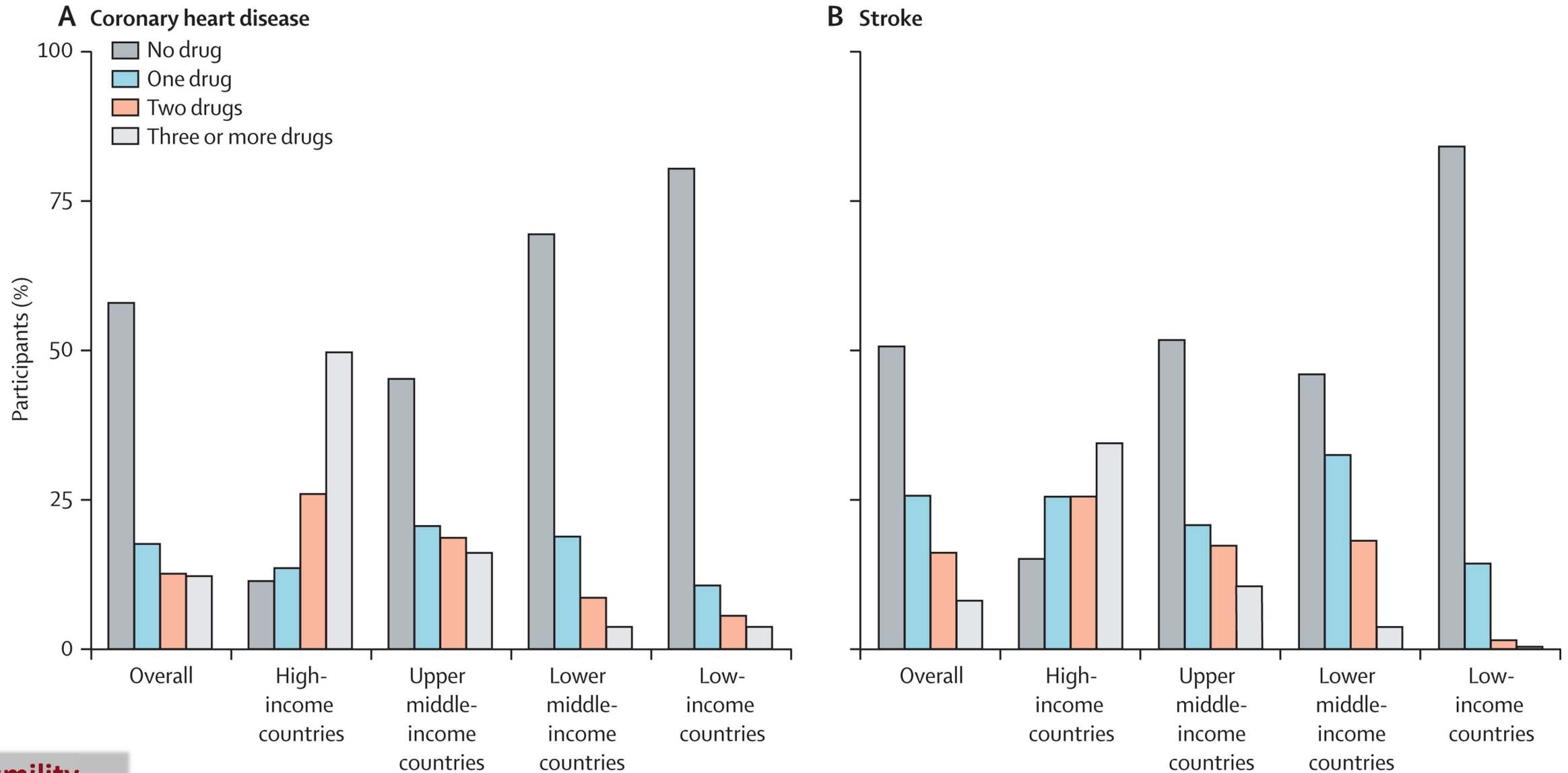


44% participant race/ethnicity  
not reported

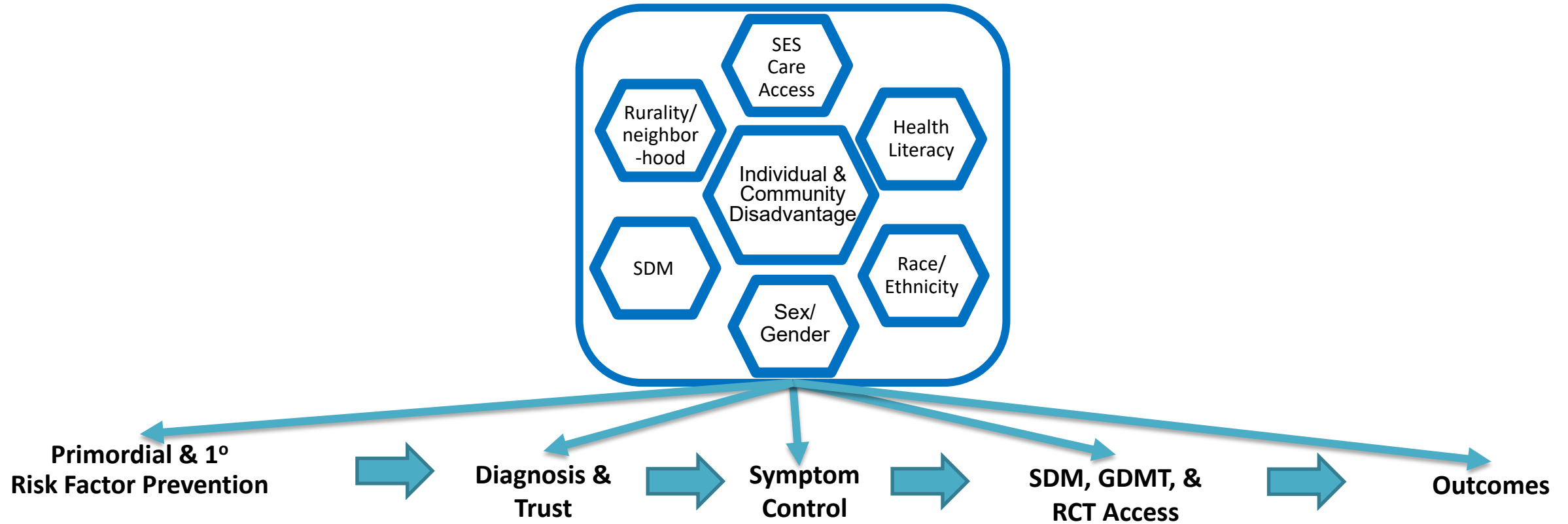


# Underutilization of Evidenced-Based Secondary Prevention

## PURE Study: Lowest use in Low Income Countries



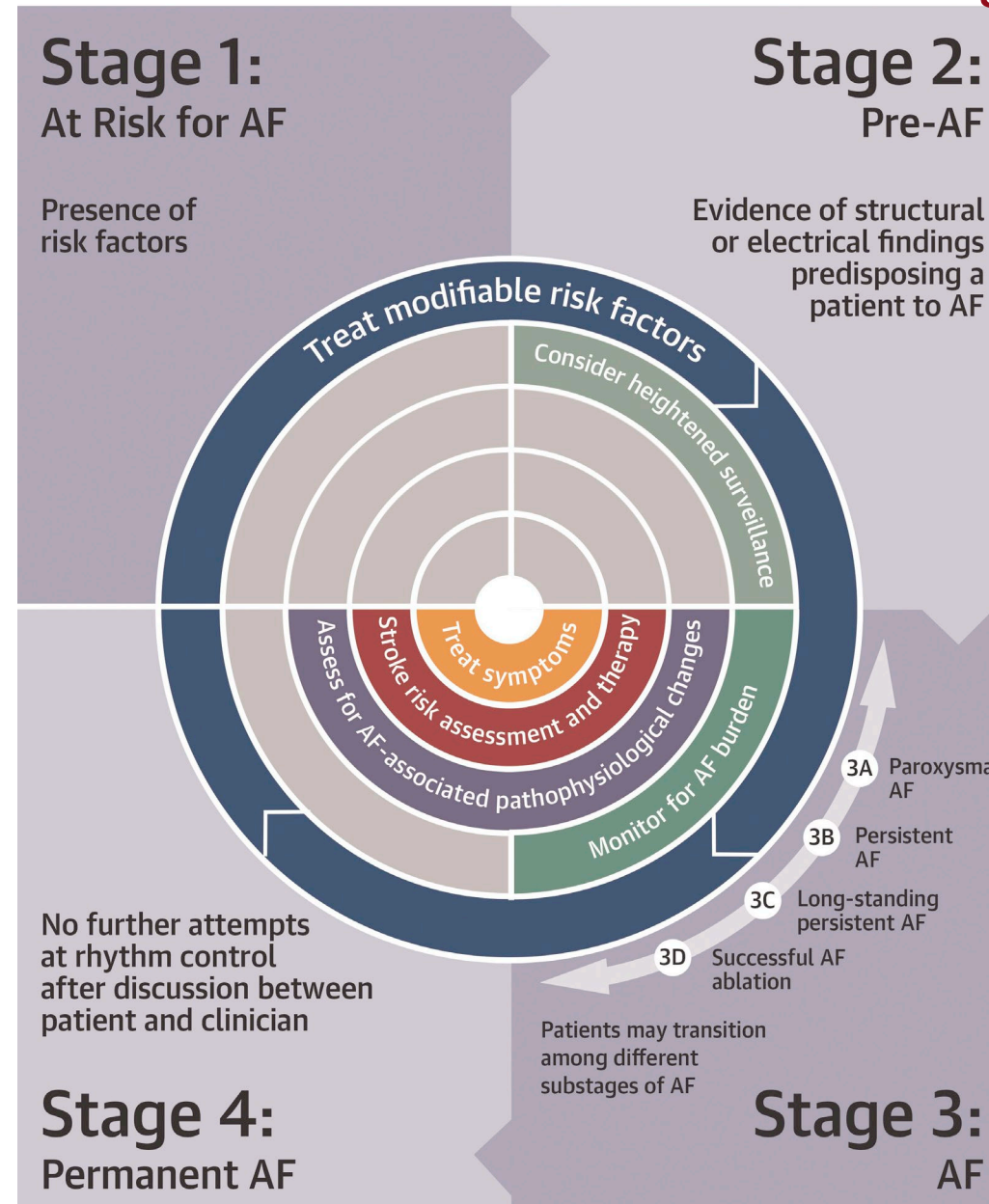
# NHLBI Workshop AF SDOH Cross-Cutting Research Opportunities



**Marked inequities amplified by SDOH across the lifecourse of AF**

# ACC/AHA/AACP/HRS Atrial Fibrillation Guidelines

## Management Strategies for New Classification of AF – Stages Across the Lifecourse



Future

# ACC/AHA/AACP/HRS Atrial Fibrillation Guidelines

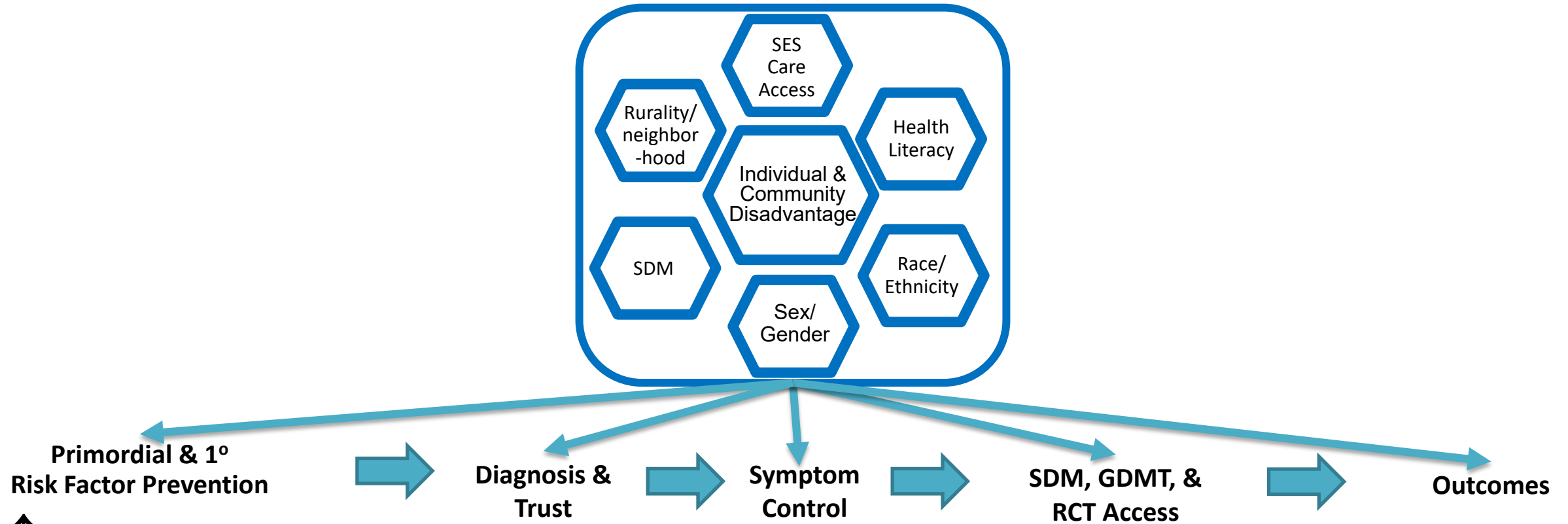
## Recommendation to Address Health Inequities & Barriers to AF Management

| Recommendation to Address Health Inequities and Barriers to AF Management |      |                                                                                                                                                                                                                                                                                                                                                                                              |
|---------------------------------------------------------------------------|------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| COR                                                                       | LOE  | Recommendation                                                                                                                                                                                                                                                                                                                                                                               |
| 1                                                                         | B-NR | 1. Patients with AF, regardless of sex <sup>1</sup> and gender diversity, race and ethnicity, <sup>2</sup> or adverse social determinants of health (SDOH), <sup>3,4*</sup> should be equitably offered guideline-directed stroke risk reduction therapies as well as rate or rhythm control strategies and LRFM as indicated to improve quality of life (QOL) and prevent adverse outcomes. |

\*Including lower income, lower education, inadequate or lack of insurance coverage, or rurality

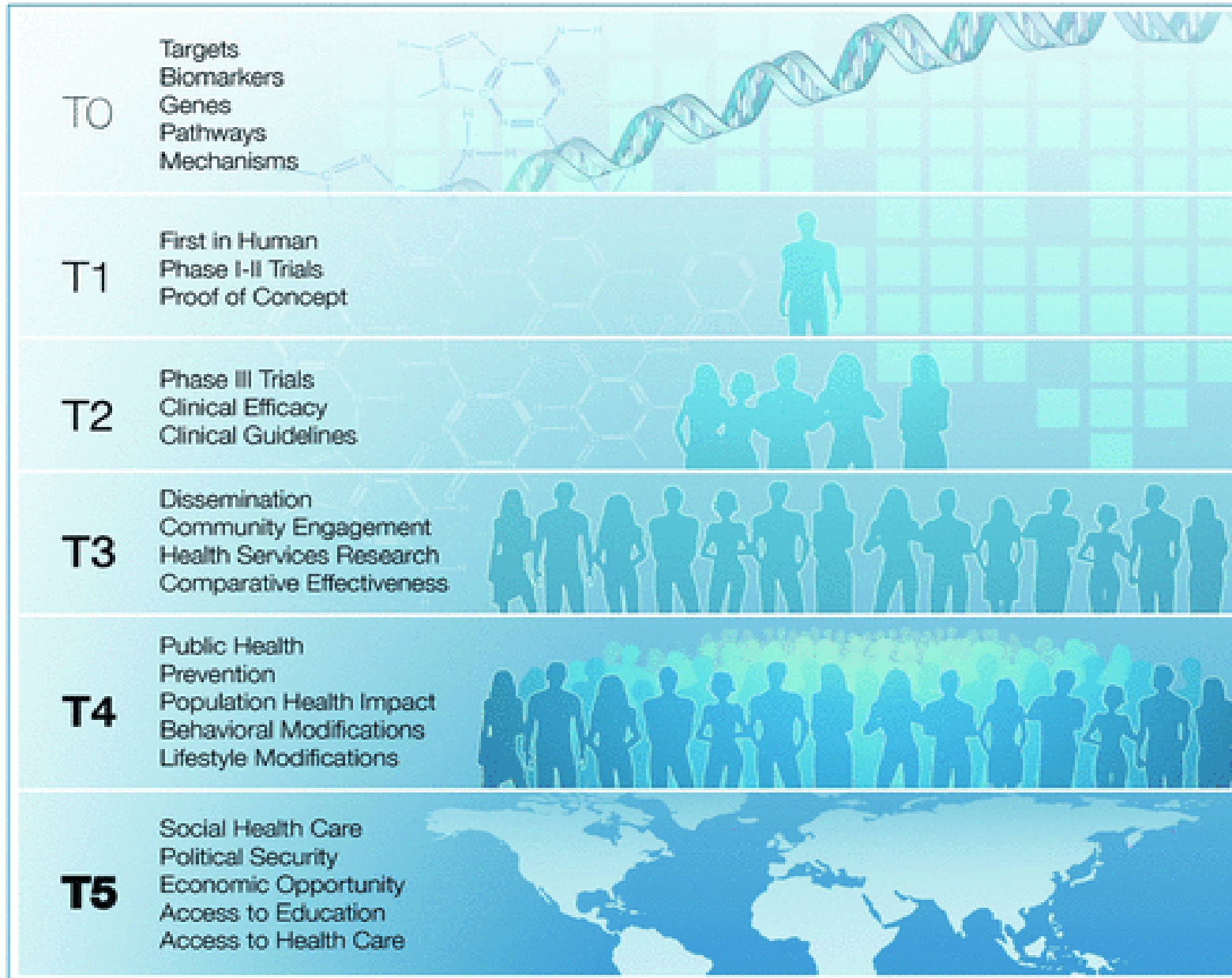


# NHLBI Workshop AF SDOH Cross-Cutting Research Opportunities



- **↑ Diversity**
  - Recruitment & retention diverse patients in observational & pragmatic studies
  - Settings
- Develop innovative methods to analyze multiple intersectional identities & cumulative disadvantage across the life course
- Pragmatic studies to test multilevel strategies mitigate SDOH across all stages AF

# Continuum of Clinical & Translational Science



Bench

Bedside

Guidelines

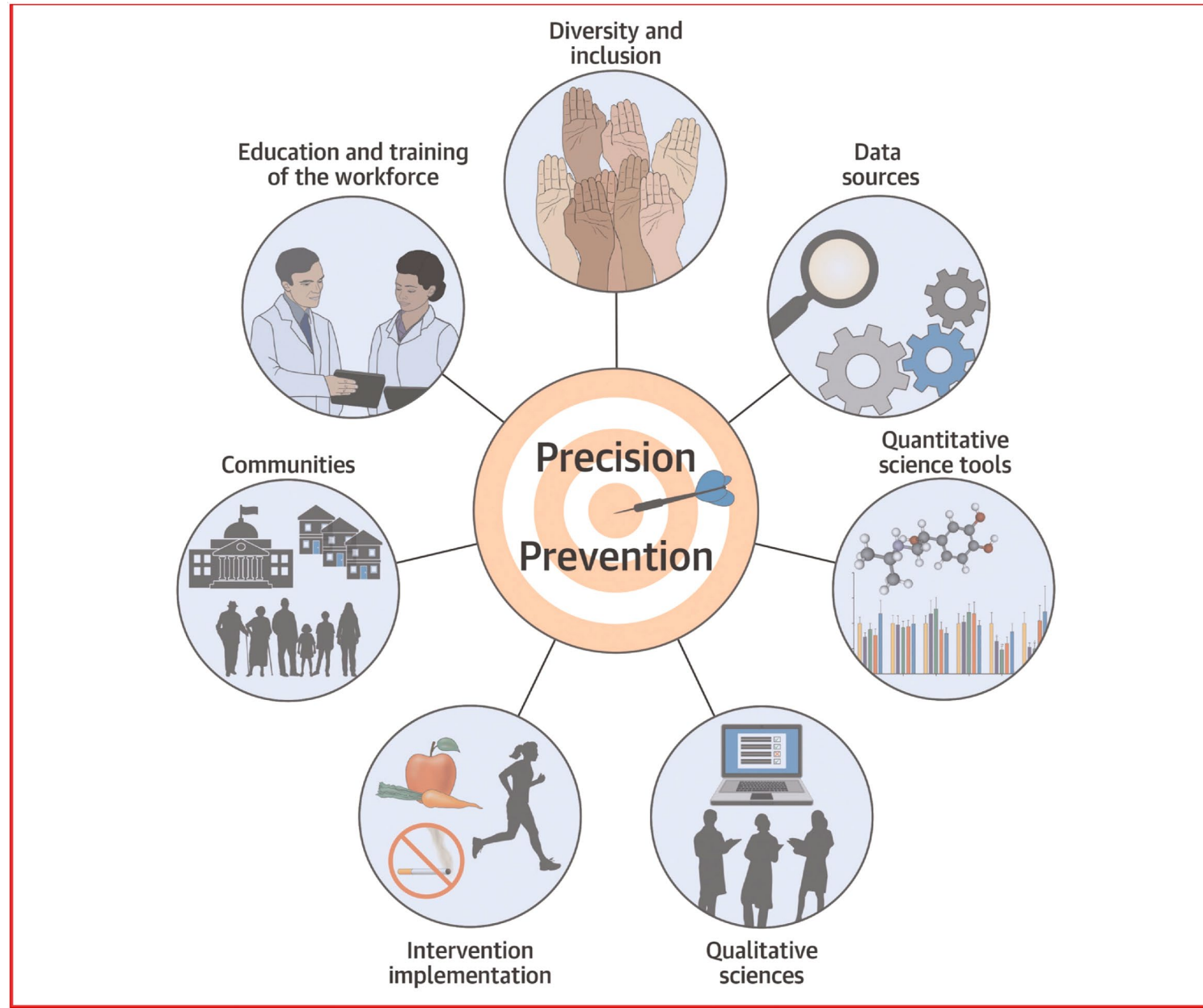
Community

Public Health

Global Village

# NHLBI Workshop: Research Opportunities to ↓ CV Health Disparities

## Precision Medicine in Individuals & Precision Public Health in Communities



Pearson *JACC: Advances*.  
2024;3:100759