Cardiometabolic Health of South Asian Americans

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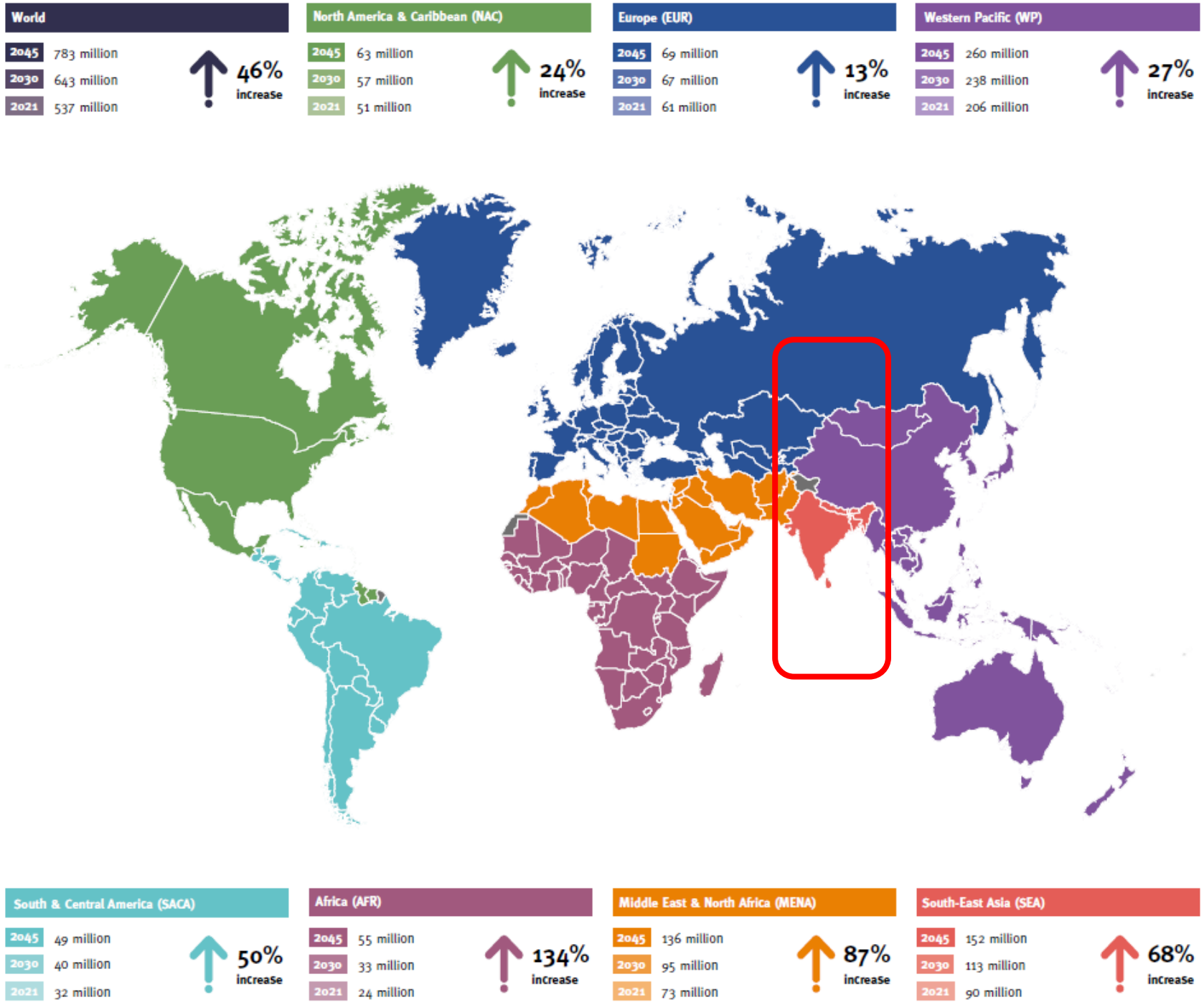
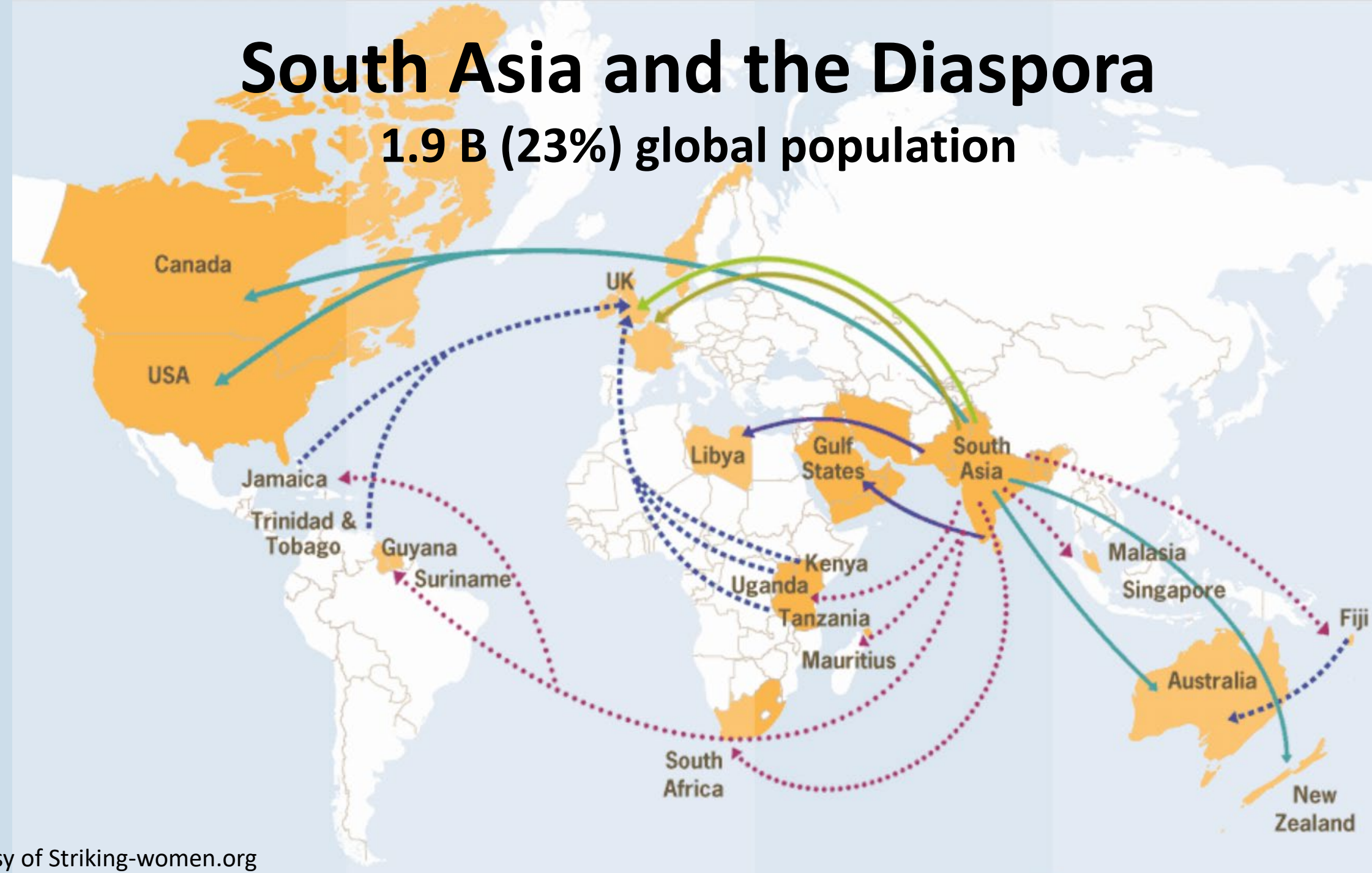
- Estimated 537 M people with diabetes globally
- 80% living in low and middle income countries
- South Asia is at the epicenter



IDF Atlas, 2021

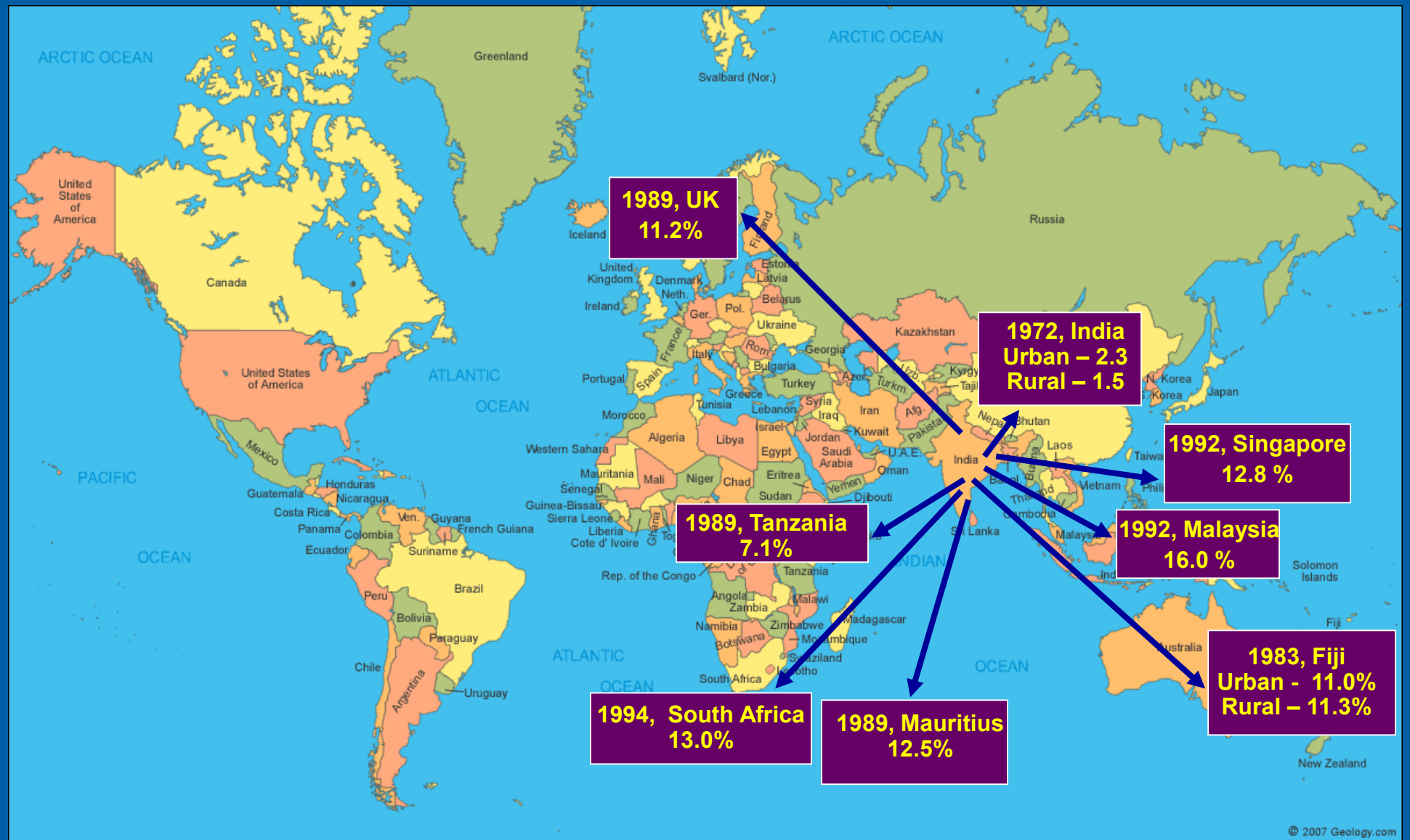
South Asia and the Diaspora

1.9 B (23%) global population



Courtesy of Striking-women.org

Earliest observations of heightened risk of diabetes in South Asians were seen in immigrant Indians



“Asian American”

23 countries of origin

Census 2020

≈ 24 M (7.2%)

↑ 39% from Census 2010

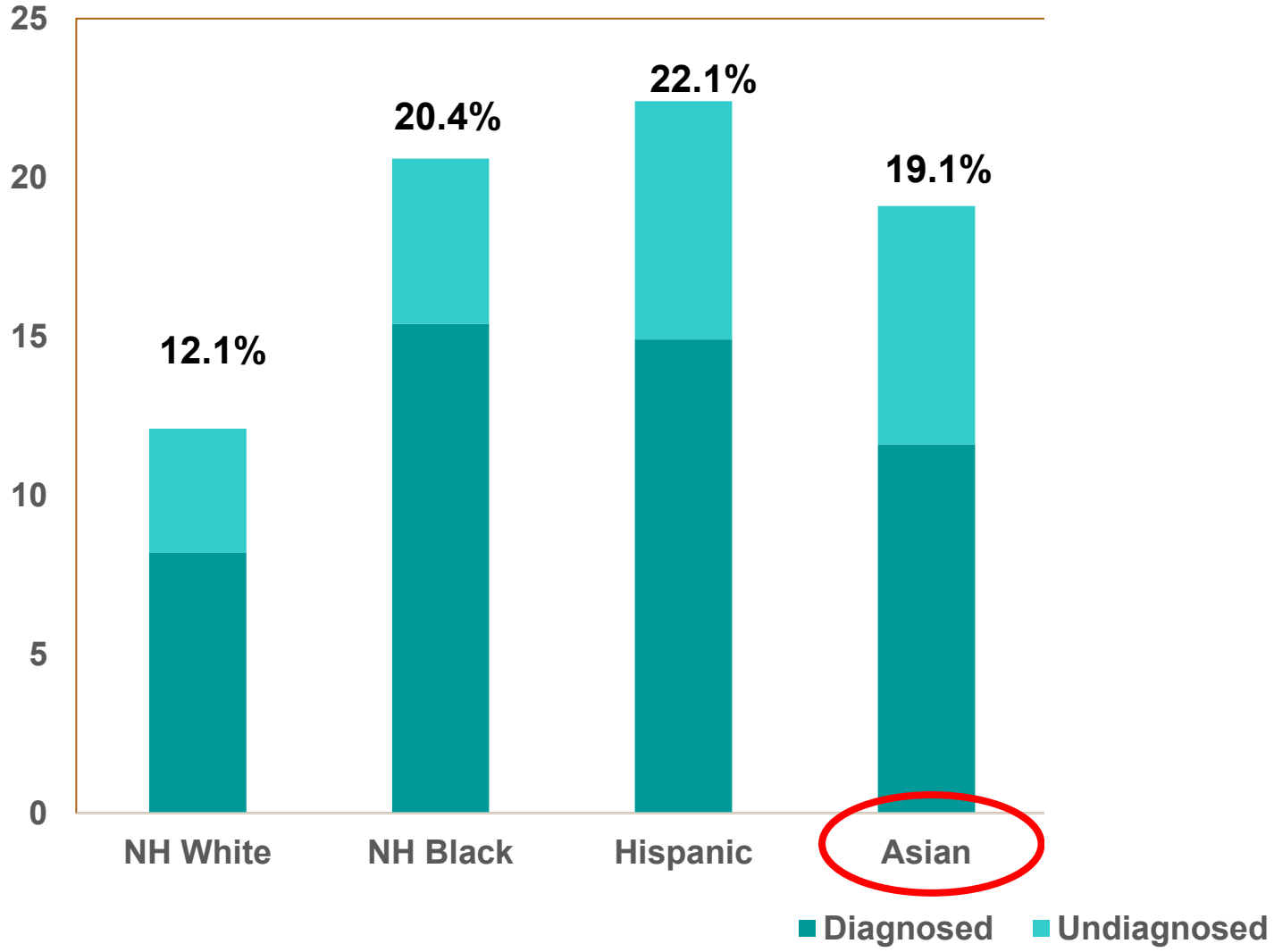
2022: 6 largest Asian subgroups*:

- Chinese: 5.5 M
- Asian Indian: 4.9 M
- Filipino: 4.5 M
- Vietnamese: 2.3 M
- Korean: 2.1 M
- Japanese: 1.6 M

*alone or in combination with another group

NHANES data: 2011 – 2016

Diabetes Prevalence: Age and Sex adjusted



Cheng, Kanaya, Araneta, *JAMA,* 2019

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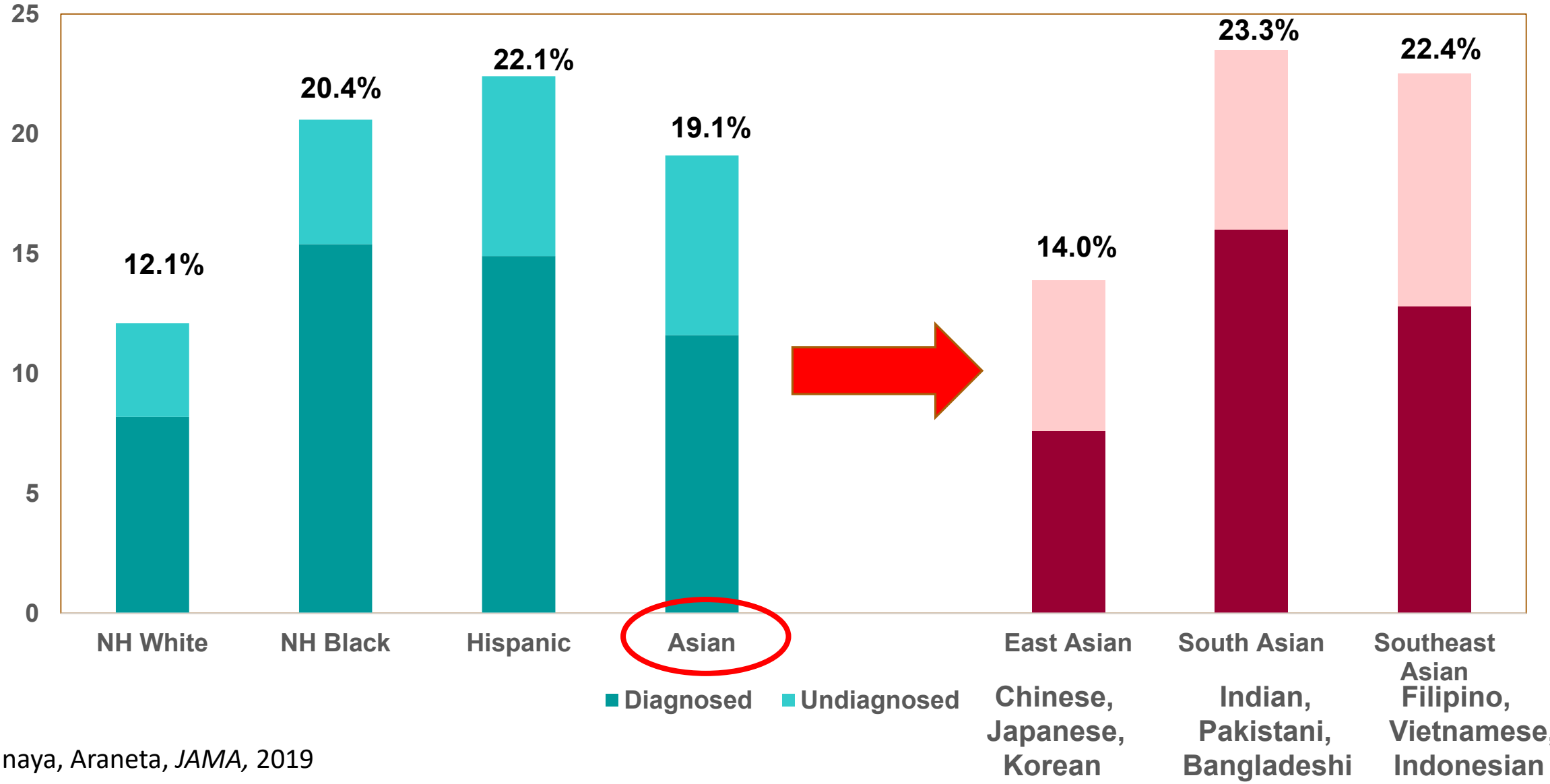
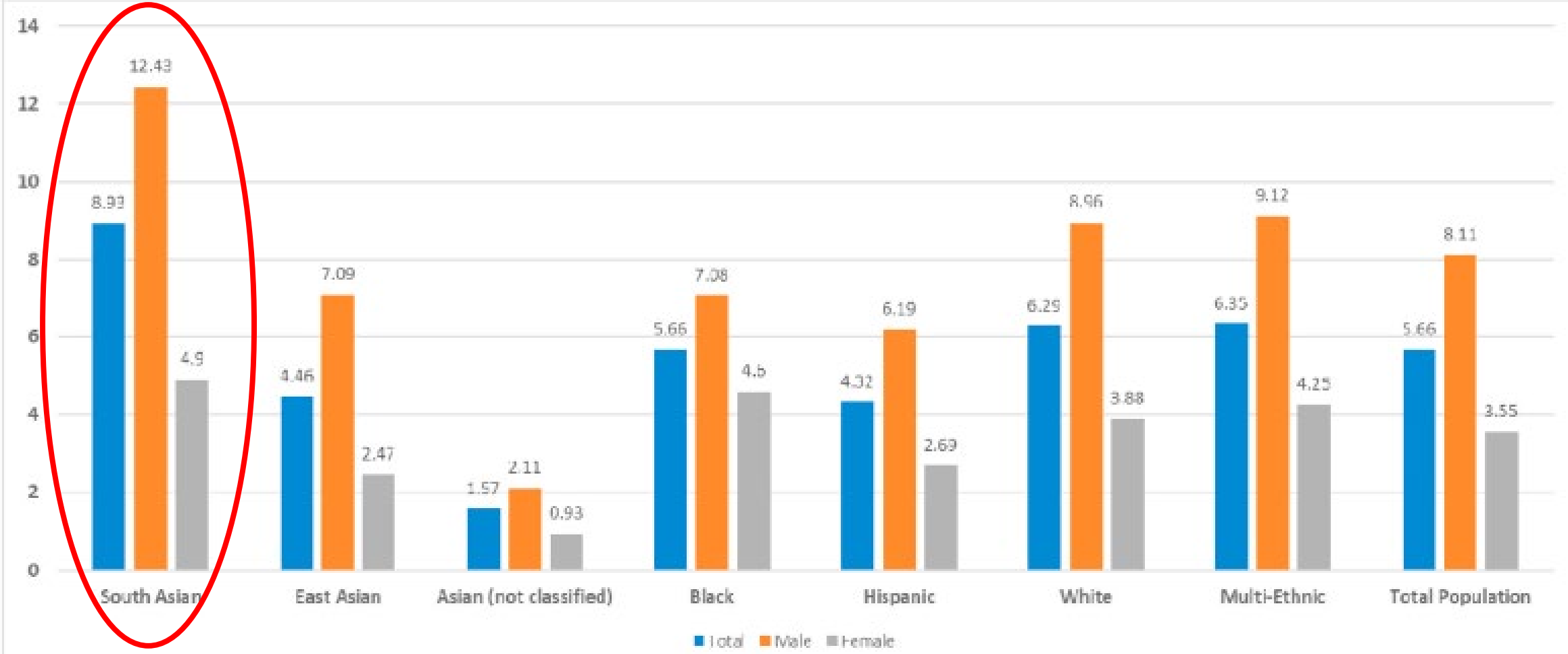
Diabetes Prevalence: Age and Sex adjusted



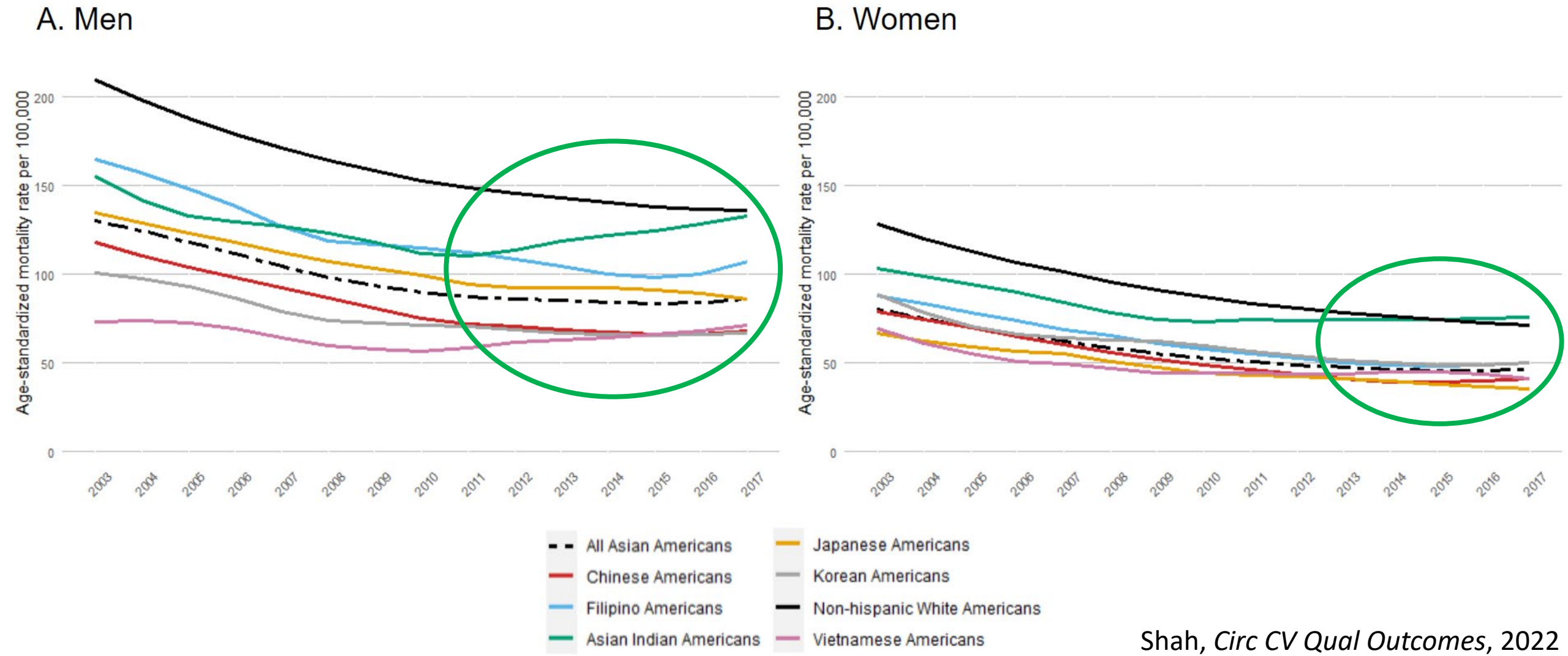
Cheng, Kanaya, Araneta, *JAMA,* 2019

Kaiser: 10 year incidence of heart disease by group 2006-2016



Pursani, *Atherosclerosis*, 2020

U.S. Ischemic Heart Disease mortality
NCHS, 2008-2017



Shah, *Circ CV Qual Outcomes*, 2022

Mediators of Atherosclerosis in South Asians Living in America

South Asian Americans

- Ages 40-84 years
- No known cardiovascular disease
- 2 sites: UCSF and Northwestern U
- Only longitudinal cohort of US South Asians

www.masalastudy.org

Mediators of Atherosclerosis in South Asian Living in America

South Asian Americans

White Americans

Black Americans

Hispanic Americans

Chinese Americans

MESA

Multi-Ethnic Study of Atherosclerosis

MASALA Study Timeline

MPIs: Drs. Alka Kanaya, Namratha Kandula, Nadia Islam

Exam 1

Glucose Tolerance Test
CT scans
Carotid Ultrasound

Exam 2

Glucose Tolerance Test
CT scan
Social Networks

Exam 1A

Glucose Tolerance Test
CT scan

Exam 3

Echocardiogram
Vascular stiffness
Endothelial function

2010 - 2013 | **2015 - 2018** | **2021 - 2024**

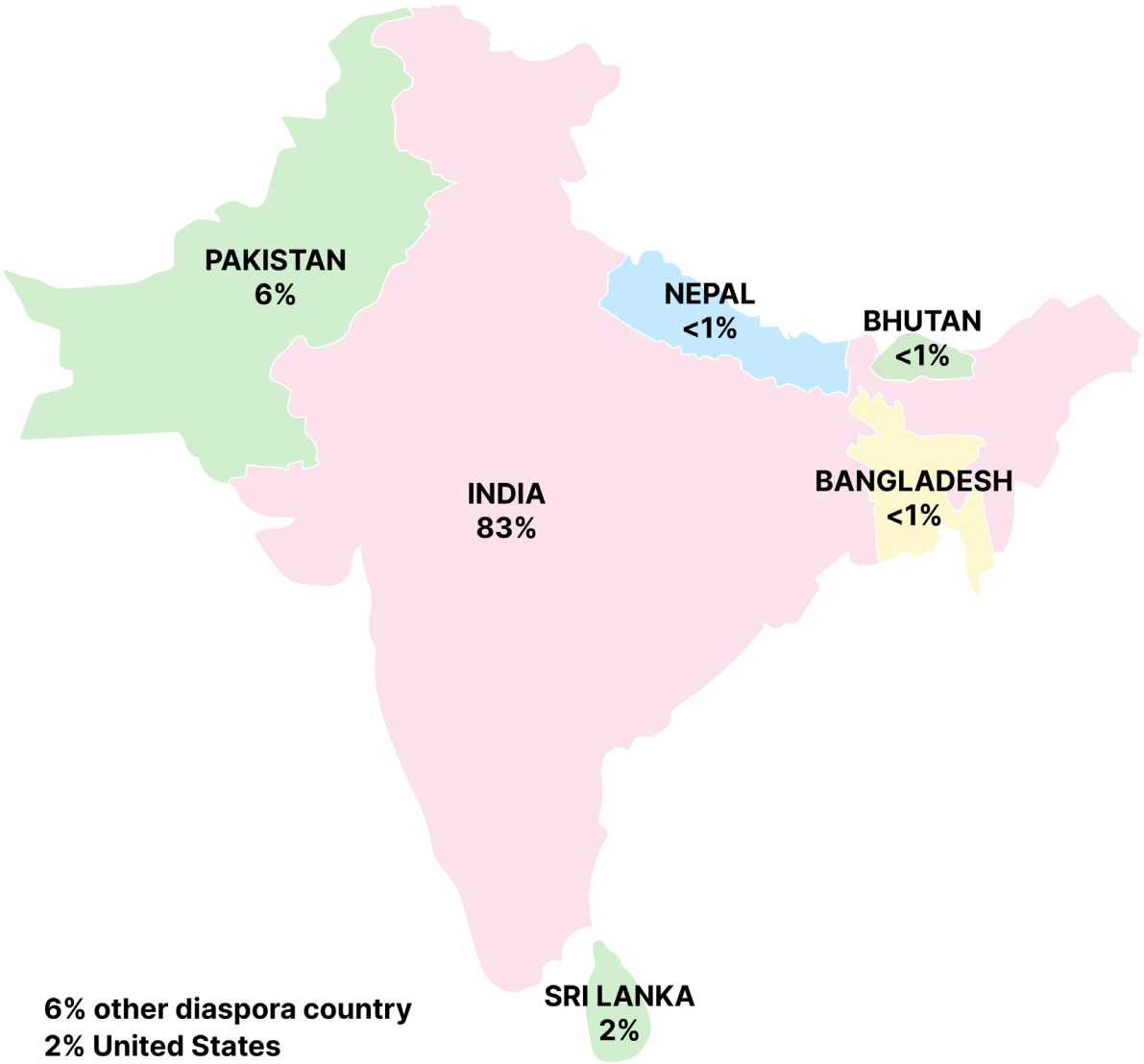
906 participants | **749** | **+258**

Wave B

Enrolling 1,150:
-Bangladeshi
-Pakistani

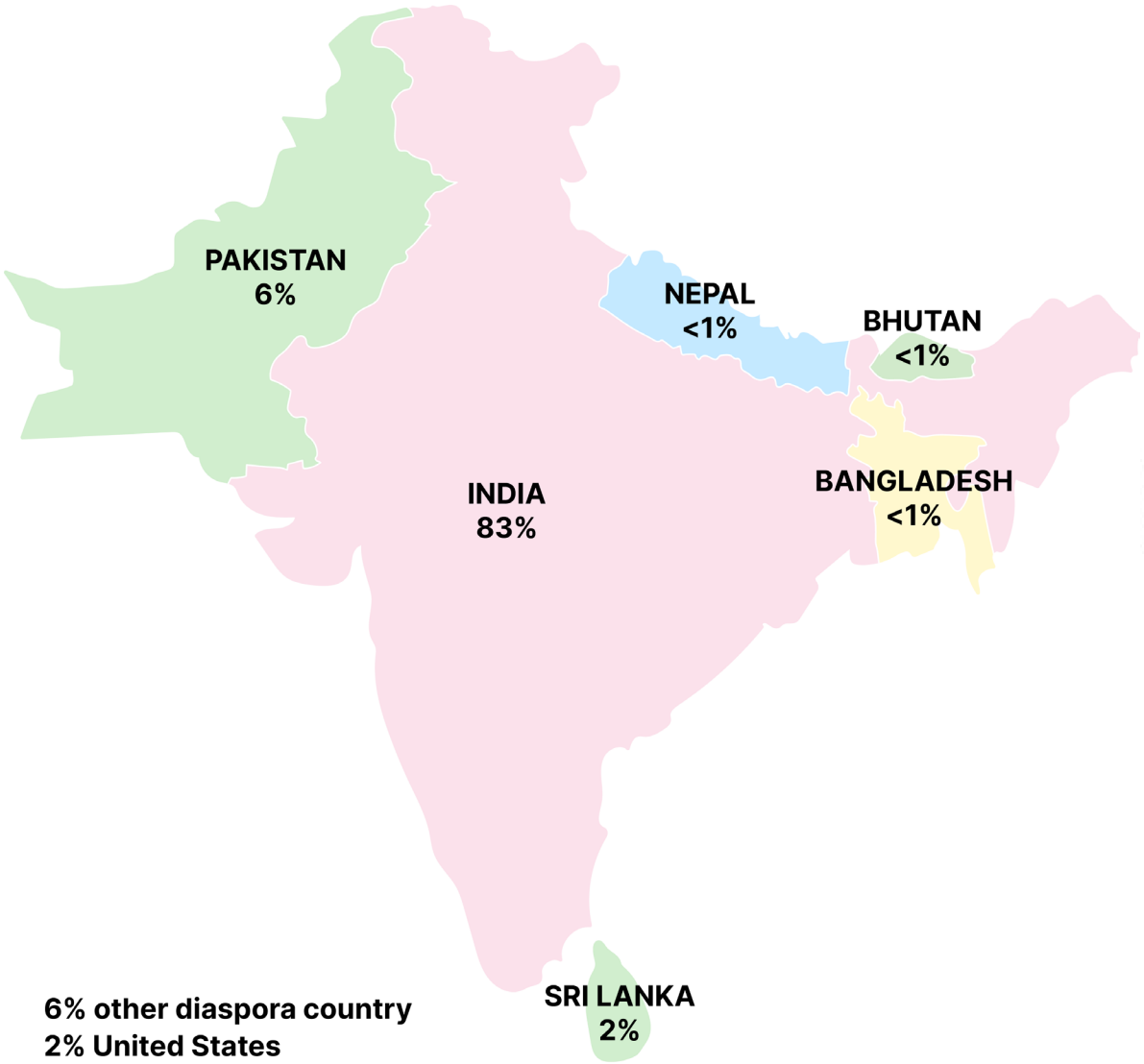
Current Cohort size: 1,164
Projected Cohort size: 2,300

98% are immigrants



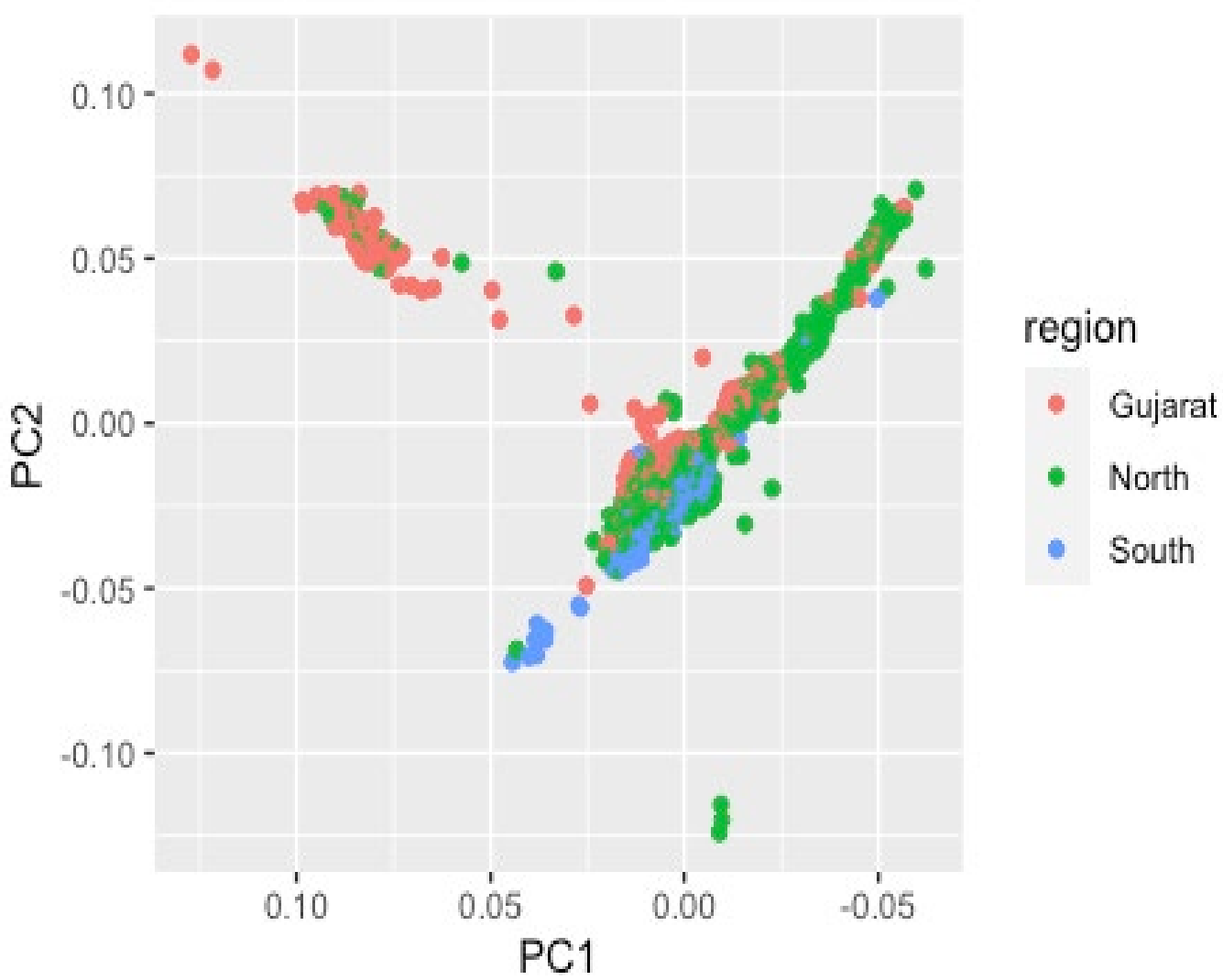
6% other diaspora country
2% United States

98% are immigrants

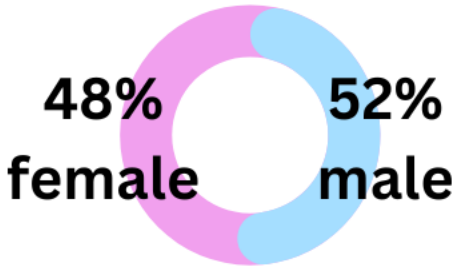


6% other diaspora country
2% United States

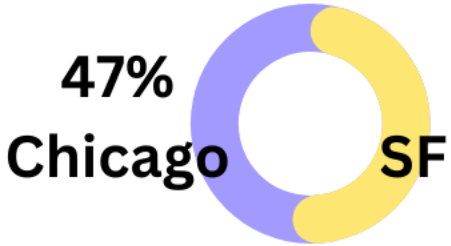
Genetic Ancestry



Who?

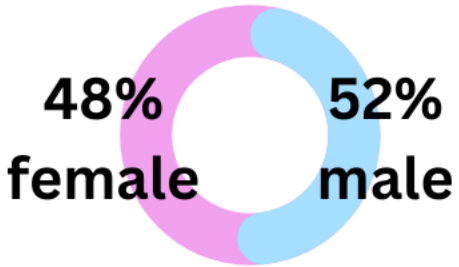


Gender

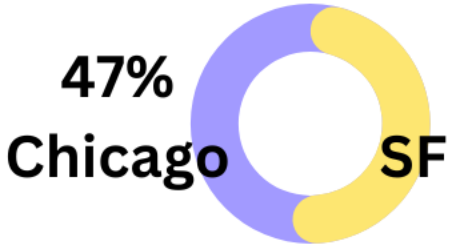


Study Site

Who?



Gender



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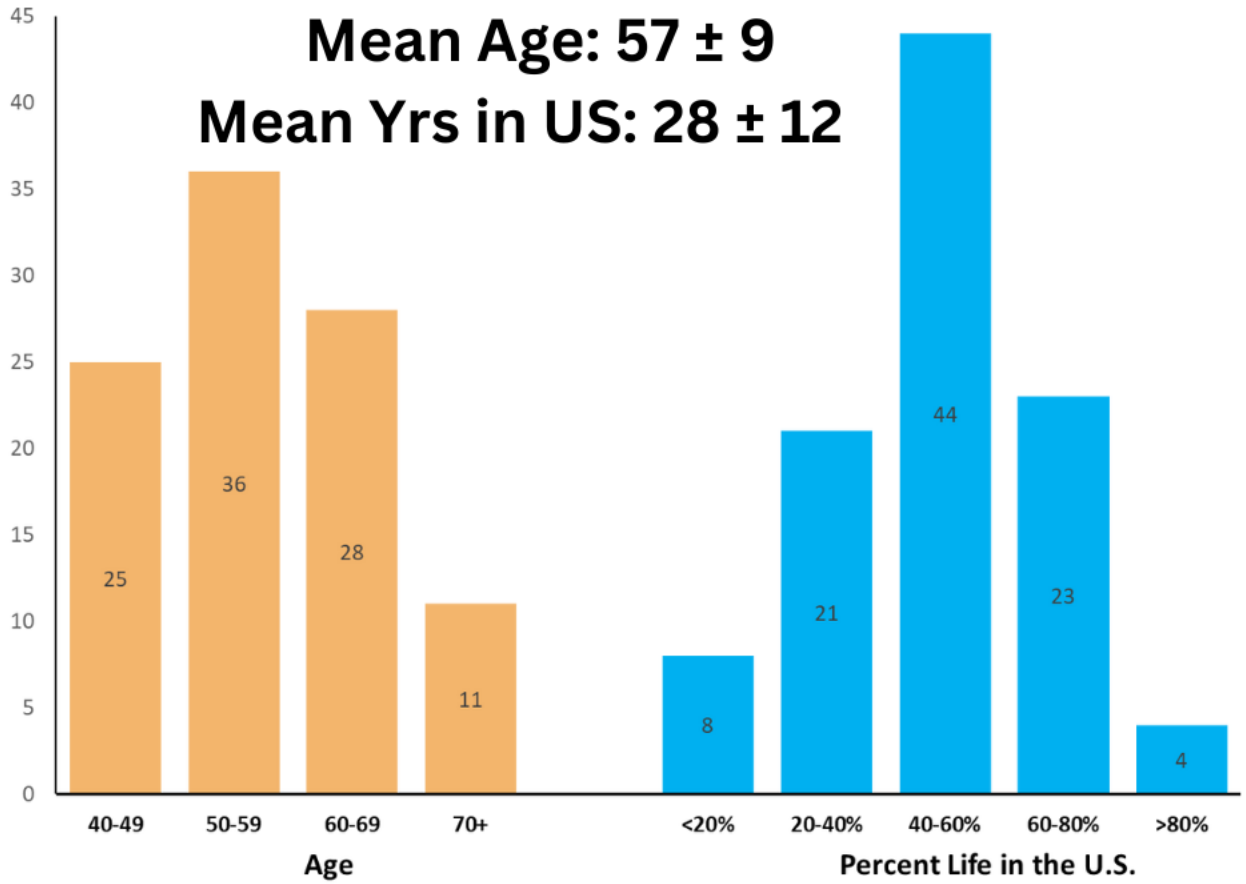
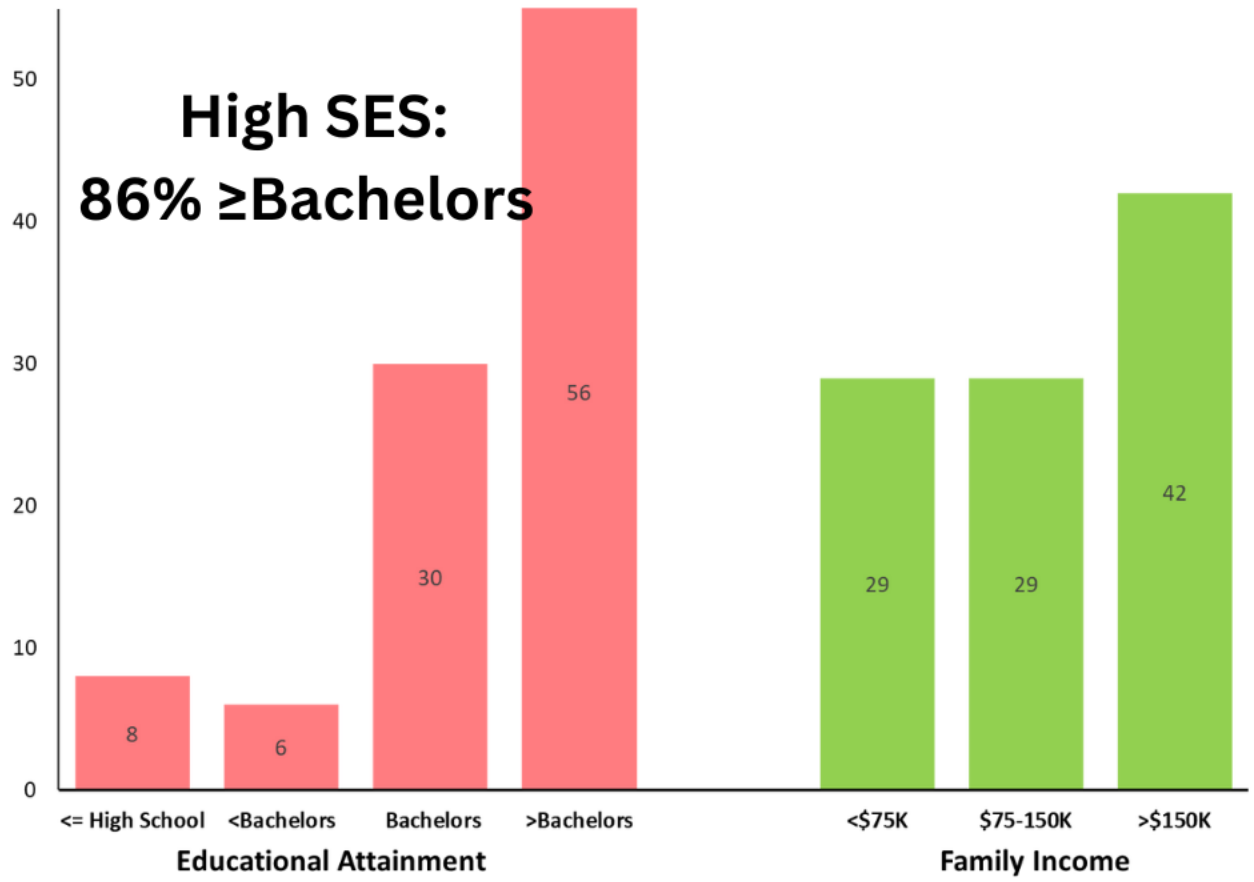


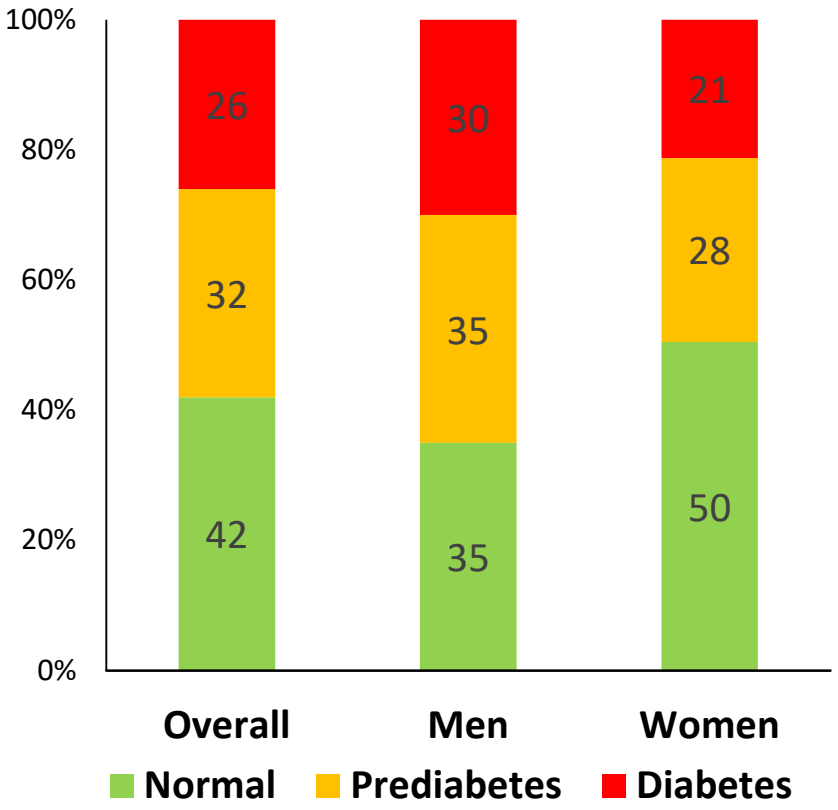


Roadmap

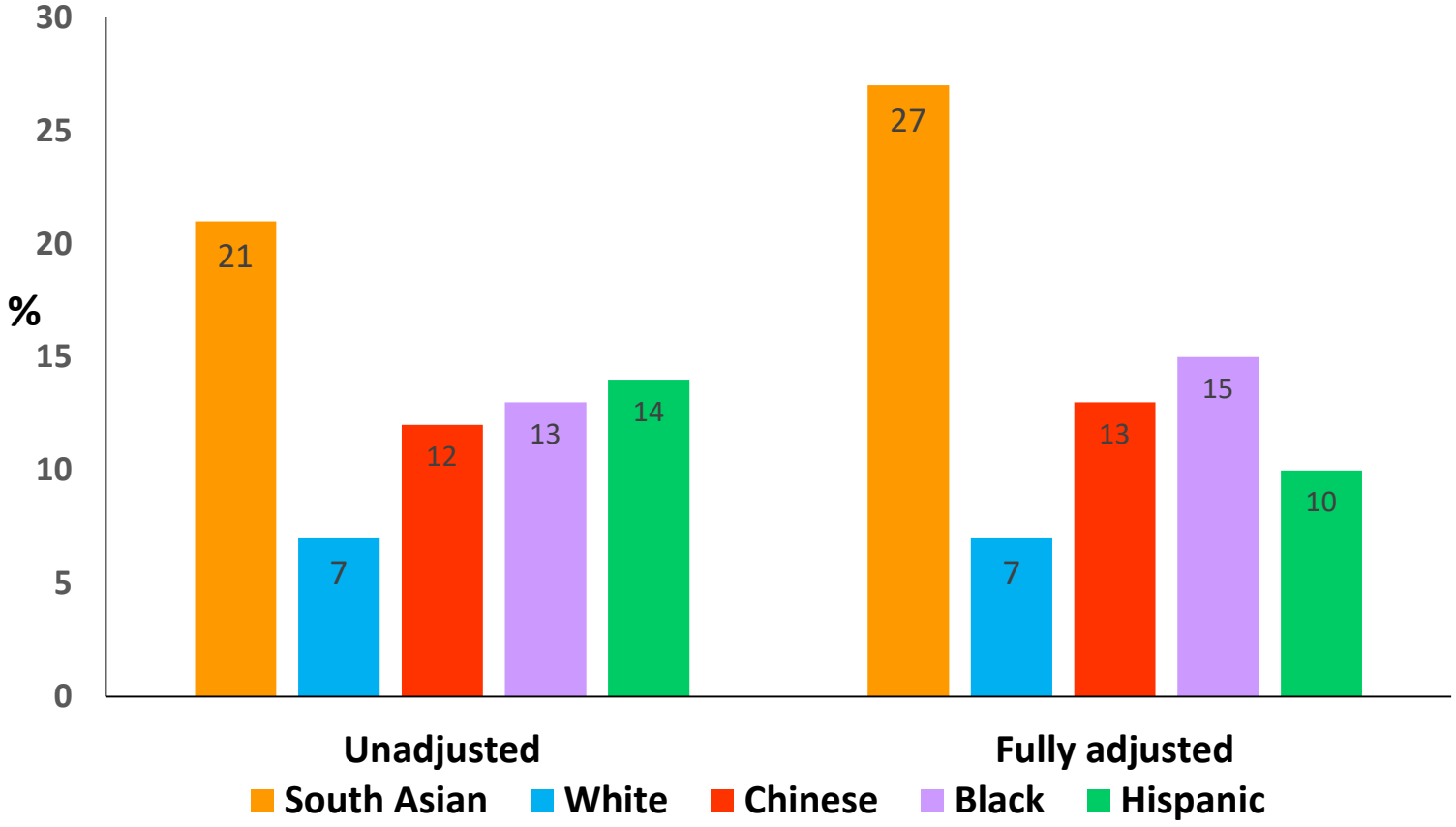
1. Diabetes
2. Body Composition
3. Atherosclerosis and other risk factors
4. Modifiable factors

Diabetes Prevalence

South Asians: Glucose Tolerance



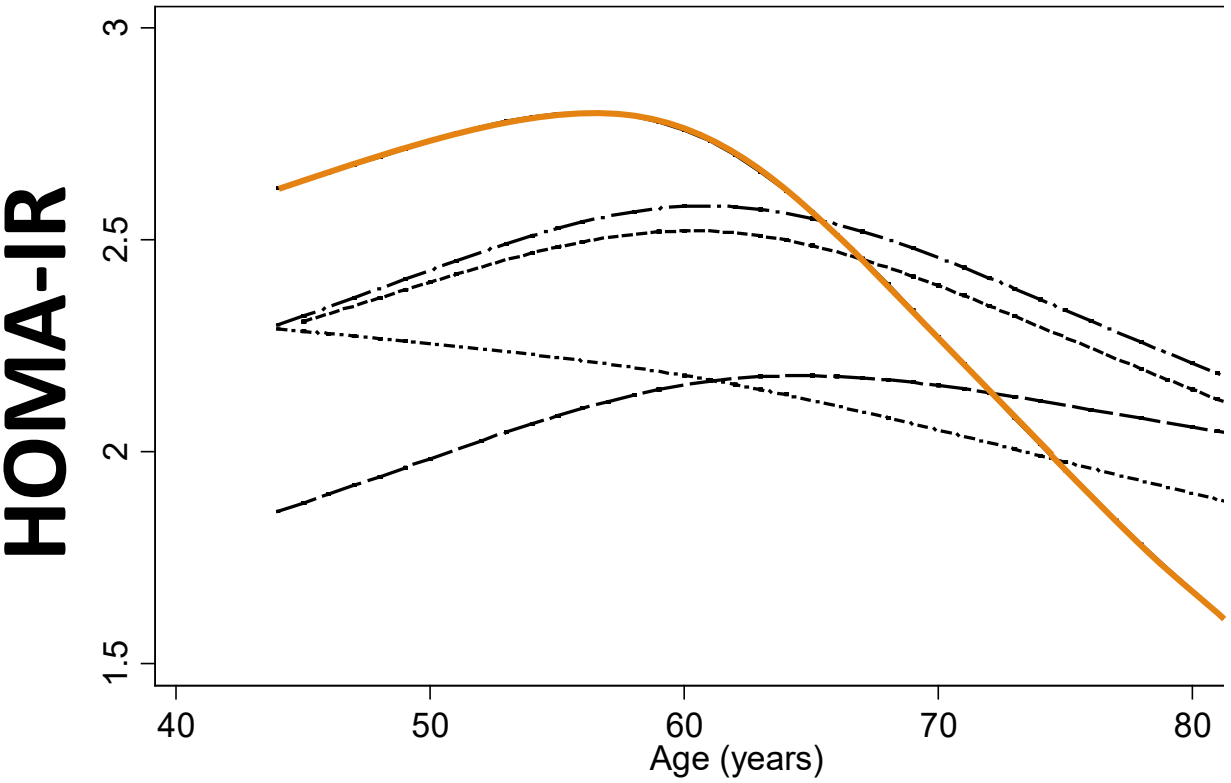
Diabetes in South Asians vs. MESA groups

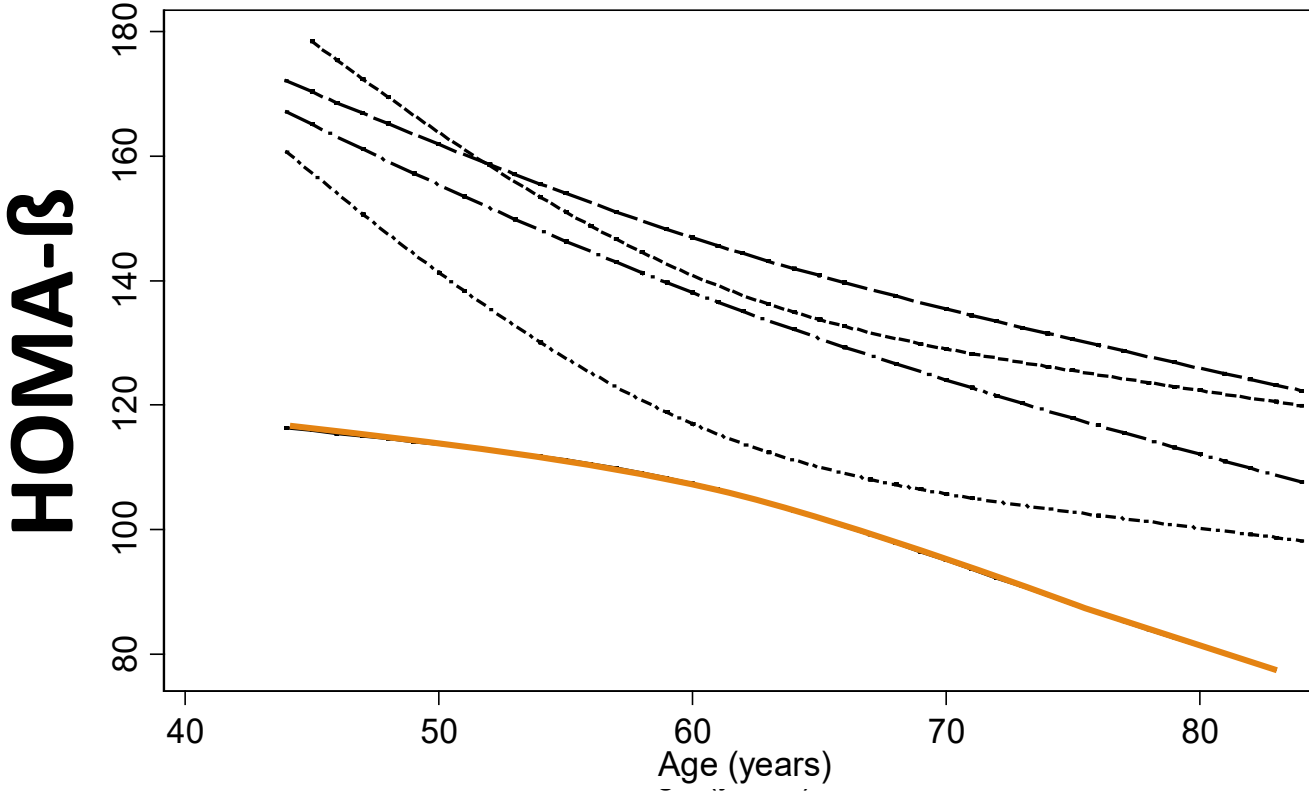


Kanaya, *Diabetes Care*, 2014

Flowers, *Diabetes Care*, 2019

More Insulin Resistance and Lower ß Cell function

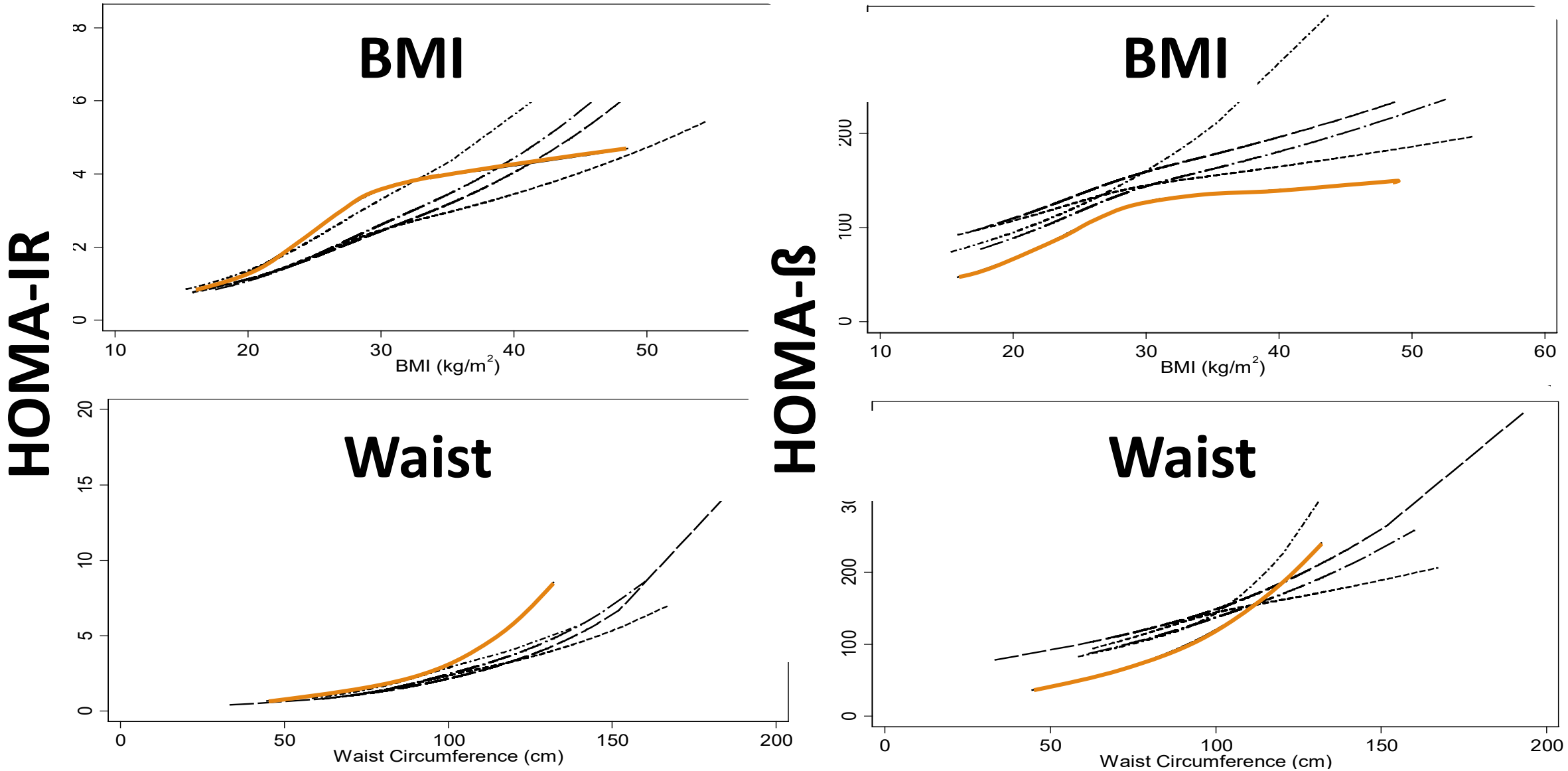




South Asians
Whites
African Americans
Latinos
Chinese

Kanaya, *Diabetes Care*, 2014

…and across all BMI and Waist circumference



MESA and MASALA diabetes subtypes

- 1,293 participants with T2DM

  240 White, 387 Black, 324 Hispanic, 125 Chinese, 217 South Asian
- 5 variables: age, BMI, HbA1c, HOMA-IR, and HOMA-B
- Compare distribution of subtypes
- Future diabetes complications (kidney, coronary artery calcium)

Banks, *JCEM*, 2021

Type 2 diabetes: 5 distinct subtypes

Cluster 1: Older age at onset (44%)

Cluster 2: Severe hyperglycemia (26%)

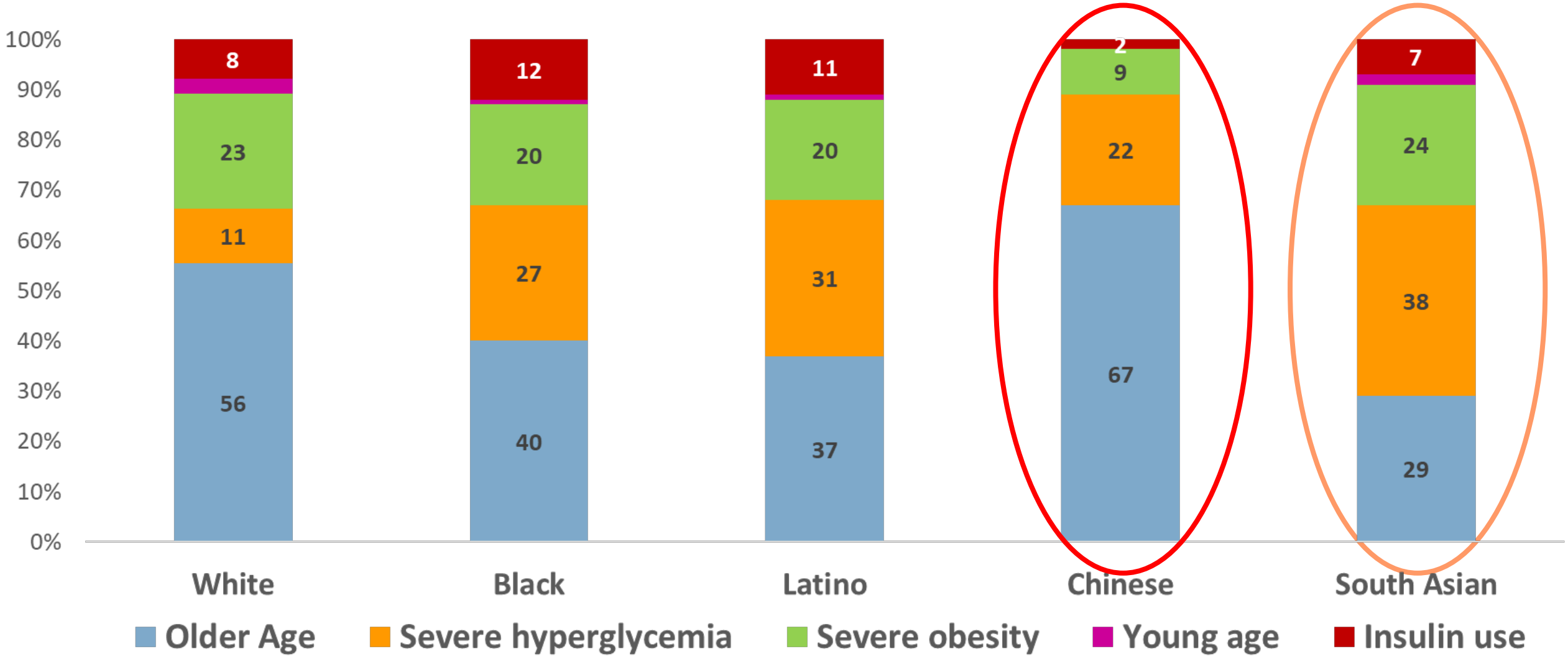
Cluster 3: Severe obesity (20%)

Cluster 4: Insulin use (9%)

Cluster 5: Younger age at onset (1%)

Banks, *JCEM*, 2021

Distributions of Subtypes by Race/Ethnic Group

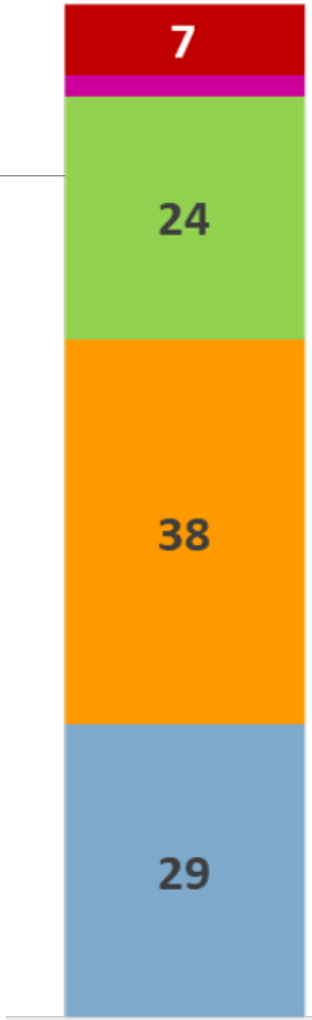


Longitudinal Outcomes by Subtype …and why does subtype matter?

1. **Severe hyperglycemia (38%):** highest incident CAC
   - consider newer agents (SGLT2i or GLP1a) to lower CVD risk

2. **Older age at onset (29%):** least aggressive (few outcomes)
   - May need less medications or less tight control

3. **Severe Obesity (24%):** no higher CKD or atherosclerosis
   - weight loss, metformin, TZDs



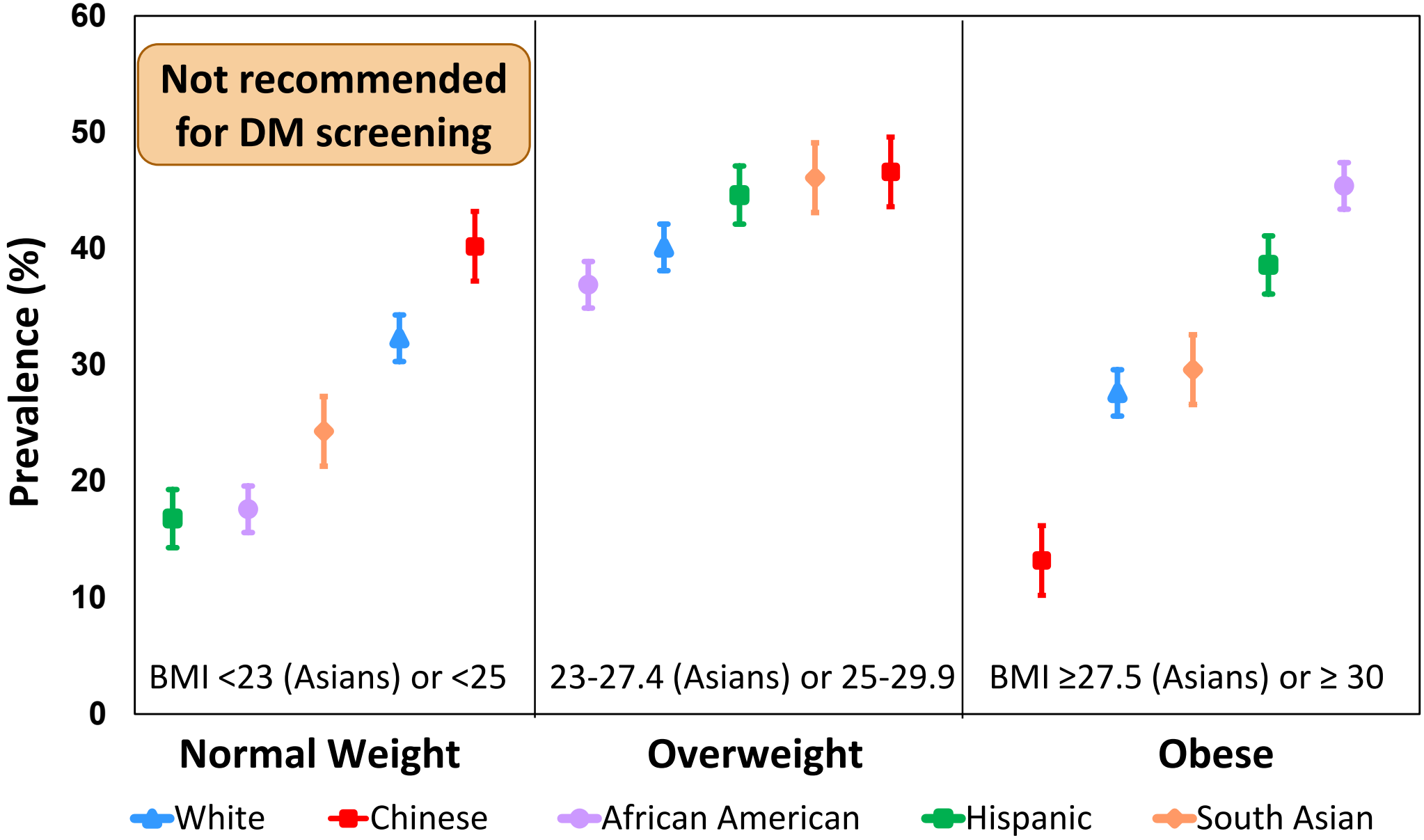
Banks, *JCEM*, 2021

Asian Populations

Non-Asian Populations

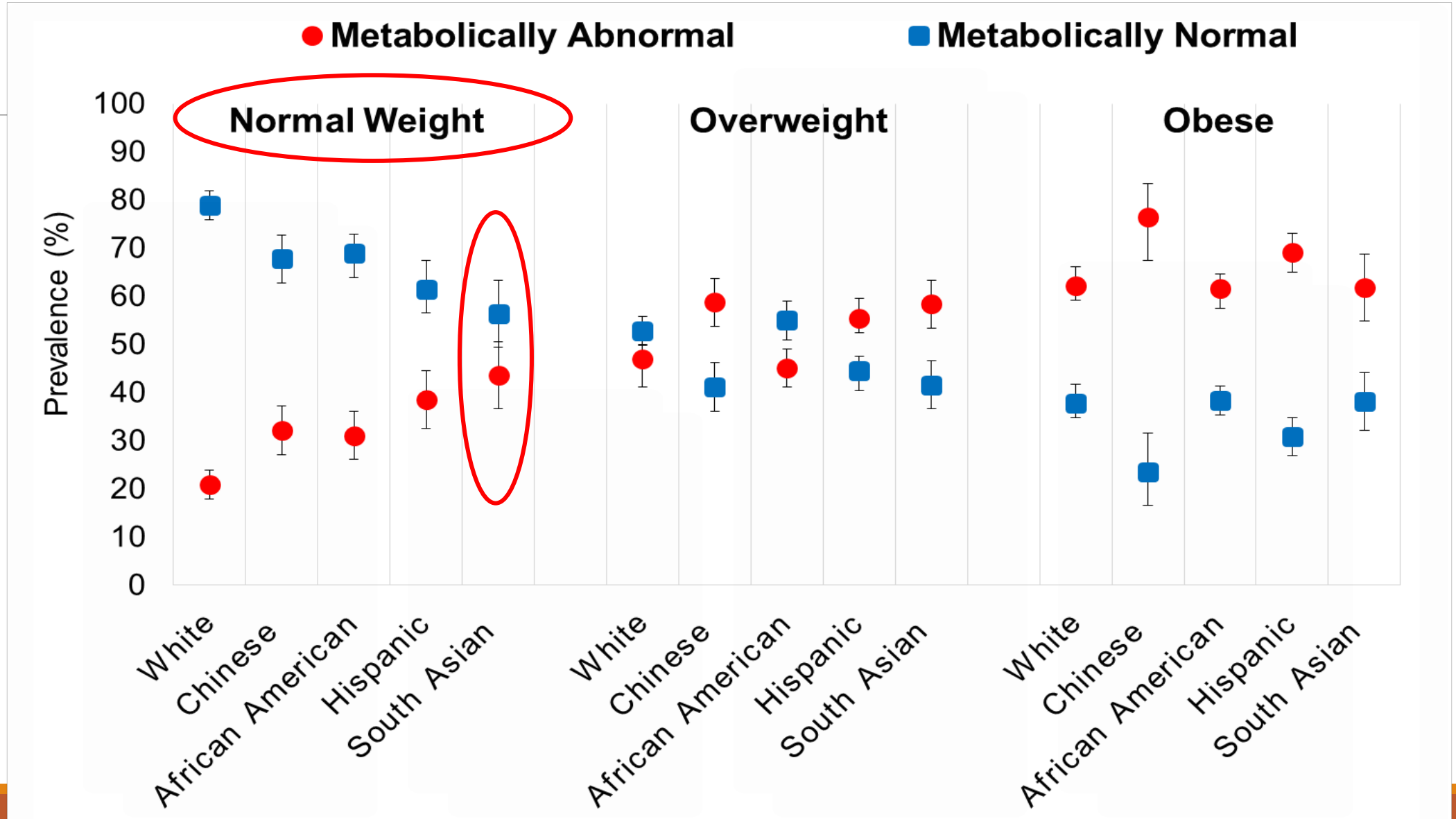
Varghese, *Primary Care Diab*, 2022

Body Mass Index Categories



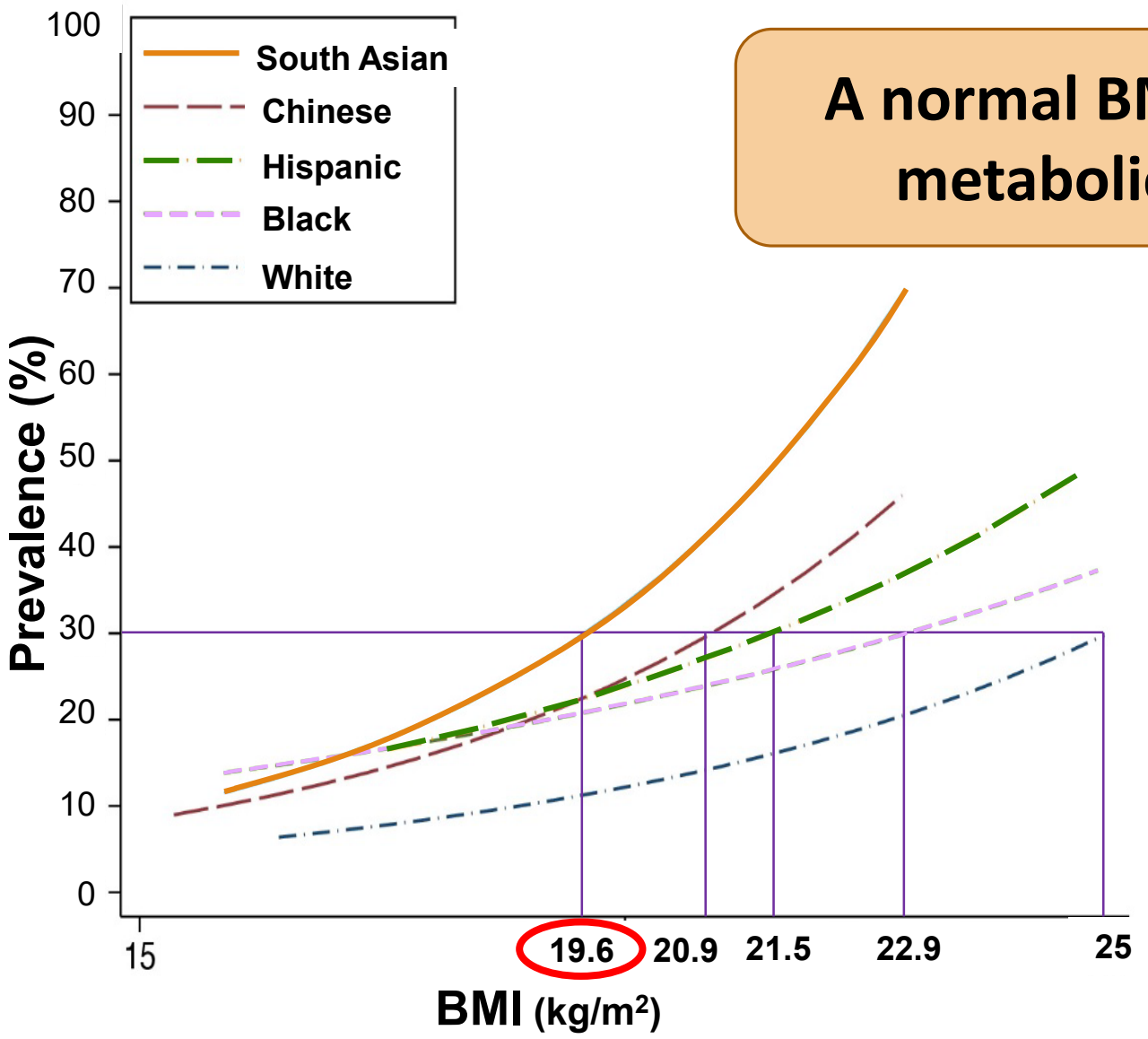
Gujral, *Annals Int Med*, 2017

Metabolic Status by BMI and Race/Ethnicity



Gujral, *Annals Int Med*, 2017

South Asian BMI 19.6 ≈ White BMI 25



A normal BMI ≠ low risk of metabolic risk factors

Gujral, *Annals Int Med*, 2017

Hidden Fat Stores

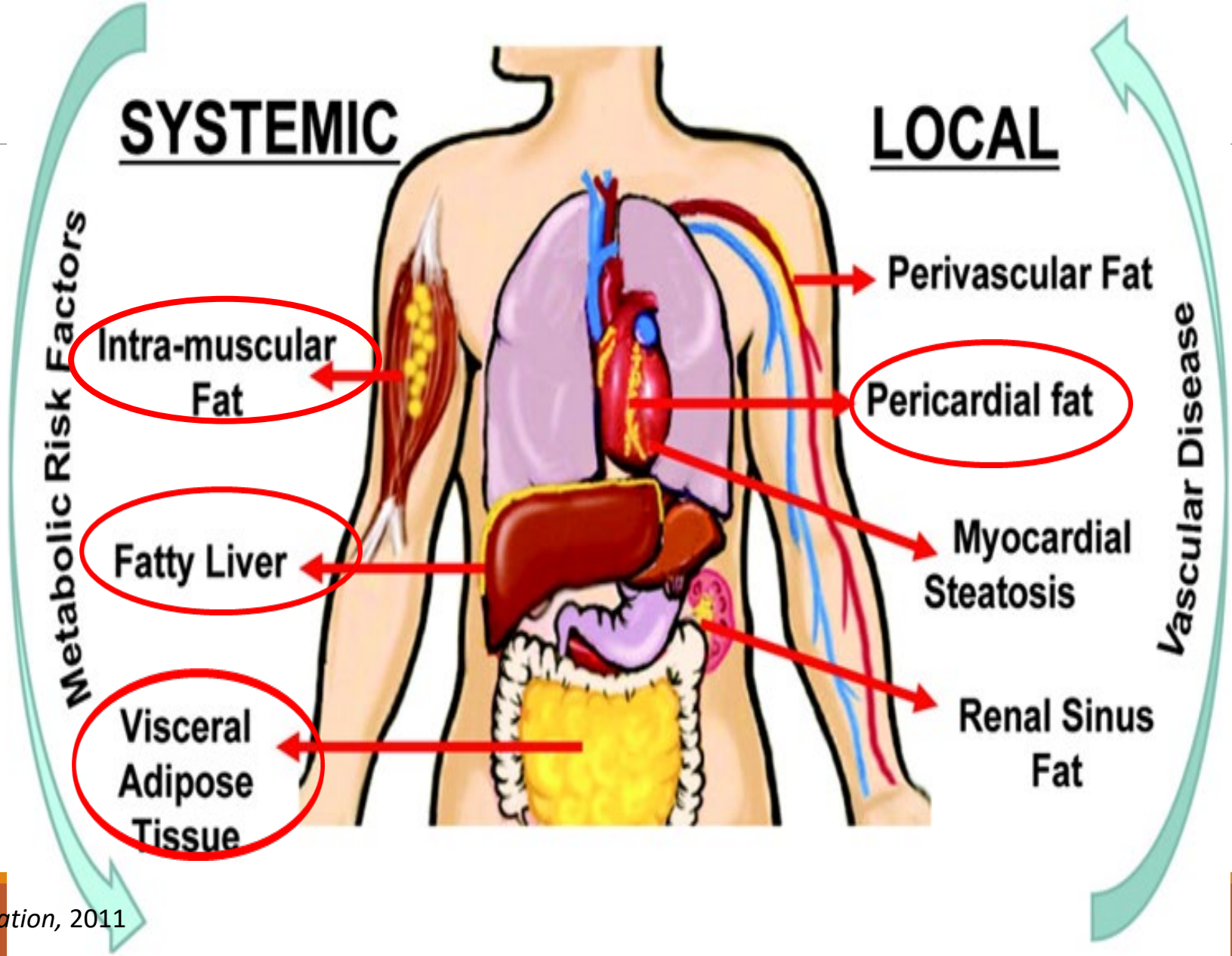
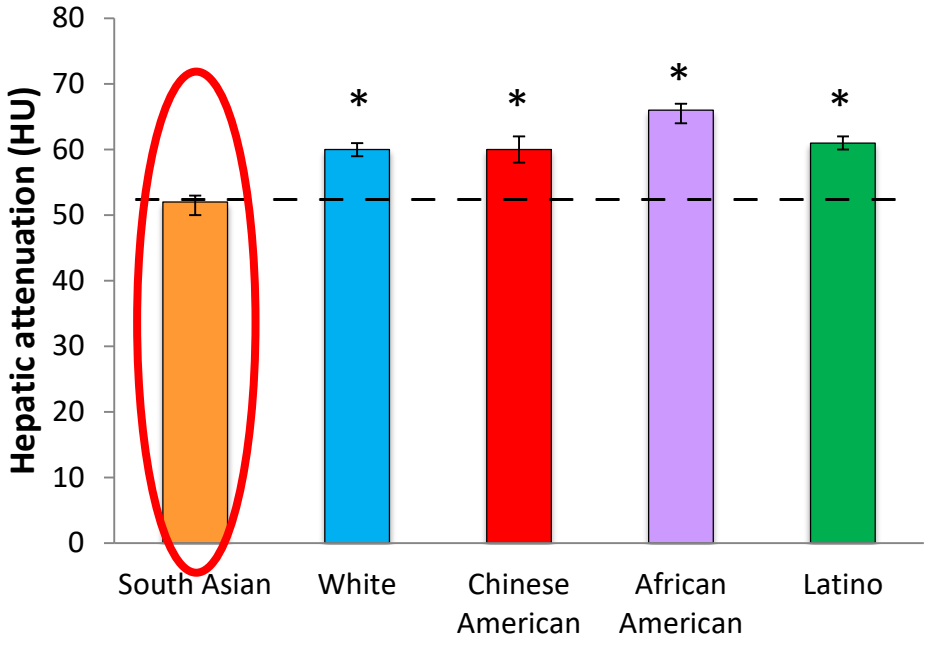
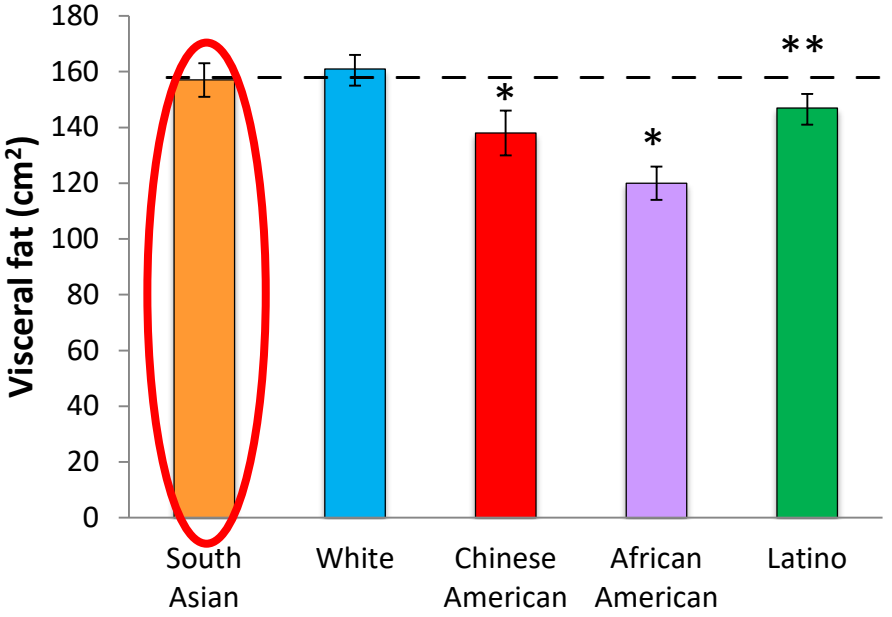
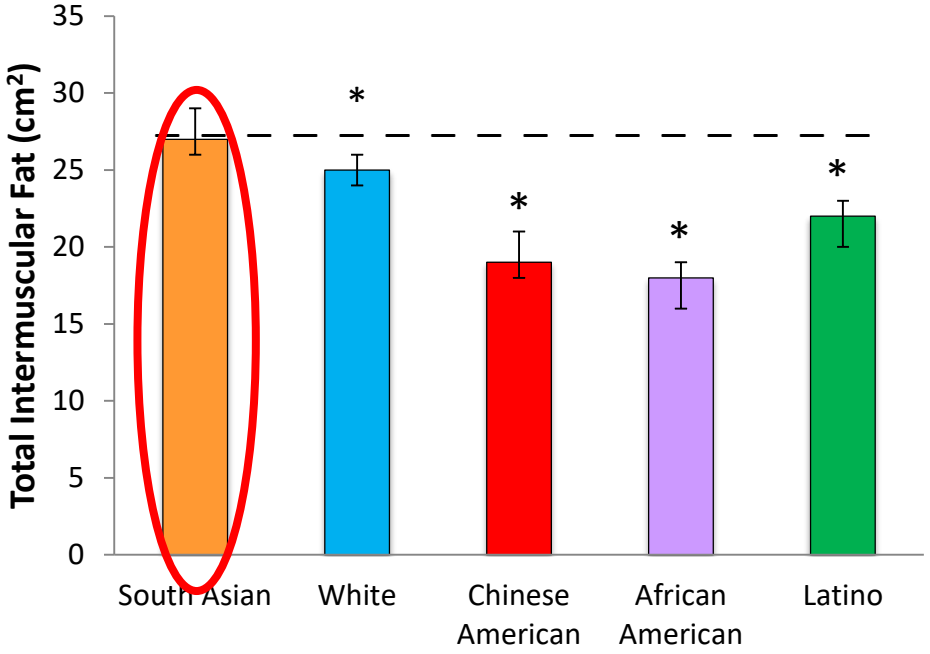


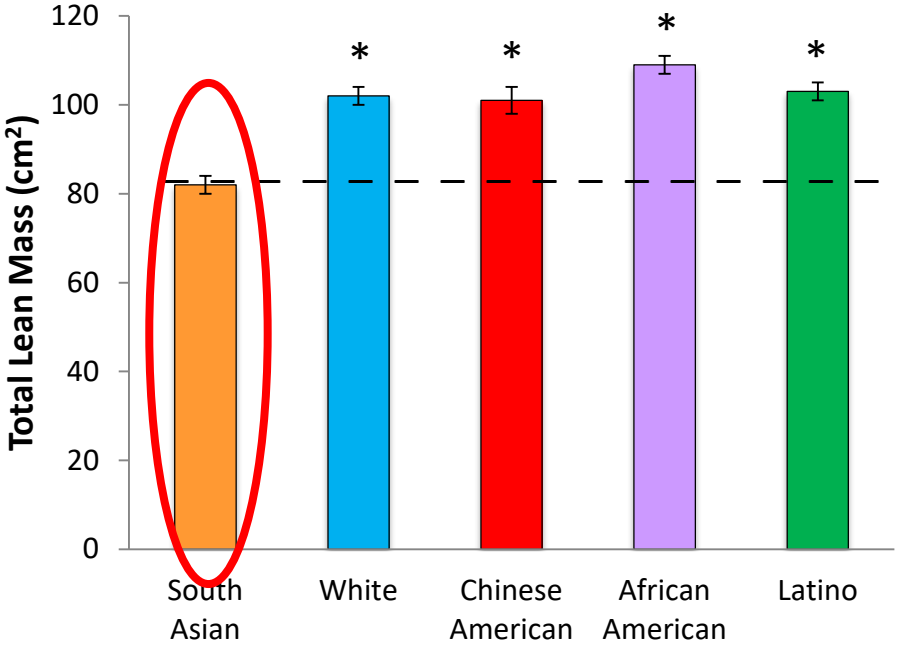
Image courtesy of AHA, *Circulation,* 2011

South Asians store fat in the wrong areas





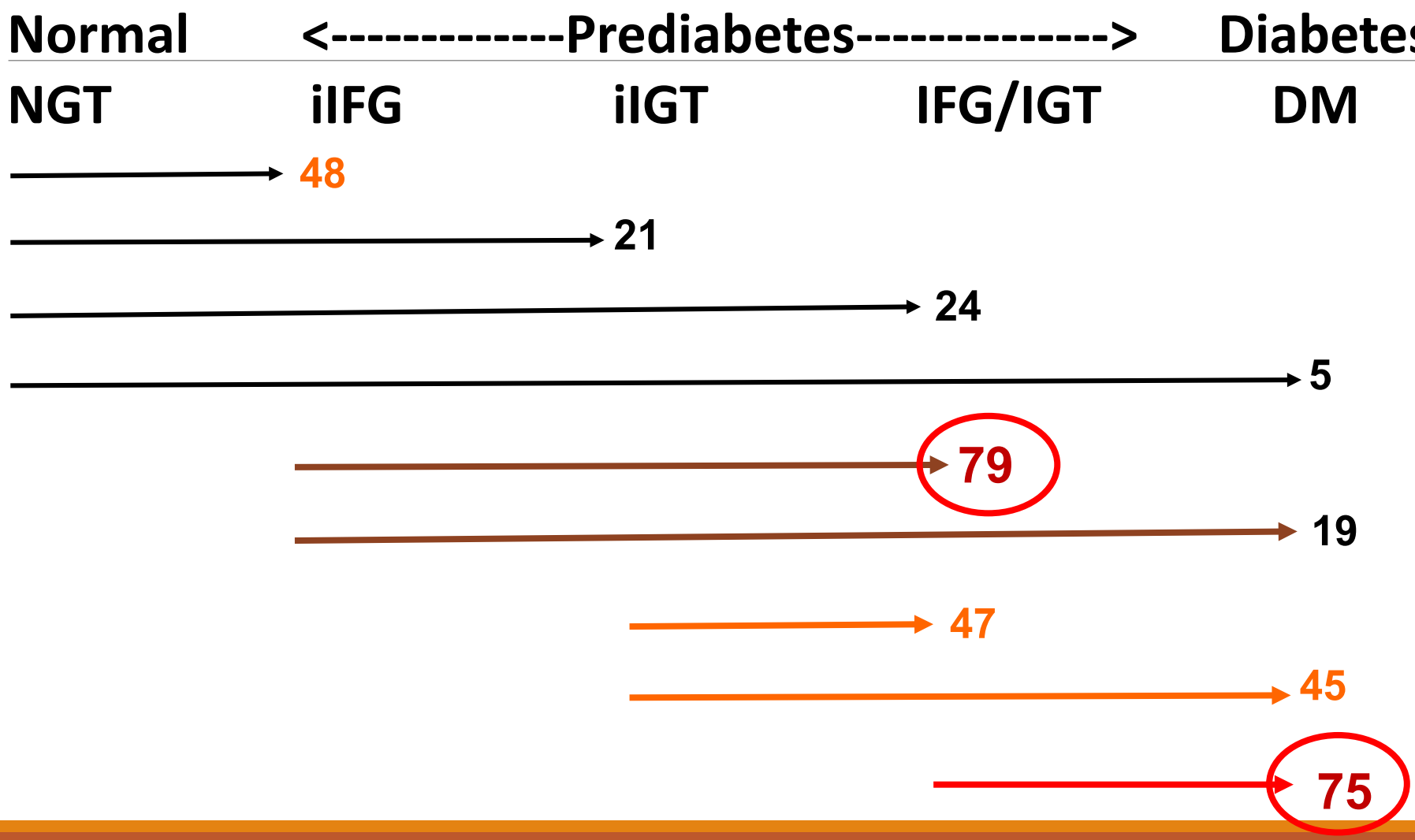




Shah, *Intl J Obes*, 2016

Glycemic Progression Rates

per 1,000 person-years



Overall Diabetes Incidence 19.9

Gujral, *BMJ Open Diab Res Care*, 2020

Predictors of Glycemic Progression

Final Model	Any Glycemic Progression OR (95% CI)
Age, years	1.04 (0.84 - 1.28)
Male sex	1.15 (0.76 - 1.75)
Visceral Fat area, cm^2	**1.34 (1.05 - 1.71)**
Hepatic attenuation (HU)	**0.69 (0.55 - 0.87)**
Hypertension	**2.28 (1.49 - 3.49)**

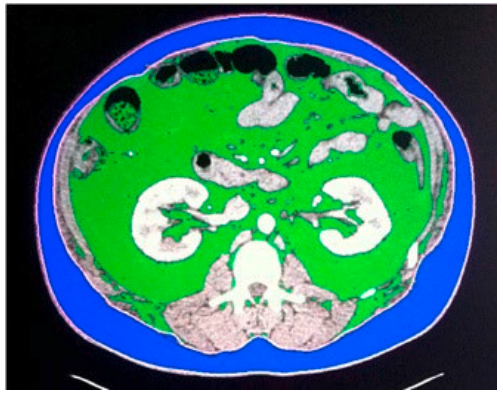
→ **NGT progression to PreDM or DM**

→ **PreDM progression to DM**

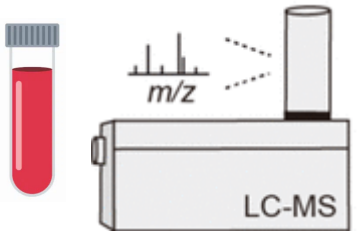
Gujral, *BMJ Open Diab Res Care*, 2020

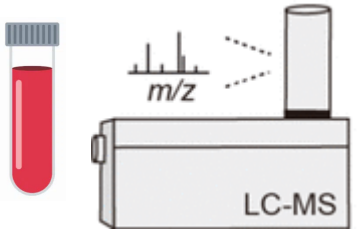
Metabolite risk scores for ectopic fat predict T2DM

Liver steatosis



Visceral fat





267 metabolites = MET-Liver score

313 metabolites = MET-Visc score

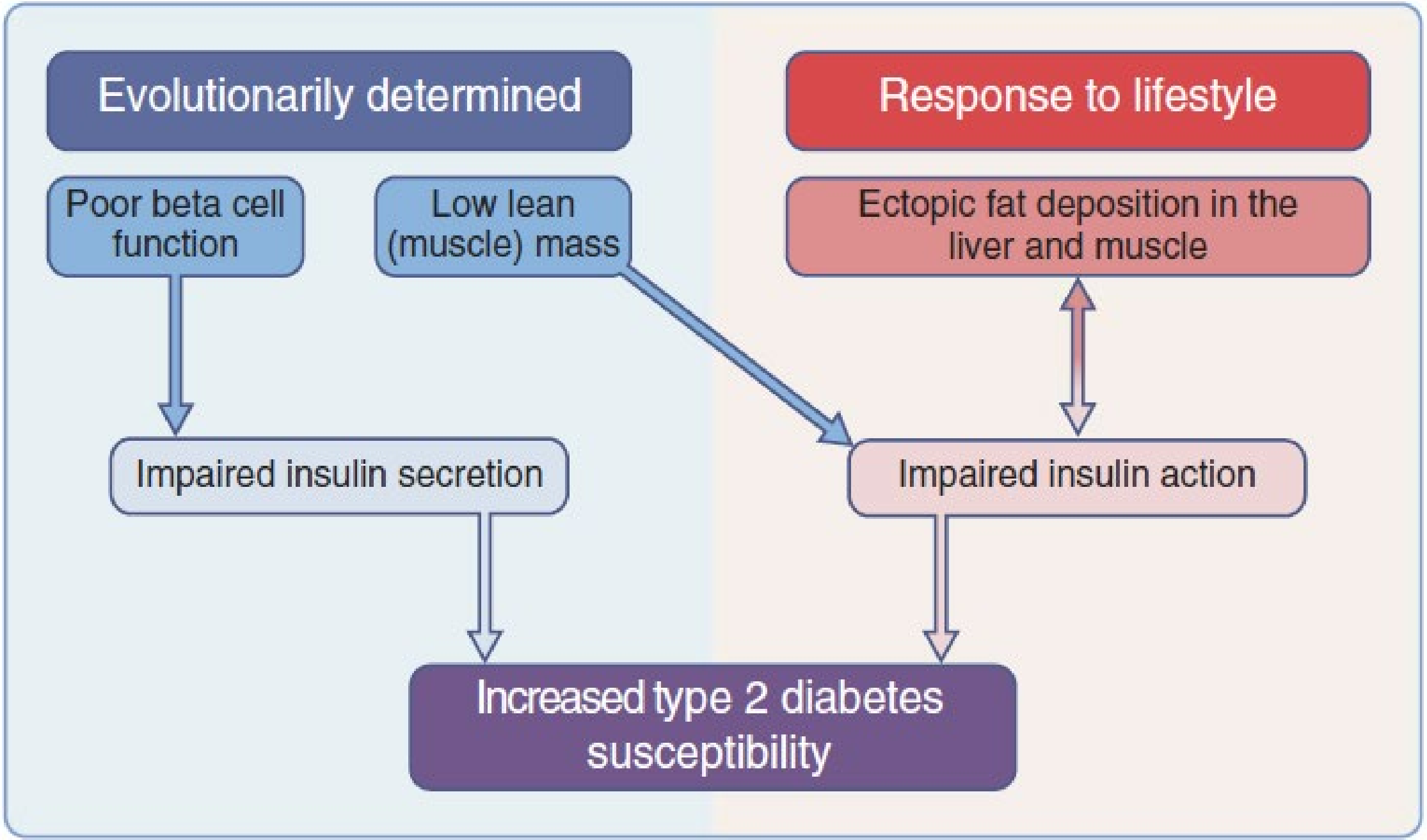
**OR 1.87 (1.06-3.27), p=0.03

***OR 2.38 (1.34-4.25), p<0.001

Incident Diabetes*

*adjusted for age, gender, site, BMI, energy intake, AHEI-2010, physical activity, use of lipid-lowering meds, and CT-measures of respective fat depot

Gadgil, *Intl J Obesity*, 2024



Narayan & Kanaya, *Diabetologia*, 2020

Cholesterol comparisons

(among non-medication users)

(mg/dl)	SA n=634	White n=2162	Black n=1581	Latino n=1285	Chin. n=685
Total Chol.	197±33	199±35	191±36*	199±38	194±31
LDL	120±29	120±30	118±33	121±33	117±28
HDL	51±14	53±16	52±15	47±13*	49±13*
TG	131±76	130±90	103±68*	154±92*	140±83*

* p<0.001 in comparison to SA, adjusted by sex and age

Lipoprotein(a) Comparison

	SA n=906	White n=2622	Black n=1893	Latino n=1496	Chin. n=803
Lp(a), mg/dl	17 (9-33)	13 (6-30)*	35 (20-62)*	13 (6-29)*	13 (8-23)*

However:

- Lp(a) was not associated with atherosclerosis (CAC, CIMT)
- Lp(a) was not associated with aortic valve calcification
- Higher Lp(a) was associated with an increase in CAC density over time

* p<0.001 in comparison to SA, adjusted by sex and age

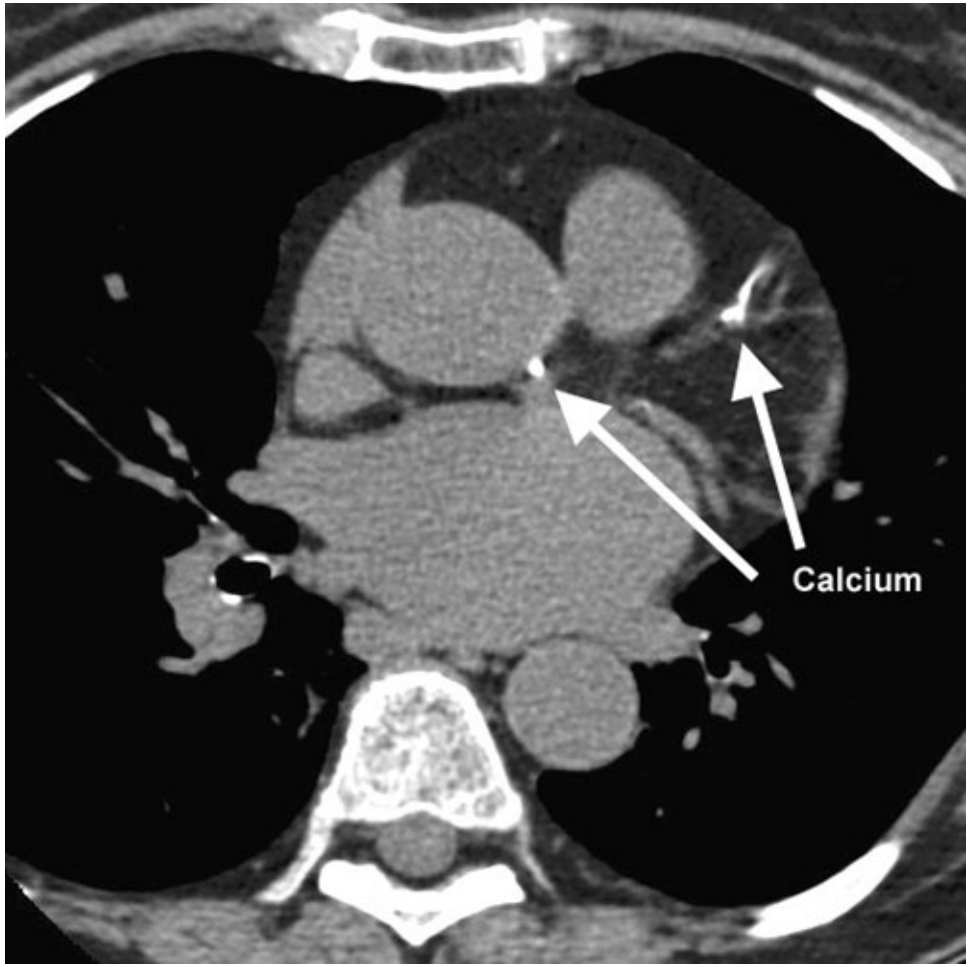
Huffman, *Am J Cardiol*, 2019
Makshood, *Atherosclerosis*, 2020
Bhatia, *Atherosclerosis*, 2022

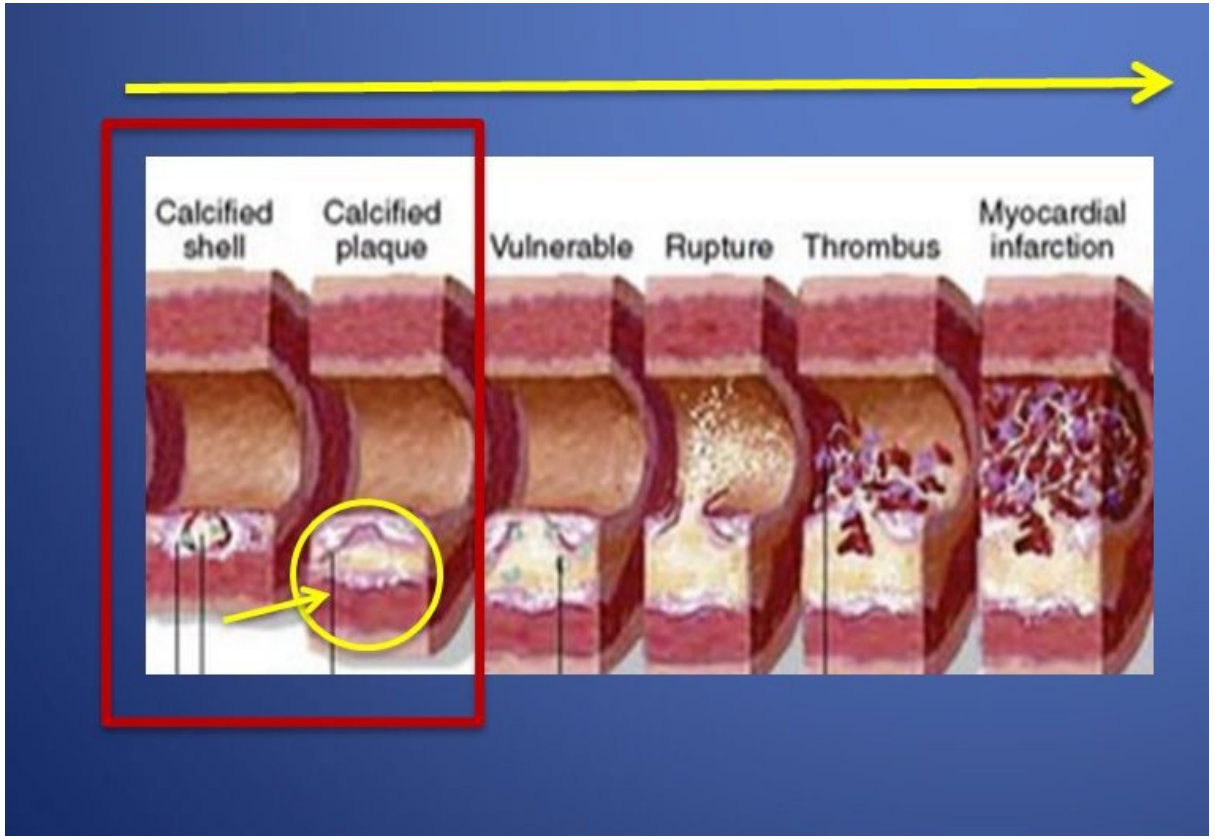
Metabolic Biomarker Comparisons

	SA n=906	White n=2622	Black n=1893	Latino n=1496	Chin. n=803
hsCRP, µg/ml	1.2 (0.6-2.8)	1.6 (0.6-4.0)*	1.7 (0.7-4.0)*	1.9 (0.8-4.9)*	0.7 (0.3-1.8)*
TNF-α, pg/ml	2.6 (1.9-3.6)	4.7 (3.4-6.4)*	4.5 (3.4-6.4)*	4.7 (3.7-6.4)*	4.2 (3.2-5.7)*
Adiponectin, ng/ml	11.8±6.6	23.9±14.0*	18.2±12.4*	19.6±11.6 *	17.1± 12.5*
Resistin, ng/ml	21.8± 11.8	16.1± 5.3*	18.0±13.7*	16.1±6.7*	15.3±7.5*

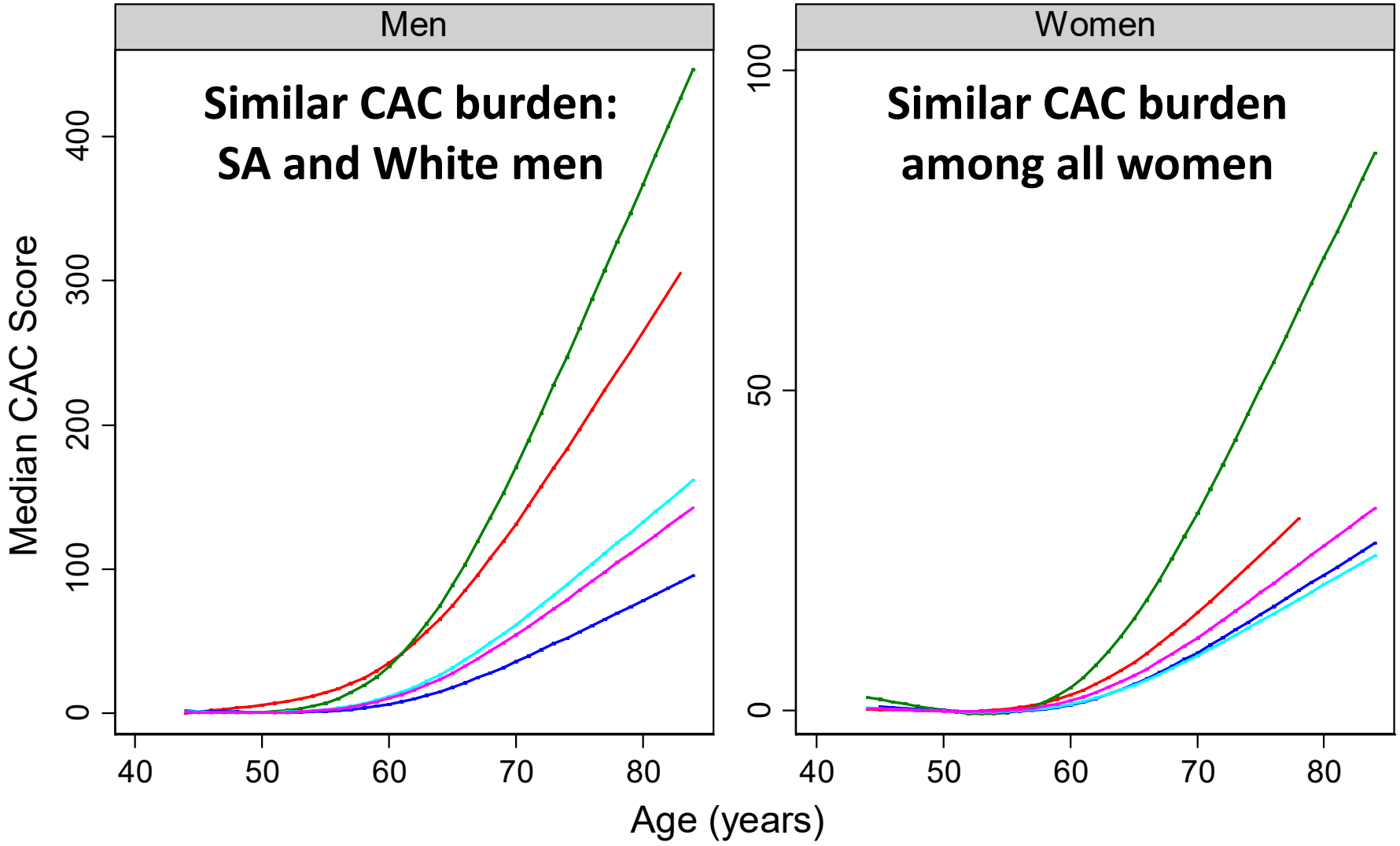
* p<0.001 in comparison to SA, adjusted by sex and age

Subclinical Atherosclerosis:
Coronary Artery Calcium (CAC)



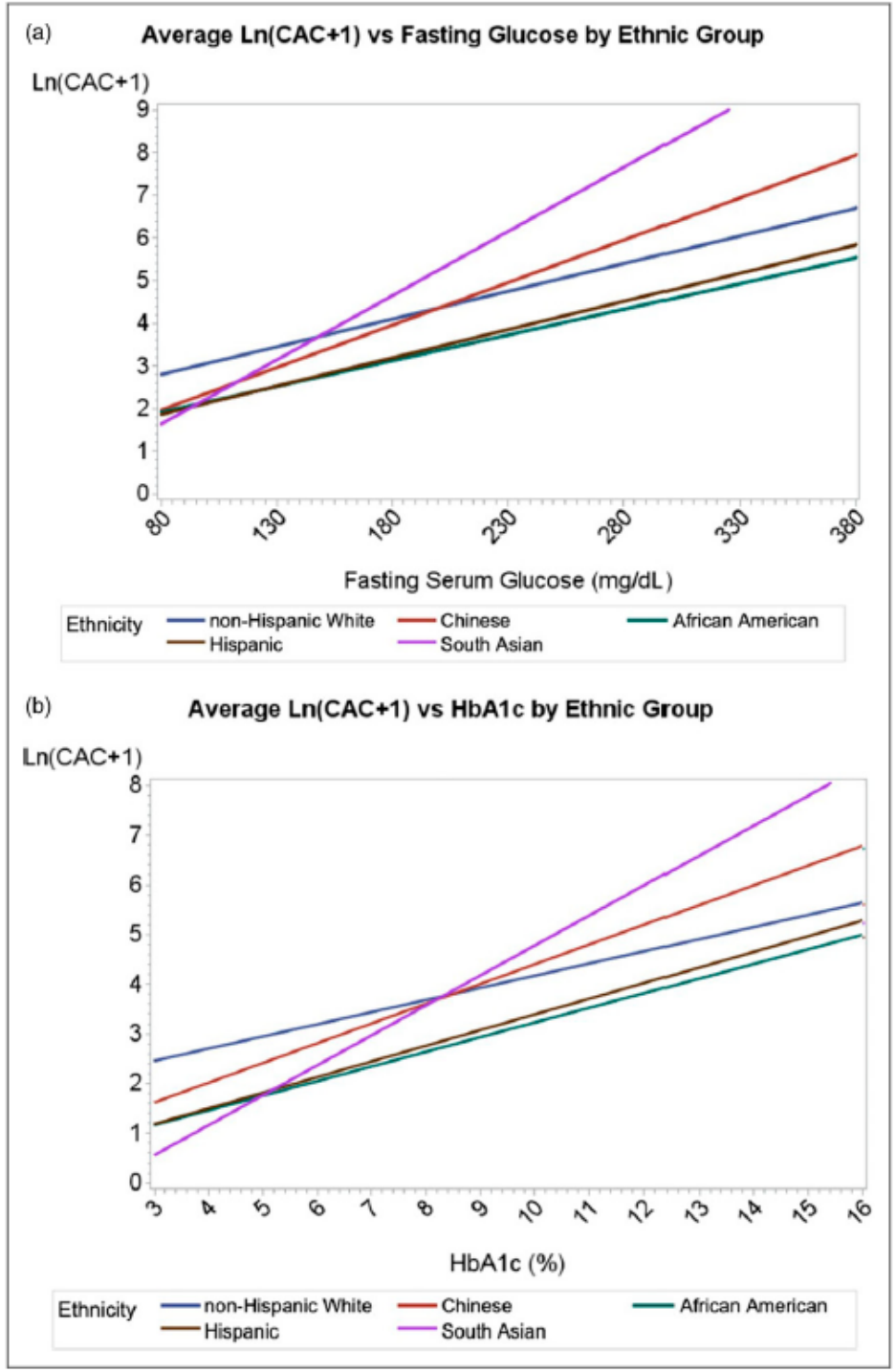


Coronary Artery Calcium



Kanaya, *J Clin Exp Res Cardiol,* 2014

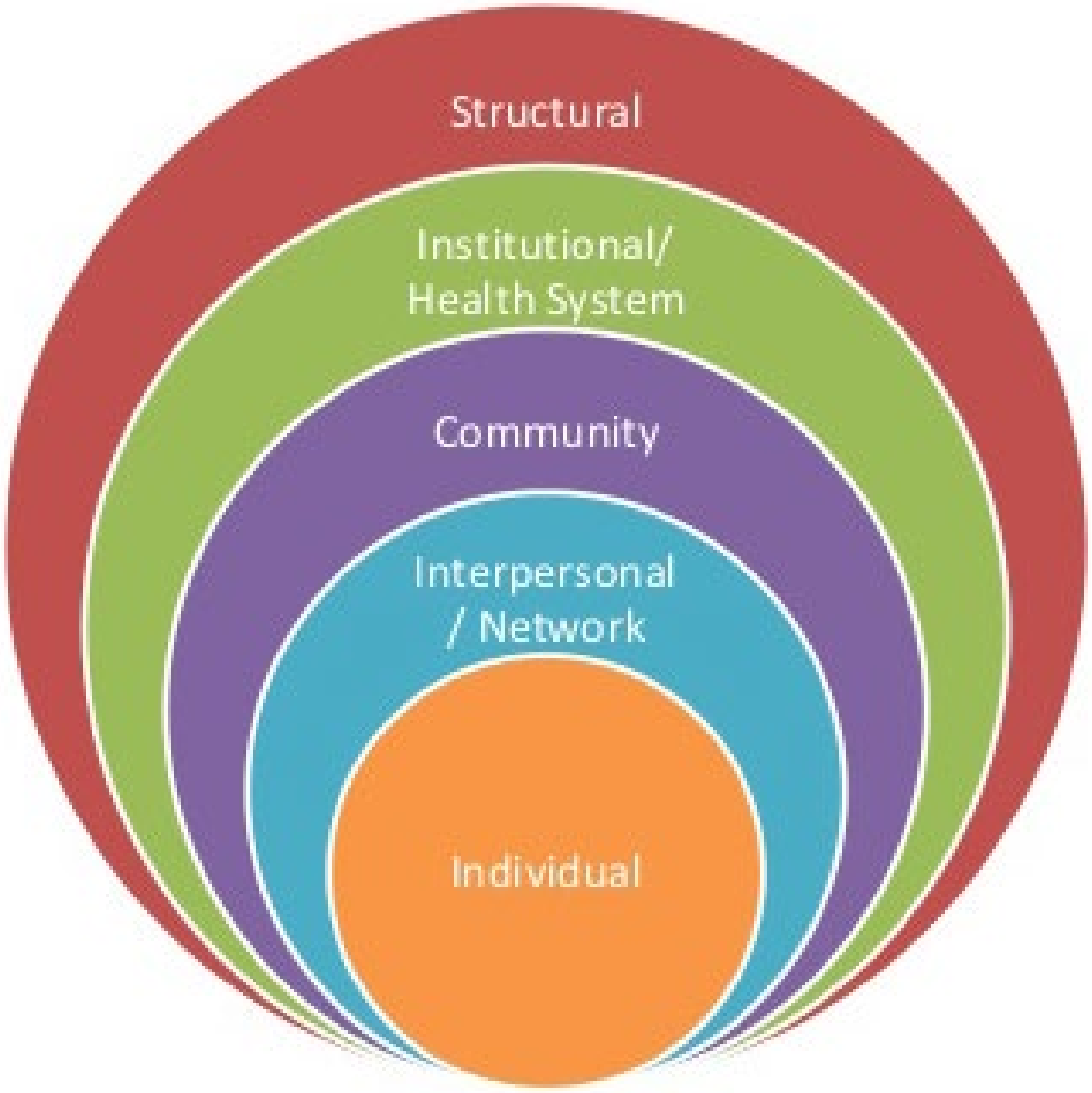
The effect of glycemia on CAC was strongest in South Asians, followed by Chinese, and NH Whites



Premoydhin, *Diab Vasc Dis Res*, 2023

Roadmap

1. Diabetes
2. Body Composition
3. Atherosclerosis and other risk factors
4. **Modifiable factors**



Societal level:

- Social determinants
- Environment
- Health care

Interpersonal level:

- Acculturation
- Social networks

Individual level:

- Diet
- Physical activity

Dietary Patterns:

- 164 item SHARE FFQ
- combined items into 29 groups
- weighted by serving size




	ANIMAL PROTEIN	FRIED SNACKS, SWEETS, HIGH-FAT DAIRY	FRUITS, VEGETABLES, NUTS, LEGUMES
+	Alcohol, coffee, eggs, fish, pasta, pizza, poultry, red meat, refined grains, vegetable oil	Added fat, butter/ghee, fried snacks, high-fat dairy, sugar-sweetened beverages, legumes, potatoes, refined grains, rice, snacks, sweets	Fruit, fruit juice, legumes, low-fat dairy, vegetable oil, nuts, vegetables, whole grains
	↑ total, LDL cholesterol ↑ weight and waist, ↑ liver fat	↓ HDL cholesterol ↑ HOMA-IR	↓ Hypertension ↓ Metabolic syndrome

Gadgil, *J Nutrition*, 2015

Dietary Patterns:

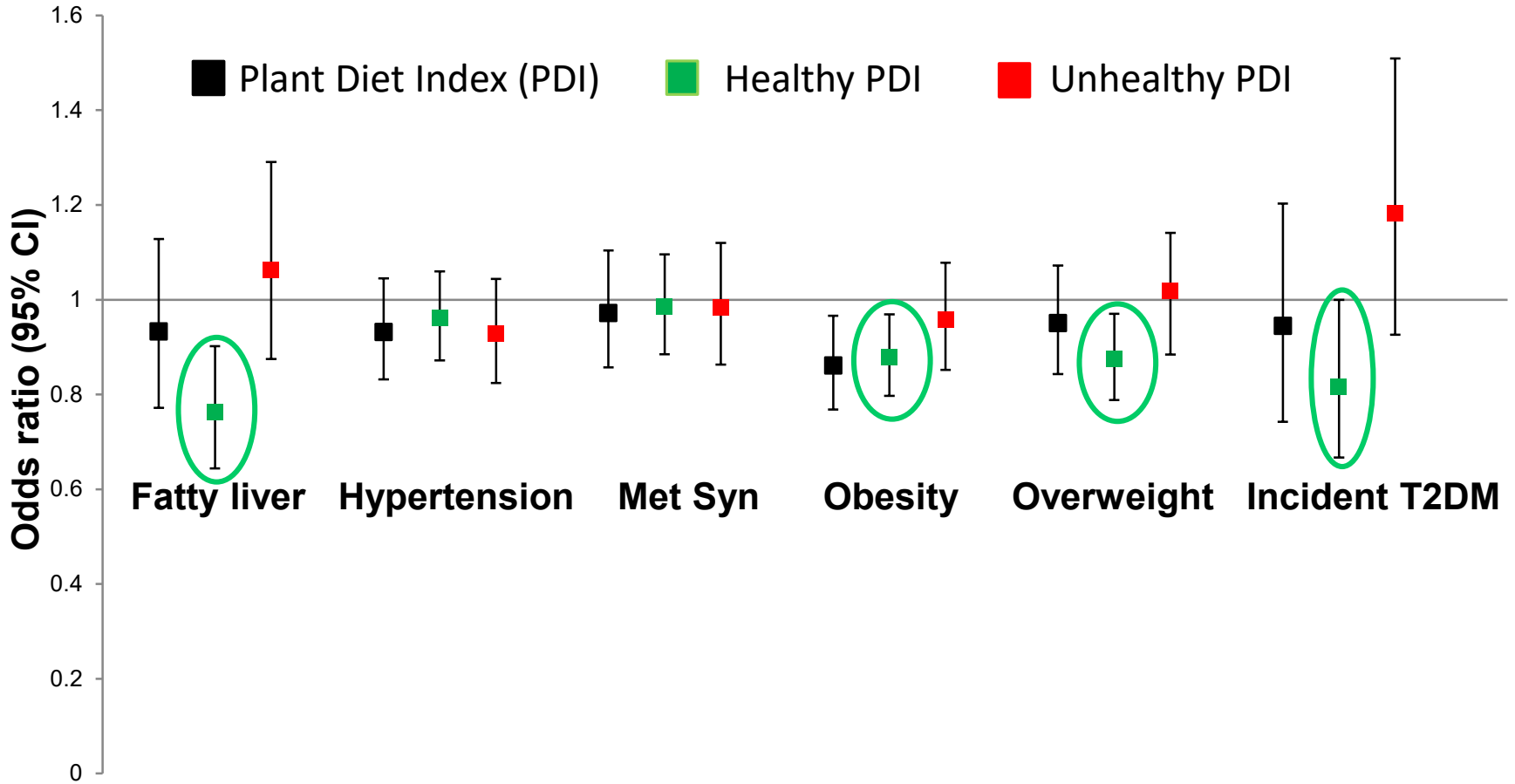
ANIMAL PROTEIN	FRIED SNACKS, SWEETS, HIGH-FAT DAIRY	FRUITS, VEGETABLES, NUTS, LEGUMES
61 metabolites: -Ceramides -Sphingomyelins -Acylcarnitines -High PUFAs	12 lipids: -Low abundance of PUFAs	5 metabolites: proline betaine
↑ total, LDL cholesterol ↑ weight and waist, ↑ liver fat	↓ HDL cholesterol ↑ HOMA-IR	↓ Hypertension ↓ Metabolic syndrome

National Phenome Centre

Gadgil, *J Nutrition*, 2015
Gadgil, *J Nutrition*, 2022

Plant-based diets: Healthy and Unhealthy

Plant-based foods	
Healthy	**Less Healthy**
Whole grains	Refined grains
Fresh fruits	Fruit juices
Vegetables	Potatoes
Herbs/spices	Deep fried snacks
Nuts	Coconut
Legumes	Sweets/desserts
Tea & coffee	Sugar sweetened beverages



Bhupathiraju, *Am J Clin Nutr*, 2022

Physical Activity

- SA had lowest exercise compared to MESA groups
- Lower among those with diabetes

- More minutes of sedentary behavior → Incident DM

Shah, *Annals Epidemiology*, 2015

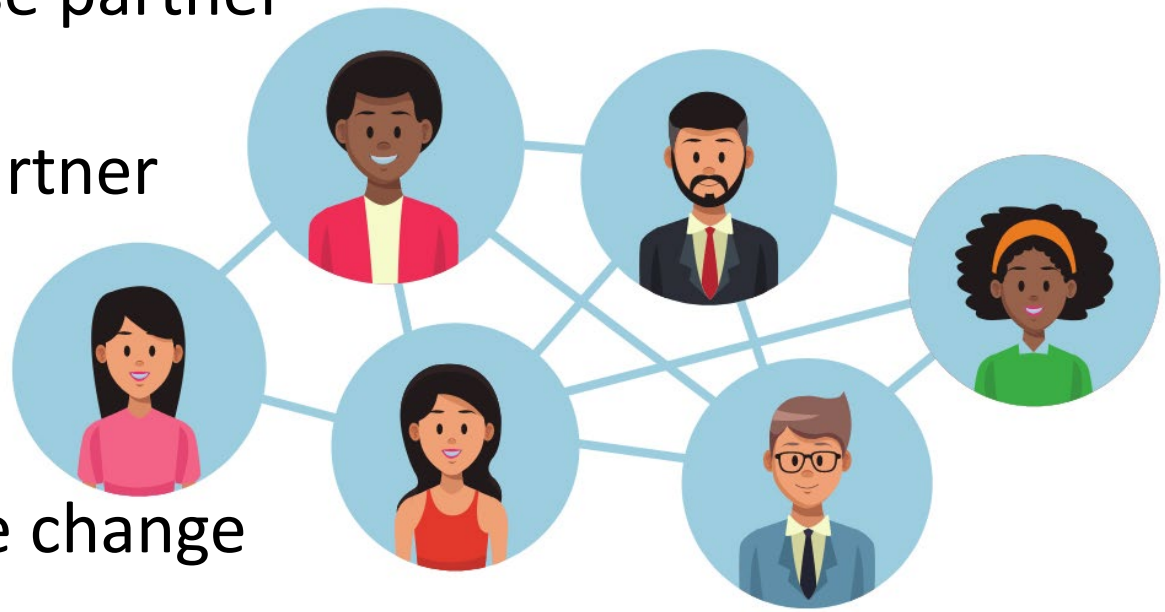
Social Interactions influence Physical Activity

Men:

- Exercise more with a non-spousal exercise partner

Women:

- Exercise more with spouse as exercise partner



Qualitative results:

- Adult children are influencers for lifestyle change

Thanawala, *J Phys Act Health,* 2020
Ram, *Ethnicity & Health*, 2020

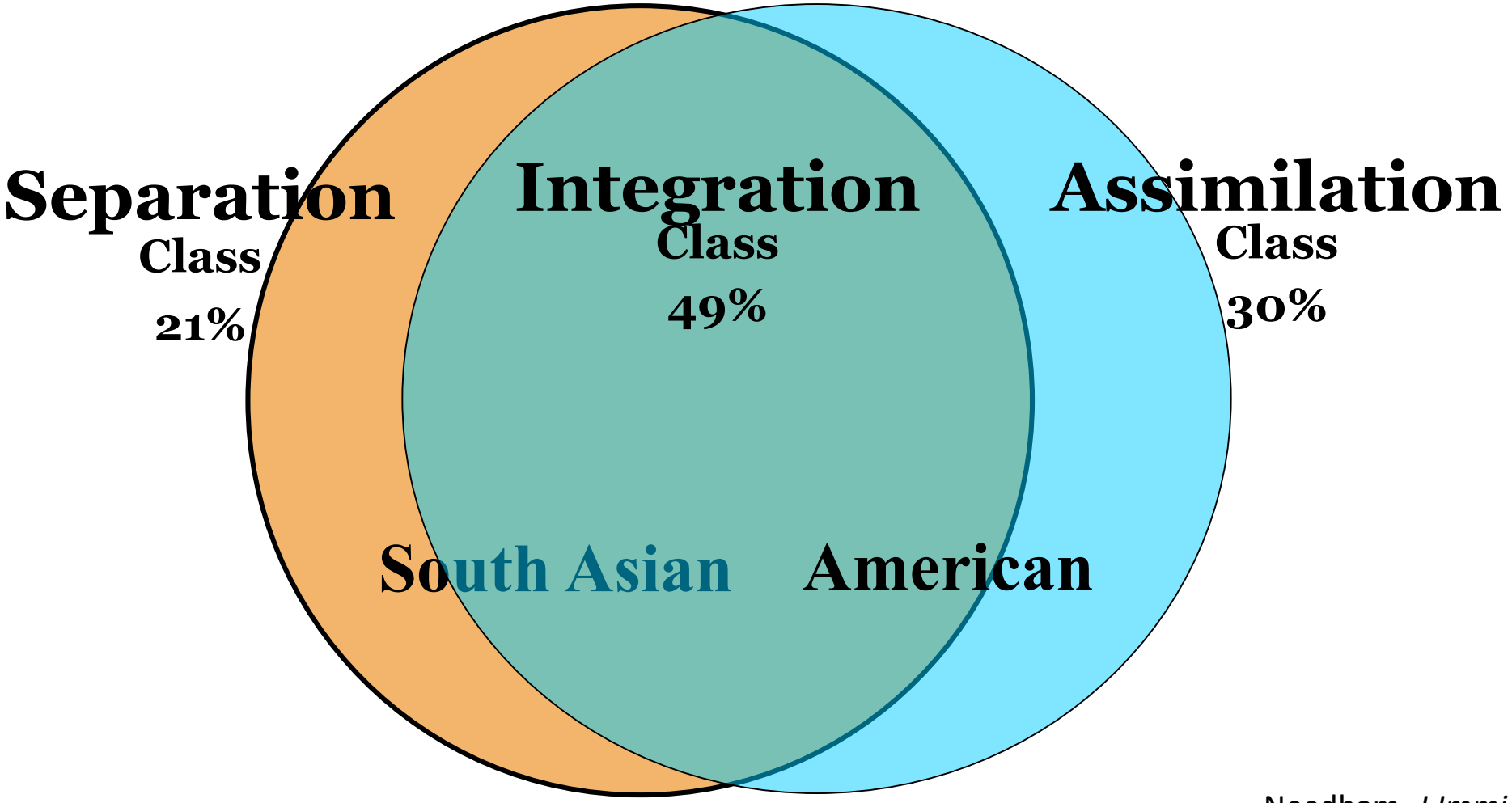
"Acculturation"

Cultural items collected:

1. Length of US residency
2. English language proficiency
3. Foods eaten at home
4. Foods eaten outside of home
5. Frequency of social, cultural, religious engagements
6. Frequency of shopping at SA markets
7. Race/ethnicity of friends
8. Language of TV, radio, print media
9. Traditional cultural beliefs scale

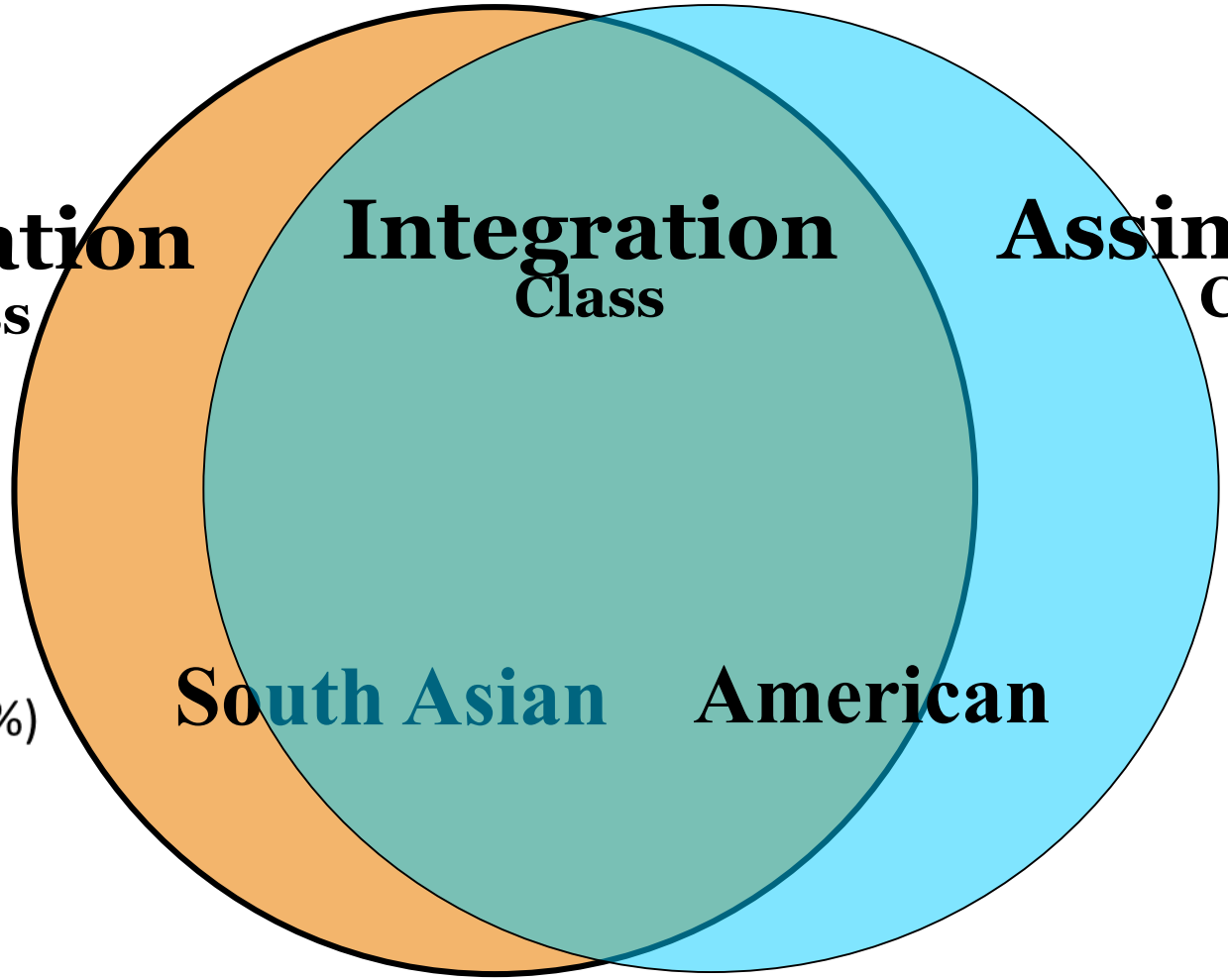
Acculturation Strategies

Acculturation Strategies



Needham, *J Immig Min Health*, 2016
Elliott, *Epidemiology*, 2020

Acculturation Strategies



↑ women (57%)
↓ years in US (22)
↓ SES
↓ exercise
↓ tobacco/alcohol
Traditional SA diet (56%)

↑ years in US (32)
↑ SES
↑ exercise
↑ tobacco/alcohol
Animal protein diet (56%)

Needham, *J Immig Min Health*, 2016
Elliott, *Epidemiology*, 2020

Prevalent Cardiometabolic Factors

	Separation Class (Most South Asian)	Integration Class (Bicultural)	Assimilation Class (Most American)
BMI, kg/m^2	26.7	26.1	25.7
Waist, cm	95	94	92
Glucose tolerance:			
Normal, %	34	38	44
Prediabetes	35	34	33
Diabetes	31	28	23
Hypertension, %	48	45	38
Fatty liver, %	18	11	13

‘South Asians’ are not a Monolith

Image courtesy of *The Juggernaut*, May 2021

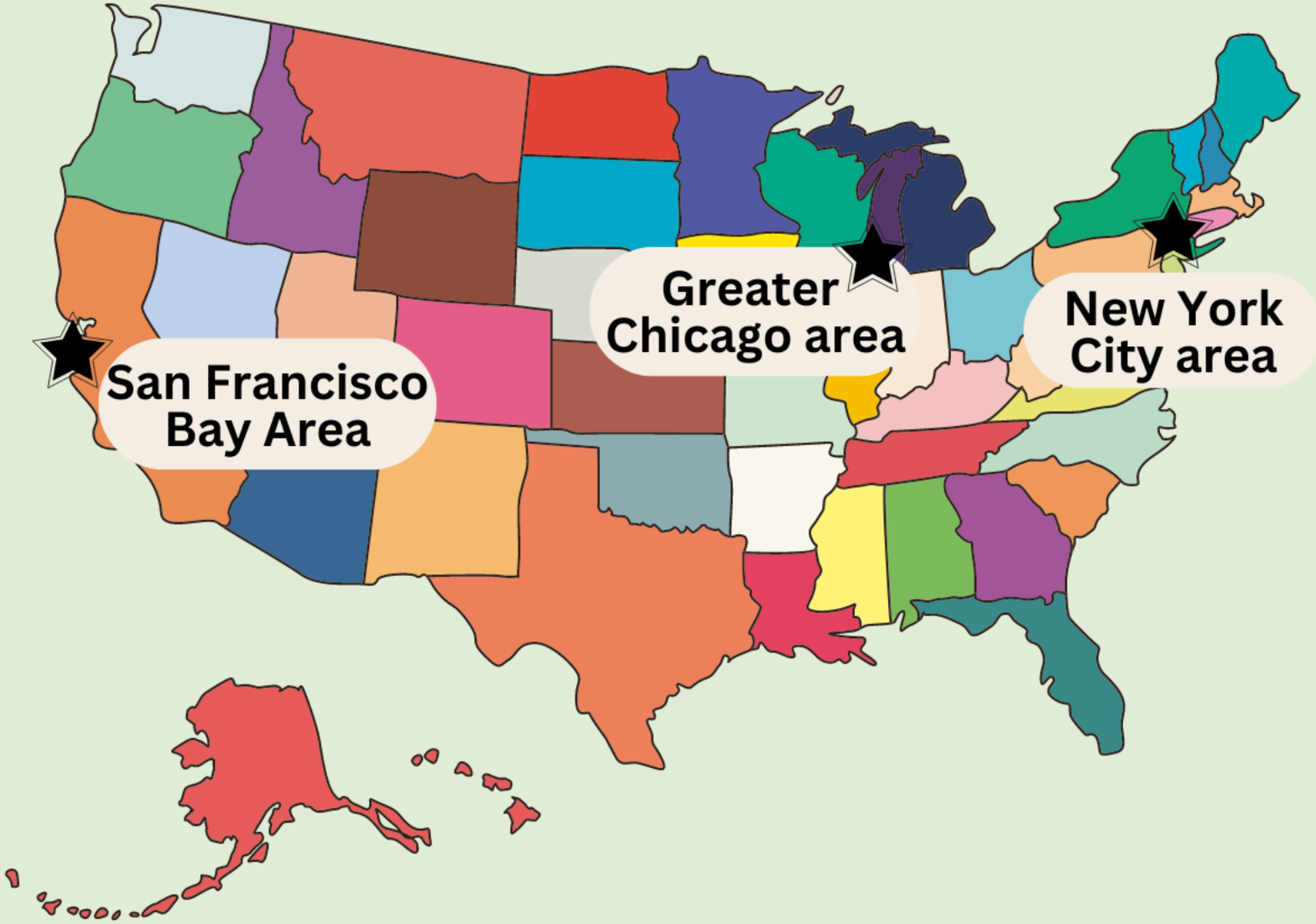
MASALA Study Expansion

New participants:

- 600 Bangladeshi
- 600 Pakistani
- 965 Indians (enrolled)

Goals:

Compare risk profiles of the 3 largest SA subgroups with other U.S. groups



Conclusions

1. South Asians have high T2D prevalence, more ß cell dysfunction, IR and ectopic fat, and lower muscle mass. SA have a rapid transition from prediabetes to diabetes.

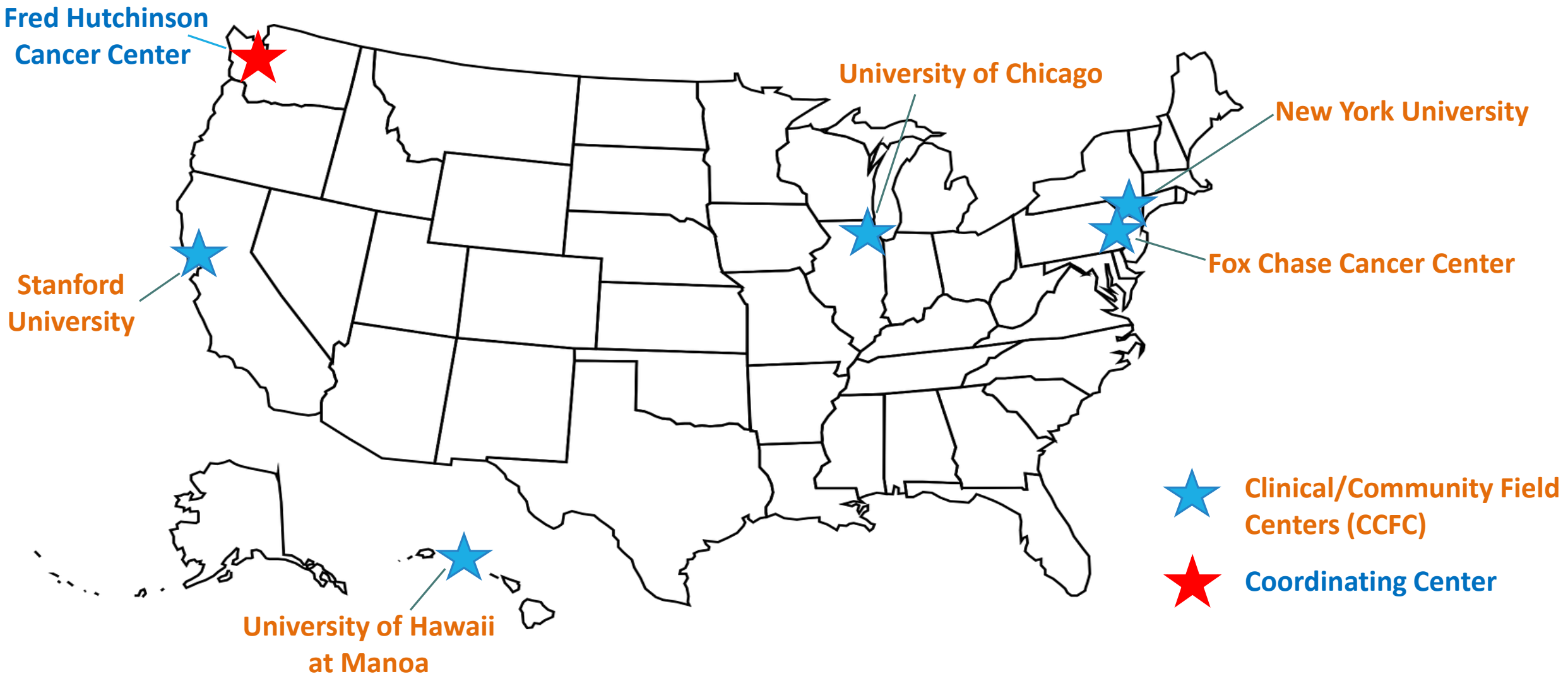
2. Lp(a) and CAC burden are high

3. Many modifiable risk factors…leverage social networks for lifestyle change

4. Risk factors vary dramatically among Asian American groups.

5. Longitudinal data provides many novel insights

New Asian American, Native Hawaiian, and Pacific Islander Prospective Cohort Study: The MOSAAIC Study



Thank you to our participants,
study staff, investigators, and funders of MASALA!