

Coronary artery Disease in Indians



*Indian Cultural Center, Marlton, NJ
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Vijay R. Marwaha, MD, MBA, FACC, FSCAI

The Cardiovascular Centers

750 Route 73 South, Suite 309A, Marlton, NJ 08053

(856)872-3636

<http://www.thecardiovascularcenters.com>

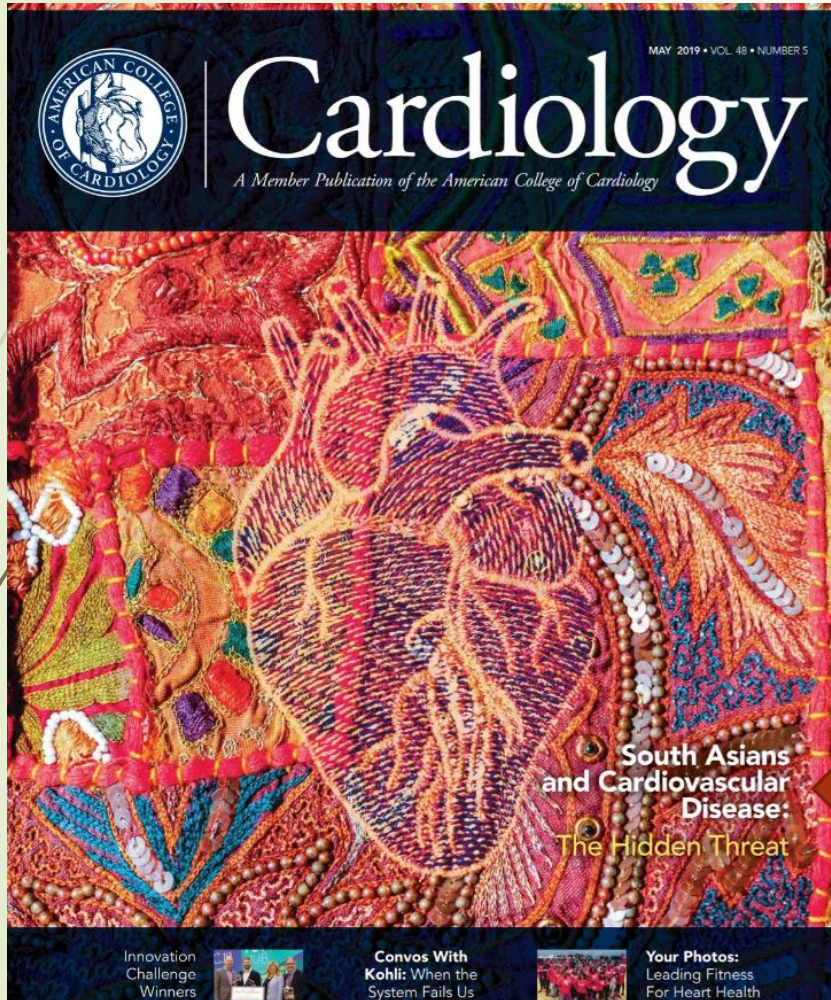
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South Asians & Heart Disease

Is it a secret? **NO**



- **South Asians** represent approximately 25 percent of the world's population – yet they account for 60 percent of the world's heart disease patients.

The MASALA study

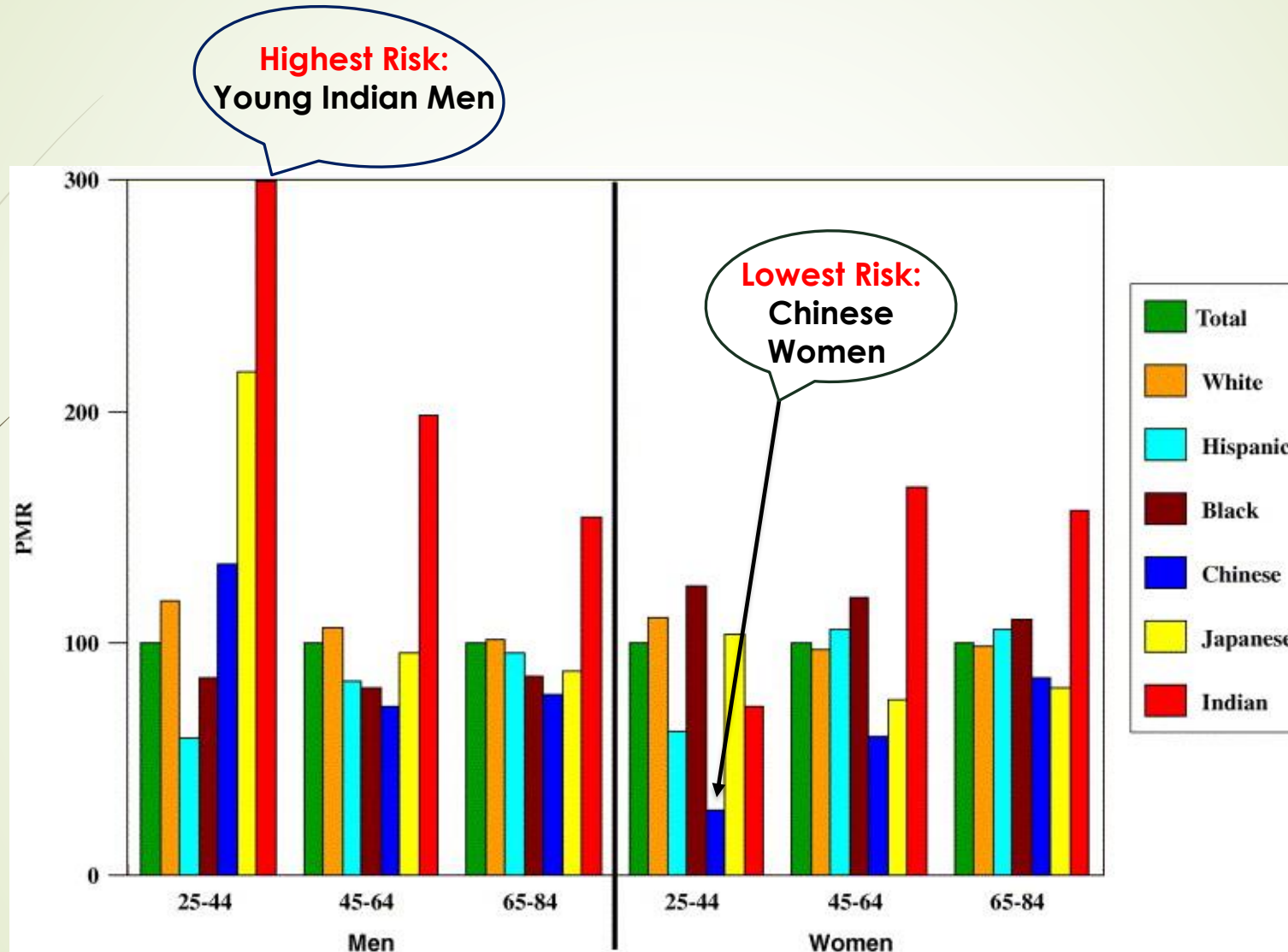
- Mediators of Atherosclerosis in South Asians Living in America
- Conducted by two university clinical field centers (University of California, San Francisco and Northwestern University).
- The study is funded by the National Heart, Lung, and Blood Institute.

FACTS: INDIANS & HEART DISEASE EPIDEMIC

- ▶ India accounts for approximately **60%** of the world's heart disease burden¹, **despite having less than 20%** of the world's population.
- ▶ Heart disease is the **number one cause of mortality** and a **silent epidemic** among Indians.
- ▶ India, particularly the city of Hyderabad in the state of Andhra Pradesh, is currently the **diabetic capital of the world**².
- ▶ When heart disease strikes Indians, it tends to do so at an **earlier age** (almost 33% earlier) and with **higher mortality rates** than other demographics.
- ▶ **Heart attacks in Indian men:**
 - ▶ **50%** of all occur HEART ATTACKS **under 50 years of age**
 - ▶ **25%** occur **under 40 years of age**
- ▶ Indian women have high mortality rates from cardiac disease as well.
- ▶ Healthy South Asians: **"At Risk"** Healthy People

Mortality Rates by Ethnic Group, Gender & Age

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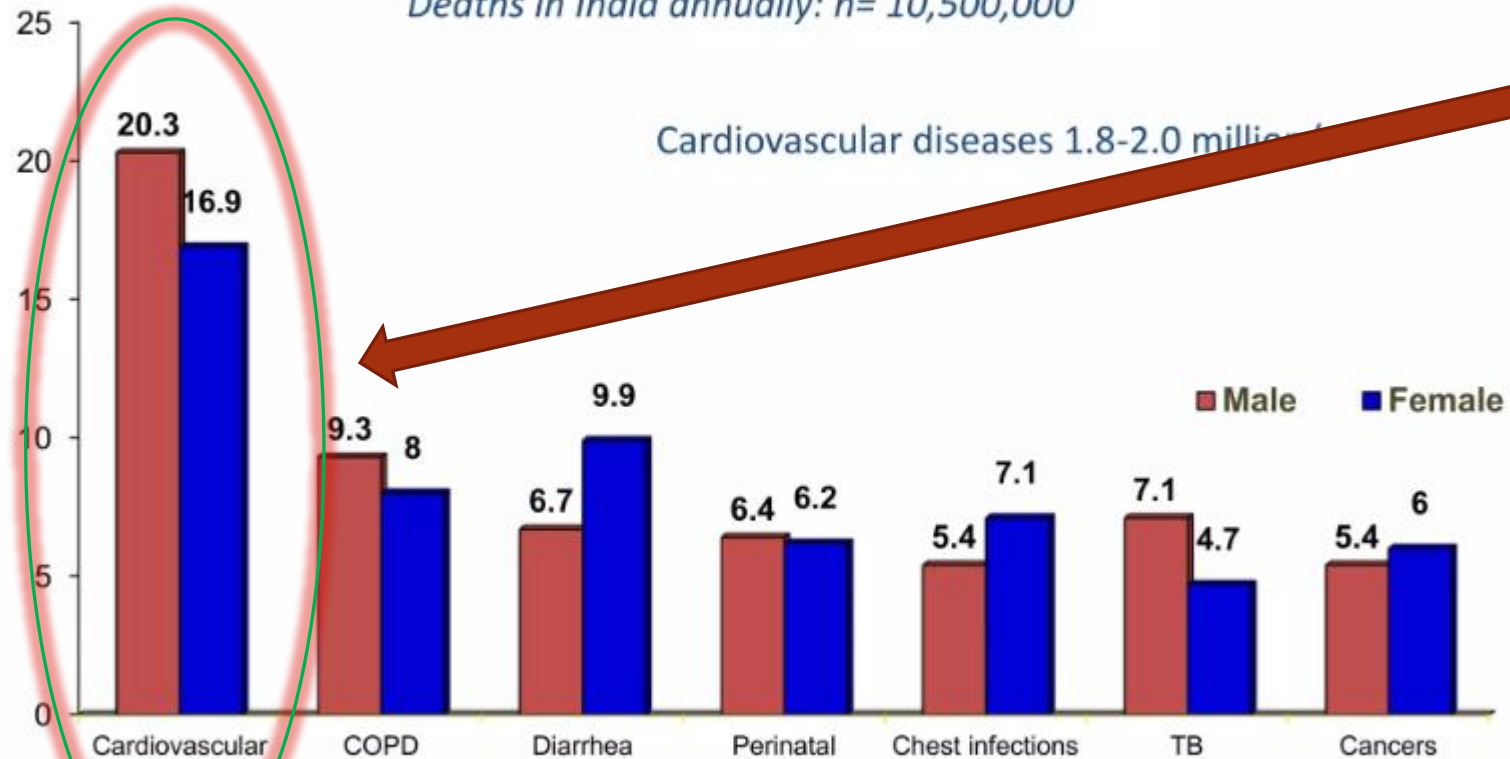


WHERE ARE ALL THE YOUNG PEOPLE IN THE AUDIENCE TODAY?

CVDs are Largest Causes of Death in India

Million Death Study

Analysis of cause of deaths in 1.1 million homes and 113,692 persons in all States
Deaths in India annually: n= 10,500,000



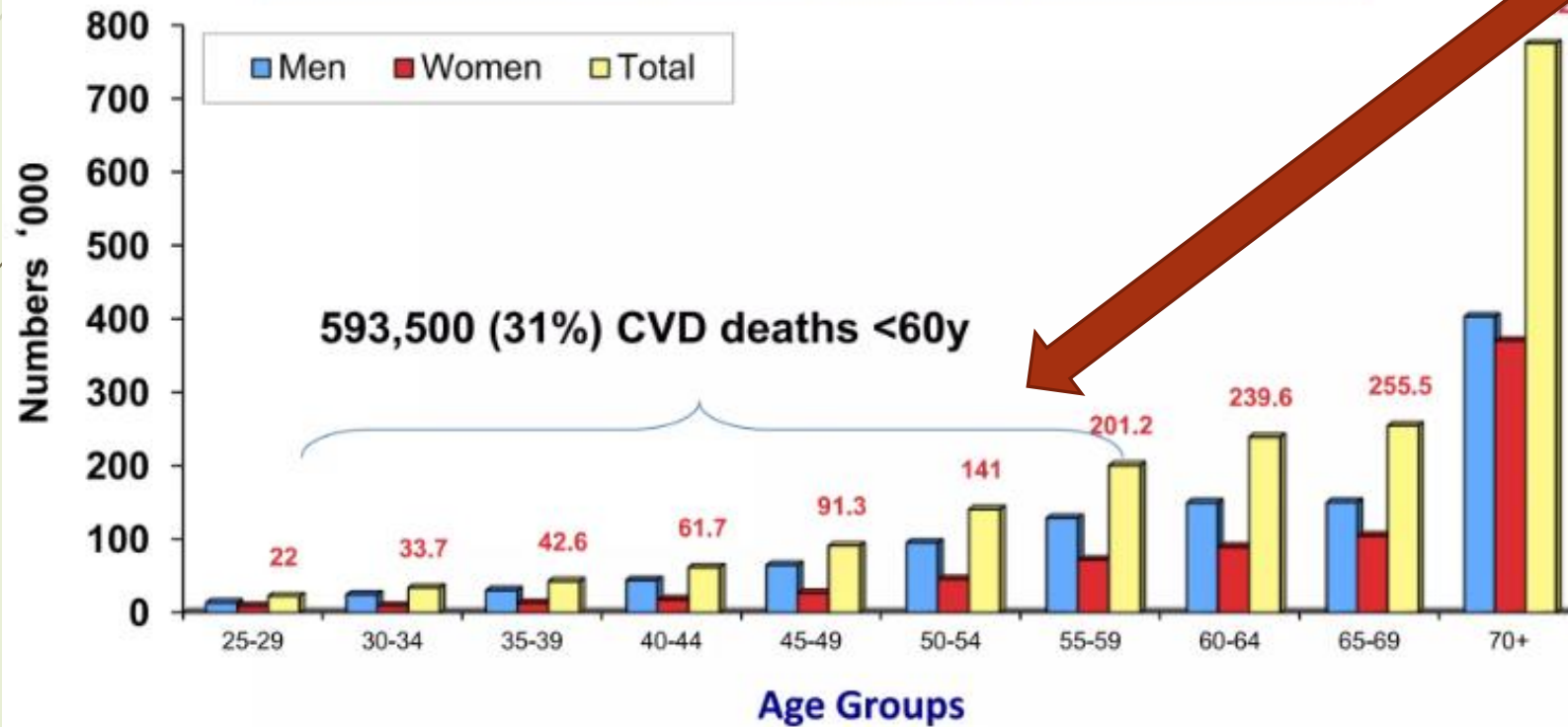
Registrar General of India. 2009

Gupta R, et al. World J Cardiol. 2012;4:112-120

~ 20% of
deaths
are from
Heart
Disease.

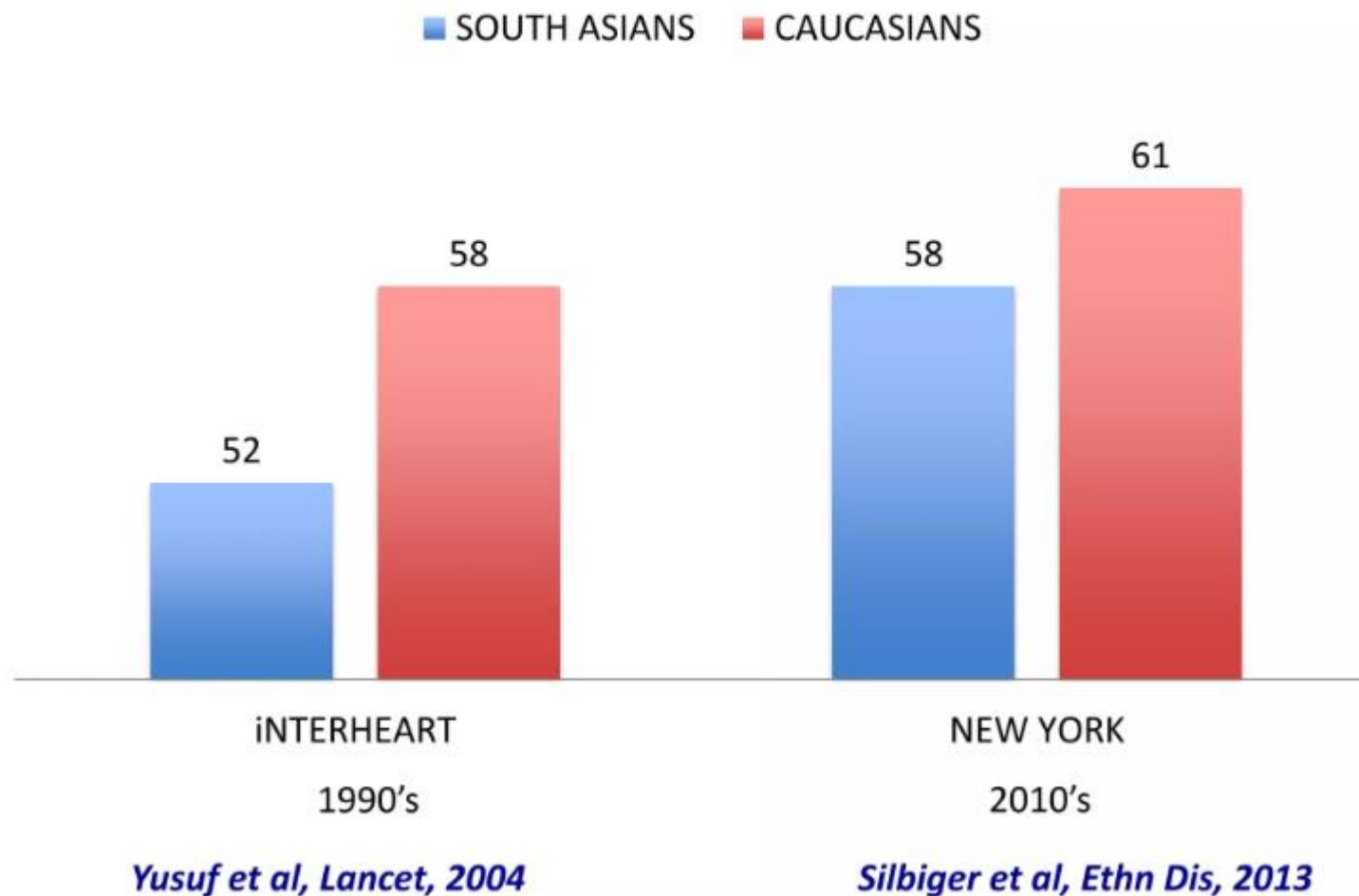
High Premature CVD Mortality in India

Total CVD deaths >15 years in 2010: 1,887,000
(M 1,116,000; F 770,000)



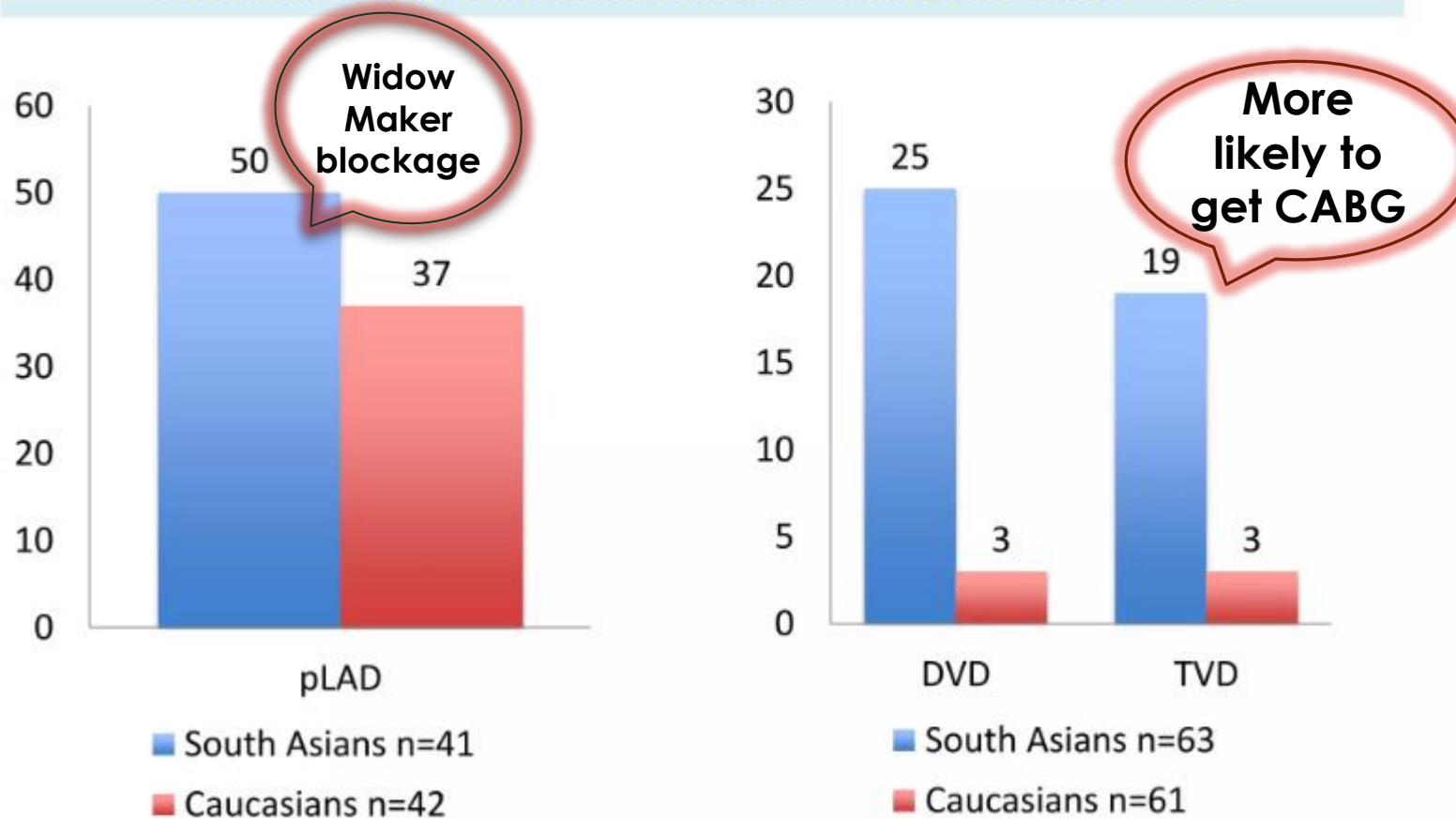
~ 31% of
heart
disease is
premature

Premature Acute Coronary Syndromes in South Asians: Younger Age of Onset



South Asians develop symptomatic heart disease earlier than whites

Coronary Angiographic Findings in South Asians vs Caucasians in UK and US



Tillin et al. Int J Cardiol. 2008;129:406-13

Hasan et al. Am J Cardiovasc Dis. 2011;1:31-7

Indians get more **severe & higher risk** blockages

WHAT MAKES SOUTH ASIANS MORE DANGEROUS HEART PATIENTS?

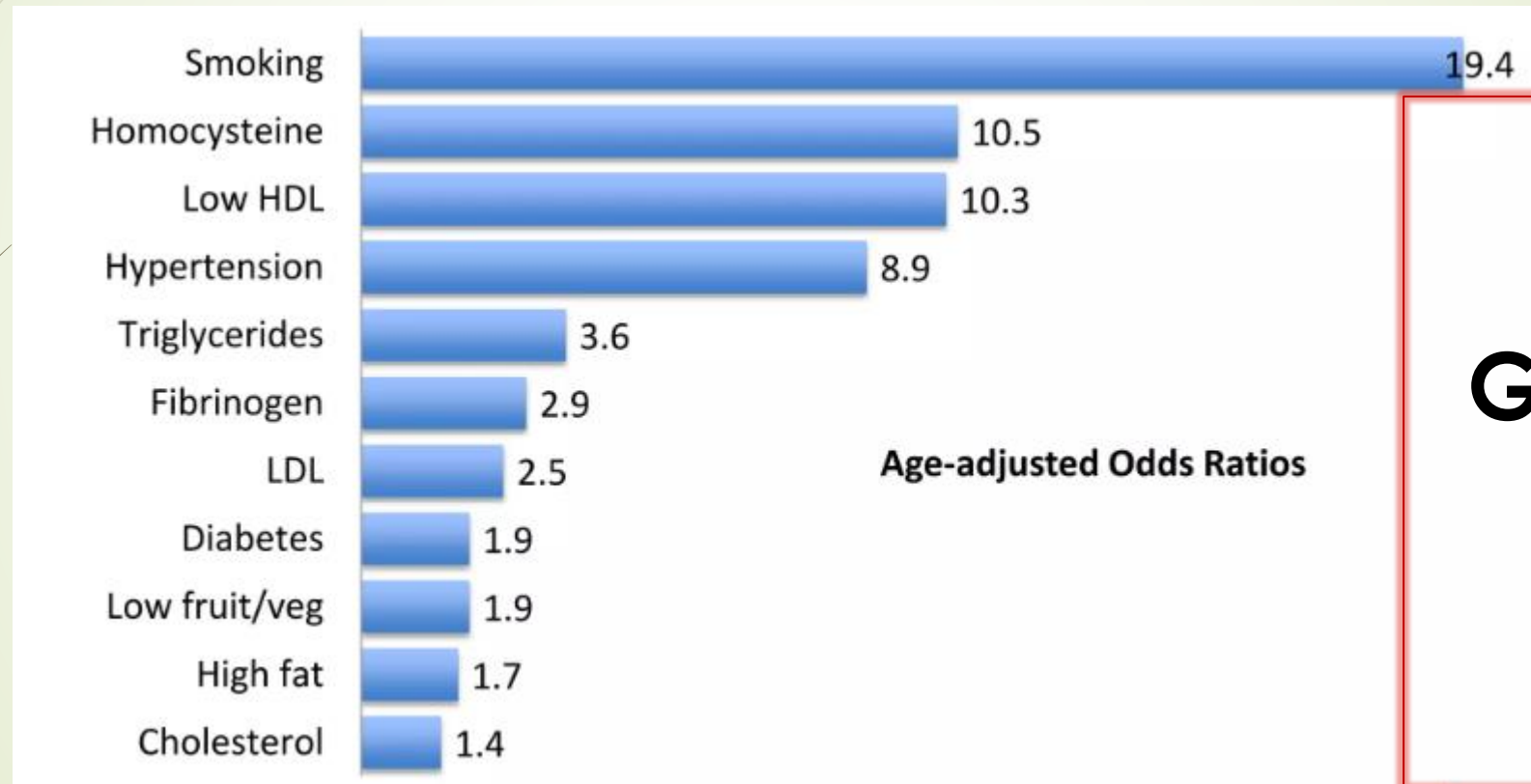
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Phenotypic Uniqueness of South Asian CAD

- Premature atherosclerotic disease
- Small arteries
- Severe atherosclerosis in the young
 - More TVD as compared to Caucasians at younger age
 - Diffuse and distal disease
- Greater prevalence of LV dysfunction at presentation
- Difficult PCI and complex CABG surgery
 - Bifurcation lesions
 - Endarterectomy more common
 - LV and MV repair

Kaul U, et al. Indian J Med Res. 2010; 132:543-8

RISK FACTORS OF PREMATURE CAD (< 50 YEARS) IN INDIANS



And
GENETICS
(NEXT SLIDE)

Lipoprotein(a) is an important genetic risk factor for coronary artery disease in Asian Indians

Genetics of CAD: Indian Studies

JPGM
Journal of Postgraduate Medicine

Table 6: Indian genetic studies

Gene	Study design	Population	Risk allele
Apo A1-C3-A5	ASP	IARS	Apo C3-Sac1 SNP
GHRd3	ASP	IARS	DD allele with increased HDL-C levels
High levels of CRP	ASP	IARS	Increased CRP
Plasma factor 7 glu353arg (RR, RQ, QQ)	ASP	IARS	RR and RQ associated with increased F7c activity
ApoA5-1131T>C	CC	New Delhi birth cohorts	CC
ACE I/D	CC	Hyderabad	DD
Apo E	CC	Kolkata	E4 allele
MMP3 5A/6A	CC	Hyderabad	No significant association
PON1 Q192R	CC	Punjab	RR with increased enzyme activity
PPARα Intron 7 G2528C	CC	Trivandrum	CC
MTHFR (Hinf1) AA, AV, VV	CC	Mumbai	Reduced activity in Hyperhomocysteinuria
MS (Hae II) (DD, DG, GG)	CC	Mumbai	Reduced activity in Hyperhomocysteinuria
ACE I/D	CC	North Indian	DD more frequent in MetSyn patients
209 SNPs in 31 genes of 10 QTLs	ASP	Kolkata	9 SNPs from four genes SELE, VEGFA, FBG and NFKB1

GHRd3 – Growth hormone receptor d3; MS – Methionine synthase; SELE – Selectin; VEGFA – Vascular endothelial growth factor A; FBG – Fibrinogen; NFKB1 – Nuclear factor kappa B 1. ASP – Affected sib pair analysis; CC – Case control; IARS – Indian atherosclerotic research study

The
American Journal
of Cardiology

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READERS' COMMENTS | VOLUME 88, ISSUE 2, P201-202, JULY 15, 2001

Lipoprotein(a) is an important genetic risk factor for coronary artery disease in Asian Indians

Enas A. Enas, MD

DOI: [https://doi.org/10.1016/S0002-9149\(01\)01659-9](https://doi.org/10.1016/S0002-9149(01)01659-9)

References

Article Info

Related Articles

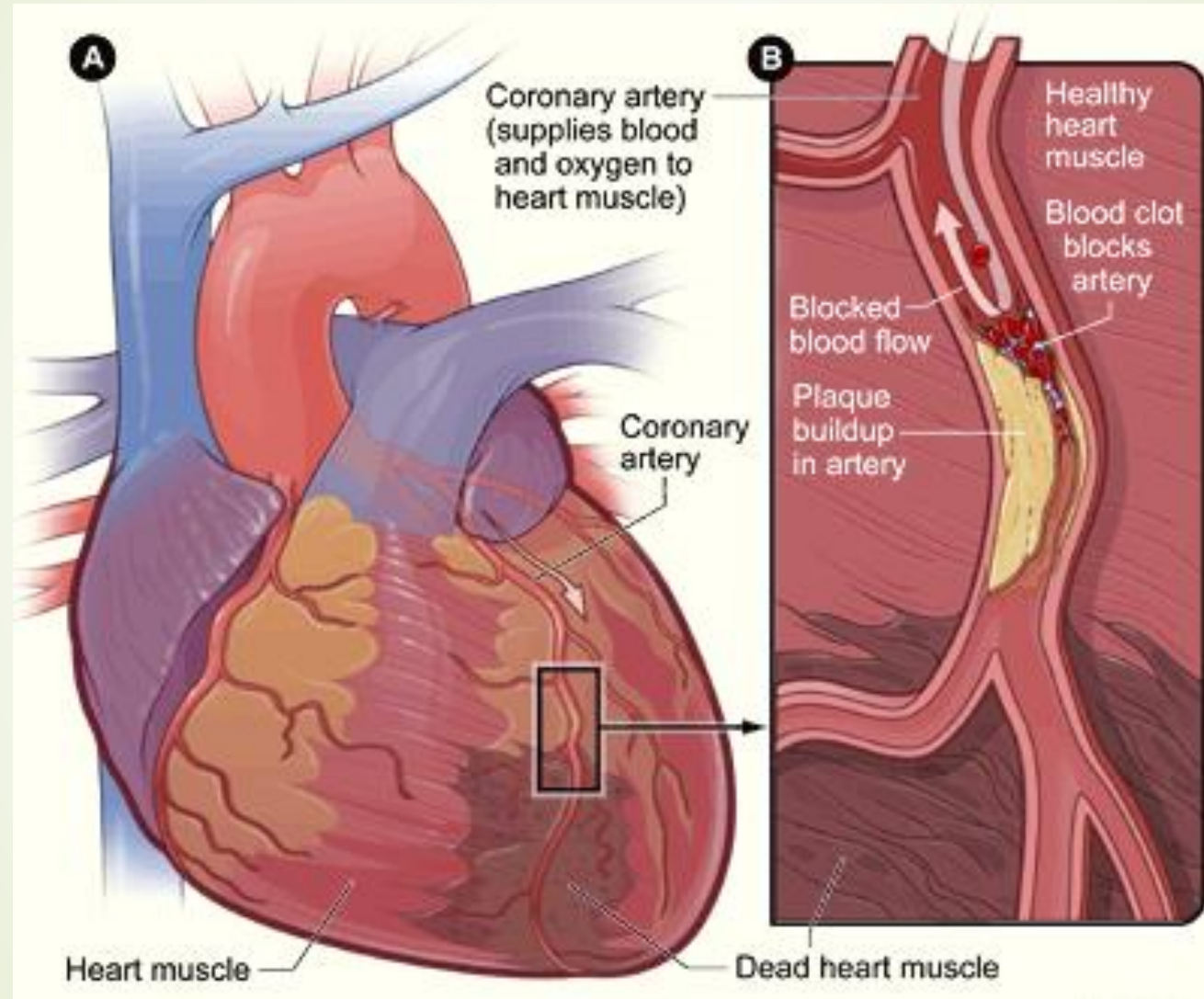
Asian Indians around the world have high rates of coronary artery disease (CAD), accompanied by a low prevalence of smoking, high cholesterol, and high blood pressure. ^{1, 2} This "Asian Indian Paradox" is best explained by the synergistic effects of glucose intolerance, atherogenic dyslipidemia, and elevated levels of lipoprotein(a) [Lp(a)]. ^{3, 4, 5} Lp(a) levels are higher in Asian Indians than in whites. ^{6, 7, 8} The Lp(a) levels in Asian Indian newborns are significantly higher than in the Chinese in Singapore, and the differences in Lp(a) levels in cord blood parallel the fourfold differences in adult CAD mortality between these 2 populations. ⁹ These data underscore the genetic determination and clinical relevance of Lp(a) in CAD among Asian Indians. Lp(a) is an independent risk factor for CAD with a relative risk of 2.7 at levels >20 mg/dl. ¹⁰ The CAD risk in patients with high Lp(a) is much greater with low high-density lipoprotein (HDL) cholesterol than with high low-density lipoprotein cholesterol. For example, the relative risk of CAD from high Lp(a) increases to 8.7 when HDL is <0.9 mmol/L versus 2.3 when LDL is >4 mmol/L. The heightened risk of CAD in Asian Indians, whose Lp(a) levels are intermediate between whites and blacks ⁵ is attributed to their low HDL, especially HDL 2b and the resulting impaired reverse cholesterol transport. ¹¹ Conversely, the lower rate of CAD in Blacks who have the highest level of Lp(a) is due to their high HDL level, which mitigates the pathologic effects of high Lp(a). ⁵

Table. Key results of the South Asian component of the INTERHEART study¹⁷

- Deaths due to acute myocardial infarction (AMI) in south Asians occur at 5-10 years earlier than western population.
- South Asian men encountering AMI were 5.6 yr younger than women.
- The higher risk for AMI in South Asians in their younger age is largely determined by the higher levels of risk factors and the nine conventional risk factors (abnormal lipids, smoking, hypertension, diabetes, abdominal obesity, psychosocial factors, consumption of fruits & vegetables, alcohol and regular physical activity) collectively explain 86 per cent of the AMI risk in south Asians.
- Abnormal Apo-B/ApoA-1 ratio and smoking are the most important risk factors.
- Low education level is associated with increased risk of AMI worldwide.
- Protective lifestyle factors such as leisure time physical activity and regular intake of fruits and vegetables are markedly lower among south Asians than western population, while harmful risk factors such as elevated ApoB/Apo A-1 ratio are higher in south Asians.

Pathogenesis of CAD

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Symptoms of CAD

- Chest pain
- Shortness of Breath
- Sweating
- Nausea/Vomiting (may be only symptoms in some diabetics, women, or elderly!)
- Neck or arm pain
- Dizziness
- What to do if you recognize these symptoms?
 - Call 911
 - If instructed by provider, may take nitroglycerin or aspirin
 - Do not try driving!

Prevention of Heart Disease

- LIVE SMART (be aware of your body and symptoms) => **what is your body telling you? Is there a problem?**
- LIVE HEALTH (Tobacco, Diet, Stress, weight)
- LIVE ACTIVE (Exercise)
- LIVE BALANCED (work, home, stress, sleep, exercise)
- AVOID TOBACCO. AVOID ALCOHOL
- KNOW OUR NUMBERS (Cholesterol, BP, BMI, Waist/Hip ration)
- TREAT YOUR RISK FACTORS (diabetes, cholesterol, weight, BP, etc)=> **no one like medications, but be smart not stubborn.**
- REDUCE STRESS (**stress causes inflammation, inflammation accelerates atherosclerosis**)
- RAISE AWARENESS (early screening & education)
- PERSONALIZED RISK EVALUATION (get tested, get treated)

Tobacco

- ▶ **Number one preventable risk factor**
- ▶ Unfortunately rates of smoking are rising among South Asians
- ▶ Companies target children at young age.



A Healthy Meal BALANCED



Not so Healthy



You are what
you eat

You are what you eat



Indians in America

Children &
Grand Children

Parents & Grand parents

Lipid Goals

- Total cholesterol goal: <200 mg/dL
- LDL (bad cholesterol) goal: <100 mg/dL
- Triglycerides Goal: <150 mg/dL
- HDL (good cholesterol) goal:
 - >40 mg/dL in men, >50 mg/dL for women

Physical Activity

- ▶ Helps lower BP, Diabetes, raises good cholesterol (HDL), manages stress, improves bone health, helps control weight
- ▶ 30 minutes of moderate activity most days of week



Obesity

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➤ **Obesity** is a major risk factor for CAD, elevated BP, high cholesterol, DM and a multitude of other health problems!

➤ **OBESITY EPIDEMIC:** Rapidly rising obesity rates within the US among all demographics.

➤ **IDEAL BMI:**

- Healthy Weight range: **18.5 to 24.9**
- Overweight: 25.0 to 29.9
- Obese: >30.0

➤ **Limitations of BMI**

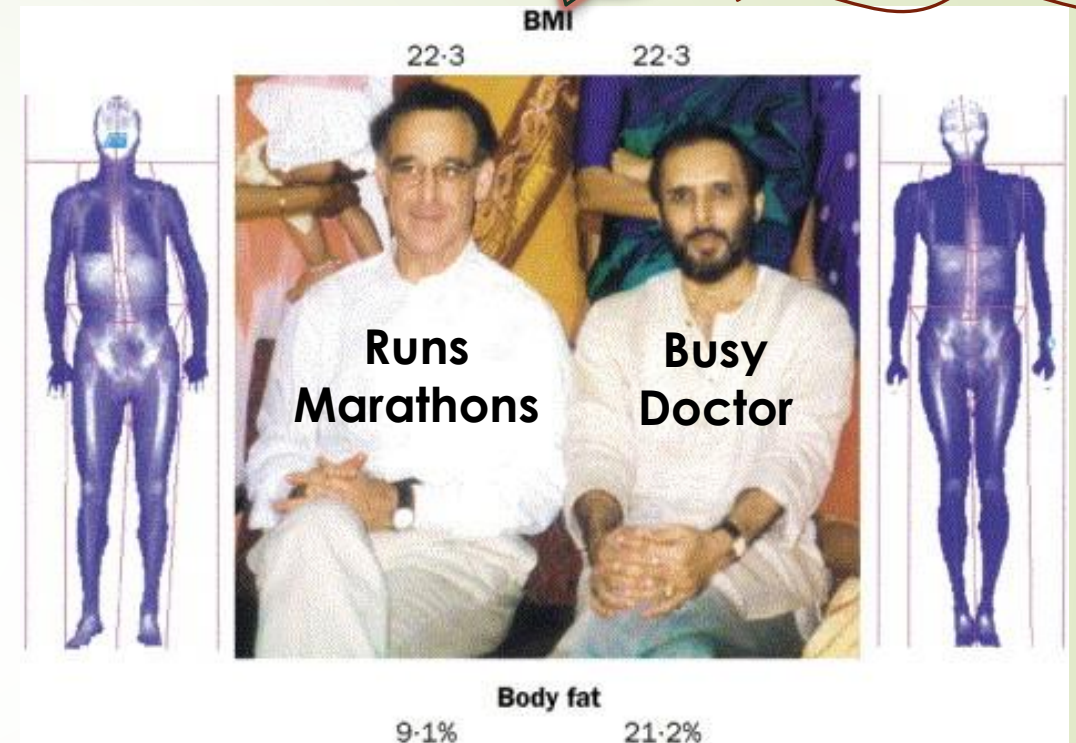
➤ **Body Fat Percentage**

- **ESSENTIAL:** Women: 10-13% Men: 2-5%
- **HEALTHY:** Women: 10-31% Men: 2-24%
- **OBESITY:** Women: > 32% Men: >25%

The WHO recommends using 23 kg/m² and 27.5 kg/m² for overweight and obesity, respectively.¹⁵

Same BMI

But DIFFERENT Body Fat %



"The two authors share a near identical body-mass index (BMI), but as dual **X-ray absorptiometry imagery** shows that is where the similarity ends. The first author ([figure, right](#)) has substantially more body fat than the second author ([figure, left](#)). Lifestyle may be relevant: the second author runs marathons whereas the first author's main exercise is running to beat the closing doors of the elevator in the hospital every morning. The contribution of genes to such adiposity is yet to be determined, although the possible relevance of intrauterine under-nutrition is supported by the first author's low birthweight. The image is a useful reminder of the limitations of BMI as a measure of adiposity across populations."

Blood Pressure

- ▶ Quick screening recommended during **ALL** healthcare visits for adults
- ▶ **Controlling hypertension reduces risk of heart disease by 25%**
 - ▶ Strategies include weight loss (i.e. via weight loss, exercise, diet), low sodium in diet, limit alcohol
- ▶ Goal BP: <120 systolic and <80 diastolic pressures
- ▶ American Heart Association
website: www.americanheart.org



The five main blood pressure ranges, as recognized by the American Heart Association, are:

- Normal: Below 120/80.
- Elevated: 120 to 129/less than 80.
- Stage 1 high blood pressure: 130 to 139/80 to 89.
- Stage 2 high blood pressure: 140 and above/90 and above.
- Hypertension crisis: above 180/above 120.

Diabetes

- ▶ Optimal fasting blood sugar is < 100 mg/dL
- ▶ Criteria for Diagnosis of Diabetes
 - ▶ Fasting glucose 126 mg/dL or higher
 - ▶ Random glucose of 200 mg/dL or higher + symptoms
 - ▶ HbA1C \geq 6.5
- ▶ Prediabetes (Glucose Intolerance): HbA1C 5.7 – 6.5
- ▶ Goal to detect patients at level of impaired fasting glucose of 100-125 mg/dL
 - ▶ Individuals at risk for diabetes can reduce their risk of developing the disease via a modest diet and exercise plan
- ▶ American Diabetes Association website: www.diabetes.org

Cardiovascular Evaluation & Testing

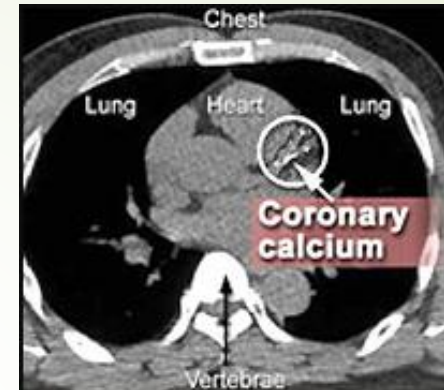
- ▶ Vitals
- ▶ Blood work (CBC, CMP, LFT, Lipid Panel, Apo B, Lipoprotien (a), Hb A1C, Thyroid, hsCRP, ESR.....)
- ▶ ECG or Electrocardiogram
- ▶ Echocardiogram
- ▶ Carotid U/S
- ▶ Evaluation of Peripheral Vascular Disease
- ▶ Coronary Low-dose CT Calcium Score Scan (Heart Scan)
- ▶ Stress testing (Exercise / Chemical, Imaging)
- ▶ Coronary CT angiography
- ▶ Cardiac catheterization or Angiography

Website: <https://www.thecardiovascularcenters.com/testing-instructions>

Cardiac Calcium Scoring (Heart Scan)

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- **The purpose of the test** is to understand your risk of heart attack or disease, taking preventive or corrective measures based on the results. **[RISK STRATIFICATION]**
- **Not indicated** for patients with previous heart disease, stents or CABG.
- A **calcium score** (sometimes called an Agatston score) is calculated based on the amount of plaque observed in the CT scan. It may be converted to a **percentile rank** based on your age and gender.
- Lower Score => Lower likelihood of a cardiac event, heart attack or presence of CAD
- NOT COVERED BY ANY INSURANCE.
- PRICE ~ \$ 100- \$125.
- Scan takes 20-30 seconds. TOTAL TIME 5-10 MINUTES.



- **Zero: No plaque.** Your risk of heart attack is low.
- **1 - 10: Small amount of plaque.** You have less than a 10 percent chance of having heart disease, and your risk of heart attack is low.
- **11-100: Some plaque.** You have mild heart disease and a moderate chance of heart attack. Your doctor may recommend other treatment in addition to lifestyle changes.
- **101 - 400: Moderate amount of plaque.** You have heart disease and plaque may be blocking an artery. Your chance of having a heart attack is moderate to high. Your health professional may want more tests and may start treatment.
- **Over 400: Large amount of plaque.** You have more than a 90 percent chance that plaque is blocking one of your arteries. Your chance of heart attack is high. Your health professional will want more tests and will start treatment.

Common Heart Medications

- ASPIRIN
- CHOLESTEROL MEDICATIONS (COMMONLY – STATINS, eg. Atorvastatin)
- BETA BLOCKERS (eg. Metoprolol, Atenolol, Carvedilol)
- Calcium Channel Blockers (Amlodipine)
- Diuretics (hydrochlorothiazide, Lasix)
- Angiotensin Converting Enzyme Inhibitors or ACE INHIBITORS (EG. Lisinopril)
- Angiotensin Receptor Blockers or ARB's (Eg. Losartan)
- Antiplatelet Agents (P2Y12 inhibitors) (eg. Clopidogrel / PLAVIX, Ticagrelor / BRILINTA or Prasugrel / EFFIENT)

LOW DOSE ASPIRIN: Yes or No? DEPENDS

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PRIMARY PREVENTION: NO HISTORY OF ASCVD

ACC/AHA primary prevention guideline **recommends:**

- **INDIVIDUALIZED APPROACH:** Low-dose aspirin **might be considered** among select adults 40 to 70 years of age who are at higher risk ASCVD risk but not at increased bleeding risk.
- Low-dose aspirin **should not be administered on a routine basis** among adults >70 years of age.
- Low-dose aspirin **should not be administered** for the primary prevention of ASCVD among adults of **any age who are at increased risk of bleeding**

SECONDARY PREVENTION: KNOWN HISTORY OF ASCVD

LOW DOSE ASPIRIN: **YES**

FULL DOSE ASPIRIN: **NO**

**ASPIRIN IS INDICATED
EXCEPT IF THERE IS A
CONTRAINDICATION.**

New Medications

- ▶ PCSK9 Inhibitors Repatha (evolocumab) // Praluent (alirocumab)
 - ▶ Injection 2 times a month
- ▶ Small interfering RNA (siRNA) therapy for LDL-C: Leqvio (Inclisiran)
 - ▶ Injection 2 times a year
- ▶ SGLT2 Inhibitors (Sodium/Glucose co-transporter 2 Inhibitor)
 - ▶ Jardiance / Farxiga / Invocana / Steglatro
- ▶ GLP-1 agonists (Glucagon-like peptide-1 agonists)
 - ▶ Victoza / Trulicity / Ozempic
- ▶ ENTRESTO: 2 medicines in one tablet: Valsartan (ARB) + Sacubitril: For heart failure
- ▶ OLD IS GOLD: Colchicine

New treatments in Development

Special interest for the South Asian Community

The American Journal of Cardiology

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References

Article Info

Related Articles

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**Lots of new
Excitement
among the
Cardiovascular
specialist treating
South Asian
population**

New Class of medications

- Antisense oligonucleotides or Small interfering ribonucleic acid (siRNA)
 - works by silencing the gene that causes liver cells to make Lp(a)
 - Inhibits the production of Lp(a)
- Lower blood levels of Lp(a) by **70-80%**.
- Normal levels are 30 mg/dL or lower.
- Statins do not lower Lipoprotien (a) levels
- **Stay tuned** => Earliest we would expect to see would be around **2025**.

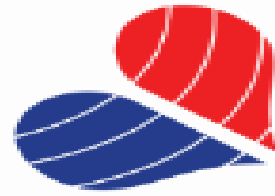
HEART HEALTH

Experimental drug lowers lipoprotein(a), a suspect in heart attacks



Summary

- ▶ CAD is a major problem, disproportionately among South Asians
- ▶ CAD is preventable
- ▶ We must IMPROVE OUTCOMES through Combination of raising awareness, education, screening, early detection, & treatment



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Dr. Vijay Marwaha
MD, MBA, FACC, FSCAI

Contact:
Phone: (856) 872-3636
Fax: (856) 872-3606

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