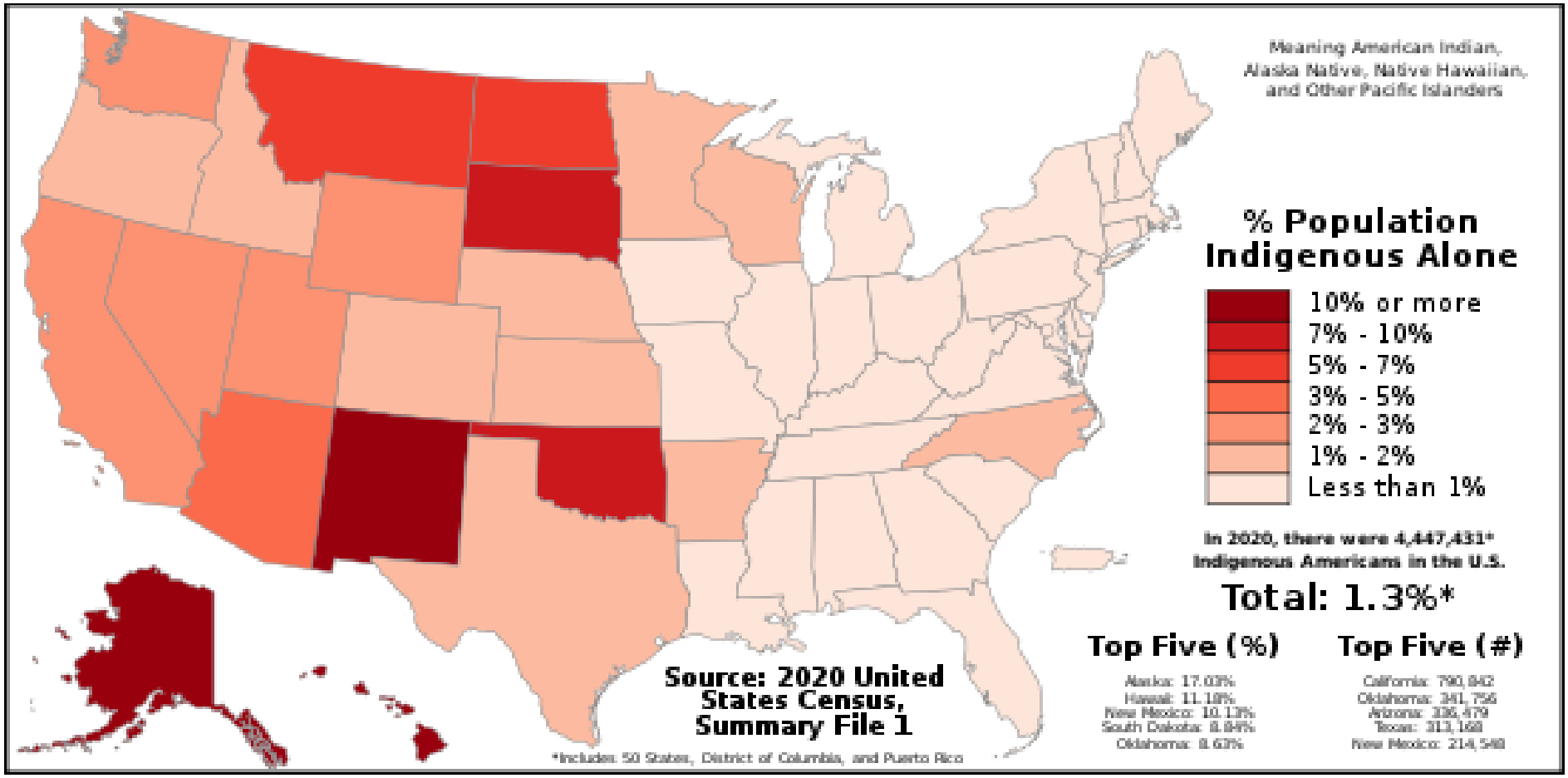
Cardiovascular Risk Stratification in American Indians

Jason Deen, MD, FAAP, FAAC
Associate Professor of Pediatrics
Adjunct Associate Professor of Medicine
Divisions of Cardiology
University of Washington

Disclosures

Why this matters . . .



Outline

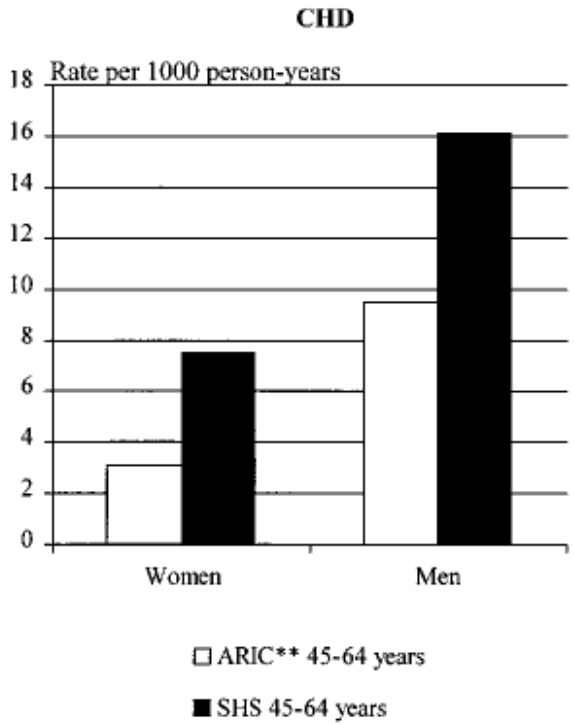
- The scope of the problem
- The successes of primary prevention
- Challenges of cardiovascular risk screening in American Indians
- American Indian-specific cardiovascular disease risk calculators
- Future directions

The scope of the problem . . .

Rising Tide of Cardiovascular Disease in American Indians

The Strong Heart Study

Barbara V. Howard, PhD; Elisa T. Lee, PhD; Linda D. Cowan, PhD; Richard B. Devereux, MD; James M. Galloway, MD; Oscar T. Go, PhD; William James Howard, MD; Everett R. Rhoades, MD; David C. Robbins, MD; Maurice L. Sievers, MD; Thomas K. Welty, MD



Circulation. 1999;99:2389-2395

The scope of the problem . . .

- AIs have an exaggerated prevalence of obesity and diabetes mellitus compared to the general population.
  - The prevalence of obesity, DM, hypertension, dyslipidemia is increasing despite elevated public awareness of CVD in AI communities

Circulation. 2014;129:399-410

Ethn Dis. 2006;16:647-652

Ann Epidemiol. 2002;12:97-106

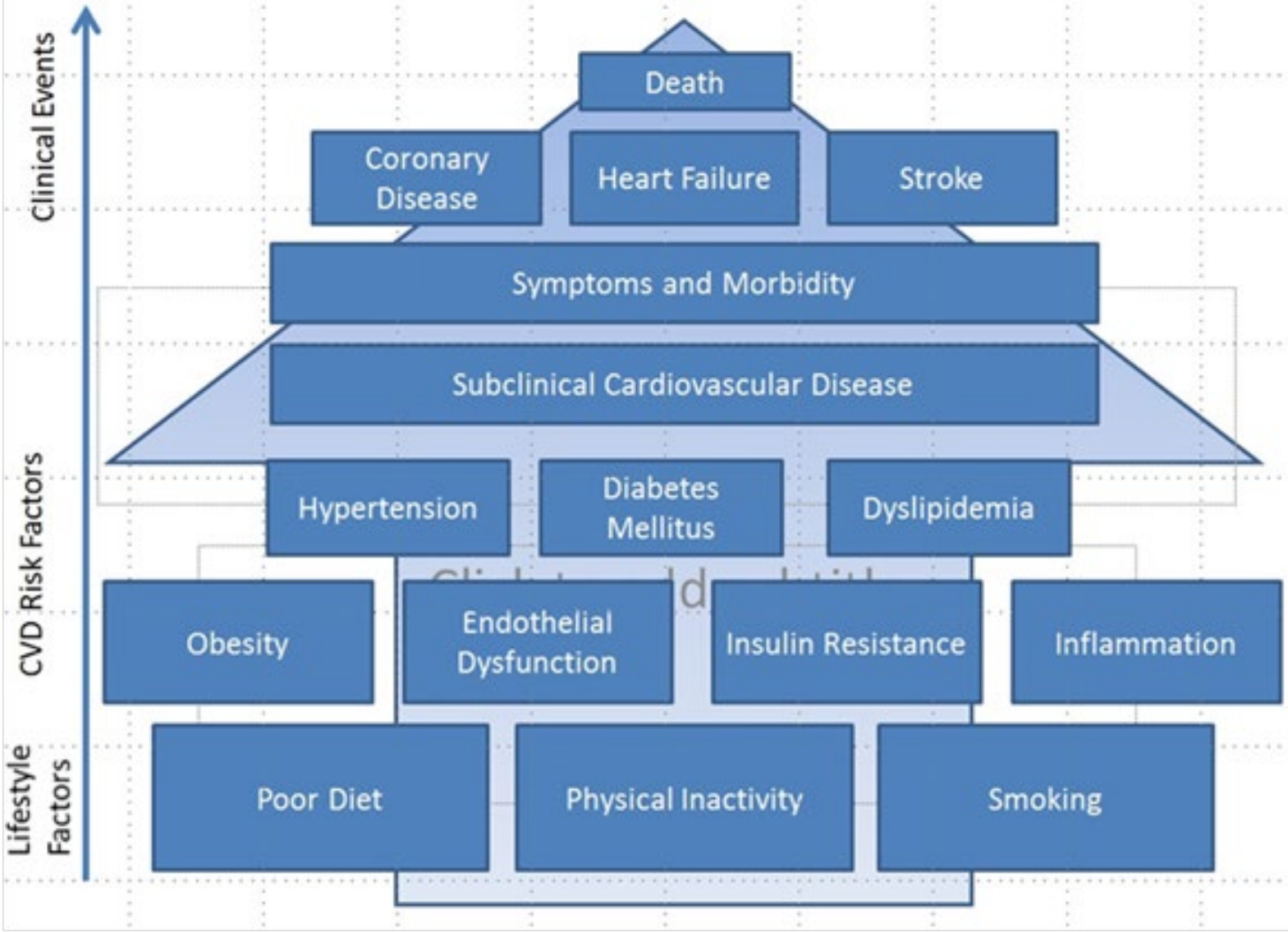
The scope of the problem . . .

- AIs have premature CVD mortality and morbidity
  - AI CVD mortality rate 20% greater than other US races
  - AIs die of CVD at younger ages
    - 36% will die before age 65 compared to 14.7% of non-Hispanic whites

Am J Public Health. 2014;104 Suppl 3:S359-367

MMWR Morb Mortal Wkly Rep. 2004;53:121-125

Primary prevention



Primary prevention

- Global CVD risk assessment and family history of CVD
  - Age, sex, smoking history, obesity, hypertension, dyslipidemia, glucose tolerance
  - These data via a global risk score estimate of CVD risk (usually a 10 year risk score)

J Am Coll Cardiol. 2010;56:e50-103

The successes of primary prevention

- From 2000 to 2010, annual CVD mortality declined 16.7% in the general US population
  - While the prevalence of CVD risk factors (particularly obesity and DM) have persisted or increased

Circulation. 2014;129:399-410

JAMA. 2014;311:806-814

Ann Intern Med. 2014;160:517-525

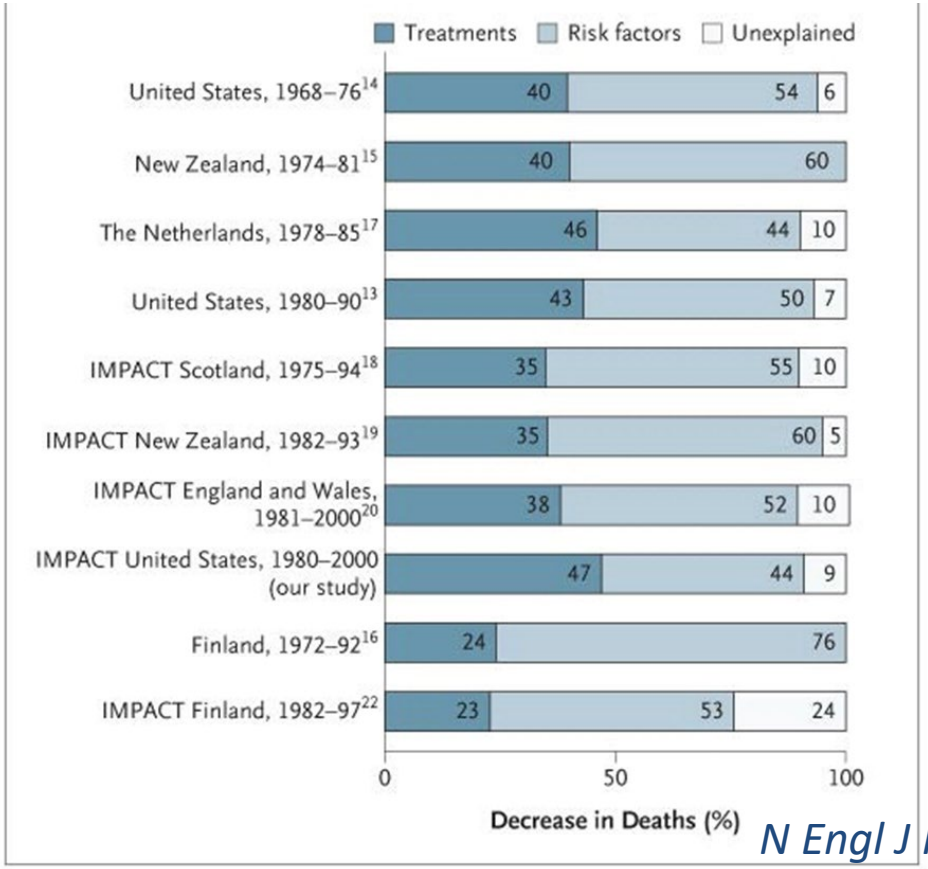
The successes of primary prevention

- Reduced CVD mortality likely due to a combination of improved primary prevention and secondary prevention.
- Best illustrated in coronary heart disease . . .

SPECIAL ARTICLE

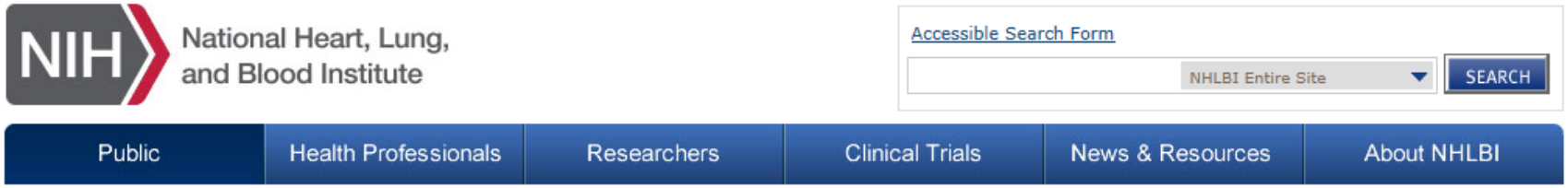
Explaining the Decrease in U.S. Deaths from Coronary Disease, 1980–2000

Earl S. Ford, M.D., M.P.H., Umed A. Ajani, M.B., B.S., M.P.H., Janet B. Croft, Ph.D., Julia A. Critchley, D.Phil., M.Sc., Darwin R. Labarthe, M.D., M.P.H., Ph.D., Thomas E. Kottke, M.D., Wayne H. Giles, M.D., M.S., and Simon Capewell, M.D.



N Engl J Med. 2007;356:2388-2398

Framingham Risk Score



Circulation 1998. 97(18): 1837-1847

The Framingham Heart Study

- Begun in 1947 in Framingham MA
  - Original (1947), offspring (1971), 3rd generation (2002)
- Generated >2000 publications
- 5,209 **white** men & women (mean age 49)

Validation of the Framingham Coronary Heart Disease Prediction Scores

Results of a Multiple Ethnic Groups Investigation

Ralph B. D'Agostino, Sr, PhD
Scott Grundy, MD, PhD
Lisa M. Sullivan, PhD
Peter Wilson, MD
for the CHD Risk Prediction Group

Context The Framingham Heart Study produced sex-specific coronary heart disease (CHD) prediction functions for assessing risk of developing incident CHD in a white middle-class population. Concern exists regarding whether these functions can be generalized to other populations.

Objective To test the validity and transportability of the Framingham CHD prediction functions per a National Heart, Lung, and Blood Institute workshop organized for this purpose.

- FRS was applied to ethnically diverse study cohorts (including the Strong Heart Study)
- FRS does not accurately estimate CHD risk for AIs (particularly women) and required recalibration for accuracy

JAMA. 2001;286:180–187

Table 2. Description of Studies Used in Evaluation*

	Men								Women				
	FHS	ARIC		PHS†	HHP	PR	SHS	CHS	FHS	ARIC		SHS	CHS
	White (n = 2439)	White (n = 4705)	Black (n = 1428)	White (n = 901)	Japanese American (n = 2755)	Hispanic (n = 8713)	Native American (n = 1527)	White (n = 956)	White (n = 2812)	White (n = 5712)	Black (n = 2333)	Native American (n = 2255)	White (n = 1601)
Age range, y	30-74	44-66	44-66	40-74	51-81	35-74	45-75	65-74	30-74	44-66	44-66	45-75	65-74
Mean age, y	48.3	54.6	53.7	57.6	61.9	54.1	55.4	69.7	49.6	53.9	53.3	56.5	69.3
Blood pressure, mm Hg													
Optimal (S<120, D<80)	20	50	27	13	18	24	27	23	35	58	33	37	28
Normal (S<130, D<85)	24	23	21	34	18	23	25	20	21	18	22	22	19
High normal (S<140, D<90)	20	14	18	30	20	18	22	22	15	11	17	17	18
Stage I Htn (S<160, D<100)	23	10	22	21	29	21	20	23	19	9	19	17	24
Stage II-IV Htn (S≥160, D≥100)	13	3	12	3	14	13	7	12	10	2	9	7	9
Total cholesterol, mg/dL‡													
<160	7	8	9	5	4	14	22	11	8	6	8	20	4
160-199	31	32	35	25	29	37	41	42	30	29	30	42	23
200-239	39	39	33	39	41	33	29	36	33	39	34	25	41
240-279	17	16	16	22	21	12	7	9	20	19	20	10	24
≥280	6	4	7	10	5	4	1	2	9	7	9	3	8
HDL-C, mg/dL‡													
<35	19	25	13	18	15	0	25	10	4	6	4	12	2
35-44	36	36	28	31	36	50	40	33	15	18	18	34	14
45-49	15	14	13	14	15	50	11	19	12	12	13	16	13
50-59	19	16	24	21	20	0	13	21	28	25	25	21	27
≥60	11	9	22	16	14	0	10	16	41	40	40	16	45
Diabetes	5	6	14	5	14	7	42	15	4	6	17	51	10
Current smoking	40	24	38	16	32	44	40	12	38	25	25	30	15
5-Year CHD Rate	0.0373	0.0317	0.0322	0.2020	0.0279	0.0123	0.0301	0.0743	0.0139	0.0091	0.0163	0.0102	0.0275

*Table entries are percentages of sample with the exception of age. FHS indicates Framingham Heart Study; ARIC, Atherosclerosis Risk in Communities Study; PHS, Physicians' Health Study; HHP, Honolulu Heart Program; PR, Puerto Rico Heart Health Program; SHS, Strong Heart Study; CHS, Cardiovascular Health Study; S, systolic; D, diastolic; Htn, hypertension; and HDL-C, high-density lipoprotein cholesterol.

†PHS is a nested case-control study with 1-to-4 matching of cases to controls.

‡To convert mg/dL to mmol/L, multiply values for total cholesterol and HDL-C by 0.0259.

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High normal (S<140, D<90)	20	14	18	30	20	18	22	22	15	11	17	17	18
Stage I Htn (S<160, D<100)	23	10	22	21	29	21	20	23	19	9	19	17	24
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Diabetes	5	6	14	5	14	7	42	15	4	6	17	51	10
Current smoking	49	24	39	16	32	44	49	12	39	25	25	39	15
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‡To convert mg/dL to mmol/L, multiply values for total cholesterol and HDL-C by 0.0259.

AHA Scientific Statement

Identification of Obesity and Cardiovascular Risk in Ethnically and Racially Diverse Populations

A Scientific Statement From the American Heart Association

Goutham Rao, MD, FAHA; Tiffany M. Powell-Wiley, MD, MPH, FAHA; Irma Ancheta, PhD, FAHA; Kristen Hairston, MD; Katherine Kirley, MD, MS; Scott A. Lear, PhD; Kari E. North, PhD; Latha Palaniappan, MD, MS, FAHA; Milagros C. Rosal, PhD; on behalf of the American Heart Association Obesity Committee of the Council on Lifestyle and Cardiometabolic Health

Circulation. 2015;132:457–472

The Strong Heart Study
1988-2018

[redacted]

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Committee

32:457–472

The Strong Heart Study

- Large epidemiologic study if CVD and its risk factors in AIs
- Inception in 1988
- Includes 13 tribal communities from Arizona, Oklahoma and the Dakotas
- Phase I-VI completed with phase VII ongoing
  - Phase IV (Strong Heart Family Study) included adolescents

https://strongheartstudy.org

Unique CVD risk factors in AIs

- Albuminuria
- Elevated fibrinogen
- Left ventricular hypertrophy measured by echocardiogram *Circulation.* 1999;99:2389–2395

- Prolonged QRS duration on resting ECG in women *AJC.* 2017;119:1757-1762

Prediction of Coronary Heart Disease in a Population With High Prevalence of Diabetes and Albuminuria

The Strong Heart Study

Elisa T. Lee, PhD; Barbara V. Howard, PhD; Wenyu Wang, PhD; Thomas K. Welty, MD; James M. Galloway, MD; Lyle G. Best, MD; Richard R. Fabsitz, PhD; Ying Zhang, MD, PhD; Jeunliang Yeh, PhD; Richard B. Devereux, MD

- AI-specific, sex-stratified coronary heart disease risk calculator
- Designed for >30 years of age
- Estimated 10-year risk of developing CHD

Circulation. 2006;113(25):2897-905

SHS CHD Risk Calculator

Prediction using (select one)	◉ LDL-C and HDL-C ○ TC and HDL-C
Gender	◉ Male ○ Female
Age	
Are you currently taking hypertension medications for high blood pressure?	◉ No ○ Yes
Systolic Blood Pressure (SBP)	
LDL-C or TC (mg/dL)	
HDL-C (mg/dL)	
Do you have diabetes?	◉ No ○ Yes
Are you a current smoker?	◉ No ○ Yes
Do you have microalbuminuria?	◉ No ○ Yes
Do you have macroalbuminuria?	◉ No ○ Yes

Reset

Calcualte Your Risk

Your Estimated Risk: 0 %

https://strongheart2.ouhsc.edu/CHDcalculator/calculator.html

Fasting Plasma Glucose and Hemoglobin A_{1c} in Identifying and Predicting Diabetes

The Strong Heart Study

WENYU WANG, PHD[1]
ELISA T. LEE, PHD[1]
BARBARA V. HOWARD, PHD[2]
RICHARD R. FABSITZ, PHD[3]
RICHARD B. DEVEREUX, MD[4]
THOMAS K. WELTY, MD, MPH[5]

Association (ADA) (2) based on fasting plasma glucose (FPG) have been used for a long time. Recently, an International Expert Committee (3) recommended a

- AI-specific tool used to estimate the risk of developing diabetes
- Designed for >35 years of age
- Estimates risk of developing diabetes in the next 4 years

Diabetes Care. 2011;34:363–368

SHS DMII Risk Calculator

Predicting risk of developing incident diabetes (DM) defined by either fasting plasma glucose (FPG) or hemoglobin A1c (HbA1c) (denoted as FPG/A1C-DM), or by HbA1c only (denoted as A1C-DM), or by FPG only (denoted as FPG-DM) in the next 4 years for a person who does not currently have FPG/A1C-DM, or A1C-DM, or FPG-DM, respectively (select one).	◉ FPG/A1C-DM ○ A1C-DM ○ FPG-DM
Gender	◉ Male ○ Female
Age (year)	
Waist circumference (cm)	
Taking hypertension medications for high blood pressure?	◉ No ○ Yes
Systolic blood pressure (SBP) (mmHg)	
Diastolic blood pressure (DBP) (mmHg)	
Do you have any of sisters or brothers who had diabetes?	◉ No ○ Yes
Fasting plasma glucose (FPG) (mg/dL)	
Hemoglobin A1c (HbA1c) (%)	
Triglycerides (TG) (mg/dL)	
Urinary albumin and creatinine ratio (UACR) (mg/g)	

Reset

Calculate Your Risk

Your Estimated Risk: 0 %

https://strongheart2.ouhsc.edu/DMcalculator/calculator.html

A Longitudinal Study of Hypertension Risk Factors and Their Relation to Cardiovascular Disease

The Strong Heart Study

Wenyu Wang, Elisa T. Lee, Richard R. Fabsitz, Richard Devereux, Lyle Best, Thomas K. Welty, Barbara V. Howard

- AI-specific tool used to estimate the risk of developing hypertension
- Designed for >35 years of age
- Estimates risk of developing hypertension in the next 4 years

Hypertension. 2006;47:403–409

SHS HTN Risk Calculator

Predicting risk of developing incident hypertension in the next 4 years for a person who does not currently have hypertension.	◉ Hypertension
Age (year)	
Weight (lb)	
Height (in)	
Systolic blood pressure (SBP) (mmHg)	
Diastolic blood pressure (DBP) (mmHg)	
Do you currently drink more than two (if male) or one (if female) serving of alcohol per day?	◉ No ○ Yes
Do you have any parents who had hypertension?	◉ No ○ Yes
Are you currently on diabetes medications?	◉ No ○ Yes
Fasting plasma glucose (FPG) (mg/dL)	
Do you have micro-albuminuria?	◉ No ○ Yes
Do you have macro-albuminuria?	◉ No ○ Yes

Reset

Calculate Your Risk

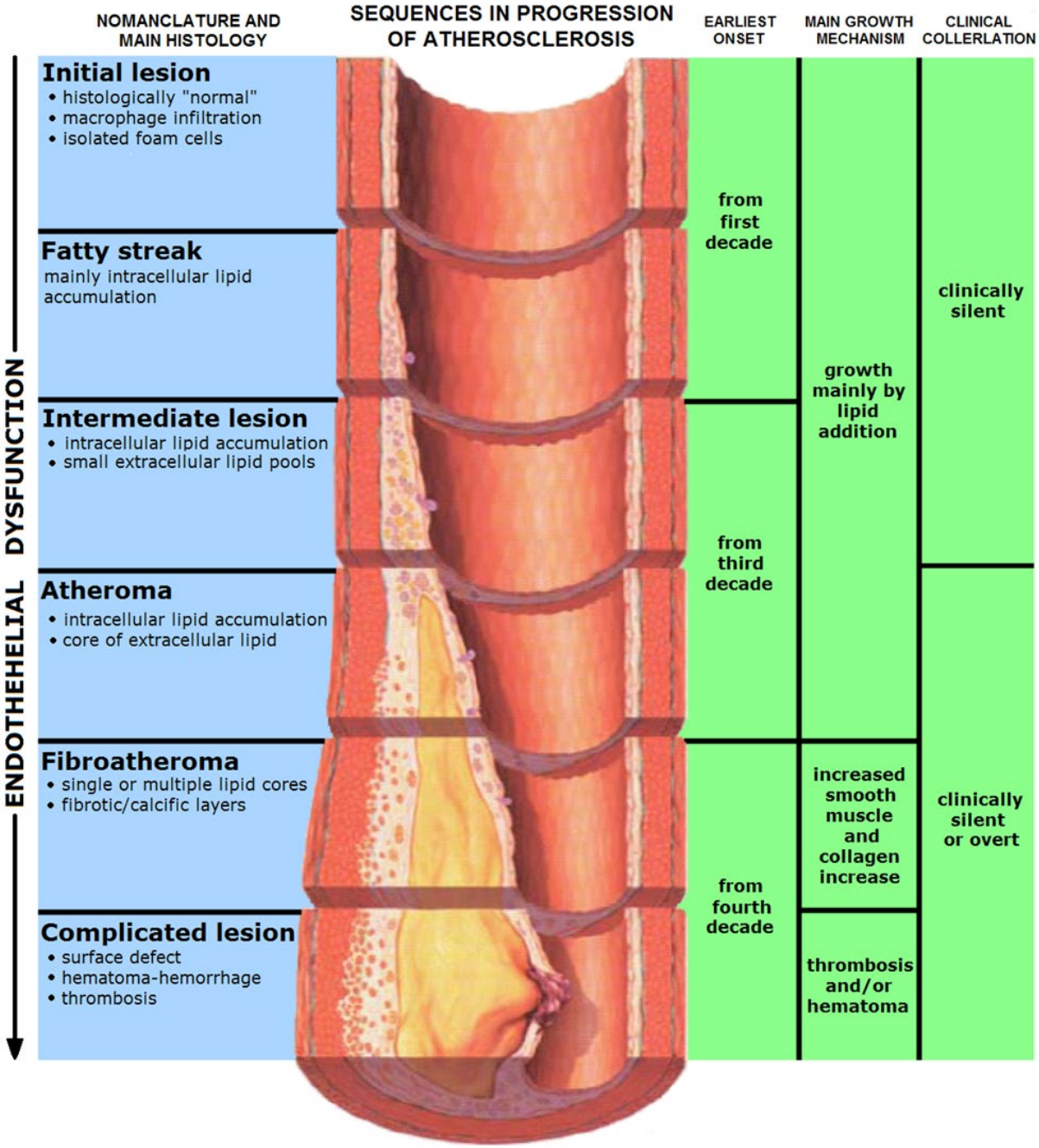
Your Estimated Risk: 0 %

https://strongheart2.ouhsc.edu/HTNcalculator/calculator.html

Future directions . . .

Future directions . . .

Atherosclerosis is a pediatric disease!


NOMANCLATURE AND MAIN HISTOLOGY
SEQUENCES IN PROGRESSION OF ATHEROSCLEROSIS
EARLIEST ONSET
MAIN GROWTH MECHANISM
CLINICAL COLLERLATION
ENDOTHEHELIAL DYSFUNCTION
Initial lesion
• histologically "normal"
• macrophage infiltration
• isolated foam cells
Fatty streak
mainly intracellular lipid accumulation
Intermediate lesion
• intracellular lipid accumulation
• small extracellular lipid pools
Atheroma
• intracellular lipid accumulation
• core of extracellular lipid
Fibroatheroma
• single or multiple lipid cores
• fibrotic/calcific layers
Complicated lesion
• surface defect
• hematoma-hemorrhage
• thrombosis
from first decade
from third decade
from fourth decade
growth mainly by lipid addition
increased smooth muscle and collagen increase
thrombosis and/or hematoma
clinically silent
clinically silent or overt

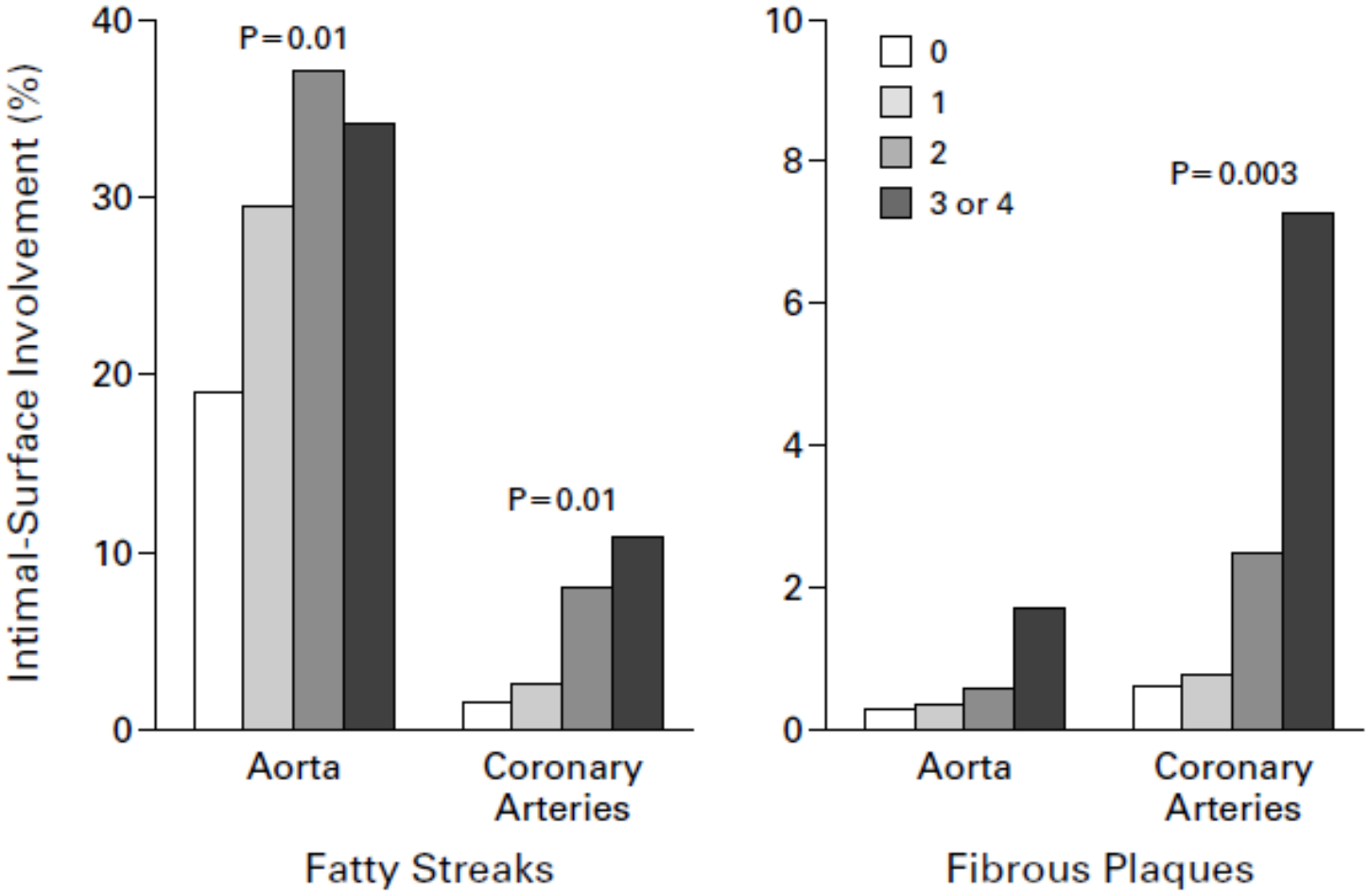
The New England Journal of Medicine

ASSOCIATION BETWEEN MULTIPLE CARDIOVASCULAR RISK FACTORS AND ATHEROSCLEROSIS IN CHILDREN AND YOUNG ADULTS

GERALD S. BERENSON, M.D., SATHANUR R. SRINIVASAN, PH.D., WEIHANG BAO, PH.D., WILLIAM P. NEWMAN III, M.D., RICHARD E. TRACY, M.D., PH.D., AND WENDY A. WATTIGNEY, M.S., FOR THE BOGALUSA HEART STUDY

- Autopsies performed on 204 patients aged 2–39 years
- Patients died of accidental causes
- Antemortem CV risk factors known in 93 subjects
- Risk factors correlated with extent of atherosclerosis present

NEJM 1998;338:1650-6


Intimal-Surface Involvement (%)
40
30
20
10
0
P=0.01
P=0.01
Aorta
Coronary Arteries
Fatty Streaks
10
8
6
4
2
0
0
1
2
3 or 4
P=0.003
Aorta
Coronary Arteries
Fibrous Plaques

Overweight and Obesity Among North American Indian Infants, Children, and Youth

LAWRENCE M. SCHELL[1,2,3] and **MIA V. GALLO**[1,2]

[1]Center for the Elimination of Minority Health Disparities, University at Albany, A&S 237, Albany, New York

[2]Department of Anthropology, University at Albany, A&S 237, Albany, New York

[3]Department of Epidemiology and Biostatistics, University at Albany, School of Public Health, One University Place, Rensselaer, New York

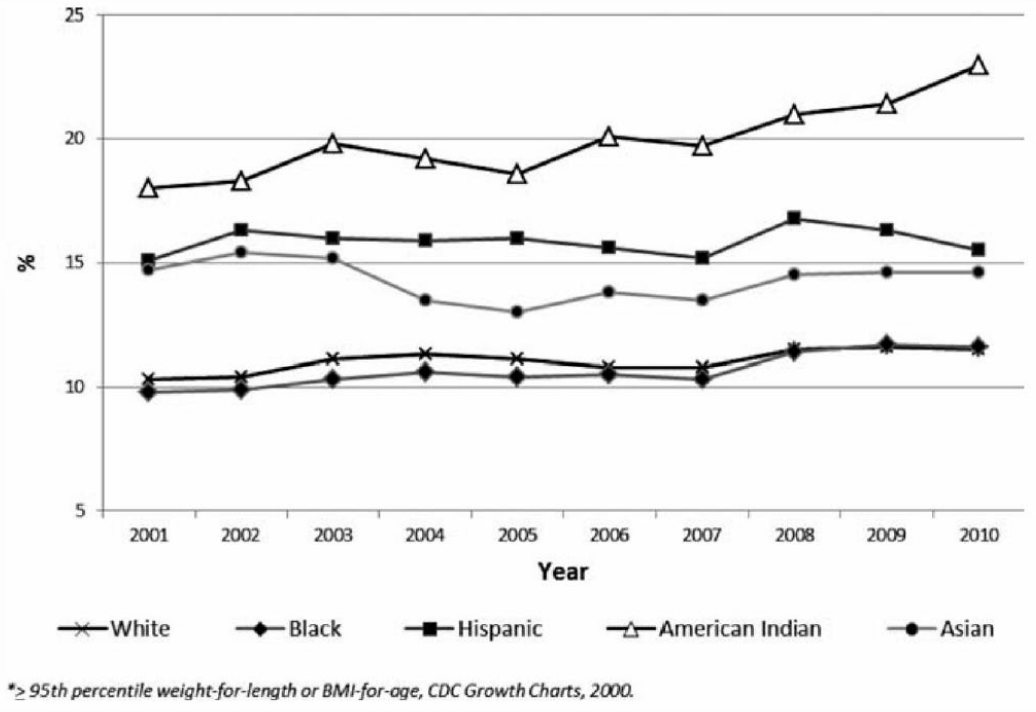


Fig. 2.
Prevalence of obesity trends among 2- to 5-year olds, by race/ethnicity.

Am J Hum Biol. 2012;24(3):302-314

The NEW ENGLAND JOURNAL of MEDICINE

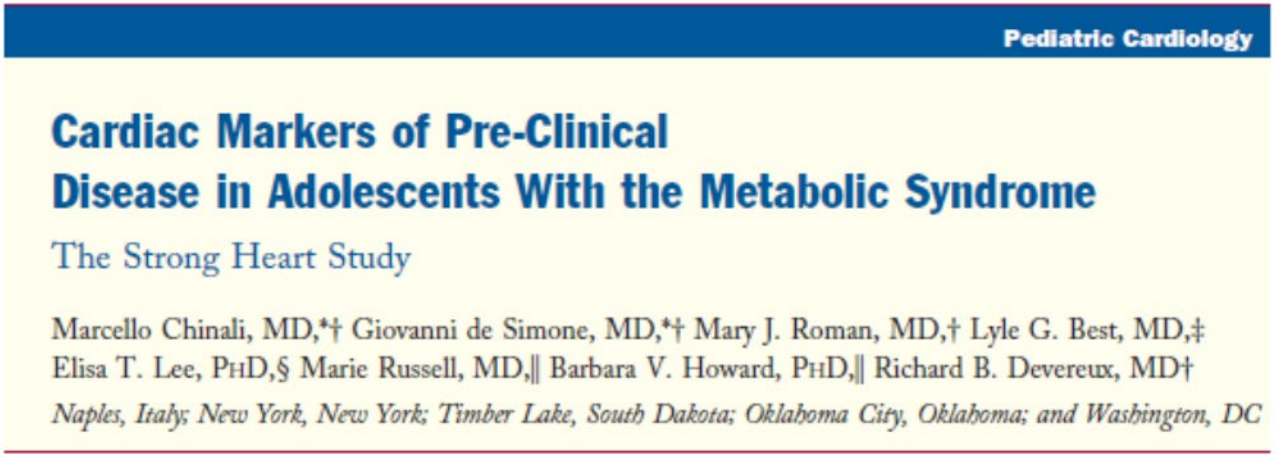
ESTABLISHED IN 1812 FEBRUARY 11, 2010 VOL. 362 NO. 6

Childhood Obesity, Other Cardiovascular Risk Factors, and Premature Death

Paul W. Franks, Ph.D., Robert L. Hanson, M.D., M.P.H., William C. Knowler, M.D., Dr.P.H., Maurice L. Sievers, M.D., Peter H. Bennett, M.B., F.R.C.P., and Helen C. Looker, M.B., B.S.

- Obesity (with subsequent development of glucose intolerance and HTN) was associated with premature endogenous mortality

N Engl J Med. 2010;362:485-493



Pediatric Cardiology

Cardiac Markers of Pre-Clinical Disease in Adolescents With the Metabolic Syndrome

The Strong Heart Study

Marcello Chinali, MD,*† Giovanni de Simone, MD,*† Mary J. Roman, MD,† Lyle G. Best, MD,‡ Elisa T. Lee, PHD,§ Marie Russell, MD,‖ Barbara V. Howard, PHD,‖ Richard B. Devereux, MD†

Naples, Italy; New York, New York; Timber Lake, South Dakota; Oklahoma City, Oklahoma; and Washington, DC

- 24.9% of AI adolescents have metabolic syndrome
  - vs. 12.9% of Hispanic teens, 10.9% of white teens and 2.5% of African American teens
  - Metabolic syndrome is associated with a 2x risk of CVD and a 5x risk of DM

J Am Coll Cardiol. 2008;52:932-938

Circulation. 2004;110:2494-2497

Circulation. 2005;112(20): p. 3066-3072

J Am Coll Cardiol. 2010;56(14)1113-1132

J Am Coll Cardiol. 2007;49(4):403-414

Early predictors of obesity and cardiovascular risk among American Indian children

Sara M Lindberg[1*], **Alexandra K Adams**[2], and **Ronald J Prince**[2]

Sara M Lindberg: smlindberg@wisc.edu

[1*]UW Center for Women's Health and Health Disparities Research, University of Wisconsin-Madison, 310 N. Midvale Blvd., Suite 201 Madison, WI 53705

[2]Department of Family Medicine, University of Wisconsin-Madison

- 471 AI children from Wisconsin, aged 5-8
- 47% were overweight or obese
- **BMI largely determined by age 1**

Matern Child Health J. 2012;16:1879-86

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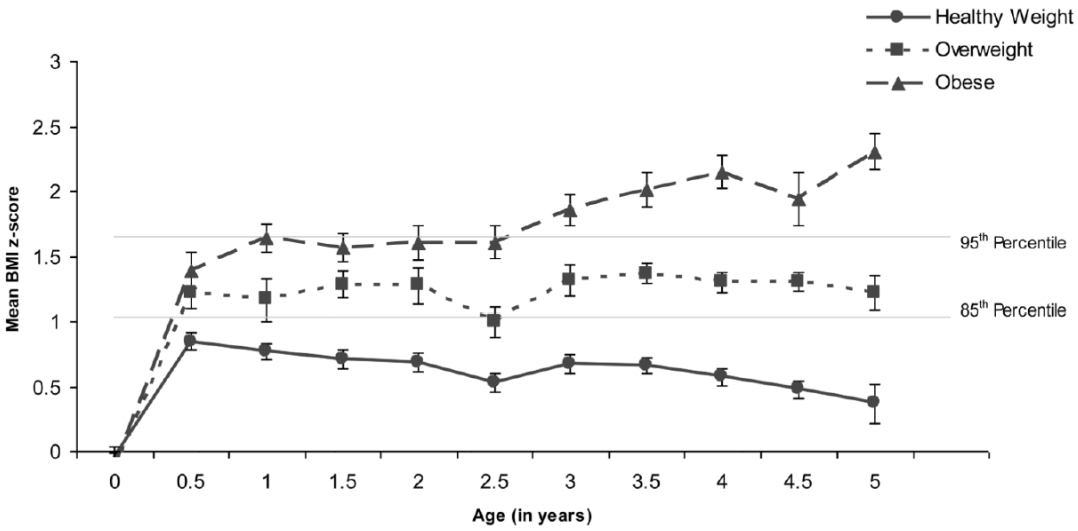

Figure 1.
Growth Trajectories from Birth to Age 5 by BMI Category at Health Screening

Matern Child Health J. 2012;16:1879-86

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- At 5-8 years old, overweight or obese infants had greater odds of:
  - Overweight (OR: 3.42)
  - Obesity (OR: 3.36)
  - Elevated low-density lipoprotein (OR: 1.64)

Matern Child Health J. 2012;16:1879-86

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- Significant predictors of BMI at age 1 year included:
  - Macrosomia (OR: 4.38)
  - Excess gestational weight gain (OR: 1.64)
  - Early termination of breastfeeding (OR: 1.66)

Matern Child Health J. 2012;16:1879-86

Perinatal effects on adult CVD

- CV system seem susceptible to injury from gestation through adulthood
- Maternal effects linked to exaggerated offspring CVD:
  - Malnutrition
  - Chronic disease (obesity)
  - Smoking
  - Allostatic load

Nat Rev Cardiol. 2009;6:712-722

Research Article

Relationship of Childhood Abuse and Household Dysfunction to Many of the Leading Causes of Death in Adults

The Adverse Childhood Experiences (ACE) Study

Vincent J. Felitti, MD, FACP, Robert F. Anda, MD, MS, Dale Nordenberg, MD, David F. Williamson, MS, PhD, Alison M. Spitz, MS, MPH, Valerie Edwards, BA, Mary P. Koss, PhD, James S. Marks, MD, MPH

American Journal of Preventive Medicine. 1998, Volume 14, pages 245–258

Adverse childhood experiences

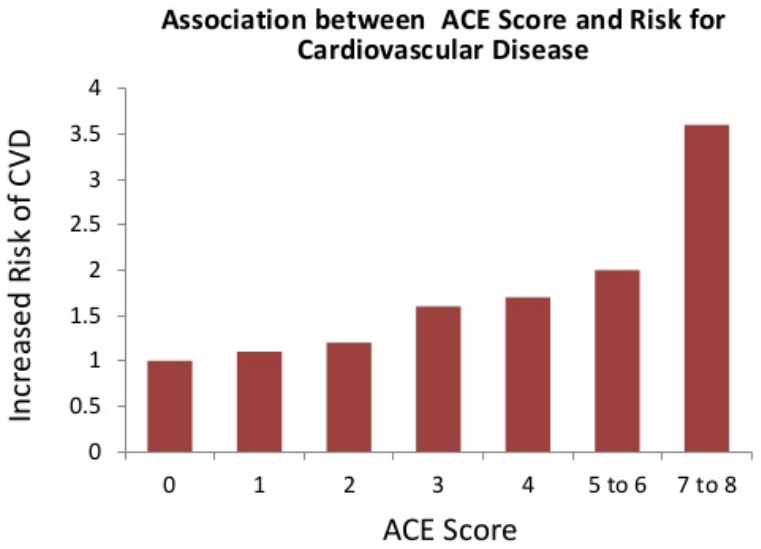
- Physical abuse
- Emotional abuse
- Sexual abuse
- Family substance abuse
- Family mental illness
- Incarcerated family member
- Parental separation/divorce
- Seeing mother physically abused
- Physical neglect
- Emotional neglect

ACE score = number of categories experienced before age 18

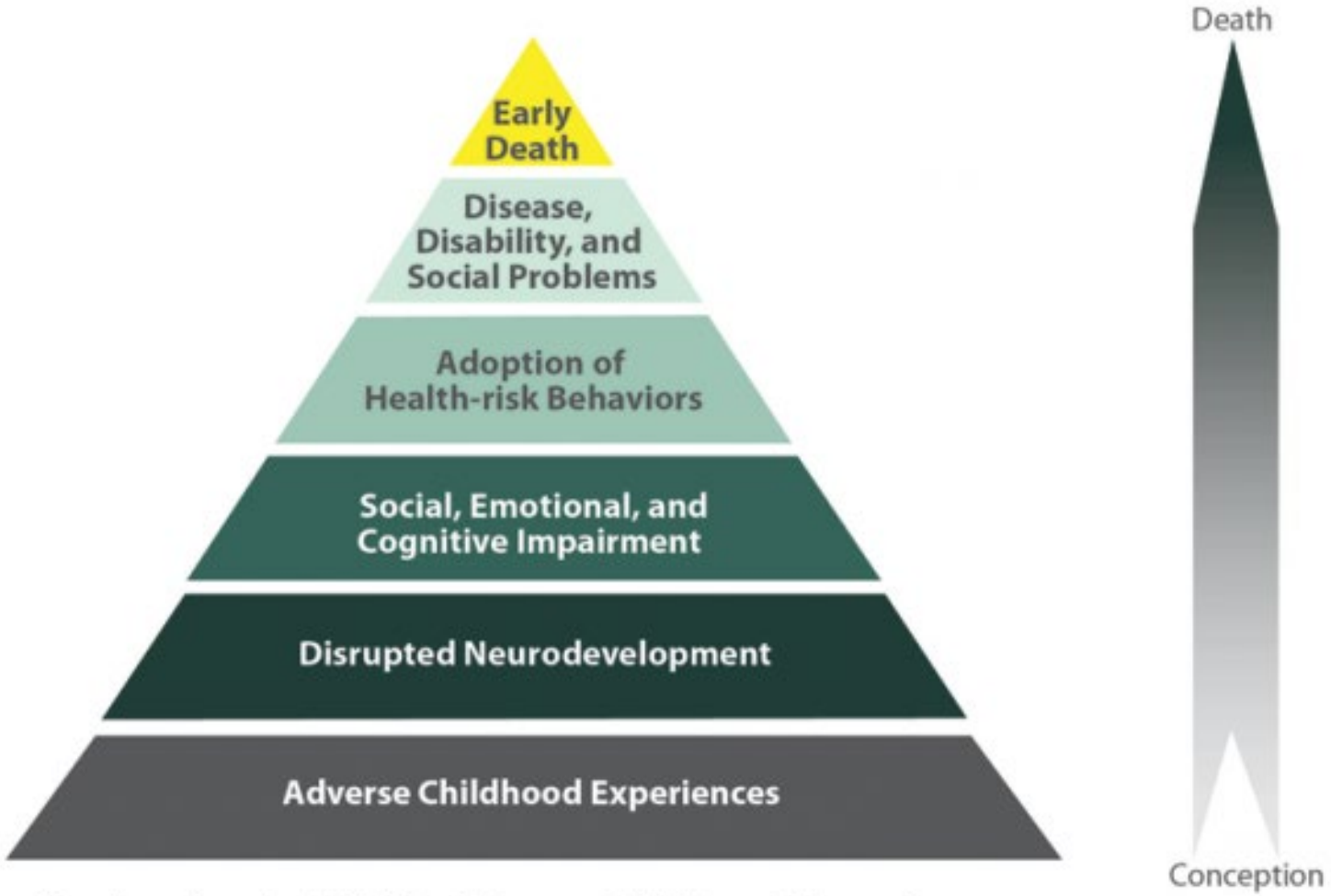
ACEs can have lasting effects on . . .

- Health (CVD, obesity, DMII, depression, cancer, STIs)
- Behaviors (smoking, EtOH, drug use)
- SES (graduation rates, academic achievement)

Graded Relationship Between ACE Score and Cardiovascular Disease



Adapted from Dong et al., 2004



Mechanism by Which Adverse Childhood Experiences Influence Health and Well-being Throughout the Lifespan

Adverse Childhood Experiences among American Indian/Alaska Native Children: The 2011-2012 National Survey of Children's Health

Mary Kay Kenney and Gopal K. Singh

- 2+ ACEs 40.3% (vs. 21.0%)
- 3+ ACEs 26.8% (vs. 11.5%)
- 4+ ACEs 16.8% (vs. 6.2%)
- 5+ ACEs 9.9% (vs. 3.3%)

Scientifica. 2016

In conclusion . . .

- American Indians have accelerated CVD mortality and morbidity
- American Indian-specific CVD risk calculators are available through the SHS website

In conclusion . . .

- AIs have early onset CVD mortality and morbidity
- CVD is a pathologic continuum which begins during gestation
- Traditional CVD risk factors are common in AI youth and are extremely prevalent with obesity
- AI youth with traditional CVD risk factors have demonstrable pathologic cardiovascular changes

Tips for family docs

- Discussions regarding pediatric obesity should begin during pre-pregnancy counseling and young well-woman visits
  - Smoking cessation
  - PHQ-9
  - Gestational diabetes/insulin resistance management
  - Focus on healthy weight gain during pregnancy

Tips for family docs

- Encourage breastfeeding
- Nutritional counseling
- Parenting skill groups/family intervention
- Assess ACE score
- Encourage physical activity/sports participation

ORIGINAL ARTICLE

Childhood Adiposity, Adult Adiposity, and Cardiovascular Risk Factors

Markus Juonala, M.D., Ph.D., Costan G. Magnussen, Ph.D., Gerald S. Berenson, M.D., Alison Venn, Ph.D., Trudy L. Burns, M.P.H., Ph.D., Matthew A. Sabin, M.D., Ph.D., Sathanur R. Srinivasan, Ph.D., Stephen R. Daniels, M.D., Ph.D., Patricia H. Davis, M.D., Wei Chen, M.D., Ph.D., Cong Sun, M.D., Ph.D., Michael Cheung, M.D., Ph.D., Jorma S.A. Viikari, M.D., Ph.D., Terence Dwyer, M.D., M.P.H., and Olli T. Raitakari, M.D., Ph.D.

- CVD outcomes among obese children who became non-obese by adulthood were similar to those who were never obese

N Engl J Med. 2011;365:1876-1885

CLINICAL PRACTICE GUIDELINE Guidance for the Clinician in Rendering Pediatric Care

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

Clinical Practice Guideline for the Evaluation and Treatment of Children and Adolescents With Obesity

Sarah E. Hampl, MD, FAAP,[a] Sandra G. Hassink, MD, FAAP,[b] Asheley C. Skinner, PhD,[c] Sarah C. Armstrong, MD, FAAP,[d] Sarah E. Barlow, MD, MPH, FAAP,[e] Christopher F. Bolling, MD, FAAP,[f] Kimberly C. Avila Edwards, MD, FAAP,[g] Ihuoma Eneli, MD, MS, FAAP,[h] Robin Hamre, MPH,[i] Madeline M. Joseph, MD, FAAP,[j] Doug Lunsford, MEd,[k] Eneida Mendonca, MD, PhD, FAAP,[l] Marc P. Michalsky, MD, MBA, FAAP,[m] Nazrat Mirza, MD, ScD, FAAP,[n] Eduardo R. Ochoa, Jr, MD, FAAP,[o] Mona Sharifi, MD, MPH, FAAP,[p] Amanda E. Staiano, PhD, MPP,[q] Ashley E. Weedn, MD, MPH, FAAP,[r] Susan K. Flinn, MA,[s] Jeanne Lindros, MPH,[t] Kymika Okechukwu, MPA[u]

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Thank you!

jason.deen@seattlechildrens.org