The Coronary Artery Risk Development in Young Adults (CARDIA) Study

and

Impact of Coronary Calcium on Young Adults

Stephen Sidney, MD, MPH
September 9, 2019
## CARDIA Study Design

<table>
<thead>
<tr>
<th>Four Field Centers</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Birmingham</td>
<td>University of Alabama</td>
<td></td>
</tr>
<tr>
<td>Chicago</td>
<td>Northwestern University</td>
<td></td>
</tr>
<tr>
<td>Minneapolis</td>
<td>University of Minnesota</td>
<td></td>
</tr>
<tr>
<td>Oakland</td>
<td>Kaiser Permanente Northern California, Division of Research</td>
<td></td>
</tr>
</tbody>
</table>

### Multicenter cohort study of evolution of CVD risk beginning in young adulthood

Funded in December 1983 by National Heart Lung and Blood Institute

5,115 participants balanced in each center by:

- Age (18-24, 25-30)
- Sex
- Race (AA/W)
- Education (≤HS, >HS)
475 deaths (9.3% of cohort) reported; 406 reviewed (as of 2/11/2019)

<table>
<thead>
<tr>
<th>Cause</th>
<th>Black</th>
<th>White</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>42</td>
<td>34</td>
<td>76</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>46</td>
<td>26</td>
<td>72</td>
</tr>
<tr>
<td>AIDS</td>
<td>26</td>
<td>23</td>
<td>49</td>
</tr>
<tr>
<td>Unintentional injury</td>
<td>18</td>
<td>14</td>
<td>32</td>
</tr>
<tr>
<td>Homicide</td>
<td>31</td>
<td>0</td>
<td>31</td>
</tr>
<tr>
<td>Unknown</td>
<td>14</td>
<td>7</td>
<td>21</td>
</tr>
<tr>
<td>Suicide</td>
<td>2</td>
<td>16</td>
<td>18</td>
</tr>
<tr>
<td>Liver disease</td>
<td>5</td>
<td>8</td>
<td>13</td>
</tr>
<tr>
<td>Kidney disease</td>
<td>10</td>
<td>3</td>
<td>13</td>
</tr>
<tr>
<td>Sepsis</td>
<td>8</td>
<td>2</td>
<td>10</td>
</tr>
</tbody>
</table>
### CARDIA Morbidity

<table>
<thead>
<tr>
<th>413 Non-fatal cardiovascular disease endpoints</th>
</tr>
</thead>
<tbody>
<tr>
<td>92 myocardial infarctions</td>
</tr>
<tr>
<td>93 strokes</td>
</tr>
<tr>
<td>73 heart failure</td>
</tr>
<tr>
<td>61 atrial fibrillation/atrial flutter</td>
</tr>
<tr>
<td>43 coronary revascularization</td>
</tr>
</tbody>
</table>
## CARDIA

### Publications

- 829 publications as of 2/22/2019
- Authors from 37 countries and over 614 institutions
- Peer-reviewed publications cited 43,624 times (average 1,363 / year)

### Presentations

- 1,208 scientific presentations at national and international meetings
# CARDIA exam components - core

<table>
<thead>
<tr>
<th>All exams</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood pressure</strong></td>
</tr>
<tr>
<td><strong>Blood lipids / other tests</strong></td>
</tr>
<tr>
<td><strong>Questionnaires</strong></td>
</tr>
<tr>
<td>Medical history</td>
</tr>
<tr>
<td>Sociodemographic</td>
</tr>
<tr>
<td>Physical activity</td>
</tr>
<tr>
<td>Tobacco</td>
</tr>
<tr>
<td>Alcohol</td>
</tr>
<tr>
<td>Illegal drugs</td>
</tr>
<tr>
<td><strong>Measurements</strong></td>
</tr>
<tr>
<td>Weight</td>
</tr>
<tr>
<td>Height</td>
</tr>
<tr>
<td>Waist circumference</td>
</tr>
</tbody>
</table>
### CARDIA Genetic Components

<table>
<thead>
<tr>
<th>DNA from Y5, Y10, Y15, Y20, Y25</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stored cells for immortalization Y15</td>
</tr>
<tr>
<td>Study funded lab (U Texas Health Science Center, Houston); three other labs</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Consortia</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARe</td>
</tr>
<tr>
<td>GENEVA</td>
</tr>
<tr>
<td>CALiCo</td>
</tr>
<tr>
<td>Exome</td>
</tr>
<tr>
<td>HeartGO</td>
</tr>
<tr>
<td>ADVANCE</td>
</tr>
<tr>
<td>CHARGE</td>
</tr>
<tr>
<td>CARDIA exam components – other</td>
</tr>
<tr>
<td>-------------------------------</td>
</tr>
<tr>
<td><strong>1 or more exams</strong></td>
</tr>
<tr>
<td>Pulmonary function testing</td>
</tr>
<tr>
<td>Echocardiogram</td>
</tr>
<tr>
<td>Coronary calcium by CT scan</td>
</tr>
<tr>
<td>Carotid ultrasound (intima media thickness)</td>
</tr>
<tr>
<td>28-day diet history</td>
</tr>
<tr>
<td>Symptom-limited graded exercise treadmill test</td>
</tr>
<tr>
<td>Urine albumin and creatinine</td>
</tr>
<tr>
<td>Cognitive function</td>
</tr>
<tr>
<td>Brain MRI (substudy)</td>
</tr>
<tr>
<td>Visceral and pericardial fat</td>
</tr>
<tr>
<td>Psychosocial questionnaires (hostility, depression, experiences of discrimination, etc.)</td>
</tr>
</tbody>
</table>
DISPARITIES
30 Year Trend, Mean SBP by Race and Sex

- AA Men
- White Men
- AA Women
- White Women


Age: 18-30

Pressure (mm Hg):
- Y0: 100
- Y2: 104
- Y5: 108
- Y7: 112
- Y10: 116
- Y15: 120
- Y20: 124
- Y25: 128
- Y30: 132

Years:
- 1985
- 1987
- 1990
- 1992
- 1995
- 2000
- 2005
- 2010
- 2015

Age:
- 18-30
- 48-60
30 Year Trend, Prevalence of Hypertension* by Race and Sex

*SBP/DBP ≥ 140/90 or using hypertensive medication

- AA Men
- White Men
- AA Women
- White Women

Years:
- 1985
- 1987
- 1990
- 1992
- 1995
- 2000
- 2005
- 2010
- 2015

Age:
- 18-30
- 48-60
30 Year Trend, Mean of BMI by Race and Sex

![Graph showing BMI trends over 30 years for AA Men, White Men, AA Women, and White Women. The graph includes data from 1985 to 2015, with age groups from 18-30 and 48-60.](image-url)

- **AA Men**: Blue line
- **White Men**: Green line
- **AA Women**: Red line
- **White Women**: Yellow line

**Years**:
- 1985
- 1987
- 1990
- 1992
- 1995
- 2000
- 2005
- 2010
- 2015

**Age Groups**:
- Age 18-30
- Age 48-60

**BMI Units**: kg/m²

-Kaiser Permanente-
30 Year Trend, Waist Circumference by Race and Sex

- AA Men
- White Men
- AA Women
- White Women

Years:
- Y0 (1985)
- Y2 (1987)
- Y5 (1990)
- Y7 (1992)
- Y10 (1995)
- Y20 (2005)
- Y25 (2010)
- Y30 (2015)

Age:
- Age 18-30
- Age 20-32
- Age 23-35
- Age 25-37
- Age 28-40
- Age 33-45
- Age 38-50
- Age 43-55
- Age 48-60

Cm:
30 Year Trend, Prevalence of Diabetes* by Race and Sex

* Definition of diabetes:
  Y0, Y7 & Y15 - Based on glucose & Rx; Y10 Based on glucose, OGTT & Rx;
  Y2 & Y5: Based on Rx; Y20 & Y25: Based on glucose, OGTT, Rx & HbA1c.
30 Year Trend, Physical Activity by Race and Sex

Exercise units

Years

Y0 Y2 Y5 Y7 Y10 Y15 Y20 Y25 Y30
Age 18-30

AA Men
White Men
AA Women
White Women

Age 48-60

Kaiser Permanente
30 Year Trend, Mean HDL by Race and Sex

- **AA Men**
- **White Men**
- **AA Women**
- **White Women**

**Axes:**
- **Y-axis:** mg/dL
- **X-axis:** Years (1985-2015)

**Legend:**
- Blue: AA Men
- Green: White Men
- Red: AA Women
- Yellow: White Women

**Graph Description:**
- The graph shows the trend of mean HDL cholesterol levels from 1985 to 2015 for AA men, white men, AA women, and white women.
- The trend is represented by lines for each group, with AA men initially having the lowest levels and white women having the highest levels.
- Over the 30-year period, there is a noticeable increase in HDL levels for all groups, with AA women showing the most significant increase.

**Additional Information:**
- **Age Range:**
  - 18-30: Years 1985-2010
  - 48-60: Years 1985-2015

**Source:** KAISER PERMANENTE
Coronary Artery Calcification

Calcification of R. coronary artery

Calcification of L. anterior descending artery
Baseline Risk Factors Predict CAC at Year 15

<table>
<thead>
<tr>
<th>Year 0 Risk Factors</th>
<th>Minimally Adjusted†</th>
<th>Multivariate Adjusted‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Age, 5 yr</td>
<td>2.54</td>
<td>(2.03–3.18)</td>
</tr>
<tr>
<td>White race</td>
<td>1.32</td>
<td>(0.99–1.75)</td>
</tr>
<tr>
<td>Male gender</td>
<td>3.35</td>
<td>(2.52–4.46)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>2.10</td>
<td>(1.58–2.78)</td>
</tr>
<tr>
<td>Above optimal cut points*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL-C ≥130 mg/dl</td>
<td>2.42</td>
<td>(1.83–3.20)</td>
</tr>
<tr>
<td>Systolic/diastolic BP ≥120/80 mm Hg</td>
<td>1.62</td>
<td>(1.21–2.16)</td>
</tr>
<tr>
<td>BMI ≥25 kg/m²</td>
<td>1.81</td>
<td>(1.38–2.38)</td>
</tr>
<tr>
<td>HDL-C &lt;40 mg/dl</td>
<td>1.46</td>
<td>(1.02–2.08)</td>
</tr>
<tr>
<td>Glucose ≥110 mg/dl</td>
<td>3.19</td>
<td>(1.29–7.88)</td>
</tr>
</tbody>
</table>

CARDIA Healthy Lifestyle Factors

<table>
<thead>
<tr>
<th>Health Lifestyle Factor score</th>
<th>= sum of HF factors present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average BMI &lt;25 kg/m²</td>
<td></td>
</tr>
<tr>
<td>Average alcohol intake 0-15 mg/day for women, 0-30 mg/day for men</td>
<td></td>
</tr>
<tr>
<td>Highest 40% of a diet score based on higher average intake of dietary potassium, calcium, and fiber, and lower intake of saturate fat</td>
<td></td>
</tr>
<tr>
<td>Highest 40% of sex-specific average physical activity score</td>
<td></td>
</tr>
<tr>
<td>Never smoking</td>
<td></td>
</tr>
</tbody>
</table>
**Low CVD Risk profile**

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absence of preexisting cardiovascular disease (CVD)</td>
</tr>
<tr>
<td>Untreated total cholesterol &lt;200 mg/dl</td>
</tr>
<tr>
<td>Untreated blood pressure &lt;120/&lt;80 mg Hg</td>
</tr>
<tr>
<td>No diabetes mellitus</td>
</tr>
<tr>
<td>No smoking</td>
</tr>
</tbody>
</table>
Age-adjusted prevalence of Low CVD Risk Profile at Year 20 by Healthy Lifestyle Factors from Year 0 - 20

Healthy Lifestyle Score and Healthy Life Score Change Predict CAC at Year 20 (2005-2006)

<table>
<thead>
<tr>
<th></th>
<th>Odds ratio</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health lifestyle score at Year 0</td>
<td>0.74</td>
<td>(0.66, 0.84)</td>
</tr>
<tr>
<td>Healthy lifestyle score change at Year 20</td>
<td>0.85</td>
<td>(0.77, 0.94)</td>
</tr>
</tbody>
</table>

Adjusted for age, sex, race, education, hypertension medication, cholesterol-lowering medication, diabetes medication

Association of Coronary artery calcification with incident CHD and Death

- Year 15: 3,043 participants, mean age 40.3 years, with assessment for CAC.
- Prevalence of CAC: 309 individuals (10.2%) with geometric mean Agatson score 21.6.
- Up to 3 CAC measurements obtain over 10 year period (Y15, Y20, Y25).
- Follow-up from Y15 for up to 12.5 years with 57 incident CHD events and 108 incident CVD events.

Ref: Carr JC et al. Association of Coronary Artery Calcium in Adults Aged 32 to 46 Years With Incident Coronary Heart Disease and Death. *JAMA Cardiol*. 2017;2(4):391-399.
Individuals Aged 32 to 46 Years With Prevalent Coronary Artery Calcium (CAC) and Progression During the Following 10 Years

**eFigure.** Cumulative Event-Free Survival for Incident Coronary Heart Disease, Unadjusted Among Participants 32 to 46 Years by CAC Score Categories

Ref: Carr et al. JAMA Cardiol. Published online February 8, 2017.
Incident CHD events by CAC score (odds ratios relative to no CAC)

Incidence Density of Coronary Heart Disease (CHD) Events per 100 Persons

Table 3. Use of Risk Factors Measured in Early Adult Life to Identify the Population Most at Risk for Developing CAC and Incidence of Coronary Heart Disease

<table>
<thead>
<tr>
<th>CAC Screening Strategy in Middle Age</th>
<th>No. (%)</th>
<th>CHD Incidence, No. (%)</th>
<th>CAC Prevalence, No. (%)</th>
<th>Cohort CAC Found by CAC Screening Strategy, No. (%)</th>
<th>No. Enrolled to Find 1 Case of CAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire eligible cohort</td>
<td>3330 (100)</td>
<td>67 (2.0)</td>
<td>964 (28.9)</td>
<td>964/964 (100.0)</td>
<td>3.5</td>
</tr>
<tr>
<td>Predicted low CAC risk</td>
<td>1665 (50.0)</td>
<td>3 (0.2)</td>
<td>219 (13.2)</td>
<td>219/964 (22.7)</td>
<td>7.7</td>
</tr>
<tr>
<td>Predicted high CAC risk</td>
<td>1665 (50.0)</td>
<td>64 (3.8)</td>
<td>745 (44.7)</td>
<td>745/964 (77.3)</td>
<td>2.2</td>
</tr>
</tbody>
</table>

Ref: Carr JC et al. JAMA Cardiol. 2017;2(4):391-399
Association of Coronary artery calcification with incident CHD and Death

Bottom line:

- CAC measured at age 32 – 46 years is predictive of increased CHD over 12.5 years.
- It may be possible to develop an effective strategy for the using of CAC screening utilizing appropriate risk stratification, e.g. as suggested by Greenland, et all J Am Coll Cardiol 2018;72:734-737.)
# Proposed Decision-Making Approach to Selective Use of Coronary Artery Calcium Measurement for Risk Prediction

Using 10-year ASCVD risk estimate plus coronary artery calcium (CAC) score to guide statin therapy:

<table>
<thead>
<tr>
<th>Patient’s 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimate:</th>
<th>&lt;5%</th>
<th>5–7.5%</th>
<th>&gt;7.5–20%</th>
<th>&gt;20%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consulting ASCVD risk estimate alone</td>
<td>Statin not recommended</td>
<td>Consider for statin</td>
<td>Recommend statin</td>
<td>Recommend statin</td>
</tr>
<tr>
<td>Consulting ASCVD risk estimate + CAC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If CAC score = 0</td>
<td>Statin not recommended</td>
<td>Statin not recommended</td>
<td>Statin not recommended</td>
<td>Recommend statin</td>
</tr>
<tr>
<td>If CAC score &gt; 0</td>
<td>Statin not recommended</td>
<td>Consider for statin</td>
<td>Recommend statin</td>
<td>Recommend statin</td>
</tr>
<tr>
<td>Does CAC score modify treatment plan?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAC not effective for this population</td>
<td>CAC can reclassify risk up or down</td>
<td>CAC can reclassify risk up or down</td>
<td>CAC not effective for this population</td>
<td></td>
</tr>
</tbody>
</table>


The figure shows a modified approach to the guideline-based decision making by incorporating a consideration of coronary artery calcium (CAC) testing to reclassify a patient’s risk up or down where it would make a clinically important change in the clinical decision. Adapted with permission from Nasir et al. (90).
Association of Coronary artery calcification with left ventricular change and heart failure


- MESA - CAC progression over approximately 3 years was associated with incident HF and modestly increased LV end diastolic volume and LV end systolic volume independent of overt coronary heart disease. (Bakhshi H, et al. JAHA, 2017, Apr 20;6(4):pii: e005253).

- CAC may be useful in predicting HF and in determining the etiology of HF (Latiff MA, Budoff MJ. Future Cardiol. (2013) 9(1):1)
Figure. Linear regression analysis of the relationship between change in coronary artery calcium (CAC) score and left ventricular (LV) mass index stratified by race.
Incident heart failure

Proportion of blacks with clinical hypertension by subsequent heart failure status

Figure 1. Trajectories in Mid-Blood Pressure in the Coronary Artery Risk Development in Young Adults (CARDIA) Study

Trajectory classes identified for mid-blood pressure, their pattern by age, and number of CARDIA participants in each class.

Adjusted odds ratio of mid-BP Trajectory Groups with Coronary Calcification

Trajectory of Blood Pressure With Untreated and Treated Blood Pressure

Mean BP at Year 25:
A: <120/80 mm Hg
B: SBP 120-139 mm Hg or DBP 80-89 mm Hg
C: SBP ≥140/90 mg Hg

# Prevalence of CAC by Y25 BP Level and Antihypertensive Treatment Status

<table>
<thead>
<tr>
<th>Prevalence of CAC &gt;100 Agatston units (%)</th>
<th>Untreated</th>
<th>Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP &lt;120/&lt;80 mg Hg at Y25</td>
<td>5.3</td>
<td>10.7</td>
</tr>
<tr>
<td>SBP 120 to 129 or DBP 80 to 89 mm Hg (or 120 to 129 / &lt;80 for Participants with Diabetes) at Y25</td>
<td>7.9</td>
<td>14.8</td>
</tr>
<tr>
<td>SBP &gt; 140 or DBP &gt; 90 mm Hg (or &gt; 130 or &gt;80 for Participants with Diabetes) at Y25</td>
<td>9.9</td>
<td>12.7</td>
</tr>
</tbody>
</table>

Cumulative incidence of All-Cause Mortality by BP Group

Cumulative incidence to CVD Events by BP Group

Conclusion

- The CARDIA study has enriched our understanding of the development of cardiovascular risk, and or subclinical and clinical endpoints over a 30-year time period from young adulthood.
- Provides support for optimizing cardiovascular health when young and for the early identification and treatment of hypertension.
NHLBI REPOSITORY DATA SETS AVAILABLE TO SCIENTIFIC COMMUNITY

- Description of data on Public CARDIA website: http://www.cardia.dopm.uab.edu
- Procedures on how to request data: https://biolincc.nhlbi.nih.gov/home/
- For Information or Questions on how to request data: biolincc@imsweb.com
- For Other Information or Questions, send an email to: CARDIAdataquestions@dopm.uab.edu
A Rainy Welcome for the Summer Solstice

White House, Iran Ease Tensions

The interest in space is expected by both sides since hope for an international solution

Rising tensions between the U.S. and Iran continued to mount in recent months, with the United States imposing new sanctions on Iran, further exacerbating the already tense relations between the two nations.

U.S. Restricts Technology Exports To Chinese Supercomputer Makers

The Commerce Department on Monday said it was restricting exports of technologies that could be used to develop artificial intelligence and other advanced computing capabilities.

Where Death Rates Are Rising

After a long period of declining mortality rates, certain parts of the country are experiencing increases in death rates, particularly in rural and less affluent areas.

Heart Disease Roars Back

Younger people and women are more often at risk of heart disease, with rates increasing in these groups.

WSJ
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THE WALL STREET JOURNAL WEEKEND

SATURDAY SUNDAY, JUNE 22 - 23, 2019

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Where Death Rates Are Rising

After a half-century of improvements, middle-aged people are now more likely to die of cardiovascular disease than they were in 2011. Heart disease death rates for people aged 55-64 are especially increasing in the South, where they are already high, and in rural and smaller metro areas.

Percentage increase in heart disease death rates ages 55-64, 2010-15

<table>
<thead>
<tr>
<th>Percentage Increase</th>
<th>2%</th>
<th>10%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decrease/no change</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50 highest increases</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heart Disease Roars Back

Younger people and women are more often stricken; obesity and diabetes stall the decline

By Betsy McKay

One of America’s greatest achievements over the past century has been a huge decline in death rates from heart disease and strokes. Anti-smoking campaigns, medications to control blood pressure and cholesterol, and surgical advances have extended millions of lives, fundamentally reshaping the U.S. population.

Now, progress has stalled. That’s helping drive down life expectancy in the U.S. after decades in which each generation of Americans could expect to live longer than the one that came before.

The death rate for cardiovascular disease—which includes heart disease and strokes—has fallen just 4% since 2011 after dropping more than 70% over six decades, according to mortality statistics from the Centers for Disease Control and Prevention.

Particularly alarming is that the death rate is actually rising for middle-aged Americans.

The overall cardiovascular disease death rate is an under-recognized contributor to the recent decline in U.S. life expectancy. While that has been driven mostly by deaths.

Please turn to page A11

Source: Centers for Disease Control and Prevention
Age-adjusted mortality rates in U.S. 2000-2014

Average annual age-adjusted rate decline (%) for heart disease, stroke, & all CVD in the U.S. 2000-2011 and 2011-2014

% change in age-adjusted rates in CVD outcomes, U.S. 2011-2016

-20  -15  -10  -5   0   5   10   15   20   25

-20 -15 -10 -5  0   5   10   15   20

All CVD  Heart Disease  Stroke  Coronary heart disease  Heart failure
Total Heart Disease Mortality Rates and Number of Deaths, 2000-2017
Age-adjusted Heart Disease mortality rates in U.S. 2000-2015

Number of Deaths per 100,000 person-years

Year

Total Population

Number of Deaths


720,000 700,000 680,000 660,000 640,000 620,000 600,000 580,000 560,000 540,000 520,000

Kaiser Permanente
Percentage change in population: United States, 2015–2016

- All ages: 3.7%
- 65+: 18.9%
Decline in Mortality Rates from Heart Disease during 2000-2015, US vs KPNC


- 12-19 y: 41.3%
- 20-39 y: 32.7%
- 40-59 y: 8.9%
- ≥60 y: 3.2%
SUMMARY OF TOPICS DISCUSSED

- Heart disease and stroke mortality rates have been nearly stagnant for the past 6 years.
- There is heterogeneity in recent trends in mortality among CVD outcomes.
- The rate of CVD mortality decline has lagged in those under age 65 years and is half the decline rate that was achieved in a large integrated health care system.
- 40,000 deaths from heart disease and stroke could potentially be prevented annually among 45-64 year olds in the U.S. with appropriate treatment.
- Trends in CVD mortality rates and the number of CVD deaths may move in different directions.