Primary & Secondary Prevention of Cardiovascular Disease in Primary Care

Marshall Miller, MD
Thomas Jefferson University

Follow this and additional works at: https://jdc.jefferson.edu/fmlectures

Part of the Family Medicine Commons, and the Primary Care Commons

Let us know how access to this document benefits you

Recommended Citation
https://jdc.jefferson.edu/fmlectures/412

This Article is brought to you for free and open access by the Jefferson Digital Commons. The Jefferson Digital Commons is a service of Thomas Jefferson University's Center for Teaching and Learning (CTL). The Commons is a showcase for Jefferson books and journals, peer-reviewed scholarly publications, unique historical collections from the University archives, and teaching tools. The Jefferson Digital Commons allows researchers and interested readers anywhere in the world to learn about and keep up to date with Jefferson scholarship. This article has been accepted for inclusion in Department of Family & Community Medicine Presentations and Grand Rounds by an authorized administrator of the Jefferson Digital Commons. For more information, please contact: JeffersonDigitalCommons@jefferson.edu.
Resident Conference

TIME
Thursday, Mar 26
8:00 AM to 12:00 PM
Primary & Secondary Prevention of Cardiovascular Disease in Primary Care

Marshal N. Miller, MD
Clinical Assistant Professor
Department of Family and Community Medicine
Sidney Kimmel Medical College at Thomas Jefferson University
Disclosures

• None
Overview

• Review historical perspective and complexity of primary CVD prevention
• Discuss primary & secondary prevention of CAD and the 2019 ACC/AHA guidelines
  • Review of the evidence & primary literature
    • Focus on CV risk assessment, DM, ASA/DAPT
    • Practical guidance and management considerations
• CASES- let’s practice and discuss
What we will not be talking about:

- Diagnosis and Management of acute coronary syndromes or ischemic heart disease
- Cardiac imaging modalities for CAD stress tests, other imaging modalities
- Cardiac catheterization, CABG and Revascularization procedures
CAD Prevention and Historical Context

Previous studies suggested as much has 50% patients with CHD had no identifiable risk factors

Greenland et al(2003): 3 prospective cohort studies:

- Chicago Heart Association Detection Project (35 642 M/W 18-59)
- Multiple Risk Factor Intervention Trial (347 978 M 35-57)
- Framingham Heart Study (3295 M/W 34-59)

Main Outcomes: Fatal CHD nonfatal MI preceded by major CHD risk factors (TC >240, SBP> 140, DBP >90 mm Hg cigarette smoking, and diabetes)

Findings: For fatal CHD (n = 20 995) 87-100% had 1+ RF (87-94% 40-59y)
Non fatal MI 92% men, 87% of women
2010 AHA Model for Ideal CV Health

Get your My Life Check® Assessment now at [heart.org/mylifecheck](http://heart.org/mylifecheck).
2019 ACC/AHA Guidelines on the Primary Prevention of Cardiovascular disease
Top 10 Take-Home Messages

2019 Primary Prevention Guidelines
Top 10 Take Home Messages

1. The most important way to prevent atherosclerotic vascular disease, heart failure, and atrial fibrillation is to promote a healthy lifestyle throughout life.

How?
Top 10 Take home messages

2. A team-based care approach is an effective strategy for the prevention of cardiovascular disease. Clinicians should evaluate the social determinants of health that affect individuals to inform treatment decisions.

This includes emphasis on shared decision-making w/ patient and family
Box 1 | Accountable Health Communities
Core Health-Related Social Needs Screening Questions

Underlined answer options indicate positive responses for the associated health-related social need. A value greater than 10 when the numerical values for answers to questions 7-10 are summed indicates a positive screen for interpersonal safety.

Housing Instability
1. What is your housing situation today?
   - I do not have housing (1)
   - I am staying with others, in a hotel, in a shelter, living outside on the street, on a beach, in a car, abandoned building, bus or train station, or in a park (1)
   - I have housing today, but I am worried about losing housing in the future (1)
   - I have housing (1)

2. Think about the place you live. Do you have problems with any of the following? (check all that apply):
   - Bug infestation (scabies, bed bugs)
   - Mold
   - Lead paint or peeling paint
   - Inadequate heat
   - Oven or stove not working
   - No or not working smoke detectors
   - Water leaks
   - None of the above (1)

Food Insecurity
3. Within the past 12 months, you worried that your food would run out before you got money to buy more.
   - Often true (1)
   - Sometimes true (1)
   - Never true (0)

4. Within the past 12 months, the food you bought just didn’t last and you didn’t have money to get more.
   - Often true (1)
   - Sometimes true (1)
   - Never true (0)

Transportation Needs
5. In the past 12 months, has lack of transportation kept you from medical appointments, meetings, work or from getting things needed for daily living? (check all that apply)
   - Yes, it has kept me from medical appointments or getting medications (1)
   - Yes, it has kept me from non-medical meetings, appointments, work, or getting things that I need (1)
   - No (0)

Utility Needs
6. In the past 12 months has the electric, gas, oil, or water company threatened to shut off services in your home?
   - Yes (1)
   - No (0)
   - Already shut off (0)

Interpersonal Safety
7. How often does anyone, including family, physically hurt you?
   - Never (1)
   - Rarely (2)
   - Sometimes (3)
   - Fairly often (4)
   - Frequently (5)

8. How often does anyone, including family, insult or talk down to you?
   - Never (1)
   - Rarely (2)
   - Sometimes (3)
   - Fairly often (4)
   - Frequently (5)

9. How often does anyone, including family, threaten you with harm?
   - Never (1)
   - Rarely (2)
   - Sometimes (3)
   - Fairly often (4)
   - Frequently (5)

10. How often does anyone, including family, scream or curse at you?
   - Never (1)
   - Rarely (2)
   - Sometimes (3)
   - Fairly often (4)
   - Frequently (5)

SOURCE: The above-noted health-related social need screening items are used with permission from their respective owners.
3. Adults who are 40 to 75 years of age and are being evaluated for cardiovascular disease prevention should undergo 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimation and have a clinician-patient risk discussion before starting on pharmacological therapy, such as antihypertensive therapy, a statin, or aspirin. In addition, assessing for other risk-enhancing factors can help guide decisions about preventive interventions in select individuals, as can coronary artery calcium scanning.
## Assessment of Cardiovascular Risk

### Recommendations for Assessment of Cardiovascular Risk

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B-NR</td>
<td>1. For adults 40 to 75 years of age, clinicians should routinely assess traditional cardiovascular risk factors and calculate 10-year risk of ASCVD by using the pooled cohort equations (PCE).</td>
</tr>
<tr>
<td>IIA</td>
<td>B-NR</td>
<td>2. For adults 20 to 39 years of age, it is reasonable to assess traditional ASCVD risk factors at least every 4 to 6 years.</td>
</tr>
<tr>
<td>IIA</td>
<td>B-NR</td>
<td>3. In adults at borderline risk (5% to &lt;7.5% 10-year ASCVD risk) or intermediate risk (≥7.5% to &lt;20% 10-year ASCVD risk), it is reasonable to use additional risk-enhancing factors to guide decisions about preventive interventions (e.g., statin therapy).</td>
</tr>
</tbody>
</table>
### Recommendations for Assessment of Cardiovascular Risk

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIa</td>
<td>B-NR</td>
<td>4. In adults at intermediate risk (≥7.5% to &lt;20% 10-year ASCVD risk) or selected adults at borderline risk (5% to &lt;7.5% 10-year ASCVD risk), if risk-based decisions for preventive interventions (e.g., statin therapy) remain uncertain, it is reasonable to measure a coronary artery calcium score to guide clinician–patient risk discussion.</td>
</tr>
<tr>
<td>IIb</td>
<td>B-NR</td>
<td>5. For adults 20 to 39 years of age and for those 40 to 59 years of age who have &lt;7.5% 10-year ASCVD risk, estimating lifetime or 30-year ASCVD risk may be considered.</td>
</tr>
</tbody>
</table>
Risk Calculator 40-75yrs old
CV Risk assessment in younger Adults:
Largely based on Framingham data and 30 year/lifetime risk estimates
### Risk-Enhancing Factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Family history of premature ASCVD</strong></td>
<td>(males, age &lt;55 y; females, age &lt;65 y)</td>
</tr>
<tr>
<td><strong>Primary hypercholesterolemia</strong></td>
<td>(LDL-C 160–189 mg/dL [4.1–4.8 mmol/L]; non–HDL-C 190–219 mg/dL [4.9–5.6 mmol/L])*</td>
</tr>
<tr>
<td><strong>Metabolic syndrome</strong></td>
<td>(increased waist circumference [by ethnically appropriate cutpoints], elevated triglycerides [&gt;150 mg/dL, nonfasting], elevated blood pressure, elevated glucose, and low HDL-C [&lt;40 mg/dL in men; &lt;50 mg/dL in women] are factors; a tally of 3 makes the diagnosis)</td>
</tr>
<tr>
<td><strong>Chronic kidney disease</strong></td>
<td>(eGFR 15–59 mL/min/1.73 m² with or without albuminuria; not treated with dialysis or kidney transplantation)</td>
</tr>
<tr>
<td><strong>Chronic inflammatory conditions</strong></td>
<td>such as psoriasis, RA, lupus, or HIV/AIDS</td>
</tr>
</tbody>
</table>
Risk-Enhancing Factors

- **History of premature menopause (before age 40 y) and history of pregnancy-associated conditions that increase later ASCVD risk, such as preeclampsia**
- **High-risk race/ethnicity** (e.g., South Asian ancestry)
- **Lipids/biomarkers**: associated with increased ASCVD risk
- Persistently elevated,* primary hypertriglyceridemia (≥175 mg/dL, nonfasting);
- If measured:
  - **Elevated high-sensitivity C-reactive protein** (≥2.0 mg/L)
  - **Elevated Lp(a)**: A relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥50 mg/dL or ≥125 nmol/L constitutes a risk-enhancing factor, especially at higher levels of Lp(a).
  - **Elevated apoB** (≥130 mg/dL): A relative indication for its measurement would be triglyceride ≥200 mg/dL. A level ≥130 mg/dL corresponds to an LDL-C >160 mg/dL and constitutes a risk-enhancing factor
  - **ABI** (<0.9)
High- Sensitivity CRP and CAD

• Elevated CRP has been associated with increased risk for CVD
  • Independent of additional RFs
  • Benefit in addition to traditional CV risk estimates appears small
    • Reclassifies risk in about 1.5%
    • 1 CV event/10 yrs per 400-500 screened
  • Benefit appears highest in those with intermediate (10-20% 10yr risk)

Who should I screen?:
Consider for those at intermediate risk for whom it may impact treatment decisions

What levels are abnormal?
<1mg/L = low risk
>2-3mg/L = higher risk
Lipoprotein a (Lp(a)) and CAD

---

A. Baseline adjustment for age and sex

Baseline multivariable adjustment

C. On-statin adjustment for age and sex

D. On-statin multivariable adjustment

---

A. Baseline lipoprotein(a) events (n) Hazard ratio (95% CI) for lipoprotein(a) ≥50 mg/dL vs <50 mg/dL

<table>
<thead>
<tr>
<th>Age</th>
<th>Events (n)</th>
<th>Hazard ratio (95% CI) for lipoprotein(a) ≥50 mg/dL vs &lt;50 mg/dL</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;60 years</td>
<td>2038</td>
<td>1.0 (0.95-1.05)</td>
<td>0.73</td>
</tr>
<tr>
<td>60 to &lt;70 years</td>
<td>2714</td>
<td>1.2 (0.99-1.43)</td>
<td>0.05</td>
</tr>
<tr>
<td>≥70 years</td>
<td>1099</td>
<td>1.2 (0.97-1.53)</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Sex

| Female | 4645 | 1.2 (1.19-1.35) | 0.07 |

Smoking status

| Other | 4777 | 1.3 (1.14-1.53) | 0.04 |

Synthetic blood pressure

| <120 mm Hg | 953 | 1.2 (1.05-1.43) | 0.03 |
| 120 to <140 mm Hg | 2172 | 1.3 (1.09-1.55) | 0.04 |
| ≥140 mm Hg | 2610 | 1.4 (1.13-1.73) | 0.04 |

LDL-C

| <3 mmol/L | 993 | 1.1 (0.99-1.38) | 0.45 |
| 3 to <4 mmol/L | 3272 | 1.3 (0.14-1.24) | 0.25 |
| ≥4 mmol/L | 2958 | 1.3 (1.13-1.57) | 0.11 |

HDL cholesterol

| <1 mmol/L | 2806 | 1.1 (0.94-1.37) | 0.47 |
| 1 to <2 mmol/L | 1354 | 1.2 (1.01-1.44) | 0.07 |
| ≥2 mmol/L | 906 | 1.4 (1.18-1.66) | 0.05 |

Body mass index

| <25 kg/m² | 894 | 1.2 (1.01-1.17) | 0.07 |
| 25 to <30 kg/m² | 2152 | 1.2 (0.10-1.08) | 0.34 |
| ≥30 kg/m² | 506 | 1.2 (1.00-1.30) | 0.02 |

---

B. Baseline lipoprotein(a) events (n) Hazard ratio (95% CI) for lipoprotein(a) ≥50 mg/dL vs <50 mg/dL

<table>
<thead>
<tr>
<th>Age</th>
<th>Events (n)</th>
<th>Hazard ratio (95% CI) for lipoprotein(a) ≥50 mg/dL vs &lt;50 mg/dL</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;60 years</td>
<td>970</td>
<td>1.6 (1.4-1.9)</td>
<td>0.008</td>
</tr>
<tr>
<td>60 to &lt;70 years</td>
<td>2229</td>
<td>1.6 (1.4-1.9)</td>
<td>0.01</td>
</tr>
<tr>
<td>≥70 years</td>
<td>404</td>
<td>1.6 (1.2-1.9)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Sex

| Male | 2058 | 1.5 (1.2-1.9) | 0.08 |

Smoking status

| Other | 2193 | 1.5 (1.2-1.9) | 0.07 |

Synthetic blood pressure

| <120 mm Hg | 446 | 1.6 (1.2-1.9) | 0.07 |
| 120 to <140 mm Hg | 934 | 1.7 (1.4-2.1) | 0.03 |
| ≥140 mm Hg | 1047 | 1.8 (1.5-2.1) | 0.02 |

LDL-C

| <3 mmol/L | 460 | 1.7 (1.2-2.4) | 0.07 |
| 3 to <4 mmol/L | 799 | 1.8 (1.3-2.4) | 0.07 |
| ≥4 mmol/L | 1314 | 1.7 (1.3-2.2) | 0.04 |

HDL cholesterol

| <1 mmol/L | 1278 | 1.8 (1.4-2.3) | 0.04 |
| 1 to <2 mmol/L | 859 | 1.9 (1.5-2.3) | 0.03 |
| ≥2 mmol/L | 394 | 1.8 (1.3-2.4) | 0.08 |

Body mass index

| <25 kg/m² | 382 | 1.9 (1.5-2.5) | 0.03 |
| 25 to <30 kg/m² | 506 | 1.6 (1.3-2.0) | 0.05 |
| ≥30 kg/m² | 216 | 1.6 (1.2-2.1) | 0.05 |
Lp(a) and CAD

• Statin (+/- ezetimibe) therapy not effective in lowering Lp(a)- and may increase

• PCSK9 Ab’s have been associated w/ 25% reduction in Lp(a) and reductions mortality and risk for MI
  • Limited by costs- consider stratifying use to those with high Lp(a) and LDL above goal
Lp(a) and CAD- Who to Test?

- No clear consensus but elevated Lp(a) clearly associated w/ CAD risk
  - Consider in non-diabetics 40-75yr at intermediate risk (to start statin)
  - Those with primary LDL>190—inc’d risk of Lp(a) excess or premature ASCVD
  - Those who cannot reach LDL goals with appropriate intensity statin (+/- ezetimibe) to consider PCSK9Ab
Apolipoprotein B (ApoB) and CAD

- Apo B is the major apolipoprotein in LDL+VLDL.
- Non-HDL is used as a surrogate
- Some studies have suggested ApoB is a more potent marker of CVD risk than LDL or non-HDL
- Others have shown non-HDL and ApoB levels are highly corelated
  - Less so with HyperTG
- When to consider ApoB:
  - To assess risk for ASCVD for patients with persistent hypertriglyceridemia (>200 mg/dL) despite statin +/- fibrate therapy
ABI and PAD screening in Cardiovascular Disease

• A 2005 meta-analysis of 9 studies found ABI <0.9 is specific (92%) but not sensitive (16%) for predicting incident cardiovascular disease (LR 2.53%), CV death (LR 5.6)

• Better for ruling in than ruling out CVD
• Presence of PAD is ASCVD equivalent and would warrant treatment as such
Coronary Artery Calcium Scoring

Adding CAC to traditional CV risk calculators yielded risk estimates 8-9% higher for those participants who had CV events vs non-events

Calculator

N=6,783. Red dashed line shows 7.5% risk.
Table 6. Selected Examples of Candidates for CAC Measurement Who Might Benefit from Knowing Their CAC Score is Zero

CAC Measurement Candidates Who Might Benefit from Knowing Their CAC Score Is Zero

- Patients reluctant to initiate statin who wish to understand their risk and potential for benefit more precisely
- Patients concerned about need to reinstitute statin therapy after discontinuation for statin-associated symptoms
- Older patients (men 55–80 y of age; women 60–80 y of age) with low burden of risk factors (S4.4-42) who question whether they would benefit from statin therapy
- Middle-aged adults (40–55 y of age) with PCE-calculated 10-year risk for ASCVD 5% to <7.5% with factors that increase their ASCVD risk, although they are in a borderline risk group.
CAC and CV risk: Take home Points

- Consider in adults at intermediate risk (≥7.5-%<20% 10-year ASCVD) or selected adults at borderline risk (5-%<7.5% 10-year ASCVD)
- CAC < 1 is highly predictive of low 10 yr. CV risk (most useful in ruling out significant CAD risk)
- CAC >100 is predictive of at least intermediate risk

Limitations:
- Not covered by most insurance companies ($100-400)
- Radiation risk
Take home points:

• For patients at intermediate ASCVD risk consider:
  • Advanced biomarker testing --Hs-CRP, Lp(a) (best data), apoB
  • ABI
  • Coronary Artery calcium scoring
  
... After assessing for risk enhancing conditions IF it will change management/risk classification
Top 10 Take Home Messages

4. All adults should consume a healthy diet that emphasizes the intake of vegetables, fruits, nuts, whole grains, lean vegetable or animal protein, and fish and minimizes the intake of trans fats, red meat and processed red meats, refined carbohydrates, and sweetened beverages. For adults with overweight and obesity, counseling and caloric restriction are recommended for achieving and maintaining weight loss.
Top 10 Take Home Messages

5. Adults should engage in at least 150 minutes per week of accumulated moderate-intensity physical activity or 75 minutes per week of vigorous-intensity physical activity.
Americans and Exercise:

<table>
<thead>
<tr>
<th>Intensity</th>
<th>METs</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedentary behavior*</td>
<td>1–1.5</td>
<td>Sitting, reclining, or lying; watching television</td>
</tr>
<tr>
<td>Light</td>
<td>1.6–2.9</td>
<td>Walking slowly, cooking, light housework</td>
</tr>
<tr>
<td>Moderate</td>
<td>3.0–5.9</td>
<td>Brisk walking (2.4–4 mph), biking (5–9 mph), ballroom dancing, active yoga, recreational swimming</td>
</tr>
<tr>
<td>Vigorous</td>
<td>≥6</td>
<td>Jogging/running, biking (≥10 mph), singles tennis, swimming laps</td>
</tr>
</tbody>
</table>
6. For adults with type 2 diabetes mellitus, lifestyle changes, such as improving dietary habits and achieving exercise recommendations, are crucial. If medication is indicated, metformin is first-line therapy, followed by consideration of a sodium-glucose cotransporter 2 inhibitor or a glucagon-like peptide-1 receptor agonist.

Top 10 Take Home Messages
Fig. 2. Treatment of T2DM for Primary Prevention of CVD

- **HbA1c > 6.5% consistent with T2DM**
  - **YES**
    - Dietary counselling regarding key aspects of a heart-healthy diet (Class I)
    - At least 150 minutes/week of moderate to vigorous physical activity (Class I)
    - Aggressive treatment of other CVD risk factors
  - **NO**
    - Consideration of metformin as first-line pharmacologic therapy to improve glycemic control and reduce CVD risk (Class IIa)

- **HbA1c < 7.0% after lifestyle therapies and metformin?**
  - **NO**
    - Further management of diabetes per primary care provider or endocrinology
  - **YES**
    - Reinforce the importance of diet and physical activity and continue current management
    - Does the patient have other CVD risk factors? (Class IIb)
      - **NO**
      - Consideration may be given to an SGLT-2 inhibitor or a GLP-1R agonist to improve glycemic control and reduce CVD risk (Class IIb)
### Metformin and CVD Risk Reduction

<table>
<thead>
<tr>
<th>Aggregate Endpoint</th>
<th>p for Metformin vs Other Intensive</th>
<th>Patients with Aggregate Endpoints</th>
<th>Absolute Risk (events per 1000 patient-years)</th>
<th>Log-rank 2p</th>
<th>RR (95% CI)</th>
<th>Favours Metformin or Intensive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any diabetes-related endpoint</td>
<td>p=0.0034</td>
<td>Metformin: 98</td>
<td>Conventional: 160</td>
<td>29.8</td>
<td>0.0023</td>
<td>0.68 (0.53–0.87)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intensive: 380</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes-related death</td>
<td>p=0.11</td>
<td>Metformin: 28</td>
<td>Conventional: 160</td>
<td>7.5</td>
<td>0.017</td>
<td>0.58 (0.37–0.91)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intensive: 103</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>p=0.021</td>
<td>Metformin: 50</td>
<td>Conventional: 89</td>
<td>12.5</td>
<td>0.011</td>
<td>0.52 (0.31–0.87)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intensive: 150</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>p=0.12</td>
<td>Metformin: 39</td>
<td>Conventional: 73</td>
<td>11.0</td>
<td>0.01</td>
<td>0.41 (0.29–0.61)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intensive: 139</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>p=0.082</td>
<td>Metformin: 12</td>
<td>Conventional: 23</td>
<td>8.8</td>
<td>0.013</td>
<td>1.58 (0.92–2.72)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intensive: 60</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>p=0.62</td>
<td>Metformin: 6</td>
<td>Conventional: 9</td>
<td>1.6</td>
<td>0.57</td>
<td>1.74 (0.82–3.69)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intensive: 12</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microvascular</td>
<td>p=0.39</td>
<td>Metformin: 24</td>
<td>Conventional: 38</td>
<td>7.7</td>
<td>0.049</td>
<td>1.71 (0.71–4.08)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intensive: 74</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Graphical Representation:**

- **D1:** Represents the baseline risk.
- **1:** Represents the intermediate risk.
- **10:** Represents the highest risk.

---

**Legend:**

- **Metformin:** Favorable results for Metformin treatment compared to conventional.
- **Intensive:** Favorable results for Intensive treatment compared to conventional.
2017 Meta-analysis of 13 RCTs
Metformin vs Placebo:
• All outcomes, with the exception of stroke, favored metformin. None significant
• Effect sizes:
  • All-cause mortality 0.96 (95% CI 0.84, 1.09)
  • CV Death 0.97 (95% CI 0.80, 1.16)
  • MI 0.89 (95% CI 0.75, 1.06)
  • Stroke 1.04 (95% CI 0.73, 1.48)
  • PVD 0.81 (95% CI 0.50, 1.31)

Table 1. Effects of Metformin Compared With Sulfonylurea Monotherapy on Long-Term All-Cause Mortality and Cardiovascular Mortality and Morbidity

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Range in RR From RCTs</th>
<th>Range in RD From RCTs</th>
<th>Adjusted HR From Observational Studies</th>
<th>Strength of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>0.5 to 1.0 (2 studies [15, 16])</td>
<td>-0.0% to -0.1% (2 studies [15, 16])</td>
<td>0.5 to 0.8 (7 studies* [17-23])</td>
<td>Low</td>
</tr>
<tr>
<td>CVD mortality</td>
<td>0.6 to 0.7 (2 studies [15, 16])</td>
<td>-2.9% to -0.1% (2 studies [15, 16])</td>
<td>0.6 to 0.9 (3 studies [19, 21, 24])</td>
<td>Moderate</td>
</tr>
<tr>
<td>CVD morbidity</td>
<td>0.7 to 1.6 (2 studies [15, 16])</td>
<td>-0.4% to 10.1% (2 studies [15, 16])</td>
<td>0.3 to 0.9 (5 studies† [19, 20, 22, 25, 26])</td>
<td>Low</td>
</tr>
</tbody>
</table>

CVD = cardiovascular disease; HR = hazard ratio; RCT = randomized, controlled trial; RD = risk difference; RR = relative risk.
* One additional retrospective cohort study reported an odds ratio of 0.9 (27).
† One additional case-control study reported an odds ratio of 0.8 (28).
# SGLT-2 Inhibitors and CVD Risk Reduction

<table>
<thead>
<tr>
<th>Patients with atherosclerotic cardiovascular disease</th>
<th>EMPA-REG OUTCOME</th>
<th>CANVAS Program</th>
<th>DECLARE TIMI 58</th>
<th>Fixed effects model for atherosclerotic cardiovascular disease (p=0.0002)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment (%)</td>
<td>4687</td>
<td>3756</td>
<td>3474</td>
<td>0.86 (0.74-0.99)</td>
</tr>
<tr>
<td>Placebo (%)</td>
<td>2333</td>
<td>2500</td>
<td>3500</td>
<td></td>
</tr>
<tr>
<td>Events / 1000 patient-years (%)</td>
<td>777</td>
<td>756</td>
<td>1020</td>
<td></td>
</tr>
<tr>
<td>HR</td>
<td>37.4</td>
<td>34.1</td>
<td>26.9</td>
<td></td>
</tr>
<tr>
<td>Weight (%)</td>
<td>43.9</td>
<td>41.3</td>
<td>43.0</td>
<td></td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>19.4</td>
<td>32.4</td>
<td>30.2</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patients with multiple risk factors</th>
<th>CANVAS Program</th>
<th>DECLARE TIMI 58</th>
<th>Fixed effects model for multiple risk factors (p=0.038)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment (%)</td>
<td>1447</td>
<td>5360</td>
<td>1.01 (0.86-1.26)</td>
</tr>
<tr>
<td>Placebo (%)</td>
<td>215</td>
<td>539</td>
<td>1.00 (0.87-1.15)</td>
</tr>
<tr>
<td>Events / 1000 patient-years (%)</td>
<td>15.8</td>
<td>13.4</td>
<td></td>
</tr>
<tr>
<td>HR</td>
<td>15.5</td>
<td>13.3</td>
<td></td>
</tr>
<tr>
<td>Weight (%)</td>
<td>25.9</td>
<td>24.1</td>
<td></td>
</tr>
<tr>
<td>HR (95% CI)</td>
<td>25.9</td>
<td>24.1</td>
<td></td>
</tr>
</tbody>
</table>

**Cardiovascular benefits**
- Glucose
- Body weight & fat
- Blood pressure
- Uric acid
- LDL-cholesterol
- HDL-cholesterol
- Genital infections
- Dehydration
- Acute kidney injury
- Low risk of hypoglycemia
- Albuminuria
- Normoglycemic nephropathy

**Disadvantages**

**Advantages**

- Cardiovascular Outcome Trials
  - Completed: EMPA-REG OUTCOME (empagliflozin), CANVAS (canagliflozin)
  - Ongoing: DECLARE TIMI 58 (dapagliflozin), VERTIS CV (ertugliflozin)
GLP-1 Agonists and CVD Risk Reduction

- Significant reductions to 3 point MACE, CV mortality and all cause
- No overall inc. in Aes

Limitations:
- Only patients w/ known CAD included in trials
- No clear evidence of fatal and non-fatal MI reduction
Comparison of DM drug classes in CV Disease Outcomes

Fig. 1. Cardiovascular outcome trials with DPP4 inhibitors, GLP1 receptor agonists, and SGLT2 inhibitors. SAVOR TIMI, Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus-Thrombolysis in Myocardial Infarction; EXAMINE, Examination of Cardiovascular Outcomes with Alogliptin versus Standard of Care; TECOS, Trial Evaluating Cardiovascular Outcomes with Sitagliptin; ELIXA, Evaluation of Lixisenatide in Acute Coronary Syndrome; LEADER, Liraglutide Effect and Action in Diabetes: Evaluation of cardiovascular outcome Results; SUSTAIN-6, a Trial to Evaluate Cardiovascular and Other Long-term Outcomes with Semaglutide in Subjects with Type 2 Diabetes; EXSCEL, Exenatide Study of Cardiovascular Event Lowering; EMPA-REG OUTCOME, Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients; CANVAS, Canagliflozin Cardiovascular Assessment Study.
7. All adults should be assessed at every healthcare visit for tobacco use, and those who use tobacco should be assisted and strongly advised to quit.
Aspirin should be used infrequently in the routine primary prevention of ASCVD because of lack of net benefit.
# Aspirin Use

## Recommendations for Aspirin Use

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIb</td>
<td>A</td>
<td>1. Low-dose aspirin (75-100 mg orally daily) might be considered for the primary prevention of ASCVD among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk.</td>
</tr>
<tr>
<td>III: Harm</td>
<td>B-R</td>
<td>2. Low-dose aspirin (75-100 mg orally daily) should not be administered on a routine basis for the primary prevention of ASCVD among adults &gt;70 years of age.</td>
</tr>
<tr>
<td>III: Harm</td>
<td>C-LD</td>
<td>3. Low-dose aspirin (75-100 mg orally daily) should not be administered for the primary prevention of ASCVD among adults of any age who are at increased risk of bleeding.</td>
</tr>
</tbody>
</table>
ASA for Primary Prevention of CAD

- ASCEND: RCT of 15,480 patients with DM, no known CAD (mean f/u 7.4 years)
  - Most pts on statin(75%), HTN Tx
  - 12% lower risk for CV events
  - 29% higher major bleeding risk

<table>
<thead>
<tr>
<th>Type of Event</th>
<th>Aspirin (N=7740)</th>
<th>Placebo (N=7740)</th>
<th>Rate Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular Outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonfatal myocardial infarction</td>
<td>191 (2.5)</td>
<td>193 (2.5)</td>
<td>0.99 (0.80–1.20)</td>
<td>0.69</td>
</tr>
<tr>
<td>Nonfatal presumed ischemic stroke</td>
<td>202 (2.6)</td>
<td>229 (3.0)</td>
<td>0.85 (0.73–1.00)</td>
<td>0.08</td>
</tr>
<tr>
<td>Vascular death excluding intracranial hemorrhage</td>
<td>257 (3.5)</td>
<td>271 (3.5)</td>
<td>0.91 (0.75–1.10)</td>
<td>0.49</td>
</tr>
<tr>
<td>Any serious vascular event excluding TIA</td>
<td>542 (7.0)</td>
<td>587 (7.6)</td>
<td>0.93 (0.82–1.03)</td>
<td>0.25</td>
</tr>
<tr>
<td>TIA</td>
<td>186 (2.3)</td>
<td>197 (2.5)</td>
<td>0.74 (0.68–0.81)</td>
<td>0.00</td>
</tr>
<tr>
<td>Any serious vascular event including TIA</td>
<td>658 (8.5)</td>
<td>743 (9.6)</td>
<td>0.88 (0.79–0.97)</td>
<td>0.01</td>
</tr>
<tr>
<td>Any arterial revascularization</td>
<td>340 (4.4)</td>
<td>384 (5.0)</td>
<td>0.86 (0.76–1.02)</td>
<td>0.10</td>
</tr>
<tr>
<td>Any serious vascular event or revascularization</td>
<td>831 (10.8)</td>
<td>915 (12.1)</td>
<td>0.86 (0.76–0.97)</td>
<td>0.00</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
<td>55 (0.7)</td>
<td>45 (0.6)</td>
<td>1.22 (0.82–1.81)</td>
<td>0.003</td>
</tr>
<tr>
<td>Sight-threatening bleeding in eye</td>
<td>57 (0.7)</td>
<td>64 (0.8)</td>
<td>0.89 (0.62–1.27)</td>
<td>0.16</td>
</tr>
<tr>
<td>Serious gastrointestinal bleeding</td>
<td>137 (1.8)</td>
<td>101 (1.3)</td>
<td>1.36 (1.05–1.75)</td>
<td>0.002</td>
</tr>
<tr>
<td>Other major bleeding</td>
<td>74 (1.0)</td>
<td>43 (0.6)</td>
<td>1.70 (1.18–2.44)</td>
<td>0.003</td>
</tr>
<tr>
<td>Any major bleeding</td>
<td>314 (4.1)</td>
<td>245 (3.2)</td>
<td>1.29 (0.99–1.59)</td>
<td>0.12</td>
</tr>
</tbody>
</table>
ASA for Primary Prevention of CAD

- Based on this data USPSTF made grade B rec for adults 50-59 w/ >10% 10yr ASCVD risk (C for 60-69 and I for <50 or >70yo)
- ASA has failed to show robust benefit across multiple study groups for primary prevention (low ABI, DM)

22% dec in non-fatal MI, 6% all cause
ASA for Primary Prevention of CAD

- Despite reducing evidence of benefits NNT to prevent ASCVD event > NNH via bleeding event

- Consider ASA If: No factors increasing bleeding risk, ASCVD risk >10% and/or patient is unable to control other ASCVD risk factors - shared decision making with patient
How Do we Assess Bleeding Risk?

- Hx of previous GI bleed/PUD
- Hx of ICH/other significant bleed
- age >70 years,
- Thrombocytopenia
- coagulopathy
- CKD
- Concurrent use of:
  - NSAIDS, Steroids, DOACs/warfarin, SSRI


• [http://www.aspiringuide.com](http://www.aspiringuide.com)
9. Statin therapy is first-line treatment for primary prevention of ASCVD in patients with elevated low-density lipoprotein cholesterol levels ($\geq 190$ mg/dL), those with diabetes mellitus, who are 40 to 75 years of age, and those determined to be at sufficient ASCVD risk after a clinician-patient risk discussion.
**Primary Prevention:**
Assess ASCVD Risk in Each Age Group
Emphasize Adherence to Healthy Lifestyle

**Age 0-19 y**
Lifestyle to prevent or reduce ASCVD risk
Diagnosis of familial Hypercholesterolemia → statin

**Age 20-39 y**
Estimate lifetime risk to encourage lifestyle to reduce ASCVD risk
Consider statin if family history premature ASCVD and LDL-C ≥160 mg/dL (≥4.1 mmol/L)

**Age 40-75 y**
LDL-C ≥190 mg/dL (≥4.9 mmol/L)
No risk assessment; High-intensity statin (Class I)

Diabetes mellitus and age 40-75 y
Moderate-intensity statin (Class I)

Diabetes mellitus and age 40-75 y
Risk assessment to consider high-intensity statin (Class IIa)

Age >75 y
Clinical assessment, Risk discussion

**ASCVD Risk Enhancers:**
- Family history of premature ASCVD
- Persistently elevated LDL-C ≥160 mg/dL (≥4.1 mmol/L)
- Chronic kidney disease
- Metabolic syndrome
- Conditions specific to women (e.g., preeclampsia, premature menopause)
- Inflammatory diseases (especially rheumatoid arthritis, psoriasis, HIV)
- Ethnicity (e.g., South Asian ancestry)

**Lipid/ Biomarkers:**
- Persistently elevated triglycerides (≥175 mg/dL, ≥2.0 mmol/L)

In selected individuals if measured:
- hs-CRP ≥2.0 mg/L
- Lp(a) levels >50 mg/dL or >125 nmol/L
- apoB ≥130 mg/dL
- Ankle-brachial index (ABI) <0.9

**Risk discussion: Emphasize lifestyle to reduce risk factors (Class I)**
- <5% “Low Risk”
- 5% - <7.5% “Borderline Risk”
- ≥7.5% - <20% “Intermediate Risk”
- ≥20% “High Risk”

**Risk discussion: If risk enhancers present then risk discussion regarding moderate-intensity statin therapy (Class IIIb)**
- If risk estimate + risk enhancers favor statin, initiate moderate-intensity statin to reduce LDL-C by 30% - 49% (Class I)

**Risk discussion: Initiate statin to reduce LDL-C ≥50% (Class I)**

If risk decision is uncertain:
Consider measuring CAC in selected adults:
CAC = zero (lowers risk; consider no statin, unless diabetes, family history of premature CHD, or cigarette smoking are present)
CAC = 1-99 favors statin (especially after age 55)
CAC = 100+ and/or ≥75th percentile, initiate statin therapy
Nonpharmacological interventions are recommended for all adults with elevated blood pressure or hypertension. For those requiring pharmacological therapy, the target blood pressure should generally be <130/80 mm Hg.
Figure 4. BP Thresholds and Recommendations for Treatment

BP indicates blood pressure; and CVD, cardiovascular disease.
### Table 7. Best Proven Nonpharmacological Interventions For the Prevention and Treatment of Hypertension

<table>
<thead>
<tr>
<th>Nonpharmacological Intervention</th>
<th>Goal</th>
<th>Approximate Impact on SBP</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight loss</td>
<td>Weight/body fat</td>
<td>-5 mm Hg</td>
<td>(S4.4-2)</td>
</tr>
<tr>
<td>Healthy diet</td>
<td>DASH dietary pattern‡</td>
<td>-11 mm Hg</td>
<td>(S4.4-7, S4.4-8)</td>
</tr>
<tr>
<td>Reduced intake of dietary sodium</td>
<td>Dietary sodium</td>
<td>-5/6 mm Hg</td>
<td>(S4.4-12, S4.4-10)</td>
</tr>
<tr>
<td>Enhanced intake of dietary potassium</td>
<td>Dietary potassium</td>
<td>-4/5 mm Hg</td>
<td>(S4.4-14)</td>
</tr>
<tr>
<td>Nonpharmacological Intervention</td>
<td>Goal</td>
<td>Approximate Impact on SBP</td>
<td>Reference</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>------</td>
<td>---------------------------</td>
<td>-----------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hypertension</td>
<td>Normotension</td>
</tr>
<tr>
<td>Physical activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aerobic</td>
<td>-90–150 min/wk 65%–75% heart rate reserve</td>
<td>-5/8 mm Hg</td>
<td>-2/4 mm Hg</td>
</tr>
<tr>
<td>Dynamic resistance</td>
<td>-90–150 min/wk 50%–80% 1 rep maximum 6 exercises, 3 sets/exercise, 10 repetitions/set</td>
<td>-4 mm Hg</td>
<td>-2 mm Hg</td>
</tr>
<tr>
<td>Isometric resistance</td>
<td>-4 × 2 min (hand grip), 1 min rest between exercises, 30%–40% maximum voluntary contraction, 3 sessions/wk 8–10 wk</td>
<td>-5 mm Hg</td>
<td>-4 mm Hg</td>
</tr>
<tr>
<td>Moderation in alcohol intake</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>In individuals who drink alcohol, reduce alcohol† to: Men: ≤2 drinks daily Women: ≤1 drink daily</td>
<td>-4 mm Hg</td>
<td>-3 mm Hg</td>
</tr>
</tbody>
</table>
What’s the data for intensive BP control?

<table>
<thead>
<tr>
<th>A</th>
<th>Blood pressure difference (mm Hg)</th>
<th>Relative risk (95% CI)</th>
<th>Weight (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HOT (1998)⁶</td>
<td>-2.6/1.1</td>
<td>0.82 (0.69-0.91)</td>
<td>20.0</td>
</tr>
<tr>
<td>HIPS-405 (1995)⁷</td>
<td>-0.85/0.05</td>
<td>0.80 (0.63-1.01)</td>
<td>22.9</td>
</tr>
<tr>
<td>ARCBS (1999)⁵</td>
<td>-1.50/0.65</td>
<td>0.88 (0.90-0.95)</td>
<td>3.7</td>
</tr>
<tr>
<td>REIN (1993)⁴</td>
<td>-0.12/0.15</td>
<td>1.00 (0.99-1.01)</td>
<td>5.3</td>
</tr>
<tr>
<td>HOT (2003)⁶</td>
<td>-1.30/0.68</td>
<td>0.90 (0.77-1.07)</td>
<td>4.1</td>
</tr>
<tr>
<td>REIN (1993)⁴</td>
<td>-0.01/0.02</td>
<td>1.00 (0.99-1.01)</td>
<td>0.5</td>
</tr>
<tr>
<td>HOT (2003)⁶</td>
<td>-0.01/0.02</td>
<td>1.00 (0.99-1.01)</td>
<td>1.1</td>
</tr>
<tr>
<td>VANN (2004)⁷</td>
<td>-0.12/0.01</td>
<td>0.88 (0.88-0.89)</td>
<td>10.0</td>
</tr>
<tr>
<td>ACCOMO (2003)⁴</td>
<td>-0.12/0.01</td>
<td>0.88 (0.88-0.89)</td>
<td>3.9</td>
</tr>
<tr>
<td>HOT (2003)⁶</td>
<td>-0.12/0.01</td>
<td>0.88 (0.88-0.89)</td>
<td>3.9</td>
</tr>
<tr>
<td>SPITS (2001)⁶</td>
<td>-0.11/0.04</td>
<td>0.87 (0.87-0.88)</td>
<td>2.1</td>
</tr>
<tr>
<td>NHF et al. (2001)⁷</td>
<td>-0.01/0.01</td>
<td>0.99 (0.99-1.00)</td>
<td>0.0</td>
</tr>
<tr>
<td>PAST (2001)⁶</td>
<td>-0.20/0.24</td>
<td>0.82 (0.76-0.88)</td>
<td>0.0</td>
</tr>
<tr>
<td>Overall</td>
<td>-0.20/0.24</td>
<td>0.82 (0.76-0.88)</td>
<td>0.0</td>
</tr>
</tbody>
</table>

**Table 2.** Primary and Secondary Outcomes and Renal Outcomes.²

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intensive Treatment</th>
<th>Standard Treatment</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All participants</td>
<td>(N = 4678)</td>
<td>(N = 4683)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary outcome⁴</td>
<td>243 (5.2)</td>
<td>319 (6.8)</td>
<td>2.19</td>
<td>0.75 (0.64-0.89)</td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>97 (2.1)</td>
<td>116 (2.5)</td>
<td>0.78</td>
<td>0.83 (0.64-1.09)</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>40 (0.9)</td>
<td>40 (0.9)</td>
<td>0.27</td>
<td>1.00 (0.64-1.53)</td>
</tr>
<tr>
<td>Stroke</td>
<td>62 (1.3)</td>
<td>70 (1.5)</td>
<td>0.47</td>
<td>0.89 (0.63-1.25)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>62 (1.3)</td>
<td>100 (2.1)</td>
<td>0.67</td>
<td>0.62 (0.45-0.84)</td>
</tr>
<tr>
<td>Death from cardiovascular causes</td>
<td>37 (0.8)</td>
<td>65 (1.4)</td>
<td>0.43</td>
<td>0.57 (0.38-0.85)</td>
</tr>
<tr>
<td>Death from any cause</td>
<td>155 (3.3)</td>
<td>210 (4.5)</td>
<td>1.40</td>
<td>0.73 (0.60-0.90)</td>
</tr>
<tr>
<td>Primary outcome or death</td>
<td>332 (7.1)</td>
<td>423 (9.0)</td>
<td>2.90</td>
<td>0.78 (0.67-0.90)</td>
</tr>
<tr>
<td>Participants with CKD at baseline</td>
<td>(N = 1330)</td>
<td>(N = 1316)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Composite renal outcome⁴</td>
<td>14 (1.1)</td>
<td>15 (1.1)</td>
<td>0.96</td>
<td>0.89 (0.62-1.27)</td>
</tr>
<tr>
<td>≥50% reduction in estimated GFR⁴</td>
<td>12 (0.9)</td>
<td>11 (0.8)</td>
<td>0.91</td>
<td>0.87 (0.56-1.38)</td>
</tr>
<tr>
<td>Long-term dialysis</td>
<td>9 (0.5)</td>
<td>10 (0.8)</td>
<td>0.91</td>
<td>0.57 (0.39-0.84)</td>
</tr>
<tr>
<td>Kidney transplantation</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incident albuminuria⁴</td>
<td>49 (3.5)</td>
<td>59 (0.0)</td>
<td>0.70</td>
<td>0.72 (0.48-1.07)</td>
</tr>
<tr>
<td>Participants without CKD at baseline</td>
<td>(N = 3352)</td>
<td>(N = 3345)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥50% reduction in estimated GFR to &lt;60 ml/ min/1.73 m²⁴</td>
<td>127 (3.8)</td>
<td>37 (1.2)</td>
<td>0.35</td>
<td>3.49 (2.04-10.1)</td>
</tr>
<tr>
<td>Incident albuminuria⁴</td>
<td>110 (2.1)</td>
<td>153 (1.6)</td>
<td>2.33</td>
<td>0.81 (0.63-0.90)</td>
</tr>
</tbody>
</table>

⁴ CI denotes confidence interval, and CKD chronic kidney disease.
⁵ The primary outcome was the first occurrence of myocardial infarction, acute coronary syndrome, stroke, heart failure, or death from cardiovascular causes.
⁶ The composite renal outcome for participants with CKD at baseline was the first occurrence of a reduction in the estimated GFR of 50% or more, long-term dialysis, or kidney transplantation.
⁷ Reductions in the estimated GFR were confirmed by a second laboratory test at least 90 days later.
⁸ Incident albuminuria was defined as a doubling of the ratio of urinary albumin (in milligrams) to creatinine (in grams) from less than 10 at baseline to greater than 10 during follow-up. The denominators for number of patients represent those without albuminuria at baseline.
⁹ No long-term dialysis or kidney transplantation was reported among participants without CKD at baseline.
Take home points re: Treatment goals

- BP target <130/80 w/ pharmacotherapy if:
  - 10 year ASCVD risk >10%
  - CKD
  - DM2

- Data suggests this may contribute to reduction in major CV events and MI but overall mortality benefit unclear
2019 ACC/AHA Guidelines on the Primary Prevention of Cardiovascular disease
Clinic Evaluation of Patients with Stable CAD (SIHD)

• At least Annual Follow up:
  • a. Assessment of symptoms and clinical function;
  • b. Surveillance for complications: heart failure and arrhythmias
  • c. Monitor risk factors: re-assess lifestyle & medical therapy

• IF evidence of MI or worsening HF: asses LVEF and segmental wall motion by echocardiography or radionuclide imaging
  • Consider resting 12-lead ECG at 1-year or longer if symptoms stable
  • No evidence for routine echo in stable patients with normal EF
Secondary Prevention: Guidelines Directed Medical Therapy

- **Lifestyle modifications**
  - Physical activity, weight mgmt, dietary mod, tobacco cessation, ETOH moderation
- **Lipid management** as per 2018 AHA/ACC guidelines (high-or moderate-intensity statin)
- **HTN management:** Goal BP <130/80 (especially if DM or CKD)
  - include ACEi (or ARB) and/or beta blockers. Other meds as need to achieve BP goal.
- **Optimize diabetic control** A1c<7% (metformin+ GLP1 or SGLT2i)
- **Antiplatelet therapy** - ASA 81mg (A,Clopidogrel (B) if contraind.)
Secondary Prevention: Guideline Directed Medical Therapy (Goal: prevent second event)

- HTN management: Goal BP <130/80 (especially if DM or CKD)
  - BP targets somewhat controversial
  - ACEi/ARB (Hx of MI, CHF/LV dysf/CKD, DM)
  - Beta blocker: Hx of MI, angina, LV dysfunction
  - Adjuncts:
    - Aldosterone antagonist if LV dysf (<40%EF)
    - Calcium channel blocker if angina
  - Optimize diabetic control A1c<7% (B) (SDM older patients)
    - metformin+ GLP1 or SGLT2i (Avoid Thiazolidinediones)
Comparison of DM drug classes in CV Disease Outcomes

Fig. 1. Cardiovascular outcome trials with DPP4 inhibitors, GLP1 receptor agonists, and SGLT2 inhibitors. SAVOR TIMI, Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus-Thrombolysis in Myocardial Infarction; EXAMINE, Examination of Cardiovascular Outcomes with Alogliptin versus Standard of Care; TECOS, Trial Evaluating Cardiovascular Outcomes with Sitagliptin; ELIXA, Evaluation of Lixisenatide in Acute Coronary Syndrome; LEADER, Liraglutide Effect and Action in Diabetes: Evaluation of cardiovascular outcome Results; SUSTAIN-6, a Trial to Evaluate Cardiovascular and Other Long-term Outcomes with Semaglutide in Subjects with Type 2 Diabetes; EXSCEL, Exenatide Study of Cardiovascular Event Lowering; EMPA-REG OUTCOME, Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients; CANVAS, Canagliflozin Cardiovascular Assessment Study.
Use of Beta Blockers to Prevent MI, CV death:

- Beta-blocker:
  - 3 years in all patients with normal LV function after MI or ACS (IB)
  - all patients with LV systolic dysfunction (EF ≤ 40%) with heart failure or prior MI
    - carvedilol, metoprolol succinate, or bisoprolol: demonstrated mortality benefit (IA)
  - Consider for all other patients with CAD
DAPT: Dual Antiplatelet Therapy

- No indication unless recent MI, PCI, CABG
- All patients with CAD s/p ACS
  - 12 mo DAPT (regardless of intervention)
- SIHD requiring intervention:
  - BMS: >1mo
  - DES >6 mo
  - CABG: 12 mo (less clear data)
- Consider longer duration if thrombotic risk > bleeding risk
Duration of DAPT: Ischemia vs Bleeding Risk

*Consider PPI for those at inc. bleeding risk (I-Hx GIB, IIa-other inc risk)
Cardiac Rehabilitation

- Meta-analysis of 48 RCTs of exercise interventions (med duration 3mo):
  - 20% reduction in all-cause mortality
  - 26% reduction in CV mortality
  - Non-sig but fav. Trends:
    - nonfatal MI, CABG, PCI

- No difference between the mortality rate effects of exercise-only and more comprehensive cardiac rehabilitation interventions, and the benefits were independent of actual amount and intensity of exercise.

When to Refer:

- Recent ACS s/p CABG or PCI @ hospital d/c or TOC (IA)
- Dx in last 1 yr:
  - ACS s/p CABG or PCI (IA)
  - chronic angina (IB)
  - PAD (IA)
  - Clinically stable outpatients with diagnosis of heart failure (IIa/B)

- Can substitute home based cardiac rehab program for low risk patients (IA)
Pharmacotherapy for Chronic Anginal Sx:

- 1\textsuperscript{st} line: Beta blockers (IB)
- 2\textsuperscript{nd} line: Calcium channel blockers or long-acting nitrates (IB) 
  -if unable to tolerate BB
- Add: Calcium channel blockers or long-acting nitrates if persistent sx on BB
- Sublingual nitroglycerin or nitroglycerin spray is recommended for immediate relief
Checklist for your patients with CAD:

- ASA therapy?
- Indication for DAPT?
  - ACS/PCI/CABG in last 12 mo
- Beta blocker?
- ACEi/ARB?
- High intensity statin?
- Diabetic control?
  - If A1c >7 consider GLP1, SGLT-2
- Tobacco cessation?
- ETOH moderation/cessation
- Depression/socioeconomic screening
- Physical activity/weight mgmt
- Eval chronic angina?
  - BB, CCB or nitrate
- Assess for interval MI, sx of worsening HF
Coronary Artery Disease: CASES in Primary Prevention
Case 1

• 55yo Male with PMH HTN, DM, remote PUD, tobacco use presents for a NPV TOC visit after recent stay in OSH with a recent STEMI of LAD managed with PCI and DES stent. Echocardiogram prior to discharge showed EF of 35%.
• Labs: A1c 8.8%, LDL 186, TG 255, HDL 30, Cr 1.2
VS: HR 82, BP 150/92, BMI 43

His current meds are:
ASA 81mg, Clopidogrel 75mg daily, Metformin 1000mg BID, Lisinopril 40mg, Atorvastatin 40mg, Furosemide 20mg daily

1. How would you counsel this patient?
2. What management recs would you make?
Case 2

- 52yo AAF Female presents to your office to establish care. Her PMH is significant for HTN, Depression and HIV. Her BP is 130/76. BMI 32
- Her meds are as follows: Chlorthalidone 25mg, Darunavir/ritonavir + Descovy (TAF/Emtricitabine), Sertraline 100mg
- She is a non-smoker
- She is reluctant to change any meds

- Labs:
  - Tot Chol: 205
  - HDL 35
  - LDL 126
  - A1c: 6.0%
  - Cr 1.4 (CrCl 49)
  - VL <40, CD4 450

- Assess her ASCVD 10yr risk
- Discuss any medication changes or additional testing.
Case 3

• 56yoM w/ PMH severe Hip OA DM2, CAD s/p NSTEMI w/ PCI and DES 3 months ago comes to you for pre-operative evaluation an clearance. He has completed cardiac rehab program and is symptom free on the following meds:
  • ASA 81mg, Atorvastatin 40mg, metoprolol XL 50mg daily, Lisinopril 20mg daily, clopidogrel 75mg daily, metformin 1000mg BID, lantus 20 units daily

1. Any other information to you want to know?
2. Would you make any changes to his medication regimen?
3. How would you counsel him regarding his procedure?
Perioperative management & DAPT in CAD
Case 4

- 47yo Caucasian Male presents to your office to review his biometric screening results:
  - TC: 250, HDL 30, LDL 170, TG 250, A1c 5.8%, BP 138/86
  - He is a non-smoker, his BMI is 36, and he has been taking ASA 81 mg for the last 6 mo after his brother died at 54 from MI

- He wants to do EVERYTHING to reduce his CV risk. How would you counsel him? Additional testing? Meds?
Case 5

- 75yo AA Female who present for routine follow up. She has a remote hx of MI treated with PCA in her 50s, HTN, DM, CKD, GERD. She is a former smoker and quit 15 yrs ago. Echo last year showed EF 45%. Her BP is 140/86 on exam.
- Labs: A1c: 8%, LDL 66, HDL 40, Tot Chol: 180, Cr 1.4 (CrCl 40)
- Meds: ASA 81mg, Atorvastatin 80mg, Metformin 100mg BID, Metoprolol 50mg, lisinopril 20mg, Omeprazole 40mg

- Would you make any changes to he regimen? Considerations?
References

- American College of Cardiology, American Heart Association. ASCVD Risk Estimator. Available at: https://tools.acc.org/ldl/ascvd_risk_estimator/index.html#!/calulate/estimator. 2192018
References

- O’Donoghue ML, et al. Lipoprotein(a), PCSK9 Inhibition, and Cardiovascular Risk Insights From the FOURIER Trial Circulation, Volume 139, Issue 12, 19 March 2019, Pages 1483-1492. https://doi.org/10.1161/CIRCULATIONAHA.118.037184
References

• Doobay AV & Anand SS. Sensitivity and Specificity of the Ankle-Brachial Index to Predict Future Cardiovascular Outcomes. Arteriosclerosis, Thrombosis, and Vascular Biology, Volume 25, Issue 7, 1 July 2005, Pages 1463-1469


References
