MHIF Research Highlights: DECEMBER 2018

Notable Milestones & First Enrollments

• Dr. Paul Sorajja, National PI for early feasibility study of Left Atrial shunt implanted MHI’s first device on November 20th - assisted by Lynelle Schneider, PA. Congrats Team!

• Dr. Karol Mudy and team for enrolling 35 patients in the HeartMate LVAD clinical study; the product is now FDA approved!

FEATURED MHIF STUDIES
Open for Enrollment and Referrals!

ASAP-SVG for coronary artery disease
CONTACT: Pamela Morley, 612-863-6066

MINT for myocardial ischemia & transfusion
CONTACT: Rose Peterson, 612-863-6051

XIENCE 90 for patients at high risk of bleeding who need coronary stents
CONTACT: Amy McMeans, 612-863-3895

MARK YOUR CALENDARS

Time to Run… or volunteer!

MHIF is proud to sponsor the Valentine’s 5K with Twin Cities in Motion. Mark your calendar!
Sat., Feb. 9, Lake Nokomis!

Raising Awareness of Valvular Disease!

MHIF is hosting a second annual Mechanics of a Healthy Heart event for patients.
Thurs, Feb. 21, Golden Valley Country Club!

CONGRATULATIONS

To Dr. Stephen Bradley who published in JAMA Network Open:
“Hypothermia for Out of Hospital Cardiac Arrest”

SHOUT OUT TO…

Drs. Hryniewicz, Grey & Saxena for participating in a heart-healthy discussion at The Marsh!
Minneapolis Heart Institute Foundation® Cardiovascular Grand Rounds

Title: A 2018 Cardiovascular Prevention Update
Speaker(s): Michael D. Miedema, MD, MPH
   Director of Cardiovascular Prevention
   Minneapolis Heart Institute® at Abbott Northwestern Hospital
Date: December 10, 2018
Time: 7:00 – 8:00 AM
Location: ANW Education Building, Watson Room

OBJECTIVES
At the completion of this activity, the participants should be able to:
1. Identify the important changes included in the 2018 ACC/AHA cholesterol guidelines.
2. Describe the cardiovascular benefits of the new diabetes medications.
3. Recall the latest research on risk assessment for cardiovascular disease.

ACCREDITATION
Physician - Allina Health is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. Allina Health designates this live activity for a maximum of 1.0 AMA PRA Category 1 Credit(s)™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Nurse - This activity has been designed to meet the Minnesota Board of Nursing continuing education requirements for 1.0 hours of credit. However, the nurse is responsible for determining whether this activity meets the requirements for acceptable continuing education.

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Moderator(s)/Speaker(s)
Dr. Michael Miedema has disclosed that he DOES NOT have any real or apparent conflicts with any commercial interest as it relates to presenting their content in this activity/course.

Planning Committee
Dr. Alex Campbell, Jake Cohen, Jane Fox, Dr. Mario Gössl, Dr. Kevin Harris, Dr. Kasia Hryniewicz, Rebecca Lindberg, Amy McMeans, Dr. Michael Miedema, Dr. JoEllyn Moore, Pamela Morley, Dr. Scott Sharkey, and Jolene Bell Makowesky have disclosed that they DO NOT have any real or apparent conflicts with any commercial interest as it relates to the planning of this activity/course. Dr. David Hurrell has disclosed the following relationship –Boston Scientific: Chair, Clinical Events Committee.
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Bristol-Myers Squibb  Janssen Pharmaceutical Companies of Johnson & Johnson

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Each attendee at an activity is responsible for determining whether an activity meets their requirements for acceptable continuing education and should only claim those credits that he/she actually spent in the activity.

Maintaining these details are the responsibility of the individual.

PLEASE SAVE A COPY OF THIS FLIER AS YOUR CERTIFICATE OF ATTENDANCE.

Signature: __________________________________________________________________________

My signature verifies that I have attended the above stated number of hours of the CME activity.

Allina Health - Learning & Development - 2925 Chicago Ave - MR 10701 - Minneapolis MN 55407
2018 Cardiovascular Prevention Update

Michael D Miedema MD MPH
Director of Cardiovascular Prevention
Minneapolis Heart Institute
December 10, 2018

Objectives

- Aspirin
- Cholesterol Guidelines
- Diabetes
- Cardiovascular Genetics
3 Recent Large ASA Trials

• ASCEND
• ARRIVE
• ASPREE

Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus

The ASCEND Study Collaborative Group

• 15,480 Individuals with diabetes but without known CVD
• Mean Age ~ 63 years
• Mean follow-up 7.4 years
• Aspirin 100mg vs placebo
A modest 12% relative risk reduction for a first serious vascular event
Effect of Aspirin on Cardiovascular Events and Bleeding in the Healthy Elderly


19,114 Individuals age ≥ 70 years and free of CVD
100mg ASA vs Placebo
Median Follow-up 4.7 years

Figure 1. Cumulative Incidence of Cardiovascular Disease.
Table 3. Major Hemorrhagic Events.*

<table>
<thead>
<tr>
<th>End Point</th>
<th>Overall (N=15,314)</th>
<th>Aspirin (N=9,925)</th>
<th>Placebo (N=5,389)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of participants with event</td>
<td>no. of participants with event</td>
<td>rate per 1000 person-yr</td>
<td>no. of participants with event</td>
<td>rate per 1000 person-yr</td>
</tr>
<tr>
<td>Major hemorrhage†</td>
<td>626</td>
<td>161</td>
<td>8.6</td>
<td>265</td>
<td>6.2</td>
</tr>
<tr>
<td>Intracranial bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>179</td>
<td>107</td>
<td>2.5</td>
<td>72</td>
<td>1.7</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>77</td>
<td>43</td>
<td>1.0</td>
<td>34</td>
<td>0.8</td>
</tr>
<tr>
<td>Subdural or extradural hemorrhage</td>
<td>61</td>
<td>39</td>
<td>0.9</td>
<td>22</td>
<td>0.5</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage‡</td>
<td>32</td>
<td>18</td>
<td>0.4</td>
<td>14</td>
<td>0.3</td>
</tr>
<tr>
<td>Extracranial bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper gastrointestinal bleeding</td>
<td>137</td>
<td>89</td>
<td>2.1</td>
<td>48</td>
<td>1.1</td>
</tr>
<tr>
<td>Lower gastrointestinal bleeding</td>
<td>127</td>
<td>73</td>
<td>1.7</td>
<td>54</td>
<td>1.3</td>
</tr>
<tr>
<td>Bleeding at another site§</td>
<td>189</td>
<td>101</td>
<td>2.4</td>
<td>88</td>
<td>2.1</td>
</tr>
<tr>
<td>Fatal bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatal major hemorrhage</td>
<td>52</td>
<td>28</td>
<td>0.7</td>
<td>24</td>
<td>0.6</td>
</tr>
<tr>
<td>Fatal hemorrhagic stroke</td>
<td>26</td>
<td>13</td>
<td>0.3</td>
<td>13</td>
<td>0.3</td>
</tr>
</tbody>
</table>
12,546 Individuals at moderate CVD risk
- Men > 55 years with 2 CVD risk factors
- Women > 60 years with 3 CVD risk factors
10-year CVD Risk ~17%
Median Follow-up ~ 5 years
ASA 100mg vs Placebo

Primary Outcome: 4.29% vs 4.48%, P-value 0.60
Any GI bleeding: 0.97% vs 0.46%, p-value 0.007

Myocardial Infarction: 1.52% vs 1.78%, p-value 0.23
Why the change in benefit?

- Change in Population


Dariush Mozaffarian et al. Circulation. 2015;131:e29-e322
Why the change in benefit?

- Change in Populations
- Change in Outcomes

How does CVD first present?

George et al. Circulation. 2015
Why the change in benefit?

- Change in Populations

- Change in Outcomes

- Change in Analysis

Per protocol Analysis

|                      | Event A | Event B | p-value
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction</td>
<td>37 (98%)</td>
<td>72 (84%)</td>
<td>0.53 (0.36, -0.79); p=0.0014</td>
</tr>
<tr>
<td>Non-fatal myocardial infarction</td>
<td>32 (84%)</td>
<td>60 (53%)</td>
<td>0.55 (0.36, -0.84); p=0.0056</td>
</tr>
</tbody>
</table>

ARRIVE Trial, Lancet, 2018
Should we use ASA for primary prevention?

- Patients > 70 years
  - No

- Patients at low CVD risk
  - No

- Patients at elevated bleeding risk
  - No

- Patients 40-69 years old at elevated CVD risk who place a significant value on reducing CVD risk
  - Maybe

Objectives

- Aspirin
- Cholesterol Guidelines
- Diabetes
- Cardiovascular Genetics
2018 Cholesterol Guidelines - 4 Statin Groups

- Known ASCVD
- LDL-C >190mg/dl
- Individuals with Diabetes
- Primary Prevention – Elevated risk (>7.5%)
### TRS 2P Risk Indicators

<table>
<thead>
<tr>
<th>Risk Indicator</th>
<th>Points</th>
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<tbody>
<tr>
<td>CHF</td>
<td>1</td>
</tr>
<tr>
<td>HTN</td>
<td>1</td>
</tr>
<tr>
<td>Age ≥75</td>
<td>1</td>
</tr>
<tr>
<td>DM</td>
<td>1</td>
</tr>
<tr>
<td>Prior Stroke</td>
<td>1</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>1</td>
</tr>
<tr>
<td>PAD</td>
<td>1</td>
</tr>
<tr>
<td>eGFR &lt;60</td>
<td>1</td>
</tr>
<tr>
<td>Smoking</td>
<td>1</td>
</tr>
<tr>
<td><strong>Maximum Possible</strong></td>
<td><strong>9</strong></td>
</tr>
</tbody>
</table>

### CV Death, MI or CVA at 7 Years

- **p-interaction = 0.010**
- **Risk Category**
  - Low: 13.3%, 14.0%
  - Intermediate: 21.5%, 19.3%
  - High: 40.2%, 33.9%


### Clinical ASCVD

**ASCVD not at very high-risk**

- **Healthy Lifestyle**
- **Age ≤75 y**
  - High-intensity statin (Goal: LDL-C ≤50 mg/dl (≤1.3 mmol/l), adding ezetimibe may be reasonable (Class IIa))
- If high-intensity statin not tolerated, use moderate-intensity statin (Class I)

**Very high-risk ASCVD**

- **Age >75 y**
  - If on maximal statin therapy and LDL-C ≥70 mg/dl (≥1.8 mmol/l), initiation of moderate- or high-intensity statin is reasonable (Class IIa)
  - Continuation of high-intensity statin is reasonable (Class IIa)
  - If on maximal statin and LDL-C ≥70 mg/dl (≥1.8 mmol/l), adding ezetimibe is reasonable (Class IIa)
  - If PCSK9-I is considered, add ezetimibe to maximal statin before adding PCSK9-I (Class I)
  - Dashed arrow indicates RCT-supported efficacy, but is less cost effective

- If on clinically judged maximal LDL-C lowering therapy and LDL-C ≥70 mg/dl (≥1.8 mmol/l), or non-HDL-C ≥160 mg/dl (≥4.1 mmol/l), adding PCSK9-I is reasonable (Class IIa)
### Table 4. Very High-Risk* of Future ASCVD Events

**Major ASCVD Events**
- Recent ACS (within the past 12 mo)
- History of MI (other than recent ACS event listed above)
- History of ischemic stroke
- Symptomatic peripheral arterial disease (history of claudication with ABI <0.85, or previous revascularization or amputation)

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### Table 4 continued

**High-Risk Conditions**
- Age ≥65 y
- Heterozygous familial hypercholesterolemia
- History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event(s)
- Diabetes mellitus
- Hypertension
- CKD (eGFR 15-59 mL/min/1.73 m²)
- Current smoking
- Persistently elevated LDL-C (LDL-C ≥100 mg/dL [≥2.6 mmol/L]) despite maximally tolerated statin therapy and ezetimibe
- History of congestive HF
MHIF CV Grand Rounds – Dec. 10, 2018

4 Statin Groups

- Known ASCVD
- LDL-C >190mg/dl
- Individuals with Diabetes
- Primary Prevention – Elevated risk (>7.5%)
Implications of Coronary Artery Calcium Testing Among Statin Candidates According to American College of Cardiology/American Heart Association Cholesterol Management Guidelines

MESA (Multi-Ethnic Study of Atherosclerosis)
CAC distribution Across Spectrum of 10 Year Risk Score Among those >7.5% Risk Score

Nasir et al. JACC 2015

Event Rates only >7.5% in those with CAC>100

Nasir et al. JACC 2015
Other Considerations

- Monitor Response
  - Class 1 – LOE A

- Non-fasting lipid panels for routine screening

- Excellent evidence for statin safety
Clinical ASCVD
- High Intensity Statin
- Goal LDL<70mg/dl
- Very-High risk consider:
  - Ezetimibe
  - PCSK9

LDL>190mg/dl
- High Intensity Statin
- Goal LDL<100mg/dl
- Ezetimibe
- PCSK9

Diabetes
- Moderate Intensity Statin
- Consider high intensity if high risk

ASCVD Risk >5%
- Moderate intensity Statin
- High intensity statin if high risk (>20%)
- If risk is 5-20% and decision is uncertain – consider CAC

### Recommendations for Statin Safety and Statin-Associated Side Effects

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>III: No Benefit</td>
<td>B-R</td>
<td>Coenzyme Q10 is not recommended for routine use in patients treated with statins or for the treatment of SAMS.</td>
</tr>
<tr>
<td>III: No Benefit</td>
<td>C-LD</td>
<td>In patients treated with statins, routine measurements of creatine kinase and transaminase levels are not useful.</td>
</tr>
</tbody>
</table>
Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia

- 8,149 Patients
- CVD or DM + other risk factors
- 4.9 years of follow-up
- On statin
- Elevated Trig's

25% Relative risk reduction for CVD event (4.8% ARR!)
Summary

**Clinical ASCVD**
- High Intensity Statin
- Goal LDL<70mg/dl
- Very-High risk consider:
  - Ezetimibe
  - PCSK9

**LDL>190mg/dl**
- High Intensity Statin
- Goal LDL<100mg/dl
- Ezetimibe
- PCSK9

**Diabetes**
- Moderate Intensity Statin
- Consider high intensity if high risk

**ASCVD Risk >5%**
- Moderate intensity Statin
- High intensity statin if high risk (>20%)
- If risk is 5-20% and decision is uncertain – consider CAC

---

**Objectives**

- Aspirin
- Cholesterol Guidelines
- Diabetes
- Cardiovascular Genetics
Prevalence of Diabetes Mellitus

- ~12% of US Adults
- Significant heterogeneity across demographics (Figure)
- Type II DM accounts for 90-95% of all cases of DM in the US
- ~34% (81.6 million US adults) have pre-diabetes

Age-adjusted Prevalence of physician diagnosed diabetes mellitus in adults > 20 years of age by race/ethnicity and years of education (NHANES 2011-2014).

Diabetes is a major risk factor for CVD
Primary Prevention of Cardiovascular Disease with a Mediterranean Diet

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Combined Mediterranean Diet</th>
<th>Control Diet</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>17/178</td>
<td>64/907</td>
<td>0.69 (0.51-0.94)</td>
<td>0.02</td>
</tr>
<tr>
<td>Female</td>
<td>72/213</td>
<td>47/462</td>
<td>0.73 (0.58-1.01)</td>
<td>0.04</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;70 yr</td>
<td>65/172</td>
<td>47/154</td>
<td>0.75 (0.52-1.09)</td>
<td>0.04</td>
</tr>
<tr>
<td>&gt;70 yr</td>
<td>57/213</td>
<td>47/462</td>
<td>0.71 (0.51-0.98)</td>
<td>0.03</td>
</tr>
<tr>
<td>Diabetes</td>
<td>54/272</td>
<td>47/154</td>
<td>0.87 (0.53-1.41)</td>
<td>0.63</td>
</tr>
<tr>
<td>Yes</td>
<td>12/243</td>
<td>16/189</td>
<td>0.71 (0.51-0.96)</td>
<td>0.03</td>
</tr>
</tbody>
</table>
UKPDS

- 32% reduction in Primary Outcome
- 42% reduction in Diabetes-related death
- 36% reduction in All-cause Mortality
Insulin vs Insulin/Metformin

390 Patients with Type II DM on insulin randomized to metformin or placebo and followed for 4.3 years.


• Lower Hgb A1C
• Less Insulin Use
• Lower BMI


• The overall data support metformin as first-line therapy in type II DM
  • More significant improvements in A1C
  • No associated weight gain
  • Less Hypoglycemia
  • Better CVD outcomes (compared to sulfonylureas)
Improving glycemic control - CVD Benefit

- Sulfonylureas
- Metaglinides
- DPP-4 Inhibitors
- Alpha glucosidase inhibitors
- Thiazolidinediones
- Insulin

Intensive Glucose Control ≠ Reduced CVD Events

ADVANCE Trial

11,140 Patients, A1C 6.5% vs 7.3%

VADT

1,791 Patients, A1C 6.9% vs 8.4%

NEJM 2008

NEJM 2009
Intensive Glucose Control ≠ Reduced CVD Events

**ACCORD – Primary Outcome**

**ACCORD – ALL-Cause Mortality**

10,251 Patients, A1C 6.4% vs 7.5%

*Significant weight gain in intensive group

**Medications to reduce CVD risk**

**SGLT-2 Inhibitors**
- Empagliflozin (EMPA-REG)
- Canagliflozin (CANVAS)
- Dapagliflozin (DECLARE)

**GLP-1 Receptor**
- Liraglutide (LEADER)
- Semaglutide (SUSTAIN-6)
- Albiglutide (Harmony)
SGLT-2 Inhibitors

- Reduction in Hgb A1C ~0.5-0.6%
- Decreased body weight
- Decreased BP
- Increased HDL
- Decreased triglycerides
- No hypoglycemia

Ahmed et al, EHJ 2017

Empagliflozin, Cardiovacular Outcomes, and Mortality in Type 2 Diabetes

- N=7,028
- Median Follow-up 3.1 Years
- Adults with type II DM and known CVD
- Mean age 63.1 years
- Mean Hgb A1C 8.1%
- Primary Outcome: CVD Death, non-fatal MI, non-fatal stroke
14% Reduction in Non-fatal MI, non-fatal stroke and CVD Death

38% Reduction in CVD Death
MHIF CV Grand Rounds – Dec. 10, 2018

- N=10,142
- Median Follow-up 2.4 years
- Individuals with type II DM and CVD or high risk for CVD
- Mean Age 63 years
- Baseline A1C 8.2%
- Primary End-Point: Cardiovascular Death, non-fatal MI, non-fatal stroke
• 33% reduction in heart failure hospitalizations

**Graph:**

- **Title:** Death from Cardiovascular Causes, Nonfatal Myocardial Infarction, or Nonfatal Stroke
- **Patients with an Event (%)**
- **Weeks since Randomization**
- **No. at Risk: Placebo**
- **Placebo:** 4347, 4259, 4153, 4061, 3942, 3826, 3705, 3574, 3437, 3288, 3131, 2968, 2805, 2636, 2460, 2283, 2111, 1831, 1641
- **Placebo:** 3672, 3562, 3453, 3345, 3237, 3129, 3021, 2913, 2805, 2697, 2589, 2481, 2373, 2265, 2157, 2049, 1941, 1833
- **Canagliflozin:** 5795, 5672, 5562, 5453, 5345, 5237, 5129, 5021, 4913, 4805, 4697, 4589, 4481, 4373, 4265, 4157, 4049, 3941

**References:**

- The New England Journal of Medicine
- Original Article
- Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes

- 17,160 patients
- 4.2 years follow-up
- Co-Primary End-Points
CENTRAL ILLUSTRATION: Sodium-Glucose Co-Transporter-2 Inhibitors in Patients With and Without Cardiovascular Disease

<table>
<thead>
<tr>
<th>Event</th>
<th>Risk Factors Without Prior Cardiovascular Disease</th>
<th>Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>With prior cardiovascular disease</td>
<td>0.56 (0.44, 0.70)</td>
</tr>
<tr>
<td></td>
<td>Without prior cardiovascular disease</td>
<td>0.56 (0.50, 0.63)</td>
</tr>
<tr>
<td></td>
<td>With prior cardiovascular disease</td>
<td>0.72 (0.63, 0.82)</td>
</tr>
<tr>
<td></td>
<td>Without prior cardiovascular disease</td>
<td>0.61 (0.48, 0.78)</td>
</tr>
<tr>
<td></td>
<td>With prior cardiovascular disease</td>
<td>0.63 (0.57, 0.70)</td>
</tr>
<tr>
<td></td>
<td>Without prior cardiovascular disease</td>
<td>0.56 (0.50, 0.62)</td>
</tr>
</tbody>
</table>

*Diagnosis of AMI, unstable angina, stroke, heart failure, transient ischemic attack, coronary revascularization (CABG or PCI) or occlusive peripheral artery disease prior to index drug initiation favor sodium-glucose co-transporter-2 inhibitors → favor other glucose-lowering drugs

Glucagon-like Peptide-1 receptor agonists

- Reduction in Hgb A1C
- Weight Loss
- Decreased BP
- Decreased LDL
- Decreased inflammation
- GI side effects

N=9,340
Median Follow-up 3.8 years
Individuals with type II DM and CVD or high risk for CVD
Mean Age 63 years
Baseline A1C 8.2%
Primary End-Point: Cardiovascular Death, non-fatal MI, non-fatal stroke
Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes

Steven P. Marso, M.D., Stephen C. Bari, M.D., Agostino Consoli, M.D.,
Fredy G. Eliaishewitz, M.D., Esteban Jilani, M.D., Lawrence A. Leber, M.D.,
Ildiko Lingnay, M.D., M.P.H., M.S.C.S., Julio Rosenstock, M.D.,
Jochen Seufert, M.D., Ph.D., Mark L. Warren, M.D., Vincent Woo, M.D.,
Ole H. Hansen, M.Sc., Anders J. Holf, M.D., Ph.D., Jonas Petterson, M.D., Ph.D.,
and Tina Vilhelm, M.D., D.M.Sc, for the SUSTAIN-6 Investigators*

- N=3,297
- Median Follow-up 2.1 years
- Individuals with type II DM and CVD or high risk for CVD
- Mean Age 62 years
- Baseline A1C 8.7%
- Primary End-Point: Cardiovascular Death, non-fatal MI, non-fatal stroke

*SUSTAIN 6 Trial, NEJM, 2016

*Increased risk for GI side effects
2018 ACC Expert Consensus Decision Pathway on Novel Therapies for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes and Atherosclerotic Cardiovascular Disease

A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways

Endorsed by the American Diabetes Association

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**Figure 3** Approach to Managing Patients With Established ASCVD and T2D

- **Yes**
  - In the patient ≥ 18 y/o and have all of the following?
    - T2D
    - Established clinical ASCVD
  - Insufficient evidence to recommend SGLT2 inhibitor or GLP-1RA for ASCVD risk reduction.

- **No**
  - Do any of the following apply to the patient?
    - CSII
    - Ongoing pregnancy
    - Currently breastfeeding.
  - Consider the timing of starting a SGLT2 inhibitor or GLP-1RA (Table 10/11).

- **Yes**
  - Do not start SGLT2 inhibitor or GLP-1RA at this time.

- **No**
  - Insist discussion incorporating patient and clinician preferences and priorities (see Table 11).

- **Patient does not wish to start SGLT2 inhibitor or GLP-1RA at this time.**

- **SGLT2 inhibitor is selected** (see Table 7 for dosing, Table 8 for contraindications).

- **GLP-1RA is selected** (see Table 6 for dosing, Table 8 for contraindications).

- **Start SGLT2 inhibitor:**
  - Empagliflozin is currently preferred.
  - For dosing, see Table 7.
  - No titration required.
  - Adjust other antihyperglycemic agents as indicated.

- **Start GLP-1RA:**
  - Liraglutide is currently preferred.
  - For dosing, see Table 6.
  - Initiate slowly to avoid nausea.
  - Adjust other antihyperglycemic agents as indicated.

- **Continue to monitor response to therapy** (see Section 8.4 and Table 12).
Objectives

- Aspirin
- Cholesterol Guidelines
- Diabetes
- Cardiovascular Genetics

The NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Genetic Risk, Adherence to a Healthy Lifestyle, and Coronary Disease

Amit V. Khera, M.D., Connor A. Emdin, D.Phil., Isabel Drake, Ph.D., Pradeep Natarajan, M.D.; Alexander G. Bick, M.D., Ph.D., Nancy R. Cook, Ph.D., Daniel I. Chaitman, Ph.D., Usman Baber, M.D., Roxana Mehran, M.D., Daniel J. Rader, M.D., Valentin Fuster, M.D., Ph.D., Eric Boerwinkle, Ph.D., Olle Melander, M.D., Ph.D., Marju Orho-Melander, Ph.D., Paul M Ridker, M.D., and Sekar Kathiresan, M.D.
Figure 3. 10-Year Coronary Event Rates, According to Lifestyle and Genetic Risk in the Prospective Cohorts.

Shown are standardized 10-year cumulative incidence rates for coronary events in the three prospective cohorts, according to lifestyle and genetic risk. Standardization was performed to cohort-specific population averages for each covariate. The bars represent 95% confidence intervals.

Khera et al, JACC, 2016
Summary

- Aspirin for primary prevention
  - Should not be routinely used
  - Can be considered in select high risk patients
  - Should generally be avoided in elderly populations
- Cholesterol
  - Statin – ezetimibe – PCSK9 for individuals at high ASCVD Risk
  - CAC scoring for those who are uncertain about their risk
- Diabetes
  - Consider SGLT-2 inhibitor or GLP-1R for individuals with type II DM at high ASCVD risk
- Polygenic risk scores
  - Not quite ready for clinical use
  - ♦ But likely will be soon
Thank you