Secondary Prevention Therapies for Acute/Chronic Coronary Syndromes Part IV

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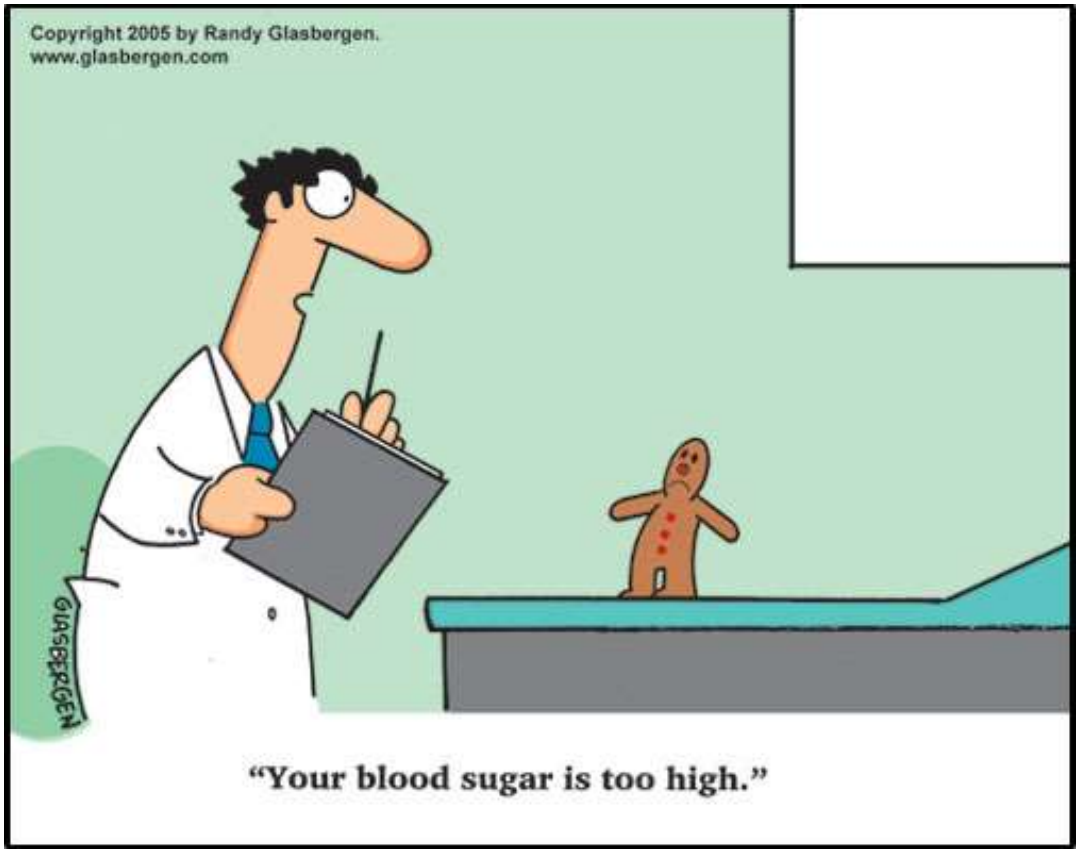
Spring 2021

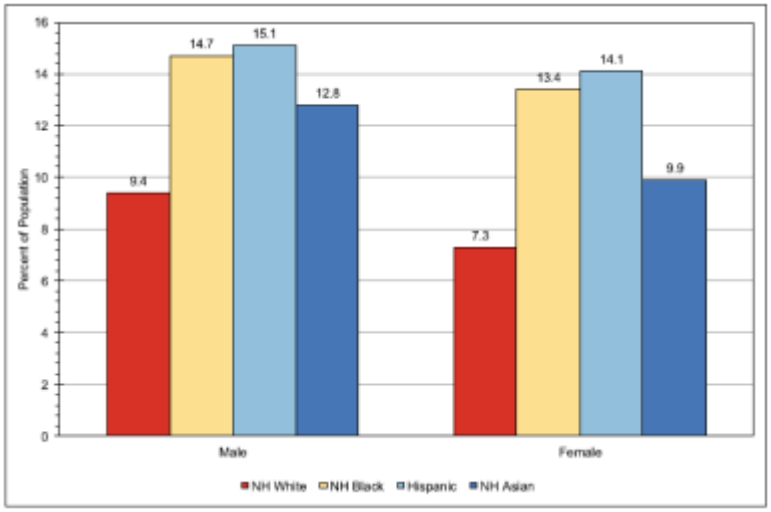
D is for:

- Diet
- Diabetes
- Depression



Diabetes and CHD

- Between 2013-2016, ~ 26M adults (9.8%) had DM, 9.4M (3.7%) had undiagnosed DM, and 91.8M (37.6%) had prediabetes.
- Why is diabetes considered a risk equivalent?
  - Patients with DM have higher number of risk factors:
    - HTN
    - Dyslipidemia: low HDL, high TG, high LDL
  - Patients with DM have more coronary arteries affected by atherosclerosis
    - Plaques are more likely to rupture due to having thin fibrous caps, large lipid core, and more inflammatory cells



Heart and Stroke Statistics- 2021 Update. Circulation 2021;143:e254-743

D: Diabetes

- Why is diabetes considered a risk equivalent continued?
  - DM creates a pro-thrombotic state:
    - Endothelial cells produce more tissue factor (major procoagulant that is found in atherosclerotic plaques)
    - Platelets more likely to aggregate
    - Increased Factor VII levels (procoagulant)
    - Decreased Protein C levels (anticoagulant)
    - Decreased Antithrombin III levels (anticoagulant)
- CHD accounts for 75% of death in patients w/DM
- Type II DM increases risk of coronary mortality by two-fold for men and three-fold for women

D: Diabetes

- ACC/AHA recommends:
  - Lifestyle modifications including daily physical activity, weight management, BP and lipid control
  - **Metformin** as first-line agent if not contra-indicated
  - SGLT2 inhibitors or GLP-1 receptor agonists recommended as part of glucose-lowering regimen to reduce MACE, HF, CV death, and CKD progression
    - SGLT2 inhibitors: empagliflozin, dapagliflozin, canagliflozin
    - GLP-1 RA: liraglutide, semaglutide
  - Target A1c </= 7%
    - 7-7.9% may be considered for older adults
    - Need to consider risks associated with hypoglycemia

2012 SIHD guidelines; 2013 Secondary Prevention in Older Adults; 2020 Standards of Med Care in Diabetes

FIRST-LINE Therapy is Metformin and Comprehensive Lifestyle (including weight management and physical activity)

INDICATORS OF HIGH-RISK OR ESTABLISHED ASCVD, CKD, OR HF†

NO

CONSIDER INDEPENDENTLY OF BASELINE A1C OR INDIVIDUALIZED A1C TARGET

TO AVOID THERAPEUTIC INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)

IF A1C ABOVE INDIVIDUALIZED TARGET PROCEED AS BELOW

ASCVD PREDOMINATES

- Established ASCVD
- Indicators of high ASCVD risk (age ≥55 years with coronary, carotid or lower extremity artery stenosis >50%, or LVH)

PREFERABLY

GLP-1 RA with proven CVD benefit[1]

OR

SGLT2i with proven CVD benefit[1] if eGFR adequate[2]

If A1C above target

If further intensification is required or patient is now unable to tolerate GLP-1 RA and/or SGLT2i, choose agents demonstrating CV safety:

- For patients on a GLP-1 RA, consider adding SGLT2i with proven CVD benefit[1]
- DPP-4i if not on GLP-1 RA
- Basal insulin[4]
- TZD[5]
- SU[6]

HF OR CKD PREDOMINATES

- Particularly HFrEF (LVEF <45%)
- CKD: Specifically eGFR 30-60 mL/min/1.73 m² or UACR >30 mg/g, particularly UACR >300 mg/g

PREFERABLY

SGLT2i with evidence of reducing HF and/or CKD progression in CVOTs if eGFR adequate[3]

OR

If SGLT2i not tolerated or contraindicated or if eGFR less than adequate[2] add GLP-1 RA with proven CVD benefit[1]

If A1C above target

- Avoid TZD in the setting of HF

Choose agents demonstrating CV safety:

- For patients on a SGLT2i, consider adding GLP-1 RA with proven CVD benefit[1]
- DPP-4i (not saxagliptin) in the setting of HF (if not on GLP-1 RA)
- Basal insulin[4]
- SU[6]

COMPELLING NEED TO MINIMIZE HYPOGLYCEMIA

DPP-4i	GLP-1 RA	SGLT2i[2]	TZD
If A1C above target			
SGLT2i[2] **OR** TZD	SGLT2i[2] **OR** TZD	GLP-1 RA **OR** DPP-4i **OR** TZD	SGLT2i[2] **OR** DPP-4i **OR** GLP-1 RA

If A1C above target

Continue with addition of other agents as outlined above

If A1C above target

Consider the addition of SU[6] **OR** basal insulin:

- Choose later generation SU with lower risk of hypoglycemia
- Consider basal insulin with lower risk of hypoglycemia[7]

COMPELLING NEED TO MINIMIZE WEIGHT GAIN OR PROMOTE WEIGHT LOSS

GLP-1 RA with good efficacy for weight loss[8] — EITHER/OR — SGLT2i[2]

If A1C above target

SGLT2i[2]	GLP-1 RA with good efficacy for weight loss[8]

If A1C above target

If quadruple therapy required, or SGLT2i and/or GLP-1 RA not tolerated or contraindicated, use regimen with lowest risk of weight gain

PREFERABLY

DPP-4i (if not on GLP-1 RA) based on weight neutrality

If DPP-4i not tolerated or contraindicated or patient already on GLP-1 RA, cautious addition of:

• SU[6] • TZD[5] • Basal insulin

COST IS A MAJOR ISSUE[9-10]

SU[6]	TZD[10]

If A1C above target

TZD[10]	SU[6]

If A1C above target

- **Insulin therapy** basal insulin with lowest acquisition cost

OR

- Consider DPP-4i **OR** SGLT2i with lowest acquisition cost[10]

1. Proven CVD benefit means it has label indication of reducing CVD events
2. Be aware that SGLT2i labelling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use
3. Empagliflozin, canagliflozin and dapagliflozin have shown reduction in HF and to reduce CKD progression in CVOTs. Canagliflozin has primary renal outcome data from CREDENCE. Dapagliflozen has primary heart failure outcome data from DAPA-HF
4. Degludec or U100 glargine have demonstrated CVD safety
5. Low dose may be better tolerated though less well studied for CVD effects
6. Choose later generation SU to lower risk of hypoglycemia, Gilmepiride has shown similar CV safety to DPP-4i
7. Degludec / glargine U300 < glargine U100 / detemir < NPH insulin
8. Semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
9. If no specific comorbidities (i.e. no established CVD, low risk of hypoglycemia and lower priority to avoid weight gain or no weight-related comorbidities)
10. Consider country- and region-specific cost of drugs. In some countries TZDs relatively more expensive and DPP-4i relatively cheaper

† Actioned whenever these become new clinical considerations regardless of background glucose-lowering medications.

LVH = Left Ventricular Hypertrophy; HFrEF = Heart Failure reduced Ejection Fraction

UACR = Urine Albumin-to-Creatinine Ratio; LVEF = Left Ventricular Ejection Fraction

D is for:

- Diet
- Diabetes
- Depression

D: Depression

- Depression may be an independent risk factor for CV related death
  - Depressive symptoms associated with symptom burden, physical function, disease-specific quality of life, and perceived overall health in patients with CHD (The Heart and Soul Study)
  - Anxiety and depression can increase the risk for events in patients with CHD
  - Moderate to severe depression pre-CABG and persistent post-op depression increases risk of death 2-fold compared to non-depressed CABG patients
  - Older adults may have 4 times the risk of dying 4 months post ACS

JAMA 2003;290:215-221; Lancet 2003;362:604-9; Arch Gen Psych 2008;65:62-71

D: Depression

- ACC/AHA recommends:
  - For patients with CHD (including recent CABG or MI), it is reasonable to screen for depression
  - Guidelines do not specify which anti-depressant therapy to use:
    - SSRIs have anti-platelet effects, so use caution in patients taking anti-platelet and anticoagulant therapies
    - Avoid SNRIs in patients with HFrEF
    - Bupropion may be reasonable in patients with depression and continued tobacco use

ACC/AHA 2011 Secondary Prevention Update; 2012 SIHD guidelines; 2013 Secondary Prevention in Older Adults; 2015 CABG Update

E is for:

- **Education**
- **Exercise**

E: Education

American Heart Association.
Learn and Live.

- ACC/AHA recommends:
  - Pathophysiology
  - Risk factors
  - Prognosis
  - Treatments and adherence
  - Risk factor reduction
  - Physical activity

CARDIAC REHABILITATION
Take Your Recovery To Heart

Monitoring Efficacy of Cardiac Medications

American Heart Association. Learn and Live.

- Anginal episodes
- Nitroglycerin use
- Exercise tolerance
- Vital signs
- Therapy goals
- Medication side effects

E: Exercise

- ACC/AHA recommends:
  - 30-60 minutes of moderate-intensity aerobic activity daily (≥ 5 days/week) supplemented by increases in daily lifestyle activities (like walking, housework, gardening)
  - Expanding exercise to include resistance training 2 days/week may be reasonable
  - Patients should be counseled to report and be evaluated for symptoms related to exercise

ACC/AHA 2007 CSA Focused Update; 2011 Secondary Prevention Update; 2012 SIHD Guideline; 2019 ESC CCS Guideline

F is for:

- **inFLUenza**
- **Fish Oil Supplements**

F: Influenza Vaccination

- ACC/AHA recommends:
  - All patients with CVD should receive yearly influenza vaccine with other high risk patient populations
  - Why?
    - Influenza infection can exacerbate heart disease and cause complications (including death)
    - 2013 meta-analysis found that flu vaccination reduced risk of CV events by 48% in the following year
    - 2018 study from Canada demonstrated 6-fold increase risk of MI within 7 days of influenza diagnosis
    - Flu shots also reduce length of hospitalization, medical costs, and work absenteeism

ACC/AHA 2007 CSA Focused Update; 2011 Secondary Prevention Guideline; 2012 SIHD Guideline; JAMA 2013;310:1711-1720; NEJM 2018;378:345-353; 2019 ESC CCS Guideline

F is for:

- inFLUenza
- **Fish Oil Supplements**

F: Fish Oil Supplements (omega 3-fatty acids)

- **GISSI-Prevenzione trial:**
  - Enrolled 11,324 patients surviving recent MI to fish oil 1g/day or vitamin E supplementation
  - Significantly lower risk of overall death (14%), CV-related death (30%), and sudden cardiac death (45%) with fish oil
  - MOA: anti-arrhythmic and anti-inflammatory effects (low doses), lowers triglycerides (high doses)

De Caterina. NEJM 2011;364:2439-50

F: Fish Oil Supplements

- ACC/AHA recommends for:
  - Primary prevention of CHD:
    - Lack of consensus on current evidence to recommend omega-3 PUFA supplements in patients at high CVD risk (Class III: no benefit vs Class IIb: reasonable)
  - Secondary prevention of CHD:
    - May reduce CHD death in patient with prior CHD but does not reduce the incidence of recurrent non-fatal MI (Class IIa: reasonable)
  - Secondary prevention of outcomes in HFrEF:
    - May reduce risk of hospitalizations and death (Class IIa: reasonable)

Science Advisory from AHA on Fish Oil Supplementation and Prevention of Clinical CV Disease Circ;2017;135:e867-884

Fish Oil and CHD Reduction

- Recent meta-analysis of 10 trials involving 77,917 patients demonstrated that fish oil supplementation for a mean of 4.4 years had no significant association with reductions in fatal or nonfatal CHD or any major vascular events.
  - ***Authors concluded that results provide no support for current recommendations to use fish oil supplements for the prevention of fatal CHD or any CV disease in patients who have or at high risk of developing CVD.***

Aung et al. JAMA Cardiol 2018;3:225-233

F: Fish Oil Dosing for Secondary Prevention

- Recommended: 1 gram/day (combination EPA and DHA)

(typical fish oil label)

FISH OIL

Serving Size 1 Softgel
Servings Per Container 100

Amount Per Serving		
Calories	10	
Calories from Fat	10	
Total Fat	1 g	2%*
Cholesterol	5 mg	2%
Vitamin E (as mixed tocopherols)	1 IU	3%
Fish Oil	1000 mg	†
EPA (Eicosapentaenoic Acid)	180 mg	†
DHA (Docosahexaenoic Acid)	120 mg	†

INGREDIENTS: Gelatin, Glycerin, Enteric Coating (Sodium Alginate, Stearic Acid).

ALLERGEN INFORMATION: CONTAINS FISH (ANCHOVY, MACKEREL, SARDINE) INGREDIENTS.

SUGGESTED USE: As a dietary supplement, take 1-2 softgels, up to 3 times daily, with meals.

1000mg of fish oil looks good, right?
Take a closer look.

Add the EPA and DHA together:

180mg of EPA
+ 120mg of DHA

300mg of total EPA:DHA

This omega 3 supplement only contains 300mg of active EPA:DHA. Inactive fats make up the remaining 700mg.

http://www.sfh.com/pdf/howtoreadlabels_sfh.pdf

Therapies that Lack Evidence and Should not be Recommended

- Postmenopausal HRT
- Anti-oxidant supplements: Vitamins C, E, and beta-carotene
- Other supplements: Folic acid, vitamin B6, vitamin B12, garlic, coenzyme Q10, selenium, chromium
- Supplement use:
  - Common in cardiac patients 26-42%
  - Supplements used (in order of frequency): MVI, Ca, Vit E, Vit C, Vit B complex

Bin and Kiat. Ev-based Complement Alt Med 2011;632829. Epub 2010 Oct 13.

Thank you!