Information Overload in Chronic Coronary Disease

C. Michael White, Pharm.D., FCP , FCCP, FASHP
Distinguished Professor and Chair, Pharmacy Practice
UConn School of Pharmacy, Storrs, CT

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Disclosure

- The presenter has no financial or nonfinancial, real of perceived conflicts of interest germane to this talk. The content is primarily derived from standard American Heart Association and American College of Cardiology Guidelines for the Treatment of Chronic Cardiac Disease with general added information from standard product labeling.

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At the conclusion of this program, the successful student will be able to:

1. Determine if a patient has chronic cardiac disease (CCD).
2. Identify lifestyle modifications that can reduce the risk of CCD.
3. Identify therapies that can reduce final health outcomes for specific CCD patient types to design successful drug regimens.
4. Describe how the steps in the PPCP process can be applied when reviewing a cardiac patient.

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Patients with proven ≥70% stenosis (atherosclerotic plaques) in coronary artery(ies) before or after treatment

Patients with angina pectoris during exertion

Patients with an acute coronary syndromes (unstable angina, NSTEMI, STEMI) in the past

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Best Recommendation

Worst Recommendation

SIZE OF TREATMENT EFFECT

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	CLASS IIa *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	CLASS IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	CLASS III *No Benefit* or CLASS III *Harm* Procedure/Test / Treatment COR III: No benefit — Not Helpful / No Proven Benefit COR III: Harm — Excess Cost w/o Benefit or Harmful / Harmful to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations	should is recommended	is reasonable can be useful/effective/beneficial	may/might be considered may/might be reasonable	COR III: No Benefit COR III: Harm

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Dietary Recommendations

Dietary Recommendations

COR	LOE	Nutrition
1	B-R	1. In patients with CCD, a diet emphasizing vegetables, fruits, legumes, nuts, whole grains, and lean protein is recommended to reduce the risk of CVD events.*[1-4]
2a	B-NR	2. In patients with CCD, reducing the percentage of calories from saturated fat (<6% of total calories) and replacing with dietary monounsaturated and polyunsaturated fat, complex carbohydrates, and dietary fiber can be beneficial to reduce the risk of CVD events.*[1-6]
2a	B-NR	3. In patients with CCD, minimization of sodium (<2,300 mg/d; optimally 1,500 mg/d) and minimization of processed meats (eg, cured bacon, hot dogs) can be beneficial to reduce the risk of CVD events.*[2,3,6,7]
2a	B-NR	4. In patients with CCD, limiting refined carbohydrates (eg, containing <25% whole grain by weight, including refined cold ready-to-eat breakfast cereal, white bread, white rice), and sugar-sweetened beverages (eg, soft drinks, energy drinks, fruit drinks with added sugars) can be beneficial to reduce the risk of CVD events.*[2-4,6,8]
3: Harm	B-NR	5. In patients with CCD, the intake of *trans* fat should be avoided because *trans* fat is associated with increased morbidity and mortality rates.*[9,10]
		Nutrition Supplements
3: No Benefit	B-NR	6. In patients with CCD, the use of nonprescription or dietary supplements, including omega-3 fatty acid, vitamins C, D, E, beta-carotene, and calcium, is not beneficial to reduce the risk of acute CVD events.[11-22]

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COR	LOE	RECOMMENDATIONS
1	A	1. In patients with CCD, tobacco use should be assessed at every health care visit to facilitate identification of those who may benefit from behavioral or pharmacologic interventions.*[1-3]
1	A	2. Patients with CCD who regularly smoke tobacco should be advised to quit at every visit.*[4]
1	A	3. In patients with CCD who regularly smoke tobacco, behavioral interventions are recommended to maximize cessation rates in combination with pharmacotherapy, including bupropion, varenicline, or combination long- and short-acting nicotine replacement therapy (NRT).*[5-7]
2b	B-R	4. In patients with CCD who regularly smoke tobacco, varenicline may be considered versus bupropion or NRT to increase cessation rates.[6]
2b	B-R	5. In patients with CCD who regularly smoke tobacco, the short-term use of nicotine-containing e-cigarettes may be considered to aid smoking cessation, although the risk of sustained use and unknown long-term safety may outweigh the benefits.[8-10]
3: Harm	B-NR	6. Patients with CCD should avoid secondhand smoke exposure to reduce risk of cardiovascular events.*[11,12]

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Substances of Abuse

Substances of Abuse Impact on ACS Risk

TABLE 9 Substances With Abuse Potential and Adverse Cardiovascular Effects for Patients With CCD*

Substance	Potential Adverse Cardiovascular Effects
Alcohol	■ J-shaped relationship between alcohol intake and cardiovascular risk in observational studies but limited by confounding.[18] ■ Heavy alcohol use and binge drinking associated with increased morbidity and mortality rates.[9,10,19] ■ May increase serum triglycerides. ■ Potential drug-drug interactions with cardiovascular therapies.
Cocaine, methamphetamine	■ Stimulation of the sympathetic nervous system.[5,20] ■ Platelet activation and aggregation.[20] ■ Increased myocardial oxygen demand.[5] ■ Can present with cocaine-associated chest pain. ■ MI risk independent of route of administration.[21]
Opioids	■ Possible association with risk of MI in chronic use.[22] ■ High potential for dependence and abuse with chronic use. ■ Potential for drug-drug interactions with cardiovascular therapies.
Marijuana	■ Stimulation of the sympathetic nervous system. ■ Platelet activation. ■ Endothelial dysfunction. ■ Carbon monoxide toxicity from smoking and inhalatation.[12] ■ Route of administration may impact toxicity, with edible products associated with fewer acute cardiovascular symptoms.[23]

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Alcohol Use

Substance Abuse and Alcohol Use

COR	LOE	RECOMMENDATIONS
1	C-LD	1. Patients with CCD should be routinely asked and counseled about substance use to reduce ASCVD events.[1-5]
2a	B-NR	2. In patients with CCD who consume alcohol, it is reasonable to limit alcohol intake (≤1 drink/d for women, ≤2 drinks/d for men) to reduce cardiovascular and all-cause death.[6-8]
3: No Benefit	B-NR	3. Patients with CCD should not be advised to consume alcohol for the purpose of cardiovascular protection.[9,10]

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Self Assessment Question

- A female patient is interested in lifestyle modification. Which of the following would you recommend?

a. Switch from EVOO to coconut oil
b. Switch from smoking weed to doing crystal methamphetamine
c. Limit alcohol to a maximum of 1 drink a day

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Self Assessment Question

- A female patient is interested in lifestyle modification. Which of the following would you recommend?

a. Switch from EVOO to coconut oil

b. Switch from smoking weed to doing crystal methamphetamine

c. Limit alcohol to a maximum of 1 drink a day

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CCD Treatment to Reduce Final Health Outcomes

	Mechanism	Who Should Receive?	Notes
Antiplatelets	⇩ Platelet thrombus formation	All patients not on OAC	• ASA or P2Y12i for all not on OAC • DAPT (ASA + P2Y12i) for awhile after ACS (12 mo) or PCI (6 mo)
Statin	⇩ LDL	All patients	• High intensity statins for all • Moderate intensity if cannot tolerate high • Low if you cannot tolerate moderate
Ezetimibe and/or PCSK9i	⇩ LDL	Patients not achieving LDL goal (<70mg/dL) on statin alone	• Add ezetimibe if not at LDL goal on statin • Add PCSK9i is not at LDL goal on statin + ezetimibe in "very high-risk patients"
GLP-1 or SGLT2i	⇩HbA1c, weight	Patients with DM2 (either), HF (either), or obesity (GLP-1)	• SGLT2i preferred in HFrEF • GLP-1 (+/- GIP) preferred in weight loss
Colchicine	⇩ hsCRP	Patients with high hsCRP (>3mg/dL) level	• If patient has RA, SLE, Crohn's, UC, Plaque psoriasis, use specific treatments

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CCD Treatment to Reduce Final Health Outcomes

	Mechanism	Who Should Receive?	Notes
GDMT for Hypertension	⇩ BP	Patients with BP >130/80mmHg	• BB preferred if angina symptoms • BB + ACEi or BB + ARB if post-ACS or HFrEF • Thiazides, CCBs, ACEi, or ARB preferred options if no ACS or HFrEF
Beta-Blockers	⇩ HR, Inotropy, BP	All patients after MI or with HFrEF	• Proven mortality benefits post-MI or with HFrEF • Metoprolol succinate or carvedilol if HFrEF
ACEi or ARB (± neprolysin i)	⇩ AT2 effects, BP	All patients after MI or with HFrEF	• Proven mortality benefits post-MI or with HFrEF
Aldosterone Antagonist	⇩ Aldosterone effects	Post-MI patients with S/S HF and LVEF <40%	• Proven mortality benefits + ACEi or ARB in post-MI patients with HFrEF or diabetes mellitus
Varenicline (± nicotine replacement)	⇩ Smoking	Current smokers	• Varenicline more effective than NRT but combo better than either alone • Bupropion + NRT if no varenicline

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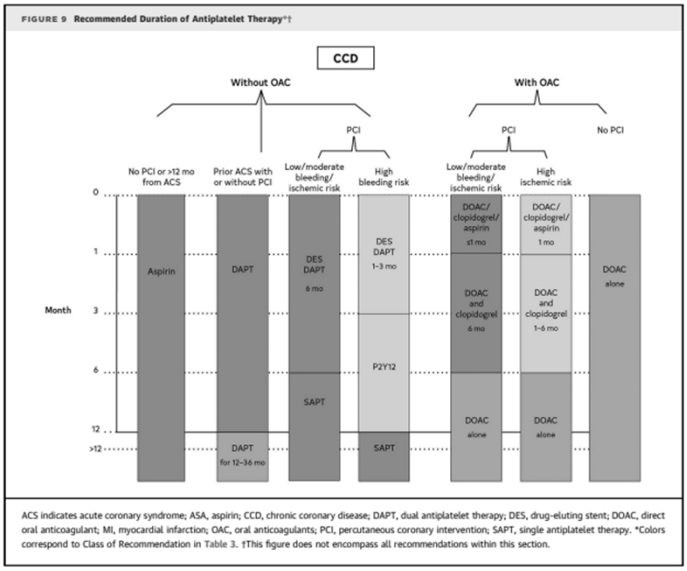
Antiplatelets and Anticoagulants

- Everyone with CCD needs SAPT or DOAC for life
- Antiplatelet preferred for CCD over OAC but some people on OAC already
- After PCI for most: DAPT for 6 mo
  - PCI + DOAC: DAPT + DOAC for 1 mo, P2Y12i + DOAC 5 mo, then DOAC alone
  - PCI w/o OAC but high risk of bleeding: DAPT 3 mo, P2Y12i 9 mo, then SAPT
- After ACS – DAPT for 1 yr
  - Then SAPT or DAPT until 36 mo and then SAPT thereafter
  - ACS + DOAC: DAPT + DOAC for 1 mo, P2Y12i + DOAC 5 mo, then DOAC alone



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Aspirin

- COX-1 effects = reduced Txa2, reduced risk of platelet aggregation
  - Doses 81 to 325mg maximize COX-1 blockade
- COX-2 effects = reduced PGI in endothelium, increased risk of platelet aggregation
  - Doses >650 mg COX-2 negates COX-1 platelet effects
    - More inflammatory pain relief at these doses
- Both lower and higher dose ASA increases gastric ulcer risk
  - A COX-1 phenomenon

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P2Y12i

- Dosing: No loading doses for CCD w/o ACS
  - Clopidogrel: 300-600mg load then 75mg daily
  - Prasugrel: 60mg load then 10mg daily
    - 5mg daily if <60kg or >74 years
  - Ticagrelor: 180mg load then 90mg twice daily
- Metabolic Pathways:
  - Clopidogrel – CYP2C19 substrate (needs activation)
    - Avoid use in genetic poor metabolizers for CYP2C19
  - Ticagrelor – CYP3A4 substrate, PGP Inhibitor, mild CYP3A4 inhibitor
    - Avoid with potent CYP3A4 inhibitors
    - Monitor digoxin serum levels closely
  - Prasugrel – Substrate for multiple CYP enzymes: No significant kinetic interactions

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Aspirin or P2Y12i Contraindications and Precautions

- Contraindications: Active GI or other serious bleed, very recent PUD (<4 weeks), hemophilia
  - ASA only: severe NSAID induced bronchoconstriction
    - P2Y12i can be used in bronchoconstriction patients
- DC 7 d before major surgery (discuss risk and benefit with cardiologist)
- Prasugrel might increase solid tumor formation
- Ticagrelor causes SOB related to adenosine MOA (transient, tolerance occurs)
- Prasugrel can't use standard dose if > 74 years (higher risk of ICH, use 5 mg)
- GI upset not an ASA contraindication
  - Enteric coating can reduce discomfort but slow absorption (don't use EC during ACS)
  - P2Y12i an alternative for chronic therapy to ASA for GI upset

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Don't Use Strong COX-2 Inhibiting NSAIDs for Musculoskeletal Pain while on ASA if Possible

- NSAIDs with high relative COX-2 selectivity should not be used for chronic musculoskeletal discomfort when APAP, nonacetylated salicylates or nonselective NSAIDs provide acceptable relief (P2Y12 agents are ASA alternative in NSAIDs unavoidable)

Table 1. NSAID Selectivity

More COX-1 Selective	Nonselective	5–50–fold COX-2 selective[a]	>50-fold COX-2 selective[a]
Ketorolac (Acular) Flurbiprofen (Ocufen) Ketoprofen (Generic) Indomethacin (Indocin) Aspirin (Generic) Naproxen (Aleve) Tolmetin (Generic) Piroxicam (Feldene) Meclofenamate (Generic)	Ibuprofen (Advil, Motrin) Fenoprofen[b] (Nalfon) Sodium salicylate (Generic) Diflunisal (Generic)	Sulindac (Clinoril) Diclofenac (Cambia) Celecoxib (Celebrex) Meloxicam[c] (Mobic) Etodolac (Generic)	Etoricoxib[d] (Arcoxia) Lumiracoxib[d] (Prexige)
Increased gastrointestinal effects ◄——► Increased cardiovascular effects			

[a]Listed in order of increasing COX-2 selectivity
[b]Equipotent for COX-1 and COX-2 selectivity
[c]At higher doses, COX-2 selectivity decreases and COX-1 inhibition increases[5]
[d]Not yet approved by the FDA

COX, cyclooxygenase; FDA, Food and Drug Administration; NSAID, non-steroidal anti-inflammatory drug

J Am Coll Cardiol. 2014 Dec 23;64(24):e139

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Self Assessment Question

- A patient had a PCI procedure and is currently receiving chronic therapy with rivaroxaban for a genetic chronic clotting disorder called Factor V Leiden. What antiplatelet therapy should be added to the DOAC?

a. DAPT for 6 months, then SAPT for 6 months, then remove the DOAC and just use SAPT therapy alone
b. SAPT for 1 year, then just remove the SAPT and use the DOAC therapy alone
c. DAPT for 1 month, then SAPT for 5 months, then remove the SAPT and just use DOAC therapy alone

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Self Assessment Question

- A patient had a PCI procedure and is currently receiving chronic therapy with rivaroxaban for a genetic chronic clotting disorder called Factor V Leiden. What antiplatelet therapy should be added to the DOAC?

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c. DAPT for 1 month, then SAPT for 5 months, then remove the SAPT and just use DOAC therapy alone

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- Everyone with CCD gets high intensity statins
  - If high not tolerated, try moderate dose
  - If moderate not tolerated, try low dose
- If LDL ≥70 mg/dL, ezetimibe can be added to statin
- If LDL ≥70 mg/dL, PCSK9i can be added to statin + ezetimibe in "very high risk" patients
- If statin contraindicated, PCSK9i is first line LDL reducer, can add ezetimibe if LDL remains ≥70 mg/dL
- Icosapent ethyl (EPA omega-3 FA) can be added if LDL <100mg/dL, but TGs are still elevated >150 mg/dL to further reduce VLDL

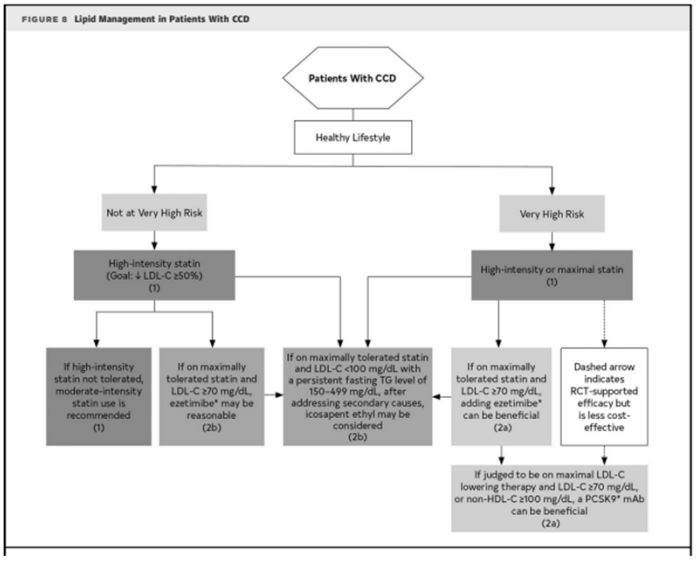

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TABLE 11 High-, Moderate-, and Low-Intensity Statin Therapy*

	High Intensity	Moderate Intensity	Low Intensity
LDL-C Lowering†	≥50%	30%–49%	<30%
Statins	**Atorvastatin (40 mg‡), 80 mg** **Rosuvastatin 20 mg (40 mg)**	**Atorvastatin 10 mg** (20 mg) **Rosuvastatin** (5 mg) **10 mg** **Simvastatin 20–40 mg**§	Simvastatin 10 mg
		Pravastatin 40 mg (80 mg) **Lovastatin 40 mg** (80 mg) Fluvastatin XL 80 mg **Fluvastatin 40 mg BID** Pitavastatin 1–4 mg	**Pravastatin 10–20 mg** **Lovastatin 20 mg** Fluvastatin 20–40 mg

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Very High or High ASCVD Risk

TABLE 10 Very High-Risk* of Future ASCVD Events

Definition of Very High-Risk*
History of multiple major ASCVD events
OR
One major ASCVD event **AND** ≥2 high-risk conditions
Major ASCVD Events
Recent ACS (within the past 12 mo)
History of MI (other than recent ACS events listed above)
History of ischemic stroke
Symptomatic peripheral artery disease (history of claudication with ABI <0.85, or previous revascularization or amputation)[51]
High-Risk Conditions
Age ≥65 y
Familial hypercholesterolemia†
History of previous coronary artery bypass graft surgery or percutaneous coronary intervention outside of the major ASCVD event(s)
Diabetes
Hypertension
Chronic kidney disease (eGFR, 15–59 mL/min/1.73 m²)[35,29]
Current tobacco smoking
Persistently elevated LDL-C ≥100 mg/dL despite maximally tolerated statin therapy and ezetimibe
History of congestive heart failure

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Colchicine

COR	LOE	RECOMMENDATION
2b	B-R	1. In patients with CCD, the addition of colchicine for secondary prevention may be considered to reduce recurrent ASCVD events.[1,2]

- Colchicine 0.5 mg PO daily is FDA approved for reducing ASCVD events in CCD patients with elevated hsCRP
- Adverse events:
  - Gastrointestinal issues: Diarrhea, nausea, vomiting
  - Sore throat
  - Muscle pain, weakness
  - Numbness or tingling in fingers or toes
  - Unusual bleeding
  - Rash, itching
- Covered in detail in gout lecture

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GLP-1 Agonist and SGLT2i Therapy in CCD

COR	LOE	RECOMMENDATIONS
1	A	1. In patients with CCD who have type 2 diabetes, the use of either an SGLT2 inhibitor[1-8] or a GLP-1 receptor agonist[9-17] with proven cardiovascular benefit is recommended to reduce the risk of MACE.
1	A	4. In patients with CCD and heart failure with LVEF ≤40%, use of an SGLT2 inhibitor is recommended to reduce the risk of cardiovascular death and heart failure hospitalization[19-22] and to improve QOL,[23,24] irrespective of diabetes status.[a]
2a	B-R	6. In patients with CCD and heart failure with LVEF >40%, use of an SGLT2 inhibitor can be beneficial in decreasing heart failure hospitalizations[27,28] and to improve QOL,[4,29] irrespective of diabetes status.

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2a	B-R	3. For patients with CCD and overweight or obesity in whom pharmacologic therapy is warranted for further weight reduction, a GLP-1 receptor agonist can be beneficial in addition to counseling for diet and physical activity,[11,12] and it is reasonable to choose semaglutide over liraglutide.[13,14]
2a	B-NR	4. In patients with CCD and severe obesity who have not met weight loss goals with lifestyle and pharmacologic intervention, and who have acceptable surgical risk, referral for consideration of a bariatric procedure is reasonable for weight loss and cardiovascular risk factor reduction.[15-18]
3: Harm	B-R	5. In patients with CCD, use of sympathomimetic weight loss drugs is potentially harmful.[19]

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COR	LOE	RECOMMENDATIONS
1	A	1. In adults with CCD, nonpharmacologic strategies are recommended as first-line therapy to lower BP in those with elevated BP (120-129/<80 mm Hg) (see Table 12).*[1-9]
1	B-R	2. In adults with CCD who have hypertension, a BP target of <130/<80 mm Hg is recommended to reduce CVD events and all-cause death.*[10-14]
1	B-R	3. In adults with CCD and hypertension (systolic BP ≥130 and/or diastolic BP ≥80 mm Hg), in addition to nonpharmacological strategies, GDMT angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARB), or beta blockers[15-17] are recommended as first-line therapy for compelling indications (eg, recent MI or angina), with additional antihypertensive medications (eg, dihydropyridine calcium channel blockers [CCB], long-acting thiazide diuretics, and/or mineralocorticoid receptor antagonists) added as needed to optimize BP control.*[13,18]

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COR	LOE	RECOMMENDATIONS
1	A	1. In patients with CCD and LVEF ≤40% with or without previous MI, the use of beta-blocker therapy is recommended to reduce the risk of future MACE, including cardiovascular death.[1-3]
1	A	2. In patients with CCD and LVEF <50%, the use of sustained release metoprolol succinate, carvedilol, or bisoprolol with titration to target doses is recommended in preference to other beta blockers.*[1,3-8]
2b	B-NR	3. In patients with CCD who were initiated on beta-blocker therapy for previous MI without a history of or current LVEF ≤50%, angina, arrhythmias, or uncontrolled hypertension, it may be reasonable to reassess the indication for long-term (>1 year) use of beta-blocker therapy for reducing MACE.[9-15]
3: No Benefit	B-NR	4. In patients with CCD without previous MI or LVEF ≤50%, the use of beta-blocker therapy is not beneficial in reducing MACE, in the absence of another primary indication for beta-blocker therapy.†[16-19]

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ACEi or ARB

COR	LOE	RECOMMENDATIONS
1	A	1. In patients with CCD who also have hypertension, diabetes, LVEF ≤40%, or CKD, the use of ACE inhibitors, or ARBs if ACE inhibitor-intolerant, is recommended to reduce cardiovascular events.[1-5]
2b	B-R	2. In patients with CCD without hypertension, diabetes, or CKD and LVEF >40%, the use of ACE inhibitors or ARBs may be considered to reduce cardiovascular events. [6-10]

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Self Assessment Question

- A patient with CCD is determined to have "high risk" of experiencing an ASCVD event. The patient cannot receive high or even moderate intensity statin due to a history of significant rises in liver enzymes 8-10 weeks after initiation on two occasions. Which is true of the patient's recommended lipid regimen?

a. The patient needs high intensity statin regardless of the liver issues and ezetimibe should be added if the LDL on the statin is over 70mg/dL

b. The patient could receive a low intensity statin + a PCSK9 inhibitor and if the LDL remains over 70mg/dL, ezetimibe can be added

c. The patient could receive a PCSK9 inhibitor and if the LDL remains over 70mg/dL, ezetimibe can be added

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Self Assessment Question

- A patient with CCD is determined to have "high risk" of experiencing an ASCVD event. The patient cannot receive high or even moderate intensity statin due to a history of significant rises in liver enzymes 8-10 weeks after initiation on two occasions. Which is true of the patient's recommended lipid regimen?

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c. The patient could receive a PCSK9 inhibitor and if the LDL remains over 70mg/dL, ezetimibe can be added

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HIV or Autoimmune Diseases

CCD in HIV or Autoimmune Dx

COR	LOE	RECOMMENDATIONS
		HIV
1	B-R	1. In adults with CCD and HIV, antiretroviral therapy is beneficial to decrease the risk of cardiovascular events.[1,2]
2a	B-R	2. In adults with CCD and HIV, it is reasonable to choose antiretroviral therapy regimens associated with more favorable lipid and cardiovascular risk profiles with consideration of drug-drug interactions.[3-5]
3: Harm	C-LD	3. In adults with CCD and HIV, lovastatin or simvastatin should not be administered with protease inhibitors as this may cause harm.[6,7]
		Autoimmune Disorders in CCD
2a	C-LD	4. In adults with CCD and rheumatoid arthritis, initiation and maintenance of disease-modifying anti-rheumatoid drugs is beneficial to decrease the risk of cardiovascular events.[8-11]
2b	C-LD	5. In adults with CCD and autoimmune diseases, treatment with biologics and other immune modulating therapies that reduce disease activity may be considered to decrease the risk of cardiovascular events.[10,11]
3: Harm	C-LD	6. In patients with CCD and rheumatoid arthritis, high-dose glucocorticoids should not be used long term if alternative therapies are available because of increased cardiovascular risk.[11,12]

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Best Antiretrovirals for the Heart

Which Antiretrovirals to Choose?

TABLE 23 Common Antiretroviral Therapy Drugs and Effects on Lipid Levels

Class	Drug	Effect on Blood Lipids
Protease inhibitors	Atazanavir	Increases HDL-C and decreases LDL-C levels
	Darunavir	Increases HDL-C levels
	Fosamprenavir	Hypertriglyceridemia
	Ritonavir*	Increases HDL-C levels
	Saquinavir	Neutral
	Tipranavir	Dyslipidemia
NRTIs	Abacavir	Increases total cholesterol, LDL-C, and HDL-C levels
	Lamivudine	Increases total cholesterol, LDL-C, and HDL-C levels
	Tenofovir fumarate disoproxil	Lowers LDL levels
	Zidovudine	Hypertriglyceridemia
NNRTIs	Efavirenz	Increases total cholesterol, LDL-C, HDL-C, and triglyceride levels
	Nevirapine	Neutral or decreases lipid levels
	Rilpivirine	Neutral
Integrase inhibitors	Dolutegravir	Neutral
	Raltegravir	Increases HDL levels

Adapted from Hsue PY et al.© by permission from Springer Nature, Copyright 2019.
*Although ritonavir is a protease inhibitor, this drug is generally used as a pharmacokinetic enhancer.
HDL indicates high-density lipoprotein; HDL-C, high-density lipoprotein cholesterol; LDL, low-density lipoprotein; LDL-C, low-density lipoprotein cholesterol; NNRTI, nonnucleoside reverse-transcriptase inhibitor; and NRTI, nucleoside reverse-transcriptase inhibitor.

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Stable Anginal Attack in CCD

Location:
- Sternum alone or radiating to:
  - Jaw and left arm
  - Gut and back

Quality:
- Squeezing, tightness, pressing pain
- Burning Sensation
- Gradual onset and offset

Duration: 5-30 min (with cessation of activity)

Precipitants: Exercise, anger, exercise + meal

Nitro relief: Yes, before 3 SL NTG

Some people have SOB as a symptom, especially the elderly

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CCD Treatment w/ Stable Angina but no Previous ACS

	Mechanism of Benefit	Terminate Angina Attack	Prevent Angina Attack	Reduce Severity of Angina Attack
SL or Spray NTG	⇩ Venodilator (see below)	++++		
Negative Chronotrope	⇩ Myocardial O2 demand		++++	++++
Venodilator	⇩ Venous return and O2 demand (Slight Coronary Dilation)		+++	+++
Arteriolar Dilator	Dilate coronary arteries ⇧ O2 supply		+++	+++
Ranolazine	⇩ Myocardial O2 demand		++	++
PCI	⇧ O2 supply		++++	++++

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Stable Angina Attack Treatment Algorithm: Steps Are Sequential

- 1. Add NTG for acute events
  - SL for most, spray for those with xerostomia
- 2. Stop meds & treat conditions that exacerbate angina (stimulants [cocaine, amphetamines, synthetic cathinones], check TSH levels, check catecholamine levels)

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3. Chronic pain reliever
   Beta-blocker or NonDHP CCB, titrate to appreciable dose or HR 50-60 bpm
4. Adjunctive DHP or long-acting nitrate
   DHP + Non-DHP CCB not recommended
   BB + Non-DHP CCB, increased heart block risk
5. Revascularization: PCI or CABG
6. Adjunctive ranolazine

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Chronic Angina Medications

- Can't be used for acute attacks, not fast enough onset
- Decrease number of subsequent attacks and severity of attacks when taken chronically
- Rate controlling medications (beta-blockers, Non-DHP CCBs) better than pure vasodilators (DHP CCBs, isosorbide or patch NTG)
  - More effective to decrease demand than boost supply
    - Target HR is 50-60 bpm for rate controllers

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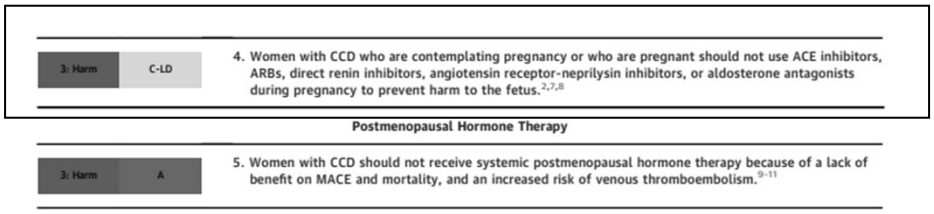
Drug Therapy in Pregnancy and Menopause



3: Harm	C-LD	4. Women with CCD who are contemplating pregnancy or who are pregnant should not use ACE inhibitors, ARBs, direct renin inhibitors, angiotensin receptor-neprilysin inhibitors, or aldosterone antagonists during pregnancy to prevent harm to the fetus.[2,7,8]

Postmenopausal Hormone Therapy

3: Harm	A	5. Women with CCD should not receive systemic postmenopausal hormone therapy because of a lack of benefit on MACE and mortality, and an increased risk of venous thromboembolism.[9-11]

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Self Assessment Question

- Why can't metoprolol tartrate be used to terminate a new onset angina pectoris event?

a. Because the onset of action is 30 minutes, and the maximum effect is felt 2 hours after ingestion
b. Because I am a pharmacist and I said so, that's why
c. Because metoprolol does not work on the coronary arteries and only coronary dilators can be used for acute angina pectoris events

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PPCP – Gather and Assess

- Gather the needed information:
  - Demographics, chief complaint, HPI, PMH, SH, FH, substance list (meds, supplements, substances of abuse), labs
- Assess the information by looking for Drug Related Problems:
  - Drug w/o indication
  - Indication w/o drug
  - Improper (sub-optimal) drug selected
  - Use with contraindication
  - Duplication of therapy
  - Overdose or underdose (including wrong dose due to renal or liver dx)
  - Improper duration
  - Adverse events
  - Drug interactions/incompatibilities

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PPCP – Gather and Assess

- Does the patient have CCD or just risk factors for CCD?
  - Positive stress test or angiogram shows coronary stenosis >70%
  - Angina pectoris
  - ACS or history of ACS
    - If ACS, are they within 12 months of the event?
- Did the person have PCI?
  - If yes, are they within 6 months of the event?
- With ACS or PCI, is the patient taking an OAC?
- Is the patient on drugs, supplements or substances that can make CCD worse? (Contraindications/Adverse Events)
  - If so, why? What are the alternatives?

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PPCP - Assess

- Is patient on all the drug classes that can reduce his risk of ACS or slow progression of cardiac disease? (Indication w/o drug)
  - If not, why not (contraindications, drug interactions)?
  - Is the dosing of these drugs appropriate to start, what is the titration schedule, and the criteria to titrate? (Underdose/Overdose, Improper Duration)
  - Is the dose appropriate for the patients CrCl, liver function, etc? (Overdose/Underdose)
  - Is the specific drug being used or considered the best one for the patient? (Duplication, Improper Drug Selection)
- Is patient on all the initial drugs needed to control both acute anginal attacks (if applicable) and to control future attacks? (Indication w/o drug)
  - If not, why not?
  - Is the dosing of these drugs appropriate to start, what is the titration schedule, and the criteria to titrate?
  - Is the dose appropriate for the patients CrCl, liver function, etc?
  - Is the specific drug being used or considered the best one for the patient?

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PPCP - Assess

- Would the addition of a newly indicated drug make an existing drug suboptimal or unnecessary to continue? (Duplication of therapy / drug w/o indication)
  - Would the dosing of an existing drug need to change with the addition of another therapy? (overdose or underdose)
- Are there any signs or symptoms of adverse drug events with existing substances? (ADEs)
- Are their any signs, symptoms, or indications of drug interactions with existing substances? (DIs)

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PPCP - Assess

- Some specific CCD questions:
  - Is the patient a smoker, diabetic, obese, HF, collagen vascular disorder, HIV, elevated hsCRP?
    - Are they on drugs to treat them? Are they the best ones? Are they dosed appropriately?
  - Does the patient have contraindications for any lipid therapy, what is the latest LDL level?
    - Can they tolerate high dose statins? Are they candidates for ezetimibe, PCSK9is or icosapent ethyl?
    - Is one statin better than another for this patient?
  - Are there drug-drug interactions or drug incompatibilities?
  - Dose patient have collagen vascular disease, elevated hsCRP, or HIV?
    - Are the drugs to treat these disorders compatible with CCD outcomes?
  - Are any drugs problematic in pregnancy?

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PPCP - Plan

- What is the plan?
- What drugs are being added, which taken away, what is the dosing of each initially and how (and how often) will it be monitored and titrated?
  - Adherence (all drugs)
    - Every follow-up visit/refill (every 6-12 mo)
  - Heart rate and PR interval (BBs and nonDHP-CCBs)
    - If hospitalized, check at Cmax after first dose (~2h after dosing) and then if hospitalized, daily for 2-3 days until Css achieved
    - Outpatient, check at every visit (30 d, 90 d, every 6-12 mo)
    - If patient complains of dizziness or new onset lethargy, check pulse and blood pressure. if low (<50 bpm of <100/60mmHg), bring patient to get an ECG and BP
  - Blood pressure (ACEi, ARB, BB, CCBs, nitrates)
    - If hospitalized, check at Cmax after first dose (~2h after dosing) and then if hospitalized, daily for 2-3 days until Css achieved)
    - Outpatient for HTN patients, wait 30 days after each dosage change or new therapy, then every visit once controlled (every 6-12 mo)
    - If patient complains of dizziness or new onset lethargy, have patient check pulse and blood pressure. if low (<50 bpm of <100/60mmHg), bring patient to get an ECG and BP
  - LDL (ezetimibe, PCSK9is)
    - 30 d after ACS
    - 60-90 days after every LDL drug dosage change or therapy added until patient at right LDL level, then every 6-12 mo
  - TGs (icosapent ethyl)
    - 30 d after ACS
    - 60 days after every LDL drug dosage change or therapy added until patient at right LDL level, then every 6-12 mo

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PPCP - Plan

- GI distress (colchicine)
  - Have patient call if severe N/V/D, check at every visit (6-12 mo)
- hsCRP (Colchicine)
  - If the hsCRP is elevated at baseline, add colchicine (unless uncontrolled collagen vascular dx) and recheck in 30-60 days
- Suicidal ideation (varenicline)
  - Have patient call if suicidal ideation occurs, check at every visit (6-12 mo)
- Smoking cessation efficacy
  - Start with varenicline, if smoking goal not met at 3 months, add nicotine replacement therapy (assess at 3 mo)
- Cough (ACEis)
  - Have patient call if dry nagging cough intolerable, check at every visit (6-12 mo)
- Bleeding (antiplatelets, OACs)
  - Have patient call if bleeding is moderate to severe
  - Check for reports of bleeding and bruising at every visit, check HCT or Hb every 6-12 mo
- Anginal attack frequency and severity (BB, CCBs, nitrates, ranolazine)
  - Check 2 weeks after each dosage change or new drug added until angina control achieved, then every visit (6-12 mo)
  - Increase to appreciable dose BB or Non-DHP CCB before adding new therapy
  - If HR 50-60 bpm, increasing BB or Non-DHP CCB dose unlikely to provide more benefit (add DHP-CCB, nitrate, or ranolazine)
- QTc interval (ranolazine)
  - Check at baseline and after Css (around days 3-5), check every year unless new symptoms like severe dizziness or fainting occur, then check ASAP
  - If QTc interval exceeds 500ms, stop ranolazine (and other QTc interval prolonging drugs)
- Signs of ACS
  - If new onset chest pain (not fitting their stable angina pattern), patient comes to ED right away

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PPCP – Implement and Follow-Up

- Present findings to team, write orders/scripts, write labs, etc
- Create follow-up appointments of sufficient times to monitor
- Discuss when and how patients should alert you of signs and symptoms in between visits

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Self Assessment Question

- Why is it important to follow the PPCP process when assessing a patient for potential drug related problems?

a. It helps structure an assessment to be sure that important drug related problems are not missed
b. It is the process that major pharmacy organizations agreed upon and is the basis of showing regulators, clinicians, patients, payers and insurers how we provide unique services to patients
c. Both these answers are correct

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Conclusions

Chronic cardiac disease (aka ASCVD) can include those with coronary artery stenosis (>70%) but no symptoms, angina pectoris, or patients after the peri-ACS period (w/in 72 hours of the onset of an ACS event)

There are drug therapies for acute pain relief during an anginal attack (NTG SL or spray) and to reduce the number and severity of future attacks (BBs, CCBs, LA NTG, ranolazine) and there are specific patient factors making one option better than another

There are drugs that can reduce the risk of ACS events, some are used in everyone while others are used if specific patient criteria is met

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