2016 Ambulatory Care Specialty Examination Review Course
Complex Case: Cardiovascular Disease 1
"GOUCH… My toe is killing me, and I can't afford this drug"

Joseph J. Saseen, PharmD, FASHP, FCCP, BCPS, BCACP
Professor and Vice Chair University of Colorado Skaggs School of Pharmacy & Pharmaceutical Sciences
Aurora, Colorado
Clinical Pharmacy Specialist University of Colorado Hospital, Department of Family Medicine
Denver, Colorado

Learning Objectives:

At the conclusion of this session, given a patient case, the participant should be able to

- Correctly answer case-based questions about appropriate ambulatory treatment for a complex patient with multiple medical problems, including dyslipidemia, gout, hypertension, obesity, and sexual dysfunction.
- Identify effective methods of managing affordability and cost-effectiveness issues for an underserved patient.
- Identify and recommend appropriate resource organizations/groups to assist a specific patient.

Format: Today's session will use a series of audience response questions to engage the audience and to prepare participants to answer similar questions on an ambulatory care board certification examination. The facilitator will discuss practical management strategies and the scientific rationale that supports these strategies.

Premise: Participants in this course are pharmacists who practice in a variety of outpatient health system settings. You are responsible for evaluating and monitoring the patient's therapy. You are responsible for providing comprehensive patient management and education. For this case scenario you are a clinical pharmacist practicing in a federally qualified health center (FQHC) that is a family medicine clinic. This FQHC is affiliated with 8 other clinics, has outpatient medical records (an electronic health record [EHR]), and each clinic has an outpatient pharmacy with 340B drug pricing. This is not an integrated health system, and hospital and specialty services are not available within this FQHC. Some patients included in this FQHC have Medicaid, some are not insured, and nearly all patients have limited income. Clinical pharmacists provide chronic disease management (e.g., diabetes, hypertension), dietary/exercise counseling, and recommendations to improve medication use and affordability.

PATIENT CASE Date: **March, 2015**

Initials	DOB/Age	Sex	Race/Ethnicity	Source
SR	59 y.o.	M	Caucasian	Patient and electronic health record (EHR)

Chief Complaint/History of Present Illness (CC/HPI) (including symptom analysis for CC):

"My toe is very painful, and I can't afford this drug."

SR awoke this morning with pain in his toe, which is visibly inflamed (red, swollen and warm to touch). He describes the acute pain as 6/10. He was diagnosed by his provider early today with acute gouty arthritis during an acute care visit. His provider has just prescribed colchicine (Colcrys® 0.6-mg tablets, #30; 1.2 mg initially, then 0.6 mg every hour thereafter up to a maximum of 8 tablets for this attack) to treat his acute gouty arthritis, but SR could not afford it when he went to his community pharmacy (the price was more than $200 and not covered by his insurance without prior authorization). He asked his provider for "Vicodin", but was told that colchicine is better and his provider was not comfortable prescribing a narcotic. When seen today, SR presented with elevated BP (164/96, 162/94 mm Hg), which both he and his provider attributed to his acute pain. He came back to clinic for an alternative to Colcrys®, or free samples, and was referred to the clinical pharmacist. As of 2014, this FQHC does not utilize sample medications, but patients may be able to obtain medication coupons if available on the Internet or acquire medications through patient assistance programs. SR is being evaluated in a 30-minute visit time slot with clinical pharmacy. He has been a patient in this FQHC since September 2012.

The provider ordered routine laboratory tests this morning, including a comprehensive metabolic panel (CMP), thyroid stimulating hormone (TSH), fasting lipid panel (FLP), complete blood count (CBC), hemoglobin A1c, and urinalysis; however, the patient was not fasting, and he reported eating breakfast (an egg sandwich with bacon and cheese) 2 hours before the blood sample was drawn.

Past Medical History (major illnesses and surgeries)
From Medical Record
Obesity x 30 years
Hypertension x 20 years
Dyslipidemia x 10 years
GERD x 3 years

Prescription/OTC Medications

Start Date	Drug Name/Strength/Regimen	Indication
9/2013	Omeprazole 20 mg orally daily	GERD
9/2013	Rosuvastatin 20 mg orally daily (samples until 1/2014; then discontinued)	Dyslipidemia
1/2015	Lovastatin 20 mg orally daily	Dyslipidemia
9/2013	Olmesartan 20 mg orally daily (samples until 1/2014; then discontinued)	Hypertension
1/2015	Hydrochlorothiazide 12.5 mg orally daily	Hypertension
Vaccinations: Influenza virus vaccine Fall 2014		Pharmacy(ies) Used: Walmart Pharmacy

RX Payment: Private Insurance (prefers generics, unsure of his copay, but is a percentage for brand-name medications)	Meds Admin by: Self

Drug Allergies/Adverse Effects: NKDA

Family Medical History: CAD (father had MI at 50 years), type 2 diabetes (mother and sister)

Social History	Residence: lives with wife (apartment)	Occupation: Facilities management
Smoking: former cigarettes smoker (quit 20 years ago)		EtOH: 2 to 3 beers daily, mostly regular beer or microbrews

Illicit Drugs: Never	Diet: Reports eating 3 meals per day usually and snacks throughout the day. Does not follow a very strict diet, but was instructed several years ago to reduce calorie and salt intake. Exercise: Owns a stationary bike.
Education: High School graduate	Family/Social Environment: Lives with his wife; has 1 son and 2 daughters; 4 grandchildren; all children live in the area

Review of Systems: Per HPI – severe toe pain, wanted Vicodin from his provider and cannot afford Colcrys that was prescribed

Objective Data (observations/vital signs/physical examination/labs)

General: pleasant male in NAD; A&0 x 3
BP 164/96, 162/94 mm Hg HR 80 bpm, regular RR 12/min T=98.8°F (oral)
Height = 5' 8" Weight = 215 lb (was 200 lb 5 years ago)
BMI =32.7 kg/m^2 Waist circ. 44"

Physical Exam – Overweight man. No rales or rhonchi. No lower extremity edema bilaterally. No chest pain or shortness of breath currently. R toe red, warm, painful (6/10), no tophi.

Diagnostics Tests:
Joint aspiration of toe not performed.

Laboratory Tests (measured today) – NOT FASTING

CMP:	Na = 140 mmol/L	K = 4.2 mmol/L	Cl = 102 mmol/L	CO3 = 28 mmol/L
	BUN = 8 mg/dL	SCr = 1.22 mg/dL	Glucose = 92 mg/dL	
	Uric Acid = 10.1 mg/dL			
	AST = 40 U/L	ALT = 42U/L		
TFT:	TSH = 0.88 mIU/L			
FLP:	Total Chol = 189 mg/dL	LDL-C = 100 mg/dL	HDL-C = 38 mg/dL	TG = 255 mg/dL
CBC:	WBC = 12.0 x 10^9/L	Hgb = 14.5 g/dL	Hct = 43.0%	Plt = 250 x 10^9/L
A1c:	5.7 %			
U/A:	Alb/Cr = 17 mg/g			

Presentation Questions and Continuation of Case

1. Assuming this patient has affordable access to all of the following agents, which is the most appropriate to use for treating his acute gouty arthritis attack?
   a. Prednisone 60 mg orally daily
   b. Naproxen 500 mg orally twice daily
   c. Colchicine 1.2 mg orally then 0.6 mg 1 hour later
   d. Indomethacin 75 mg orally twice daily

Patient Interview:
SR is distracted and hard to interview. You focus the interview, reconcile his medications, and gather the following information:

- He has had 4 similar gout episodes over the past year, the pain eventually decreases in response to Vicodin (OTC acetaminophen does not work well); pain relief is his goal
- Reports drinking 2 to 3 beers daily, does not follow any specific diet, does not use his stationary bike
- He has a new home BP monitor, but does not use it, does not want to talk about his hypertension because of pain
- Upon direct questioning to reconcile his medications, SR states he is not taking hydrochlorothiazide or lovastatin (ran out); takes omeprazole regularly because he has heartburn often
- He does not understand benefits of treating his conditions
- Expressed concern regarding cost of medications in general

2. In addition to lifestyle modifications, which of the following recommendations should be implemented to reduce SR's risk of recurrent gouty arthritis?
   a. Start allopurinol 100 mg orally daily today
   b. Start allopurinol 100 mg orally daily as soon as his gout attack is completely resolved
   c. Start allopurinol 100 mg orally daily 4 weeks after his gout attack is completely resolved
   d. Implement intense dietary changes, then reevaluate

Care Plan for SR today

After gaining his trust, you agree to the following treatment plans, in collaboration with the provider:

- Acute Gouty Arthritis: Your FQHC pharmacy has colchicine and SR is eligible for PAP; colchicine 1.2 mg orally now, 0.6 mg in 1 hr then 0.6 mg daily; agrees to general basic dietary changes (less beer and red meat)
- Prevention of Gout: Start allopurinol 100 mg orally daily
- Hypertension and Dyslipidemia: Refuses to start medications; agrees to measure BP at home, keep a diary and come back in 2 weeks
- Provide patient resources regarding diseases and medication discounts

Case SR – Follow Up #1

- Interview: 5 weeks later, gout pain improved within 2 days, resolved now. Asking for febuxostat, not allopurinol because granddaughter found information that it is better. Cut back beer to 1 daily. Started using his bike 2 times weekly for 20 minutes.
- Medication Reconciliation: Reports adherence to colchicine 0.6 mg daily, allopurinol 100 mg daily, omeprazole 20 mg daily
- Additional data:
  - Home BP measurement diary not completed; measured three times, all in high 150's/90's. Agrees that it is too high.
- Vital signs:
  - BP 162/94, 160/94 mm Hg HR 78 bpm
  - Wt 213 lb BMI 32.4 kg/m^2
- Laboratory measurements
  - SCr 1.15 mg/dL, Uric Acid 7.9 mg/dL
  - 10-year atherosclerotic cardiovascular disease (ASCVD) risk score 13.5% (50% lifetime risk)

3. Which of the following is the most appropriate antihypertensive regimen to start in SR?
   a. Chlorthalidone 25 mg orally daily
   b. Losartan 50 mg orally daily
   c. Lisinopril/hydrochlorothiazide 10 mg/12.5 mg orally daily
   d. Amlodipine/benazepril 5 mg/10 mg orally daily

4. Which of the following combination antihypertensive regimens is the safest and most efficacious in lowering BP? [note, this is not related to this case]
   a. Felodipine with irbesartan
   b. Losartan with ramipril
   c. Hydrochlorothiazide with triamterene
   d. Amlodipine with diltiazem

5. Which of the following is the most appropriate lipid-lowering regimen for SR at this time?
   a. No drug therapy, low-fat and low cholesterol diet for 3 months then reevaluate FLP
   b. Start pravastatin 40 mg orally daily
   c. Start simvastatin 80 mg orally daily
   d. Restart lovastatin 20 mg orally daily at night with food

6. SR is started on a moderate-intensity statin regimen. Which of the following serum laboratory tests should be measured in 3 months?
   a. Fasting lipid panel
   b. Liver enzymes
   c. Creatine kinase
   d. A1C
   e. All of the above

Care Plan for SR – Follow up #1

- Prevention of Gout: Increase allopurinol to 200 mg orally daily; colchicine 1.2 mg orally, 0.6 mg in 1 hr if attack occurs
- Hypertension: Motivational interviewing to establish goals; start amlodipine/benazepril 5/10 mg orally daily, continue home BP monitoring
- Dyslipidemia: Agrees to start atorvastatin 20 mg orally daily
- Lifestyle: Agrees to continue exercise and visit dietician at FQHC

Case SR – Follow Up #2

- Interview: Back 3 months later after 2 phone follow ups. Feels good, implemented several lifestyle changes, willing to continue more. No gout attacks in past month.
- Medication Reconciliation: Reports adherence to medications:
  - Colchicine 0.6 mg daily, allopurinol 200 mg daily, omeprazole 20 mg daily, amlodipine/benazepril 10/20 mg orally daily (increased with phone follow-up), atorvastatin 20 mg daily. Has not had to use prn colchicine.
- Additional data
  - Home BP measurement diary shows regular measurements; mean from past week 128/74 mm Hg.
- Vital signs:
  - BP 132/78, 130/76 mm Hg HR 74 bpm
  - Wt 208 lb BMI 31.6 kg/m^2
- Laboratory measurements
  - SCr 1.10 mg/dL, Serum potassium 4.8 mmol/L
  - Uric Acid 5.8 mg/dL
  - FLP: TC 135 mg/dL, HDL-C 45 mg/dL, LDL-C 80 mg/dL

7. Two months ago, SR's home BP values were consistently above his goal of < 140/90 mm Hg. At that time, his amlodipine/benazepril dose was increased. If a third antihypertensive medication is to be added to his regimen in the future, which of the following would be the most appropriate third agent?
   a. Aliskiren
   b. Metoprolol succinate
   c. Chlorthalidone
   d. Hydralazine

Case SR – Follow Up #3

- Interview: Back 6 months later for a routine evaluation and influenza vaccination. Feels good, eating well (restricts calories and sodium, eats a low saturated fat diet), 1-2 beers daily but only on weekends. Biking 4 to 5 times weekly for 45 minutes. No gout attacks since starting allopurinol.
- Medication Reconciliation: Reports adherence to medications:
  - Allopurinol 200 mg daily, omeprazole 20 mg daily, amlodipine/benazepril 10/20 mg orally daily, atorvastatin 20 mg daily
  - Has stopped colchicine as instructed at last visit
- Additional data
  - Home BP measurement diary with regular measurements; average from last month 127/75 mm Hg
- Vital signs:
  - BP 130/78, 128/80 mm Hg HR 74 bpm
  - Wt 200 lb BMI 30.4 kg/m^2
- Laboratory measurements
  - SCr 1.10 mg/dL, Serum potassium 4.8 mmol/L

8. SR feels as though his weight loss has plateaued, and he is interested in a medication for weight loss. Which of the following would result in the greatest amount of weight loss?
   a. Orlistat
   b. Lorcaserin
   c. Naltrexone and bupropion
   d. Phentermine and topiramate

9. While interviewing SR, he reports having problems with erectile dysfunction (ED) and has been using a friend's vardenafil 10 mg 1 hour before intercourse. It works well but only lasts an hour. Which of the following would be the most effective ED treatment for SR?
   a. Swith to sildenafil orally 30 minutes before intercourse
   b. Switch to tadalafil orally daily regardless of intercourse
   c. Start low-dose transdermal testosterone daily
   d. Replace amlodipine with carvedilol and reevaluate

References (BOLD font = references for review)

Gout

1. Khanna D, Khanna PP, Fitzgerald JD et al. 2012 American College of Rheumatology guidelines for management of gout. Part 2: therapy and antiinflammatory prophylaxis of acute gouty arthritis. *Arthritis Care Res*. 2012; 64:1447-61. http://www.ncbi.nlm.nih.gov/pubmed/23024029. (Accessed 2015 February 15)

2. Khanna D, Fitzgerald JD, Khanna PP et al. 2012 American College of Rheumatology guidelines for management of gout. Part 1: systematic nonpharmacologic and pharmacologic therapeutic approaches to hyperuricemia. *Arthritis Care Res*. 2012; 64:1431-46. http://www.ncbi.nlm.nih.gov/pubmed/23024028. (Accessed 2015 February 15)

3. Saseen JJ, Agashivala N, Allen RR et al. Comparison of patient characteristics and gout-related health-care resource utilization and costs in patients with frequent versus infrequent gouty arthritis attacks. *Rheumatology*. 2012; 51:2004-12. http://www.ncbi.nlm.nih.gov/pubmed/22829689. (Accessed 2015 February 15)
4. Terkeltaub RA, Furst DE, Bennett K et al. High versus low dosing of oral colchicine for early acute gout flare: Twenty-four-hour outcome of the first multicenter, randomized, double-blind, placebo-controlled, parallel-group, dose-comparison colchicine study. *Arthritis Rheum*. 2010; 62:1060-8. http://www.ncbi.nlm.nih.gov/pubmed/20131255. (Accessed 2015 February 15)
5. Richette P, Bardin T. Gout. *Lancet*. 2010; 375:318-28. http://www.ncbi.nlm.nih.gov/pubmed/19692116. (Accessed 2015 February 15)
6. Kesselheim AS, Solomon DH. Incentives for drug development--the curious case of colchicine. *N Engl J Med*. 2010; 362:2045-7. http://www.ncbi.nlm.nih.gov/pubmed/20393164. (Accessed 2015 February 15)
7. Becker MA, Schumacher HR Jr, Wortmann RL et al. Febuxostat compared with allopurinol in patients with hyperuricemia and gout. *N Engl J Med*. 2005; 353:2450-61. http://www.ncbi.nlm.nih.gov/pubmed/16339094. (Accessed 2015 February 15)
8. Borstad GC, Bryant LR, Abel MP et al. Colchicine for prophylaxis of acute flares when initiating allopurinol for chronic gouty arthritis. *J Rheumatol*. 2004; 31:2429-32. http://www.ncbi.nlm.nih.gov/pubmed/15570646. (Accessed 2015 February 15)

340B Drug Pricing

9. U.S. Department of Health and Human Services - Health Resources and Services Administration (HRSA). 340B Drug Pricing Program. http://www.hrsa.gov/opa/. (Accessed 2015 February 15)

Patient Assistance Programs

10. The Official U.S. Government Site for Medicare. Pharmaceutical Assistance Program. http://www.medicare.gov/pharmaceutical-assistance-program/. (Accessed 2015 February 15)

11. Needy Meds. http://www.needymeds.org/index.htm. (Accessed 2015 February 15)

Lifestyle Management

12. **Eckel RH, Jakicic JM, Ard JD et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart**

Association Task Force on Practice Guidelines. *Circulation*. 2014; 129(25 suppl 2):S76-99. http://www.ncbi.nlm.nih.gov/pubmed/24222015. (Accessed 2015 February 15)

Hypertension

13. Weber MA, Schiffrin EL, White WB et al. Clinical practice guidelines for the management of hypertension in the community: A statement by the American Society of Hypertension and the International Society of Hypertension. *J Clin Hypertens*. (Greenwich) 2014; 16(1):14-26.

14. James PA, Oparil S, Carter BL et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA*. 2014; 311:507-20. http://www.ncbi.nlm.nih.gov/pubmed/24352797. (Accessed 2015 February 15)

15. Kidney Disease Improving Global Outcomes (KDIGO). Summary of Recommendation Statements. *Kidney Int Suppl*. 2012; 2:341-2. http://www.ncbi.nlm.nih.gov/pubmed/25018959. (Accessed 2015 February 15)

16. American Diabetes Association (ADA). Standards of medical care in diabetes--2015: summary of revisions. *Diabetes Care*. 2015; 38(Suppl 1):S4. http://www.ncbi.nlm.nih.gov/pubmed/25537706. (Accessed 2015 February 15)

17. Jamerson K, Weber MA, Bakris GL et al. Benazepril plus amlodipine or hydrochlorothiazide for hypertension in high-risk patients. *N Engl J Med*. 2008; 359:2417-28. http://www.ncbi.nlm.nih.gov/pubmed/19052124. (Accessed 2015 February 15)

18. Pickering TG, White WB, American Society of Hypertension Writing Group. When and how to use self (home) and ambulatory blood pressure monitoring. *J Am Soc Hypertens*. 2008; 2:119-24. http://www.ncbi.nlm.nih.gov/pubmed/20409893. (Accessed 2015 February 15)

19. Pickering TG, Hall JE, Appel LJ et al. Recommendations for blood pressure measurement in humans and experimental animals: Part 1: blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. *Hypertension.* 2005; 45:142-61. http://www.ncbi.nlm.nih.gov/pubmed/15611362. (Accessed 2015 February 15)

20. Calhoun DA, Jones D, Textor S et al. Resistant hypertension: diagnosis, evaluation, and treatment: a scientific statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research. *Circulation*. 2008; 117:e510-26. http://www.ncbi.nlm.nih.gov/pubmed/18574054. (Accessed 2015 February 15)

21. Makani H, Bangalore S, Desouza KA et al. Efficacy and safety of dual blockade of the renin-angiotensin system: meta-analysis of randomised trials. *BMJ*. 2013; 346:f360. http://www.ncbi.nlm.nih.gov/pubmed/23358488. (Accessed 2015 February 15)

22. Wright JT, Williamson JD, Whelton PK et al. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373:2103-16. http://www.ncbi.nlm.nih.gov/pubmed/26551272 (Accessed 2016 January 10)

Dyslipidemia

23. Stone NJ, Robinson JG, Lichtenstein AH et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014; 129(25 suppl 2):S1-45. http://www.ncbi.nlm.nih.gov/pubmed/24222016. (Accessed 2015 February 15)

24. Rosenson RS, Baker SK, Jacobson TA et al. An assessment by the Statin Muscle Safety Task Force: 2014 update. *J Clin Lipidol*. 2014; 8(3 suppl):S58-71. http://www.ncbi.nlm.nih.gov/pubmed/24793443. (Accessed 2015 February 15)

25. Jacobson TA, Ito MK, Maki KC et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: part 1 - executive summary. *J Clin Lipidol*. 2014; 8:473-88. http://www.ncbi.nlm.nih.gov/pubmed/25234560. (Accessed 2015 February 15)

26. Jacobson TA. NLA Task Force on Statin Safety--2014 update. *J Clin Lipidol*. 2014; 8(3 suppl):S1-4. http://www.ncbi.nlm.nih.gov/pubmed/24793438. (Accessed 2015 February 15)

27. Goff DC Jr., Lloyd-Jones DM, Bennett G et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014; 129:S49-73. http://www.ncbi.nlm.nih.gov/pubmed/24222018. (Accessed 2015 February 15)

28. Guyton JR, Bays HE, Grundy SM et al. An assessment by the Statin Intolerance Panel: 2014 update. *J Clin Lipidol*. 2014; 8(3 suppl):S72-81. http://www.ncbi.nlm.nih.gov/pubmed/24793444. (Accessed 2015 February 15)

29. Cannon CP, Blazing MA, Giugliano RP et al. Ezetimibe added to statin therapy after acute coronary syndromes. *N Engl J Med.* 2015;372(25): 2387-97. http://www.ncbi.nlm.nih.gov/pubmed/26039521 (Accessed 2016 January 10)

Obesity

30. Jensen MD, Ryan DH, Apovian CM et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Circulation.* 2014; 129(25 suppl 2):S102-38. http://www.ncbi.nlm.nih.gov/pubmed/24222017. (Accessed 2015 February 15)

31. Citrome L. Lorcaserin, phentermine topiramate combination, and naltrexone bupropion combination for weight loss: the 15-min challenge to sort these agents out. *Int J Clin Pract*. 2014; 68:1401-5. http://www.ncbi.nlm.nih.gov/pubmed/25418525. (Accessed 2015 February 15)

REMS

32. U.S. Food and Drug Administration. Approved Risk Evaluation and Mitigation Strategies (REMS). http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111350.htm. (Accessed 2015 February 15)

Erectile Dysfunction

33. Levine GN, Steinke EE, Bakaeen FG et al. Sexual activity and cardiovascular disease: a scientific statement from the American Heart Association. *Circulation* 2012; 125:1058-72. http://www.ncbi.nlm.nih.gov/pubmed/22267844. (Accessed 2015 February 15)

34. Martin-Morales A, Haro JM, Beardsworth A et al. Therapeutic effectiveness and patient satisfaction after 6 months of treatment with tadalafil, sildenafil, and vardenafil: results from the erectile dysfunction observational study (EDOS). *Eur Urol*. 2007; 51:541-50; discussion 50. http://www.ncbi.nlm.nih.gov/pubmed/17084518. (Accessed 2015 February 15)

35. Montague DK, Jarow JP, Broderick GA et al. Chapter 1: The management of erectile dysfunction: an AUA update. *J Urol*. 2005; 174:230-9. http://www.ncbi.nlm.nih.gov/pubmed/15947645. (Accessed 2015 February 15)

Complex Case: Cardiovascular Disease 1 "GOUCH... My toe is killing me, and I can't afford this drug"

Joseph J. Saseen, PharmD, FASHP, FCCP, BCPS, BCACP
Professor and Vice Chair
University of Colorado Skaggs School of Pharmacy & Pharmaceutical Sciences
Aurora, Colorado
Clinical Pharmacy Specialist
University of Colorado Hospital, Department of Family Medicine
Denver, Colorado

Disclosure

- I have nothing to disclose related to the content of this presentation.

Learning Objectives

- Correctly answer case-based questions about appropriate ambulatory treatment for a complex patient with multiple medical problems, including dyslipidemia, gout, hypertension, obesity, and sexual dysfunction.
- Identify effective methods of managing affordability and cost-effectiveness issues for an underserved patient.
- Identify and recommend appropriate resource organizations/groups to assist a specific patient.

Premise

- You are a clinical pharmacist practicing in a federally qualified health center (FQHC) that is a family medicine clinic
- This FQHC is affiliated with 8 other clinics, has outpatient medical records (an electronic health record [EHR]), and each clinic has an outpatient pharmacy with 340B drug pricing medications; hospital and specialty services are not available within this FQHC
- Some patients have Medicaid, some are not insured, and nearly all patients have limited income
- Clinical pharmacists provide chronic disease management (e.g., diabetes, hypertension), dietary/exercise counseling, and recommendations to improve medication use and affordability

Case - SR

- 59 year old Caucasian man
- Chief Complaint
  - "My toe is killing me, and I can't afford this drug"
- Past Medical History
  - Obesity x 30 years
  - Hypertension x 20 years
  - Dyslipidemia x 10 years
  - GERD x 3 years
- Social History
  - ETOH (2 to 3 beers daily); former smoker (quit 20 years ago)

Case – HPI (today)

- SR awoke this morning with pain in his toe which is red, swollen and warm to touch. He describes it as 6/10.
- Diagnosed by his provider early today with acute gouty arthritis. Has just been prescribed colchicine, but could not afford it when he went to his community pharmacy. He asked his provider for "Vicodin", but was told colchicine is better. Patient also presented today with elevated BP (164/96, 162/94 mm Hg), which was attributed to his acute pain.
- He came back to clinic and was referred to the clinical pharmacist. He is being evaluated in a 30-minute visit time slot.

Current Medications (today)

- Hydrochlorothiazide 12.5 mg orally daily
- Lovastatin 20 mg orally daily at night
- Omeprazole 20 mg orally daily
- Acetaminophen 500 mg orally four times daily as needed for pain

Case – Laboratory Values (today)

- Measured today (patient was not fasting):
  - Comprehensive metabolic panel (CMP)
  - Thyroid stimulating hormone (TSH)
  - Fasting lipid panel (FLP)
  - Complete blood count (CBC)
  - A1c
  - Urinalysis

Laboratory Measurements (today)

- CMP
  - Na = 140 mmol/L
  - K = 4.2 mmol/L
  - Cl = 102 mmol/L
  - CO_3 = 28 mmol/L
  - BUN = 8 mg/dL
  - SCr = 1.22 mg/dL
  - Glucose = 92 mg/dL
  - Uric Acid = 10.1 mg/dL
  - AST = 40 U/L
  - ALT = 42U/L
- TSH = 0.88 mIU/mL
- FLP
  - Total Cholesterol = 189 mg/dL
  - LDL-C = 100 mg/dL
  - HDL-C = 38 mg/dL
  - TG = 255 mg/dL
- CBC
  - WBC = 12.0 x 10^9 per liter (L)
  - Hgb = 14.5 g/dL
  - Hct = 43.0%
  - Plt = 250 x 10^9 per liter (L)
- A1c = 5.7 %
- Alb/Cr = 17 mg/g

Physician Evaluation - (today)

VITAL SIGNS

- BP 164/96, 162/94 mm Hg HR 80 bpm, reg
- RR 12/min Temp 98.8 °F (oral)
- Ht 5'8" Wt 215 lb Waist circ. 44" BMI 32.7 kg/m^2
- FAMILY HX: CAD, type 2 diabetes
- DIET: Reduce calories and limit sodium intake
- EXERCISE: Stationary bike

PHYSICAL EXAM

- GENERAL: Overweight man; severe pain in R toe
- Extremities: R toe red, warm, painful (6/10), no tophi

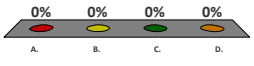
Other findings were essentially normal

Setting Priorities for SR

- Format of Interviewing:
  - Establish effective and open communication
  - Identify barriers to care
  - Determine patient goals
- Gather data missing from the EHR (e.g., from patient, family members, provider, pharmacy)
- Assure medication reconciliation
- Establish short-term targets, immediate priorities and long term goals
- Provide patient specific resources

Question 1:
Assuming this patient has affordable access to all of the following agents, which is the most appropriate to treat his acute gouty arthritis attack?

A. Prednisone 60 mg orally daily
B. Naproxen 500 mg orally twice daily
C. Colchicine 1.2 mg orally then 0.6 mg 1 hour later
D. Indomethacin 75 mg orally twice daily



Drugs that Raise Serum Urate

Commonly Prescribed	Less Common
• Diuretics (esp. thiazides) • Nicotinic Acid • Ethanol • Low-dose salicylates (minimal) • Cyclosporine • Tacrolimus	• Levodopa • Cytotoxic chemotherapy (several) • Pyrazinamide • Ethambutol • Teriparatide • Ribavirin and interferon

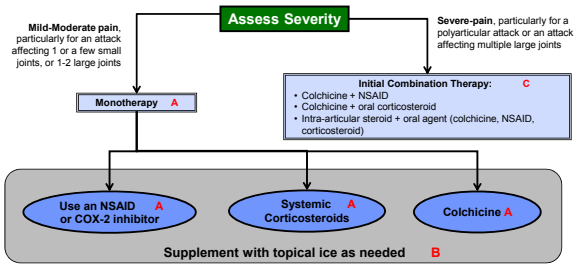
Richette P et al. *Lancet.* 2010; 375:318–28.

American College of Rheumatology: Dietary Recommendations for Gout

	Recommendation	Evidence Level
Avoid	Organ meats high in purines (e.g., sweetbreads, liver, kidney)	B
	High fructose corn syrup sodas, other beverages, foods	C
	Alcohol overuse (> 2 servings/day, men; > 1 women)	B
	Any alcohol during periods of frequent gout attacks, or advanced gout under poor control	B
Limit	Serving sizes of beef, lamb, pork, high purine content seafood (e.g., sardines, shellfish)	B
	Servings of naturally sweet fruit juices, table sugar; sweetened beverages and desserts; table salt	C
	Alcohol (particularly beer) in all gout patients	B

Khanna D et al. *Arthritis Care & Research.* 2012; 64(10):1431-1446.
Khanna D et al. *Arthritis Care & Research.* 2012; 64(10):1447-1461.

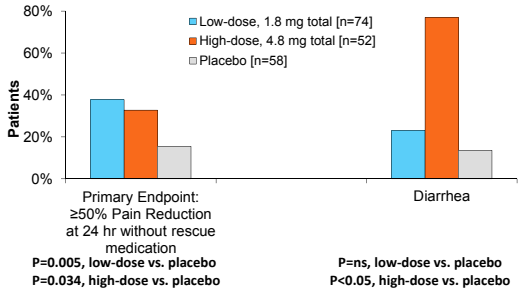
Management of an Acute Gout Attack



LETTER indicates level of evidence

Khanna D et al. *Arthritis Care & Research.* 2012; 64(10):1431-1446.
Khanna D et al. *Arthritis Care & Research.* 2012; 64(10):1447-1461.

Acute Gout Flare Receiving Colchicine Evaluation (AGREE)



P=0.005, low-dose vs. placebo
P=0.034, high-dose vs. placebo

P=ns, low-dose vs. placebo
P<0.05, high-dose vs. placebo

Terkeltaub RA et al. Arthritis & Rheumatism 2010;62(4):1060-1068.

The Curious Case of Colchicine

- July 2009: FDA approved brand-name colchicine (Colcrys) with other generic versions removed from the market; the price increased from pennies to $4.85 per pill
- January 2015: Authorized generic colchicine 0.6 mg capsules (Mitigare) by West-Ward
- January 2015: Announced availability of generic colchicine 0.6 mg tablets (Colcrys) by Prasco in collaboration with Takeda Pharmaceuticals Inc.

Kesselheim AS et al. *N Engl J Med.* 2010; 362(22):2045-7.
http://www.west-ward.com/news.php?id=62
http://www.medpagetoday.com/Rheumatology/GeneralRheumatology/49493.

Patient Assistance Programs (PAP)

- Eligibility criteria must be met with proof of income and finances usually required
- Some are specifically for patients with or without prescription coverage
- Cannot be used for participants in government programs (e.g., Medicare)
- Several Internet resources:
  - www.medicare.gov, manufacturer's websites, www.needymeds.org

340B Drug Pricing Programs

- Drug manufacturers required to provide outpatient drugs at significantly reduced prices
- Eligible organizations:
  - Nonprofit health care organizations with certain federal designations or funded by specific Federal programs
  - E.g., FQHCs, Ryan White HIV/AIDS Programs, disproportionate Share Hospitals, safety net providers
- Eligible patients must receive health care services other than drugs from the 340B covered entity (exception for state-operated/funded AIDS drug purchasing assistance programs)

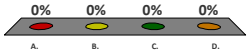
http://www.hrsa.gov/opa/

SR Patient Interview

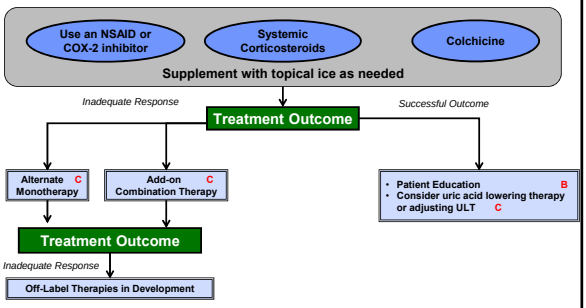
- You focus the interview with SR, reconcile his medications, and gather the following information:
  - 4 similar gout episodes over the past year, the pain eventually decreases with Vicodin; pain relief is his goal
  - Drinks 2 to 3 beers daily, does not follow any specific diet, does not use his stationary bike
  - Has a new home BP monitor, but does not use it, does not want to talk about his hypertension because of pain
  - Not taking hydrochlorothiazide or lovastatin (ran out); takes omeprazole regularly for frequent heartburn
  - Does not understand benefits of treating his conditions
  - Concerned with cost of medications

Question 2:
In addition to lifestyle modifications, which of the following recommendations should be implemented to reduce SR's risk of recurrent gouty arthritis?

A. Start allopurinol 100 mg orally daily today
B. Start allopurinol 100 mg orally daily as soon as his gout attack is resolved
C. Start allopurinol 100 mg orally daily 4 weeks after his gout attack is completely resolved
D. Implement intense dietary changes, then re-evaluate



Management of an Acute Gout Attack



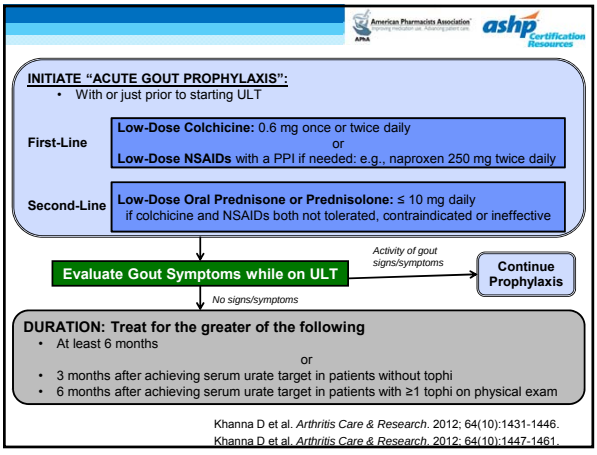
Khanna D et al. *Arthritis Care & Research*. 2012; 64(10):1431-1446.
Khanna D et al. *Arthritis Care & Research*. 2012; 64(10):1447-1461.

Prevention of Recurrent Gout

Urate-Lowering Therapy (ULT):

- Serum urate target of <6 mg/dL (<5 mg/dL for some)
  - Measure every 2 to 5 weeks until target achieved
- Indicated with established gout diagnosis and:
  1. Tophus or tophi by exam or imaging study
  2. Frequent gouty arthritis attacks (≥2 attacks/year)
  3. Chronic Kidney Disease (CKD) stage 2 or worse
  4. Past urolithiasis

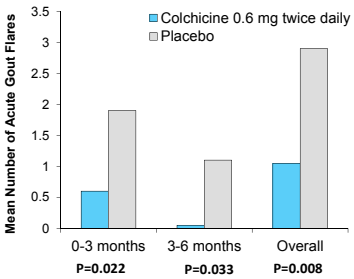
Khanna D et al. *Arthritis Care & Research*. 2012; 64(10):1431-1446.
Khanna D et al. *Arthritis Care & Research*. 2012; 64(10):1447-1461.



Khanna D et al. *Arthritis Care & Research*. 2012; 64(10):1431-1446.
Khanna D et al. *Arthritis Care & Research*. 2012; 64(10):1447-1461.

Colchicine for Acute Gout Prophylaxis When Initiating Allopurinol

- Randomized trial in 43 patients with gout who were starting allopurinol therapy



Borstad GC et al. *J Rheumatol.* 2004; 31:2429-32.

Care Plan for SR (today)

- **Acute Gouty Arthritis**
  - FQHC pharmacy has colchicine and SR is eligible for PAP
  - Colchicine 1.2 mg orally now, 0.6 mg in 1 hr
  - Colchicine 0.6 mg daily thereafter
  - Agrees to basic dietary changes (less beer and red meat)
- **Prevention of Gout**
  - Start allopurinol 100 mg orally daily
- **Hypertension and Dyslipidemia**
  - Refuses to start medications; agrees to measure BP at home, keep a diary and come back in 2 weeks
- **Provide patient resources**

Patient Specific Resources

- Disease
  - Most national organizations have free patient resources for disease awareness and education
    - e.g., American Heart Association, National Lipid Association
- Affordable Medications
  - www.helprx.info/ or www.goodrx.com/
  - Sites to avoid listed at: www.nabp.net/programs/consumer-protection/buying-medicine-online/not-recommended-sites

Case SR – Follow Up #1

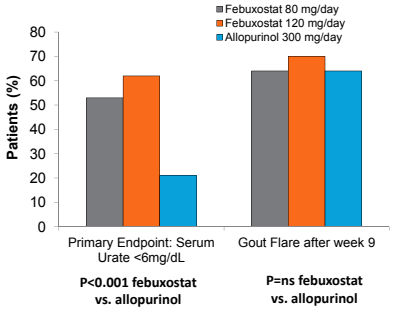
- Interview
  - 5 weeks later, gout pain improved within 2 days, resolved now. Asking for febuxostat instead of allopurinol because granddaughter says it is better. Cut back beer to 1 daily. Started using his bike 2 times weekly for 20 minutes.
- Medication Reconciliation
  - Reports adherence to colchicine 0.6 mg daily, allopurinol 100 mg daily, omeprazole 20 mg daily

Case SR – Follow Up #1

- Additional data
  - Home BP measurement diary not completed; measured three times, all in high 150's/90's. Agrees that it is too high.
- Vital signs:
  - BP 162/94, 160/94 mm Hg — HR 78 bpm
  - Wt 213 lb — BMI 32.4 kg/m^2
- Laboratory measurements
  - SCr 1.15 mg/dL, Uric Acid 7.9 mg/dL
  - 10-year atherosclerotic cardiovascular disease (ASCVD) risk score 13.5% (50% lifetime risk)

Febuxostat Compared with Allopurinol

- Randomized trial in 762 patients with gout and serum urate ≥ 8 mg/dL for 52 weeks



Becker MA et al. *N Engl J Med.* 2005; 353(23):2450-61.

Lesinurad

Approved Dec 2015

- Inhibits uric acid transporter 1 [URAT1] and organic anion transporter 4 [OAT4]; reduces uric acid resorption and lowers serum uric acid
- Indication: In combination with a xanthine oxidase inhibitor to treat hyperuricemia in patients with gout who are not at their serum urate target
  - 200 mg po once daily (only dose)
  - Do not use if CrCl is <45 mL/min or kidney transplant; may cause acute kidney failure
- Clinical data:
  - Uric acid reduction of ~ 1 mg/dL, higher rates of target achievement but no impact on gout attacks

Zurampic Package Insert; AstraZeneca Pharmaceuticals Inc, Wilmington, DE. December 2015.

ACC/AHA Guideline: Lifestyle Management to Reduce BP

Dietary Pattern

- Emphasize vegetables, fruits, whole grains; low-fat dairy, poultry, fish, legumes, nontropical vegetable oils, and nuts; limit sweets, sugar-sweetened beverages, red meats (e.g., DASH, USDA Food Pattern, AHA Diet)
- Lower sodium intake (maximum 2400 mg/day; 1500 mg/day can be better; at least reduce by 1000 mg/day)

Physical Activity

- Engage in aerobic physical activity 3–4 sessions/week, 40-minute sessions, moderate-to vigorous-intensity

Eckel RH et al. *Circulation.* 2014; 129[[suppl 2]:s76-s99.

Goal BP Recommendations

ASH/ISH Guidelines	JNC 8 Report
Age < 80 years:	**Age < 60 years:**
• <140/90 mm Hg	• <140/90 mm Hg
Age ≥ 80 years:	**Age ≥ 60 years:**
• <150/90 mm Hg	• <150/90 mm Hg*
• <140/90 mm Hg if diabetes or CKD	• <140/90 mm Hg if diabetes or CKD

*If pharmacologic treatment results in lower achieved SBP (e.g., <140 mm Hg) and is well tolerated and without adverse effects, treatment does not need to be adjusted

Weber MA et al. J Hypertens. 2014; Jan;32(1):3-1. James PA et al. JAMA. 2014; 311(5):507-20.

Antihypertensive Agents

Traditional "First-Line"

- Angiotensin Converting Enzyme Inhibitor (ACEI)
- Angiotensin Receptor Blocker (ARB)
- Beta-Blocker
- Calcium Channel Blocker (CCB)
- Diuretic (chlorthalidone, hydrochlorothiazide)

Alternatives

- Aldosterone Antagonist (e.g., spironolactone)
- Alpha Antagonist
- Centrally Acting Alpha Agonist
- Direct Arterial Vasodilator Direct Renin Inhibitor (aliskiren)
- Rauwolfia Alkaloid (reserpine)

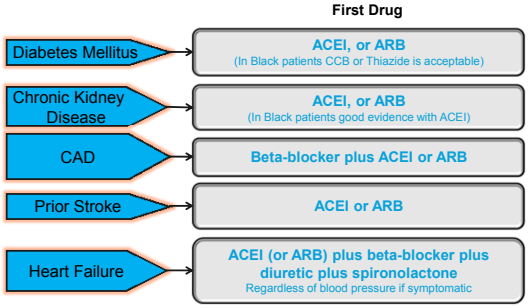
Drug Therapy Recommendations

Without compelling indications/special cases

- First-line agent (ACEI, ARB, CCB and/or thiazide)
  - Stage 1 (BP ≥140-159/90-99 mm Hg)
    - Monotherapy or combination therapy
  - Stage 2 (BP ≥160/100 mm Hg)
    - Start with 2 drug combination therapy
- Options with greatest degree of BP lowering
  - Black: CCB or thiazide
  - Non-Black age <60 yr: ACEI or ARB

Weber MA et al. J Hypertens. 2014; Jan;32(1):3-1. James PA et al. JAMA. 2014; 311(5):507-20.

Compelling Indications/Special Cases



Weber MA et al. *J Hypertens.* 2014 Jan; 32(1):3-15.

Kidney Disease: Improving Global Outcomes Clinical Practice Guideline

- Management of BP in CKD
  - Non-dialysis patients

Urine Albumin Excretion per 24 hrs	BP Goal (mm Hg)	Treatment
< 30 mg	≤ 140/90	Not specified
30 to 300 mg	≤ 130/80	ACE-I or ARB
> 300 mg	≤ 130/80	ACE-I or ARB

Please cite: Kidney Disease: Improving Global Outcomes. *Kidney Int Suppl*. 2012; 2:341-2.

"JNC 8" Report: Strategies for Dosing Antihypertensive Agents

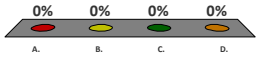
Strategy	Description	Comments
A	Start 1 drug, titrate to maximum dose, and then add a second drug	• Use ACEI, ARB, CCB, or thiazide-type diuretic
B	Start 1 drug and then add a second drug before achieving maximum dose of the initial drug	• May minimize side effects
C	Begin with 2 drugs at the same time, either as 2 separate pills or as a fixed dose combination pill	• Especially if BP ≥160/100 mm Hg (BP ≥20/10 mm Hg above goal)

Always avoid combination of an ACEI with ARB!

James PA et al. *JAMA*. 2014; 311(5):507-20.

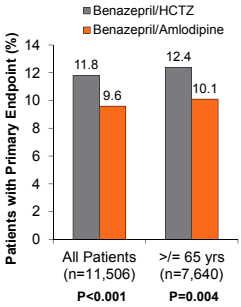
Question 3:
Which of the following is the most appropriate antihypertensive regimen to start in SR?

A. Chlorthalidone 25 mg orally daily
B. Losartan 50 mg orally daily
C. Lisinopril/hydrochlorothiazide 10 mg/12.5 mg orally daily
D. Amlodipine/benazepril 5 mg/10 mg orally daily



ACCOMPLISH Trial

- Randomized, double-blind, controlled trial*
  - Benazepril/HCTZ vs. Benazepril/Amlodipine
- 11,506 patients with hypertension and:
  - Age ≥ 60 yr; or 55-59 yr if ≥ 2 CV diseases or target organ damage
  - SBP ≥ 160 mm Hg or on BP medication
- Primary endpoint: CV events

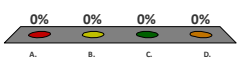


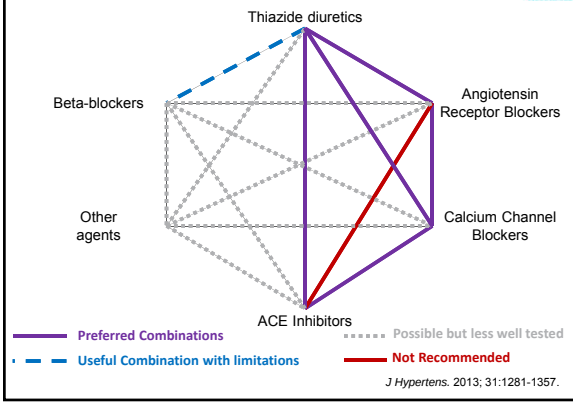
*Dosages titrated, as tolerated, to benazepril 40 mg/day, HCTZ 25 mg/day, amlodipine 10 mg/day

Jamerson K et al. *N Engl J Med*. 2008; 359:2417-28.

Question 4:
Which of the following combination antihypertensive regimens is the safest and most efficacious in lowering BP?

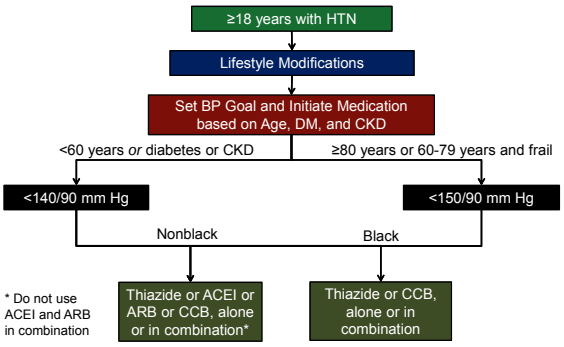
A. Felodipine with irbesartan
B. Losartan with ramipril
C. Hydrochlorothiazide with triamterene
D. Amlodipine with diltiazem





J Hypertens. 2013; 31:1281-1357.

Hypertension Treatment Algorithm



James PA et al. *JAMA*; 2014; 311(5):507-20.
Weber MA et al. *J Clin Hypertens* (Greenwich) 2014;16(1):14-26.

Systolic Blood Pressure Intervention Trial (SPRINT)

- An unmasked, open-label randomized controlled trial in 9361 patients with SBP ≥ 130 mm Hg, 50 yrs or older with one or more additional CV risk factor
  - Intensive treatment: SBP <120 mm Hg
  - Standard treatment: SBP <140 mm Hg
- Patients with serious comorbidities were excluded (e.g., diabetes, prior stroke, left ventricular dysfunction)
- Results:
  - Primary outcome of CV events lower with intensive treatment
    - 1.65% vs. 2.19% per year (HR 0.75; 95% CI 0.64-0.89; P<0.001)
- BP measurement techniques, adverse effects and lack of a reduction in stroke have complicated clinical applications

Wright JT, et al. *N Engl J Med*. 2015;373:2103-16.

AHA/ASA Newsroom: *Hypertension Guideline Writing Process Underway*

- Multi-disciplinary writing panel led by ACC/AHA to update 12-year-old recommendations
- Will update the 2003 guideline, officially the JNC 7, which was empaneled by the NHLBI
- Nine additional medical societies are partners
- A separate evidence review committee will develop a systematic review on specific critical questions, which will inform recommendations in this **2016 Guideline on the Management of Hypertension**

http://newsroom.heart.org/news/hypertension-guideline-writing-process-underway

Primary Message in the 2013 ACC/AHA Blood Cholesterol Guideline

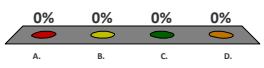
*The panel makes **no recommendations** for or against specific **LDL-C or non-HDL-C targets** for primary or secondary prevention of ASCVD*

Stone JJ et al. *Circulation*. 2014; 129[suppl 2]:S1-S45

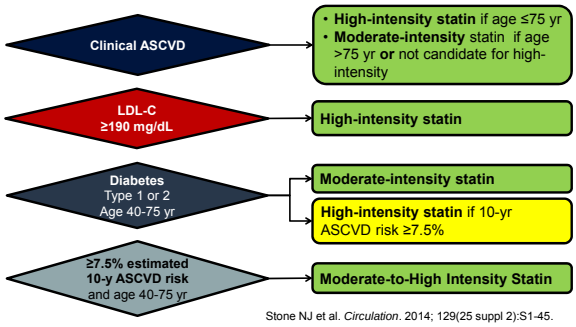
Question 5:

Which of the following is the most appropriate lipid-lowering regimen for SR at this time?

A. No drug therapy, low-fat and low cholesterol diet for 3 months then reevaluate FLP
B. Start pravastatin 40 mg orally daily
C. Start simvastatin 80 mg orally daily
D. Restart lovastatin 20 mg orally daily at night with food



4 Statin Benefit Groups



Stone NJ et al. *Circulation*. 2014; 129(25 suppl 2):S1-45.

ACC/AHA: Statin Intensity

High-Intensity	Moderate-Intensity	Low-Intensity
Daily dose lowers LDL–C on average, by ~ ≥ 50%	Daily dose lowers LDL–C on average, by ~ 30 to <50%	Daily dose lowers LDL–C on average, by <30%
Atorvastatin (40)–80 mg **Rosuvastatin 20** *(40)* **mg**	**Atorvastatin 10** *(20)* **mg** **Rosuvastatin** *(5)* **10 mg** **Simvastatin 20–40 mg** **Pravastatin 40** *(80)* **mg** **Lovastatin 40 mg** *Fluvastatin XL 80 mg* **Fluvastatin 80 mg** *Pitavastatin 2–4 mg*	*Simvastatin 10 mg* **Pravastatin 10–20 mg** **Lovastatin 20 mg** *Fluvastatin 20–40 mg* *Pitavastatin 1 mg*

Specific statins and doses are noted in **bold** that were evaluated in randomized controlled trials. Statins and doses that are approved by the U.S. FDA but were not tested in the RCTs reviewed are listed in *italics*. All doses are daily doses given once daily except fluvastatin should be dosed 40 mg twice daily (for moderate-intensity LDL-C lowering)

Stone NJ et al. *Circulation*. 2014; 129(25 suppl 2):S1-45.

ACC/AHA: Primary Prevention, no DM and LDL-C 70-189 mg/dL

Class I Recommendations	Level of Evidence
The pooled cohort equations should be used to estimate 10 year ASCVD risk for individuals with an LDL-C between 70 to 189 mg/dL without clinical ASCVD to guide initiation of statin therapy	B
Adults age 40 to 75 years without clinical ASCVD or DM and a 10 yr ASCVD risk ≥ 7.5% should be treated with a moderate-to-high intensity statin therapy	A

Class IIa Recommendations	Level of Evidence
Reasonable to offer moderate intensity statin to adults 40 to 75 years of age with LDL-C 70-189 mg/dL, without clinical ASCVD or DM and a 10 year ASCVD risk of 5 to < 7.5%	B

Stone NJ et al. *Circulation*. 2014; 129(25 suppl 2):S1-45.

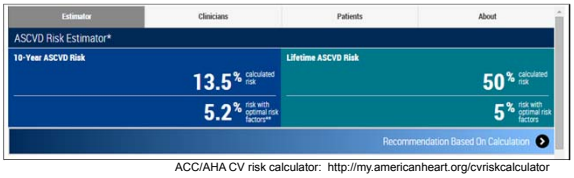
ACC/AHA Guideline on the Assessment of Cardiovascular Risk

- Pooled Cohort Equations
- Predicts 10-year risk in age 40 to 79 years (and 30-year or "lifetime risk" in age 20 to 59 years) of ASCVD:
  - Nonfatal/Fatal Myocardial Infarction
  - Nonfatal/Fatal Stroke
- Information required:
  - Age, sex, race, total cholesterol, HDL-C, systolic BP, antihypertensive medication use, diabetes status, smoking status

ACC/AHA CV risk calculator: http://my.americanheart.org/cvriskcalculator

ASCVD Risk Score

- Ex: 59-year-old White man. Non-smoker. BP is 162/94, 160/94 mm Hg (mean SBP 161 mm Hg) not on drug therapy. TC = 189 mg/dL, HDL-C = 38 mg/dL, no lipid-lowering therapy.



ACC/AHA CV risk calculator: http://my.americanheart.org/cvriskcalculator

Dyslipidemia Medications: Effects on Lipoprotein Concentrations

	LDL-C	HDL-C	TG
Statins	↓18-55%	↑5-15%	↓7-30%
Bile acid sequestrants	↓15-30%	↑3-5%	↑0-10%
Nicotinic acid	↓5-25%	↑15-35%	↓20-50%
Fibric Acids	↓5-↑20%	↑10-20%	↓20-50%
Cholesterol absorption inhibitor	↓13-20%	↑3-5%	↓5-11%
Long-chain omega-3 fatty acid drugs	↓6-↑25%	↓5-↑7%	↓19-44%
PCSK9 Inhibitors	↓40-72%	↑0-10%	↓0-17%

Jacobson TA et al. *J Clin Lipidol.* 2014; 8:473-88.
Shimada YJ and Cannon CP. *European Heart Journal*. 2015; 36(36):2415-24.

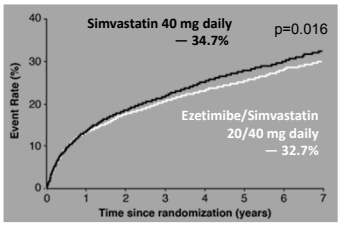
ACC/AHA: Other Recommendations

- Non-Statins
  - No data supporting routine use with statin therapy to further reduce ASCVD events
  - For statin candidates who are completely statin intolerant, it is reasonable to use nonstatins that have been shown to reduce ASCVD events
- No recommendations regarding initiating or discontinuing statins in NYHA Class II-IV ischemic systolic heart failure or maintenance hemodialysis

Stone NJ et al. *Circulation*. 2014; 129(25 suppl 2):S1-45.

IMPROVE-IT

- Double-blind randomized trial in acute coronary syndrome (n=18,144)
- Age ≥50 years with LDL-C 50-125 mg/dL (50-100 if on lipid-lowering therapy)
- Simvastatin or ezetimibe/simvastatin for 4.9 years
- Mean LDL-C values:
  - 69.9 vs. 53.2mg/dL



7-year event rates for primary endpoint of CV events

Cannon CP et al. *N Engl J Med.* 2015;372:2387-97.

PCSK9 Inhibitors: Role in Therapy

- Alirocumab and Evolocumab FDA approval:
  - Adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (FH) or clinical atherosclerotic cardiovascular disease, who require additional lowering of LDL-C
  - Evolocumab also approved for homozygous FH

	Dosing
Alirocumab (Praluent)	75 – 150 mg sq every 2 weeks
Evolocumab (Repatha)	140 sq every 2 weeks or 420 mg once monthly in homozygous FH patients

- Use in statin intolerance is debated and evolving

Praluent Package Insert; Sanofi-Aventis U.S. LLC, Bridgewater, NJ. July 2015.
Repatha Package Insert; Amgen Inc, Thousand Oaks, CA. August 2015.

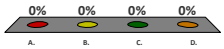
National Lipid Association (NLA) Recommendations

Risk Category	Non-HDL-C Primary Target (mg/dL)	LDL-C Primary Target (mg/dL)	Apo B Optional, Secondary Target (mg/dL)
• Low, moderate or high	<130	<100	<90
• Very High	<100	<70	<80

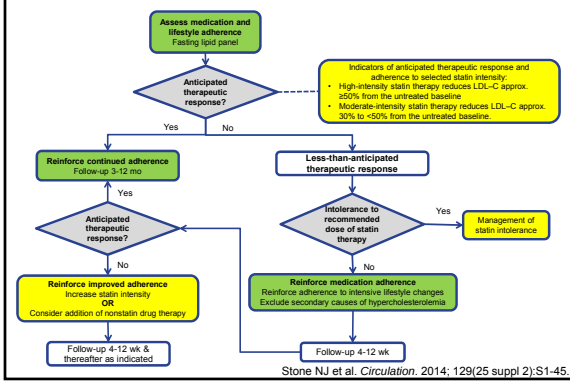
Jacobson TA et al. J Clin Lipidol. 2014; 8:473-88.

Question 6:
SR is started on a moderate-intensity statin regimen. Which of the following serum laboratory tests should be measured in 3 months?

A. Fasting lipid panel
B. Liver enzymes
C. Creatine kinase
D. A1C
E. All of the above



ACC/AHA: Ongoing Lipid Monitoring



Stone NJ et al. *Circulation*. 2014; 129(25 suppl 2):S1-45.

NLA Statin Muscle Safety Task Force

Spectrum of statin-associated muscle adverse events
Myalgia – unexplained muscle discomfort with normal creatine kinase (CK) level
Myopathy – muscle weakness (not pain), not necessarily with elevated CK
Myositis – muscle inflammation
Myonecrosis – muscle enzyme (**creatine kinase [CK]** elevation) • Mild >3-fold greater than untreated baseline or normal upper limit* • Moderate ≥10-fold greater than untreated baseline or normal upper limit* • Severe ≥50-fold greater than untreated baseline or normal upper limit*
Myonecrosis with myoglobuminuria or acute renal failure – increase in serum creatinine ≥ 0.5 mg/dL (clinical rhabdomyolysis)
* adjusted for age, race and sex

Rosenson RS et al. *J Clin Lipidol*. 2014; 8(3 suppl):S58-71.

NLA Statin Muscle Safety Task Force: Stain Intolerance

Definition

- Inability to tolerate at least 2 statins, one at the lowest starting daily dose AND another at any daily dose
- Symptoms (real/perceived) or abnormal lab result temporally related to statin use, reversible upon discontinuation, reproducible with re-challenge

Management Options

- Stop statin for 2-4 weeks if mild myonecrosis or worse
  - Work up secondary causes (hypothyroidism, vitamin D deficiency, myopathy)
  - If symptoms resolve, restart same or different statin at lower dose
  - Use lower statin dose or once/ twice weekly atorvastatin or rosuvastatin (5-10 mg)
  - Use a nonstatin

Guyton JR et al. *J Clin Lipidol*. 2014; 8(3 suppl):S72-81.
Rosenson RS et al. *J Clin Lipidol*. 2014; 8(3 suppl):S58-71.

Care Plan for SR – Follow up #1

- **Prevention of Gout**
  - Increase allopurinol to 200 mg orally daily; colchicine 1.2 mg orally, 0.6 mg in 1 hr if attack occurs
- **Hypertension**
  - Motivational interviewing to establish goals
  - Start amlodipine/benazepril 5/10 mg orally daily, continue home BP monitoring
- **Dyslipidemia**
  - Agrees to start atorvastatin 20 mg orally daily
- **Lifestyle**
  - Agrees to continue exercise and visit dietician at FQHC

Case SR – Follow Up #2

- Interview
  - Back 3 months later after 2 phone follow ups.
  - Feels good, implemented several lifestyle changes, willing to continue more.
  - No gout attacks in past month
- Medication Reconciliation
  - Reports adherence to medications:
    - Colchicine 0.6 mg daily, allopurinol 200 mg daily, omeprazole 20 mg daily, amlodipine/benazepril 10/20 mg orally daily (increased with phone follow-up), atorvastatin 20 mg daily. Has not had to use prn colchicine.

Case SR – Follow Up #2

- Additional data
  - Home BP measurement diary shows regular measurements; mean from past week 128/74 mm Hg.
- Vital signs:
  - BP 132/78, 130/76 mm Hg
  - HR 74 bpm
  - Wt 208 lb
  - BMI 31.6 kg/m^2
- Laboratory measurements
  - SCr 1.10 mg/dL, Serum potassium 4.8 mmol/L
  - Uric Acid 5.8 mg/dL
  - FLP: TC 135 mg/dL, HDL-C 45 mg/dL, LDL-C 80 mg/dL

BP Self Measurement Devices: Clinical Implications

- Improved medication adherence and BP control
- Accurate documentation may be problematic:
  - Patients might omit or fabricate readings
  - Devices with internal memory are optimal
- Patients must follow correct procedures:
  - Patient preparation same as office measurements
  - 3 readings separated by 1 minute; average values

dabl® Educational Trust http://www.dableducational.com Pickering TG et al. *Hypertension*. 2005; 45:142-61.

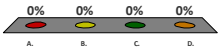
ASH: Position Paper Home and Ambulatory BP Monitoring

	Office BP Monitoring	Ambulatory BP Mentoring	Self-BP Monitoring
Predicts Events	Yes	Yes	Yes
Initial Diagnosis	Yes	Yes	Yes
Detect White Coat HTN	No	Yes	Yes
Evaluate Therapy	Yes	Yes (limited repeat use)	Yes
Normal Limit (mm Hg)	140/90	130/80 (24 hr) 135/85 (awake) 120/80 (asleep)	135/85
Cost	Low	High	Low
Reimbursement	Yes	Partial	No

Pickering TG et al. *J Am Soc Hypertens*. 2008; 2(3):119-24.

Question 7:
Two months ago, SR's home BP values were consistently above his goal of < 140/90 mm Hg. At that time, his amlodipine/benazepril dose was increased. If a third antihypertensive medication is to be added to his regimen in the future, which of the following would be the most appropriate third agent?

A. Aliskiren
B. Metoprolol succinate
C. Chlorthalidone
D. Hydralazine



Resistant Hypertension: AHA Scientific Statement

- Definition:
  - Patients not at their goal BP on 3 or more antihypertensive agents (ideally, at full doses, one of which is a diuretic), or
  - Patient requiring 4 or more antihypertensive agents to treat hypertension, even if they are at their goal BP
- Causes may include: Improper BP measurement, volume overload, drug-induced or other causes (e.g. non-adherence), and secondary hypertension

Calhoun DA, et al. *Circulation*. 2008;117:e510-526.

Resistant Hypertension: AHA Scientific Statement

Pharmacotherapy Options:

- Assure appropriate diuretic therapy
  - Chlorthalidone instead of hydrochlorothiazide
  - Aldosterone antagonist (e.g., spironolactone)
  - Loop diuretic (only if decreased renal function)
- Optimize current agents
  - Switch metoprolol to carvedilol or labetalol
- Additional pharmacotherapy options
  - Alternative antihypertensive agent
  - Dihydropyridine with non-dihydropyridine CCB

Calhoun DA, et al. *Circulation*. 2008;117:e510-526.

The Obesity Society/ACC/AHA Guideline for Managing Overweight/Obese Adults

- Sustained 3%–5% weight loss can result in meaningful reductions in triglycerides, blood glucose, A1c, and risk of type 2 diabetes
- Greater weight loss will reduce BP, improve LDL–C and HDL–C, and reduce need for medications to control comorbidities
- Initial goal loss of 5%-10% of baseline weight within 6 months

Jensen MD et al. *Circulation*. 2014; 129(25 suppl 2):S102-38.

The Obesity Society/ACC/AHA Guideline for Managing Overweight/Obese Adults

Dietary Pattern

- Prescribe a diet to achieve reduced calorie intake for obese or overweight individuals
  - 1200 to 1500 kcal/day, women; 1500 to 1800 kcal/day, men
  - 500 kcal/day or 750 kcal/day energy deficit
  - Evidence-based diets to create an energy deficit
  - Preferably refer to a nutrition professional for counseling

Bariatric Surgery

- BMI ≥40 kg/m^2 or BMI ≥35 kg/m^2 with obesity-related comorbidity who are motivated and who have not responded to behavioral treatment +/- pharmacotherapy

Jensen MD et al. *Circulation*. 2014; 129(25 suppl 2):S102-38.

Case SR – Follow Up #3

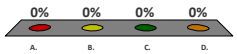
- Interview
  - Back 6 months later for a routine evaluation and influenza vaccination. Feels good, eating well (restricts calories and sodium, eats a low saturated fat diet), 1-2 beers daily but only on weekends. Biking 4 to 5 times weekly for 45 minutes. No gout attacks since starting allopurinol.
- Medication Reconciliation
  - Reports adherence to medications:
    - Allopurinol 200 mg daily, omeprazole 20 mg daily, amlodipine/benazepril 10/20 mg orally daily, atorvastatin 20 mg daily
    - Has stopped colchicine as instructed at last visit

Case SR – Follow Up #3

- Additional data
  - Home BP measurement diary with regular measurements; average from last month 127/75 mm Hg
- Vital signs:
  - BP 130/78, 128/80 mm Hg HR 74 bpm
  - Wt 200 lb BMI 30.4 kg/m^2
- Laboratory measurements
  - SCr 1.10 mg/dL, Serum potassium 4.8 mmol/L

Question 8:
SR feels as though his weight loss has plateaued and he is interested in a medication for weight loss. Which of the following would result in the greatest amount of weight loss?

A. Orlistat
B. Lorcaserin
C. Naltrexone and bupropion
D. Phentermine and topiramate



Pharmacotherapy for Obesity

- Orlistat
  - Reversible lipase inhibitor
- Lorcaserin
  - Serotonin 5-HT$_{2C}$ receptor agonist
- Phentermine and topiramate
  - Sympathomimetic amine anorectic, antiepileptic
- Naltrexone and bupropion
  - Opioid antagonist , aminoketone antidepressant

Newer Obesity Medications

- Indications:
  - Adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with BMI ≥ 30 kg/m2 (obese), or ≥ 27 kg/m2 (overweight) with ≥ 1 weight-related comorbidity (e.g., hypertension, dyslipidemia, type 2 diabetes)
- Stop therapy after 12 weeks if a minimum amount of weight loss is not achieved

Citrome L. Int J Clin Pract. 2014; 68(12):1401-5.

Efficacy of Newer Obesity Medications

	% of patients losing ≥ 5% body weight			% of patients losing ≥ 10% body weight		
	Active	Placebo	NNT	Active	Placebo	NNT
Lorcaserin 10 mg twice daily	46.4	22.1	5	21.9	8.4	8
Phentermine and topiramate 15 mg/92 mg daily	69.0	19.7	2	47.7	7.0	3
Naltrexone and bupropion 16 mg/180 mg twice daily	46.6	22.9	5	25.2	9.7	7

http://www.medscape.com/viewarticle/836453?nlid=73663_745&src=wnl_edit_medp_phar&uac=39775MJ&spon=30

Liraglutide (Saxenda) for Obesity

- Indication: BMI ≥ 30 kg/m^2 (obese), or ≥ 27 kg/m^2 (overweight) with ≥ 1 weight-related comorbidity
- Dosing: titrate to 3 mg subcutaneously daily, stop if 4% weight loss not achieved by week 16
- Not approved in type 2 diabetes; should not be used with insulin
- Total body weight loss at 56 weeks:
  - 62.3% lost ≥ 5%; 33.9% lost ≥ 10%
- Required REMS program (communication plan)

U.S. Food and Drug Administration.
http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm427913.htm

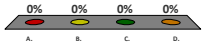
Risk Evaluation and Mitigation Strategies (REMS)

- Phentermine/topiramate ER (Qsymia) capsules require REMS elements
- All REMS elements
  - Medication Guide
  - Communication Plan
  - Elements to Assure Safe Use
  - Implementation System
  - Timetable for Assessments

U.S. Food and Drug Administration. Approved Risk Evaluation and Mitigation Strategies (REMS). (URL in handout)

Question 9:
While interviewing SR, he reports having problems with erectile dysfunction (ED) and has been using a friend's vardenafil 10 mg 1 hour before intercourse. It works well but only lasts an hour. Which of the following would be the most effective ED treatment for SR?

A. Switch to sildenafil 30 minutes before intercourse
B. Switch to tadalafil orally daily regardless of intercourse
C. Start low-dose transdermal testosterone daily
D. Replace amlodipine with carvedilol and reevaluate



PDE-5 Inhibitors

	Sildenafil	Vardenafil	Avanafil	Tadalafil
Half-life (hr)	4-5			18
Duration of action (hr)	4			24-36

- All are generally efficacious, high satisfaction
  - Tadalafil may be slightly more effective, but may have increased adverse effects; patients may prefer tadalafil over others
  - If fail one PDE-5 inhibitor, can try another
- Okay to use in patients with stable CV disease
  - Contraindicated with nitrates; caution with typical alpha blockers
- Other options: Alprostadil, testosterone replacement for hypogonadism; surgery or devices

Martin-Morales A et al. *Eur Urol.* 2007; 51:541-50.
Govier F et al. *Clin Ther.* 2003; 25:2709-23.
Eardley I et al. *BJU Int.* 2005; 96:1323-32.