

Clinical Pearls for Cardiovascular Disease in the Elderly

Hypertension

Christie Schumacher, PharmD, BCPS, BCACP, BC-ADM, CDE
Associate Professor, Pharmacy Practice
Director, PGY2 Ambulatory Care Residency Program
Midwestern University Chicago College of Pharmacy
Clinical Pharmacist, Advocate Medical Group

Heart Failure

Alexandra Goncharenko, PharmD, BCPS, BCCP
Clinical Pharmacist, Heart Failure, Chronic Disease
Management, Anticoagulation
Advocate Medical Group

Hyperlipidemia

Daniel Majerczyk, Pharm.D., BCPS, BC-ADM, CACP
Assistant Professor of Clinical Sciences
Roosevelt University College of Pharmacy
Clinical Pharmacy Specialist, Loyola Medicine -
MacNeal Family Medicine Residency Program

Diabetes Mellitus

Liz Van Dril, PharmD, BCPS
Clinical Assistant Professor, Department of Pharmacy Practice
University of Illinois at Chicago College of Pharmacy
Clinical Pharmacist, Internal Medicine/Managed Care
University of Illinois Hospital and Health Sciences System



Disclosures

- Drs. Goncharenko, Van Dril, Majerczyk and Schumacher have no conflicts of interest to disclose related to the content of this presentation

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Learning Objectives for Pharmacists

1. Compare and contrast treatment regimens for the management of hypertension in the elderly based on primary literature and the 2017 ACC/AHA Hypertension guidelines.
2. Examine recommendations for the use of statins as primary and secondary prevention in patients over 75 years of age as defined by the 2018 ACC/AHA Multisociety Guideline on the Management of Blood Cholesterol.
3. Develop a treatment plan for the management of chronic heart failure in an elderly patient utilizing the 2017 ACC/AHA/HFSA Focused Update Guideline for the Management of Heart Failure.
4. Design a safe and effective medication regimen for a patient with cardiovascular disease and diabetes.

Meet MM

MM is an 81-year-old AA man who presents to clinic for a physical and follow-up.

Past medical history: hypertension (HTN), heart failure reduced ejection fraction (HFrEF), peripheral vascular disease (PVD), and type 2 diabetes mellitus (T2DM).

Vital signs: BP of 156/86 mmHg, with a repeat BP of 154/86 mmHg, and a HR of 88 bpm.



Meet MM

Lab results:

Scr 0.9 mg/dL
eGFR 47 ml/min/1.73m²
Na⁺ 143 mg/dL
K⁺ 4.8 mmol/L
LDL 134 mg/dL
Triglycerides 176 mg/dL
A1c 7.8%

ECHO: EF 25-30%

Medication list:

lisinopril 40 mg daily
spironolactone 25 mg daily
furosemide 20 mg twice daily
glipizide 5 mg twice daily
metformin 1000 mg twice daily
aspirin 81 mg daily



Hypertension Management in the Elderly

Christie Schumacher, PharmD, BCPS, BCACP, BC-ADM, CDE
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Prevalence of HTN with Increasing Age

Age	≥ 130/80 or antihypertensive medication ¹		≥ 140/90 or antihypertensive medication ¹	
	Men	Women	Men	Women
20 – 44	30%	19%	11%	10%
45 – 54	50%	44%	33%	27%
55 – 64	70%	63%	53%	52%
65 – 74	77%	75%	64%	63%
75 +	79%	85%	71%	78%

¹BP cutpoints for definition of hypertension in the present guideline

²BP cutpoints for definition of hypertension in JNC7

Hypertension 2018;71(8):e13-e25



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ACC/AHA Blood Pressure Goal for Older Adults

Goal BP (mmHg)	Population	Recommendation
< 130 (SBP)	Ambulatory, community dwelling, noninstitutionalized patients ≥ 65 years of age	Medication recommendations depend on comorbid conditions described on previous slides If no comorbid conditions present, may choose thiazide diuretic, dihydropyridine CCB or ACEI/ARB based on patient specific characteristics

Hypertension 2018;71(8):e13-e25



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The SPRINT Trial

Population	9361 patients ≥ 50 years of age with at least one CV risk factor or with renal disease (no diabetes); 25% of patients were ≥ 75 years old
Regimen	Randomized to intensive treatment arm (goal SBP <120 mmHg) or standard treatment arm (goal SBP <140 mmHg)
Primary Endpoint	Composite endpoint of MI, other ACS, stroke, HF or death from any cause
Results	<ul style="list-style-type: none"> Terminated early after 3.26 years Mean SBP 121.5 mmHg in intensive treatment group vs. 134.6 mmHg in standard treatment group Composite endpoint in the intensive group was significantly lower than in the standard treatment group <ul style="list-style-type: none"> 1.65% per year vs 2.19% per year (HR 0.75, 95% CI, 0.64 – 0.89, p < 0.001) Intensive treatment arm had a 38% ↓ in HF, a 30% ↓ in CV events, a 43% ↓ in death from CV causes and a 27% ↓ in all-cause mortality Serious adverse events occurred in 38.3% of patients in the intensive treatment group and 37.1% of patients in the standard treatment group (p = 0.25)
Conclusion	Among patients at high risk for CV events, but without diabetes, targeting a SBP <120 mmHg, as compared with <140 mmHg, resulted in lower rates of fatal and nonfatal major cardiovascular events and death from any cause; however, at the expense of increased rates of certain adverse events

N Engl J Med. 2015;373:2103-2116



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The SPRINT Senior Analysis

Patients ≥ 75 years-old (n=2636)

- Mean age 79.9 years
- 37.9% women
- Median follow-up 3.14 years

Patients classified by frailty

- 13.3% fit
- 55.6% less fit
- 31.1% frail

JAMA. 2016;315:2673-2682

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SPRINT vs. SPRINT Senior

Outcome	SPRINT HR (95% CI) p-value	SPRINT NNT	SPRINT-SENIOR HR (95% CI) p-value	SPRINT-SENIOR NNT
Primary outcome ¹	0.75 (0.64 – 0.89) p < 0.001	61	0.66 (0.51 – 0.85) p = 0.001	27
Primary Outcome + all cause mortality	0.78 (0.67 – 0.90) p < 0.001	52	0.68 (0.54 – 0.84) p < 0.001	21
Heart failure	0.62 (0.45 – 0.84) p = 0.002	123	0.62 (0.40 – 0.95) p = 0.03	67
Death from any cause	0.73 (0.6 – 0.90) p = 0.003	90	0.67 (0.49 – 0.91) p = 0.009	41

HR = hazards ratio; CI = confidence interval; NNT = number needed to treat
¹The primary outcome was the first occurrence of myocardial infarction, acute coronary syndrome, stroke, heart failure or death from cardiovascular causes.

N Engl J Med. 2015;373:2103-2116
 JAMA. 2016;315:2673-2682

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SPRINT vs. SPRINT Senior

Safety Outcome	SPRINT HR p-value	SPRINT NNH	SPRINT-SENIOR HR p-value	SPRINT-SENIOR NNH ¹
Serious adverse event	1.04 p = 0.25	-	0.99 p = 0.09	-
Hypotension	1.67 p = 0.001	100	1.71 p = 0.07	-
Electrolyte abnormality	1.35 p = 0.02	125	1.51 p = 0.06	-
Injurious fall	0.95 p = 0.71	-	0.91 p = 0.61	-
Acute kidney injury or acute kidney failure	1.66 p < 0.001	63	1.41 p = 0.061	-

HR = hazards ratio; NNH = number needed to harm
¹Not statistically different; however, not powered to detect a difference

N Engl J Med. 2015;373:2103-2116
 JAMA. 2016;315:2673-2682

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Clinical Considerations for Treatment in the Elderly Population

- Intensive SBP target ↓ risk of cardiovascular disease (CVD) and mortality
 - Larger benefit in SPRINT-SENIOR trial
- Lower SBP of < 130 mmHg applies to ambulatory community dwelling patients
- Institutionalized patients should have an individualized SBP goal
 - Consider disease burden, comorbidities and life expectancy
 - Consider relaxed SBP goal of < 150 mmHg or < 140 mmHg, if tolerated

Hypertension 2018;71(6):e13-e15

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Isolated Systolic Hypertension (ISH)

Definition: SBP ≥140 mmHg and DBP <90 mmHg

More common in elderly, but reason for this effect in aging not well understood

Due to ↓ flexibility of the arterial wall

↑PP = ↑ arterial stiffness and is correlated with ↑ risk of cardiovascular mortality

Elevated pulse pressure (PP = SBP - DBP) reflects extent of CVD

High SBP in elderly = major risk factor for CVD, stroke and CKD progression

Hypertension 2018;71(6):e13-e15

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Managing ISH

Dihydropyridine calcium channel blockers (DHP CCB) and thiazide and thiazide-like diuretics are preferred antihypertensives

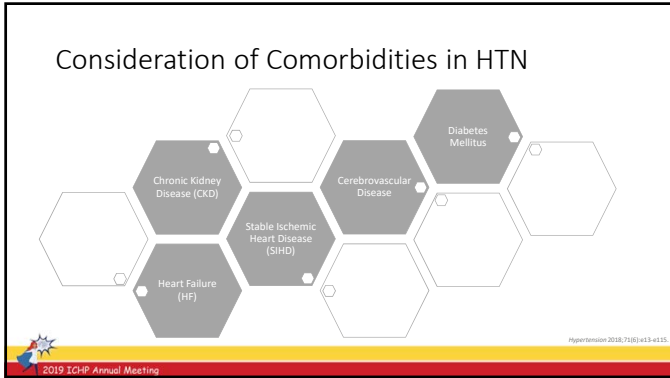
- Data strongest with indapamide (HYVET trial) and chlorthalidone (SHEP trial)
- DHP CCBs, such as amlodipine, more commonly used over thiazide diuretics
- Minimize risk of electrolyte abnormalities and urinary frequency issues

Angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) have benefit when added on to either DHP CCBs or thiazide diuretics

- Data more impressive when compelling indication present

Hypertension 2018;71(6):e13-e15

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Stable Ischemic Heart Disease

Goal BP (mmHg)	Recommendation
<130/80	<p>First-line therapy for compelling indications (previous MI, stable angina)</p> <ul style="list-style-type: none"> • BB and ACEI/ARB <p>Second line therapy options:</p> <ul style="list-style-type: none"> • Dihydropyridine CCB • Thiazide diuretic • Aldosterone antagonists (AA)

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Heart Failure with Reduced Ejection Fraction (HFrEF)

Goal BP (mmHg)	Recommendation
<130/80	<p>First-line therapy</p> <ul style="list-style-type: none"> • ACEI/ARB/ARNI[†] and BB <ul style="list-style-type: none"> • Carvedilol, metoprolol succinate or bisoprolol • Additional mortality reducing therapies to be used after ACEI/ARB and BB <ul style="list-style-type: none"> • Aldosterone antagonist (AA) • Hydralazine + isosorbide dinitrate (black patients) <p>Volume overload? + loop diuretics*</p>

†ARNI = angiotensin receptor blocker + neprilysin inhibitor (sacubitril/valsartan)
*NSA + hospitalizations or ↑ mortality

2019 ICHP Annual Meeting Hypertension 2018; 71(5):e13-e15

Heart Failure with Preserved Ejection Fraction (HFpEF)

Goal BP (mmHg)	Recommendation
<130/80	<p>First-line therapy:</p> <ul style="list-style-type: none"> • ACEI/ARB and BB <p>Second line therapy:</p> <ul style="list-style-type: none"> • AA or nondihydropyridine CCB

*Note: Volume overload? + loop diuretics**

*No ≥ hospitalizations or ≥ mortality

Hypertension 2018; 71(6):e13-e15

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Diabetes Mellitus (DM)

Goal BP (mmHg)	Population	Recommendation
<130/80	DM <u>without</u> albuminuria*	Thiazide diuretic, dihydropyridine CCB or ACEI/ARB
	DM <u>with</u> albuminuria*	ACEI/ARB Dihydropyridine CCB and thiazide diuretic should be selected after ACEI/ARB, if tolerated

*Albuminuria: ≥300 mg/day or urinary albumin-to-creatinine ratio ≥300 mg/g creatinine

Hypertension 2018; 71(6):e13-e15

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Secondary Stroke Prevention

Goal BP (mmHg)	Population	Recommendation
<130/80	History of stroke or TIA	<p>Thiazide diuretic or ACEI/ARB OR Combination of thiazide diuretic + ACEI</p> <p>Dihydropyridine CCB should be selected after ACEI and thiazide diuretic</p>

Patients should be restarted or started on initial antihypertensive therapy the first few days after the index event to reduce the risk of recurrent stroke or other vascular events

Hypertension 2018; 71(6):e13-e15

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Patient Case: MM

81-year-old AA man who presents to clinic for a physical and follow-up.

PMH: HTN, HFrEF, T2DM, PVD

Vital signs: BP of 156/86 mmHg, with a repeat BP of 154/86 mmHg, and a HR of 88 bpm

Lab results from last week: Scr 0.9 mg/dL, eGFR 47 ml/min/1.73m², Na⁺ 143 mg/dL, K⁺ 4.8 mmol/L, LDL 134 mg/dL, triglycerides 176 mg/dL and A1c of 7.8%

Current medication regimen: lisinopril 40 mg daily, spironolactone 25 mg daily, furosemide 20 mg twice daily, glipizide 5 mg twice daily, metformin 1000 mg twice daily, and aspirin 81 mg daily




What is MM's blood pressure goal?



Which medication (including appropriate dose) would you recommend to better control MM's BP?




What counseling points should be provided to MM regarding his new medication?



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Hyperlipidemia Management in the Elderly

Daniel Majerczyk, Pharm.D., BCPS, BC-ADM, CACP
Assistant Professor of Clinical Sciences
Roosevelt University College of Pharmacy
Clinical Pharmacy Specialist, Loyola Medicine - MacNeal Family Medicine Residency Program



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2018 (ACC/AHA) Cholesterol Guidelines

Evidence-based/patient-centered approach to the assessment and treatment of ASCVD

- Updated November 2018

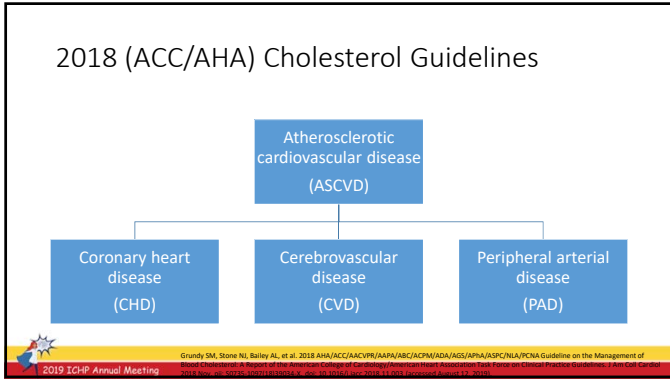
Patients with clinical ASCVD are stratified into two subgroups:

- "Very high-risk"
- "Not very high risk"
- This is based on the patient's history of major ASCVD event/s and high-risk condition/s



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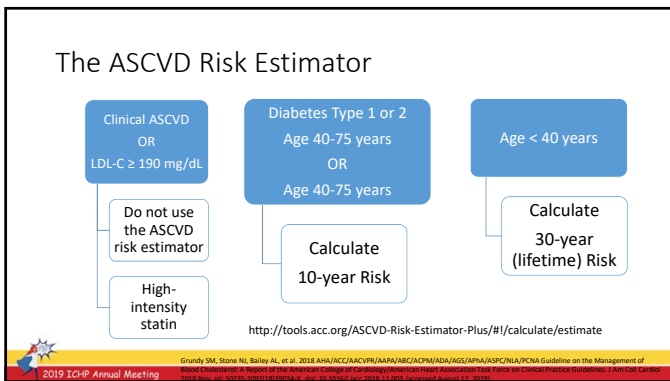
Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APHA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019;73(25):e179-e350.

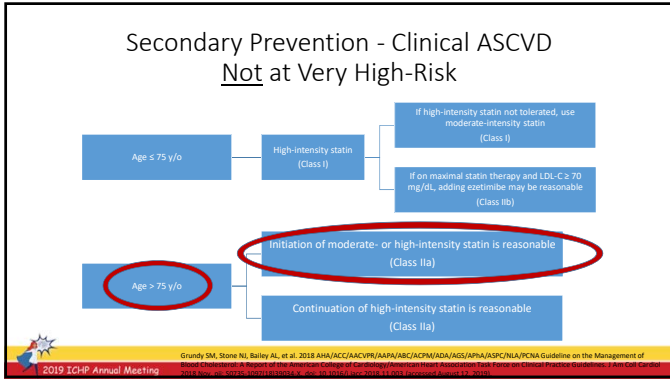


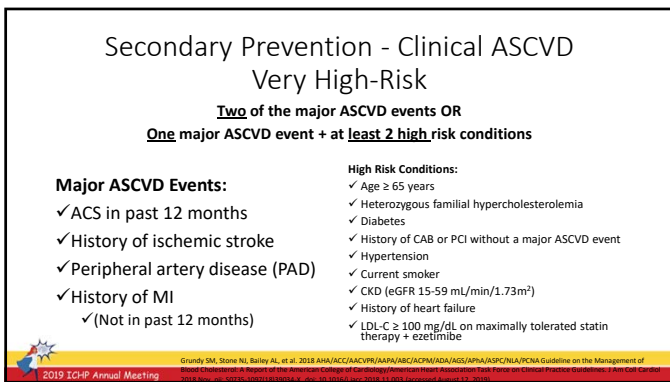
Statin Intensity – Daily Doses

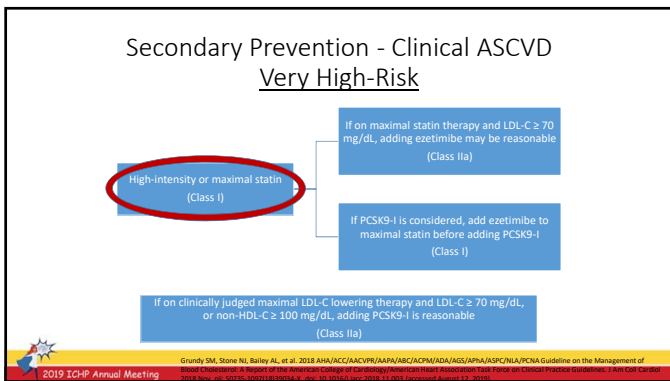
Statin Intensity		
High-intensity ↓ LDL-C ≥ 50%	Moderate-intensity ↓ LDL-C 30-49%	Low-intensity ↓ LDL-C < 30%
Atorvastatin 40 mg, 80 mg Rosuvastatin 20 mg, 40 mg	Atorvastatin 10 mg, 20 mg Fluvastatin 40 mg bid Fluvastatin XL 80 mg Lovastatin 40 mg Pitavastatin 1 mg, 2 mg, 4 mg Pravastatin 40 mg, 80 mg Rosuvastatin 5 mg, 10 mg Simvastatin 20 mg, 40 mg	Fluvastatin 20 mg, 40 mg Lovastatin 20 mg Pravastatin 10 mg, 20 mg Simvastatin 10 mg

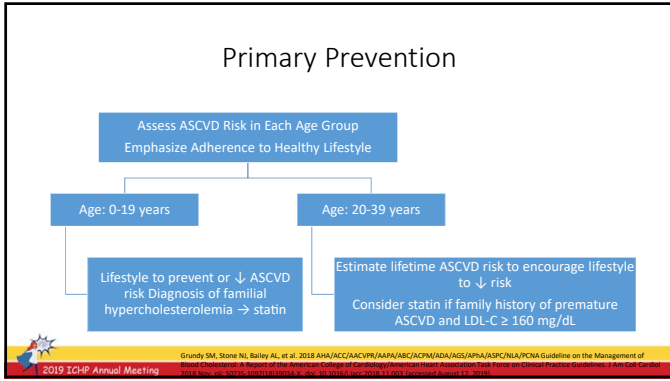
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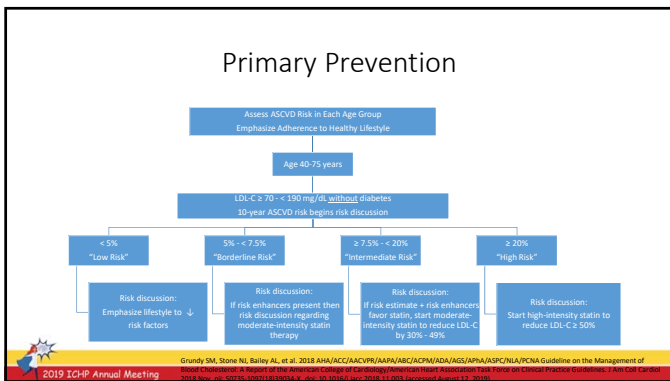


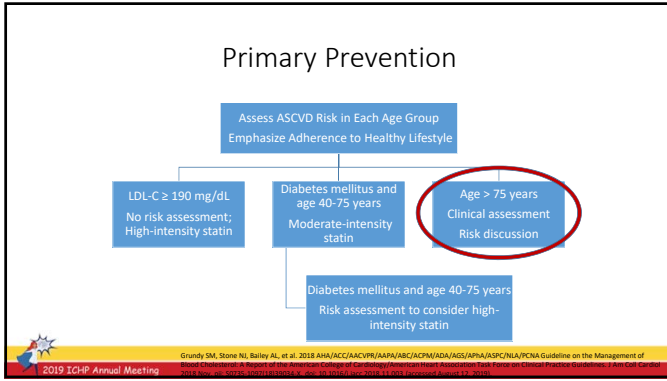


Primary Prevention

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

Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2019;72(13):e103-e145. doi:10.1016/j.jacc.2018.11.011. Epub 2018 Dec 14. PMID: 30579601





Back to MM....

- **PMH:**
 - Hypertension
 - Heart failure reduced ejection fraction (EF 25-30%)
 - Peripheral vascular disease (PAD)
 - Type 2 diabetes mellitus
- **Vital:**
 - BP: 156/86 mm/Hg with a repeat BP: 154/86 mm/Hg
 - HR: 88 bpm
- **Labs:**
 - Scr 0.9 mg/dL
 - eGFR 47 ml/min/1.73m²
 - Na⁺ 143 mg/dL
 - K⁺ 4.8 mmol/L
 - LDL 134 mg/dL
 - TG 176 mg/dL
 - A1c 7.8%

- **Medications:**
 - lisinopril 40 mg daily
 - spironolactone 25 mg daily
 - carvedilol 3.125 mg twice daily
 - furosemide 20 mg twice daily
 - glipizide 5 mg twice daily
 - metformin 1000 mg twice daily
 - aspirin 81 mg daily
- **Other important factors:**
 - Age \geq 65 years

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Statin Intensity – Daily Doses

Statin Intensity		
High-intensity ↓ LDL-C \geq 50%	Moderate-intensity ↓ LDL-C 30-49%	Low-intensity ↓ LDL-C < 30%
<div style="border: 2px solid red; border-radius: 50%; width: 100%; height: 100%; display: flex; align-items: center; justify-content: center;"> <p>Atorvastatin 40 mg, 80 mg Rosuvastatin 20 mg, 40 mg</p> </div>	<p>Atorvastatin 10 mg, 20 mg Fluvastatin 40 mg bid Fluvastatin XL 80 mg Lovastatin 40 mg Pitavastatin 1 mg, 2 mg, 4 mg Pravastatin 40 mg, 80 mg Rosuvastatin 5 mg, 10 mg Simvastatin 20 mg, 40 mg</p>	<p>Fluvastatin 20 mg, 40 mg Lovastatin 20 mg Pravastatin 10 mg, 20 mg Simvastatin 10 mg</p>

Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APMA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2019;72(13):e103-e145. doi:10.1016/j.jacc.2018.11.011. Epub 2018 Dec 14. PMID: 30579620.

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Current medication regimen: lisinopril 40 mg daily, spironolactone 25 mg daily, furosemide 20 mg twice daily, glipizide 5 mg twice daily, metformin 1000 mg twice daily, and aspirin 81 mg daily



What is this patient's ASCVD risk score?



What medication (including appropriate dose) would you recommend to reduce MM's risk of a future cardiovascular event?



Heart Failure in the Elderly

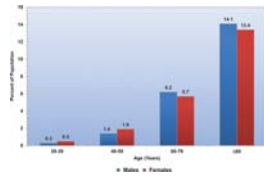


Alexandra Goncharenko, PharmD, BCPS, BCCP
Clinical Pharmacist
Heart Failure, Chronic Disease, Anticoagulation
Advocate Medical Group

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Heart Failure in the US

- 6.5 million Americans over the age of 20 have heart failure



- Expected to rise to 8 million by 2030

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Heart Disease and Stroke Statistics—2018 Update: A Report From the American Heart Association
Volume 137, Number 12, December 13, 2018
<https://www.ahajournals.org/doi/full/10.1161/STR.118.315864>

Heart Failure in the US

- 1,000,000 new cases of heart failure annually and incidence rates increase with advanced age
- More than 70% of hospitalizations for HF are among 65 years and older
- Survival after the onset of HF in older adults has improved with guideline-directed medical treatments and risk factor management but still remains high
 - 1-year survival 20.2%
 - 5-year survival 52.6%
- In 2012, total cost for HF was estimated to be \$30.7 billion Projections suggest that by 2030, the total cost of HF will increase almost 127%, to \$69.7 billion

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Heart Disease and Stroke Statistics—2018 Update: A Report From the American Heart Association
Volume 137, Number 12, December 13, 2018
<https://www.ahajournals.org/doi/full/10.1161/STR.118.315864>

Definition and Diagnosis of Heart Failure

- “A complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood.”
- HFrEF versus HFpEF
- Difficult to recognize symptoms in elderly versus young adults
 - dyspnea, fatigue, exercise intolerance, fluid retention
- Evidence of cardiac dysfunction of either systolic or diastolic origin on a transthoracic echocardiogram
- Elevated plasma BNP/NT-proBNP levels
 - Less specific in older adults

2019 ICHP Annual Meeting Yancy, C, et al. 2013 ACC/AHA Guideline for the Management of Heart Failure. J Am Coll Cardiol. 2013;61(4):e1-110.

Heart Failure Classifications

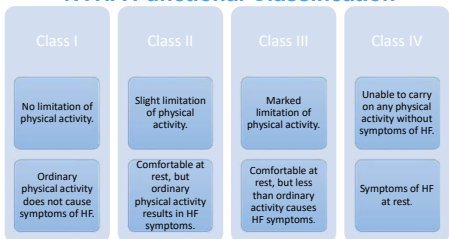
ACC/AHA Stages of HF

- Stage A • At high risk for HF but without structural heart disease or symptoms of HF
- Stage B • Structural heart disease but without signs or symptoms of HF
- Stage C • Structural heart disease with prior or current symptoms of HF
- Stage D • HF refractory to medical therapy, marked symptoms at rest, and requiring specialized interventions

2019 ICHP Annual Meeting Yancy, C, et al. 2013 ACC/AHA Guideline for the Management of Heart Failure. J Am Coll Cardiol. 2013;61(4):e1-110.

Heart Failure Classifications

NYHA Functional Classification

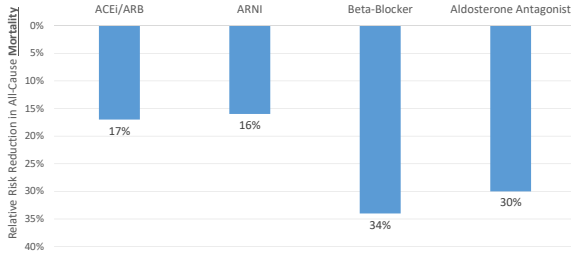


2019 ICHP Annual Meeting Yancy, C, et al. 2013 ACC/AHA Guideline for the Management of Heart Failure. J Am Coll Cardiol. 2013;61(4):e1-110.

Guideline-Directed Medical Therapy ("GDMT")

Image removed due to copyright. Refer to citation:
Yancy CW, Januzzi JL Jr, et al. J Am Coll Cardiol 2017;71.
<http://www.onlinejacc.org/content/early/2017/12/12/j.jacc.2017.11.025>

Benefits of Evidence-Based Therapies for Patients With Heart Failure and Reduced Ejection Fraction



Guideline-Directed Medical Therapy

TABLE 1 Starting and Target Doses of Select Guideline-Directed Medical Therapy for HF (3,13)


	Starting dose	Target dose
Beta-blockers		
Bisoprolol	1.25 mg twice daily	10 mg once daily
Carvedilol	3.75 mg twice daily	25 mg twice daily for weight < 80 kg and 30 mg twice daily for weight > 80 kg
Metoprolol succinate	12.5–25 mg/d	200 mg daily
ARNI		
Sacubitril/valsartan	240/26 mg/d	970/101 mg twice daily
ACEI		
Captopril	6.25 mg 3x/daily	30 mg 3x/daily
Benazepril	10 mg twice daily	40 mg twice daily
Lisinopril	10 mg daily	20–40 mg daily
Ramipril	5 mg daily	10 mg daily
MRB		
Canesartan	4–8 mg daily	32 mg daily
Losartan	25–50 mg daily	100 mg daily
Valsartan	40 mg twice daily	160 mg twice daily
Aldosterone antagonists		
Eplerenone	25 mg daily	50 mg daily
Spironolactone	12.5–25 mg daily	25–50 mg daily
Vasodilators		
Hydrochloric	25 mg 3x/daily	75 mg 3x/daily
Isosorbide dinitrate*	20 mg 3x/daily	40 mg 3x/daily
Fixed-dose combination isosorbide dinitrate/hydralazine†	20 mg/17.5 mg 3x/daily	2 tablets 3x/daily
Inotropes		
Dobutamine	2.5–5 mg twice daily	Titrate to heart rate 50–60 bpm. Maximum dose 7.5 mg twice daily

Sacubitril/Valsartan – Clinical Pearls

- Sacubitril = neprilysin inhibitor
- Either switched from ACE inhibitor or ARB or started “de novo”
- Dispensing pharmacy should be informed to delete all refills of prior ACE inhibitor or ARB prescriptions
- Available in 3 doses
- Dosing schedule is TWICE daily

Image removed due to copyright
 Entresto (sacubitril/valsartan) [full prescribing information], East Hanover, NJ: Novartis; July 2015.

Sacubitril/Valsartan – Clinical Pearls

24/26 mg	49/51 mg	97/103 mg
<ul style="list-style-type: none"> • Low dose ACEI - Equivalent of <10 mg of enalapril twice daily • Low dose ARB - Equivalent of valsartan <80 mg twice daily • ACEI/ARB naïve • Severe renal impairment (eGFR <30 mL/min/1.73 m²) • Moderate hepatic impairment (Child-Pugh Class B) • Elderly (age ≥75 years) 	<ul style="list-style-type: none"> • Moderate- or high-dose ACEI - Equivalent of enalapril ≥10 mg twice daily • Moderate- or high-dose ARB - Equivalent of valsartan ≥80 mg twice daily 	<ul style="list-style-type: none"> • Titrate every 2 weeks to the target dose 

Sacubitril/Valsartan – Clinical Pearls

- Titration Schedule:
 - Double the dose every 2 weeks as tolerated
- Monitoring:
 - Vital signs
 - Potassium
 - Renal function
- Contraindications:
 - Within 36 hours of ACEI use
 - Angioedema or known hypersensitivity with an ACEI or ARB previously
 - Pregnancy/Lactation
 - Severe hepatic impairment (Child-Pugh C)
 - Concomitant aliskiren use in patients with diabetes

Sacubitril/Valsartan – Clinical Pearls

Patient Counseling and Education:

- Inform clinic immediately if this medication is not affordable.
- Must have a 36-hour washout period when switching from or to an ACE inhibitor
- Signs and symptoms of angioedema and get emergency help right away if these symptoms occur.
- Low blood pressure may be more common. Call clinic if any new dizziness or lightheadedness, or develop extreme fatigue.
- Laboratory monitoring will be completed at every visit and periodically thereafter.
- Tell doctor right away if patients plan to or become pregnant due to possible harm to unborn baby.



Safe Prescribing and Use of Sacubitril/Valsartan (Entresto)

Concurrent treatment with an ACE inhibitor or ARB:
 Increased risk of angioedema when used together. Do not use together.
 Increased risk of hypotension when used together. Use cautiously.

Discontinue ACE Inhibitor:
 Stop ACE inhibitor 36 hours before starting Entresto.

Discontinue ARB:
 Stop ARB 36 hours before starting Entresto.

Prevent Potential Errors:
 Review each patient's drug list for ACE inhibitors or ARBs. Do not use together.

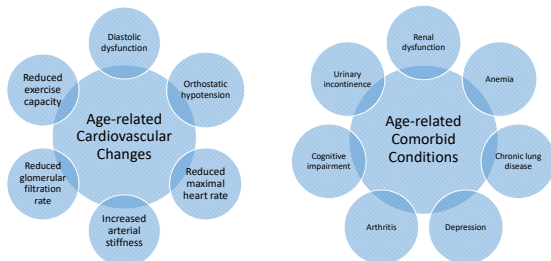
Work With Pharmacists:
 Pharmacist may be helpful in identifying potential drug interactions.

Educate Patients:
 Review patient education for key information.

Drug Class	Drug Name	Form	Strength	Frequency	Notes
ACE Inhibitor	Lisin	Tablet	10, 20, 30, 40, 50, 60, 80, 100	Once daily	Do not use with Entresto
ARB	Losartan	Tablet	25, 50, 100	Once daily	Do not use with Entresto
ARB	Valsartan	Tablet	40, 80, 160	Once daily	Do not use with Entresto
ARB	Candesartan	Tablet	8, 16, 32, 48, 64, 96, 128, 192	Once daily	Do not use with Entresto
ARB	Azilsartan	Tablet	20, 40, 80	Once daily	Do not use with Entresto
ARB	Telmisartan	Tablet	20, 40, 80	Once daily	Do not use with Entresto
ARB	Eprosartan	Tablet	600, 1200	Once daily	Do not use with Entresto
ARB	Irbesartan	Tablet	75, 150, 300	Once daily	Do not use with Entresto
ARB	Olmesartan	Tablet	5, 10, 20, 40	Once daily	Do not use with Entresto
ARB	Losartan	Tablet	25, 50, 100	Once daily	Do not use with Entresto
ARB	Valsartan	Tablet	40, 80, 160	Once daily	Do not use with Entresto
ARB	Candesartan	Tablet	8, 16, 32, 48, 64, 96, 128, 192	Once daily	Do not use with Entresto
ARB	Azilsartan	Tablet	20, 40, 80	Once daily	Do not use with Entresto
ARB	Telmisartan	Tablet	20, 40, 80	Once daily	Do not use with Entresto
ARB	Eprosartan	Tablet	600, 1200	Once daily	Do not use with Entresto
ARB	Irbesartan	Tablet	75, 150, 300	Once daily	Do not use with Entresto
ARB	Olmesartan	Tablet	5, 10, 20, 40	Once daily	Do not use with Entresto



Complexity of Heart Failure Management in the Elderly



Heart Failure Treatment in the Elderly

- The upper range for inclusion in HF clinical trials has typically been age 75 ± 5 years
- There are essentially no randomized data for drugs or devices in patients older than age 80 years
- Observational data support similar treatment benefits in older patients, but also suggest higher risks of adverse events
- Optimal doses for older patients may be lower than those studied in trials or tolerated in younger patients
- Elderly patients may require more frequent visits and laboratory monitoring during dose titration and more gradual dose changes



Patient Case: MM


- MM returns to clinic for a heart failure management visit and blood pressure check. He complains of increasing shortness of breath and can only walk 1 block, down from his usual 3 blocks. In addition, he has been sleeping on an extra pillow every night
- Vital signs: BP of 120/74 mmHg on the L arm, with a repeat BP of 124/76 mmHg on the R arm, and a HR of 68 bpm
- Laboratory results from last week: Scr 1.0 mg/dL, eGFR 48 ml/min/1.73m², Na⁺ 141 mg/dL, K⁺ 4.9 mmol/L, and A1C of 7.8%
- Current medication regimen: lisinopril 40 mg daily, carvedilol 25 mg twice daily, spironolactone 25 mg daily, furosemide 20 mg twice daily, glipizide 5 mg twice daily, metformin 1000 mg twice daily, atorvastatin 20 mg daily, and aspirin 81 mg daily




What ACC/AHA Stage and what NYHA Class is MM's heart failure?



What guideline-recommended medication therapy change (drug name and dose) would you recommend to optimize MM's regimen?





What are important counseling points to review with MM prior to initiating Sacubitril/Valsartan (Entresto)?



Diabetes Mellitus and Cardiovascular Disease in the Elderly

Liz Van Dril, PharmD, BCPS
Clinical Assistant Professor, Department of Pharmacy Practice
University of Illinois at Chicago College of Pharmacy
Clinical Pharmacist, Internal Medicine/Managed Care
University of Illinois Hospital and Health Sciences System



Tight Glycemic Control in Older Adults

Benefits

Risks

↓ Microvascular Complications

Accounts for 25% of all emergency department hospitalizations in older adults treated with antihyperglycemic agents

Hospitalizations due to hypoglycemia > hyperglycemia in Medicare population

© Eng J / Med 2009; 360:129-35
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The Evidence: Intensive Glycemic Control

Currie et al. (2010)

- Primary outcome: all-cause mortality
- Mean age: 64.1 years
- Elevated or reduced A1c associated with:
 - ↑ All-cause mortality
 - Risk greater in insulin-treated group
 - ↑ Large-vessel cardiac events
- Oral combination therapy with a wide A1c range may be safer with regard to all-cause mortality

U-Shaped Association between A1c and Mortality

Source: 2010;370:483-93
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Considerations for Glycemic Goals in the Elderly

Disease Duration

Life Expectancy

Presence of Macrovascular Complications

Comorbidity Burden

Cognitive Status

Functional Status

Diabetes Care 2018;41:53-61
J Am Geriatr Soc 2013;61(11):2021-6
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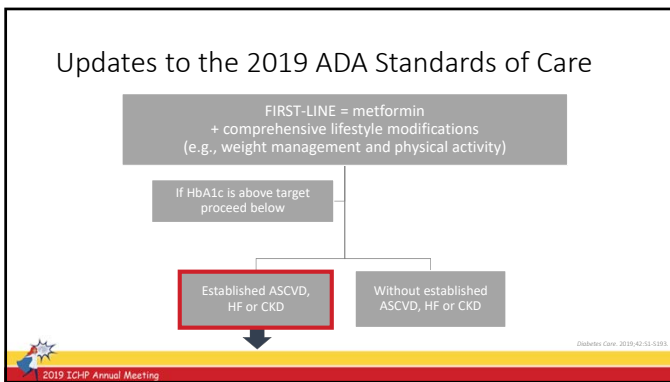
Glycemic Treatment Goals in Older Adults

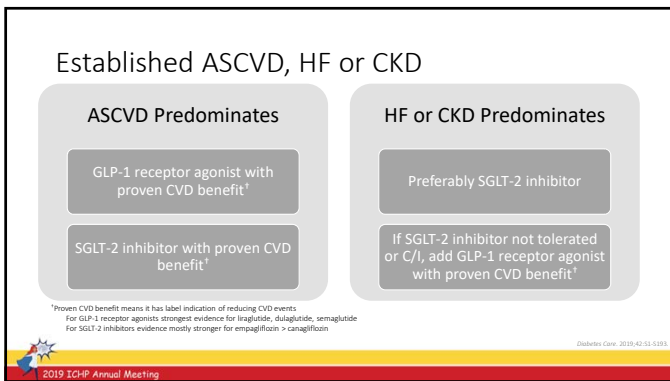
Health Status	Rationale	A1C goal	Fasting or Preprandial Glucose	Bedtime Glucose
Healthy (few comorbidities)	Longer life expectancy	<7.5%	90-130 mg/dL	90-150 mg/dL
Complex/Intermediate (multiple comorbidities*)	Intermediate life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0%	90-150 mg/dL	100-180 mg/dL
Very Complex/Poor Health**	Limited life expectancy makes benefit uncertain	<8.5%	100-180 mg/dL	110-200 mg/dL

*≥3 coexisting chronic illnesses (e.g., arthritis, cancer, HF, HTN, depression, emphysema, falls, incontinence, stage ≥3 CKD, MI, and stroke) or ≥2 instrumental ADL impairments or mild-to-moderate cognitive impairment
 **Long-term care or end-stage chronic illnesses (e.g., NYHA class III-IV HF or oxygen-dependent lung disease, CKD requiring dialysis, or metastatic cancer), or moderate-to-severe cognitive impairment or ≥2 ADL dependencies

Diabetes Care 2019;42(S1):S193

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Established ASCVD

ASCVD Predominates

- GLP-1 receptor agonist with proven CVD benefit¹
 - For GLP-1 receptor agonist strongest evidence for
 - liraglutide (LEADER)
 - dulaglutide (REWIND)
 - semaglutide (SUSTAIN-6)
- SGLT-2 inhibitor with proven CVD benefit²
 - For SGLT-2 inhibitor evidence mostly stronger for:
 1. empagliflozin (EMPA-REG OUTCOME)
 2. canagliflozin (CANVAS + CANVAS-R)

*Proven CVD benefit means it has label indication of reducing CVD events

Diabetes Care 2019;42(11):E193

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HF or CKD

HF or CKD Predominates

- Preferably SGLT-2 inhibitor
 - EMPA-REG OUTCOME**
 - ↓ 35% HF hospitalization
 - ↓ 39% incident or worsening nephropathy¹
 - CANVAS + CANVAS-R**
 - ↓ 33% HF hospitalization
 - ↓ 40% Composite renal outcome²
 - DECLARE-TIMI 58**
 - ↓ 27% HF hospitalization
 - ↓ 47% Composite renal outcome³
- If SGLT-2 inhibitor not tolerated or C/I, add GLP-1 receptor agonist with proven CVD benefit⁴

*Proven CVD benefit means it has label indication of reducing CVD events

Diabetes Care 2019;42(11):E193

1. Progression to macroalbuminuria (AACE-300 mg/dL), doubling of SCr + decrease in eGFR (per MDRD) <45 mL/min/1.73m², HF hospitalization or renal death

2. Sustained >40% decrease in eGFR, HF hospitalization or renal death

3. >40% decrease in eGFR to <45 mL/min/1.73m², new ESRD or renal death

4. Engl J Med. 2015;373(22):2117-26

5. Engl J Med. 2016;375(6):323-34

6. Engl J Med. 2012;367(10):944-53

7. Engl J Med. 2015;363(4):347-57

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Updates to the 2019 ADA Standards of Care

FIRST-LINE = metformin + comprehensive lifestyle modifications (e.g., weight management and physical activity)

If HbA1c is above target proceed below

- Established ASCVD, HF or CKD
- Without established ASCVD, HF or CKD**

Diabetes Care 2019;42(11):E193

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Without Established ASCVD, HF or CKD

Minimize Hypoglycemia	Minimize Weight Gain or Promote Weight Loss	Cost is Major Issue
DPP-4i	GLP-1-RA with good efficacy for weight reduction [†]	SU [‡]
GLP-1-RA	SGLT-2i	TZD
SGLT-2i		
TZD		

[†]semaglutide > liraglutide > dulaglutide > exenatide > lixisenatide
[‡]Choose later generation SU with lower risk of risk of hypoglycemia (i.e., glipizide or glimepiride)

Diabetes Care 2019;42:51-5193

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Antihyperglycemic Therapy in Older Adults

- Increased risk of hypoglycemia**
 - Medication classes with low risk of hypoglycemia are preferred
- Overtreatment**
 - Common in older adults and should be avoided
- Deintensification**
 - Simplification of complex regimens is recommended, with consideration of individualized A1C targets

Diabetes Care 2019;42:51-5193

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Deprescribing Complex Insulin Regimens

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    graph TD
      A[Basal +/- mealtime insulin] --> B[Basal insulin]
      A --> C[Mealtime insulin]
      D[Premixed insulin] --> E[Use 70% of total daily dose as basal only once daily in the morning]
      E --> F[Add noninsulin agents as follows:  
eGFR ≥45 mL/min/1.73m2 → start metformin and ↑dose q 2 weeks as tolerated  
eGFR <45 mL/min/1.73m2, already taking metformin, or metformin not tolerated → consider second line agent]
      B --> G[Change to morning administration]
      G --> H[Titrate based on fasting SMBG over 1 week  
50% readings above goal: ↑2 units  
>2 readings <80 mg/dL: ↓2 units]
      C --> I[Mealt ime dose >10 units; ↓dose by 50% + add noninsulin agent]
      C --> J[Mealt ime dose ≤10 units; discontinue + add noninsulin agent(s)]
      I --> K[Titrate mealtime dose down, while increasing noninsulin agent(s) dose]
      K --> F
      J --> F
  
```

Diabetes Care 2019;42:51-5193

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Clinical Considerations

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Back to MM

MM returns to clinic for a heart failure management visit and blood pressure check. He states he is feeling much better, can walk even further now and is back to his “old self.”

Vital signs: BP of 118/64 mmHg, with a repeat BP of 116/62 mmHg, and a HR of 68 bpm

Laboratory results from last week: Scr 0.8 mg/dL, eGFR 47 ml/min/1.73m², Na⁺ 140 mg/dL, K⁺ 4.7 mmol/L, and A1c of 7.8%


Current medication regimen: sacubitril/valsartan 97/103 mg twice daily, carvedilol 25 mg twice daily, spironolactone 25 mg daily, furosemide 20 mg twice daily, glipizide 5 mg twice daily, metformin 1000 mg twice daily, atorvastatin 20 mg daily, and aspirin 81 mg daily

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Does MM require any additional medication changes today to optimize his chronic disease state management? If so, which medication changes would you recommend today and why?


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Do any of his other medications require an adjustment?




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What counseling points should be provided to MM regarding his new medication?



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Clinical Pearls for Cardiovascular Disease in the Elderly

<p>Hypertension</p> <p>Christie Schumacher, PharmD, BCPS, BCACP, BC-ADM, CDE Associate Professor, Pharmacy Practice Director, PGY2 Ambulatory Care Residency Program Midwestern University Chicago College of Pharmacy Clinical Pharmacist, Advocate Medical Group</p>	<p>Heart Failure</p> <p>Alexandra Goncharenko, PharmD, BCPS, BCCP Clinical Pharmacist, Heart Failure, Chronic Disease Management, Anticoagulation Advocate Medical Group</p>	
<p>Hyperlipidemia</p> <p>Daniel Majerczyk, Pharm.D., BCPS, BC-ADM, CACP Assistant Professor of Clinical Sciences Roosevelt University College of Pharmacy Clinical Pharmacy Specialist, Loyola Medicine - MacNeal Family Medicine Residency Program</p>	<p>Diabetes Mellitus</p> <p>Liz Van Driel, PharmD, BCPS Clinical Assistant Professor, Department of Pharmacy Practice University of Illinois at Chicago College of Pharmacy Clinical Pharmacist, Internal Medicine/Managed Care University of Illinois Hospital and Health Sciences System</p>	



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Clinical Pearls for Cardiovascular Disease in the Elderly

1. An 85-year-old man presents to clinic for chronic disease management. His medical history is significant for hypertension, stage IV chronic kidney disease and type 2 diabetes. His vital signs include a BP of 146/86 mmHg, with a repeat BP of 144/84 mmHg, and a HR of 78 bpm. Laboratory results show Scr 2.3 mg/dL, eGFR 28 mL/min/1.73m², Na⁺ 143 mg/dL and K⁺ 4.5 mmol/L. His medication regimen includes lisinopril 40 mg daily, atorvastatin 40 mg daily, sitagliptin 25 mg daily and aspirin 81 mg daily. What is this patient's systolic BP goal?
 - a. < 120 mmHg
 - b. < 130 mmHg
 - c. < 140 mmHg
 - d. < 150 mmHg

LO1. Compare and contrast treatment regimens for the management of hypertension in the elderly based on primary literature and the 2017 ACC/AHA Hypertension guidelines.

2. Which of the following medications would you recommend to better control this patient's blood pressure?
 - a. Carvedilol 3.125 mg twice daily
 - b. Furosemide 20 mg twice daily
 - c. Hydrochlorothiazide 12.5 mg daily
 - d. Amlodipine 2.5 mg daily

LO1. Compare and contrast treatment regimens for the management of hypertension in the elderly based on primary literature and the 2017 ACC/AHA Hypertension guidelines.

3. Which of the following medications would be expected to lower LDL-C by at least 50%?
 - a. Lovastatin 40 mg
 - b. Pravastatin 20 mg
 - c. Pravastatin 80 mg
 - d. Rosuvastatin 20 mg

LO2. Examine recommendations for the use of statins as primary and secondary prevention in patients over 75 years of age as defined by the 2018 ACC/AHA Multisociety Guideline on the Management of Blood Cholesterol.

4. Which of the following patients over the age of 75 would be indicated for a high-intensity statin?
 - a. A patient with peripheral arterial disease, type 2 diabetes, and current tobacco use
 - b. A patient with chronic kidney disease and hypertension
 - c. A patient with heart failure and hypertension
 - d. A patient with type 2 diabetes and LDL-C of 68 mg/dL

LO2. Examine recommendations for the use of statins as primary and secondary prevention in patients over 75 years of age as defined by the 2018 ACC/AHA Multisociety Guideline on the Management of Blood Cholesterol.

5. 82-year-old AA man presents to Heart Failure Clinic for post hospital follow-up. He was recently discharged after being diagnosed with new onset Heart Failure with Reduced Ejection Fraction (HFrEF). LVEF on echocardiogram 25%. Your assessment reveals NYHA Functional Class II symptoms and he is euvolemic. Blood pressure is 110/75 mmHg and heart rate is 74 bpm. Pertinent labs include potassium 5.1 mmol/L, BUN 20, creatinine 1.2 mg/dL, eGFR 50 mL/min/1.73m². His current medications include lisinopril 20mg daily and furosemide 80mg daily. What change should be made to the patient's guideline-directed medical therapy at today's visit?
 - a. Decrease lisinopril 10mg daily
 - b. Start metoprolol succinate 25mg daily
 - c. Discontinue lisinopril 20mg daily and start Entresto® 49/51mg twice daily after a 36-hour washout period
 - d. Start spironolactone 25mg daily

LO3. Develop a treatment plan for the management of chronic heart failure in an elderly patient utilizing the 2017 ACC/AHA/HFSA Focused Update Guideline for the Management of Heart Failure.

6. Which of the following statements is true regarding the use of Entresto®?
- a. Entresto® is associated with less hypotension than ACE inhibitors and ARBs
 - b. The use of Entresto® requires a 36-hour washout period when transitioning from losartan
 - c. Clinical trial data showed that Entresto® reduced hospitalizations and HF symptoms but had no effect on mortality
 - d. Entresto® should be titrated no faster than every 2 weeks

LO3. Develop a treatment plan for the management of chronic heart failure in an elderly patient utilizing the 2017 ACC/AHA/HFSA Focused Update Guideline for the Management of Heart Failure.

7. A 76-year-old man presents to clinic for chronic disease management. He has a medical history significant for type 2 diabetes, hypertension, obesity and myocardial infarction 6 months ago. His current medications include saxagliptin 2.5 mg daily, metoprolol succinate 200 mg daily, lisinopril 40 mg daily, atorvastatin 80 mg daily and aspirin 81 mg daily. His most recent A1c from 2 weeks ago was 8.1%. His labs are within normal limits, except for SCr, which is 2.2 mg/dL and eGFR 28 mL/min/1.73m². His physician would like to change his antihyperglycemic regimen to reduce his cardiovascular risk. Which of the following would you recommend for this patient?
- a. Continue saxagliptin and start dapagliflozin
 - b. Stop saxagliptin and start liraglutide
 - c. Stop saxagliptin and start sitagliptin
 - d. Continue saxagliptin and start exenatide

LO4. Design a safe and effective medication regimen for a patient with cardiovascular disease and diabetes.

8. A 68-year-old African American woman presents to your practice for chronic disease management. She has a past medical history significant for type 2 diabetes, hypertension, and heart failure with preserved ejection fraction. Her vitals today are 142/84 mmHg and 144/86 mmHg on repeat. Her labs are within normal limits except for SCr, which is 1.3 mg/dL and eGFR 49 mL/min/1.73m². Her most recent A1c from last week was 7.9%. According to the most recent recommendations from the 2019 ADA Standards of Care, which of the following medications would be most appropriate to initiate after metformin?
- a. Semaglutide 0.25 mg weekly
 - b. Alogliptin 12.5 mg daily
 - c. Empagliflozin 10 mg daily
 - d. Pioglitazone 15 mg daily

LO4. Design a safe and effective medication regimen for a patient with cardiovascular disease and diabetes.

Answer Key: 1) B; 2) D; 3. D; 4. A; 5. B; 6. D; 7. B; 8. C