CARDIOLOGY PRACTICE GUIDELINES WHAT WE NEED TO KNOW TO GUIDE PATIENT CARE

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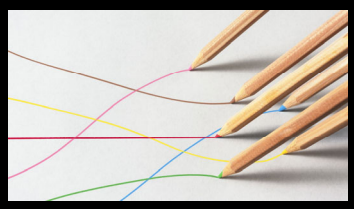


OBJECTIVES

- Examine, discuss and apply current Cardiology Guidelines for
  - Primary Prevention of CV disease
  - Treating Hyperlipidemia
  - Treating Atrial Fibrillation
  - Treating Heart Failure

NEW GUIDELINES

- Assessing Cardiovascular Risk
- Hyperlipidemia Guidelines
- Heart Failure Guidelines
- Atrial Fibrillation Guidelines

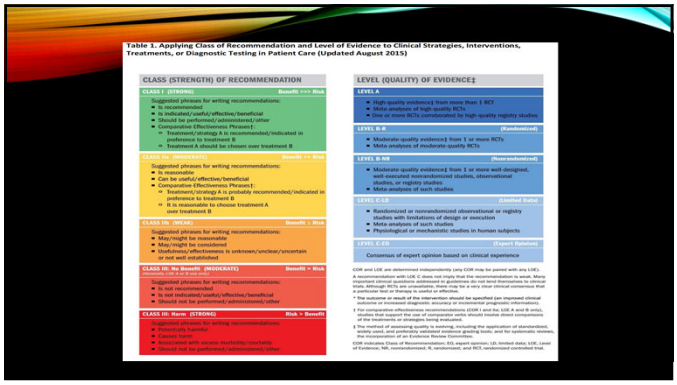
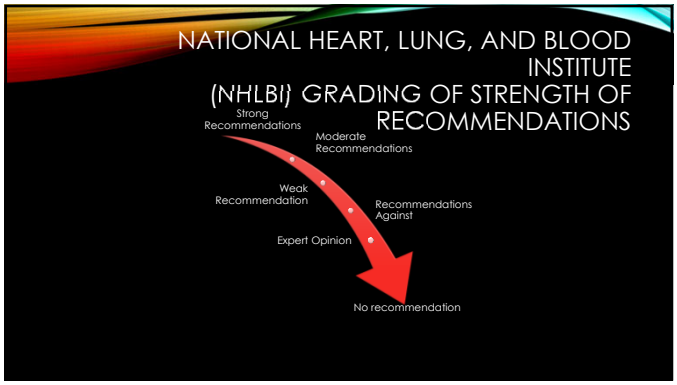
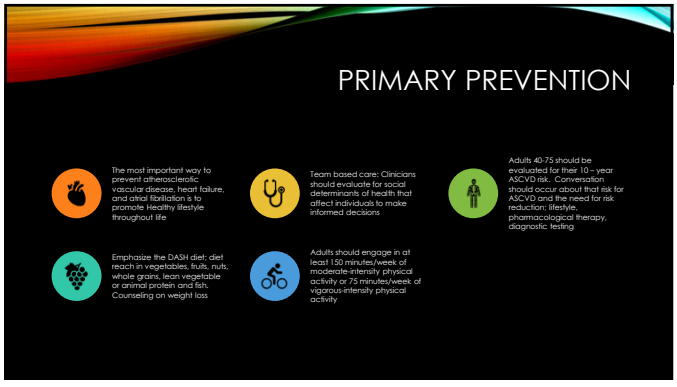


Table 1. Applying Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care (Updated August 2015)
CLASS (STRENGTH) OF RECOMMENDATION
CLASS I (STRONG)
Benefit >>> Risk
Suggested phrases for writing recommendations:
Is recommended
Is indicated/useful/effective/beneficial
Should be performed/administered/other
Comparative-Effectiveness Phrases†:
Treatment/strategy A is recommended/indicated in preference to treatment B
Treatment A should be chosen over treatment B
CLASS IIa (MODERATE)
Benefit >> Risk
Suggested phrases for writing recommendations:
Is reasonable
Can be useful/effective/beneficial
Comparative-Effectiveness Phrases†:
Treatment/strategy A is probably recommended/indicated in preference to treatment B
It is reasonable to choose treatment A over treatment B
CLASS IIb (WEAK)
Benefit ≥ Risk
Suggested phrases for writing recommendations:
May/might be reasonable
May/might be considered
Usefulness/effectiveness is unknown/unclear/uncertain or not well established
CLASS III: No Benefit (MODERATE)
Benefit = Risk
Suggested phrases for writing recommendations:
Is not recommended
Is not indicated/useful/effective/beneficial
Should not be performed/administered/other
CLASS III: Harm (STRONG)
Risk > Benefit
Suggested phrases for writing recommendations:
Is potentially harmful
Causes harm
Associated with excess mortality/morbidity
Should not be performed/administered/other
LEVEL (QUALITY) OF EVIDENCE‡
LEVEL A
High-quality evidence§ from more than 1 RCT
Meta-analysis of high-quality RCTs
One or more RCTs corroborated by high-quality registry studies
LEVEL B-R
(Randomized)
Moderate-quality evidence§ from 1 or more RCTs
Meta-analyses of moderate-quality RCTs
LEVEL B-NR
(Nonrandomized)
Moderate-quality evidence§ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
Meta-analyses of such studies
LEVEL C-LD
(Limited Data)
Randomized or nonrandomized observational or registry studies with limitations of design or execution
Meta-analyses of such studies
Physiological or mechanistic studies in human subjects
LEVEL C-EO
(Expert Opinion)
Consensus of expert opinion based on clinical experience
COR and LOE are determined independently (any COR may be paired with any LOE).
A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Even though RCTs are not available, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.
* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).
† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.
‡ The method of assessing quality is evolving, including the application of standardized, widely used grading schemes, algorithms, and online tools, and for systematic reviews, the incorporation of an Evidence Review Committee.
COR indicates Class of Recommendation; ED, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.


NATIONAL HEART, LUNG, AND BLOOD INSTITUTE (NHLBI) GRADING OF STRENGTH OF RECOMMENDATIONS
Strong Recommendations
Moderate Recommendations
Weak Recommendation
Recommendations Against
Expert Opinion
No recommendation


PRIMARY PREVENTION
The most important way to prevent atherosclerotic vascular disease, heart failure, and atrial fibrillation is to promote Healthy lifestyle throughout life
Team based care: Clinicians should evaluate for social determinants of health that affect individuals to make informed decisions
Adults 40-75 should be evaluated for their 10 – year ASCVD risk. Conversation should occur about that risk for ASCVD and the need for risk reduction: lifestyle, pharmacological therapy, diagnostic testing
Emphasize the DASH diet: diet reach in vegetables, fruits, nuts, whole grains, lean vegetable or animal protein and fish. Counseling on weight loss
Adults should engage in at least 150 minutes/week of moderate-intensity physical activity or 75 minutes/week of vigorous-intensity physical activity

PRIMARY PREVENTION

- Adults with DM T2, lifestyle changes are crucial. If medication is indicated, Metformin is 1st line followed by sodium-glucose cotransporter 2 inhibitor or a glucagon-like peptide-1 receptor agonist
- Every adult should be assessed at every healthcare visit for tobacco use
- Aspirin should be used INFREQUENTLY in routine primary prevention of ASCVD due to lack of benefit
- Statin therapy is 1st line treatment for primary prevention of ASCVD in patients with elevated LDL >/= 190 mg/dl, those with DM, who are 40 – 75 yrs of age, and those determined to be at sufficient ASCVD risk after a risk discussion
- Nonpharmacological interventions are recommended for all adults with elevated BP or HTN. Target BP should be < 130/80 mm/Hg

Stone et al., 2018, ACC/AHA Primary Prevention Guideline

EMPHASIS ON PATIENT CENTERED APPROACH

- Team based
- Shared decision making
- Social determinants
  - Screen for psychosocial stressors
  - Health literacy
  - Social and cultural influences
  - Potential barriers
  - Risk for DM, HTN
  - Obesity/Wt loss
  - Support to stop tobacco use

Stone et al., 2018, ACC/AHA Primary Prevention Guideline

RISK-ENHANCING FACTORS FOR CLINICIAN-PATIENT RISK REDUCTION

- Family history of premature ASCVD (males < 55, Females <65)
- Primary hypercholesterolemia (LDL-C 160-189)
- Metabolic syndrome (waist circumference > 40" in men, > 35 " women) Triglycerides > 150 nonfasting, HTN, Hyperglycemia, low HDL (< 40 in men, < 50 in women) tally of 3 or more makes the diagnosis
- CKD (GFR 15-59mL/min with or without albuminuria; not treated with HD or transplant
- Chronic Inflammatory conditions (psoriasis, RA, SLE, HIV/AIDS)
- H/O premature menopause (before 40) h/o pregnancy associated conditions such as preeclampsia

Stone et al., 2018, ACC/AHA Primary Prevention Guideline

RISK-ENHANCING FACTORS FOR CLINICIAN-PATIENT RISK REDUCTION

- High-risk race/ethnicity (south Asian ancestry)
- Lipids/biomarkers
  - Persistent (3 measurements) elevated primary hypertriglyceridemia (>/= 175 mg/dl, nonfasting)
  - Elevated HS C-RP (> 2.0)
  - Elevated Lp(a) >/= 50 mg/dL: relative indication for + family h/o premature ASCVD
  - Elevated apoB (>/= 130 mg/dL) relative indication for its measurement for Triglyceride >/= 200 mg/dL. A level of >/= 130mg/dL corresponds with LDL-C > 160 mg/dL and constitutes a risk-enhancing factor
  - ABI (<0.9)

Stone et al., 2018, ACC/AHA Blood Primary Prevention Guideline

DEFINING INTENSITY OF PHYSICAL ACTIVITY

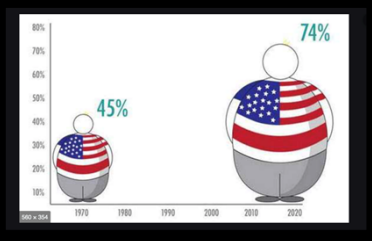
- Sitting is the new smoking
- Watch apps to tell you when to stand
- Meetings now have requirements for every hour of sitting there must be 3 minutes of standing or movement
- Remember the exercise requirement?
- For pre-op evaluation, pts are asked if they can walk up a flight of stairs without any CV symptoms. Must be able to do at least 4 METS of greater

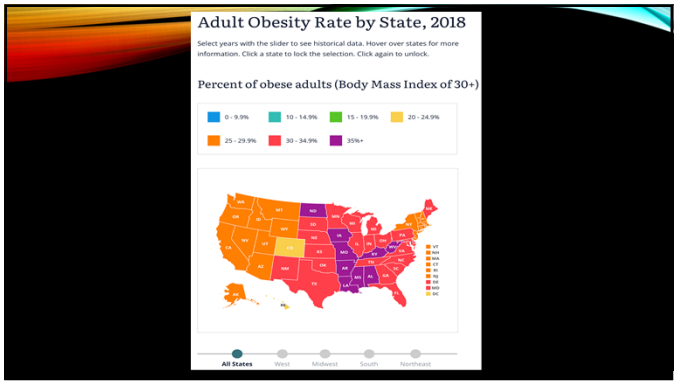
Intensity	METs	Examples
Sedentary behavior*	1-1.5	Sitting, reclining, or lying; watching television
Light	1.6-2.9	Walking slowly, cooking, light housework
Moderate	3.0 -5.9	Brisk walking (2.4–4 mph), biking (5–9 mph), ballroom dancing, active yoga, recreational swimming
Vigorous	>6	Jogging/running, biking (>10 mph), singles tennis, swimming laps

*Sedentary behavior is defined as any waking behavior characterized by an energy expenditure ≤1.5 METs while in a sitting, reclining, or lying posture. Standing is a sedentary activity in that it involves ≤1.5 METs, but it is not considered a component of sedentary behavior.

MET indicates metabolic equivalent; and mph, miles per hour.

OBESITY IN THE USA





Rank	State	Adult Obesity Rate 2018
1	Mississippi	39.5%
1	West Virginia	39.5%
3	Arkansas	37.1%
4	Louisiana	36.8%
5	Kentucky	36.6%
6	Alabama	36.2%
7	Iowa	35.3%
8	North Dakota	35.1%
9	Missouri	35.0%
10	Oklahoma	34.8%
10	Texas	34.8%
12	Kansas	34.4%
12	Tennessee	34.4%
14	South Carolina	34.3%
15	Indiana	34.1%
15	Nebraska	34.1%
17	Ohio	34.0%

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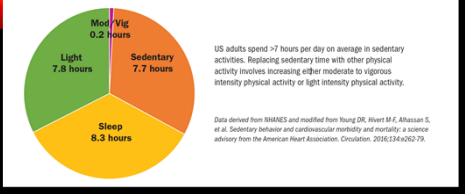
8	North Dakota	35.1%
9	Missouri	35.0%
10	Oklahoma	34.8%
10	Texas	34.8%
12	Kansas	34.4%
12	Tennessee	34.4%
14	South Carolina	34.3%
15	Indiana	34.1%
15	Nebraska	34.1%
17	Ohio	34.0%

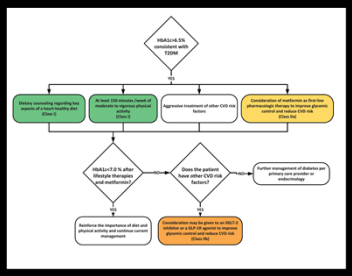


US adults spend >7 hours per day on average in sedentary activities. Replacing sedentary time with other physical activity involves increasing either moderate to vigorous intensity physical activity or light intensity physical activity.

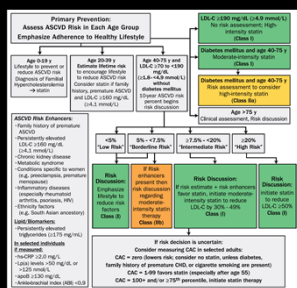
Data derived from NHANES and modified from Young DR, Hivert M-F, Alhassan S, et al. Sedentary behavior and cardiovascular morbidity and mortality: a science advisory from the American Heart Association. Circulation. 2016;134:e262-79.

HOURS PER DAY SPENT IN VARIOUS STATES OF ACTIVITY

TREATMENT OF DMT2



PRIMARY PREVENTION



SPECIFIC RISK FACTORS

Diabetes-Specific Risk Enhancers That Are Independent of Other Risk Factors in Diabetes Mellitus

- Long duration (≥10 years for T2DM or ≥20 years for type 1 diabetes mellitus)
- Albuminuria ≥30 mcg albumin/mg creatinine
- eGFR <60 mL/min/1.73 m2
- Retinopathy
- Neuropathy
- ABI <0.9

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 [published online ahead of print November 10, 2018]. Circulation. doi: 10.1161/CIR.0000000000000625

ABI indicates ankle-brachial index; eGFR, estimated glomerular filtration rate; and T2DM, type 2 diabetes mellitus.

DIAGNOSTIC TESTING TO HELP

Selected Examples of Candidates for Coronary Artery Calcium Measurement Who Might Benefit From Knowing Their Coronary Artery Calcium Score Is Zero

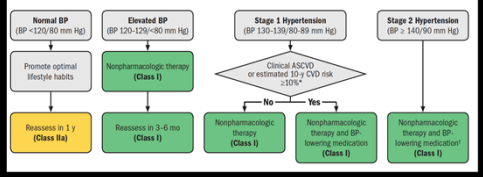
- Patients reluctant to initiate statin who wish to understand their risk and potential for benefit more precisely
- Patients concerned about need to reinstitute statin therapy after discontinuation for statin -associated symptoms
- Older patients (men 55–80 y of age; women 60–80 y of age) with low burden of risk factors who question whether they would benefit from statin therapy
- Middle-aged adults (40–55 y of age) with PCE-calculated 10-year risk of ASCVD 5% to <7.5% with factors that increase their ASCVD risk, although they are in a borderline risk group.

Caveats: If patient is at intermediate risk and if a risk decision is uncertain and a coronary artery calcium score is obtained, it is reasonable to withhold statin therapy unless higher-risk conditions, such as cigarette smoking, family history of premature ASCVD, or diabetes mellitus, are present and to reassess coronary artery calcium score in 5 to 10 years. Moreover, if coronary artery calcium scoring is recommended, it should be performed in facilities that have current technology and expertise to deliver the lowest radiation possible.

ASCVD indicates atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; and PCE, pooled cohort equations.

HIGH BLOOD PRESSURE

BP Thresholds and Recommendations for Treatment



	Nonpharmacological Intervention	Dose	Approximate Impact on SBP Hypertension	Nonhypertension
Weight loss	Weight/body fat	Best goal is ideal body weight, but aim for at least a 1 kg reduction in body weight for most adults who are overweight. Expect about 1 mm Hg for every 1 kg reduction in body weight.	-5 mm Hg	-2/3 mm Hg
Healthy diet	DASH dietary pattern	Consume a diet rich in fruits, vegetables, whole grains, and low-fat dairy products, with reduced content of saturated and total fat.	-11 mm Hg	-3 mm Hg
Reduced intake of dietary sodium	Dietary sodium	Optimal goal is ~1500 mg/d, but aim for at least a 1000-mg/d reduction in most adults.	-5/6 mm Hg	-2/3 mm Hg
Enhanced intake of dietary potassium	Dietary potassium	Aim for 3500–5000 mg/d, preferably by consumption of a diet rich in potassium.	-4/5 mm Hg	-2 mm Hg
Physical activity	Aerobic	• 90–150 min/wk • 65%–75% heart rate reserve	-5/8 mm Hg	-2/4 mm Hg
	Dynamic resistance	• 90–150 min/wk • 50%–80% 1 rep maximum • 8 exercises, 3 sets/exercise, 10 repetitions/set	-4 mm Hg	-2 mm Hg
	Isometric resistance	• 4 × 2 min (hand grip), 1 min rest between exercises, 30%–40% maximum voluntary contraction, 3 sessions/wk • 8–10 wk	-5 mm Hg	-4 mm Hg
Moderation in alcohol intake	Alcohol consumption	In individuals who drink alcohol, reduce alcohol^ to: • Men: ≤2 drinks daily • Women: ≤1 drink daily	-4 mm Hg	-3 mm Hg

NONPHARMACOLICAL INTERVENTIONS

TOBACCO USE

							NOTE: The FDA has issued a removal of black box warnings about neuropsychiatric events.	
Nicotine replacement (NRT): 5 forms (3 OTC, nasal spray/oral inhaler by prescription) Cigarettes smoked per day (CPD) can guide dosing. 1 CPD ≈ approx. 1-2 mg of nicotine Note: Use caution with all NRT products for patients with recent (≤2 weeks) MI, serious arrhythmia, or angina; patients who are pregnant or breastfeeding; and adolescents							Bupropion (Zyban [GlaxoSmithKline], Wellbutrin SR [GlaxoSmithKline])	Varenicline (Chantix [Pfizer])
Dosing	**Patch: 21 mg, 14 mg, or 7 mg**	**Gum: 2 mg or 4 mg**	**Lozenge: 2 mg or 4 mg**	**Nasal spray: 10 mg/mL**	**Oral inhaler: 10 10-mg cartridge**		**Tablet: 150 mg SR**	**Tablet: 0.5 mg or 1 mg**
Dose and duration can be titrated on the basis of response	Starting dose: 21 mg for >10 CPD; 14 mg for <10 CPD	Starting dose: 4 mg if first tobacco use is ≤30 min after waking; 2 mg if first tobacco use is >30 min after waking; maximum of 20 lozenges or 24 pieces of gum per day. Chew and park gum*		Starting dose: 1-2 doses/h (1 dose = 2 sprays); maximum of 40 doses/d	Starting dose: Puff for 20 min per cartridge every 1-2 h; maximum 6-16 cartridges/d; taper over 3-6 mo^		150 mg once daily (am) for 3 d; then 150 mg twice daily; may use in combination with NRT	0.5 mg once daily (am) for 3 d; then 0.5 mg twice daily for 4 d; then 1 mg twice daily (use start pack followed by continuation pack) for 3-6 mo
Precautions	Local irritation possible; avoid with skin disorders; may remove for sleep if needed	Hiccups/dyspepsia possible; avoid food or beverages 15 min before and after use		Local irritation possible; avoid with nasal or reactive airway disorders	Cough possible; avoid with reactive airway disorders		Avoid with history/risk of seizures, eating disorders, MAO inhibitors, or CYP 2D6 inhibitor	Nausea common; take with food. Renal dosing required. Very limited drug interactions; near-exclusive renal clearance.

ASPIRIN USE

Recommendations for Aspirin Use

COR	LOE	Recommendations
IIb	A	1. Low-dose aspirin (75-100 mg orally daily) might be considered for the primary prevention of ASCVD among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk.
III: Harm	B-R	2. Low-dose aspirin (75-100 mg orally daily) should not be administered on a routine basis for the primary prevention of ASCVD among adults >70 years of age.
III: Harm	C-LD	3. Low-dose aspirin (75-100 mg orally daily) should not be administered for the primary prevention of ASCVD among adults of any age who are at increased risk of bleeding.

MANAGEMENT OF BLOOD CHOLESTEROL

WHAT'S NEW IN THE GUIDELINE?

- Focus on ASVD Risk Reduction: 4 Statin Benefit Groups
- A New Perspective on LDL-C and/or Non-HDL-C Treatment Goals
- Global Risk Assessment of Primary Prevention
- Safety Recommendations
- Role of Biomarkers
- Future Updates to the Blood Cholesterol Guideline

Stone et al., 2018, ACC/AHA Blood Cholesterol Guideline

HOW TO REDUCE ASCVD THROUGH CHOLESTEROL MANAGEMENT

- Emphasize Heart Healthy Lifestyle
- Patients with Clinical ASCVD, reduce LDL-C with high-intensity statin therapy
- Patients at very high-risk for ASCVD; threshold for LDL-C is 70 mg/dL
- Patients with severe primary hypercholesterolemia (LDL-C >/= 190) without calculating 10 year ASCVD risk, begin high-intensity statin therapy
- Patients 40-75 with DM and LDL-C >/= 70, start moderate-intensity statin therapy without calculating 10-year ASCVD risk

HOW TO REDUCE ASCVD THROUGH CHOLESTEROL MANAGEMENT

Patients 40-75 evaluated for primary ASCVD prevention should have a clinician-patient risk discussion prior to starting therapy

Patients 40-75 without DM and LDL-C levels >/= 70, at a 10 year ASCVD risk of >/= 7.5%, start moderate-intensity statin if the discussion favors statin therapy

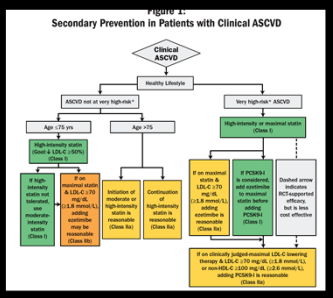
HOW TO REDUCE ASCVD THROUGH CHOLESTEROL MANAGEMENT

Patients 40-75 without DM and LDL-C >/= 70 mg/dL – 189 mg/dL at a 10 year ASCVD risk of >/= 7.5% to 19.9% and statin therapy is uncertain, consider measuring CAC

Assess adherence and percentage response to LDL-C lowering medication and lifestyle changes with repeat lipid measurements 4-12 weeks after statin initiation or dose adjustment, repeat every 3-12 months as needed

SECONDARY PREVENTION

First statin Benefit Group



SEVERE HYPERCHOLEEROLEMIA

- Second Statin Group

Recommendations for Primary Severe Hypercholesterolemia [LDL-C ≥190 mg/dL (≥4.9 mmol/L)]

COR	LOE	Recommendations
I	B-R	1. In patients 20 to 75 years of age with an LDL-C level of 190 mg/dL or higher (≥4.9 mmol/L) maximally tolerated statin therapy is recommended.
IIa	B-R	2. In patients 20 to 75 years of age with an LDL-C level of 190 mg/dL or higher (≥4.9 (mmol/L) who achieve less than 50% reduction in LDL-C while receiving maximally tolerated statin therapy and/or have an LDL-C level of 100 mg/dL (≥2.6 mmol/L) or higher, ezetimibe therapy is reasonable.
IIb	B-R	3. In patients 20 to 75 years of age with a baseline LDL-C 190 mg/dL or higher (≥4.9 mmol/L), who achieve less than a 50% reduction in LDL-C levels and have fasting triglycerides 300 mg/dL or lower (≤3.4 mmol/L) while taking maximally tolerated statin and ezetimibe therapy, the addition of a bile acid sequestrant may be considered.
IIb	B-R	4. In patients 30 to 75 years of age with heterozygous FH and with an LDL-C level of 100 mg/dL or higher (≥2.6 mmol/L) while taking maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered.
IIb	C-LD	5. In patients 40 to 75 years of age with a baseline LDL-C level of 220 mg/dL or higher (≥5.7 mmol/L) who achieve an on-treatment LDL-C level of 130 mg/dL or higher (≥3.4 mmol/L) while receiving maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered.
Value Statement: Uncertain Value (B-NR)		6. Among patients with FH without evidence of clinical ASCVD taking maximally tolerated statin and ezetimibe therapy, PCSK9 inhibitors provide uncertain value at mid-2018 US list prices.

ADULT DM

Third Statin Group

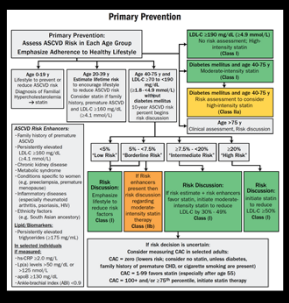
Diabetes-specific Risk Enhancers That Are Independent of Other Risk Factors in Diabetes

Table 5

- Long duration (≥10 years for type 2 diabetes or ≥ 20 years for type 1 diabetes)
- Albuminuria ≥30 mcg albumin/mg creatinine
- eGFR <60 ml/min/1.73 m^2
- Retinopathy
- Neuropathy
- ABI <0.9

PRIMARY PREVENTION OVER THE LIFE SPAN

Fourth Statin Benefit Group



WHAT TO DISCUSS WITH YOUR PATIENTS?

- Family history of premature ASCVD
- Primary Hypercholesterolemia
- Metabolic syndrome
- Chronic Kidney disease
- Chronic inflammatory conditions
- History of premature menopause
- High risk ethnicities
- Lipid Biomarkers

INITIATING THERAPY

ASCVD Risk Assessment	• Assign to statin treatment group; use ASCVD risk estimator plus* ○ In lower risk primary prevention adults 40-75 years with LDL-C ≥70 mg/dL (≥1.8 mmol/L). ○ Not needed in secondary prevention, LDL-C ≥190 mg/dL (≥4.9 mmol/L) and those 40-75 years with diabetes. • Assess other patient characteristics which influence risk. See Risk Enhancing Factors *(Section 4.4.1.3 and Table 6)* • Assess coronary artery calcium *(section 4.4.1.4)* if risk decision uncertain and additional information is needed to clarify ASCVD risk ○ Use decision tools to explain risk (ASCVD risk estimator plus- http://tools.acc.org/ASCVD-Risk-Estimator-Plus, Mayo Clinic Statin Choice Decision Aid)

ESTIMATING RISK

Personal screen shot LBailey

THERE'S AND APP FOR THAT

- https://ccccalculator.ccctracker.com/

CARDIOVASCULAR RISK ASSESSMENTS

- Framingham: 10 year risk and 30 year risk
- QRISK2 (NICE Guidelines)
- MESA Risk Score Calculator
- National Heart, Lung and Blood Institute
- ACC/AHA ASCVD Risk Calculator
- NCEP ATP III

http://cvdrisk.nhlbi.nih.gov/http://www.cvdriskcalculator.com
/https://www.mesa-nhlbi.org/CACReference.aspx
http://www.framinghamheartstudy.org/
http://www.nhlbi.nih.gov/files/docs/guidelines/atglance.pdf
Stone et al. (2018)
http://cvdrisk.nhlbi.nih.gov/

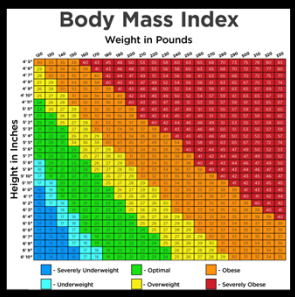
INITIATING THERAPY

Clinician-Patient Shared Decision making

Lifestyle Modifications	• Review lifestyle habits (diet, physical activity, weight/BMI, tobacco use) • Endorse a healthy lifestyle and provide relevant advice/materials/referrals (CardioSmart, AHA Life's Simple 7, NLA Patient Tear Sheets, PCNA Heart Healthy Toolbox, cardiac rehab, dietitian, smoking cessation program)
Potential Net Clinical Benefit of Pharmacotherapy	• Recommend statins as first-line therapy • Consider the combination of statin and non-statin therapy in select patients • Discuss potential risk reduction from lipid-lowering therapy • Discuss the potential for adverse effects/drug-drug interactions
Cost Considerations	• Discuss potential out-of-pocket cost of therapy to the patient (e.g., insurance plan coverage, tier level, copayment)
Shared Decision Making	• Encourage patient to verbalize what was heard (personal ASCVD risk, available options and their risk/benefit) • Invite the patient to ask questions, express values/preferences, state ability to adhere to lifestyle changes and medications • Refer patients to trustworthy materials to aid in their understanding of issues regarding risk decisions • Collaborate with the patient to determine therapy and follow-up plan

LIFESTYLE CHANGES

Reality Check

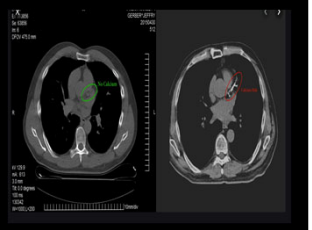


CORONARY ARTERY CALCIUM MEASUREMENT

TABLE 1

Categories of coronary artery calcium scores

Score	Category
0	No atherosclerosis
1–99	Mild disease
100–399	Moderate disease
≥ 400	Severe disease



TREATMENT CONSIDERATIONS

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

CONCERNS FOR SIDE EFFECTS

Statin Associated Side Effects	Frequency	Predisposing Factors	Quality of Evidence
Statin Associated Muscle Symptoms (SAMS) • Myalgias (CK normal)	Infrequent (1%-5%) in RCTs/frequent (5%-10%) in observational studies and clinical setting	Age, female, low BMI, high- risk medications (CYP3A4 inhibitors, OATP1B1 inhibitors), comorbidities (HIV, renal, liver, thyroid, pre-existing myopathy), Asian descent, excess alcohol, high levels of physical activity and trauma.	RCTs cohorts/observational
• Myositis/Myopathy (CK >ULN) with concerning symptoms/objective weakness	Rare		RCTs cohorts/observational
• Rhabdomyolysis (CK >10xULN + renal injury)	Rare		RCTs Cohorts/observational
• Statin-associated autoimmune myopathy (SAAM) (HMGCR Ab's, incomplete resolution)	Rare		Case reports
New onset Diabetes Mellitus	Depends on population; more frequent if diabetes mellitus risk factors such as BMI ≥30, fasting blood glucose ≥100 mg/dL, metabolic syndrome or A1c ≥6% are present	Diabetes risk factors/ metabolic syndrome High-intensity statin therapy	RCTs/Meta-analyses

CONCERNS FOR SIDE EFFECTS

Statin Associated Side Effects	Frequency	Predisposing Factors	Quality of Evidence
Liver • Transaminase elevation 3xULN	Infrequent		RCTs/cohorts/observational Case reports
• Hepatic Failure	Rare		
CNS • Memory/Cognition	Rare		Case reports; no increase in memory/cognitive problems in three large scale RCTs
Cancer	No definite association		RCTs/meta-analyses
Other • Renal Function • Cataracts • Tendon Rupture • Hemorrhagic Stroke • Interstitial Lung Disease • Low Testosterone	Unfounded Unfounded Unfounded Unfounded Unfounded Unfounded		

WHAT ABOUT CHILDREN?

	Acceptable	Borderline	Abnormal
TC	<170 mg/dL (<4.3 mmol/L)	170-199 mg/dL (4.3-5.1 mmol/L)	≥200 mg/dL (≥5.1 mmol/L)
Triglycerides: 0-9 y	<75 mg/dL (<0.8 mmol/L)	75-99 mg/dL (0.8-1.1 mmol/L)	≥100 mg/dL (≥1.1 mmol/L)
Triglycerides: 10-19 y	< 90 mg/dL (<1.0 mmol/L)	90-129 mg/dL (1.0-1.5 mmol/L)	≥130 mg/dL (≥1.4 mmol/L)
HDL-C	>45 mg/dL (>1.2 mmol/L)	40-45 mg/dL (1.0-1.2 mmol/L)	<40 mg/dL (<1.0 mmol/L)
LDL-C	<110 mg/dL (<2.8 mmol/L)	110-129 mg/dL (2.8-3.3 mmol/L)	≥130 mg/dL (≥3.4 mmol/L)
Non-HDL-C	<120 mg/dL (<3.1 mmol/L)	120-144 mg/dL (3.1-3.7 mmol/L)	≥145 mg/dL (≥3.7 mmol/L)

ETHNICITY CONSIDERATIONS

Ethnic/racial groupings	Asian-Americans*	Hispanic/Latino-Americans†	Blacks African-Americans	Comments
Evaluation				
ASCVD issues informed by ethnicity	South Asian and East Asian ASCVD risk varies by country of origin; Individuals from South Asia (see below) have increased ASCVD risk	Race and country of origin together with socioeconomic status and acculturation level may explain risk factor burden more precisely e.g. ASCVD risk is higher among individuals from Puerto Rico than from Mexico.	ASCVD risk assessment in black women shows increased ASCVD risk compared to their otherwise similar white counterparts	Heterogeneity in risk according to racial/ethnic groups and within racial/ethnic groups. Native American/Alaskan populations have high rates of risk factors for ASCVD compared to non-hispanic whites.
Lipid issues informed by ethnicity	Lower levels of HDL-C compared to whites Higher prevalence of LDL-C among Asian Indians, Filipinos, Japanese, and Vietnamese compared to whites. An increased prevalence of high TGs was seen in all Asian American subgroups	Hispanic/Latino women have higher prevalence of low HDL-C compared to Hispanic/Latino men	Higher levels of HDL-C and lower levels of triglycerides (TG) than in Non-Hispanic Whites or Mexican-Americans.	All ethnic groups appear to be at greater risk for dyslipidemia, but important to identify those with more sedentary behavior and less favorable diet.
Metabolic issues informed by ethnicity	Increased Metabolic Syndrome (MetS) seen with lower waist circumference than in whites. DM develops at a lower lean body mass and at earlier age (19-21)	DM disproportionately present compared to whites and blacks. Increased prevalence MetS, DM in Mexican Americans compared to whites & Puerto Ricans.	Increased DM and hypertension	Increased prevalence of DM. Features of MetS vary by ethnicity. Waist circumference, not weight, should be used to determine abdominal adiposity when possible

ETHNICITY CONSIDERATIONS

Ethnic/racial groupings	Asian-Americans*	Hispanic/Latino-Americans†	Blacks/ African-Americans	Comments
Risk Decisions				
Pooled Cohort Equations (PCE)	No separate PCE available; use PCE for whites. PCE may underestimate ASCVD risk in South Asians PCE may overestimate risk in East Asians	No separate PCE available; use PCE for non-Hispanic whites. If African American ancestry also, then use PCE for blacks	Use PCE for blacks	Country specific race/ethnicity, along with socio-economic status, may affect estimation of risk of PCE
Coronary Artery Calcium (CAC) Score	In terms of CAC burden, South Asian men were similar to non-Hispanic white men, but higher CAC when compared to blacks, Latinos and Chinese Americans. South Asian women had similar CAC to whites and other ethnic women, although CAC burden higher in older age	CAC predicts similarly in whites and those who identify as Hispanic/ Latino	In MESA, CAC score was highest in whites and Hispanic men, with blacks having significantly lower prevalence and severity of CAC.	Risk factor differences in MESA between ethnicities didn't fully explain variability in CAC However, CAC predicted ASCVD events over and above traditional risk factors in all ethnicities

ETHNICITY CONSIDERATIONS

Ethnic/racial groupings	Asian-Americans*	Hispanic/Latino-Americans†	Blacks/ African-Americans	Comments
Treatment (continued)				
Intensity of Statin therapy and Response to LDL-C lowering	Japanese patients may be sensitive to statin dosing. In an open-label, randomized primary prevention trial, Japanese participants had a reduction in CVD events with low-intensity doses of pravastatin as compared to placebo. In a secondary prevention trial, Japanese participants with CAD benefitted from a moderate-intensity doses of pitavastatin.	No sensitivity to statin dosage compared to non-Hispanic white or black individuals	No sensitivity to statin dosage compared to non-Hispanic white individuals	Using a lower statin intensity in Japanese patients may give results similar to those seen with higher intensities in non-Japanese patients
Safety	Higher rosuvastatin plasma levels in Japanese, Chinese, Malay, and Asian-Indians compared to whites. FDA recommends a lower starting dose (5 mg of rosuvastatin in Asians vs. 10 mg in whites). Caution urged as dose uptitrated.	No specific safety issues with statins related to Hispanic/Latino ethnicity	Baseline serum CK values are higher in blacks than in whites. The 95th percentile race/ethnicity specific and sex-specific serum CK normal levels are available for assessing changes in serum CK.	Clinicians should take Asian ethnicity into account when prescribing dose of rosuvastatin (see package insert). In adults of East Asian descent, other statins should be used preferentially over simvastatin.

2019 FOCUSED GUIDELINES FOR MANAGEMENT OF PATIENTS WITH ATRIAL FIBRILLATION

AFIB CLASSIFICATIONS

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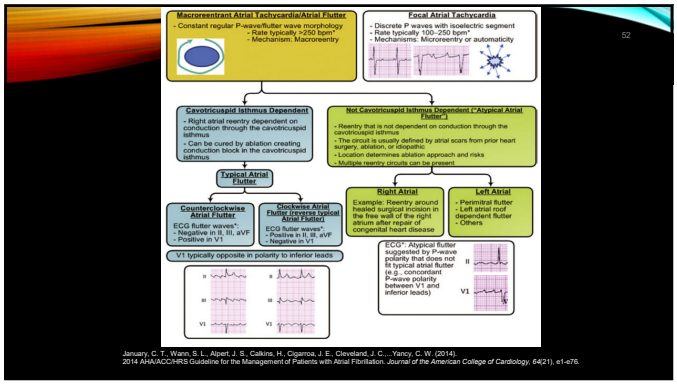
- Described in terms of duration
  - Paroxysmal
    - AF terminates spontaneously or with intervention within 7 days of onset. Episodes may reoccur
  - Persistent
    - Continuous AF > 7 days
  - Long Standing Persistent
    - Continuous AF > 12 months
  - Permanent
    - Joint decision to stop further attempts to maintain sinus

January, C. T., Wann, S. L., Alpert, J. S., Calkins, H., Cigarroa, J. E., Cleveland, J. C., ...Yancy, C. W. (2014). 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation. *Journal of the American College of Cardiology, 64*(21), e1-e76.

AANP 2015

BIG NEWS

- The Term "*nonvalvular AF*" is no longer used



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January, C. T., Wann, S. L., Alpert, J. S., Calkins, H., Cigarroa, J. E., Cleveland, J. C.,...Yancy, C. W. (2014). 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation. *Journal of the American College of Cardiology, 64*(21), e1-e76.

PROGNOSIS

53

- AF is associated with an increased long term risk of stroke
- AF is associated with an increased risk for developing HF
- AF is associated with all cause mortality, especially in women
- AF patients have double the mortality rate as compared with those in sinus rhythm

Fuster, V., Ryden, L. E., Cannom, D. S., Crijns, H. J., Ellenbogen, K. A., Halperin, J. L.,...Wann, L. S. (2011). 2011 ACCF/AHA/HRS Focused Updates Incorporated Into the ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation. *Journal of the American College of Cardiology, 57*(11), e101-e198.

PROGNOSIS

54

- The rate of ischemic stroke among patients with nonvalvular AF avg 5% per year
- AF is a strong independent risk factor for mortality
- One and six strokes occurs in patients with AF
- In HF studies, the annual risk due to AF was 1.5% in persons 50-59 and 23.5% in ages 80-89

Fuster, V., Ryden, L. E., Cannom, D. S., Crijns, H. J., Ellenbogen, K. A., Halperin, J. L.,...Wann, L. S. (2011). 2011 ACCF/AHA/HRS Focused Updates Incorporated Into the ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation. *Journal of the American College of Cardiology, 57*(11), e101-e198.

ETIOLOGIES AND FACTORS PREDISPOSING TO A FIB

- Electrophysiological abnormalities
  - Enhanced automaticity (focal AF)
  - Conduction abnormality (re-entry)
- Atrial pressure elevation
  - Mitral or tricuspid valve disease
  - Myocardial disease (systolic or diastolic disease)
  - Semi lunar Valvular abnormalities (causing ventricular hypertrophy
  - Systemic or pulmonary HTN (pulmonary Hypertrophy)
  - Intracardiac tumors or thrombi

Foster, V., Ryden, L. E., Cannom, D. S., Crijns, H. J., Ellenbogen, K. A., Halperin, J. L., ... Wann, L. S. (2011). 2011 ACCF/AHA/HRS Focused Updates Incorporated Into the ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation. Journal of the American College of Cardiology, 57(11), e101-e198.

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ETIOLOGIES AND FACTORS PREDISPOSING TO A FIB

- Atrial Ischemia
  - CAD
- Drugs
  - Alcohol
  - Caffeine
  - Illicit drugs
- Endocrine
  - Hyperthyroidism
  - Pheochromocytoma
- Inflammatory or infiltrative disease
  - Pericarditis
  - Amyloidosis
  - Myocarditis
  - Age-induced atrial fibrotic changes

Foster, V., Ryden, L. E., Cannom, D. S., Crijns, H. J., Ellenbogen, K. A., Halperin, J. L. Wann, L. S. (2011). 2011 ACCF/AHA/HRS Focused Updates Incorporated Into the ACC/AHA/ESC 2006 Guidelines for the Management of Patients with Atrial Fibrillation. Journal of the American College of Cardiology, 57(11), e101-e198.

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ETIOLOGIES AND FACTORS PREDISPOSING TO A FIB

- Changes in autonomic tone
  - ↑ parasympathetic activity
  - ↑ sympathetic activity
- Primary or metastatic diseases in or adjacent to the atrial wall
- Postoperative
  - Cardiac, pulmonary, esophageal
- Congenital heart disease
- Neurogenic
  - SAH
  - Non-hemorrhagic, major stroke
- Idiopathic
- Familial AF
- Renin-Angiotensin-Aldosterone System

January, C. T., Wann, S. L., Alpert, J. S., Calkins, H., Cigarroa, J. E., Cleveland, J. C., ... Yancy, C. W. (2014). 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation. Journal of the American College of Cardiology, 64(21), e1-e76.

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PATHOLOGY OF THROMBUS FORMATION

- Thrombotic material associated with AF most frequently is due turbulent flow in LAA
- This is not seen using transthoracic echo
- For AF that is > 48 hours long, risk increases
- Virchow's triad of stasis applies
  - Triad of stasis
  - Endothelial dysfunction
  - Hypercoagulable state

Geerts WH, Bergqvist D, Pineo GF et al. Prevention of venous thromboembolism: American College of Chest Physicians evidence-based clinical practice guidelines (8th Edition). Chest 2008;133:381S–453S.

59

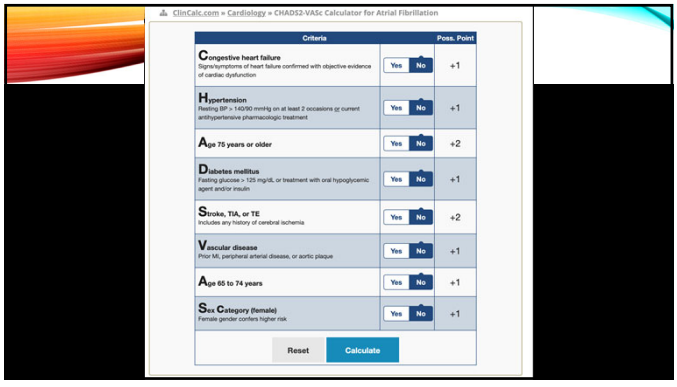
ASSESSING STROKE RISK

$CHADS_2$ -> CHA_2DS_2VASc

CHADS2 Risk	Score	CHA2DS2-VASc Risk	Score
CHF	1	CHF or LVEF ≤ 40%	1
Hypertension	1	Hypertension	1
Age > 75	1	Age ≥ 75	2
Diabetes	1	Diabetes	1
Stroke or TIA	2	Stroke/TIA/ Thromboembolism	2
		Vascular Disease	1
		Age 65 - 74	1
		Female	1

From ESC AF Guidelines.
http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/guidelines-afib-FT.pdf

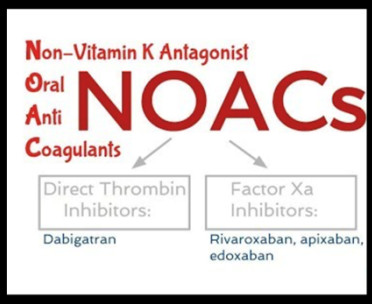
AANP 2015



SELECTION OF ANTITHROMBOTIC REGIMEN

- NOACs are recommended over Warfarin where eligible except in those patients with moderate – severe mitral stenosis or a mechanical valve

DRUGS APPROVED FOR AFIB



BALANCING RISKS AND BENEFITS

- For patient with AF and an elevated CHA_2DS_2-VASc score of 2 or greater in men or 3 or greater in women, oral anticoagulants are recommended I
  - Warfarin
  - Dabigatran
  - Rivaroxaban
  - Apixaban
  - Edoxaban

DRUG - Year (generic name)	Pradaxa - 2010 (dabigatran)	Xarelto - 2011 (rivaroxaban)	Eliquis - 2012 (apixiban)	Savaysa - 2015 (edoxaban)
MECHANISM	Direct thrombin inhibitor	Factor Xa inhibitor	Factor Xa inhibitor	Factor Xa inhibitoran
INDICATIONS	Nonvalvular a-fib VTE Rx & prevention	Nonvalvular a-fib VTE Rx & prevention	Nonvalvular a-fib VTE Rx & prevention	Nonvalvular a-fib
DOSING	A-fib: 150mg bid VTE: heparin x 5d then Pradaxa 150 bid VTE prevent: 150 bid	A-fib: 20mg qd VTE: 15mg bid x 21d then 20mg qd VTE prevent: 20 qd	A-fib: 5mg bid VTE: 10mg bid x 7d then 5mg bid VTE prevent: 2.5 bid	A-fib: 60mg qd iff CrCl 50-95
- Renal dosing	75mg bid if CrCl 15-30	15mg qd if CrCl 15-50	2.5mg bid if 2 of age ≥80, weight ≤60kg, Cr ≥1.5	30mg qd if CrCl 15-50
BLEED RISK	PMH: Age>75, cancer prior bleed Meds: NSAID, aspirin antiplatelet drug Lab: Cr>1.2, anemia	PMH: Age>75, cancer prior bleed Meds: NSAID, aspirin antiplatelet drug Lab: Cr>1.2, anemia	PMH: Age>75, cancer prior bleed Meds: NSAID, aspirin antiplatelet drug Lab: Cr>1.2, anemia	PMH: Age>75, cancer prior bleed Meds: NSAID, aspirin antiplatelet drug Lab: Cr>1.2, anemia
- Monitoring	High if PTT >2xULN or or if ECT >3xULN Thrombin time	Proportional to PT, anti-factor Xa assay	anti-factor Xa assay	Proportional to PT
INTERACTIONS	Ketoconazole, rifampin	Ketoconazole, rifampin, Ritonavir, verapamil, diltiazem, Tagamet,EES	Ketoconazole, rifampin, Ritonavir, itraconazole, Biaxin	rifampin
REVERSAL	Charcoal if took <2h Mod.: FFP 2-4u, IVF cryoprecipitate 10u Bad :Praxbind or PCC,	Charcoal if took <2h Mod.: FFP 2-4u cryoprecipitate 10u Bad :PCC, (factor 7)	Charcoal if took <2h Mod.: FFP 2-4u cryoprecipitate 10u Bad :PCC, (factor 7)	Charcoal if took <2h Mod.: FFP 2-4u cryoprecipitate 10u Bad :PCC, (factor 7)
- Dialysable?	Yes	No	No	No
- Half-life	~15 hours	~7 hours	~12 hours	~12 hours
OTHER	Higher risk of GI bleed	Avoid if ↑INR from liver disease		

Abbreviations: Cr = creatinine, CrCl = creatinine clearance, ECT = ecarine clotting time, FFP = fresh frozen plasma, PT = prothrombin time, PTT = , TT = thrombin time, ULN = upper limit of normal, VTE = venous thromboembolism

NOACS

Table 1: Laboratory Monitoring of NOACs

NOAC	Preferred Method	In an Emergency
Dabigatran	1. Ecarin clotting time 2. Dilute thrombin time	APPT (preferably with specific calibrated reagents)
Rivaroxaban	Anti-factor Xa	PT (preferably with specific calibrated reagents)
Apixaban	Anti-factor Xa	Dilute PT
Edoxaban	Anti-factor Xa	Few firm data

APTT = activated partial thromboplastin time; NOAC = non-vitamin K oral anticoagulant; PT = prothrobin time.

REVERSAL AGENTS

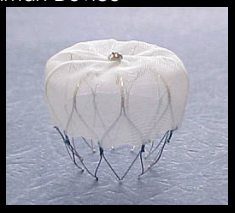
- Dabigatran
  - Idarucizumab I
- Apixaban and Rivaroxaban
  - Andexaet Alfa IIa

PERCUTANEOUS APPROACHES TO OCCLUDE THE LEFT ATRIAL APPENDAGE

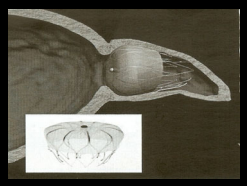
- Percutaneous LAAO should be considered for those AF patients at an increased risk of stroke who have contraindication to long-term anticoagulation and who are at high risk of thromboembolic events IIb

LEFT ATRIAL APPENDAGE DEVICE

Watchman Device



Placed in LAA



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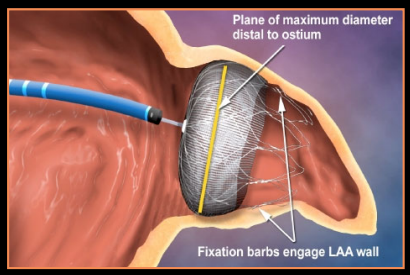
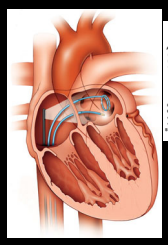
WATCHMAN LAA CLOSURE DEVICE IN SITU

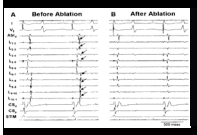


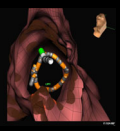
CATHETER ABLATION IN AFIB

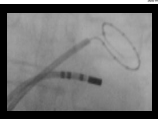
- Catheter ablation of AF is reasonable in symptomatic AF patient with HF and reduced LVEF IIa

PV ANTRUM ISOLATION: CATHETER ABLATION ICE+CIRCULAR MAPPING CATHETER









COMPLICATING ACUTE CORONARY SYNDROME

- If triple therapy is prescribed post-stent placement, clopidogrel is preferred over prasugrel IIa
- Double therapy with $P2Y_{12}$ inhibitor and dose adjusted vitamin K antagonist is reasonable in post-stenting IIa
- Double therapy with clopidogrel and low-dose rivaroxabn (15 mg daily) may be reasonable post-stenting IIa
- Double therapy with a $P2Y_{12}$ inhibitor and dabigatran 150 mg twice daily is reasonable post-stenting IIa
- If triple therapy is prescribed for patients with AF who are at increased risk of stroke and who have undergone PCI with stenting for ACS, a transition to double therapy at 4-6 weeks may be considered IIB

P2Y12 INHIBITORS

Table 4 Comparison of pharmacological characteristics of major P2Y12 receptor antagonists

Characteristics	Clopidogrel	Prasugrel	Ticagrelor	Cangrelor
Receptor blockage	Irreversible	Irreversible	Reversible	Reversible
Route of administration	Oral	Oral	Oral	Intravenous
Frequency	Once daily	Once daily	Twice daily	Continuous micropump infusion
Prodrugs	Yes	Yes	No[a]	No
Effective	2–8 h	30 min–4 h[b]	30 min–4 h[b]	2 min
Expiration	7–10 days	7–10 days	3–5 days	30–60 min
Interaction with CYP targeted drugs	CYP2C19	None	CYP3A4/5	None
Indications	ACS undergoing PCI and stable coronary heart disease	ACS undergoing PCI	All ACS	ACS undergoing PCI

[a], although most ticagrelor-mediated anti-platelet effects are immediate effects, about 30-40% of these effects originate from their active metabolite (AR-C124910XX); [b], depending on the clinical setting.

DEVICE DETECTION OF AF AND AFLUTTER

- In patient with cardiac implantable electronic devices, atrial high rate episodes (AHREs) should prompt further evaluation I

In patients with cryptogenic stroke in whom long-term external ambulatory monitoring is inconclusive, implantation of a cardiac monitor is reasonable to detect silent AF IIa

WEIGHT LOSS

- Weight Loss and risk factor modification is recommended for overweight/obese patients with Afib I

BALANCING RISKS AND BENEFITS LOE I

- NOACs are recommended over warfarin in NOAC- eligible patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve
- Among patients treated with warfarin, the INR should be determined at least weekly during initiation of OAC and at least monthly after achieving therapeutic range
- In patients with AF except with moderate-to-severe mitral stenosis or a mechanical heart valve, the CHA_2DS_2-VASc score is recommended for assessment of stroke
- For patients with AF who have a mechanical heart valve, warfarin is recommended
- Selection of anticoagulant should be based on the risk of thromboembolism, irrespective of whether the AF pattern is paroxysmal, persistent, or permanent

BALANCING RISKS AND BENEFITS LOE I

- Renal function and hepatic function should be evaluated before initiation of a NOAC and re-evaluated at least annually
- In patients with AF, anticoagulant therapy should be individualized on the basis of shared decision-making after discussion of the absolute risks and relative risks of stroke and bleeding, as well as the patient's values and preferences
- Patients with atrial flutter, anticoagulant therapy is recommended according to the same risk profile used for AF
- Patients with AF excluding those with moderate-severe mitral stenosis or mechanical heart valve, who are unable to maintain a therapeutic INR with Warfarin, use of a NOAC is recommended

BALANCING RISKS AND BENEFITS

- For patients with AF (excluding moderate-severe mitral stenosis or mechanical heart valve and a CHA_2DS_2-VASc score of 0 in men and 1 in women, it is reasonable to omit anticoagulant therapy

BALANCING RISKS AND BENEFITS

- Patients with AF with a CHA_2DS_2-VASc score of 2 or greater in men or 3 or greater in women and who have end-stage CKD; Creatinine clearance < 15mL/mi or on dialysis, it may be reasonable to prescribe warfarin or apixaban
- Patient with AF (except with moderate to severe mitral stenosis or mechanical heart valve and moderate to sever CKD (serum creat >/= 1.5 mg/dL [apixaban], CrCl 15 to 30 mL/min [dabigatran] with elevated CHA_2DS_2-VASc score , treatment with reduced doses of direct throbin or factor Xa inhibitors may be considered

BALANCING RISKS AND BENEFITS

- Patients with AF except for moderate-to-severe mitral stenosis or a mechanical heart valve and CHA_2DS_2-VASc score of 1 in men and 2 in women, prescribing an OAC to reduce thromboembolic stroke risk may be considered
- End stage CKD or on dialysis, the direct thrombin inhibitor dabigatran or the factor Xa inhibitors rivaroxaban or edoxaban are not recommended due to lack of evidence that benefit exceeds risk
- Direct thrombin inhibitor dabigatran should not be used in patients with AF and a mechanical heart valve

BALANCING RISKS AND BENEFITS

- If interruption of oral anticoagulation is needed in patients with Chronic AF with a mechanical heart valve; unfractionated heparin or LMWH is recommended
- Any bridging should balance the risks of stroke and bleeding and the duration of time a patient will not be anticoagulated

OTHER CONSIDERATIONS

- Urgent direct-current CV of new-onset AF in the setting of ACS is recommended for hemodynamic compromise, ongoing ischemia, or inadequate HR control
- IV BB can be used for those not hemodynamically unstable or who have bronchospasm
- Administration of amiodarone or digoxin may be considered to slow a RVR response in patients with ACS and AF associated with severe LV dysfunction, HF, or hemodynamically unstable
- Nondihydropyridine CC may be considered to slow a RVR in patients with ACS and AF if no evidence of HF or hemodynamic instability

HF GUIDELINES

DEFINITION OF HEART FAILURE

- Complex clinical syndrome
- Result from any structural or functional impairment of ventricular filling or ejection of blood
- May result from disorders of the pericardium, myocardium, endocardium, heart valves, or great vessels or certain metabolic abnormalities

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2018 ACCF/AHA DEFINITIONS FOR HF

Classification	EF%	Description
I HF with reduced EF (HFrEF)	≤ 40	Referred to systolic HF
II HF with preserved EF (HFpEF)	≥ 50	Referred to diastolic HF
a. HFpEF, boderline	41-49	Intermediate group similar to HFrEF
b. HFpEF, improved	> 40	This subset of patients with HFpEF previously had HFrEF. They have improvement or recovered EF and may be clinically distinct from those with peristently preserved or reduced EF

Yancy et al. (2016)

DEFINITION OF HF

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms and Signs	Symptoms and Signs	Symptoms and Signs
	2	LVEF < 40%	LVEF 40 – 49%	LVEF > 50%
	3		1. Elevated Levels of NT-proBNP 2. At least on additional criterion: a. relevant structural heart disease (LVH &/or LAE) b. Diastolic dysfunction	1. Elevated levels of NT-proBNP 2. At least on additional criterion: a. Relevant structural heart disease (LVH &/or LAE) b. Diastolic Dysfunction

Poinkowski et al. (2016)

COMPARISON OF ACCF/ AHA STAGES OF HF AND NYHA FUNCTIONAL CLASSIFICATIONS

ACCF/AHA Stages of HF		NYHA Functional Classifications	
A	**At high risk for HF but without structural heart disease (HD) or symptoms of HF**	NONE	
B	Structural HD but without Signs or symptoms of HF	I	No limitations of physical activity.
C	Structural HD with prior or current Symptoms of HF	I	No limitations of physical activity
		II	Slight limitations
		III	Marked limitations
		IV	Limitations with any activity without symptoms of HF, or symptoms of HF at rest
D	Refractory HF requiring specialized interventions		Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest

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HEART FAILURE WITH PRESERVED EJECTION FRACTION HFMREF AND HFPEF AS DEFINED AS EF 40-71%

- Patients characterized by *preserved LV function* may not have an entirely normal EF
- Criteria to define the syndrome of HFpEF
  - Evidence of preserved or LVEF
  - Evidence of abnormal LV diastolic dysfunction determined by Doppler ECHO
  - Evidence of abnormal LV diastolic dysfunction by left heart catheterization

IMPORTANT RISK FACTORS

- Hypertension
  - Single most important modifiable risk factor
- Diabetes Mellitus
  - Obesity and insulin resistance
- Metabolic syndrome
  - Abdominal adiposity, hypertriglyceridemia, low HDL, HTN and Fasting Hyperglycemia
- Atherosclerotic Disease
  - Coronary, cerebral or peripheral blood vessel disease

MEASUREMENT OF NATRIURETIC PEPTIDES

- BNP or NT-proBNP levels *should be* assessed in all patients suspected of having HF **when the diagnosis is uncertain**
- BNP & NT-proBNP can be helpful with risk stratification
- Determination of BNP or NT-proBNP is ***not*** **recommended** as a routine part of evaluation for structural heart disease in patients at risk ***without*** signs/symptoms of HF

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SELECTED CAUSES OF AN ELEVATED BNP

Cardiac
HF, including RV syndrome Acute Coronary syndrome Hear Muscle disease, including LVH Valvular Heart diseases Atrial Fibrillation Cardiac Surgery CV
Noncardiac
Advanced age Anemia Renal failure Pulmonary: OSA, Severe pneumonia, PAH Critical illness Bacterial Sepsis Severe Burns Toxic Metabolic insults, including Cancer, Chemo and envenomation

BIOMARKERS BNP OR NT-PROBNP

- Ambulatory Patients
  - May be helpful with presentation of dyspnea to support clinical decision making
  - May be helpful in establishing prognosis in severity of chronic HF
- Hospitalized/Acute Care
  - Useful for clinical decision making if uncertain

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SELECTED CAUSES OF AN ELEVATED BNP

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OTHER BIOMARKERS THAT MAY BE HELPFUL

- Myocardial Injury: Troponin T or I
- Myocardial Fibrosis: soluble ST2 and Galectin-3
- HsCRP
- Oxidative Stress: Nitrous Oxide

CARDIAC IMAGING

CXR	TTE	TEE
• Safe accessible • Cost	• 2 & 3 dimensional • Method of choice	• Not ordered routinely • suspect of aortic dz

CARDIAC IMAGING

Stress Echocardiography	Cardiac MRI (CMR)	CT (SPECT)
• Assess for ischemic causes • Look for diastolic dysfunction	• Gold Standard • Good for assessing myocardial fibrosis • Differentiate ischemic vs non-ischemic	• Assess ischemia or viability • Good for detection of cardiac amyloidosis

CARDIAC IMAGING

PET	Heart Cath	CCTA
• Ischemia • Viability • Limited availability • Radiation exposure	• HF that is determined to be ischemic • Considered for patients with High test probability of CAD	• Low intermediate pre test probability of CAD in patients with HF • Non-invasive means to visualize coronary anatomy in patients with HF

RECOMMENDATIONS TO PREVENT OR DELAY OVERT HF

- Treat HTN aggressively (IA)
- Treat with Statins (I A)
- Smoking cessation (I A)
- Treat risk factors (IIa C)

RECOMMENDATIONS TO PREVENT OR DELAY OVERT HF

- For DM TII consider starting Empagliglozin (IIa C)
- Start an ACE-I for asymptomatic pts with and without h/o MI (I C)
- ACE-I Should be started in patients with stable CAD to prevent HF (IIa B)
- Beta blockers started in asymptomatic LV Systolic dysfunction & h/o MI to prolong life (I B)

RECOMMENDATIONS TO PREVENT OR DELAY OVERT HF

- ICD recommended in patients (I B)
  - Asymptomatic LVEF ≤ 30% d/t ischemia who are at least 40 days post acute MI
  - Asymptomatic NICM ≤30% who receive OMT to prevent SCD

MEDICATIONS

- ACE/ARB
- Beta Blockers
- Aldosterone Antagonist
- Vasodilators
- Diuretics
- Digoxin
- ARNI

ACE Inhibitors and ARBs used in HF

Drug	Initial Daily Dose	Maximum Dose
Ace Inhibitors		
Captopril	6.25 mg tid	50 mg tid
Enalapril	2.5 mg bid	10 to 20 mg bid
Fosinopril	5 to 10 mg daily	40 mg daily
Lisinopril	2.5 to 5 mg daily	20 to 40 mg daily
Perindopril	2 mg daily	8 to 16 mg
Quinapril	5 mg daily	20 mg daily
Ramipril	1.25 to 2.5 mg daily	10 mg daily
Trandolapril	1 mg daily	4 mg daily
ARBs		
Candesartan	4 to 8 mg daily	32 mg daily
Losartan	25 to 50 mg daily	50 go 150 mg daily
Valsartan	20 to 40 mg bid	160 mg bid

Yancy et al. (2017)

ACE INHIBITOR OR ARB

- Start Low and titrate to target dose
- Assess renal function and potassium within 7-10 days of starting and uptitrating
- Need to be cautious in the elderly due to orthostatic hypotension
- Class effect

- Cautions and contraindications
  - Creat $\geq$ 3 mg/dl
  - K > 5.0 mEq/L
  - Systolic < 80 mm/Hg
  - Bilateral RAS

BETA BLOCKERS

- Can not assume class effect
- Bisoprolol-β1
  - CIBIS III RCT - 2005
- Metoprolol Succinate – β1
  - MERIT-HF RCT - 1999
- Carvediolol – β1, β2, a1
  - CAPRICORN RCT – 2001
  - Comet RCT - 2003

- Unless in HF, initiate prior to starting or getting to target dose of ACE or ARB
- Use cautiously in acute HF unless due to tachyarrhythmia
- If hypotension occurs use opposite of ACE
- Fatigue is guaranteed but evaluate for other causes.

Yancy et al. (2017)

RESEARCH BASED BETA BLOCKERS AND DOSES

Drug	Initial daily dose	Maxium dose(s)
Beta Blockers		
Bisoprolol	1.25 mg daily	10 mg daily
Carvedilol	3.125 mg bid	50 mg bid
Carvedilol	10 mg daily	80 mg daily
Metoprolol Succinate (CR/XL)	12.5 to 25 mg daily	200 mg daily

Yancy et al. (2017)

ALDOSTERONE ANTAGONIST

- ACCF/AHA 2013 HF guidelines
- Class I, A Recommendation
- LVEF ≤ 35% with NYHA Class II-IV HF to reduce Morbidity and mortality
- Creatinine should be less than 2.5 mg/dl or < for men and less than 2.0 mg/dl or < in women or GFR > 30 mL/min/1.73m^2

ALDOSTERONE CLINICAL EFFECTS AND WHY WE WANT TO BLOCK IT'S AFFECTS

- Promotes retention of Sodium
- Promoted loss of potassium and magnesium
- Potentiates catecholamines
- Inhibits the parasympathetic nervous system
- Decreases arterial compliance
- Promotes direct remodeling
- Has prothrombotic properties
- Causes vascular inflammation and injury

ALDOSTERONE ANTAGONISTS

- The landmark RALES trial (**R**andomized **A**ldactone **E**valuation **S**tudy) showed a 30% reduction in all-cause mortality as well as a reduced risk of SCD and HF hospitalizations with the use of spironolactone in patients with chronic HFrEF and LVEF < 35%. Eplerenone has been shown to reduce all-cause deaths, CV deaths, or HF hospitalizations in wider range of patient with HF*r*EF.

ALDOSTERONE ANTAGONISTS

Drug Dosing for Aldosterone Receptor Antagonists

	Eplerenone		Spironolactone	
eGFR (mL/min/1.73 m²)	≥ 50	30 to 49	≥ 50	30 to 49
Initial dose (only if K^+ ≤ 5 mEq/L)	25 mg daily	25 mg QOD	12.5 to 25 mg daily	12.5 mg daily or QOD
Maintenance dose (after 4 wk for K^+ ≤ 5 mEq/L)	50 mg daily	25 mg daily	25 mg daily	12.5 to 25 daily

Adapted from Butler et al.

Yancy et al. (2017)

MONITORING FOR ALDOSTERONE ANTAGONIST

- To reduce the delay in onset: may load with dosing 2-3 times daily for FIRST day
- Stop or interrupt therapy if Potassium is > 5 mEq/L or Serum Creatinine is > 4 mg/dl
- If GFR is 31-50ml/min use lowest dose
- If GFR is < 30ml: DO NOT USE
- K levels and renal function should be monitored at 3 days, 1 wk, after initiation or increase, then 2-4 weeks for 3 months, then q 3 months for the first year then twice yearly
- When monitoring Renal function and considering for HF treatment
  - Creat should be ≤ 2.5 mg/dl in men
  - Creat should be ≤ 2 mg/dl in women

HYDRALAZINE AND ISOSORBIDE DINITRATE

- Class I LOE A
  - The combination of hydralazine and isosorbide dinitrate is recommended to reduce morbidity and mortality for African Americans with NYHA class III – IV HFrEF receiving optimal therapy with ACE Inhibitors and beta blockers, unless contraindicated
- Class IIa LOE B
  - A combination of hydralazine and isosorbide dinitrate can be useful to reduce morbidity and mortality in patients with current or prior symptomatic HFrEF who cannot be given an ACE Inhibitor or ARB because of drug intolerance, hypotension or renal insufficiency, unless contraindicated

Yancy et al. (2017)

HYDRALAZINE AND ISOSORBIDE DINITRATE

Fixed Dose Combination	37.5 mg hydralazine/20mg isosorbide dinitrate 3 times daily	75 mg hydralazine/40 mg isosorbide dinitrate 3 times daily	225 mg hydralazine/90 mg isosorbide dinitrate daily
Hydralazine and Isosorbide dinitrate	Hydralazine: 25 mg to 50 mg, 3 -4 times daily and isosorbide dinitrate: 20 to 30 mg 3 to 4 times daily	Hydralazine: 300 mg daily in divided doses and isosorbide dinitrate: 120 mg daily in divided doses	NA

Yancy et al. (2017)

ETICS

Drug	Initial Daily Dose	Maximum Total daily Dose	Duration of Action
Loop diuretics			
Bumetanide	0.5 to 1.0 once or twice	10 mg	4-6 hours
Furosemide	20 to 40 mg once or twice	600 mg	6—8 hours
Torsemide	10 to 20 mg once	200 mg	12-16 hours
Thiazide Diuretics			
Chlorothiazide	250 to 500 mg once or twice	1000mg	6-12 hours
Hydrochlorothiazide	25 mg once or twice	200 mg	6-12 hours
Chlorthalidone	12.5 to 25 mg once	100 mg	24-72 hours
Indapmide	2.5 mg once	5 mg	36 hours
Metolazone	2.5 mg once	20 mg	12 – 24 hours
Potassium Sparing Diuretics			
Amiloride	5 mg once	20 mg	24 hours
Spironolactone	12.5 to 25 mg once	50 mg	1-3 hours
Triamterene	50 to 75 mg twice	200 mg	7-9 hours
Sequential nephron blockade			
Metolazone	2.5 to 10 mg once plus loop diuretic	NA	NA
Hydrochlorothiazide	25 to 100 mg once or twice plus loop diuretic	NA	NA
Chlorothiazide (IV)	500 to 1000 mg once plus loop diuretic	NA	NA

Yancy et al. (2017)

DIURETIC THERAPY

Considerations

- Outpatient weight loss of 0.5 to 1.0 kg per day
- Adjustable diuretic dosing
- Use with moderate sodium restriction

Diuretic Resistance

- Reasons
  - High sodium intake
  - NSAIDS
  - Severe Renal impairment
  - Renal hypoperfusion
- Strategies
  - IV
  - Different Loop
  - Addition of Thiazide diuretic

LOOP DIURETICS

	Bumetanide	Furosemide	Torsemide
Equivalent doses	1 mg	40 mg	20 mg
Escalating dosing outpatient	Double home dose for 3-5 days	Double home dose for 3-5 days	Double home dose for 3-5 days
Escalating dosing inpatient	PO dose to IV and administer daily, increase to desired affect	PO dose to IV and administer twice daily (better absorption if dosed twice daily if GFR low)	PO dose IV once daily, increase to desired affect
Monitor lytes	Baseline and with change in dosing or daily if hospitalized	Baseline and with change in dosing or daily if hospitalized	Baseline and with change in dosing or daily if hospitalized

Yancy et al. (2017)

DIGOXIN

- Digoxin can be beneficial in patients with HFrEF, unless contraindicated, to decrease hospitalization
- Consider for selected patients
- Treatment for 1-3 months can often improve symptoms, HRQOL and exercise tolerance
- Should be on other GDMT first and added later
- Do not use in patients with significant AV block unless they have a PPM
- Use cautiously with other meds that can depress the AV node function or affect Digoxin levels (amiodarone or a beta blocker)

DIGOXIN MONITORING AND CONSIDERATIONS

- GFR > 50 mL/min: no dosage adjustment
- GFR 10-50 mL/min: reduce 25-75% of normal dose
- GFR < 10 mL/min: reduce 10-25% normal dose
- Periodic ECG to assess for desired affect
- Digoxin serum levels should be drawn within 5-7 days
- After dose change: 7-10 days
- ESRD: may take 15-20 days to reach steady state

OTHER THINGS TO CONSIDER IN HF

- Anticoagulation may be considered in patients who have additional risk such as PAF, AF and risk for cardioembolic stroke *(Class I)*
- Selection of an anticoagulant for permanent or persistent AF should be based on each individual patient need (Class I)
- Recommend risk stratifying using $CHADS_2$ or CHADS2-VASc for OAC considerations
- Use of low-dose ASA in systolic HF patients with no prior MI or known CAD remains unknown
- Statins show no benefit for HF patients unless known to have HLP
- Omega-3 poly unsaturated fatty acid (PUFA) supplementation is reasonable to use for adjunctive therapy to reduce CV hospitalization
- Coenzyme Q 10, carnitine, taurine, and antioxidants: no added benefit to date

ARNI

- Sacubitril and Valsartan
  - Entresto
    - Angiotensin II Receptor Blocker
      - Inhibits vasoconstriction
    - Neprilysin Inhibitor
      - Prodrug, inhibits neprilysin via active metabolite LBQ657

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ARNI

- Disease related concerns and use with caution with the following
  - Aortic or mitral valve stenosis
  - Heart failure: Look at other meds, renal fx, hepatic fx
  - Hepatic impairment: moderate reduce dose
  - Renal artery stenosis; use with caution
  - Renal impairment: adjust dose
  - Elderly: Adjust for those ≥ 75

IVABRADINE CORLANOR

- Category: CV Agent I_f *Channel inhibitor*
- Use based on SHIFT trial
- Used for pts intolerant or unable to uptitrate traditional B blocker
- Used in pts with NYHC II-IV HFrEF (SHIFT < 35%)
- Affects SA node, not AV or IV Conduction
- Pure HR lowering drug, inhibiting cardiac pacemaker funny current
- May reduce HF readmissions

IVABRADINE CORLANOR

- Dosing
  - HF: 5 mg twice daily or 2.5 mg twice daily (h/o conduction defect) Max dose 7.5 mg BID
    - Watch for SA node dysfunction and bradycardia
  - Off label use: Stable Angina: 2.5 mg to max of 7.5 mg twice daily
    - Stop drug if angina not improved
  - No renal adjustments for CrCl ≥ 15 ml/min
  - Use with caution for CrCl < 15 ml/min

OTHER THINGS TO CONSIDER IN HF DRUGS AND THINGS THAT DO NOT PROVE THEY HELP HFREF

- Nutritional supplements as treatment for HF are not recommended
- Most Calcium Channel blockers except for Amlodipine
- Most antiarrhythmics, NSAIDS, or thiazolidinediones
- Long-term infused positive inotropic drugs unless used as palliation for ESD

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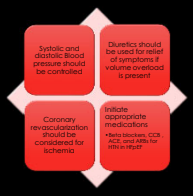
STRATEGIES FOR ACHIEVING OPTIMAL GDMT

- Uptitrate in small increments
- Strategize patients who may need more frequent visits
- Monitor VS
- Alternate adjustments of different medication classes
- Monitor Renal Function and electrolytes
- Patients may complain of symptoms of fatigue and weakness
- Discourage sudden DC of therapy
- Carefully review doses and other meds
- Consider temporary adjustments to uptitrate other meds
- Educate your patients and families

RECOMMENDATIONS FOR TREATMENT OF HFPEF



Yancy C et al. Circulation 2013;128:e240-e327

It should not be the symptoms
that trigger you to act,
but the science
that triggers you to think
early and often

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Thank you for listening
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