SARS-CoV-2 virus; COVID-19 illness, Cardiovascular Considerations

Management of Heart Failure and Cardiovascular Complications

- Updates and Review of HFrEF/HFpEF Inpatient and Outpatient Management

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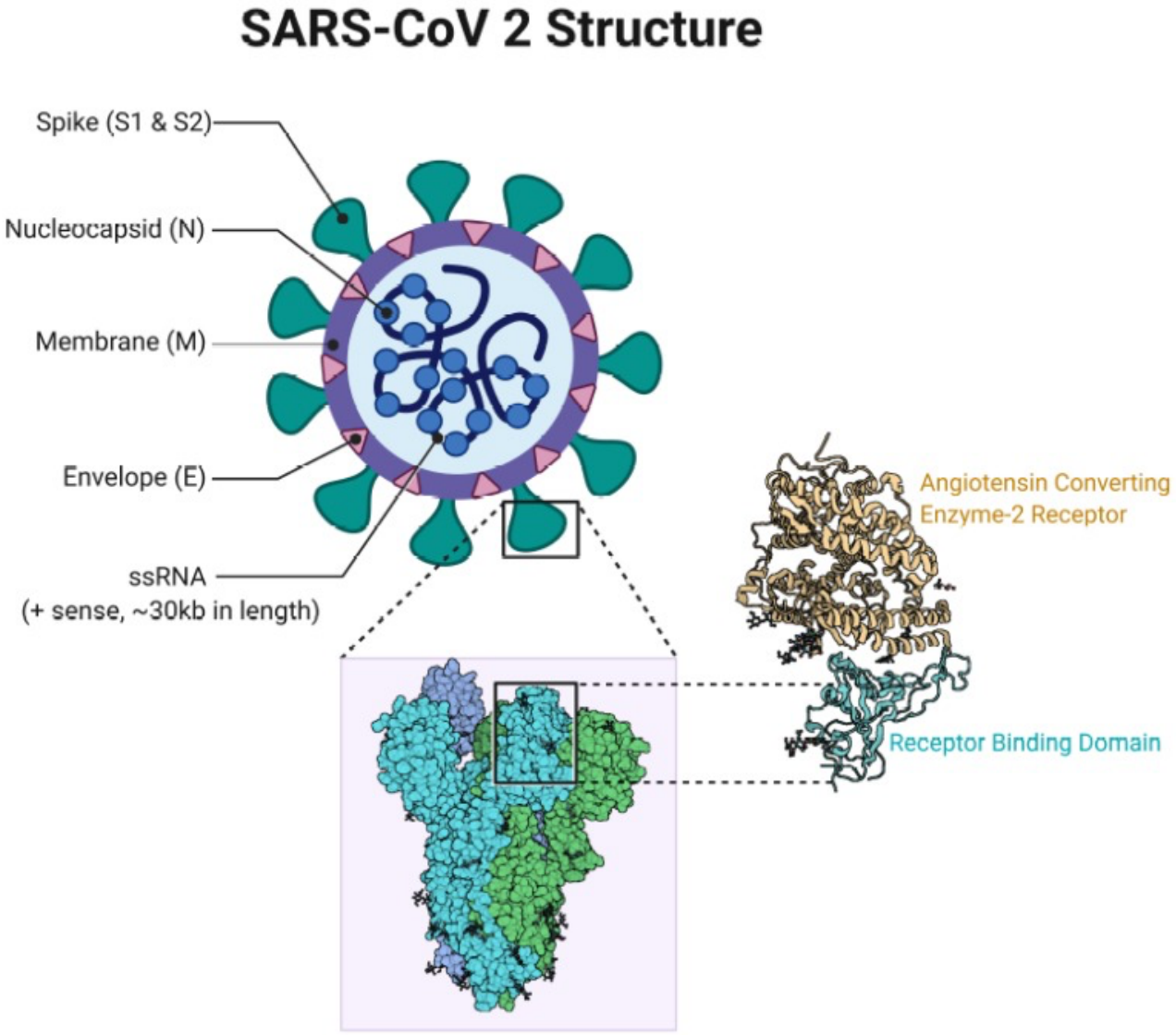
- 2 April 2020

SARS-CoV-2



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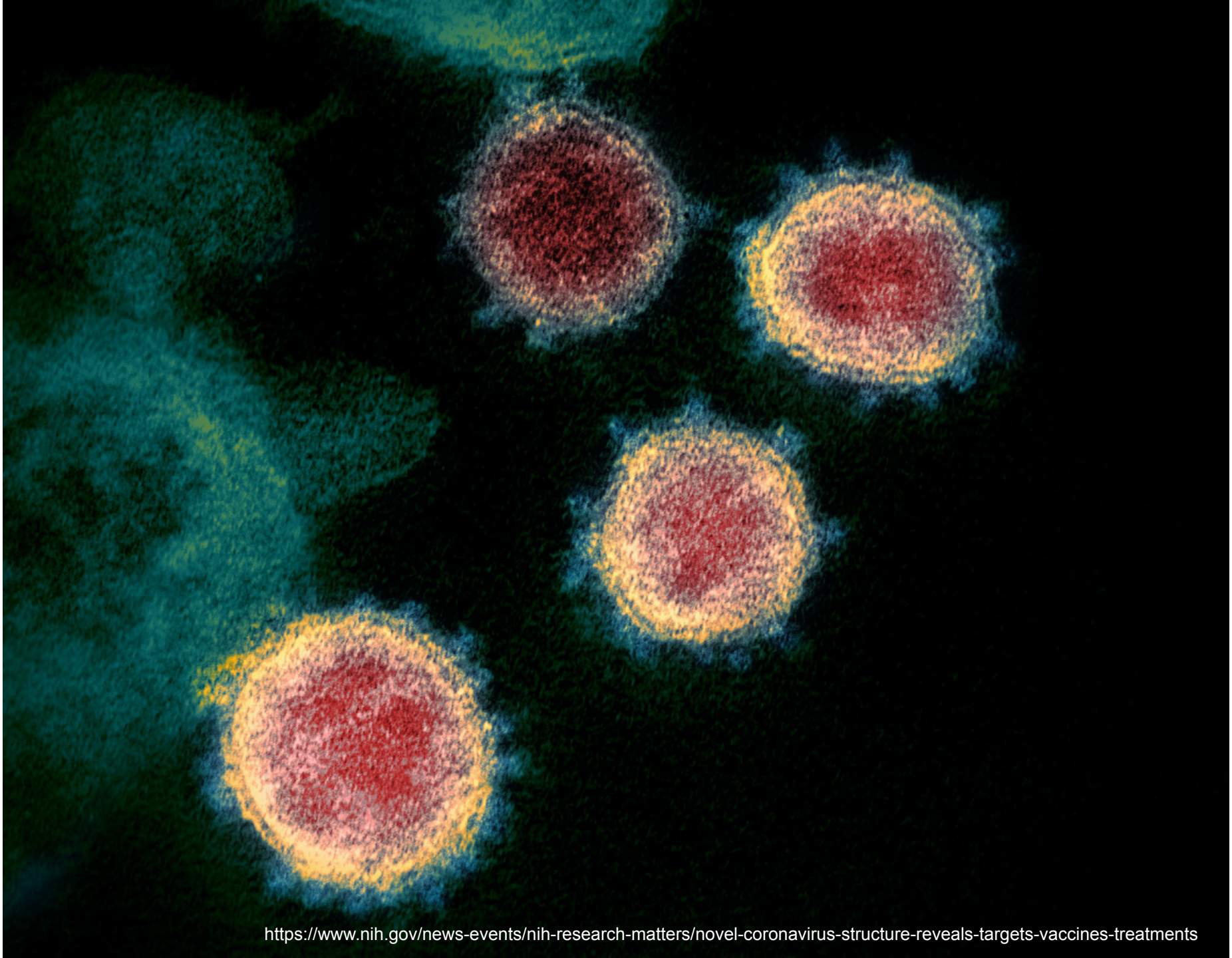


https://www.nih.gov/news-events/nih-research-matters/novel-coronavirus-structure-reveals-targets-vaccines-treatments

Modes of Transmission - WHO 29 Mar 2020

Community Modes of transmission of the COVID-19 virus
Respiratory infections can be transmitted through droplets of different sizes: when the droplet particles are >5-10 μm in diameter they are referred to as respiratory droplets, and when then are <5μm in diameter, they are referred to as droplet nuclei.[1] According to current evidence, COVID-19 virus is primarily transmitted between people through respiratory droplets and contact routes.[2-7] In an analysis of 75,465 COVID-19 cases in China, airborne transmission was not reported.[8]

Healthcare settings: **Airborne transmission may be possible in specific circumstances and settings** in which procedures or support treatments that generate aerosols are performed; i.e., endotracheal intubation, bronchoscopy, open suctioning, administration of nebulized treatment, manual ventilation before intubation, turning the patient to the prone position, disconnecting the patient from the ventilator, non-invasive positive-pressure ventilation, tracheostomy, and cardiopulmonary resuscitation.

In Italy and Spain, 8-12% of COVID cases are healthcare workers.

https://www.who.int/news-room/commentaries/detail/modes-of-transmission-of-virus-causing-covid-19-implications-for-ipc-precaution-recommendations

COVID-19 Resources

- https://www.cdc.gov/coronavirus/2019-nCoV/hcp/index.html
- https://www.who.int/health-topics/coronavirus#tab=tab_1
- https://www.naccho.org/membership/lhd-directory?searchType=standard&lhd-state=AK#card-filter

Clinical Practice Guidelines

- https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html
- https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19?topicRef=8350&source=related_link
- https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=17&cad=rja&uact=8&ved=2ahUKEwjlhIae-sfoAhXKPn0KHcyvBB8QFjAQegQIChAB&url=https%3A%2F%2Fhealth.mil%2FReference-Center%2FTechnical-Documents%2F2020%2F03%2F24%2FDoD-COVID-19-Practice-Management-Guide&usg=AOvVaw0Y1IaAlvOg9oKEf2H7D97a

Case Fatality Rates

- Subject to numerator/denominator
- Infection fatality rate is likely 0.7% or less
- Case Fatality Rate by Age (Chinese data)
- 80+, 0.148, 14.8%
- 70-79, 0.08, 8%
- 60-69, 0.036, 3.6%
- 50-59, 0.013, 1.3%
- 40-49, 0.004, 0.4%
- < 40, 0.002, < 0.2%

- Italian Data: 11264/11857 deaths 60+, 95%

https://www.statista.com/statistics/1105061/coronavirus-deaths-by-region-in-italy/

COVID-19 Symptoms (?% without robust symptoms, 15%, 25%, ??50% - unclear)

- Fever 91% (44% at admission, 89% developed a fever at some point in their hospitalization)
- Cough 67% (typically nonproductive, but varies)
- Fatigue 51%
- Dyspnea 30%
- Gastrointestinal up to 50%
- Anosmia/Dysgeusia
- Myalgias, Headache, Nasal Congestion, Pharyngitis, other

COVID-19 Testing and Imaging

- Initial CXR may not be abnormal
- CT is more sensitive (up to 97% in a study)
- https://www.escardio.org/Education/COVID-19-and-Cardiology
- https://www.youtube.com/embed/jcXiQo7NneM?rel=0&autoplay=1
- RT-PCR COVID-19 False Negative Rates may be 30% or higher

COVID-19 Cardiovascular Considerations

- Markedly Increased Risk of Morbidity and Mortality with Comorbid Illnesses (n=46 248)
- Hypertension, OR 2.36 for severe illness
- Diabetes, at least OR 1.6 (Chinese data, death 7.3% versus 0.9%)
- Obesity, elevated risk, BMI > 40 very high risk
- Respiratory System Illness, OR 2.46
- Ischemic Heart Disease
- Cardiomyopathy/Heart Failure, OR 3.42

COVID-19 Cardiovascular Considerations

- Published case reports from the Chinese Centers for Disease Control indicate patients with underlying comorbid conditions have a heighted risk for contracting COVID-19 and a worse prognosis; depending on the report, between 25% and 50% of COVID-19 patients present with underlying conditions
- Case fatality rates for comorbid patients are materially higher than the average population:

o Cancer: 5.6%
o Hypertension:6.0%
o Chronic respiratory disease: 6.3%
o Diabetes:7.3%
o Cardiovascular disease: 10.5%

https://www.acc.org/~/media/665AFA1E710B4B3293138D14BE8D1213.pdf

COVID-19 Cardiovascular Complications

- Acute myocardial injury - absence of hsTnT is an excellent prognostic feature
- (Peri?)myocarditis (LV/RV/BiV) - 7-33% of deaths
- Acute coronary syndrome (Type II NSTEMI)
- Arrhythmias (15-20% overall) (45-50% in the ICU)
    - Tachyarrhythmias (all kinds)
    - Bradyarrhythmias (sinus arrest, heart block, asystole)
- Takotsubo-like syndrome
- Heart failure, up to 25% (52 versus 12%, nonsurvivors/ survivors)

http://www.onlinejacc.org/content/accj/early/2020/03/18/j.jacc.2020.03.031.full.pdf

Testing Considerations

- D-Dimer (> 1gm/L) OR 18.4 for non survival
- 71% of non survivors met criteria for DIC
- Elevated hsTnT predicts more severe illness and non survival
- Elevated BNP

Treatment Considerations

- Simvastatin is contraindicated with lopinavir/ritonavir. Use atorvastatin and rosuvastatin at reduced dose.
- Remdesivir - unknown cardiac effects. 1/175 pts loaded during the Ebola crisis had hypotension and cardiac arrest
- chloroquine results in CYP2D6 inhibition; beta-blockers metabolized via CYP2D6 (such as metoprolol, carvedilol, propranolol, or labetalol) can have increased concentration of drug requiring careful monitoring for heart rate and blood pressure
- Rare risk of TdP with hydroxychloroquine and chloroquine
- ACE/ARB agents - may be protective? Continued therapy is recommended for compelling indications. No increased adverse outcomes noted when data were adjusted. Hold for typical reasons.
- NSAIDs are heart poison, regardless of COVID-19. Avoid use in cardiac patients as you would normally.
- NSAIDS most likely do not worsen outcomes in non cardiac patients.

Treatment Considerations

- Ribavirin has no direct cardiovascular toxicity
- lopinavir/ritonavir may result in QT and PR interval prolongation
- Hydroxychloroquine and Chloroquine may result in QTc prolongation
- Some risk factors for QT prolongation: ETOH use, LVH, structural cardiac disease, behavioral health medications
- Antivirals may interact with DOACs, warfarin
- lopinavir/ritonavir may lead to clopidogrel ineffectiveness

Other Recommendations

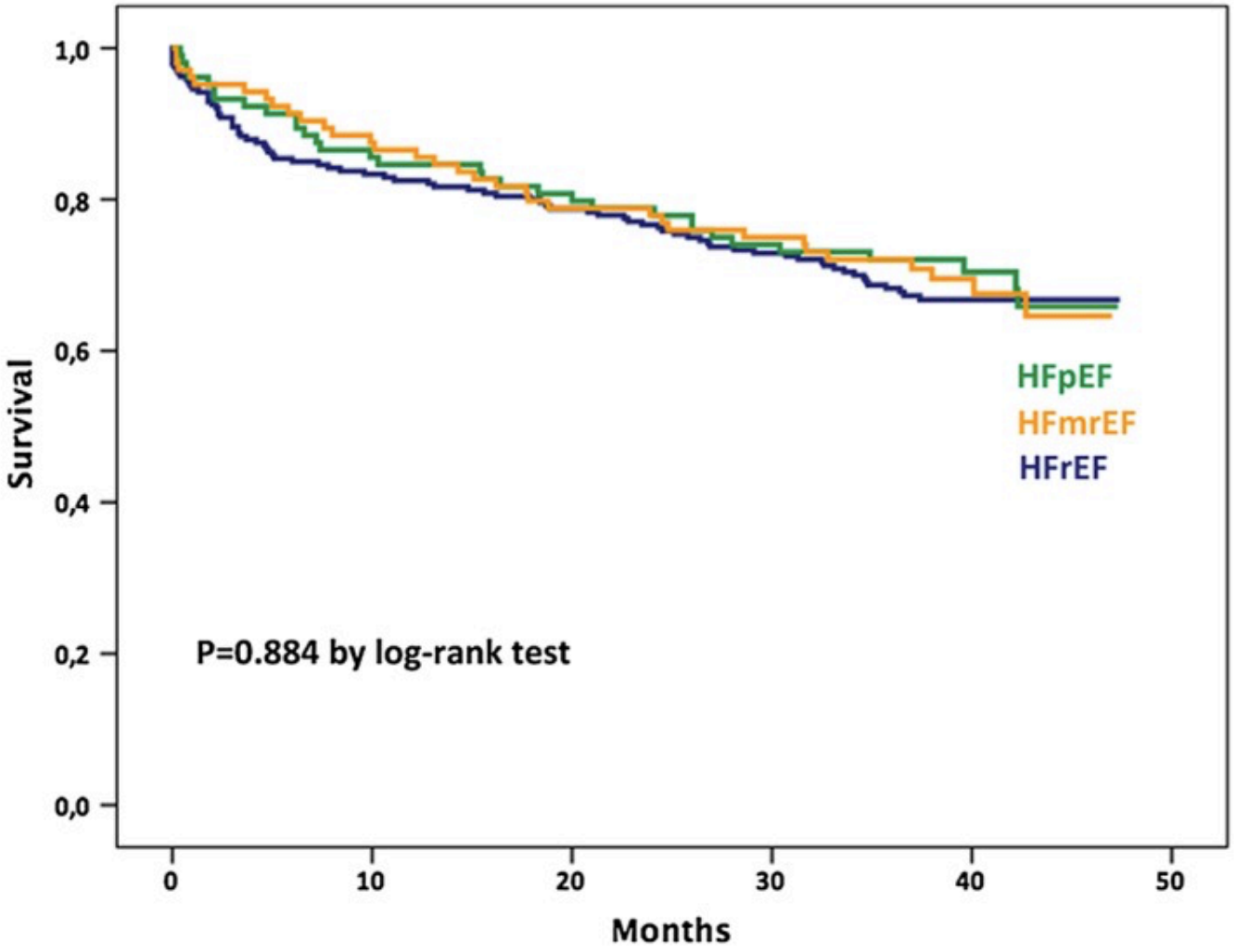
- Seasonal influenza vaccination rates for adults are 45% in the US (only slightly higher in high risk patients)
- Coinfection has been reported and may impact severity
- Alaska has one of the lowest adult influenza vaccination rate (approximately 40%), AN/AI adults (37.6%)
- Pneumococcal vaccine rate > 65y/o, 67%
- Patients will ask: should I wear a mask? High risk groups.
- Broad use of surgical masks might reduce transmission (influenza data).
- Not generally effective to protect an individual patient FROM the illness, but will reduce viral shedding into the environment from ill patients (influenza data)
- Broad use of N95 masks would very likely reduce transmission, but would exacerbate shortages in healthcare facilities. N2 rated: Much more effective in preventing infection in an individual high risk patient when used properly.
- CDC is reviewing recommendations for SARS-CoV2 mask wear by the public
- https://www.cdc.gov/flu/professionals/infectioncontrol/maskguidance.htm

https://www.cdc.gov/flu/fluvaxview/coverage-1819estimates.htm https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3591312/

CURRENT HEART FAILURE TERMINOLOGY (ACC/ESC)

- HFrEF - heart failure reduced ejection fraction
- HFpEF - heart failure preserved ejection fraction
- HFiEF - heart failure improved ejection fraction
- HFrecEF - heart failure recovered ejection fraction
- HFmrEF - heart failure midrange ejection fraction

Figure 2



Kaplan–Meier survival curves for patients with heart failure and reduced, mild, range or preserved ejection fraction.

ESC Heart Fail. 2017 May; 4(2): 99–104.

HFPEF

- Visually normal ejection fraction, 50%+
- Classic case: elderly woman with hypertension
- Treat underlying and exacerbating conditions
- Do not use: digoxin, nitrates, PDE-Is for HFpEF (ineffective or harm)
- Volume management
- TOPCAT trial supports MRAs for reduction in hospitalization risk, if: eGFR > 30mL/min, K < 5, BNP elevated, and pt can be monitored closely. Hyperkalemia risk of nearly 20%.

HF$_{mr}$EF

- Mildly reduced ejection fraction, 40-50%
- Similar to HFpEF
- Treat underlying and exacerbating conditions
- If HFrEF->HFiEF/HFmrEF, continue GDMT medications.
- Volume management

HF$_{REC}$EF

- LVEF was less than 50%, now >50%
- Should we stop their medications?
- We were data deficient. Then came a landmark 51 patient trial.
- TRED-HF (pilot)
- https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(18)32825-3/fulltext
- Half deteriorated. Do not stop their medications (for now).
- Caveats and exceptions.

SGLT2 INHIBITORS

- Increased urinary glucose excretion
- Lower blood pressure
- No significant change in cholesterol
- Nephroprotective: macroalbuminuria 5, creatinine 1.1, RRT 0.3
- In patients in the EMPA-REG trial (high risk for CV events), decreased a composite endpoint by 1.6% ARR (driven by decreased CV death) (FDA label changed 2016)
- Decreased weight, waist circumference, uric acid

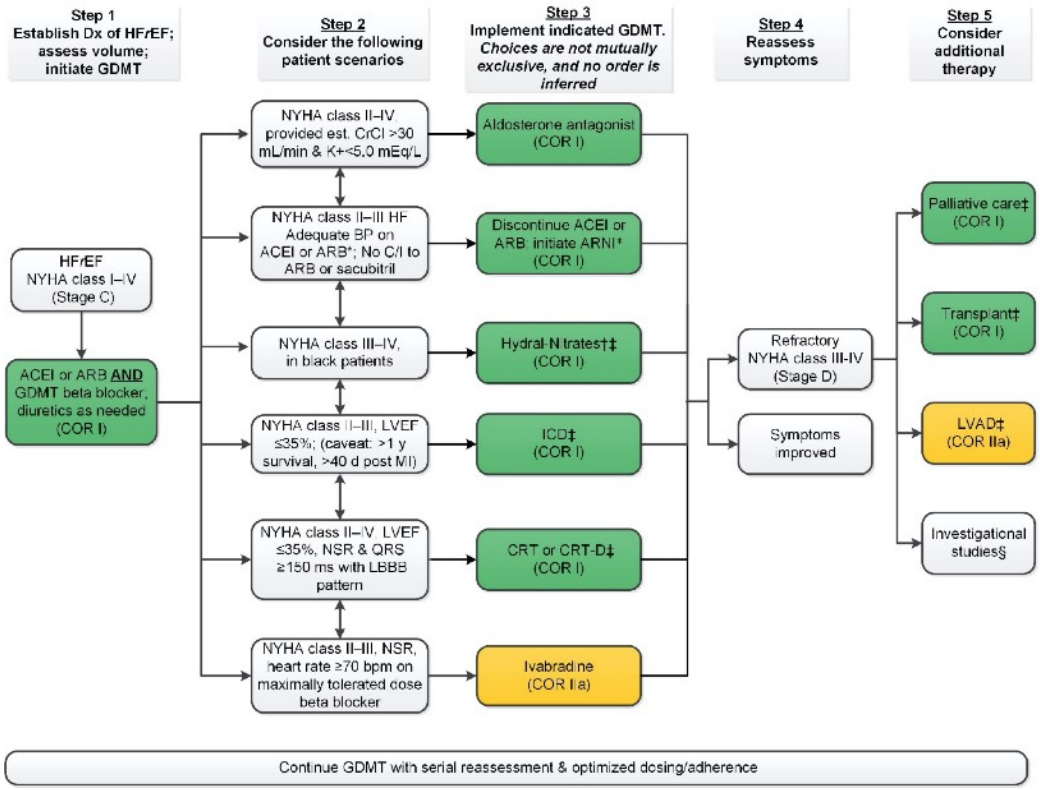
SGLT2 INHIBITORS - HEART FAILURE

- Diuretics
- Lower blood pressure
- DAPA-HF - reduced CHF adverse outcomes in non diabetics
- Dapagliflozin, Empagliflozin (secondary outcomes in EMPA-REG and DECLARE-TIMI)
- EMPEROR-Reduced, EMPEROR-Preserved (finishing Jun 20)
- Fast tracked Empagliflozin for review of CHF indication

AHA Heart Failure Stages

- STAGE A at risk – HTN, DM2, Drug use, Obesity, CAD, Valvular Heart Disease
- STAGE B Structural abnormalities without symptoms
    - Ex: Screening TTE, LVEF 40-45%, no symptoms, trastuzumab therapy
- STAGE C Clinical Heart Failure (symptoms past or present)
- STAGE D Refractory heart failure

Ambulatory Treatment of HFrEF Stage C and D



†Hydral-Nitrates green box: The combination of ISDN/HYD with ARNI has not been robustly tested. BP response should be carefully monitored.
‡See 2013 HF guideline.
§Participation in investigational studies is also appropriate for stage C, NYHA class II and III HF.
ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor-blocker; ARNI, angiotensin receptor-neprilysin inhibitor; BP, blood pressure; bpm, beats per minute; C/I, contraindication; COR, Class of Recommendation; CrCl, creatinine clearance; CRT-D, cardiac resynchronization therapy–device; Dx, diagnosis; GDMT, guideline-directed management and therapy; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; ICD, implantable cardioverter-defibrillator; ISDN/HYD, isosorbide dinitrate hydral-nitrates; K+, potassium; LBBB, left bundle-branch block; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSR, normal sinus rhythm; and NYHA, New York Heart Association.

2019 ACC Expert Consensus Decision Pathway on Risk Assessment, Management, and Clinical Trajectory of Patients Hospitalized With Heart Failure:

- Admission
- Trajectory Check
- Oral Therapies
- Discharge
- Follow-Up Visit

https://www.acc.org/latest-in-cardiology/ten-points-to-remember/2019/09/11/15/51/2019-acc-expert-consensus-decision-pathway-on-hf

Ten Points To Remember

1. Each stage of a heart failure admission is an opportunity to improve outcomes
   - admission/emergency department to the first post-discharge follow-up
2. Clinical trajectory of HF should be evaluated continuously during admission.
   1) improving towards target
   2) stalled after initial response
   3) not improved/worsening
   The major target of management is decongestion:
   improvement in signs and symptoms, decrease in natriuretic peptides, and decrease in weight.
3. Evaluation of the long-term trajectory of heart failure should be performed: initial assessment, review on the day of transition to oral therapy, re-assess at the first follow-up visit.

https://www.acc.org/latest-in-cardiology/ten-points-to-remember/2019/09/11/15/51/2019-acc-expert-consensus-decision-pathway-on-hf

Ten Points To Remember

4. Comorbid conditions, such as diabetes, pulmonary disease, renal disease, and frailty, is a key component of the comprehensive initial assessment. Comorbidities are highly prevalent in heart failure patients, increase heart failure severity, and contribute to decompensation
5. Risk factors, such as nonadherence, degree of decongestion, and appropriateness and tolerance of guideline-directed medical therapy: assess and mitigate
6. The transition day, when therapy changes from intravenous diuretics to oral, is a critical point
>>>Determining the effectiveness of the diuretic regimen is key. Observation on the intended discharge diuretic regimen for ≥24 hours is associated with significant reductions in 30- and 90-day mortality.<<<
Patient education, caregiver education, and plans for discharge should be arranged.

https://www.acc.org/latest-in-cardiology/ten-points-to-remember/2019/09/11/15/51/2019-acc-expert-consensus-decision-pathway-on-hf

Ten Points To Remember

7. Discharge day: avoid starting new therapies. Ensure that the follow up plan is assured. Educate again.
8. Discharge planning: Ensure that hospital course and trajectory are effectively communicated in documentation. Goals of care, consideration of palliative care should be communicated to the receiving outpatient team.
9. Post-discharge visit: ideally within 7 days; reassess, reeducate, review (medications), readmission (assess for risk).
10. Palliative care consultation is important to consider with an unfavorable trajectory

https://www.acc.org/latest-in-cardiology/ten-points-to-remember/2019/09/11/15/51/2019-acc-expert-consensus-decision-pathway-on-hf

Readmission Risk (20-30% within 30 days)

- This is a very vexing problem. Some of the best hospital systems have had significant difficulty impacting readmission rates.
- Inadequate decongestion is a significant predictor of readmission and death
- Diurese to a euvolemic state whenever possible. Review prior ‘dry’ weights, prior natriuretic peptide levels.

Reducing Readmission Strategies

- Schedule follow-up physician appointments;
- Provide one-to-one inpatient education;
- Make follow-up calls or have pts seen 24-72 hours postdischarge and again at 25-30 days post-discharge;
- Employing the teach-back approach; and
- Promote in-home follow up and teaching reinforcement with home care programs.

https://www.aha.org/case-studies/2014-10-10-reducing-heart-failure-readmissions

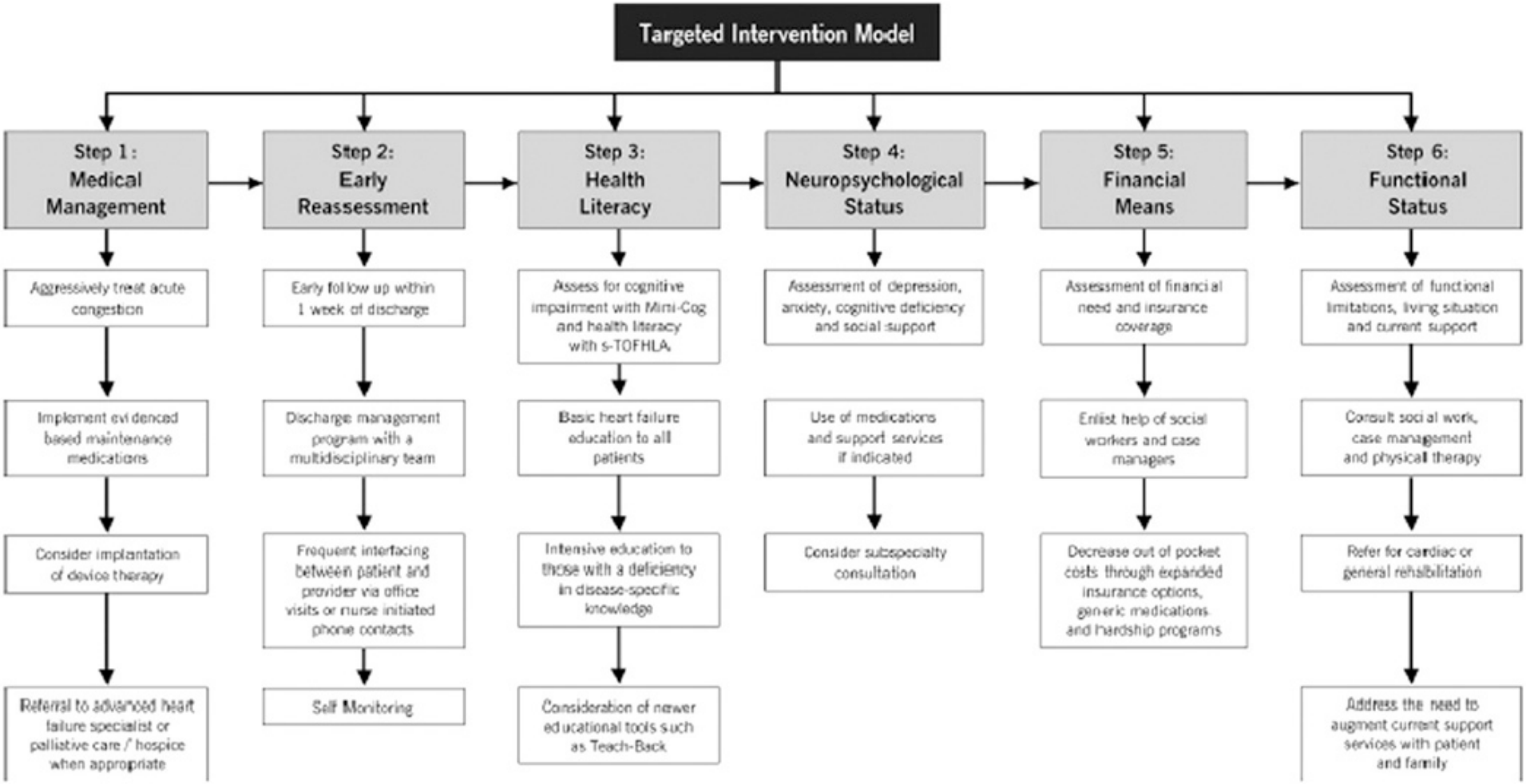


Fig. 2 Overview of a targeted intervention model

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4783289/

Heart Failure Toolkit Links

- American Heart Association
- https://www.heart.org/en/professional/quality-improvement/target-heart-failure/strategies-and-clinical-tools
- American College of Cardiology
- https://www.acc.org/tools-and-practice-support/clinical-toolkits/heart-failure-practice-solutions

Decongestion Strategies (1 of 2)

- Start early
- Give 2-2.5x their furosemide equivalent dose IV BID
- Example - oral furosemide dose 20mg
- Give 40mg IV BID (equivalent to 80mg po BID)
- Reassess in 30-90min
- Bolus dosing versus continuous (no difference)
- Up to 3-5L/first day, subsequent days as tolerated by BP
- BUN/Creatinine may rise, stay the same, or decrease
- Undertreatment is more common than over treatment

https://acphospitalist.org/archives/2018/09/does-door-to-diuretic-time-matter.htm

Decongestion Strategies (2 of 2)

- Role of intravenous nitrates:
  - Hypertensive patients
  - Some evidence for benefit, increased diuretic response
  - Initial dose: 5-10mcg/min NTG (range 10-200mcg/min)
  - Avoid with tachycardia, RV failure, obstructive valve disease
- Goals: JVP < 8cm H_2O, hemoconcentration, trace to no edema, no orthopnea
- Add MRA, thiazide for diuretic resistance or to help balance electrolytes
- Tolvaptan (consider in significantly hyponatremic patients), short term use

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4659502/

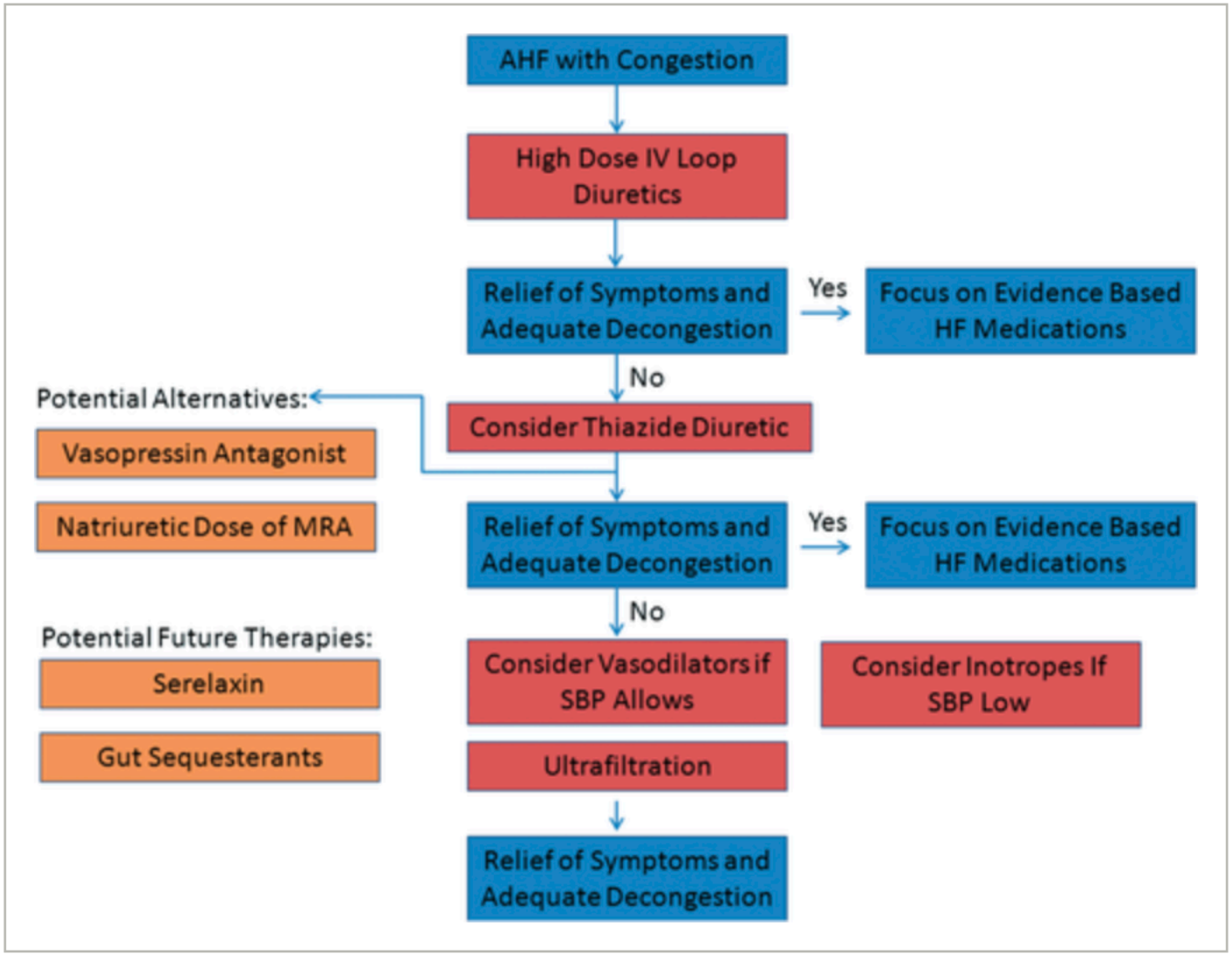


Figure 6

Open in figure viewer | PowerPoint

An approach to managing congestion in acute heart failure (HF) patients. MRA, mineralocorticoid receptor antagonist; SBP, systolic blood pressure.

Newer therapies: Ivabradine

- Inhibits the I_f or I_{kf} current (funny current) in the SA node
- Is not a beta blocker and does not appear to affect autonomic functions other than HR
- SR, HR > 70 on maximal medical therapy or intolerant of beta-blockers
- Not used in acute patients
- 2.5mg to 5mg BID
- Well tolerated; phosphenes (visual phenomena)

Pharmacological Treatment for Stage C HF With Reduced EF

Ivabradine

LOR: IIa	**LOE: B-R**	Ivabradine can be beneficial to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HF*r*EF (LVEF ≤35%) who are receiving GDEM*, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest.

*In other parts of the document, the term “GDMT” has been used to denote guideline-directed management and therapy. In this recommendation, however, the term “GDEM” has been used to denote this same concept in order to reflect the original wording of the recommendation that initially appeared in the “2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure”.

Neprilysin MMPE

- Neprilysin membrane bound metalloproteinase/ endopeptidase
- Probably modulates CHF via increasing the activity of the natriuretic peptide system (cannot follow BNP)
- Nesiritide as an isolated therapy did not improve outcomes
- Sacubitril/Valsartan is a neprilysin inhibitor plus a very bioavailable ARB

Paradigm HF

- Sacubitril/valsartan versus enalapril
- Was shown to be superior to ACE (enalapril)
- Decreased hospital admissions by 20% and all cause mortality by 18%
- Recommended by AHA/JACC guidelines in symptomatic NYHA Class 2/3 HFrEF pts
- MUST not be used with ACE-I (fatal in early studies of animals) Must stop ACE for 36 hours prior to starting sacubitril/ valsartan

SACUBITRIL/VALSARTAN - ACUTE HF PIONEER-HF TRIAL 2018

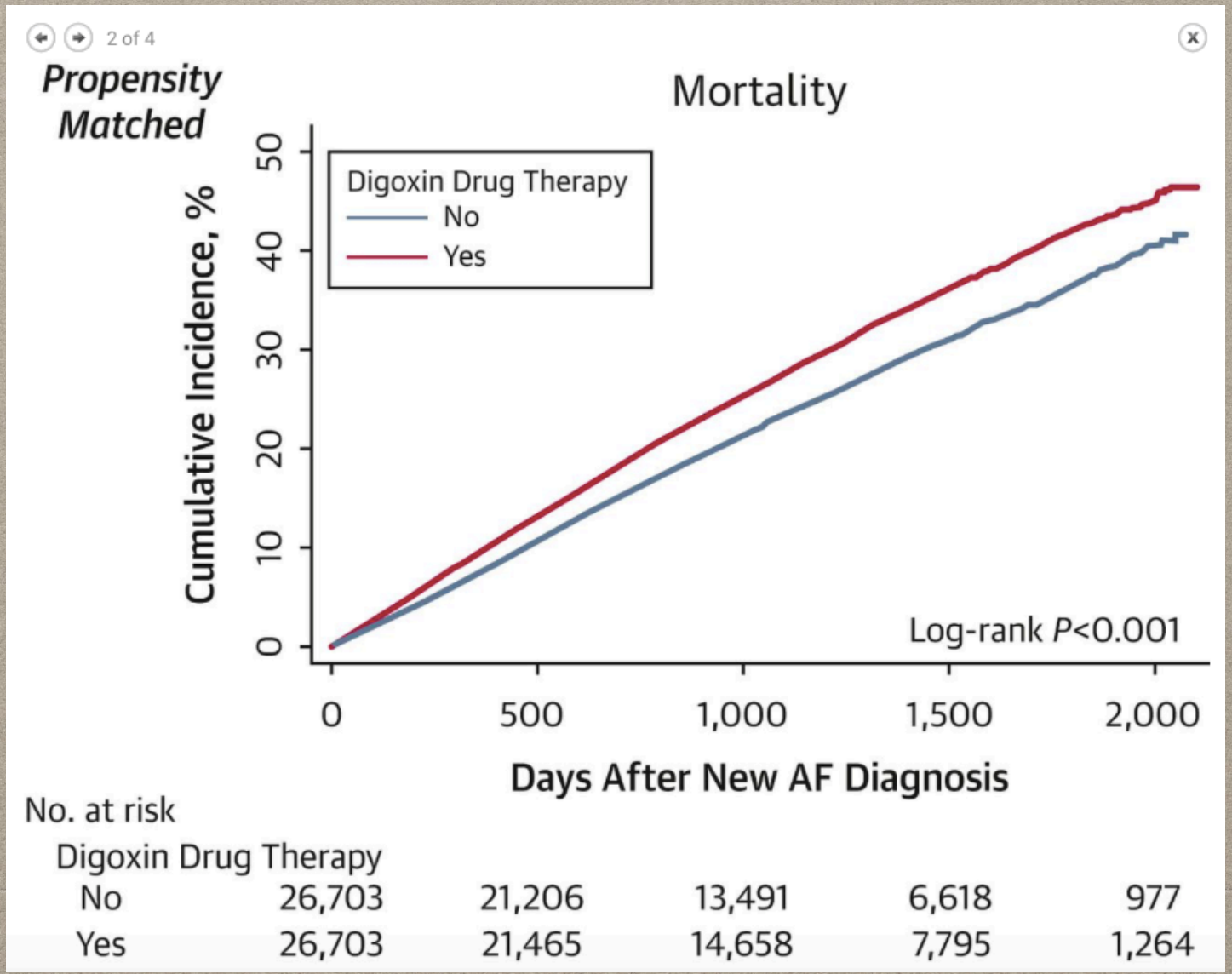
- NEJM 11 Nov 2018
- Angiotensin–Neprilysin Inhibition in Acute Decompensated Heart Failure
- After hemodynamic stabilization, patients were randomly assigned to receive sacubitril–valsartan (target dose, 97 mg of sacubitril with 103 mg of valsartan twice daily) or enalapril (target dose, 10 mg twice daily)
- Conclusions: Among patients with heart failure with reduced ejection fraction who were hospitalized for acute decompensated heart failure, the initiation of sacubitril–valsartan therapy led to a greater reduction in the NT-proBNP concentration than enalapril therapy. Rates of worsening renal function, hyperkalemia, symptomatic hypotension, and angioedema did not differ significantly between the two groups.

DIGOXIN

- Data from multiple trials: AFFIRM, ROCKET AF, ARISTOTLE, meta-analyses, DIG trial
- Do not use in normal LVEF AF - harm
- Do not use in HFpEF - ineffective/harm
- Avoid with CKD/varying CrCl
- Keep the levels below 1, (0.8 to 0.9) - death risk rises as the serum concentration rises

INCREASED MORTALITY ASSOCIATED WITH DIGOXIN IN CONTEMPORARY PATIENTS WITH ATRIAL FIBRILLATION

Journal of the American College of Cardiology
Volume 64, Issue 7, August 2014



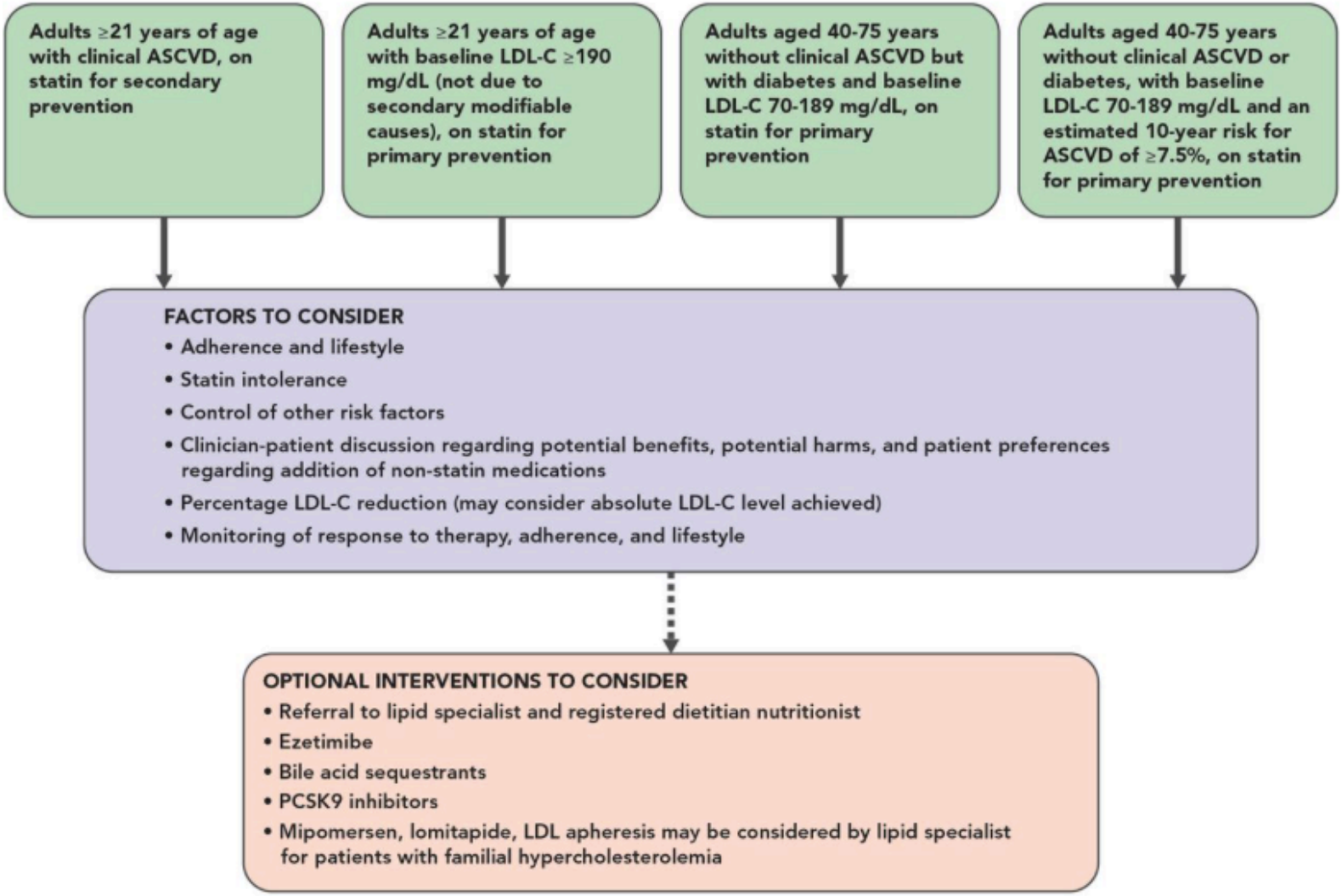
No. at risk

Digoxin Drug Therapy					
No	26,703	21,206	13,491	6,618	977
Yes	26,703	21,465	14,658	7,795	1,264

STAGE D HFREF

- If Pt is a candidate for advanced therapies then this should be explored
- If Pt is not then other options including palliation should be explored
- Palliation could include inotropic support

PATIENT POPULATIONS ADDRESSED: 4 STATIN BENEFIT GROUPS



Abbreviations: ASCVD = atherosclerotic cardiovascular disease, LDL = low-density lipoprotein, LDL-C = low-density lipoprotein cholesterol, PCSK9 = proprotein convertase subtilisin/kexin 9.

Major causes of dilated cardiomyopathy

Ischemia
Infectious diseases
Viral Coxsackievirus
Cytomegalovirus
HIV
Varicella
Hepatitis
Epstein-Barr
Echovirus
Other
Bacterial
Streptococci-rheumatic fever
Typhoid fever
Diphtheria
Brucellosis
Psitticosis
Rickettsial disease
Lyme disease
Mycobacterial-fungal
Histoplasmosis
Cryptococcosis
Parasitic
Toxoplasmosis
Trypanosomiasis
Shistosomiasis
Trichinosis
Deposition diseases
Hemochromatosis
Amyloidosis

Medications
Chemotherapeutic agents
Anthracyclines
Cyclophosphamide
Trastuzumab
Antiretroviral drugs
Zidovudine
Didanosine
Zalcitabine
Phenothiazines
Chloroquine
Clozapine
Toxins
Ethanol
Cocaine
Amphetamines
Cobalt
Lead
Mercury
Carbon monoxide
Beryllium
Electrolyte abnormalities
Hypocalcemia
Hypophosphatemia
Uremia
Nutritional deficiencies
Thiamine
Selenium
Carnitine

Rheumatologic diseases
Systemic lupus
Scleroderma
Giant cell arteritis
Endocrinologic disorders
Thyroid hormone excess or deficiency
Growth hormone excess or deficiency
Pheochromocytoma
Diabetes mellitus
Cushing's disease
Genetic with or without neuromuscular disease
Duchenne's muscular dystrophy
Myotonic dystrophy
Friedreich's ataxia
and others
Miscellaneous
Peripartum cardiomyopathy
Tachycardia
Sarcoidosis
Familial cardiomyopathies
Sleep apnea
Autoimmune myocarditis
Radiation
Calcium overload
Oxygen free radical damage

Etiologic classification of cardiomyopathy-I

Infectious
Bacterial
Diptheria*
Tuberculosis*
Typhoid fever*
Rheumatic fever*
Scarlet fever*
Meningococcal*
Pneumococcal
Gonococcal
Brucellosis
Tetanus
Meliodosis
Tularemia
Pertussis
Spirochetal
Syphilis
Leptospirosis*
Lyme disease*
Rickettsial
Typhus
Rocky mountain spotted fever*
Q fever
Viral
Poliomyelitis*
Influenza*
Mumps*
Rubella*
Rubeola*
Variola*
Varicella*
Epstein-Barr*

Viral (cont'd)
Coxsackievirus*
Echovirus*
Cytomegalovirus*
Hepatitis*
Rabies*
Mycoplasma*
Psittacosis*
Herpes
Encephalitis
Arboviruses*
Mycotic
Actinomycosis
Blastomycosis
Moniliasis
Aspergiliosis
Histoplasmosis*
Coccidiomycosis
Cryptococcosis*
Candidiasis
Protozoal
South American
trypanosomiasis*
African trypanosomiasis*
Toxoplasmosis*
Malaria
Amebiasis
Leishmaniasis
Balantidiasis
Sarcosporidiosis
Helminthic
Trichiniasis*
Echinococcosis

Helminthic (cont'd)
Schistosomiasis*
Ascariasis
Heterophydiasis
Filariasis
Paragonimiasis
Strongyloidiasis
Cysticercosis
Visceral larva migrans
Toxins and drugs
Adriamycin*
Amphetamine*
Antimony
Arsenic*
Carbon monoxide
Carbon tetrachloride
Catecholamines*
Cobalt*
Cocaine*
Cyclophosphamide
Emetine
Ethyl alcohol*
Lithium
Lead
Methysergide
Phenothiazine drugs
Phosphorus*
Tricyclic antidepressants
Zidovudine*
Radiation*•

* Conditions that may manifest clinically as dilated cardiomyopathy.
• Conditions that may manifest clinically as restrictive cardiomyopathy by daggers.
Δ Conditions that may manifest clinically as hypertrophic cardiomyopathy (These designations are neither obligatory nor exclusive).
Adapted with permission from Abelmann, WH. Introduction to Atlas of Heart Diseases, Vol. II: Cardiomyopathies, Myocarditis and Pericardial disease, Abelmann, WH (Ed), Current Medicine, Philadelphia, 1995, p. 1.

Etiologic classification of cardiomyopathy-II

Genetic
Genetic hypertrophic cardiomyopathyΔ•
Genetic dilated cardiomyopathy*
Metabolic
Endocrine
Acromegaly*•Δ
Thyrotoxicosis*
Hypothyroidism*•Δ
Pheochromocytoma*•Δ
Diabetes melllitus
Familial storage diseases
Glycogen storage diseases*Δ
Refsum disease
Niemann-Pick disease
Hand-Schuller-Christian disease
Fabry's disease*Δ
Gangliosiderosis
Gaucher's disease*•
Sandhoff's disease*
Mucopolysaccharidosis*
Hunter's syndrome
Hurler's syndrome
Nutritional
Beriberi*
Kwashiokor*
Pellagra
Selenium deficiency
(Keshan's disease)*
Other
Hypokalemia*
Carnitine deficiency*
Uremia*

Hematologic/oncologic
Hematologic disorders
Leukemia*
Myeloma
Sickle cell anemia*
Anemia*
Henoch-Schonlein purpura*
Neoplastic diseases
Primary neoplasms•
Metastatic neoplasms•
Deposits
Hemochromatosis*•
Oxalosis
Ochronosis
Amyloid disease•
Heredofamilial neurologic and neuromuscular diseases
Progressive muscular dystrophy (Duchenne)*
Limb-girdle muscular dystrophy (Erb)*
Fascioscapulohumeral dystrophy (Landouzy-Dejerine)
Humeroperoneal ataxia
Friedreich's ataxia Δ
Myotonia atrophica (Steinert)*
Myasthenia gravis
Chronic progressive external opthmoplegia (Kearns-Savre)
Familial centronuclear myopathy
Juvenile progressive spinal muscular atrophy (Kugelberg-Welander)
NeurofibromatosisΔ

Endomyocardial diseases
Endomyocardial fibrosis*•
Hypereosiinophilic heart disease
(Loffler's)•
Endocardial fibroelastosis*•
Inflammatory
Connective tissue diseases
Rheumatoid heart disease*
Ankylosing spondylitis
Systemic lupus erythematosus*
Scleroderma*•
Dermatomyositis*
Periarteritis nodosa
Granulomatous
Sarcoid*
Wegener's granulomatosis*
Granulomatous myocarditis*
Other inflammation
Giant cell myocarditis*
Hypersensitivity myocarditis*

* Conditions that may manifest clinically as dilated cardiomyopathy.
• Conditions that may manifest clinically as restrictive cardiomyopathy by daggers.
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Examples of different diseases that cause cardiomyopathies

HCM	DCM	ARVC	RCM	Unclassified
Familial				
Familial, unknown gene	Familial, unknown gene	Familial, unknown gene	Familial, unknown gene	Left ventricular non-compaction
Sarcomeric protein mutations	Sarcomeric protein mutations (see HCM)	Intercalated disc protein mutations	Sarcomeric protein mutations	Barth syndrome
β myosin heavy chain	Z-band	Plakoglobin	Troponin I (RCM +/- HCM)	Lamin A/C
Cardiac myosin binding protein C	Muscle LIM protein	Desmoplakin	Essential light chain of myosin	ZASP
Cardiac troponin I	TCAP	Plakophilin 2	Familial amyloidosis	α-dystrobrevin
Troponin-T	Cytoskeletal genes	Desmoglein 2	Transthyretin (RCM + neuropathy)	
α-tropomyosin	Dystrophin	Desmocollin 2	Apolipoprotein (RCM + nephropathy)	
Essential myosin light chain	Desmin	Cardiac ryanodine receptor (RyR2)	Desminopathy	
Regulatory myosin light chain	Metavinculin	Transforming growth factor-$_{\beta}$3 (TGF$_{\beta}$3)	Pseuxanthoma elasticum	
Cardiac actin	Sarcoglycan complex		Haemochromatosis	
α-myosin heavy chain	CRYAB		Anderson-Fabry disease	
Titin	Epicardin		Glycogen storage disease	
Troponin C	Nuclear membrane			
Muscle LIM protein	Lamin A/C			
Glycogen storage disease (eg, Pompe; PRKAG2, Forbes', Danon)	Emerin			
Lysosomal storage diseases (eg, Anderson-Fabry, Hurler's)	Mildly dilated CM			
Disorders of fatty acid metabolism	Intercalated disc protein mutations (see ARVC)			
Carnitine deficiency	Mitochondrial cytopathy			
Phosphorylase B kinase deficiency				
Mitochondrial cytopathies				
Syndromic HCM				
Noonan's syndrome				
LEOPARD syndrome				
Friedreich's ataxia				
Beckwith-Wiedermann syndrome				
Swyer's syndrome				
Other				
Phospholamban promoter				
Familial amyloid				

Examples of different diseases that cause cardiomyopathies

HCM	DCM	ARVC	RCM	Unclassified
Non-familial				
Obesity	Myocarditis (infective/toxic/immune)	Inflammation?	Amyloid (AL/prealbumin)	Tako Tsubo cardiomyopathy
Infants of diabetic mothers	Kawasaki disease		Scleroderma	
Athletic training	Eosinophilic (Churg Strauss syndrome)		Endomyocardial fibrosis	
Amyloid (AL/prealbumin)	Viral persistence		Hypereosinophilic syndrome	
	Drugs		Idiopathic	
	Pregnancy		Chromosomal cause	
	Endocrine		Drugs (serotonin, methysergide, ergotamine, mercurial agents, busulfan)	
	Nutritional - thiamine, carnitine, selenium, hypophosphataemia, hypocalcaemia		Carcinoid heart disease	
	Alcohol		Metastatic cancers	
	Tachycardiomyopathy		Radiation	
			Drugs (anthracyclines)	

ARVC: arrhythmogenic right ventricular cardiomyopathy; DCM: dilated cardiomyopathy; HCM: hypertrophic cardiomyopathy; RCM: restrictive cardiomyopathy.

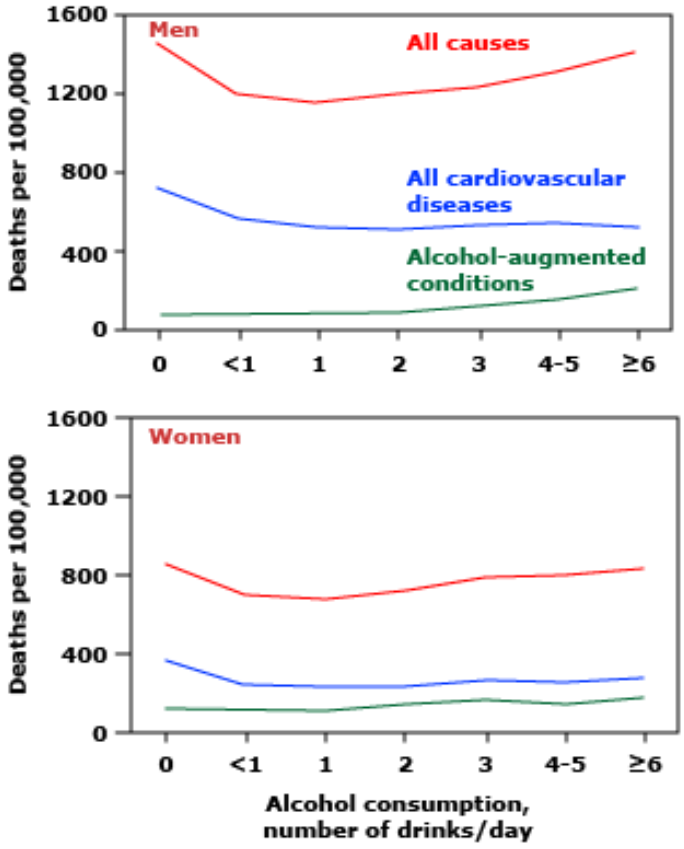
Non-familial types of cardiomyopathy

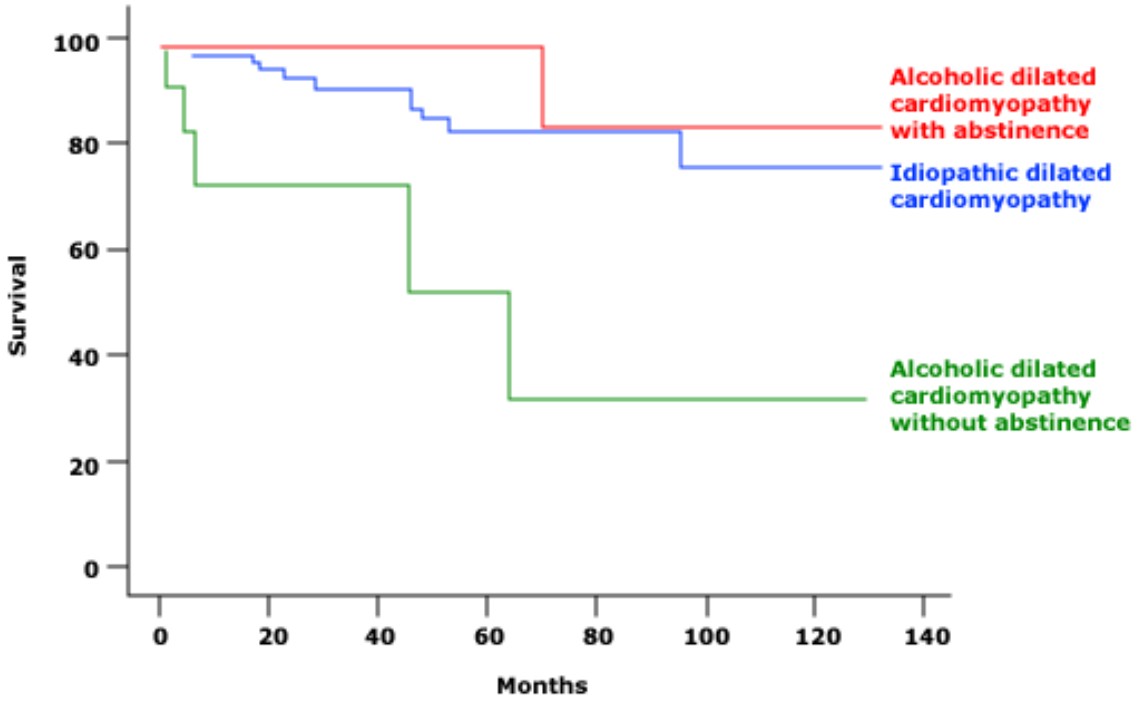
HCM	DCM	ARVC	RCM	Unclassified
Obesity Infants of diabetic mothers Athletic training Amyloid (AL/prealbumin)	Myocarditis (infective/toxic/immune) Kawasaki disease Eosinophilic (Churg Strauss syndrome) Viral persistence Drugs Pregnancy Endocrine Nutritional - thiamine, carnitine, selenium, hypophosphataemia, hypocalcaemia Alcohol Tachycardiomyopathy	Inflammation?	Amyloid (AL/prealbumin) Scleroderma Endomyocardial fibrosis ▪ Hypereosinophilic syndrome ▪ Idiopathic ▪ Chromosomal cause ▪ Drugs (serotonin, methysergide, ergotamine, mercurial agents, busulfan) Carcinoid heart disease Metastatic cancers Radiation Drugs (anthracyclines)	Takotsubo cardiomyopathy

HCM: hypertrophic cardiomyopathy; DCM: dilated cardiomyopathy; ARVC: arrhythmogenic right ventricular cardiomyopathy; RCM: restrictive cardiomyopathy.

ETOH Cardiomyopathy

- Direct toxic effect of ETOH (apoptosis, free radical damage)
- Nutritional effects: Thiamine deficiency and others
- Toxic effects from additives in ETOH beverages (rare)
- ETOH and metabolite acetaldehyde are toxic to myocardium





Natural History IDCM

- Symptomatic (NYHA Class III-IV) (Based on older retrospective and tertiary referral data)
  - ¼ death within 1 year
  - ½ death within 5 years
- More recently, studies suggest improved survival
  - 5 year mortality 20%, average
  - Pediatric data similar, more variable
- Mild dilatation more favorable
- Recent onset
  - ¼ improve spontaneously

Diuretics

- Mild volume excess – thiazides may be sufficient
- Often, loop diuretics are necessary
  - Furosemide: bioavailablity varies significantly - decreased absorption with small bowel edema
  - Torsemide: more predictable bioavailability, may be favored, approx 2-4x potency
  - Bumetanide: less commonly used, approx 20-40x potency
- Dietary sodium intake can overpower diuretics easily
- Careful monitoring of weight, renal function, electrolytes
- As in renal disease, knowing a dry weight is essential – pts may need intermittent or ‘sliding-scale therapy’

Beta-Adrenergic Receptor Blockade

- Negative chronotropic effect
  - Decreases myocardial oxygen demand
- Reduces myocardial damage from catecholamines
- Improves diastolic relaxation
- Increase LVEF
- Decrease LV Mass
- Inhibits sympathetically mediated vasoconstriction
- Increases myocardial beta-adrenoreceptor density
- Improves calcium handling at slower rates
- Inhibition of negative remodeling
- Reduces risk of ventricular arrhythmias
- carvedilol (maintains CO, decreases peripheral resistance)
- nebivolol (NO dependent vasodilator effects, antioxidant)

Anticoagulation

- **Justified in atrial fibrillation, previous history of embolic events, mural thrombus**
- **2013 guidelines: not without any of the above**

Antiarrhythmics

- Pts with systolic dysfunction at high risk for VT/ VF/SCD
- Most antiarrhythmics are negative inotropes
- Not recommended for asymptomatic and nonsustained arrhythmias (beta blockers only)
- Reserved for sustained VT, VF, survivors of SCD, recurrent or sustained atrial arrhythmias with hemodynamic instability or severe symptoms – WITH an ICD in place
- Amiodarone - neutral mortality

Drugs That May Cause or Exacerbate Heart Failure

A Scientific Statement From the American Heart Association

ABSTRACT: Heart failure is a common, costly, and debilitating syndrome that is associated with a highly complex drug regimen, a large number of comorbidities, and a large and often disparate number of healthcare providers. All of these factors conspire to increase the risk of heart failure exacerbation by direct myocardial toxicity, drug-drug interactions, or both. This scientific statement is designed to serve as a comprehensive and accessible source of drugs that may cause or exacerbate heart failure to assist healthcare providers in improving the quality of care for these patients.

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On behalf of the American

Heart failure (HF) remains the leading discharge diagnosis among patients ≥65

Digoxin: No Effect on Mortality in AF

Circulation. 2016;134:00–00. DOI: 10.1161/CIR.0000000000000426 August 9, 2016

Table 1. Prescription Medications That May Cause or Exacerbate HF

Drug or Therapeutic Class	Association With HF		Magnitude of HF Induction or Precipitation	Level of Evidence for HF Induction or Precipitation	Possible Mechanism(s)	Onset	Comments
	Causes Direct Myocardial Toxicity	Exacerbates Underlying Myocardial Dysfunction					
Analgesics							
COX, nonselective inhibitors (NSAIDs)		x	Major	B	Prostaglandin inhibition leading to sodium and water retention, increased systemic vascular resistance, and blunted response to diuretics	Immediate	
COX, selective inhibitors (COX-2 inhibitors)		x	Major	B			
Anesthesia medications							
Inhalation or volatile anesthetics							
Desflurane		x	Major	B	Myocardial depression, peripheral vasodilation, attenuated sympathetic activity	Immediate	Sole induction alone is not generally used because of hemodynamic instability and airway irritation in patients with HF
Enflurane		x	Major	B			
Halothane		x	Major	B			
Isoflurane		x	Major	B			
Sevoflurane		x	Major	B			
Intravenous anesthetics							
Dexmedetomidine		x	Moderate	B	α_2-Adrenergic agonist	Immediate	
Etomidate		x	Moderate	B	Suppression of adrenal function		Not generally used for maintenance of anesthesia
Ketamine		x	Major	B	Negative inotrope		
Propofol		x	Moderate	B	Negative inotrope, vasodilation		

Heart Failure: Guideline For the Management of

publish date: **Jun 05, 2013**

focused update: **Apr 28, 2017**

Go to JACC article | Download PDF

Quick Reference

These items break the guidelines down into easy-to-use summaries.

- 2017 Focused Update
- 2017 Key Points to Remember
- 2013 Executive Summary
- 2013 Pocket Card Printed
- 2013 Pocket Guide Digital
- 2013 Key Points to Remember

Slides

Find all the guideline recommendations in PowerPoint format here.

- 2017 Slide Set
- 2013 Slide Set

Perspectives

Need a quick summary of the guideline? Access the guideline commentary.

- 2017 News Story

Education

Test your in-depth knowledge of this guideline with CME, CE and MOC educational activities.

- Guideline Education

Apps and Tools

Use these for critical decision making at the point-of-care.

- 2013 Heart Failure Toolkit

Patient Resources

Increase patient knowledge and motivation with these resources.

- 2017 CardioSmart Patient Summary

CardioSmart
American College of Cardiology

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Mar 07, 2018

Climate change may increase heart attack risk, a Michigan study suggests.

Heart Failure
AN ACC CLINICAL TOOLKIT

Symptom and Activity Level Assessment
(Outpatient Setting)

Guideline Recommended Practice

In general, patients with LV dysfunction or HF present to the healthcare provider in 1 of 3 ways:

1. **Decreased exercise tolerance.**
   - Complaints of tolerance reduction due to dyspnea and/or fatigue on exertion.
2. **Fluid retention.**
   - Complaints of leg or abdominal swelling, difficulty lying flat, or weight gain as primary or only symptom.
3. **With no symptoms or symptoms of another cardiac or non-cardiac disorder.**

Assessing Symptom and Activity Level

Recording NYHA Class should occur at each office visit to quantify the degree of functional limitation imposed by HF.

New York Heart Association (NYHA) Classifications

NYHA Class	Symptoms
I	No limitation of physical activity. Ordinary physical activity (e.g., walking , climbing stairs) does not cause symptoms of HF.
II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF.
III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity, e.g. walking short distances (20-100 yards), causes symptoms of HF.
IV	Unable to carry on any physical activity without symptoms of HF, or, symptoms of HF at rest.

Performance Measure Reporting

What's Being Measured

Percentage of all patient visits, ≥ 18 years of age with a diagnosis of heart failure, which have documented quantitative results of current activity level and clinical symptoms evaluations.

How to Satisfy this Measure

Document the results of both the *current activity level* and *clinical symptoms* of your HF patients (≥ 18 years) at each office visit.

Exceptions are made for those with documentation of medical reason(s) for not evaluating both components (eg, severe cognitive or functional impairment).

For registry users, documentation must include assignment of a New York Heart Association (NYHA) Class: NYHA Class I, NYHA Class II, NYHA Class III, or NYHA Class IV (see table on the left).

Non-registry users must provide either NYHA Class assignment OR the completion of a valid, reliable, disease-specific instrument, such as:

- Kansas City Cardiomyopathy Questionnaire
- Minnesota Living with Heart Failure Questionnaire
- Chronic Heart Failure Questionnaire