

Inclusion of Older Adults in Clinical Trials

The View from Heart and Vascular Research

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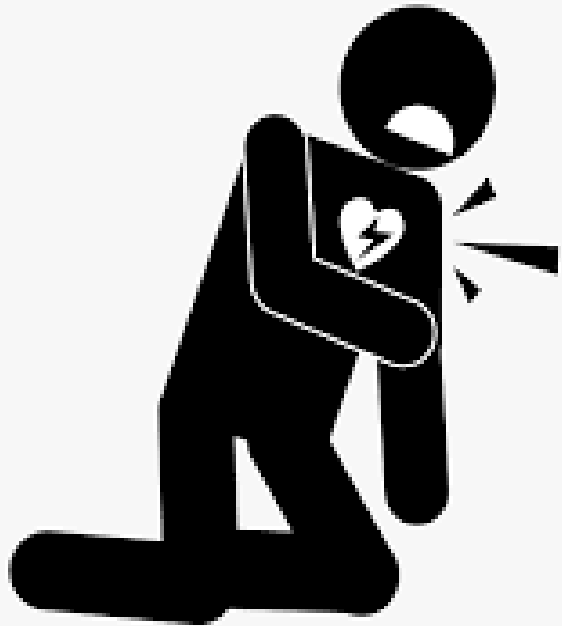
Chair, Geriatric Cardiology Section, University of Pittsburgh Medical Center

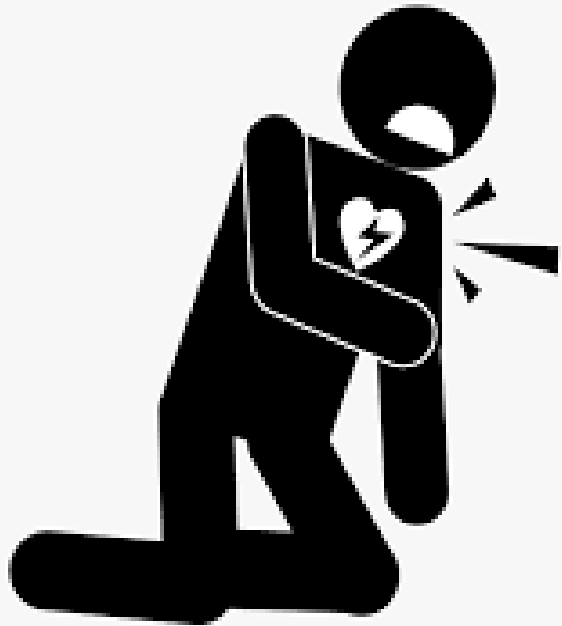
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So how should we integrate care? Geriatric Cardiology

- Diagnosis
 - Multimorbidity
- Risk Assessment
 - Multimorbidity
 - Frailty
 - Cognition
 - Biological
- Disease Management
 - Multimorbidity
 - Pharmacology
 - Function, Cognition, Rehabilitation
 - Quality of life

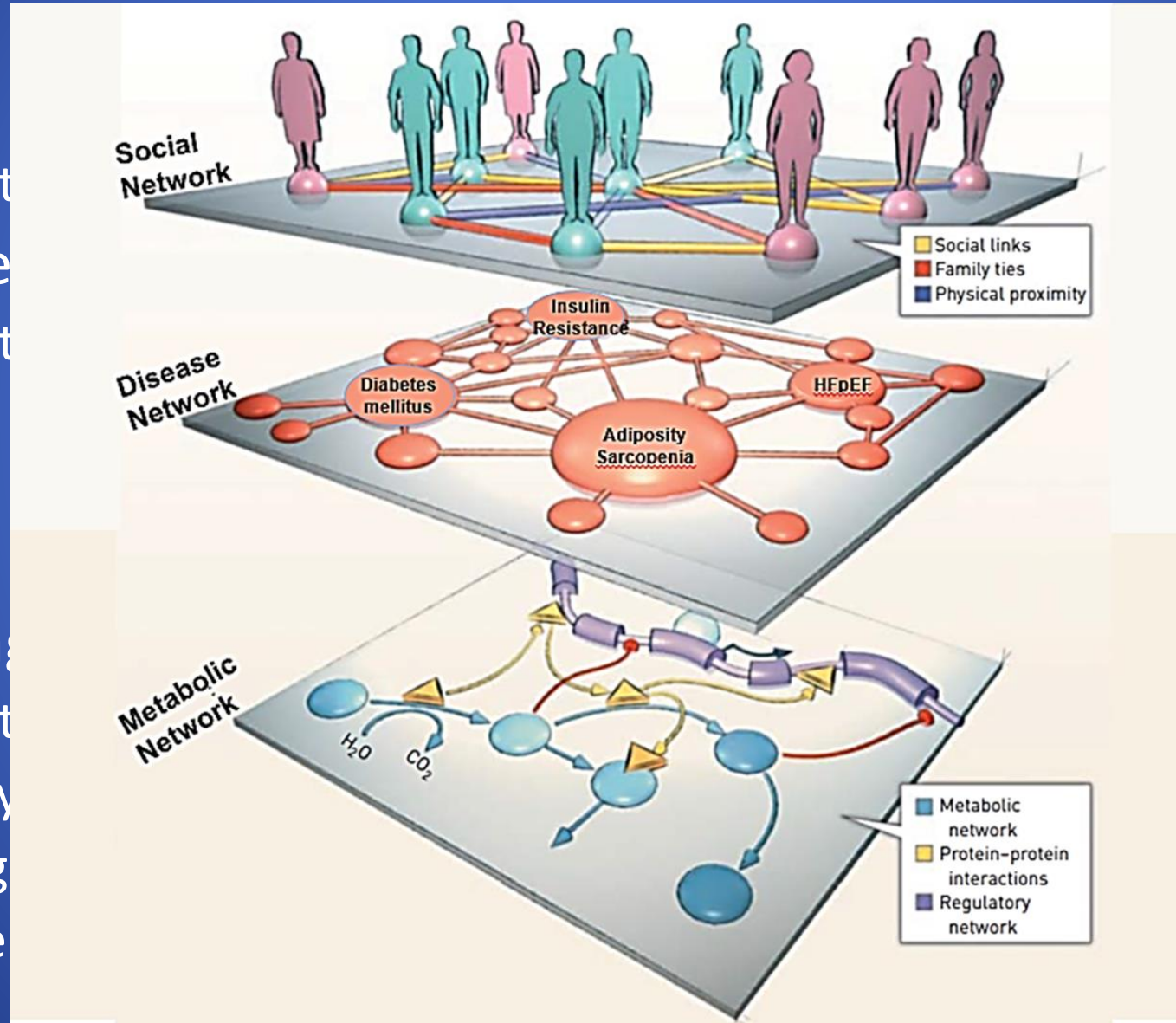


- Process of care
 - Transfers
 - Palliative Care
- Psychosocial

U13: Integration of Geriatrics Principles into the Care of Older Adults with Cardiovascular Disease
Presented at The American College of Cardiology, 2-10-2015

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Process of care
transfers
collaborative Care
biopsychosocial

Building a Choir

 Society of Geriatric Cardiology



AMERICAN
COLLEGE *of*
CARDIOLOGY

Geriatric Cardiology Section (GCS)

- Member Value: Commitment to quality of care
 - Commitment to professionalism and educational trainees
 - Broad avenue of dissemination at national meetings
 - Foundation to support educational initiatives
- **Essentials of Cardiovascular Care for Older Adults**
 - Case-based educational initiative
 - Fostering mentoring cardiology fellows and education, inclusive of geriatricians
 - Dissemination throughout ACC's State Chapters with programs (GCS and local speakers)
 - Foundation with CardioSmart, a patient-facing portal

COUNCIL PERSPECTIVES

THE PRESENT AND FUTURE

JACC COUNCIL PERSPECTIVES

Cardiovascular Biomarkers and Imaging in Older Adults



JACC Council Perspectives

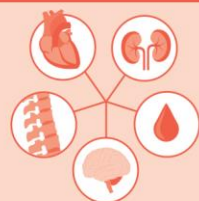
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Marcel E. Salive, MD, MPH,^{i,*} Michael W. Rich, MD,^j for the Geriatric Cardiology Section Leadership Council

ABSTRACT

Whereas the burgeoning population of older adults is intrinsically vulnerable to cardiovascular disease, the utility of many

CENTRAL ILLUSTRATION Redefining Cardiovascular Disease as a Clinical Challenge Amid Multimorbidity

Treating Multimorbidity in Older Adults with Cardiovascular Disease (CVD)



Current separate disciplinary approach:

- Focus on dominant cardiac issue; non-cardiac comorbid diseases are separate and secondary
- Limited integration across or between conditions
- Lack of standardized approach
- Treatment provided by separate specialists, primary care physician, and care extenders

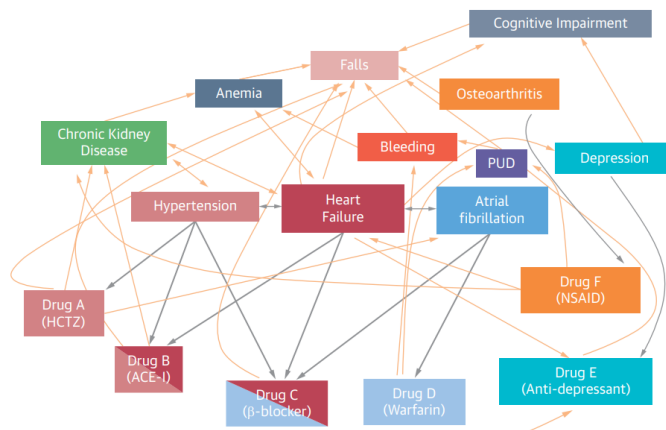
Recommended multidisciplinary approach:

- Focus on identifying preferences and goals and providing preference-sensitive options
- Integration between conditions and specialties
- Overall integrated care plan
- Treatment provided by multidisciplinary team; linked electronic health records

Forman, D.E. et al. J Am Coll Cardiol. 2018;71(19):2149-61.

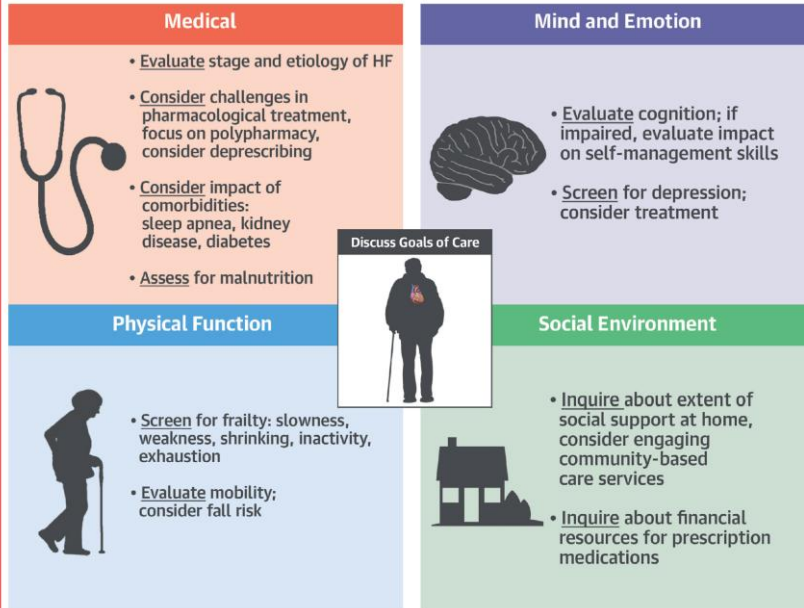
Differences between current disease-specific paradigm and the emerging patient-specified goal directed care approach: the latter seeks to address issues emanating from cardiovascular disease in a context of multimorbidity.

FIGURE 2 Diseases and Medications Impacting One Another in Multimorbidity



Forman, D.E. et al. J Am Coll Cardiol. 2018;71(19):2149-61.

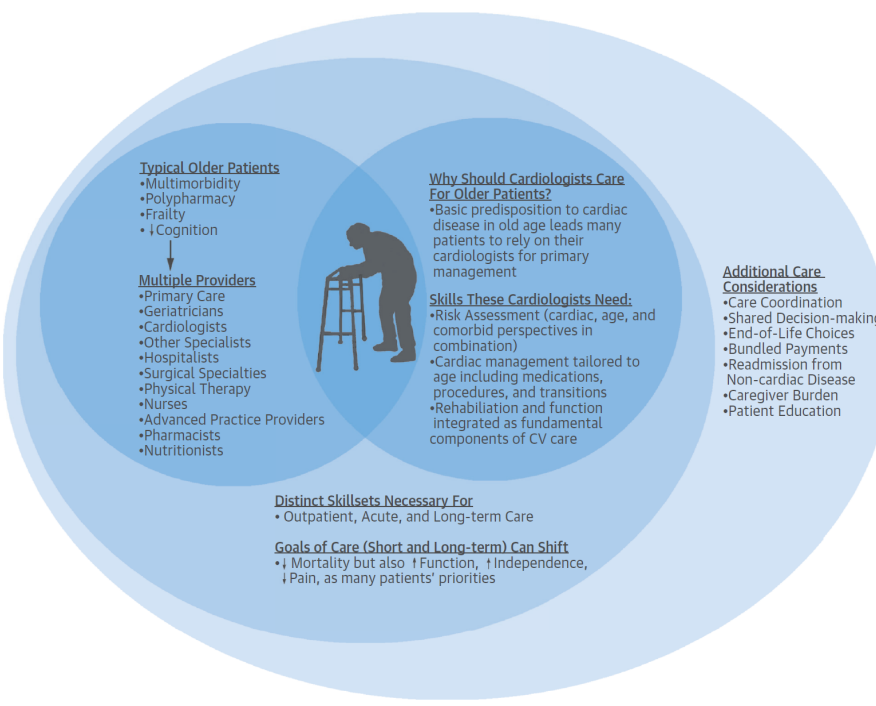
CENTRAL ILLUSTRATION Domain Management Approach to HF in the Geriatric Patient



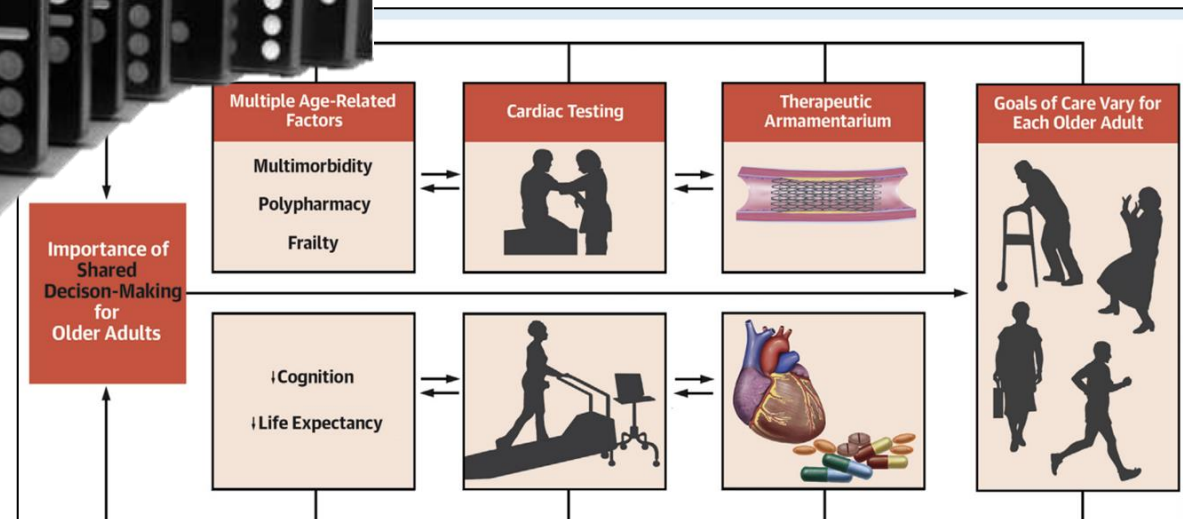
Gorodeski, E.Z. et al. J Am Coll Cardiol. 2018;71(17):1921-36.

Clinicians caring for older adults with HF should consider using this 4-domain framework in their routine clinical work. When utilized, this holistic model can address the unique multidimensional needs and vulnerabilities of this population. HF = heart failure.

CENTRAL ILLUSTRATION Future of Geriatric Cardiology: Proposed Care Model and Skillsets Required by Cardiologists Caring for Geriatric Patients

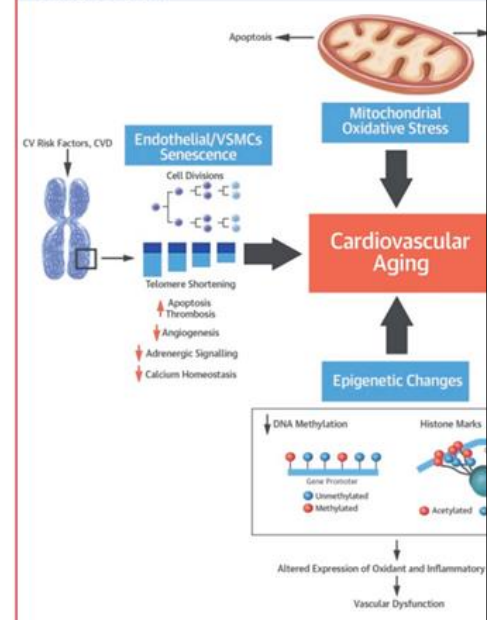


Bell, S.P. et al. J Am Coll Cardiol. 2015; 66(11):1286-99.

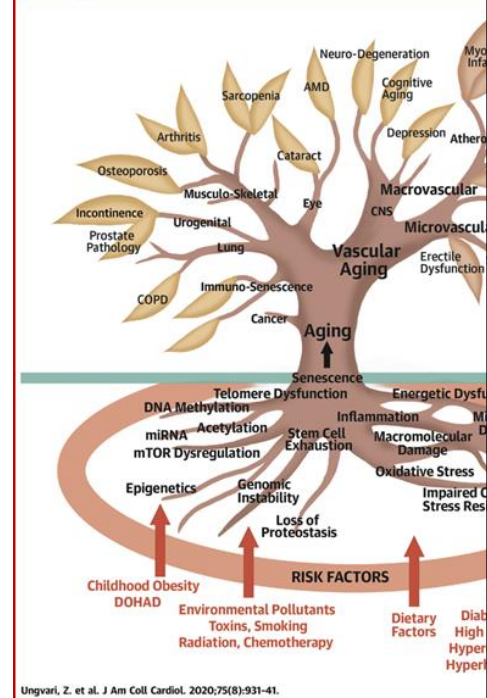


Forman, D.E. et al. J Am Coll Cardiol. 2020;76(13):1577-94.

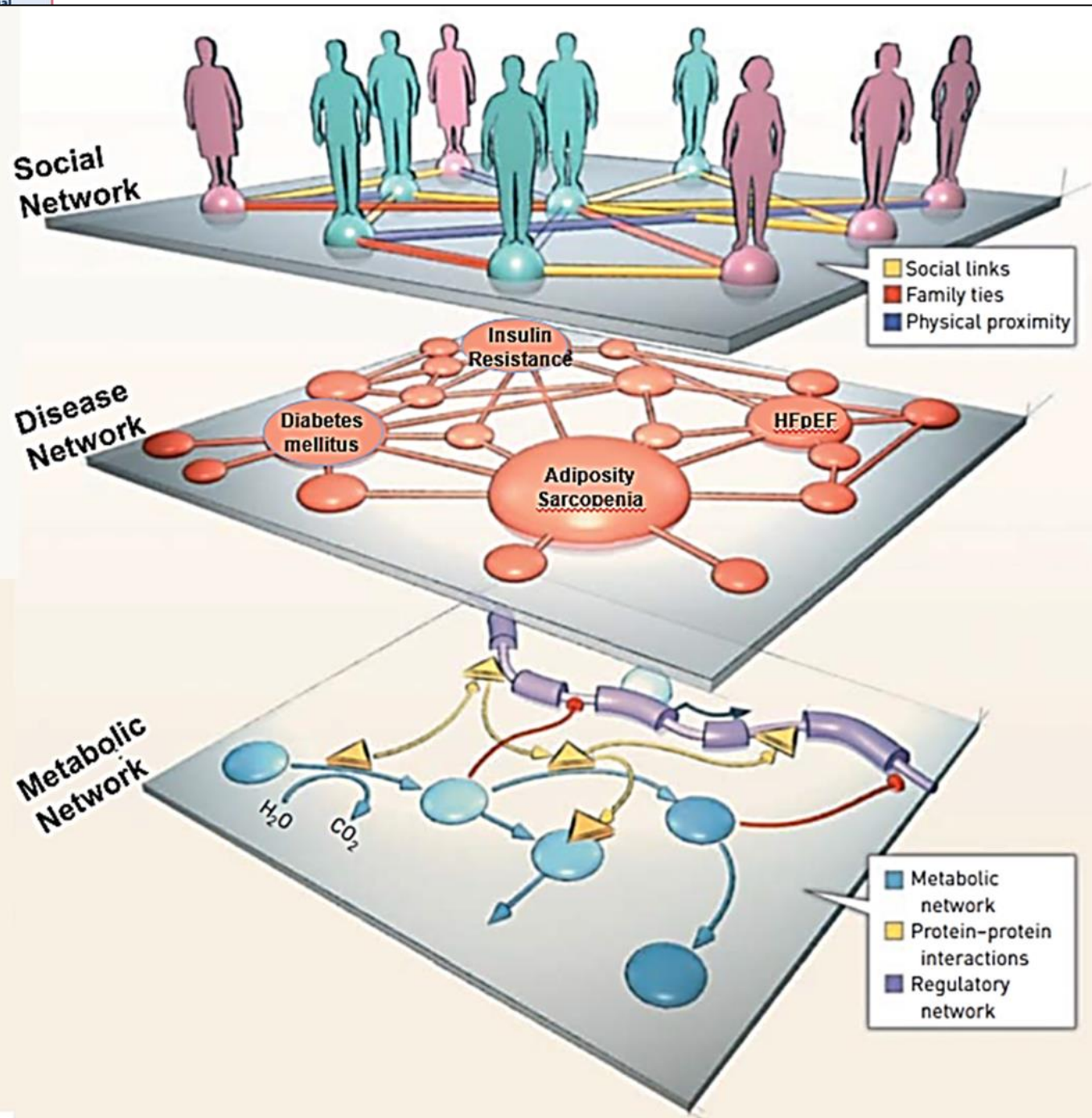
CENTRAL ILLUSTRATION: Molecular Hallmarks of CV Aging (Cellular Senescence, Genomic Instability, Chromatin Remodeling, and Mitochondrial Oxidative Stress)



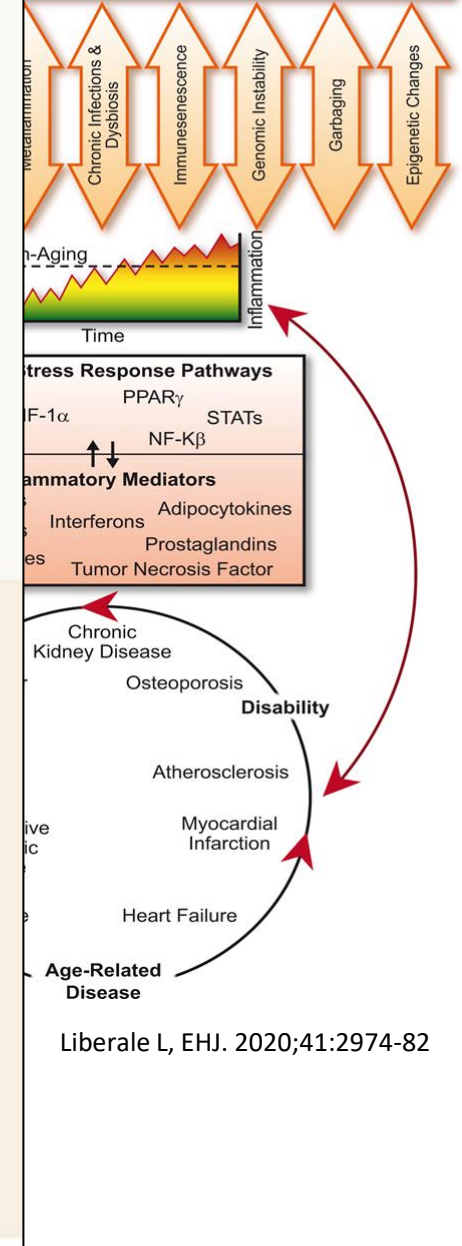
Paneni, F. et al. J Am Coll Cardiol. 2017;69(15):1952-67.



Ungvari, Z. et al. J Am Coll Cardiol. 2020;75(8):931-41.



AGING



Liberale L, EHJ. 2020;41:2974-82



National Institute
on Aging

NIA: Pivotal Research in Cardiology in the Elderly (PRICE) (1999-2008)

NIA: Integration of Geriatrics Principles into the Care of Older Adults with Cardiovascular Disease (2014-2018)

NIA: Pepper Centers, T32 grants, Nathan Shock Centers

NIA: Grants for Early Medical/Surgical Specialists' Transition to Aging Research (GEMSSTAR) Clinician-Scientists Transdisciplinary Aging Research (Clin-STAR) Coordinating Center

NIA: Building a Research Infrastructure to Develop Generalizable Evidence (BRIDGE) Geriatric Cardiology (?)

2018

AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol

4.4.4. Primary Prevention in Other Age Groups

4.4.4.1. Older Adults

Recommendations for Older Adults		
Referenced studies that support recommendations are summarized in Online Data Supplements 18 and 19 .		
COR	LOE	Recommendations
IIb	B-R	1. In adults 75 years of age or older with an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), initiating a moderate-intensity statin may be reasonable (S4.4.4.1-1–S4.4.4.1-8)
IIb	B-R	2. In adults 75 years of age or older, it may be reasonable to stop statin therapy when functional decline (physical or cognitive), multimorbidity, frailty, or reduced life-expectancy limits the potential benefits of statin therapy (S4.4.4.1-9).
IIb	B-R	3. In adults 76 to 80 years of age with an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), it may be reasonable to measure CAC to reclassify those with a CAC score of zero to avoid statin therapy (S4.4.4.1-10, S4.4.4.1-11).

Grundy SM, Stone NJ, et al. 2018 Cholesterol Clinical Practice Guidelines

Where are we now?

Prevention

- ASPREE: Aspirin in Reducing Events in the Elderly
- SPRINT: Systolic Blood Pressure Intervention Trial
- PREVENTABLE: Pragmatic Evaluation of Events And Benefits of Lipid-lowering in Older Adults
- TAME: Targeting Aging with Metformin

Secondary Therapy

- Cardiac Rehabilitation: MACRO (Modified Application of Cardiac Rehabilitation for Older Adults)
- Heart Failure: REHAB-HF
- CHD: Senior Rita and Fire Trial
- Amyloid, HFpEF
- Valvular Heart Disease
- PAD
- Afib
- Deprescribing
- Decision-Making



PREVENTABLE

- Atorvastatin 40 mg: Polypharmacy vs. the right pill and the right dose
- Challenges to motivate 20,000 older adults and their providers to participate in this trial
- Culture shift of the DCRI armamentarium to focus on cognition and ADLs



Modified Application of Cardiac Rehabilitation for Older Adults

- Shift from a disease model of care to patient-oriented management, with the patient more important than the program, and outcomes focused on function rather than cardiorespiratory fitness.
- Challenge of harmonizing endpoints with concurrent NHLBI trials

Challenges 1: Novel endpoints are difficult to assess

- Frailty, Function, Fatigue, Cognition, Physical Activity, ADLs, Quality of Life
- Body Composition, cellular physiology
- Senescence, Autophagy, Proteostasis, Proteomics, Metabolomics, Transcriptomics, Microbiomics, Bioenergetics

Fidelity, logistics, and costs are formidable challenges...

Challenges 2: Operational complexities are considerable

- Difficulty of assessing older adults encumbered by geriatric limitations:
 - Impeding effects of multimorbidity, frailty, cognitive limits, sensory limits, socioeconomic constraints on enrollment and/or adherence
 - ↓ Feasibility of Logistics
 - ↓ Feasibility of Apps, Wearables, Internet-based techniques
- Motivating the very old adults for research: Why do it? Time and fear.
- Motivating CVD clinicians to value research for their very old patients
- AE/SAE may be prohibitive

Challenges 3: Heterogeneity of Older Adults

Geriatric parameters rarely standardized and/or comparable to norms:

- Frail to robust, Resiliency
- Function, Body Composition, Nutrition, Sleep, Cognition, Falls, Incontinence, Sensory Impairment
- Comprehensive regimens of medications (Prescription and OTC)
- Self-Efficacy, Independence
- Social Determinants (Post-Acute and Long-term care)

Challenges 4: Conceptual

- Is there a biologic threshold when benefits are less likely to occur?
 - Should there be an upper age cutoff?
- Endpoints: Disability vs. cardiovascular endpoints?
- Trajectories of age hard to assess

Summary: *Inclusion of older patients as an evolving paradigm shift*

- It is happening: Multiple trials, growing momentum
 - Compelling rationale
 - Fortuitous timing of TAVR...
- Consensus, Education, Transdisciplinary Science
 - Support of the NIA, Hartford (science, education, funding impetus)
 - Support of the ACC and AGS (home, education, dissemination both clinical and research)
 - Support of the Journals (prioritization, dissemination)
 - Support of the Guidelines (emphasis, mandate for science)
- Inclusion of older study patients is happening, but remains a work in progress as many challenges remain

Thank you

- Sue Zieman
- Mike Rich