

Prevention in Focus Webinar Series

Welcome! We will begin shortly.

Better Measurement of Multimorbidity: What's New and What Funding is Available?



Jerry Suls, Ph.D.
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Marcel Salive, M.D.
National Institute on
Aging

Introduction by Carrie Klabunde, Ph.D., Senior Scientific Advisor
NIH Office of Disease Prevention

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Better Measurement of Multimorbidity: What's New and What Funding is Available?



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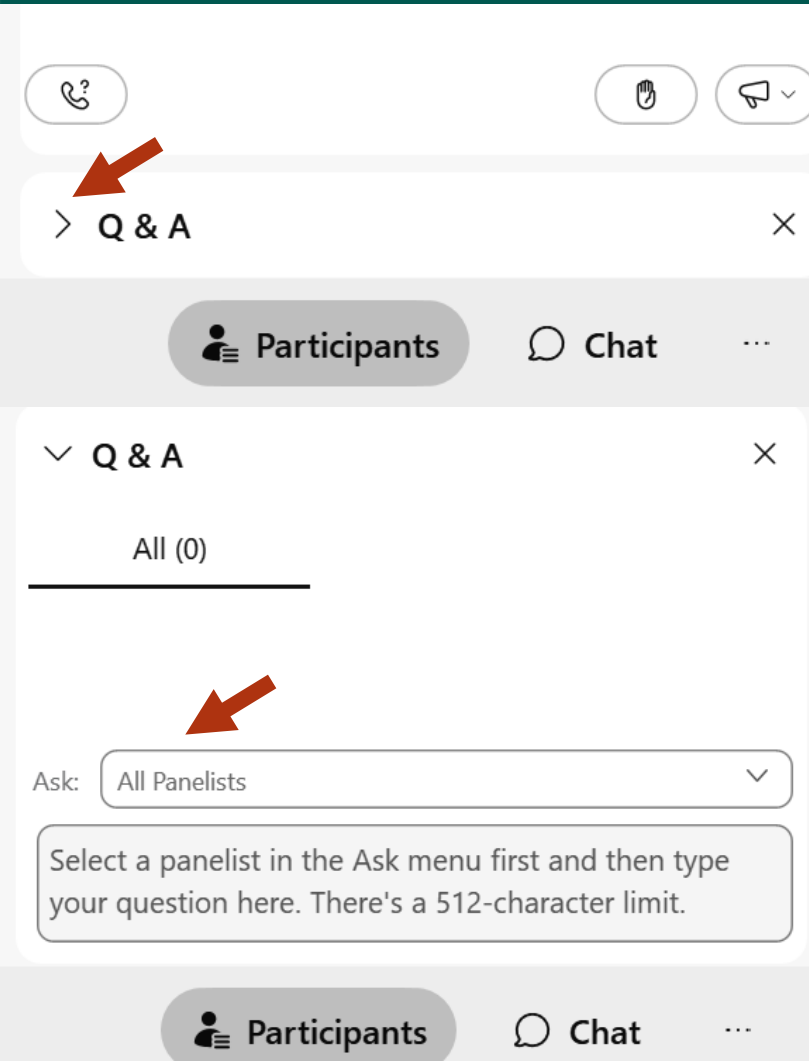
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Upcoming Q&A Session

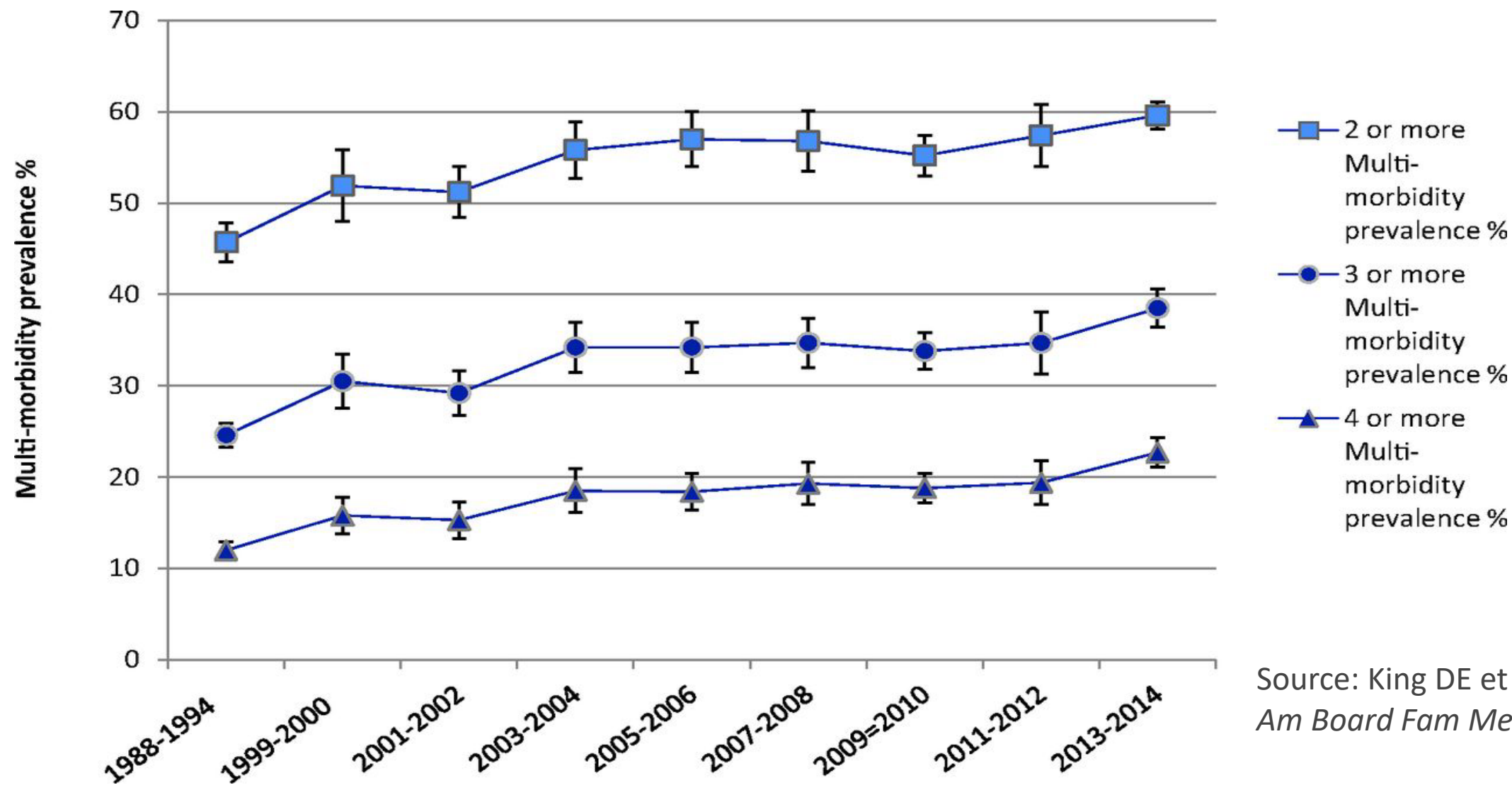
Please send us your questions
via the **Q&A pod** directed to
All Panelists

Please use the Chat pod to request technical assistance

Background

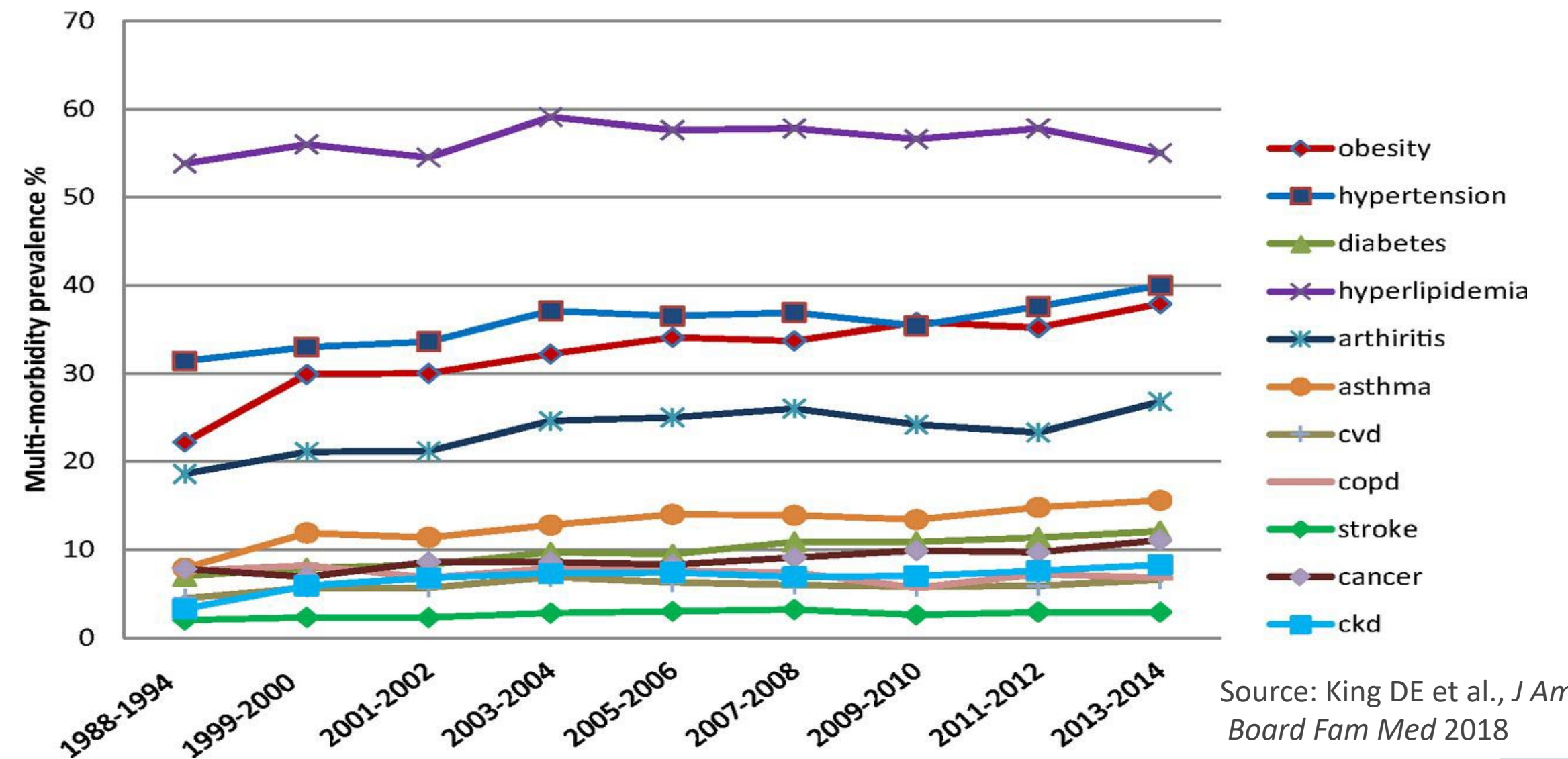
- Multimorbidity is defined as the co-occurrence of two or more chronic conditions, or multiple chronic conditions (MCCs).
- In the U.S. population, the prevalence of multimorbidity is increasing:
 - NHANES data for 1988-2014 show that multimorbidity has increased over time (e.g., **60%** of adults aged ≥ 20 had 2 or more chronic conditions in 2014 vs. **46%** in 1988)
- Multimorbidity is both challenging and resource-intensive to assess and address.
- In 2016, the National Institutes of Health (NIH) Office of Disease Prevention formed a trans-NIH Scientific Interest Group on Comorbidity, to provide a forum for NIH policy and program officials to assess and advance cross-cutting research on multimorbidity.
 - This group convened a Multimorbidity Methods workshop in 2018 and published three papers summarizing measures, emerging methods, and research opportunities.

Age-standardized trends in multimorbidity prevalence for participants 20 years or older, NHANES 1988-2014



Source: King DE et al., *J Am Board Fam Med* 2018

Age-standardized prevalence of chronic conditions in participants 20 years or older, NHANES 1988-2014



Source: King DE et al., *J Am Board Fam Med* 2018

Trans-NIH Funding Opportunity Announcements

- **PAR-20-179: Advancing Research To Develop Improved Measures and Methods for Understanding Multimorbidity (R01 Clinical Trial Optional)**
 - Participating organizations: ODP, NCI, NIA, NIDCD, NIDCR, NCCIH, NICHD, ORWH
 - Updated Expiration Date: January 8, 2024
- **PAR-20-180: Identifying Innovative Mechanisms or Interventions That Target Multimorbidity and its Consequences (R01 Clinical Trial Optional)**
 - Participating organizations: ODP, NCI, NIA, NIDCD, NIDA, NIMH, NIMHD, NINR, NCCIH, OBSSR, NICHD, ORWH
 - Updated Expiration Date: January 8, 2024

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Better Measurement of Multimorbidity: What's New and What Funding is Available?



Jerry Suls, Ph.D.
Northwell Health

Considerations in Measuring Multimorbidity: Purpose, Data Sources, Established and Emerging Methodologies

Jerry Suls PhD

Professor

Institute for Health Systems Science

Feinstein Institutes for Medical Research/Northwell Health

New York, New York

- No Conflicts to Report

Design: Instruments were reviewed and guidance developed during a special expert workshop sponsored by the National Institutes of Health on September 25–26, 2018.

The objective was to describe a broad range of instruments and data sources available to assess multimorbidity and offer guidance about selecting appropriate measures

Types of Measures:

Medical Records & Clinical Assessments

Administrative Claims

Patient Report Data Outside a Population Survey Context

Public Health Survey Data

*Adapted from: Jerry Suls, PhD, Elizabeth A. Bayliss, MD, MSPH, Jay Berry, MD, MPH, Arlene S. Bierman, MD, MS, Elizabeth A. Chrischilles, PhD, Tilda Farhat, PhD, MPH, Martin Fortin, MD, MSc, CMFC, Siran M. Koroukian, PhD, Ana Quinones, PhD, Jeffrey H. Silber, MD, PhD, Brian W. Ward, PhD, Melissa Wei, MD, MPH, MS, Deborah Young-Hyman, PhD, and Carrie N. Klabunde, PhD, MHS, MBA. *Medical Care*, 2021, 59 (8), 743-756. doi: 10.1097/MLR.0000000000001566*

Table 1. Representative Instruments for Measuring Multimorbidity

Name of Measure/Tool	Original Purpose for Creating	Data Source	Number of Conditions Included	Type of Conditions Included	Population for Development/Use
Cumulative Illness Rating Scale	Assess patients' physical impairment	Clinician severity ratings based on clinic visit or chart review	13 body systems	Chronic, physical	Adults
Cumulative Illness Rating Scale-G	Assess older patients' physical impairment	Clinician severity ratings based on clinic visit or chart review	14 body systems -relevant to older adults	Chronic, physical	Older adults
Charlson Co-morbidity Index (CCI)	Assess multimorbidity to predict mortality	Presence of selected (ICD-9) diagnoses in medical chart	19 conditions	Chronic, mainly physical	Adults
CCI adaptation Romano	Predict postop mortality in hospital or 6 wks post discharge	ICD-9 diagnoses from claims data with broader definitions of some conditions	17 conditions	Chronic, mainly physical	Adults
CCI adaptation Quan	Predict mortality in hospitals	ICD-10 diagnoses from claims data with expanded definitions	12 conditions	Chronic, physical	Adults

Name of Measure	Original Purpose	Data Source	Number of conditions included	Type of conditions included	Population for use/development
CCI adaptation Klabunde	Predict future treatment in cancer populations	Inpatient & outpatient administrative claims data	19 conditions	Chronic	Adult
Elixhauser Index (EI)	Categorize patient comorbidities to predict hospital resource use & mortality	Presence of selected (ICD-9) conditions from administrative claims data	30 conditions	Chronic	Adults
EI adaptation van Walraven	Predict mortality in hospitals	Weighted scores (based on regression weights) from claims data	30 conditions	Chronic	Adults

Ambulatory Care Groups (ACG)²⁵	Predict use of ambulatory health services within specific population groups	Assignment of ACG categories (i.e., diagnoses that cluster based on expected health services use) from claims data	5,000+ ICD-9-CM codes; patients classified into 51 categories based on disease cluster, age and sex	Chronic	Adults
Hierarchical Condition Categories (HCC)-CMS model	Predict health expenditure risk for Medicare capitation costs and private health care plans	Assignment of categories by physicians in inpatient and outpatient settings from claims data	15,000+ ICD-9-CM codes mapped to diagnostic groups and aggregated into 70 HCCs	Chronic	Adults

Name of Measure	Original Purpose	Data Source	Number of conditions included	Type of conditions included	Population for use/development
Chronic Disease Score (CDS)	Predict health care utilization, cost & mortality	Database of pharmacy fills for 6 months	28 disease categories with weightings based on regression models	Chronic, physical and mental health	Adults
CDS adaptation RxRisk	Identify chronic diseases & predict future health care costs	Algorithm used to identify drugs dispensed from outpatient pharmacy data	Prescriptions linked to 57 conditions or clinical groups	Chronic, physical and mental health	Adults & children
Self-Administered Comorbidity Questionnaire (SCQ)	Assess comorbidity for clinical & health services research settings	Patients in medical & surgical clinics	13 problems & option of reporting 3 others. Also, whether they receive txt & does problem limit activities	Chronic, physical and mental health (only depression)	Adults

Name of Measure	Original Purpose	Data Source	Number of Conditions	Type of Conditions	Population
Fortin, Almirall, Nicholson Questionnaire	Document the presence of chronic conditions	Patient report in primary care or research participants; data can also be abstracted from EHR via ICD-10 codes	20 conditions selected for their relevance to primary care, patient impact, prevalence. Conditions described in general language, understandable, inclusive, and self-explanatory.	Chronic, physical and mental health	Adults
Multimorbidity-Weighted Index (M. Wei)	Assess the relationship of chronic diseases or conditions on physical functioning	Survey of three large, national cohorts of community-dwelling young to older adults (e.g., HRS)	81 conditions	Chronic	Young through older adults

Name of Measure	Original Purpose	Data Source	Number of conditions included	Type of conditions included	Population for use/development
National Health Interview Study (NHIS)	Monitor trends in illness and disability and track progress toward achieving U.S. health objectives	Cross-sectional, nationally representative survey of civilian, noninstitutionalized adults and children that includes questions about diseases, and chronic and comorbid health conditions	Inquire about eight general disease categories (some broken down into finer categories); additional diseases are captured through supplemental questions for certain survey years	Chronic, physical and mental health	Adults & Children
National Ambulatory Medical Care Survey (NAMCS)	Obtain objective, reliable information about the provision and use of ambulatory medical care services	Cross-sectional, nationally-representative survey of visits to non-federally employed office-based physicians that includes items on patients' diseases, and chronic and comorbid health conditions	Primary diagnosis and up to four other diagnoses abstracted from medical records, and coded using ICD-CM; indicators for 20+ chronic conditions	Chronic, physical and mental health	Adults & Children

Table 2. Related Constructs to Enhance Multimorbidity Measurement

Construct	Description	Measurement
Childhood Adversity	Adverse Childhood Events (ACE) - stressful events, adversity or trauma that may include physical, verbal and sexual abuse; physical and emotional neglect; witnessing violence; or growing up in a dysfunctional environment or extreme poverty.	Measures assess children/youth contemporaneously or adults retrospectively. Repetitive and cumulative exposures are often summed and serve as predictors of chronic conditions. ACE assessments include survey questions and specific questionnaires (e.g., Adverse Childhood Experiences International Questionnaire) administered by self-report, external observers (parents or clinicians), or interviewers.
Functional Limitations	Many adults with chronic conditions also have functional limitations in strength, upper or lower body mobility, and basic and instrumental activities of daily living.	Measures include respondent self-reports or interview responses to questions about difficulties with specific tasks, often grouped in the following categories: strength limitations, upper body limitations, lower body limitations (Activities of Daily Living and Instrumental Activities of Daily Living). Claims-based measures include mobility limitations, etc.
Geriatric Syndromes	Geriatric syndromes refer to heterogeneous clinical conditions, including – but not limited to – falls, persistent dizziness, and urinary incontinence “that do not fit into discrete disease categories.”	May be evaluated with the Comprehensive Geriatric Assessment or via self-report for visual impairment (fair or poor), hearing impairment (fair or poor); depressive symptoms (CESD)
Health-Related Quality of Life (HRQOL)	Patient reports about health domains related to physical, cognitive, and emotional function; pain; vitality; and wellbeing represents a summative measure of the patient's subjective health perspective.	The Short Form-36 can discriminate between and within individuals over the life course in community-dwelling and clinic-based studies. Has contributed to the development of multimorbidity measures and as an outcome of multimorbidity. Other examples include the CDC’s HRQOL–14 Healthy Days Measure.

Table 3. Matching Purpose to Multimorbidity Measurement Approach and Instrument Selection: Examples

Purpose		Instrument Options
1	Assess multimorbidity in primary care patients, including patients with low health literacy	Brief patient report questionnaires: • SCQ-13 closed- + 3 open-ended questions on health problems • Questionnaire by Fortin and colleagues includes 20 conditions relevant and prevalent in primary care
2	Estimate presence/severity of multimorbidity with minimal technology in hospital settings based on clinicians' brief assessment	Questionnaires based on patient exams or medical records: • CIRS-13 body systems; each rated for severity on a 5-point scale with ratings summed to yield a cumulative severity score
3	Obtain an overall index of incidence/severity of multimorbidity in hospital or clinic(s) for (1) descriptive purposes; (2) to serve as predictor (moderator/covariate) of another outcome (e.g., health costs, re-hospitalization, 1-year mortality)	Clinical assessments abstracted from EHR systems: • CCI-17 medical diagnoses; simple disease counts used as an index or as an overall severity score
4	Obtain an overall index of incidence/severity of multimorbidity on a larger scale, such as a health care system, for (1) descriptive purposes; (2) to serve as predictor (moderator/covariate) of another outcome (e.g., health costs, re-hospitalization, 1-year mortality).	Administrative claims data or EHR: • CCI or CCI adaptations • EI-binary code for 30 conditions; EI adaptation yields a continuous quantitative score

Purpose		Instrument Options
5	Predict health care utilization and costs, hospitalization, or mortality with baseline prescription drug use for medical conditions (as a proxy of multimorbidity) in hospitals or health care systems.	Administrative claims data from pharmacies: • CDS-empirically derived condition weights to classify people into chronic disease groups based on prescription fills • RxRisk-identifies chronic conditions and predicts health care costs
6	Predict the morbidity, mortality, health care utilization of patients in large health care systems (obtain representative samples).	Administrative claims data or EHR: • Combine diagnosis and medication-based indices to obtain a cumulative index of multimorbidity
7	Compare cumulative and comparative predictive ability of multimorbidity, functional limitations and geriatric syndromes to predict health outcomes (obtain representative samples).	Combine data sources and use regression/classification and regression trees: • Interview responses of Health and Retirement Study participants to list of chronic conditions, functional limitations, and geriatric syndromes to predict health outcomes • Function-related indicators in Medicare claims
8	Assess cumulative disease burden and physical functioning in young to older community-dwelling adults.	EHR using all diagnoses as separate predictors: • MWI-presence of 81 conditions on physical functioning

Purpose		Instrument Options
9	Assess prognosis of patients from history of illness.	Patient reports: • EI-treats each diagnosis as a separate predictor using individual ICD-9 codes • HCUP or Veterans Affairs data warehouse-provides large samples
10	Estimate prevalence or predict health outcomes, including health care costs of multimorbidity in ambulatory health care settings.	Administrative claims data or EHR: • ACG system uses ICD diagnosis codes to classify a patient into one of 51 categories based on disease cluster, age, and sex • HCC system, originally designed to predict Medicare beneficiaries' medical expenditures, ranks diagnoses into categories that represent conditions with similar cost patterns; higher categories represent higher predicted healthcare costs, resulting in higher risk scores
11	Estimate the prevalence of multimorbidity in large representative population samples when clinical specificity or rare conditions are less critical	Various approaches include: • Public health surveys administered in person, online or by mail/phone • National claims databases • Medicare Chronic Conditions Dashboard

Some Emerging Measurement Approaches

Qualifying CoMorbidity Sets (QCS) – Jeffrey Silber

Multimorbidity Index (MMI) – Farokh Alemi

Omics & Network Medicine - Gaby Kastenmuller

Classification and Regression Tree (CART) –Siran Koroukian

Based on Suls, J., Salive, M., Koroukian, S., Silber, J., Kastenmuller, G., Alemi, F., & Klabunde, C. (2022). Emerging approaches to multiple chronic condition assessment. *Journal of the American Geriatrics Society*. 70(9):2498-2507. doi: 10.1111/jgs.17914. Epub 2022 Jun 14. PMID: 35699153; PMCID: PMC9489607.

Qualifying Comorbidity Sets (QCSs)—Jeffrey Silber MD, PhD, University of Pennsylvania

Silber JH, Reiter JG, Rosenbaum PR et al. Defining multimorbidity in older surgical patients. Med Care 2018;56:701-710.

Aim: QCSs help identify *specific* comorbidity combinations associated with poor outcomes (e.g., patient's 30-day mortality rate after surgery).

Example of Application setting: Identify an inpatient population with Medicare Claims for 12-months prior to hospitalization.

Procedure:

Step 1. Create QCS lists of single, double- or triple-comorbidity combinations that double the odds of 30-day mortality vs. general population undergoing the same procedure.

QCS Procedure Continued

Step 2. Review the patient's comorbidities from EHR using at least a 12- month look-back

Step 3. check QCSs list for General Surgery in the elderly.

Step 4. Find a match between the patient's medical conditions with entry on QCS list.

Example: For a 70-yr old admitted for cholecystectomy with a history of COPD and CHF (a QCS for general surgery), the QCS conferred a 2.54 increased 30-day mortality compared to the general patient population receiving the same procedure (with or without QCSs

Now for Another Emerging
Approach

Prevention in Focus Webinar Series

Better Measurement of Multimorbidity: What's New and What Funding is Available?



Siran M. Koroukian, Ph.D.
Case Western Reserve University

Applying Classification and Regression Tree (CART) Analysis in Multimorbidity Research

Siran M. Koroukian, Ph.D.

NIA Webinar on Multimorbidity

December 19, 2022



Multiple Chronic Conditions: A Strategic Framework

Optimum Health and Quality of Life
for Individuals with Multiple Chronic Conditions

Objective B: Understand the epidemiology of multiple chronic conditions—Limited research has yielded information about the constellations of conditions that are most prevalent and most important in terms of disability among individuals with MCC. Additional research identifying the most common patterns of MCC can help in targeting specific interventions for specific subgroups and monitoring the impact of those interventions. Such research should utilize public program (e.g., Medicare) and other existing datasets.



U.S. Department of Health & Human Services

December 2010

The questions before us are:

- How to sift through massive amounts of data; and
- How to identify constellations of conditions that are most prevalent and most important in terms of disability (or any other outcome) in individuals with MCC?

Challenge in using
traditional
statistical methods

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- How to sift through massive amounts of data; and
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Challenge in using
traditional
statistical methods

The word “Constellation”
is critically important
here, because most prior
studies have evaluated
health outcomes in
relation to one condition
at a time

The questions before us are:

- How to sift through massive amounts of data; and
- How to identify constellations of conditions that are most prevalent and most important in terms of disability (or any other outcome) in individuals with MCC?

Why constellations of conditions?

- Chronic conditions often co-occur (e.g., diabetes, hypertension, eye problems, and peripheral vascular disease)
- Their effects on a given outcome may vary depending on:
 - Sociodemographic characteristics (e.g., age, sex);
 - Place of residence;
 - Health-related social needs; and
 - The presence other health-related conditions:
 - Functional limitations (upper/lower body limitations; ADL and/or IADL limitations)
 - Geriatric syndromes (e.g., cognitive decline, urinary incontinence)

Important limitations in previous studies:

- Multivariable models examine the association between a given condition and the outcome, *one condition at a time*
 - For example, holding other variables in the model constant, is diabetes associated with increased risk of self-reported worse health in two years?
We need to move away from looking at one condition at a time, and create models that better represent real-life situations
- Most previous studies have relied on a-priori hypotheses.
 - When it comes to identifying conditions that are associated with certain outcomes, we need to allow for conditions to *emerge empirically*:
Data-driven approach → What do the data say?

Proposed solution: CART analysis

- Developed by Breiman, CART is a machine learning technique using *recursive* partitioning that considers all possible splits from all possible variables
- It starts with a ***parent*** node and splits into binary ***child*** nodes by examining all independent variables and selecting the ones that yield the most homogeneous groups relative to a study outcome (i.e., when no more homogeneous clusters can be obtained)
 - *Recursive*, because the variable that is the most strongly associated with the outcome is selected for the next split
- Each child node becomes a parent node, and the splitting continues until a terminal node is reached, i.e., when no more homogeneous clusters can be obtained

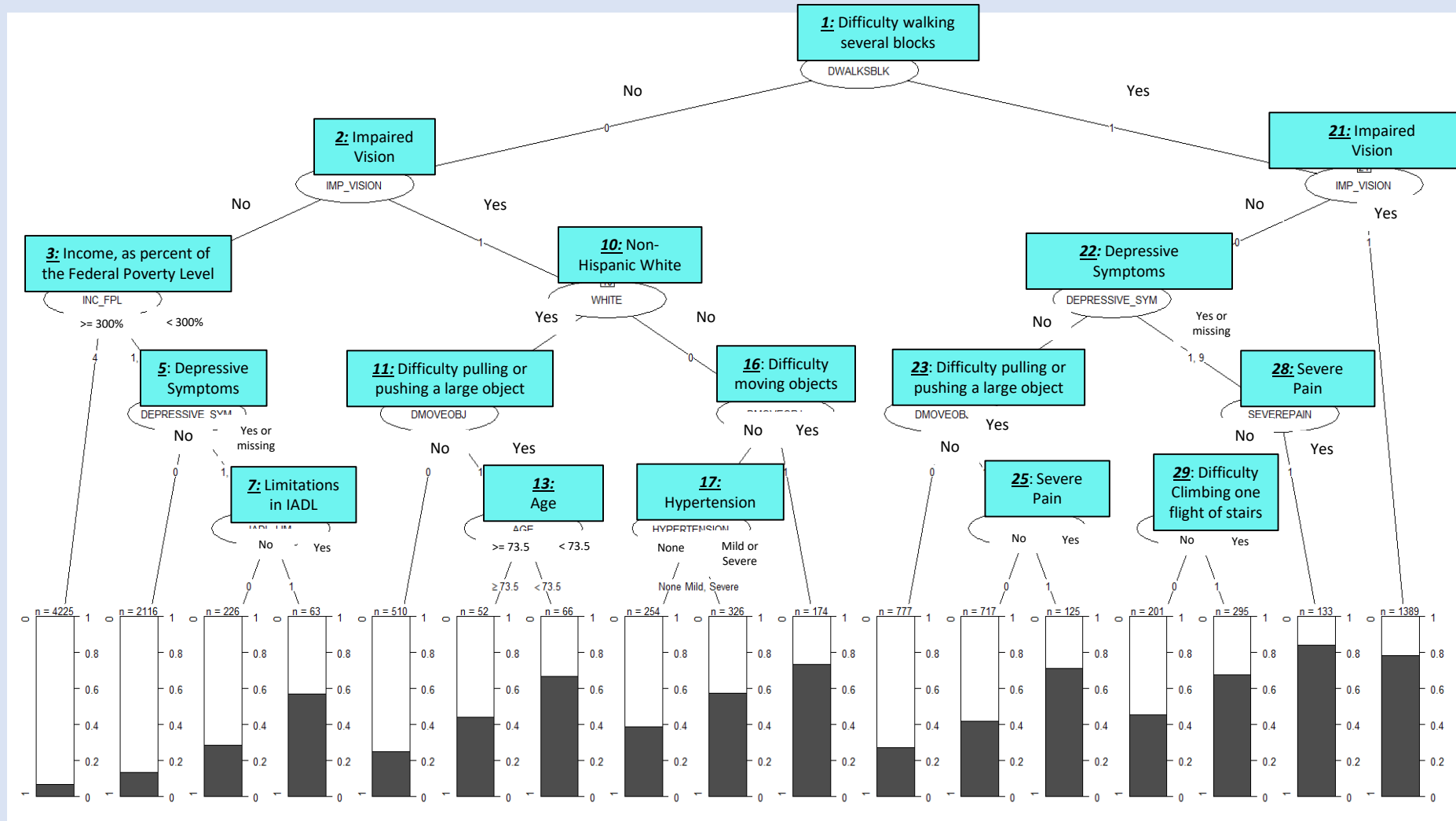
Quick notes on modeling

- '*RPART*' package in R
- Choose the split points, based on the *Gini Index* and the *entropy* (measures of purity to ensure that residual sum of squared difference between observed and predicted values are minimized)
- Choose the tree depth and the minimum size in the terminal nodes
- Pruning the tree to avoid overfitting by specifying the *complexity parameter (cp)*
 - the '*CARET*' package helps to choose the optimal cp for cross-validation accuracy

Examples of CART models

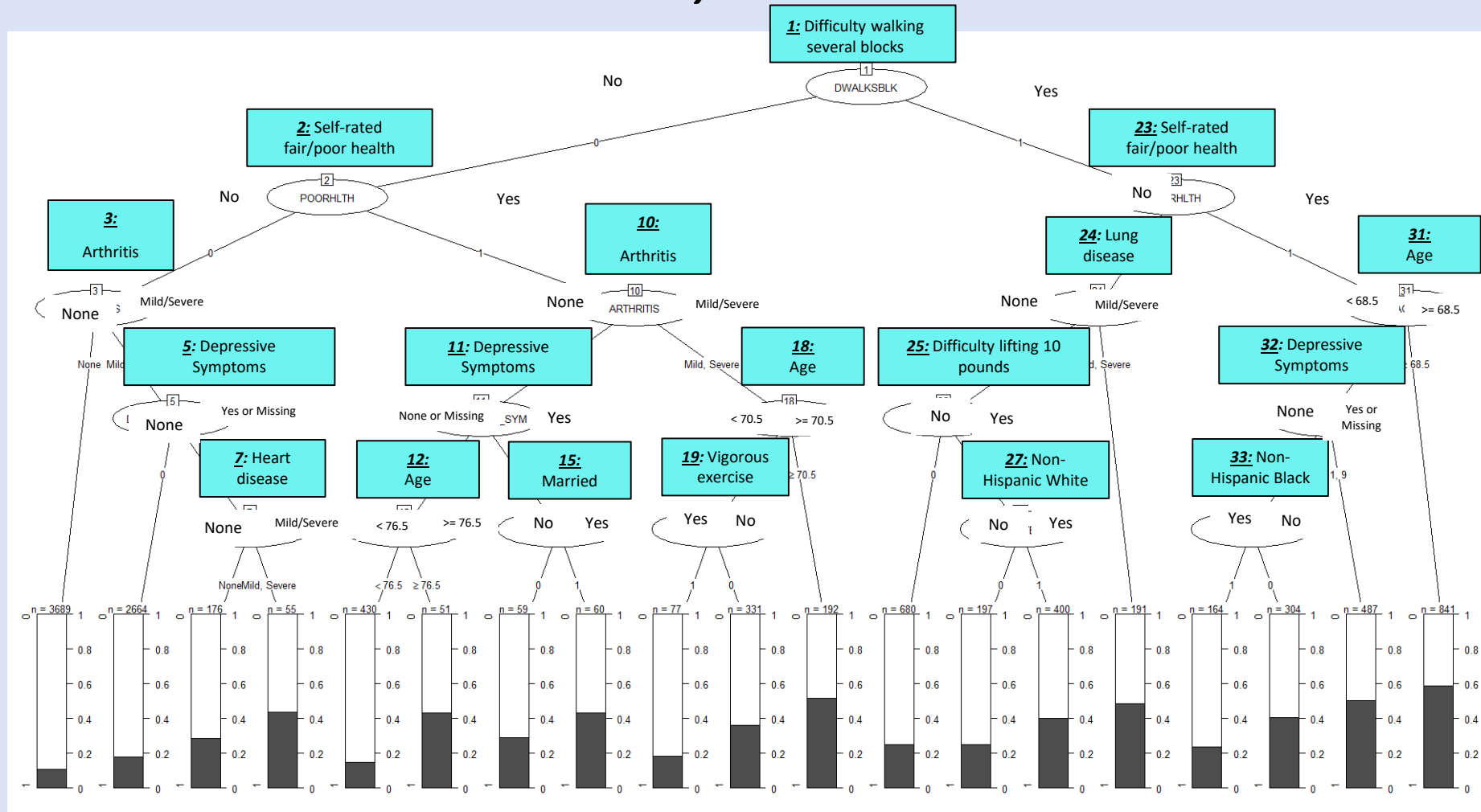
Outcome: Self-reported Fair/Poor Health

Health and Retirement Study



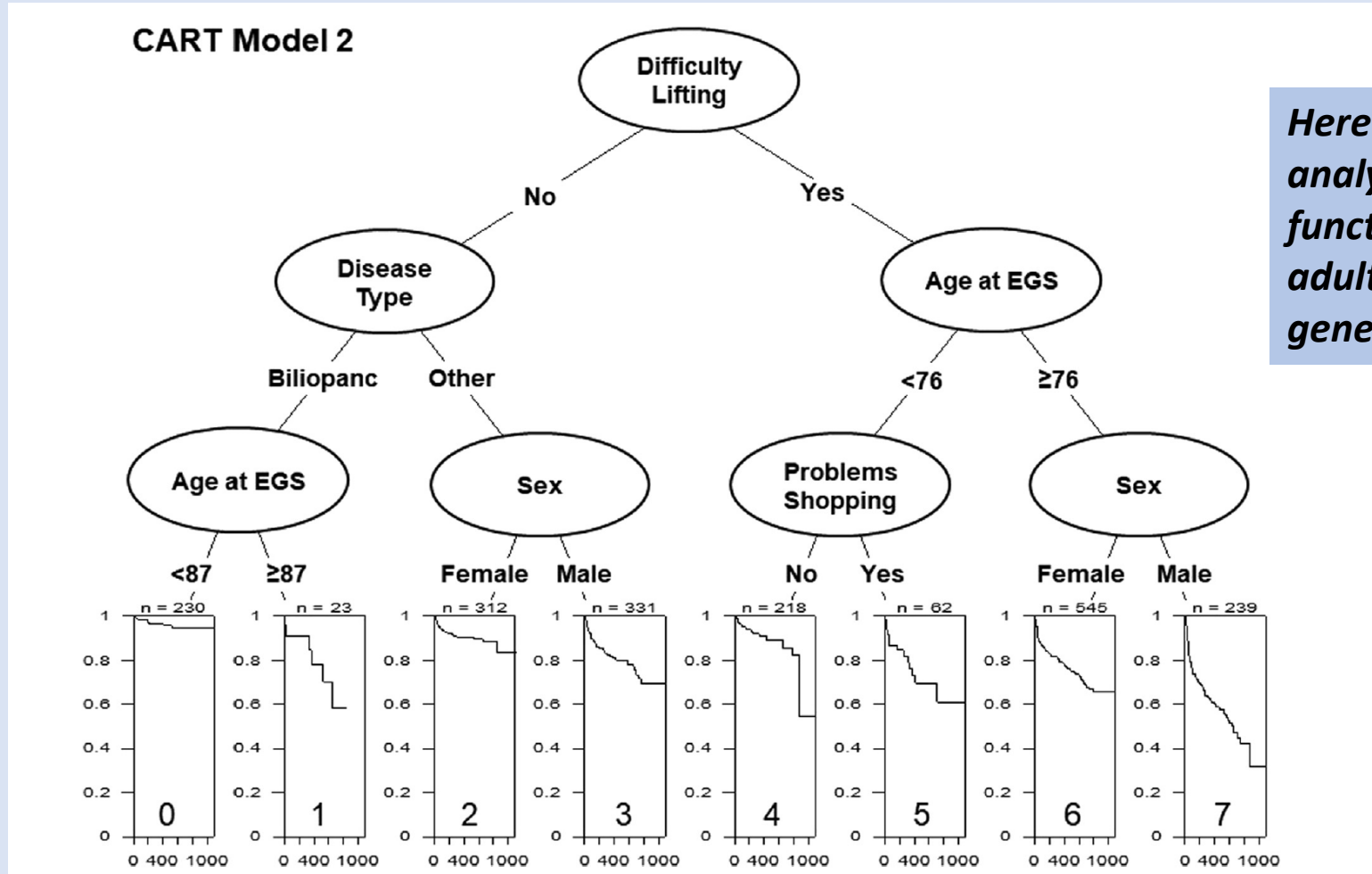
Outcome: Two-year Self-Reported Health Decline

Health and Retirement Study



CART is also highly versatile, and does not depend on the distribution of the outcome variable

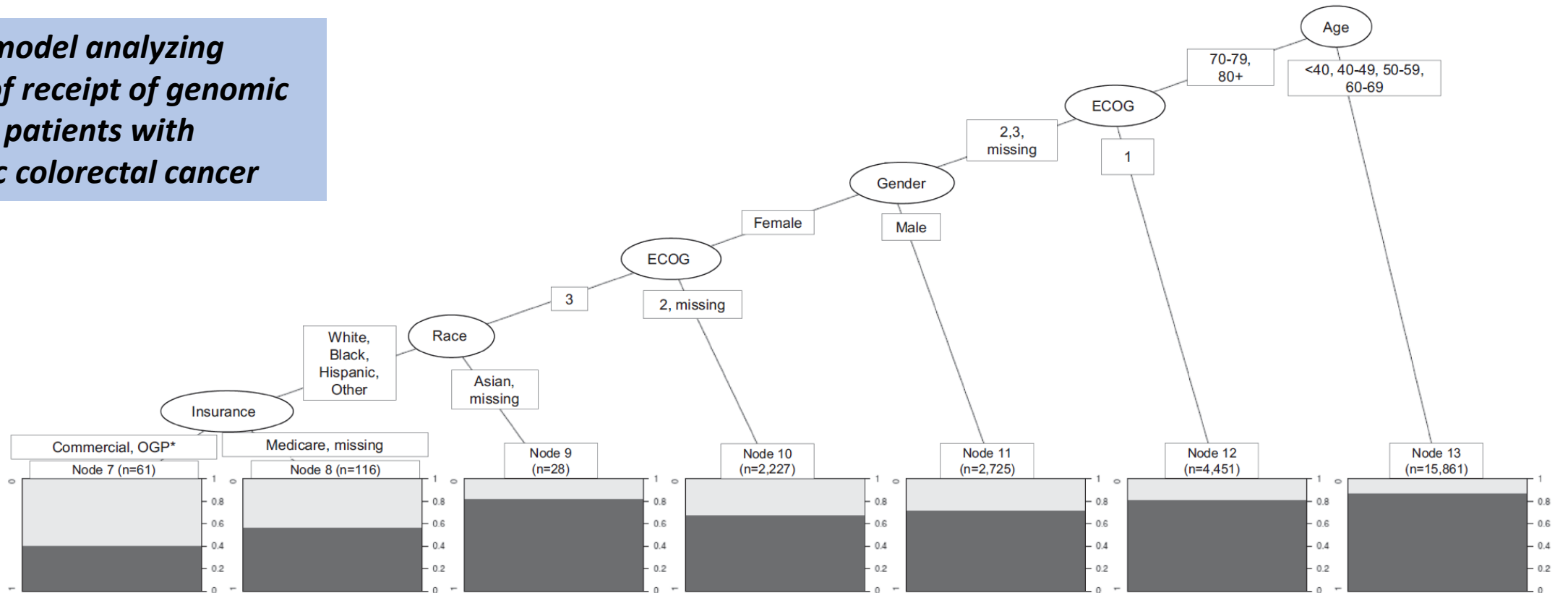
Medicare Beneficiary Survey – Medicare data



Here is an example with survival analysis, looking at components of functional limitations in older adults undergoing emergency general surgery

CART can also be used in many different contexts (not just in multimorbidity research) *FlatironHealth data*

***Here is a model analyzing
patterns of receipt of genomic
testing by patients with
metastatic colorectal cancer***



Advantages of the CART approach

- Identify ***phenotypes*** consisting of combinations of different conditions (as well as other factors that may be included in the model – e.g., demographics) that are most closely associated with the study outcome
 - ***These phenotypes are empirically emerging – “what do the data say?”***
- The visual representation of the results from the CART analysis is easy to interpret and communicate to others

Limitations of the CART approach

- Results from CART may not be robust, especially when the sample size is small, or when variables are strongly correlated with each other
 - → Random forest approach, which identifies the most important variables using subsets of the data, as well as bootstrapping
 - → K-fold validation whereby the data is divided into k subsets, and the tree is derived in all by one of the subsets. The tree is then applied to the remaining subsets to estimate the extent of misclassification.

Where do we go from here?

- In MM research, the use of CART as a predictive tool is still under exploration; but the CART is excellent for identifying constellations of conditions for hypothesis generation and further exploration
- More work needs to go into incorporating time-varying covariates in our models
- In multimorbidity research, machine learning has not been a mainstream approach, and we are behind in applying methods in high-dimensional data analysis that have been (or are being) developed in other disciplines (e.g., research involving genetics or even consumer research)
 - *We need to be open minded to cross-disciplinary pollination of methods and ideas*

Acknowledgments

- Nicholas K. Schiltz, Ph.D.
- Wyatt P. Bensken, Ph.D.

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Better Measurement of Multimorbidity: What's New and What Funding is Available?



Marcel Salive, M.D.
National Institute on Aging



Better Measurement of Multimorbidity:

What's new? What funding is available?

Marcel Salive, M.D.
National Institute on Aging
December 19, 2022



National Institute
on Aging

Disclaimer: These are my opinions
and not necessarily representing
those of NIH, NIA or DHHS

I have no conflicts to disclose.

Outline of talk

- Background/motivation
- Conceptual framework for multimorbidity
- Recent Multimorbidity research
- Recommendations for MM research
- Opportunities for MM research funding

Measuring Multimorbidity: Matching the Instrument and the Purpose (background)

- Purpose:
 - Identify the best available instruments and measures
 - Propose recommendations for use of particular instruments or measures that are appropriate for the purpose and the data source
 - Identify areas of research needs and gaps
- Planning Committee and Funding: Tilda Farhat (NIMHD), Carrie Klabunde (ODP), Marcel Salive (NIA), Jerry Suls (NCI), Deborah Young-Hyman (OBSSR)
- Held at NIA Sept 25-26, 2018, webcast

Keynote Presentations

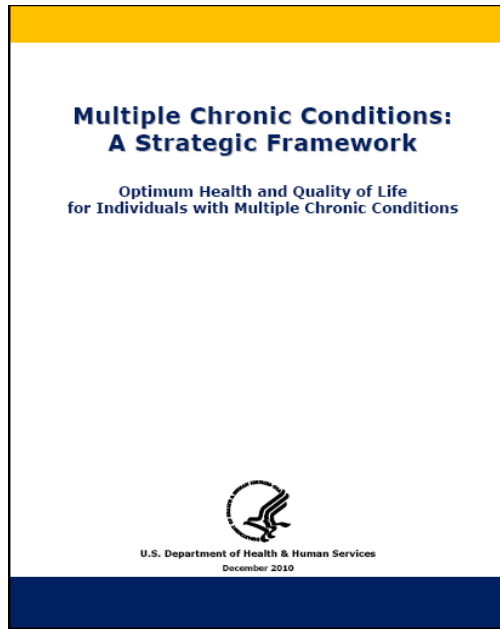
- Dr. Cynthia Boyd, Johns Hopkins University
 - “Why Assess Multimorbidity?”
 - *To improve the well-being of people living with multimorbidity*
- Dr. Claudia Steiner, Kaiser Permanente Colorado
 - “Overview of Multimorbidity Measures”
 - *There is no gold standard on how to measure multimorbidity*
 - *Measure of choice depends on the outcome of interest and, often, on what’s in the database*

“Treating an Illness Is One Thing.
What About a Patient With Many?”



New York Times, March 31, 2009
Image: Brendan Smialowski for the New York Times

Overarching Goals from 2010



1. Foster health care and public health system changes to improve the health of individuals with multiple chronic conditions



2. Maximize the use of proven self-care management and other services by individuals with multiple chronic conditions

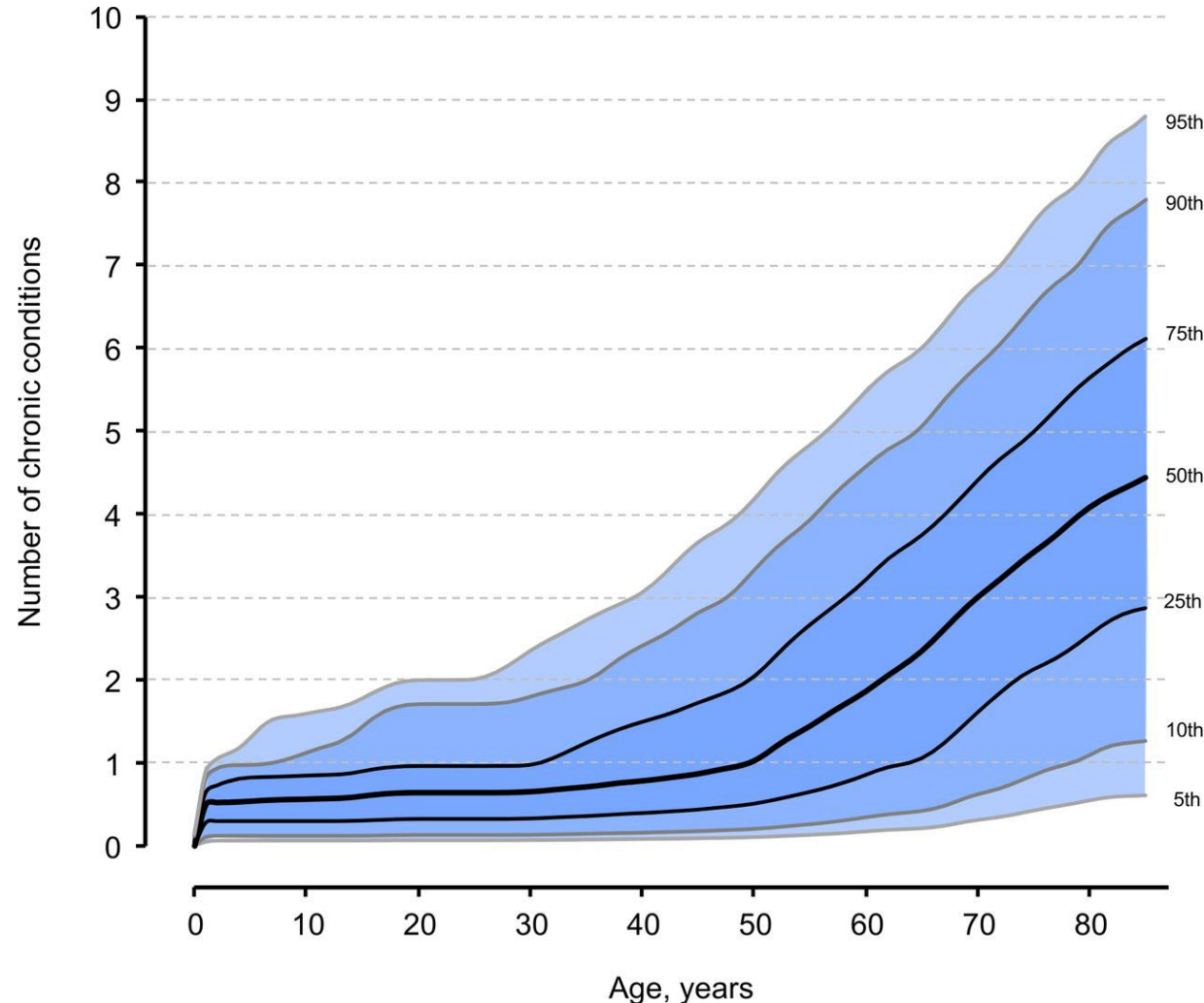


3. Provide better tools and information to health care, public health, and social services workers who deliver care to individuals with multiple chronic conditions



4. Facilitate research to fill knowledge gaps about, and interventions and systems to benefit, individuals with multiple chronic conditions

Accumulation of chronic conditions with age (sexes, all race and ethnicity groups combined)



Assigning multimorbidity percentiles to persons in a population may be a simple and intuitive tool

- assess relative health status, &
- predict short-term mortality,
- especially in younger persons and in women

Multimorbidity in the older population: prevalence and spending

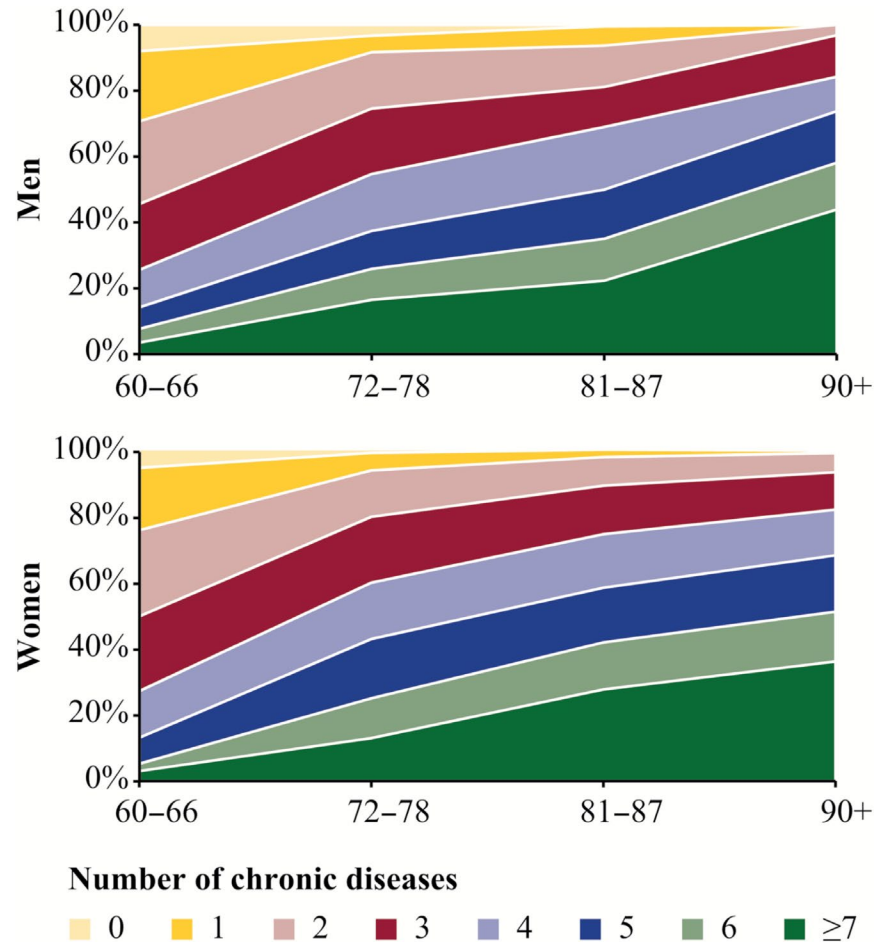
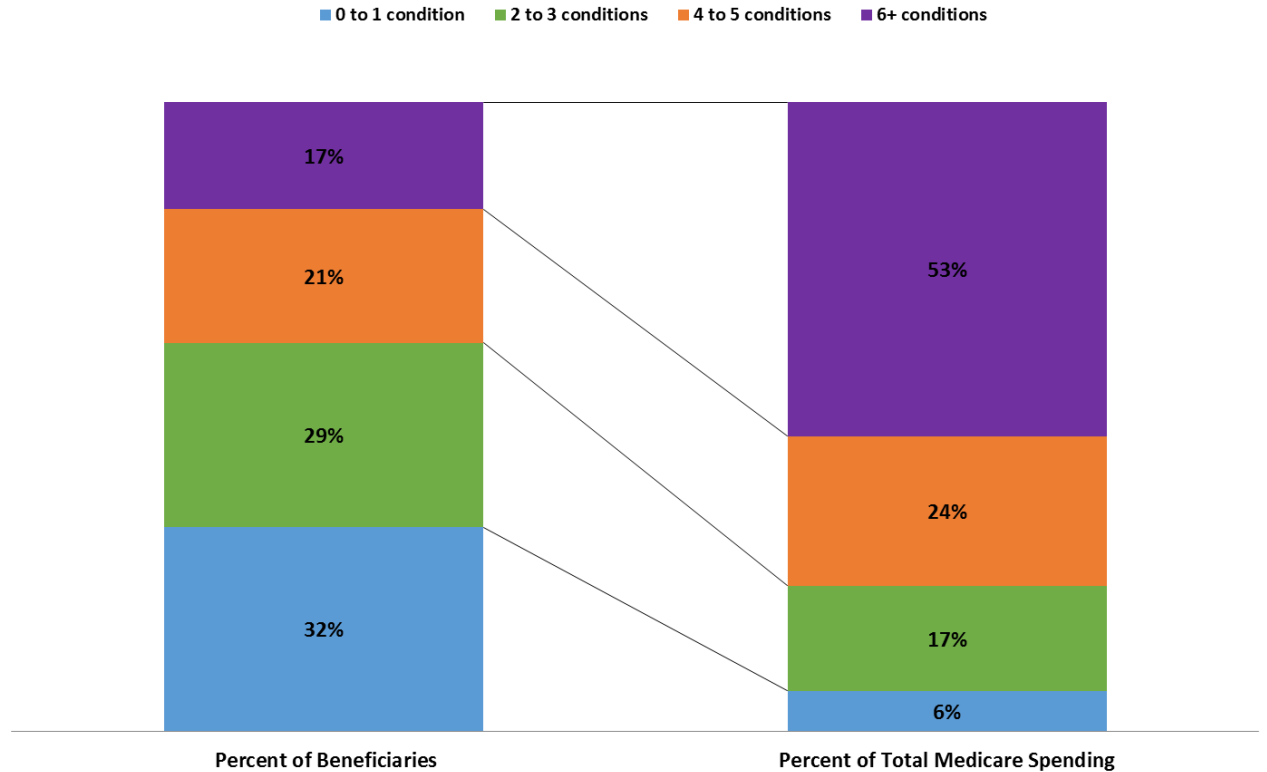


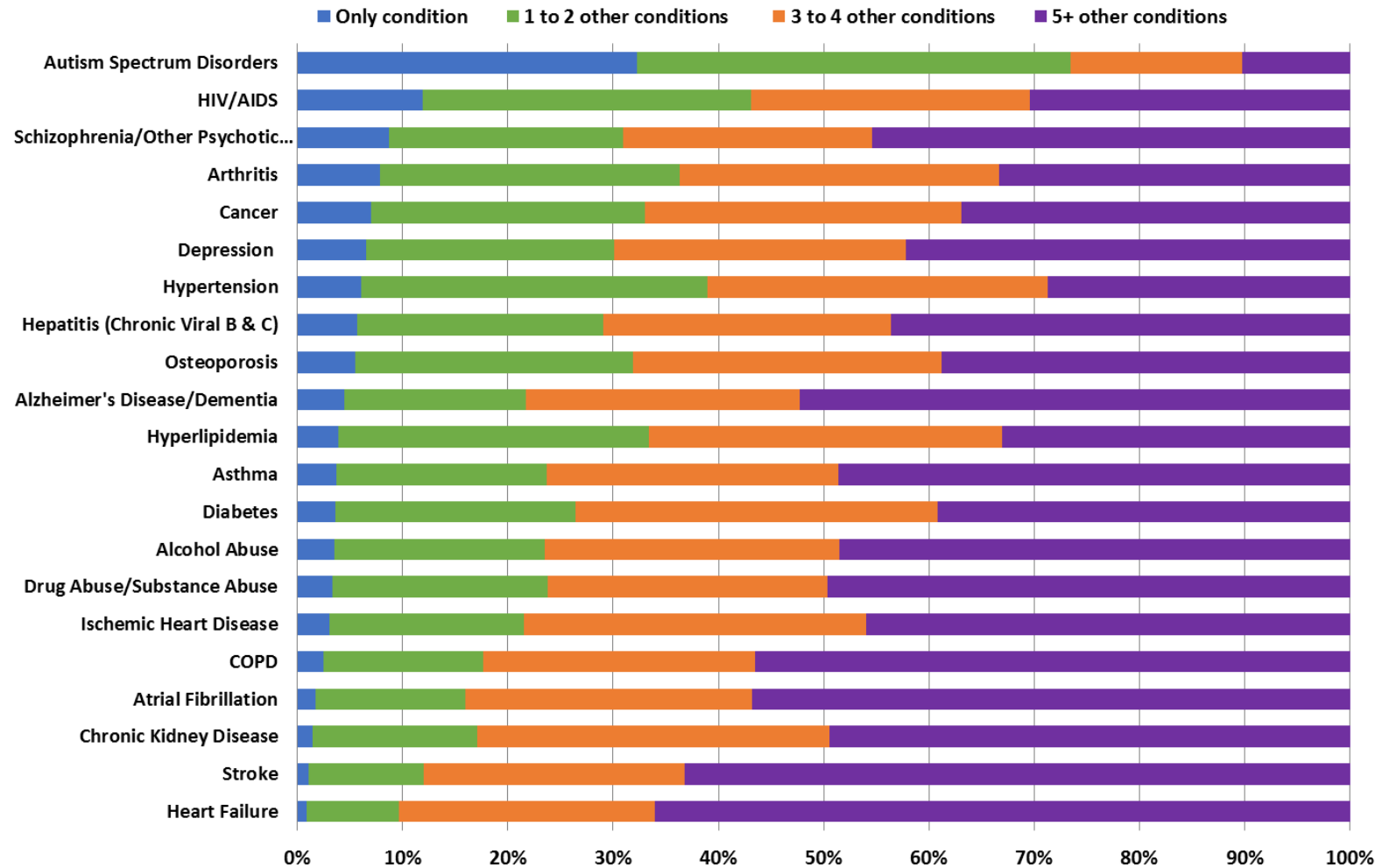
Figure 13: Distribution of Medicare Fee-for-Service Beneficiaries and Medicare Spending by Number of Chronic Conditions: 2017



From: Assessing and Measuring Chronic Multimorbidity in the Older Population: A Proposal for Its Operationalization
 J Gerontol A Biol Sci Med Sci. 2016;72(10):1417-1423. doi:10.1093/gerona/glw233
 Open Access article

Medicare fee-for-service beneficiaries, US, 2017
 Source: [CMS.gov](https://www.cms.gov)

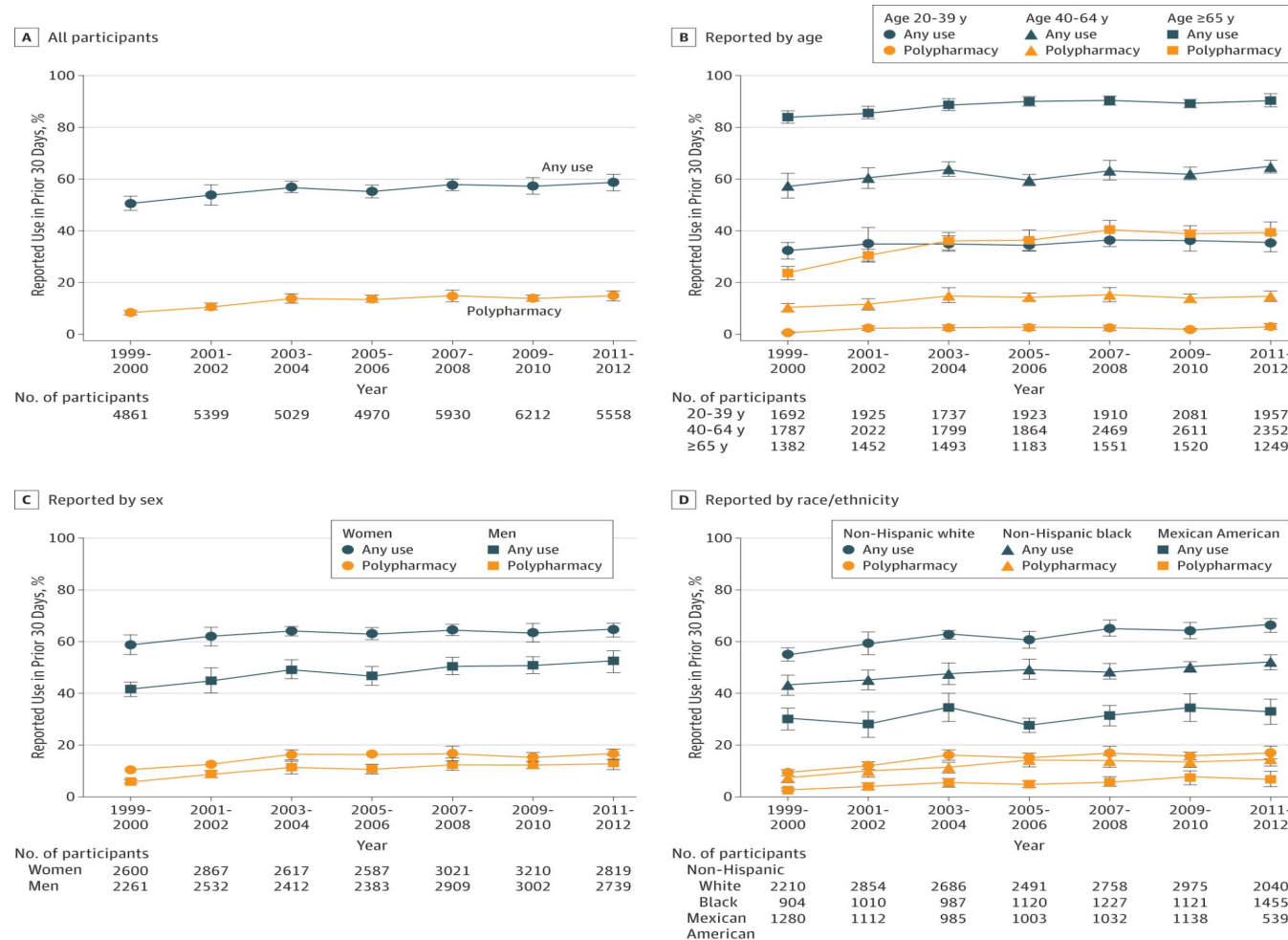
Figure 15: Co-morbidity among Chronic Conditions for Medicare Fee-for-Service Beneficiaries : 2017



Medicare fee-for-service beneficiaries, US, 2017

Source: [CMS.gov](https://www.cms.gov)

Trends in Prescription Drug Use Among Adults United States, 1999-2012



59% adults 18+ used any prescription-prior 30 days.
39% adults aged 65+ reported polypharmacy (5+ drugs).

These results exclude the nursing home population.
Source: NHANES

Types of Multimorbidity

Concordant

- Part of same overall pathophysiology
- May have related management plans

Discordant

- Unrelated to each other in pathogenesis or management

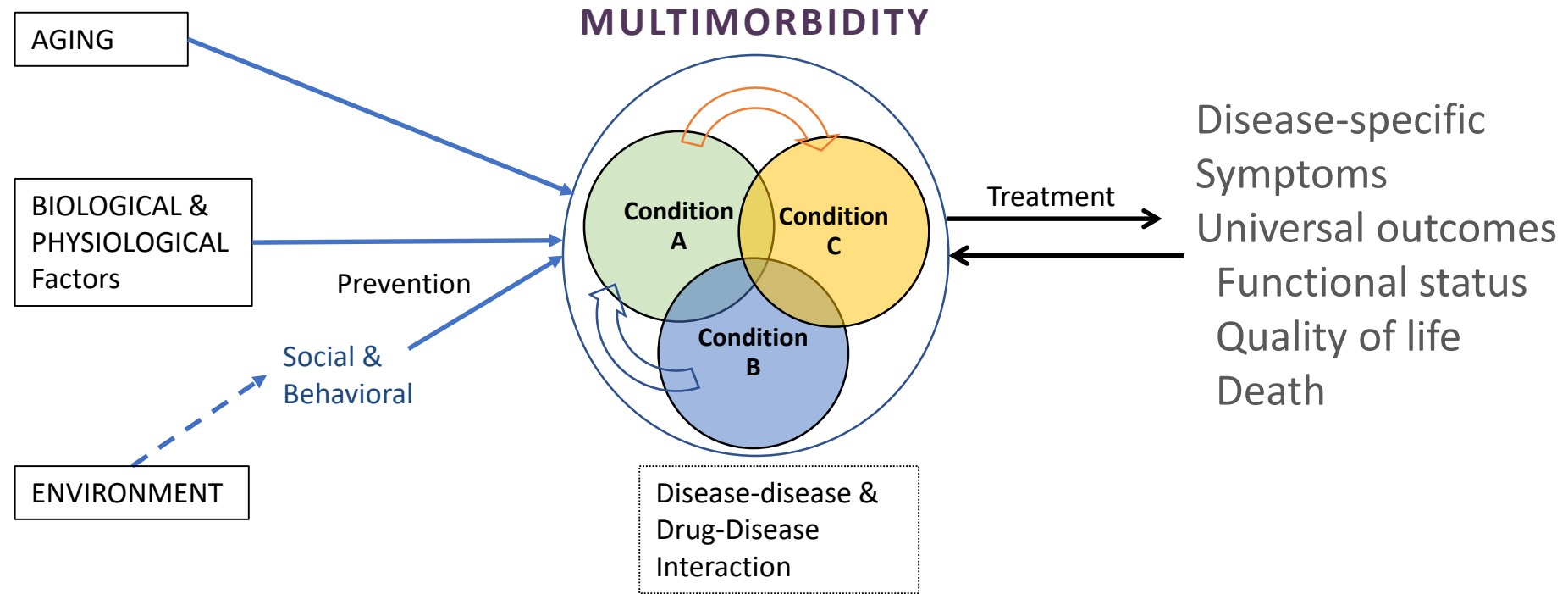
Clinically Dominant

- Drive management
 - End-stage
 - Severely symptomatic
 - Recently Diagnosed

Symptomatic vs Asymptomatic

- Focus on symptoms vs prevention of sequelae

Multimorbidity Research Framework



Salive et al. *Medical Care* 2021;59: 622-624. adapted from Clin Geriatr Med. 2016 May;32:399-407.



Multimorbidity and COVID-19 risk (n=360k UK Biobank)

- Multimorbidity index includes 12 chronic conditions
- Multimorbidity twice as common in severe COVID-19 cases (25% vs 11%), clusters more common; adjusted odds ratio 1.9
- Highest risk among those with chronic kidney disease and diabetes.

Chudasama et al. *BMC Infect Dis* (2021) 21:908.

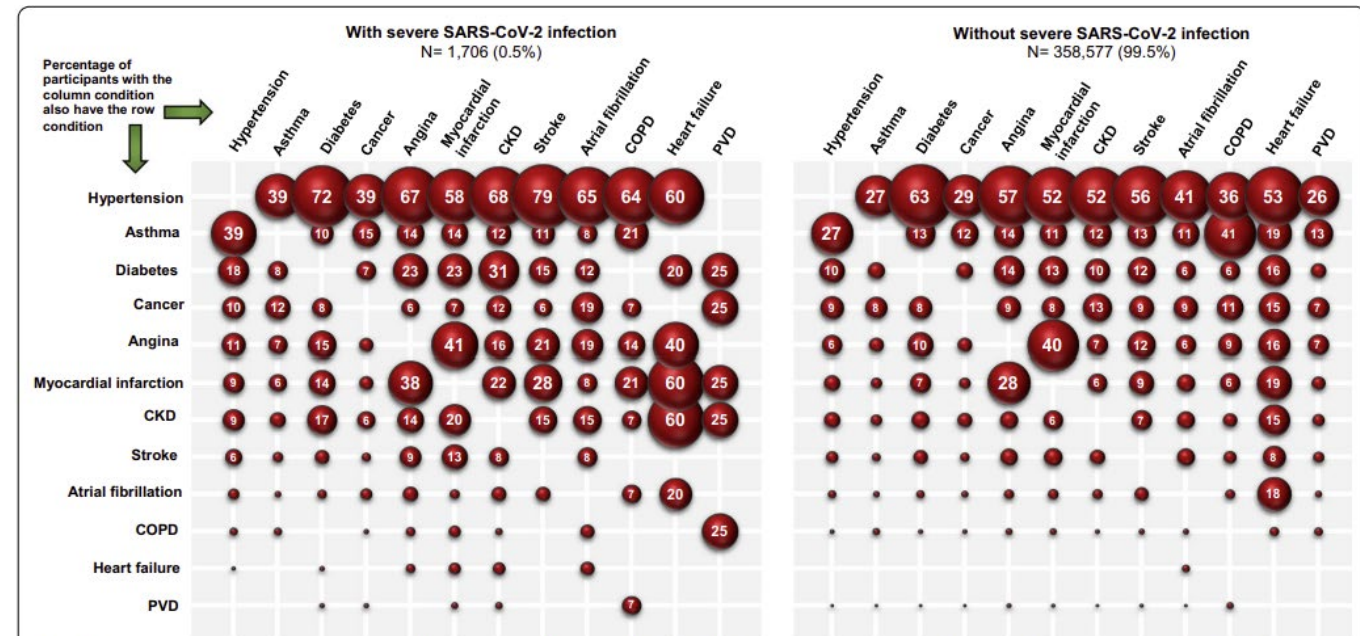


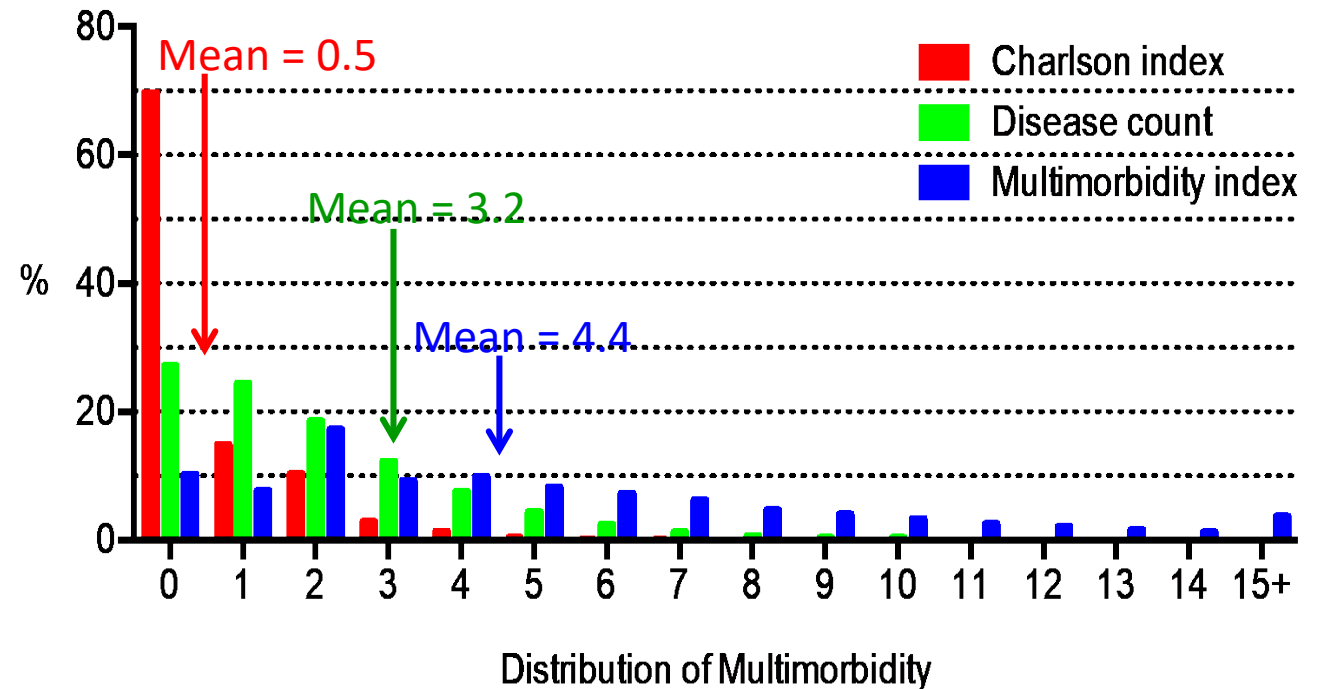
Fig. 1 Two most common pre-existing multimorbidity index conditions in UK Biobank participants with and without severe SARS-CoV-2 infection (March 16 to July 26, 2020). CKD

Risk of severe SARS-CoV-2 infection (hospitalisation or death)	Crude OR (95% CI)	Adjusted OR (95% CI)
≥ 1 vs. 0 (reference)	2.02 (1.84, 2.23)	1.65 (1.49, 1.82)
≥ 2 vs. < 2 (reference)	2.59 (2.32, 2.89)	1.91 (1.70, 2.15)
≥ 3 vs. < 3 (reference)	3.29 (2.76, 3.92)	2.02 (1.68, 2.43)
≥ 4 vs. < 4 (reference)	4.47 (3.28, 6.09)	2.25 (1.64, 3.09)

Multimorbidity index conditions include: angina, asthma, atrial fibrillation, cancer, chronic kidney disease, chronic obstructive pulmonary disease, diabetes mellitus, heart failure, hypertension, myocardial infarction, peripheral vascular disease, and stroke

Multimorbidity Weighted Index (MWI)

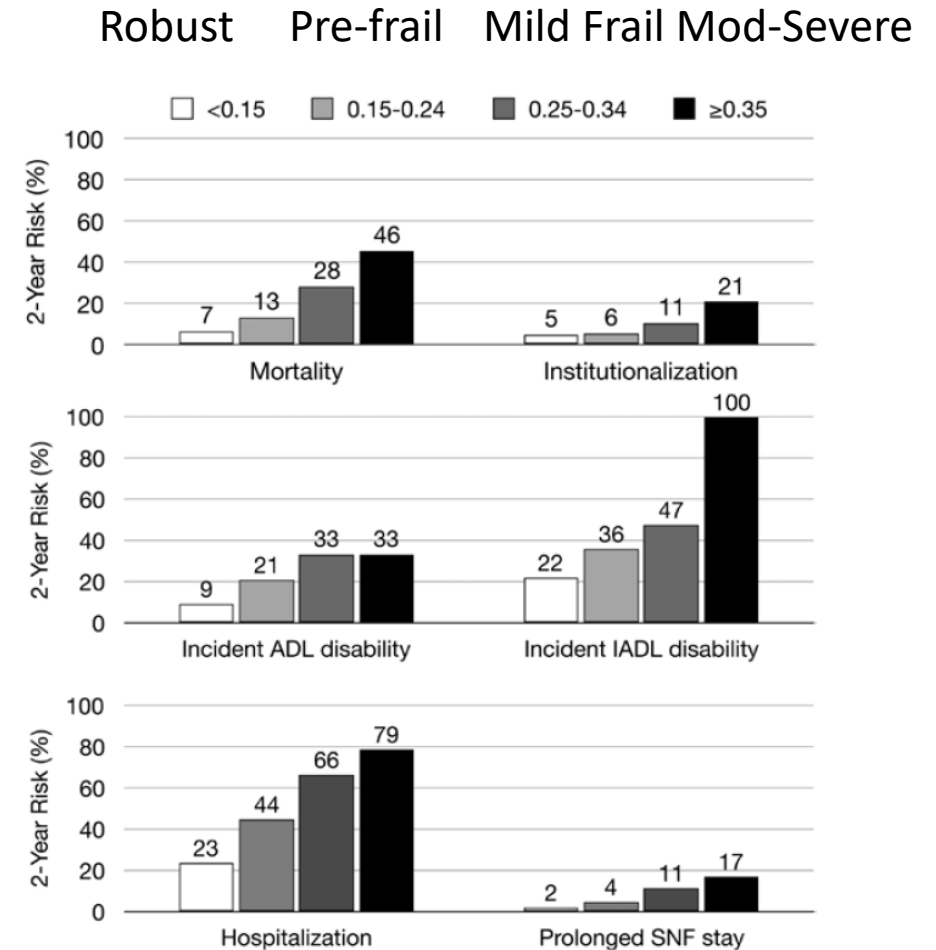
- Data from Short Form-36 in the Nurses' Health Study 1 and 2, and Health Professionals Follow-up Study and 72 self-reported conditions
- Mean MWI score was 4.8 (median, 3.7; range, 0–53), and the mean number of comorbid conditions was 3.3 (median, 2.8; range, 0–34).
- Simple disease count is unlikely to capture the full impact of multimorbidity on health-related quality of life



Wei et al. Am J Epidemiol. 2017;187(1):103-112
Wei et al. Am J Epidemiol. 2016;184(5):357-65.

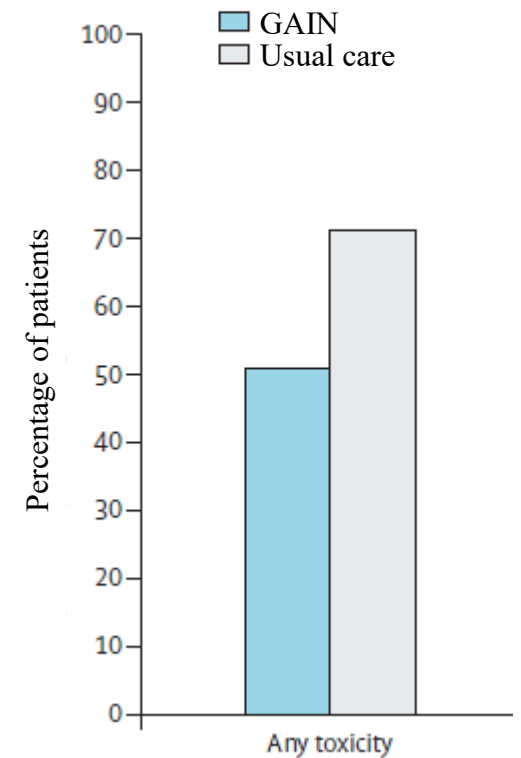
Claims-Based Frailty Index

- Estimated from Medicare claims data in the past year using deficit-accumulation approach
- Uses inpatient, outpatient, SNF, home health, carrier, DME data
- Validated against 2008 Health and Retirement Study wave
- Useful for identifying persons with poor physical function and greater risks of adverse outcomes



Personalized geriatric assessment in older patients with cancer reduces chemotherapy toxicity and reduces falls

- Older adults are at higher risk of complications from cancer treatment
- Geriatric Assessment INtervention (GAIN) evaluates health status in older adults and recommends personalized interventions across a variety of domains:
 - Functional status, comorbidities, multiple medications, symptoms, psychological status, social activity, social support, nutrition, cognition, and spiritual well-being
- Two randomized trials tested the effectiveness of GAIN in older adults undergoing cancer treatment in 605 patients in a cancer center, or in 718 patients from 40 oncology practices
- GAIN prevented serious chemotherapy toxicity by 10-26% in both trials
- In one trial GAIN reduced falls by 42%, and in the other, increased advance directive completion by 15% with no effect on survival.



Li et al. *JAMA Oncol.* 2021;7(11):e214158. Mohile et al *Lancet* 2021; 398: 1894–904.
NIA grants K24AG055693, K24AG056589 and R33AG059206

Deprescribing potentially inappropriate medications is efficacious and safe



You may be at risk IF

You are taking one of the following sedative-hypnotic medications:

☐ Alprazolam (Xanax®)	☐ Diazepam (Valium®)	☐ Quazepam
☐ Chlorazepate	☐ Estazolam	☐ Temazepam (Restoril®)
☐ Chlordiazepoxide	☐ Flurazepam	☐ Triazolam (Halcion®)
☐ Chlordiazepoxide-amitriptyline	☐ Loprazolam	☐ Eszopiclone (Lunesta®)
☐ Clidinium-Chlordiazepoxide	☐ Lorazepam (Ativan®)	☐ Zaleplon (Sonata®)
☐ Clobazam	☐ Lormetazepam	☐ Zolpidem (Ambien®, Intermezzo®, Edluar®, Sublinox®, Zolpimist®)
☐ Clonazepam (Rivotril®, Klonopin®)	☐ Nitrazepam	☐ Zopiclone (Imovane®)
☐ Oxazepam (Serax®)		






STEP-BY-STEP TAPERING-OFF PROGRAM

We recommend that you follow this schedule under the supervision of your doctor or pharmacist to taper off **your sedative-hypnotic medication**.

WEEKS	TAPERING SCHEDULE							✓
	MO	TU	WE	TH	FR	SA	SU	
1 and 2								
3 and 4								
5 and 6								
7 and 8								
9 and 10								
11 and 12								
13 and 14								
15 and 16								
17 and 18								

EXPLANATIONS

 Full dose
  Half dose
  Quarter of a dose
  No dose

10 You May Be at Risk

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<http://deprescribing.org/resources/deprescribing-information-pamphlets/>

JAMA Intern Med. 2014;174:890-8. JAMA. 2018;320(18):1889-1898.

Potential for cross-NIH multimorbidity studies

- Biological basis for multimorbidity
 - Hallmarks of aging studies
 - Other potential underlying causes
- Comparative studies-epidemiological
- Evaluating interventions—composite endpoint of multimorbidity
 - Incorporate standardized screening/diagnosis
 - Incorporate disease severity measures
 - Include geriatric syndromes

Multimorbidity Research Priorities-older adults

Themes

- Screening and assessment tools
- Outcomes
- Interventions
- Health services research
- Analytical approaches to studying

Priorities

- Health-related quality of life
- Assessment tools (to assess, e.g., symptom burden, quality of life, function)
- Risk stratification
- Data harmonization across healthcare systems
- Epidemiological methods of addressing longitudinal data, missing data, and information censoring

A National Platform to Advance Transdisciplinary Aging Research



The Clinician-Scientists Transdisciplinary Aging Research (Clin-STAR) Coordinating Center provides a national platform for clinicians focusing their careers on aging research in order to improve patient-centered care for older adults across specialties and disciplines.

MCC Funding Opportunities

The NIA has prioritized research pertaining to older adults with multiple chronic conditions (MCC)

Active Funding Announcements involve many Institutes and Centers:

[PAR-20-179](#): Advancing Research To Develop Improved Measures and Methods for Understanding Multimorbidity (R01 Clinical Trial Optional)

[PAR-20-180](#): Identifying Innovative Mechanisms or Interventions that Target Multimorbidity and Its Consequences (R01 Clinical Trial Optional)

[PAR-21-308](#): Pragmatic Trials for Dementia Care and Caregiver Support (R61/R33 –Clinical Trial Required)

NOTE that investigator-initiated MCC research could go to parent R01, R21 and R03 announcements

Recently closed RFAs:

[RFA-AT-22-001](#): NIH Health Care Systems Research Collaboratory - Pragmatic and Implementation Trials of Embedded Interventions

[RFA-AG-23-032](#): Network for Personalization of Diagnostic Tests for AD/ADRD in Older Adults with Multiple Chronic Conditions (MCCs)

Conclusions

- Growing focus on multimorbidity
- Underlying biology may provide clues for prevention
- Many challenges for disease ascertainment, recording
- Opportunities abound for MCC research funding at NIH

Further Information

- NIA Division of Geriatrics & Clinical Gerontology
 - 301-496-6761
 - <https://www.nia.nih.gov/research/dgcg>

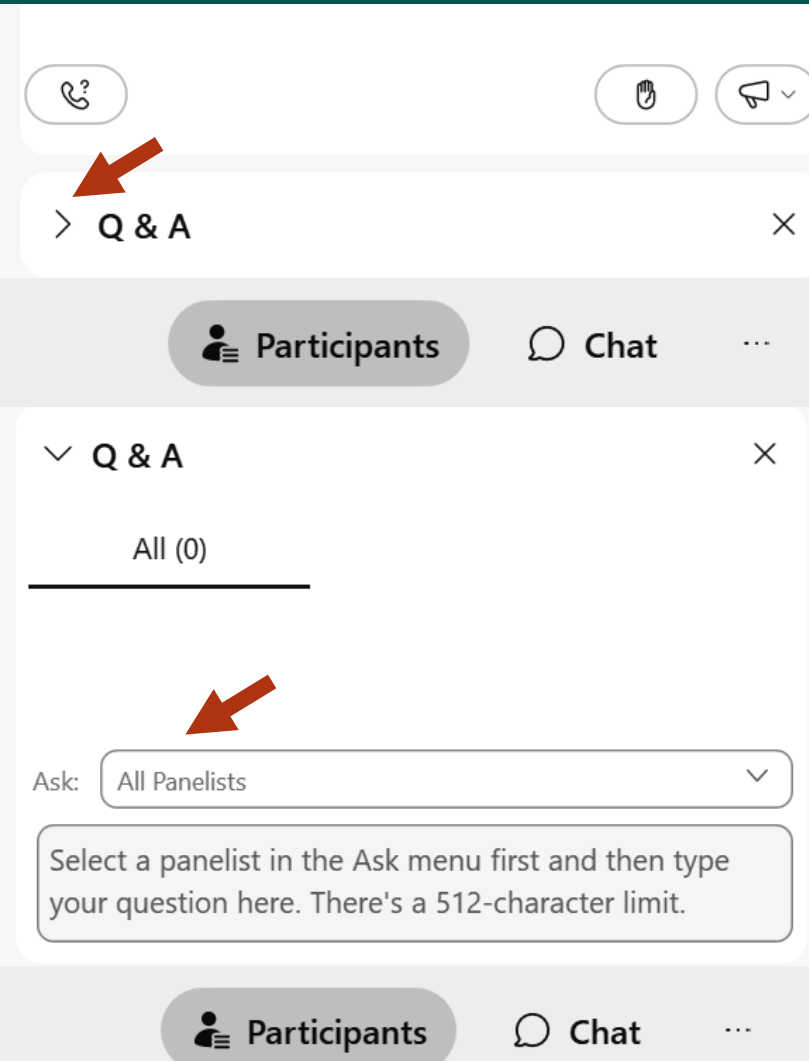


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All Panelists



Thank You!

Please register for our next webinar
on January 19th!



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