When More than One Outcome Matters: A Method for Precise Accounting of Multiple Chronic Conditions in a Case Study of Patients with Obstructive Airway Disease

Heather Allore, PhD
Professor, Director of Biostatistics, Program on Aging

Terrence E. Murphy, PhD
Assistant Professor of Medicine, Geriatrics
Your attendee ID helps the host interact and manage your attendance in the webinar.

It can be found in **Event Info tab**:

**Event info Tab:**

![WebEx Event Center](image)

**HMORN-OAIC AGING Webinars Demo**

- **Host:** Kathryn Anzuoni
- **Audio connection:** US Toll: +1-415-655-0002
- **Access code:** 669 408 159
- **Attendee ID:** 1
- **Event number:** 669 408 159
- **Host key:** 907320
How to ask a question

- When you would like to interact with the presenter
  - Type your questions in the Q&A box:
    - Hosts will acknowledge questions in order
If you are having technical issues

- Type your questions in the chat box:

- Hosts will communicate via chat to try and fix any technical issues
When More than One Outcome Matters: A Method for Precise Accounting of Multiple Chronic Conditions in a Case Study of Patients with Obstructive Airway Disease

Aging Initiative Webinar - April 19, 2017
An exciting opportunity exists to build upon the collective and complementary knowledge, resources, and capabilities of the HCSRN and the OAICs to develop an interdisciplinary research agenda focused on older adults with multiple chronic conditions under a new HCSRN-OAICs AGING ("Advancing Geriatrics Infrastructure & Network Growth") Initiative.

Supported by: R24 AG045050 (NIA)
Why Multiple Outcomes?

• Most important life decisions consider multiple outcomes
  – Healthcare Systems:
    • Accessibility
    • Cost
    • Quality

• Decisions on healthcare of older persons
  – Potential need for ongoing provider care
  – Patient’s quality of life
Methods for Considering Multiple Outcomes?

• Most studies assess a single primary outcome
  – Sometimes a secondary/tertiary outcome

• No consensus on the best ways to statistically evaluate multiple, concurrent outcomes
  – Joint modeling of Outcomes
  – Joint Latent Trajectory Modeling

• Typically consider a few outcomes in parallel
  – Look for consistency and complementary insight
Multiple Chronic Conditions (MCC)

- In medical research of older person we study how MCC affect patient centered outcomes.
- Also, how MCC may contribute to utilization.
- We interpret MCC as including diseases such as cancer and diabetes.
A Precise Accounting of the Contributions of Multiple Chronic Conditions to an Outcome

• A useful method would:
  – estimate the individual, additive contributions of each coexisting condition
  – account for a fairly large number (10-30) of co-occurring conditions
  – be model driven with good face validity
Average Attributable Fraction (AAF): A Useful Method for Dichotomous Outcomes and Conditions

- AAF accounts for coexisting risk factors (Eide and Gefeller, 1995; Gefeller, et al. 1998)

- Good face validity
  - Model based
  - Additive contributions of multiple conditions

- Can address many conditions/covariates (Murphy et al. 2012 and Allore et al. 2016)
What is the Average Attributable Fraction for a Condition?

- Explains the proportion of outcomes potentially prevented by its removal
  - E.g., among older U.S. adults with obstructive airway disease, removal of COPD would eliminate 22% of the reported cases of incident decline in perceived health

- Improves on Attributable Fraction of Levin (1959) in accounting for overlap among conditions (non-additive)

- Sum of AAF from multiple conditions ≤100%
AAF of a Given Condition Depends On Two Characteristics

• Both directly from data
• Prevalence of condition
  • Higher prevalence can lead to higher AAF
• Association with outcome
  • Stronger associations can yield higher AAF
Example from Index Pilot Study

• Patient-Centered Outcomes:
  • ≥ 7 days in bed
  • Incident loss of mobility
  • Incident decline in perceived health

• Asthma
  • Highly prevalent (63%)
  • only associated with ≥ 7 days in bed

• COPD
  • Highly prevalent (55%)
  • Associated with all 3 outcomes
## Average Attributable Fractions of Patient Centered Outcomes

<table>
<thead>
<tr>
<th>Patient-Centered Outcomes</th>
<th>ASTHMA (prev 63%)</th>
<th>COPD (prev 55%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥7 days in bed</td>
<td>8.2%</td>
<td>17.7%*</td>
</tr>
<tr>
<td>Incident Loss of Mobility</td>
<td>0.00%</td>
<td>11.4%*</td>
</tr>
<tr>
<td>Incident Decline in Perceived Health</td>
<td>0.00%</td>
<td>22.0%**</td>
</tr>
</tbody>
</table>

* second highest AAF of 12 conditions  
** largest AAF of 12 conditions

**Asthma:** High Prevalence + Weak Association = Low AAF  
**COPD:** High Prevalence + Strong Association = High AAF
How To Calculate Average Attributable Fraction (1)

• Identify extant combinations of conditions
  – Build a design matrix of these combinations
  – Identify all the subsets of these combinations

• Build a good logistic model of outcome
  – Conditions of interest
  – Plausible, significant interactions of conditions
  – Clinically important covariates
How To Calculate Average Attributable Fraction (2)

• Each person has a unique set of conditions
• Calculate reduction in probability of outcome by removing condition of interest
• Repeat for each subset of person’s conditions
• Average across all person-conditions
• Cross-sectional (AAF) or longitudinal (LE-AAF)
AAF Has Been Applied to a Growing Range of Outcomes

• Mortality
  (Tinetti et al, 2012)

• Pneumonia requiring hospitalization
  (Juthani-Mehta et al, 2013)

• Outcomes Important to Patients with COPD and their providers in our Pilot Study
  • four healthcare utilization outcomes
  • three patient-centered outcomes
  (Murphy et al, under review)
Original Motivation: Mortality in Older Adults

• National Center for Health Statistics (NCHS)
  – Algorithmic rules applied to death certificate data
  – Single condition chosen as cause
  – Encourage citation of certain categories
    • Cancer
    • CVD
  – Some conditions systematically underestimated
    • Dementia
    • Injury
  – Don’t consider multiple chronic conditions (MCC)
Wanted a More Objectively Informed Approach

• Empirical method with good properties
  – Systematic consideration of MCCs
  – Drawing from longitudinal information
  – Want contributions from individual conditions
    • Whether individually occurring or in combinations

• Average Attributable Fraction
  – Achieves these goals
<table>
<thead>
<tr>
<th>Disease Category</th>
<th>NCHS Reported Percentage of Deaths</th>
<th>LE-AAF Prop Contribution (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>30.4</td>
<td>17.4 (10.8, 23.0)</td>
</tr>
<tr>
<td>Cancer</td>
<td>22.0</td>
<td>7.6 (6.3, 8.9)</td>
</tr>
<tr>
<td>Cerebrov/Stroke</td>
<td>7.4</td>
<td>2.9 (1.4, 4.2)</td>
</tr>
<tr>
<td>Lower Resp/Lung</td>
<td>6.0</td>
<td>13.6 (11.6, 16.3)</td>
</tr>
<tr>
<td>Alzh / Dementia</td>
<td>3.7</td>
<td>7.1 (5.9, 8.2)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3.1</td>
<td>Not in top ten</td>
</tr>
<tr>
<td>Pneum/Influenza</td>
<td>3.0</td>
<td>4.8 (4.1, 5.8)</td>
</tr>
<tr>
<td>Renal / kidney</td>
<td>2.0</td>
<td>4.8 (3.9, 5.7)</td>
</tr>
<tr>
<td>Unint Injuries</td>
<td>2.0</td>
<td>3.0 (2.1, 4.0)</td>
</tr>
<tr>
<td>Septicemia</td>
<td>1.5</td>
<td>1.8 (1.4, 2.3)</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>Not in top 10</td>
<td>3.1 (1.5, 4.5)</td>
</tr>
<tr>
<td>All other causes</td>
<td>19</td>
<td>33.9 (residual)</td>
</tr>
</tbody>
</table>

(Murphy et al, Statistics in Medicine, 2012)
COPD’s Average Attributable Fraction from multiple chronic conditions (CAAFE)

Geisinger and Yale O.A.I.C. (Pepper Center)
CAAFE Team Affiliations

- Heather Allore (Yale)
  - PI of Parent Study using MEPS
  - Arc-COPD (Absolute Risk Calculator for COPD)
- Gail McAvay (Yale)
  - Epidemiologist for Arc-COPD and CAAFE
- Terrence E. Murphy (Yale)
  - PI of CAAFE
- Paul Simonelli (Geisinger)
  - Pulmonologist
- Jason Stamm (Geisinger)
  - Pulmonologist
Funding

• The Aging Initiative
  • R24 AG045050 (NIA/HMORN)
  • PI: Jerry Gurwitz, MD

• Absolute Risk Calc. for COPD (ArcCOPD)
  • R01 AG047891 (NIA)
  • PI: Heather Allore, PhD

• Yale OAIC
  • P30AG21342 (NIA)
  • PI: Tom Gill, MD
Motivation for CAAFE

• U.S. Adults with Obstructive Airway Disease
  – Asthma
  – COPD
  – Both

• High burden of MCCs

• High utilization of healthcare

• Strong effect on quality of life

• Understudied medical condition
Objective and Data Source

• Want proportions of attributable outcomes
  • From COPD and Asthma
  • And 10 commonly co-occurring medical conditions
  • Need large national cohort with COPD/Asthma
  • Need data on MCCs

• Medical Expenditure Panel Survey (MEPS)
  • Large, representative sample with COPD or Asthma
  • Detailed information on comorbidity
  • Restricting to persons $40 \leq \text{age} \leq 85$ years
  • $(N=3486$ at round 1).
Sample from MEPS

Medical Expenditure Panel Survey (MEPS)
Total Sample with Statistical Weight Present:
N=89087

N=52032; age less than 40 years
N=189; missing diagnostic information
N=33092; did not have COPD or asthma
N=288; missing smoking information

Asthma or COPD
Aged 40-85 years
N=3486

Asthma Alone
N=1585 (45.5%)

COPD Alone
N=1294 (37.1%)

Asthma and COPD
N=607 (17.4%)
Definition of COPD

• We designate persons with COPD from having one or both of two identifiable conditions in round 1 of MEPS:

  – Chronic Bronchitis:
    • In the last 12 months have you been diagnosed for chronic bronchitis?

  – Emphysema:
    • Have you ever been diagnosed with emphysema?
Definition of Asthma and other Chronic Conditions

• Asthma:
  • ever been diagnosed or still have asthma?

• Other Chronic Conditions:
  • ever been told by an MD or other provider that you have this condition?
Healthcare Utilization Outcomes in MEPS (incidence over 1 year)

- Any cause visit to the ER
  - (30%)

- Any cause Hospitalization
  - (21%)

- ≥ 6 Outpatient visits
  - (50%)

- Respiratory Hospitalization
  - (5.5%)
Patient Centered Outcomes in MEPS (incidence over 1 year)

- ≥ 7 days of disability in past year
  - (27%)

- Incident loss of mobility
  - (14%)

- Incident worsening of perceived health
  - (17%)
Baseline prevalence of 12 Medical Conditions in our MEPS Sample (Round 1)

- Angina (10%)
- Arthritis (58%)
- Asthma (63%)
- Cancer (20%)
- Cognitive Decline (15%)
- COPD (55%)
- Coronary HD (17%)
- Diabetes (23%)
- HTN (62%)
- Lung Cancer (1.4%)
- MI (12%)
- Stroke (11%)
Healthcare Utilization

- COPD largest contributor in 3 of 4 outcomes
- Arthritis second largest contributor
- Cognitive Impairment and Diabetes contribute to all 4 outcomes
- Hypertension contributes to 3 of 4 outcomes
Interpreting the AAFs of COPD for Healthcare Utilization Outcomes

• Removing COPD from U.S. adults with obstructive airway disease would potentially reduce incidence by:

  a. Any ER visit – reduce by 20.1%
  b. Any Hospitalization – reduce by 19.4%
  c. ≥ Six Outpatient Visits – reduce by 5.9%
  d. Respiratory Hospitalization – reduce by 14.9%
Interpreting the AAFs of Arthritis for Healthcare Utilization Outcomes

• Removing Arthritis from U.S. adults with obstructive airway disease would potentially reduce incidence by:

  a. Any ER visit – reduce by 15.0%

  b. Any Hospitalization – reduce by 17.2%

  c. ≥ Six Outpatient Visits – reduce by 19.7%

  d. Respiratory Hospitalization – reduce by 11.1%
Patient Centered Outcomes

- Arthritis largest contributor in 2 of 3 outcomes
- COPD second largest contributor
- Cognitive Impairment and Stroke contribute to all 3 outcomes
Interpreting the AAFs of Arthritis for Patient-Centered Outcomes

- Removing Arthritis from U.S. adults with obstructive airway disease would potentially reduce incidence by:
  a. ≥ Seven Disability Days – reduce by 23.7%
  b. Incident Loss of Mobility – reduce by 29.2%
  c. Incident Decline in Perceived Health – reduce by 15.0%
Interpreting the AAFs of COPD for Patient-Centered Outcomes

• Removing COPD from U.S. adults with obstructive airway disease would potentially reduce incidence by:

  a. ≥ Seven Disability Days – reduce by 17.7%

  b. Incident Loss of Mobility – reduce by 11.4%

  c. Incident Decline in Perceived Health – reduce by 22.0%
Conclusions

• COPD
  • largest contributor to utilization of healthcare

• Arthritis
  • largest contributor to patient-centered outcomes

• Other significant contributors
  • Cognitive impairment
  • Diabetes
  • Hypertension
  • Stroke

• Twelve medical conditions accounted for:
  • 52% to 61% of four healthcare utilization outcome
  • 53% to 68% of three patient-centered outcomes
Conclusions

• Multiple Outcomes
  • Consistent results across two domains
    – Healthcare utilization (4 outcomes)
    – Patient-centered (3 outcomes)

• A few conditions dominate
  • COPD and Arthritis

• AAF for dichotomous outcomes and conditions

• Clinical message:
  • Prioritize treatment of lung disease
  • Musculoskeletal important to most outcomes
  • A few high (diabetes, HTN) and low (cognitive impairment / stroke) prevalence conditions important
References

When More than One Outcome Matters

Heather Allore, PhD
Professor Yale School of Medicine
Program on Aging
School of Public Health
Department of Biostatistics
Acknowledgments

Funding sources supported this work NIA’s Claude D. Pepper OAIC at Yale University School of Medicine (P30AG021342), Yale Alzheimer’s Disease Research Center (P50 AG047270), R21 AG021342 (Tinetti & Allore), R01AG047891 (Allore), R24 AG045050 (Gurwitz).

Disclosure
Dr. Allore has no conflicts of interest.
KEEP CALM AND LOVE BIOSTATISTICS
Universal Health Outcomes

- One approach to analyzing data of persons with multiple chronic conditions (MCC) is the use of cross-condition, universal health outcomes.

- Universal health outcomes (e.g. self-rated health, survival and function) refer to outcomes that are noticed by, and meaningful to, patients and that are affected by all health conditions.

- Older adults often value more than a single outcome.
Health Outcome Prioritization as a Tool for Decision Making Among Older Persons With Multiple Chronic Conditions

<table>
<thead>
<tr>
<th>Health Outcome Ranking</th>
<th>First (Most Important)</th>
<th>Second</th>
<th>Third</th>
<th>Fourth</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Independence</td>
<td>Pain relief</td>
<td>Symptom relief</td>
<td>Staying alive</td>
<td>270 (76)b</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Symptom relief</td>
<td>Pain relief</td>
<td>Staying alive</td>
<td>104 (39)c</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Staying alive</td>
<td>Symptom relief</td>
<td>Pain relief</td>
<td>76 (28)c</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pain relief</td>
<td>Staying alive</td>
<td>Symptom relief</td>
<td>38 (14)c</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Staying alive</td>
<td>Pain relief</td>
<td>22 (8)c</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pain relief</td>
<td>Staying alive</td>
<td>19 (7)c</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Staying alive</td>
<td>11 (4)c</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staying alive</td>
<td>Independence</td>
<td>Pain relief</td>
<td>Symptom relief</td>
<td>40 (11)b</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Independence</td>
<td>Symptom relief</td>
<td>Pain relief</td>
<td>13 (33)c</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pain relief</td>
<td>Independence</td>
<td>Symptom relief</td>
<td>13 (33)c</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Symptom relief</td>
<td>Independence</td>
<td>Pain relief</td>
<td>7 (18)c</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Independence</td>
<td>Pain relief</td>
<td>5 (13)c</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pain relief</td>
<td>2 (5)c</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain relief</td>
<td>Independence</td>
<td>Symptom relief</td>
<td>Staying alive</td>
<td>26 (7)b</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Symptom relief</td>
<td>Independence</td>
<td>Staying alive</td>
<td>11 (42)c</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Staying alive</td>
<td>Symptom relief</td>
<td>Staying alive</td>
<td>7 (27)c</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Independence</td>
<td>Symptom relief</td>
<td>Independence</td>
<td>4 (15)c</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Staying alive</td>
<td>Symptom relief</td>
<td>Independence</td>
<td>3 (12)c</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pain relief</td>
<td>Independence</td>
<td>1 (4)c</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Staying alive</td>
<td>Pain relief</td>
<td>21 (6)b</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Independence</td>
<td>Staying alive</td>
<td>11 (52)c</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Staying alive</td>
<td>Pain relief</td>
<td>4 (19)c</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pain relief</td>
<td>Independence</td>
<td>3 (14)c</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Staying alive</td>
<td>Pain relief</td>
<td>2 (10)c</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pain relief</td>
<td>Independence</td>
<td>1 (5)c</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a Percentages do not add up to 100% because of rounding.
b Percentage of total participants (N=357).
c Percentage of health outcome ranked first.

Analytic Challenges to Assess Treatments

- Condition-specific outcomes are inadequate to assess treatments in those with MCC.
- Number of possible combinations of conditions and treatments.
- There often multiple recommended medications for each condition, these medications may change over time.
- As person’s health changes, their response to medications may change.
- Methods that account for changes in medications and outcomes over time are needed to determine the contribution of common medications to outcomes important to patients.
Interpretation of LE-AAF methodology

› Analytical technique that can handle large numbers of variables that may change over time.
› Provides an absolute amount that an outcome may be changed should the condition or medication be removed (or present).
› This informs at the population (or healthcare system) level that amount of change in the outcome that might be expected from a “perfect” treatment or elimination of a condition.
Treatments in the Setting of Multiple Chronic Conditions

- 20% receive ≥1 “guideline” medication that may harm coexisting condition (Lorgunpai, Tinetti PLoS ONE, 2014)
- Risk of adverse effects increase 10%/drug reaching ~ 100% with 10 drugs (Gandhi, NEJM, 2003)
- Medicare beneficiaries differ significantly from the cardiovascular clinical trial participants used to inform Medicare coverage decisions.
  - Clinical trial participants, compared with beneficiaries, are more likely to be younger (60.1 vs 74.7 years), male (75.4% vs 41.8%), and non-US residents (60% vs 0%). The clinical trials, moreover, rarely included outcome stratification by age, sex, and race. (Dhruva & Redberg, Arch Int Med, 2008)
<table>
<thead>
<tr>
<th>Study Condition:</th>
<th>Atrial Fibrillation</th>
<th>Coronary Artery Disease</th>
<th>Depression</th>
<th>Diabetes</th>
<th>Heart Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=662</td>
<td>N=1658</td>
<td>N=656</td>
<td>N=1670</td>
<td>N=516</td>
</tr>
<tr>
<td>Sociodemographic:</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Age &gt; 80</td>
<td>32.5</td>
<td>26.8</td>
<td>20.5</td>
<td>19.1</td>
<td>32.6</td>
</tr>
<tr>
<td>Female</td>
<td>45.3</td>
<td>36.2</td>
<td>65.1</td>
<td>49.5</td>
<td>46.5</td>
</tr>
<tr>
<td>Caucasian</td>
<td>95.3</td>
<td>92.2</td>
<td>91.0</td>
<td>85.3</td>
<td>91.5</td>
</tr>
<tr>
<td>Yearly Income &lt; $25,000</td>
<td>44.7</td>
<td>44.0</td>
<td>54.0</td>
<td>47.7</td>
<td>55.4</td>
</tr>
<tr>
<td>Prescription Drug Coverage</td>
<td>69.3</td>
<td>69.2</td>
<td>67.3</td>
<td>70.1</td>
<td>68.4</td>
</tr>
<tr>
<td>Risk factors:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body Mass Index &gt; 30</td>
<td>19.8</td>
<td>21.5</td>
<td>22.2</td>
<td>33.9</td>
<td>23.6</td>
</tr>
<tr>
<td>Impairments:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive</td>
<td>8.9</td>
<td>8.0</td>
<td>16.2</td>
<td>6.4</td>
<td>10.3</td>
</tr>
<tr>
<td>Study Conditions:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>-</td>
<td>21.5</td>
<td>14.8</td>
<td>13.5</td>
<td>43.2</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>54.2</td>
<td>-</td>
<td>38.4</td>
<td>37.8</td>
<td>68.6</td>
</tr>
<tr>
<td>Depression</td>
<td>14.4</td>
<td>14.0</td>
<td>-</td>
<td>12.4</td>
<td>18.8</td>
</tr>
<tr>
<td>Diabetes</td>
<td>34.1</td>
<td>39.0</td>
<td>32.1</td>
<td>-</td>
<td>45.3</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>33.4</td>
<td>21.9</td>
<td>15.3</td>
<td>14.2</td>
<td>-</td>
</tr>
<tr>
<td>Co-existing Conditions:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>78.7</td>
<td>91.2</td>
<td>78.0</td>
<td>87.6</td>
<td>82.6</td>
</tr>
<tr>
<td>Hypertension</td>
<td>92.3</td>
<td>92.3</td>
<td>90.4</td>
<td>92.6</td>
<td>95.9</td>
</tr>
<tr>
<td>Kidney disease</td>
<td>10.7</td>
<td>12.9</td>
<td>9.0</td>
<td>11.0</td>
<td>22.1</td>
</tr>
<tr>
<td>Thromboembolic Disease</td>
<td>7.6</td>
<td>4.9</td>
<td>4.3</td>
<td>3.1</td>
<td>7.0</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>54.8</td>
<td>54.5</td>
<td>60.4</td>
<td>51.5</td>
<td>54.7</td>
</tr>
<tr>
<td>Condition(s)</td>
<td>Beta Blocker</td>
<td>Calcium Channel Blocker</td>
<td>Clopid</td>
<td>Metform</td>
<td>RAS Blocker</td>
</tr>
<tr>
<td>---------------------------</td>
<td>--------------</td>
<td>-------------------------</td>
<td>--------</td>
<td>---------</td>
<td>-------------</td>
</tr>
<tr>
<td>Coexisting Conditions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AF-CAD-HL-HTN (N=910)</td>
<td>72.7</td>
<td>42.7</td>
<td>25.5</td>
<td></td>
<td>66.8</td>
</tr>
<tr>
<td>AF-DM-HL-HTN (N=633)</td>
<td>72.2</td>
<td>45.3</td>
<td>21.6</td>
<td>31.1</td>
<td>68.4</td>
</tr>
<tr>
<td>AF-DEP-HL-HTN (N=407)</td>
<td>68.3</td>
<td>45.2</td>
<td>18.4</td>
<td></td>
<td>60.7</td>
</tr>
<tr>
<td>AF-HF-HL-HTN (N=689)</td>
<td>72.1</td>
<td>42.7</td>
<td>21.9</td>
<td></td>
<td>68.5</td>
</tr>
<tr>
<td>DEP-CAD-HL-HTN (N=877)</td>
<td>66.9</td>
<td>42.4</td>
<td>30.0</td>
<td></td>
<td>64.8</td>
</tr>
<tr>
<td>DEP-DM-HL-HTN (N=797)</td>
<td>57.5</td>
<td>40.0</td>
<td>34.3</td>
<td></td>
<td>68.4</td>
</tr>
<tr>
<td>DEP-HF-HL-HTN (N=548)</td>
<td>70.8</td>
<td>40.1</td>
<td></td>
<td></td>
<td>67.2</td>
</tr>
<tr>
<td>DM-CAD-HL-HTN (N=1471)</td>
<td>73.7</td>
<td>40.4</td>
<td>32.8</td>
<td>32.8</td>
<td>71.2</td>
</tr>
<tr>
<td>DM-HF-HL-HTN (N=863)</td>
<td>74.4</td>
<td>40.0</td>
<td>30.7</td>
<td></td>
<td>72.0</td>
</tr>
<tr>
<td>HF-CAD-HL-HTN (N=1129)</td>
<td>77.1</td>
<td>40.2</td>
<td>32.0</td>
<td></td>
<td>70.8</td>
</tr>
</tbody>
</table>
LE-AAF for Good to Excellent Self-Rated Health

A positive value is the additive contribution to good to excellent SRH and a negative value is additive contributes to poor to fair.

b 95% CI is the 95% confidence interval derived from 300 bias-corrected and accelerated bootstrap pseudo-samples.

c Estimates are adjusted for the control variables: year, age, gender, race, ethnicity, income, smoking, obesity, prescription drug insurance, incontinence, use of assistive device, hearing impairment, vision impairment, cognitive impairment, and Elixhauser comorbidity score (≥2).


<table>
<thead>
<tr>
<th>Condition</th>
<th>Unadjusted Model</th>
<th>Adjusted Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation</td>
<td>-1.19 (-1.96, -0.53)</td>
<td>-0.67 (-1.41, 0.08)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>-3.51 (-5.06, -2.49)</td>
<td>-2.13 (-3.55, -1.06)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>-3.50 (-4.40, -2.82)</td>
<td>-1.89 (-2.69, -1.22)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>-3.63 (-4.63, -2.64)</td>
<td>-2.25 (-3.21, -1.05)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>-8.48 (-11.95, -5.56)</td>
<td>-5.08 (-8.82, -1.77)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>8.52 (6.46, 10.37)</td>
<td>4.58 (2.61, 6.56)</td>
</tr>
<tr>
<td>Kidney disease</td>
<td>-1.90 (-2.49, -1.42)</td>
<td>-1.56 (-2.15, -1.05)</td>
</tr>
<tr>
<td>Depression or Anxiety</td>
<td>-6.66 (-7.60, -5.80)</td>
<td>-4.25 (-5.24, -3.35)</td>
</tr>
<tr>
<td>PE and Venous thrombosis</td>
<td>-0.75 (-1.08, -0.47)</td>
<td>-0.50 (-0.85, -0.22)</td>
</tr>
</tbody>
</table>

Total for conditions: -21.10 -13.74
Total for conditions absolute values: 38.14 22.91

<table>
<thead>
<tr>
<th>Medication</th>
<th>Unadjusted Model</th>
<th>Adjusted Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renin-angiotensin system blocker</td>
<td>0.73 (0.18, 1.26)</td>
<td>0.49 (-0.08, 1.08)</td>
</tr>
<tr>
<td>Statin</td>
<td>0.17 (-0.44, 0.61)</td>
<td>0.08 (-0.66, 0.52)</td>
</tr>
<tr>
<td>Thiazide</td>
<td>-1.25 (-1.77, -0.75)</td>
<td>-1.17 (-1.74, -0.64)</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>0.17 (-0.31, 0.73)</td>
<td>-0.12 (-0.59, 0.44)</td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>-0.24 (-0.61, 0.15)</td>
<td>-0.22 (-0.58, 0.15)</td>
</tr>
<tr>
<td>SSRI/SNRI</td>
<td>-0.42 (-0.75, -0.17)</td>
<td>-0.15 (-0.47, 0.12)</td>
</tr>
<tr>
<td>Metformin</td>
<td>-0.08 (-0.32, 0.11)</td>
<td>-0.09 (-0.34, 0.11)</td>
</tr>
<tr>
<td>Warfarin</td>
<td>-0.16 (-0.42, 0.11)</td>
<td>-0.35 (-0.61, -0.08)</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>-0.23 (-0.43, -0.05)</td>
<td>-0.21 (-0.40, -0.05)</td>
</tr>
</tbody>
</table>

Total for medications: -1.31 -1.74
Total for medications absolute values: 3.47 2.87

Overall total: -22.41 -15.48
Overall total absolute values: 41.60 25.79
Mortality

› Longitudinal time-varying models of study medications and conditions on the universal health outcome mortality.

› All individual conditions were fit with a set of multivariable Cox regression models for time until death with censoring of survivors at the end of their follow-up. Analyses were repeated for subsets of coexisting conditions.

› A person entered the risk set for a condition at the first annual interview in which the condition was present. Each condition- or coexisting conditions- model included the main effects of each medication indicated for the conditions, as well as time-varying main effects for the remaining study conditions and time-varying interactions between the remaining conditions and their indicated medications

› Further we calculated the contribution of medications and each conditions using the HD LE-AAF
Adjusted hazard ratios of death associated with guideline recommended cardiovascular drugs for older adults with chronic conditions.

Tinetti et al. BMJ 2015;351
Heart failure was the condition that made the largest contributor (39%) to mortality. Beta blockers, renin-angiotensin system blockers, thiazides and statins contributed to improved survival by 10.4%, 9.3%, 7.2% and 7.2% respectively.

Most cardiovascular medications contributed independently to survival, heart failure and atrial fibrillation.

The effects were similar by age.

8,578 Medicare Current Beneficiary Survey participants with baseline from 2005 to 2009 up to three yearly in-person follow-up interviews with two or more of the conditions.
While chronic conditions have been associated with disability in physical activities, it is unclear whether the guideline-recommended medications prescribed for these conditions alter these associations.

Physical activities: 1) writing/handling objects, 2) extending arms above shoulder, 3) stooping/kneeling/crouching, 4) lifting/carrying 4.5 kg, 5) walking ¼ mile or 2-3 blocks

Disability was defined as being unable to perform the activity.

An interval-censored survival analysis using a complementary log-log link, was estimated, with repeated observations for each participant until the time of decline or end of follow-up.

Functional Disability
Functional Decline Based on Low <7 or ≥7 Polypharmacy

Medication:
- Beta Blocker:
  - Atrial fibrillation
  - Coronary artery disease
  - Heart failure
- Dihydropyridine Calcium Channel Blocker:
  - Atrial fibrillation
- Nondihydropyridine Calcium Channel Blocker:
  - Atrial fibrillation
- Metformin:
  - Diabetes
- Renin-angiotensin blocker:
  - Coronary artery disease
  - Diabetes
  - Heart failure
- Serotonin reuptake inhibitor:
  - Depression
- Statin:
  - Coronary artery disease
  - Diabetes

Hazard Ratio for Decline in Function

Low Polypharmacy

High Polypharmacy

p-value for interaction
- p=0.84
- p=0.52
- p=0.69
- p=0.15
- p=0.21
- p=0.07
- p=0.14
- p=0.38
- p=0.05
- p=0.43
- p=0.58
- p=0.01
26.7% of older adults are hospitalized annually, with the longest LOS 5.2d, at the highest cost/stay $13,000.

39.1% of Medicare beneficiaries are hospitalized resulting in $14.3M.

Persons with dementia have twice the hospitalization rates (Phelan JAMA 2012). The majority of inpatients with dementia experience significant adverse outcomes including functional disability, hospital re-admission and mortality.

Evidence suggests that some hospital admissions and their complications are potentially avoidable.

~ 30% of admissions among older adults attributed to inappropriate prescribing

Inappropriate prescribing include polypharmacy, exposure to high risk medications (i.e. anticholinergics and Beers) that lead to functional decline in older people.

Medications are the most reversible cause of decline in cognitive and physical function in older adults.
OBJECTIVE: To test whether an intervention of systematic CGA, followed by the transitional care bridge program, improved activities of daily living (ADLs) compared with systematic CGA alone.

DESIGN, SETTING, AND PARTICIPANTS
- Double-blind, multicenter, randomized clinical trial conducted at 3 hospitals with affiliated home care organizations in the Netherlands between September 1, 2010, and March 1, 2014.
- 674 enrolled were 65 years or older, acutely hospitalized to a medical ward for at least 48 hours with an Identification of Seniors at Risk–Hospitalized Patients score of 2 or higher
- Randomized stratified by study site and Mini-Mental State Examination score (<24 vs24).

INTERVENTIONS
- The transitional care bridge program intervention was started during hospitalization by a visit from a community care registered nurse (CCRN)
- Continued after discharge with home visits at 2 days and at 2, 6, 12, and 24 weeks.
- The CCRNs applied the CGA care and treatment plan.
### Table 3. Differences Between the Intervention Arm and the CGA-Only Control Arm for ADL and Cognition

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention (LS Mean (95% CI))</th>
<th>CGA Only (Baseline)</th>
<th>CGA Only (6 Months)</th>
<th>P Value for Treatment x Time Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>6 Months</td>
<td>Baseline</td>
<td>6 Months</td>
</tr>
<tr>
<td>ADL&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.81 (1.63-1.99)</td>
<td>2.00 (1.78-2.23)</td>
<td>1.89 (1.71-2.07)</td>
<td>1.92 (1.69-2.15)</td>
</tr>
<tr>
<td>ADL&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.83 (1.59-2.07)</td>
<td>3.66 (3.40-3.92)</td>
<td>1.92 (1.68-2.16)</td>
<td>3.80 (3.54-4.06)</td>
</tr>
<tr>
<td>MMSE&lt;sup&gt;c&lt;/sup&gt;</td>
<td>22.2 (21.3-23.0)</td>
<td>24.8 (23.8-25.8)</td>
<td>22.4 (21.6-23.3)</td>
<td>25.1 (24.1-26.1)</td>
</tr>
</tbody>
</table>

**Abbreviations:** ADL, activities of daily living; CGA, comprehensive geriatric assessment; LS, least squares; MMSE, Mini-Mental State Examination.

<sup>a</sup> As measured with the 6-item Katz Index of ADL<sup>21</sup> Estimates are the adjusted LS means (95% CIs) for the number of ADL that were disabled at 2 weeks before hospitalization and at 6 months after admission (see the Statistical Analysis subsection of the Methods section) using a linear mixed-effects model with random participant-specific intercepts and center and stratification factor MMSE score (<24 vs ≥24).

<sup>b</sup> Represents a sensitivity analysis in which decedents were assigned a score of 7 on the Katz Index of ADL.

<sup>c</sup> Cognitive functioning, measured with the 11-item MMSE.<sup>20</sup> Estimates are the adjusted LS means (95% CIs) for the MMSE score at the time of hospital admission and at 6 months after admission (see the Statistical Analysis subsection of the Methods section) using a linear mixed-effects model with random participant-specific intercepts and center.
Mortality From Admission to 6 Months After Admission: survival curves from a Cox proportional hazards regression analysis adjusted for study site and cognitive functioning (Mini-Mental State Examination Score, <24 vs ≥24). Significant protective intervention effects were observed for 1-month mortality and 6-month mortality. CGA (comprehensive geriatric assessment).
Figure 1. Individual survival curves for two white women (W1 and W2) aged 75 with frailty at baseline and disparate histories of disability from three models: separate survival model with no adjustment for disability (A), separate survival model with adjustment for disability (B), and joint model of survival and disability (C).

Panel A: DIC = 5067
Panel B: DIC = 5061
Panel C: DIC = 5004

W2’s Ordinal Disability from 91 months: 00000000001000000000000100000000End
W1’s Ordinal Disability from 91 months: 000000211012222222222222222222222222End
(0 = No disability, 1 = Mild disability, 2 = Severe disability)

DIC = deviance information criterion where lower values indicate better model fit
Complicated Self-Care Conditions

- ADL trajectories with a 5-year follow-up to determine whether diabetes and heart disease, were associated with increased disability, and evaluated whether these trajectories differed by dementia status.

- Data from the National Health and Aging Trends Study, a nationally representative sample of Medicare beneficiaries ages ≥65 years from 2011-2015 (N=7,609) was used. In-person interviews included ADLs and cognitive status.

- Trajectories of ADLs and attrition over 5 years were jointly estimated using group-based trajectory modeling.

- Trajectories of ADLs were associated with CSC and dementia using multinomial logistic regression adjusting for baseline participant characteristics.
### Number of Activities of Daily Living Disabled

<table>
<thead>
<tr>
<th>Year of National Health &amp; Aging Trends Study</th>
<th>Severe Disability (N=991)</th>
<th>Mild Disability (N=1,232)</th>
<th>No Disability (N=5,386)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>National percentage: 9.7%</td>
<td>National percentage: 13.9%</td>
<td>National percentage: 76.3%</td>
</tr>
<tr>
<td>2013</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Severe disability (N=991)**
  - US National Estimate: 3,441,485
  - National percentage: 9.7%

- **Mild disability (N=1,232)**
  - US National Estimate: 4,922,933
  - National percentage: 13.9%

- **No disability (N=5,386)**
  - US National Estimate: 26,941,212
  - National percentage: 76.3%
Severe disability: 770,873 (22.4%)
Mild disability: 2,173,973 (44.2%)
No disability: 14,510,375 (53.9%)
Mild disability trajectory group versus no disability group

- No diabetes, no heart disease, no dementia: Adjusted Odds Ratio (95% CI) 1.10 (0.82-1.48)
- Diabetes, no heart disease, no dementia: Adjusted Odds Ratio (95% CI) 1.33 (1.04-1.70)*
- Diabetes, heart disease, no dementia: Adjusted Odds Ratio (95% CI) 1.39 (0.92-2.10)
- No diabetes, no heart disease, possible dementia: Adjusted Odds Ratio (95% CI) 1.39 (1.06-1.83)*
- No diabetes, heart disease, possible dementia: Adjusted Odds Ratio (95% CI) 1.27 (0.75-2.14)
- Diabetes, no heart disease, possible dementia: Adjusted Odds Ratio (95% CI) 1.67 (1.04-2.67)**
- Diabetes, heart disease, possible dementia: Adjusted Odds Ratio (95% CI) 2.56 (1.26-5.20)*
- No diabetes, no heart disease, probable dementia: Adjusted Odds Ratio (95% CI) 2.76 (1.97-3.88)****
- No diabetes, heart disease, probable dementia: Adjusted Odds Ratio (95% CI) 1.44 (0.70-2.95)
- Diabetes, no heart disease, probable dementia: Adjusted Odds Ratio (95% CI) 1.30 (0.77-2.20)
- Diabetes, heart disease, probable dementia: Adjusted Odds Ratio (95% CI) 2.28 (0.85-6.11)

Severe disability trajectory group versus no disability group

- No diabetes, no heart disease, no dementia: Adjusted Odds Ratio (95% CI) 5.09 (1.71-15.15)**
- Diabetes, no heart disease, no dementia: Adjusted Odds Ratio (95% CI) 4.46 (2.57-7.74)****
- Diabetes, heart disease, no dementia: Adjusted Odds Ratio (95% CI) 2.30 (1.19-4.4)*
- No diabetes, no heart disease, possible dementia: Adjusted Odds Ratio (95% CI) 6.31 (4.25-9.37)****
- No diabetes, heart disease, possible dementia: Adjusted Odds Ratio (95% CI) 2.41 (1.33-4.35)**
- Diabetes, no heart disease, possible dementia: Adjusted Odds Ratio (95% CI) 4.17 (2.05-8.48)***
- Diabetes, heart disease, possible dementia: Adjusted Odds Ratio (95% CI) 1.99 (0.98-4.06)
- No diabetes, no heart disease, probable dementia: Adjusted Odds Ratio (95% CI) 1.39 (0.92-2.10)
- No diabetes, heart disease, probable dementia: Adjusted Odds Ratio (95% CI) 1.33 (1.04-1.70)*
- Diabetes, no heart disease, probable dementia: Adjusted Odds Ratio (95% CI) 1.10 (0.82-1.48)
- Diabetes, heart disease, probable dementia: Adjusted Odds Ratio (95% CI) 0.96 (0.60-1.53)
9,237 Americans age 65 or older from the Health and Retirement Study, who were observed biennially from 1998 to 2010.

Distinct patterns of joint trajectories of physical, emotional, and cognitive functioning exist in old age. There were significant socioeconomic differences in the joint trajectories, with education-based inequality in health converging in later old age.

Further research identifying strategies to alleviate the disproportionate burden of poor multidimensional health trajectories in lower socioeconomic groups is important.
Ongoing Work

› Joint models are being created in a pairwise manner using non-linear mixed effects and MCMC models.

› These are joined across the universal health outcomes.

› Individualized Absolute Risk Calculator for Persons with Multiple Chronic Conditions
  – An innovative methodology that will have wide-spread application regarding individualized absolute risk calculations for patient-centered competing outcomes.
Individualized Absolute Risk Calculator

### COPD Outcomes Absolute Risk Calculator

**Patient Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>67</td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
</tr>
<tr>
<td>Race</td>
<td>White</td>
</tr>
<tr>
<td>Hispanic ethnicity</td>
<td>Yes</td>
</tr>
<tr>
<td>Education</td>
<td>High School</td>
</tr>
<tr>
<td>Income</td>
<td>$15,001-$35,000</td>
</tr>
<tr>
<td>Marital Status</td>
<td>Widowed</td>
</tr>
</tbody>
</table>

**Coexisting Conditions**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Present</th>
<th>Absent</th>
<th>Not known</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angina</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysrhythmias</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart Failure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other Cardiovascular disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung cancer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone or Cartilage Disorder</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive Impairment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressive Symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual Impairment</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Treatment(s)**

- Beta-Agonist-Inhaled
- Inhaled Anticholinergic
- Steroids-Inhaled
- Steroids-Oral
- Smoking Cessation

**Outcome(s)**

- ADL Disability
- IADL Disability
- Need for Assistive Device
- Mobility Disability
- Social Limitation
- Hospitalization
- Worsening Perceived Health
- Disability Bed Days

**Calculate Absolute Risk**

### Absolute Risk of Competing Outcomes

**Treatment: Steroids-Inhaled**

- ADL Disability: 0.10
- Worsening Perceived Health: 0.20
- Hospitalization: 0.05

**Treatment: Smoking Cessation**

- ADL Disability: 0.08
- Worsening Perceived Health: 0.12
- Hospitalization: 0.04

[Guide to interpreting these findings](#)
Thank you
For questions about the AGING Initiative or today’s webinar, please contact:

Kathryn.Anzuoni@meyersprimary.org