Multimorbidity and Polypharmacy

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Speaker Disclosures

Dr. Little has no financial relationship(s) to disclose.

Learning Objectives

By the end of the session, participants will be able to:

• Define multimorbidity and describe its impacts
• Identify factors related to patient complexity and treatment burden
• Utilize patient-level interventions to reduce treatment burden in polypharmacy
• Describe the current evidence base and future research directions of multimorbidity
• Apply aspects of successful patient-centered interventions into practice
Defining good health and care from the perspective of persons with multimorbidity: results from a qualitative study of focus groups in eight European countries.


“...it’s true, I am sick, but the disease is not me. I don't want to be reduced to my diseases.”
-- Focus Group Participant, Austria

“So I would have wished for a doctor that, to put it this way, had the overview of the whole human being, that he shouldn’t treat a heart disease just in isolation, you have another disease, and a third…”
-- Focus Group Participant, Norway

Co-morbidity versus Multimorbidity

INDEX DISEASE WITH ONE OR MORE CONDITIONS

HTN
HLD
Coronary Artery Disease
Insulin Resistance

CODEXISTENCE OF TWO OR MORE CHRONIC DISEASES

Major Depression
CKD
Arthritis
Osteoporosis

Co-occurrence of three or more chronic conditions affecting three or more body systems within one person, without defining an index condition'.

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Why is multimorbidity so difficult to discuss?

• Still a topic with a small evidence base (only became a MeSH term in 2018)

• Clinical guidelines are single-disease focused and “cookbook” medicine leads to polypharmacy and treatment burden

• What are the “right” outcomes?

Prevalence

• Reported ranges 3.5%-100%

• Using NHANES data from 1988-2014
  • 5541 participants in the 2013 to 2014 cycle
  • 59.6% had 2 morbidities
  • 38.5% had 3 morbidities
  • 22.7% had 4 morbidities.

• Prevalence of ≥2 morbidities was higher in those aged 65 years or older, female, non-Hispanic white or black, with health insurance, and under poverty

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**Figure 1.** Age-standardized trends in multi-morbidity prevalence for participants 20 years or older from NHANES 1988–2014 by number of morbidities.

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Impact

- Multimorbidity is associated with
  - lower quality of life
  - lower physical function
  - higher acute admission rates
  - increased polypharmacy
  - increased treatment burden
  - increased healthcare costs

- Multimorbidity increases mortality

Risk Factors for Multimorbidity

- Mental Illness (especially depression)
- Lower socioeconomic status
- Tobacco use
- Obesity
- Physical inactivity

The Significant Role of Depression

| Table 2. Association between diagnostic group and chronic diseases |
|-----------------------------|-----------------------------|-----------------------------|
|                              | Number of chronic disease    | Multimorbidity              |
|                              | (FR) 95% CI P value | (OR) 95% CI P value         |
| Controls                     |                   |                             |
| Psychological diagnosis      |                   |                             |
| Depression                   |                   |                             |
| Reference                    |                   |                             |
| Reference                    |                   |                             |
| Physical inactivity          |                   |                             |

Frailty

- 70% of frail adults also have multimorbidity
- 1/5 of adults with multimorbidity also have frailty
- Multimorbidity increases risk of frailty nearly twofold

Multimorbidity and Patient Complexity

- Multiple Chronic Conditions is only one aspect of medical complexity

Multimorbidity in the Nursing Home Setting

- Highly prevalent, under studied
- ¼ newly admitted nursing home residents have mental-physical multimorbidity (MPM)
  - Care needs differ
  - More likely younger, male, unmarried
  - High number of clinically relevant neuropsychiatric symptoms

A. M. A. van den Brink et al. International Psychogeriatrics (2017), 29(6), 1037–1047
Who is more medically complex?

Two 72 year old men recently discharged to SNF from the hospital after suffering heart attacks. They were both given medications to control blood pressure and lipids, and advised to take aspirin, as well as to quit smoking. While in the hospital, they were also diagnosed with diabetes, and given much information about changing diet and exercising.

Mr. Jones is European American, lives in an inner city impoverished neighborhood with a sick wife who requires much care, works as a janitor, and has limited health insurance benefits.

Mr. Smith is African American, lives in a suburban neighborhood, has a stable employment situation with good health insurance benefits, and has a supportive family.
Multimorbidity and Patient Complexity

- Multiple Chronic Conditions is only one aspect of medical complexity
- Five key issues:
  - Patient preferences
  - Contextual factors
  - Dynamics
  - Acute shocks
  - Resilience


Treatment Burden Adds to Medical Complexity

- Condition A + Condition B + Condition C = Treatment A + Treatment B + Treatment C

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Antecedents and Consequences of Treatment Burden

- More common in women and older adults
- Increased in depression, anxiety, diabetes, functional incapacity, poor symptom control, no caregiver, longer duration of illness, and high number of medications
- High treatment burden leads to non-adherence and poor post-SNF outcomes

Sav et al. Health Expectations, 18, pp.312–324

Treatment Burden Framework

- Patients identify four burden of treatment issues:
  - Administration – burdens in correctly delivering or taking treatment
  - Effects – unwanted or unintended symptoms or consequences of the prescribed treatment
  - Access – patients’ efforts or difficulty obtaining treatment in a timely, convenient or affordable manner
  - Monitoring – trouble complying with the monitoring required for effective or safe use of medication

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Treatment Burden in NH Residents

- For every $1 spent on medications in nursing homes, $1.33 was spent on treating ADR
  Boom et al. Arch Int Med 1997;157:2089-2096
- In the 30 days following SNF discharge
  - Fatigue was positively associated with treatment burden
  - Caregiver support partially mediated the effect
- LTC residents rated a lower number of needs but a higher rate of unmet needs compared to nursing staff.
  - Unmet needs positively associated with depression and anxiety
  - Unmet needs negatively associated with social participation
Minimizing Risk of Treatment: First Do No Harm

What is the optimal combination of drugs in a multi-morbidity context?


Break-out Exercise

For a person aged 65-75 with type 2 diabetes, heart failure, and chronic obstructive pulmonary disease, which drugs would you recommend as the OPTIMAL BASIC THERAPY?
Multimorbidity and Appropriate Prescribing

- ADR risk prediction tools lack sufficient predictive value to be useful in daily clinical practice
- Multiple NH studies to reduce polypharmacy have been done with many positive but also mixed results
  - No one intervention has consistently proven effective
  - A multi-faceted approach is likely more effective
  - Need more research on clinical decision support systems

The delicate choice of optimal basic therapy for multimorbid older adults

- Cross-sectional study
  - Mostly pharmacists responded
  - 10% geriatricians
- Little consensus
  - Median number of recommended drugs: 10 (6-13)
  - 21.6% >2 medications or classes with a contraindicated interaction (but none of the geriatricians did)
- What is appropriate polypharmacy??

Polypharmacy in Multimorbidity

- Disease clusters leading to highest polypharmacy rates
  - CHF with osteoporosis
  - CKD with COPD
  - CKD with osteoporosis

- Physical activity inversely associated with polypharmacy in older multimorbid adults


1. How is it going to **ACT** on my patient?

2. How is it going to **MOVE THROUGH** my patient?

**Pharmacodynamics & Pharmacokinetics**

- **Serum albumin**
  - Major drug binding protein
  - Acute phase reactant
  - Highly protein bound drugs affected (e.g. phenytoin, warfarin, NSAIDs)

- **Ordering serum drug levels in older patients?**
  - Therapeutic ranges routinely may not be accurate guide to determine toxicity or efficacy, especially in acute or chronic inflammation

**A Word on Protein Binding**

- Fat soluble drugs have *longer half-life* with increased Vd
  - side effects mainly after reaching steady state.
  - e.g. amiodarone, desipramine, diazepam, haloperidol

- Water soluble drugs distribute *less effectively* with decreased Vd
  - higher plasma concentration, side effects mainly with initial doses.
  - e.g. digoxin, aminoglycosides, atenolol, sotalol, theophylline, lithium, sedative-hypnotics

**Volume of Distribution (Vd)**

Phase 1 Metabolism: Cytochrome P450 (CYP)

- Substrates: metabolized by particular P450 enzymes
- Inhibitors: impair the ability of specific P450 enzymes to metabolize their target substrates
- Inducers: increase the production of particular P450 enzymes
82 year old man in the hospital for acute MI, given haloperidol for agitation:

- **CYP 2D6**
  - *Haloperidol*
  - Metoprolol (Active)
  - Metabolite (Inactive)

75 year old woman, lives in assisted living facility

- History of DM, UI, chronic LBP, one previous NSTEMI, and HLD
- Admitted for new onset atrial fibrillation and recurrent MI
- Medications prior to admission:
  - glyburide
  - losartan
  - cyclobenzaprine
  - oxybutinin (extended release)
  - simvastatin
  - metoprolol
  - aspirin
75 year old woman, with new onset a fib and MI

- During her hospitalization, started on amiodarone clopidogrel
- On discharge to SNF, she is in NSR, has no complaints.
- Within two weeks:
  - had two episodes of hypoglycemia
  - became more lethargic
  - fell twice
  - lower than her usual blood pressure
  - constipation and dry mouth
  - muscle aches

<table>
<thead>
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<th>Substrates</th>
<th>Inhibitors</th>
<th>Substrate side effects</th>
</tr>
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<tbody>
<tr>
<td>1A2</td>
<td>cyclobenzaprine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2C9</td>
<td>glyburide</td>
<td></td>
<td></td>
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<tr>
<td>2C19</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>2D9</td>
<td>metoprolol</td>
<td>simvastatin</td>
<td></td>
</tr>
<tr>
<td>3A4</td>
<td>losartan</td>
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<td>simvastatin</td>
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### CYP Enzymes Substrates Inhibitors Substrate side effects

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<td>falls, lethargy</td>
</tr>
<tr>
<td>2C9</td>
<td>glyburide</td>
<td>amiodarone, clopidogrel</td>
<td>hypoglycemia</td>
</tr>
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<td>metoprolol</td>
<td>amiodarone</td>
<td>Myopathy</td>
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<td>3A4</td>
<td>losartan, cyclobenzaprine</td>
<td>amiodarone</td>
<td>low blood pressure, falls, lethargy, myopathy, dry mouth, constipation</td>
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Re-consider new medications from hospital AND/OR NonRx methods for neck pain, change to Metformin, Pravastatin, Trospium.

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### Deprescribing in Multimorbidity

- Evidence limited – evidence-based recommendations for stopping medications only possible for bisphosphonates
  

- PRIMUM Trial (pragmatic clustered RTC)
  - Medication regimens unstable over a 3-6 mo time period
Evidence Base and Research Priorities

Multimorbidity and Key Research Priorities

Given the heterogeneity of multimorbidity, the initial focus of research should be on the determinants of clusters that are most common and of greatest impact. (Academy of Medical Sciences, April 2018)
Cluster diagnoses

Table 1. Summary of disease patterns, disease combinations, and common diseases in multimorbidity.

<table>
<thead>
<tr>
<th>Disease patterns</th>
<th>Disease combinations</th>
<th>Common diseases</th>
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<tbody>
<tr>
<td>Cardiovascular and metabolic diseases</td>
<td>Hypertension combined with other conditions (e.g., hyperlipidemia, diabetes), cancer</td>
<td>Diabetes, Heart disease, Sleep disorders, Obesity, Depression, COPD, Stroke</td>
</tr>
<tr>
<td>Mental health-related problems</td>
<td>Hypertension combined with other conditions (e.g., hyperlipidemia, diabetes, cancer)</td>
<td>Arthritis, Depression, COPD, Stroke</td>
</tr>
<tr>
<td>Neurological disorders</td>
<td>Arthritis combined with hypertension, CVD, hyperlipidemia, diabetes, and mental health problems</td>
<td>Arthritis, Depression, COPD, Stroke</td>
</tr>
<tr>
<td>Arthritis combined with arthritis, CVD, and diabetes</td>
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<tr>
<td>Arthritis combined with arthritis, CVD, and diabetes</td>
<td>A disease related to arthritis, CVD, hyperlipidemia, diabetes, and mental health problems</td>
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Core Outcome Set for Multimorbidity Research

- Minimum that should be measured and reported in all clinical trials of a specific condition or conditions.
- 17 core outcomes identified by experts through Modified-Delphi

Table 3. Core Outcome Set for Multimorbidity (COOmb): 17 Outcomes by Group

- Highest scoring outcomes
  - Health-related quality of life
  - Mental health
  - Morbidity
  - Health-related quality of life
  - Mental health
  - Morbidity
  - Activities of daily living
  - Self-care and health behaviors
  - Self-management behavior
  - Social support
  - Physical activity and function
  - Physical function
  - Physical activity
  - Consultation-related confidence
  - Shared decision making
  - Prioritization
  - Health system
  - Health care use
  - Costs

Multimorbidity and Public Health Prioritization

WHO Recommendations

- Make changes at a policy level
- Take a systems approach
- Identify people in need of extra support
- Prioritize care coordination and self management support
- Simplify treatment regimens

2016 Cochrane Review of 18 RCTs

- Overall the results regarding the effectiveness of interventions were mixed.
  - Modest improvements in mental health outcomes
  - Modest improvements in functional outcomes

- Are these the right type of studies to do for this topic?


2018 Systematic Review and Meta-Analysis

- To identify effective multimorbidity interventions
- To determine which components optimize impact

2/25 studies in PALTC
  - Dementia and Depression cluster
  - Case manager coordination of care and Education of IPT

**Integrated Care Programs**

- “Real-work care practices”
- 30 models
  - Chronic Care Model
  - Guided Care Model
  - Ariadne Principles
- **Person-centered Care**
- Evidence of benefit lacking in PALTC continuum

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**Multimorbidity and Patient-Centered Care: What Patients Want**

- Social relationships
- A positive frame of mind or resilience
- Enjoyment of life
- Maintaining independence.
Minimally Disruptive Medicine (MDM)

“A patient-centred approach to care that focuses on achieving patients’ goals for life and health while imposing the smallest possible treatment burden on their lives.”

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Assessing Patient-Centeredness

- Limited evidence of how to do this well and quickly
- Available tools developed for single-disease or specific contexts, not multimorbidity or polypharmacy
- Outcome Prioritization Tool: remaining alive, maintaining independence, reducing pain, and reducing other symptoms.

JJGT van Summeren, et al. Br J Gen Pract 2017; DOI: https://doi.org/10.3399/bjgp17X690485

FIGURE 1. CKD and comorbidities and their implications for patients, clinicians and health systems.

Role of the Leadership Team

Steps to strengthen safety culture:

- Leadership walk rounds, whereby senior managerial and clinical leaders “walk the floor”
- Starting team meetings with a patient story
- Using reflective practice to focus on safety issues
- Mechanisms for reporting safety issues, such as through regular team meetings.

Thank you!