

50th ESCP PRAGUE SYMPOSIUM 2022

Population ageing and trends in multimorbidity, polypharmacy in Europe and other countries

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Outline

• What are multimorbidity and polypharmacy?

Multimorbidity

- Defined as the co-occurrence of 2 or more chronic conditions
- Observed in >60% of older adults
- It often causes negative health outcomes
- It challenges the organization of the health care systems

Multimorbidity





Comorbidity of 10 common conditions

* Percentage who do not have one of 39 other conditions in the full count

Guthrie B et al. BMJ 2012;345:bmj.e6341



BMC Public Health 2014

BM



Objectives of preliminar ICARE4OLD analyses

CARE 4 06

- Within care dependent older adults:
- <u>Identify</u> subgroups of individuals sharing the same patterns of chronic disease
- <u>Validate</u> such findings across different countries and

care settings (Home Care and Nursing Home)

Methods



CARE 400

- $\,\circ\,$ Two settings: home care and nursing home
- \circ Older adults aged 60 years or older
- o Countries: Canada, Italy, Finland and New Zealand
- \circ First assessment between 2014 and 2018 through the comprehensive

geriatric assessments tools interRAI HC and LTCF





Total sample: 177,000

Results

A 5-class solution was chosen as the best model for both HC and NH

5 classes	Over expressed diseases	Naming of the classes	
	Chronic obstructive pulmonary disease		
1	Congestive heart failure	Cardio-pulmonary	
	Coronary heart disease	uiseases	
2	Other dementia	Other dementias	
	Anxiety		
3	Bipolar	Psychiatric conditions	
	Depression		
Λ	Hemiplegia	Stroka / Hamiplagia	
4	Stroke	Stroke / Herripiegia	
5	Alzheimer disease	Alzheimer dementia	

Characteristics of the Canada dataset, HC setting									
Characteristics	Total sample N=25000	Cardio-pulmonary diseases N=2137 (9%)	Other dementias N=4230 (17%)	Psychiatric conditions N=12342 (49%)	Stroke / Hemiplegia N=1878 (8%)	Alzheimer dementia N=4413 (18%)			
Females	60%	70.8%	59.5%	62.7%	49.1%	52.1%			
Age (mean (SD)	81.2 (9,1)	77.6 (9.4)	83.9 (7.5)	80.8 (9.4)	79.9 (9.2)	82.1 (8.7)			
ADL									
Mild-moderate	32.4%	32.8%	41.3%	30.1%	30.3%	31%			
Severe	23.9%	24.1%	28.8%	20.9%	32.4%	23.6%			
CPS > 1	77.6%	83.9%	99.2%	69.4%	84%	73.8%			
Total number of diseases									
3+ diseases	31.2%	87%	32.1%	8%	48.4%	60.4%			

ADL = Activities of Daily Living, CPS = Cognitive Performance Scale

Polypharmacy

US

... The highest prevalence of medication use was among persons aged at least 65 years, of whom 12% took at least 10 medications

Kaufman et al. JAMA 2002

The prevalence of polypharmacy (use of \geq 5 prescription drugs) **increased from an** estimated 8.2% in 1999-2000 to 15% in 2011-2012

Sweden

Kantor et al. JAMA 2015

... mean number of drugs was 7.9 for age group 70-79 y, 9.3 for age group 80-89 y and 9.7 for age group 90 y or older

Hovstadius B et al. BMC Clin Pharmacol. 2009

NH Europe

Polypharmacy was observed in 2,000 (49.7%) residents and excessive polypharmacy in 979 (24.3%) residents.

Onder G et al. J Gerontol A Biol Sci Med Sci. 2013

N. duuree			% M	en					% Wo	omen		
N. arugs	65-69	70-74	75-79	80-84	≥85	Tot	65-69	70-74	75-79	80-84	≥85	Tot
1	10,9	7,1	5,0	3,7	3,6	6,6	9,4	6,2	4,4	3,4	4,0	5,6
2	11,8	8,7	6,6	5,1	4,4	7,9	11,0	8,1	6,1	4,8	4,9	7,1
3	11,4	9,4	7,7	6,3	5,5	8,5	11,4	9,2	7,5	6,2	6,0	8,2
4	10,7	9,7	8,4	7,4	6,6	8,9	11,0	9,7	8,4	7,4	7,2	8,8
5	9,6	9,4	8,8	8,2	7,6	8,9	9,9	9,5	8,9	8,2	8,0	9,0
6	8,5	8,9	8,8	8,5	8,2	8,6	8,8	9,0	8,8	8,6	8,5	8,7
7	7,2	8,1	8,4	8,4	8,4	8,0	7,5	8,2	8,4	8,6	8,5	8,2
8	6,1	7,1	7,7	8,0	8,1	7,2	6,2	7,2	7,8	8,1	8,1	7,5
9	5,0	6,0	6,8	7,4	7,6	6,4	5,2	6,2	6,9	7,5	7,5	6,6
10+	18,8	25,6	31,9	37,1	40,1	29,0	19,6	26,8	32,7	37,2	37,2	30,3

Rapporto Osmed anziani 2020



		Prevalence of use (%)											
Drug class	Men							Women					
	65-69	70-74	75-79	80-84	≥85	Tot	65-69	70-74	75-79	80-84	≥85	Tot	
PPI	35,4	45,6	49,6	58,5	66,5	<u>47,9</u>	37,1	47,2	50,7	58,7	62,7	<u>50,3</u>	
Anti-hypertens.	59,0	71,6	75,3	86,9	95,5	<u>73,9</u>	54,8	69,3	74,8	86,2	92,0	74,0	
Antibiotics	43,9	49,5	49,2	54,9	63,5	<u>50,3</u>	48,2	51,8	49,0	52,4	57,5	51,6	

					Preva	lence	of us	e (%)				
Drug class			Μ	en					Wor	nen		
	65-69	70-74	75-79	80-84	≥85	Tot	65-69	70-74	75-79	80-84	≥85	Tot
PPI	35,4	45,6	49,6	58,5	66,5	<u>47,9</u>	37,1	47,2	50,7	58,7	62,7	<u>50,3</u>
Anti-hypertens.	59,0	71,6	75,3	86,9	95,5	<u>73,9</u>	54,8	69,3	74,8	86,2	92,0	74,0
Antibiotics	43,9	49,5	49,2	54,9	63,5	<u>50,3</u>	48,2	51,8	49,0	52,4	57,5	<u>51,6</u>
Urinary	19,7	29,1	34,5	42,1	47,3	31,7	0,3	0,4	0,4	0,5	0,4	0,4
Anti-osteopor.	9,0	12,7	15,2	19,3	22,4	14,3	44,1	51,1	50,4	52,7	44,8	48,4
Pain killers	7,6	10,0	12,0	15,6	18,3	11,5	10,5	14,6	17,7	22,4	23,2	17,1
Anti-depress.	6,6	8,5	10,6	14,6	19,5	10,6	13,3	16,4	18,8	23,8	27,0	19,3

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Urinary	19,7	29,1	34,5	42,1	47,3	31,7	0,3	0,4	0,4	0,5	0,4	0,4
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Pain killers	7,6	10,0	12,0	15,6	18,3	11,5	10,5	14,6	17,7	22,4	23,2	17,1
Anti-depress.	6,6	8,5	10,6	14,6	19,5	10,6	13,3	16,4	18,8	23,8	27,0	19,3
Antidiabetics	16,7	21,2	22,3	23,8	21,6	20,6	11,1	15,3	16,9	18,9	17,6	15,6
Statins	32,5	41,3	43,1	46,1	38,6	39,6	28,7	37,6	39,5	41,3	30,5	35,2
NSAIDs	26,2	30,0	28,7	30,3	28,6	28,6	33,0	38,2	36,6	37,2	30,8	35,1

Interactions – Italian Population

	Total (≥6	5 years)	65-74	75-84	≥85
	n.	%	(%)	(%)	(%)
2 o + drugs increasing	910 000	6.6	17	Q 1	0.5
risk of bleeding	910.000	0,0	4,7	0,1	5,5
2 o + drugs causing QT	247 720	1 Q	1 /	2.0	26
prolongation	247.720	1,0	1,4	2,0	2,0
2 o + drugs increasing					
the risk of acute renal	1.301.647	9,5	8,2	10,9	10,3
failure					

Rapporto Osmed anziani 2020

Outline

- What are multimorbidity and polypharmacy?
- Approaches?

Potentially serious drug-drug interactions between drugs recommended by clinical guidelines for 3 index conditions and drugs recommended by each of other 11 other guidelines



Dumbreck et al BMJ 2015

Decision Making for Older Adults With Multiple Chronic Conditions: American Geriatrics Society Guiding Principles



Journal of the American Geriatrics Society, Volume: 67, Issue: 4, Pages: 665-673



Italian Guidelines on MM and polypharmacy

...persons with multimorbidity are heterogeneous, and their global health status and risk of negative outcomes may vary largely... strategies for patients' stratification are needed to identify the most demanding and complex-to-treat groups, i.e., those that might benefit most from individualized and integrated healthcare approaches. ...

Onder G et al. Aging Clin Exp Res 2021

Italian Guidelines on MM and polypharmacy

<u>Recommendation</u>. The Frailty Index can be used to identify persons with multimorbidity at risk of unplanned hospital admissions. <u>Recommendation</u>. Among patients hospitalized or discharged from hospital, validated tools such as the Clinical Frailty Scale, Frailty Index, and Multidimensional Prognostic Index are recommended for identifying those with multimorbidity and limited life expectancy. <u>Recommendation</u>. In community-dwelling persons, the Charlson Comorbidity Index, Frailty Index, and gait speed test can be used to identify those with multimorbidity and limited life expectancy.

Onder G et al. Aging Clin Exp Res 2021

AGS guiding principles

Elicit and incorporate patient (and family/caregiver) preferences into medical decision making.

Recognize the limitations of the evidence base, and interpret and apply the medical literature specifically for this population.

Frame clinical management decisions within the context of harms, burdens, benefits, and prognosis (eg, remaining life expectancy, functional status, and quality of life).

Consider treatment complexity and feasibility when making clinical management decisions.

Use strategies for choosing therapies that optimize benefit, minimize harm, and enhance quality of life.

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Goal-Oriented Patient Care — An Alternative Health Outcomes Paradigm

David B. Reuben, M.D., and Mary E. Tinetti, M.D.

... focus on a patient's individual health goals within or across a variety of dimensions (e.g., symptoms; physical functional status, including mobility; and social and role functions) and determine how well these goals are being met...

Rubern DB NEJM 2012

Goal oriented care

1. Individually desired rather than universally applied health states;

2.It **simplifies decision making** for patients with multiple conditions by focusing on outcomes that span conditions and aligning treatments toward common goals

3. It prompts patients to articulate which health states are important to them and their relative priority



Association of Patient Priorities–Aligned Decision-Making With Patient Outcomes and Ambulatory Health Care Burden Among Older Adults With Multiple Chronic Conditions

Intervention: Patient priorities care, an approach to decision-making that includes patients' identifying their health priorities (ie, specific health outcome goals and health care preferences) and clinicians aligning their decision-making to achieve these health priorities.

Tinetti ME et al. JAMA IM 2019

Association of Patient Priorities–Aligned Decision-Making With Patient Outcomes and Ambulatory Health Care Burden Among Older Adults With Multiple Chronic Conditions

Results: Compared with UC patients, PPC patients were more likely to have medications stopped (OR, 2.05; 95% CI, 1.43-2.95) and less likely to have self-management tasks (OR, 0.59; 95% CI, 0.41-0.84) and diagnostic tests (OR, 0.22; 95% CI, 0.12-0.40) ordered.

Conclusions: This study's findings suggest that aligning care with patients' priorities may improve outcomes for patients with multiple chronic conditions.

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Treatment of non dementia illness in patients with dementia

Problems	Consequences	Responses
Cognition and language	Decreased decision-making capacity Increased caregiver burden Increased risk of diagnostic procedures Adherence problems Difficulty reporting adverse effects Difficulty titrating medicines based on reporting by patient	Consider altered risk-benefit ratio balancing safety and autonomy Adjust communication strategies
Decreased life expectancy	Decreased potential benefit	Consider altered risk-benefit ratio Reserve therapy/screening for those with sufficient life expectancy to realize benefit
Exclusion from studies	Increased uncertainty about effects of therapy in this group	Policy changes to include patients with dementia in appropriate studies

Brauner et al. JAMA 2000



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Concerns about older persons' ability to adhere to complex medication regimens

Concern	Representative Quotation
Historical evidence of inability to adhere	Also I factor in adherence to even a basic treatment. If they cannot manage a basic treatment, the one I am giving them, I am not going to complicate it further by adding something to get to the goal range.
Difficulty understanding medications	Whenever [patients] are confused about what medications they are on that suggests a problem. When they can not tell you what the medications either by name or description, and they are confused about when they are supposed to take them
Availability of social support	Often what you are doing is assessing someone's personality and their abilities to integrate complicated information and goals and if you have a patient who is limited you are obviously not going to push the meds nearly as hard unless there is somebody else in the picture who can administer them.
	I look at their functioning as a whole and also whether or not they live alone, their support system, have help.
	Fried, T. R. et al. Arch Intern Med 2010

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Avoid un-necessary drugs Herbal medications



Herbal meds:

- Not regulated
- No proofs of safety and efficacy
- Contamination
- Concentration (?)
- Side effects

Onder G et al. JACC 2017 Onder G et al. JAMA 2016

Multimorbidity overview	NICE Pathways
Adult with 2 or more long- term health conditions	
2 General principles	6 Patient and service user experience
3 Identifying people who may benefit from an approach to care that takes account of multimorbidity	NICE Guidelines Multimorbidity
Assessing frailty	 Discuss the purpose of an approach to care that takes account of multimorbidity Establish disease and treatment burden
Delivering an approach to care that takes account of multimorbidity	 Establish patient goals, values and priorities Review medicines and other treatments
5 4	taking into account evidence of likely benefits and harms
	 Agree an individualised management plan with the person

Italian guidelines on multimorbidity

To achieve optimal outcomes in persons with multimorbidity and/or polypharmacy, the following principles concerning the interaction of healthcare professionals and patients are recommended:

1. Identify health trajectories, clinical care needs, and person preferences for their care plan.

2. Agree on an **individualized care plan** that takes into account the interaction between chronic disease and drug treatments, as well as personal preferences about care and living environment.

3. Educate patients and/or caregivers about the use of medications and support self-management of treatment, while increasing their knowledge on the risks and benefits of polypharmacy and providing information about deprescribing procedures.

Onder G et al. Aging Clin Exp Res 2021

Italian guidelines on multimorbidity

To implement an optimal approach to patients with multimorbidity and/or polypharmacy, healthcare professionals should consider the following principles:

1. Contextualize the scientific evidence.

2. Assess the benefit/risk ratio of using specific guidelines for single diseases, in light of the patients' clinical and social care characteristics and personal preferences.

3. Use drugs with documented efficacy, at the minimum effective dose, with the lowest number of dosage units and daily administrations.

4. Look out for adverse drug reactions due to **drug interactions** (including drug-drug, drug-disease, drug-food, drug-dietary supplement interactions)

Onder G et al. Aging Clin Exp Res 2021

Outline

- What are multimorbidity and polypharmacy?
- Approaches?
- Biology of multimorbidity

Biological Mechanisms of Multimorbidity?

 Biological mechanisms of aging increases the susceptibility of aged individuals to several chronic diseases and loss of function



Time and the Metrics of Aging

Age

Ferrucci et al. Circ Res 2018

Inflammaging



Ferrucci et al Nature Reviews Cardiology 2018

Biological Mechanisms of Multimorbidity?

- Biological mechanisms of aging increases the susceptibility of aged individuals to several chronic diseases and loss of function
- These mechanisms are not fully defined

The hallmarks of aging

A major challenge is to dissect the interconnectedness between the candidate hallmarks and their relative contributions to aging, with the final goal of identifying pharmaceutical targets to improve human health during aging, with minimal side effects.



Lopez-Otin et al. Cell 2013

Biological Mechanisms of Multimorbidity?

- Biological mechanisms of aging increases the susceptibility of aged individuals to several chronic diseases and loss of function
- These mechanisms are not fully defined
- Therapies developed to target such shared 'drivers' have the potential to delay the onset and progression of multiple chronic diseases and functional decline

SCIENTIFIC DISCOVERY AND THE FUTURE OF MEDICINE Aging as a Biological Target for Prevention and Therapy

Nir Sarzilai, MD Institute for Aging esearch, Albert Einstein College of Medicine, Brons, New York.

IEWPOINT

Ana Maria Coervo, MD, PhD Institute for Aging Research, Albert Einstein Colliege of Medicine, Bronx, New York.

Steve Austad, PhD Department of Biology. The University of Alahima at Banningham.

edented aging of the human population in the 21st cenquality of later life throughout the developed world. Fortunately, research has shown that fundamental aging processes can be targeted by nutritional, genetic, and pharmacologic interventions to enhance and extend both health and longevity in experimental animal models. These findings clearly demonstrate that the biological rate of aging can be slowed.

biological aging processes will prevent, or at a minidiseases and debilities that are typically observed in older adults.12 For example, interventions that extend the life span of mice often also prevent or slow the progress of

Chronic health problems related to the unprec- another. If biological aging processes are the fundamental cause of virtually all major medical diseases and tury threaten to disrupt economies and degrade the conditions in individuals, then targeting those processes holds promise to ameliorate many of these diseases and conditions as a group

Opinion

Aging Processes Can Be Targeted

One of the main geroscience accomplishments is to highlight a small number of major "pillars," interacting molecular and physiological processes that underlie the biology The geroscience hypothesis, for which there is abun-of aging, for instance, metabolism, proteostasis, macrodant evidence in animal models. links these biological dis-molecular damage, inflammation, adaptation to stress, coveries to human health by proposing that targeting epigenetics, and stem cells and their regeneration.1 The key feature of this conceptual framework is that these promum delay, the onset and progression of multiple chronic cesses are understood to be tightly interrelated. These findings have emerged from the remarkable progress made in recent years in dissecting aging processes in model organisms.

JAMA Sept 2018

TAME trial – Aging as a target



TAME will mark a paradigm shift, moving from treating each medical condition to targeting aging per se

Barzilai N et al. Cell Metabolism 2016

TAKE HOME MESSAGE

- Multimorbidity highly prevalent
- Polipharmacy consequence of multimorbidity
- Individualized approach of multimorbidity
- Understanding of biological mechanisms is important to target interventions