Defining and classifying multimorbidity to inform guideline development and clinical practice: From complexity to clarity

Определение и категоризация мультиморбидности для поддержки клинической практики разработки клинических рекомендаций: от сложности до ясности

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Janne Estill – Declaration of conflicts of interest

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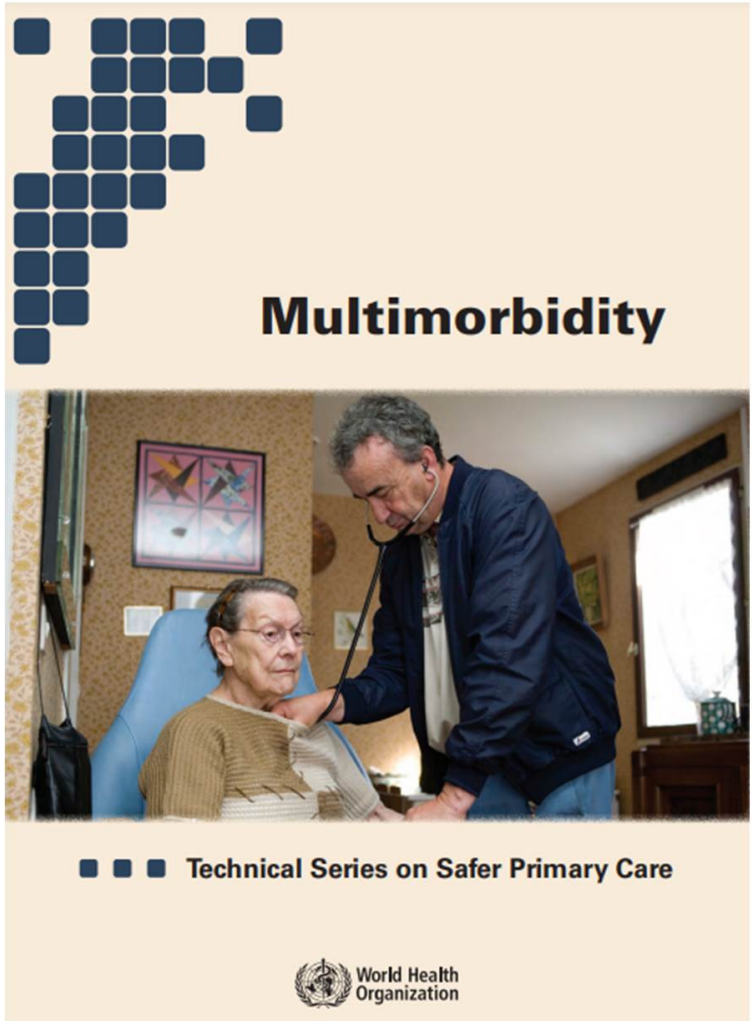
- **No financial conflicts of interest**

What is multimorbidity?



"The coexistence of two or more chronic conditions in the same individual" (WHO, 2016)

More precise term: *multiple long-term conditions*

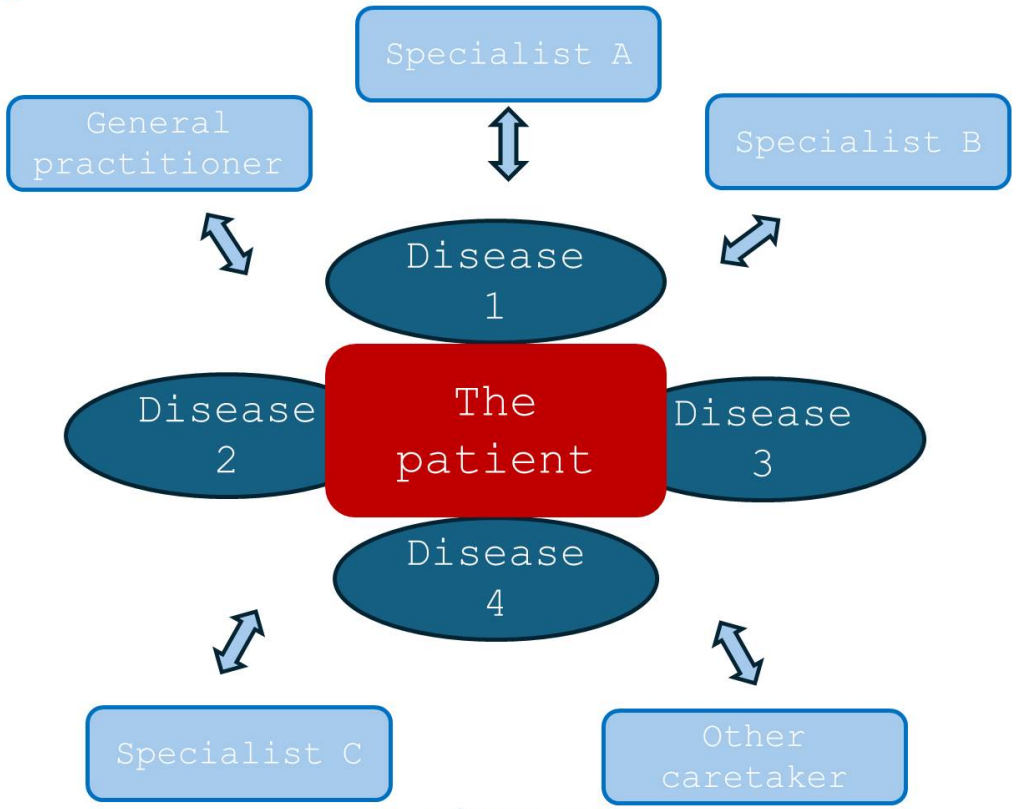
NIH National Library of Medicine
National Center for Biotechnology Information

MeSH

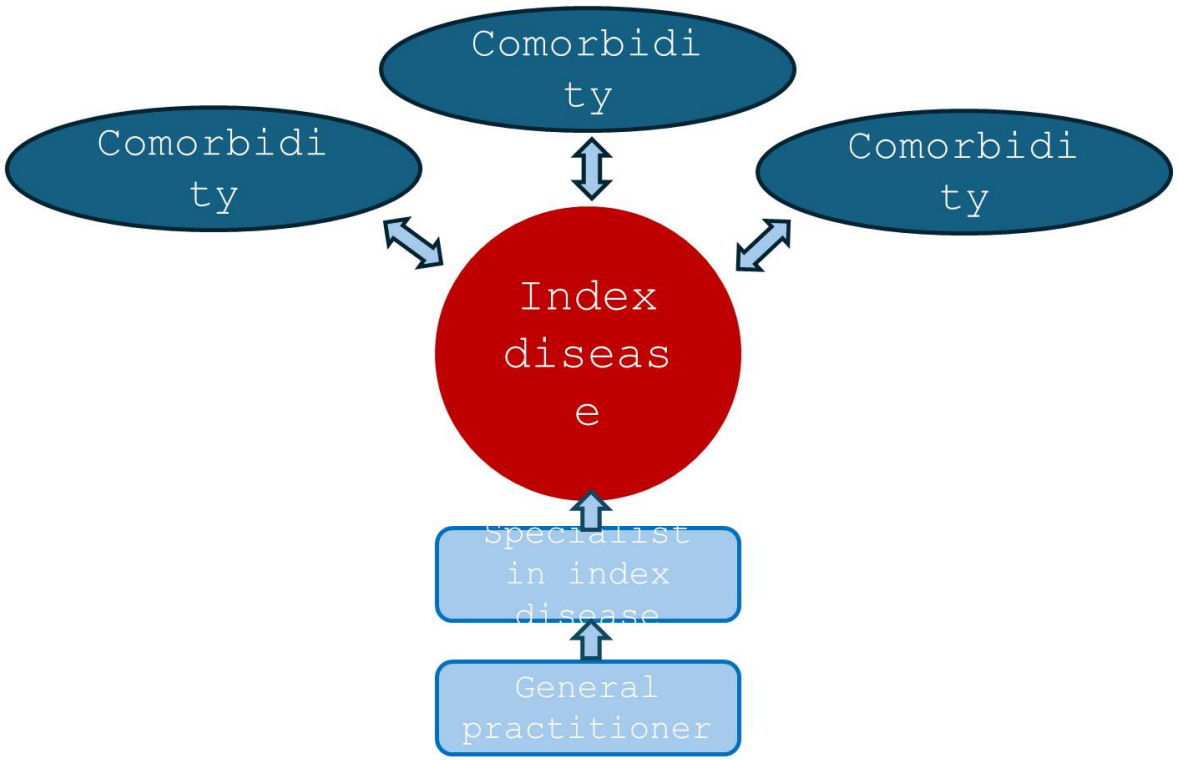
"The complex interactions of several co-existing diseases" (National Library of Medicine, 2018)

Multimorbidity vs comorbidity

Multimorbidity – the situation of the patient

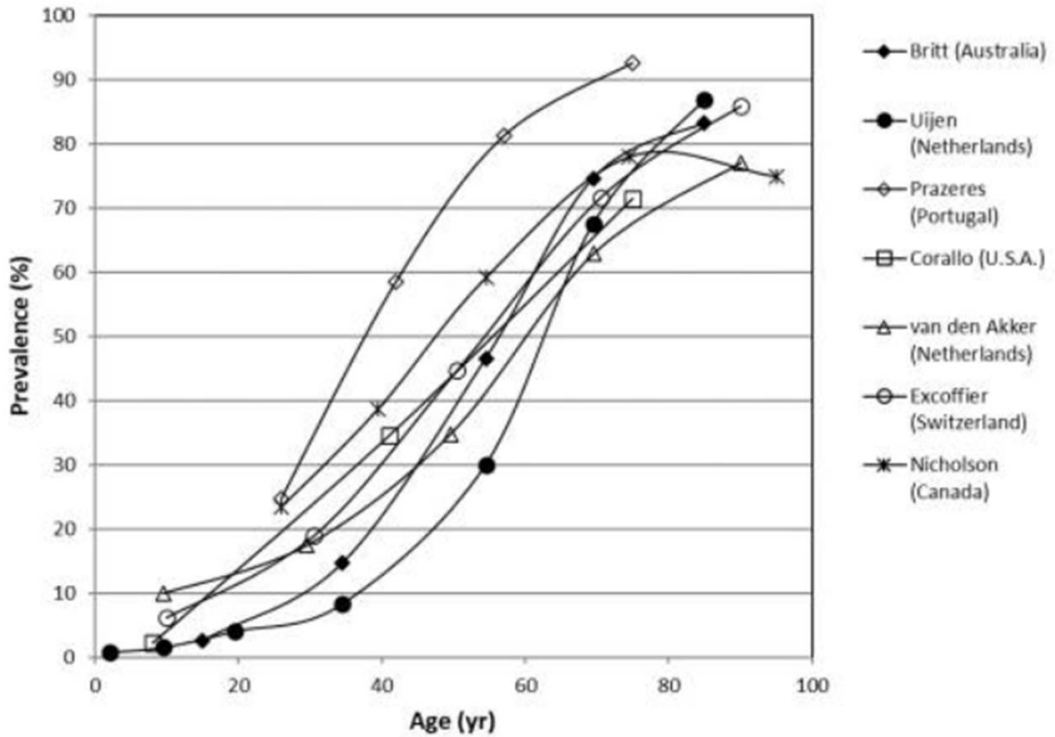


Comorbidity – other diseases except the disease of interest



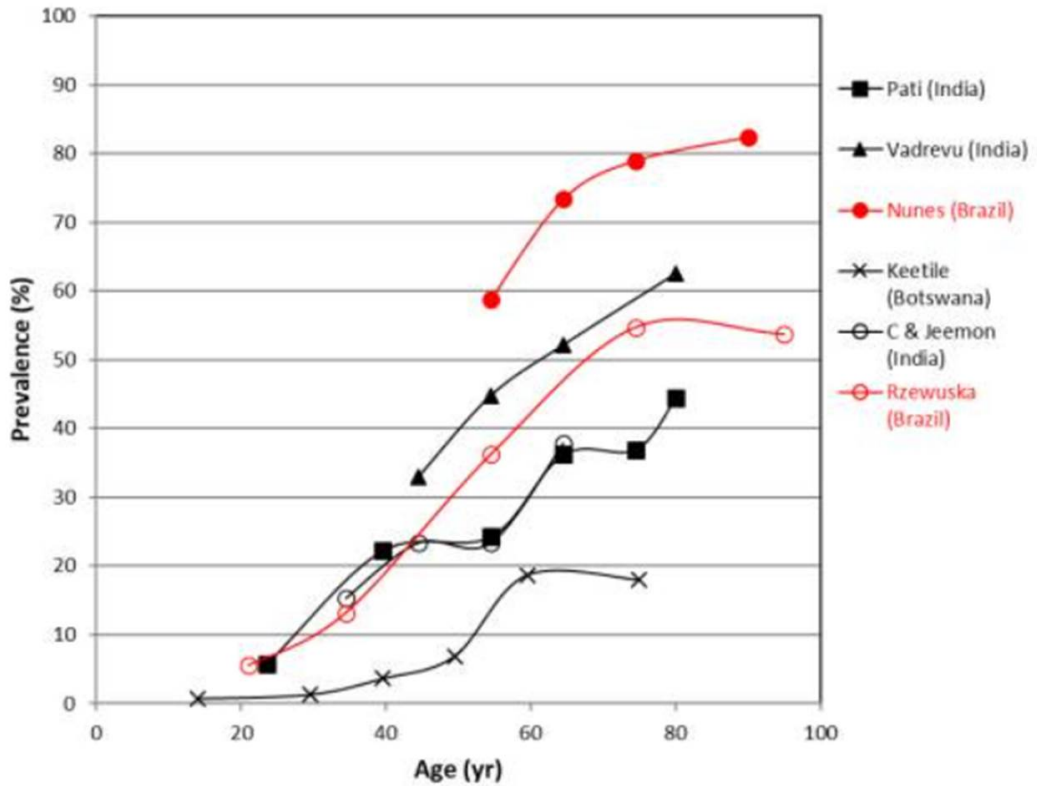
Prevalence of multimorbidity

- Multimorbidity affects most heavily **the elderly,** but it exists in all age groups including children



Skou ST *et al* 2022 Nat Rev Dis Primers

- **One third of the world's adult population** has multimorbidity



Do we need a categorization of multimorbidity?

Let's assume there are 300 diseases (with a rough categorization)

- **1 trillion** combinations of 2 to 6 diseases
- Impossible to develop guidelines for all possible combinations
- Current care based primarily on single-disease guidelines

Patient

Individualized care

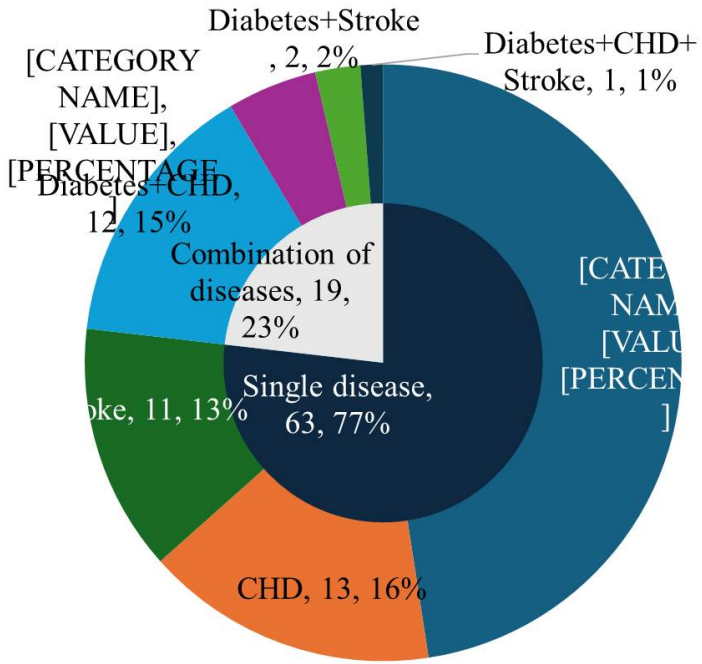
Difficult to find evidence to support clinical management

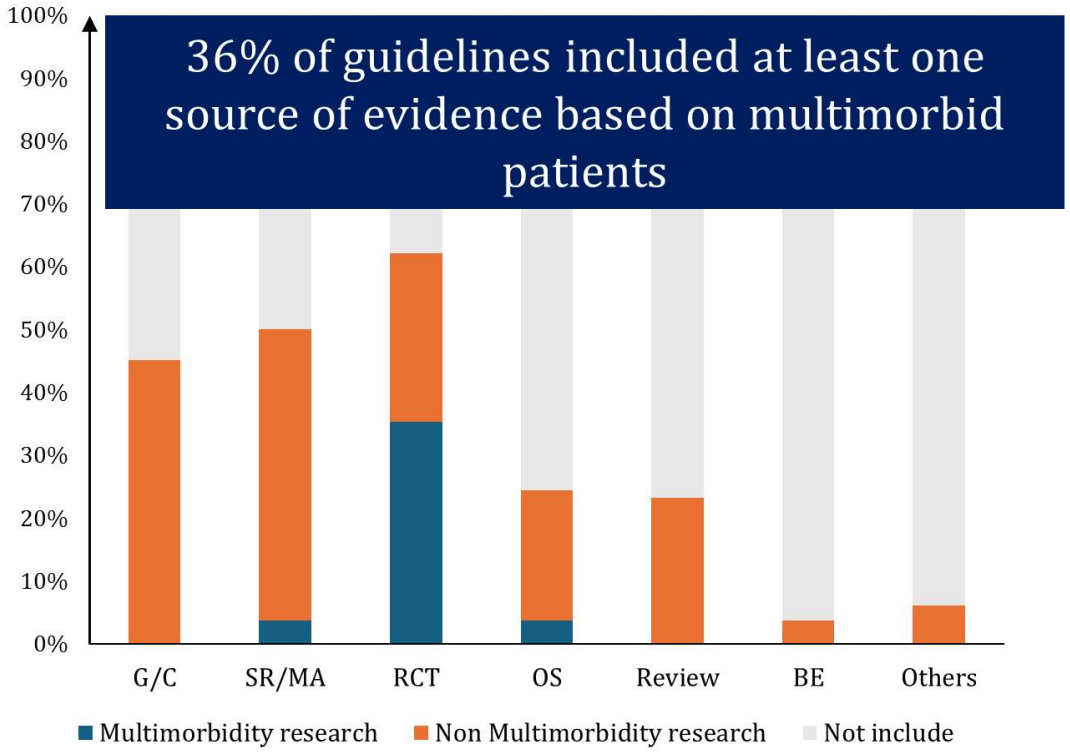
Strongly **evidence-based** approach

But the evidence is almost always **indirect**

Disease

Even guidelines for common combinations have severe limitations





Wang Z *et al* (under review)

Even guidelines for common combinations have severe limitations

- *"The heterogeneity of the multimorbid population, which affect both elder and younger people, make guidelines application difficult. While clustering or identifying multimorbidity patterns may help, the issue remains far more complex."*

- *"A 2021 review showed only a few Dutch guidelines contained usable recommendations on comorbidity—nothing much has changed since then."*

- *"When the evidence is unclear, guidelines may say 'ask the patient'—but how can a clinician and patient decide in five minutes what experts couldn't agree on in a year?"*

- *"We need studies with real life evidence from a broader range of patients that can be translated into recommendations for different subgroups."*

Citations from interviews on multimorbidity experts - Wang Z *et al* (under review)

Measuring multimorbidity – four major approaches

Disease count	Grouping of diseases by co-occurrence	Weighted indices	Identification of homogenous groups
✓ Simple to calculate and understand	✓ Can define common forms of multimorbidity	✓ E.g. **Charlson comorbidity index**	✓ **Concordant and discordant multimorbidity**
• Reflects (to some extent) the severity	✓ Can inform patient-centered care	• Reflects well the severity of the condition	✓ Accounts for synergies in management
• Unidimensional measure and often oversimplification	• Identifies common combinations where guidelines needed	• Not informative for management purposes	✓ Accounts for pathophysiological pathways
• Not informative for management purposes	• Does not account for pathophysiologi		✗ Ignores co-occurrence based on complex reasons

Lefèvre *et al* 2014 Rev Epidemiol Sante Publique

How to define concordant and discordant multimorbidity?

Concordant multimorbidity = ...

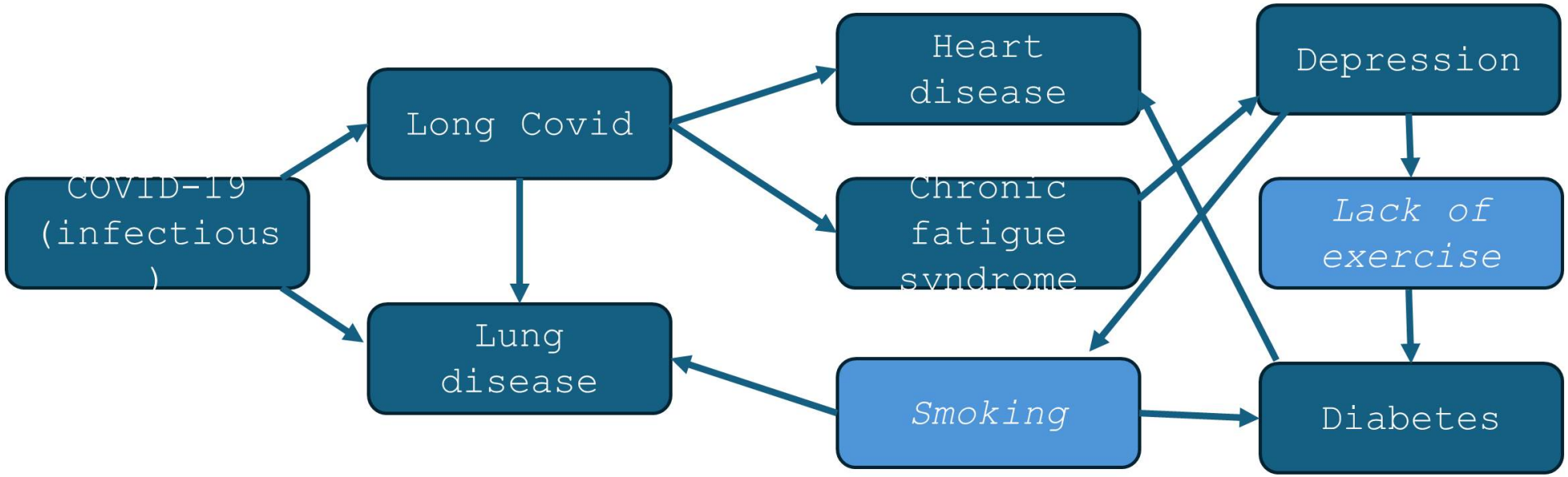
- ...The patient's conditions are from the same disease system
- ...There is a clear link in the pathophysiological mechanisms of the patient's diseases
- ...The treatment of the different diseases has synergies instead of conflicts
- ...The conditions are all either non-communicable only, infectious only, or mental only

Discordant multimorbidity = non-concordant

Or: can we say that any multimorbidity is concordant?

How to define concordant and discordant multimorbidity?

It is possible to find a link or common risk factor for almost any pair of conditions – so does it make sense to distinguish between "concordant" and "discordant"?



If we want clarity for multimorbidity, we need a classification system that...

- Focuses primarily on the **patients' needs** but also considers the biological and medical background
- Supports the collection of **evidence** and development of **dedicated guidelines and recommendations** for the most urgently needed multimorbidity profiles
- Serves as a key milestone towards truly **patient-centred** care

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First step – define concordant multimorbidity

Simple definition

Disease system

- Simple and unambiguous
- Implies (usually) synergies in treatment

Examples

- Cardiometabolic multimorbidity (cardiovascular diseases, diabetes, stroke, kidney disease...)
- Respiratory multimorbidity (asthma, COPD, ...)

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But how about discordant multimorbidity?

No easy way for classification!

Pathophysiologically unrelated and no treatment synergies

But: some forms of discordant multimorbidity can be very common

Let's look at data!

But how about discordant multimorbidity?

CHARLS 中国健康与养老追踪调查 China Health and Retirement Longitudinal Study

2018 dataset: almost 20,000 patients aged 45 years and above with chronic conditions: **almost 9000 (45%) are multimorbid**

14 chronic diseases

- Cardiometabolic and related diseases: Hypertension, heart disease, dyslipidemia, diabetes, kidney disease, liver disease, stroke
- Respiratory diseases: Asthma, chronic lung disease
- Other diseases and conditions: Arthritis, digestive disease, memory-related disease, psychiatric problems, cancer

http://charls.pku.edu.cn/en/

But how about discordant multimorbidity?

Latent class analysis of ~7000 individuals with **discordant** multimorbidity

Name of classes	Cardiac metabolic diseases and related diseases							Arthritis	Digestive disease	Respiratory diseases		Other diseases			Share of the population	Number of individuals
	Hypertension	Heart disease	Dyslipidemia	Diabetes	Kidney disease	Liver disease	Stroke	Arthritis	Digestive disease	Chronic lung disease	Asthma	Memory related disease	Psychiatric problems	Cancer		
Digestive-comorbid conditions class	38.3%	23.7%	24.4%	11.1%	14.3%	11.3%	5.4%	64.7%	100.0%	10.0%	0.6%	2.4%	3.4%	2.8%	37.7%	2753
Arthritis-cardiometabolic class	64.7%	23.7%	29.9%	17.6%	12.4%	6.4%	8.9%	95.1%	0.0%	7.6%	1.4%	4.3%	3.2%	5.5%	26.8%	1959
Respiratory-comorbid conditions class	40.6%	30.9%	16.9%	8.4%	14.5%	11.6%	4.7%	60.4%	47.1%	88.8%	40.3%	3.5%	5.5%	3.9%	21.5%	1572
Multisystem morbidity class	82.3%	70.3%	76.1%	47.5%	35.1%	21.9%	29.4%	69.0%	65.2%	37.2%	18.6%	25.6%	15.4%	6.3%	14.0%	1022

But how about discordant multimorbidity?

Latent class analysis of ~7000 individuals with **discordant** multimorbidity

Digestive-comorbid condition-cluster	**Arthritis-cardiometabolic cluster**	**Respiratory-comorbid condition-cluster**	**Multisystem morbidity cluster**
• Everyone has **digestive disease** • Hypertension, heart disease, dyslipidemia common • Most common discordant cluster	• Almost everyone has **arthritis** • Two thirds have hypertension • Heart disease, dyslipidemia and diabetes also frequent	• Almost 90% have **chronic lung disease** • Many other frequent conditions: arthritis, digestive disease, asthma, hypertension,	• **More than half have hypertension, heart disease, dyslipidemia, arthritis, digestive disease** • 14% of all discordant multimorbidity

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The way towards a proper classification?

- Combination of theory and data – **theoretical disease system based** categorization of concordant multimorbidity and **data-driven** categorization of discordant multimorbidity
- Approaches that utilize "big data" and more powerful methods (Gaussian mixture models, different forms of machine/deep learning)
- **International collaboration needed** to have more comprehensive data sources and truly generalizable definitions

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Conclusion

- Multimorbidity can have a simple definition – but it is an extremely complex concept
- Multimorbidity affects about a third of the world's population – but evidence-based medicine still tends to focus on **diseases** instead of **patients**
- Currently, no universal categorization scheme for multimorbidity
- Our initiative: combine **theory- and data-driven approaches** to define a multimorbidity classification system that can serve as the basis for evidence collection and guideline development

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- The **Guidelines International Network** (GIN) Multimorbidity Working Group

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Thank you!
Спасибо за внимание!

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