

# **“L'APPROCCIO GENERALISTA NELLA CURA DEI PAZIENTI AD ALTA COMPLESSITÀ”**



*Azienda Provinciale  
per i Servizi Sanitari  
Provincia Autonoma di Trento*



## **Teoria e epidemiologia della multimorbilità**

**Raffaele Landolfi**

Medicina Interna  
Fondazione Policlinico Gemelli

# Outline

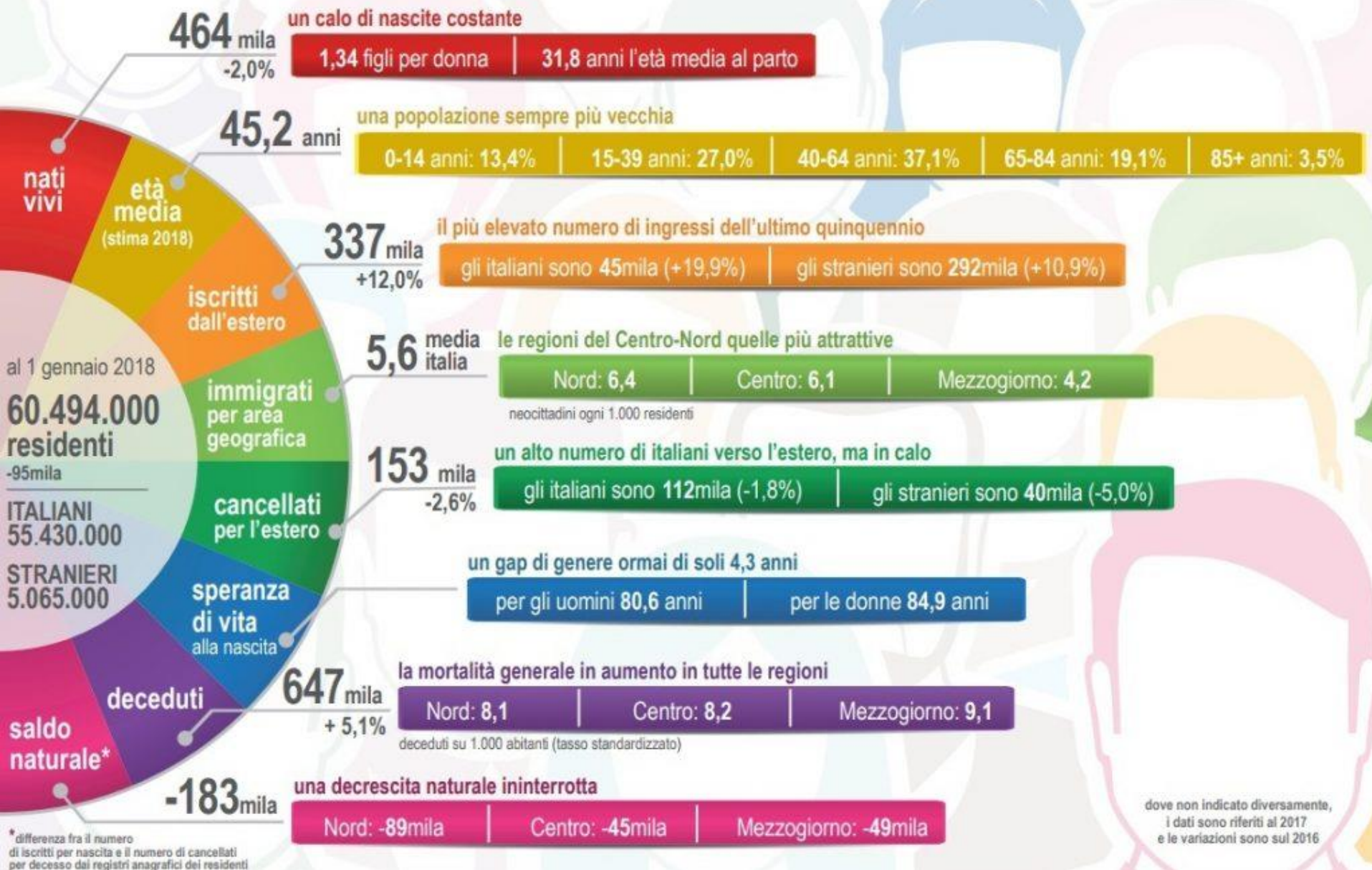
- Tsunami epidemiologico
- Inflamm-aging e malattie età-associate
- Epidemiologia della multimorbilità
- Impatto della multimorbilità
- Crisi/insufficienza della EBM
- Da precision medicine a precision care
- Multimorbilità e frailty
- Il caso scompenso cardiaco
- Verso una nuova forma di assistenza

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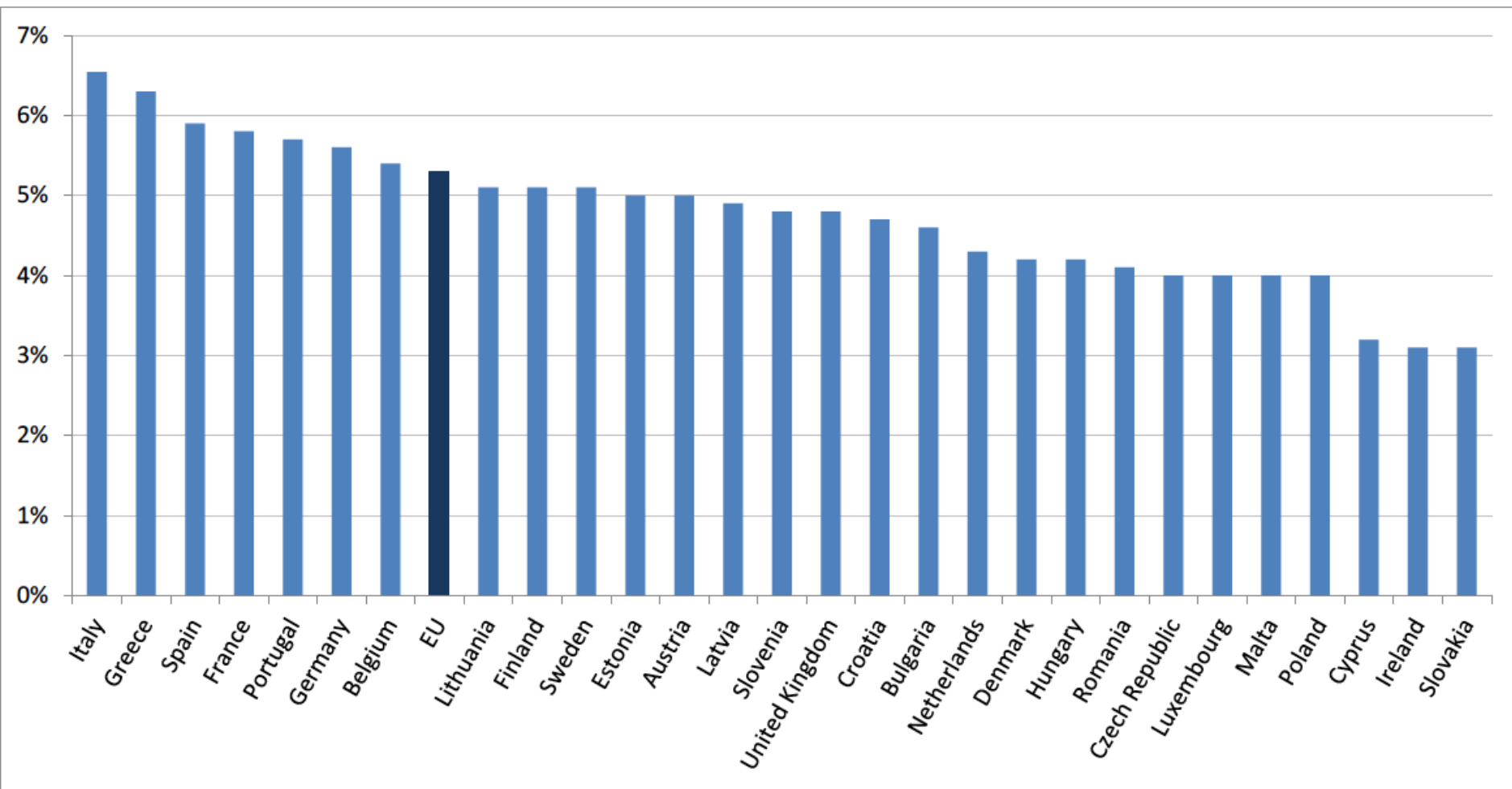
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# Indicatori demografici. Stime per l'anno 2017

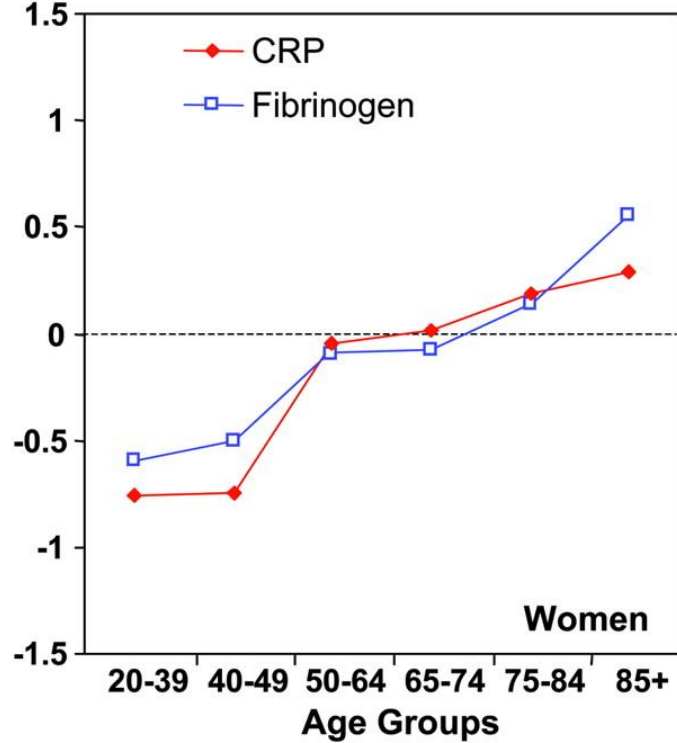
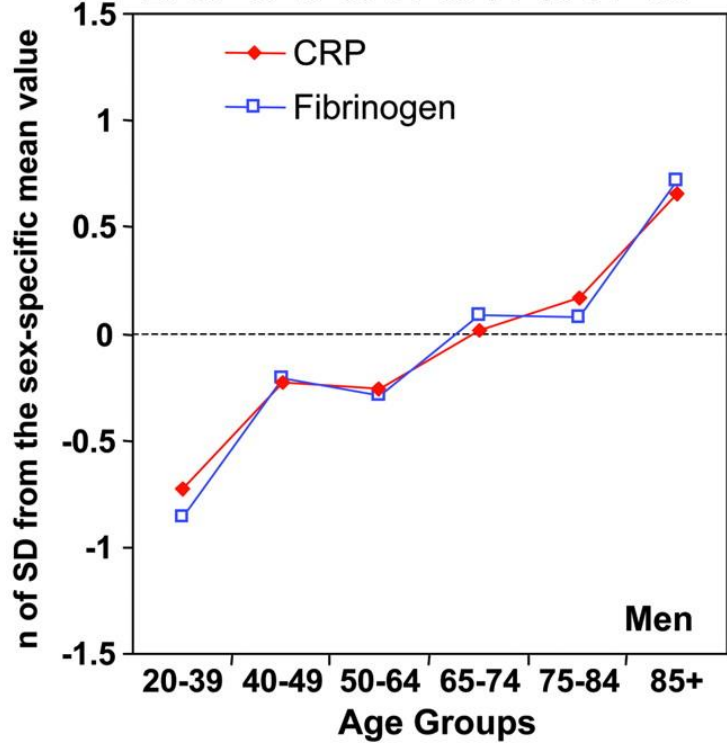
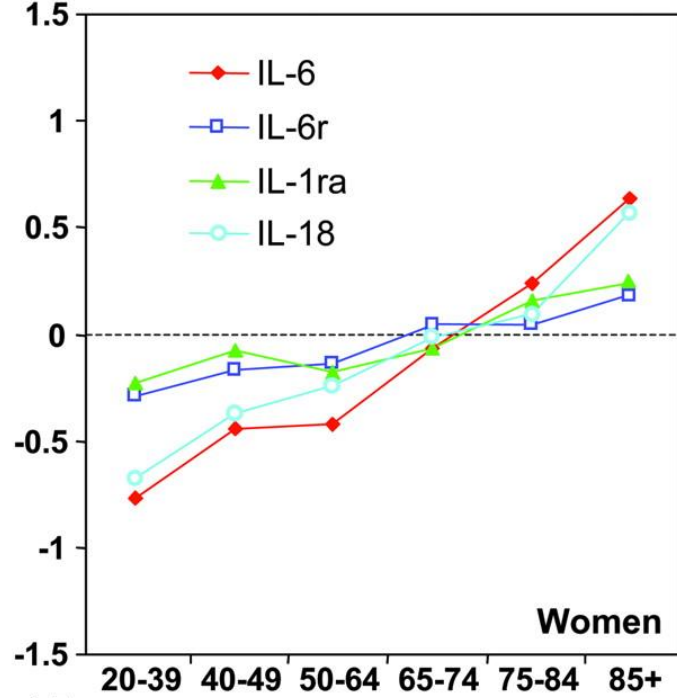
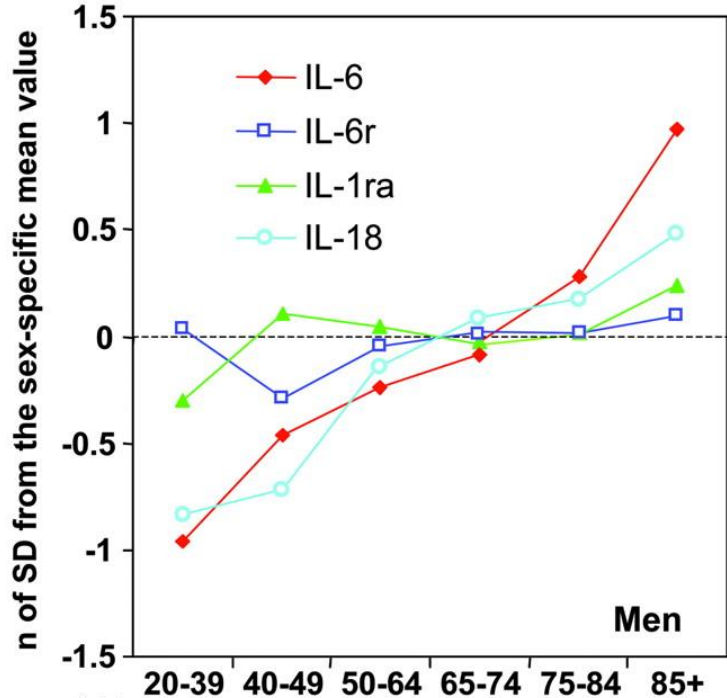


### Share of people aged 80 or over in the EU Member States, 2015



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# Uncontrolled Inflammation Is a Pathological Feature of Common Diseases



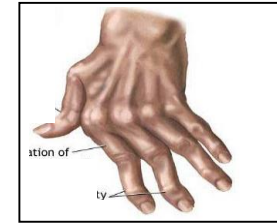
## Cardinal signs of inflammation:

- Calor (heat)
- Rubor (redness)
- Tumor (swelling)
- Dolor (pain)

*Excessive  
Uncontrolled*



## Rheumatoid arthritis



## Cardiovascular diseases

(Atherosclerosis)

## Neurological disorders

(Alzheimer's, Parkinson's)

## Inflammatory bowel diseases

(Colitis, Crohn's)

## Asthma

## Cancer

## Diabetes

## Autoimmune diseases

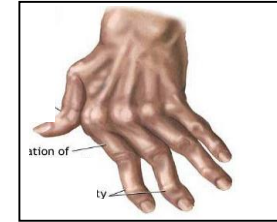
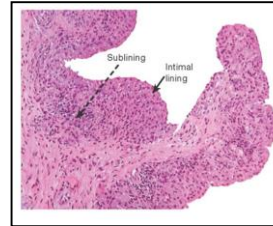
# Uncontrolled Inflammation Is a Pathological Feature of Common Diseases



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## Rheumatoid arthritis



## Cardiovascular diseases

(Atherosclerosis)

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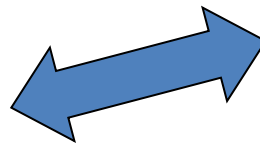
Asthma

Cancer

Diabetes

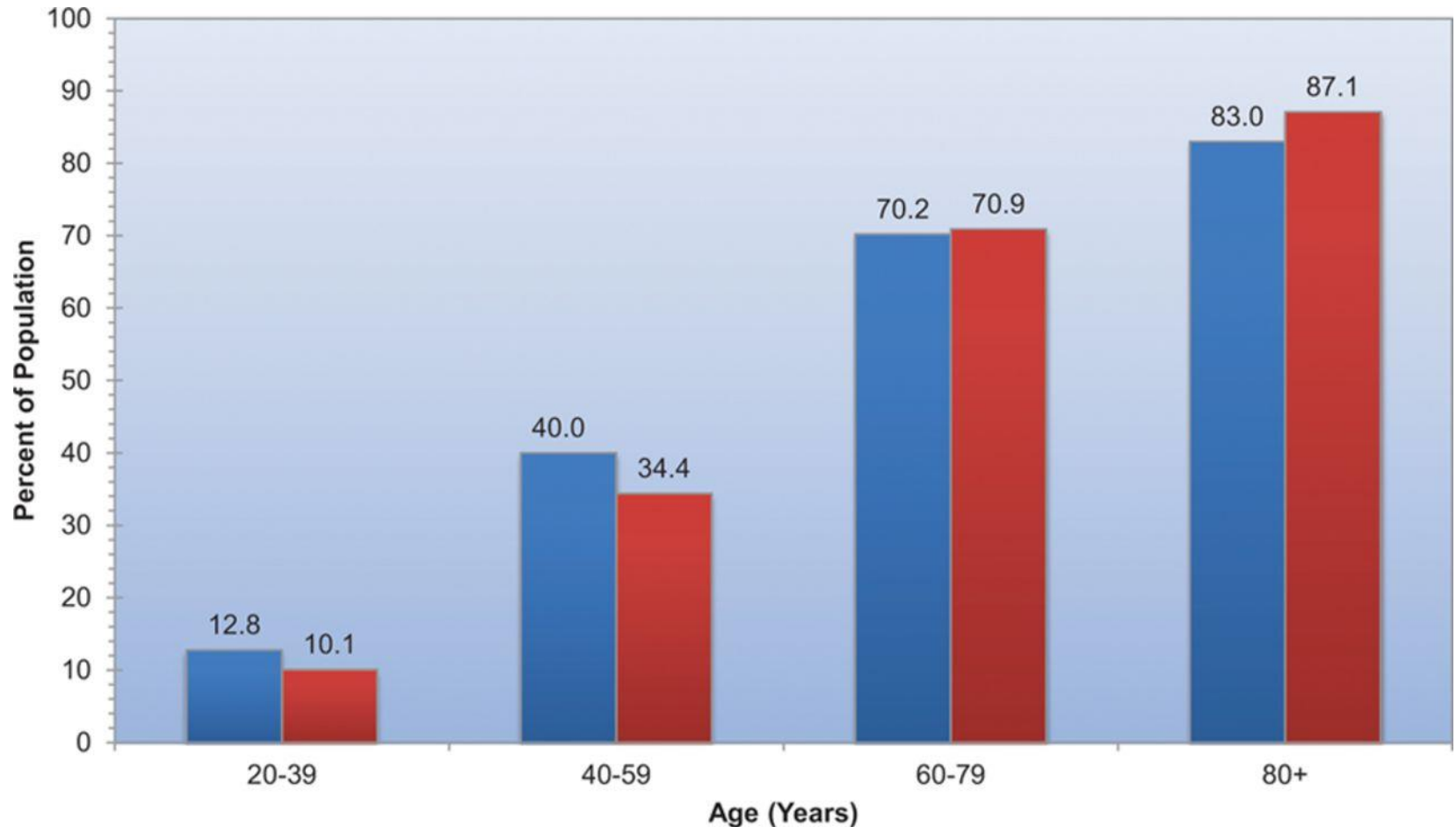
Autoimmune diseases

# AGING



# Prevalence of cardiovascular disease

(National Health and Nutrition Examination Survey: 2007–2010)



Go A S et al. *Circulation*. 2014;129:e28-e292

■ Men ■ Women



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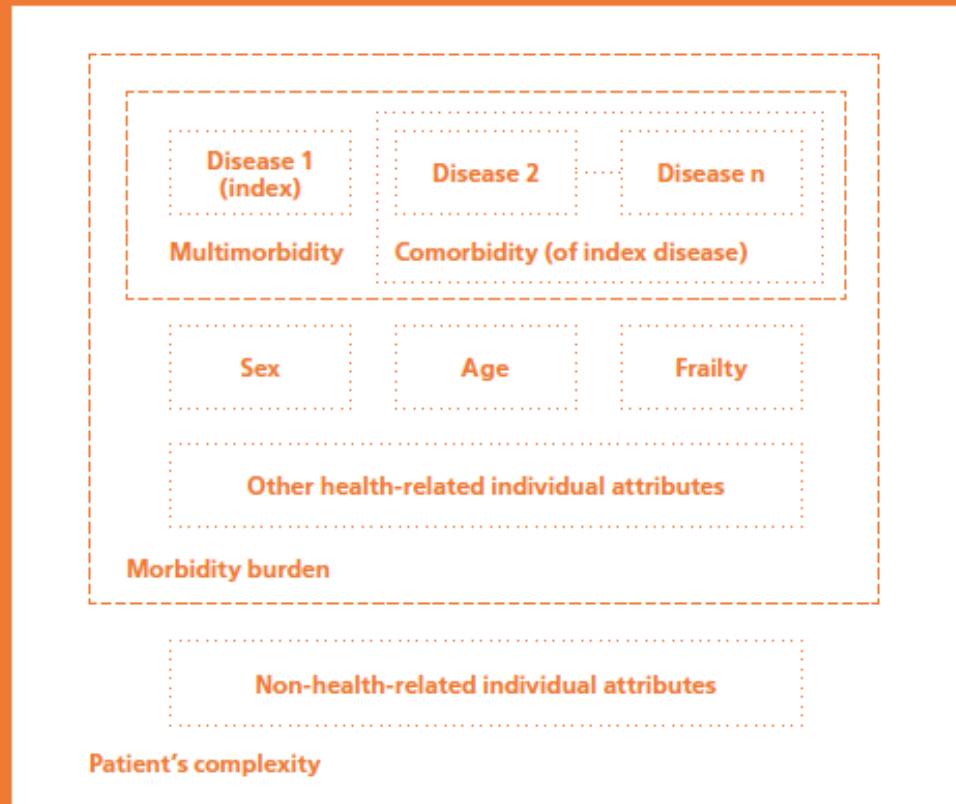
Not having an agreed definition of multimorbidity has hampered research and patient care.



**Comorbidity is the co-existence of other conditions with an index condition that is the specific focus of attention.**

**Multimorbidity is the co-existence of several conditions where none are considered an index condition that is the specific focus of attention.**

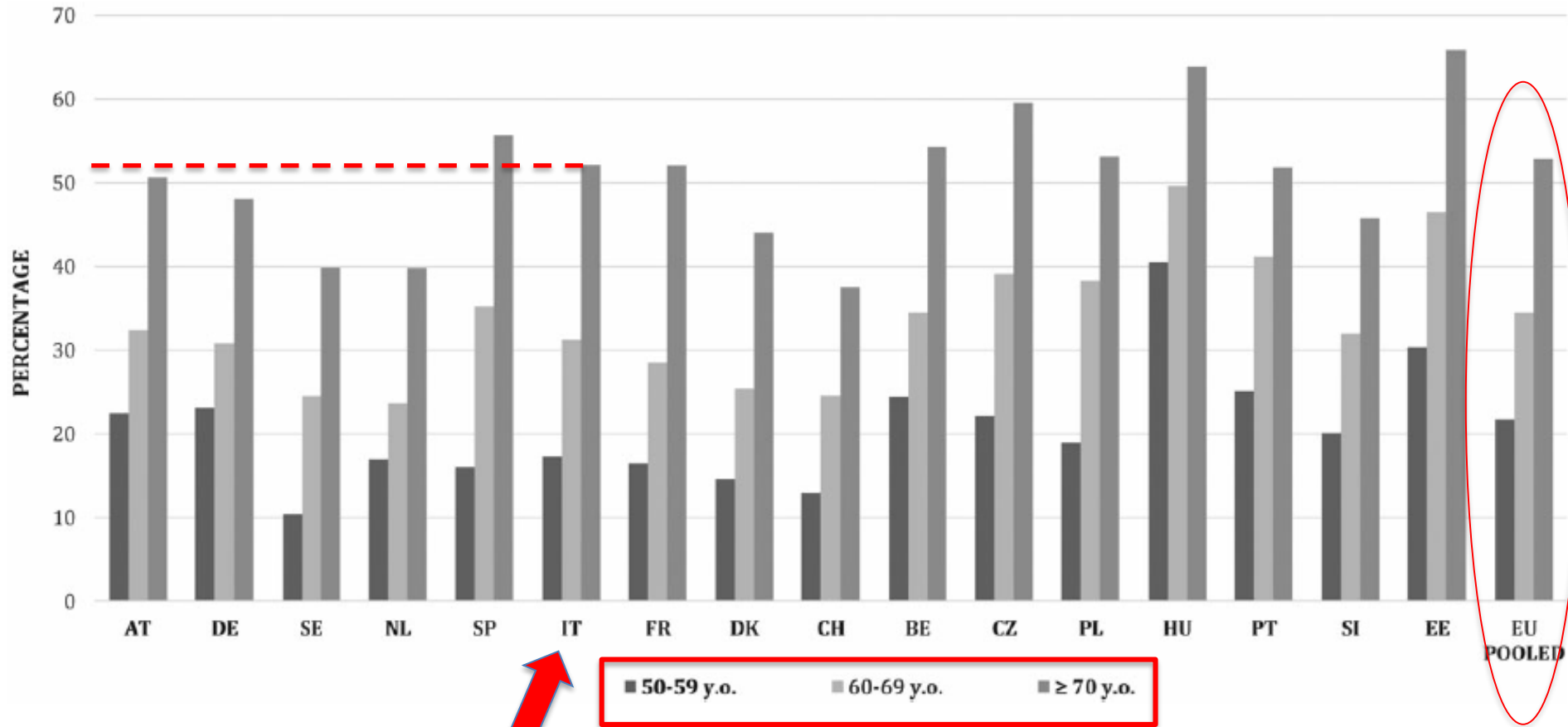
Multimorbidity is therefore a highly heterogeneous concept, and can be used to describe a wide array of patients experiencing a multitude of different combinations of conditions. As described in **Section 2.1.2**, co-existing conditions can be similar in their origin and/or treatment (concordant multimorbidity) or appear to be unrelated from each other (discordant multimorbidity). Multimorbidity constitutes a more generic, patient-centred concept and in doing so also acknowledges that the impact of a condition is influenced not only by health-related characteristics but also by socioeconomic, cultural, and environmental factors, and patient behaviour.



# Associations between multimorbidity, healthcare utilisation and health status: evidence from 16 European countries

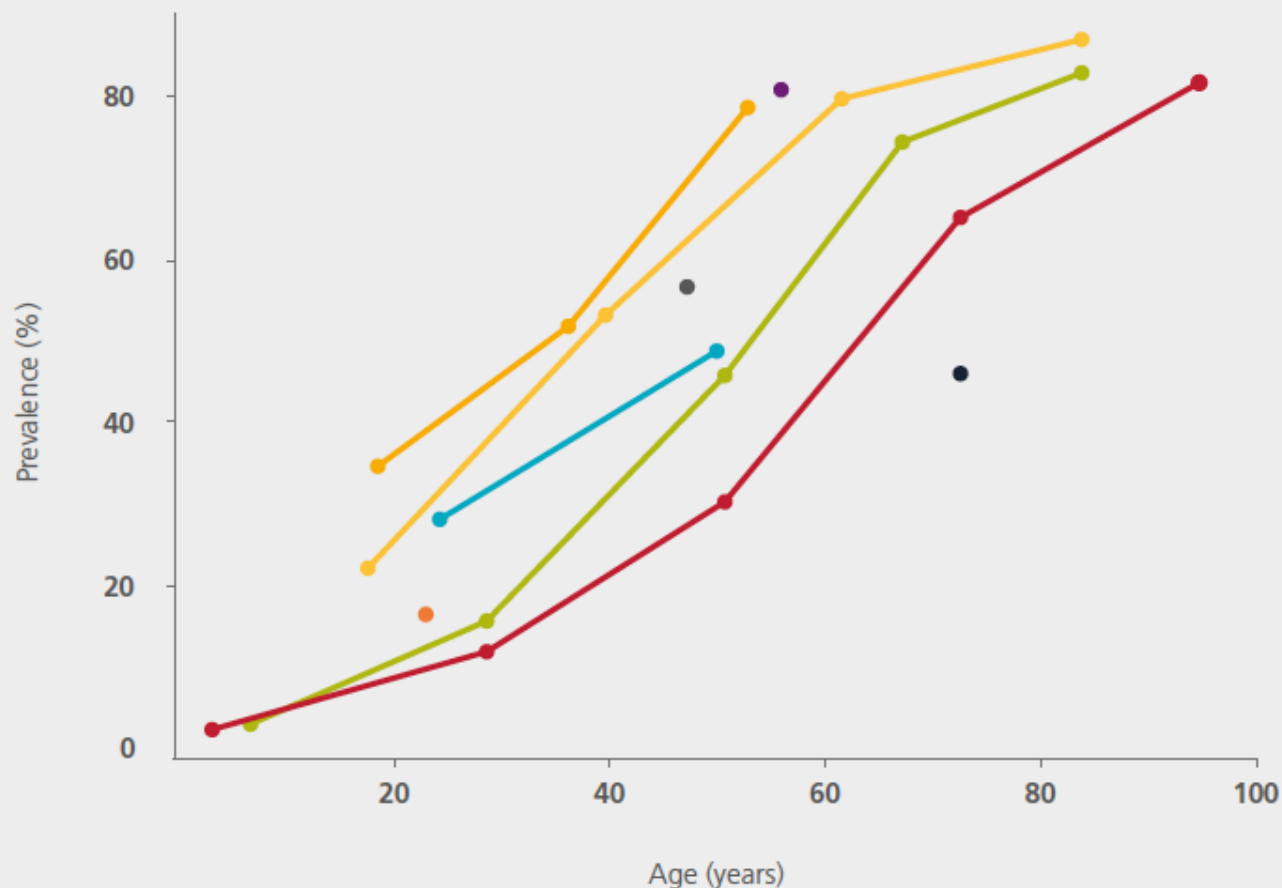
*Age and Ageing* 2016; **45**: 431–435

2 or more chronic conditions



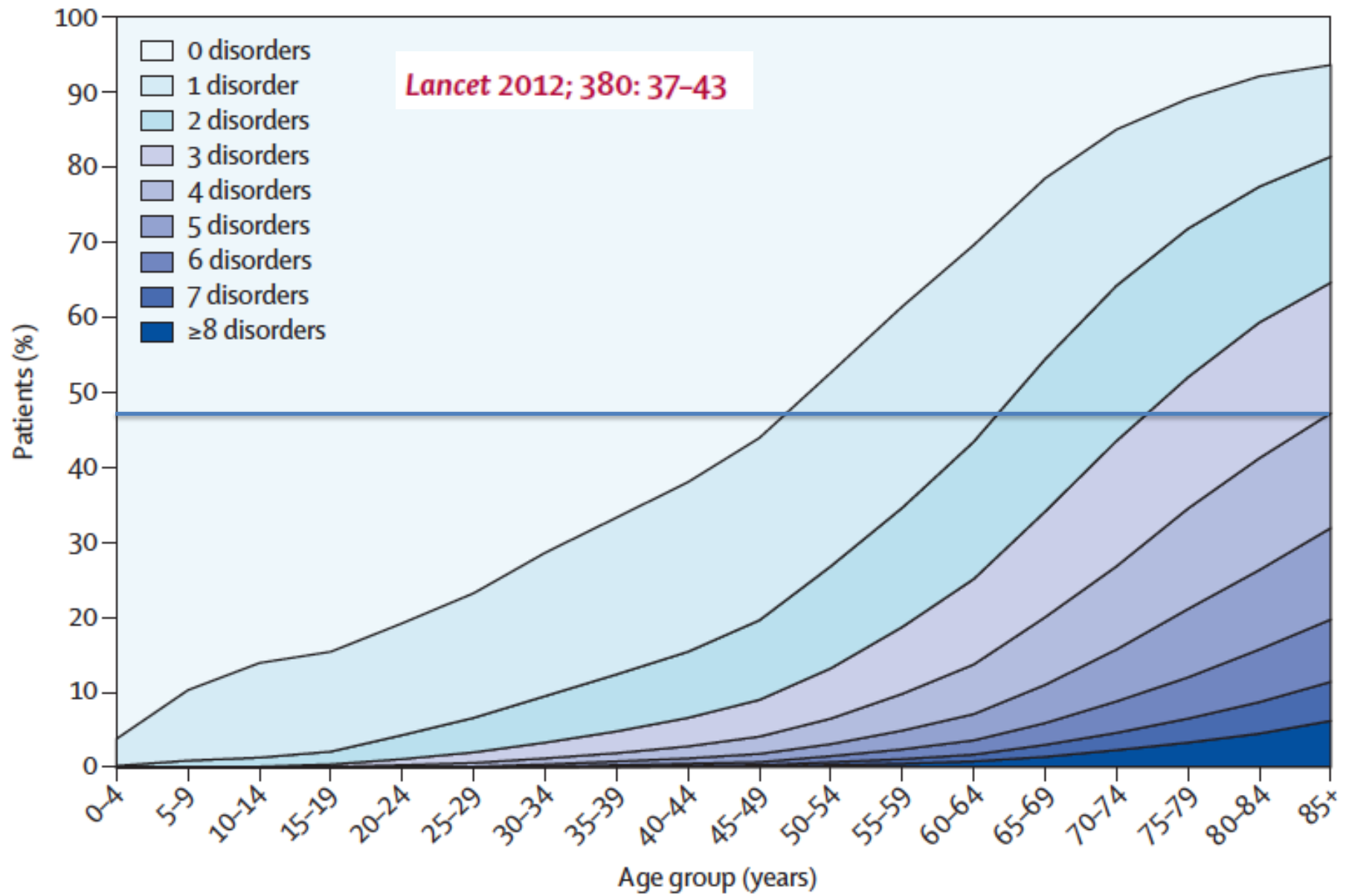
# Multimorbidity: a priority for global health research

April 2018



- Abete 2004
- Barnett 2012
- Britt 2008
- Kadam 2007
- Macleod 2004
- Muggah 2012
- Naessens 2011
- Van der Akker 2006
- Violan 2013

# Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study





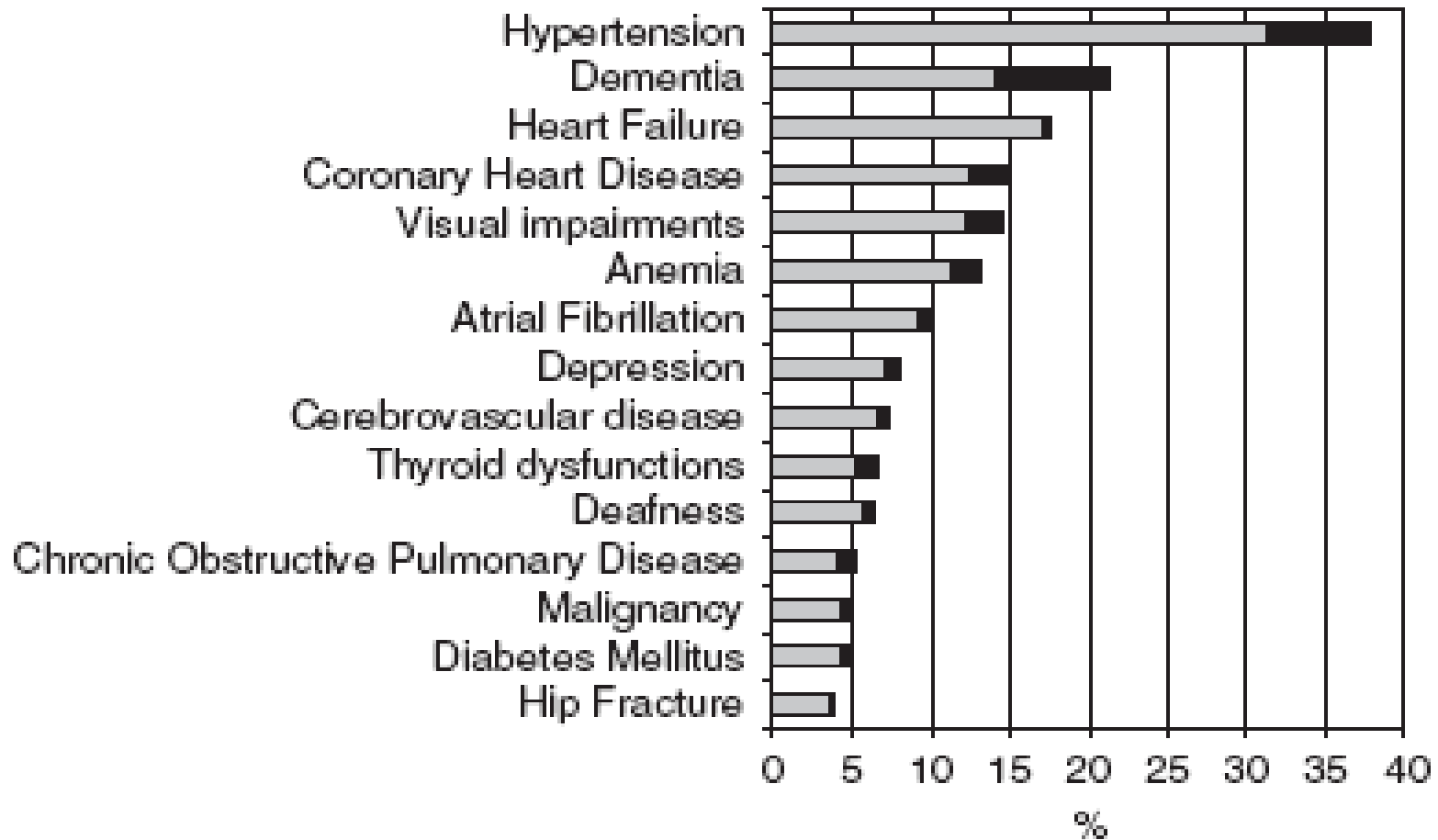
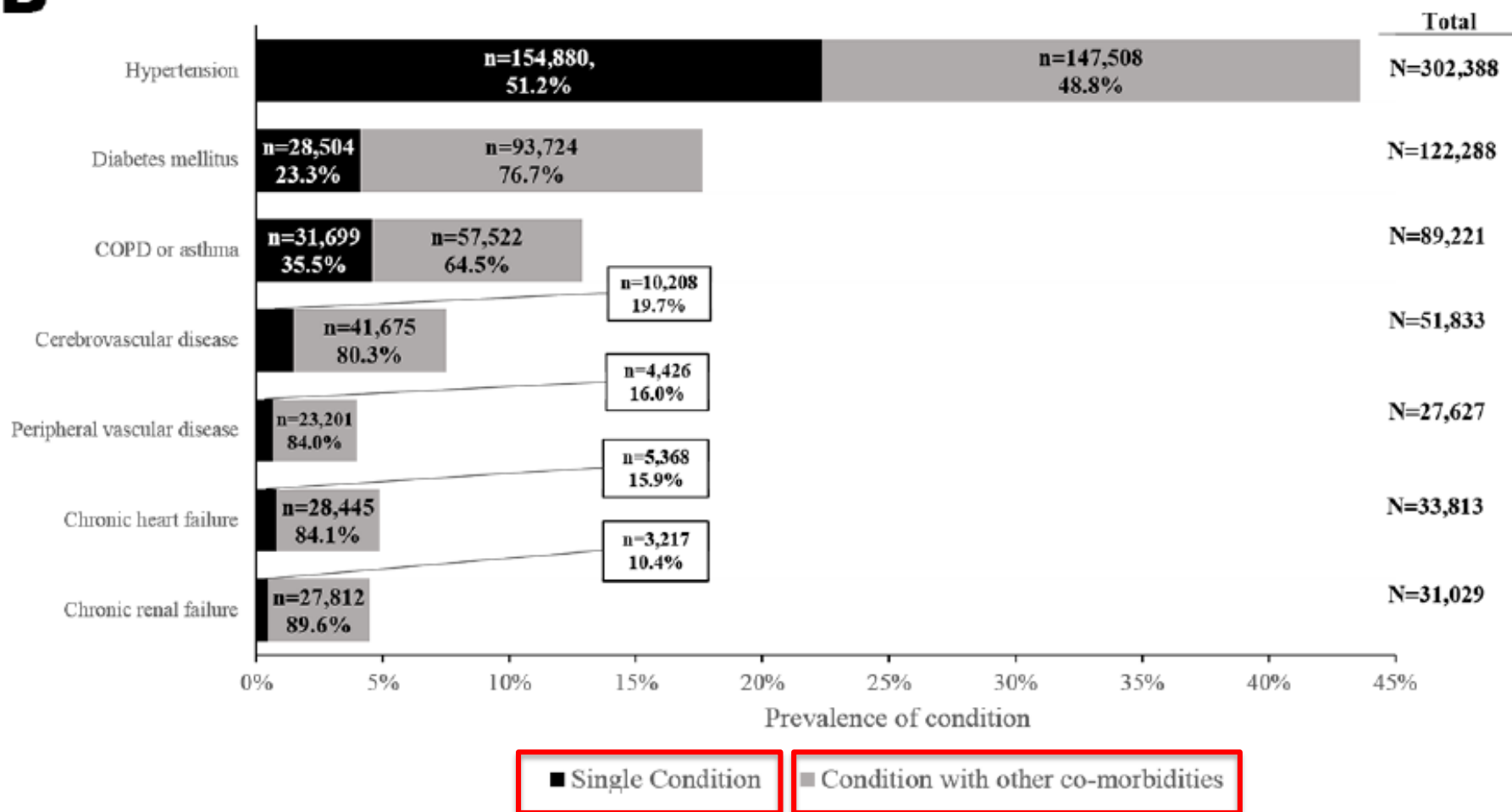


Figure 1. Prevalence per 100 of most frequent chronic diseases occurring independently of comorbidity (gray + black) or without any comorbidity (black).

# Multimorbidity and survival for patients with acute myocardial infarction in England and Wales: Latent class analysis of a nationwide population-based cohort

**B**

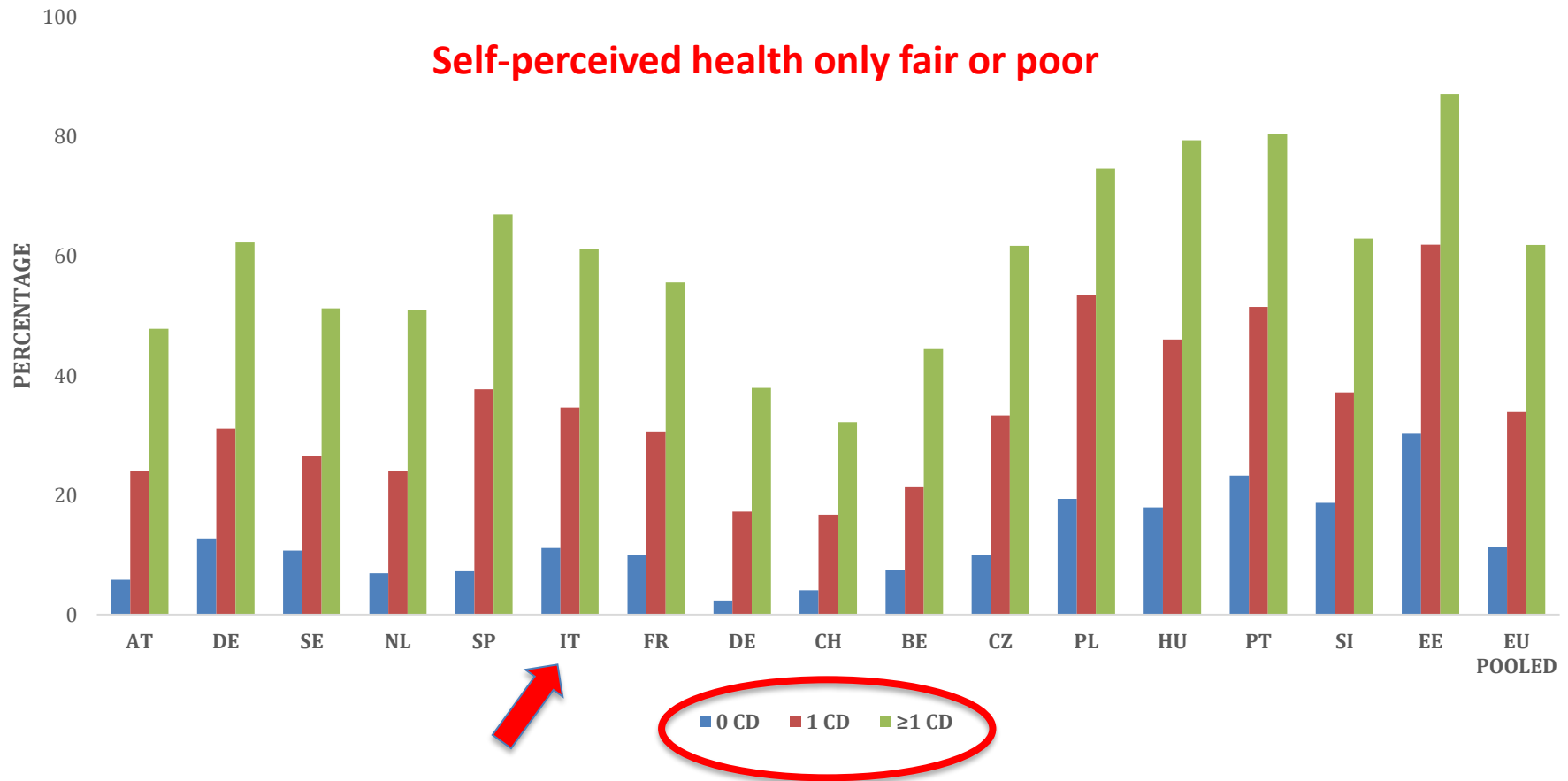


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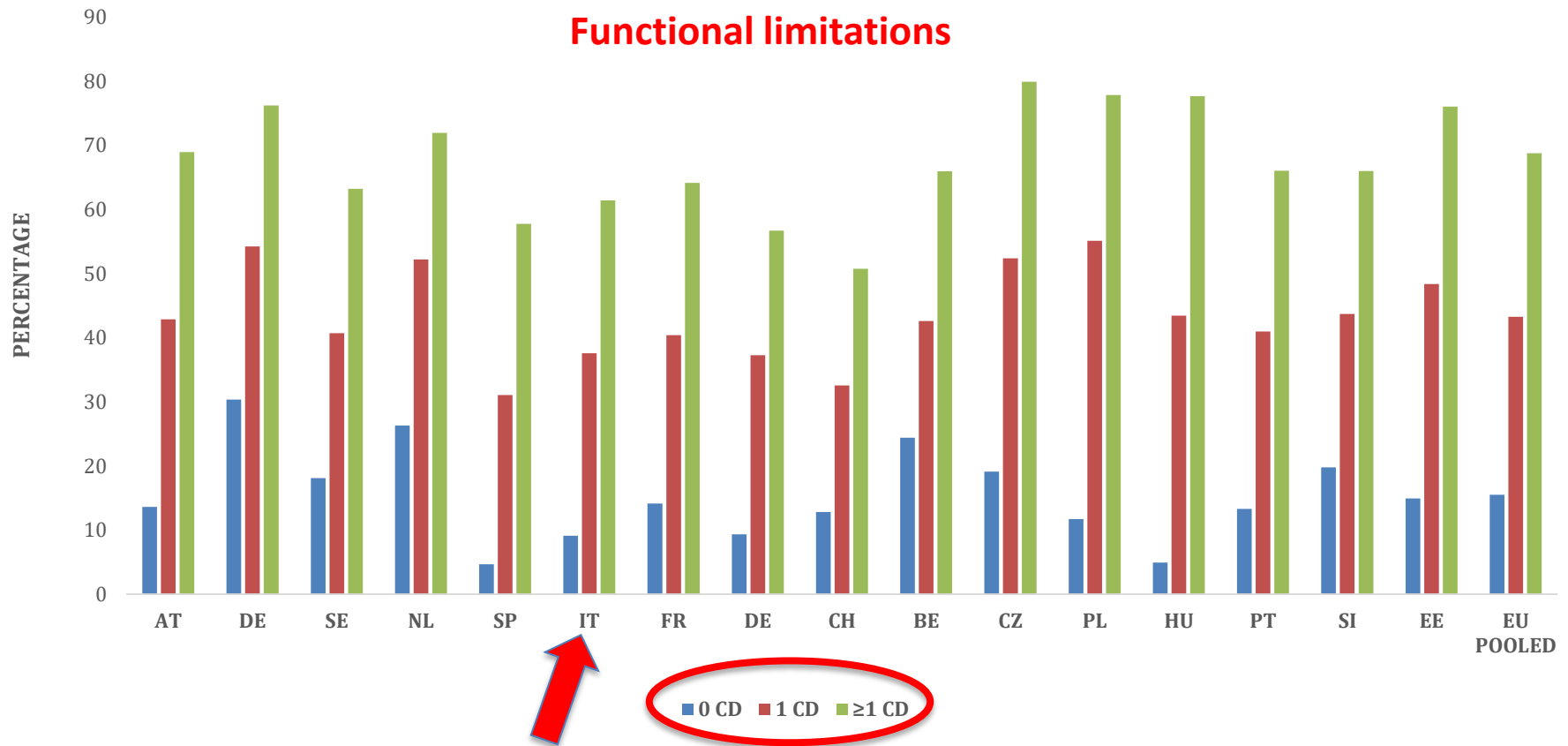
# Associations between multimorbidity, healthcare utilisation and health status: evidence from 16 European countries

*Age and Ageing* 2016; **45**: 431–435

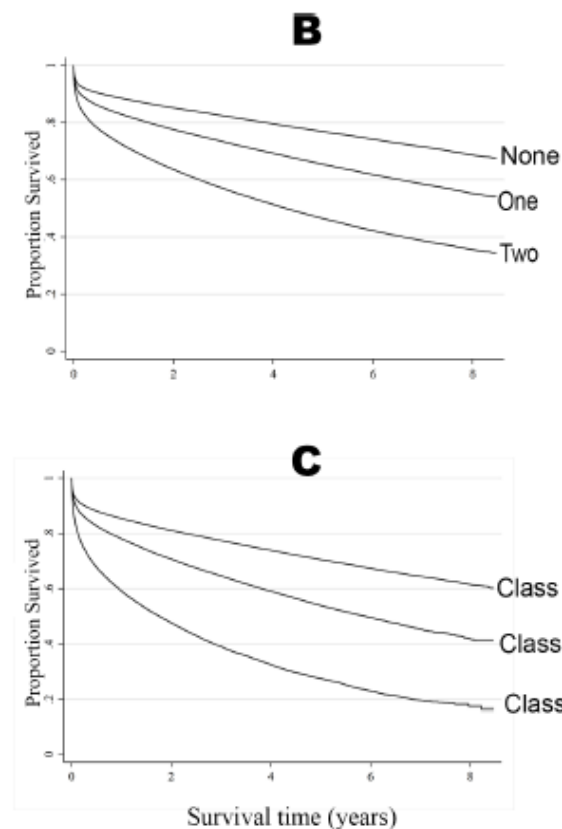
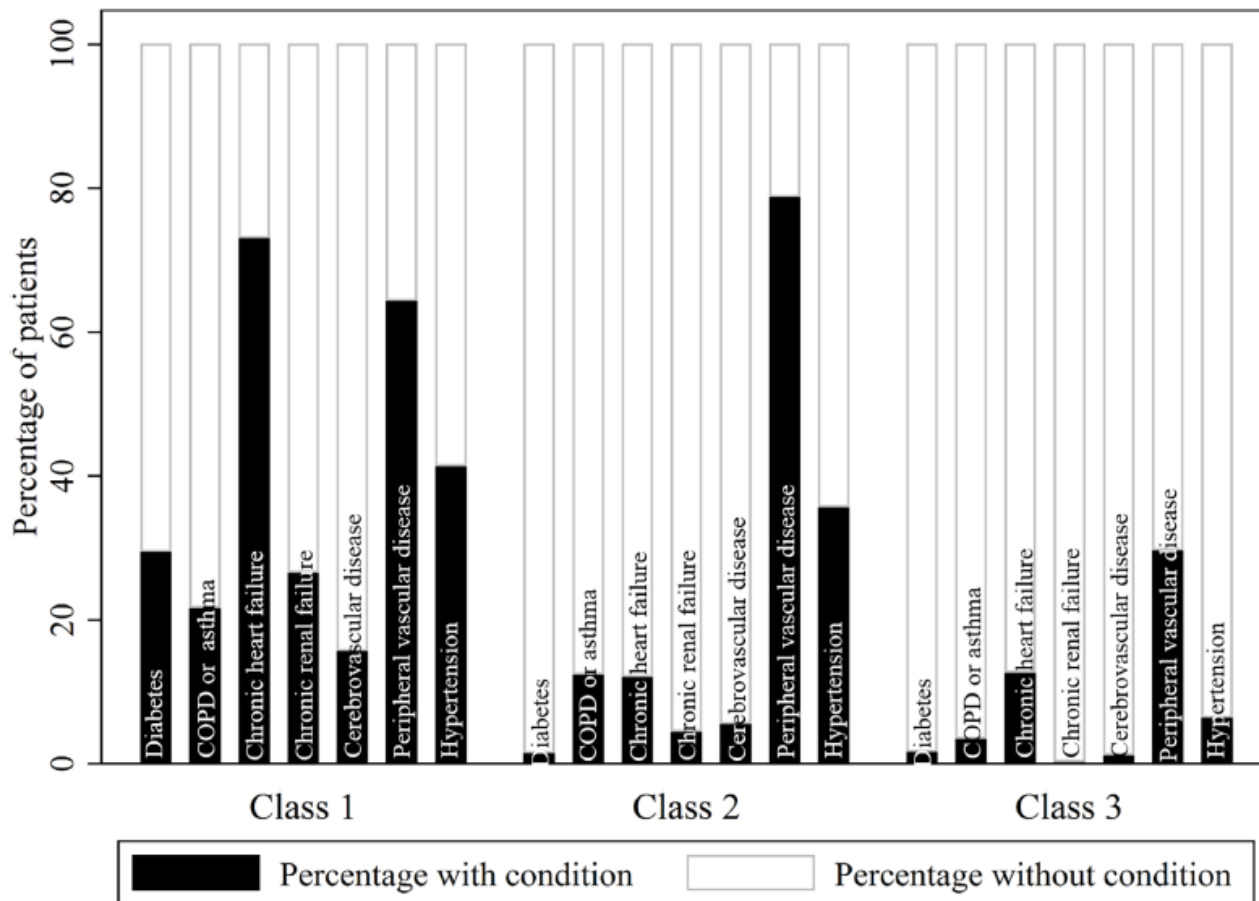


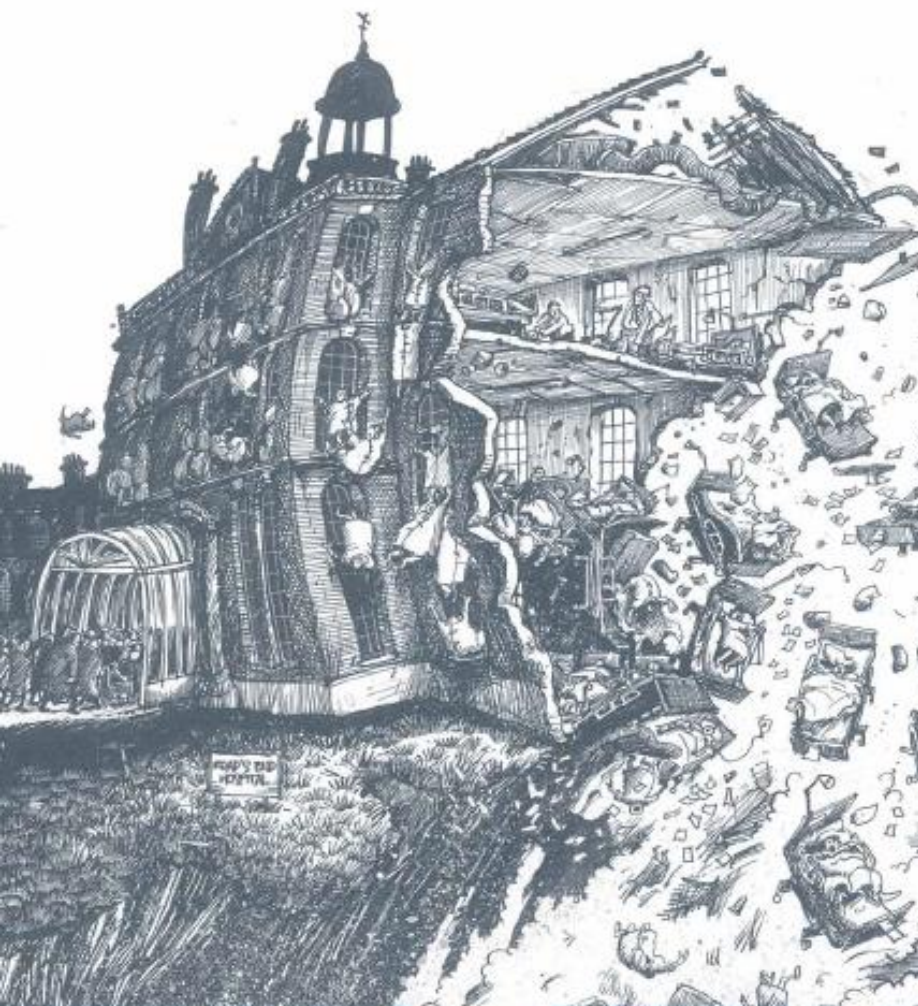
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# Multimorbidity and survival for patients with acute myocardial infarction in England and Wales: Latent class analysis of a nationwide population-based cohort





Unsurprisingly, the demographic of hospital inpatients has also changed substantially in the 64 years since the NHS was created. An increasing number of patients are older and frail, and around 25% of inpatients have a diagnosis of dementia. The reality of care in our hospitals has changed considerably. Nearly two thirds (65%) of people admitted to hospital are over 65 years old. People over 65 occupy more than 51,000 acute care beds at any one time, accounting for 70% of bed days.<sup>5,3</sup> Hospital Episode Statistics (HES) show a 65% increase in secondary care episodes for those over 75 during the past 10 years, compared with 31% for those aged 15–59.<sup>4</sup>

People over 85 years old account for 25% of bed days – increased from 22% over the past 10 years. This equates to more than five bed days per annum, compared to only one fifth of a bed day each year for those under 65.<sup>5</sup> People over 85 tend to spend around eight days longer in hospital than those under 65 – 11 days compared to three.<sup>3</sup>

Despite patients over 65 making up the larger share of the hospital population, the system continues to treat older patients as a surprise, at best, or unwelcome, at worst. Much more

Hospitals on the edge?  
The time for action



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# The End of the Disease Era

Mary E. Tinetti, MD, Terri Fried, MD

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## Disease-Oriented Model

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Clinical decision making is focused primarily on the diagnosis, prevention, and treatment of individual diseases. Discrete pathology is believed to cause disease; psychological, social, cultural, environmental and other factors are secondary factors, not primary determinants of disease. Treatment is targeted at the pathophysiologic mechanisms thought to cause the disease(s). Symptoms and impairments are best addressed by diagnosing and treating “causative” disease(s). Relevant clinical outcomes are determined by the disease(s). Survival is the usual primary focus of disease prevention and treatment.

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## Integrated, Individually Tailored Model

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Clinical decision making is focused primarily on the priorities and preferences of individual patients. Health conditions are believed to result from the complex interplay of genetic, environmental, psychological, social, and other factors. Treatment is targeted at the modifiable factors contributing to the health conditions impeding the patient’s health goals. Symptoms and impairments are the primary foci of treatment even if they cannot be ascribed to a discrete disease. Relevant clinical outcomes are determined by individual patient preference. Survival is one of several competing goals.

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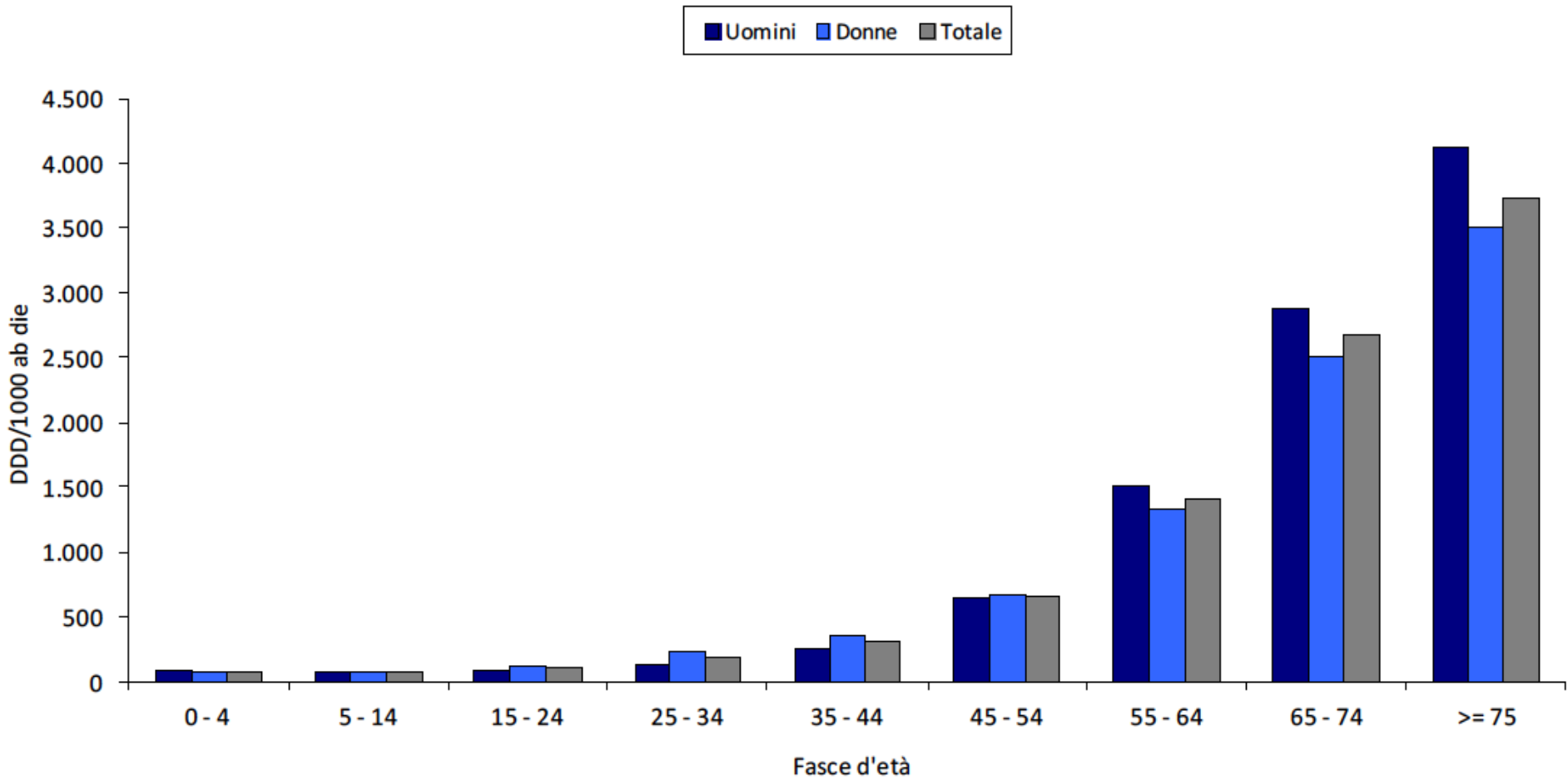


## Multiple health problems in elderly people

The problem is that in health care the specialist medical view predominates. And, as a direct result, multiple diagnoses lead almost inevitably to polypharmacy as each condition is treated in perverse isolation from the others.

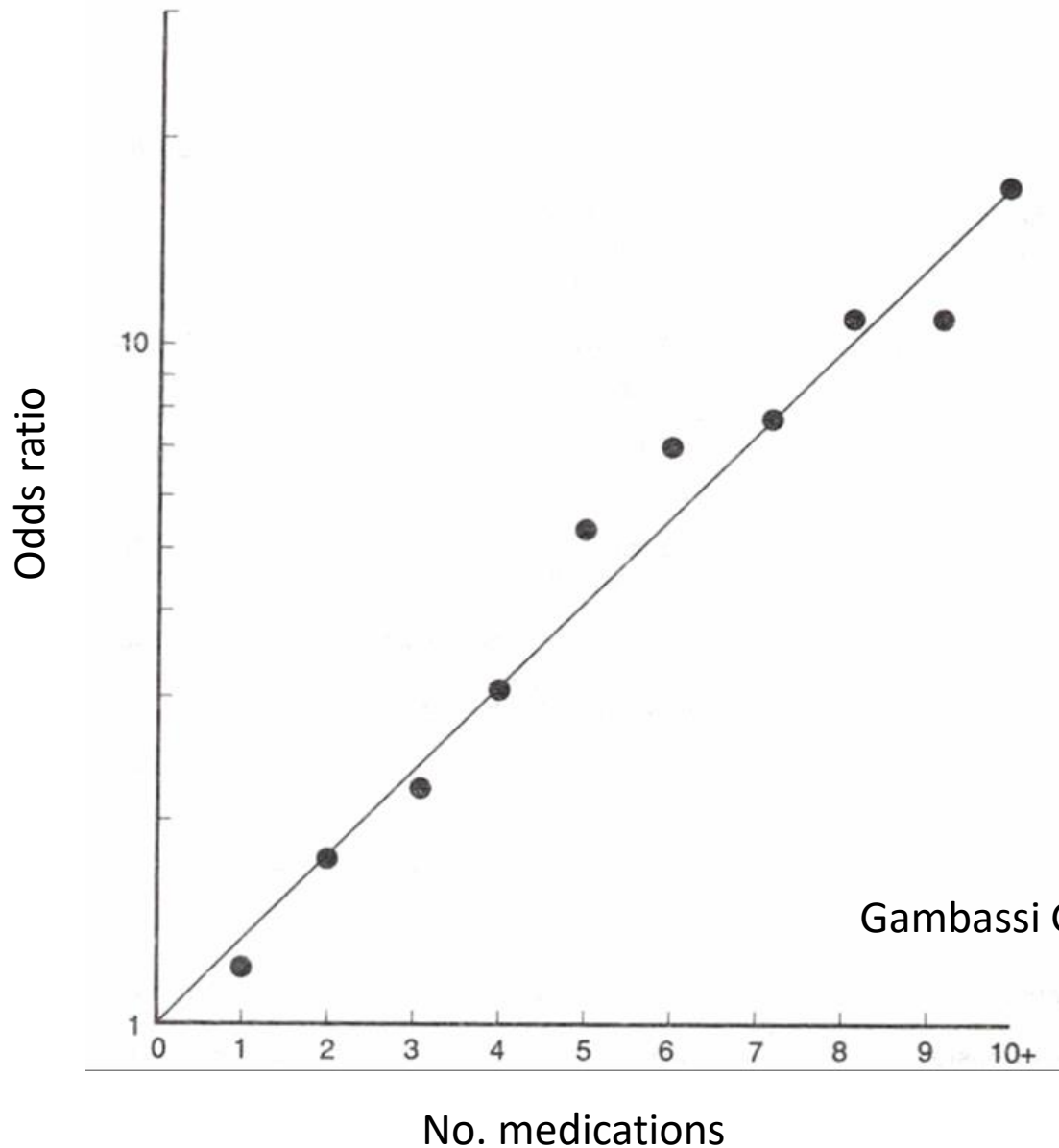
Research findings are extrapolated from younger age groups and interpreted overoptimistically in the context of what inevitably are limited life expectancies. As a direct result, older people are taking an ever increasing number of prescribed drugs, but because of diminished physiological reserve they are also more susceptible to adverse drug reactions and interactions. Nevertheless, the all too easy accusation of age discrimination means that the limited time available for older people to derive clinical benefit is not seen as a legitimate reason for “underprescribing.”

# Farmacoterapia





# Adverse drug reactions



# Eligibility Criteria of Randomized Controlled Trials Published in High-Impact General Medical Journals

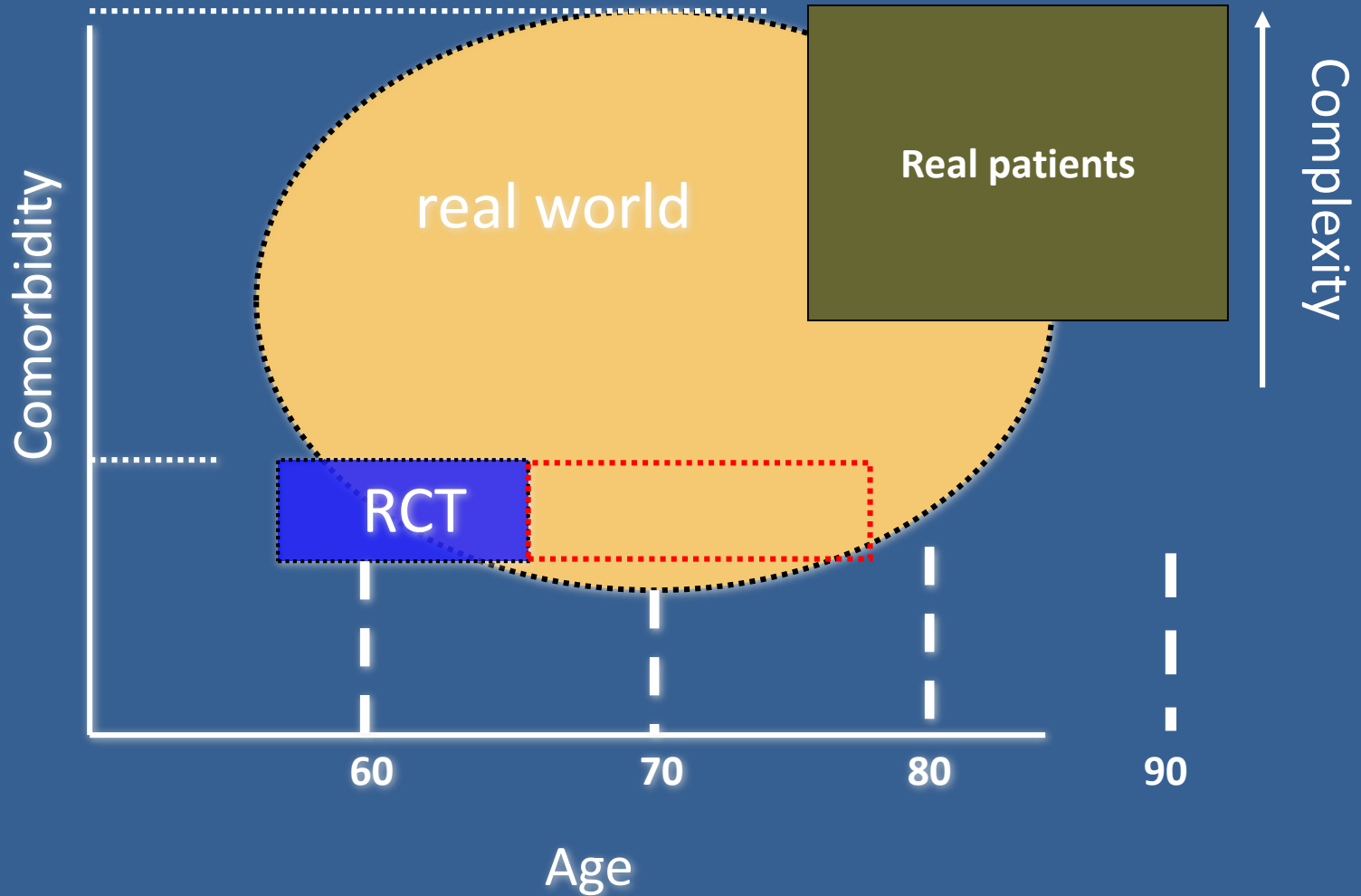
*JAMA. 2007;297:1233-1240*

- I pazienti risultavano esclusi in base a:

età	72.1% dei trial
sesto femminile	47.0% dei trial
<input type="text"/> <b>multimorbilità</b>	81.3% of trials
polifarmacoterapia	54.1% of trials

- I trials sui farmaci tendono ad escludere più facilmente, così come quelli sponsorizzati dall'industria farmaceutica.

# Evidence-B(i)ased Medicine



**SOUNDING BOARD**

**Potential Pitfalls of Disease-Specific Guidelines  
for Patients with Multiple Conditions**

Mary E. Tinetti, M.D., Sidney T. Bogardus, Jr., M.D., and Joseph V. Agostini, M.D.



Comment

[www.thelancet.com](http://www.thelancet.com) Vol 367 February 18, 2006

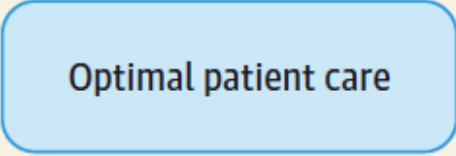
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Comorbidity and guidelines: conflicting interests



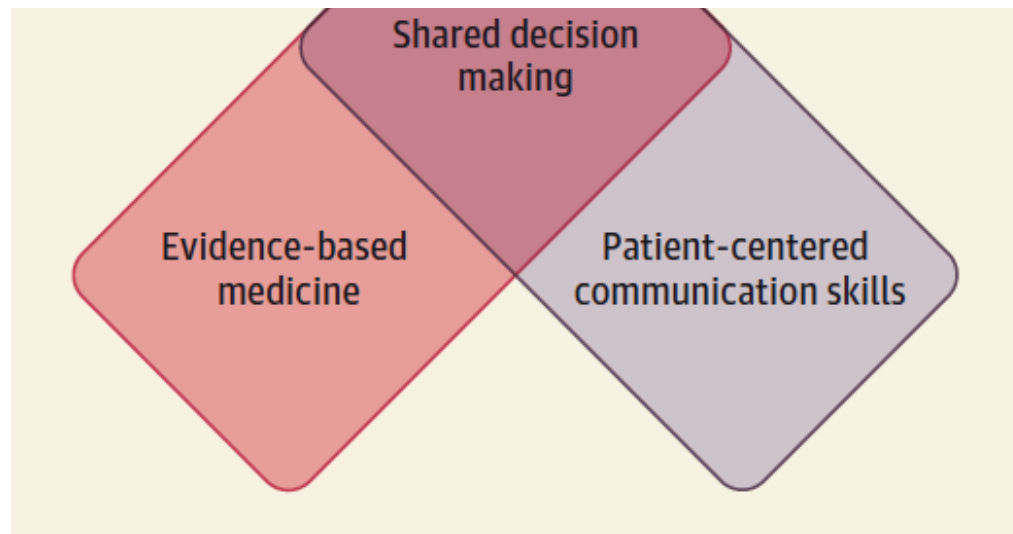
# The Connection Between Evidence-Based Medicine and Shared Decision Making

JAMA October 1, 2014 Volume 312, Number 13



Optimal patient care

Without shared decision making, EBM can turn into evidence tyranny.

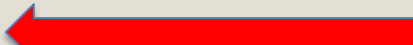


# Evidence based medicine: a movement in crisis?

*BMJ* 2014;348:g3725 doi: 10.1136/bmj.g3725 (Published 13 June 2014)

Despite these and many other successes, wide variation in implementing evidence based practice remains a problem. For example, the incidence of arthroscopic washout of the knee joint, whose benefits are unproved except when there is a known loose body, varies from 3 to 48 per 100 000 in England.<sup>13</sup> More fundamentally, many who support evidence based medicine in principle have argued that the movement is now facing a serious crisis (box 1).<sup>14 15</sup> Below we set out the problems and suggest some solutions.

## Box 1: Crisis in evidence based medicine?

- The evidence based “quality mark” has been misappropriated by vested interests
  - The volume of evidence, especially clinical guidelines, has become unmanageable
  - Statistically significant benefits may be marginal in clinical practice
  - Inflexible rules and technology driven prompts may produce care that is management driven rather than patient centred
  - Evidence based guidelines often map poorly to complex multimorbidity
- 

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# Management Reasoning Beyond the Diagnosis

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By contrast, management reasoning is primarily a task of prioritization, shared decision making, and monitoring, and is typically more complex.

**Author:** David A. Cook,  
MD, MHPE, Division of  
General Internal  
Medicine, Mayo Clinic  
College of Medicine,

**JAMA** Published online May 10, 2018

# Better management of patients with multimorbidity

We have argued that multimorbidity introduces clinical uncertainty in a way that is unlikely to be resolved by ever more sophisticated guidelines. Doctors must therefore embrace clinical judgment based on their assessment of a patient's needs. This requires time to deal with more than one problem at a time and coordination of care in ways that promote long term or at least medium term relationships between doctors and patients. This approach will inevitably emphasise the importance of generalist skills, whether among primary care doctors or those who specialise in the care of older people.

## Key messages

Clinicians need to be free to exercise professional judgment in their management of patients with multimorbidity

Patients need to determine treatment priorities and the goals of medical care

Clinicians should provide continuity of care for people with complex long term problems

# A Physician = Emotion + Passion + Science

Robert H. Brook, MD, ScD

JAMA, December 8, 2010<sup>hood that the  
tually be read,</sup>

## The art of medicine

### Narrative evidence based medicine

We are coming to see that the three fundamental tensions upon which medicine finds itself—known/unknown, universal/particular, body/self—are reflected in the three circles of EBM. Clinical evidence examines the known and unknown. Clinical circumstances integrate the universal and particular. Patients' values speak to both body and self. By virtue of its capacity to recognise the tensions fully, narrative medicine can lend to evidence-based medicine the *methods* of respecting its three circles of attention. It is not through dearth of desire but dearth of methods that EBM has yet to achieve attention to all three circles. With narrative medicine's methods, EBM can indeed be true to all its promises.

## Multimorbidity: clinical assessment and management

Multimorbidity: assessment, prioritisation and management of care for people with commonly occurring multimorbidity

NICE guideline NG56

Methods, evidence and recommendations

September 2016

Final.

Commissioned by the National Institute for Health and Care Excellence

### General principles

1. Be aware that multimorbidity refers to the presence of 2 or more long-term health conditions, which can include:
  - defined physical and mental health conditions such as diabetes or schizophrenia
  - ongoing conditions such as learning disability
  - symptom complexes such as frailty or chronic pain
  - sensory impairment such as sight or hearing loss
  - alcohol and substance misuse.
2. Be aware that the management of risk factors for future disease can be a major treatment burden for people with multimorbidity and should be carefully considered when optimising care.
3. Be aware that the evidence for recommendations in NICE guidance on single health conditions is regularly drawn from people without multimorbidity and taking fewer prescribed regular medicines.
4. Think carefully about the risks and benefits, for people with multimorbidity, of individual treatments recommended in guidance for single health conditions. Discuss this with the patient alongside their preferences for care and treatment.

# Interventions for improving outcomes in patients with multimorbidity in primary care and community settings


We identified 18 RCTs examining a range of complex interventions for people with multimorbidity. Nine studies focused on defined comorbid conditions with an emphasis on depression, diabetes and cardiovascular disease. The remaining studies focused on multimorbidity, generally in older people. In 12 studies, the predominant intervention element was a change to the organisation of care delivery, usually through case management or enhanced multidisciplinary team work. In six studies, the interventions were predominantly patient-oriented, for example, educational or self-management support-type interventions delivered directly to participants. Overall

## Authors' conclusions

This review identifies the emerging evidence to support policy for the management of people with multimorbidity and common comorbidities in primary care and community settings. There are remaining uncertainties about the effectiveness of interventions for people with multimorbidity in general due to the relatively small number of RCTs conducted in this area to date, with mixed findings overall. It is possible that the findings may change with the inclusion of large ongoing well-organised trials in future updates. The results suggest an improvement in health outcomes if interventions can be targeted at risk factors such as depression, or specific functional difficulties in people with multimorbidity.



# Approach for Achieving Effective Care for High-Need Patients

Patient Subpopulation	Drivers of Costs
Children with complex needs: severe impairment in at least 4 categories (including learning and mental functions, communication, motor skills, self-care, hearing, or vision) or at least 2 categories in addition for need of enteral or parental feeding or ventilatory support	Substantial spending in acute care settings with long-term hospital stays, often driven by lack of appropriate resources in the community coupled with inability of families to manage their care and supervision without intensive support
Nonelderly disabled adults: adults <65 y old with physical or cognitive disability	High levels of spending on drugs, long-term care support, and services and high burden of mental health disease and substance abuse
 Frail elderly individuals: adults ≥65 y of age with ≥2 frailty markers (eg, gait abnormality, malnutrition, failure to thrive, cachexia, debility, difficulty walking, or history of falls)	Most spending is related to hospitalizations, including preventable hospitalizations, and subsequent post-acute care use, including short-term rehabilitation centers, skilled nursing facilities, and home health services
 Patients with major complex chronic conditions: patients with ≥2 complex chronic conditions (eg, congestive heart failure, chronic kidney disease, or chronic obstructive pulmonary disease).	Most spending was related to the use of outpatient services across multiple specialty services followed by spending related to hospitalizations
 Patients with less severe but multiple chronic conditions: patients with <6 chronic conditions (and ≤2 major complex chronic conditions)	High levels of spending in the outpatient setting with relatively low levels of spending in the acute care setting with patients at increased risk for developing major chronic conditions in future with subsequent increased risk of spending
Patients with advancing illness: patients with terminal illness (eg, advanced cancer) or near end of life	Substantial variation in spending depending on underlying illness, including specialized treatment for cancer or intensive hospital-level care for patients with an end-stage organ disease process

# Precision medicine to precision care: managing multimorbidity

The gap between traditional disease-focused medicine and patients' needs is growing as the burden of multimorbidity increases.<sup>1</sup> This mismatch, which stems from both successes (eg, increasing life expectancy and advances in biomedicine) and failures (eg, underinvestment in prevention and focus on managing discrete disease rather than what matters to each patient), results in fragmented care, suboptimal health outcomes, and avoidable harms for patients with multiple chronic conditions. Although multimorbidity is common among older adults (aged  $\geq 65$  years), it is also common in younger populations.

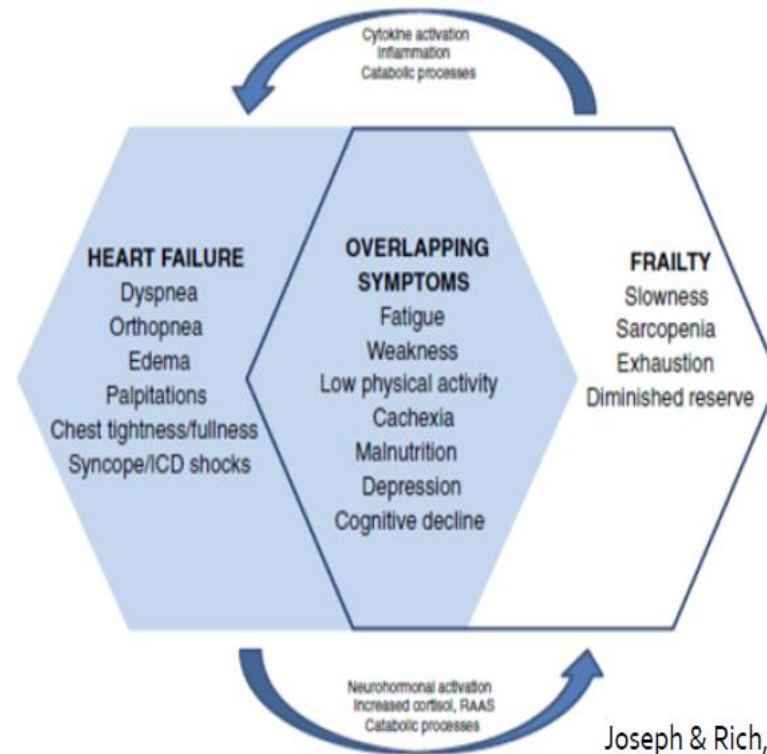
In the USA in 2010, over 60% of adults aged 65 years or more had two or more chronic conditions as did a third of adults aged 45–64 years.<sup>2</sup> Socioeconomically disadvantaged individuals have a higher burden of multimorbidity, and they develop multiple chronic conditions 10–15 years earlier than do those who are more socioeconomically advantaged.<sup>3</sup> People with multimorbidity are common users of health care, generate high costs, and are at increased risk for adverse events. Most of these individuals are cared for by practitioners with inadequate expertise in geriatrics or multimorbidity.

Multimorbidity is the most common condition managed in practice. Health-care delivery must be transformed to provide precision care to people with multimorbidity. Accomplishing this transition will require a change in practice, research, and policy from disease-specific to patient-centred models of care delivery.

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# Overlapping Symptoms of HF and Frailty



Joseph & Rich, 2017

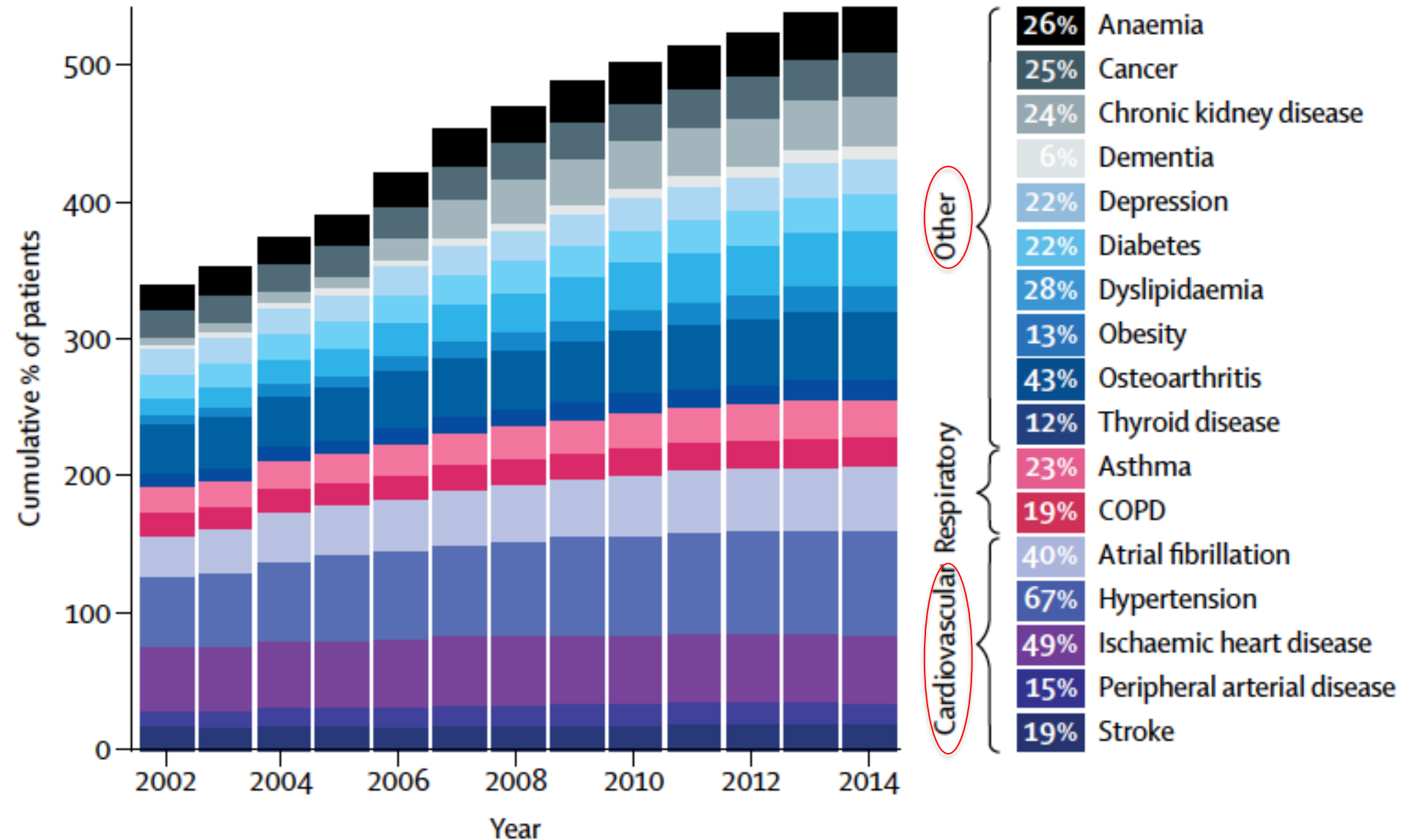
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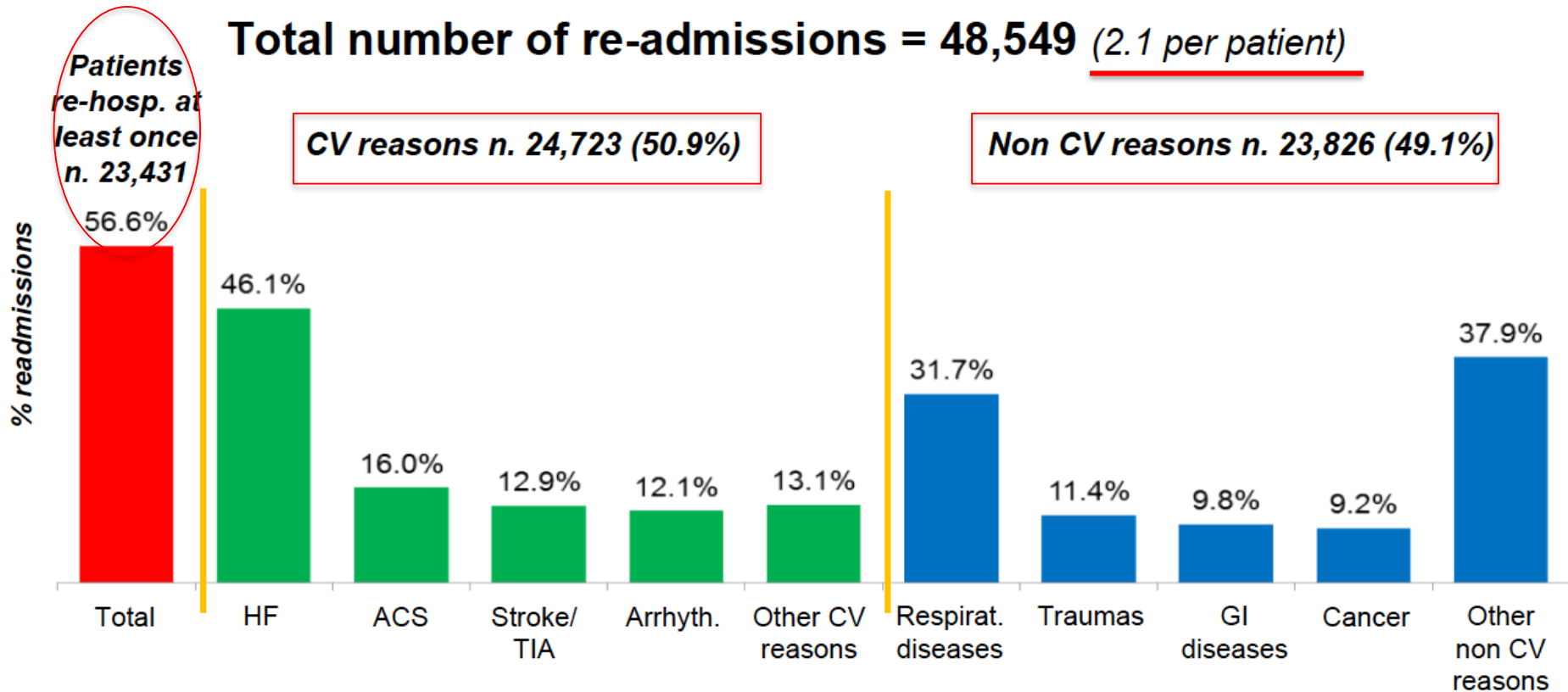
# Temporal trends and patterns in heart failure incidence: a population-based study of 4 million individuals

## B Individual comorbidities

*Lancet 2018; 391: 572-80*



**Total number of re-admissions = 48,549 (2.1 per patient)**



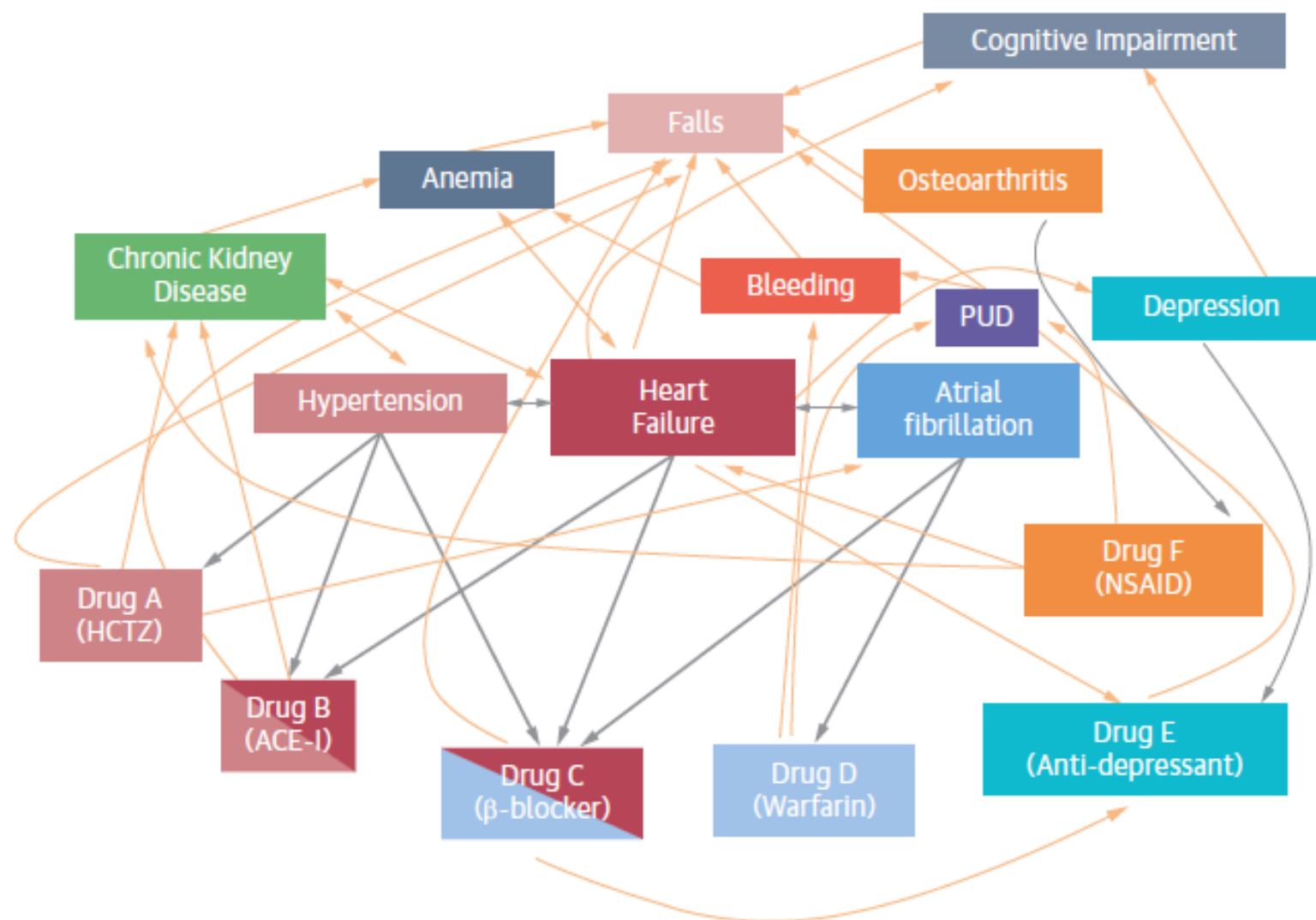
HF=Heart failure; ACS=Acute coronary syndrome; TIA=Transient ischemic attack; CV=Cardiovascular; GI=Gastrointestinal

# Multimorbidity in Older Adults With Cardiovascular Disease

JACC VOL. 71, NO. 19, 2018

MAY 15, 2018:2149-61

## Diseases and Medications Impacting One Another in Multimorbidity





# Multimorbidity in Older Adults With Cardiovascular Disease

JACC VOL. 71, NO. 19, 2018

MAY 15, 2018:2149-61

## Treating Multimorbidity in Older Adults with Cardiovascular Disease (CVD)



CVD



Comorbid diseases

### Current separate disciplinary approach:

- Focus on dominant cardiac issue; non-cardiac comorbid diseases are separate and secondary
- Limited integration across or between conditions
- Lack of standardized approach
- Treatment provided by separate specialists, primary care physician, and care extenders



### Recommended multidisciplinary approach:

- Focus on identifying preferences and goals and providing preference-sensitive options
- Integration between conditions and specialties
- Overall integrated care plan
- Treatment provided by multidisciplinary team; linked electronic health records

Differences between current disease-specific paradigm and the emerging patient-specified goal directed care approach: the latter seeks to address issues emanating from cardiovascular disease in a context of multimorbidity.

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- Tsunami epidemiologico
- Inflamm-aging e malattie età-associate
- Epidemiologia della multimorbilità
- Impatto della multimorbilità
- End of disease era e EBM
- Da precision medicine a precision care
- Multimorbilità e frailty
- Il caso scompenso cardiaco
- **Verso una nuova forma di assistenza**

# Making more of multimorbidity: an emerging priority



Multimorbidity would seem a relatively straightforward term, denoting multiple medical conditions within a single patient. Yet an Academy of Medical Sciences report, *Multimorbidity: a priority for global health research*, published in April, 2018, suggests that competing definitions in the medical literature have impeded research and improvements in patient care. The report recommends that a path forward must include a standardised definition that can be incorporated into research agendas to identify the evidence gaps and to inform the organisation of health-care systems globally.

Multimorbidity, as emphasised by the authors, is distinct from comorbidity because there is no primary or index condition. Frailty is a related construct in ageing populations, but is different since patients with multimorbidity might not necessarily be frail. Researchers

Most of the evidence on multimorbidity has come from cross-sectional studies sampling specific populations in various settings. The report largely focuses on where the research agenda must be extended, including refining descriptive epidemiology, especially for LMICs and younger patients, and underscoring the need for longitudinal cohort data to understand clustering of conditions across the lifespan. But it also highlights the challenges for patients and clinicians. The majority of health-care systems are organised to treat single conditions. For patients with multimorbidity, that can mean interfacing with multiple health-care providers, increased risk of inappropriate polypharmacy from lack of provider communication, and potentially suboptimal care.

To update health-care systems in the face of the increasing burden of multimorbidity will require a shift for



Jenkinson/Getty Images

## To update health-care systems in the face of the increasing burden of multimorbidity will require a shift for physicians from specialists to generalists, likely through

and is the norm in this age group in high-income countries. It is also more prevalent in women, possibly because of greater exposure to the adverse effects of poverty. Multimorbidity is increasing globally, likely driven by the ageing population but also by factors such as high body-mass index, urbanisation, and the growing burden of NCDs (such as type 2 diabetes) and tuberculosis in low- and middle-income countries (LMICs). Predictably, certain morbidities cluster together, such as coronary heart disease and cerebrovascular disease. These conditions are called concordant multimorbidities since they can share a common aetiology. Depression, cardiometabolic disorders, and musculoskeletal disorders are most commonly present within multimorbidity clusters. Notably, multimorbidity clusters comprising concurrent physical and mental

Although not yet well characterised, multimorbidity is extremely costly to individuals and health-care systems. While actively engaging in efforts to adapt to increasing demand, identifying the determinants of the acceleration of multimorbidity is crucial. Appreciating that multimorbidity clusters are linked with the increase in NCDs is essential as well. The report backs up the findings and recommendations in *The Lancet's* Taskforce on NCDs and Economics, also published this month, highlighting greater investment in prevention and control of NCDs to disrupt the cycle of chronic illness and economic impoverishment.

The multimorbidity perspective adds a timely dimension, suggesting an important window of opportunity to curtail this complex and expanding challenge. Aggressively targeting NCDs as preventable and with identifiable (and

For *Multimorbidity: a priority for global health research* see <https://acmedsci.ac.uk/policy/policy-projects/multimorbidity>

The *Lancet's* Taskforce on NCDs and Economics see <http://www.thelancet.com/series/taskforce-ncds-and-economics>



Future  
hospital:  
Caring for  
medical  
patients



Setting higher standards

# Putting patients first: realising Francis' vision

Royal College of Physicians' response  
to the final report of the Mid Staffordshire  
NHS Foundation Trust Public Inquiry

# Choosing Wisely<sup>®</sup>

*An initiative of the ABIM Foundation*



PREVENTING  
OVERDIAGNOSIS  
Winding back the harms of too much medicine



LESS  
IS MORE  
- = +  
MEDICINE

 The **JAMA** Network



# Family Medicine Forum (FMF), 2016, Vancouver

LESS  
IS MORE  
- = +  
MEDICINE

- misuse of evidence 
- imbalance of power 
- entitlement & patient satisfaction 
- medicalization 
- fear of uncertainty 
- fear of death and illness 
- fear of litigation 
- perverse incentives 
- industry pressure, corruption 
- new technology 
- magical thinking 
- herd mentality 

## Factors in Health Care

- EBM evidence-based medicine 
- patient-centred care 
- fully-informed consent 
- population health 
- comfort with uncertainty 
- strong relationships 
- taking time 
- cost awareness 
- professionalism & accountability 
- measuring quality 
- efficiency 
- safety & common sense

### INAPPROPRIATENESS

*choosing unwisely, overdiagnosis,  
wrong care, overtreatment,  
undertreatment, too much medicine*

### APPROPRIATENESS

*Less is More, 'Goldilocks' healthcare,  
choosing wisely, high-value care,  
#rightcare, minimally-disruptive medicine*



The NEW ENGLAND  
JOURNAL of MEDICINE

“ We believe that a shift toward the acknowledgment and acceptance of uncertainty is essential — for us as physicians, for our patients, and for our health care system as a whole. Only if such a revolution occurs will we thrive in the coming medical era. ”

Arabella L. Simpkin, B.M., B.Ch., M.M.Sc, and Richard M. Schwartzstein, M.D.  
N Engl J Med 2016; 375:1713-1715 November 3, 2016 DOI: 10.1056/NEJMp1606402

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**THE GOOD PHYSICIAN  
TREATS THE DISEASE; THE  
GREAT PHYSICIAN TREATS  
THE PATIENT WHO HAS THE  
DISEASE**

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WILLIAM OSLER



# Summary

- Invecchiamento della popolazione associato ad aumentata prevalenza della multi-morbilità
- Impatto enorme della multi-morbilità sulla qualità della vita e sull'utilizzo di risorse
- Necessità di rivedere il modello di assistenza specializzato per patologie
- Uso ragionato delle evidenze scientifiche
- Centralità del paziente nelle scelte terapeutiche e nella definizione delle priorità di trattamento