

# The cluster medicine approach

(Evaluating the feasibility of RCTs in elderly with multimorbidity)

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# HISTORY OF GERIATRIC MEDICINE

1900

Signs  
symptoms

Acute diseases

Chronic diseases

2000 - on



THE REAL WORLD

FRIBIDITY

GENEIT

EXITY



**'Complex information can  
be best recognized as patterns'**

Vogt W and Nagel D, Clin Chem 1992

**<DATA REDUCTION>**  
(helpful despite a reduction  
also of information)

**PATTERNS OR CLUSTERS OF DISEASES:  
THE CO-OCCURRENCE OF 2 OR MORE SPECIFIC CHRONIC  
DISEASES**

**THE STUDY OF THE DISTRIBUTION OF CO-OCCURRING DISEASES  
IN THE POPULATION AND THE IDENTIFICATION AND**

# Statistical methods

**Proportion of pairs or triades of diseases:**

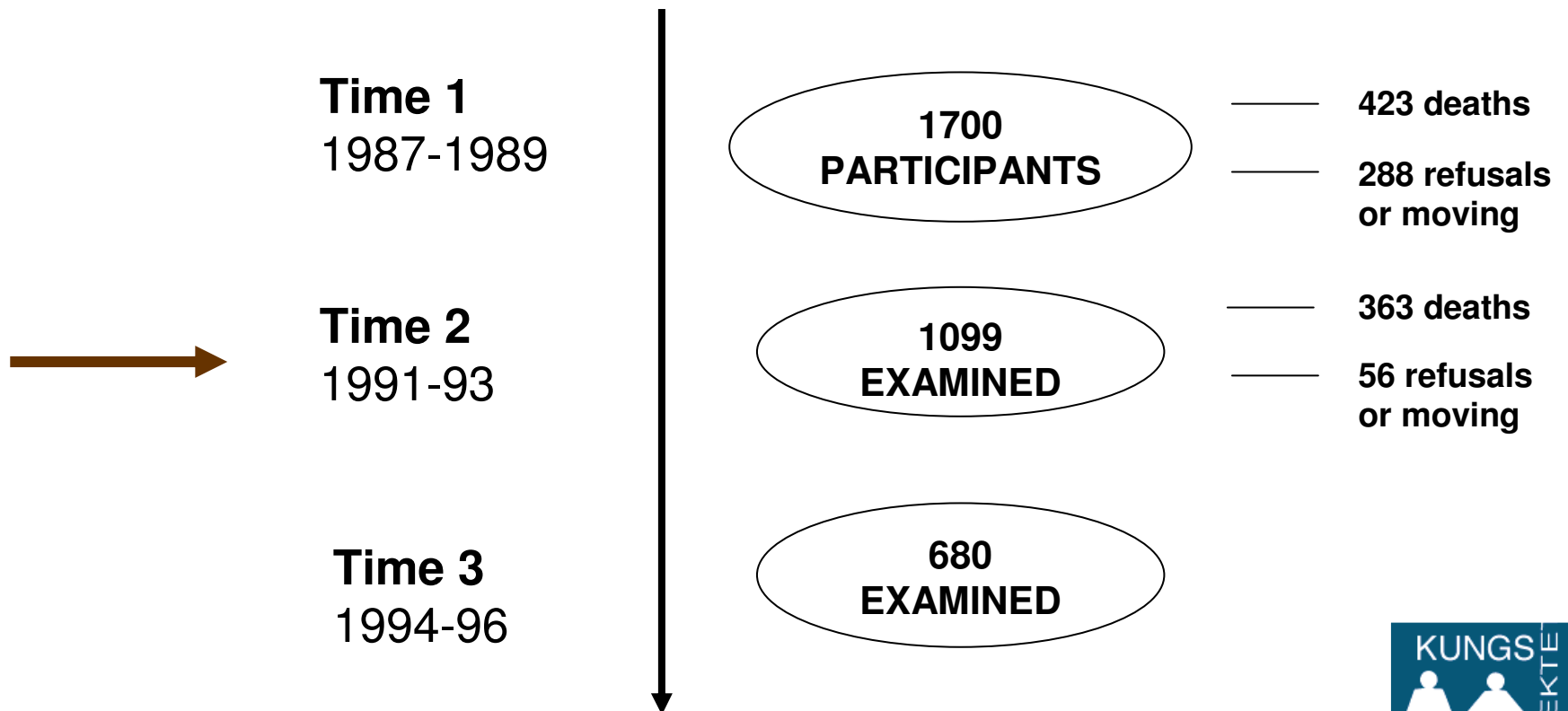
many calculations/large samples

**Ratio of Observed / Expected Prevalence (multimorbidity coefficient):**  
degree to which comorbid diseases exceed the chance level

**Odds Ratio, Risk Ratio:** statistical issues (i.e. multiple comparisons)  
overestimation of the effect size

# Study design of the Kungsholmen Project

2368  $\geq$  75 years  
Living in the KUNGSHOLMEN area (born  $\leq$  1912)

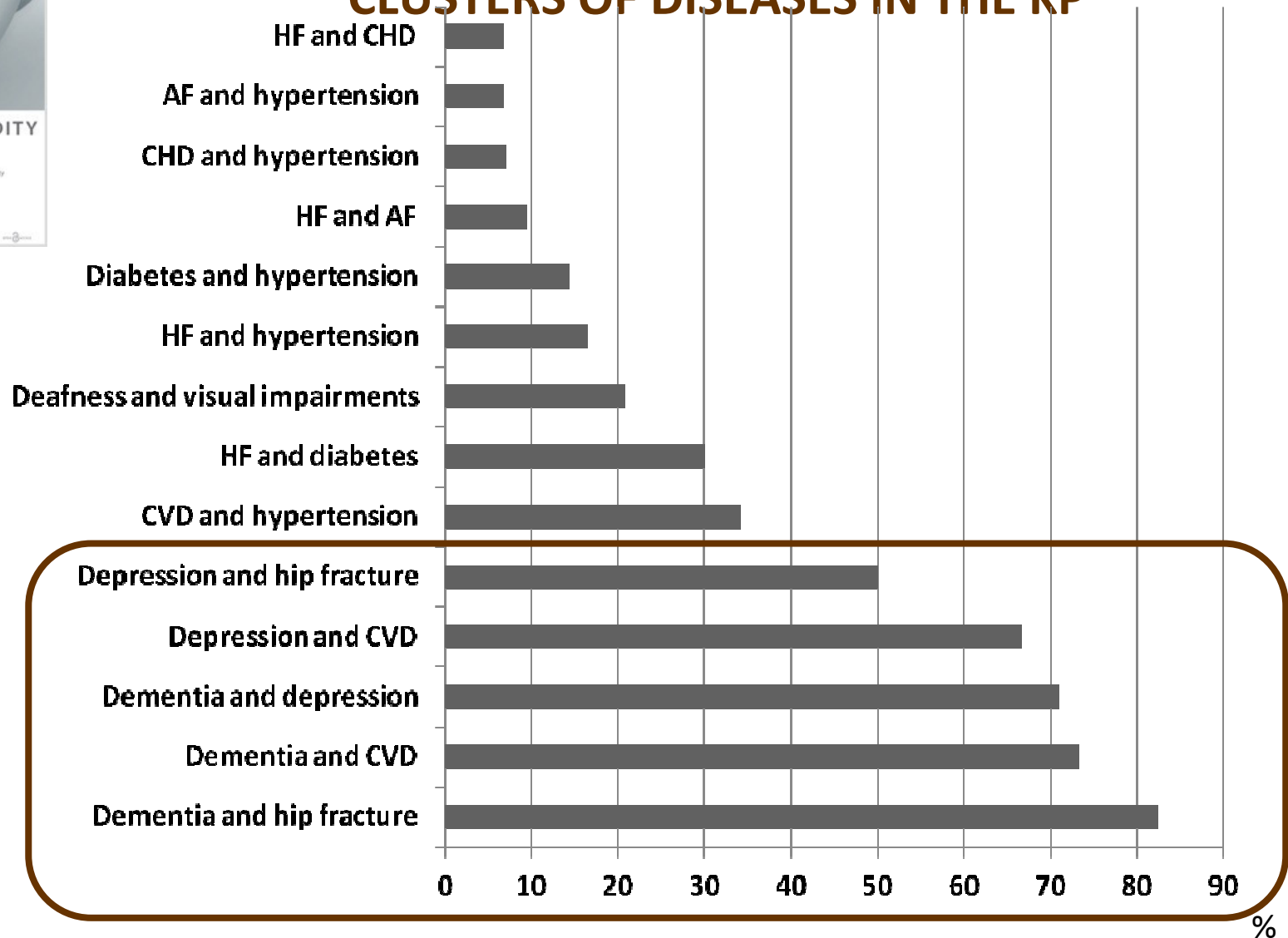


# RATIO OF OBSERVED/EXPECTED PREVALENCE OF PAIRS OF DISEASES

	Prevalence per 100		
	Observed	Expected	Ratio O/E
Heart failure & CHD	5.6	2.6	2.2
Heart failure & Atrial fibrillation	3.8	1.8	2.1
Heart failure & diabetes	1.8	0.9	2.0
Hypertension & Heart failure	15.1	6.7	2.3
Dementia & depression	3.0	1.7	1.8
Dementia & hip fracture	1.7	0.8	2.1
Dementia & CVD	2.7	1.6	1.7
Depression & CVD	1.1	0.6	1.8
Depression & hip fracture	0.6	0.3	2.0

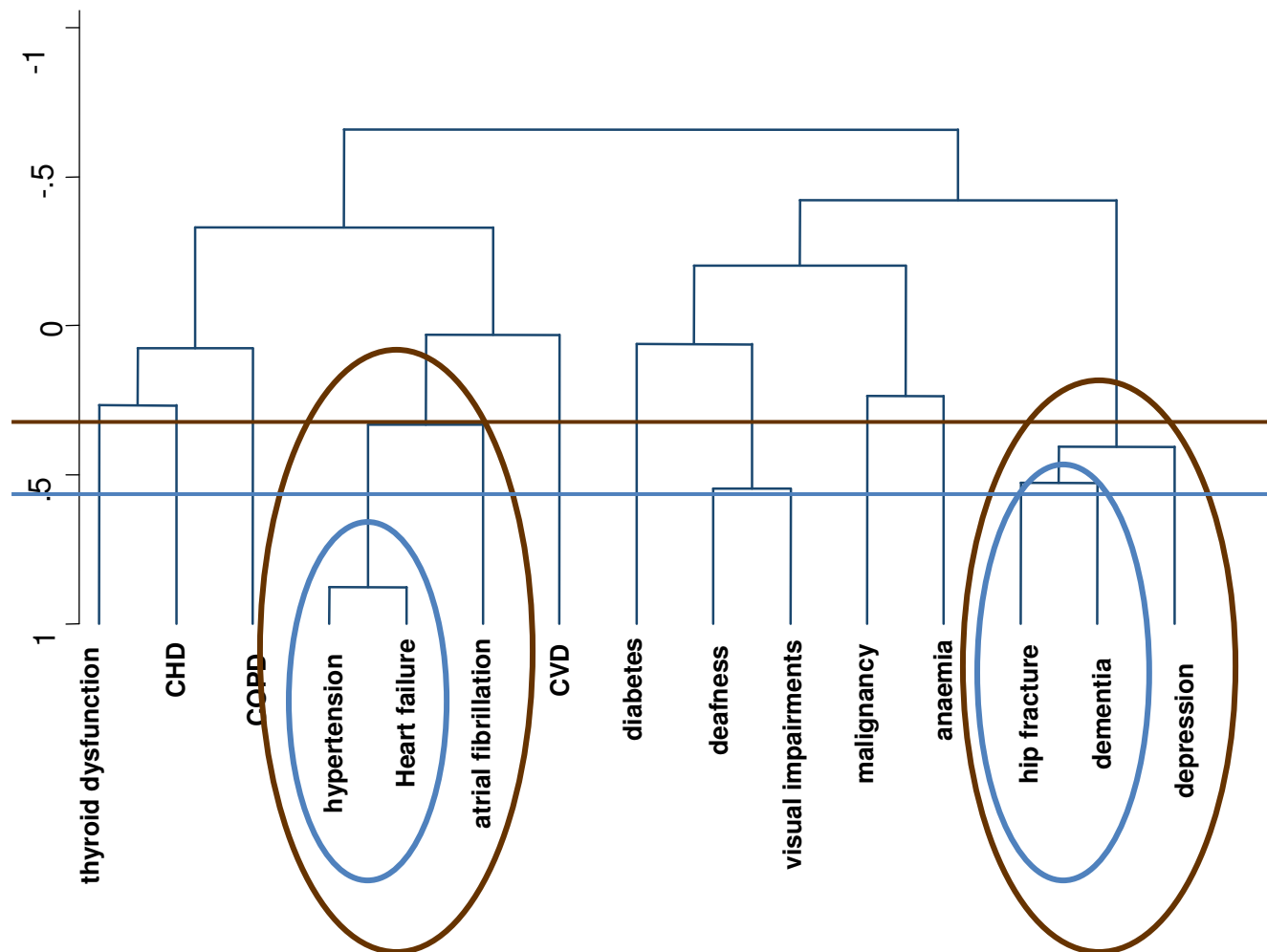


# PREVALENCE OF DISABILITY ACCORDING TO DIFFERENT CLUSTERS OF DISEASES IN THE KP



# CLUSTER ANALYSIS: CLUSTERING IS THE GROUPING OF SIMILAR OBJECTS BY USING ALGORITHMS. IT IS BEST SEEN AS HYPOTHESIS-GENERATING RATHER THAN -SOLVING.

Similarity measure



CHD=coronary heart diseases  
 CVD=cerebrovascular diseases  
 COPD=chronic obstructive pulmonary diseases



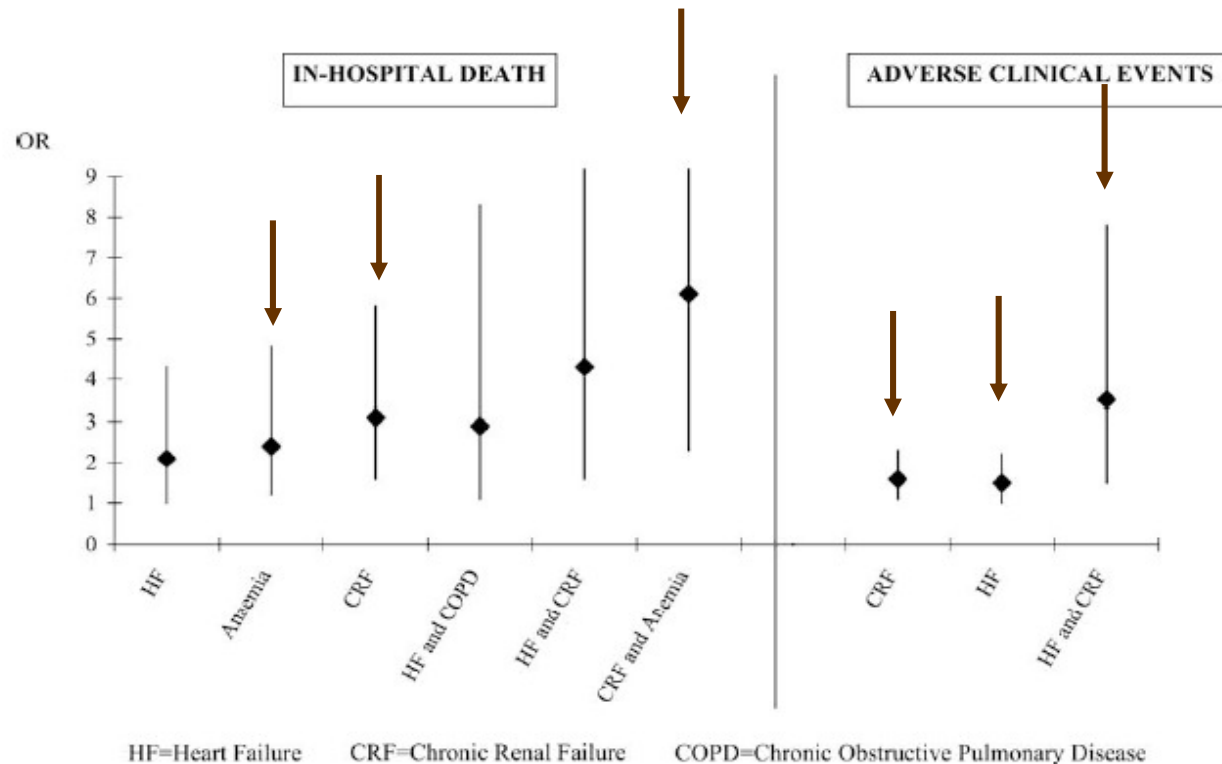


## THE RE.PO.SI. STUDY

- **Designed by the Italian Society of Internal Medicine and the Mario Negri Pharmacological Institute (Milan)**
  - **Cross-sectional (2008 e 2010) and Longitudinal Study (2010)**
  - **38 Internal Medicine and Geriatric Wards in Italy in 2008 and 70 in 2010**
  - **4 weeks, one/season**
  - **1155 patients, 65+ yrs, in 2008 and 1400 in 2010**
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## In-Hospital Death and Adverse Clinical Events in Elderly Patients According to Disease Clustering: The REPOSI Study

A. Marengoni,<sup>1</sup> F. Bonometti,<sup>1</sup> A. Nobili,<sup>2</sup> M. Tettamanti,<sup>2</sup> F. Salerno,<sup>3</sup> S. Corrao,<sup>4</sup> A. Iorio,<sup>5</sup> M. Marcucci,<sup>5</sup>  
P.M. Mannucci,<sup>6</sup> for the Italian Society of Internal Medicine (SIMI) Investigators\*



**FIG. 2.** Odds ratio (OR) and 95% confidence intervals for in-hospital death and adverse clinical events during hospitalization due to different clusters of diseases. Models adjusted for age, gender, education, number of drugs, and severe dependency. HF, Heart failure; CRF, chronic renal failure; COPD, chronic obstructive pulmonary disease.



Original article

## Association between clusters of diseases and polypharmacy in hospitalized elderly patients: Results from the REPOSI study

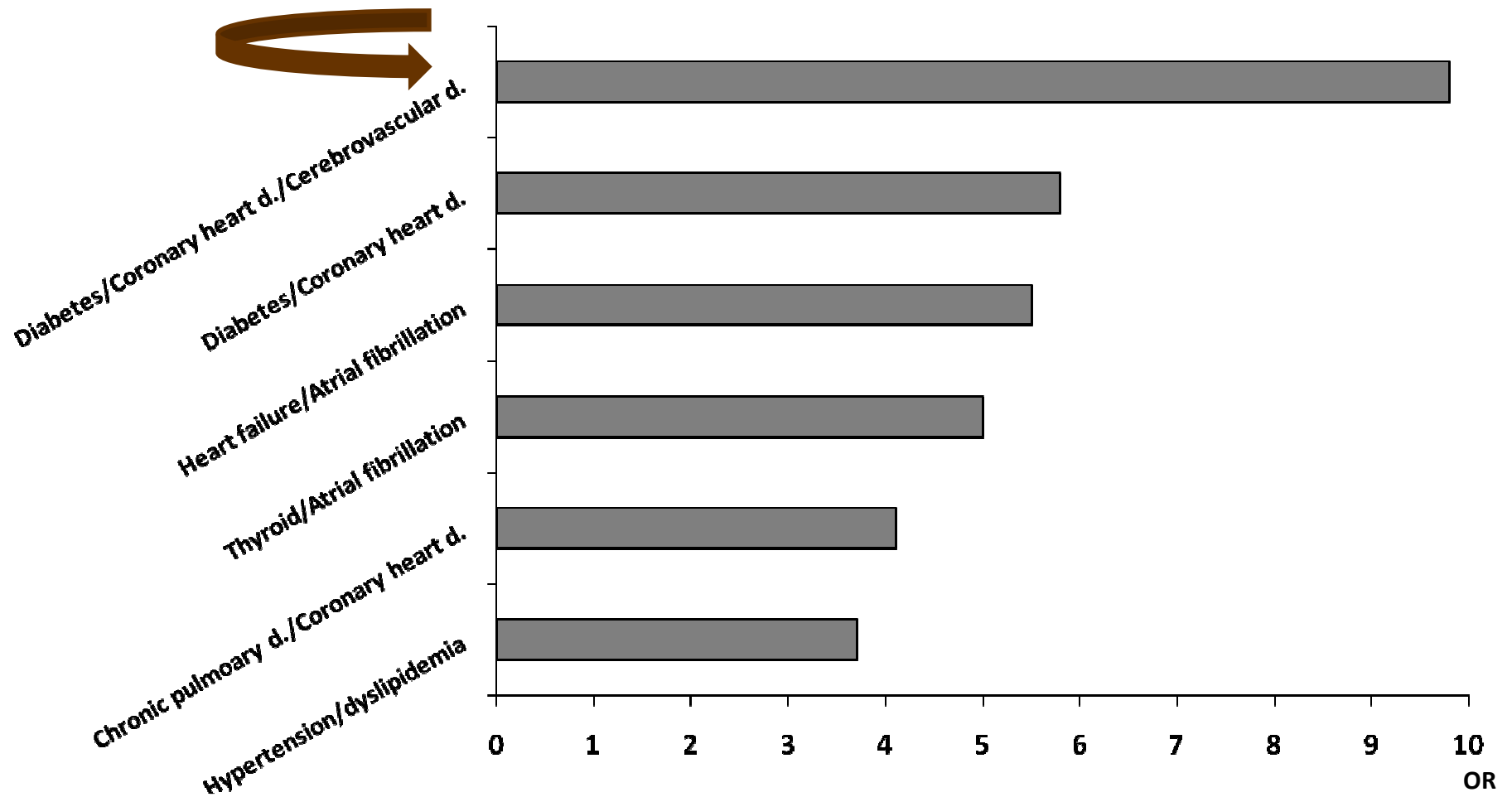


Diseases	OR	95% CI
Hypertension	2.3	1.8-2.9
Diabetes mellitus	1.9	1.4-2.8
Coronary heart disease	4.0	2.7-6.1
Atrial fibrillation	2.7	1.9-3.7
Chronic pulmonary disease	1.9	1.3-2.9
Cerebrovascular disease	1.5	1.1-2.0
Malignancy	0.6	0.4-0.9
Dyslipidemia	2.4	1.6-3.7
Chronic renal failure	2.1	1.3-3.3
Thyroid diseases	2.4	1.4-4.1
Heart failure	3.6	1.6-8.1



Original article

## Association between clusters of diseases and polypharmacy in hospitalized elderly patients: Results from the REPOSI study



Adjusted for age, gender, Charlson Index, participating centers

# CLUSTERS OF DISEASES AND ANTICHOLINERGIC BURDEN

Anticholinergic Cognitive Burden scale (ACB)

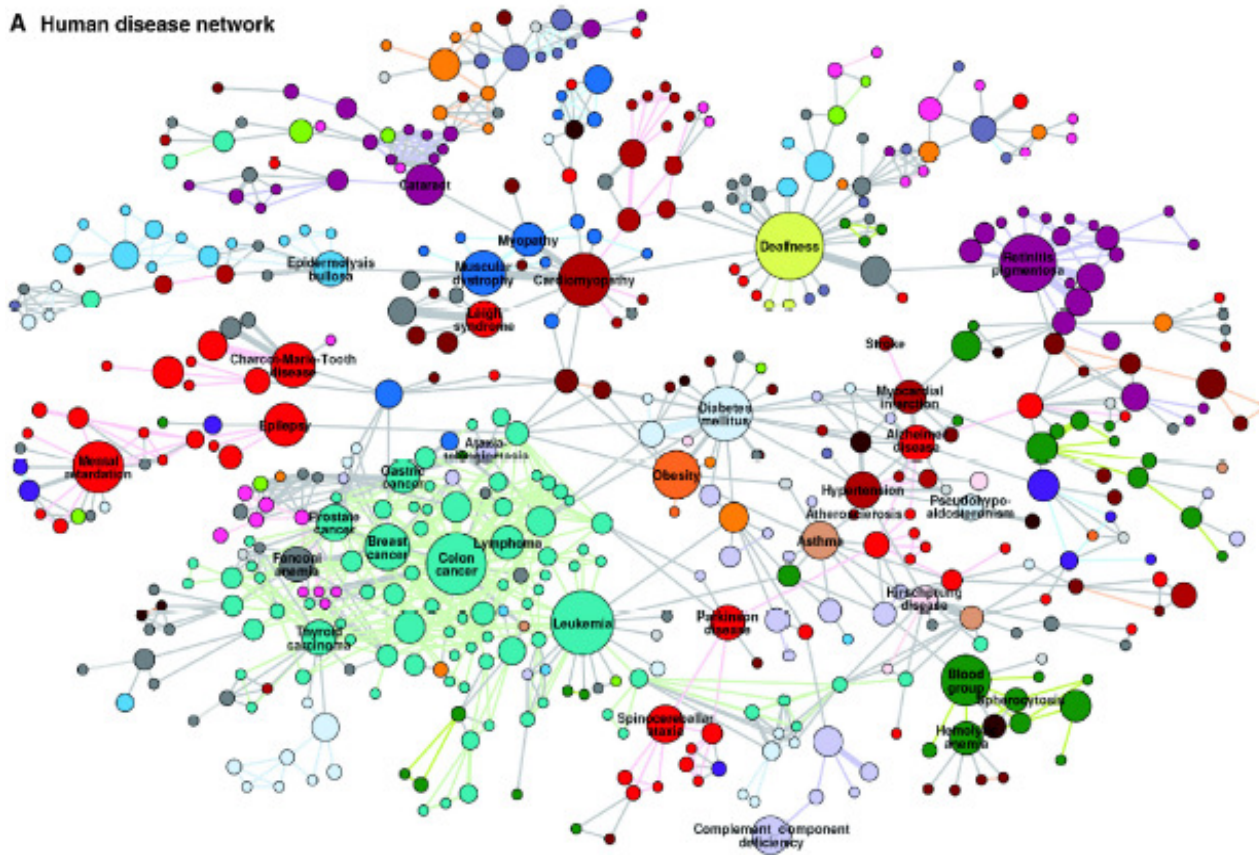
Clusters	Mean score ACB (sum score)	Number of patients treated with anticholinergic drugs (%)
1	2 (78)	32 (82.0)
2	1.4 (21)	9 (56.3)
3	1.1 (35)	7 (22.6)
4	1.7 (125)	64 (87.7)

Unpublished data

# NETWORK MEDICINE:

'a network-based approach to human disease'

A Human disease network



'Uncovering links between disease help us understand how different phenotypes are linked at the molecular level, but also help us to comprehend why certain groups of diseases arise together'

'...one can also link disease pairs on the basis of the directly observed coexistence between them, thereby obtaining a phenotypic disease network...'

# RESEARCH HYPOTHESES

**MAY DIFFERENT OUTCOMES/PROGNOSIS IN MULTIMORBID ELDERLY BE BETTER EXPLAINED BY DISEASE CLUSTERS?**

**MAY STUDIES ON SELECTED DISEASE CLUSTERS EXPLAIN:**

- **HIGHER RISK OF ADVERSE DRUG EVENTS?**
- **DIFFERENT RESPONSIVENESS?**
- **DIFFERENT COSTS?**

**IDEALLY, CAN WE DESIGN A CLINICAL TRIAL AIMING TO CHANGE THE CHAIN OF EVENTS (REDUCE OR SLOW DOWN DISEASE CLUSTERING)?**

**OUTCOMES NOT BASED ON DISEASE SPECIFIC INDICATORS BUT GOAL ORIENTED PATIENTS CARE: INDEPENDENCY , QUALITY OF LIFE, ..**