Aging, multimorbidity and polypharmacy:
which strategies for the Third Millennium
Milan, September 25th 2013

Cluster and Network Medicine

Alessandra Marengoni, MD, PhD

UO Geriatria, Spedali Civili, Brescia

Department of Clinical and Experimental Science

UNIVERSITÀ DEGLI STUDI DI BRESCIA

i. History and Present

ii. Cluster Medicine

iii. Network medicine

iv. The future

History

Oslerian formalism: disease is defined on the basis of the organ system in which symptoms are manifest, and in which pathology is correlated.

This approach to **disease by disease** diagnosis, prognosis, and treatment has served the medical establishment and society well for many years but vastly overgeneralizes pathophenotypes.

William Osler (1849-1919)

"Father of Modern Medicine"

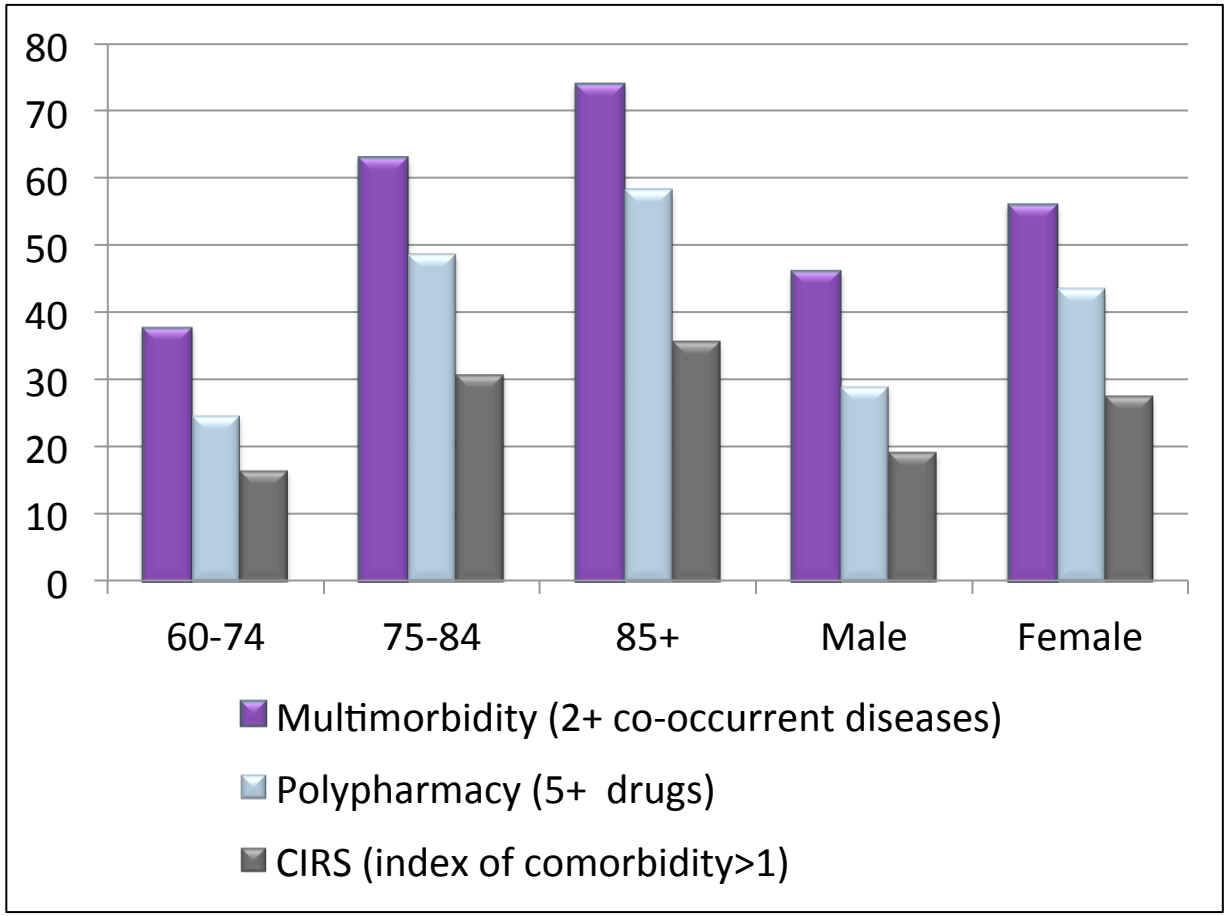
"the effective, moving, vitalizing work of the world is done between the ages of twenty-five and forty''

Sir William Osler, "The Fixed Period", farewell address at Johns Hopkins Medical School, 1905

Present

Prevalence per 100 of different measures of health status according to age groups and gender. The Swedish National Aging and Care Project.

Unpublished data
Poster n. P-21



PERTURBATORS OF HEALTH STATUS

Stress persistent/ transient

Acute, transient disease

Inflammation persistent/ transient

Chronic disease 1

Patient

Chronic disease 2

Chronic disease 3

Aging

Time span

Polypharmacy persistent/ transient

CLUSTER MEDICINE

A SYSTEM OF DISEASES PERSPECTIVE

DISEASE BY DISEASE PERSPECTIVE

COMPLEX SYSTEM

NETWORK MEDICINE

ONE CAUSE/ ONE DISEASE

DEFINITION OF CLUSTER

Clusters are defined as the co-occurrence of two or more SPECIFIC diseases in the same individual

According to the European Forum for Primary Care, an important first step to generate an evidence base for actual clinical practice is focusing on the systematic associations or clusters of diseases.

http://calliope.nivel.nl/pdf/EuropeanForumforPrimaryCareresponse_120419_Final.pdf.

According to the National Institute for Health and Clinical Excellence (NICE) this information is essential for developing guidelines or framework for clinical treatment of patients affected by multiple diseases.

http://www.nice.org.uk/newsroom/news/NICEshouldProduceGuidanceOnMultipleMorbidities.jsp

LITERATURE ON MULTIMORBIDITY CLUSTERS

John R, et al. Patterns and impact of comorbidity and multimorbidity among community-resident American Indian elders. Gerontologist 2003

Cornell et al. Multimorbidity clusters: clustering binary data from a large administrative medical database. Appl Multiv Res 2007

Marengoni A, et al. Patterns of chronic multimorbidity in the elderly population. J Am Geriatr Soc 2009

Schäfer I, et al. Multimorbidity patterns in the elderly: a new approach of disease clustering identifies complex interrelations between chronic conditions. PLoS One 2010

Newcomer SR et al. Identifying subgroups of complex patients with cluster analysis. Am J Manag Care 2011

Kirchberger I, et al. Patterns of multimorbidity in the aged population. Results from the KORA-Age Study. PLoS One 2012

Schäfer I, et al. The influence of age, gender and socio-economic stuatus on multimorbidity patterns in primary care. First results from the multicare cohort study. BMC Health Serv Res 2012

Prados-Torres A, et al. Multimorbidity patterns in primary care: interactions among chronic diseases using factor analysis. PLoS One 2012

García-Olmos L, et al. Comorbidity patterns in patients with chronic diseases in general practice. PLoS One 2012

Kirchberger I, et al. Patterns of multimorbidity in the aged population. Results from the KORA-Age study. PLoS One 2012

Francesc Formiga et al. Patterns of comorbidity and multimorbidity in the oldest old: The Octabaix Study. EJIM 2013

REJUVENATION RESEARCH
Volume 13, Number 4, 2010

DOI: 10.1089/rej.2009.1002

In-Hospital Death and Adverse Clinical Events in Elderly Patients According to Disease Clustering: The REPOSI Study

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

European Journal of Internal Medicine 22 (2011) 597–602

Contents lists available at SciVerse ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Original article

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

Gerontology

Clinical Section / Original Paper

Gerontology 2013;59:307–315
DOI: 10.1159/000346353

Received: September 12, 2012
Accepted: December 3, 2012
Published online: January 25, 2013

Comparison of Disease Clusters in Two Elderly Populations Hospitalized in 2008 and 2010

A. Marengoni[a] A. Nobili[b] C. Pirali[a] M. Tettamanti[b] L. Pasina[b] F. Salerno[c] S. Corrao[d] A. Iorio[g] M. Marcucci[g] C. Franchi[e] P.M. Mannucci[f] on behalf of REPOSI Investigators

POSSIBLE IMPLICATIONS OF CLUSTER MEDICINE

- New research hypotheses on possible shared pathological pathways for clusters of specific diseases can be developed
- Prevention, especially secondary prevention can be implemented
- Groups of people at high risk of adverse outcomes can be identified
- Polypharmacy, adverse drug reactions and potentially inappropriate medications can be different in different diseases' clusters
- Financial resources could be better distributed; in fact, cost of specific clusters of diseases can be additive or multiplicative
- The severity of a disease can be approximated by its connection with other specific diseases for patients with the same number of diagnoses
- Once the triggering event promoting the clustering of diseases has been identified, trials could be designed in order to change the chain of events

Network Definition

Network science is the study fields of the collection, management, analysis, interpretation, and presentation of relational data

The aim of network science is to simplify complex systems

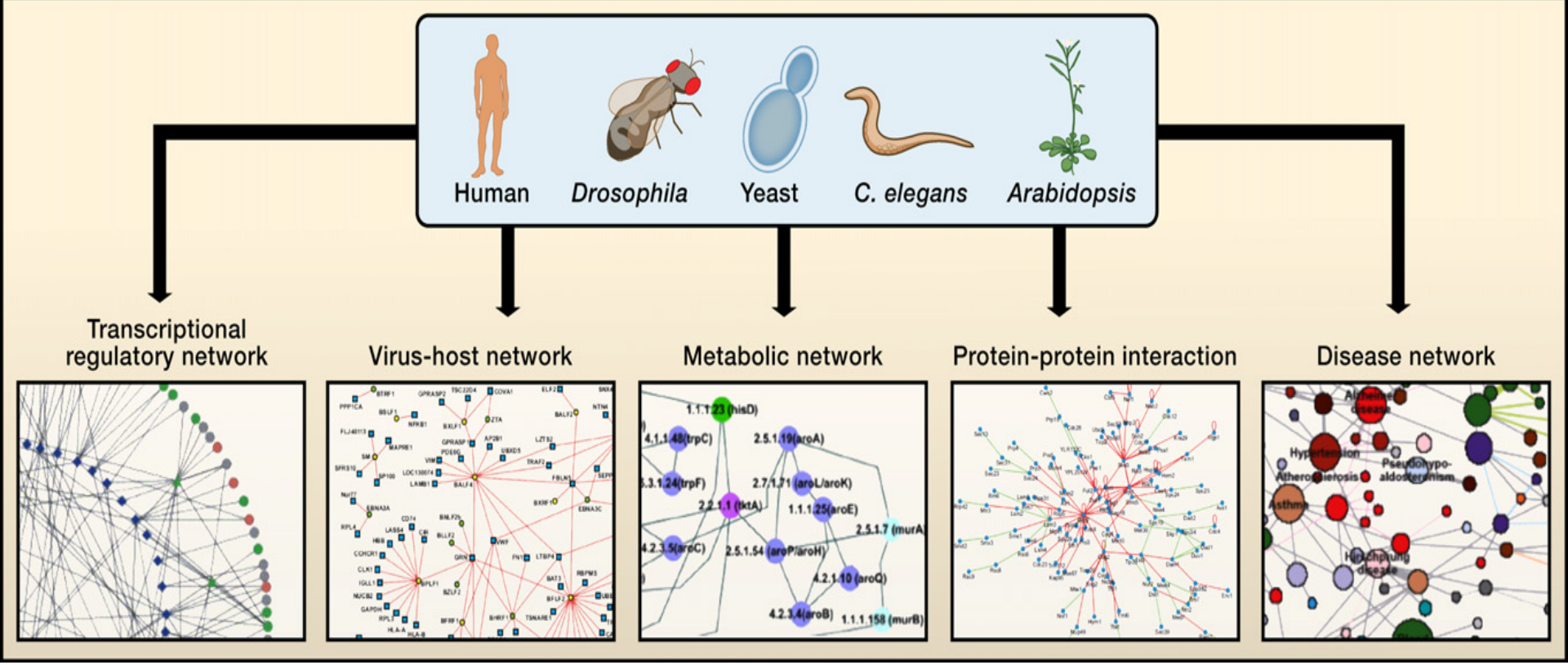
A network can be viewed as a collection of linked nodes, whose distribution can range from random to highly clustered

At the heart of a network there is dependence, both between and within variables

The presence of one tie may influence the presence of another

As regards cellular systems, the nodes are protein, RNA and gene sequences

The edges are physical and functional interactions amongst them



Nodes are either a transcription factor or a DNA regulatory element and edges represent the link between them	Viruses have evolved mechanisms to perturb the intracellular networks to their advantages	Attempt to describe all possible biochemical reactions for a particular cell	Nodes represent proteins and edges a physical interaction between two proteins

Vidal et al. Cell 2011

Networks and human diseases

Why mechanisms underlying genotype-fenotype relationships are only partially explained?

Every disease is the result of the complex nonlinear dynamic network of genomic, proteomic and environmental factors linked to yield different clinical phenotypes

Phenotypes arise from the pathological perturbation of one or more biological networks (genes, proteins, metabolism)

Possible implications of network approach in human diseases

Analysis of network perturbations by pathogens

Global relationship between diseases with associated gene and molecular networks

The so-called off-target effect of drugs, which often leads to a drug's withdrawal from the market is a reflection of the failure to consider any pharmacological agent in holistic context, perturbating a network.

Failure of the majority of clinical trials, i.e., Alzheimer's disease, based on one cause – one disease idea

The link between cluster and network medicine

Human Molecular Genetics, 2011, Vol. 20, No. 3 **510–527**
doi:10.1093/hmg/ddq496
Advance Access published on November 15, 2010

Comparison of an expanded ataxia interactome with patient medical records reveals a relationship between macular degeneration and ataxia

Juliette J. Kahle[1], Natali Gulbahce[5,6,†], Chad A. Shaw[1], Janghoo Lim[1,‡], David E. Hill[5], Albert-László Barabási[5,7] and Huda Y. Zoghbi[1,2,3,4,*]

Spinocerebellar ataxias 6 and 7 (SCA6 and SCA7) are neurodegenerative disorders caused by expansion of CAG repeats encoding polyglutamine (polyQ) tracts in CACNA1A, the alpha1A subunit of the P/Q-type calcium channel, and ataxin-7 (ATXN7), a component of a chromatin-remodeling complex, respectively. We hypothesized that finding new protein partners for ATXN7 and CACNA1A would provide insight into the biology of their respective diseases and their relationship to other ataxia-causing proteins. We identified 118 protein interactions for CACNA1A and ATXN7 linking them to other ataxia-causing proteins and the ataxia network. To begin to understand the biological relevance of these protein interactions within the ataxia network, we used OMIM to identify diseases associated with the expanded ataxia network. We then used Medicare patient records to determine if any of these diseases co-occur with hereditary ataxia. We found that patients with ataxia are at 3.03-fold greater risk of these diseases than Medicare patients overall. One of the diseases comorbid with ataxia is macular degeneration (MD). The ataxia network is significantly ($P = 7.37 \times 10^{-5}$) enriched for proteins that interact with known MD-causing proteins, forming a MD subnetwork. We found that at least two of the proteins in the MD subnetwork have altered expression in the retina of *Ataxin-7*$^{266Q/+}$ mice suggesting an *in vivo* functional relationship with ATXN7. Together these data reveal novel protein interactions and suggest potential pathways that can contribute to the pathophysiology of ataxia, MD, and diseases comorbid with ataxia.

http://barabasilab.neu.edu/courses/phys5116/ — Network Science Course - 2...

File Modifica Visualizza Preferiti Strumenti ?

Siti suggeriti — Ulteriori componenti ...

Pagina — Sicurezza — Strumenti

NETWORK SCIENCE

Welcome to the Network Science course website.
Please tune in for updates, messages, homework assignments and useful links.

The lectures will take place on Mondays and Wednesdays, 5:30 – 7:20 PM

At the Center for Complex Network Research
Northeastern University Physics Department
110 Forsyth Street, Boston, MA 02115
Hint: Its on the 5th floor of the Charles A. Dana building.
Use the elevator on the left.

The course will be presented by Prof. Albert-László Barabási
and assisted by Dr. Baruch Barzel
network visualizations by Prof. Mauro Martino

INFORMATION
syllabus & course schedule

HOMEWORK
assignment & solution

http://www.barabasilab.com/

IT 16:04 12/09/2013