System medicine e complessità in medicina

GF Gensini

Pisa, 16 novembre 2013

Evidence-Based Medicine

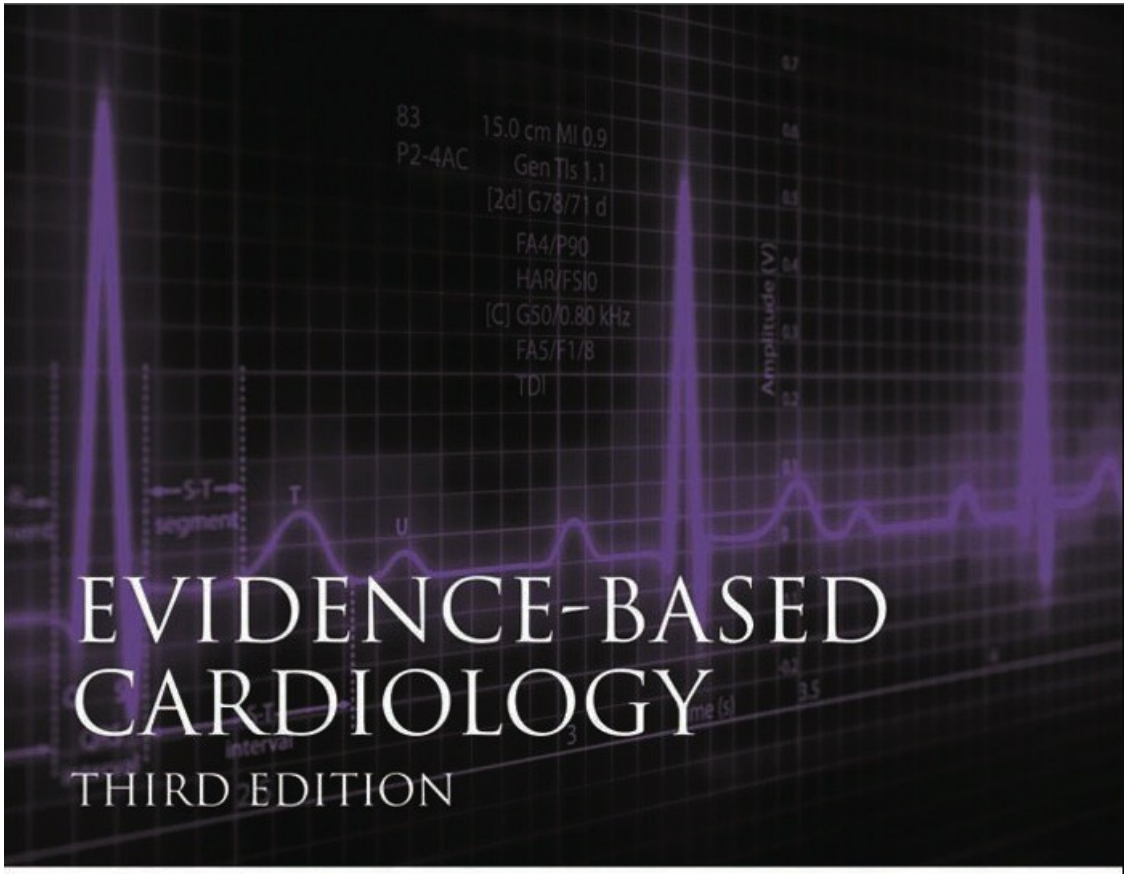
A New Approach to Teaching the Practice of Medicine

Evidence-Based Medicine Working

Practising EBM

- Formulating **answerable clinical questions**
- Searching for the **best evidence**
- Critical **appraisal** of the evidence
- **Applying evidence** to patients

Knowledge Translation Clearinghouse, Canada
St. Michael's Hospital and the University of Toronto, Faculty of Medicine.



Edited by
Salim Yusuf
John A. Cairns
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Ernest L. Fallen
Bernard J. Gersh

2010

WILEY-BLACKWELL

BMJ|Books

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Scandinavian Simvastatin Survival Study (4S)

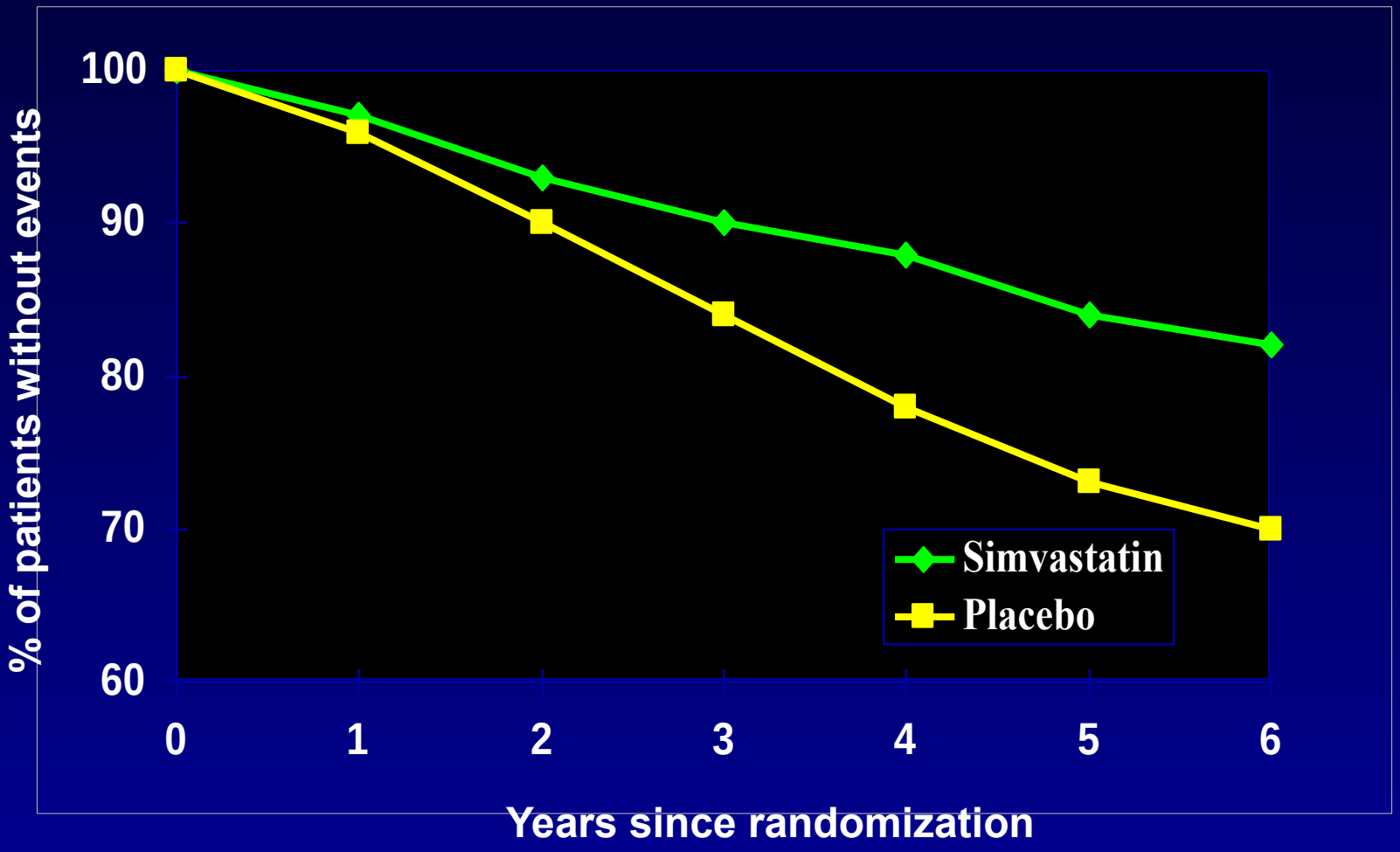
The Lancet, Vol 344, November 19, 1994

Design

- Double-blind, randomized, placebo-controlled
  - 94 centers in 5 countries
  - 4,444 men and women 35 to 70 years of age
  - Inclusion Criteria: **Prior MI** and/or angina pectoris
  - Total Cholesterol: 212-309 mg/dL
  - Follow-up: until 440 deaths occurred.

The Lancet, Vol 344, November 19, 1994

Coronary Death and Nonfatal MI



The Lancet, Vol 344, November 19, 1994

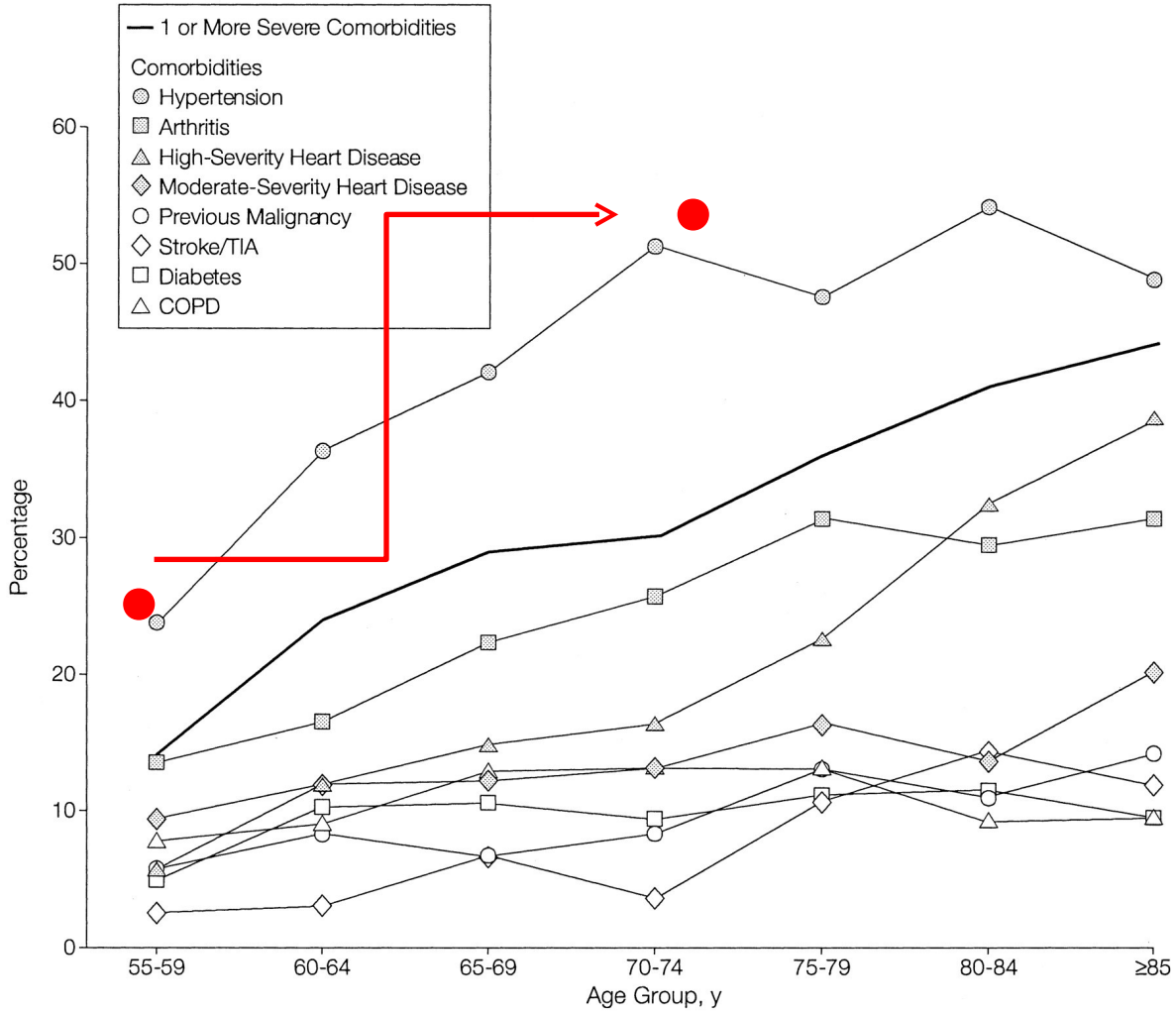
Baseline Characteristics

	Placebo (n=2223)	Simvastatin (n=2221)
Mean age (years)-men	**58.1**	**58.2**
Mean age (years)-women	**60.5**	**60.5**
Angina only	21%	21%
MI only	62%	63%
Both angina and MI	17%	16%
Hypertension	**26%**	**26%**
Smoker	27%	24%
TC (mg/dL)	260	260
LDL (mg/dL)	180	180

The Lancet, Vol 344, November 19, 1994

Importance of co-morbidity

Prevalence and age trends for selected co-morbidities



Holmes 2003

….in questi 20 anni che cosa è cambiato

- Progressivo **invecchiamento** della popolazione
- Aumento dei pazienti con **comorbilità** multiple - **multimorbilità**
- Queste categorie di pazienti sono **solitamente non incluse** nei trial clinici

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LA MEDICINA CLASSICA

- **Concetto di malattia**
- La medicina ha coniato il concetto di ‘malattia’ e aderisce a questo concetto nella sua attività.
- **Le malattie definite come ontologie in medicina rappresentano il risultato di un processo di consenso talora recentemente esplicito, in precedenza più frequentemente implicito, relativamente alla definizione di un’ontologia.**

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LA MEDICINA CLASSICA

- Il ragionamento diagnostico assume così le caratteristiche del riconoscimento di un'impronta digitale: si ricercano i **punti di identità** fra malattia conosciuta e situazione clinica del paziente e, quando i punti di identità superano un certo numero, si definisce la **diagnosi (approccio euristico al problema)**.

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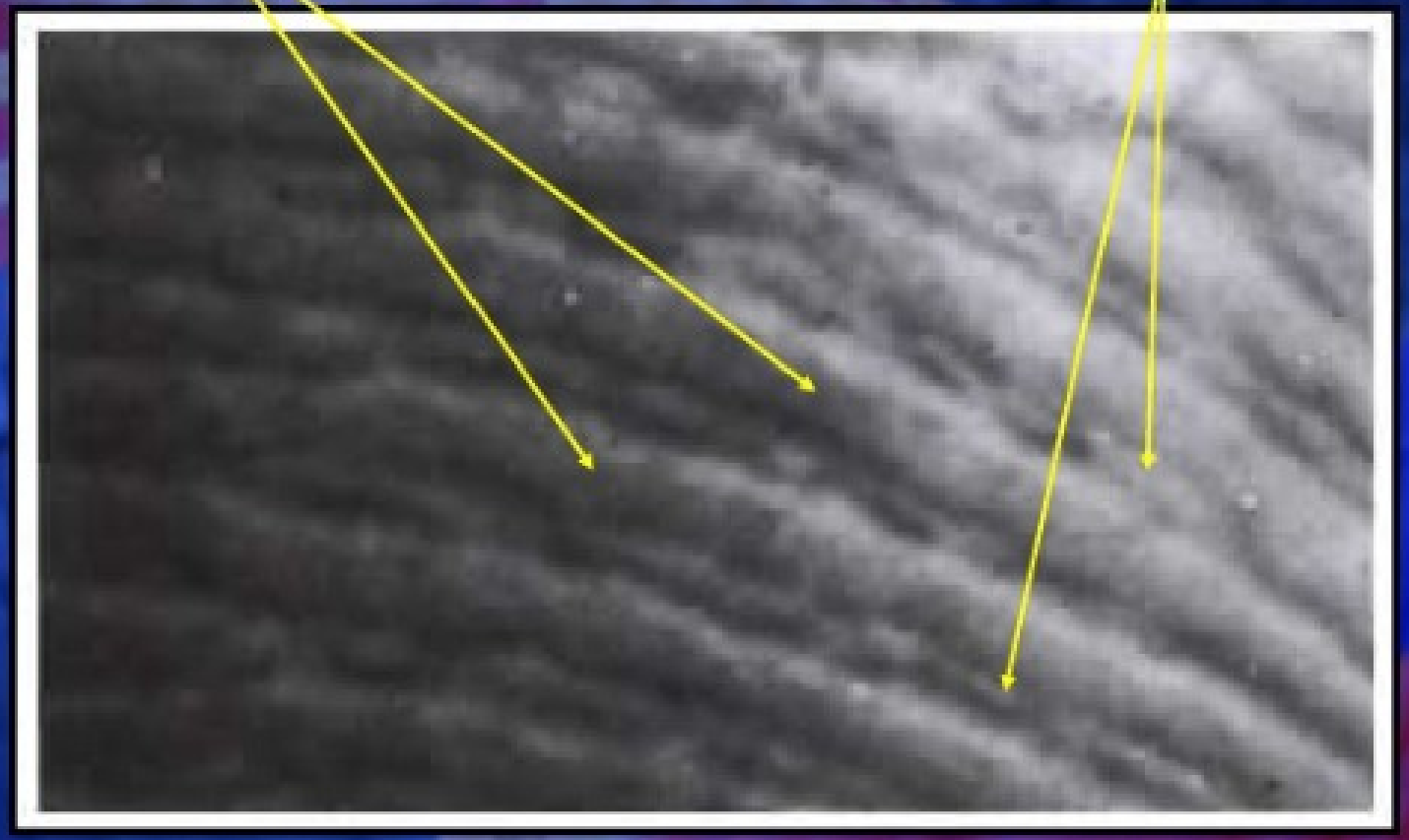
DEPARTMENT OF JUSTICE
FEDERAL BUREAU OF INVESTIGATION
FIDELITY
BRAVERY
INTEGRITY

Ridge

Valley



WHAT IS A FINGERPRINT?

A fingerprint is a pattern of friction ridge details, that are comprised of ridges and valleys.

A Ridge – is a high.

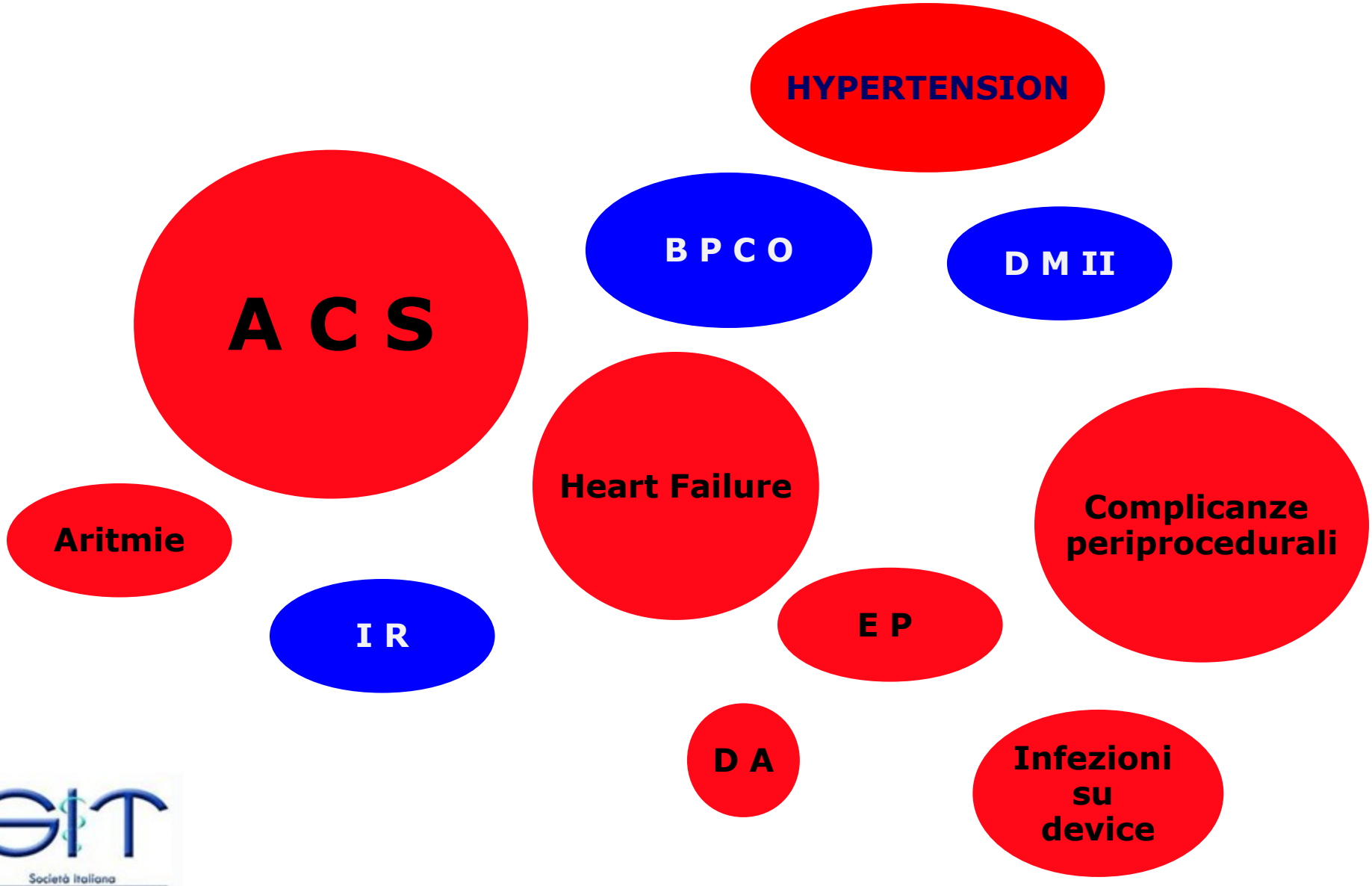
A Valley – is a depression or low.

Friction ridges are also found on our palms, feet and toes.

POINTS OF IDENTIFICATION

- United States — No Set Number
- England — 16
- France — 17
- Germany — 12

Il fenotipo clinico complesso



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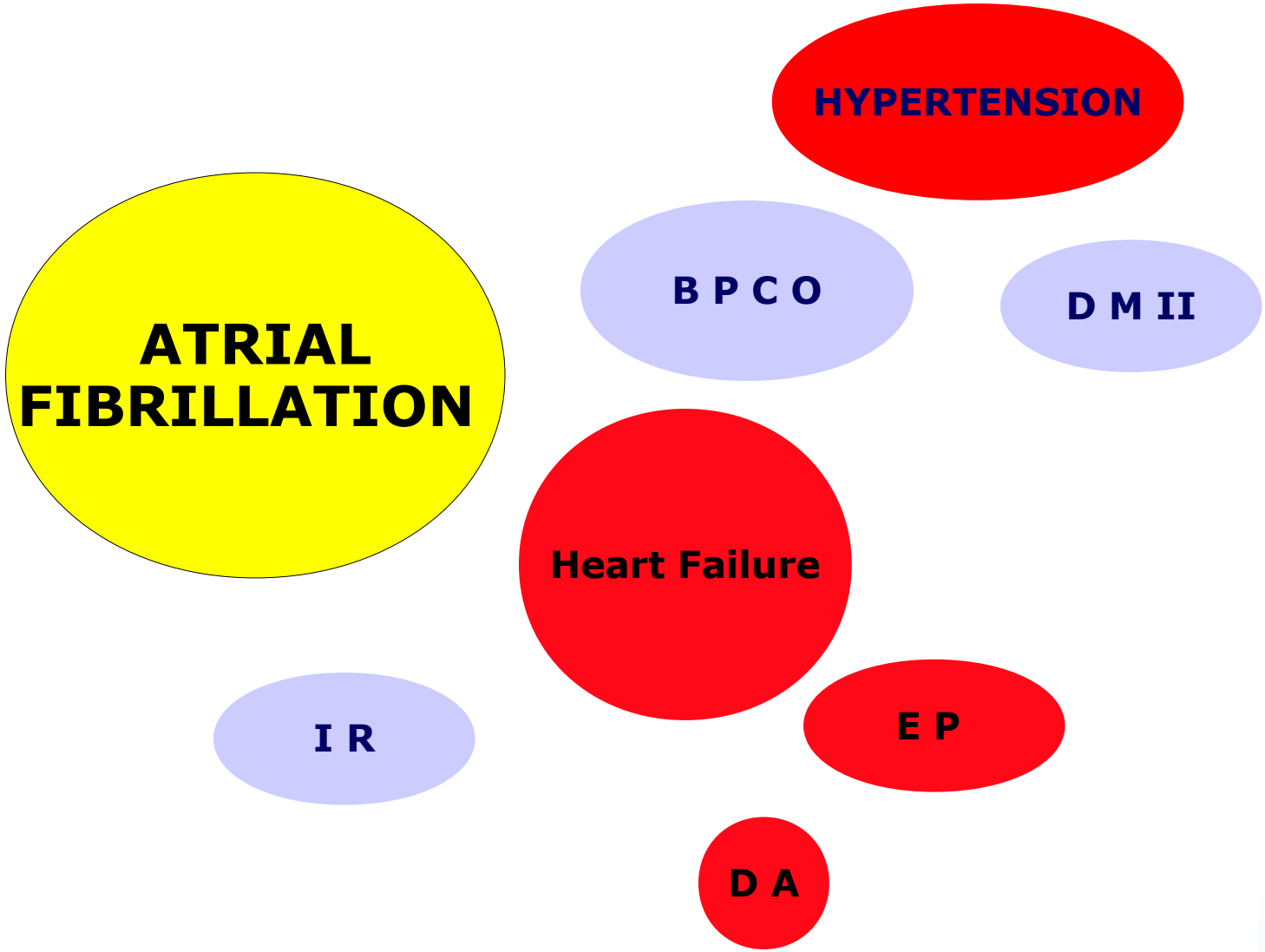
Il fenotipo clinico complesso



- Il **singolo malato** – potenzialmente sempre, ma in particolare oggi con il progressivo invecchiamento della popolazione – si può presentare con un **quadro clinico complesso** in rapporto alla coesistenza di più condizioni morbose.

- Questo complica e rende più **difficile**, e talora **impossibile**, il processo di **identificazione di una di queste malattie** con la condizione **complessiva** del paziente.

Un approccio elementare alla complessità

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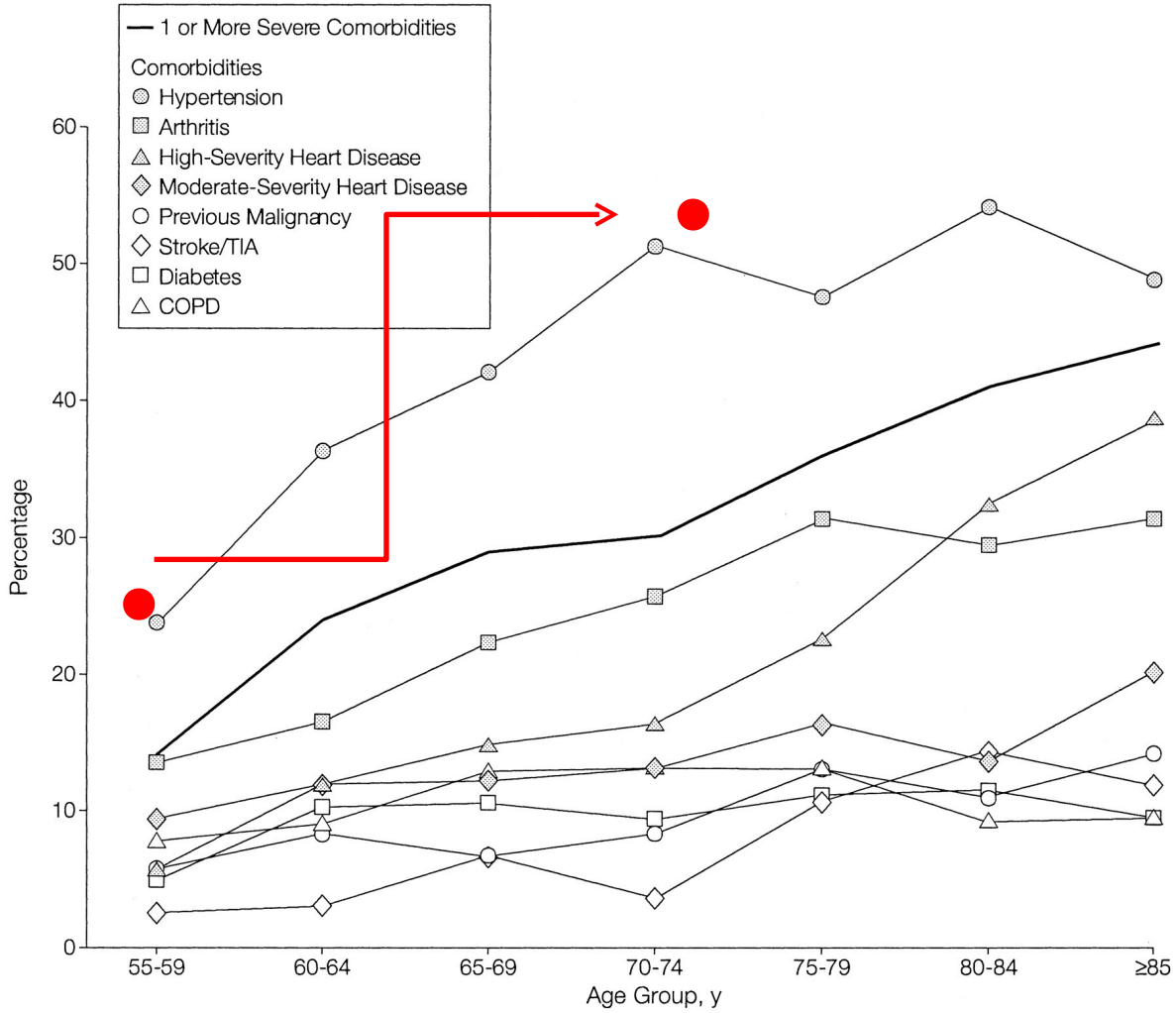
Importance of co-morbidity

Prevalence and age trends for selected co-morbidities



Holmes 2003

Some common measures of comorbidity

- **Disease Count (DC) (!!!?)**
- **Charlson Index (CI)**
- **Index of Co-Existent Diseases (ICEDDS) ← Index of Disease Severity (IDS)**
- **Geriatric Index of Comorbidity (GIC)**

J Chron Dis Vol. 40, No. 5, pp. 373–383, 1987
Printed in Great Britain.

0021-9681/87 $3.00 + 0.00

A NEW METHOD OF CLASSIFYING PROGNOSTIC COMORBIDITY IN LONGITUDINAL STUDIES: DEVELOPMENT AND VALIDATION

MARY E. CHARLSON,* PETER POMPEI, KATHY L. ALES and C. RONALD MACKENZIE

Clinical Epidemiology Unit, Department of Medicine, Cornell University Medical College, 1300 York Avenue, New York, NY 10021, U.S.A.

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Evaluation of co-morbidity
Charlson co-morbidity index (1987)

Index 1

Chronic obstructive pulmonary diseases

Cardiovascular diseases:
myocardial infarction, cardiac decompensation, angina pectoris, peripheral arterial disease, intermittent claudication, abdominal aneurysm
Cerebrovascular diseases:
cerebrovascular accident
Hypertension (medically treated)

Diabetes mellitus

Auto-immune disease
Peptic ulceration
Dementia
Liver function disturbances

Index 2

Hemiplegia
Kidney function disturbances (moderate/severe)
Diabetes mellitus with terminal organ damage
Tumours: solid tumours, leukemia, lymphoma

Index 3

Liver function disturbances (moderate/severe)

Index 6

AIDS
Metastatic cancer

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Etimologia della complessità

- Complesso, complicato e semplice sono termini che vengono tutti dalla stessa radice indoeuropea: plek- (parte, piega, intreccio).Da **plek**- derivano, in latino:
- Il verbo **plicare** = piegare

  Il verbo **plectere** = intrecciare

  Il suffisso –**plex** = parte
- La parola **semplice** = sine plex…

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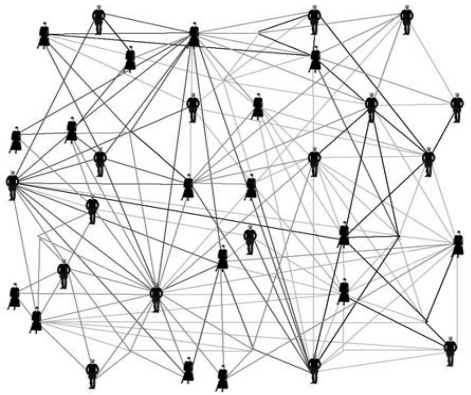
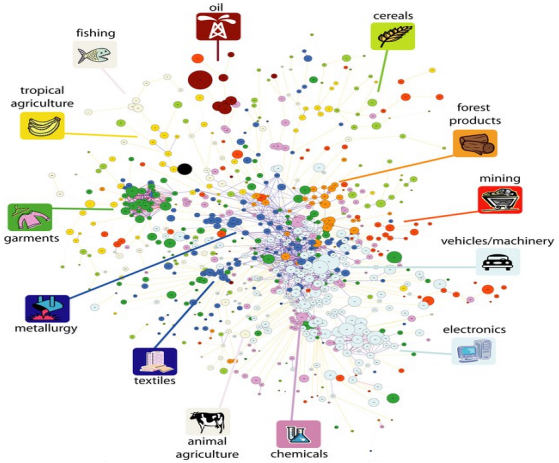
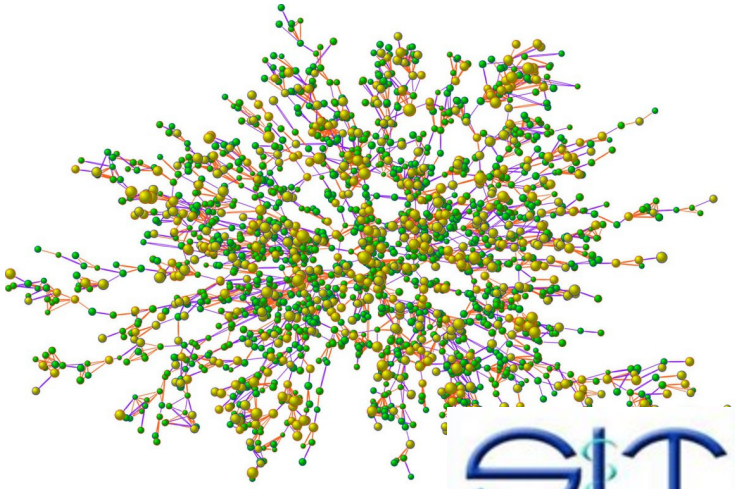
Complex Systems

- A complex system is a system composed of interconnected parts that **as a whole** exhibit **one or more properties** (behavior among the possible properties) **not obvious from the properties** of the **individual parts** .







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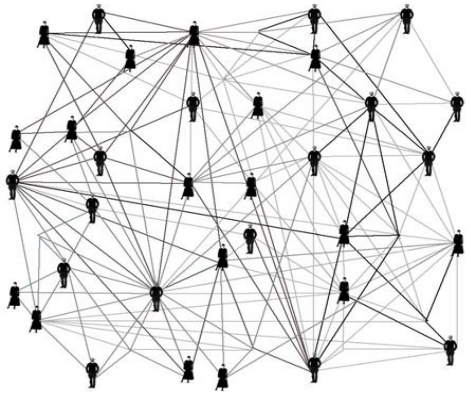
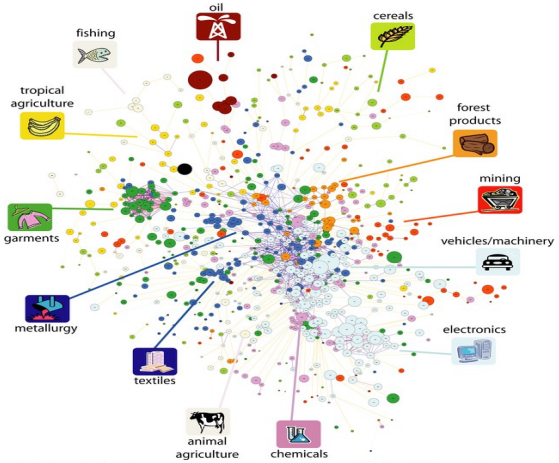
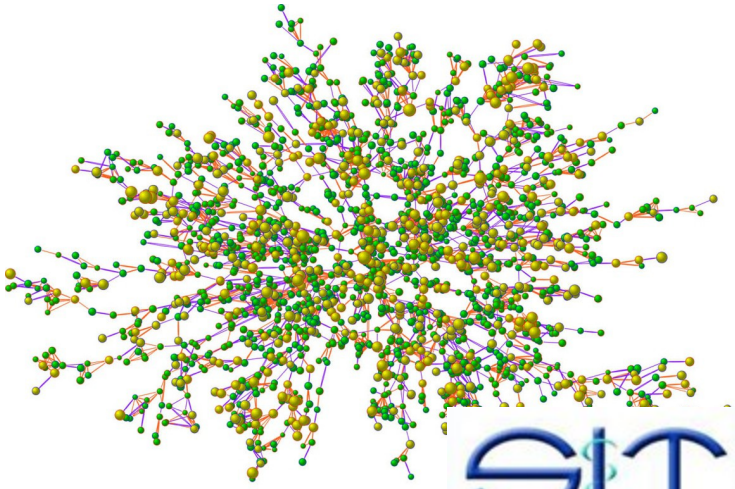
Complex Systems

- Examples of complex systems include **social systems**, **human economies**, **nervous systems**, **cells and living things**, including human beings.







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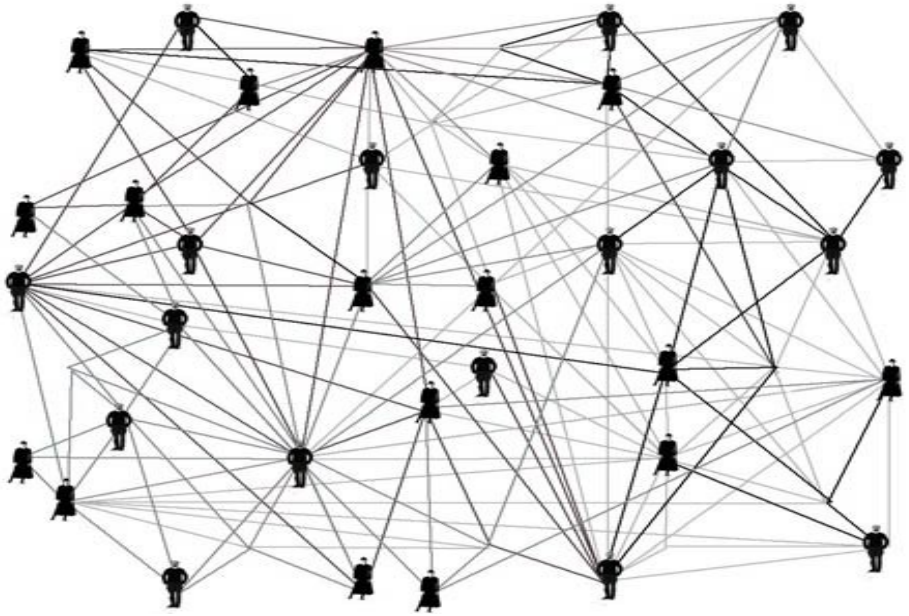

It's Twitter, not the 'Turkish Spring': Turkish PM Recep Tayyip Erdogan blames 'extremists' after fourth day of protests

The Prime Minister rejected comparisons with the Arab Spring wave of protests as first death during unrest is reported

JAMES LEGGE | MONDAY 03 JUNE 2013

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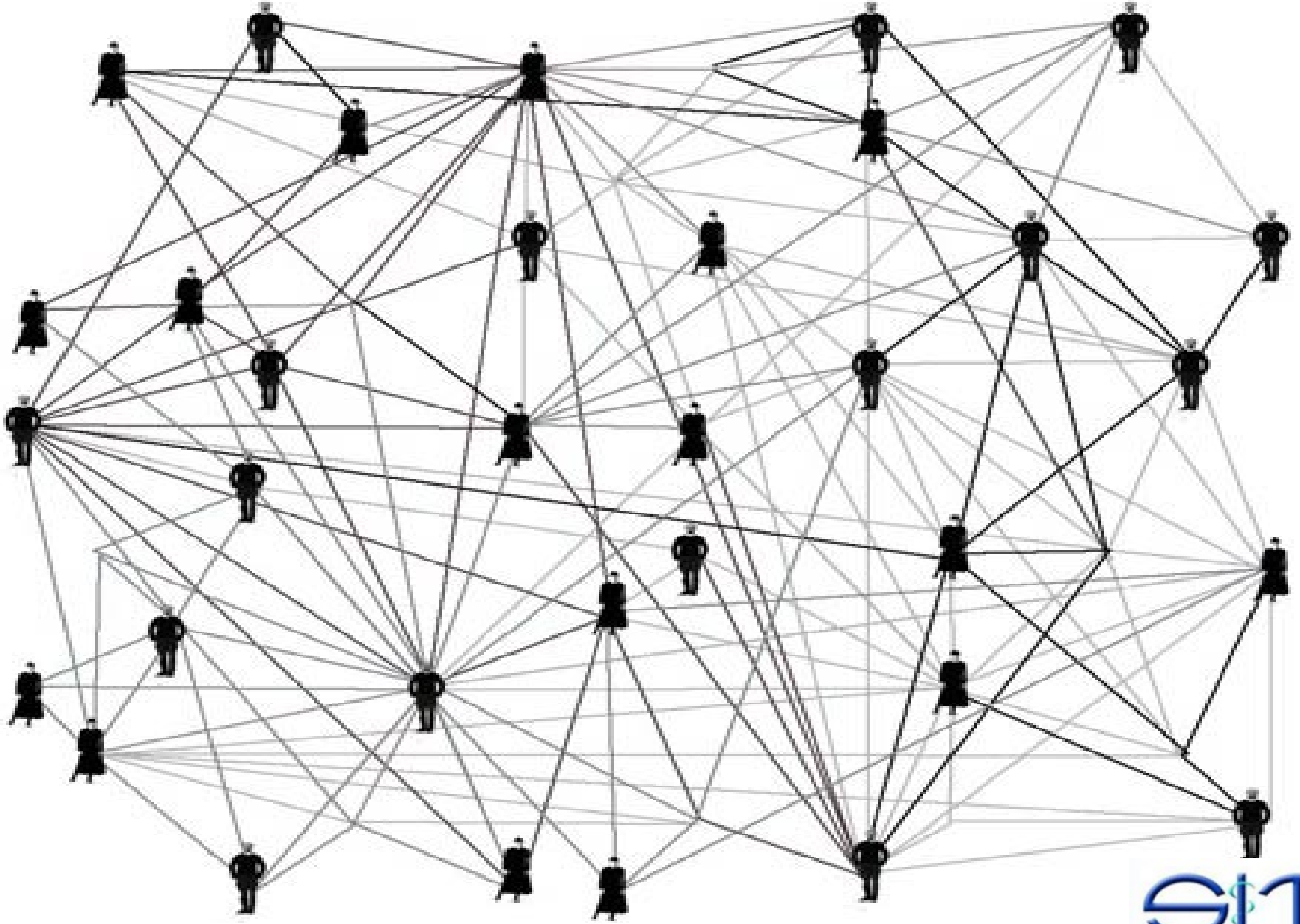

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Turkish Leader Says Protests Will Not Stop Plans for Park

New York Times - Jun 3, 2013

In his remarks, Mr. **Erdogan** criticized **Twitter**, which became an important conduit of news — and unfounded rumors — about the ...

Protests in Turkey

New York Times - Jun 2, 2013

He decried **Twitter** and social media as "a menace," and he accused Turkey's secular opposition of fomenting the protests. The protests began ...

Police Retreat as Protests Expand Through Turkey

New York Times - Jun 1, 2013

Many of the protesters, some of whom voted for Mr. **Erdogan**, said his leadership had become increasingly dictatorial. In a **Twitter** message late ...

Mr. Erdogan, whose party has accused opposition parties of stoking the protests, weighed in on Twitter in the late afternoon: "Wherever they try to hit us, we will stand tall and strong."

The explanation **alternative to reductionism** that
has received much recent attention,
due to systems biology, is the **systems perspective**

Rather than dividing a complex problem into its component parts**, the systems perspective appreciates the holistic and composite characteristics of a problem** and evaluates the problem with the use of computational and mathematical tools..

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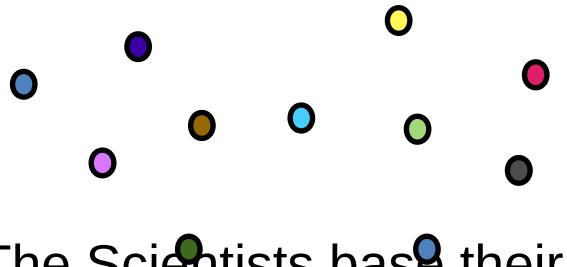
The systems perspective is rooted in the assumption that the forest cannot be explained by studying the trees individually.

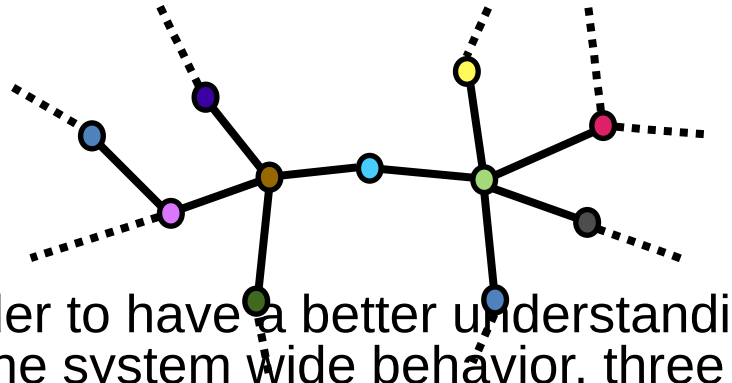
Reductionism vs System approach

Reductionism



- The Scientists base their research on a principle hypothesis that complex systems can be understood by seeking out its most fundamental constituents.
- **Complex problems are resolved by dividing them into smaller, simpler and more tractable units.**
- In the last 50 years, the reductionist approach of has been successful in revealing the chemical basis of numerous

System approach



In order to have a better understanding of the system wide behavior, three factors need to be considered:

Context: the inclusion of all components involved in a process (and their interactions).

Time: to consider the changing characteristics of each component.

Space: to account for the topographic relationships between and among

New York Times 18 sep 2007

Dr. Michael Stern reported in the June issue of Emergency Medicine.

By JANE E. BRODY

Published: September 18, 2007

A 78-year-old woman was found unconscious on the floor of her apartment by a neighbor who checked on her. The woman could not remember falling but told doctors that before going to bed she had abdominal pain and nausea and had produced a black stool, after which she had palpitations and felt lightheaded.

New York Times 18 sep 2007

Her medical history included

- **high blood pressure,**
- **coronary artery disease,**
- **atrial fibrillation,**
- **congestive heart failure and**
- **osteoarthritis**. She also had
- a **cold** with a
- **productive cough.**

For **each** condition, she had been prescribed a **different drug**, and she was taking a few over-the-counter remedies on her own.

New York Times 18 sep 2007

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New York Times 18 sep 2007

PERSONAL HEALTH

The 'Poisonous Cocktail' of Multiple Drugs

These were the medications:

- **Beta-blocker** to control high blood pressure.
- **Digitalis** to help the heart pump and control its rhythm.
- **Coumadin** to prevent a stroke caused by blood clots.
- **Furosemide**, a potent diuretic to lower blood pressure.
- **Statins** to lower serum cholesterol.
- **Baby aspirin** to reduce cardiac risk from blood clots.
- **Cox-2 inhibitor** for arthritis pain.
- **antidepressant** for depression and anxiety.
- **Diazepam**, as needed, to help her sleep.
- **Levofloxacin**, an antibiotic for the cough.
- **Ibuprofen** for body aches.
- **Cough medicine.**

New York Times 18 sep 2007

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New York Times 18 sep 2007

PERSONAL HEALTH

The 'Poisonous Cocktail' of Multiple Drugs

This is what doctors call polypharmacy, otherwise known as a "poisonous cocktail" of **many drugs that can interact in dangerous ways and cause side effects** that can be far worse than the diseases they are treating. Elderly people are especially vulnerable because they often have several medical problems for which they see **different doctors, each prescribing drugs**, often without knowing what else the patient is taking.

The woman described above passed out because she had **a bleeding stomach ulcer** from a combination of drugs that **irritate the stomach**, **Cox-2** inhibitor , ibuprofen and aspirin, and **thin the blood**, coumadin and aspirin, **made worse** by an antibiotic that raises blood levels of coumadin.

EVIDENZE ?

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POPOLAZIONI CAUCASOIDI			AFRICANE			DELL'ASIA CONTINENTALE	
MEDITERRANEI	NORDEUROPEI	INDIANI	JU/HUA BOSCIMANI	MASAI	PIGMEI	CINESI	TIBETANI








FAMIGLIA DI LINGUE INDOEUROPEE	KHOISAN	NILO-SAHARIANE	NIGER-CONGOLESI	SINO-TIBETANE

	ARTICHE	AMERICANE		DEL PACIFICO			
COREANI	INUIT	AZTECHI	YANOMAMI	POLINESIANI	MAORI	MELANESIANI	AUSTRALIANI





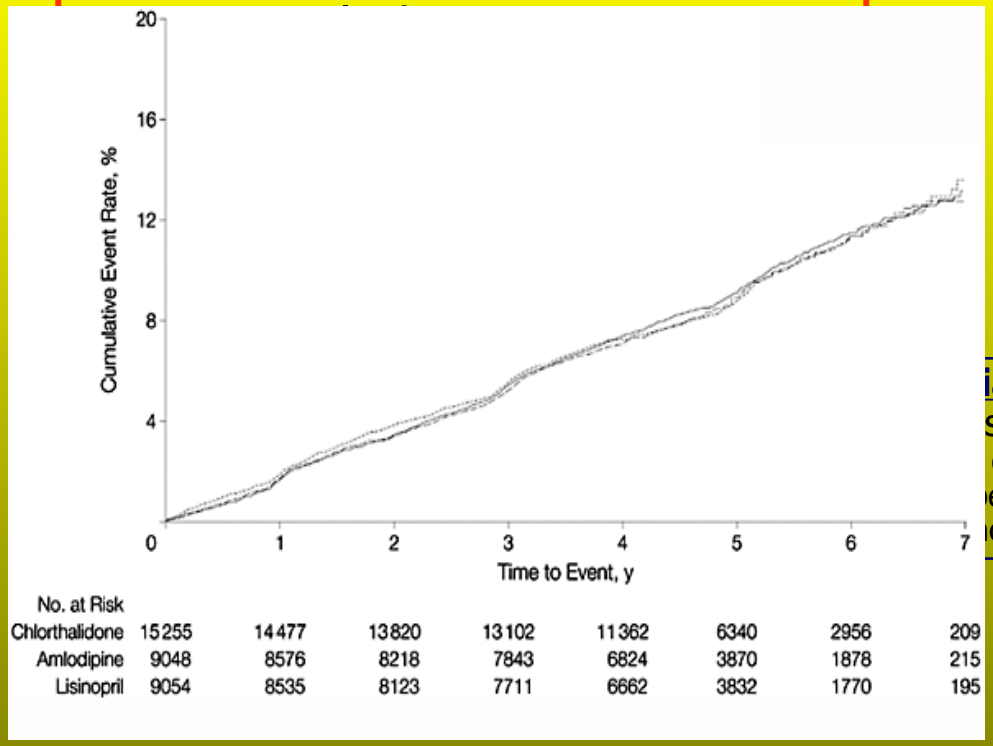



COREANE	ESCHIMO-ALEUTINE	AMERINDE	AUSTRONESIANE	INDO-PACIFICHE	AUSTRALIANE

ALLHAT

Cumulative Event Rates for the Primary Outcome

(Fatal Coronary Heart Disease or Nonfatal Myocardial Infarction)



ia
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other CVD,
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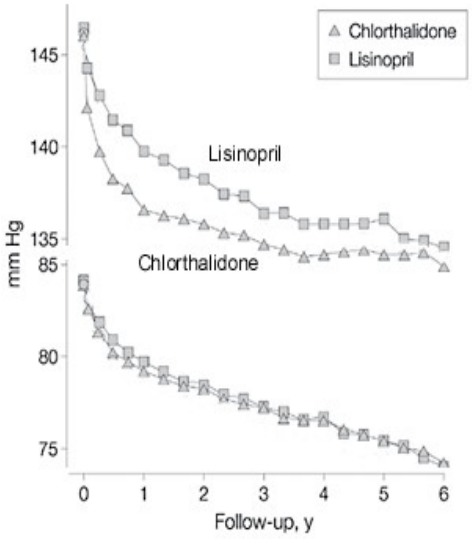
ALLHAT Collaborative Research Group. JAMA. 2002; 288: 2981-97

ALLHAT

Effects of ACE inhibitor based and Diuretic based treatments on Blood Pressure and Outcomes



Lisinopril vs Chlortalidone

Outcomes	***RR (95% CI)***
CV mortality	-
All cause mortality	1.00 (0.94-1.06)
Myocardial infarction	0.99 (0.91-1.08)
Stroke	**1.19** (1.02-1.30)*
Heart failure	**1.20** (1.09-1.34)*

** = p<0.01*

35% of enrolled patients were blacks

ALLHAT Collaborative Research Group. JAMA. 2002; 288: 2981-97

ALLHAT—All Hit or All Miss? Key Questions Still Remain

Franz H. Messerli, MD, and Michael A. Weber, MD

… black patients did not do well when randomized to lisinopril; most glaringly, the incidence of stroke was 40% higher than while receiving chlorthalidone.

The American Journal of Cardiology Vol. 92 August 1, 2003

Chlortalidone vs Lisinopril

	stroke	**BP (mmHg)**
All patients	- 15%	- 2 mmHg
Blacks	**- 40%**	**- 4 mmHg**
effect of race	$p<0.01$	

ALLHAT Collaborative Research Group. JAMA. 2002; 288: 2981-97

BI-DIL

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 11, 2004 VOL. 351 NO. 20

Combination of Isosorbide Dinitrate and Hydralazine in Blacks with Heart Failure

Anne L. Taylor, M.D., Susan Ziesche, R.N., Clyde Yancy, M.D., Peter Carson, M.D., Ralph D'Agostino, Jr., Ph.D., Keith Ferdinand, M.D., Malcolm Taylor, M.D., Kirkwood Adams, M.D., Michael Sabolinski, M.D., Manuel Worcel, M.D., and Jay N. Cohn, M.D., for the African-American Heart Failure Trial Investigators*

conclusions

The addition of a fixed dose of isosorbide dinitrate plus hydralazine to standard therapy for heart failure including neurohormonal blockers is efficacious and increases survival among black patients with advanced heart failure.

Circulation. 2007;115:1747-1753

An Evolving Scenario

Integrated Care supported by ICT

ICT as enabler of a new model of care

4P medicine

Predictive

Personalized

Preventive

Participatory

Efficient patient management

Modulation of disease progress

Società Italiana Telemedicina @ Sanità Elettronica

La complessità di un elemento clinico:

La dispnea

Società Italiana
Telemedicina & Sanità Elettronica

DISPNEA ACUTA (ENTRO POCHI MINUTI)

Cause polmonari

- Pneumotorace
- Embolia polmonare
- Asma, broncospasmo o patologia reattiva delle vie aeree
- Inalazione di un corpo estraneo
- Lesione tossica delle vie aeree (p. es., inalazione di cloro, solfuro di idrogeno)

Cause cardiache

- Ischemia miocardica acuta o infarto
- Disfunzione o rottura dei muscoli papillari
- Insufficienza cardiaca

Altre cause

- Paralisi del diaframma
- Disturbo d'ansia con iperventilazione

DISPNEA SUBACUTA (ENTRO ORE O GIORNI)

Cause polmonari

- Polmonite
- Esacerbazione di BPCO

Cause cardiache

- Angina o coronaropatia
- Versamento pericardico o tamponamento

DISPNEA CRONICA (DA ORE AD ANNI)

Cause polmonari

- Patologia polmonare ostruttiva
- Patologia polmonare restrittiva
- Patologia polmonare interstiziale
- Versamento pleurico

Cause cardiache

- Insufficienza cardiaca
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Altre cause

- Anemia
- Decondizionamento fisico

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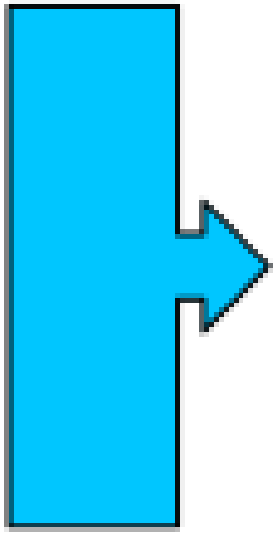
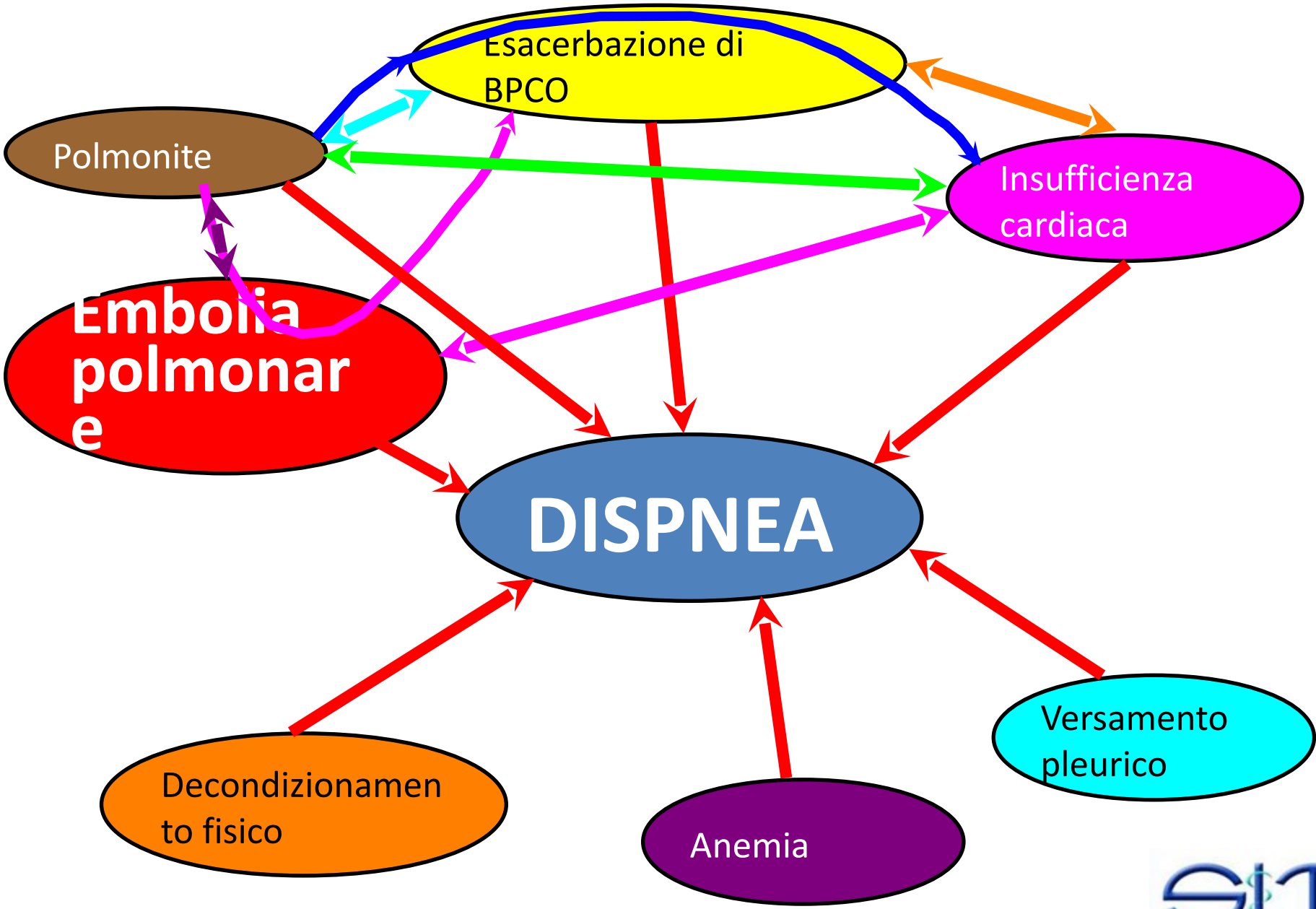
- **Embolia polmonare**
- Insufficienza cardiaca
- Polmonite
- Esacerbazione di BPCO
- Versamento pleurico
- Anemia
- Decondizionamento fisico



DISPNEA


Esacerbazione di BPCO
Polmonite
Insufficienza cardiaca
Embolia polmonare
DISPNEA
Decondizionamento fisico
Anemia
Versamento pleurico

An Evolving Scenario

Integrated Care supported by ICT

ICT as enabler of a new model of care

4P medicine

Predictive

Personalized

Preventive

Participatory

Efficient patient management
Modulation of disease progress

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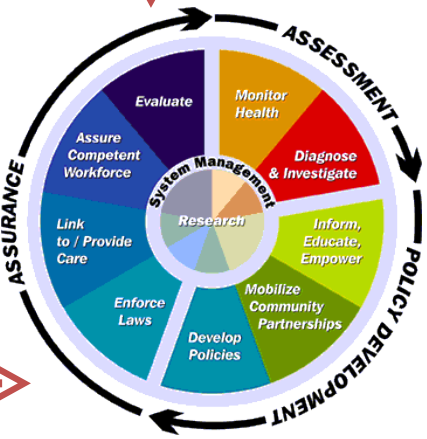
Paziente

Medico

Complessità iatrogena

Farmaco



Sistema sanitario

An Evolving Scenario

Integrated Care supported by ICT

ICT as enabler of a new model of care

4P medicine

Predictive

Personalized

Preventive

Participatory

Efficient patient management
Modulation of disease progress

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The NEW ENGLAND JOURNAL of 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.

GUIDELINES

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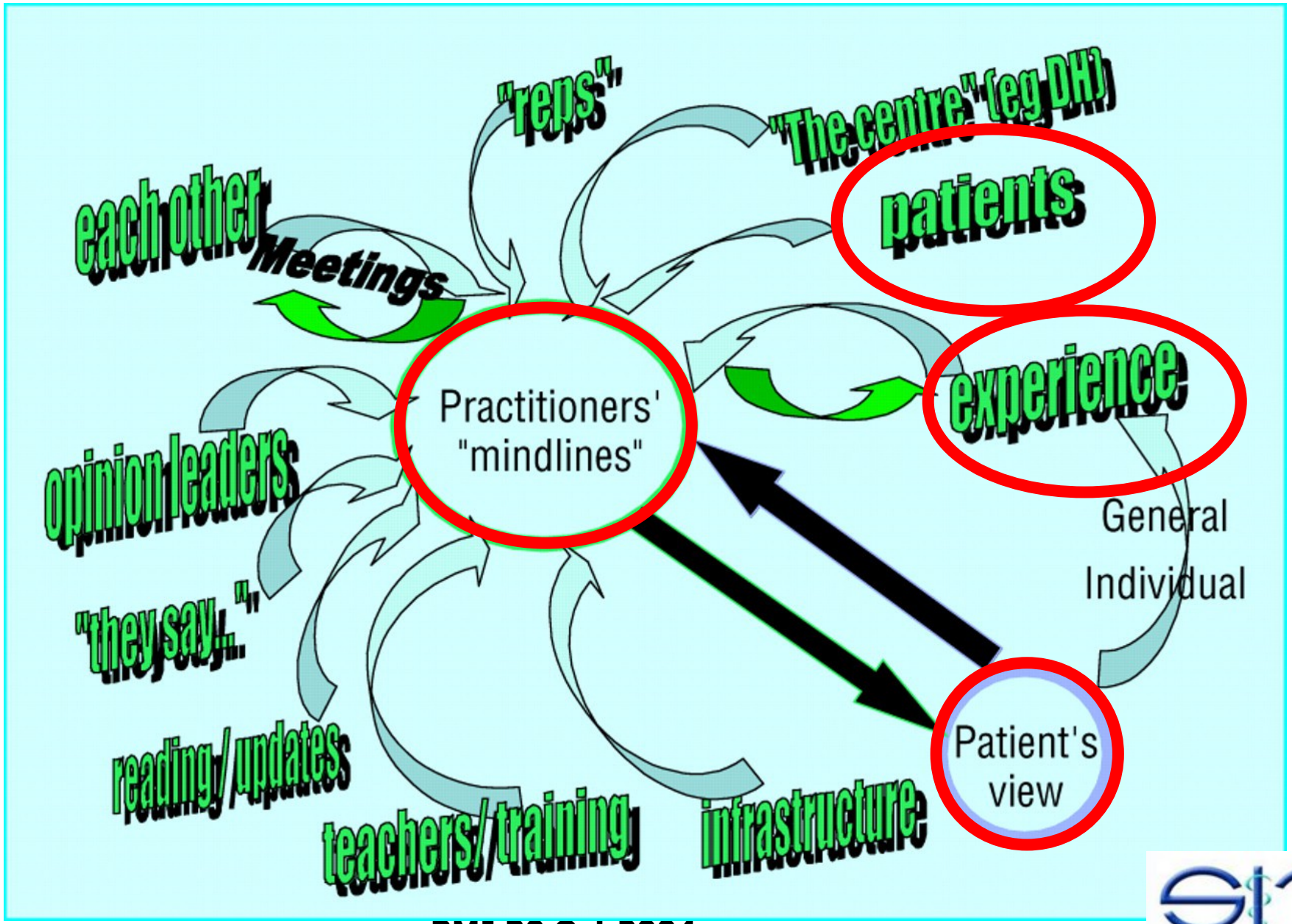
MINDLINES

Construction of mindlines



BMJ 30 Oct 2004

An Evolving Scenario

Integrated Care supported by ICT

ICT as enabler of a new model of care

4C medicine

Continuous processes

Communication

Collaboration

Confidentiality

4P medicine

Predictive

Personalized

Preventive

Participatory

Efficient patient management
Modulation of disease progress

Società Italiana
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Target personalizzato di HbA1c

Dott. Pier lorenzo Franceschi
Medico Medicina Generale

Type 2 diabetes is associated with serious complications

Diabetic Retinopathy

Leading cause of blindness in adults[1,2]

Diabetic Nephropathy

Leading cause of end-stage renal disease[3,4]

Stroke

2- to 4-fold increase in cardiovascular mortality and stroke[5]

Cardiovascular Disease

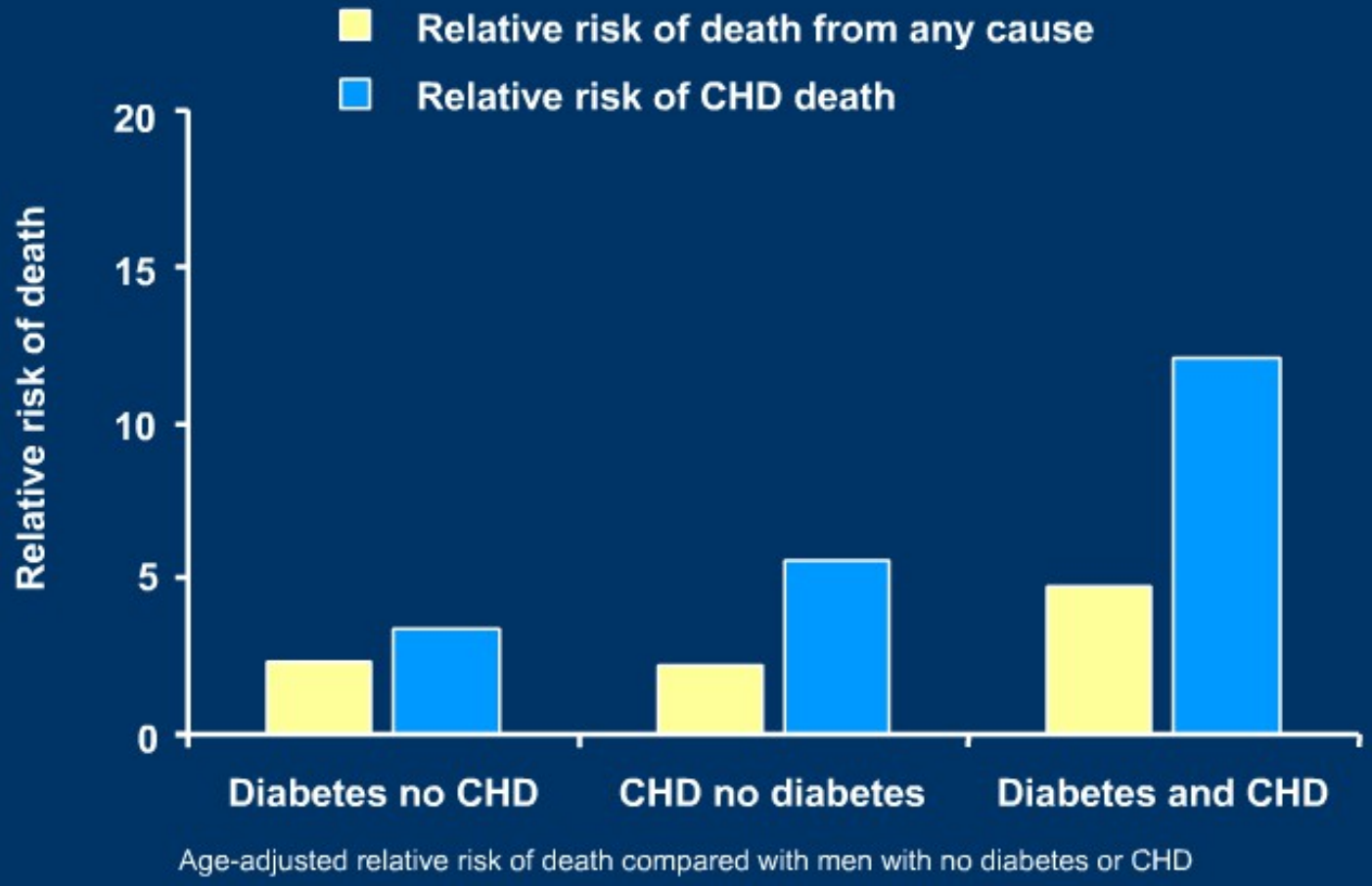
8/10 individuals with diabetes die from CV events[6]

Diabetic Neuropathy

Leading cause of non-traumatic lower extremity amputations[7,8]

[1]UK Prospective Diabetes Study Group. *Diabetes Res* 1990; 13:1–11. [2]Fong DS, *et al. Diabetes Care* 2003; 26 (Suppl. 1):S99–S102. [3]The Hypertension in Diabetes Study Group. *J Hypertens* 1993; 11:309–317. [4]Molitch ME, *et al. Diabetes Care* 2003; 26 (Suppl. 1):S94–S98. [5]Kannel WB, *et al. Am Heart J* 1990; 120:672–676. [6]Gray RP & Yudkin JS. Cardiovascular disease in diabetes mellitus. In *Textbook of Diabetes* 2nd Edition, 1997. Blackwell Sciences. [7]King's Fund. *Counting the cost*. The real impact of non-insulin dependent diabetes. London: British Diabetic Association, 1996. [8]Mayfield JA, *et al. Diabetes Care* 2003; 26 (Suppl. 1):S78–S79.

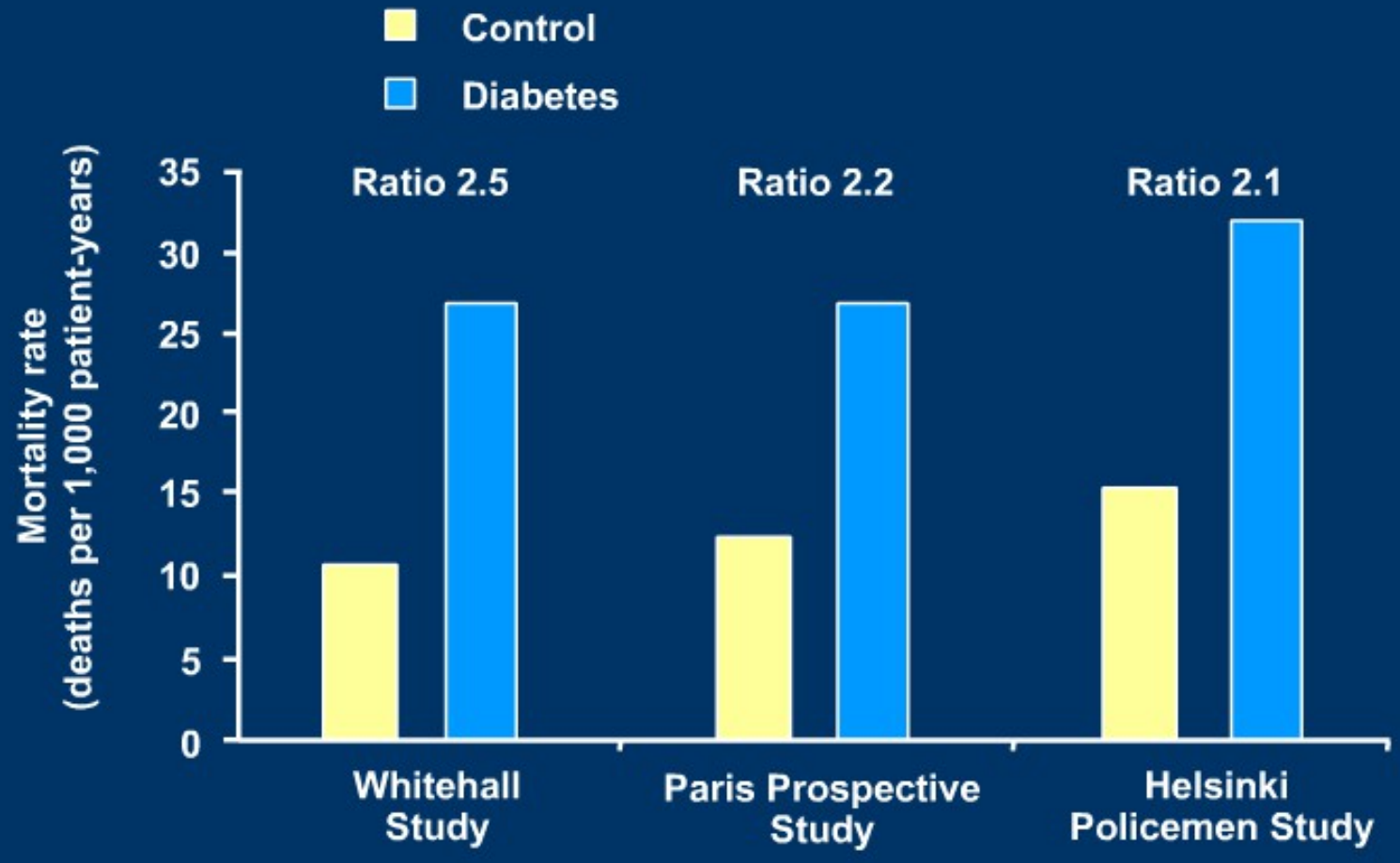
Individuals with diabetes are at increased risk of cardiovascular mortality



Age-adjusted relative risk of death compared with men with no diabetes or CHD

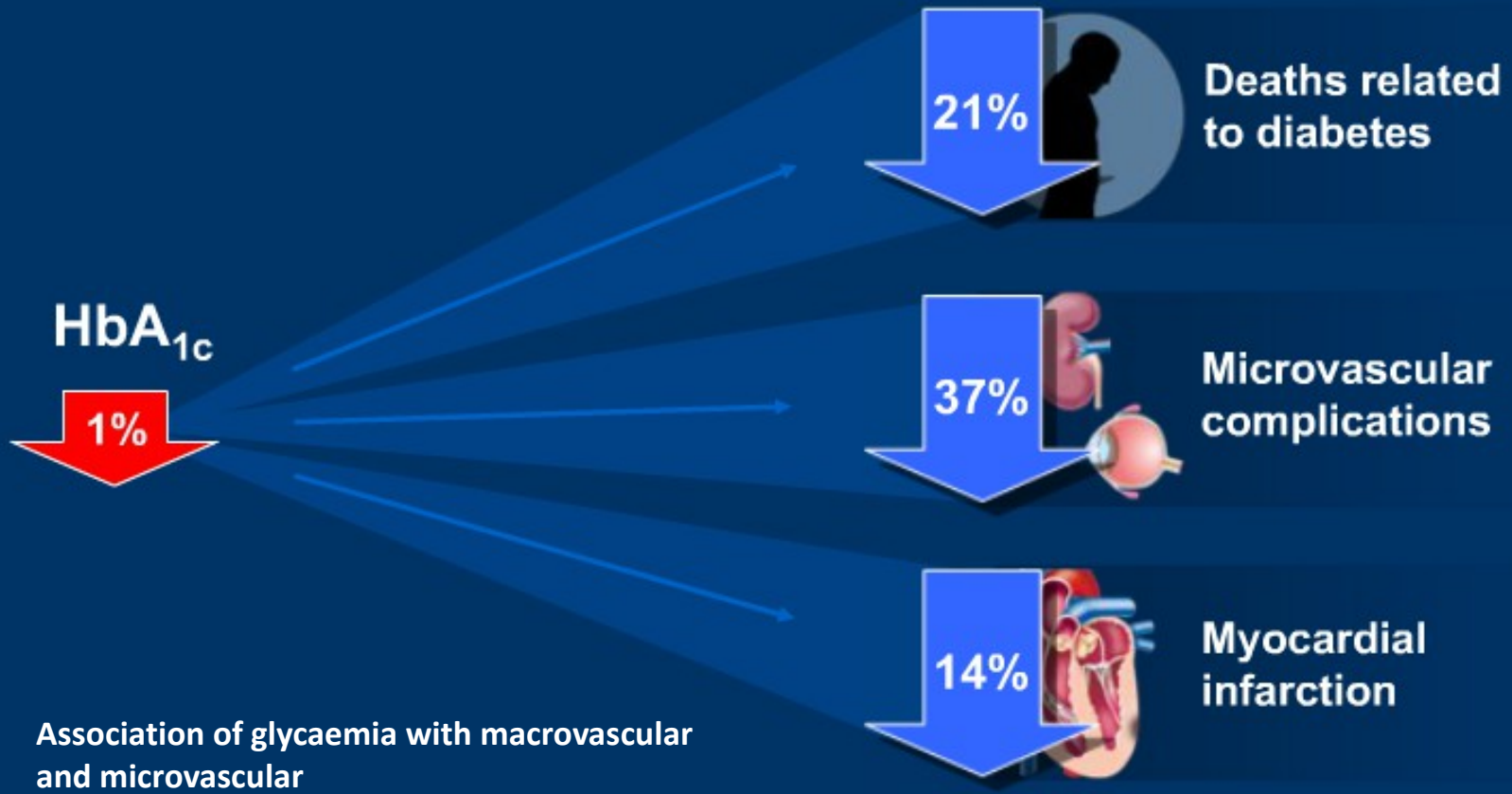
Lotufo P, *et al. Arch Intern Med* 2001; 161:242–247.

Mortality rate is doubled in individuals with diabetes



Balkau B, *et al. Lancet* 1997; 350:1680.

Lowering HbA_{1c} reduces the risk of complications



Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study

BMJ 2000; 321 doi: http://dx.doi.org/10.1136/bmj.321.7258.405
(Published 12 August 2000) Cite this as: **BMJ** 2000;321:405

Endocrinetoday

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Healio › Endocrinology › Diabetes › News

Examining the relationship between HbA1c, mortality

Endocrine Today, March 2010

Yehuda Handelsman, MD; Zachary T. Bloomgarden, MD

AAFP

Home Page > CME Center > Live Courses & Conferences > Conferences > AAFP Live! > Diabetes and Ca
Q&A > 1. Mortality decreases linearly with lower HbA1C (even <6%), but an increase in mortality was

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DM-CVD Q&A

Diabetes Monitoring

1. What percentage of persons with metabolic syndrome or prediabetes go on to develop diabetes?
2. What will be the best action to take for a patient with elevated HbA1c ≥6.5 but normal fasting glucose?
3. In diabetic patients with microalbuminuria who are already on an ACEI or ARB whose BP is well controlled (<130/80 mm Hg), do you recommend any changes?
4. Regarding HbA1c, is in-office

Self-Study

Put your CME to work

Printer-friendly version

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1. Mortality decreases linearly with lower HbA1C (even <6%), but an increase in mortality was noted in the ACCORD trial in the tight control group. Why is this? What do I do with my diabetic patients who maintain an HbA1c of 5.8 and have no symptoms? Would you back off on drug therapy?

THE LANCET

Search for in All Fields GO Advance

Survival as a function of HbA_{1c} in people with type 2 diabetes: a retrospective cohort study

A1c Targets for Patients with Diabetes and Heart Disease

Relationship of A1c and mortality in heart failure patients with diabetes.

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Nutr Metab Cardiovasc Dis. 2012 May 25. [Epub ahead of print]

HbA1c levels and all-cause mortality in type 2 diabetic patients: Epidemiological evidence of the need for personalised therapeutic targets.

Monami M, Vitale V, Lamanna C, Bartoli N, Martelli D, Zannoni S, Antenore A, Toffanello G, Marchionni N, Mannucci E.

Section of Geriatric Cardiology and Medicine, Department of Cardiov

Abstract

BACKGROUND AND AIM: The aim of the present case-
haemoglobin (HbA1c) and mortality in type 2 diabetic pat

METHODS AND RESULTS: A nested case-control study
outpatients) by sampling controls from the risk sets. Cas
of the cohort who were at risk for the same follow-up time
of diabetes (±5 years), and Charlson's Comorbidity Score
proportion of patients with each HbA1c class (<6.5%, 6.5
recorded. The lowest risk of death was observed in the H
a higher risk. The risk associated with a low (<6.5%) HbA
sample.

CONCLUSIONS: The present study suggests that glyca
considering age, co-morbidity and duration of diabetes. C
older, frail patients.

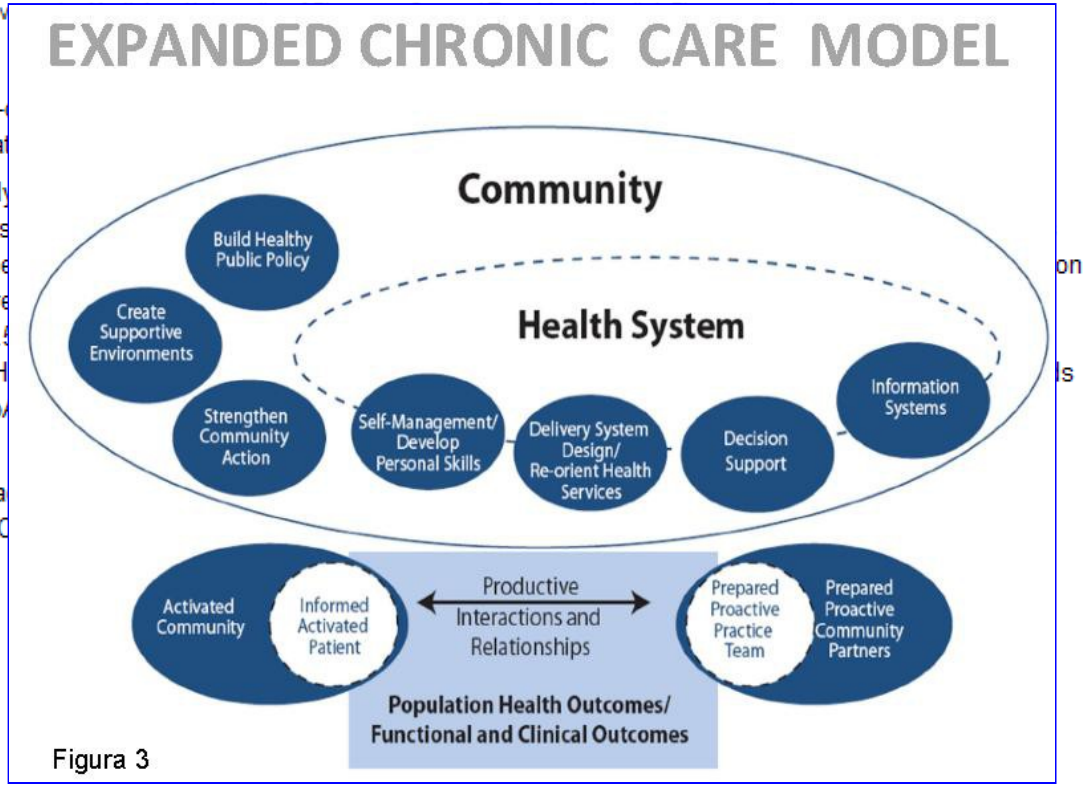


Figura 3

PERSONALIZED

GENOME

The personal genome--the future of personalised medicine?

LANCET may 2010

Società Italiana
Telemedicina @ Sanità Elettronica

Clinical assessment incorporating a personal genome

Euan A Ashley, et al., Lancet, May 1°, 2010

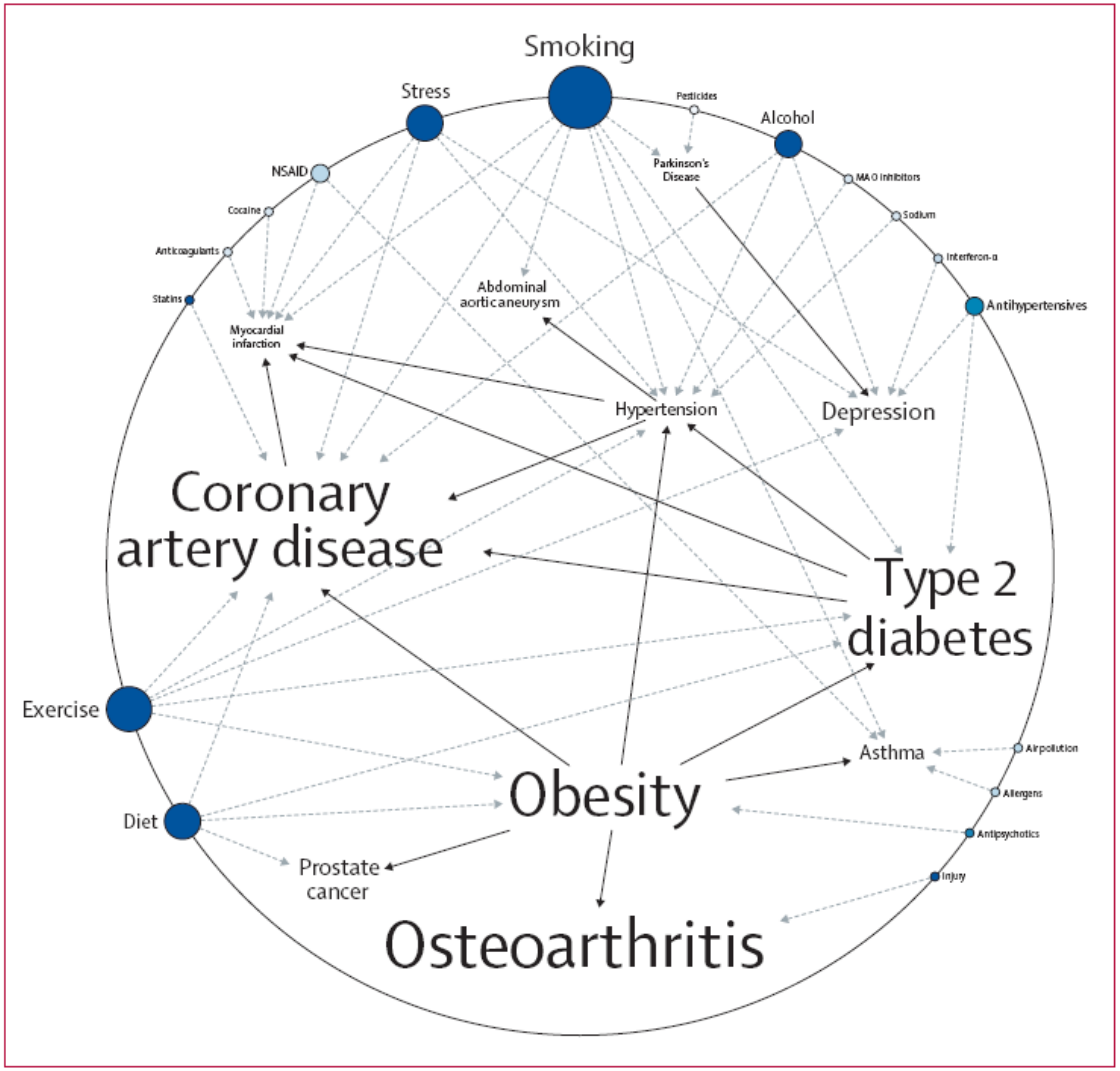
Findings Analysis of 2·6 million single nucleotide polymorphisms and 752 copy number variations showed increased genetic risk for myocardial infarction, type 2 diabetes, and some cancers. We discovered rare variants in three genes that are clinically associated with sudden cardiac death—*TMEM43*, *DSP*, and *MYBPC3*. A variant in *LPA* was consistent with a family history of coronary artery disease. The patient had a heterozygous null mutation in *CYP2C19* suggesting probable clopidogrel resistance, several variants associated with a positive response to lipid-lowering therapy, and variants in *CYP4F2* and *VKORC1* that suggest he might have a low initial dosing requirement for warfarin. Many variants of uncertain importance were reported.

Interpretation Although challenges remain, our results suggest that whole-genome sequencing can yield useful and clinically relevant information for individual patients.

Funding National Institute of General Medical Sciences; National Heart, Lung And Blood Institute; National Human Genome Research Institute; Howard Hughes Medical Institute; National Library of Medicine, Lucile Packard Foundation for Children's Health; Hewlett Packard Foundation; Breetwor Family Foundation.

Clinical assessment incorporating a personal genome

Euan A Ashley, et al., Lancet, 2010



Reducing Uncertainty:
A fifth P : PRECISION MEDICINE

Researchers and health-care providers must have **access to vary large sets of health and disease-related data linked to individual patients**. These data are also critical for the development of the **Information Commons**, the Knowledge Network of Disease, and the development and validation of the **New Taxonomy**, different from the usual **Disease-based Taxonomy**.

Società Italiana Telemedicina @ Sanità Elettronica

Geographical **I**nformation **S**ystem

System **M**edicine

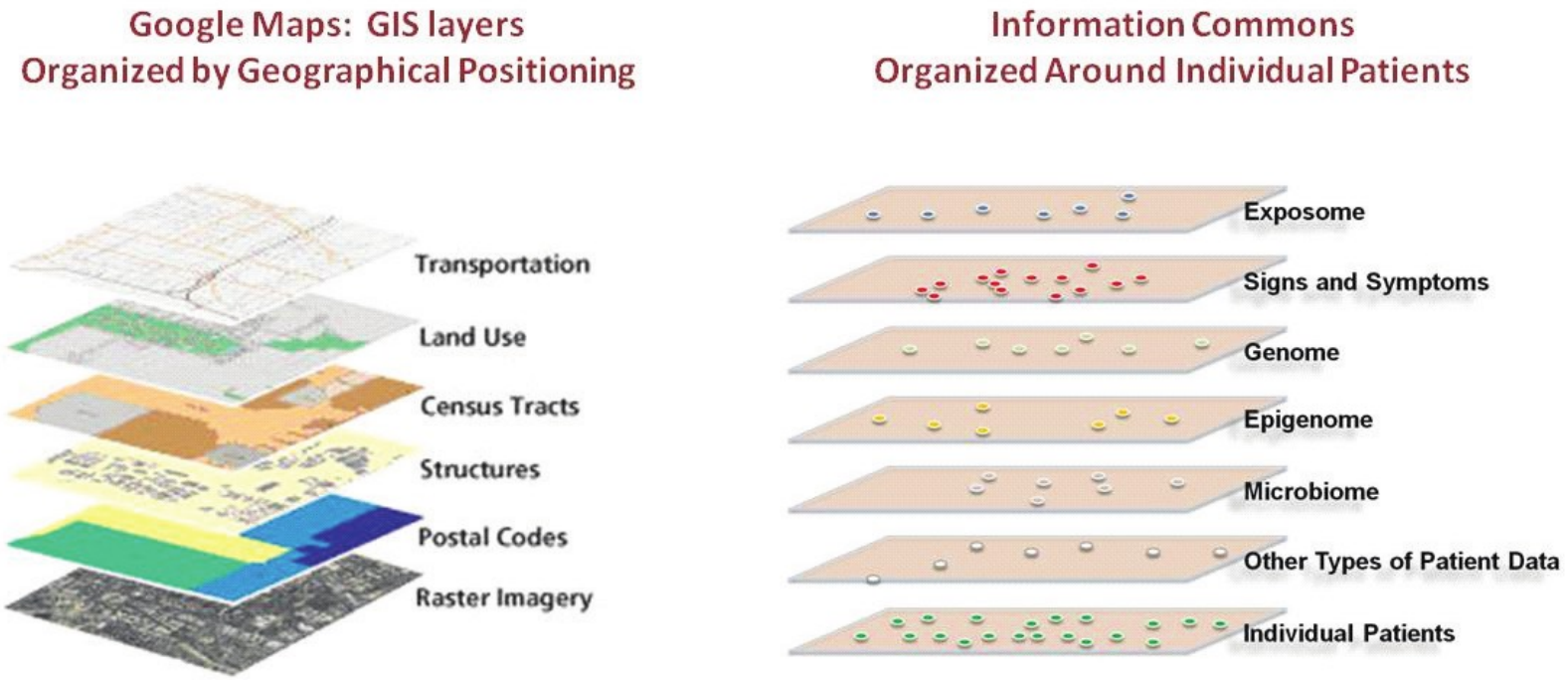
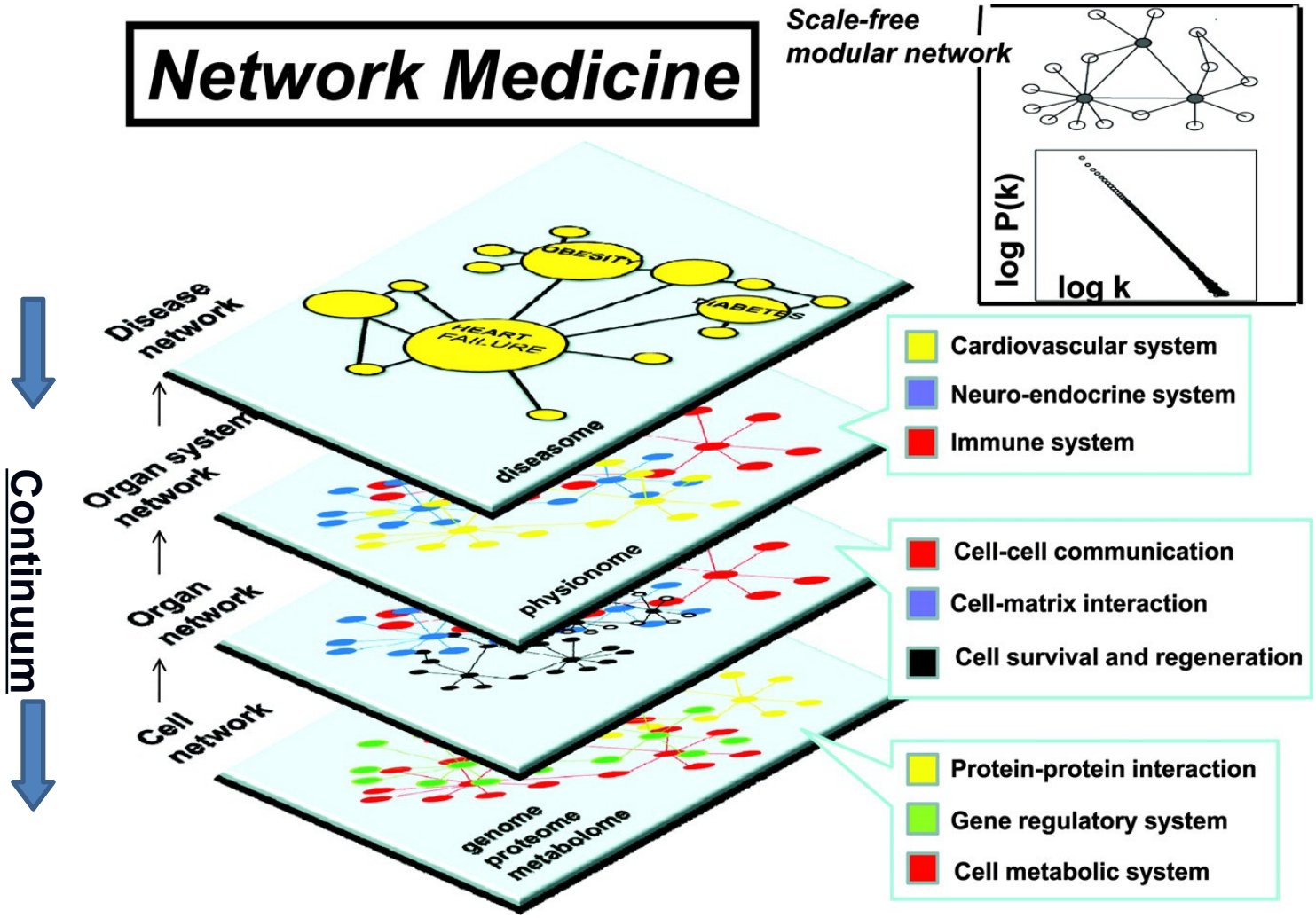


FIGURE 1-2 An Information Commons might use a GIS-type structure.
The proposed, individual-centric Information Commons (right panel) is somewhat analogous to a layered GIS (left panel). In both cases, the bottom layer defines the organization of all the overlays. However, in a GIS, any vertical line through the layers connects related snippets of information since all the layers are organized by geographical position. In contrast, data in each of the higher layers of the Information Commons will overlay on the patient layer in complex ways (e.g., patients with similar microb and symptoms may have very different genome sequences).
SOURCE: FPA 2011 (left panel).

Figure 1-2
Bitmapped

Systems biology approach to medicine creates network medicine.

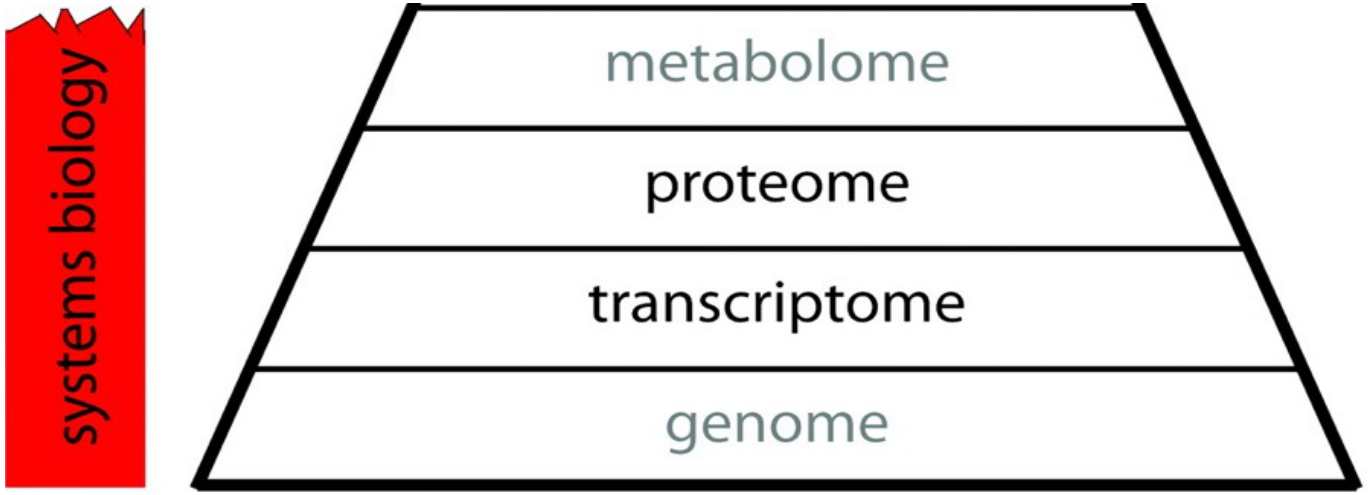


De Keulenaer G W , Brutsaert D L Circulation 2011;123:1996-2005

American Heart Association
Learn and Live

System approach to disease states

- The use of systems biology approaches to characterize disease states is just at the beginning stages.Application of systems biology to disease states will occur at multiple organizational levels with a simultaneous focus on gene network, transcriptome network, protein network and metabolic networks.



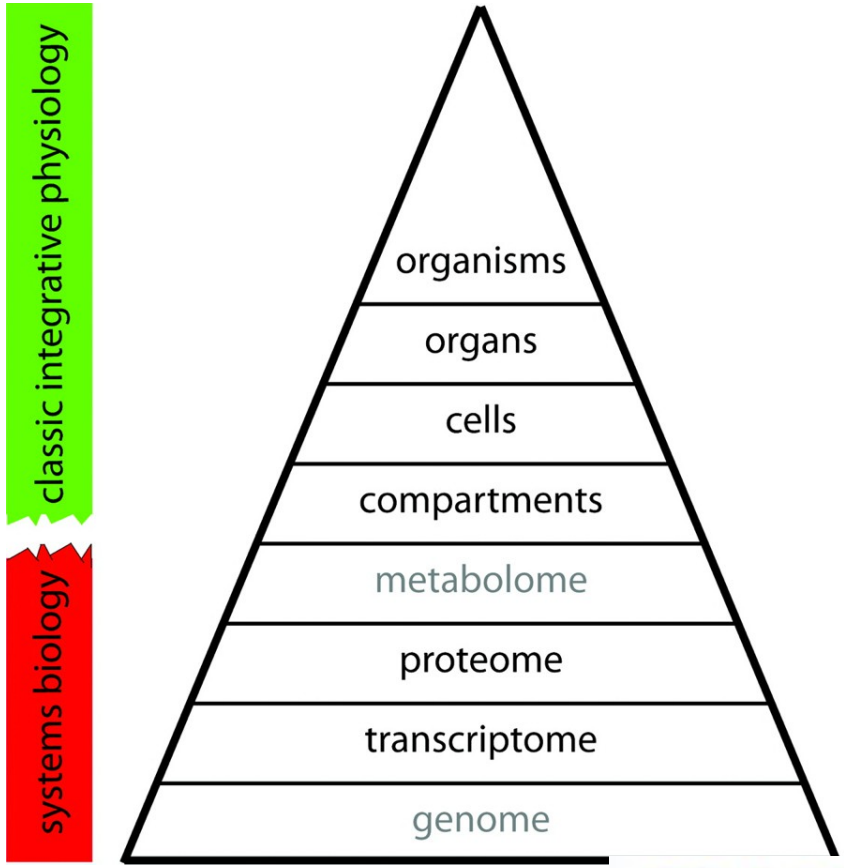
System approach to disease states

- Delineation of the systems biology of various cardiovascular diseases, including **heart failure**, is particularly challenging due to the **involvement of multiple organ systems in these disorders, each with a particular systems biology.**

- Human heart failure is a syndrome involving multiple clinical phenotypes which share an undetermined number of common pathophysiological mechanisms.

- Each of these clinical phenotypes is characterized by multiorgan derangements involving multiple biochemical pathways and numerous molecular elements in each phenotype.

- Clearly, pathophysiological changes would involve **numerous biomedomic domains**, each requiring detailed description.



Towards System Medicine

Genomic/Transcriptomic

Sensoring

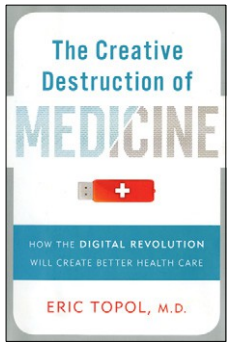
Proteomic

Metabolomic

Social Network

Book

Medicine 2.0



The Creative Destruction of Medicine: How the Digital Revolution Will Create Better Healthcare
Eric Topol. Basic Books, 2012.
Pp 303. US$27·99.
ISBN 0465025501

Watch Eric Topol talk about *The Creative Destruction of Medicine* at http://www.booktv.org/Watch/13279/The+Creative+Destruction+of+Medicine+How+the+Digital+Revolution+Will+Create+Better+Health+Care.aspx

"One of our passengers needs medical attention. If there are any doctors on board, please ring your call button." A doctor was quickly escorted to the passenger having chest pains. He pulled out his smartphone, but rather than making a phone call, he got the passenger to place his fingers on the sensors on the back of his custom iPhone that measures pulse; the real-time electrocardiogram displayed on the iPhone indicated a heart attack. The plane made an unscheduled landing and the patient lived. Science fiction? No. It's already happened, and the doctor in question was influential cardiologist Eric Topol, Director of the Scripps Translational Science Institute.

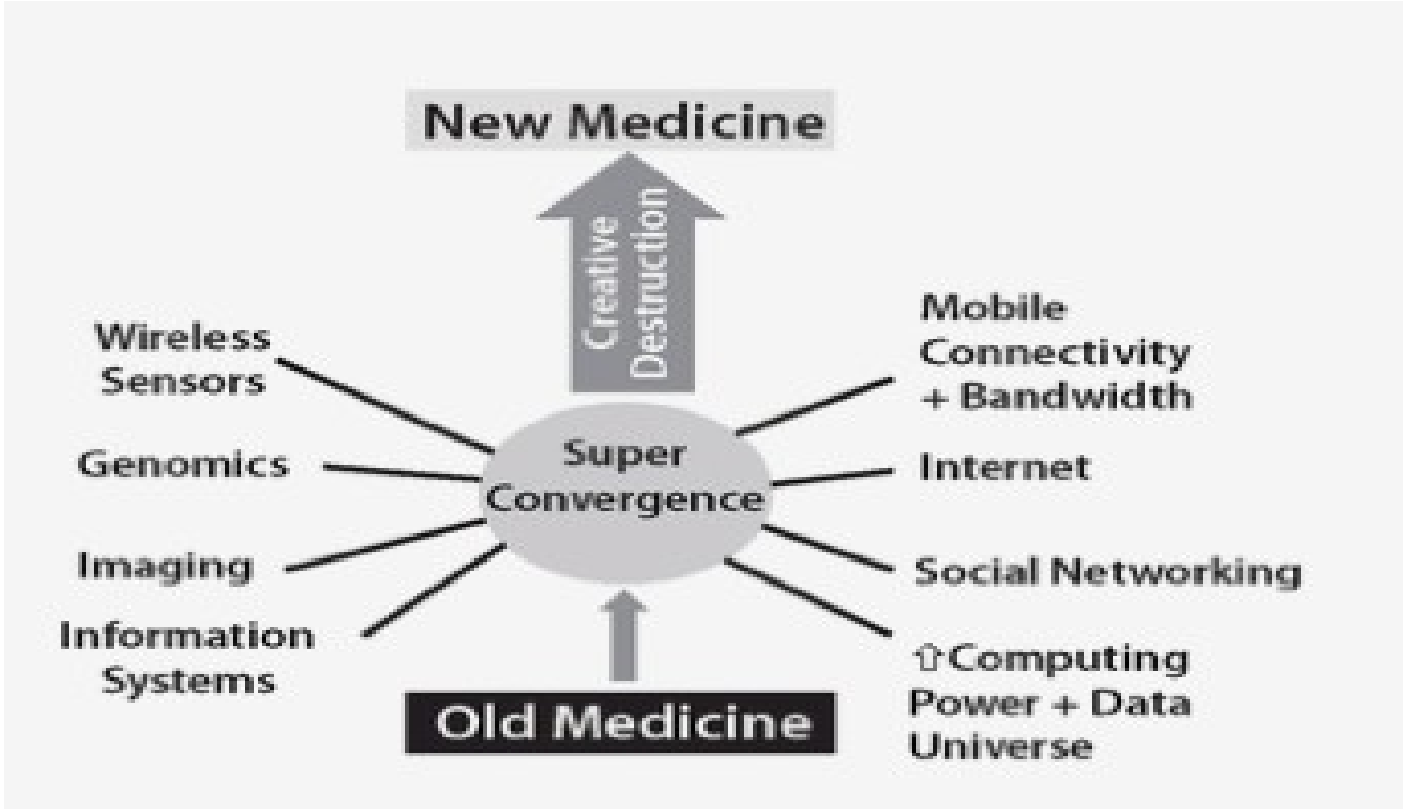
In *The Creative Destruction of Medicine*, Topol argues that the digital revolution will fundamentally change the way medicine is practised. He proposes that the convergence of genomics screening out those predisposed to rare but serious side-effects; and showing which patients cannot metabolise clopidogrel and convert it to an active drug. Topol suggests that such approaches would not only improve patient care but would also mean huge savings for the US health system. He does caution that "Currently the ability to sequence is way out in front of our ability to interpret the data", and admits that genomics has not yet delivered the goods with regard to identifying disease susceptibility. But if genomics does start delivering as Topol predicts, this could greatly accelerate the penetration of the

"'...medicine can and will be rebooted and reinvented one individual at a time'."

themselves. Physicians can use smartphones to monitor the continuous vital signs of patients living in different cities. A sophisticated smartphone app that uses a wireless sonogram sensor allows physicians to help spot leaky heart valves and other heart conditions that would traditionally require expensive hospital imaging. In his own practice, Topol uses this in place of a stethoscope, but points to its potential use for mammograms in breast cancer.

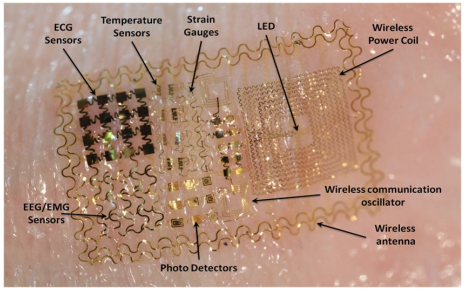
A lot of health information, such as vital signs, glucose levels, and other diagnostic data, can now be collected by individuals using wireless technologies that work on commercially available smartphones. One of my friends who recently had a jaw relocation for sleep apnoea was surprised to learn from Topol's book that she could monitor her own brainwaves during sleep with her

Figura 1. La trasformazione dalla medicina di oggi (vecchia e statica) alla nuova medicina personalizzata, resa possibile dalle nuove tecnologie ICT applicate alla persona.



Towards System Medicine

Genomic/Transcriptomic



Sensoring

Proteomic

Metabolomic

Social Network

Quaderni del Ministero della Salute

ISSN 2038-5293

23

n. 23, settembre-ottobre 2013

Criteri di appropriatezza clinica, tecnologica e strutturale nell'assistenza del paziente complesso

Ministero della Salute

Quaderni del Ministero della Salute 23

Criteri di appropriatezza clinica, tecnologica e strutturale nell'assistenza del paziente complesso

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THE END OF THE UNIVERSITY AS WE KNOW IT

by Nathan Harden

Everyone knows that change is coming to higher education, but few realize just how destructive (and creative) the