System Medicine, e-health e mobile health in Oncologia

GF Gensini

Trento, 18 settembre 2015

1992: Evidence Based Medicine

Evidence-Based Medicine

A New Approach to Teaching the Practice of Medicine

Evidence-Based Medicine Working Group D. Sackett et al

2420 JAMA, November 4, 1992—Vol 268, No. 17

evidence
open access journal published by the GIMBE Foundation

Editoriale

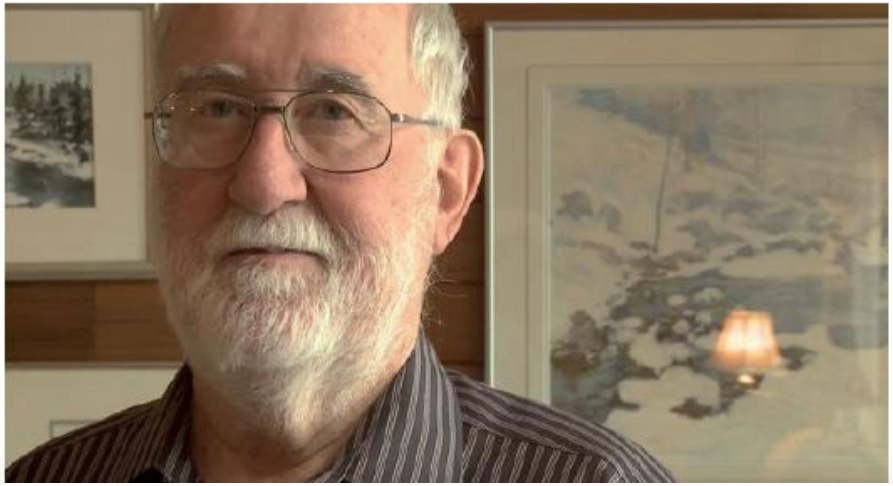
OPEN ACCESS

David Sackett: addio al padre dell'Evidence-based Medicine

Antonino Cartabellotta[1*]

[1]Medico, Fondazione GIMBE

Il "gigante tra i giganti" ci ha lasciati il 13 maggio 2015 e tutto il mondo lo ha ricordato[1-13]. Ecco il mio doveroso omaggio all'uomo che ha illuminato la mia vita professionale, ha ispirato la nascita del Gruppo Italiano per la Medicina Basata sulle Evidenze, la costituzione della Fondazione GIMBE e mi ha onorato con la sua ultima lettera agli amici.



centre for Evidence-Based Medicine TORONTO

http://ktclearinghouse.ca/cebm/

EBM is the integration of

- **best research evidence with**
- **clinical expertise and**
- **patient values.**

What kind of evidence?.

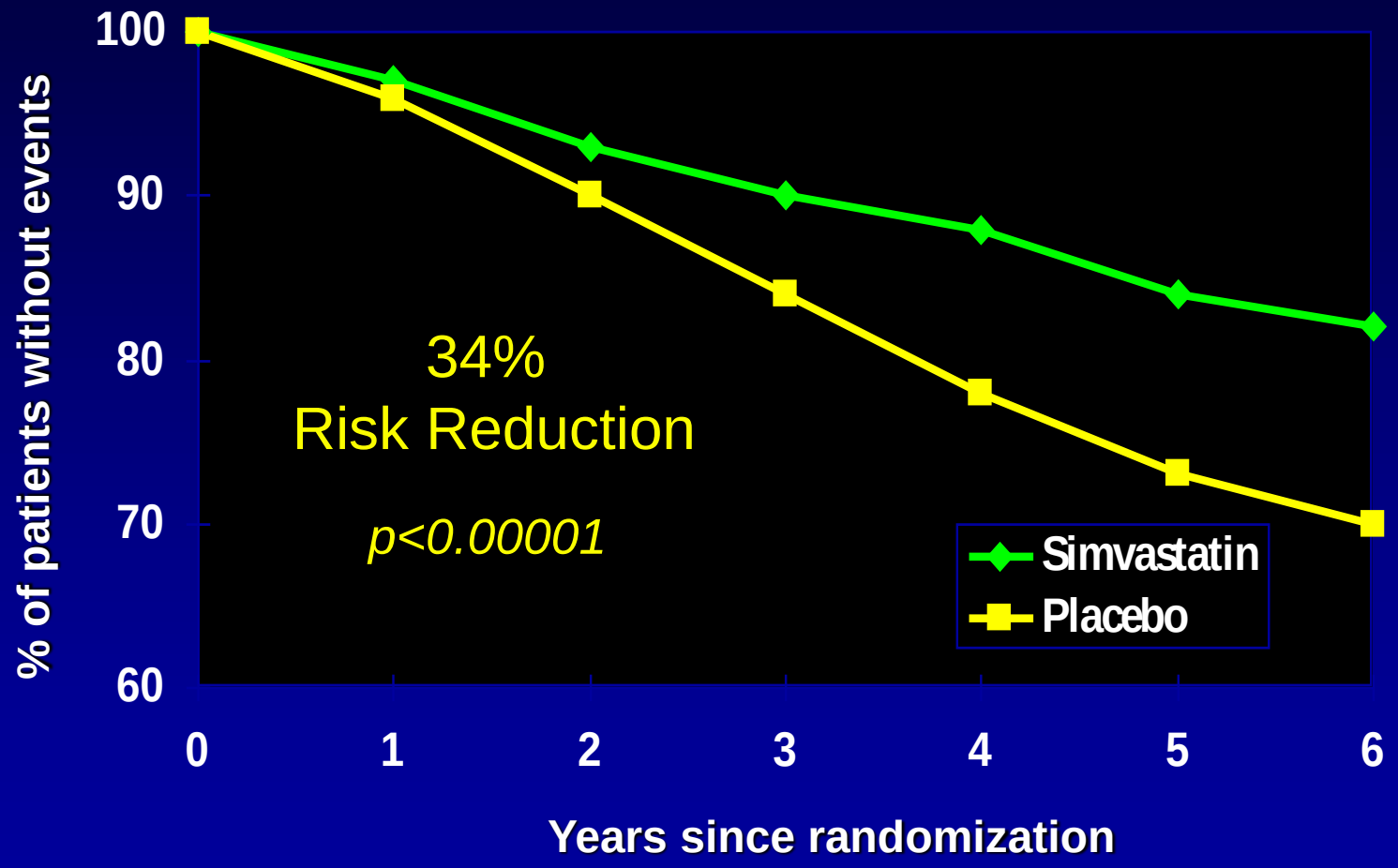
Simple, disease-related evidence

1994: an example of simple Evidence

Scandinavian Simvastatin Survival Study (4S)

The Lancet, Vol 344, November 19, 1994

Coronary Death and Nonfatal MI



Inclusion Criteria: **Prior MI** and/or angina pectoris

The Lancet, Vol 344, November 19, 1994

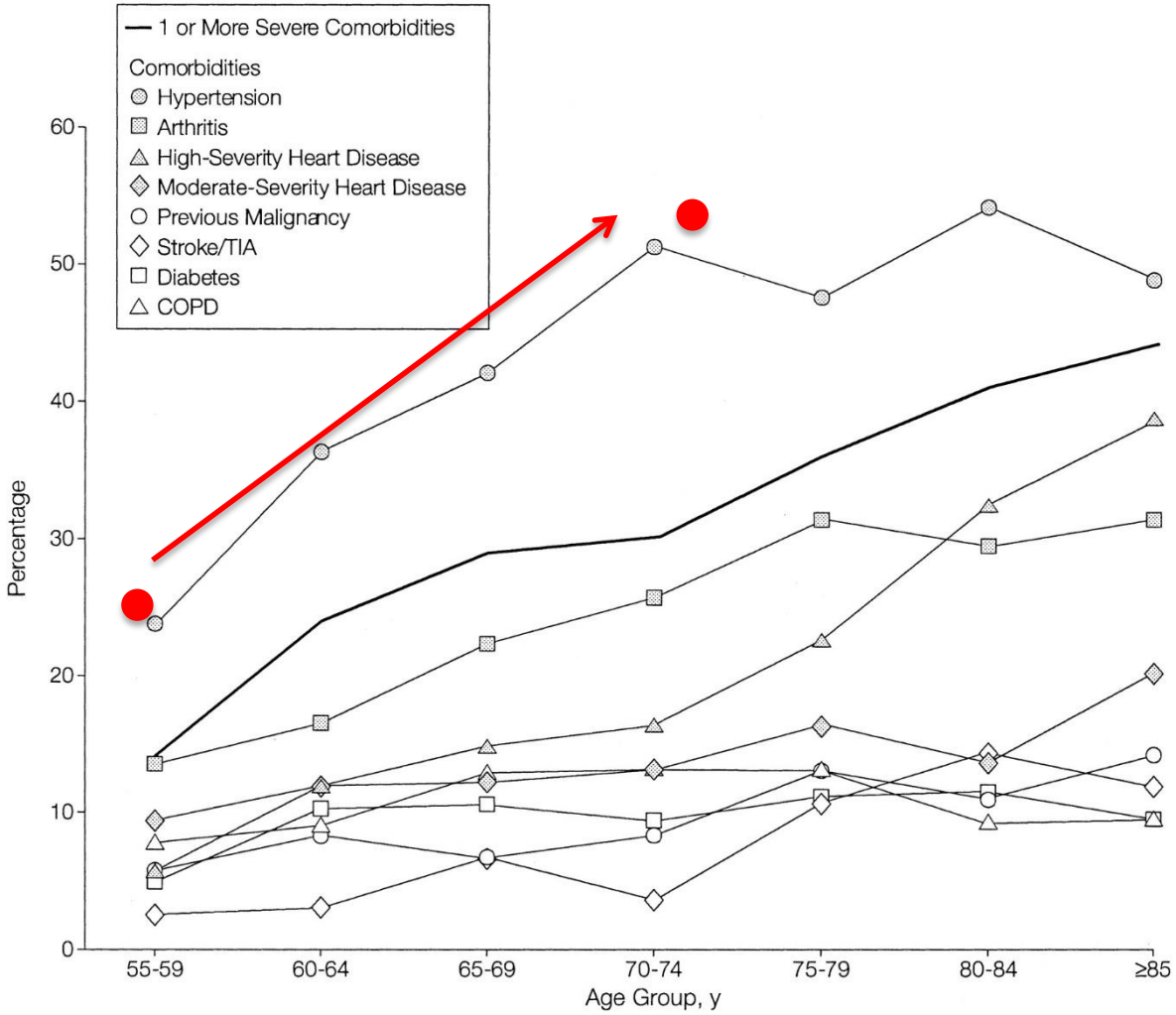
Baseline Characteristics

	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

….Changes occurred since 1992

- **Ageing**
- **Increased comorbidities - multimorbidities**
- These patients are usually **not included** in clinical trials

The “new” patients

The **unknown** “new” patients

JAMA The Journal of the American Medical Association

Home Current Issue All Issues Online First Specialties & Topics CME Mu

March 21, 2007, Vol 297, No. 11 »

« Previous Article Next Article »

Review | March 21, 2007

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

A Systematic Sampling Review FREE

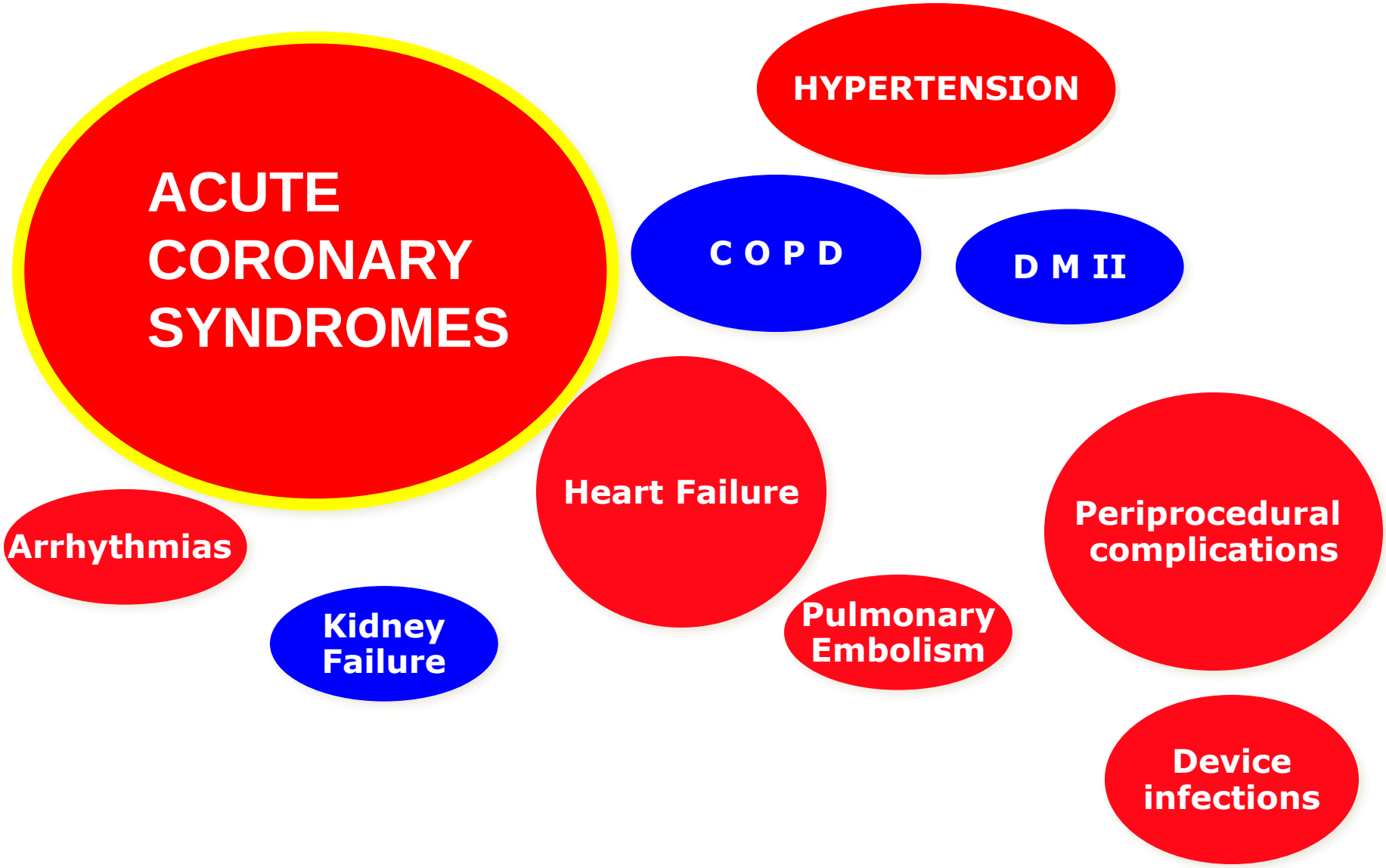
Causes of failure to enrol in the trial

- **Age** >75 (**72.1%**)
- **Comorbidities** (**81.3%**)
- **Polypharmacotherapy** (**54.1%**)

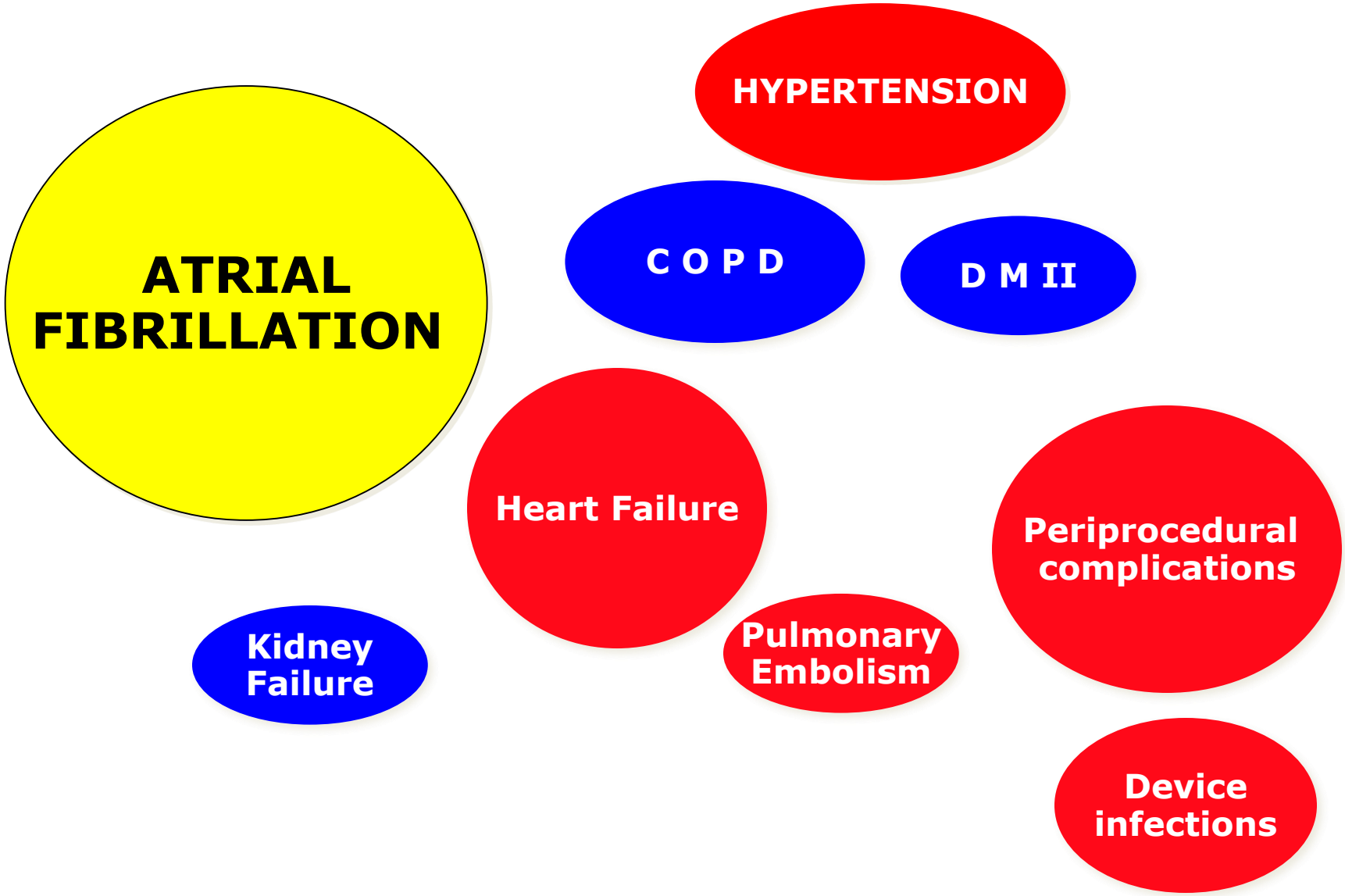
UNIVERSITÀ CATTOLICA del Sacro Cuore

Van Spall HG, 2007

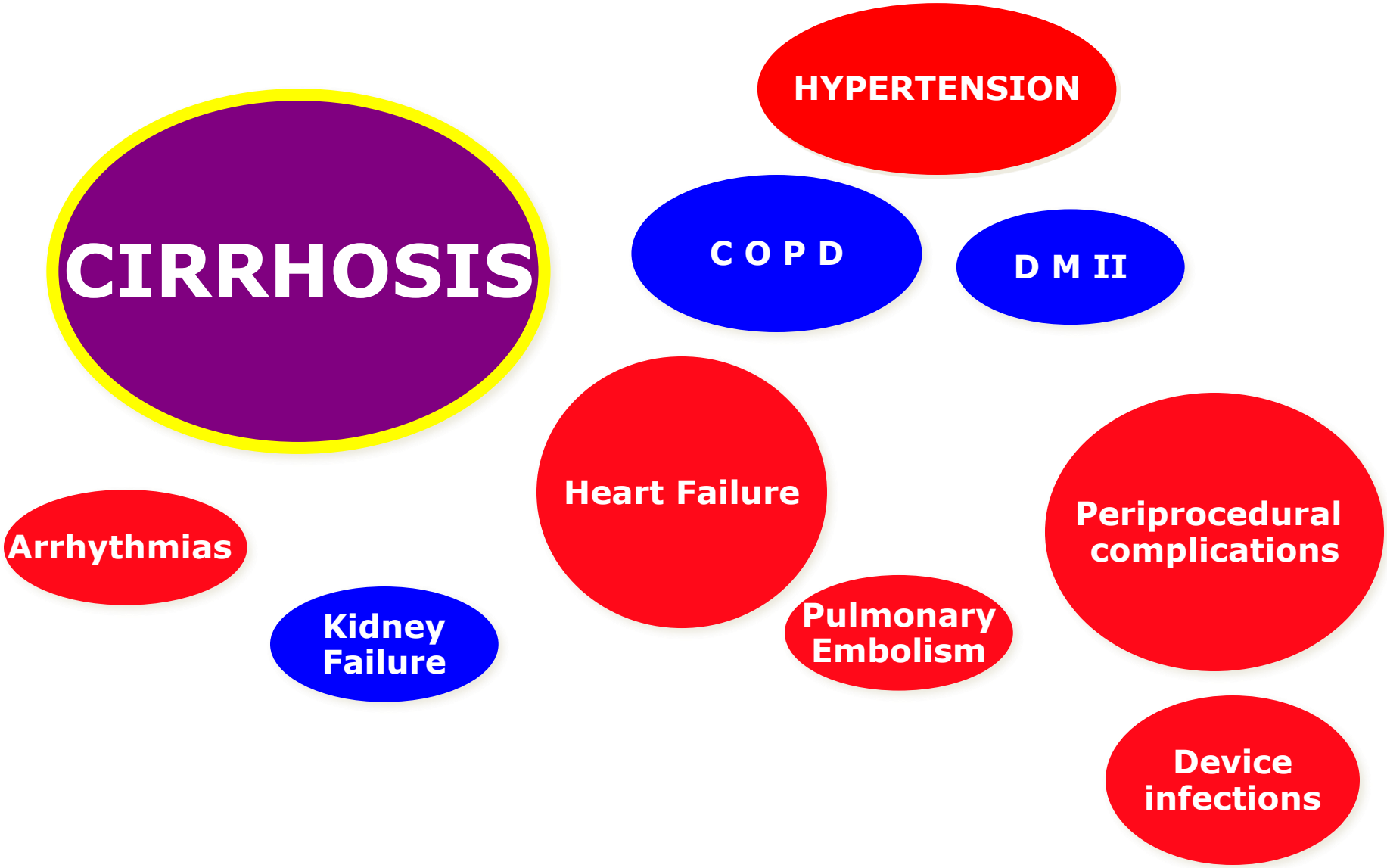
The complex clinical phenotype



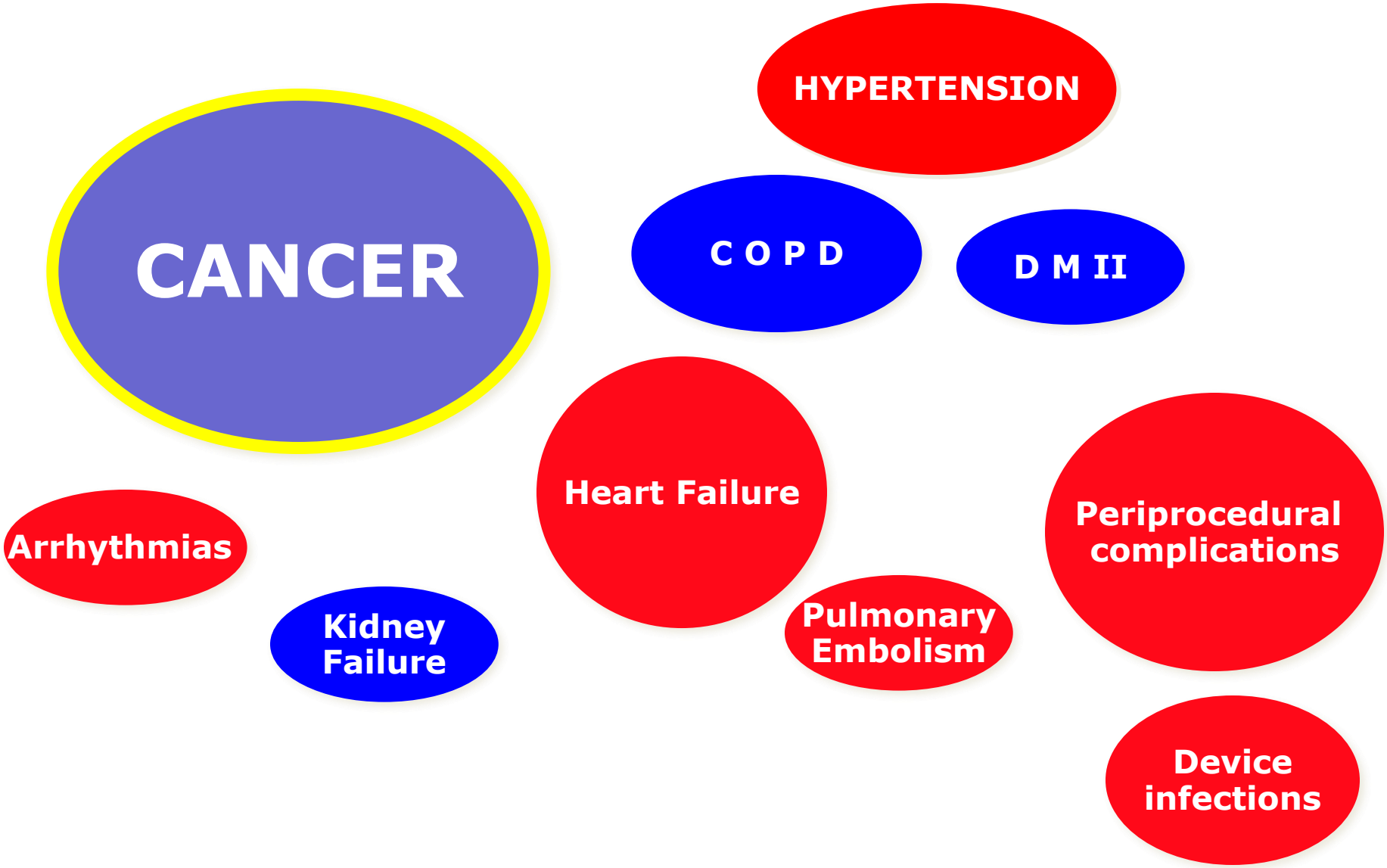
The complex clinical phenotype



The complex clinical phenotype



The complex clinical phenotype



An elementary approach to complexity

Some common measures of comorbidity

- **Disease Count (DC) (!!!?)**
- **Charlson Index (CI)**
- **Index of Co-Existent Diseases ($ICED_{DS}$) ← 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.

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

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…

Etimologia della complessità

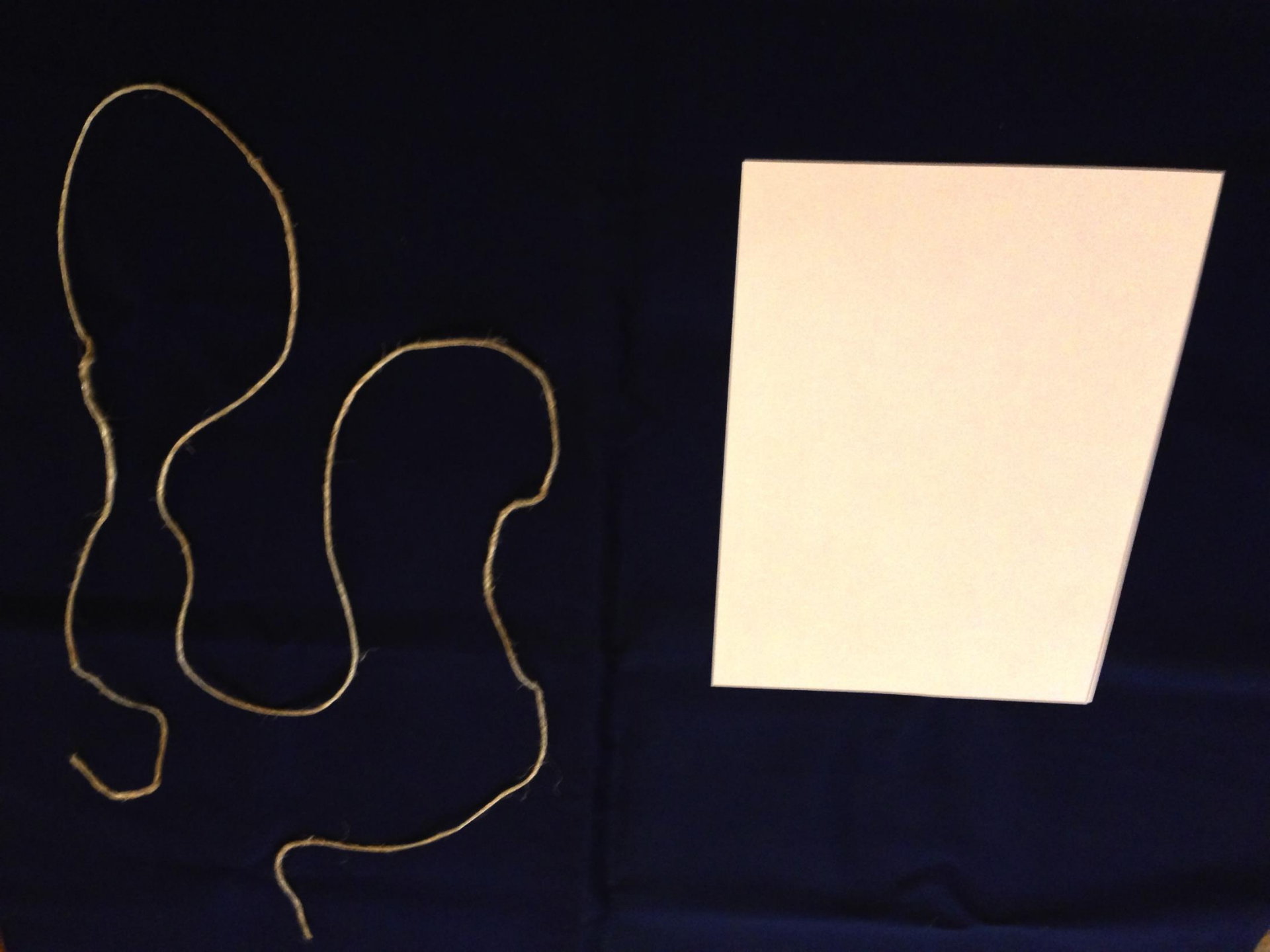
- Da cum- + plicare deriva: **Complicatus**

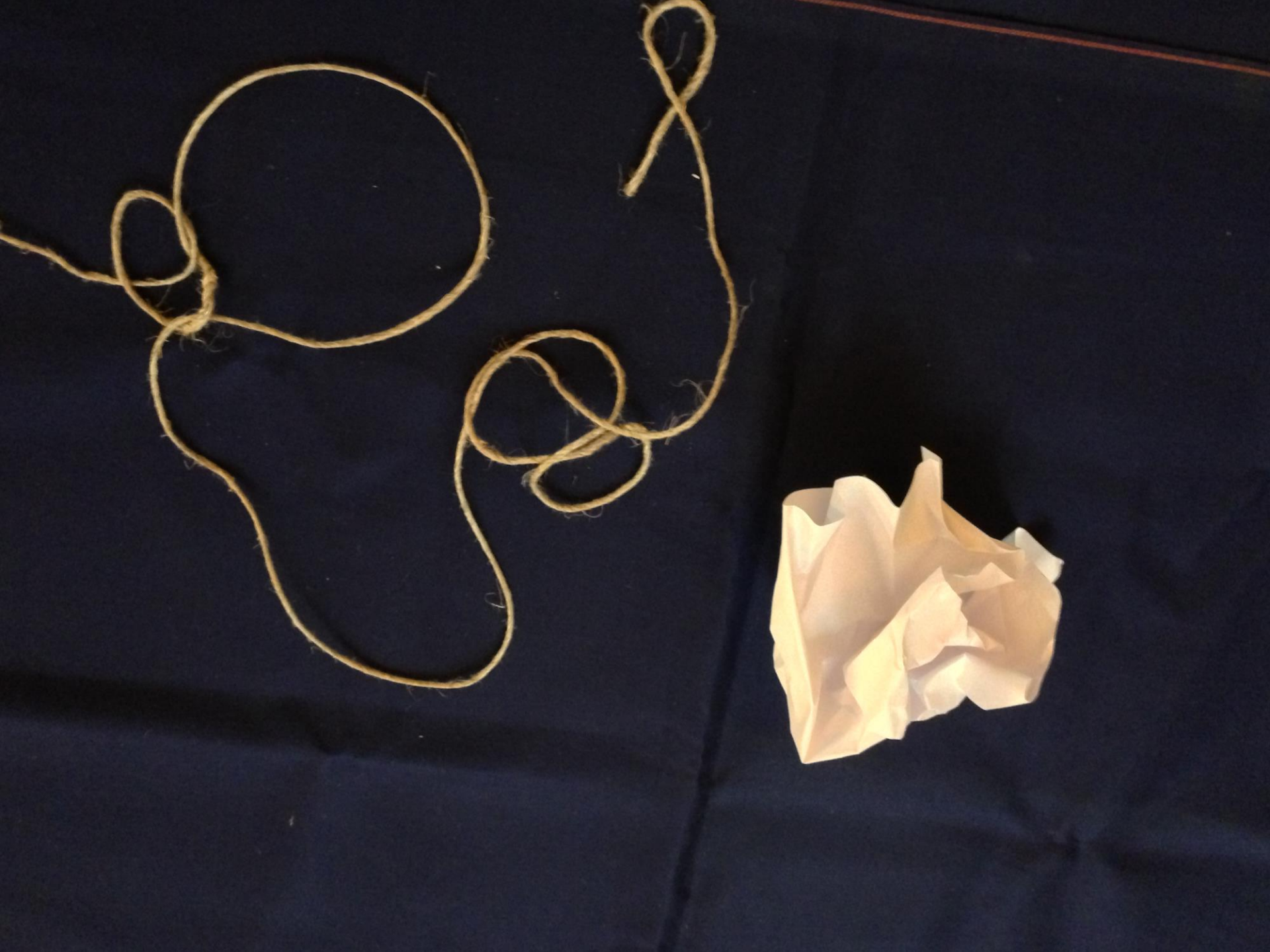
Ovvero: complicato (con pieghe)

Può essere “spiegato”

- Da cum- + plectere deriva: **Complexus**
  Ovvero: complesso (**con intrecci**)
- Non può essere “spiegato”

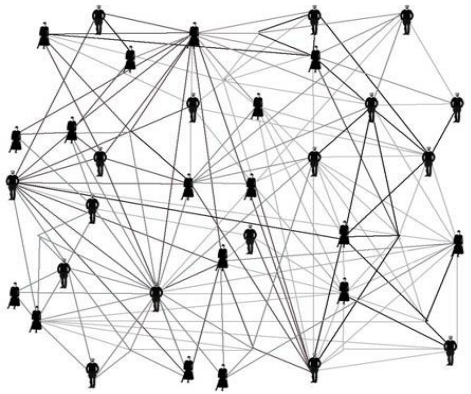
- Da **sine- + -plex** deriva: **Simplex**• Ovvero: semplice (senza pieghe)• Né complicato, né complesso

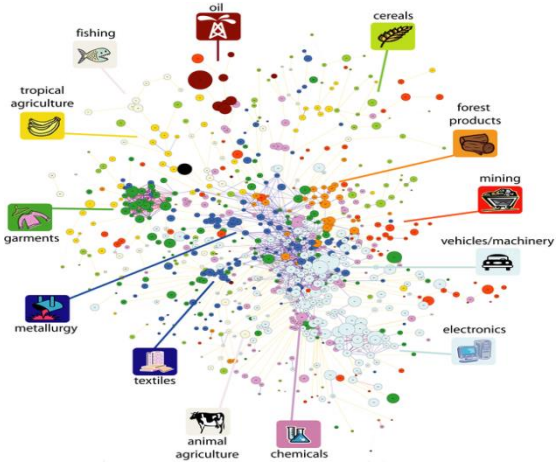


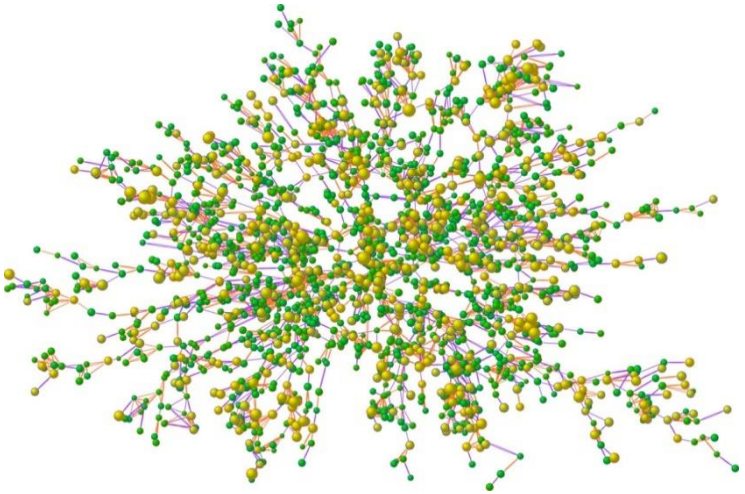


Complex Systems

- 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** .





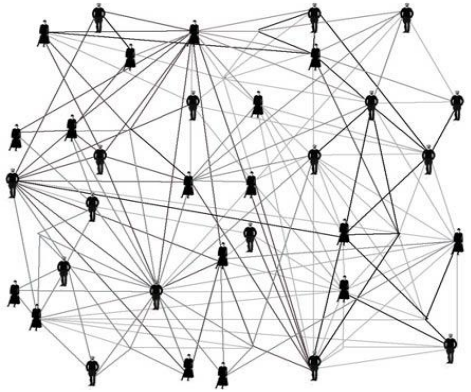


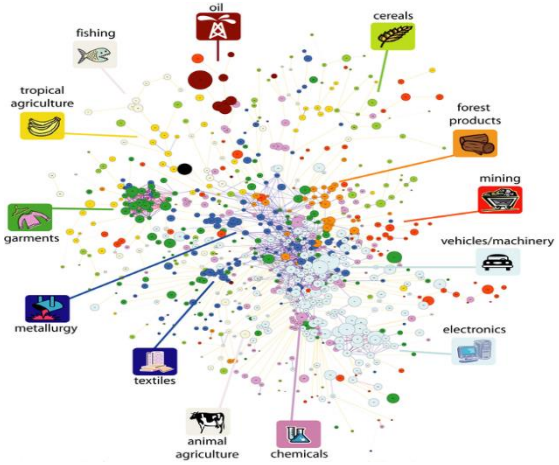
The systems perspective is rooted in the assumption that

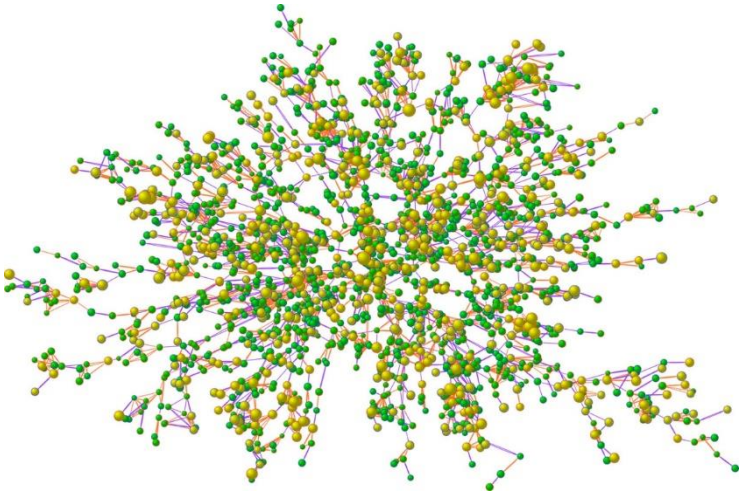
- **the forest cannot be explained by studying**
- **the trees individually.**

Complex Systems

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

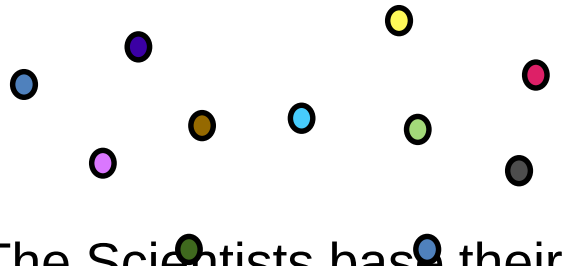






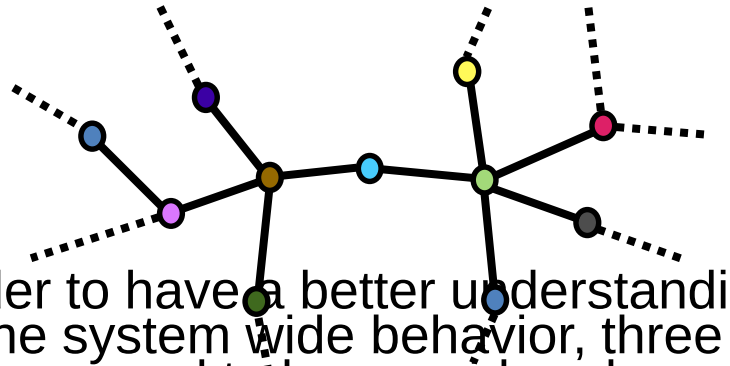
Reductionism vs System approach

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).

Space: to account for the topographic relationships between and among components.

Time: to consider the changing characteristics of each component

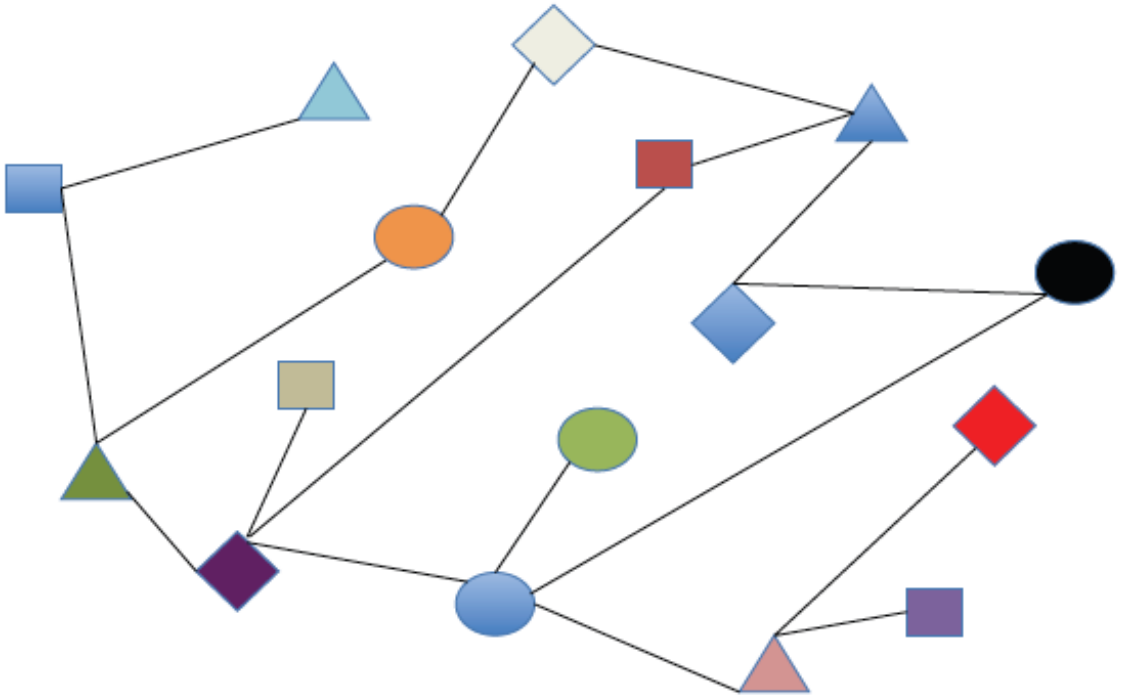
Hindawi Publishing Corporation
Molecular Biology International
Volume 2015, Article ID 698169, 8 pages
http://dx.doi.org/10.1155/2015/698169

Review Article

Systems Medicine: The Application of Systems Biology Approaches for Modern Medical Research and Drug Development

Duncan Ayers[1,2] and Philip J. Day[2]

[1]*Centre for Molecular Medicine and Biobanking, University of Malta, Msida MSD 2080, Malta*
[2]*Faculty of Medical & Human Sciences, The University of Manchester, Oxford Road, Manchester M13 9PL, UK*



Conventional (reductionist) approach

(i) Focuses on individual key molecular players (nodes)

(ii) Investigations are not time/space-inclusive

(iii) Generalised research according to medical condition

Systems approach

(i) Focuses on dynamic molecular interactions (lines)

(ii) Investigations are time/space-inclusive

(iii) Bespoke research according to individual patient

FIGURE 1: Overview of the main concepts for conventional (reductionist) and systems approaches to modern medical research.

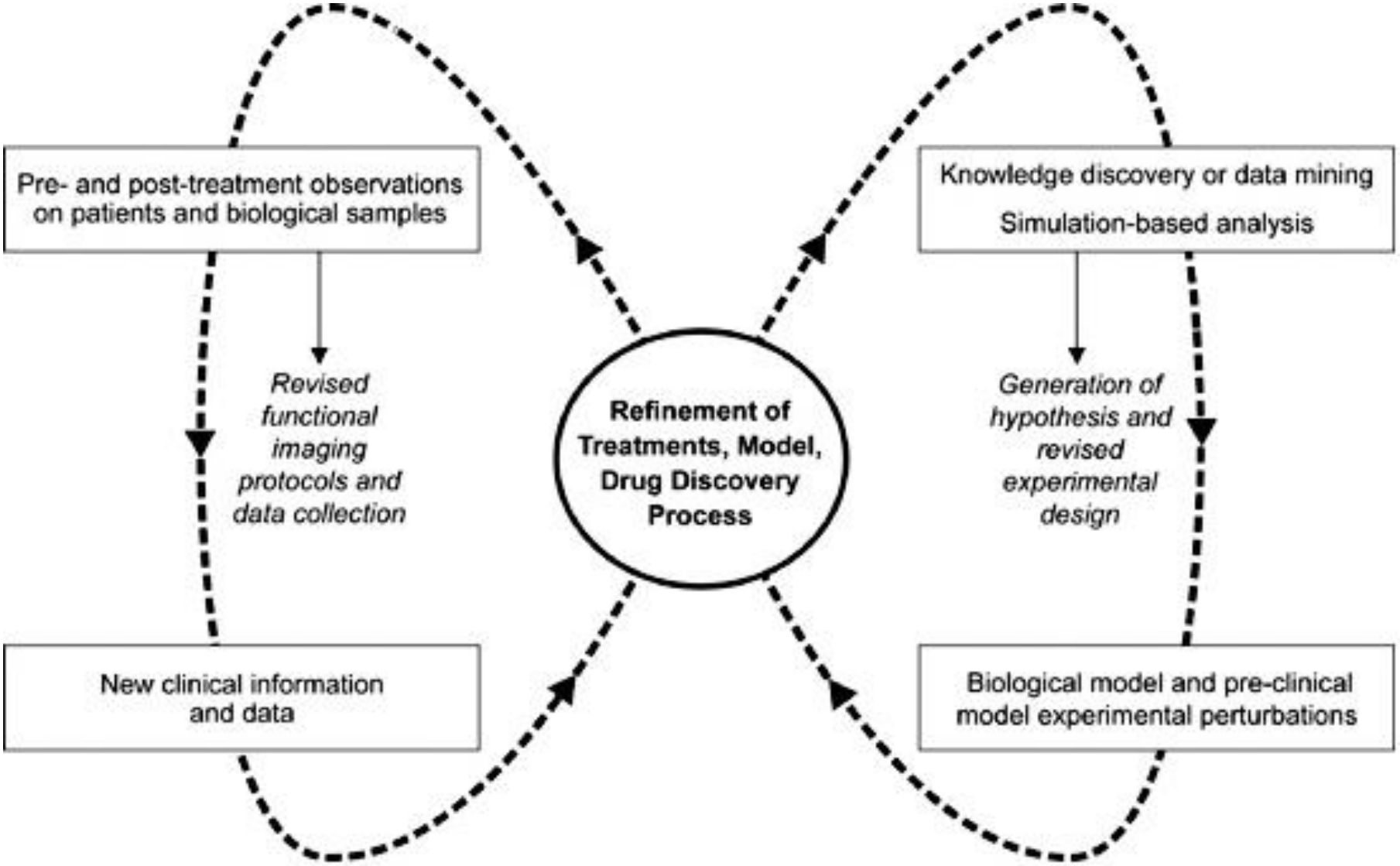
www.nature.com/clinicalpractice/onc

Systems medicine in oncology

José Costa

systems medicine integrates seven approaches,

1. **disease-focused units** that combine clinical expertise with conceptual insight into medical problems. These units identify the necessary patient population and build high quality bio-repositories linked to clinical databases.
2. **quantitative analytical sciences**, mathematical modeling and computational biology are central to data acquisition, mining and display, biophysical analyses, and **multiscale in-silico modeling.**
3. **diagnostic imaging**, nuclear medicine, and functional imaging collectively provide digitized high-density macroanatomical and functional data sets.
4. **analytical laboratory technologies** enable multimodality and quantitative interrogation of tissues and biological fluids at the **molecular level**, as well as high-density **morphological** data sets at the tissue and cellular levels.
5. **instrumentation and methodology** development adapt, design, and optimize the 'omics' methodologies required to move applications into the clinical environment.
6. **bio-engineering generates novel ways to obtain quantitative information** from patient samples and develops new methods of delivering and targeting drugs
7. **information technology and computing databases** provide the high-performance computing and high-speed infrastructure required to move, distribute, analyze, archive and manage **massive amounts of 'omics' data**, and to support the overall process and to implement specific projects.


Pre- and post-treatment observations on patients and biological samples
Revised functional imaging protocols and data collection
New clinical information and data
Refinement of Treatments, Model, Drug Discovery Process
Knowledge discovery or data mining
Simulation-based analysis
Generation of hypothesis and revised experimental design
Biological model and pre-clinical model experimental perturbations

Editorial

For reprint orders, please contact reprints@expert-reviews.com

New molecular oncology-changing era: prospects and challenges of cancer genome and integrative systems biology

Expert Rev. Anticancer Ther. 11(1), 5–8 (2011)

"At the end of the first postgenomic decade, we are now facing a genomic revolution. The use of massively parallel genome sequencing technology for the simultaneous analysis of millions of genetic variants across the genome permits the identification of causal mutations underlying common human disorders."

Conclusion

Advances in cancer biology and molecular oncology have resulted in an evidence-based standardization of multimodal treatment, including modern cytotoxic and biologic agents. This therapeutic strategy has improved survival of patients with solid cancers. Nonetheless, the rates of drug resistance, treatment failure and mortality still remain alarmingly high.

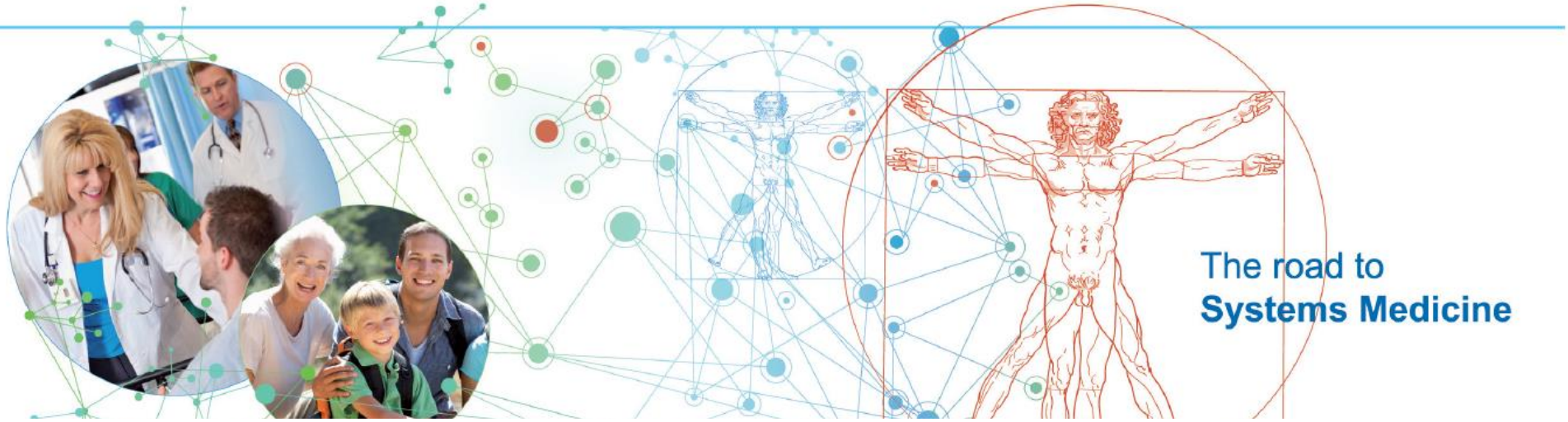
The latest developments in systems biology approaches provide a global understanding of how complex interactions of biological and environmental systems drive tumorigenesis, tumor growth and metastasis. This new era of molecular networks-based research might change oncological practice in the future.

Expert Rev. Anticancer Ther. 11(1), (2011)

CASYM EUROPE

Coordinating Action Systems Medicine
Implementation of Systems Medicine across Europe

SEVENTH FRAMEWORK PROGRAMME



Clinical needs in oncology and cardiovascular diseases as drivers for a Systems Medicine approach

REPORT

May 2014

The complexity of diagnosis

Up till now the decisional process in medicine entailed a "chain of exclusions" (guided by *evidence-based medicine)* of other diseases **in order to reach a diagnosis.**

One example is the "heuristic" thought: the highly experienced physician searches his memory for the pattern most similar to the one in question, in this way ruling out all the others.

Faced with complexity, the hierarchical exclusion process must be associated with the ability to include the various elements, as they all contribute to the genesis of the disease pattern.

The "inclusive" approach is therefore the only approach that respects the entirety of the "descriptors" necessary for guaranteeing the effectiveness of clinical medicine.

Nevertheless, there is another element typical of clinical medicine that cannot be overlooked: the **converging of different clinical conditions into one single dominant clinical element** (dyspnoea, fever, anaemia).

Il Manuale Merck dei Segni e Sintomi

Una guida sintetica e pratica all'eziopatogenesi, all'iter diagnostico e al trattamento

Robert S. Porter, MD, Editor
Justin L. Kaplan, MD, Senior Assistant Editor
Barbara P. Homeier, MD, Assistant Editor

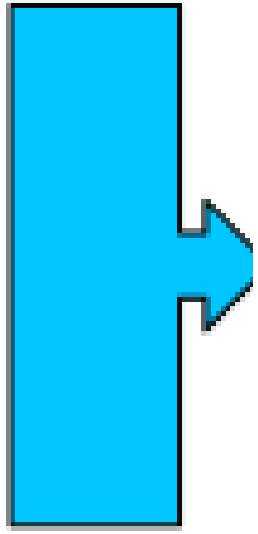
Springer

Edizione originale pubblicata da **Merck Research Laboratories**
Divisione di MERCK & CO., INC.
Whitehouse Station, NJ
2008

The complexity of one clinical element:

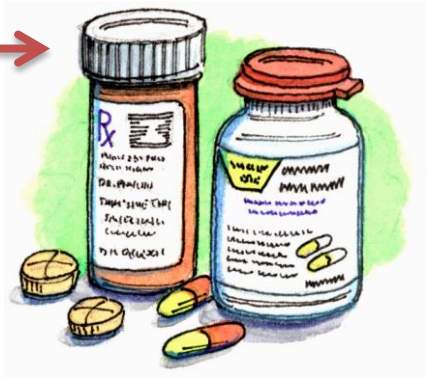
Dyspnoea

- Pulmonary embolism
- Heart failure
- Pneumonia
- Exacerbation of COPD
- Pleural effusion
- Anaemia
- Physical deconditioning



DYSPNOEA

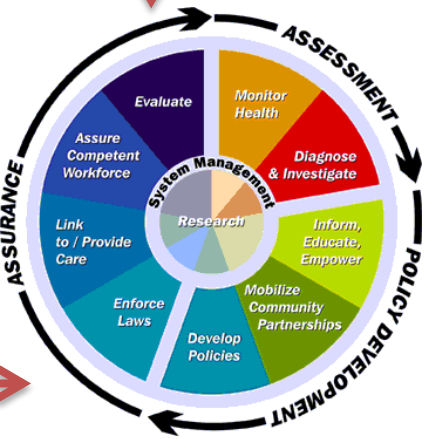
Patient



Physician

Iatrogenic complexity

Medicines



Health system

- Pulmonary embolism
- Heart failure
- Pneumonia
- Exacerbation of COPD
- Pleural effusion
- Anaemia
- Physical deconditioning

DYSPNOEA

TICAGRELOR

An Evolving Scenario

Integrated Care supported by ICT

ICT as enabler of a new model of care

ELECTRONIC HEALTH

- Electronic health dossier
- Patient summaries
- Computerised clinical charts
- Electronic prescriptions
- Telematic certifications
- Telematic medicine....

….BIG DATA….CLOUD COMPUTING

Huge ubiquitous availability of clinical data to be mutually shared and integrated within the health system

An Evolving Scenario

Integrated Care supported by ICT

ICT as enabler of a new model of care

4P medicine

Predictive

Preventive

Participatory

Personalized

Leroy Hood 2010

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

NUFFIELD DEPARTMENT OF
PRIMARY CARE
HEALTH SCIENCES

UNIVERSITY OF
OXFORD

Evidence-Based Medicine: A movement in crisis?

Professor Trish Greenhalgh FMedSci

Florence, 12th February 2015

A real case:
Mrs Patel, age 83 “feels unwell”

- Quinine 300 mg at night “**for my cramps**”
- Cholecalciferol 1 capsule daily **“for my bones”**
- Ramipril 5 mg daily **“for my blood pressure”**
- Simvastatin 40 mg daily **“for my cholesterol”**
- Aspirin / clopidogrel 75+100 mg daily **“for my blood”**
- Bisoprolol 10 mg daily **“after my heart attack”**
- Metformin 1g twice daily **“for my diabetes”**

Mrs Patel: Questions

1. What are her (many) **diagnoses**?
2. In Asian women over 80 with condition X, what is the **benefit** of drug Y and what are the **harms**?
3. In Asian women over 80 with multi-morbidity, **how does the benefit-harm balance change** as each additional drug gets added?
4. How do I go about **de-prescribing**?
5. How can I **share decisions** with Mrs Patel?

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.

N ENGL J MED 351;27 WWW.NEJM.ORG DECEMBER 30, 2004

An Evolving Scenario

Integrated Care supported by Information Communication Technology

ICT as enabler of a new model of care

P4 medicine

Predictive

Preventive

Participatory

Personalized

Efficient patient management
Modulation of disease progress

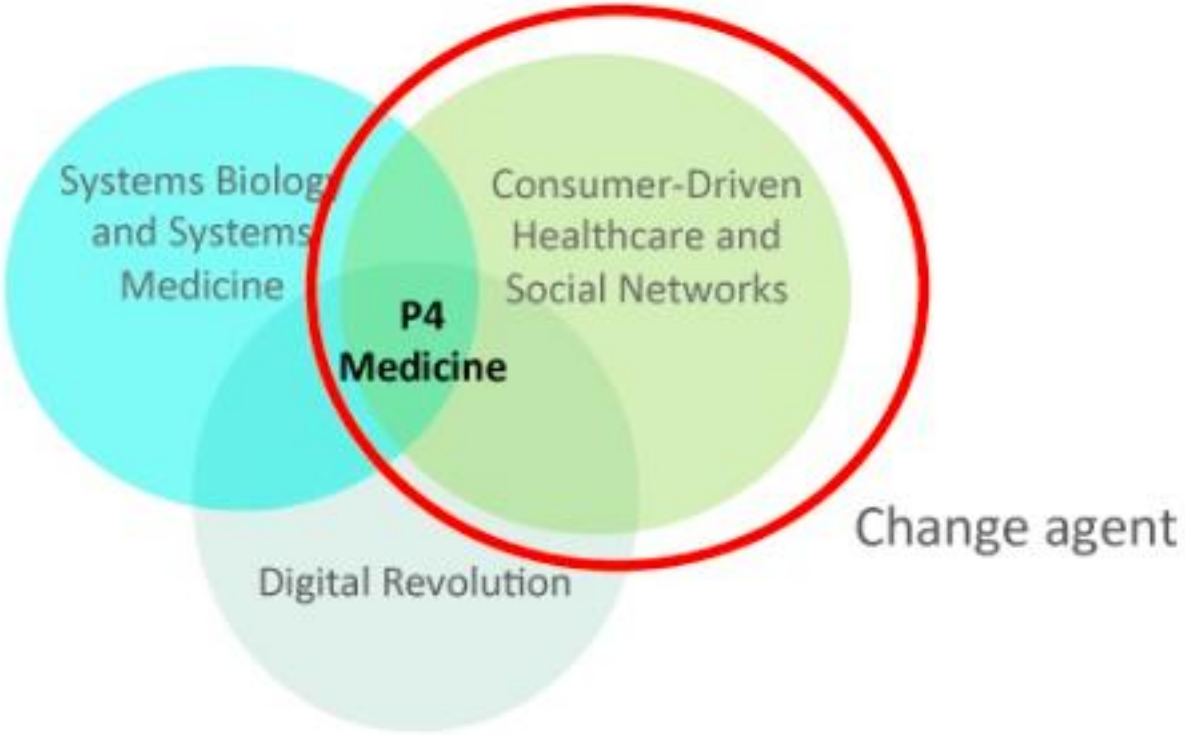
LEROY HOOD, MD, PHD

Co-founder and Chairman P4 Medicine institute

Dr. Leroy Hood is a world-renowned scientist, inventor, entrepreneur and visionary. His discoveries have permanently changed the course of biology, and revolutionized the understanding of genetics, life, and human health.

Dr. Hood created the technological foundation for the sciences of genomics (study of genes) and proteomics (study of proteins) through the invention of five groundbreaking instruments and by explicating the potentialities of genome and proteome research into the future through his pioneering of the fields of systems biology and systems medicine. Hood's instruments not only pioneered the deciphering of biological information,

The convergence of systems biology, the digital revolution and consumer-driven healthcare is transforming medicine from its current reactive mode, which is focused on treating disease, to a P4 Medicine mode, which is medicine that is predictive, preventive, personalized and participatory.



3.3• The potential of personalized medicine

There is the potential for biobanks to be key tools in enabling personalized medicine and for this to become a common approach within Europe. Personalized Medicine or 'P4 Medicine' involves the following characteristics [8,9,11,29]:

1. "*personalization*" which reflects the individual "digital genome";

2. "*predictivness*" which is due to the ability to predict the risk of certain diseases based on "personal genome" information in combination with lifestyle data, age, sex, occupation etc.;

3. "*preventiveness*" that is based on individualized risk prediction,

4. this requires an active "*participation*" of the individual concerned in proactively maintaining their health.

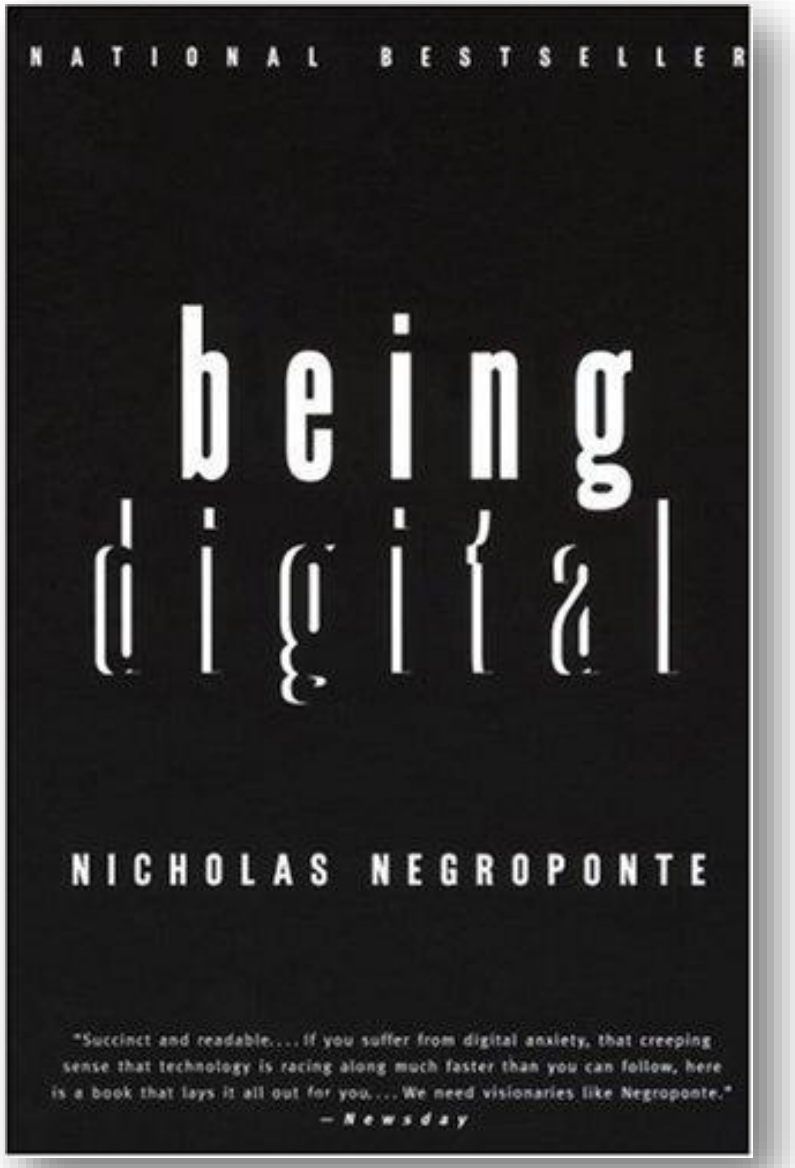
European Commission

EUR 25302 — Biobanks for Europe - A Challenge for Governance

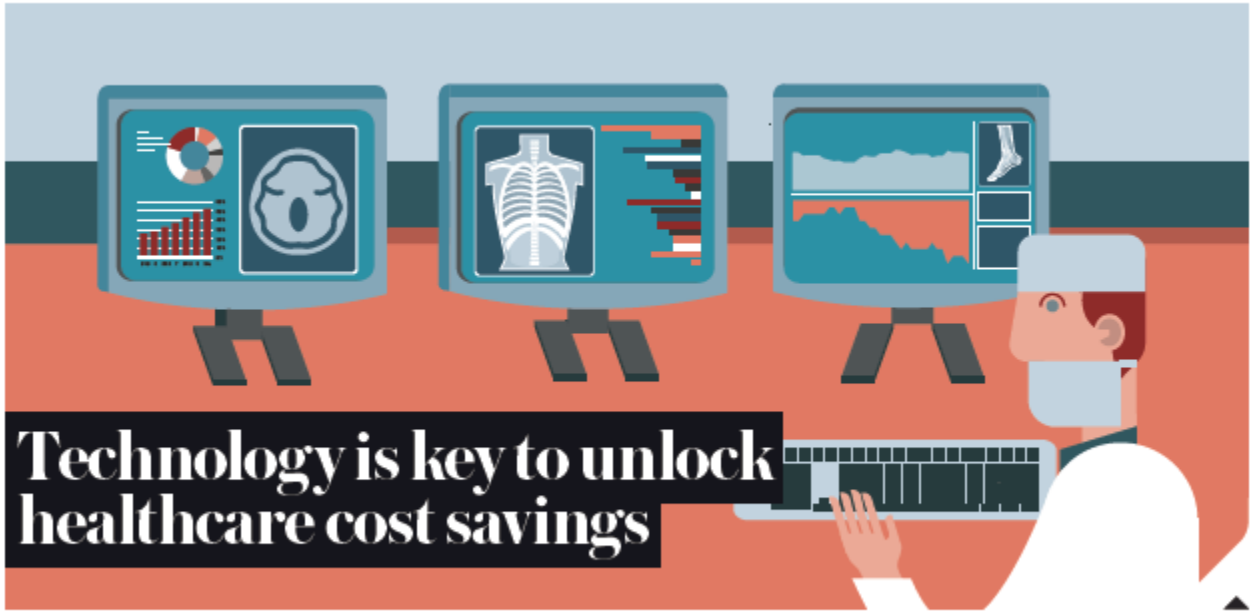
Luxembourg: Publications Office of the European Union

2012 — 63 pp — 17.6 x 25 cm

ISBN 978-92-79-22858-2
doi:10.2777/68942



By Nicholas Negroponte The founder of the MIT Media Lab



Technology is key to unlock healthcare cost savings

As the UK population ages and more people live with illness, provision of healthcare must adapt to meet the new challenge, writes **Lilian Anekwe**

Connected healthcare, incorporating latest technologies, will improve outcomes

15%

forecast global increase in long-term illness, 2010-2020

Source: World Health Organization

3m

people targeted for telehealth and telecare

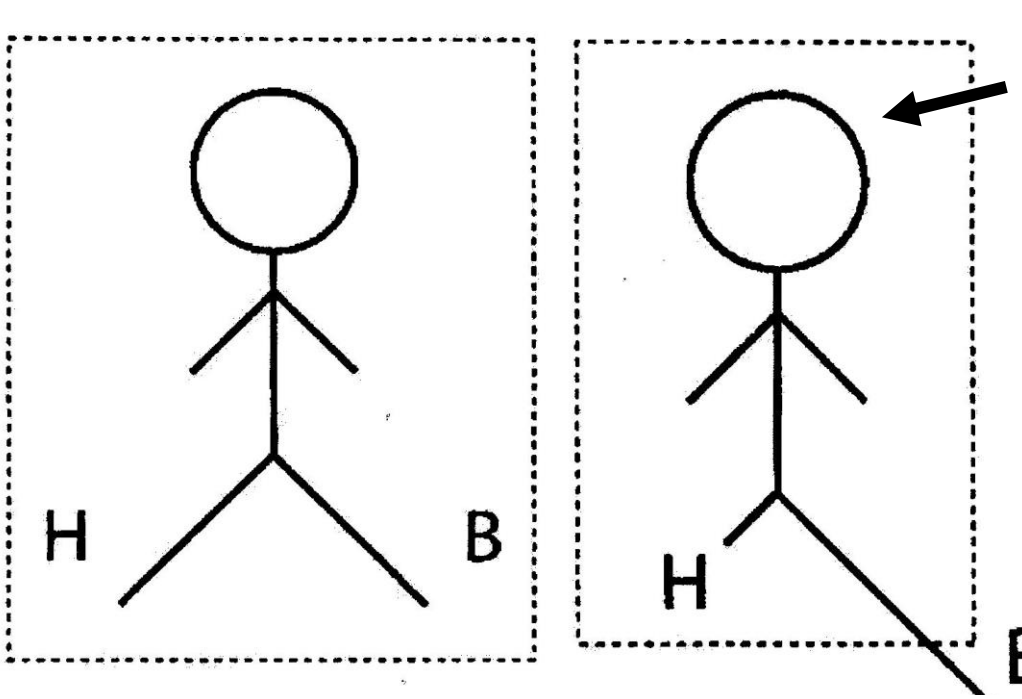
Source: Department of Health

80%

of face-to-face interactions with the NHS are unnecessary

Source: Healthcare Informatics Congress 2011

The patient as a person



Today's medicine

B: Biomedical model; H: Humanistic model

Hetlevik I. Evidence-based medicine in general practice: a hindrance to optimal medical care? Scand J Prim Health Care 2004; 22: 136-40

The Case for

PERSONALIZED MEDICINE

We shed light on the demonstrated benefits of personalized medicine and describe the pathway for its widespread adoption to improve healthcare.

"Over the past decade, we have unlocked many of the mysteries about DNA and RNA…This knowledge isn't just sitting in books on the shelf nor is it confined to the workbenches of laboratories. We have used these research findings to pinpoint the causes of many diseases, such as sickle cell anemia, cystic fibrosis, and chronic myelogenous leukemia. Moreover, scientists have translated this genetic knowledge into several treatments and therapies prompting a bridge between the laboratory bench and the patient's bedside."

Senator Barack Obama *Illin*

Introductory remarks on the Genomics and Personalized Medicine Act (S.976)
March 23, 2007

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**.

Toward Precision Medicine NCR 2011

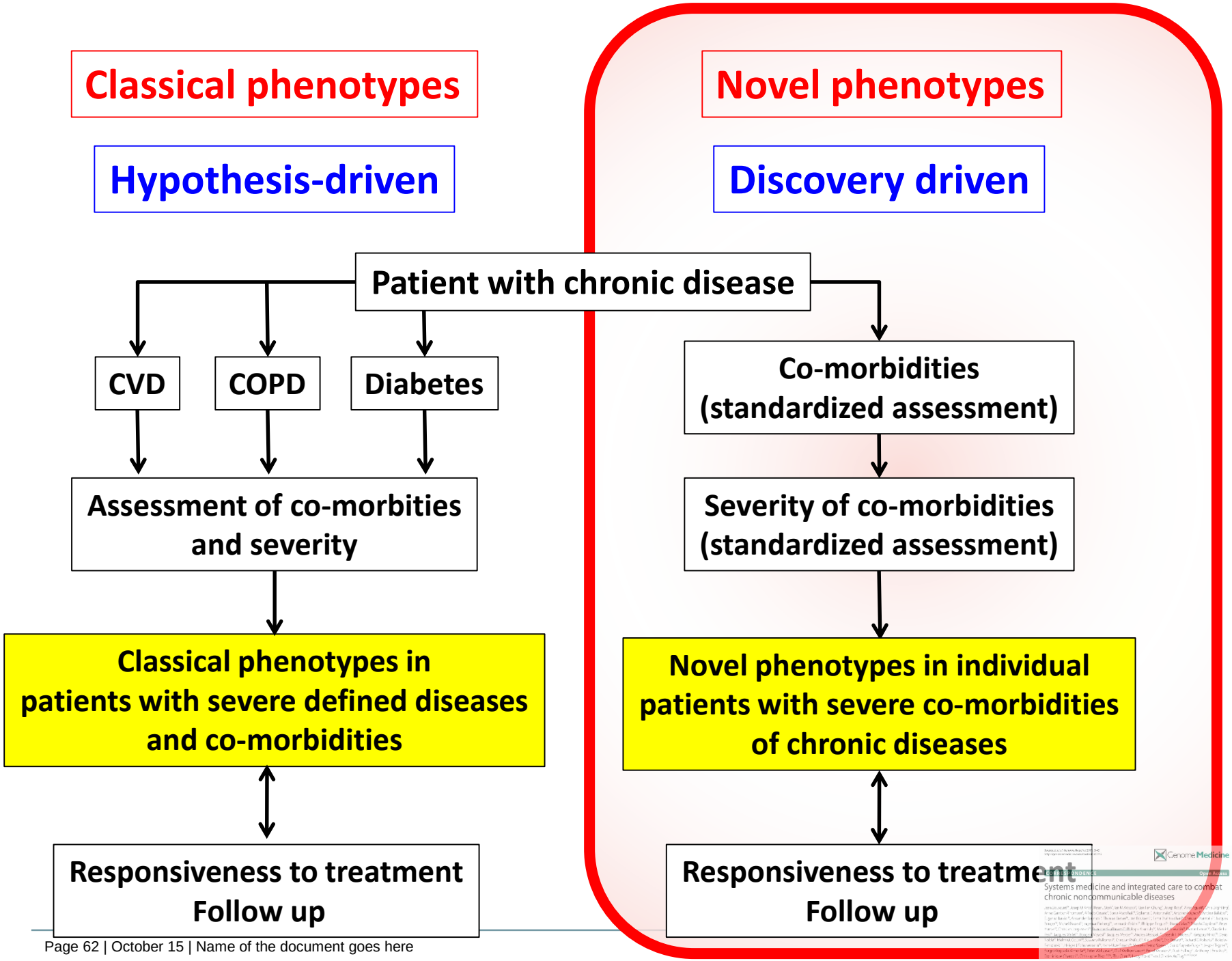
Toward Precision Medicine:
Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease

Committee on A Framework for Developing a New Taxonomy of Disease

Board on Life Sciences

Division on Earth and Life Studies

NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES


Classical phenotypes
Novel phenotypes
Hypothesis-driven
Discovery driven
Patient with chronic disease
CVD
COPD
Diabetes
Co-morbidities (standardized assessment)
Assessment of co-morbities and severity
Severity of co-morbidities (standardized assessment)
Classical phenotypes in patients with severe defined diseases and co-morbidities
Novel phenotypes in individual patients with severe co-morbidities of chronic diseases
Responsiveness to treatment Follow up
Responsiveness to treatment Follow up

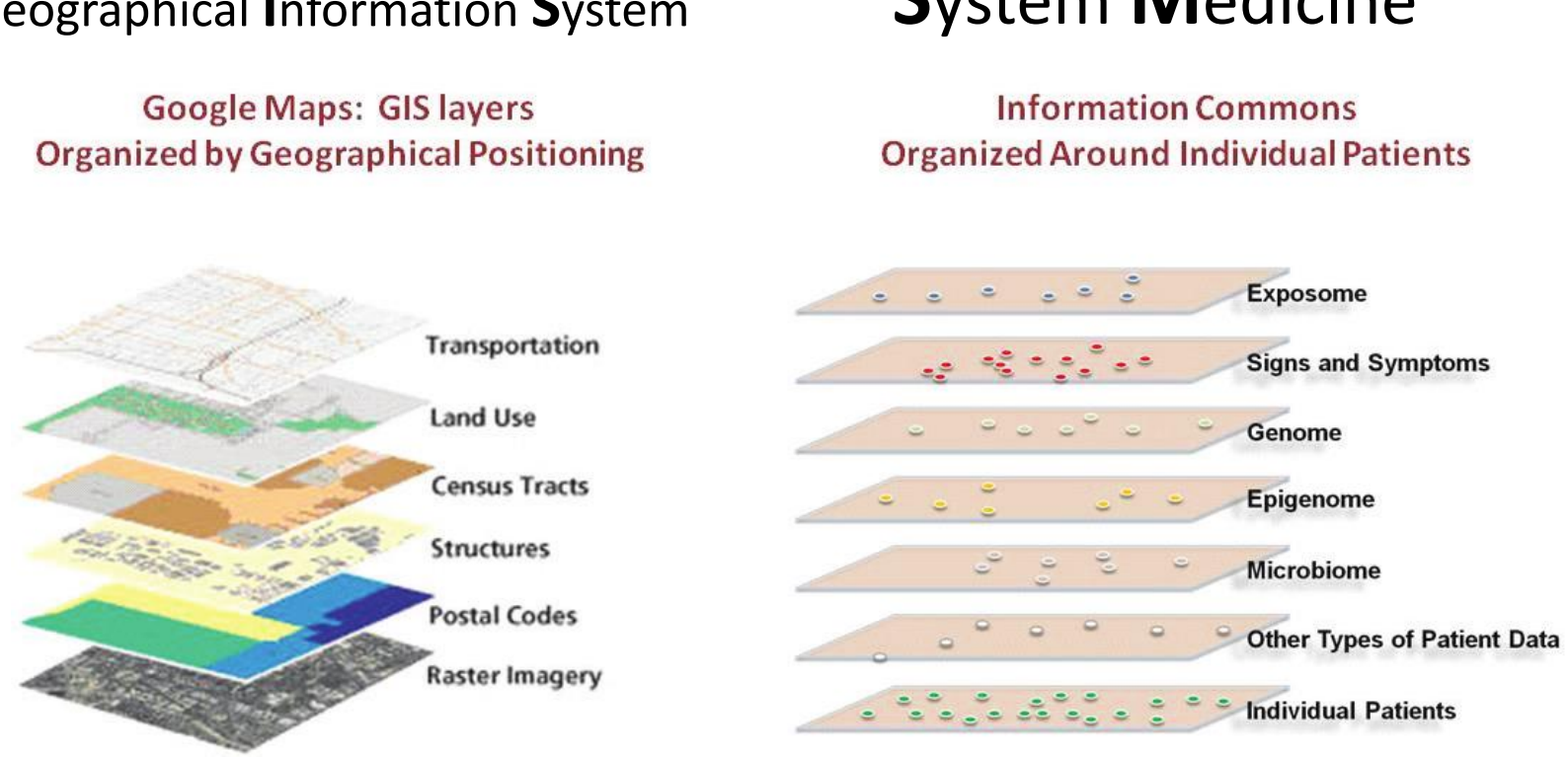
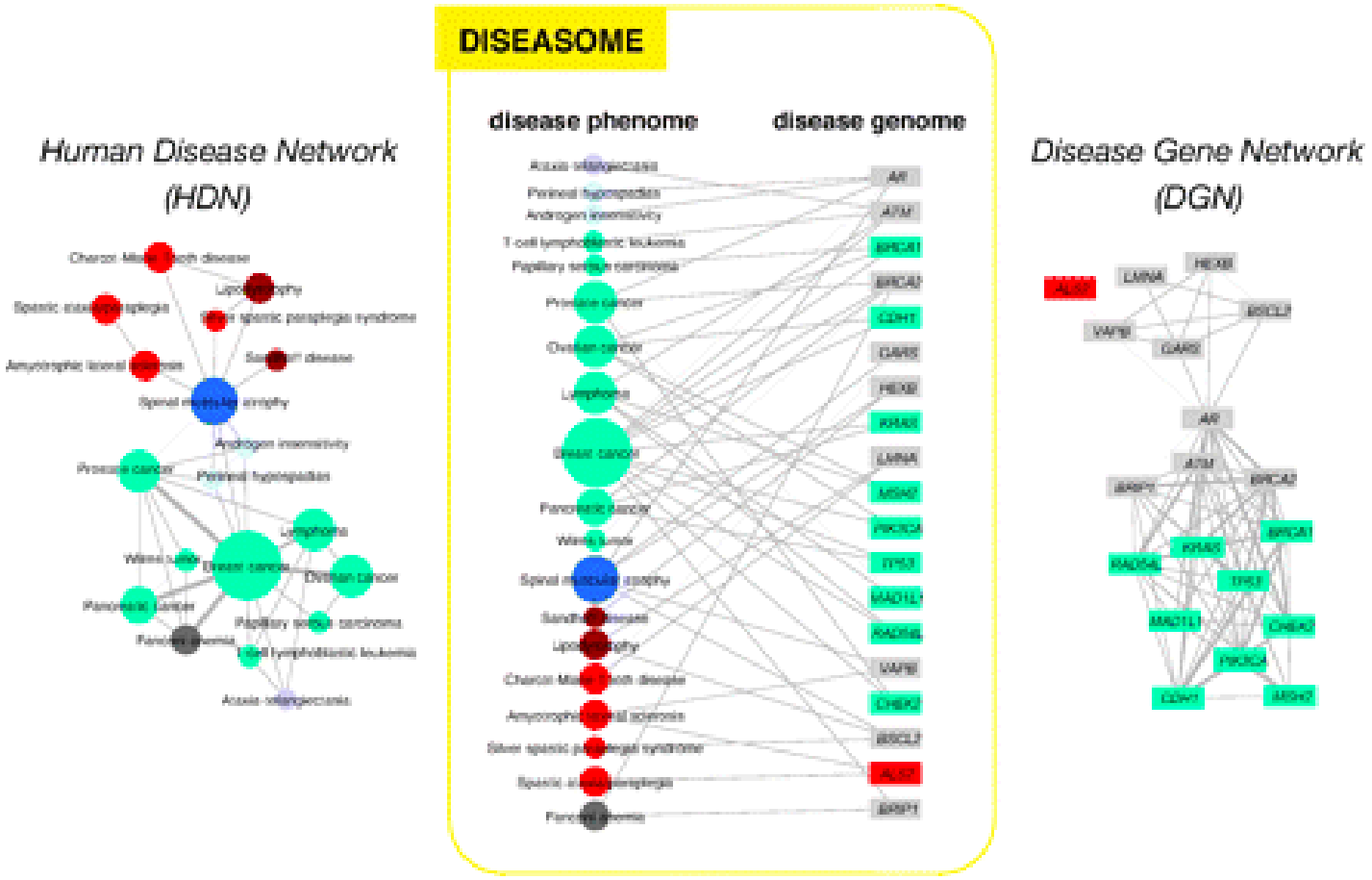
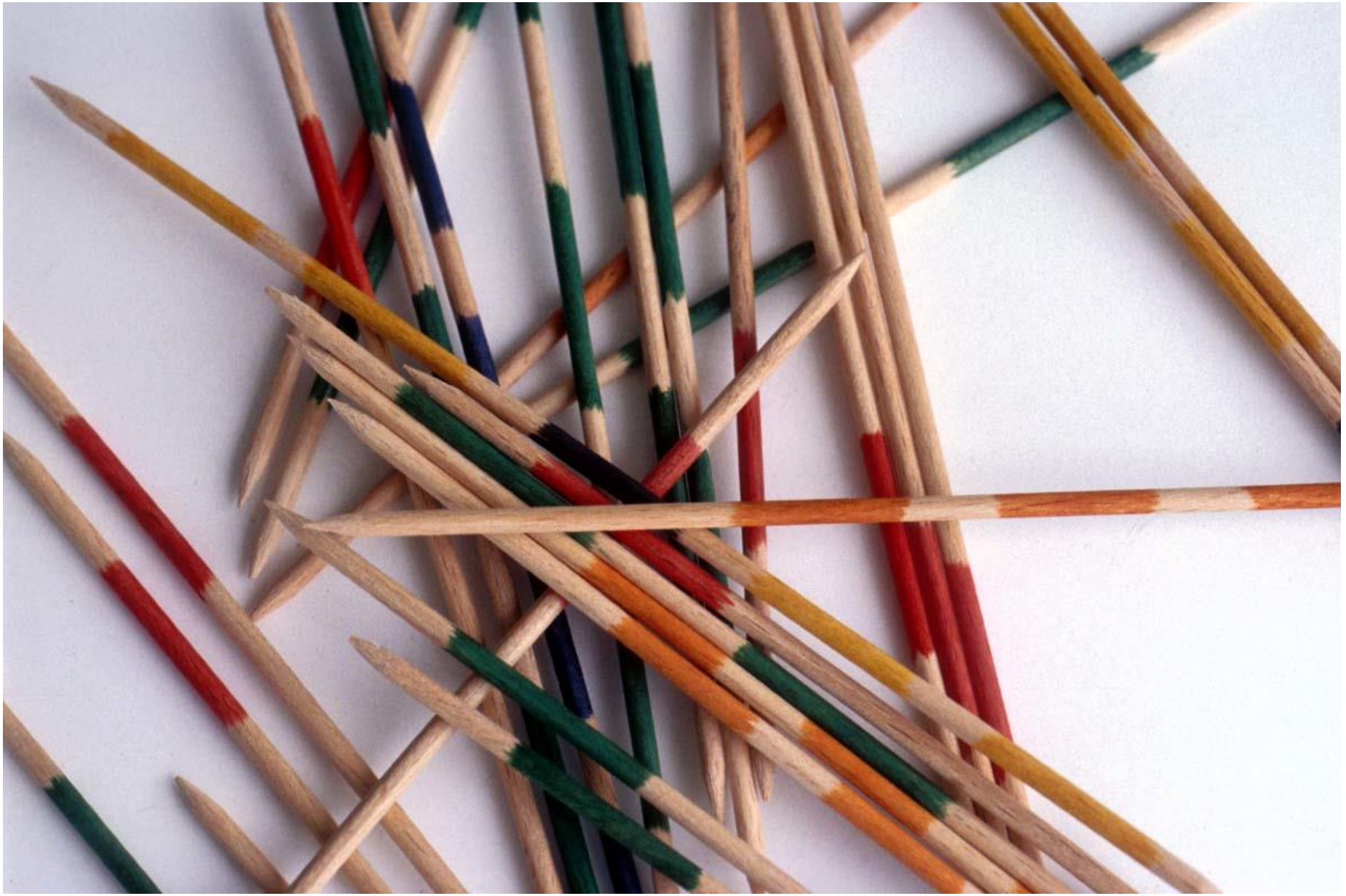
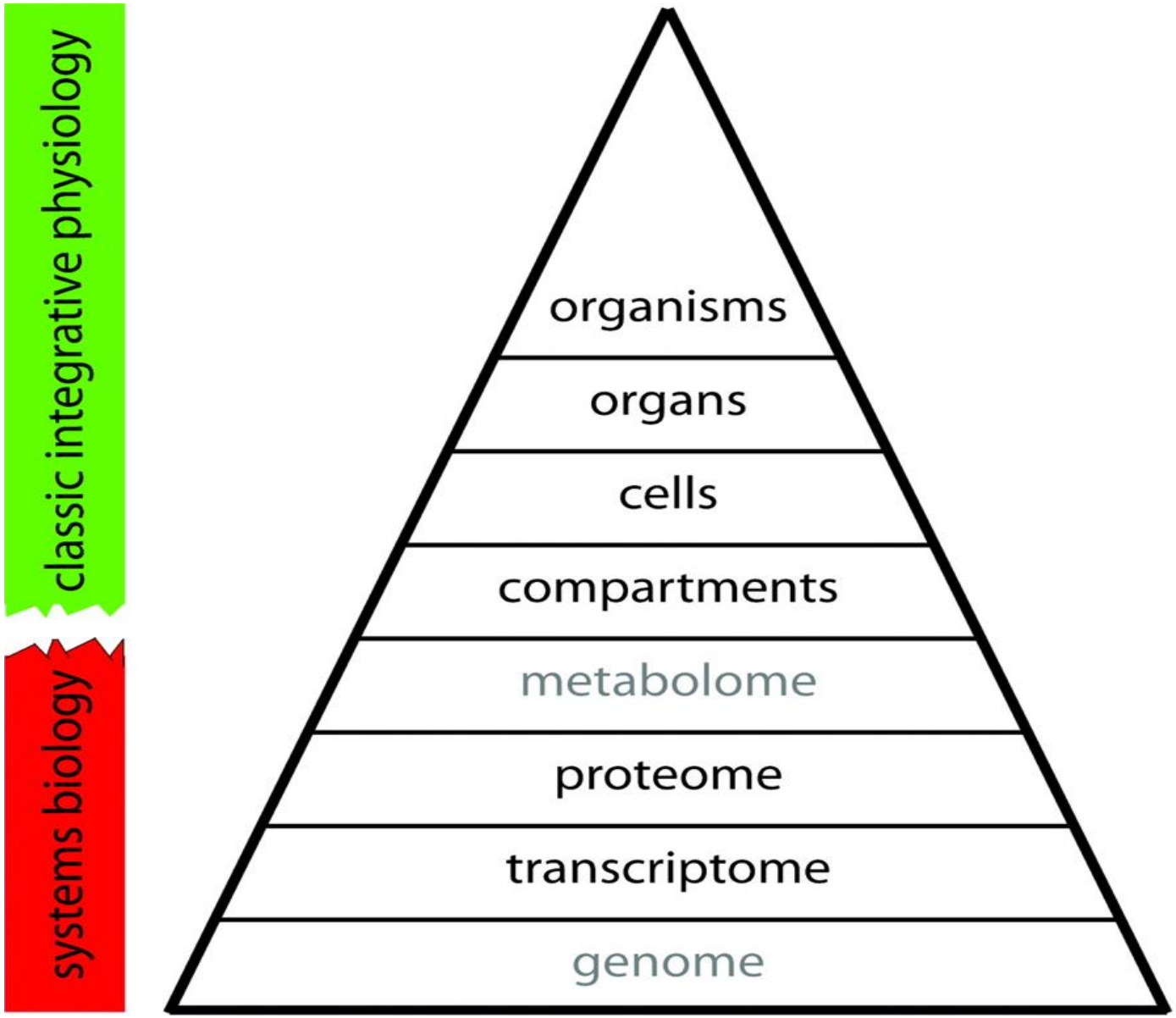


FIGURE 1-2 An Information Commons might use a GIS-type structure.
The proposed, individual-centric Information Commons (right panel) is somewhat analogous to a layered GIS (left panel). In both cases, the bottom layer defines the organization of all the overlays. However, in a GIS, any vertical line 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 microbiomes and symptoms may have very different genome sequences).
SOURCE: FPA 2011 (left panel).


DISEASOME
disease phenome
disease genome
Human Disease Network
(HDN)
Disease Gene Network
(DGN)
Androgen insensitivity
Lymphoma
Ovarian cancer
Pancreatic cancer
Papillary serous carcinoma
Acute myelogenous leukemia
AR
ATM
BRCA1
BRCA2
CDH1
GARS
HEXB
KRAS
LMNA
MSH2
PIK3CA
TP53
RAD51
RAD54L
VAPB
CHEK2
BSCL2
ALS2
BAP1
LMNA
HEXB
BSCL2
VAPB
GARS
AR
ATM
BRCA2
BAP1
KRAS
BRCA1
RAD54L
TP53
MAD1L1
CHEK2
PIK3CA
CDH1
MSH2

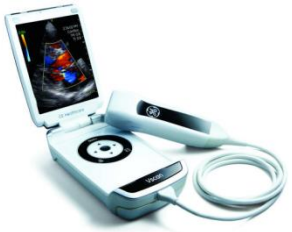


System approach to disease states



Towards System Medicine

Genomic/Transcriptomic

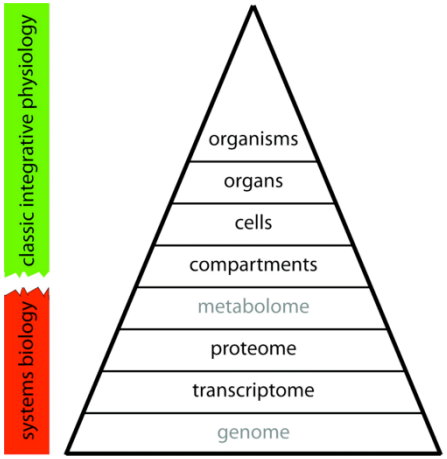


Sensoring

Proteomic

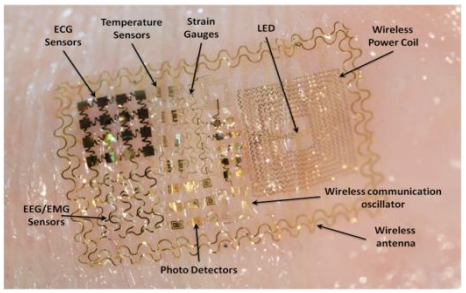
Metabolomic

Social Network



Towards System Medicine

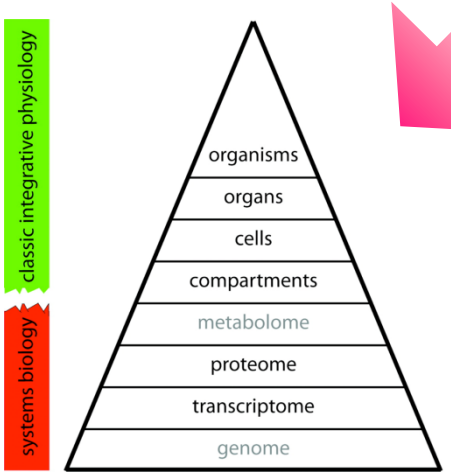
Genomic/Transcriptomic



Sensoring

Proteomic

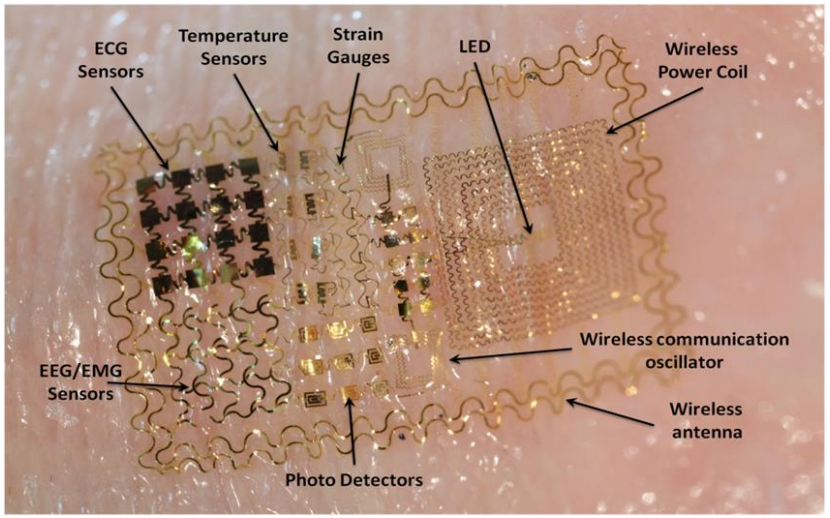
Metabolomic



Social Network

Phenotyping behaviour

- The **study of behaviour** is a special challenge for phenomics as it depends on both context and time, and it is obviously very variable.
- Currently available technologies combine tracking systems based on **GPS** (global position systems), **accelerometers**, and tools for monitoring the **neuronal activity**. The study of human behaviour can also be carried out via the use of **web-** and **smartphone-**based instruments.



CERN

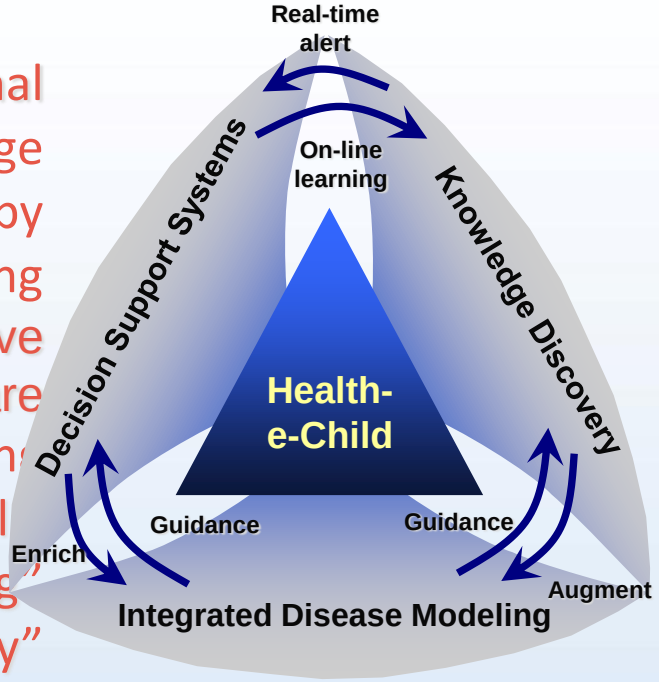
(GENEVE)

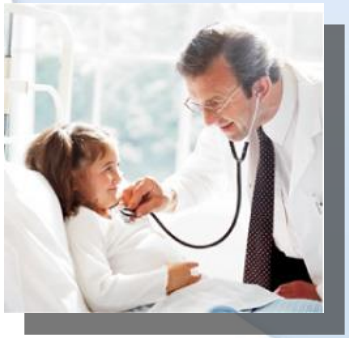
to *Accelerating Science and Innovation*

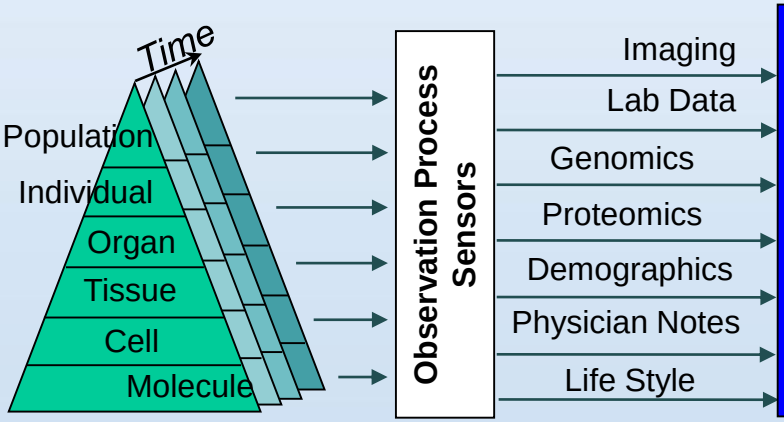

Running jobs: 246791
Transfer rate: 13.98 GiB/sec
Data SIO, NOAA, U.S. Navy, NGA, GEBCO
© 2012 Google
US Dept of State Geographer
© 2009 GeoBasis-DE/BKG
Google

Health-e-Child at a Glance

- Establish multi-site, vertical, and longitudinal integration of data, information and knowledge
- Develop a GRID based platform, supported by robust search, optimisation and matching
- Build enabling tools and services that improve patient care
- Two main use case scenarios leveragin disease model
  - "Aiding the Clinician in Decision Making"
  - "Clinical Studies, Knowledge Discovery"







Information Society Technologies

Similarity Search

Measurement of Pulmonary Trunk

Temporal Modelling

RV and LV Automatic Modelling

Visual Data Mining

Surgery Planning

Genetics Profiling

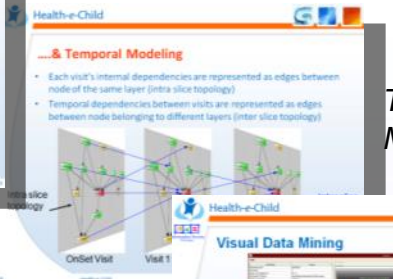
Personalised Simulation

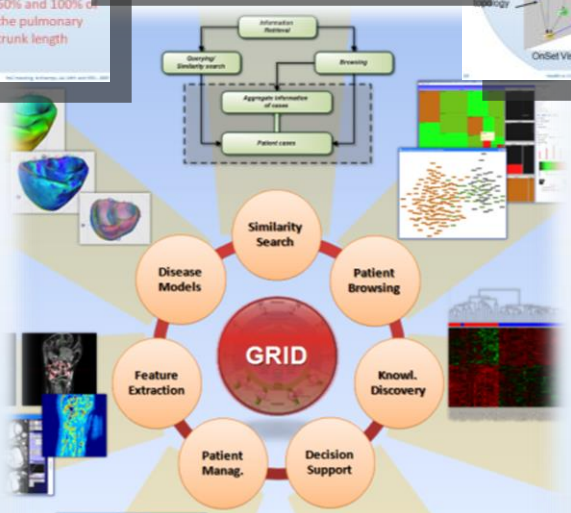
Treatment Response

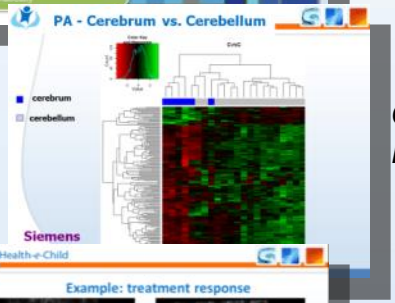
Semantic Browsing

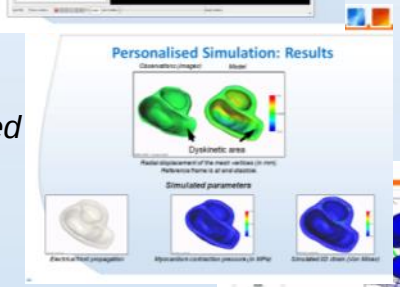
Inferring Outcome

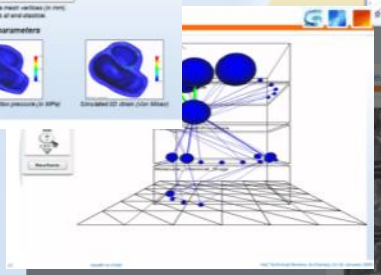
Biomechanical Models
Tumor Growth Modelling

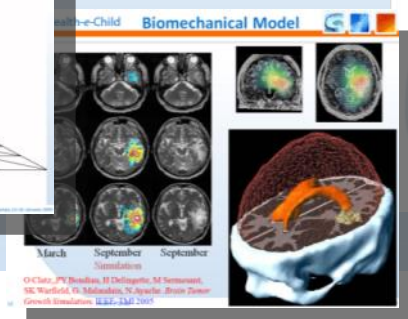


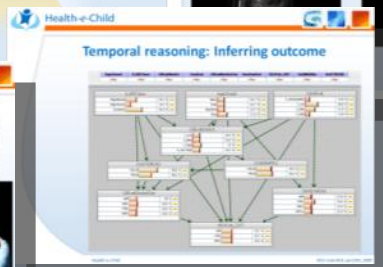












Summary

- The importance of IT will increase the more personalized medicine becomes reality
  - to automatically process and analyze the data (genetics, proteomics but also imaging)
  - to provide access to large annotated patient data bases
- Health-e-Child has developed a multi-site system infrastructure supporting vertical data integration and offering both generic and specific tools
  - to discover new knowledge
  - to aid in decision making
- These are the first steps in a long journey towards support for effective, personalized healthcare in the 21st century.

Digital Health Live is about

- thinking big,
- thinking holistically and
- thinking differently.

Un anno fa ha sbaragliato i campioni umani di quiz televisivi. Ora **Watson viene sperimentato nei grandi ospedali americani.** *È solo il primo passo:* **il calcolatore Ibm,** *che legge un milione di libri al secondo, sa adattarsi al progresso delle conoscenze E presto* **dalle diagnosi potrebbe spingersi a suggerire una cura**

Il super computer debutta in corsia

la Repubblica
GIOVEDÌ 27 DICEMBRE 2012

L'intervista

Antonino Mazzone: "Mi fido solo dell'occhio clinico"

"Ma il ruolo del medico non può essere sostituito"

Watson integrates on a large scale:

- **Clinical** data,
- **Research** data,
- **Medical guidelines** and
- **Personal Clinical Wisdom**.

Watson is a deep question answering natural-language computer system, a very complex and sophisticated, healthcare oriented, software, it is in an advanced stage of development. Its developers have chosen ***oncology*** as a medical area for the starting of their efforts. They have started with few specific subfields of cancer diagnosis and therapy:

(i) **Lung adeno-carcinomas**; Breast cancer; Prostate cancer (Memorial Sloan-Kettering).

(ii) **Leukemias** (MD Anderson).

The supercomputer has incorporated (*and made manageable in an integrated way*) thousands of sources, including scientific journal articles, national guidelines, individual-hospital best practices, clinical trials, and even textbooks. Probably we have behind Watson a very important work of preclinical / clinical database standardization and accessibility (especially in collaboration with the large Cancer Centers mentioned above). We can expect that to implement sufficiently standardized electronic medical files will be an input prerequisite also at a European level. On this wavelength was a 2013 recommendation of the "Academy of Medical Royal Colleges" (UK). **Watson interfaces with electronic medical records, it has the capability to read and "comprehend" case notes (natural language processing).**

“Tonight, I'm launching **a new Precision Medicine Initiative** to bring us closer to curing diseases like **cancer and diabetes** — and to give all of us access to the **personalized information** we need to keep ourselves and our families **healthier**.”

President Barack Obama, State of the Union Address, January 20, 2015

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

FEBRUARY 26, 2015

A New Initiative on Precision Medicine

Francis S. Collins, M.D., Ph.D., and Harold Varmus, M.D.

… Although the precision medicine initiative will probably yield its greatest benefits years down the road, there should be some notable near-term successes. In addition to the results of the cancer studies described above, studies of a large research cohort exposed to many kinds of therapies may provide early insights into pharmacogenomics — **enabling the provision of the right drug at the right dose to the right patient.**

Opportunities to identify persons with rare loss of function mutations that protect against common diseases may point to attractive drug targets for broad patient populations. And observations of beneficial use of mobile health technologies may improve strategies for preventing and managing chronic diseases. …

The Precision Medicine Initiative: Data-Driven Treatments as Unique as Your Own Body

Lindsay Holst

January 30, 2015
09:19 AM EST

Share This Post

E-Mail
Tweet
Share
+


THE PRECISION MEDICINE INITIATIVE

Right now, most medical treatments are designed for the average patient.

But one size doesn't fit all, and treatments that are very successful for some patients don't work for others. **Think about it:**

- If you need glasses, you aren't assigned a generic pair. You get a prescription customized for you.
- If you have an allergy, you get tested to determine exactly what you're allergic to.
- If you need a blood transfusion, it has to match your precise blood type.


THE PRECISION MEDICINE INITIATIVE

BMJ

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

ANALYSIS

Evidence Based Medicine Renaissance

ESSAY

Evidence based medicine: a movement in crisis?

Trisha Greenhalgh and colleagues argue that, although evidence based medicine has had many benefits, it has also had some negative unintended consequences. They offer a preliminary agenda for the movement's renaissance, refocusing on providing useable evidence that can be combined with context and professional expertise so that individual patients get optimal treatment

Trisha Greenhalgh *dean for research impact*[1], Jeremy Howick *senior research fellow*[2], Neal Maskrey *professor of evidence informed decision making*[3], for the Evidence Based Medicine Renaissance Group

[1]Barts and the London School of Medicine and Dentistry, London E1 2AB, UK; [2]Centre for Evidence-Based Medicine, University of Oxford, Oxford OX2 6NW, UK; [3]Keele University, Staffs ST5 5BG, UK

BMJ

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

ANALYSIS

Evidence Based Medicine Renaissance

ESSAY

Evidenc risis?

Trisha Greenh cine has had many benefits, it has preliminary agenda for the moveme can be combined with context an eatment

Trisha Greenha low[2], Neal Maskrey

professor of ev cine Renaissance Group

[1]Barts and the London School of Medicine and Dentistry, London E1 2AB, UK; [2]Centre for Evidence-Based Medicine, University of Oxford, Oxford OX2 6NW, UK; [3]Keele University, Staffs ST5 5BG, UK

The NEW ENGLAND JOURNAL of MEDICINE

SOUNDING BOARD

Precision Medicine — Personalized, Problematic, and Promising

J. Larry Jameson, M.D., Ph.D., and Dan L. Longo, M.D.

This article was published on May 27, 2015, at NEJM.org.

WHAT IS PRECISION MEDICINE?

The terms precision, personalized, and individualized medicine are often used interchangeably. Many physicians contend that they have always practiced individualized and personalized medicine. We agree and, for this reason, prefer the term precision medicine to emphasize the new aspects of this field, which is being driven by new diagnostics and therapeutics.

May 27, 2015, at NEJM

We define precision medicine as treatments targeted to the needs of individual patients on the basis of

- **genetic,**
- **biomarker,**
- **phenotypic, or**
- **psychosocial** characteristics

that distinguish a given patient from other patients with similar clinical presentations.

Inherent in this definition is the goal of improving clinical outcomes for individual patients and minimizing unnecessary side effects for those less likely to have a response to a particular treatment.

May 27, 2015, at NEJM

Technological Advances as Drivers of Precision Medicine

The **convergence** of

- genetics,
- informatics, and
- imaging,

along with ***other technologies*** such as:

- cell sorting,
- epigenetics,
- proteomics, and
- metabolomics,

is rapidly expanding the scope of precision medicine by **refining the classification of disease**, often with important prognostic and treatment implications.

May 27, 2015, at NEJM

Table 1. Examples of Conditions in Which Precision Medicine Has Been Used.*

Medical Field	Disease	Biomarker	Intervention
Cancer	Chronic myeloid leukemia	BCR-ABL	Imatinib[4]
	Lung cancer	EML4-ALK	Crizotinib[3]
Hematology	Thrombosis	Factor V Leiden	Avoid prothrombotic drugs[5]
Infectious disease	HIV/AIDS	CD4+ T cells, HIV viral load	Highly active antiretroviral therapy[6]
Cardiovascular disease	Coronary artery disease	*CYP2C19*	Clopidogrel[7]
Pulmonary disease	Cystic fibrosis	*G551D*	Ivacaftor[8]
Renal disease	Transplant rejection	Urinary gene signature	Antirejection drugs[9]
Hepatology	Hepatitis C	Hepatitis C viral load	Direct-acting antiviral agents[10]
Endocrine disease	Multiple endocrine neoplasia type 2	*RET*	Prophylactic thyroidectomy[11]
Metabolic disease	Hyperlipidemia	LDL cholesterol	Statins[12]
Neurology	Autoimmune encephalitis	CXCL13	Immunotherapy[13]
Psychiatry	Alcohol-use disorder	*GRIK1*	Topiramate[14]
Pharmacogenomics	Smoking cessation	*CYP2A6*	Varenicline[15]
Ophthalmology	Leber's congenital amaurosis	*RPE65*	Gene therapy[16]

* In the biomarker column, proteins or genes that are probed to find the specific variants of interest are shown. AIDS denotes acquired immunodeficiency syndrome, HIV human immunodeficiency virus, and LDL low-density lipoprotein.

Among these new technologies, **genetics and next-generation DNA sequencing methods** are having the greatest effect.

The prospect of sequencing whole exomes or genomes for less than $1,000 reshapes our thinking about approaches to genetic testing.

The clinical implications will be greatest when the results of genetic testing are **actionable**, thus informing prognosis or treatment.

May 27, 2015, at NEJM

For example, **the molecular diagnosis of multiple endocrine neoplasia type 2** allows prophylactic thyroidectomy and regular screening for medullary thyroid cancer, pheochromocytoma, and hyperparathyroidism in affected persons; it also **spares unaffected family members** from unnecessary screening.

May 27, 2015, at NEJM

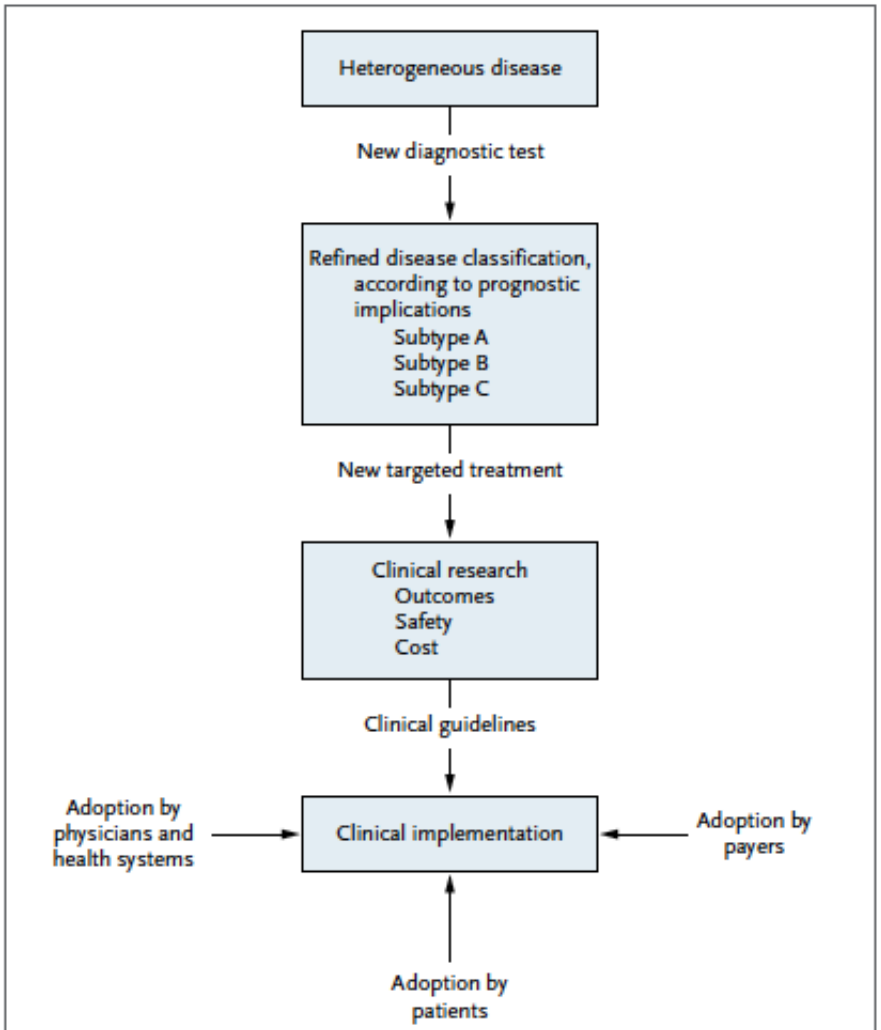
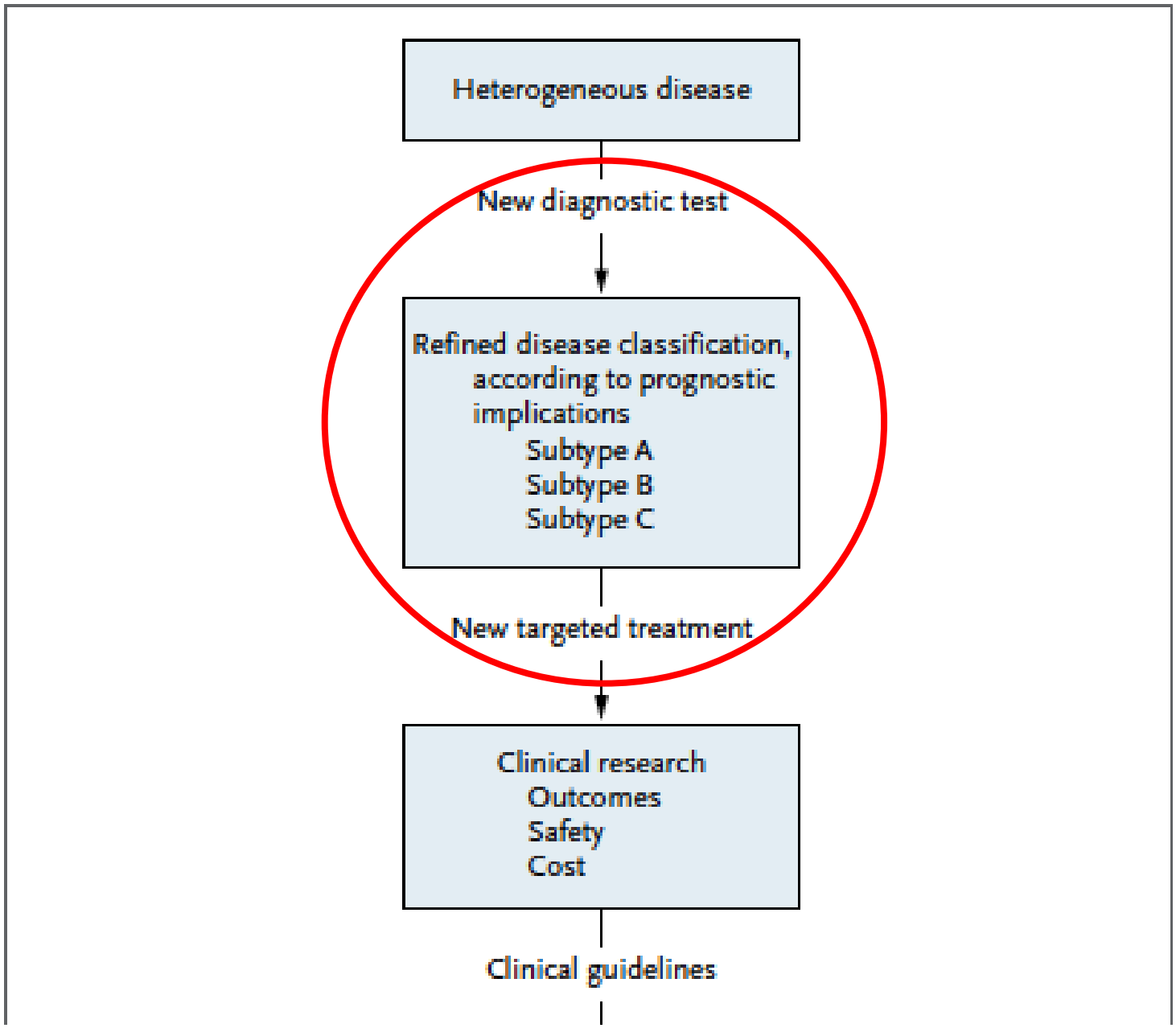


Figure 1. Scope of Precision Medicine.

The need for precision medicine is driven by the heterogeneous nature of many diseases. New diagnostic tests allow for refined classification of disease, which may have important prognostic implications. When targeted therapies are available, clinical studies can assess efficacy, safety, and cost-effectiveness, leading to revised clinical guidelines. Clinical implementation requires adoption by regulatory agencies, payers, physicians, and patients. Each of these groups has a different perspective, role, and incentive when it comes to clinical implementation.

May 27, 2015, at NEJM



May 27, 2015, at NEJM

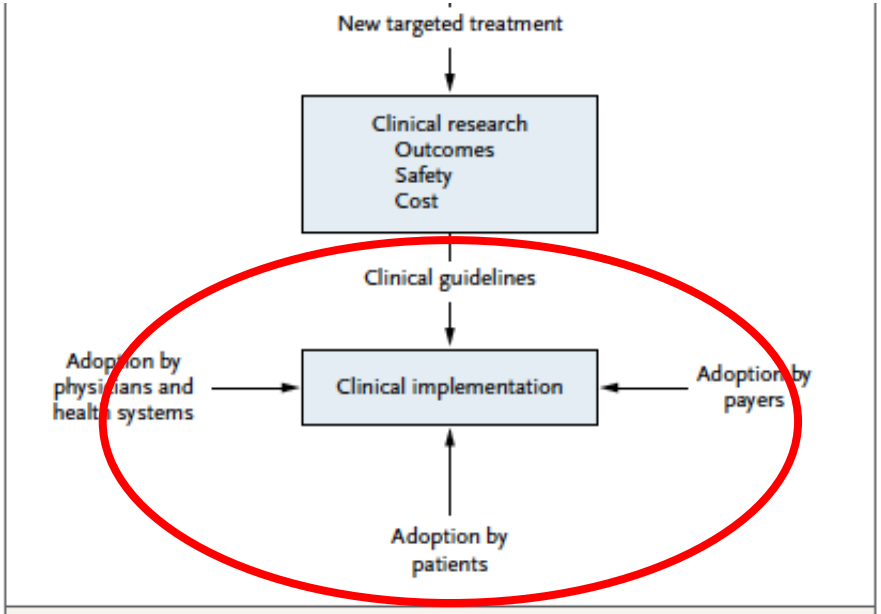


Figure 1. Scope of Precision Medicine.

The need for precision medicine is driven by the heterogeneous nature of many diseases. New diagnostic tests allow for refined classification of disease, which may have important prognostic implications. When targeted therapies are available, clinical studies can assess efficacy, safety, and cost-effectiveness, leading to revised clinical guidelines. Clinical implementation requires adoption by regulatory agencies, payers, physicians, and patients. Each of these groups has a different perspective, role, and incentive when it comes to clinical implementation.

7, 2015, at NEJM

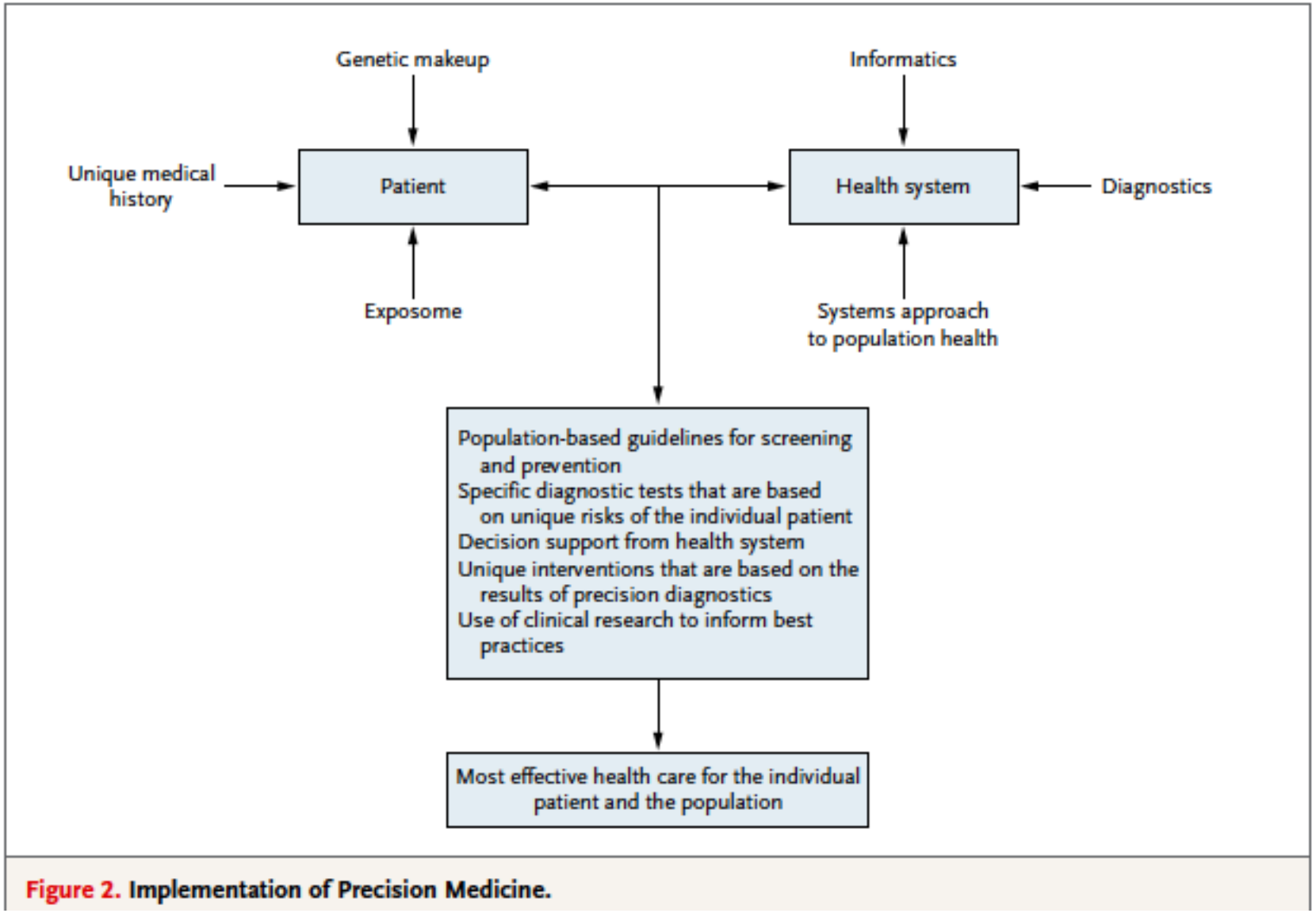


Figure 2. Implementation of Precision Medicine.

May 27, 2015, at NEJM

Precision medicine
should be viewed as a means of providing the best available health care for a population by

- **identifying the needs** and
- **improving the outcomes** of individual patients.

May 27, 2015, at NEJM

Un anno fa ha sbaragliato i campioni umani di quiz televisivi. Ora **Watson viene sperimentato nei grandi ospedali americani.** *È solo il primo passo:* **il calcolatore Ibm,** *che legge un milione di libri al secondo, sa adattarsi al progresso delle conoscenze E presto* **dalle diagnosi potrebbe spingersi a suggerire una cura**

Il super computer debutta in corsia

la Repubblica
GIOVEDÌ 27 DICEMBRE 2012

L'intervista

Antonino Mazzone: "Mi fido solo dell'occhio clinico"

"Ma il ruolo del medico non può essere sostituito"

Watson integrates on a large scale:

- **Clinical** data,
- **Research** data,
- **Medical guidelines** and
- **Personal Clinical Wisdom**.

Watson is a deep question answering natural-language computer system, a very complex and sophisticated, healthcare oriented, software, it is in an advanced stage of development. Its developers have chosen ***oncology*** as a medical area for the starting of their efforts. They have started with few specific subfields of cancer diagnosis and therapy:

(i) Lung adeno-carcinomas; Breast cancer; Prostate cancer (Memorial Sloan-Kettering).

(ii) Leukemias (MD Anderson).

The supercomputer has incorporated (*and made manageable in an integrated way*) thousands of sources, including scientific journal articles, national guidelines, individual-hospital best practices, clinical trials, and even textbooks. Probably we have behind Watson a very important work of preclinical / clinical database standardization and accessibility (especially in collaboration with the large Cancer Centers mentioned above). We can expect that to implement sufficiently standardized electronic medical files will be an input prerequisite also at a European level. On this wavelength was a 2013 recommendation of the "Academy of Medical Royal Colleges" (UK). **Watson interfaces with electronic medical records, it has the capability to read and "comprehend" case notes (natural language processing).**

Nucleic Acids Research Advance Access published November 4, 2014

Nucleic Acids Research, 2014 1
doi: 10.1093/nar/gku953

hnRNPA1 couples nuclear export and translation of specific mRNAs downstream of FGF-2/S6K2 signalling

Rajat Roy[1], Danielle Durie[2], Hui Li[3], Bing-Qian Liu[3], John Mark Skehel[4], Francesco Mauri[5], Lucia Veronica Cuorvo[6], Mattia Barbareschi[6], Lin Guo[3], Martin Holcik[2], Michael J. Seckl[1,*] and Olivier E. Pardo[1,*]

[1]Division of Cancer, Department of Surgery and Cancer, 1st Floor, ICTEM Building, Hammersmith Hospitals Campus of Imperial College London, Du Cane Road, London W12 0NN, UK, [2]Apoptosis Research Centre, Children's Hospital of Eastern Ontario Research Institute, Ottawa, Ontario, Canada, [3]Department of Biochemistry, Wuhan University, Wuhan, China, [4]Protein Analysis and Proteomics Laboratory, London Research Institute, South Mimms, EN6 3LD, UK, [5]Department of Histopathology, Hammersmith Hospital Campus, Imperial College, London W120NN, UK and [6]Department of Histopathology, S. Chiara Hospital, Trento, Italy

Possible relevance to cancer and areas for further investigation

At first sight, prior reports demonstrating the **translational repression** of XIAP and BCL-XL through HNRNPA1-heterogeneous nuclear ribonucleoprotein A1 binding would suggest that **overexpression of this RNP in cancer could be associated with reduced levels of these anti- apoptotic proteins**.
This ***should link to enhanced responsiveness to cytotoxic therapies*** and ***improved patient survival***. Instead, increased hnRNPA1 expression correlates with worse patient survival. Our data now provide a mechanism to explain this apparent conundrum.

Rajat Roy et al *Nucleic Acids Research, 42, 15 , 2014*

Regulatory agencies and payers will need to evaluate and support, when appropriate, advances in precision medicine if patients are to receive maximum benefit.

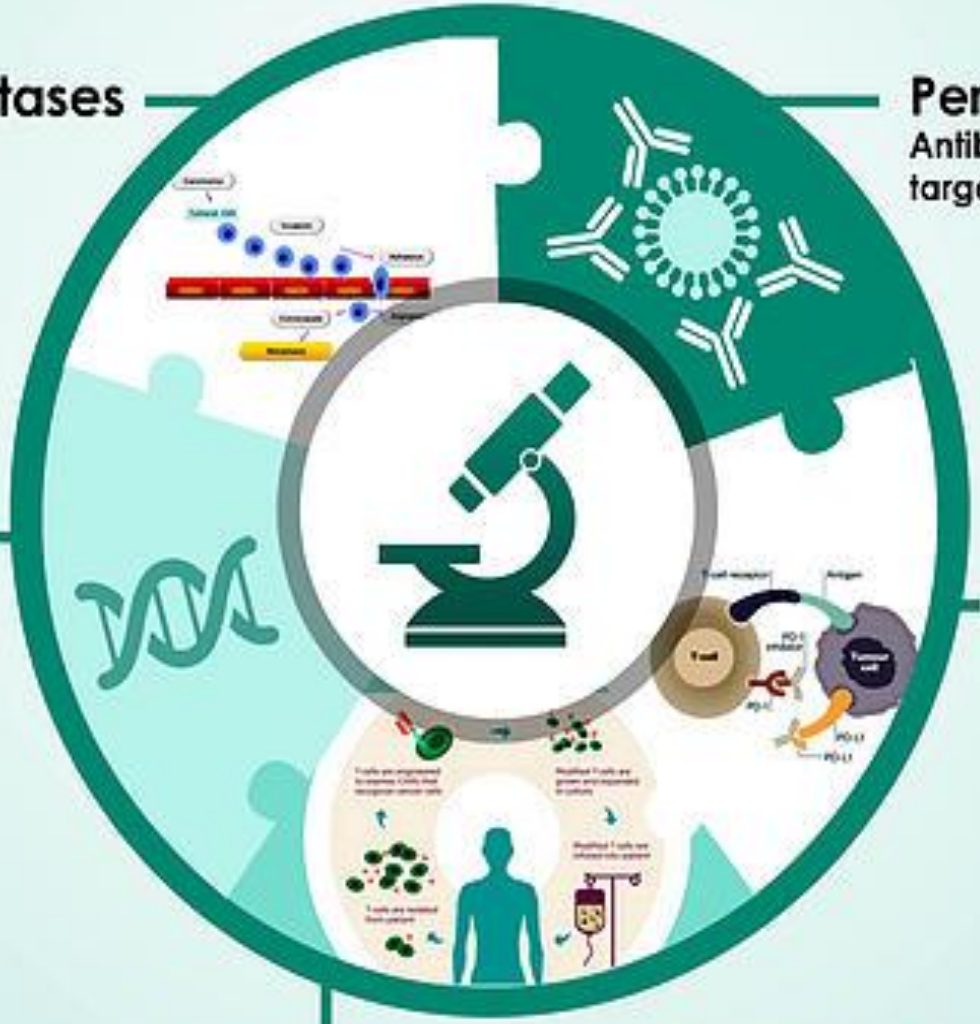
When the term precision medicine disappears from our lexicon, we will know that a revised disease classification with more targeted treatment options has become the norm.

May 27, 2015, at NEJM

The Future of Cancer Treatment

Battling Metastases
Stopping tumors from spreading

Personalized Medicine
Antibodies can be produced that target and destroy cancer cells



Epigenetic Drugs
Regulating the genes that cause cancer

Immunotherapy
Vaccines, cytokines, checkpoint inhibitors, immunomodulating drugs

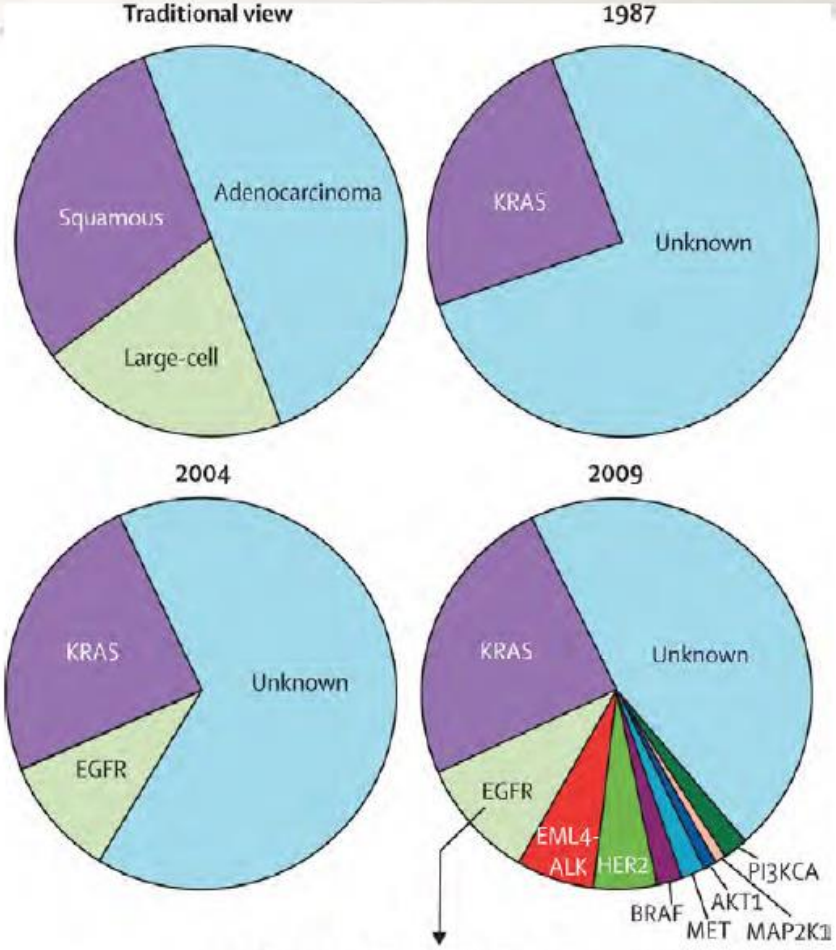
Cell Based Therapy
Immune cells are isolated, genetically re-engineered to attack the patient's tumor and re-infused

All Treatment Begins With a Diagnosis Made by Pathologists

Path Report

For more information visit www.pathreport.org

Change in View of Lung Cancer



- **Mutations associated with drug sensitivity**
  EGFR Gly719X, exon 19 deletion, Leu858Arg, Leu861Gln
- **Mutations associated with primary drug resistance**
  EGFR exon 20 insertions
- **Mutations associated with acquired drug resistance**
  EGFR Thr790Met, Asp761Tyr, Leu747Ser, Thr854Ala

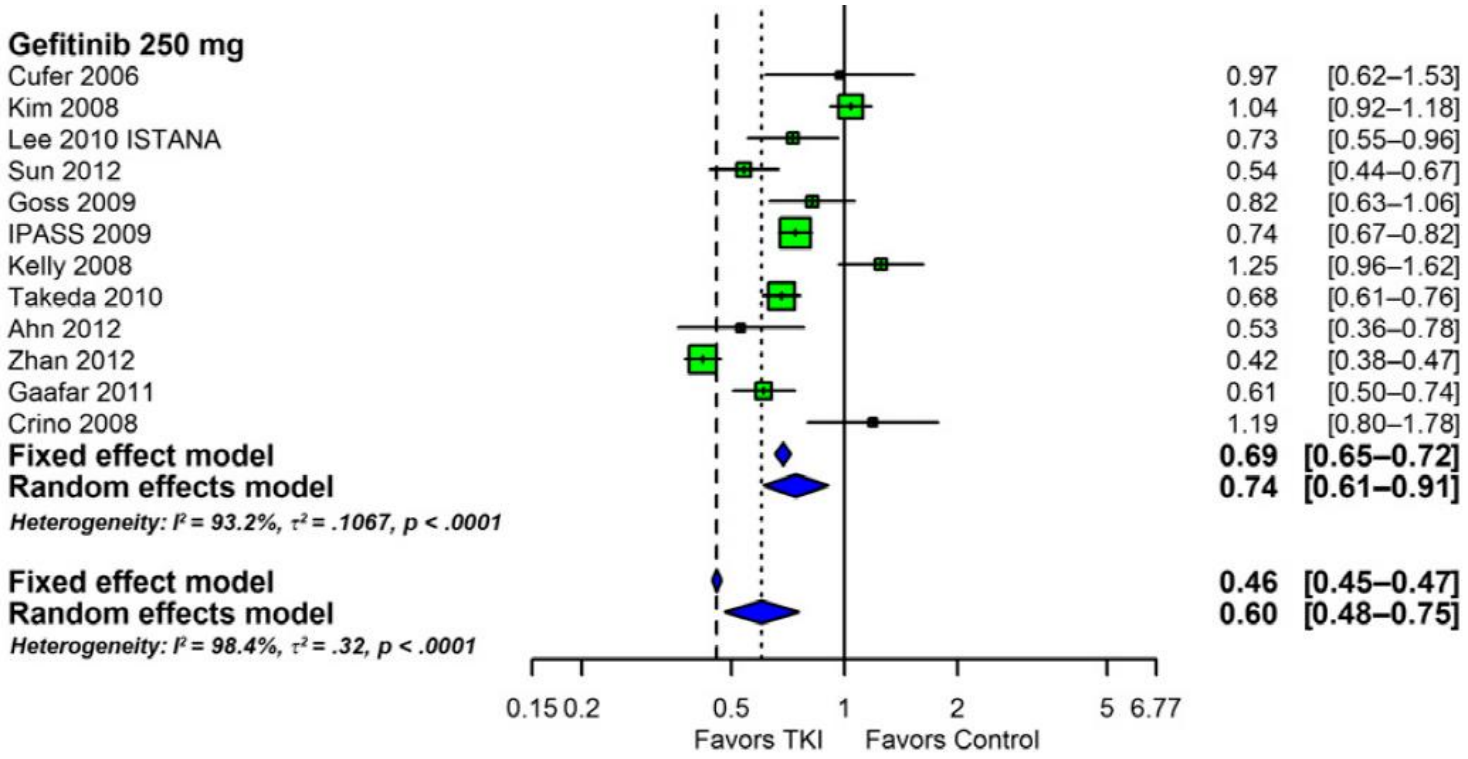
PMC
PERSONALIZED MEDICINE COALITION

Drug name (Brand name)	Biomarker	Indication
ado-trastuzumab emtansine (Kadcyla®)	*ERBB2 (HER2)*	**Breast cancer:** Indicated, as a single agent, for the treatment of patients with *HER2-positive,* metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination.
Afatinib (Gilotrif®) *cf. Table 2*	*EGFR*	**NSCLC:** Indicated for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (*EGFR*) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test.
Anastrozole (Arimidex®)	*HR*	**Breast cancer:** Indicated for i) adjuvant treatment of postmenopausal women with Hormone receptor *(HR)-positive* early breast cancer; ii) first-line treatment of postmenopausal women with HR-positive or HR unknown locally advanced or metastatic breast cancer.
Arsenic trioxide (Trisenox®)	*PML / RARĐ*	**Leukemia:** For induction of remission and consolidation in patients with acute promyelocytic leukemia (APL) whose APL is characterized by the presence of the t (15;17) translocation or *PML / RAR-alpha* gene expression.
Azathioprine (Imuran®)	*TPMT*	**Leukemia:** Guides adjustment of dose in treatment of acute lymphoblastic leukemia: Patients with inherited little or no thiopurine S-methyl-transferase (TPMT) activity are at increased risk for severe drug toxicity from conventional doses. It is recommended that consideration be given to either genotype or phenotype patients for *TPMT*.

Gefitinib and Erlotinib in Metastatic Non-Small Cell Lung Cancer: A Meta-Analysis of Toxicity and Efficacy of Randomized Clinical Trials

MAURICIO BUROTTO,[a,b] ELISABET E. MANASANCH,[c] JULIA WILKERSON,[a,b] TITO FOJO[a,b]

[a]Medical Oncology and [b]Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, USA; [c]Department of Lymphoma and Myeloma, University of Texas MD Anderson Cancer Center, Houston, Texas, USA



The Oncologist, 2015; 20:400-410

EGFR-TK mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer

Issued: August 2013

NICE diagnostics guidance 9

www.nice.org.uk/dg9

1 Recommendations

1.1 The tests and test strategies listed below are recommended as options for detecting epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutations in the tumours of adults with previously untreated, locally advanced or metastatic non-small-cell lung cancer (NSCLC), when used in accredited laboratories participating in an external quality assurance scheme. The laboratory-developed tests should be designed to detect the mutations that can be detected by one of the CE-marked tests as a minimum.

- therascreen EGFR RGQ PCR Kit (CE-marked, Qiagen)
- cobas EGFR Mutation Test (CE-marked, Roche Molecular Systems)
- Sanger sequencing of samples with more than 30% tumour cells and therascreen EGFR RGQ PCR Kit for samples with lower tumour cell contents
- Sanger sequencing of samples with more than 30% tumour cells and cobas EGFR Mutation Test for samples with lower tumour cell contents
- Sanger sequencing followed by fragment length analysis and polymerase chain reaction (PCR) of negative samples.

NICE

EGFR-TK mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer

Issued: August 2013

1.2 There was insufficient evidence for the Committee to make recommendations on the following methods:

- high-resolution melt analysis
- pyrosequencing combined with fragment length analysis
- single-strand conformation polymorphism analysis
- next-generation sequencing
- therascreen EGFR Pyro Kit (CE-marked, Qiagen).

NICE

PMC
PERSONALIZED MEDICINE COALITION

Drug name (Brand name)	Biomarker	Indication
Platinum therapies *cf. Table 2*	*ERCC1*	**Multiple cancers:** **Bladder cancer:** Low *ERCC1* expression is associated with greater survival in bladder cancer patients treated with platinum-based therapies. **Colon cancer:** In a study of advanced colorectal cancer treated with 5-fluorouracil/oxaliplatin, low *ERCC1* expression is associated with longer survival. High expression of *ERCC1* is associated with response to irinotecan therapy. **Gastric cancer:** Patients treated with (5-fluorouracil/leucovorin/oxaliplatin) regimen or first-line cisplatin-based regimens respond significantly better if they show lower levels of *ERCC1* expression. **Lung cancer:** Enzyme excision repair complementing factor 1 *(ERCC1)* helps repair DNA damage caused by platinum-based therapy. Low ERCC1 is a favorable indicator for response to platinum therapy.
Ponatinib (Iclusig®)	*BCR-ABL1*	**Leukemia:** The molecular response measured by BCR-ABL1 RT-qPCR assists in identifying suboptimal responses and can help inform the decision to switch to alternative therapies that may be more efficacious (or to pursue more stringent monitoring). Ponatinib is a kinase inhibitor, which inhibits the in vitro tyrosine kinase activity of ABL and T315I mutant ABL.
Tamoxifen (Nolvadex®) *cf. Table 2*	*ER*	**Breast cancer:** Available evidence indicates that patients whose tumors are ER positive are more likely to benefit from tamoxifen therapy.

PMC
PERSONALIZED MEDICINE COALITION

Drug name (Brand name)	Biomarker	Indication
Thioguanine (Tabloid®)	*TPMT*	**Leukemia:** Guidance for dose adjustment during treatment of acute lymphoblastic leukemia: Patients with inherited little or no *TPMT* activity are at increased risk for severe drug toxicity from conventional doses. It is recommended that consideration be given to either genotype or phenotype patients for *TPMT*.
Tositumomab (Bexxar®)	*CD20*	**Lymphoma:** Is indicated for the treatment of patients with CD20 antigen expressing non-Hodgkin's lymphoma.
Trametinib (Mekinist®) *cf. Table 2*	*BRAF*	**Melanoma:** Indicated for the treatment of patients with unresectable or metastatic melanoma with *BRAF* V600E or V600K mutations as detected by an FDA-approved test.
Trastuzumab (Herceptin®) *cf. Table 2*	*HER2 / neu receptor*	**Breast cancer:** Indicated for i) the treatment of *HER2* overexpressing breast cancer; ii) the treatment of *HER2* overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma.
Tretinoin (Vesanoid®)	*PML / RARĐ*	**Leukemia:** For induction of remission and consolidation in patients with acute promyelocytic leukemia (APL) whose APL is characterized by the presence of the t (15;17) translocation or *PML/RAR-alpha* gene expression.
Vemurafenib (ZelborafTM)	*BRAF V600E*	**Melanoma:** Indicated for the treatment of patients with unresectable or metastatic melanoma with *BRAF* V600E mutation as detected by an FDA-approved test. The *BRAF* V600E mutation is found in about half of


Toronto Won't Bid for 2024 Olympics


Facebook Is Finally Making a 'Dislike' Button


Apple Might Finally Let You Delete Those Apps You Never Use


Watch the New Trailer for the Final Season of *Downton Abbey*


This Humpback Whale Almost Crushed Kayakers


Here's Why Apple Is Offering An iPhone Upgrade Plan

How Doctors Cured This Woman's Brain Cancer

Alice Park @aliceparkny | Aug. 19, 2015

Earlier this year, TIME explored the promise of precision medicine in treating cancer patients. We featured one woman who was taking a drug typically used for melanoma to treat her brain tumor. Here's an update on how she's doing

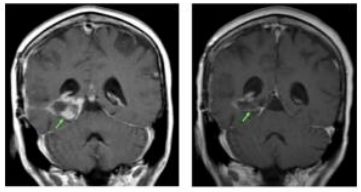
In November 2013, MaryAnn Anselmo—who was on the cover

ORIGINAL ARTICLE

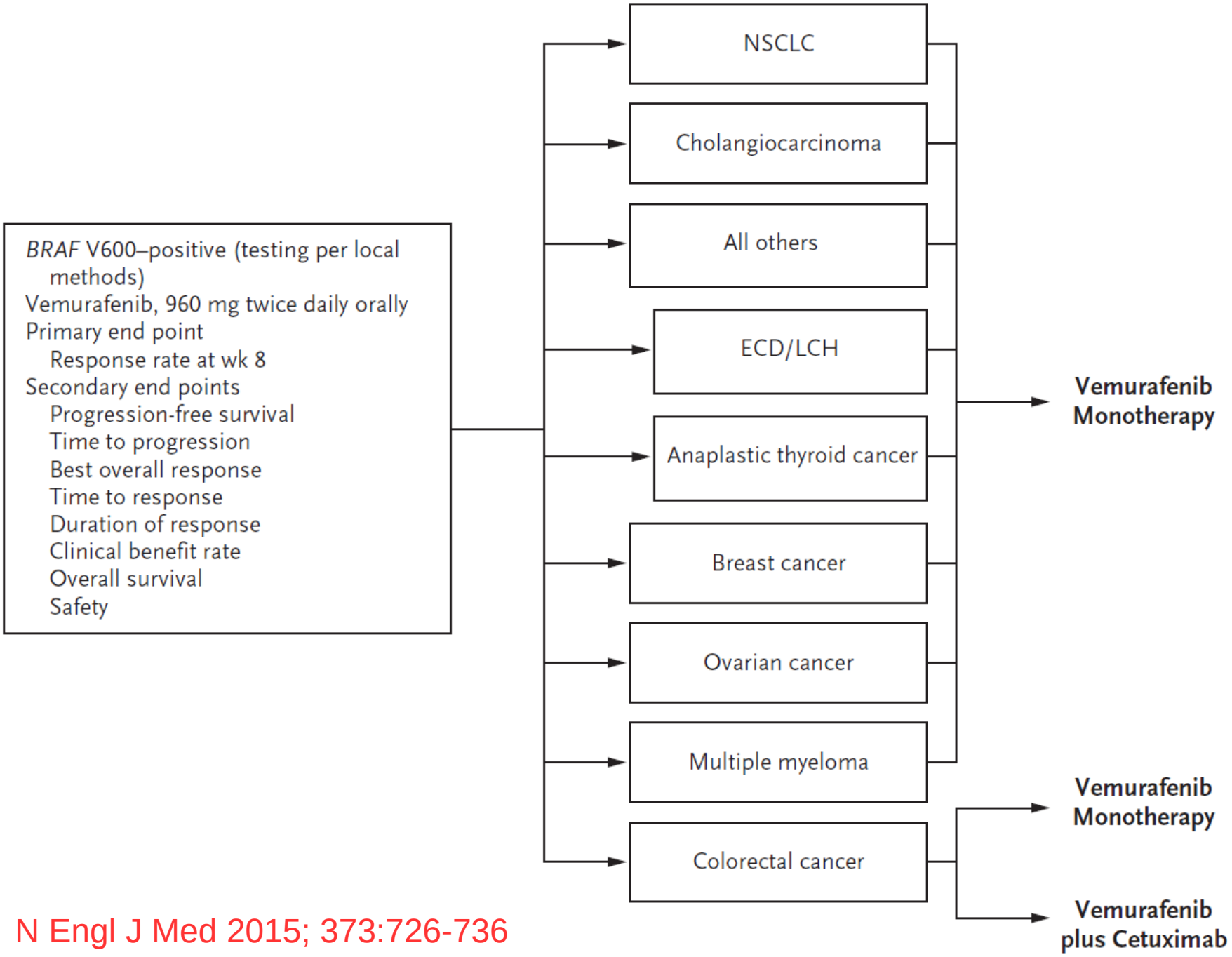
Vemurafenib in Multiple Nonmelanoma Cancers with *BRAF* V600 Mutations

David M. Hyman, M.D., Igor Puzanov, M.D., Vivek Subbiah, M.D., Jason E. Faris, M.D., Ian Chau, M.D., Jean-Yves Blay, M.D., Ph.D., Jürgen Wolf, M.D., Ph.D., Noopur S. Raje, M.D., Eli L. Diamond, M.D., Antoine Hollebecque, M.D., Radj Gervais, M.D., Maria Elena Elez-Fernandez, M.D., Antoine Italiano, M.D., Ph.D., Ralf-Dieter Hofheinz, M.D., Manuel Hidalgo, M.D., Ph.D., Emily Chan, M.D., Ph.D., Martin Schuler, M.D., Susan Frances Lasserre, M.Sc., Martina Makrutzki, M.D., Florin Sirzen, M.D., Ph.D., Maria Luisa Veronese, M.D., Josep Tabernero, M.D., Ph.D., and José Baselga, M.D., Ph.D.

The NEW ENGLAND JOURNAL of MEDICINE



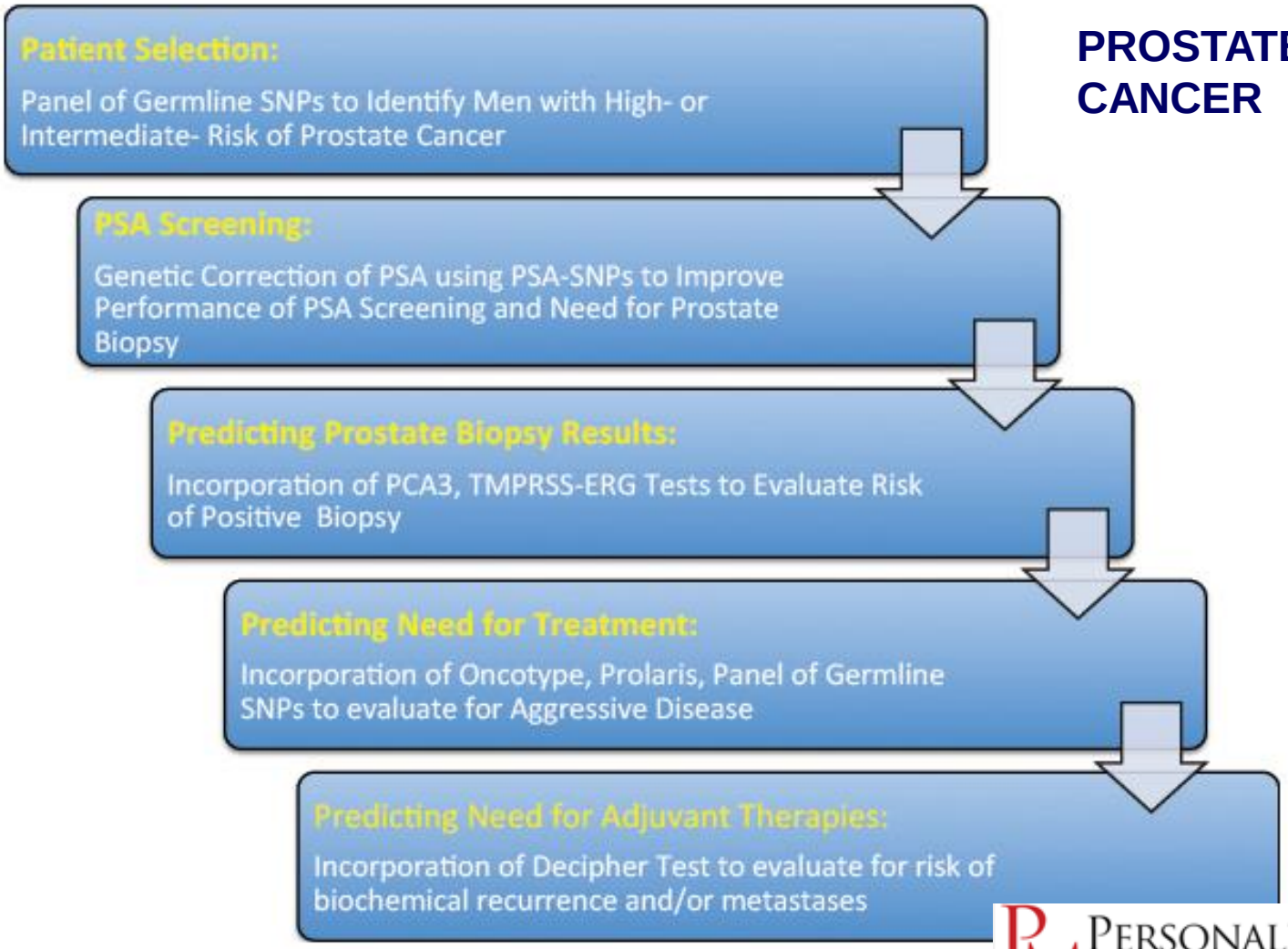
N Engl J Med 2015; 373:726-736



N Engl J Med 2015; 373:726-736

Figure

Incorporation of Genetic Testing to Improve on Current Screening and Treatment Algorithms



PROSTATE CANCER

PMO Personalized Medicine in Oncology
BIOMARKERS • IMMUNOTHERAPY • TARGETED THERAPIES • DIAGNOSTICS
August 2015

Table Commercially Available Genetic Assays Based on Somatic Mutations Within Prostate Cancer Tumors

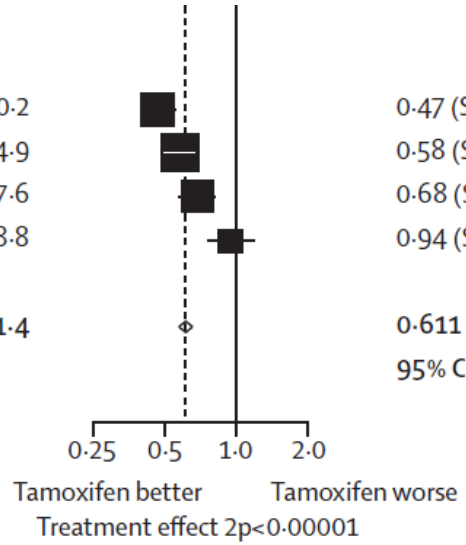
Proposed Utility	Test Name	Commercial Company	Sample	Measures	References and/or Website(s)
Distinguish between aggressive and non-aggressive prostate tumors	Prolaris	Myriad Genetics	Prostate biopsy tissue	48-gene expression panel involved in cell cycle progression	77, 82, 83 www.myriad.com/treating-diseases/prostate-cancer/
	Oncotype DX, Prostate	Genomic Health, Inc	Prostate biopsy tissue	17-gene expression panel involved in multiple pathways	78, 79 http://prostate-cancer.oncotypedx.com/en-US/prostate/professional/introducing-gps/validation-clinical-experience http://prostate-cancer.oncotypedx.com/en-US/prostate/professional/resources/bibliography
Determine need for repeat biopsy after a negative prostate biopsy	Progensa PCA3	Gen-Probe (Hologic)	Urine	PCA3 gene expression	66, 84-86 www.gen-probe.com/products-services/progensa-pca3
	Mi-Prostate Score	University of Michigan Labs	Urine, serum	TMPRSS2-ERG, PCA3, PSA	www.pathology.med.umich.edu/handbook/?search=MIPS
Determining metastasis after radical prostatectomy	Decipher	GenomeDx Biosciences	Prostate tissue	22-gene multi-pathway expression panel	87 http://genomedx.com/?s=prostate+test

Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials

*Early Breast Cancer Trialists' Collaborative Group (EBCTCG)**

Category	Events/woman-years (rate [% per year])		Tamoxifen events		Ratio of annual event rates
	Allocated tamoxifen	Allocated control	Log-rank O–E	Variance of O-E	Tamoxifen : control
(i) Time since randomisation (years) (trend χ^2_1=43·7; 2p<0·00001)					
0–1	343/10 229 (3·4)	676/9825 (6·9)	–175·3	230·2	0·47 (SE 0·05)
2–4	548/13 434 (4·1)	790/11 894 (6·6)	–168·0	304·9	0·58 (SE 0·04)
5–9	454/17 258 (2·6)	499/14 372 (3·5)	–82·5	217·6	0·68 (SE 0·06)
≥10	308/15 631 (2·0)	253/12 610 (2·0)	–7·7	128·8	0·94 (SE 0·09)
Total	1653/56 747 (2·9% per year)	2218/48 876 (4·5% per year)	–433·5	881·4	0·611 (SE 0·027; 95% CI 0·57–0·65)

99% or 95% CIs

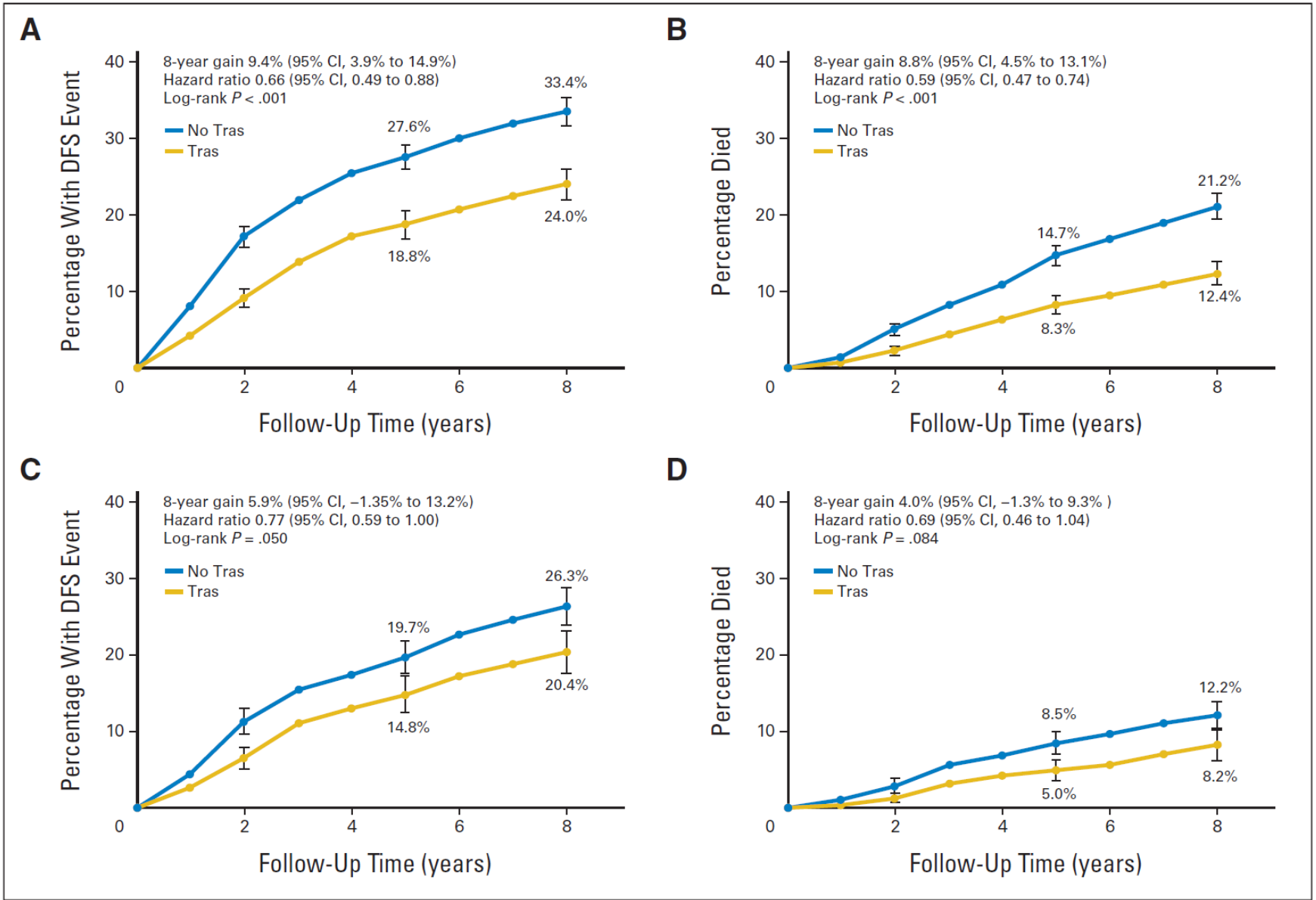


Lancet 2011; 378: 771–84

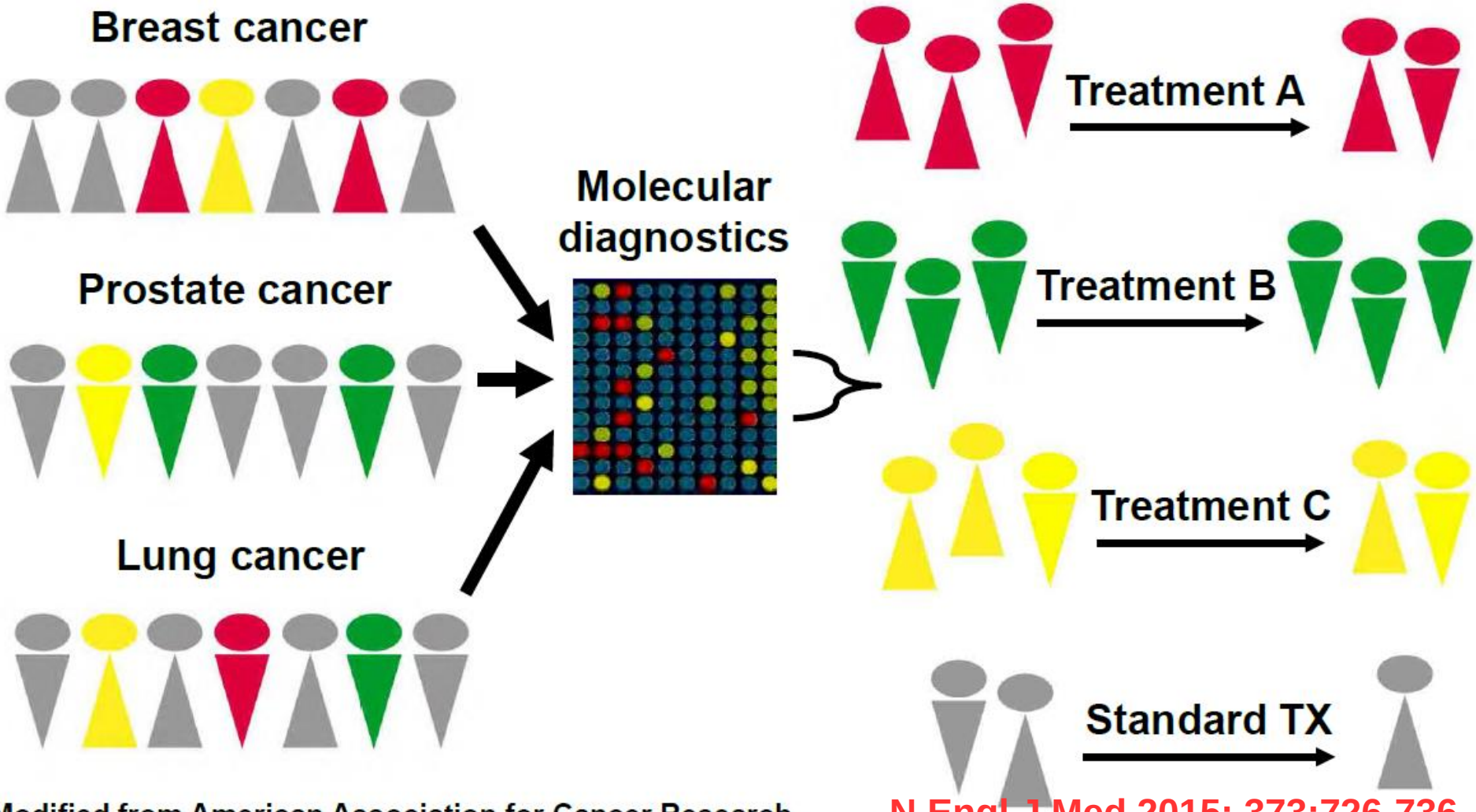
Efficacy of Adjuvant Trastuzumab for Patients With Human Epidermal Growth Factor Receptor 2–Positive Early Breast Cancer and Tumors ≤ 2 cm: A Meta-Analysis of the Randomized Trastuzumab Trials

JOURNAL OF CLINICAL ONCOLOGY

june, 2015



Precision Medicine



Modified from American Association for Cancer Research

N Engl J Med 2015; 373:726-736

BILANCIO/ Con il potenziamento della sanità digitale risparmi per 6,9 mld all'anno

Telemedicina, l'ora delle App

Gianfranco Gensini Paolo Colli Franzone

Sviluppare programmi innovativi per gestire i dati e i processi clinici

Avanti con il "digitale"! Cioè con il numerico, contare non sulla punta delle dita, come l'etimologia del termine suggerirebbe, ma con sistemi informatici, quello che è fornito dallo studio dei pazienti e richiesto dalla gestione dei loro problemi. Questa l'essenza della tanto enunciata e annunciata, ma ancora solo assai parzialmente realizzata "rivoluzione digitale" della sanità.

Addio agli eccessi di medicina difensiva

La medicina difensiva genera sovracosti stimati intorno ai **10-12 miliardi all'anno**. Oltre a «costare», la medicina difensiva influisce negativamente sulla qualità dell'assistenza sanitaria.

Medici che dichiarano di prescrivere per ragioni di medicina difensiva:	
Farmaci	53%

FORUM S@LUTE

Così l'e-health abbatte le inefficienze e fa aumentare la qualità dei servizi

La prima edizione, appena conclusa, di S@lute, il Forum della Sanità Digitale, si è ri-

Dobbiamo riuscire a immaginare e realizzare una "Rete della Salute" interamente sul Cloud, in

› Prevention and Screening
› Food
› Exercise
› Skin Safety
› Tobacco
› Screening
› Health
› Subscribe

43 Apps to help prevent cancer

Focused on Health - February 2014

From smartphone apps to interactive websites, plenty of tools exist to help you lead a healthier life. Here are some to get you started — at home and on the go. Many are free, but additional features may cost.

Exercise Apps

1. Exercise Counts Calculator (American Cancer Society): Web
2. Endomondo Sports Tracker (fitness tracker): Web / iPhone / Android / Blackberry / Windows Phone
3. Fitbit (activity and sleep tracker): Web / iPhone / Android
4. Loops (Livestrong): Web
5. MapMyFitness (fitness tracker): Web / iPhone / Android / Blackberry (See also: MapMyRun, MapMyRide, MapMyWalk, MapMyHike)
6. MyStart! Walking Paths and Tracker (American Heart Association): Web / iOS
7. Nexercise (workout game): Web/ iPhone / Android
8. Runtastic PRO (run tracker): Web / iOS / Android / Windows Phone (See also: Runtastic Six Pack Abs)
9. Target Heart Rate Calculator (American Cancer Society): Web
10. Zombies, Run! (running game): Web / iPhone /Android

Nutrition Apps

1. Calorie Counter (American Cancer Society): Web
2. Calorie Tracker (Livestrong): Web / iOS / Android / Windows Phone
3. Calorie Counter: diets & activities (calories, water and fitness tracker): iOS (See also: Calories Counter Plus: diets and activities)
4. Calories Count (calorie counter and activity tracker): Web / iOS / Android / Web / iPhone / Android
5. Lose It! (calorie counter for weight loss): Web / iOS / Android / Kindle / Nook
6. Fatsecret (calorie counter and diet and fitness tracker): Web / iPhone / Android
7. Meal makeover (healthy recipes): Web / iOS
8. MyFitnessPal (calorie counter and diet tracker): Web / iOS / Android / Windows Phone
9. Restaurant Nutrition (restaurant nutrition information): iPhone / Android
10. SuperTracker (U.S. Department of Agriculture): Web (Includes: Food-A-Pedia, Food Plans and Tracker, Physical Activity Tracker and My Weight Manager)
11. Virtual Dietitian (American Cancer Society): Web

Quit Smoking Apps

1. ASPIRE (MD Anderson): Web
2. Cigarette Calculator (American Cancer Society): Web
3. Freedom From Smoking® (American Lung Association): Web
4. MyQuit Coach (Livestrong): iPhone
5. QuitMedKit (MD Anderson): iPhone
6. SmokefreeTXT (National Cancer Institute): Text messaging
7. Smokefree Apps (National Cancer Institute): QuitSTART / NCI QuitPal / QuitGuide
8. Smoking Cost Calculator (American Cancer Society): Web
9. Tobacco Free Teens (MD Anderson): iPhone

Sun-Safety Apps

1. UV Index (Environmental Protection Agency): Web / iPhone / Android / Blackberry

Kids Apps

1. Apps for Healthy Kids (U.S. Department of Agriculture): Web

General Health Information Apps

1. CDC Health Tips (Centers for Disease Control): Text messaging
2. MD Anderson Mobile (MD Anderson): iPhone

Risk Assessment Tools

1. Breast Cancer Risk Assessment Tool (National Cancer Institute): Web / Mobile
2. Cancer Risk Check (MD Anderson): Web
3. Colorectal Risk Assessment Tool (National Cancer Institute): Web
4. Melanoma Risk Assessment Tool (National Cancer Institute): Web / Mobile
5. My Life Check (American Heart Association): Web

Screening Exams Apps

1. Find a Health Center (U.S. Department of Health & Human Services): iPhone
2. Mammogram Reminder (American Cancer Society): Web

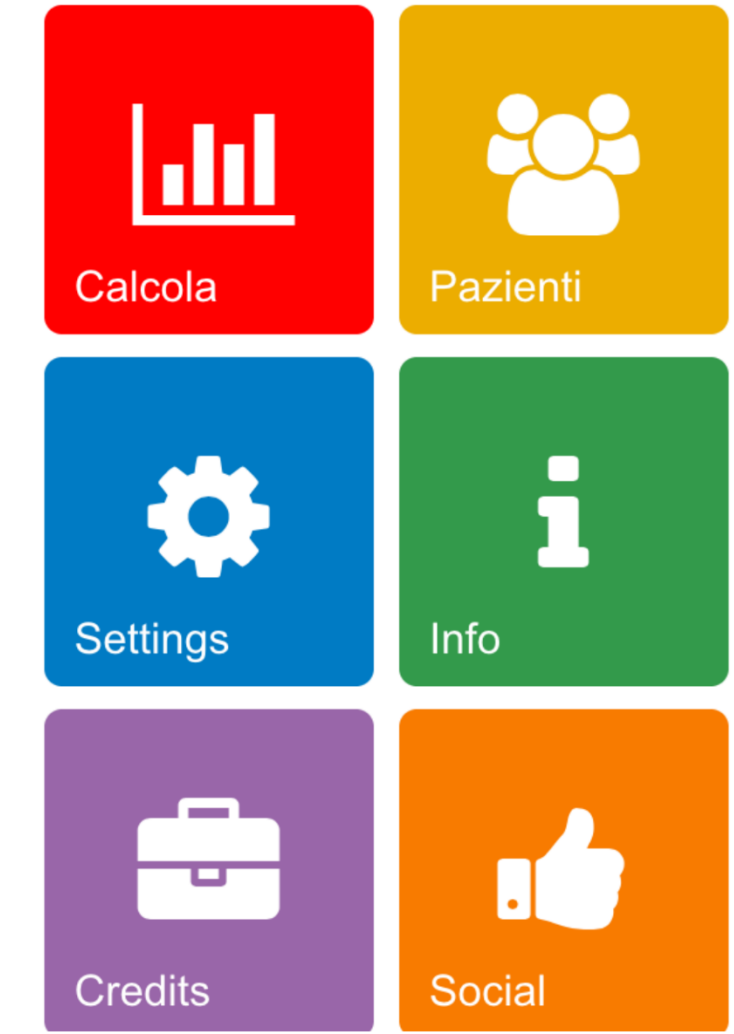
Cancer Treatment and Survivorship Apps

1. Cancer.net (American Society of Clinical Oncology): iOS / Android
2. Caring Bridge (CaringBridge.org): Web / iPhone / Android

Remember, apps, like health goals, are a personal choice. What works for you, may not work for someone else.

La borsa del medico

Visita: nessun Paziente selezionato



Next Steps in Developing the Precision Medicine Initiative

AUGUST 21, 2015 AT 7:48 PM ET BY DJ PATIL, STEPHANIE DEVANEY

Summary: The President's Precision Medicine Initiative is looking for new activities that will help make this important program a reality.

The President's Precision Medicine Initiative (PMI) is dedicated to enabling a new era of medicine through research, technology, and policies that will lead to the development of individualized, tailored treatments for patients. This vision will allow everyone to become an active participant in scientific discovery – furthering an open and inclusive model for better recruitment of and partnership with research participants. Why is this so important? We have seen incredible innovations in health care, and central to many of those advances have been people participating in research. PMI will provide the foundation that allows all Americans to sign up and share their data in a safe and responsible way, leading to scientific breakthroughs that will ultimately pave the way to better options for patients.

And that's why we want to hear from **YOU.**

Next Steps in Developing the Precision Medicine Initiative

AUGUST 21, 2015 AT 7:48 PM ET BY DJ PATIL, STEPHANIE DEVANEY

Summary: The President's Precision Medicine Initiative is looking for new activities that will help make this important program a reality.

The President's Precision Medicine Initiative (PMI) is dedicated to enabling a new era of medicine through research, technology, and policies that will lead to the development of individualized, tailored treatments for patients. This vision will allow everyone to become an active participant in scientific discovery – furthering an open and inclusive model for better recruitment of and partnership with research participants. Why is this so important? We have seen incredible

And that's why we want to hear from **YOU.**

And that's why we want to hear from **YOU.**


I WANT YOU

FOR THE PRECISION MEDICINE INITIATIVE