La Gastroenterologia nell' era della precision medicine: leader o follower?

Enzo Grossi

TOP TEN 2017

Iseo , 17 Marzo 2017

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

CONCEPT

Precision medicine:

- New taxonomic classification of diseases based on big data
- Translation of decisions and outcome prediction at individual level

NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES

THE NATIONAL ACADEMIES PRESS
Washington, D.C.
www.nap.edu

Da: Grossi Enzo
Inviato: venerdì 30 dicembre 2011 17:38
A: 'Newman, Francis'; Asadi-Zeydabadi, Masoud; Massimo Buscema; Lodwick, Weldon; Bronstein, Al
Oggetto: R: End of the year notice: Precision medicine

Dear friends, here you will find something very interesting: a recent manifesto coming from NIH which appointed a special committee to work on a innovative frame work for a definite change in the philosophical approach of health and disease management. This new impetus toward the so called **“precision medicine”** seems to point toward complexity-surfing people like us. Maybe the time is coming for our group to ride the tiger. The full book is easily downloadable following the instructions.

Best wishes for a beautiful new year.

Enzo

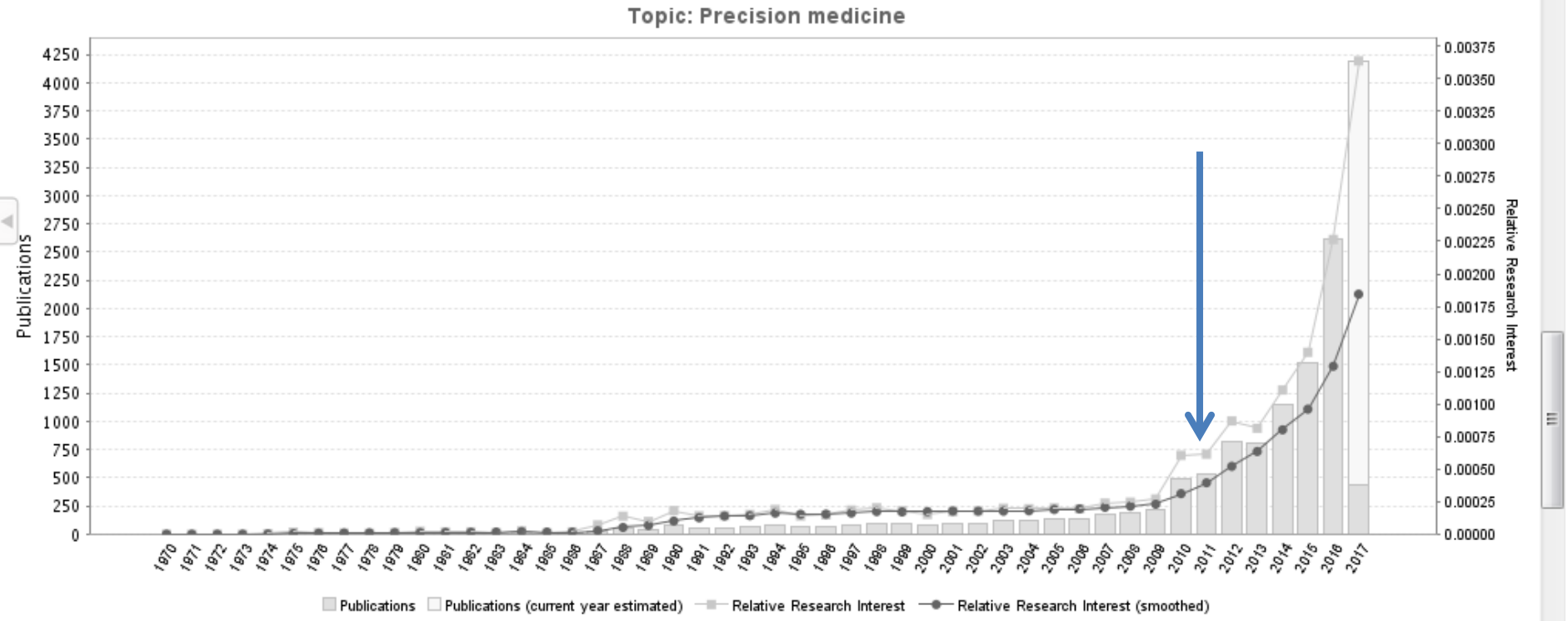
Precision medicine

find

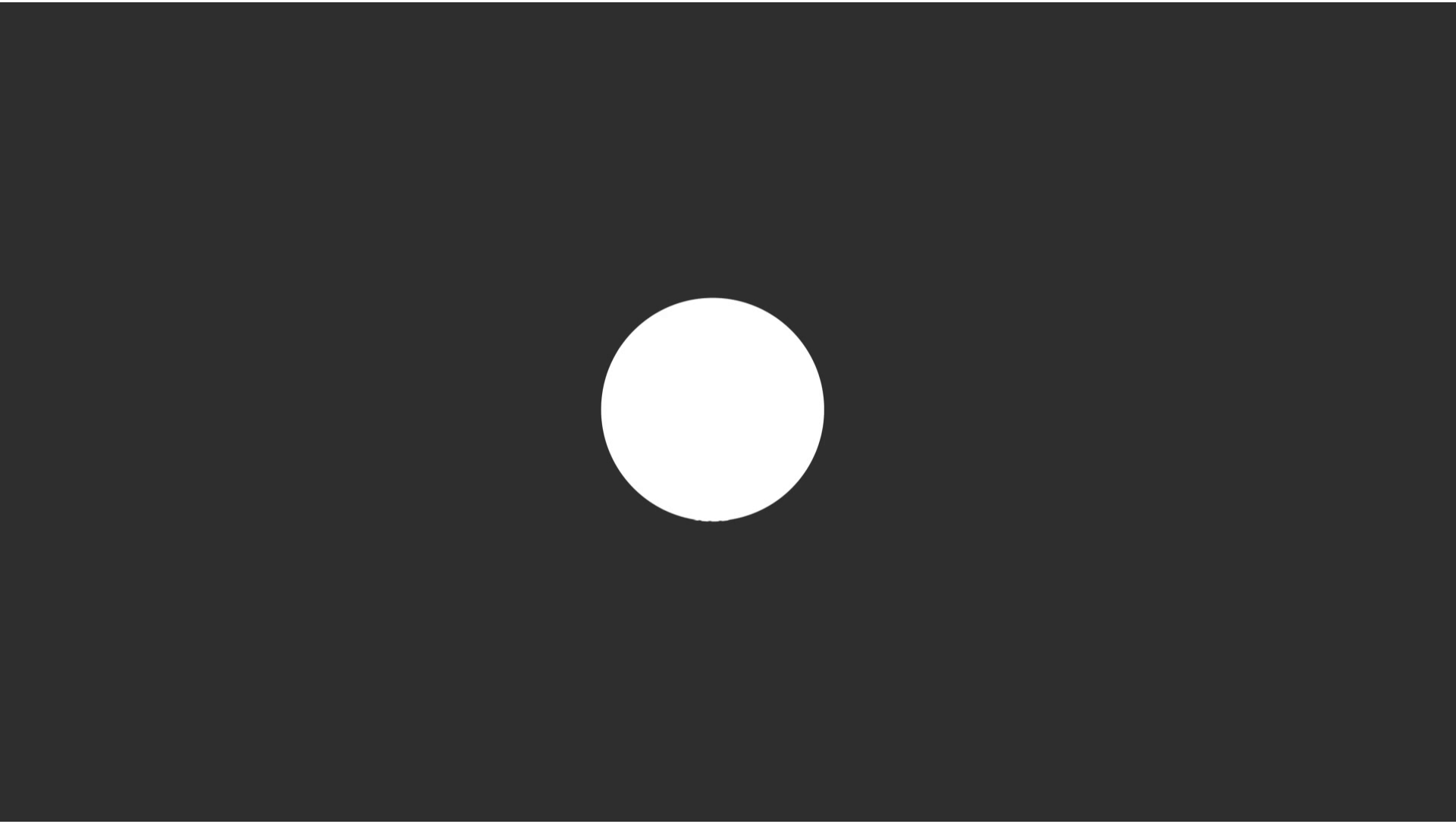
show abstracts documents statistics clipboard share export

statistics of 23,206 documents

publications over time



world map



The NEW ENGLAND JOURNAL of MEDICINE

Perspective

FEBRUARY 26, 2015

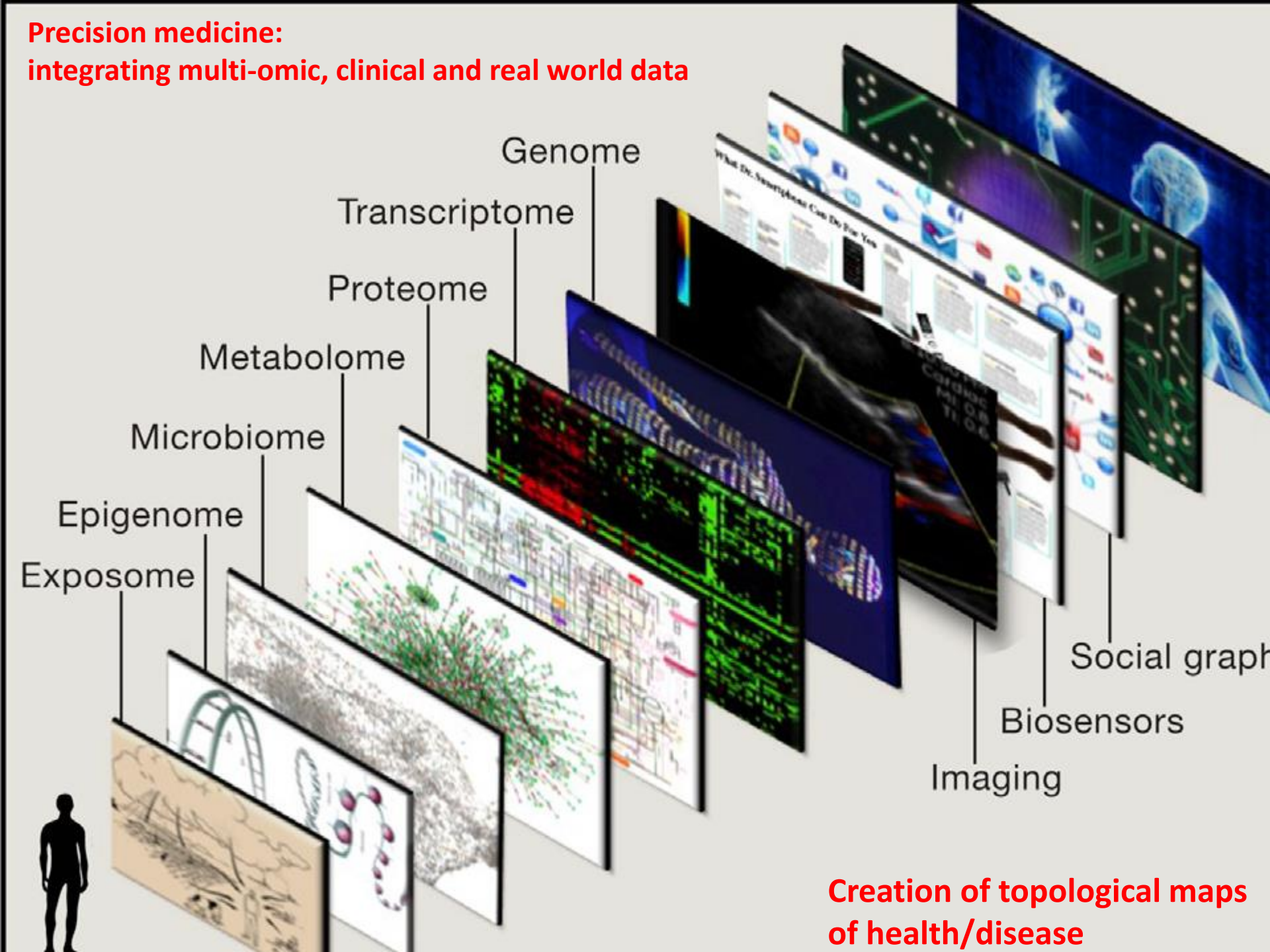
A New Initiative on Precision Medicine

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

"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

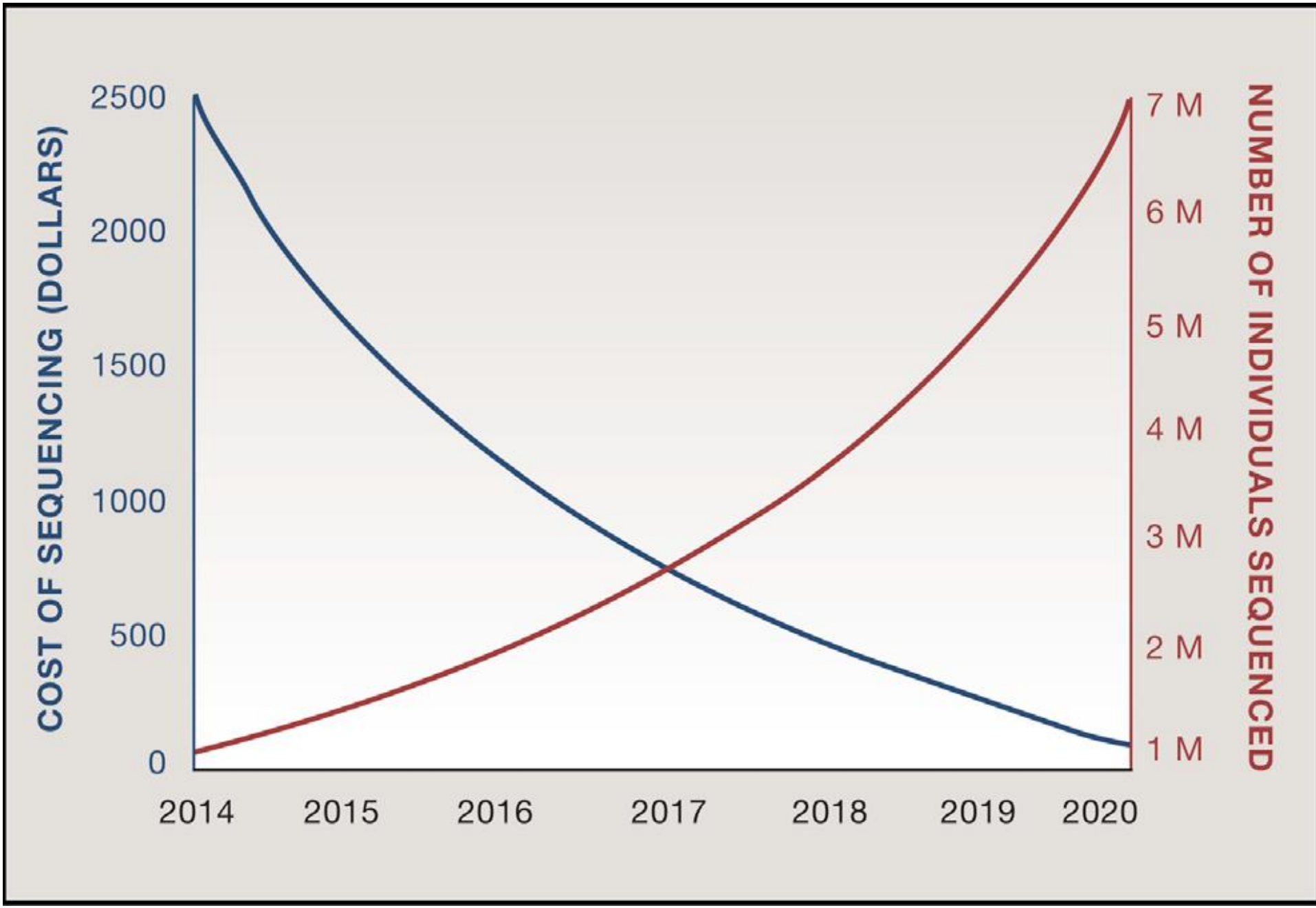
Precision medicine:
integrating multi-omic, clinical and real world data



Creation of topological maps of health/disease

Data inflation

Unit	Size	What it means
Bit (b)	1 or 0	Short for "binary digit", after the binary code (1 or 0) computers use to store and process data
Byte (B)	8 bits	Enough information to create an English letter or number in computer code. It is the basic unit of computing
Kilobyte (KB)	1,000, or 2^{10}, bytes	From "thousand" in Greek. One page of typed text is 2KB
Megabyte (MB)	1,000KB; 2^{20} bytes	From "large" in Greek. The complete works of Shakespeare total 5MB. A typical pop song is about 4MB
Gigabyte (GB)	1,000MB; 2^{30} bytes	From "giant" in Greek. A two-hour film can be compressed into 1-2GB
Terabyte (TB)	1,000GB; 2^{40} bytes	From "monster" in Greek. All the catalogued books in America's Library of Congress total 15TB
Petabyte (PB)	1,000TB; 2^{50} bytes	All letters delivered by America's postal service this year will amount to around 5PB. Google processes around 1PB every hour
Exabyte (EB)	1,000PB; 2^{60} bytes	Equivalent to 10 billion copies of *The Economist*
Zettabyte (ZB)	1,000EB; 2^{70} bytes	The total amount of information in existence this year is forecast to be around 1.2ZB
Yottabyte (YB)	1,000ZB; 2^{80} bytes	Currently too big to imagine

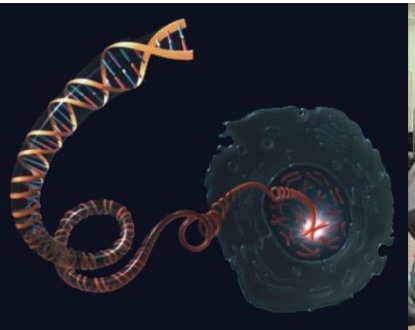

COST OF SEQUENCING (DOLLARS)
2500
2000
1500
1000
500
0
NUMBER OF INDIVIDUALS SEQUENCED
7 M
6 M
5 M
4 M
3 M
2 M
1 M
2014
2015
2016
2017
2018
2019
2020

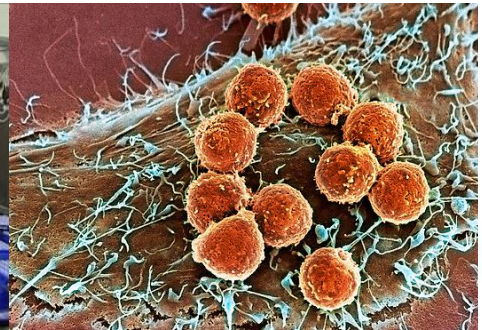
Una gara aperta tra le grandi potenze scientifiche

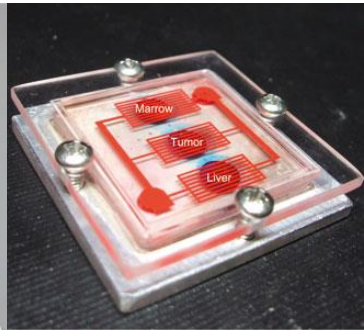
- UK (2012):100.000 casi per il genome project https://www.genomicsengland.co.uk/
- USA(2015) : PMI Cohort program (un milione di casi con multi-omics)
- Cina (2016): 100 milioni di casi sequenziati entro il 2030

Science Priorities: PMI for Oncology

- Goal: Apply tenets of precision medicine to cancer
- To reach this goal, PMI-Oncology will enable research to:
- Use NCI clinical trials as models
  - NCI-MATCH: solid tumors, lymphomas (multi-drug, multi-arm)
  - Lung-MAP: squamous cell lung cancer (multi-drug, multi-arm, randomized)
- Identify new cancer subtypes, therapeutic targets
- Test combination therapies
- Partner with private sector to test precision medicine
- Understand and combat drug resistance







The Institute for Precision Cardiovascular Medicine

The American Heart Association Institute for Precision Cardiovascular Medicine is dedicated to preserving and prolonging health. We invite you to learn more and join us.

WHAT WE DO

OUR WORK

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frontiers in Psychiatry

PERSPECTIVE
published: 29 November 2016
doi: 10.3389/fpsyt.2016.00188

Defining Precision Medicine Approaches to Autism Spectrum Disorders: Concepts and Challenges

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Focus on Toward Precision Medicine in Neurological Diseases

Ann Transl Med 2016;4(6):107

Toward precision medicine in Alzheimer's disease

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Abstract: In Western societies, Alzheimer's disease (AD) is the most common form of dementia and the sixth leading cause of death. In recent years, the concept of precision medicine, an approach for disease prevention and treatment that is personalized to an individual's specific pattern of genetic variability, environment and lifestyle factors, has emerged. While for some diseases, in particular select cancers and a few monogenetic disorders such as cystic fibrosis, significant advances in precision medicine have been made over the past years, for most other diseases precision medicine is only in its beginning. To advance the application of precision medicine to a wider spectrum of disorders, governments around the world are starting to launch Precision Medicine Initiatives, major efforts to generate the extensive scientific knowledge needed to integrate the model of precision medicine into every day clinical practice. In this article we summarize the state of precision medicine in AD, review major obstacles in its development, and discuss its benefits in this highly prevalent, clinically and pathologically complex disease.

Keywords: Precision medicine; Alzheimer's disease (AD); genomics

Imaging in the Age of Precision Medicine: Summary of the Proceedings of the 10th Biannual Symposium of the International Society for Strategic Studies in Radiology

Article *in* Radiology 279(1):150709 · October 2015
DOI: 10.1148/radiol.2015150709

….. **Because of the growing volume and complexity of imaging data, decision-support algorithms will be required to help physicians apply the most essential patient data for optimal management. These innovations will challenge traditional concepts of health care and business models.**

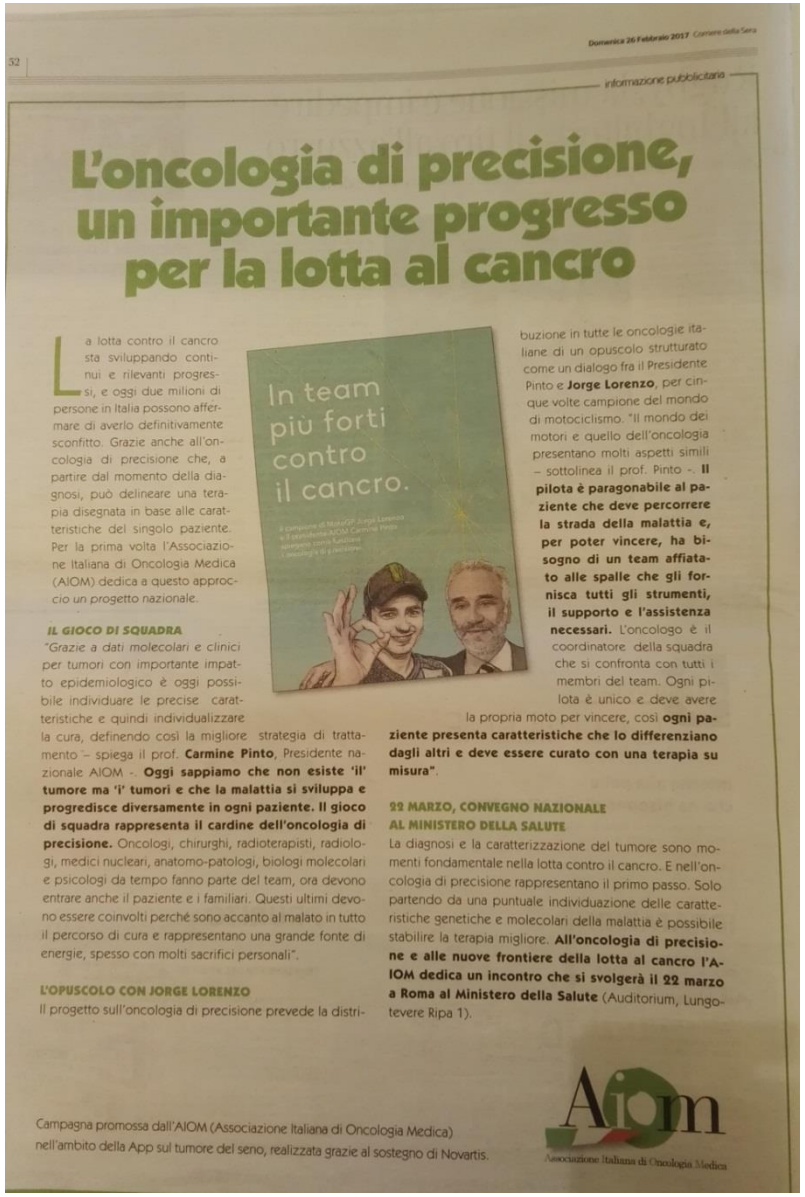
UN MANIFESTO PER L'ONCOLOGIA DI PRECISIONE

Sfide e opportunità da cogliere nei prossimi 10 anni per medici, pazienti e istituzioni

Nei dieci punti cardine del Manifesto NEXT10 si affrontano temi di grande importanza nello sviluppo prospettico dell'oncologia che vanno dalla necessità di gestire la pratica clinica in funzione del rapporto umano con il paziente alla creazione e sviluppo di reti di collaborazione e di circolazione dei saperi, che assicurino uniformità su tutto il territorio nazionale. E ancora, la gestione al meglio della tecnologia in continua evoluzione; l'incentivazione di investimenti economici per la ricerca, la realizzazione di un sistema integrato, complessivo e condiviso di registrazione dei dati e delle informazioni.

NOVARTIS

1. Precisione: una nuova fase per l'oncologia
2. Precisione: ottenere migliori risultati per i pazienti
3. Precisione: più partecipazione nella gestione della cura
4. Precisione: unire le competenze
5. Precisione: una nuova cultura della condivisione
6. Precisione: una diagnosi ad hoc
7. Precisione: la ricerca si sposa con la clinica
8. Precisione: disegnare reti che diffondono i saperi
9. Precisione: abbracciare le nuove tecnologie
10. Precisione: costruire network sostenibili



L'oncologia di precisione, un importante progresso per la lotta al cancro

La lotta contro il cancro sta sviluppando continui e rilevanti progressi, e oggi due milioni di persone in Italia possono affermare di averlo definitivamente sconfitto. Grazie anche all'oncologia di precisione che, a partire dal momento della diagnosi, può delineare una terapia disegnata in base alle caratteristiche del singolo paziente. Per la prima volta l'Associazione Italiana di Oncologia Medica (AIOM) dedica a questo approccio un progetto nazionale.

IL GIOCO DI SQUADRA

"Grazie a dati molecolari e clinici per tumori con importante impatto epidemiologico è oggi possibile individuare le precise caratteristiche e quindi individualizzare la cura, definendo così la migliore strategia di trattamento" – spiega il prof. **Carmine Pinto**, Presidente nazionale AIOM –. **Oggi sappiamo che non esiste 'il' tumore ma 'i' tumori e che la malattia si sviluppa e progredisce diversamente in ogni paziente. Il gioco di squadra rappresenta il cardine dell'oncologia di precisione.** Oncologi, chirurghi, radioterapisti, radiologi, medici nucleari, anatomo-patologi, biologi molecolari e psicologi da tempo fanno parte del team, ora devono entrare anche il paziente e i familiari. Questi ultimi devono essere coinvolti perché sono accanto al malato in tutto il percorso di cura e rappresentano una grande fonte di energie, spesso con molti sacrifici personali".

L'OPUSCOLO CON JORGE LORENZO

Il progetto sull'oncologia di precisione prevede la distribuzione in tutte le oncologie italiane di un opuscolo strutturato come un dialogo fra il Presidente Pinto e **Jorge Lorenzo**, per cinque volte campione del mondo di motociclismo. "Il mondo dei motori e quello dell'oncologia presentano molti aspetti simili – sottolinea il prof. Pinto –. **Il pilota è paragonabile al paziente che deve percorrere la strada della malattia e, per poter vincere, ha bisogno di un team affiatato alle spalle che gli fornisca tutti gli strumenti, il supporto e l'assistenza necessari.** L'oncologo è il coordinatore della squadra che si confronta con tutti i membri del team. Ogni pilota è unico e deve avere la propria moto per vincere, così **ogni paziente presenta caratteristiche che lo differenziano dagli altri e deve essere curato con una terapia su misura"**.

22 MARZO, CONVEGNO NAZIONALE AL MINISTERO DELLA SALUTE

La diagnosi e la caratterizzazione del tumore sono momenti fondamentale nella lotta contro il cancro. E nell'oncologia di precisione rappresentano il primo passo. Solo partendo da una puntuale individuazione delle caratteristiche genetiche e molecolari della malattia è possibile stabilire la terapia migliore. **All'oncologia di precisione e alle nuove frontiere della lotta al cancro l'AIOM dedica un incontro che si svolgerà il 22 marzo a Roma al Ministero della Salute** (Auditorium, Lungotevere Ripa 1).

Campagna promossa dall'AIOM (Associazione Italiana di Oncologia Medica) nell'ambito della App sul tumore del seno, realizzata grazie al sostegno di Novartis.

Aiom
Associazione Italiana di Oncologia Medica

The NEW ENGLAND JOURNAL of MEDICINE

La gastroenterologia si sta interrogando su questo?

Perspective

JUNE 5, 2014

Learning from Big Health Care Data

Sebastian Schneeweiss, M.D., Sc.D.

Gastroenterology 2017;152:53–67

Using Big Data to Discover Diagnostics and Therapeutics for Gastrointestinal and Liver Diseases

Benjamin Wooden,[1] Nicolas Goossens,[1,2] Yujin Hoshida,[1] and Scott L. Friedman[1]

[1]Division of Liver Diseases, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, New York; and [2]Division of Gastroenterology and Hepatology, Department of Medical Specialties, Geneva University Hospital, Geneva, Switzerland

Technologies such as genome sequencing, gene expression profiling, proteomic and metabolomic analyses, electronic medical records, and patient-reported health information have produced large amounts of data from various populations, cell types, and disorders (big data). However, these data must be integrated and analyzed if they are to produce models or concepts about physiological function or mechanisms of pathogenesis. Many of these data are available to the public, allowing researchers anywhere to

acetylome, lipidome, microbiome, phenome, exposome, meta-genome, and interactome are increasingly being deposited for public use.

In parallel, the widespread adoption of electronic health records[6] has generated massive amounts of digitized personal health information, as has the increasing popularity of automatic serial data acquisition from wearable devices/technologies[7] and web applications that collect patient-reported health information (eg, the www.HepCure.org

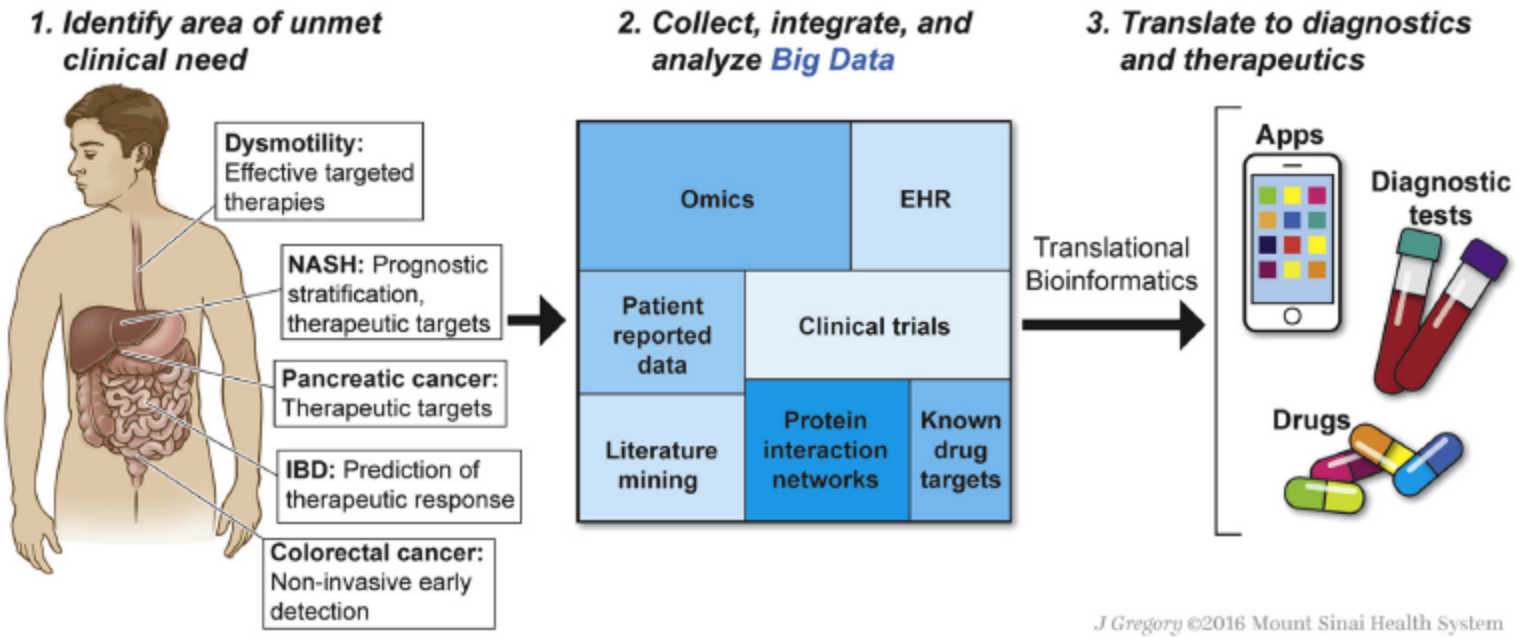


Figure 1. Big data–driven discovery in gastroenterology and hepatology. (*1*) Big data–driven discovery may provide new approaches to long-standing or emerging unmet needs in gastrointestinal and liver diseases. (*2*) Multi-domain systematically and/or automatically collected data from patients and publicly or privately available databases are integrated into a highly rich and heterogeneous dataset. (*3*) Mining of the assembled big data by specialized methodologies (translational bioinformatics) more efficiently yields diagnostic devices, tools, and/or therapeutics. NASH, nonalcoholic steatohepatitis; EHR, electronic health record.

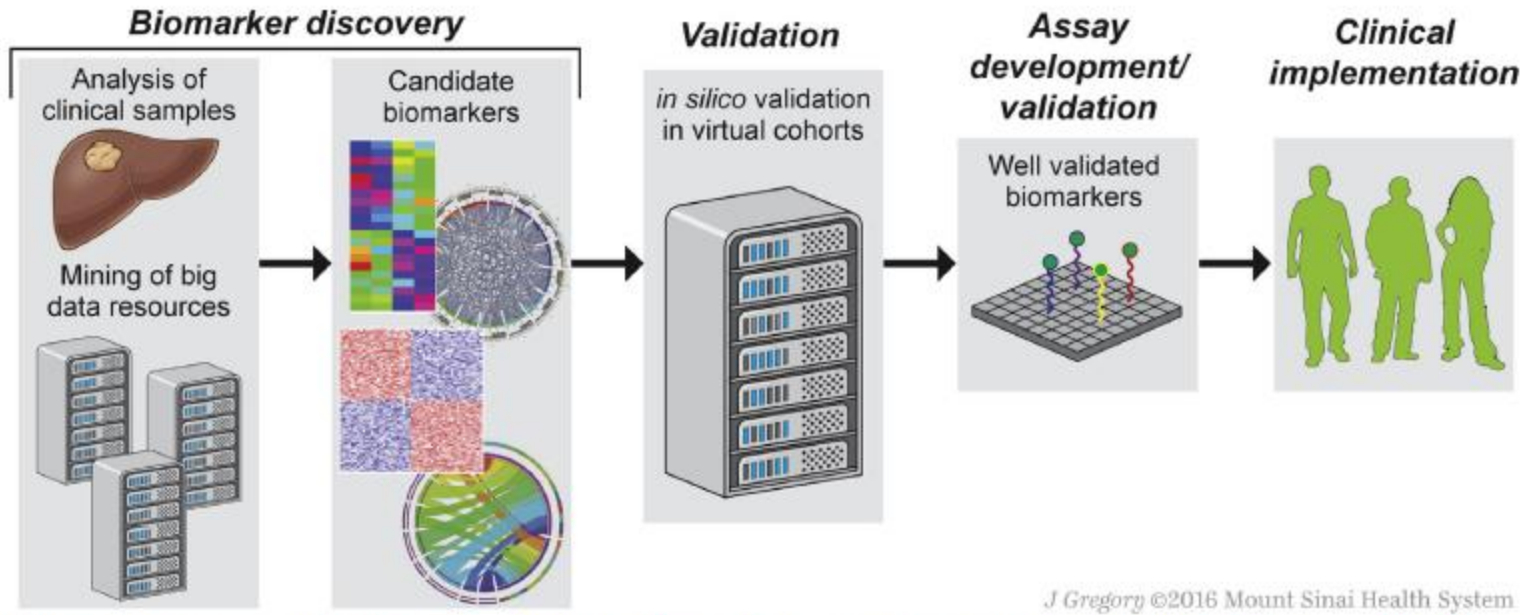


Figure 3. Big data–driven biomarker discovery. Biomarker candidates may be identified from either analysis of newly collected samples or in silico analysis of existing data from public and/or private big data repositories. Biomarker validation has traditionally been a costly process requiring assay development and prospective clinical evaluation with patients followed according to a strict protocol. By incorporating big data resources, in silico validation of a candidate biomarker can establish its clinical utility in multiple patient cohorts without conducting costly and lengthy prospective clinical trials. Only well-validated biomarkers are advanced to subsequent assay development and clinical evaluation with reduced risk of failure to show clinical utility.

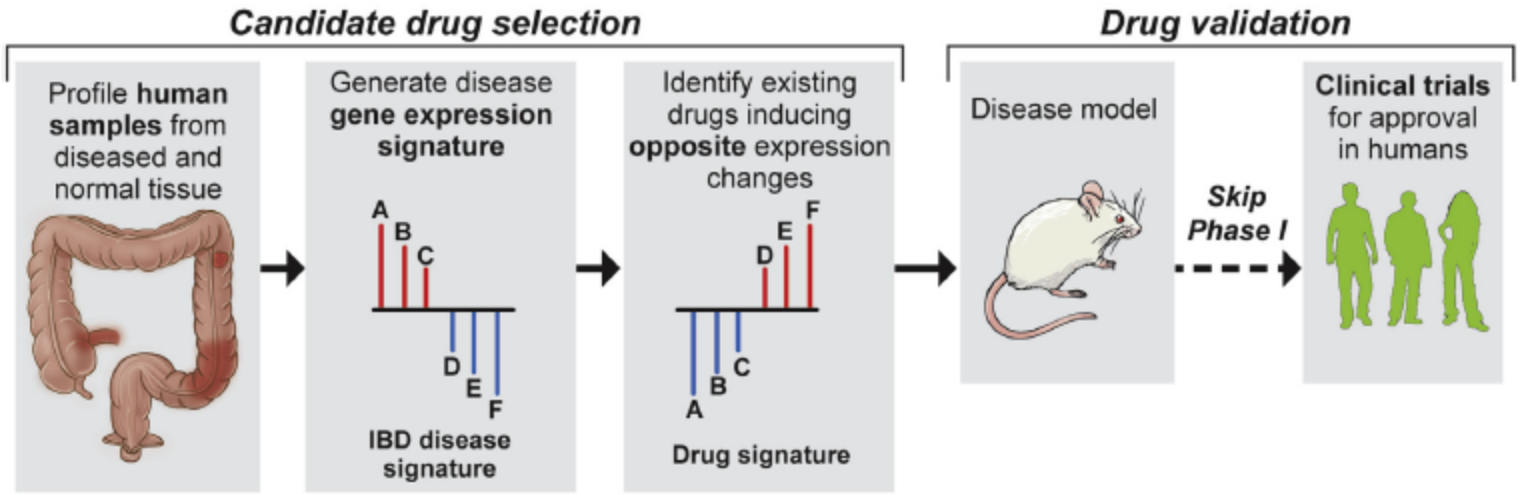
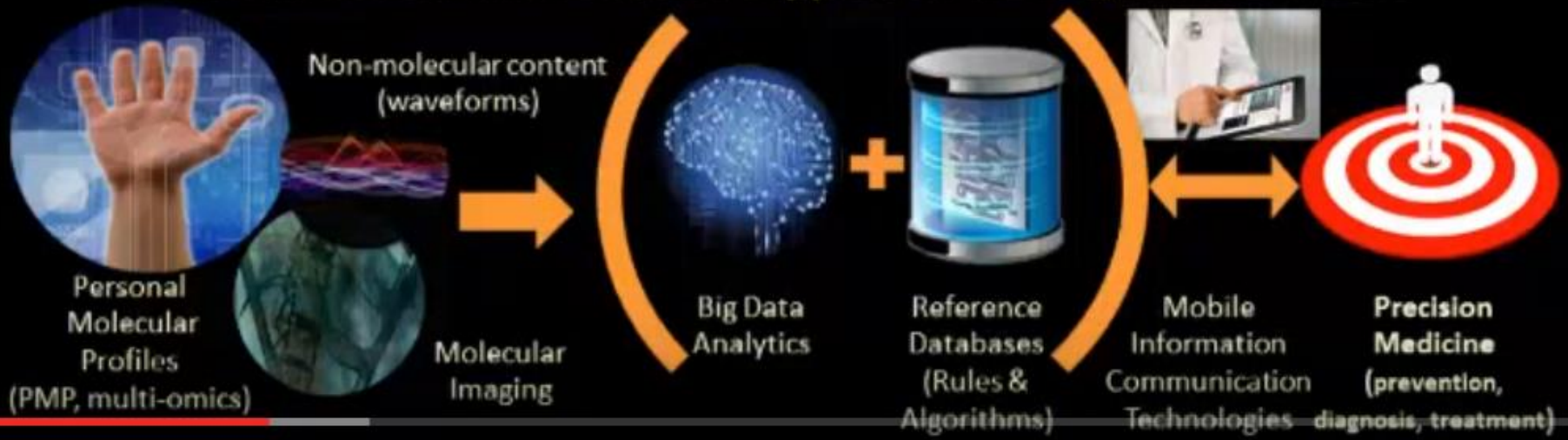


Figure 4. Big data–driven therapeutic discovery. An example of the hypothesis-free, "signature inversion" therapeutic discovery approach for IBD is shown as an example of big data–driven drug discovery (eg, Dudley et al[55]). A disease signature—a set of genes dysregulated in a coordinated manner in patients with IBD—is first identified (*left*, genes A, B, and C are up-regulated, and genes D, E, and F are down-regulated). With the IBD disease signature, a database of drug perturbation gene signatures is queried to identify compounds that modulate genes A to F in the opposite direction (ie, suppress expression of genes A, B, and C and induce expression of genes D, E, and F) and are thereby expected to antagonize the IBD disease signature. No mechanistic understanding of the associated gene dysregulation is needed for the computational compound identification. Subsequent experimental validation can confirm the predicted therapeutic effect and seek to uncover the mechanism(s) of action before proceeding to further preclinical and clinical development (*right*). Because the screening is performed using data derived from approved drugs with known toxicity profiles, clinical testing can omit phase 1 and move immediately to phase 2.

Precision Medicine - Paradigm Shift

	Yesterday	Today	Tomorrow
DATA	Symptom-based	Cohort-based	Algorithm-based
ACTIONS	Intuition Medicine	Evidence-based Medicine	Precision Medicine

Application of rules, algorithms and reference databases enables ACTIONABLE clinical decision support & PRECISE/EFFICIENT care



Il fascino dei big data

- Con i Big data non vi è alcuna necessità di una teoria a priori, di modelli o di ipotesi;
- Attraverso opportuni algoritmi i dati possono parlare da soli prescindendo da bias interpretativi.
- Tutti i pattern e le relazioni nei Big Data sono intrinsecamente significative e veritiere;
- Il significato trascende la conoscenza specifica di un certo contesto o dominio per essere interpretabile da chiunque sia in grado di decodificare una statistica o di visualizzare i dati.

R. Kitchin, Big Data, new epistemologies and paradigm shifts, Big Data & Society April–June 2014: 1–122014

REVIEW

CME

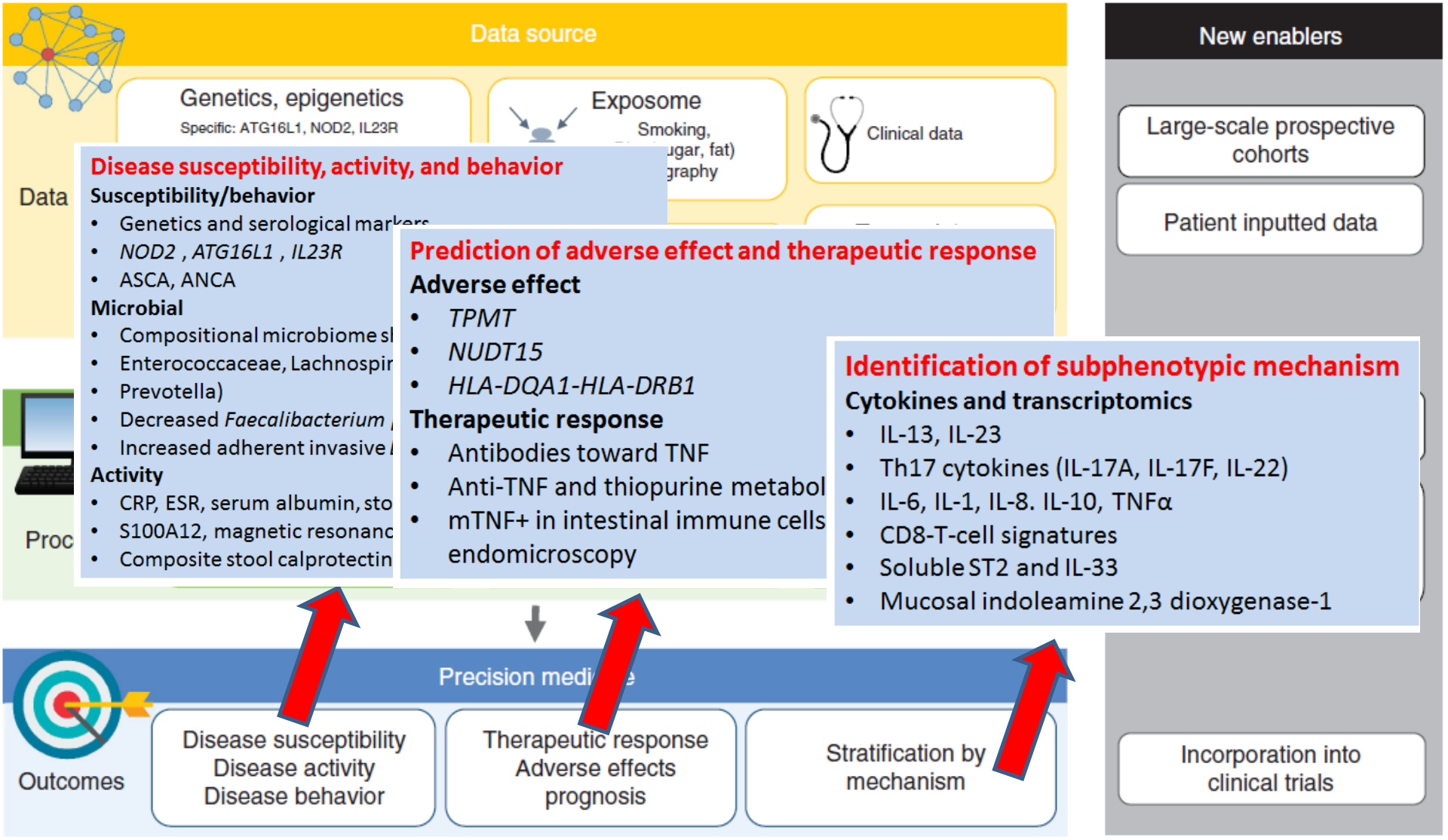
Biomarkers in Search of Precision Medicine in IBD

Ray K. Boyapati, MBBS, FRACP[1,2], Rahul Kalla, MBBS, MRCP[3], Jack Satsangi, DPhil, FRCP[3] and Gwo-tzer Ho, PhD, FRCP[1,3]

The completion of the human genome project in 2003 represented a major scientific landmark, ushering in a new era with hopes and expectations of fresh insights into disease mechanisms and treatments. In inflammatory bowel disease (IBD), many important discoveries soon followed, notably the identification of >200 genetic susceptibility loci and characterization of the gut microbiome. As "big data", driven by advances in technology, becomes increasingly available and affordable, individuals with IBD and clinicians alike yearn for tangible outcomes from the promise of "precision medicine"—precise diagnosis, monitoring, and treatment. Here, we provide a commentary on the prospects and challenges of precision medicine and biomarkers in IBD. We focus on the three key areas where precision IBD will have the most impact: (1) disease susceptibility, activity, and behavior; (2) prediction of drug response and adverse effects; and (3) identification of subphenotypic mechanisms to facilitate drug discovery and selection of new treatments in IBD.

Am J Gastroenterol 2016; 111:1682–1690; doi:10.1038/ajg.2016.441; published online 27 September 2016

IBD BIG DATA: SINK OR SWIM?



Am J Gastroenterol 2016; 111:1682–1690; doi:10.1038/ajg.2016.441; published online 27 September 2016

AP&T Alimentary Pharmacology and Therapeutics
2016 Jan;43(2):262-71.

A validated web-based tool to display individualised Crohn's disease predicted outcomes based on clinical, serologic and genetic variables

C. A. Siegel[*,†], H. Horton[‡], L. S. Siegel[§,¶], K. D. Thompson[*,†], T. Mackenzie[†], S. K. Stewart[*], P. W. Rice[¶], J. M. Stempak[**], S. Dezfoli[‡], T. Haritunians[‡], A. Levy[‡], M. Baek[‡], R. Milgrom[**], P. S. Dulai[*,†], S. R. Targan[‡], M. S. Silverberg[**], M. C. Dubinsky[††] & D. P. McGovern[‡]

[*]Dartmouth-Hitchcock Inflammatory Bowel Disease Center, Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA.
[†]Department of Medicine, Geisel School of Medicine at Dartmouth, Hanover, NH, USA.
[‡]F. Widjaja Foundation Inflammatory Bowel and Immunobiology Research Institute, Cedars-Sinai Medical Center, Los Angeles, CA, USA.
[§]Siegel Environmental Dynamics, Hanover, NH, USA.

SUMMARY

Background

Early treatment for Crohn's disease (CD) with immunomodulators and/or anti-TNF agents improves outcomes in comparison to a slower 'step up' algorithm. However, there remains a limited ability to identify those who would benefit most from early intensive therapy.

Aim

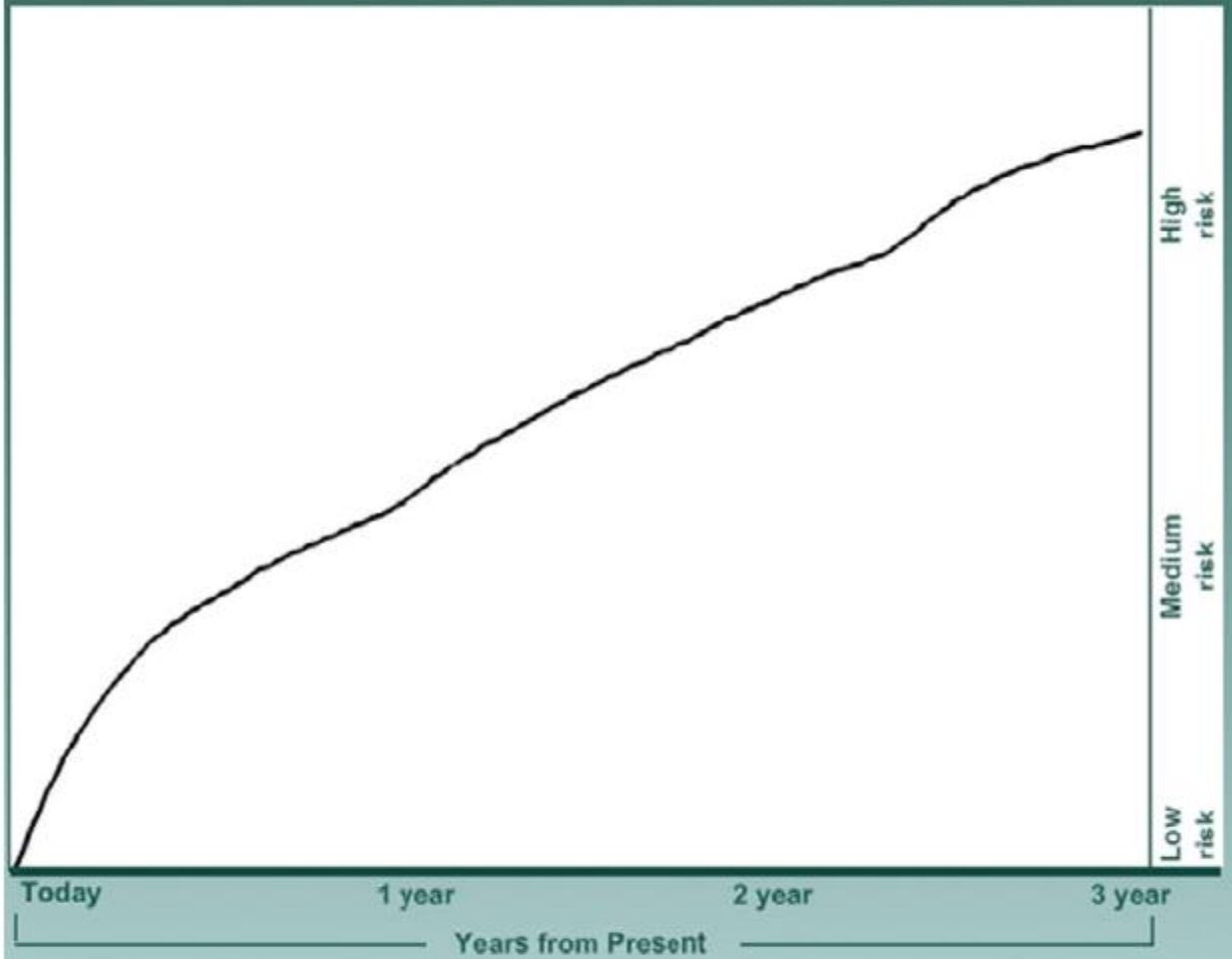
To develop a validated, individualised, web-based tool for patients and clinicians to visualise individualised risks for developing Crohn's disease complications.

Clinical data input

Patient page

Gender: Male
Diagnosis: Crohn's disease
Date of Birth: 5/1/1958

PROSPECT
Personalized Risk and Outcome Prediction Tool



Personal characterisitcs

(•) Male ( ) Female

	Month	Day	Year
Birthdate	5	1	1958
Date of Diagnosis	2	15	2010

Disease Location

- [ ] Upper GI Tract (stomach/esophagus)
- [x] Small bowel
- [x] Right colon
- [x] Transverse colon
- [x] Left colon
- [x] Perianal

Blood test markers

ASCA A 4 ASCA G 4

CBir 1 16 ANCA 20

Genetic test

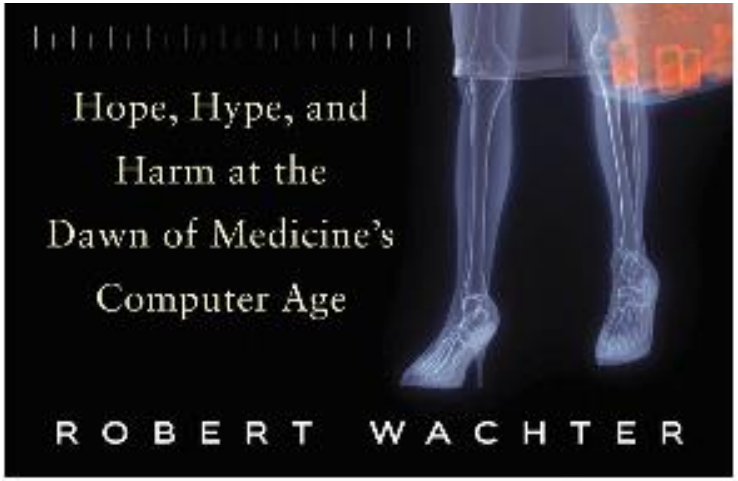
- [x] NOD2 variant

Calculate | Save Run | Manage | Logout of sim

v15.49beta

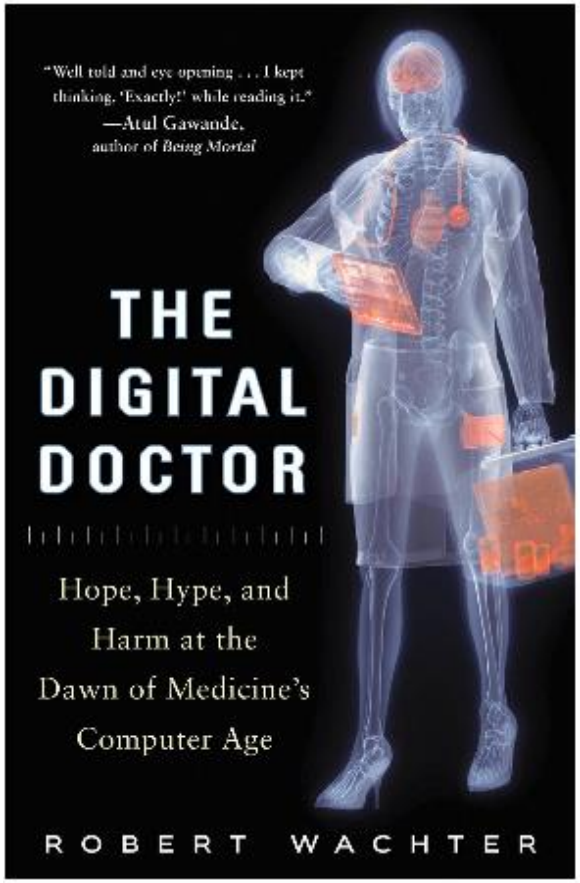
IL NUOVO GASTROENTEROLOGO ?

proteomics, metabolomics, kinomics, methylomics, acetylomics, lipidomics, microbiomics, phenomics, exposomics, meta-genomics, interactomics…



Complessità delle malattie croniche

Aumento esponenziale dei dati che descrivono un individuo



TOP TEN 2015
IN GASTROENTEROLOGIA

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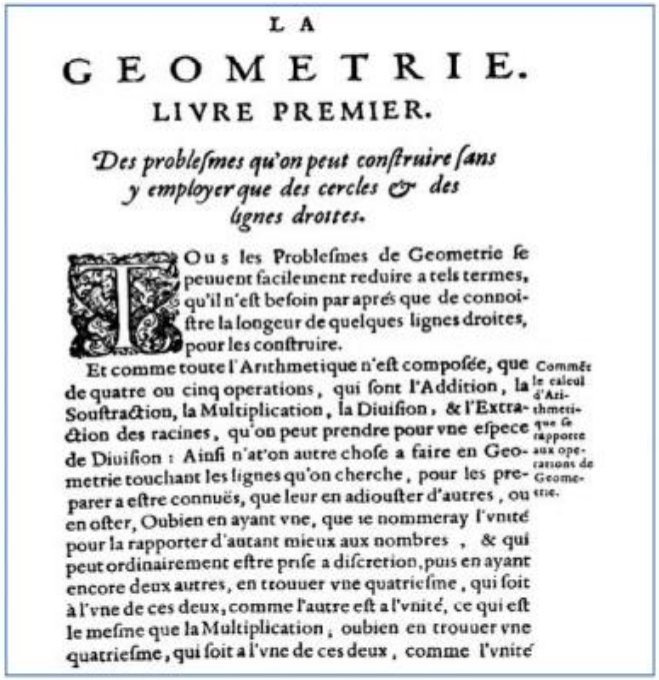
Il dilemma della Nona di Beethoven in un diagramma cartesiano



LA
GEOMETRIE.
LIVRE PREMIER.

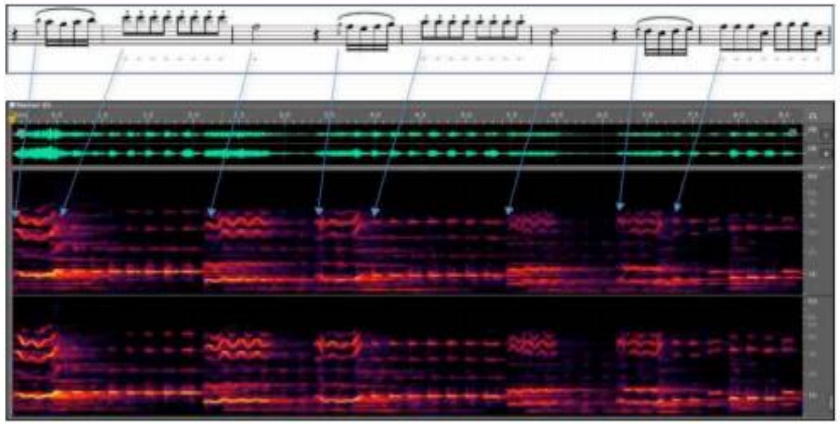
Des problesmes qu'on peut construire sans y employer que des cercles & des lignes droites.

TOus les Problesmes de Geometrie se peuuent facilement reduire a tels termes, qu'il n'est besoin par aprés que de connoistre la longeur de quelques lignes droites, pour les construire.

Et comme toute l'Arithmetique n'est composée, que de quatre ou cinq operations, qui sont l'Addition, la Souſtraction, la Multiplication, la Diuision, & l'Extraction des racines, qu'on peut prendre pour vne espece de Diuision : Ainsi n'at'on autre chose a faire en Geometrie touchant les lignes qu'on cherche, pour les preparer a estre connuës, que leur en adiouster d'autres, ou en oster, Oubien en ayant vne, que ie nommeray l'vnité pour la rapporter d'autant mieux aux nombres, & qui peut ordinairement estre prise a discretion, puis en ayant encore deux autres, en trouuer vne quatriesme, qui soit à l'vne de ces deux, comme l'autre est a l'vnité, ce qui est le mesme que la Multiplication, oubien en trouuer vne quatriesme, qui soit a l'vne de ces deux, comme l'vnité

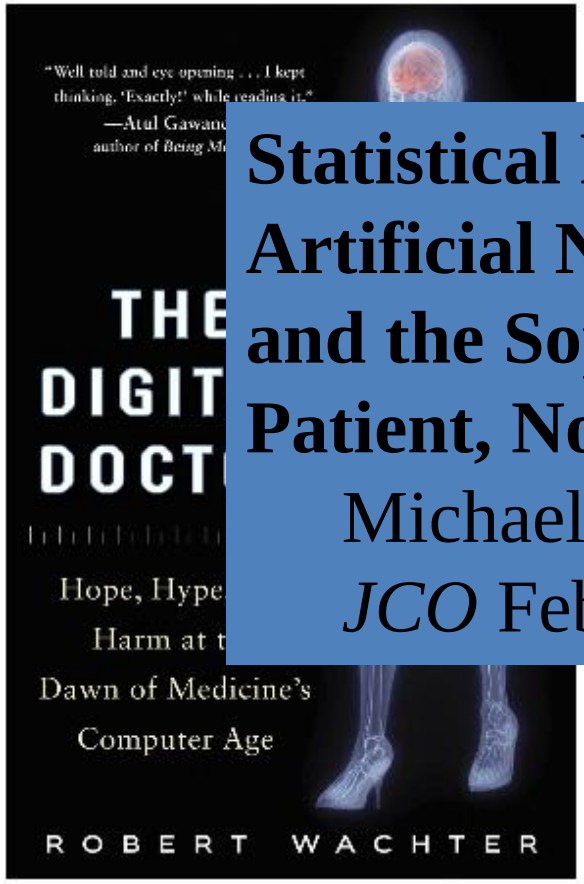
Comme le calcul d'Arithmetique se rapporte aux operations de Geometrie.

Enzo Grossi



Complessità delle malattie croniche

Aumento esponenziale dei dati che descrivono un individuo



Statistical Prediction Models, Artificial Neural Networks, and the Sophism "I Am a Patient, Not a Statistic"

Michael Kattan

JCO Feb 15 2002: 885-887.

Gastroenterologia di precisione

Uncertainty in the Era of Precision Medicine

David J. Hunter, M.B., B.S., Sc.D.

A National Research Council report on "precision medicine" explains that the term "refers to the tailoring of medical treatment to the individual characteristics of each patient." The report goes on to say, "It should be emphasized that in 'precision medicine' the word 'precision' is being used in a colloquial sense, to mean both 'accurate' and 'precise.'"[1] In the colloquial sense, "precision" also implies a high degree of certainty of an outcome, as in "precision-guided missile" or "at what precise time will you arrive?" So will precision medicine usher in an age of diagnostic and prognostic certainty?

In fact, the opposite will probably result. The new tools for tailoring treatment will demand a greater tolerance of uncertainty and greater facility for calculating and interpreting probabilities than we have been used to as physicians and patients.

Oncology has been called "the clear choice for enhancing the near-term impact of precision medicine."[2] New tools extract information from cancer genomes that include both the mutations

The NEW ENGLAND JOURNAL of MEDICINE

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CORRESPONDENCE

Limits to Precision Cancer Medicine

N Engl J Med 2017; 376:95-97 | January 5, 2017 | DOI: 10.1056/NEJMc1613563

To the Editor:

In their Sounding Board article on personalized medicine, Tannock and Hickman (Sept. 29 issue)[1] make constructive contributions toward a possible midcourse correction. Precision medicine is based on targeting a validated and genetically stable driver of disease. To date, proof-of-concept trials have not supported this premise.[2] The precision approach has worked in bacterial infections and in certain hematologic cancers that are characterized by clonal proliferation. However, solid cancer is different; local invasion and metastasis are more relevant than clonal proliferation[3] and are dependent on multiple coordinated and sequential mechanisms. The mechanistic locus resides within the stroma, and this may explain the shift in interest from the cancer cell to the stroma.[4] Noncancer cells predominate in the stroma, and here advanced imaging offers advantages in drug discovery, development, and evaluation.[5] Stromal targeting allows for the development of broad-spectrum drugs on the basis of common mechanistic denominators rather than unique mutations. A strategic rethinking may be in order since it is not possible to aim precisely at moving targets, and tumor shrinkage does not predict the inhibition of metastasis.[6]

Michael Fernandes, M.D.; Medbase, Chapel Hill, NC
Charles University, Prague, Czech Republic
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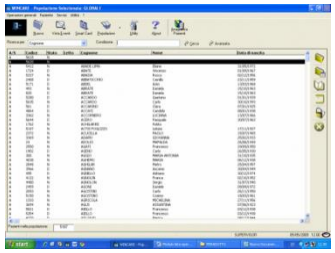
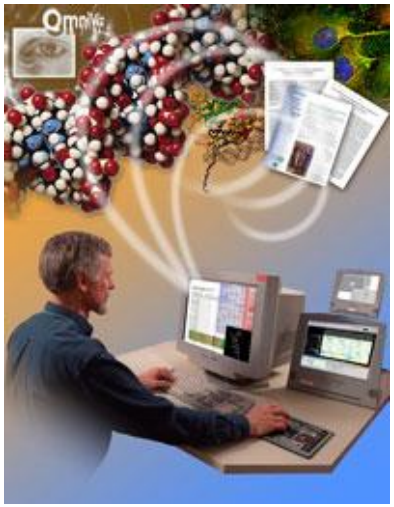
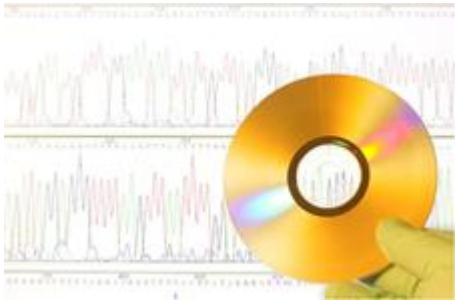
LA SFIDA: INTEGRARE TUTTE LE INFORMAZIONI RACCOLTE IN UNA GRANDE COORTE, MODELLIZZARLE E TRASFERIRLE SUL SINGOLO PAZIENTE



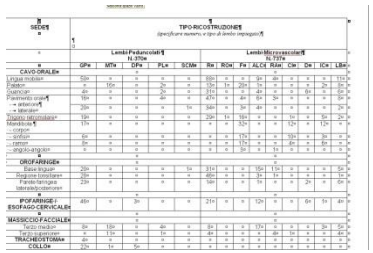
Dati clinici e demografici



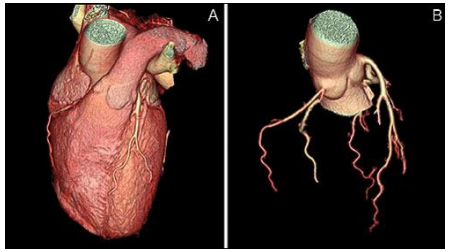


Profilo genetico

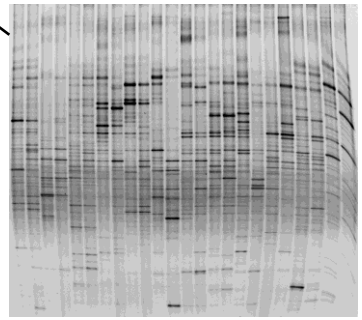
Esami di laboratorio



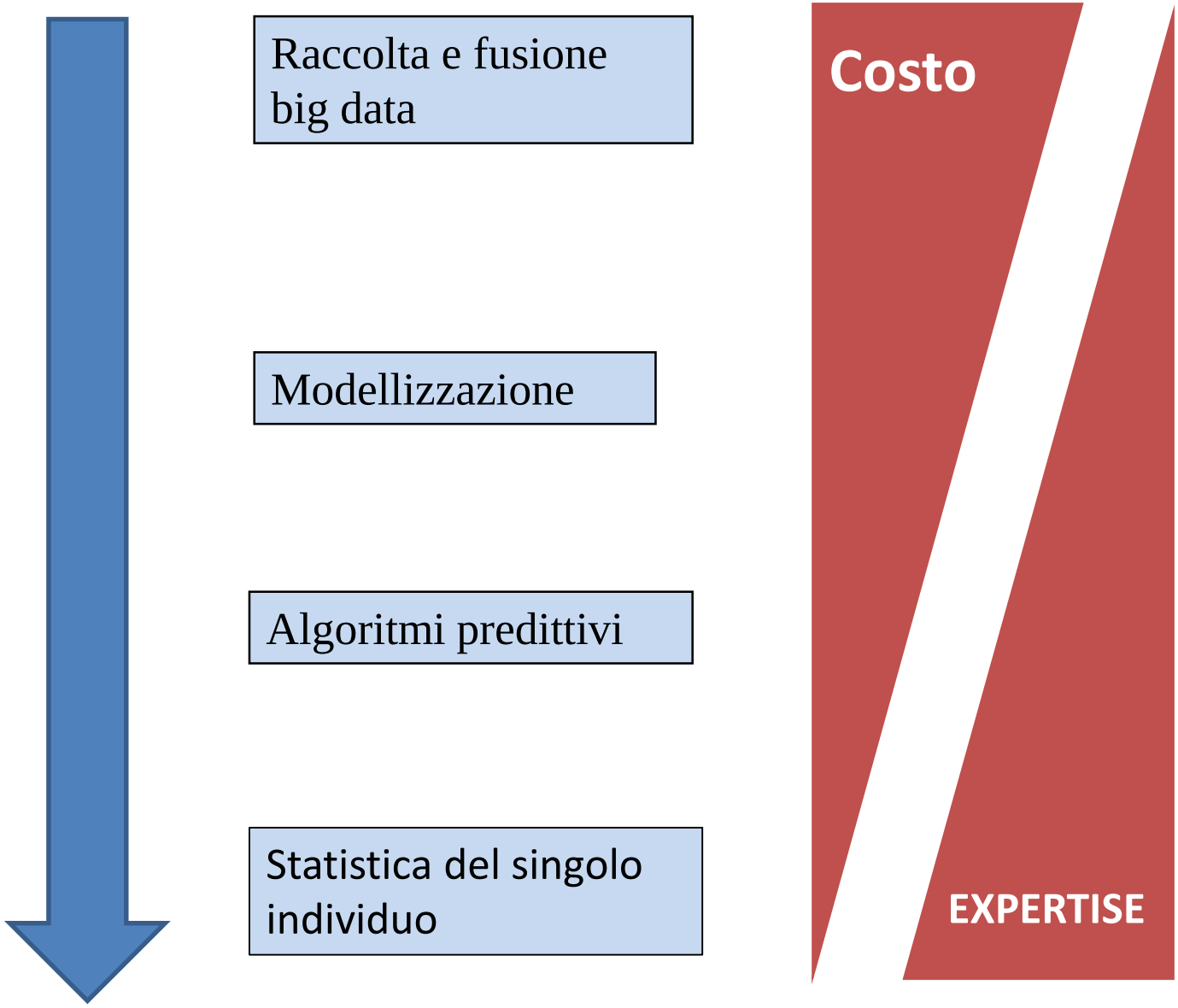
Pattern alimentare



imaging



Microbiota intestinale



Precision Medicine

The NEW ENGLAND JOURNAL of MEDICINE

PERSPECTIVE

Predicting the Future — Big Data, Machine Learning, and Clinical Medicine

Ziad Obermeyer, M.D., and Ezekiel J. Emanuel, M.D., Ph.D.

……Machine learning will dramatically improve the ability of health professionals to establish a prognosis and will improve diagnostic accuracy. They will become an indispensable tool for clinicians seeking to truly understand their patients.

Ziad Obermeyer, M.D

Ezekiel J. Emanuel M.D., Ph.D.

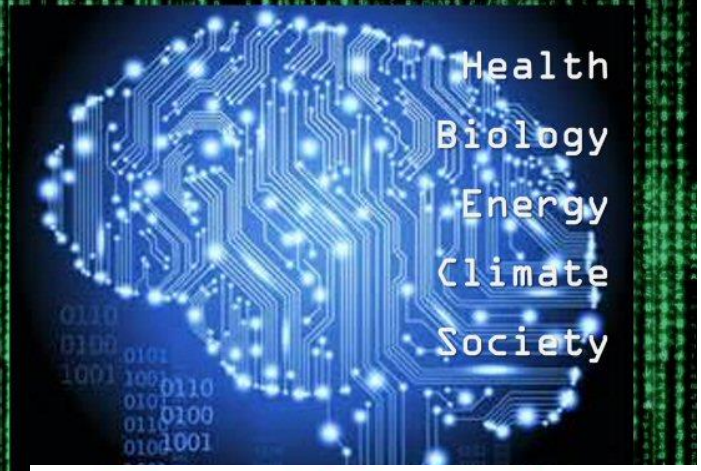
…. To be useful, data must be analyzed, interpreted, and acted on. Thus, it is algorithms — not data sets — that will prove transformative. We believe, therefore, that attention has to shift to new statistical tools from the field of machine learning that will be critical for anyone practicing medicine in the 21st century.

Predicting the Future — Big Data, Machine Learning, and Clinical Medicine

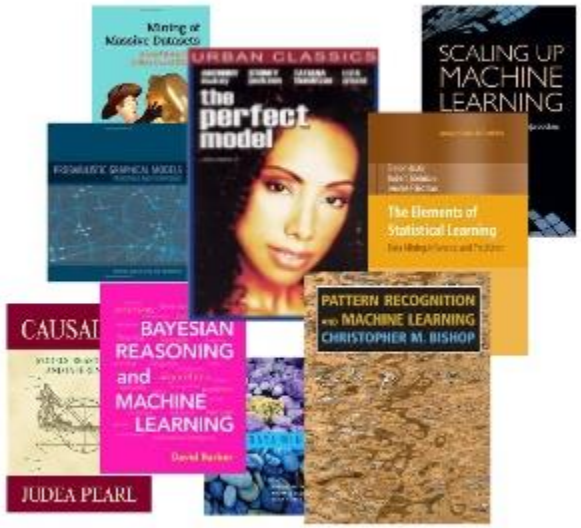
AMLS

Analytics and Machine Learning Systems

Computer Science
https://uit.no/informatikk



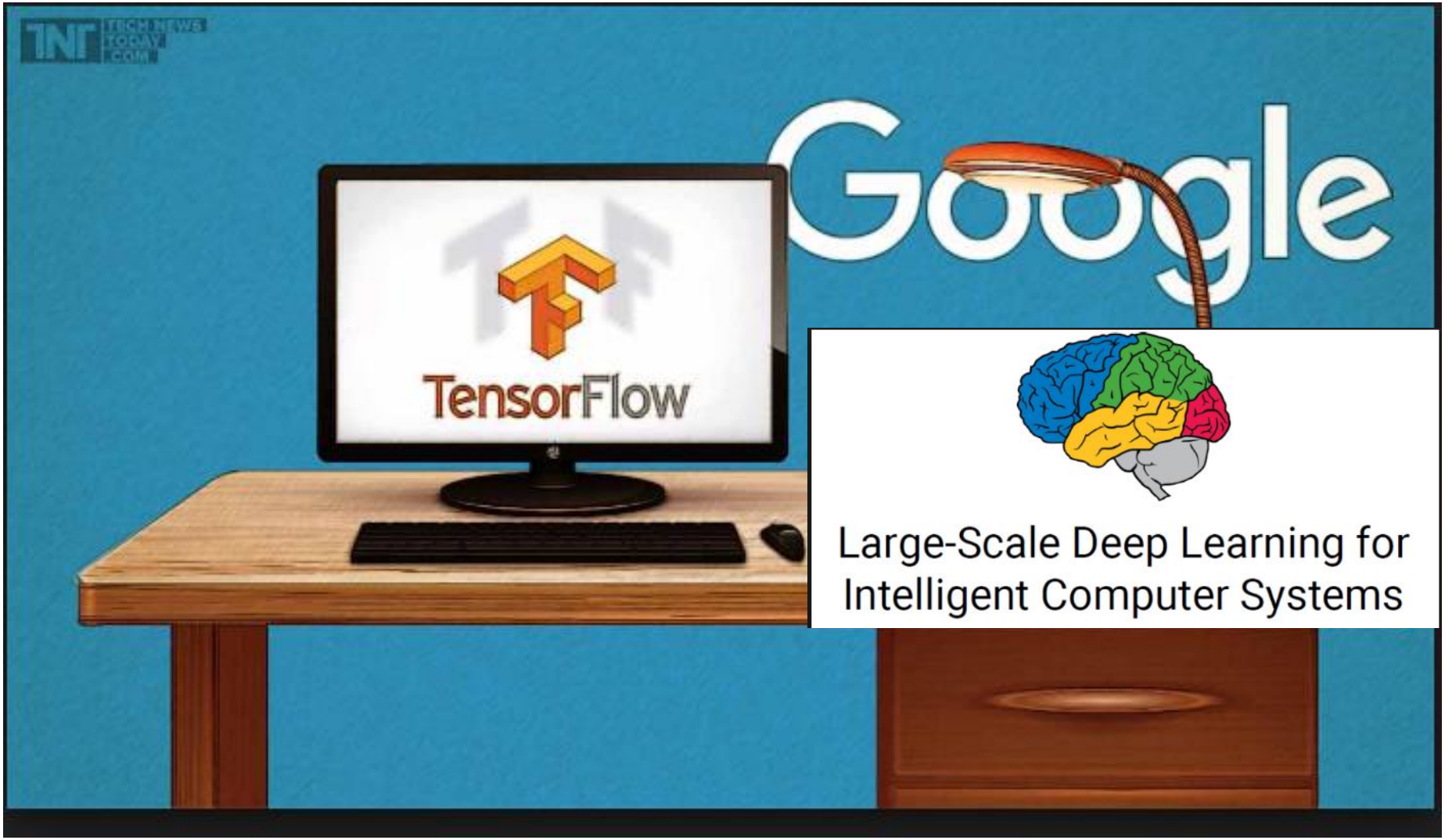
Smart Models



- Regression models (Logistic, Linear, Elastic nets)
- GBDT/RF
- SVD & other MF models
- Factorization Machines
- Restricted Boltzmann Machines
- Markov Chains & other graphical models
- Clustering (from k-means to HDP)
- Deep ANN
- LDA
- Association Rules
- …

NETFLIX

Google Artificial Intelligence Software; Available For Free



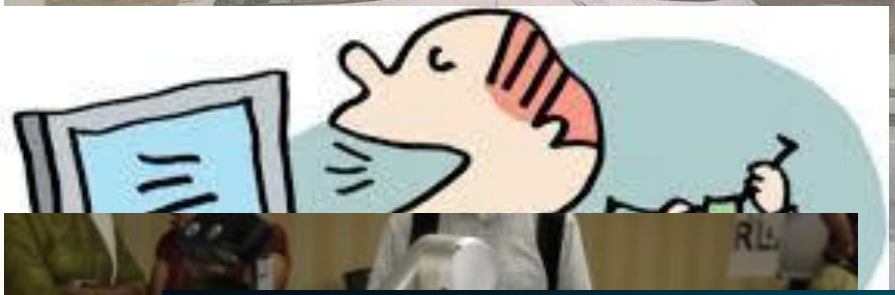
Machine learning vs classical statistics: Differences

Conventional statistics	Machine learning
• Assume that relations are linear and model data using linear combination	No
• Assume that variables are independent each other	No
• Handle preferentially homogeneous type of data	No

Machine learning vs classical statistics: Differences

Machine learning	Classical statistics
• Can employ Boolean algebra (AND, OR,NOT)	No
• Can employ fuzzy logic (IF, THEN, ELSE)	No
• Can employ conditional probabilities	No
• Use optimization strategies to model data	No
• Learn from examples	No

Application of MLS




Machine Learning Algorithms
Deep Learning
Deep Boltzmann Machine (DBM)
Deep Belief Networks (DBN)
Convolutional Neural Network (CNN)
Stacked Auto-Encoders
Ensemble
Random Forest
Gradient Boosting Machines (GBM)
Boosting
Bootstrapped Aggregation (Bagging)
AdaBoost
Stacked Generalization (Blending)
Gradient Boosted Regression Trees (GBRT)
Radial Basis Function Network (RBFN)
Neural Networks
Perceptron
Back-Propagation
Hopfield Network
Regularization
Ridge Regression
Least Absolute Shrinkage and Selection Operator (LASSO)
Elastic Net
Least Angle Regression (LARS)
Rule System
Cubist
One Rule (OneR)
Zero Rule (ZeroR)
Repeated Incremental Pruning to Produce Error Reduction (RIPPER)
Regression
Linear Regression
Ordinary Least Squares Regression (OLSR)
Stepwise Regression
Multivariate Adaptive Regression Splines (MARS)
Locally Estimated Scatterplot Smoothing (LOESS)
Logistic Regression
Bayesian
Naive Bayes
Averaged One-Dependence Estimators (AODE)
Bayesian Belief Network (BBN)
Gaussian Naive Bayes
Multinomial Naive Bayes
Bayesian Network (BN)
Decision Tree
Classification and Regression Tree (CART)
Iterative Dichotomiser 3 (ID3)
C4.5
C5.0
Chi-squared Automatic Interaction Detection (CHAID)
Decision Stump
Conditional Decision Trees
M5
Dimensionality Reduction
Principal Component Analysis (PCA)
Partial Least Squares Regression (PLSR
Sammon Mapping
Multidimensional Scaling (MDS)
Projection Pursuit
Principal Component Regression (PCR)
Partial Least Squares Discriminant Analysis
Mixture Discriminant Analysis (MDA)
Quadratic Discriminant Analysis (QDA)
Regularized Discriminant Analysis (RDA)
Flexible Discriminant Analysis (FDA)
Linear Discriminant Analysis (LDA)
Instance Based
k-Nearest Neighbour (kNN)
Learning Vector Quantization (LVQ)
Self-Organizing Map (SOM)
Locally Weighted Learning (LWL)
Clustering
k-Means
k-Medians
Expectation Maximization
Hierarchical Clustering

The use of artificial neural network in gastroenterology: the experience of the first 10 years

Edited by Fabio Pace and Vincenzo Savarino

Review in depth

Overview

Fabio Pace[a] and Vincenzo Savarino[b]

European Journal of Gastroenterology & Hepatology 2007, **19**:1043–1045

[a]Department of Gastroenterology, University Hospital L. Sacco, Milan and [b]Department of Internal Medicine, University of Genoa, Genoa, Italy

Correspondence to Professor Vincenzo Savarino, MD, Dipartimento di Medicina Interna, Università di Genova, Viale Benedetto XV, n. 6, Genova 16132, Italy
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Received 29 August 2007 **Accepted** 29 August 2007

Artificial neural networks (ANNs) are information paradigms inspired by the analytical processes of the human brain. Such systems are able to modify their internal operating structure, and the resulting analysis, in relation to a defined goal, question or functional objective. They learn to recognize the complex patterns existing between input signals and the corresponding outputs. ANNs are particularly suitable for solving problems of the nonlinear type and for analyzing complex datasets.

Introduction to artificial neural networks

Enzo Grossi[a] and Massimo Buscema[b]

The coupling of computer science and theoretical bases such as nonlinear dynamics and chaos theory allows the creation of 'intelligent' agents, such as artificial neural networks (ANNs), able to adapt themselves dynamically to problems of high complexity. ANNs are able to reproduce the dynamic interaction of multiple factors simultaneously, allowing the study of complexity; they can also draw conclusions on individual basis and not as average trends. These tools can offer specific advantages with respect to classical statistical techniques. This article is designed to acquaint gastroenterologists with concepts and paradigms related to ANNs. The family of ANNs, when appropriately selected and used, permits the maximization of what can be derived from available data and from complex, dynamic, and multidimensional phenomena, which are often poorly predictable in the traditional 'cause and effect' philosophy. *Eur J Gastroenterol Hepatol* 19:1046–1054

European Journal of Gastroenterology & Hepatology 2007, **19**:1046–1054

Keywords: artificial neural networks, diagnosis, evolutionary algorithms, nonlinearity, prognosis

[a]Bracco Spa Medical Department, Milan, Italy and [b]Semeion Research Centre for Science and Communication, Trigoria, Rome

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Received 29 August 2007 **Accepted** 29 August 2007

Artificial neural networks can classify uninvestigated patients with dyspepsia

Angelo Andriulli[a], Enzo Grossi[b], Massimo Buscema[c], Alberto Pilotto[a], Virginia Festa[a] and Francesco Perri[a]

There is consensus on investigating older patients presenting with or without alarm symptoms and/or risk factors, and irrespective of their *Helicobacter pylori* status. Remaining patients with uninvestigated dyspepsia, however, represents a 'grey' population for whom no clearly defined guidelines have been delineated. Physicians often struggle with the decision of whether or not to undertake noninvasive testing, treat dyspeptic patients empirically or perform an invasive endoscopy of the upper gastrointestinal tract. We have explored the contribution of artificial neural networks (ANNs) to provide appropriate interpretation of presenting complaints and clinical characteristics for these patients. By taking into account all the 86 recorded features of 101 dyspeptic patients, the overall predictive capability of ANNs in sorting out organic from functional disease amounted to 74.2% data, past medical history, risk factors for organic disease, and presenting abdominal complaints that each patient brings to the clinical encounter. With this ability, ANNs can be used to assist in the classification and treatment of patients with uninvestigated dyspepsia, and to bring a greater level of confidence to this process. *Eur J Gastroenterol Hepatol* 19:1055–1058 © 2007 Wolters Kluwer Health | Lippincott Williams & Wilkins.

European Journal of Gastroenterology & Hepatology 2007, 19:1055–1058

Keywords: artificial intelligence, artificial neural networks, dyspepsia, *H. pylori* infection

[a]Division of Gastroenterology, 'Casa Sollievo Sofferenza' Hospital, IRCCS, San Giovanni Rotondo, [b]Bracco Imaging S.p.A., Medical Affairs Europe, Milan and [c]Semeion Research Centre for Sciences of Communication, Rome, Italy

Assessing the severity of atrophic gastritis

Bruno Annibale and Edith Lahner

Atrophic gastritis, mainly the consequence of long-standing *Helicobacter pylori* infection, is linked to the development of gastric cancer. In the case of atrophic gastritis, severity may be mainly related to the lifetime risk of the single patient to develop gastric cancer, mostly in relation to the degree and extension of mucosal damage. As atrophic gastritis is the result of complex multifactorial interactions, the application of artificial neural networks is promising and may be useful for the identification of those patients with atrophic gastritis at higher risk for gastric malignancies. The experience of application of artificial neural networks in atrophic gastritis is still scarce. The available data suggest that these systems may contribute to identify patients with corporal metaplastic atrophic gastritis and to optimize bioptic sampling during gastroscopy. *Eur J Gastroenterol Hepatol* **19:1059–1063**

European Journal of Gastroenterology & Hepatology 2007, 19:1059–1063

Keywords: artificial neural networks, atrophic gastritis, gastric cancer, gastric malignancies, gastroscopy, *Helicobacter pylori* infection

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Tel: +39 06 49972369; fax: +39 06 4455292;
e-mail: bruno.annibale@uniroma1.it

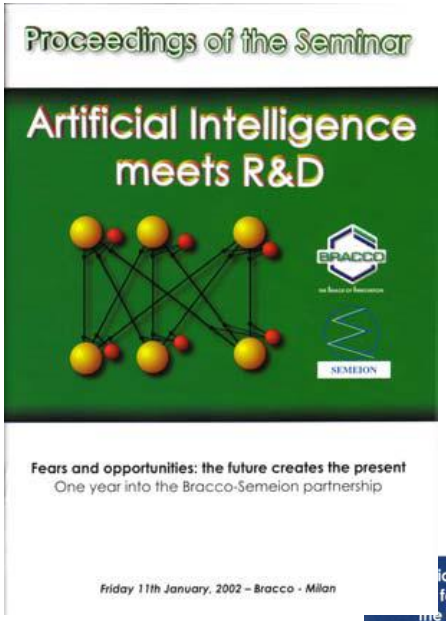
Received 29 August 2007 **Accepted** 29 August 2007

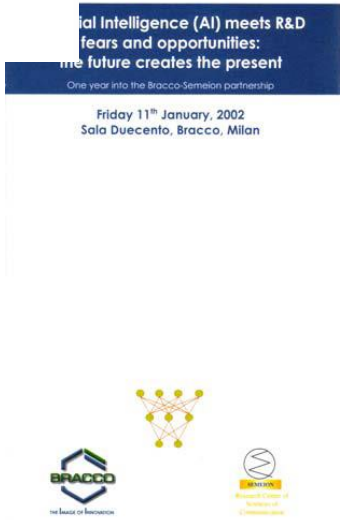
Intelligenza Artificiale in Gastroenterologia: nuovi orizzonti nella analisi e interpretazione dei dati clinici.

Federazione Società Italiane Malattie Digestive. 7° Congresso Nazionale. Simposio Satellite Bracco. Bari, 3 dicembre 2001.

Artificial Intelligence (AI) meets R&D. Fears and opportunities: the future creates the present.

Milano, 11 gennaio 2002.





PROGRAMME

Chairpersons:
M. Denaro; E. Grossi

Opening Session

9:30 - 9:45 Welcome and Introduction
M. Denaro, Bracco Imaging

9:45 - 10:30 Scientific background of dynamic adaptive systems
M. Buscema, Semeion

COFFEE break

Diagnostic Imaging

11:00 - 11:20 Ultrasound evaluation of patients at high risk of cardiovascular disease
D. Baldassarre, Osp. Niguarda Milan

11:20 - 11:35 Prediction of adverse reactions to contrast media
E. Grossi, Bracco Imaging

11:35 - 11:55 Diagnosis of Breast Cancer in Radiology
T. Vomweg, Mainz University

11:55 - 12:30 A novel CAD system for breast MRI
M. Buscema, Semeion

12:30 - 13:00 Discussion

LUNCH break (13:00 - 14:00)

Alzheimer's Disease

14:00 - 14:15 Prediction of response to donepezil
P. Mecocci, Perugia University

14:15 - 14:30 Profile of responders and non-responders to donepezil
E. Grossi, Bracco Imaging

14:30 - 14:45 A novel test for cognitive impairment
L. De Vreese, Modena University

14:45 - 15:00 Discussion

Gastroenterology

15:00 - 15:20 Diagnosis of atrophic gastritis
B. Annibale, G. Delle Fave
Rome University

15:20 - 15:40 Diagnosis of GERD in the clinical setting
F. Pace, G. B. Porro
Milan University

15:40 - 15:55 Screening of GERD in primary care
P. Dominici, Bracco Imaging

15:55 - 16:15 Evaluation of Dyspepsia
A. Andriulli, S. Giovanni Rotondo, Foggia

16:15 - 16:30 Discussion

COFFEE break

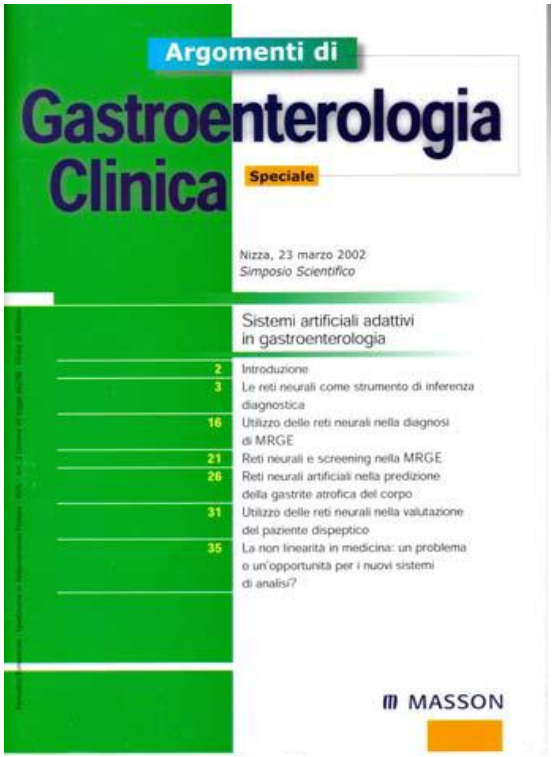
16:45 - 17:25 Overview of Bracco-Semeion cooperation
E. Grossi, Bracco Imaging

17:25 - 17:30 Conclusions
M. Denaro, Bracco Imaging

17:30 - 18:00 Overall Discussion

Pubblicazioni

Sistemi Artificiali Adattivi in Gastroenterologia.
Simposio Scientifico. Nizza, 23 marzo 2002.



Studio eMeRGE. Applicazione delle Reti Neurali nella diagnosi e prognosi della GERD.
Simposio Scientifico. Milano – Roma, 1 giugno 2002.

Available online at www.sciencedirect.com
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European Journal of Gastroenterology & Hepatology 2005, 17:605–610

PO Box 2345, Beijing 100023, China
www.wjgnet.com

World J Gastroenterol 2005;11(37):5867-5873
World Journal of Gastroenterology ISSN 1007-9327

ORIGINAL ARTICLE: Clinical Endoscopy

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Marco
Gastroi

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Study G

Proceedings UEGW Congress, Stockholm 2011

DO ERD AND NERD REFLECT THE SAME DISEASE?
A STUDY USING ARTIFICIAL NEURAL NETWORKS

E. Grossi,M. Buscema*, F. Pace**,*

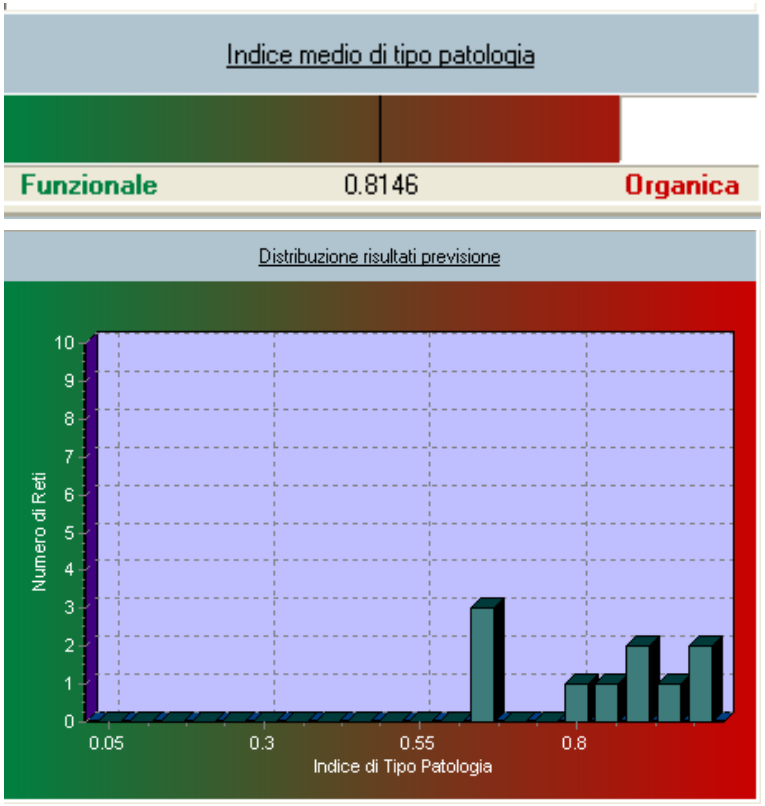
* *Semeion Research Center , Via Sersale, 117 - 00128 Roma, Italy*

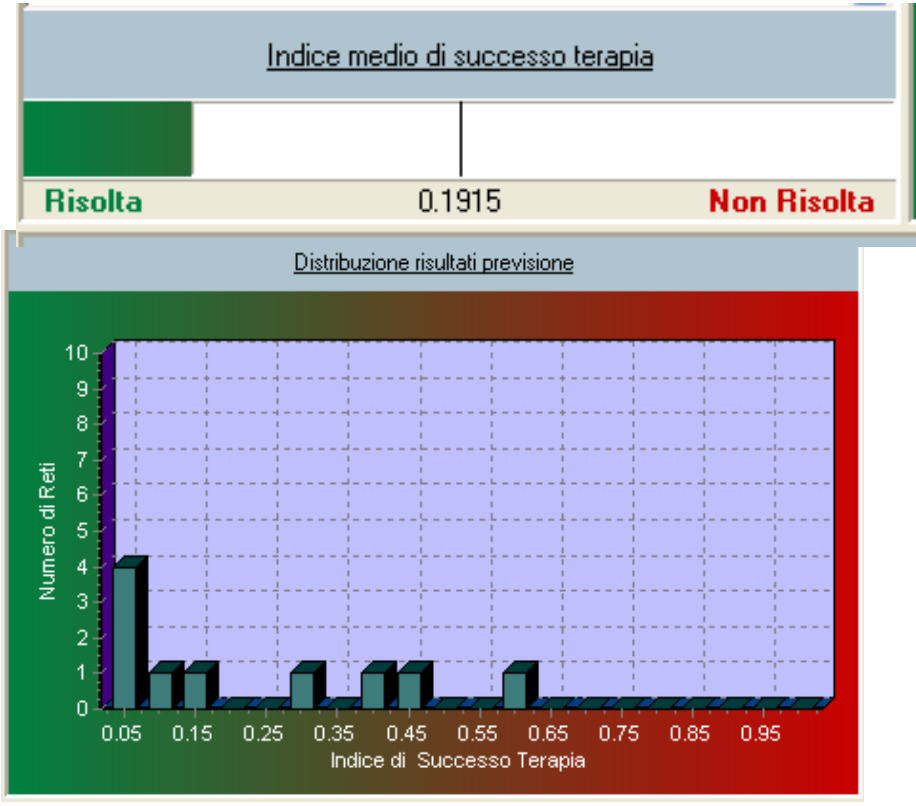
** *Gastrointestinal Unit, Ospedale Bolognini, Seriate (BG), Italy*

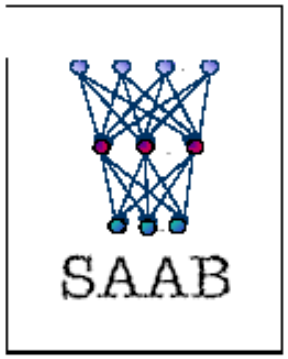
DYSP-LAB PROJECT: AN APPLICATION SOFTWARE FOR DYSPETIC SYNDROME

A special software able to classify new patients with dyspeptic symptoms into organic or functional type has been developed by Semeion Centre. The software uses 20 independent already trained artificial neural networks to classify new subjects according to 45 variables.

Pazient No. 28 male, 55 years, sent to an hospital from G.P. for epigastric pain ulcer-like.







Sistemi Artificiali Adattivi in Biomedicina

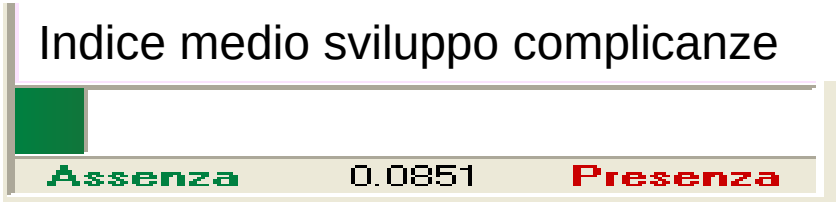
DR
Di Renzo Editore

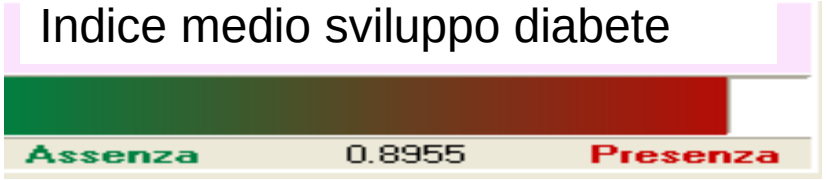
Identificazione delle variabili correlate al diabete mellito nella Pancreatite Cronica attraverso l'applicazione delle Reti Neurali Artificiali (RNA) *

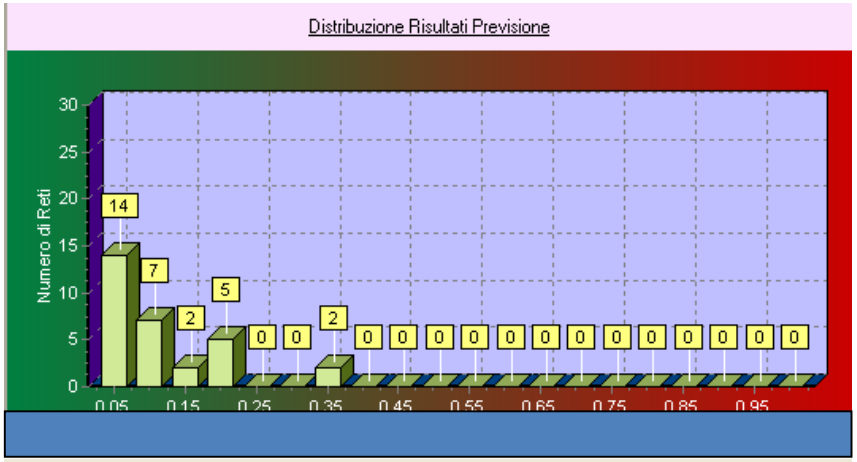
E. Gaia[1], N. Pagano[1], M. Buscema[2], M. Intraligi[2], A. Mancini[2], P. Salacone[1], C. Arduino[3], E. Grossi[4]

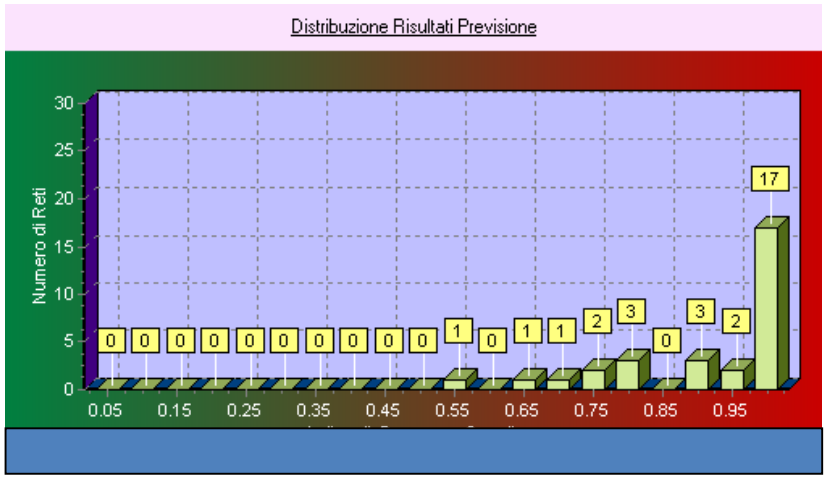
[1]Unità di Gastroenterologia, Ospedale S. Luigi, Orbassano (TO);
[2]Semeion Centro Ricerche di Scienze della Comunicazione, Roma;
[3]Istituto di Genetica, Ospedale S. Giovanni, Torino;
[4]Bracco S.p.a., Direzione Medica Farma, Milano;

- **Paziente 15, maschio , 69 anni, affetto da dolore epigastrico, calcificazioni parenchimali pancreatiche, insufficienza esocrina, polimorfismo gene CFTR.**









European Journal of Gastroenterology & Hepatology 2005, Vol 17 No 6

Artificial neural networks are able to recognize gastro-oesophageal reflux disease patients solely on the basis of clinical data

Fabio Pace[a], Massimo Buscema[b], Patrizia Dominici[c], Marco Intraligi[b], Fabio Baldi[d], Renzo Cestari[e], Sandro Passaretti[f], Gabriele Bianchi Porro[a] and Enzo Grossi[c]

Can artificial neural networks be beneficial in diagnosing gastro-oesophageal reflux disease?

Vincenzo Savarino and Pietro Dulbecco

European Journal of Gastroenterology & Hepatology 2005, **17**:599–601

Correspondence to Prof. Vincenzo Savarino.
E-mail: vsavarin@unige.it

Dipartimento di Medicina Interna e Specialità Mediche, Università degli Studi di Genova, Viale Benedetto XV, M. 6, 26132 Genova (Italy).

Bracco S.p.A.

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Valutazione del rischio di decesso per il sanguinamento gastrointestinale

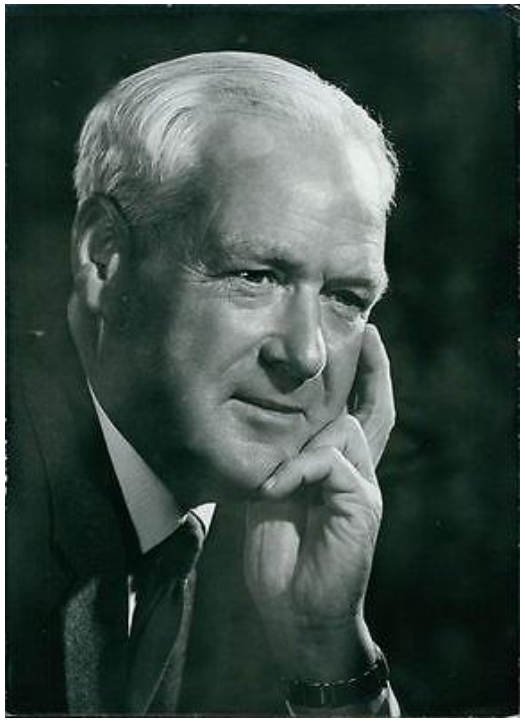
“There is an agonising and currently insoluble problem of advising individuals based on evidence gathered in populations”.

Richard Smith, Past Editor of British medical Journal

CASES JOURNAL

"We cannot necessarily, perhaps very rarely, pass from (the overall result of a clinical trial) to stating exactly what effect the treatment will have on a particular patient. But there is, surely, no way and no method of deciding that."

Austin Bradford Hill, 1952

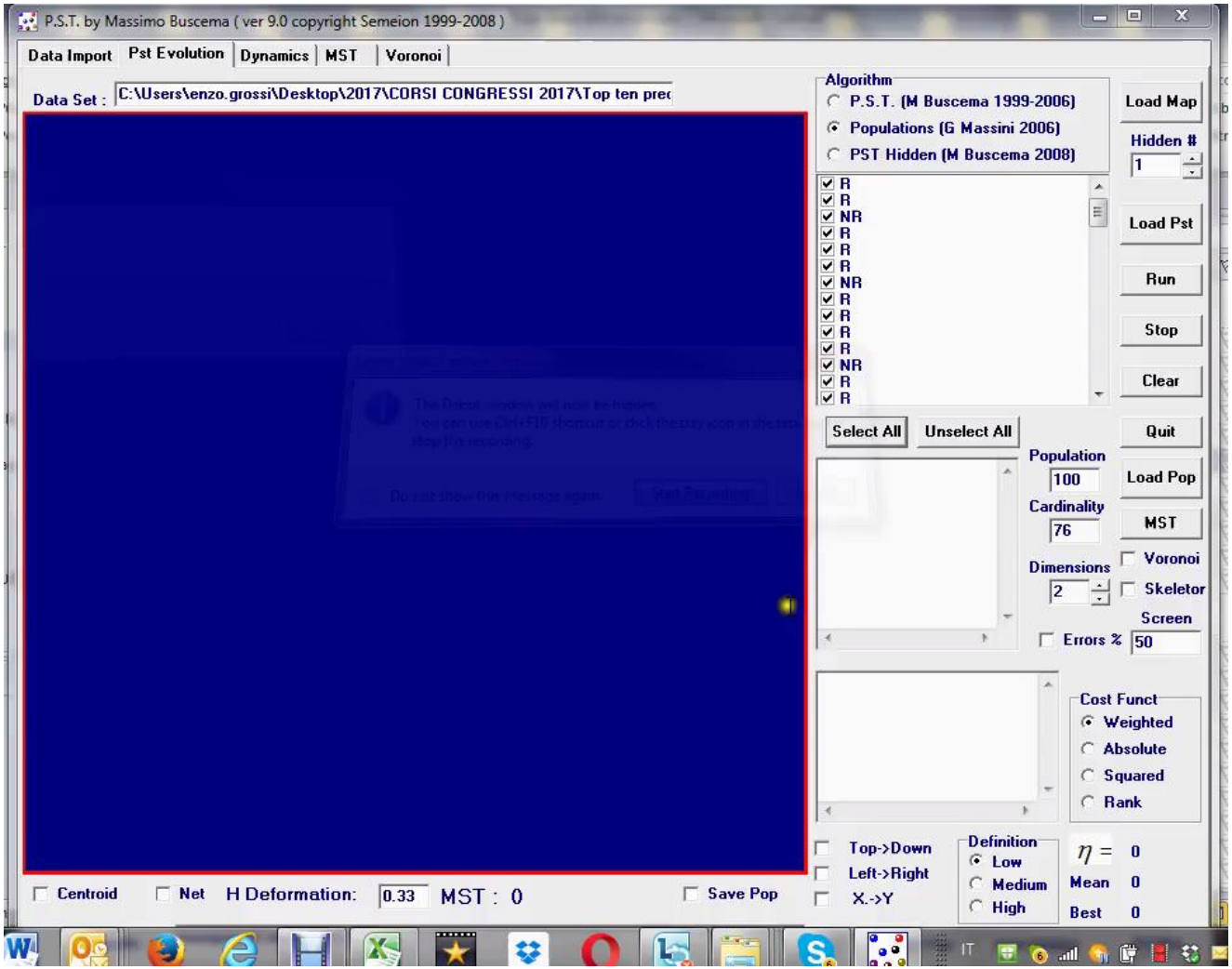


Dig Liver Dis 2005; 37 (suppl.1):S51.

Use of Artificial Neural Networks in predicting response to infliximab treatment in patients with Crohn's disease.

Kohn A, Grossi E, Mangiarotti R, Prantera C.

81 pazienti trattati con Infliximab. 45 variabili cliniche e di laboratorio.


P.S.T. by Massimo Buscema (ver 9.0 copyright Semeion 1999-2008)
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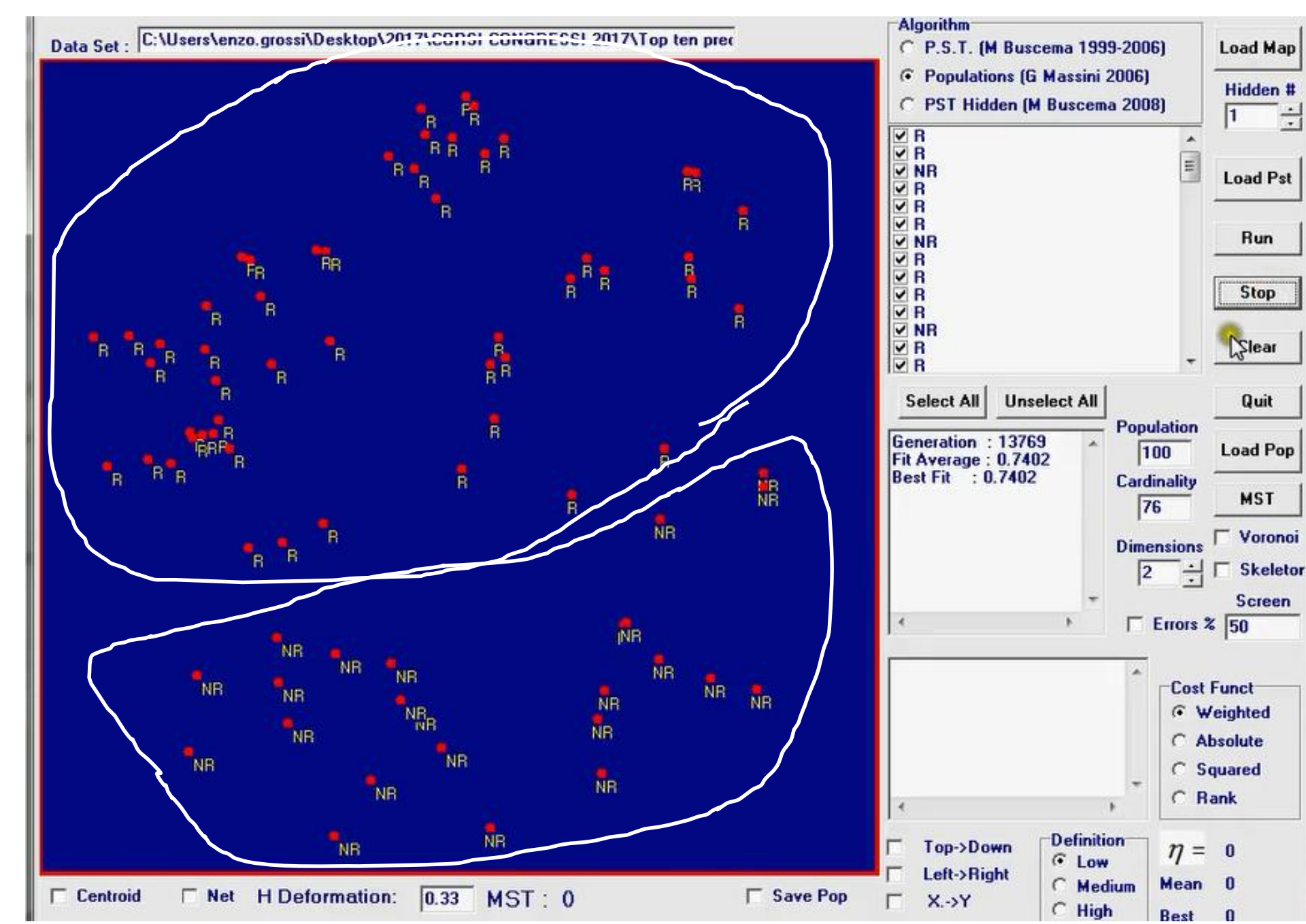
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Definition
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η = 0
Mean 0
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Conclusioni

- La medicina precisione non è ancora una pratica standard ma lo sarà probabilmente in tempi non lunghi.
- L' applicazione dei machine learning systems ai big data sembra essere l'unica via percorribile per raggiungere lo scopo.
- Molto significativa l'esperienza italiana in gastroenterologia con l'uso di machine learning systems in epoca non sospetta.
- Forse siamo stati leaders in medicina di precisione senza esserne del tutto consapevoli….

Un giorno le macchine riusciranno a risolvere tutti i problemi, ma mai nessuna di esse potrà porne uno.

(A. Einstein)