Personalisierte Medizin: Zurück zum Wort - Implikationen für die Versorgung und transaktionale Entscheidungshilfen

Tanja Krones

… doch nochmal hin zu den Grundlagen aus medizinethischer Sicht…

Personalized medicine: whats in a name? Pokorska-Bocci et al (2014)

- Individualisierte Medizin: Eigene Zellen von Patienten als Therapie (z.B. CAR –T Cells)
- Präzisionsmedizin: Kombination von molekularbiologischer Forschung und individuellen klinischen Daten für genauere molekulare Taxonomie
- Stratifizierte Medizin: Verwendung von klinischen Biomarkern mit Paarung spezifischer Patientenpopulationen
- P4 Medizin: Anwendung von Strategien der Systembiologie um Wohlbefinden biologisch zu messen und Krankheitsdispositionen zu erkennen und zu vermeiden
- Personalisierte Medizin: Anwendung von genomischen und molekularen Daten, um gezielter zu behandeln, die Entwicklung neuer Therapien zu forcieren, und individuelle Prädispositionen besser und früher zu erkennen und zu behandeln.

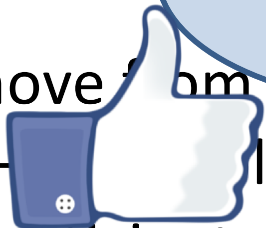
OPINION

Predictive, personalized, preventive, participatory (P4) cancer medicine

Leroy Hood and Stephen H. Friend

Hood, L. & Friend, S. H. *Nat. Rev. Clin. Oncol.* 8, 184–187 (2011); doi:10.1038/nrclinonc.2010.227

We are already in the golden age!



- “Medicine will move from a reactive to a proactive discipline over the next decade–[illegible]line that is predictive, personalized, preventive and participatory (P4). P4 medicine will be fueled by systems approaches to disease, emerging technologies and analytical tools. The ultimate promise is that the focus of medicine will be shifted from disease to wellness and that the billions of data points for each individual will define with exquisite specificity the nature of their wellness—and any transitions into disease, (…) with enormous attendant cost savings to society resulting in a lower requirement for sick leave and a concurrent increase in national productivity. (…) Many factors will converge to bring the costs of health care down in a striking manner so that the benefits of P4 medicine can be shared by rich and poor nations alike.”
- Leroy Hood & Stephen H. Friend: **Predictive, personalized, preventive, participatory (P4) cancer medicine.** Nature Reviews Clinical Oncolo[illegible] (March 2011)

Universität Zürich[UZH]

Nr. 2/2018

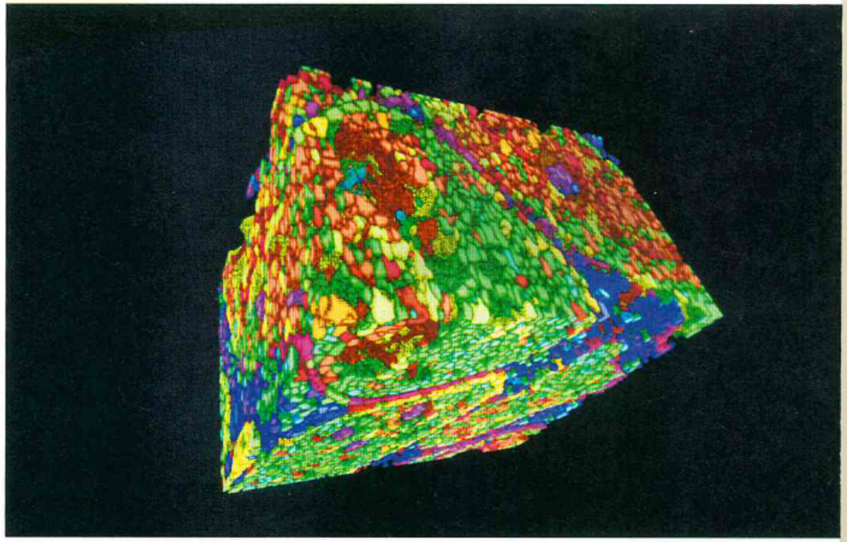
UZH magazin
Die Wissenschaftszeitschrift

EDITORIAL 2/18

Neues Magazin und präzise Medizin

Liebe UZH-Angehörige, liebe Alumni und Alumnae, liebe Wissenschaftsinteressierte

Sie halten das UZH Magazin im neuen Kleid in den Händen – wir haben die Wissenschaftszeitschrift der Universität Zürich rundum erneuert. Das gilt vor allem für Format und Layout – das UZH Magazin ist handlicher, vielfältiger und farbiger geworden. Das Heft wurde etwas verkleinert und ist



Blick in den Krebs: Differenziertes Bild von Brustkrebsgewebe.

Zitate

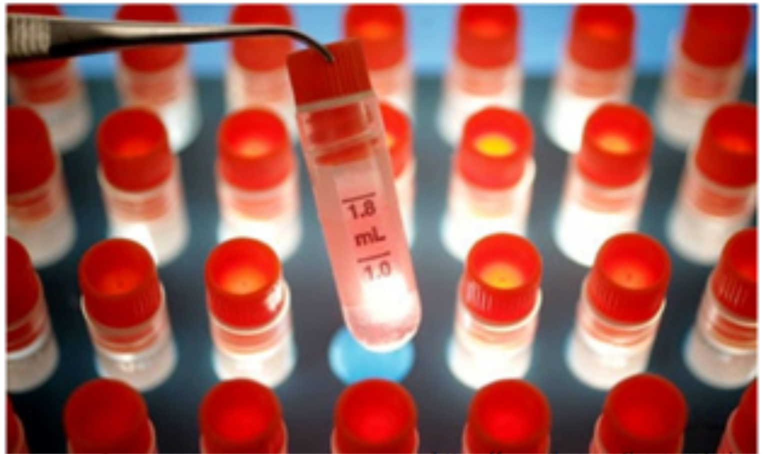
- «Menschen neigen dazu, sich falsch zu entscheiden, das gilt auch für Ärzte. Dagegen ermöglicht die digitale Mustererkennung ein hypothesenfreies Vorgehen»
- «In 10 bis 15 Jahren werden wir Krebs nicht mehr als den Horror empfinden der er heute ist»
- Durch die neuen Immuntherapien beim malignen Melanom «schnellte die Heilungsrate in die Höhe und liegt heute bei 40-50%»
- «Anfang der 1990er Jahre kannte man bei Kindern nur für eine Handvoll genetisch bedingter Krankheiten die molekulare Ursache. Heute sind es rund 3000»

4P:
Prediction, Practice, Promise or Prayer?

Die 10 Jahres Mystik

Stem cells: what happened to the radical breakthroughs?

Much was promised in the late 1990s, but the challenge of advances such as growing whole human organs has been difficult to deliver



https://www.theguardian.com/science/2013/aug/11/stem-cell-research-bioengineering

Empfehlung Journal Club
(Finde die Fehler)

nature biotechnology

A wellness study of 108 individuals using personal, dense, dynamic data clouds

Nathan D Price[1,2,6,7], Andrew T Magis[2,6], John C Earls[2,6], Gustavo Glusman[1], Roie Levy[1], Christopher Lausted[1], Daniel T McDonald[1,5], Ulrike Kusebauch[1], Christopher L Moss[1], Yong Zhou[1], Shizhen Qin[1], Robert L Moritz[1], Kristin Brogaard[2], Gilbert S Omenn[1,3], Jennifer C Lovejoy[1,2] & Leroy Hood[1,4,7]

(nathan.price@systemsbiology.org) or L.H. (hood@systemsbiology.org).

Received 16 October 2016; accepted 11 April 2017; published online 17 July 2017; doi:10.1038/nbt.3870

Fazit der Autoren


Trending: Hey, sad internet, use your imagination! If Toys R Us goes bust, pick a smaller box to shop in

Study finds Lee Hood's 'scientific wellness' approach can make people healthier

BY CLARE MCGRANE on July 17, 2017 at 8:00 am

3 Comments | Share 434 | Tweet | Share | Reddit | Email

Tickets on sale for the GeekWire Bash!

Genomics pioneer Lee Hood, left, and Maveron's Clayton Lewis, the CEO of Arivale.

Scientific wellness is a straightforward idea: use data about a person's genes, proteins and other biology, along with behavioral coaching, to keep them healthy, even preventing health problems before they arise. The approach is championed by genomics pioneer Lee Hood, and it's being pursued his latest startup, Seattle-based Arivale.

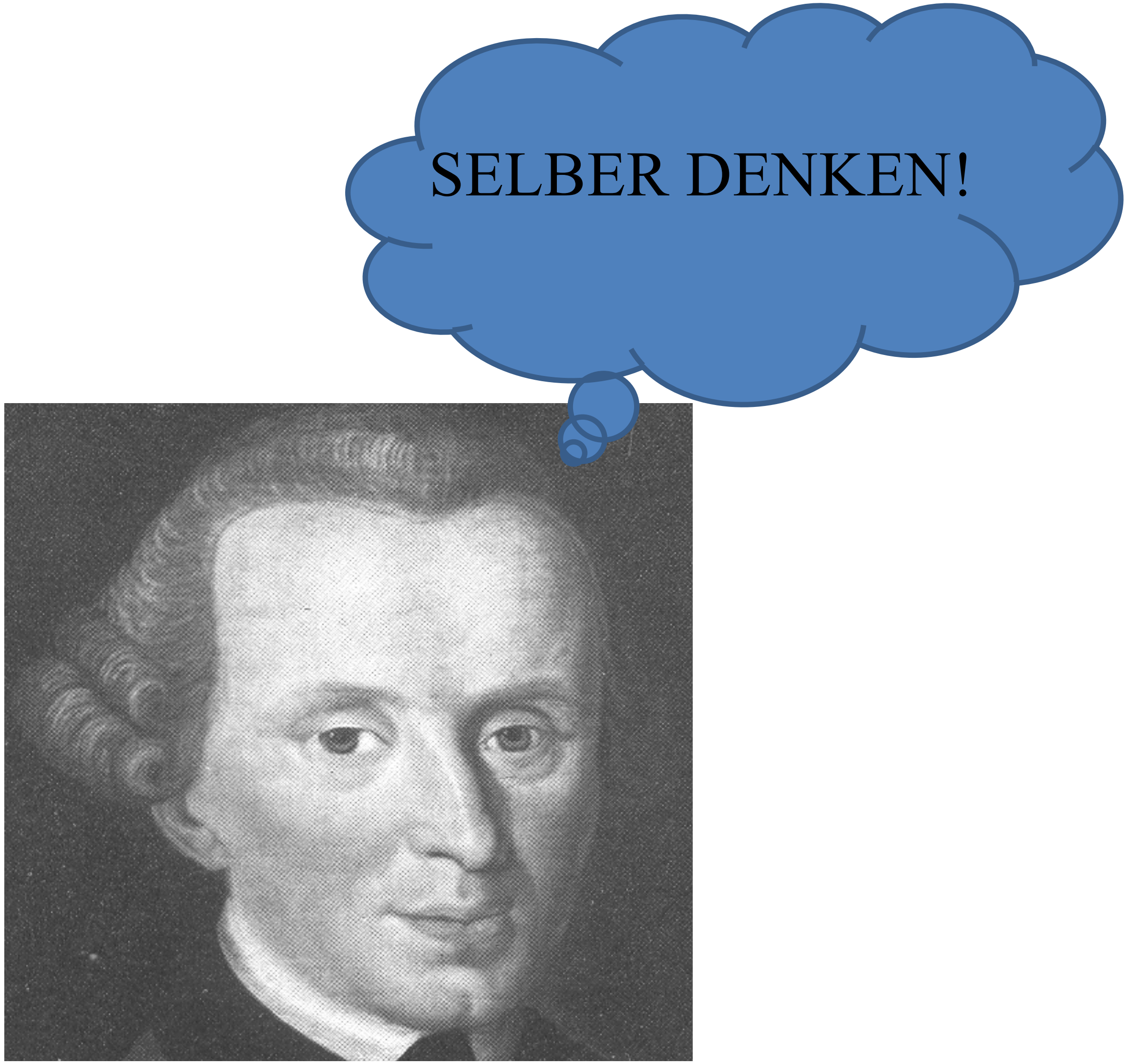
It's such a new and evolving concept that it isn't in the dictionary yet. Or Merriam

Die Rolle ethischer Erwägungen?

"There are challenges of ethics (will the accessibility of these anonymized data lead to exploitation by employers or insurance companies), and security (how will the data be protected)", p.187

Hood, L. & Friend, S. H. *Nat. Rev. Clin. Oncol*. **8**, 184–187 (2011); doi:10.1038/nrclinonc.2010.227

“Just as the Hubble Telescope provided a new view into the universe, these data sets have been transformational in providing new insights into both human biology and disease,” Hood said in a statement. “We have termed this quantitative and transformational approach Scientific Wellness, which enables individuals to improve their health and wellbeing, while generating the data necessary to optimize wellness as well as avoid or slow down the transition into certain disease states.”



Was sollen wir tun?

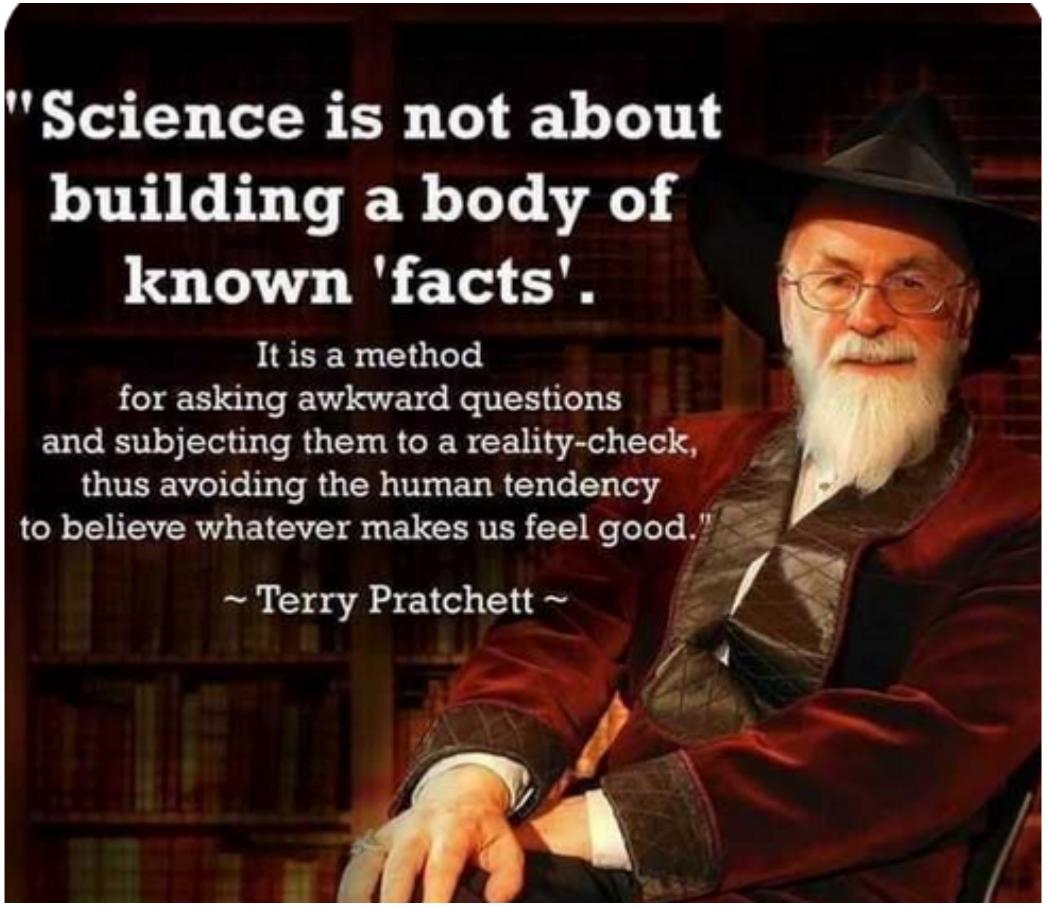
Beantwortung der Frage: Was ist Aufklärung?
Immanuel Kant, 1784

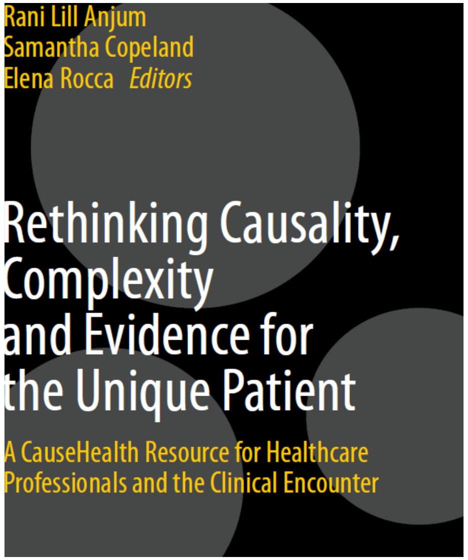
AUFKLÄRUNG ist der Ausgang des Menschen aus seiner selbstverschuldeten Unmündigkeit. **Unmündigkeit** ist das Unvermögen, sich seines Verstandes ohne Leitung eines anderen zu bedienen. **Selbstverschuldet** ist diese Unmündigkeit, wenn die Ursache derselben nicht am Mangel des Verstandes, sondern der Entschließung und des Mutes liegt, sich seiner ohne Leitung eines andern zu bedienen. *Sapere aude*! Habe Mut, dich deines **eigenen** Verstandes zu bedienen! ist also der Wahlspruch der Aufklärung.

Lehrbuch der Evidenzbasierten Medizin
Vorwort, Günter Jonitz 2006

Evidenzbasierte Medizin ist der Ausgang des Arztes aus seiner selbstverschuldeten Unmündigkeit. **Unmündigkeit** ist das Unvermögen, sich seines Verstandes ohne Leitung eines anderen zu bedienen. **Selbstverschuldet** ist diese Unmündigkeit, wenn die Ursache derselben nicht am Mangel des Verstandes, sondern der Entschließung und des Mutes liegt, sich seiner ohne Leitung eines andern zu bedienen. *Sapere aude*! Habe Mut, dich deines **eigenen** Verstandes zu bedienen!

Was können wir wissen?


"Science is not about
building a body of
known 'facts'.
It is a method
for asking awkward questions
and subjecting them to a reality-check,
thus avoiding the human tendency
to believe whatever makes us feel good."
~ Terry Pratchett ~

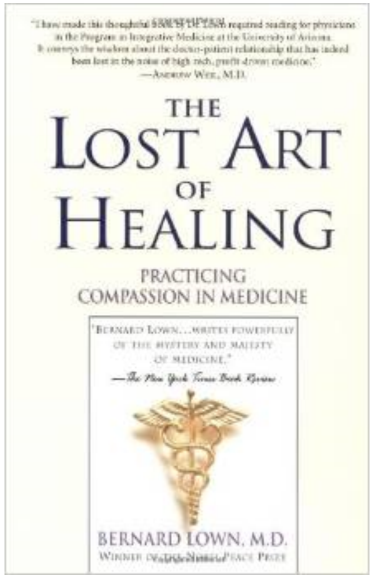


Was ist Medizin?

- Legitimation durch wissenschaftliche Basis
- Handlungswissenschaft, auf die Anwendung im Einzelfall gerichtet
- Zentrale Rolle der Praxis
- Gesundheits- und Krankheitsbezug: daher genuin normativ
- Medizin ist daher keine “Angewandte Humanbiologie“ (Paul 2006) sondern….

The nature of Medicine

«Practicing the Art and Mastering the Science»



Wissenschaft + Erfahrung + Werte

Zentraler „Gegenstand“

Patient als Subjekt (nicht Objekt)

Was ist also «gute» Medizin?

Exzellente integre Forschung,
Kritische Evaluation von Diagnose,
Prognose und Therapie,
Exzellente klinische Fertigkeiten
(manuell, kommunikativ, reflexiv),
Person-Centred Care

2 zentrale Fragen bei Therapien

1. Was sind unsere zentralen realistisch erreichbaren (Therapie)-Ziele?
(inkl. aller Alternativen)

2. Was wollen unsere Patient*innen?
(und ist er/sie bzw. die Stellvertreter wirklich bestmöglich aufgeklärt und ernsthaft einbezogen in die Evaluation von Therapiezielen und Behandlungsentscheiden?)

- 2 Fragen bei jeder Form von Behandlung, Aufklärung und Massnahmenfestlegung zur Beantwortung der klinisch-ethischen Frage

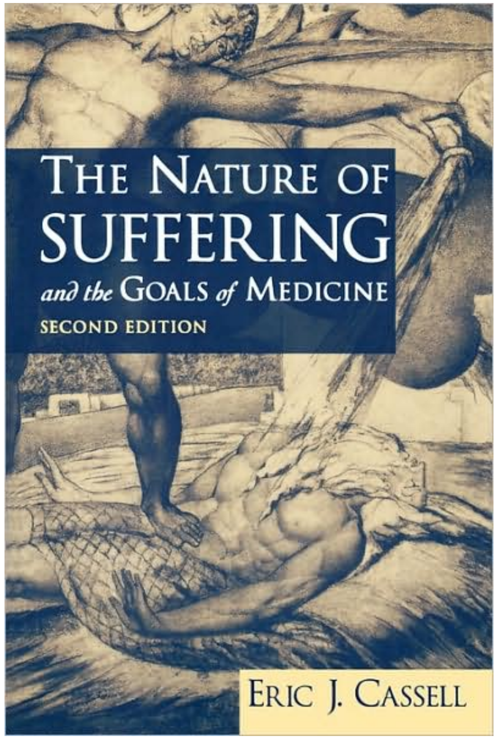
- „Was sollen wir tun“?

Goals of Medicine

1) Prevention of *premature* death
2) Prevention of disease
3) Care of the ill
4) Relief of suffering

⇒Increase quality of life

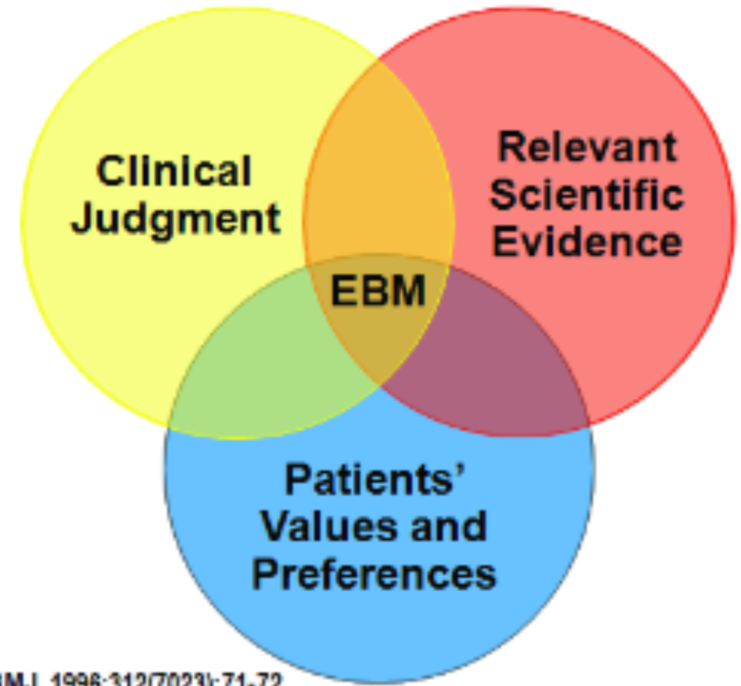
⇒and quality of death



EBM

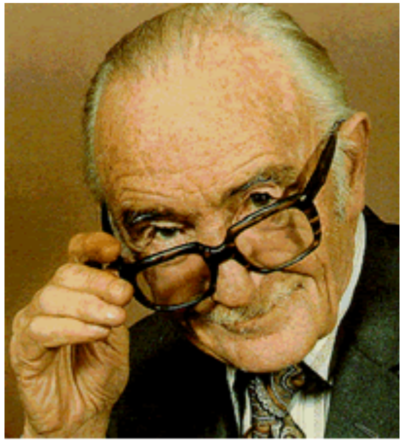
Evidence Based Medicine (EBM)

What Is Evidence-Based Medicine?



Sackett DL, et al. BMJ. 1996;312(7023):71-72.

Kritik an «naiv-positivistischem» Determinismus, u.a:



- Direktem «from bench to bedside approach» (da sicherer Patienten-Nutzen nicht von Surrogatparametern oder Beobachtungen auf Zellebene extrapolierbar);
- «Schlüssel-Schlossprinzip», «Vom Bild zur Diagnose» (Kausalitäts-Koinzidenzverwechsler, unterkomplexe Kausalitätsannahmen);
- Diagnosen als «Wahrheit» (nicht Wahrscheinlichkeit);
- Zufällige Befunde ohne oder mit unbekannter klinischer Relevanz;
- Kein Verständnis von epidemiologischen Phänomenen wie «Lead Time Bias», «Progression free survival Schätzern», «Regression to the mean»
- (…)

Erica S. Spatz, MD, MHS
Section of Cardiovascular Medicine, Yale University School of Medicine, New Haven, Connecticut; and Center for Outcomes Research and Evaluation, Yale-New Haven Hospital, New Haven, Connecticut.

Harlan M. Krumholz, MD, SM
Section of Cardiovascular Medicine, Yale University School of Medicine, New Haven, Connecticut; and Center for Outcomes Research and Evaluation, Yale-New Haven Hospital, New Haven, Connecticut.

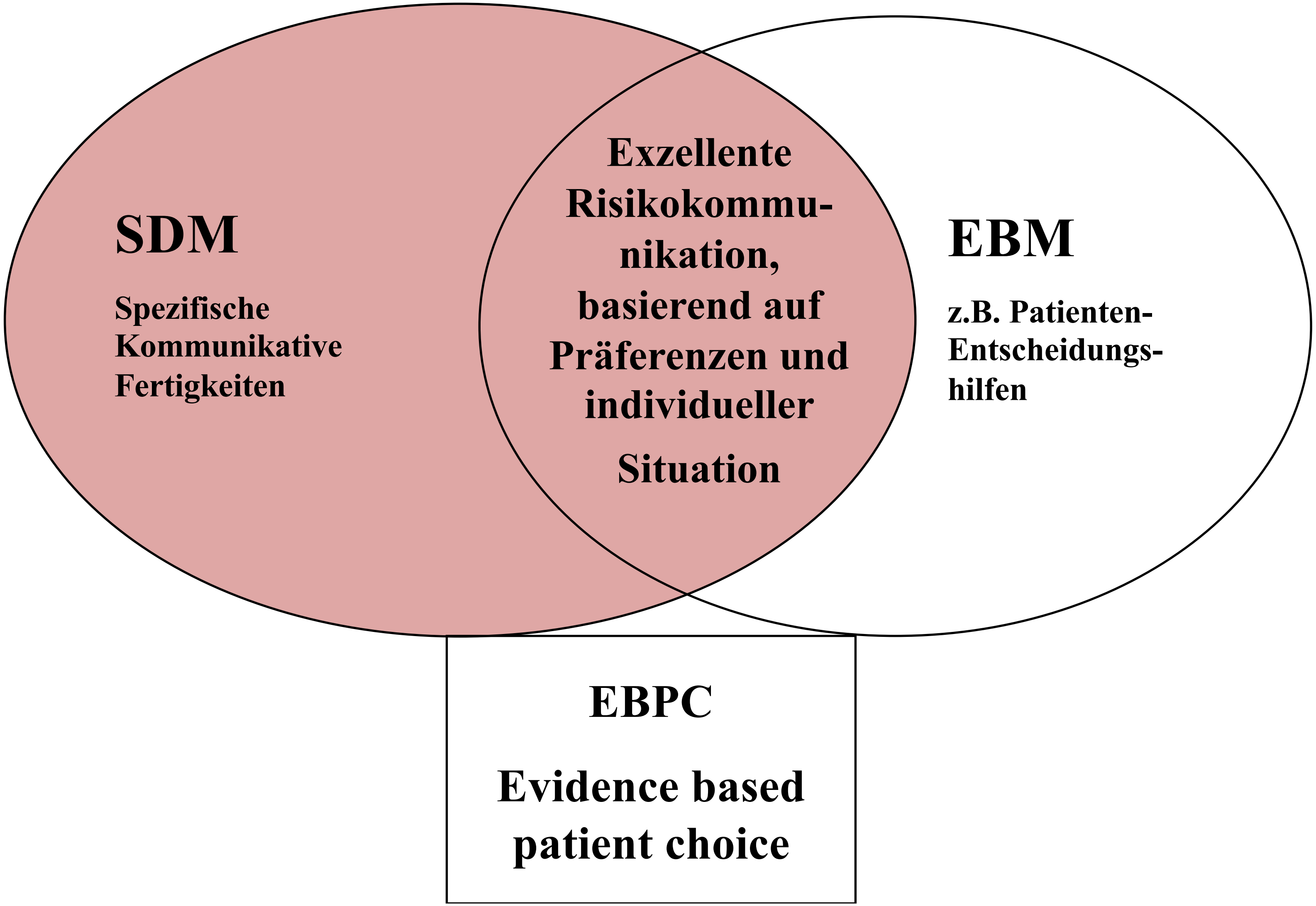
Benjamin W. Moulton, JD, MPH
Informed Medical Decisions Foundation, Healthwise Research and Advocacy, Adjunct Harvard School of Public Health, Boston, Massachusetts.

VIEWPOINT

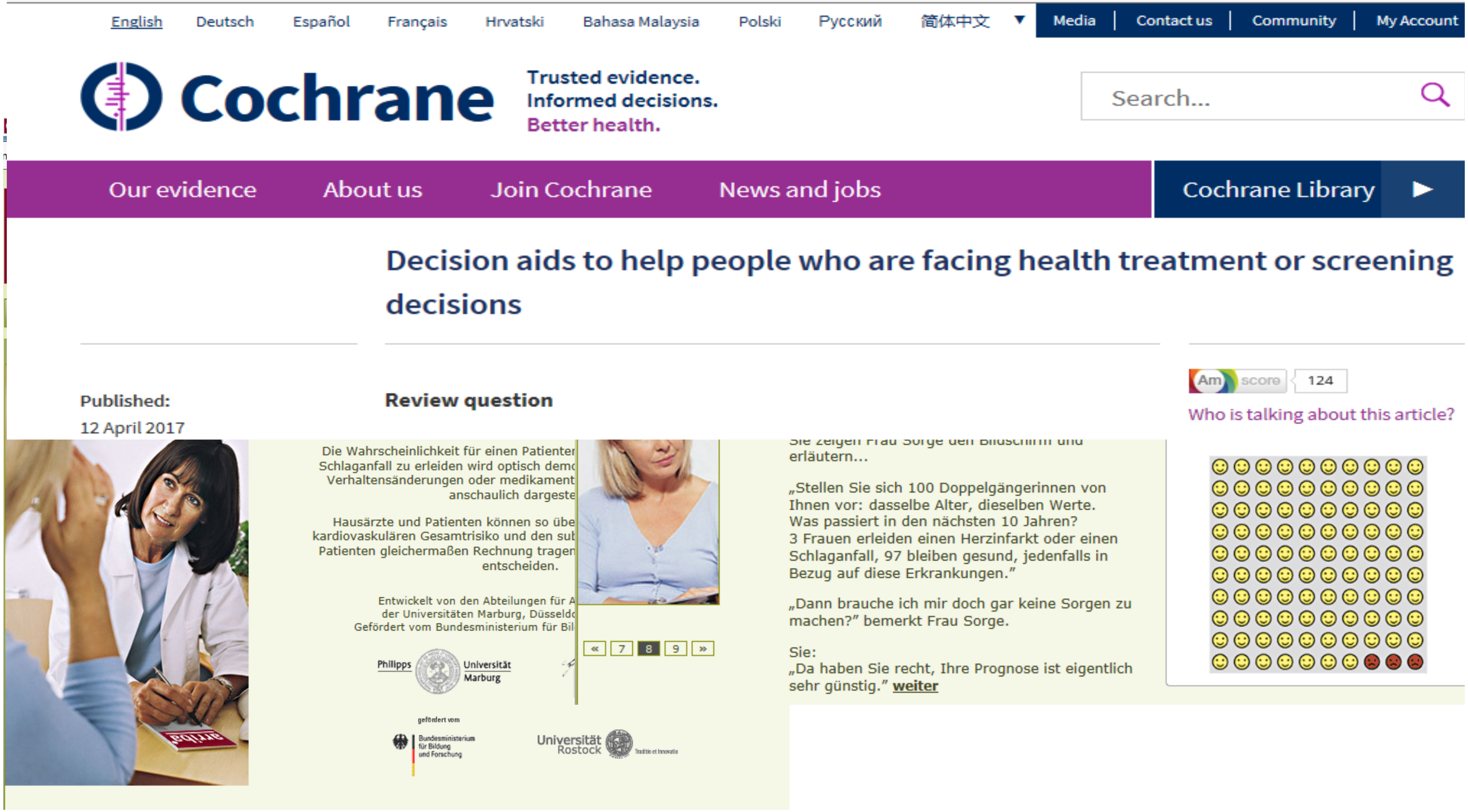
The New Era of Informed Consent
Getting to a Reasonable-Patient Standard Through Shared Decision Making

JAMA May 17, 2016 Volume 315, Number 19

SDM und EbM


SDM
Spezifische
Kommunikative
Fertigkeiten
Exzellente
Risikokommu-
nikation,
basierend auf
Präferenzen und
individueller
Situation
EBM
z.B. Patienten-
Entscheidungs-
hilfen
EBPC
Evidence based
patient choice

„Interventionen, die entwickelt werden, um Menschen zu helfen, persönliche und gut informierte Entscheidungen zu treffen, indem diese mindestens Informationen über alle Optionen und Ergebnisse enthalten, die für den Gesundheitszustand der jeweiligen Person relevant sind“ (O´Connor et al. 1999)



Life span 1
Life span 2
Efficency treatment 1
Efficiency treatment 2
Qol treatment 1
QoL treatment 2

Cost per Qaly
€ 2354
treatment1,

€ 1280
treatment 2

treatment 1
not
reimbursed

Transparency about value judgment in a decision analytic tool (the Black Box) for deciding for treatment about aneurism; B. Molewijk, 2006

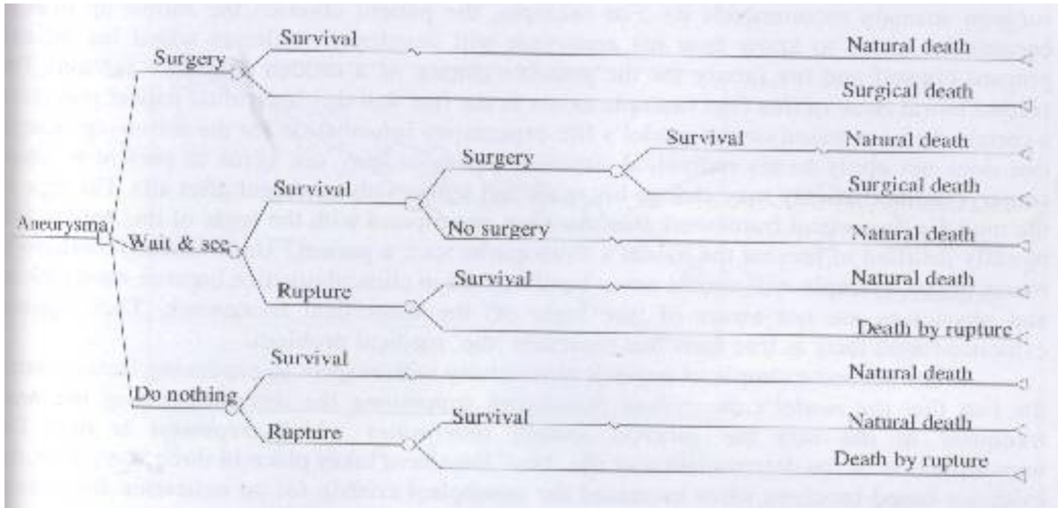
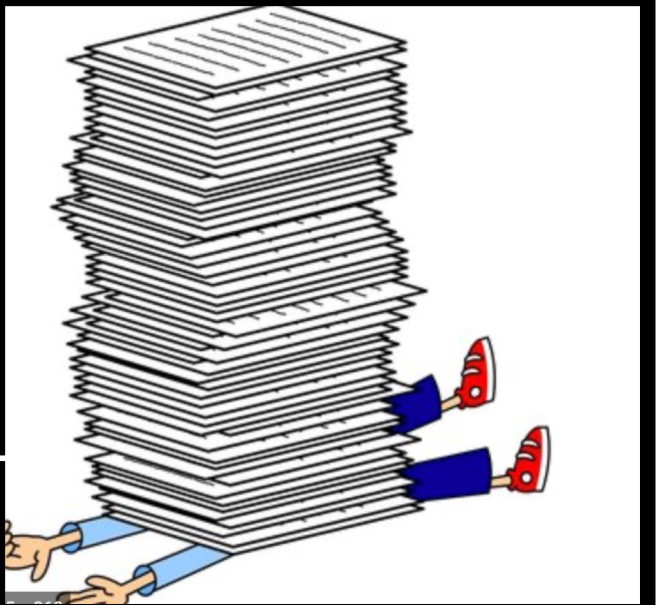


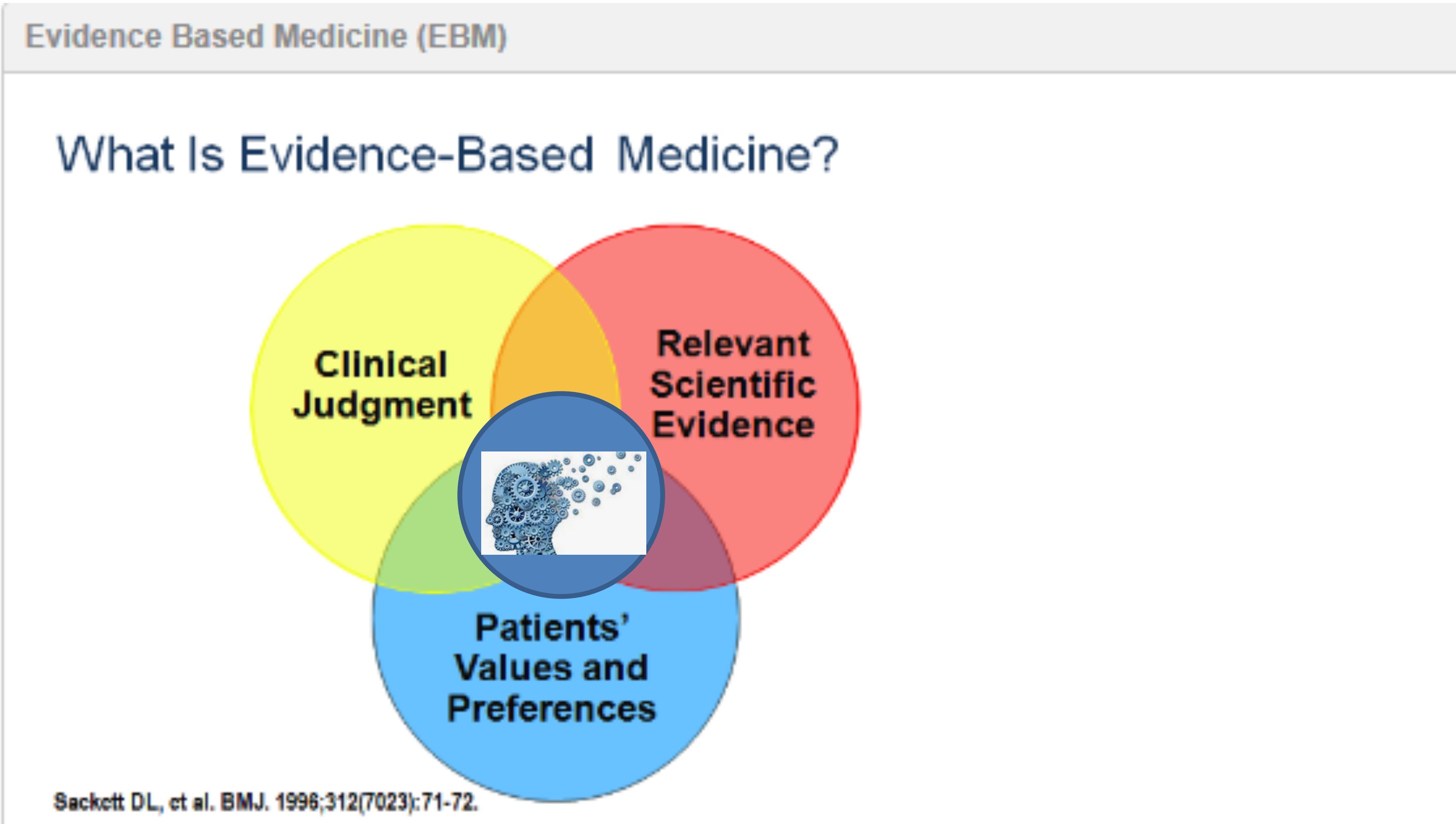
Fig. 1: The theoretical framework of a simple aneurysm decision tree.

Probleme unserer epidemiologischen Methoden und von Evidenzbasierten Entscheidungshilfen

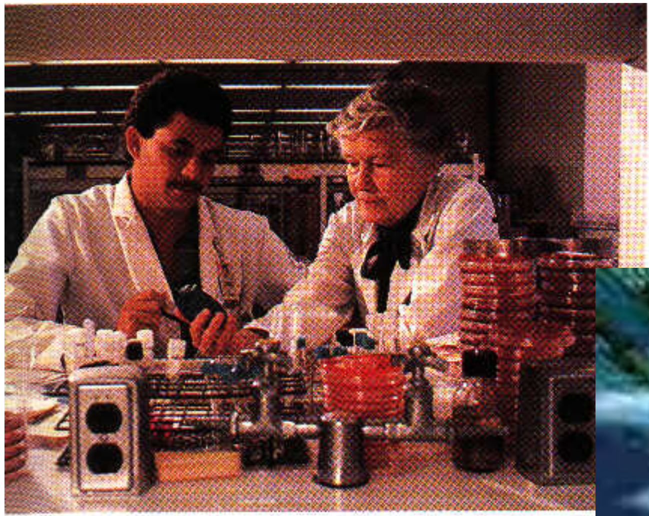


- Eher grob in Bezug auf das individuelle Risiko
- Aufwendig und langwierig, neue Evidenz zu generieren…
- Bzw. diese Up to date halten
- Noch mehr relevant bei mit viel Herzblut und wenig finanziellen Ressourcen ohne Pharmasponsoring entwickelten evidenzbasierten Entscheidungshilfen

Lösung:
Evidence based to KI-OMICS-informed or KI-OMICS based Medicine?!



Die Methodologie und der Fokus der «Personalisierten (oder «Präzisions»)- Medizin?»



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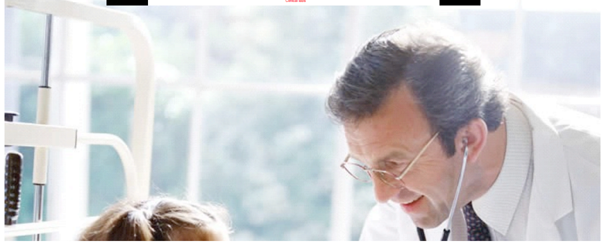


Informationswissenschaft basierend auf Biomarkern und Biosystemen auf verschiedenen «Systemleveln» von Gen/Protein/Umweltinteraktionen (omics), um schliesslich für so stratifizierte Patientengruppen individuelle Therapien festzulegen

- https://www.ibm.com/watson/health/resources/making-health-smarter-together/

IBM **Watson Health**

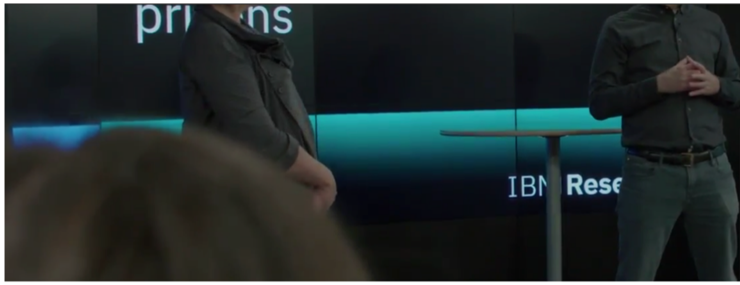
Introduction
Smarter data
Smarter technology
Smarter strategies

When you put IBM's technology and experience to work, you can focus on what matters most—the patients, citizens and members you serve.

Hide

Find out the next step on your journey to smarter health.

Take our assessment to learn about the right technology solutions for your unique needs.



Using AI to make better decisions

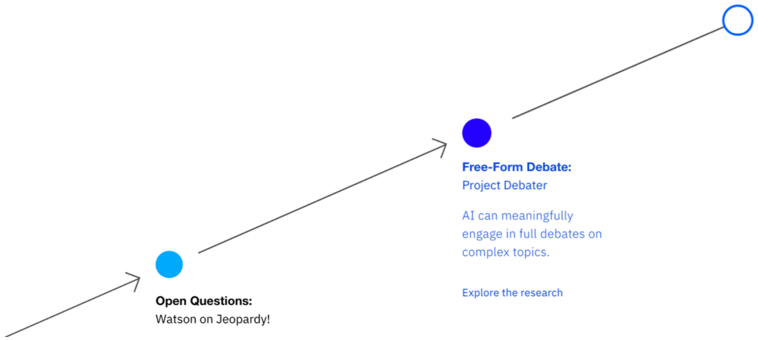
The world is awash with information, misinformation, and superficial thinking. Project Debater pushes the frontiers of AI to facilitate intelligent debate so we can build well-informed arguments and make better decisions.

Learn more

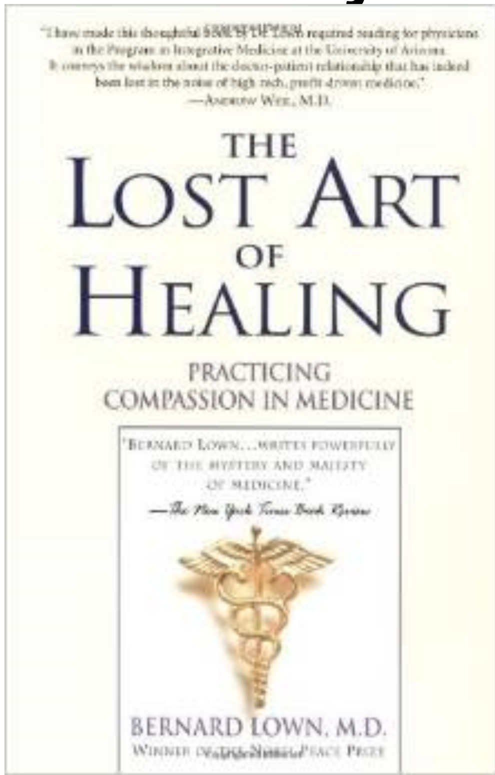
Why is Project Debater important?

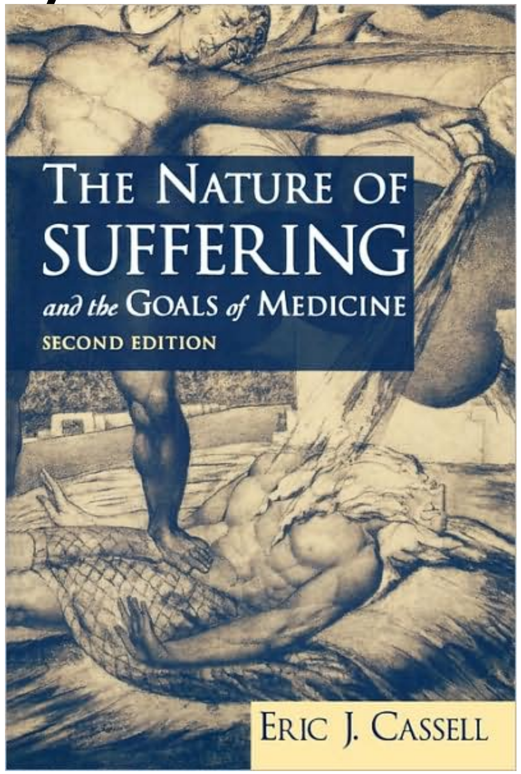
The rise of one-sided and doctored narratives is challenging society and our platforms. Too often, we talk past one another. We need a smarter way. New developments in language and reasoning in AI can help shine a light in the darkness of distorted facts to provide diverse, well-informed viewpoints—both the pro and the con.

The world is awash with information, misinformation, and superficial thinking. Project Debater pushes the frontiers of AI to facilitate intelligent debate so we can build well-informed arguments and make better decisions.



Grossartig, wenn wir so die Ziele der Medizin besser erreichen
(foster well informed choices , prevent disease, prevent harm, take better care of the ill, consider patients values, contribute to a just health care system)



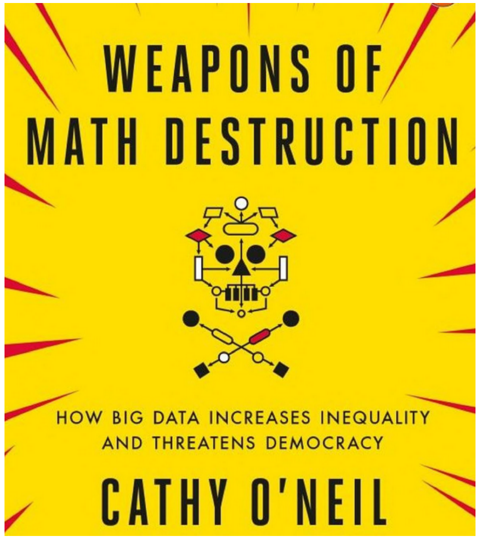


Was wissen wir bis jetzt?

Einige vielversprechende Forschungsergebnisse (v.a. in der Onkologie), die in Einzelfällen zu (sehr, sehr teuren) klinischen Standards mit begrenztem klinischen Effekt bei schwer kranken Patienten werden...

ABER

2000 Jahre Theorie und Praxis der Wissenschaft und Medizin sind nicht „out-dated“ trotz des Versprechens der 4P „revolution“



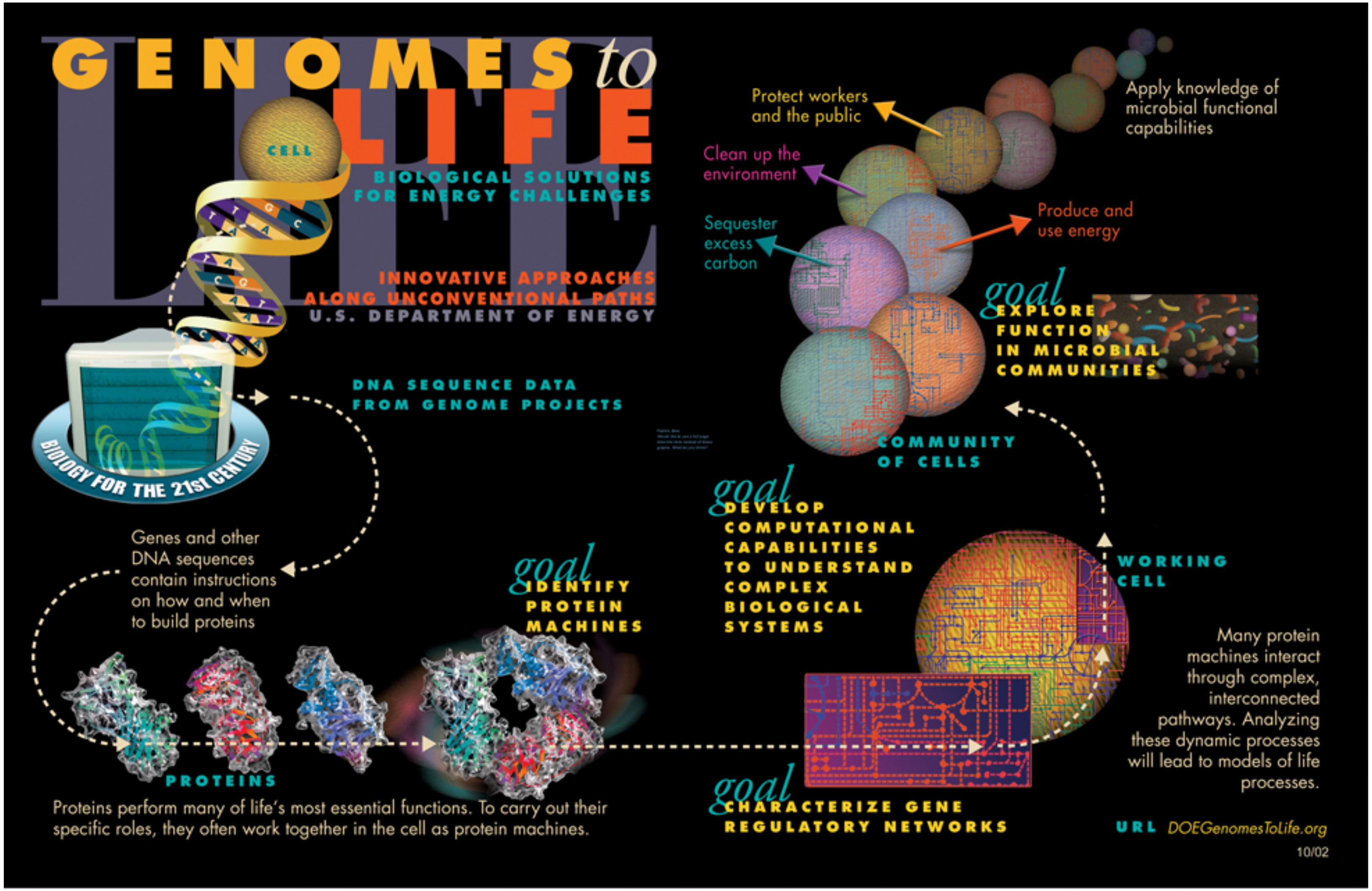
Denkanstösse zu «4P»

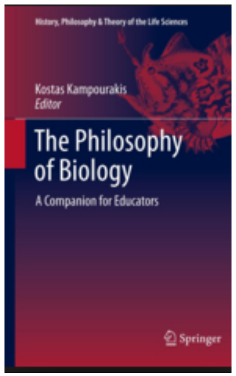
- Natur der Medizin?
- Wissenschafts-/Medizintheoretische Annahmen?
- Konzepte von Diagnose, Prognose, Krankheit, Gesundheit, Therapie, Mensch?
- Abgrenzung von Forschung und Therapie?
- Was wissen wir eigentlich?
- Wer profitiert? Wer verliert?

Welche Patienten sind im Fokus?

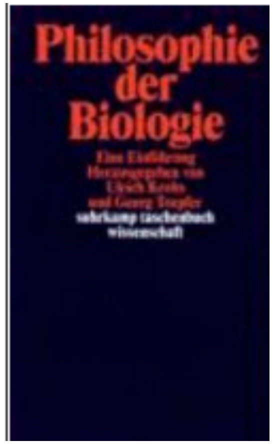
- Der multimorbide Patient?
- Der erschöpfte Patient?
- Die Intensivpatientin?
- Das verunfallte Kind?
- Die Schwangere Patientin mit Herzfehler?
- Der psychisch oder psychosomatisch erkrankte Migrant?
- Der Patient mit körperlicher Behinderung?
- Der Patient mit einer monogenetischen Erkrankung?
- Der sterbenskranke Patient?

Wo ist der Patient überhaupt?



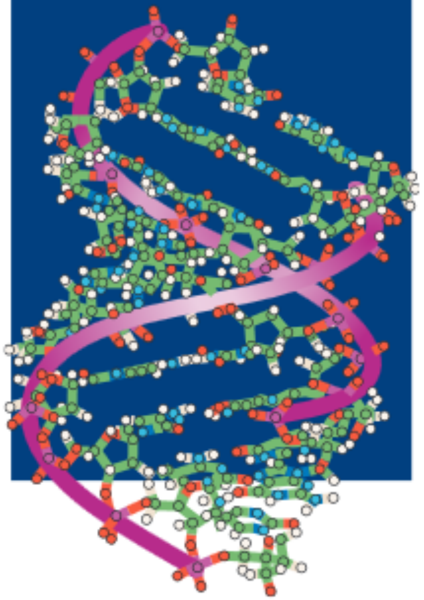


Die Herauspartialisierung des Organismus/Lebewesens in der Systembiologie



RESEARCH HIGHLIGHTS

PIONEERS OF MOLECULAR BIOLOGY



AN INTERVIEW WITH…

Sydney Brenner

Sydney Brenner was born in 1927 in South Africa, where he attended medical school. He obtained his DPhil from Oxford University, UK, and spent most of his professional career at the Laboratory of Molecular Biology at Cambridge University, UK, working with the late Francis Crick for much of that time. Brenner won the Nobel Prize in 2002 for establishing *Caenorhabditis elegans* as the widely used experimental model it is today. He presently divides his time between Cambridge, The Salk Institute, Singapore, Japan and the Howard Hughes Medical Institute Janelia Farm campus, conducting research in neurobiology and comparative genomics and mentoring young investigators.

REPORTER

VANDERBILT UNIVERSITY MEDICAL CENTER'S WEEKLY NEWSPAPER

Brenner hammers 'factory science'

BY: BILL SNYDER

From Bench to Bedside

- "The promise of the human genome is that we will have millions of targets … and we can take all the chemicals, and we can just do high-throughput analysis on all of these and find all the drugs for everything for the future … from bench to bedside. I think this is totally wrong."
- For one thing, this approach requires a "therapeutic hypothesis," that blocking a particular target could affect a physiological function or prevent a disease.
- "It is very rare that I have seen coming out of basic labs hypotheses of these kinds," Brenner argued, "mostly because most people in basic labs don't know anything about human physiology and pathology." (and Evidence based Medicine, TK)
- Beispiele: 3-Methylcrotonyl-CoA- Carboxylase Deficiency and short chain Acyl CoA Dehydrogenase (SCAT) deficiency in newborn screening
- Microdeletions in non invasive prenatal screening
- Harmful genes in every person and every embryo, like pathological findings without known significance in CT and MRI scans

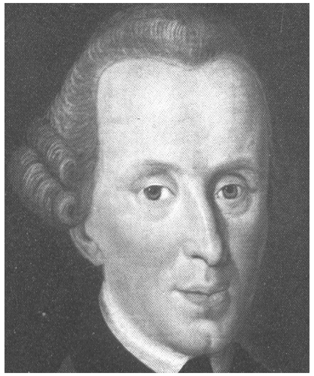
Universität Zürich[UZH]
Nr. 2/2018
UZHmagazin
Die Wissenschaftszeitschrift

«Menschen neigen dazu, sich falsch zu entscheiden, das gilt auch für Ärzte. Dagegen ermöglicht die digitale Mustererkennung ein hypothesenfreies Vorgehen».

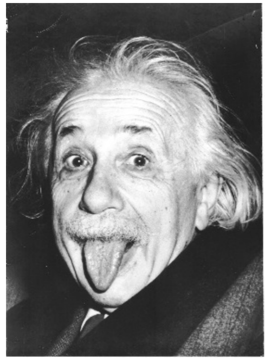
DNA Sequencing

“Sequencing the genome is like sending a man to the moon, because it’s easy. The hard part is bringing him back.”

“ The discovery of a gene, for example, doesn't necessarily mean that the protein it encodes has an important function. “You've got to have a theory on how the cell works”



Brenner finales Urteil über die «OMICS»



“Artificial intelligence combined with human stupidity.” He said that such an approach to science was **low input, high throughput, no output** – where you put garbage in and get garbage out. Instead, Dr. Brenner encouraged us to start with high input, which, he said, is what’s in your head.

- The study was conducted more than two years ago at Hood’s Institute for Systems Biology. Hood founded Arivale with the company’s CEO, Clayton Lewis, and many of the researchers behind the original study.

  The company now offers its scientific wellness program to anyone with $3,499 in their pocket, and Arivale is collecting more data to refine and further study the scientific wellness approach. In the paper, researchers said they’re aiming to recruit 100,000 people to a new study by 2020.

4 P aus meiner Sicht

- Hat Potential für die Steigerung von Patientennutzen und Vermeidung von Schaden bei bestimmten Erkrankungen
- Fokussiert aktuell auf bestimmte Patientengruppen: metabolisch (mit)-bedingte Erkrankungen, Tumorerkrankungen, genetisch (mit)-bedingte Erkrankungen)
- Ist wissenschaftstheoretisch, medizintheoretisch und –ethisch unterbestimmt
- Ist meist noch Forschung in vitro – in silico
- Macht zur Zeit mehr das messbare wertvoll als das wertvolle messbar
- Verspricht therapeutisch aktuell viel mehr als sie halten kann
- Stärkt daher die „therapeutic misconception"
- Macht Erkrankungen zu „seltenen" Erkrankungen durch Biomarkerstratifizierung
- Ist daher sehr teuer (sowohl Forschung als auch neue Therapien) auch aufgrund der EMEA Pricing und Patentierungspolitik seit 2000
- Das zentrale Moment der wissenschaftlichen kritischen Reflexion ist kaum sichtbar

A thoughtful «4 P Approach»
z.B: Green et al 2013

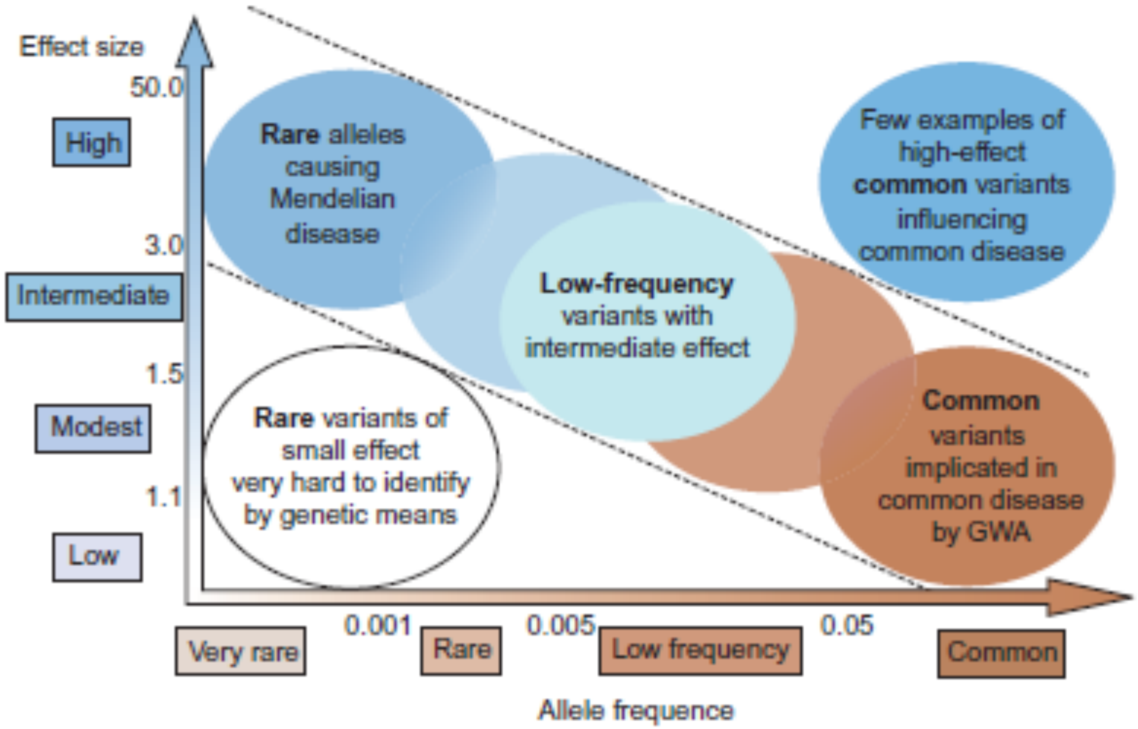
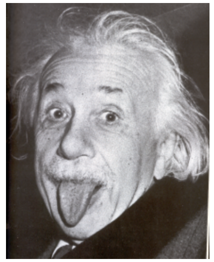


Figure 9.5 The spectrum of risk associated with rare and common genetic variants. *Figure reproduced from Manolio et al., 2009, cited in that paper as modified from a similar figure in McCarthy et al., 2008.*

Table 9.1 Potential benefits and possible limitations associated with clinical applications of whole-genome sequencing

WGS application	Potential benefits	Limitations
Molecular characterization of rare diseases	Definitive diagnosis, family planning, and familial risk assessment	Many variants of unknown significance will be identified
Individualized cancer treatment	Targeted therapeutics specific for a cancer genotype with improved outcomes	There is currently limited prognostic information available
Pharmacogenomics	Inform choice or dosage of medications	Clinical utility has not been demonstrated in most cases
Preconception and prenatal screening	Inform parents about the risk of disease in offspring	Ethical problems arising from acting on such information
Population screening for highly penetrant Mendelian disorders	Identification of diseases where surveillance or intervention could alter outcome	Limited knowledge of penetrance of disease alleles within unaffected families makes interpretation difficult
Population screening for common disease susceptibility	Increased health knowledge and potentially positive health changes	Clinical utility has not been demonstrated

Was heisst das für unseren Zugang zu transaktionalen Entscheidungshilfen?

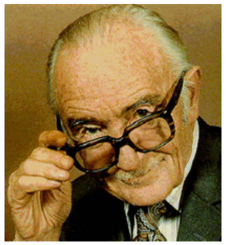


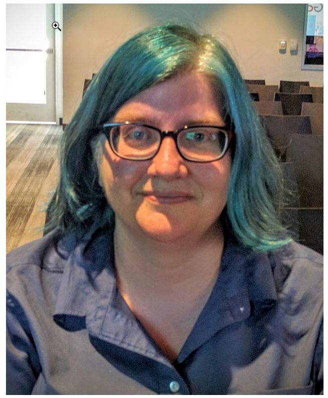
Faire Evaluation des Nutzens (=well informed choices)
von «AI» und «Omics» für

- Updates der Evidenz, Generierung von Parametern
- Biologisch-Individuell genauere prognostische oder diagnostische Aussagen
- Biologisch-Individuell angepasste Therapievorschläge

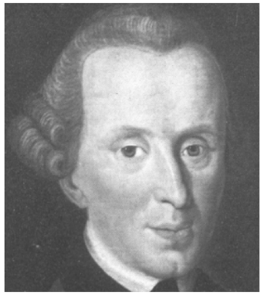
Dann medizinethisch vertretbar und sinnvoll wenn
- Transparenz in der Nutzung, der Ziele und Grenzen der AI/Omics/4P gegeben ist

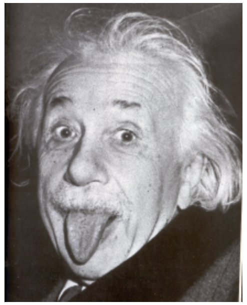
Und
- das primäre Ziel einer wohlinformierten, therapiezielorientierten Patient*innenentscheidung und gerechten Gesundheitsversorgung weiter im Fokus bleibt





Notwendige Packungsbeilage





Keep being enthusiastic in research, but critical and decent towards your own and others results

Beware of conflating research (still most of 4P) with therapy

and choose wisely for and with your patients while practising
THE ART OF MEDICINE

Zusatzfolien

nature biotechnology

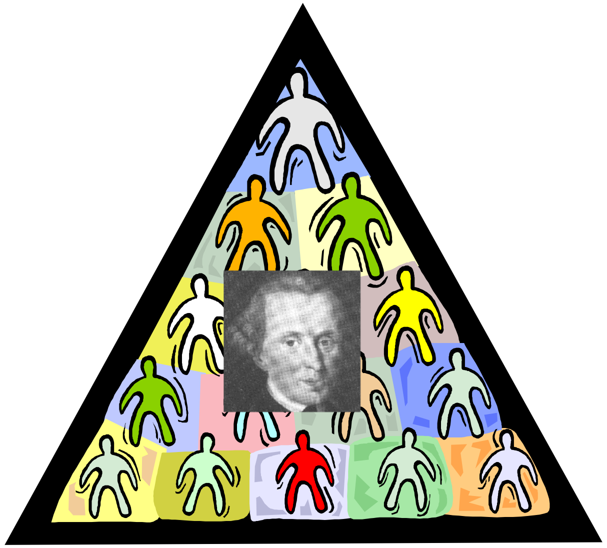
A wellness study of 108 individuals using personal, dense, dynamic data clouds

Nathan D Price[1,2,6,7], Andrew T Magis[2,6], John C Earls[2,6], Gustavo Glusman[1], Roie Levy[1], Christopher Lausted[1], Daniel T McDonald[1,5], Ulrike Kusebauch[1], Christopher L Moss[1], Yong Zhou[1], Shizhen Qin[1], Robert L Moritz[1], Kristin Brogaard[2], Gilbert S Omenn[1,3], Jennifer C Lovejoy[1,2] & Leroy Hood[1,4,7]

(nathan.price@systemsbiology.org) or L.H. (lhood@systemsbiology.org).

Received 16 October 2016; accepted 11 April 2017; published online 17 July 2017; doi:10.1038/nbt.3870

Subjekt im Zentrum der Erkenntnistheorie Wer sind die Autoren der Scientific Wellness Studie?



Hood is now pioneering new approaches to P4 medicine and most recently, has embarked on creating a P4 pilot project on 108 well individuals, that is transforming healthcare and leading to a new healthcare discipline termed scientific wellness.

P4 MEDICINE institute

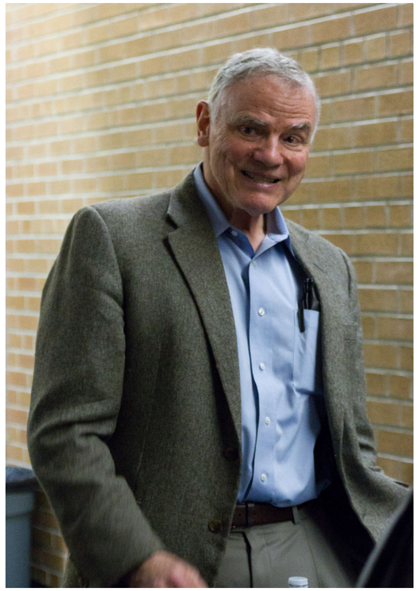
Quantifying Wellness. Demystifying Disease.

P4 MEDICINE | WHAT WE DO | MEDIA CENTER | ABOUT | BLOG

LEROY HOOD, MD, PHD

Co-founder and Chairman P4 Medicine institute

Leroy Hood geb. 10.Oktober 1938 in Montana, USA



- Studium der Biologie, Medizin und
Biochemie
- Kein praktizierender Arzt
- 1986 Erfindung des high speed DNA sequencers (HGP)
- 1990 DNA chips Arrays
- Professor für Biologie, Fokus auf Krebserkrankungen
- 2000 Gründung des Institute of System Biology
- “Hood has played a key role in founding numerous biotechnology companies, including Amgen, Applied Biosystems, Systemix, Darwin, and Rosetta.”

Motto:

“always practice biology at the leading-edge; and if you really want to change biology, develop a new technology for pushing back the frontiers of biological knowledge.”

Stephen H. Friend,
geb. 10.Dez. 1953, Connecticut, USA

- BA in Philosophie ;
- PhD in Biochemistry, MD Indiana University
- Klinische Ausbildung Childrens Hospital; Dana Faber Institute
- Faculty position in der Harvard medical School und Mass General
- Clonierung des P54 tumor suppressor Gens
- Co Founder of Rosetta; Co Vice President of Merck, new oncology unit
- CEO of «Sage Bionetworks» non profit foundation for «proof of concept« in man development.

“Recognizing that genetic datasets were too fragmented and siloed and data and model sharing was inadequate, he left Merck in 2009”

PICO

Population oder Patient, Problem:

Beschreibung der Gruppe von Patienten bzw. des Problems

Intervention = Technologien, diagnostisches/therapeutisches Verfahren: Welche Intervention ist Gegenstand der gegenwärtigen Untersuchung?

Comparison oder Control = Vergleichsintervention:

Was ist die Hauptalternative, mit der die Intervention verglichen werden kann?

Outcome = Zielgröße:

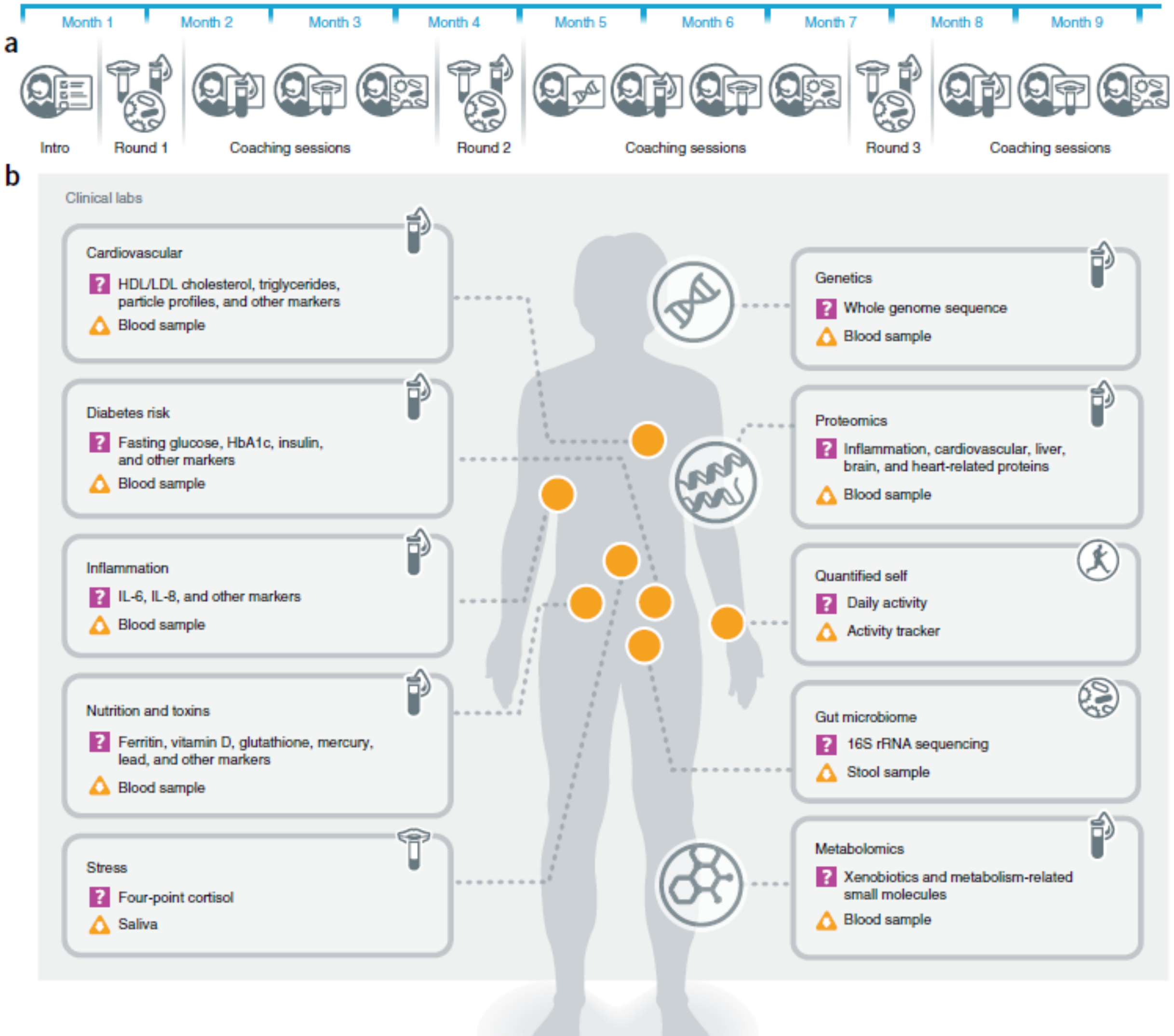
Was soll erreicht werden?

Population «Patienten»

We report the generation and analysis of personal, dense, dynamic data clouds for 108 individuals over the course of a 9-month study that we call the Pioneer 100 Wellness Project (P100). Our study included whole genome sequences; clinical tests, metabolomes, proteomes, and microbiomes at 3-month intervals; and frequent activity measurements (i.e., wearing a Fitbit). This study takes a different approach

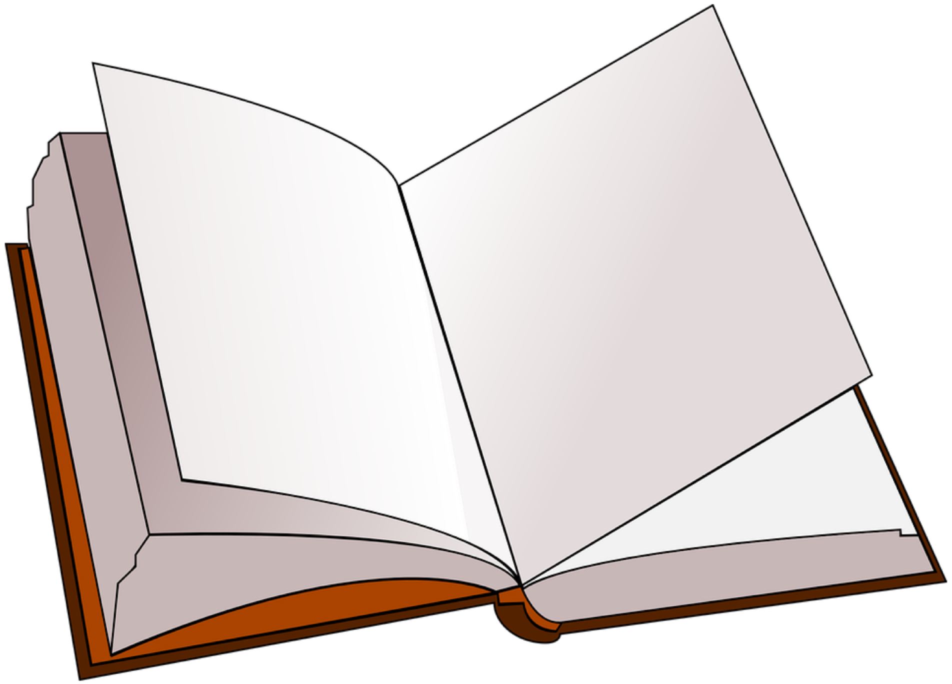
Problem

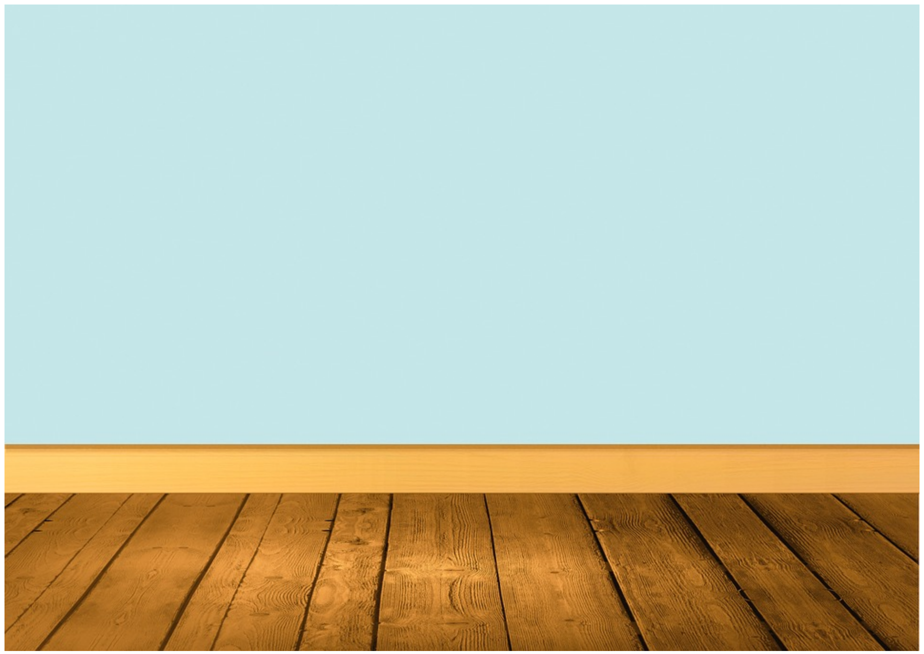
Intervention



Controls

ZWILLING
J.A.HENCKELS

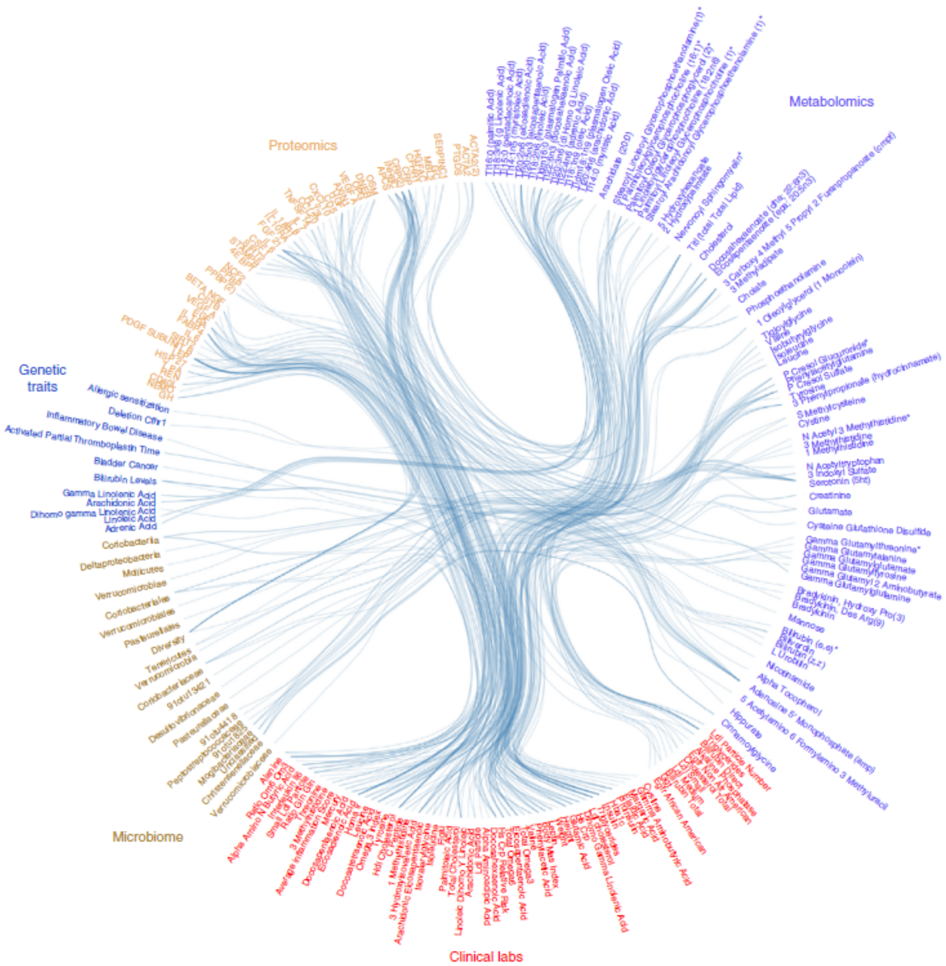




Outcome (geplant)

- Kosteneffiziente Strategien zur Ermittelung, Speicherung, und Analyse von Gesundheitsdaten über die Zeit in Kombination mit Genomic Daten
- Entwicklung und Gebrauch analytischer tools, um die Korrelationen (Interrelationen) in Handlungsanweisungen zu giessen
- Entdeckung von Mustern in den Gesundheitsdaten durch multivariate Analysen, um Korrelationen zu Wellness zu finden, bzw. zu Transitionen von Wellness zu Disease
- Herausfinden, wie man am Besten mit diesen Informationen arbeitet, Menschen informiert, indem deren Reaktionen und Feedback berichtet werden

Outcome (berichtet)



Clinical labs

Figure 2 Top 100 correlations per pair of data types. Subset of top statistically significant Spearman inter-omic cross-sectional correlations between all data sets collected in our cohort. Each line represents one correlation that was significant after adjustment for multiple hypothesis testing using the method of Benjamini and Hochberg[10] at $p_{adj} < 0.05$. The mean of all three time points was used to compute the correlations between analytes. Up to 100 correlations per pair of data types are shown in this figure. See **Supplementary Figure 1** and **Supplementary Table 2** for the complete inter-omic cross-sectional network.

Table 1 Longitudinal analysis of clinical changes by round

Clinical laboratory test		Changes in labs in participants out-of-range at baseline		
Health area	Name	*N*	Δ per round	*P*-value
Nutrition	Vitamin D	95	+7.2 ng/mL/round	7.1×10^{-25}
Nutrition	Mercury	81	−0.002 mcg/g/round	8.9×10^{-9}
Diabetes	HbA1c	52	−0.085%/round	9.2×10^{-6}
Cardiovascular	*LDL particle number (Quest)*	*30*	*+130 nmol/L/round*	9.3×10^{-5}
Nutrition	Methylmalonic acid (Genova)	3	−0.49 mmol/mol creatinine/round	2.1×10^{-4}
Cardiovascular	LDL pattern (A or B)	28	−0.16 /round	4.8×10^{-4}
Inflammation	Interleukin-8	10	−6.1 pg/mL/round	5.9×10^{-4}
Cardiovascular	Total cholesterol (Quest)	48	−6.4 mg/dL/round	7.2×10^{-4}
Cardiovascular	LDL cholesterol	57	−4.8 mg/dL/round	8.8×10^{-4}
Cardiovascular	LDL particle number (Genova)	70	−69 nmol/L/round	1.2×10^{-3}
Cardiovascular	Small LDL particle number (Genova)	73	−56 nmol/L/round	3.5×10^{-3}
Diabetes	Fasting glucose (Quest)	45	−1.9 mg/dL/round	8.2×10^{-3}
Cardiovascular	Total cholesterol (Genova)	43	−5.4 mg/dL/round	1.2×10^{-2}
Diabetes	Insulin	16	−2.3 IU/mL/round	1.5×10^{-2}
Inflammation	TNF-alpha	4	−6.6 pg/mL/round	1.8×10^{-2}
Diabetes	HOMA-IR	19	−0.56 /round	2.0×10^{-2}
Cardiovascular	HDL cholesterol	5	+4.5 mg/dL/round	2.2×10^{-2}
Nutrition	Methylmalonic acid (Quest)	7	−42 nmol/L/round	5.2×10^{-2}
Cardiovascular	Triglycerides (Genova)	14	−18 mg/dL/round	1.4×10^{-1}
Diabetes	Fasting glucose (Genova)	47	−0.98 mg/dL/round	1.5×10^{-1}
Nutrition	Arachidonic acid	35	+0.24 wt%/round	1.9×10^{-1}
Inflammation	hs-CRP	51	−0.47 mcg/mL/round	2.1×10^{-1}
Cardiovascular	Triglycerides (Quest)	17	−14 mg/dL/round	2.4×10^{-1}
Nutrition	Glutathione	6	+11 micromol/L/round	2.5×10^{-1}
Nutrition	Zinc	4	−0.82 mcg/g/round	3.0×10^{-1}
Nutrition	Ferritin	10	−14 ng/mL/round	3.1×10^{-1}
Inflammation	Interleukin-6	4	−1.1 pg/mL/round	3.8×10^{-1}
Cardiovascular	HDL large particle number	8	+210 nmol/L/round	4.9×10^{-1}
Nutrition	Copper	10	+0.006 mcg/g/round	6.0×10^{-1}
Nutrition	Selenium	6	+0.035 mcg/g/round	6.2×10^{-1}
Cardiovascular	Medium LDL particle number	20	+2.8 nmol/L/round	8.5×10^{-1}
Cardiovascular	Small LDL particle number (Quest)	14	−2.3 nmol/L/round	8.8×10^{-1}
Nutrition	Manganese	0	N/A	N/A
Nutrition	EPA	0	N/A	N/A
Nutrition	DHA	0	N/A	N/A

Generalized estimating equations (GEE) were used to calculate average changes in clinical laboratory tests over time, for those analytes that were actively coached on. The 'Δ per round' column is the average change in the population for that analyte by round adjusted for age, sex, and self-reported ancestry. 'Out-of-range at baseline' indicates the average change using only those participants who were out-of-range for that analyte at the beginning of the study. Rows in boldface indicate statistically significant improvement, while the italicized row indicates statistically significant worsening. N/A values are present where no participants were out-of-range at baseline. For example, the average improvement in vitamin D for the 95 participants that began the study out-of-range was +7.2 ng/mL per round. Several analytes are measured by both Quest and Genova; with the exception of LDL particle number, the direction of effect for significantly changed analytes was concordant across the two laboratories. An independence working correlation structure was used in the GEE. See **Supplementary Table 10** for the complete results.

Effekt

age, sex, and self-reported ancestry. The results are shown in **Table 1** and **Supplementary T**. The most significant improvements for those who began the study out of range were observed in vitamin D (+7.2 ng/mL/round), mercury (−0.002 mcg/g/round), and HbA1c (−0.085%/round). We observed consistent improvements in total cholesterol measured by both Quest and Genova (−6.4 mg/dL/round and −5.4 mg/dL/round, respectively). LDL cholesterol, measured only with Genova, significantly decreased (−4.8 mg/dL/round), while HDL cholesterol significantly increased (+4.5 mg/dL/round). Other significant improvements were observed in other diabetes risk

Fazit der Autoren

Study finds Lee Hood's 'scientific wellness' approach can make people healthier

BY CLARE MCGRANE on July 17, 2017 at 8:00 am

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Genomics pioneer Lee Hood, left, and Maveron's Clayton Lewis, the CEO of Arivale.

Scientific wellness is a straightforward idea: use data about a person's genes, proteins and other biology, along with behavioral coaching, to keep them healthy, even preventing health problems before they arise. The approach is championed by genomics pioneer Lee Hood, and it's being pursued his latest startup, Seattle-based Arivale.

It's such a new and evolving concept that it isn't in the dictionary yet. Or Merriam

Die 100 Pioniere

- Ist der befundlose Pionier eigentlich gesund?

- Ist der gesunde Pionier nur nicht ausreichend diagnostiziert?

- Ist irgend ein Pionier gesünder geworden?

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Spezialseiten

Regression zur Mitte

ch einem extrem ausgefallenen
einen Einfluss auf die
00 %.

Zum einen werden oft
deren wird bei Prognosen der
trapoliert. Der Satz „Der
nifikant über einen Zeitraum von
g der Getränke.[2] In der
: Ein Sportler zeigt
bildet wurde. Der Grund, warum
mittelmäßige Leistungen

3 Medizin

Medizin [Bearbeiten | Quelltext bearbeiten]

In der Medizin bzw. Psychologie spielt das Phänomen eine wichtige Rolle in Zusammenhang mit klinischen Studien.

Wählt man beispielsweise im Rahmen einer Reihenuntersuchung (Screening) unter Routinepatienten die Gruppe der Patienten mit den höchsten Messwerten aus, z. B. Blutdruck, und untersucht diese Gruppe zu einem späteren Zeitpunkt erneut, so werden die Patienten meistens einen Wert aufweisen, der näher am Normalwert liegt – unabhängig davon, ob in der Zwischenzeit eine Behandlung erfolgt ist.[6]

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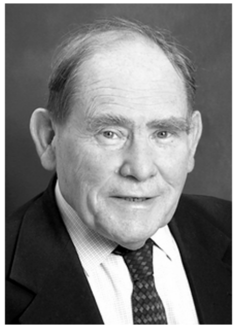
Sydney Brenner - Facts



Sydney Brenner

Born: 13 January 1927, Germiston, South Africa

Affiliation at the time of the award: The Molecular Sciences Institute, Berkeley, CA, USA

Prize motivation: "for their discoveries concerning genetic regulation of organ development and programmed cell death"

Field: genetics

Prize share: 1/3

Work

At the beginning of an organism's life, the number of cells it contains increases rapidly. New cells are formed throughout its lifetime, but cells also die in order to maintain a balance in the number of cells in existence. This process is regulated by genes and is called programmed cell death. Groundbreaking in the understanding of this phenomenon were studies on the development of the small roundworm Caenorhabditis elegans, conducted by Sydney Brenner in the mid-1970s. Sydney Brenner's work made it possible to link genetic analysis to cell division and organ formation.

Sydney Brenner

1947 Abschluss Medizin und Wissenschaft, Johannesburg
1954 Abschluss in Chemie
1956 Arbeit mit Francis Crick in Cambridge, in den nächsten Jahren zusammen Postulat des Triplets, der «messenger RNA» und des «Stop Codons» (Uracil, Adenine, Guanine)
1965 ff Forschung an *Caenorhabditis elegans als Modellorganismus für Genetik, Neurobiologie, Entwicklungsbiologie*
Pionier der Apoptoseforschung

How has molecular biology research changed in the past 50 years?

"It has changed completely. It has become much more descriptive and much less experimental. It is what I call '**low input, high throughput, no output science'**! The proponents of this kind of science claim that by generating descriptions of the behaviour of biological systems they'll be able to generate models of what's going on in them, and then refine these models. They call this 'systems biology'.

To use a simple analogy of this type of science, consider that one is sitting outside a room in which someone is playing a drum. The room is wired for sound, and using only the recording of the sounds one is trying to reconstitute the physical properties of the drum. In my mind one cannot succeed because in this **classic inverse problem**, information is lost and measurements are inaccurate."

Causality-Coincidence conflation/Lead time bias/Clinical Validity problems

- 3-Methylcrotonyl-CoA- Carboxylase Deficiency and short chain Acyl CoA Dehydrogenase (SCAT) deficiency in newborn screening
- Microdeletions in non invasive prenatal screening
- Harmful genes in every person, like pathological findings without known significance in CT and MRI scans e.g. in 1/3 of healthy 73 year old in Scotland (Sandeman et al 2013)
- Fault of Earlier detection and Progression free survival estimates

WHO Wilson & Junger „Every screning harms“:
Screening and describing without pre-test probabilities, clinical knowledge and ethical evaluation is necessarily harmful

Conflation of Research and Therapy, some Lead time bias and correlation effects in „4P“ medicine with unproven effects

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