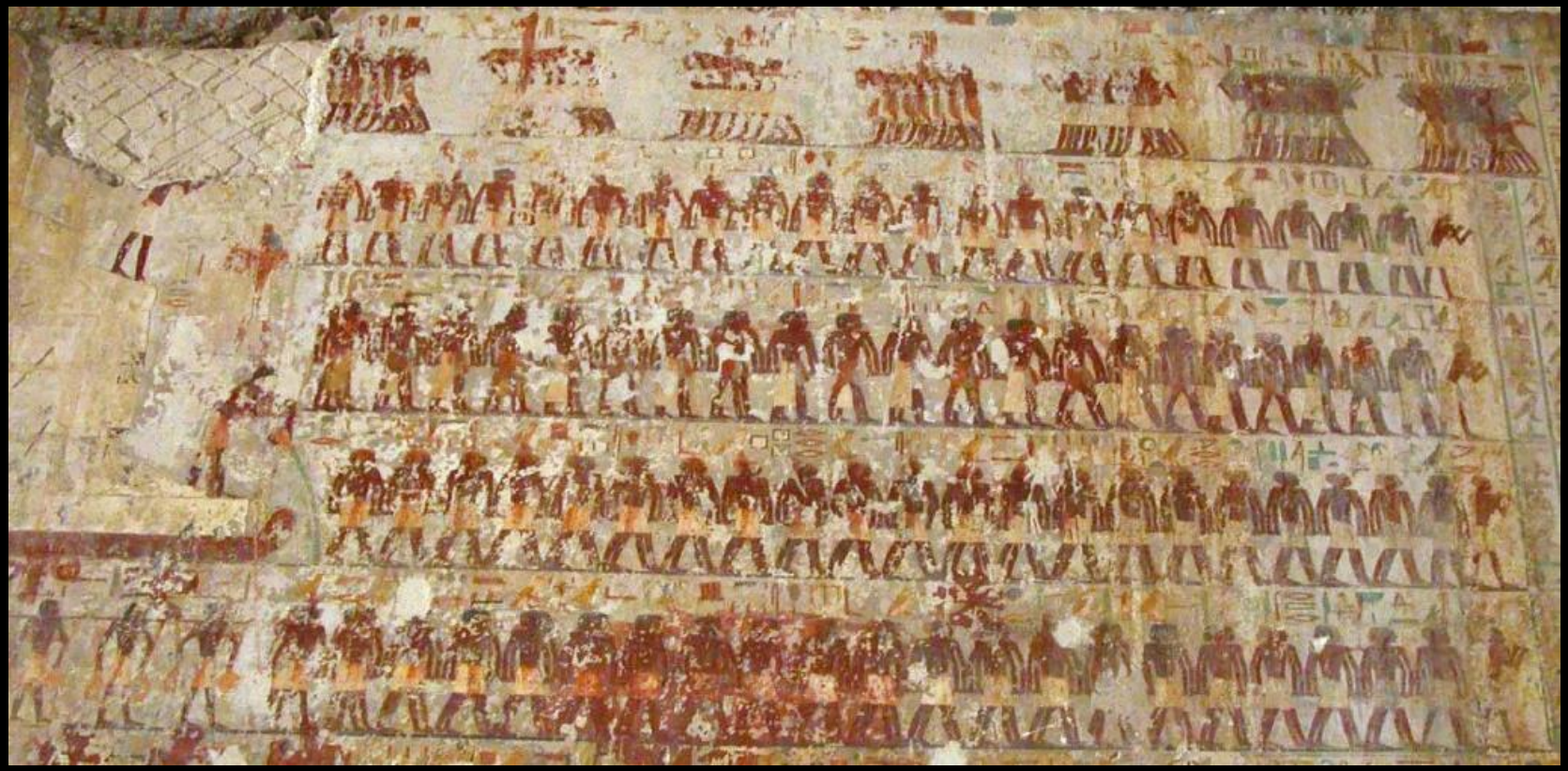
Notwendige Infrastrukturen für Transparenz, Effizienz und Nachhaltigkeit in der medizinische Forschung

Prof. Dr. Michael Krawczak

TMF - Technologie- und Methodenplattform
für die vernetzte medizinische Forschung e.V.

Christian-Albrechts-Universität zu Kiel



Wandmalerei im Grab des Djehutihotep
ca. 1900 v.Chr.

Big Data – Zukunft der Wissenschaft (?)

Big Data – Zukunft der Wissenschaft (?)

"**Big Data** is high-**volume**, high-**velocity** and/or high-**variety** information assets that demand cost-effective, innovative forms of information processing that enable enhanced insight, decision making, and process automation."

Gartner IT Glossary

Big Data – Zukunft der Wissenschaft (?)

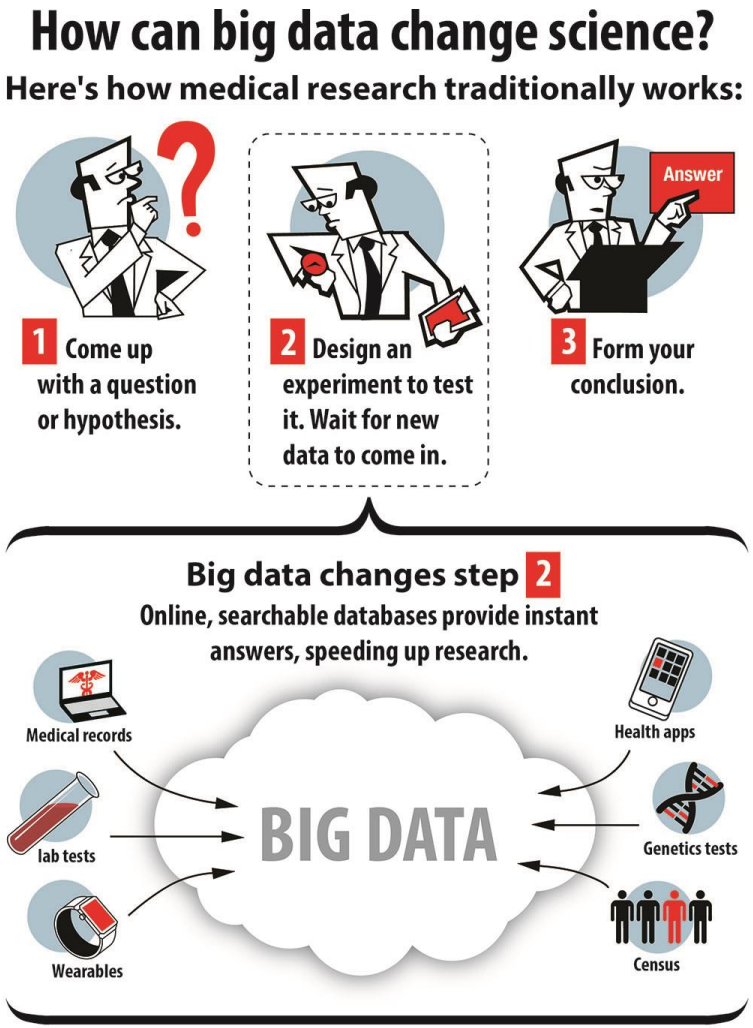
Big Data – Zukunft der Wissenschaft (?)

"All models are wrong, but some are useful."
George Box, Statistiker, University of Wisconsin

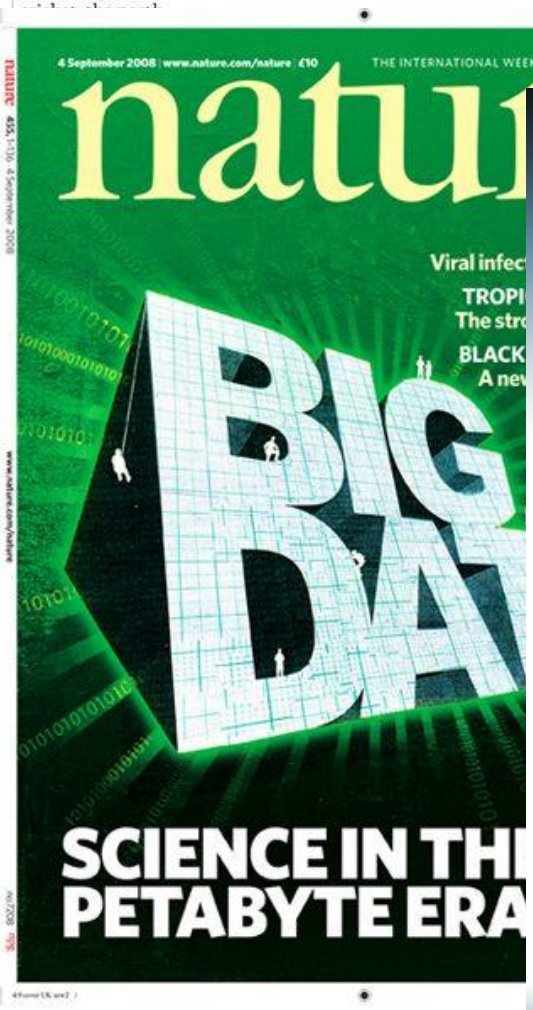
"All models are wrong, and increasingly you can succeed without them."
Peter Norvig, Director of Research, Google Inc.

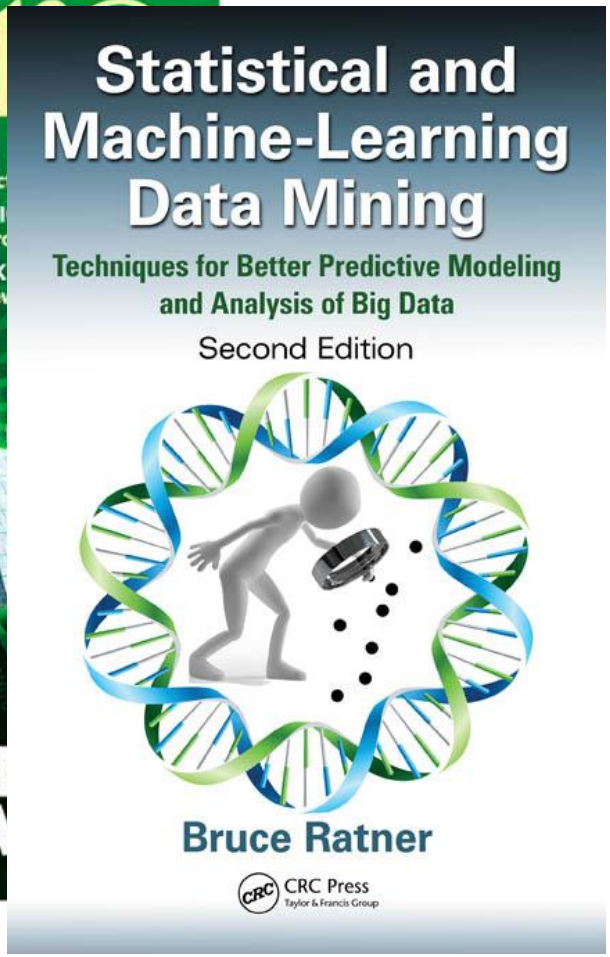
"Correlation supersedes causation, and science can advance even without coherent models, unified theories, or really any mechanistic explanation at all."
Chris Anderson, Chief Editor, Wired Magazine

Big Data – Zukunft der Wissenschaft (?)



Big Data – Zukunft der Wissenschaft (?)

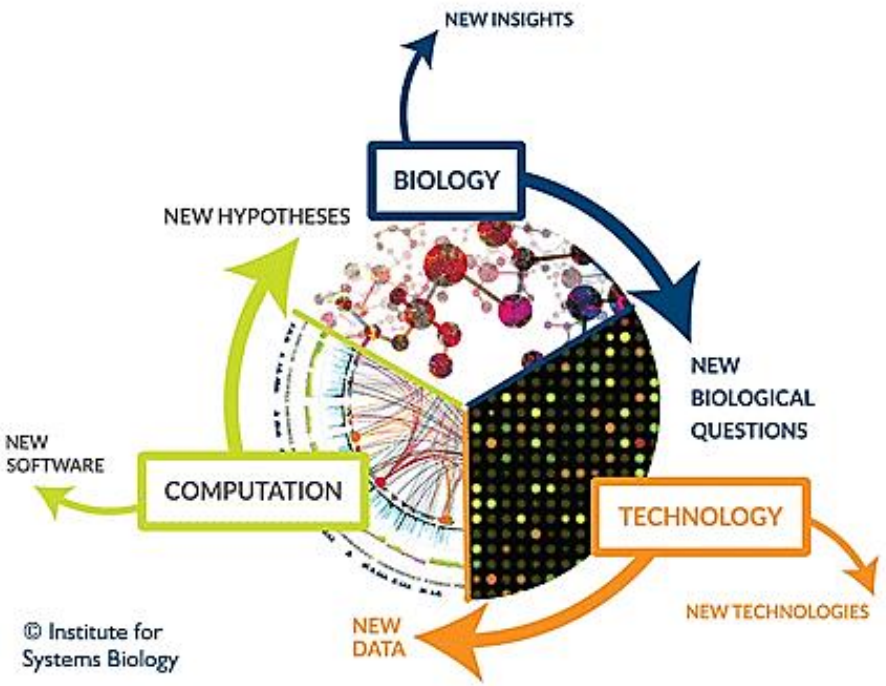




Big Data – Zukunft der Wissenschaft (?)

"**Systems Biology** is the computational and mathematical modeling of complex biological systems. [...] Systems Biology is a biology-based inter-disciplinary field of study that focuses on complex interactions within biological systems, using a holistic approach (instead of the more traditional reductionism) to biological and biomedical research."

Wikipedia



http://www.centerforsystemsbiology.org/

Big Data – Zukunft der Wissenschaft (?)

e:Med SYSTEMS MEDICINE

GEFÖRDERT VOM Bundesministerium für Bildung und Forschung

e:Med | Konsortien | Demonstratoren | Nachwuchsforschung | Querschnitt | International

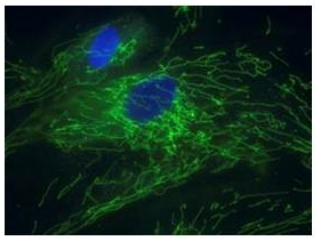
Home > Konsortien

- CancerTelSys
- CAPSyS
- CLIOMMICS
- e:AtheroSysMed
- e:Kid
- IntegraMent
- Multiscale HCC
- PANC-STRAT
- SMOOSE
- SYSIMIT
- SysINFLAME
- SysMedAlcoholism
- SYSMED-NB
- SYS-Stomach

Modul I

Konsortien der Systemmedizin

Das e:Med Modul I mit aktuell 14 interdisziplinären Forschungskonsortien der Systemmedizin ist die zentrale Maßnahme des Forschungs- und Förderkonzepts. Für Forschungsgruppen an 42 wissenschaftlichen Einrichtungen in 28 deutschen Städten sowie 3 Universitäten außerhalb Deutschlands stellt das BMBF für die ersten drei der vorgesehenen fünf Förderjahre einen Betrag von 52,3 Mio.€ zur Verfügung.



Diese interdisziplinären Forschungskonsortien bearbeiten in zahlreichen Teilprojekten an unterschiedlichen Standorten jeweils eine gemeinsame krankheitsbezogene Fragestellung anhand eines systemmedizinischen Forschungsansatzes. Hierbei arbeiten klinische Arbeitsgruppen, hochdurchsatzorientierte Teams der biomedizinischen Grundlagenforschung sowie Experten für Informationstechnologien zusammen. Sie untersuchen komplexe physiologische und pathologische Prozesse verschiedener Krebsarten, neurologischer Krankheiten und Entzündungs- sowie Herz-Kreislauf-Erkrankungen. Zentral sind hierbei die funktionelle Annotation, das Formulieren von Modellen des

Mitglieder

Hier entsteht in Kürze der e:Med Mitgliederbereich.

AKTUELLES

- Genomforschung – Quo vadis, Deutschland?
- Schlussbericht PerMediCon 2015

VERANSTALTUNGEN

- Sep. 26-30, 2015: HUPO, Vancouver
- Nov. 16-18, 2015: IHEC, Tokio

mehr

http://www.sys-med.de//

Forderungen

Forderungen

Series

Research: increasing value,

How to increase value and r
priorities are set

Iain Chalmers, Michael B Bracken, Ben Djulbegovic, Silvio Garattini
Sandy Oliver

Lancet 2014; 383: 156–65
Published Online
January 8, 2014
http://dx.doi.org/10.1016/
S0140-6736(13)62229-1

This is the first in a Series of
five papers about research

James Lind Initiative, Oxford,
UK (Sir I Chalmers DSc); School of
Public Health and School of
Medicine, Yale University,
New Haven, CT, USA
(Prof M B Bracken PhD); Center
for Evidence-Based Medicine
and Health Outcomes Research,
Division of Internal Medicine,
University of South Florida,
Tampa, FL, USA
(Prof B Djulbegovic PhD);
Department of Hematology
and Department of Health
Outcomes and Behavior, H Lee
Moffitt Cancer Center and
Research Institute, Tampa, FL,
USA (Prof B Djulbegovic);
Istituto di Ricovero e Cura a
Carattere Scientifico Istituto di
Ricerche Farmacologiche Mario
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World Bank Special Programme
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Research Training in Human
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Mental Health, Melbourne, VIC,
Australia (D W Howells PhD);
Stanford Prevention Research
Center, Department of Medicine
(Prof J P A Ioannidis MD), and
Division of Epidemiology,
Department of Health Research
and Policy (Prof J P A Ioannidis),
School of Medicine, Stanford
University, Stanford, CA, USA;
Department of Statistics,
School of Humanities and
Sciences, Stanford University,
Stanford, CA, USA
(Prof J P A Ioannidis); and
Meta-Research Innovation
Center at Stanford (METRICS),
Stanford University, Stanford,

The increase in annual global investment in biomed
important health dividends for patients and the p
achievements, partly because some studies are done
have relevance for human health. Additionally, good
as the way in which these ideas are prioritised for
should not be deemed wasteful; they are simply an in
of waste cannot be justified. In this report, we discuss
are set. We have four recommendations. First, ways
Second, the transparency of processes by which fu
making clear how they take account of the needs of po
should always be preceded by systematic assessme
research that is in progress should be strengthened
primary responsibility for reductions in waste resulti

Recommendations

1 More research on research should be done to identify factors associated with successful replication of basic research and translation to application in health care, and how to achieve the most productive ratio of basic to applied research
   - Monitoring—periodic surveys of the distribution of funding for research and analyses of yields from basic research
2 Research funders should make information available about how they decide what research to support, and fund investigations of the effects of initiatives to engage potential users of research in research prioritisation
   - Monitoring—periodic surveys of information on research funders' websites about their principles and methods used to decide what research to support
3 Research funders and regulators should demand that proposals for additional primary research are justified by systematic reviews showing what is already known, and increase funding for the required syntheses of existing evidence
   - Monitoring—audit proposals for and reports of new primary research
4 Research funders and research regulators should strengthen and develop sources of information about research that is in progress, ensure that they are used by researchers, insist on publication of protocols at study inception, and encourage collaboration to reduce waste
   - Monitoring—periodic surveys of progress in publishing protocols and analyses to expose redundant research

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commentary

Social engineering for virtual 'big science' in systems biology

Hiroaki Kitano, Samik Ghosh & Yukiko Matsuoka

A new type of big science is emerging that involves knowledge integration and collaboration among small sciences. Because open collaboration involves participants with diverse motivations and interests, social dynamics have a critical role in making the project successful. Thus, proper 'social engineering' will have greater role in scientific project planning and management in the future.

Scientific projects with large amounts of funding to achieve a defined mission are often referred to as 'big science'. Successful big science projects should have a clearly defined goal, a possible means to achieve it and a strong sociological rationale to justify public funding of such endeavors. Similarly, the type of project that can be widely supported beyond the scientific community depends on societal needs at the time.

Although most biology has been and continues to be small science, the Human Genome Project and other genome projects are considered big science in biology. A defining feature of these projects is a large-scale engineering effort designed in support of a specific scientific aim. Projects involving particle colliders and genome sequencing are essentially equipment-driven data-acquisition projects, and such projects will continue to provide new findings through equipment advances.

There is a related desire to obtain a comprehensive understanding of specific cellular systems and biological processes through high-throughput methods. Emergence of systems biology as mainstream biology is accelerating this tendency, because it often requires measurements and analysis of various large-scale and multifaceted data. At the same time, new knowledge critical for in-depth and precise understanding of systems is often derived from small science. This means that a new type of big science is needed that consolidates data and knowledge not only from large-scale projects, but also from discoveries by small science.

It is therefore inevitable that a 'virtual' big science will form, connecting large numbers of researchers around the globe to attain large-scale knowledge integration in an emergent manner. The implication is that such an initiative must have widely acceptable objectives, leadership and proper sociological design to make it sustainable.

There is an impossible number of problems that have yet to be resolved in the biomedical field, and some of these would benefit from being included in big science projects, either in a deliberate and organized or in a more emergent manner. For example, in the numerous cases of diseases for which effective cures are not available but are being proposed and developed, problems remain. Indeed, the cost of drug discovery is so high that it puts severe pressure on the public medical system and impedes access to drugs for underprivileged segments, which in turn prevents development of drugs for rare diseases or those that are prevalent in the poorest areas of the world.

The rising cost of drug discovery affects all segments of society. With increased understanding of individual genomic variations and their impacts on drug efficacy and side effects, we can envision an era of personalized medicine in which patients are selected on the basis of genetic and biochemical differences that underlie different responses to drugs. This would help patients minimize side effects and help health-care systems eliminate considerable misdirected cost. At the same time, it may also mean substantial revenue reduction for pharmaceutical companies. Research and development (R&D) as an industry, and thereby the ability to find possible cures for orphan diseases, may not be sustainable unless drastic reductions in R&D costs are achieved.

Cost and access to medical services is a critical factor for the base-of-the-pyramid segment of the population. For example, tuberculosis is still a major killer in developing countries, as 9.27 million new infections were reported in 2007 globally, with a significant percentage of them being multidrug resistant and some being extensively drug resistant[1]. Yet only a handful of drug-discovery projects exist because of the mismatch between the investment of R&D and the ability of countries where tuberculosis is prevalent to afford treatment. Unless cost-effective drug development can be achieved, those who suffer from neglected diseases will not be saved. Developing technologies to substantially mitigate these problems is socially valuable.

Knowledge integration at all levels

One of the fundamental causes of low productivity in drug discovery is a lack of in-depth understanding of the complexity of biological systems and a means of predicting potential outcomes of candidate compounds when used in cells, model animals and patients (http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/CriticalPathInitiative/CriticalPathOpportunitiesReports/ucm113411.pdf and http://www.pwc.com/gx/en/pharma-life-sciences/pharma-2020/pharma-2020-vision-path.jhtml). Proper introduction of a system- and network-oriented approach to drug discovery, with prediction capabilities even at the cellular level, is expected to rectify the situation by providing a better understanding of the biology that underlies diseases and, ultimately, by enabling us to use precise computational models of cells, organs and patients. Already, several systems biology efforts are under way and being planned.

Development of precise biological models requires integration of knowledge and data at all levels, from genomics and proteomics to imaging and physiology. Various data from high-throughput experiments provide us with genome-wide characteristics, but small-sciences data must be incorporated to gain an understanding of the detailed mechanisms. For both financial and sociological reasons, no single large-scale project can address a systems-level problem truly comprehensively. For instance, even if a large-scale project is

alue, reducing waste 3

educing waste in biomedical research
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gan, Elina Hemminki, Robert S Phillips, Julian Savulescu, Malcolm Macleod, Janet Wisely,

rch question and selection of an appropriate study design, waste can arise
nagement of biomedical research. Obtaining regulatory and governance
some and disproportionate to the conceivable risks to research participants.
entions that are assumed to be justified in the interests of patients and the
e these interests. Inefficient management of the procedural conduct of
in poor recruitment and retention of participants in well designed studies
urces of waste can be minimised if the following four recommendations
their influence to reduce other causes of waste and inefficiency in research.
uld work with researchers, patients, and health professionals to streamline
delines, and processes that govern whether and how research can be done,
the plausible risks associated with the research. Third, researchers and
fficiency of recruitment, retention, data monitoring, and data sharing in
known to reduce inefficiencies, and further research should be done to
lly, everyone, particularly those responsible for health-care systems, should
day clinical practice. Regulators and researchers should monitor adherence
blish metrics.

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research, which are elaborated upon in this Series. After identification of an important research question and selection of an appropriate study design, waste can be noticeable and quantifiable from the way in which research is regulated and managed.[2] Furthermore, foreknowledge of regulatory and management requirements can affect researchers' choice of research question and study design, resulting in unnoticed and unquantifiable waste, such that important research is identified but never addressed. Ultimately, waste arises from questions being overlooked or unnecessarily addressed, research being underpowered or done too slowly, and research being too costly.

A consensus on the need to regulate biomedical research arose from Nazi research atrocities[3] and abuses of people in mainly non-therapeutic research,[4,5] such that by the 1980s, the need for ethics review and prelicensing regulation of biomedical research involving human beings was not controversial. Similarly, published revelations of maltreatment of experimental animals in preclinical research led to it becoming more regulated.[6] Nowadays, permission to do biomedical research (regulatory approval) is needed in accordance with requirements of national or regional laws or professional authorities. Research ethics committees are independent regulators of most types of biomedical clinical research, whereas additional specific regulators oversee research involving data, devices, drugs, embryos, radiation, and tissue, among others. Regulatory functions are also undertaken by institutional bodies concerned with biomedical research governance, which is

Forderungen

Ioannidis JPA, et al. (2014) Lancet 383: 166–175.

- Standardisierung von Ressourcen und Prozeduren
- hohe methodologische Anforderungen an Publikationen
- mehr Anreize für Sorgfalt und Qualität
- Offenlegung von Methoden, Registrierung von Daten
- Anreize für Datenteilung schaffen
- Pflicht der Förderer zur Sicherung von Qualität
- Replikation fördern, Duplikation vermeiden
- bessere Ausbildung der Forscher
- bessere Kommunikation zwischen Forschern

"To maximise motivation for change, reductions of waste in research will need behavioural changes, not only from researchers, but also from publishers and regulators. These changes will need external pressure from stake holders such as funding agencies."

Forderungen

Al-Shali Salman R, et al. (2014) Lancet 383: 176–185.

- Reduzierung des administrativen Aufwands
  - Aufsichtsbehörden
  - Ethikkommissionen
  - Förderanträge
  - rechtliche Rahmenbedingungen
- konsistente Anforderungen
  - angeglichene Regeln und Verfahren

Chalmers I, et al. (2014) Lancet 383: 166–165.

- Forschung über Forschung
  - Faktoren für erfolgreiche Replikation und Translation
- Informationsquellen über Forschung

Forderungen

Kitano H, et al. (2011) Nat Chem Biol 7: 323–326.

- Konsolidierung von Daten und Wissen der “Small Science”
- Vermeidung einzelner Mega-Projekte
    - finanzielle und soziologische Gründe
- Vernetzung von Forschern zwecks Wissensintegration
- akzeptierte Ziele
- Führung und angemessenes soziologisches Design
- Anreize für die Beteiligung an gemeinschaftlichen Anstrengungen

“Social engineering will be recognized as an indispensable part of research activity in the coming years for large-scale and complex big science, because it is the people who do science, not technology or machines..”

Herausforderungen

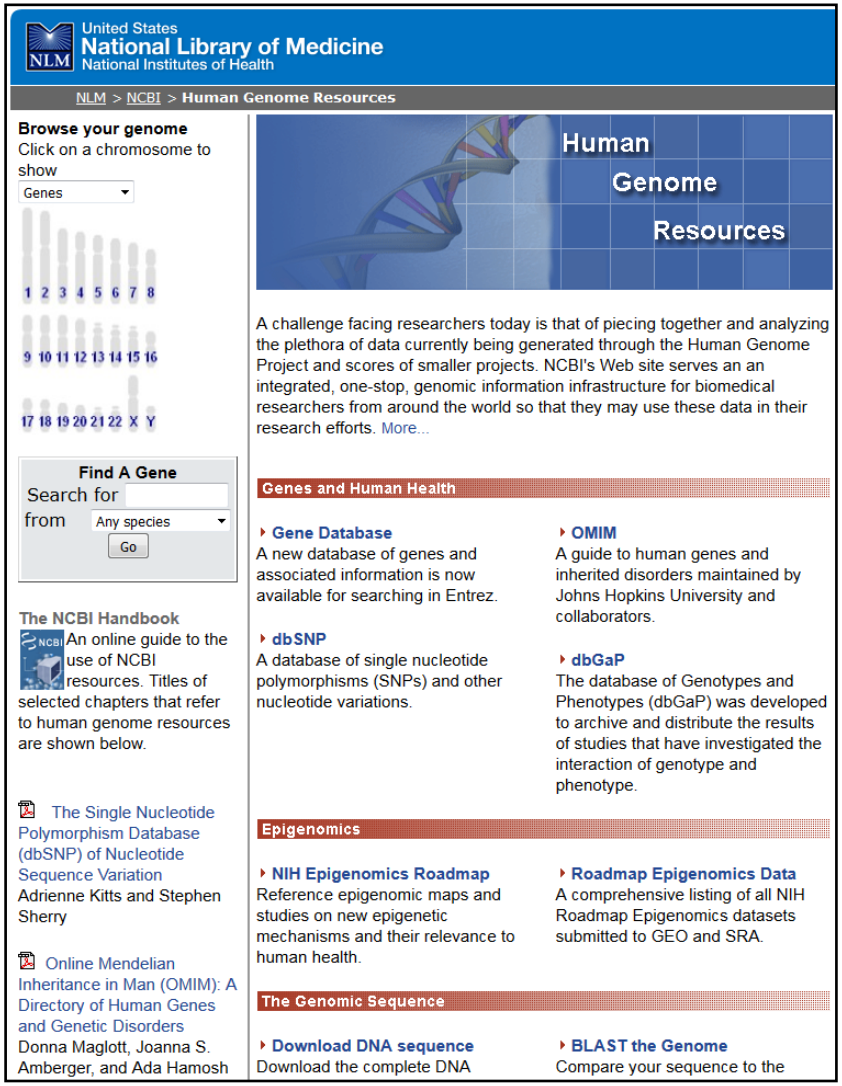
Herausforderungen

- keine übergreifenden Konzepte (weder lokal noch national)
- mangelhafte Interoperabilität
- Fehlen von Standards
- heterogene Datentypen (meist unstrukturiert)
- wenig Nutzung von Versorgungsdaten und -biomaterialien
- unklare ELSI Rahmenbedingungen
- mangelhafte institutionelle Einbettung (finanziell, strukturell)
- starke Abhängigkeit von Drittmitteln

Herausforderungen

Beispiele

Beispiele

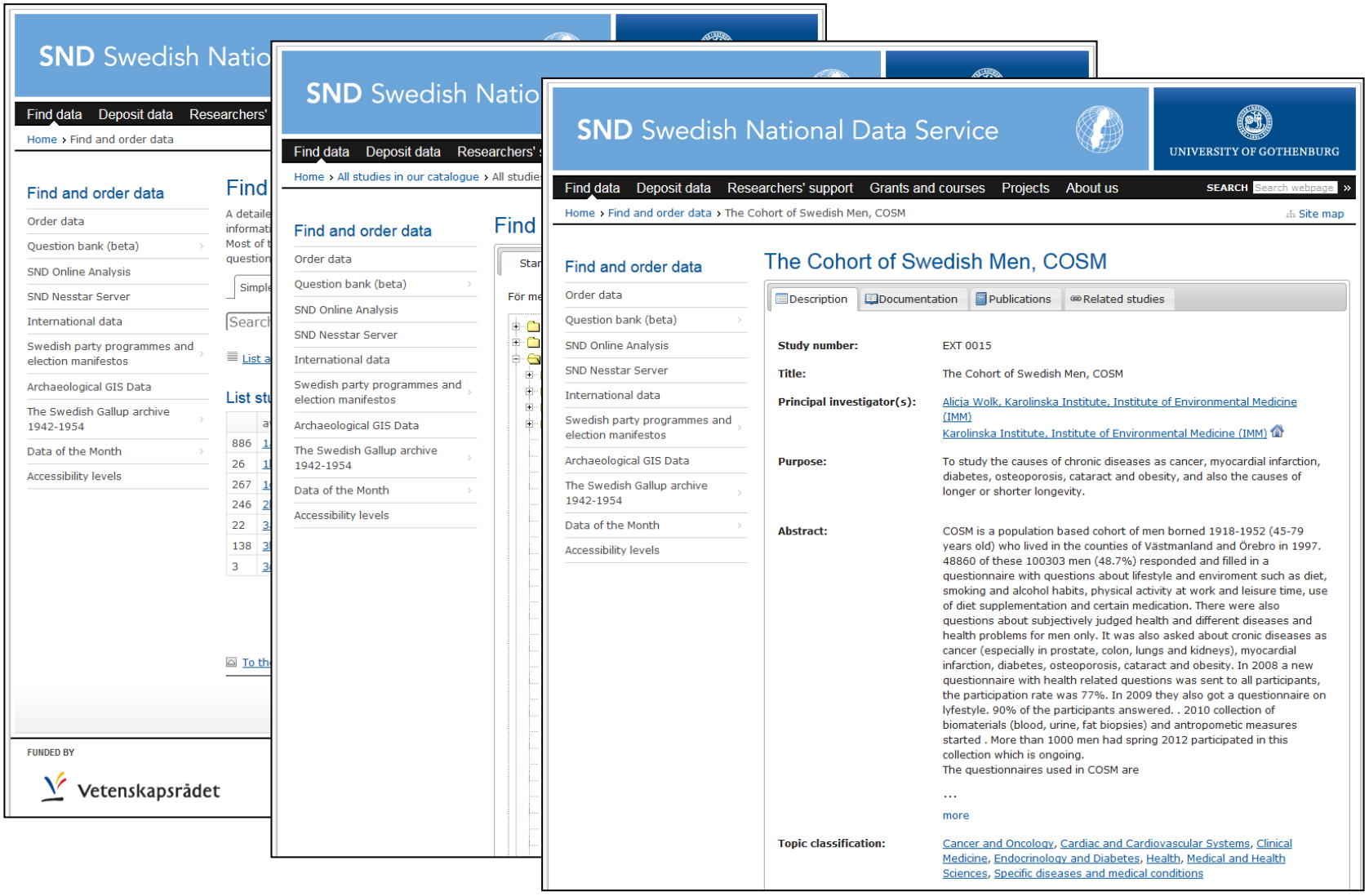


http://www.ncbi.nlm.nih.gov/genome/guide/human/resources.shtml

Beispiele

http://www.crhc.pitt.edu/

Beispiele



http://snd.gu.se

Beispiele

https://www.i2b2.org/

Beispiele

http://www.biobanken.de/

Beispiele

https://drks-neu.uniklinik-freiburg.de/drks_web/

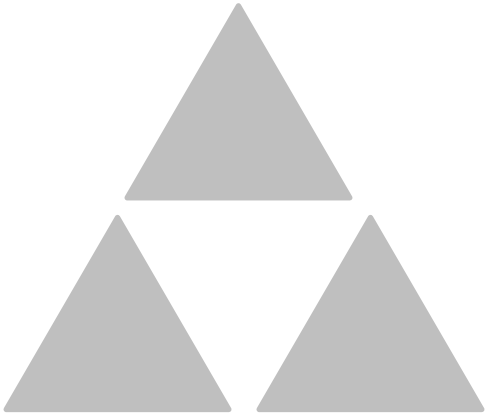
Notwendigkeiten

Notwendigkeiten

- Entwicklung lokaler und nationaler Integrationskonzepte
- Definition und Etablierung konsentierter Datenstandards
- Qualitätskontrolle für Daten und Biomaterialien
- bessere Nutzbarkeit von Daten und Biomaterialien
- Etablierung versorgungsintegrierter Forschungsinformatik und Biobanken
- generische und konsistente Antworten auf ELSI-Fragen
- strukturelle Einbindung von Medizininformatik und Biobanken
- nachhaltige Finanzierung
- Änderung der Förderungs- und Publikationsanreize
- bessere Aus- und Weiterbildungsangebote
- übergreifende Kommunikations- und Abstimmungsplattformen

Notwendigkeiten

Verfügbarkeit



Verwertbarkeit

Verknüpfbarkeit

Perspektive

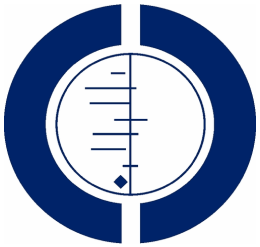
Perspektive

Bundesministerium
für Bildung
und Forschung

Nationale Initiative Medizininformatik

Workshop, 18. März 2015, Berlin
Konzept: Eils, Hahn, Jahns, Kroemer, Tolxdorf, von Kalle

- kleine Anzahl multiregionaler Kompetenzzentren
- Konzentration auf wenige Krankheiten
- Entwicklung einer forschungsorientierten Versorgungs-IT
- aktive Rolle der Krankenversorger (finanziell, strukturell)
- Definition und Abstimmung gemeinsamer Datenstandards
- Definition von Interoperabilitäts-Kriterien
- Lotsenfunktion bei der zukünftigen Auswahl von Standards und Verfahren



Cochrane
Deutschland

Herzlichen Dank für Ihre Aufmerksamkeit !