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Ethics in Genetics and Genomics Research

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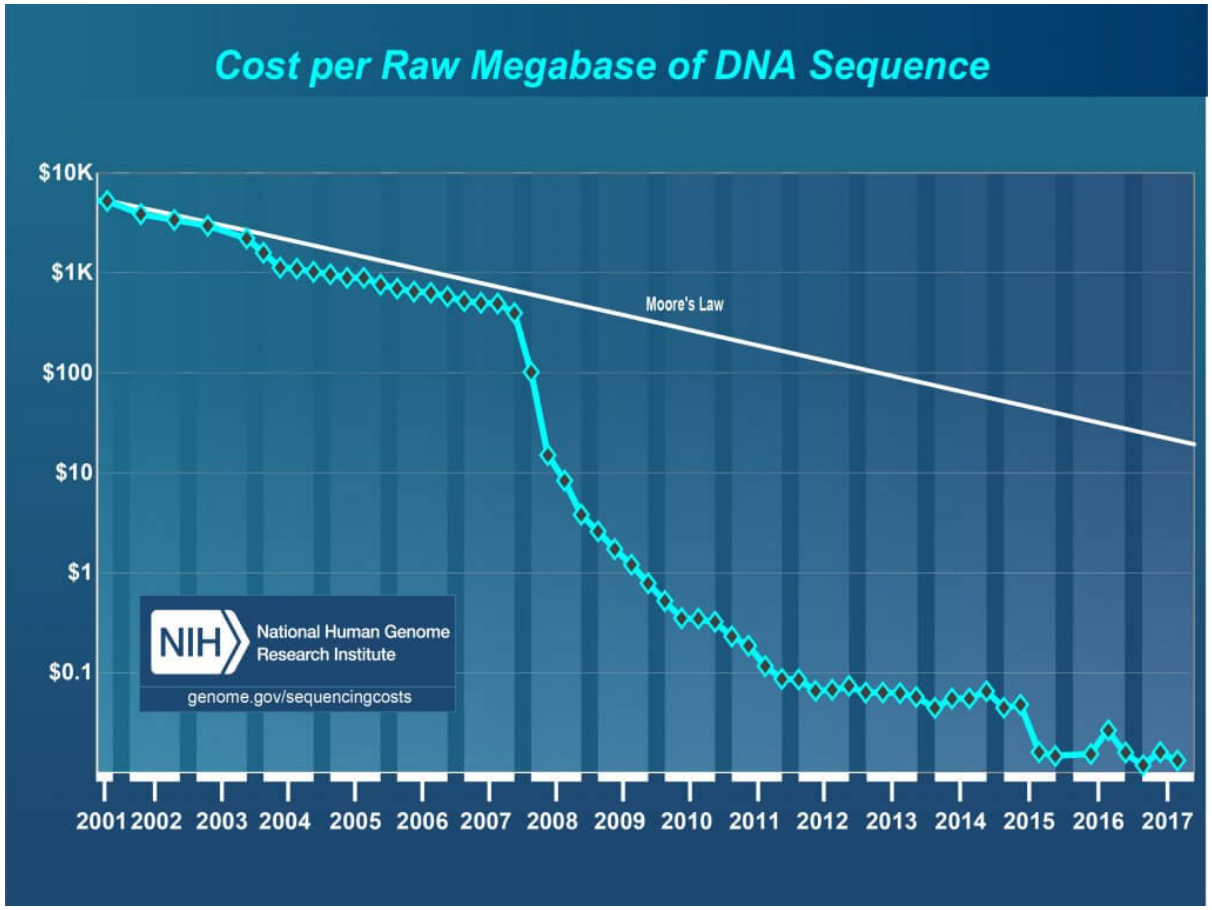
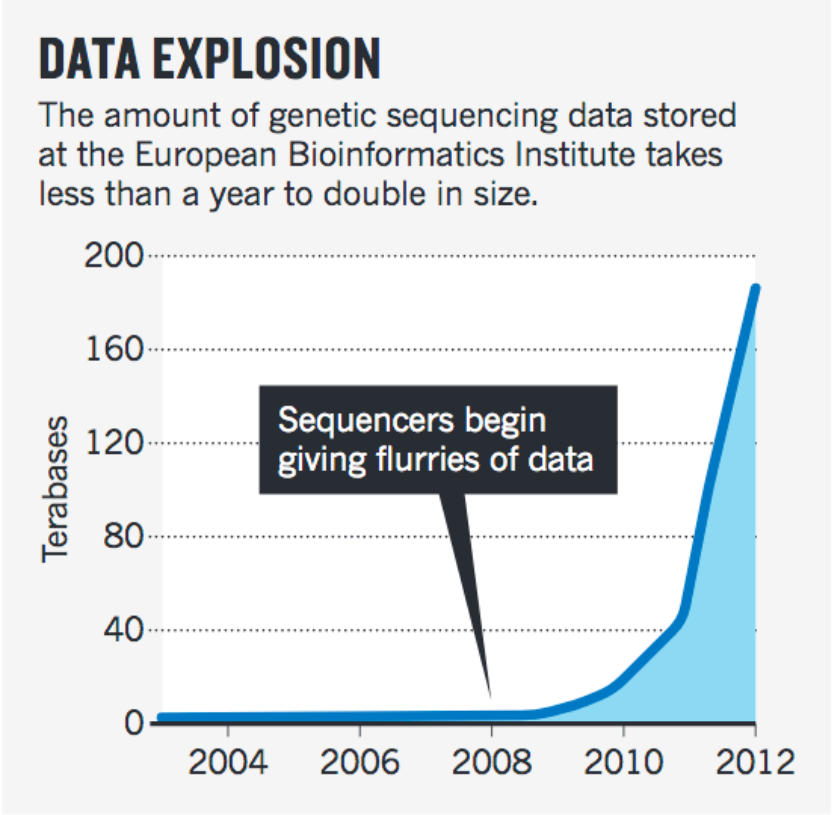
1. Cost and scale





https://www.nature.com/articles/498255a.pdf

2. Clinical care and genomic research BLURRED LINE

"flexible, permeable, and permanently shifting"

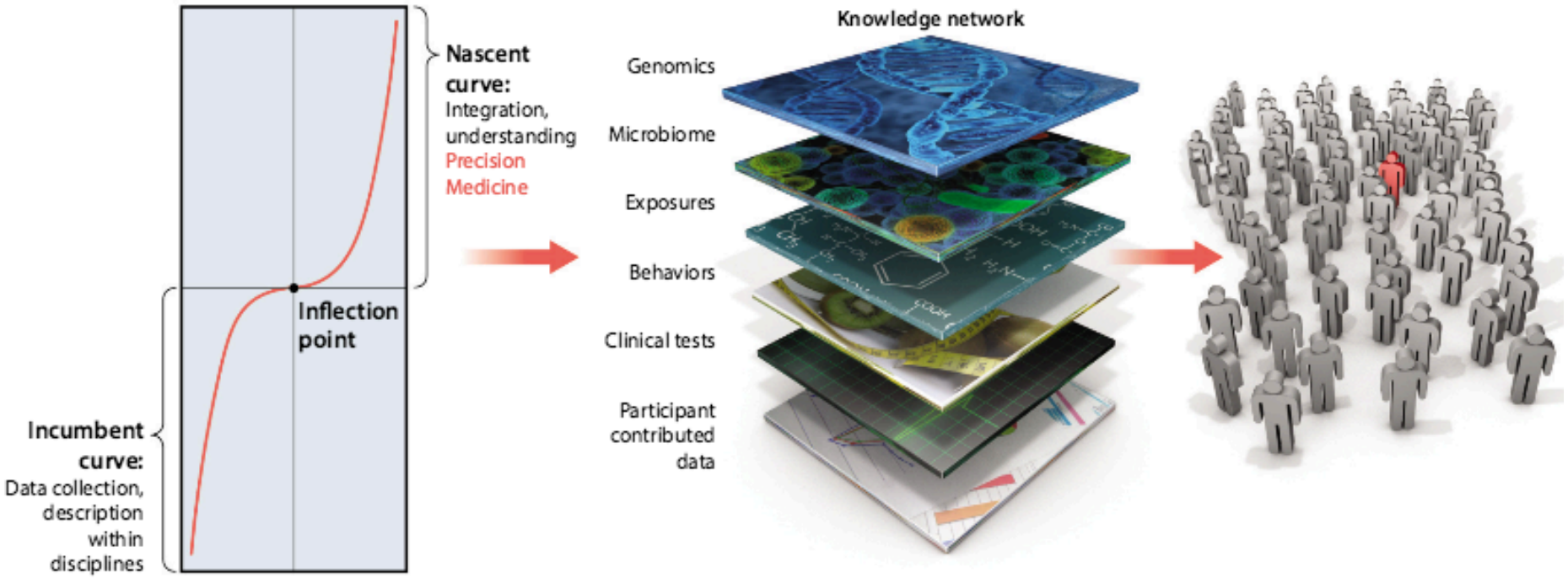
The research-clinical interface

Table 3 Characterizations of the research–clinical interface

Characterization of interface	Explication
1. Research and clinical care seen as **distinct**	Research components are clearly designated and differentiated from clinical care (e.g., consent for participation is sought by research personnel in space dedicated to research)
2. Research and clinical care seen as distinct but **interdigitated**	Despite differentiation between research and clinical care in study design, the mixing of research and clinical care leads to potential confusion, prompting efforts to distinguish the two domains (e.g., avoiding having the clinician seek research consent; research team intentionally chooses to "hand off" management to clinical team after return of research results)
3. **Negotiated or dynamically evolving** interface between research and clinical care	Decisions related to research and clinical care activities are made in a negotiated or dynamically evolving way (e.g., determining which results to disclose to a participant or whether the research budget will cover costs of testing)
4. **Translational merger** of research and clinical care	Research and clinical care cannot be separated (e.g., study results are used to direct clinical care)

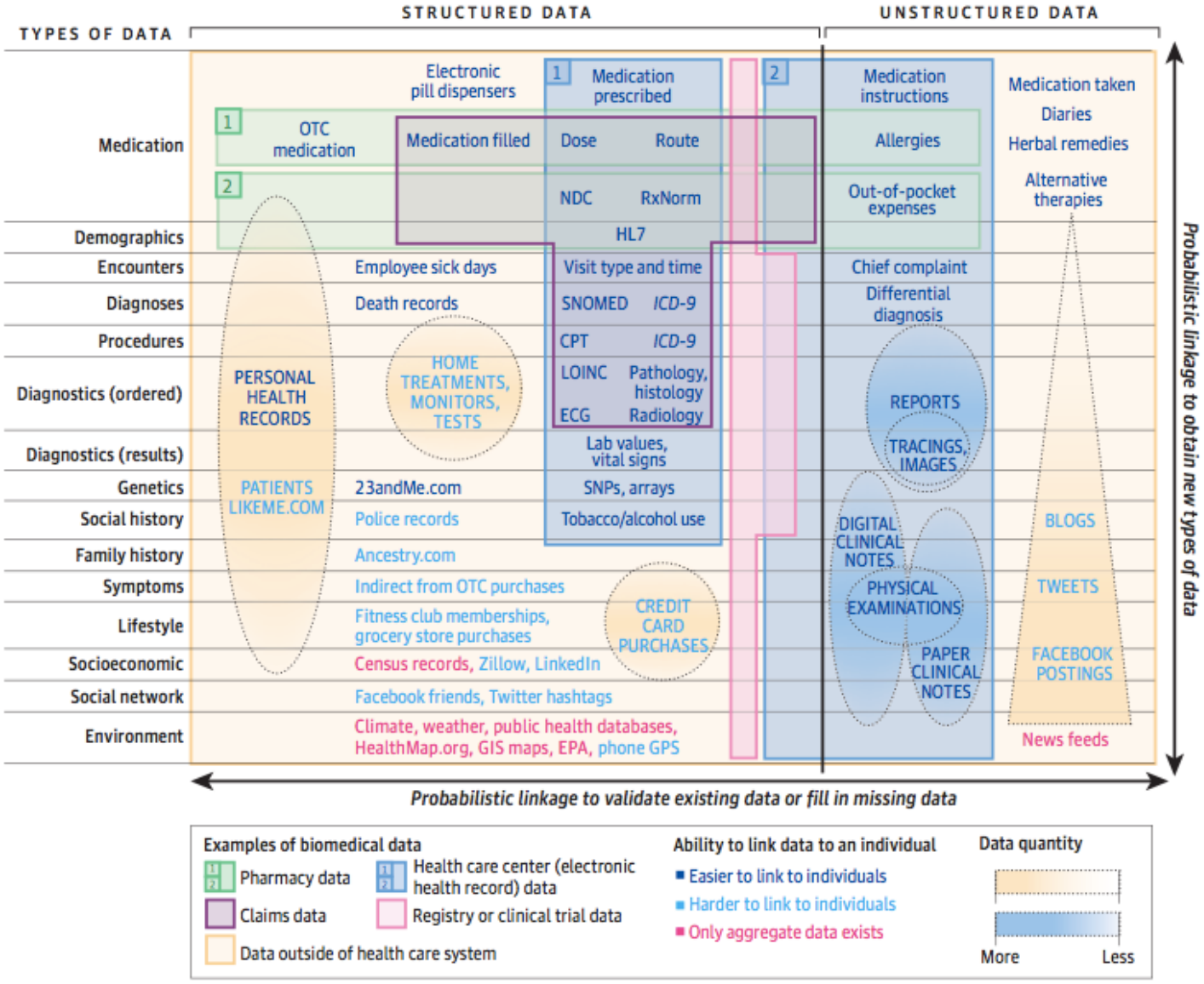
Bolded selected words signify differences among the 4 characterizations.

Precision medicine: Beyond the inflection point



Hagwood et al. Science Translational Medicine 12 Aug 2015: Vol. 7, Issue 300, pp. 300ps17

Figure. The Tapestry of Potentially High-Value Information Sources That May be Linked to an Individual for Use in Health Care



(Weber et. al ***JAMA*** 2014)

Generation genome - NHS

NHS Genomic Medicine Service

How the NHS is working to provide consistent and equitable access to genomic medicine.

National Genomic Test Directory →

100,000 Genomes Project

The world-leading initiative to sequence 100,000 genomes from people with cancer and families with rare disease.

Genomic Laboratory Hubs →

Personalised medicine

Providing better management of people's health by moving away from a 'one size fits all' approach.

Genomic resources →

3. Beyond the clinic

Best invention of the year 2008:The Retail DNA test

Everybody's doing DNA tests

Total number of people tested by consumer genetics companies through January 2019, in millions

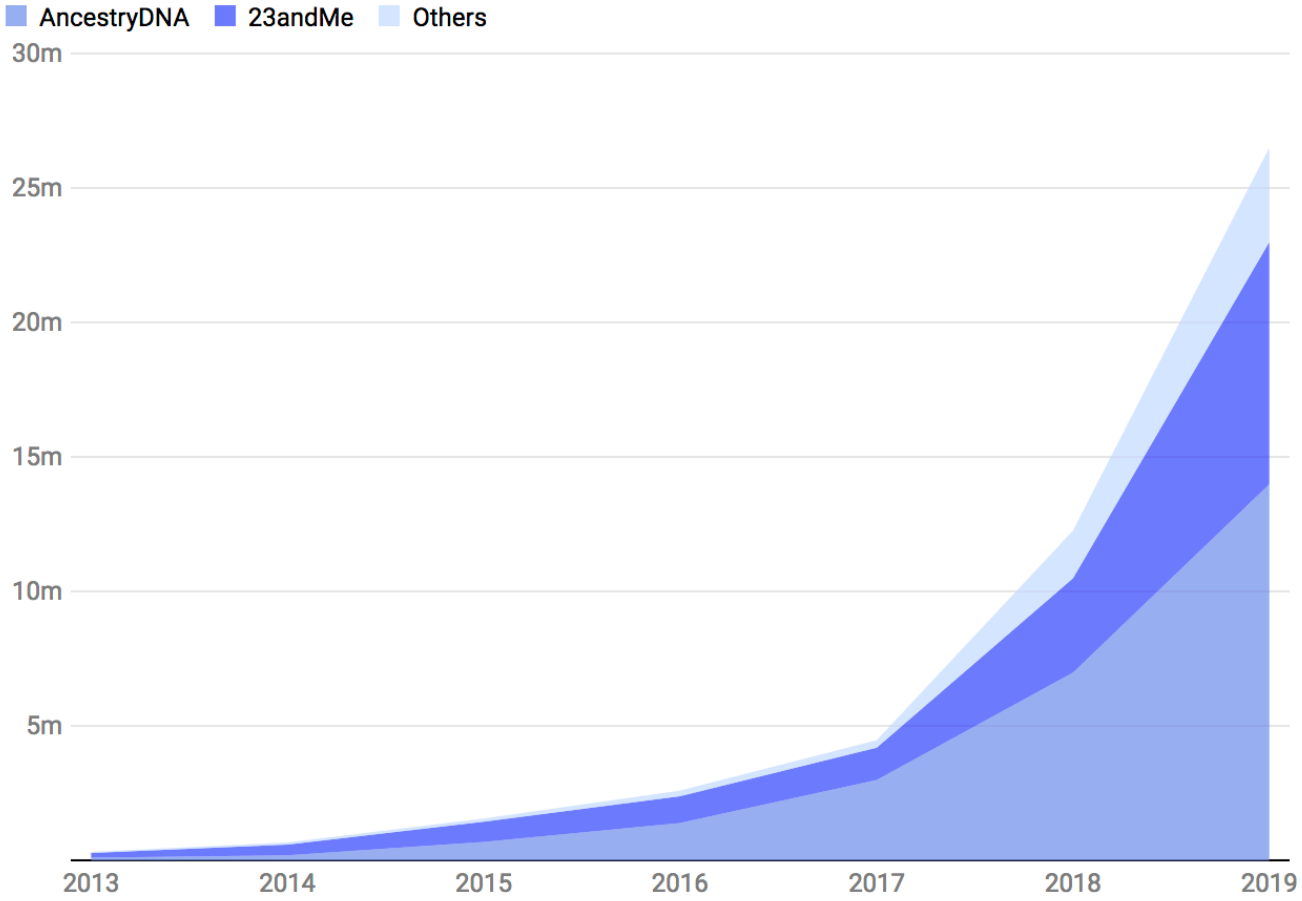
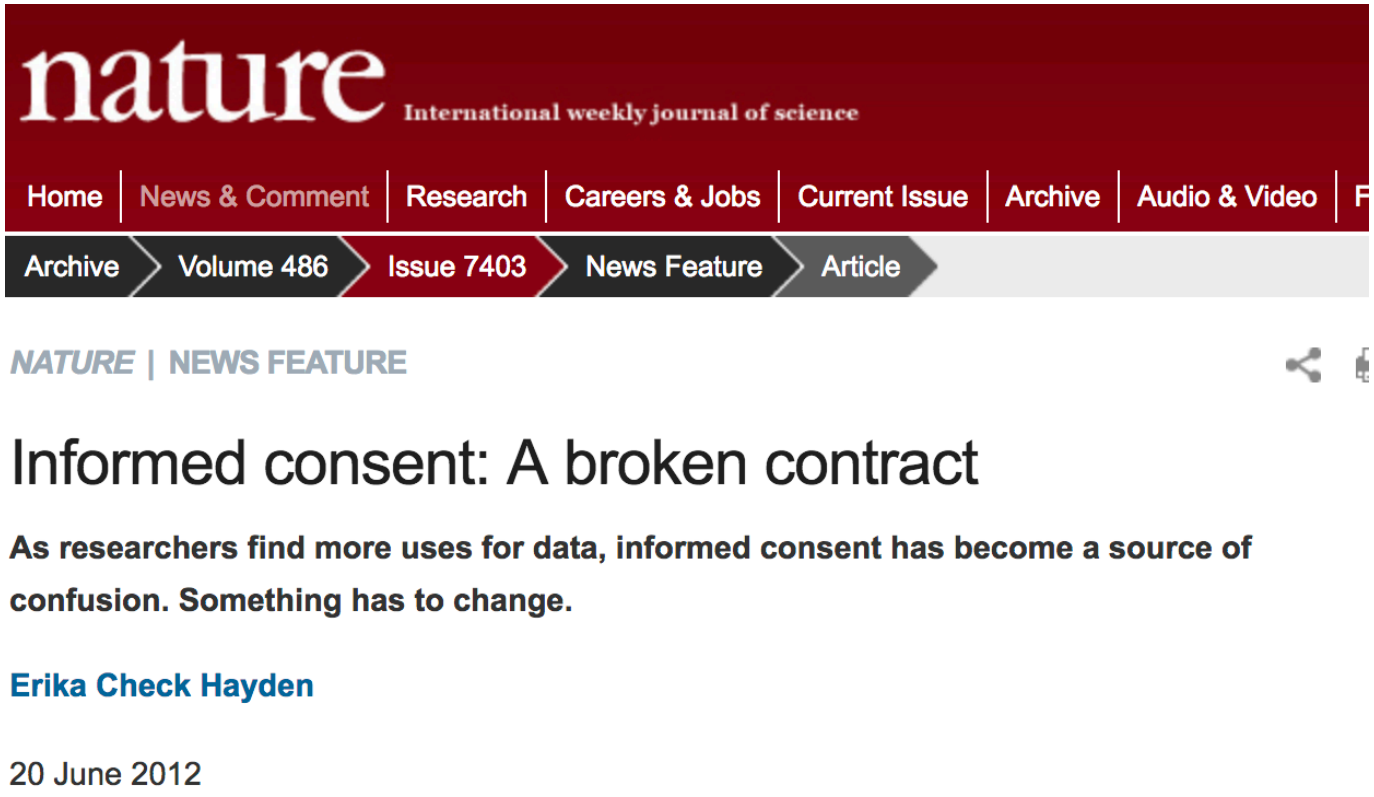


Chart: MIT Technology Review • Source: Company reports, Leah Larkin, ISOGG • Created with Datawrapper

A. CONSENT



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Archive > Volume 486 > Issue 7403 > News Feature > Article

NATURE | NEWS FEATURE

Informed consent: A broken contract

As researchers find more uses for data, informed consent has become a source of confusion. Something has to change.

Erika Check Hayden

20 June 2012

Koening, B. Have We Asked Too Much of Consent? *Hastings Center Report* 44, no. 3 (2014):33-34

The Fate of Informed Consent

The New York Times | https://nyti.ms/2m9KVyO

WELL | LIVE

Informed Patient? Don't Bet On It

By MIKKAEL A. SEKERES, M.D. and TIMOTHY D. GILLIGAN, M.D. MARCH 1, 2017

We want to let you in on a secret.

As your oncologists, we'd like to treat you with two, or three, or four different chemotherapy drugs, each of which has distinct side effects, some of which can kill you.

Or, if we were cardiothoracic surgeons, we might tell you that we need to crack your chest open to repair your damaged heart valve, and for that to happen you'll need to undergo anesthesia from which you may never wake up.

As doctors, our goal is to help you, of course, and to do no harm. But we may actually hurt you, irreversibly. Not that this happens frequently, but it might.

How does that sound? Ready to take the plunge?

The secret is that informed consent in health care is commonly not-so-well informed. It might be a document we ask you to sign, at the behest of our lawyers, in case we end up in court if a bad outcome happens. Unfortunately, it's often not really about informing you.

In schools, teachers determine what students know through tests and homework. The standard is not whether the teacher has explained how to add, but instead whether the student *can* add. If we were truly invested in whether you were informed, we'd give you a quiz, or at least ask you to repeat back to us what you heard so we could assess its accuracy. Instead, our script frequently

ELSEVIER

The American Journal of the Medical Sciences

Volume 342, Issue 4, October 2011, Pages 267-272

Symposium Article

Is Informed Consent Broken?

Gail E. Henderson PhD

A BROKEN CONTRACT

Late in May, the direct-to-consumer gene-testing company 23andMe proudly announced the impending award of its first patent. The firm's research on Parkinson's disease, which used data from several thousand customers, had led to a patent on gene sequences that contribute to risk for the disease and might be used to predict its course. Anne Wojcicki, co-founder of the company, which is based in Mountain View, California, wrote in a blog post that the patent would help to move the work "from the realm of academic

AS RESEARCHERS FIND MORE USES FOR DATA, INFORMED CONSENT HAS BECOME A SOURCE OF CONFUSION. SOMETHING HAS TO CHANGE.

BY ERIKA CHECK HAYDEN

CONSENT and the individual

Table 1

Common Features of genetic and genomic research

Common Features of Genetic and Genomic Research	Implications for Informed Consent
Indefinite storage and use of biospecimens	Research never ends; consent is forever
Unspecified future use	Uncertainty about what participant is consenting to
Stability of DNA over time	Privacy risks persist throughout lifetime
Broad sharing of samples/data	Uncertainty about privacy risks involved
Limited control over downstream access, use, and disclosure	Autonomy rights are limited
Limited right to withdraw	Can't change mind; consent is forever
Implications for family/community	Group harm

McGuire A, Beskow, L. Annu Rev Genomics Hum Genet. 2010 Sep 22; 11: 361–381.

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Consent Innovation

Least onerous - info-control + data availability	Midway		Most onerous + info-control - Data availability
	Overseen	Choice-based	
No consent **Presumed consent** (Gill 2004) **Presumed consent with opt-out** (Wendler and Emanuel 2002) **Blanket consent** (UNESCO 2001) (Tomlinson 2013) **Open consent** (Lunshof et al. 2008) **Portable legal consent** (Hayden 2012; Vayena, Mastroianni, and Kahn 2013) **Broad consent 1** = blanket + limitations (as defined in Grady et al. 2015)	**Broad consent 2** = blanket consent + safety + withdrawal + access review (Hansson et al. 2006) **Broad consent + ongoing oversight and communication** (Grady et al. 2015) **Broad consent + governance** (O'Doherty et al. 2011) **Broad consent + trusted governance system** (Koenig 2014; Garrett, Dohan, and Koenig 2015)	**Authorization model** (Caulfield, Upshur, and Daar 2003) **Tiered consent** (McGuire and Beskow 2010; Mello and Wolf 2010; Bunnik, Janssens, and Schermer 2013) **Electronic informed Consent** (FDA and DHHS 2016; Sage Bionetworks 2017) **Dynamic consent** (Kaye et al. 2012; Kaye et al. 2015; Budin-Ljøsne et al. 2017)	**Informed consent** (Faden and Beauchamp 1986; Manson and O'Neill 2007) **Consent for de-identified samples and data**

Consent and the family

J Genet Counsel (2017) 26:276–278
DOI 10.1007/s10897-016-0046-7

ORIGINAL RESEARCH

My Identical Twin Sequenced our Genome

Samantha L.P. Schilit[1] · Arielle Schilit Nitenson[2]

"Are you aware that the test results may reveal information about yourself that you would rather not know, such as predispositions for diseases that might not be curable? Are you aware that you could be subject to genetic discrimination for life insurance or long-term disability insurance? Are you aware that if the security system is breached that the electronic delivery of your results could be accessed by someone else?"

Consent and the family

- Consent and individual autonomy
- Does not consider interests of family members

- Procedures designed for individual consent
- No requirement to consult the family
- Practical difficulties in reaching family members

- Static consent does not account for complexity of decision making

Minari et al. Genome Med. 2014; 6(12): 118.

More than it meets the I ?

- deCode uses genotypes from 120,000 participants and genealogical data
- Estimates “in silico” genotypes of close relatives of volunteers
- Can deduce genotypes of entire population
- Able to identify 2,000 people with BRCA mutations

Donna Gitter- Consent for estimated data

http://www.technologyreview.com/news/536096/genome-study-predicts-dna-of-the-whole-of-iceland/

Consent and data sharing

nature International weekly journal of science

NATURE | COLUMN: WORLD VIEW

BBMRI-ERIC

We must urgently clarify data-sharing rules

Scientists have worked hard to ensure that Europe's new data laws do not harm science, but one last push is needed, says Jan-Eric Litton.

24 January 2017

Consent and data sharing

EU countries agreed to cooperate in linking genomic data across borders

THEY DID IT!

& more will too

Austria
Bulgaria
Croatia
Cyprus
Czech Republic
Estonia
Finland
Greece
Hungary
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Portugal
Slovenia
Spain
Sweden
UK

Consent and data sharing

- Data protection
- Privacy

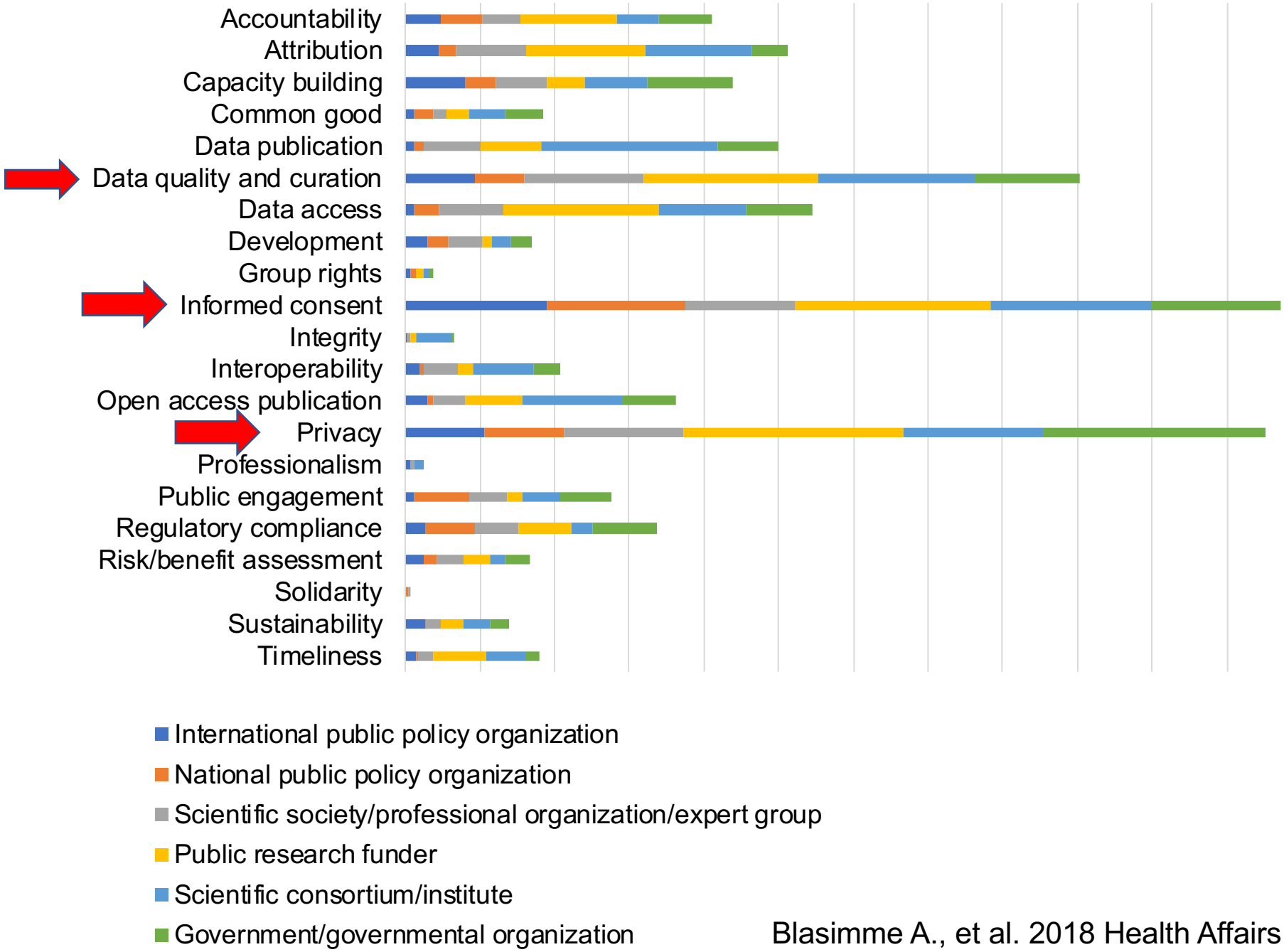
Consent and data sharing

PRECISION MEDICINE

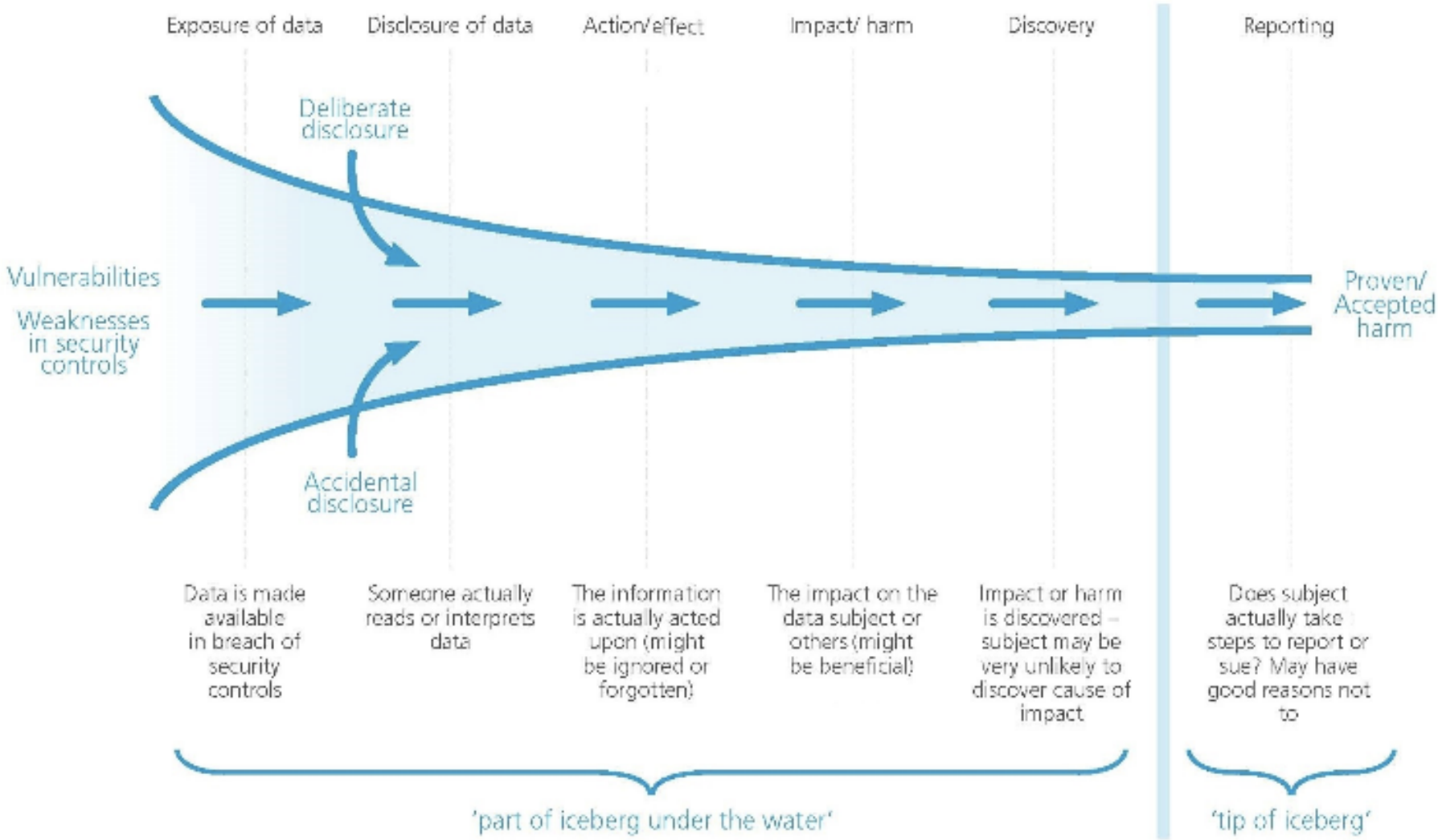
By Alessandro Blasimme, Marta Fadda, Manuel Schneider, and Effy Vayena

DOI: 10.1377/hlthaff.2017.1558
HEALTH AFFAIRS 37,
NO. 5 (2018): 702–709

Data Sharing For Precision Medicine: Policy Lessons And Future Directions



Blasimme A., et al. 2018 Health Affairs



Nuffield Council of Bioethics, 2015

"From privacy to trust"

Redefining Genomic Privacy: Trust and Empowerment

Yaniv Erlich, James B. Williams, David Glazer, Kenneth Yocum, Nita Farahany, Maynard Olson, Arvind Narayanan, Lincoln D. Stein, Jan A. Witkowski, Robert C. Kain

Published: November 4, 2014 • DOI: 10.1371/journal.pbio.1001983 • Featured in PLOS Collections

- **Transparency** creates trust
- Increased **control** enhances trust
- **Reciprocity** maintains trust

Can there be trust without privacy?

- Re-interpret privacy
- Redefine how to protect privacy
- Renegotiate trade-offs (medical research, public health)
- “The value of privacy is both to be defended and to be enhanced.” (L. Floridi)

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OPEN ACCESS Check for updates

Genes wide open: Data sharing and the social gradient of genomic privacy

Tobias Haeusermann[a], Marta Fadda[b], Alessandro Blasimme[b], Bastian Greshake Tzovaras[c], and Effy Vayena[b]

> I feel like, here is some concept of privilege that informs who is willing to share their data, like if you're wealthy and you're not worried about finding a new job and you're much more likely to say what bad thing can happen to be by doing this. And so, I feel like we end up with a lot of sequences that tend to be from people who don't have to worry about it. (participant #3, male, United States, with previous scientific involvement, no children)

> I think I would not be so open about it if I was a person of color or a transgender or … So, all of what I said before, I said in full awareness that I am an able hetero white male. (participant #13, male, Switzerland, no scientific involvement, no children)

DHEST
Department of Health Sciences and Technology

B. Return of research results

- **What** results?
- **How** to return?
- **When** to return?
- **Who** does it and to **whom**?

Return of research results

- At a minimum: return valid, medically important, actionable (discovered purposefully of by chance- no duty to hunt)
- ACMG list of genes a starting point
- Identifiable participants a requirement
- Participants must consent to receiving results (right not to know)

Return of research results

- Type 1 actionability: well-established medical actions
- Type 2 actionability: patient-initiated health-related actions
  - Individual initiatives of patients
  - Lifestyle options etc.
- Type 3 actionability: life-span decisions

Return of research results

BIG DATA & SOCIETY

Commentary

Big Data & Society
January–June 2019: 1–6

DOI: 10.1177/2053951719830111
journals.sagepub.com/home/bds
SAGE

Big Data, precision medicine and private insurance: A delicate balancing act

Alessandro Blasimme[1], Effy Vayena[1] and Ine Van Hoyweghen[2]

A person undergoes genetic testing as part of a research protocol

The project yields genetic results

According to the jurisdictions, the person may be required to disclose the results for life, disability and long-term insurance coverage

Genetic information are protected and genetic test results are allowed to be used only for medical and scientific endeavours.

Premium and coverage should not be impacted.

Genetic results cannot be used for insurance coverage under a certain financial limit (specific to each jurisdiction)

Premium and coverage should only be impacted, if the policy exceed a certain financial limit.

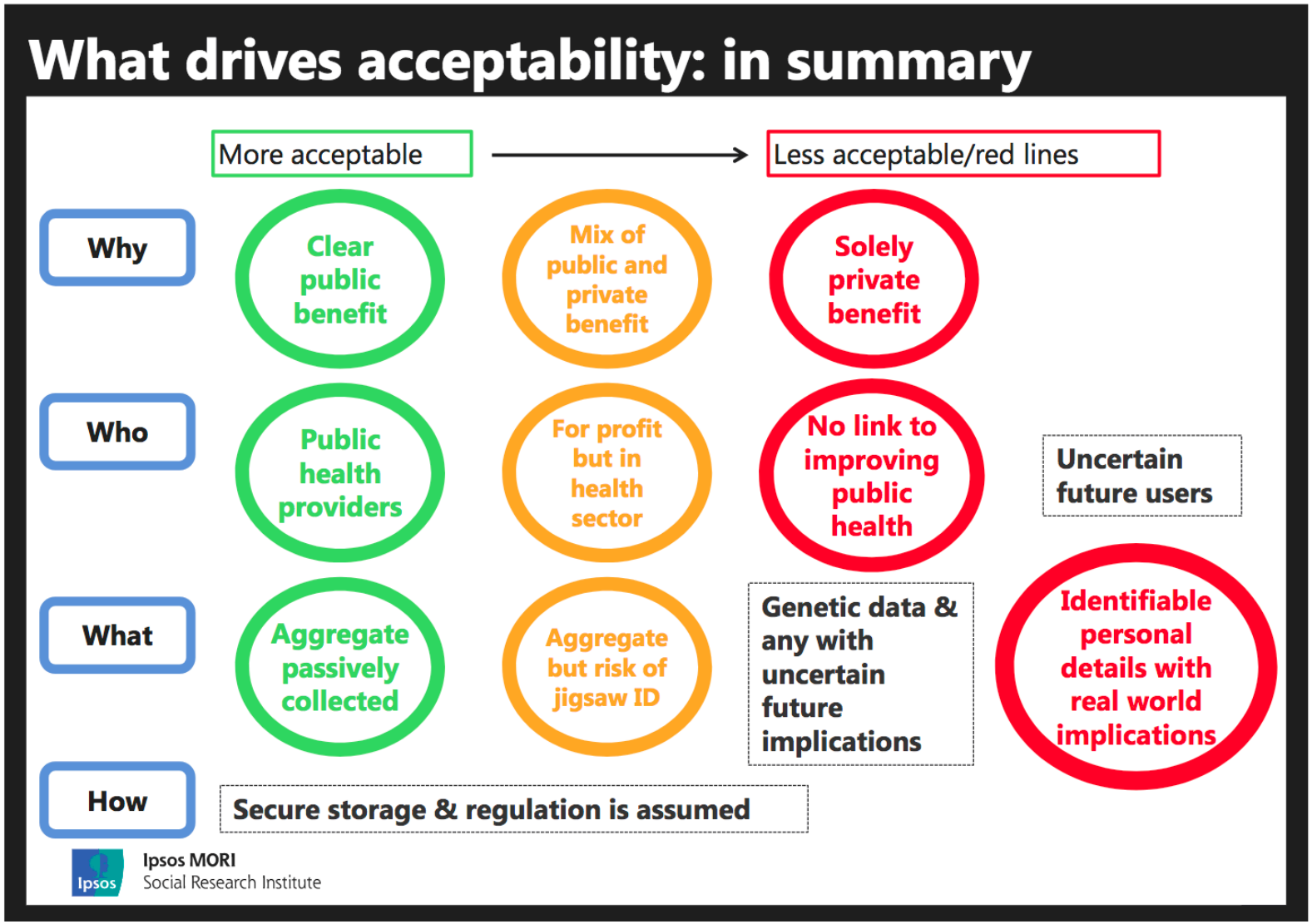
The person could end up having to disclose any genetic findings as part of the underwriting process for these kinds of insurance

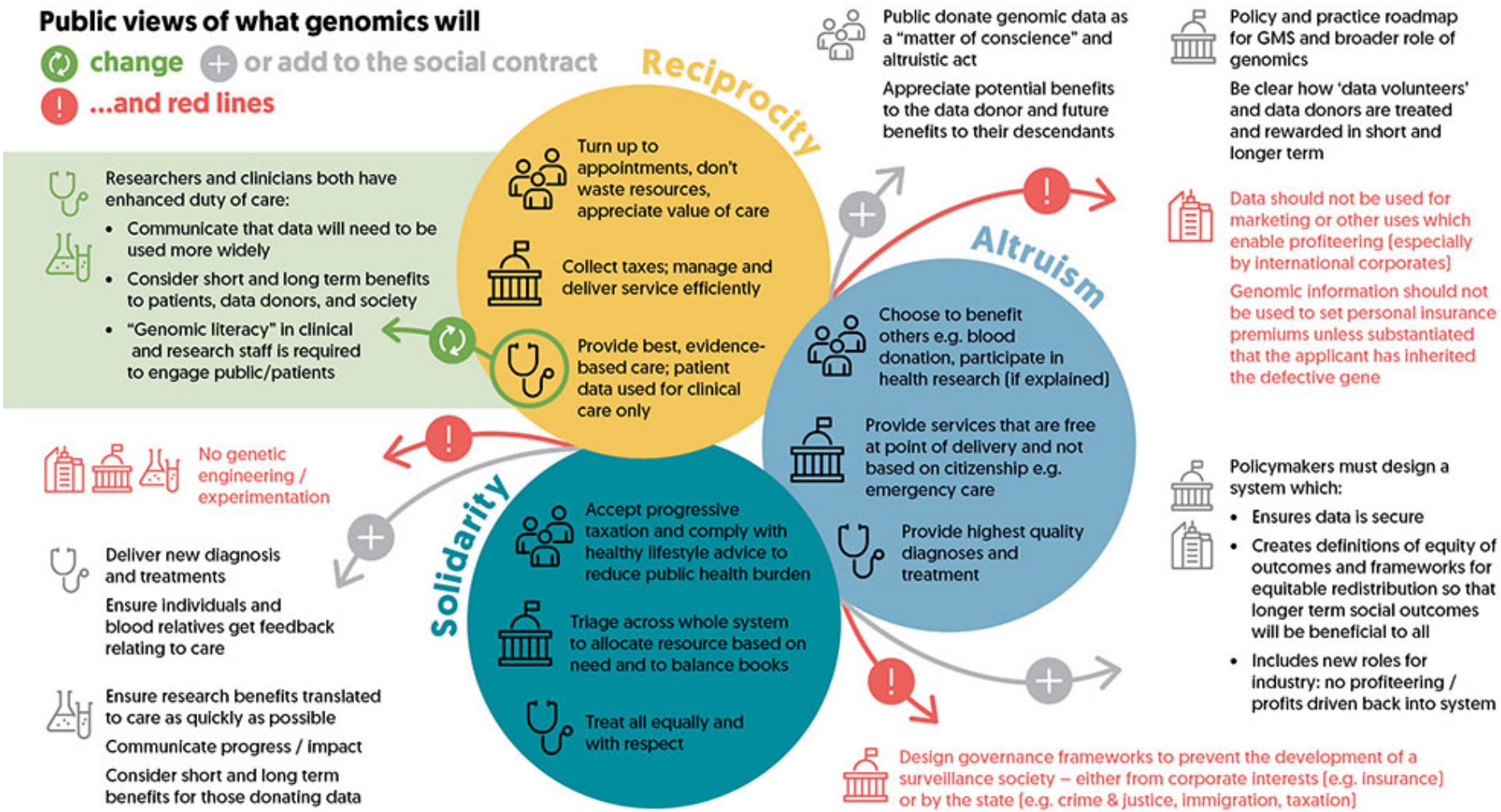
This could lead to higher premium and coverage refusal

Bélisle-Pipon JC, et al. Nature Medicine (forthcoming)

C. Public engagement

- Public dialogue
- Information
- Deliberation
- Understanding concerns
- Include in governance


What drives acceptability: in summary
More acceptable
Less acceptable/red lines
Why
Clear public benefit
Mix of public and private benefit
Solely private benefit
Who
Public health providers
For profit but in health sector
No link to improving public health
Uncertain future users
What
Aggregate passively collected
Aggregate but risk of jigsaw ID
Genetic data & any with uncertain future implications
Identifiable personal details with real world implications
How
Secure storage & regulation is assumed
Ipsos MORI
Social Research Institute



A public dialogue on genomic medicine: time for a new social contract?
Ipsos Mori April 2019

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