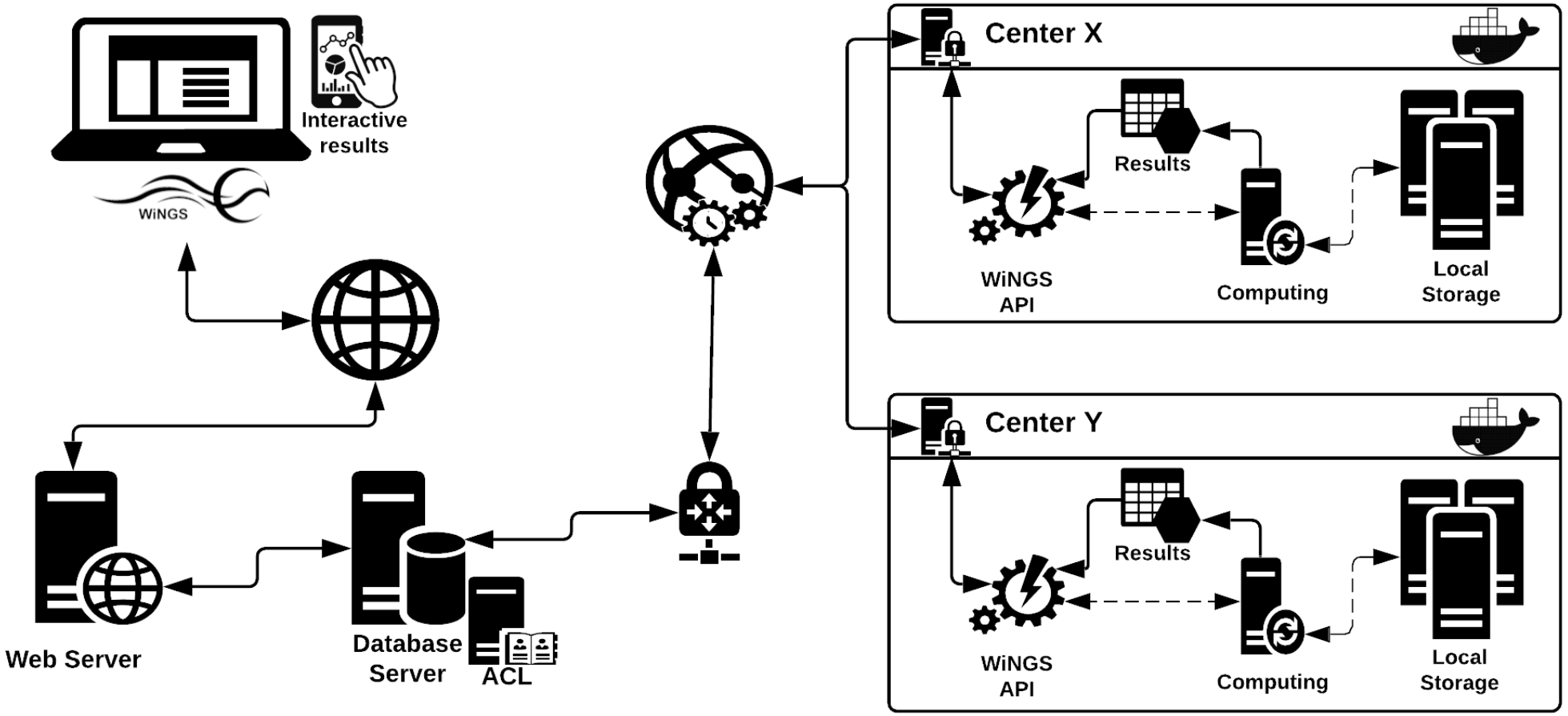
Introduction to biomedical ethics

Yves Moreau

KU LEUVEN

Federated privacy-preserving analytics




دولة الكويت ترحب بكم
Welcome To State Of Kuwait
13 CODIS Core STR Loci
with Chromosomal Positions
TPOX
D3S1358
D5S818
FGA
CSF1PO
D7S820
D8S1179
TH01
VWA
AMEL
D13S317
D16S539
D18S51
D21S11
AMEL
1 2 3 4 5 6 7 8 9 10 11 12
13 14 15 16 17 18 19 20 21 22 X Y

Eugenics: the original sin?

The Nuremberg code (1947)

1. Voluntary consent of the human subject is absolutely essential
2. The experiment must yield generalizable knowledge that could not be obtained in any other way and is not random and unnecessary in nature
3. Animal experimentation should precede human experimentation
4. All unnecessary physical and mental suffering and injury should be avoided
5. No experiment should be conducted if there is reason to believe that death or disabling injury will occur

The Nuremberg code (1947)

6. The degree of risk to subjects should never exceed the humanitarian importance of the problem
7. Risks to the subjects should be minimized through proper preparations
8. Experiments should only be conducted by scientifically qualified investigators
9. Subjects should always be at liberty to withdraw from experiments
10. Investigators must be ready to end the experiment at any stage if there is cause to believe that continuing the experiment is likely to result in injury, disability or death to the subject

Declaration of Geneva (1948)

- Modern form of Hippocratic Oath

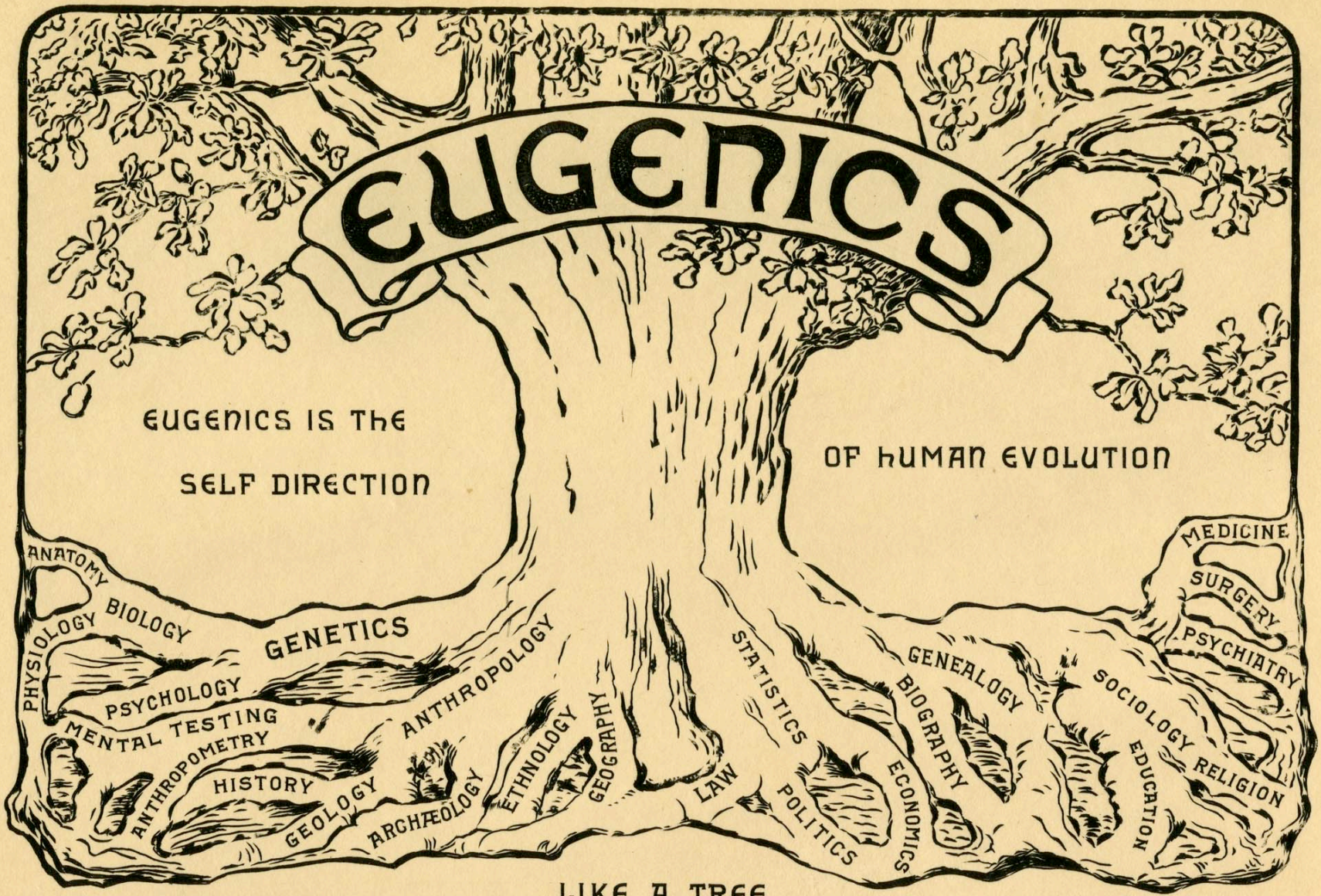
- As a member of the medical profession
  - I solemnly pledge to dedicate my life to the service of humanity;
  - The health and well-being of my patient will be my first consideration;
  - I will respect the autonomy and dignity of my patient;
  - I will maintain the utmost respect for human life;

Declaration of Geneva (1948)

- I will not permit considerations of age, disease or disability, creed, ethnic origin, gender, nationality, political affiliation, race, sexual orientation, social standing or any other factor to intervene between my duty and my patient;
- I will respect the secrets that are confided in me, even after the patient has died;
- I will practice my profession with conscience and dignity and in accordance with good medical practice;
- I will foster the honour and noble traditions of the medical profession;

Declaration of Geneva (1948)

- I will give to my teachers, colleagues, and students the respect and gratitude that is their due;
- I will share my medical knowledge for the benefit of the patient and the advancement of healthcare;
- I will attend to my own health, well-being, and abilities in order to provide care of the highest standard;
- I will not use my medical knowledge to violate human rights and civil liberties, even under threat;
- I make these promises solemnly, freely and upon my honour.



LIKE A TREE

EUGENICS DRAWS ITS MATERIALS FROM MANY SOURCES AND ORGANIZES THEM INTO AN HARMONIOUS ENTITY.

Eugenics: the original sin?

- Francis Galton (statistician)
  - Coined the term eugenics in 1883
- Alexander Graham Bell (AT&T)
- Winston Churchill (English prime minister)
- Ronald Fisher (statistician)
- Theodore Roosevelt (US president, New Deal)
- Helen Keller (first deaf-blind person to obtain a university degree)
- Francis Crick (DNA double helix)

- Large-scale sterilization campaigns


FRITZ HABER

WWI chemical warfare

WWI

- Fritz Haber
- Otto Hahn
- James Franck
- Gustav Hertz

- Victor Grignard

Post-WWI

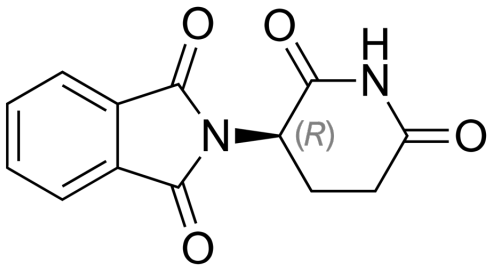
- Zyklon A
- Degesch
- IG Farben (BASF, Bayer, Hoechst, Agfa, Griesheim-Elektron, and Weiler-ter Meer & Co.)

- Veritasium episode: https://www.youtube.com/watch?v=EvknN89JoWo

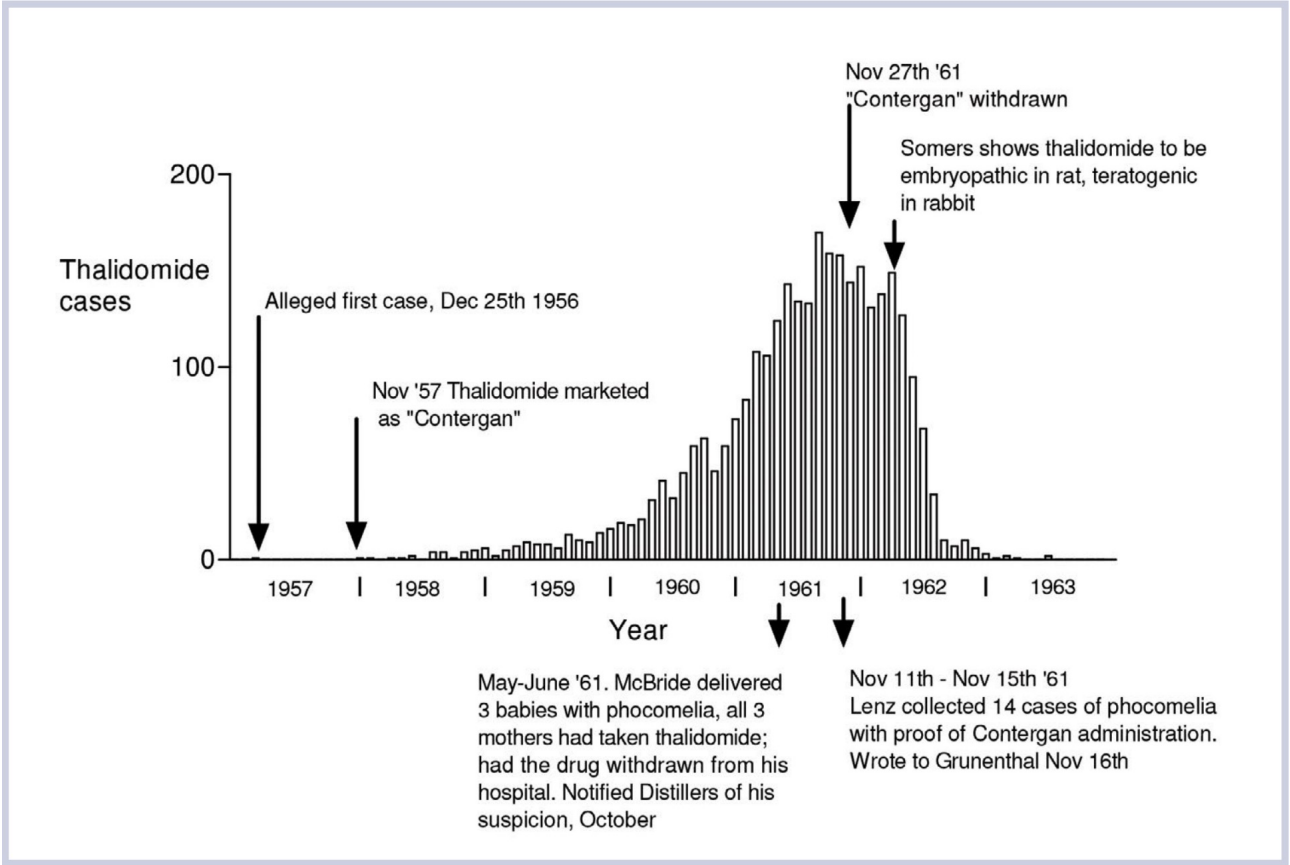
Thalidomide

- Sedative (non-addictive, hard to overdose), anti-convulsive, anti-emetic (morning sickness)

Thalidomide



- Grünenthal Co., Germany (Mückter, Ambros [sArin], Baumkötter, Staemmler, Schenck)
- 1954 patent by Keller and Kunz (early development by Ciba AG or Ambros and Mückter?!?)
- Marketed 1957
- Withdrawal 1961
- >10,000 births?
- Currently used against leprosis and myeloma



'Heroine' of FDA Keeps Bad Drug Off of Market: Vital FDA Delay Keeps Bad Drug Off of Market
By Morton Mintz Staff Reporter
The Washington Post, Times Herald (1959-1973); Jul 15, 1962;
ProQuest Historical Newspapers: The Washington Post
pg. A1

Linked to Malformed Babies

'Heroine' of FDA Keeps Bad Drug Off of Market

By Morton Mintz
Staff Reporter

This is the story of how the skepticism and stubbornness of a Government physician prevented what could have been an appalling American tragedy, the birth of hundreds or indeed thousands of armless and legless children.

The story of Dr. Frances Oldham Kelsey, a Food and Drug Administration medical officer, is not one of inspired prophesies nor of dramatic research breakthroughs.

She saw her duty in sternly simple terms, and she carried it out, living the while with insinuations that she was a bureaucratic nitpicker, unreasonable — even, she said, stupid. That such attributes could have been ascribed to her is, by her own acknowledgement, not surprising, considering all of the circumstances.

The Washington Post

DR. FRANCES O. KELSEY
. . . skepticism wins

What she did was refuse to be hurried into approving an application for marketing a new drug. She regarded its safety as unproved, despite considerable data arguing that it was ultra safe.

It was not until last April, 19 months after the application was filed with the FDA, that the terrible effects of the drug abroad were widely reported in this country. What remains to be told is how and why Dr. Kelsey blocked the introduction of the drug before those effects were suspected by anyone.

Dr. Kelsey invoked her high standards and her belief that the drug was "peculiar" against these facts:

The drug had come into widespread use in other countries. In West Germany, where it was used primarily as a sedative, huge quantities of it were sold over the counter before it was put on a prescription basis. It gave a prompt, deep, natural sleep that was not followed by a hangover. It was cheap. It failed to kill even the would-be suicides who swallowed massive doses.

And there were the reports on experiments with animals. Only a few weeks ago the American licensee told of giving the drug to rats in doses 6 to 60 times greater than the comparable human dosage. Of 1510 offspring, none was delivered with "evidence of malformation."

In a separate study, one rat did deliver a malformed offspring, but the dosage had been 1200 times the usual one. Rabbits that were injected with six times the comparable human dose also were reported to have produced no malformed births.

Recently, the FDA publicly

See DRUG, A8, Col. 1

Frances Oldham Kelsey
"said she could not help regarding thalidomide as a "peculiar drug." It troubled her that its effects on experimental animals were not the same as on humans – it did not make them sleepy."

Thalidomide

- 1968 criminal trial in Germany
- 1970 settlement
- In Germany, most compensations paid by government (2400 victims alive) – compensation waives right to sue
- IN UK, 1972 article by the Sunday Times led to change in settlement from £3.25m to £32.5m (400 victims alive)
- 2012: “We also ask for forgiveness for not reaching out to you from human to human for almost 50 years... We ask that you see our long speechlessness as a sign of the silent shock that your fate has caused us.”
- Victims argue that they are not able to access all promised compensations

Declaration of Helsinki (1964)

- Extends Nuremberg code
  - Minimize harm to the environment
  - Ensure respect for all human subjects
  - Provide appropriate access to underrepresented groups
  - Respect the welfare of animals used for research
  - Submit research protocol to the research ethics committee for approval
  - Protect the privacy of research subjects
  - Adequately inform subjects of aims, methods, and funding
  - Seek freely-given informed consent


skegee Experiment | Genealogy Roadshow
The Tuskegee experiment (1932-1972)


Deadly Deception
John Cutler
35:00 / 56:27

The Tuskegee experiment (1932-1972)

- John C. Cutler (assistant Surgeon General 58-60, Prof. U. Pittsburgh)
  - The Deadly Deception (60 min)
  - https://www.youtube.com/watch?v=3I3vPgJNFwg (03:30, 34:38, 41:15, 48:36)

- Raymond A. Vonderlehr (CDC director 1947-51)
- John R. Heller (NCI director 48-60, CEO Memorial Sloan-Kettering Cancer Center 60-63)
- Thomas Parran Jr. (Surgeon General 36-48)
- Eugene Dibble, Eunice Rivers

Moral disengagement

- Albert Bandura
- Cognitive dissonance
    - Misalignment between behavior and values
    - Cognitive strategies to reduce dissonance

Behavior

1. Moral justification
2. Advantageous comparison
3. Euphemistic labelling

Moral disengagement

Effects

4. Disregarding or misrepresenting injurious consequences

Victim

5. Dehumanization
6. Blaming the victim

Link between behavior and effect

7. Displacement of responsibility
8. Diffusion of responsibility

Double effect fallacy

- Double effect principle
  - Under what circumstances is it morally acceptable to carry out an action that has both morally positive and negative effects?
    - The nature-of-the-act condition. The action must be either morally good or indifferent.
    - The means-end condition. The bad effect must not be the means by which one achieves the good effect. Good ends do not justify evil means.
    - The right-intention condition. The intention must be the achieving of only the good effect, with the bad effect being only an unintended side effect. All reasonable measures to avoid or mitigate the bad effect must be taken.
    - The proportionality condition. There needs to be a proportionally grave reason to allow the bad effect.
- Double effect fallacy
  - Conditions for the double effect principles are not met
  - False dilemma

The Belmont report (1979)

- Birth of bioethics
- Respect for persons
  - Individuals should be treated as autonomous agents
  - Persons with diminished autonomy are entitled to additional protections
- Beneficence
  - Do no harm
  - Maximize possible benefits and minimize possible harm
- Justice
  - Requires that individuals and groups be treated fairly and equitably in terms of bearing the burdens and receiving the benefits of research

Seven pillars of clinical research

1. Autonomy
2. Non-maleficence
3. Beneficence
4. Fidelity
5. Truthfulness
6. Confidentiality
7. Justice

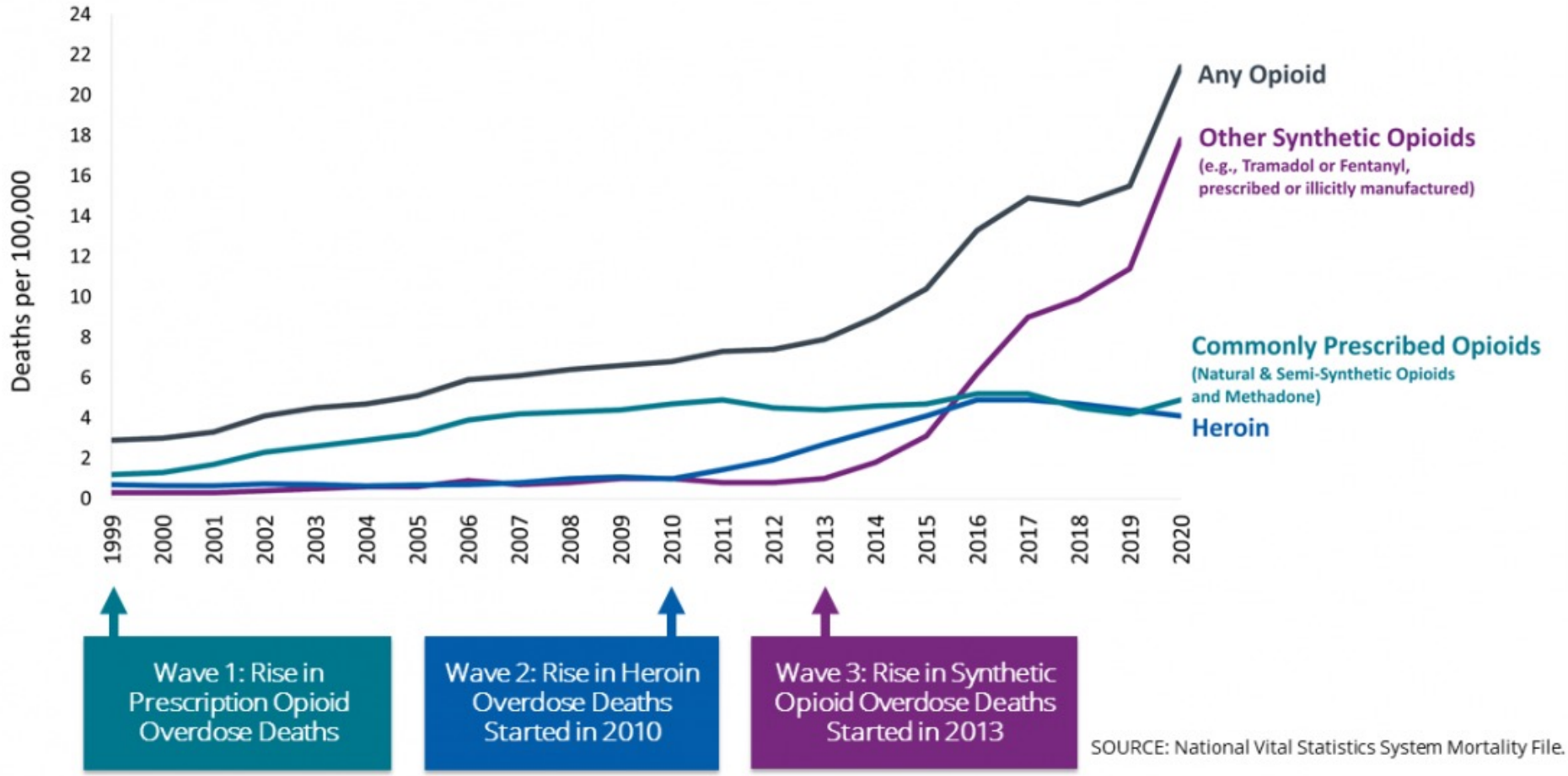
More cases

- Vioxx (Merck, 2006)
- Mediator (Servier, 2009)
- …

Year	Company	Settlement	Violation(s)	Product(s)	Laws violated (if applicable)
2012	GlaxoSmithKline[1][6]	$3 billion ($1B criminal, $2B civil)	Criminal: Off-label promotion, failure to disclose safety data. Civil: paying kickbacks to physicians, making false and misleading statements concerning the safety of Avandia, reporting false best prices and underpaying rebates owed under the Medicaid Drug Rebate Program	Avandia (not providing safety data), Wellbutrin, Paxil (promotion of paediatric use), Advair, Lamictal, Zofran, Imitrex, Lotronex, Flovent, Valtrex	False Claims Act, FDCA
2009	Pfizer[2]	$2.3 billion	Off-label promotion, kickbacks	Bextra, Geodon, Zyvox, Lyrica	False Claims Act, FDCA
2013	Johnson & Johnson[7]	$2.2 billion	Off-label promotion, kickbacks	Risperdal, Invega, Nesiritide	False Claims Act, FDCA
2012	Abbott Laboratories[8]	$1.5 billion	Off-label promotion	Depakote	False Claims Act, FDCA
2009	Eli Lilly[9]	$1.4 billion	Off-label promotion	Zyprexa	False Claims Act, FDCA
2001	TAP Pharmaceutical Products[10]	$875 million	Medicare fraud, kickbacks	Lupron	False Claims Act, Prescription Drug Marketing Act
2012	Amgen[11]	$762 million	Off-label promotion, kickbacks	Aranesp	False Claims Act, FDCA
2010	GlaxoSmithKline[12]	$750 million	Poor manufacturing practices	Kytril, Bactroban, Paxil CR, Avandamet	False Claims Act, FDCA
2005	Serono[13]	$704 million	Off-label promotion, kickbacks, monopolistic practices	Serostim	False Claims Act
2008	Merck[14]	$650 million	Medicare fraud, kickbacks	Zocor, Vioxx, Pepsid	False Claims Act, Medicaid Rebate Statute
2007	Purdue Pharma[15]	$601 million	Off-label promotion	Oxycontin	False Claims Act
2010	Allergan[16]	$600 million	Off-label promotion	Botox	False Claims Act, FDCA
2010	AstraZeneca[17]	$520 million	Off-label promotion, kickbacks	Seroquel	False Claims Act
2007	Bristol-Myers Squibb[18]	$515 million	Off-label promotion, kickbacks, Medicare fraud	Abilify, Serzone	False Claims Act, FDCA
2002	Schering-Plough[19]	$500 million	Poor manufacturing practices	Claritin	FDA Current Good Manufacturing Practices
2006	Mylan[20]	$465 million	Misclassification under the Medicaid Drug Rebate Program	EpiPen (epinephrine)	False Claims Act
2006	Schering-Plough[21]	$435 million	Off-label promotion, kickbacks, Medicare fraud	Temodar, Intron A, K-Dur, Claritin RediTabs	False Claims Act, FDCA
2004[22]	Pfizer	$430 million	Off-label promotion	Neurontin	False Claims Act, FDCA
2008	Cephalon[23]	$425 million	Off-label promotion[23]	Actiq, Gabitril, Provigil	False Claims Act, FDCA
2010	Novartis[24]	$423 million	Off-label promotion, kickbacks	Trileptal	False Claims Act, FDCA
2003	AstraZeneca[25]	$355 million	Medicare fraud	Zoladex	Prescription Drug Marketing Act
2004	Schering-Plough[26]	$345 million	Medicare fraud, kickbacks	Claritin	False Claims Act, Anti-Kickback Statute

Opioid epidemic (ongoing)

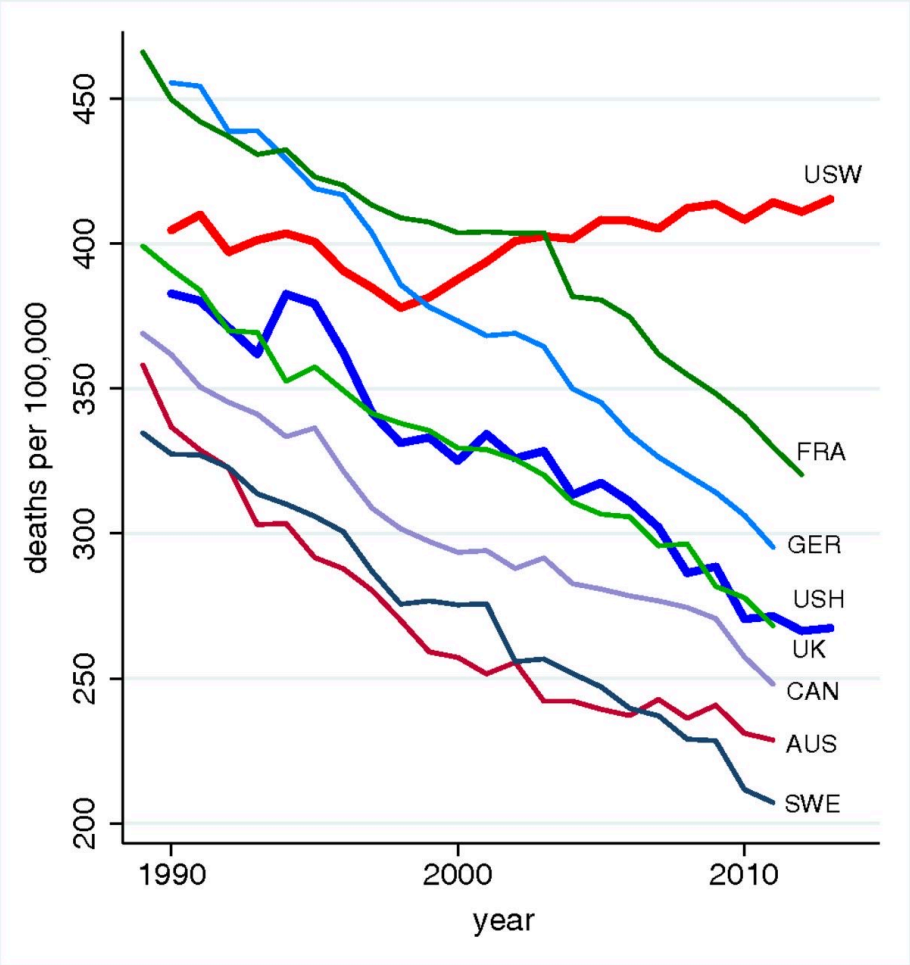
- Prescription drugs and illegal drugs
- Purdue Pharma, Johnson & Johnson, Teva, etc.



Opioid epidemic

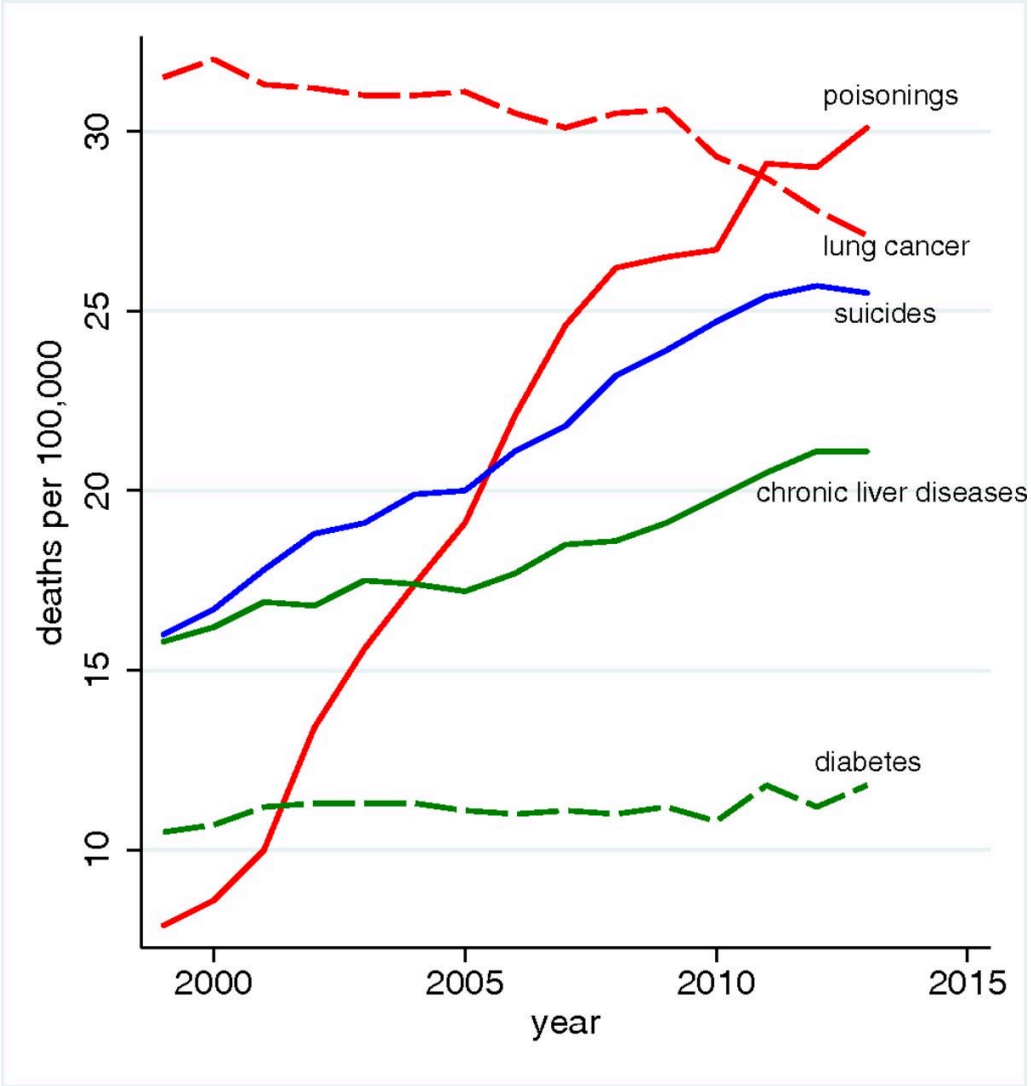
- US Department of Human Health Services
  - “In the late 1990s, pharmaceutical companies reassured the medical community that patients would not become addicted to opioid pain relievers and healthcare providers began to prescribe them at greater rates. Increased prescription of opioid medications led to widespread misuse of both prescription and non-prescription opioids before it became clear that these medications could indeed be highly addictive.”
- National Institute on Drug Abuse
  - “Of people entering treatment for heroin addiction who began abusing opioids in the 1960s, more than 80 percent started with heroin. Of those who began abusing opioids in the 2000s, 75 percent reported that their first opioid was a prescription drug. Examining national-level general population heroin data (including those in and not in treatment), nearly 80 percent of heroin users reported using prescription opioids prior to heroin.”

All-cause mortality, ages 45–54 for US White non-Hispanics (USW), US Hispanics (USH), and six comparison countries: France (FRA), Germany (GER), the United Kingdom (UK), Canada (CAN), Australia (AUS), and Sweden (SWE).



Anne Case, and Angus Deaton PNAS 2015;112:15078-15083

Mortality by cause, white non-Hispanics ages 45–54.



Anne Case, and Angus Deaton PNAS 2015;112:15078-15083

Moral disengagement

- Albert Bandura
- Cognitive dissonance
    - Misalignment between behavior and values
    - Cognitive strategies to reduce dissonance

Behavior

1. Moral justification
2. Advantageous comparison
3. Euphemistic labelling

Moral disengagement

Effects

4. Disregarding or misrepresenting injurious consequences

Victim

5. Dehumanization
6. Blaming the victim

Link between behavior and effect

7. Displacement of responsibility
8. Diffusion of responsibility

KU LEUVEN

Is technology morally neutral?

I think that technologies are morally neutral until we apply them. It's only when we use them for good or for evil that they become good or evil.

— William Gibson, 1994

Is technology morally neutral?

Science in itself is morally neutral; it comes good or evil as it is applied. Ideally, science should be applied by humanists. In this case it would be good. In actual fact it is more likely to be applied by economists, and so to turn out, if not wholly bad, at any rate a very mixed blessing. It rests with us and our descendants to decide whether we shall use the unprecedented power which science gives us for good or for bad purposes. It is in our hands to choose wisely or unwisely. Alas, that wisdom should be so much harder to come by than knowledge!

— Aldous Huxley, 1933

Is technology morally neutral?

For mechanical arts are of ambiguous use, serving as well for hurt as for remedy, and they have in a manner power both to loose and bind themselves.

— Francis Bacon, 1609

Guns don’t kill people, people kill people

- Replace “guns” with “nukes”

- Proximate cause
  - Key legal element to determine liability
  - “But for” test: If the cause had not occurred, the harm would not have occurred
  - The consequences of the action were foreseeable

per mRNA

$$\frac{dM_P}{dt} = v_s \frac{K_I^n}{K_I^n + P_N^n} - v_m \frac{M_P}{K_m + M_P}$$

PER protein (unphosph.)

$$\frac{dP_0}{dt} = k_s M_P - v_1 \frac{P_0}{K_1 + P_0} + v_2 \frac{P_1}{K_2 + P_1}$$

PER protein (monophosph.)

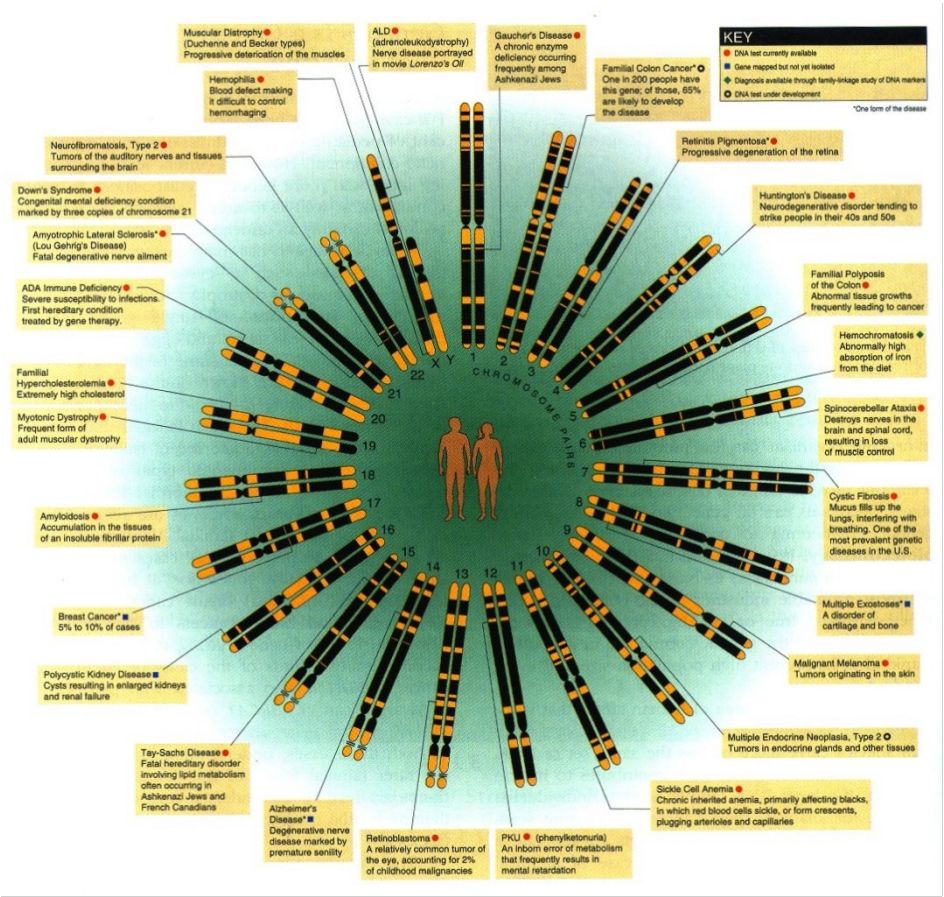
$$\frac{dP_1}{dt} = v_1 \frac{P_0}{K_1 + P_0} - v_2 \frac{P_1}{K_2 + P_1} - v_3 \frac{P_1}{K_3 + P_1} + v_4 \frac{P_2}{K_4 + P_2}$$

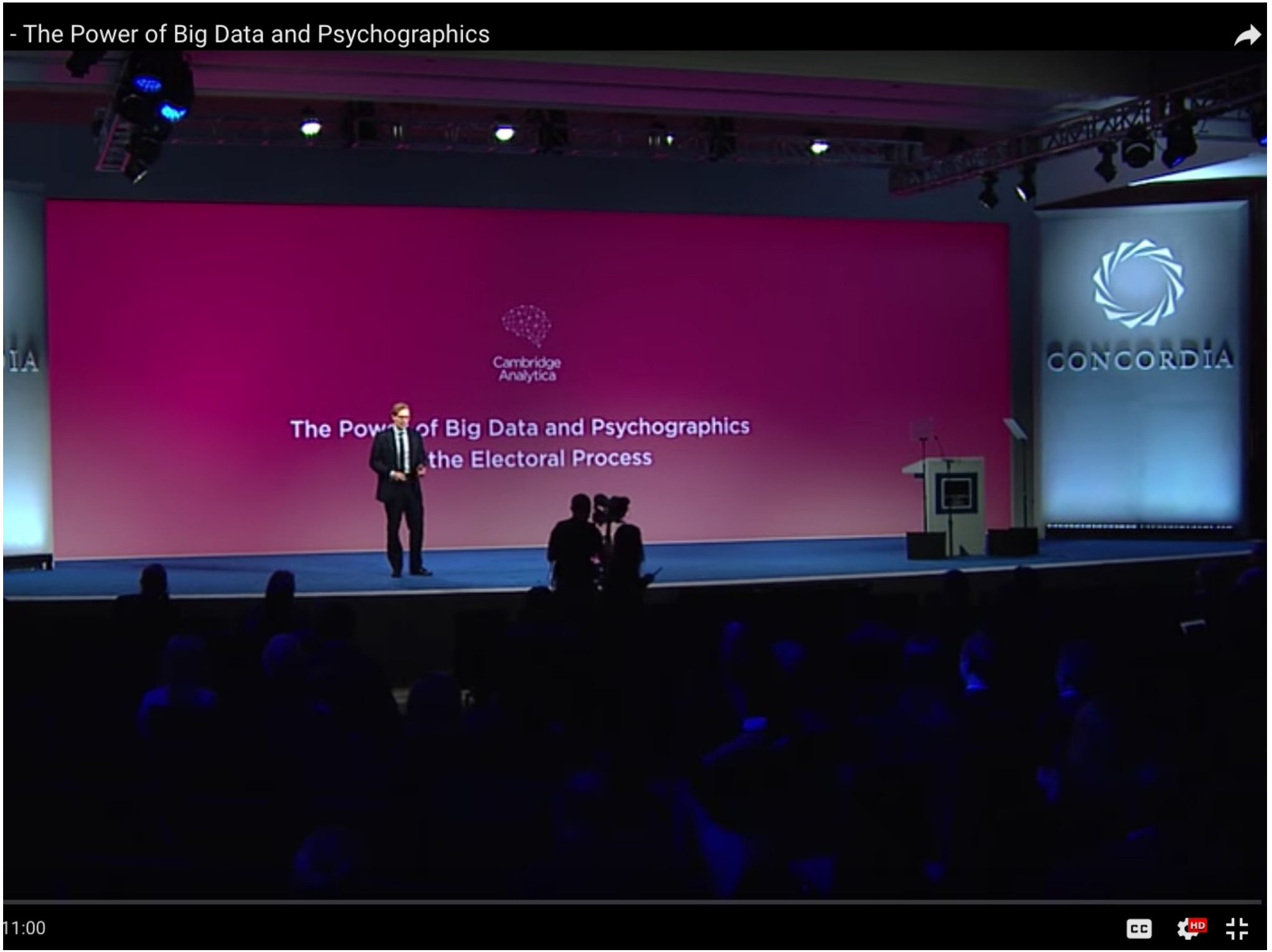
PER protein (biphosph.)

$$\frac{dP_2}{dt} = v_3 \frac{P_1}{K_3 + P_1} - v_4 \frac{P_2}{K_4 + P_2} - v_d \frac{P_2}{K_d + P_2} - k_1 P_2 + k_2 P_N$$

nuclear PER protein

$$\frac{dP_N}{dt} = k_1 P_2 - k_2 P_N$$




- The Power of Big Data and Psychographics
Cambridge Analytica
CONCORDIA
11:00

Cool, isn’t it?

Why?

Should we care?

“collect DNA [...] from non-United States persons who are detained under the authority of the United States.” 24 U.S.C. § 40702(a)(1)(A)

Credit: Salvador Gonzalez/AP

POLICY FORUM

The alleged Golden State Killer, Joseph DeAngelo, appears at his arraignment in Sacramento, California, in late April.

SCIENCE AND LAW

Is it time for a universal genetic forensic database?

Bias and privacy concerns cloud police use of genetics

By **J. W. Hazel[1,2], E. W. Clayton[1,2,3], B. A. Malin[2,4,5,6], C. Slobogin[2,3]**

obviating the need for any other DNA source (*1*). Although this move would be controversial, it may not be as dramatic as one might

ers to upload genetic data coupled with personal identifiers in order to gain insights into their genealogy. Without authorization from a court, law enforcement simply pretended to be the donor of what was, in fact, crime scene DNA. Through that ruse, officers found a match to a person in the database who was distantly related to Joseph DeAngelo, the man ultimately arrested for the crimes. Since these revelations came to light last spring, multiple law enforcement agencies have used similar long-range familial searches of publicly accessible databases to close 13 cold

O'Doherty *et al. BMC Medical Ethics* (2016) 17:54
DOI 10.1186/s12910-016-0137-x

BMC Medical Ethics

REVIEW Open Access

If you build it, they will come: unintended future uses of organised health data collections

Kieran C. O'Doherty[1*], Emily Christofides[1], Jeffery Yen[1], Heidi Beate Bentzen[2,3,4], Wylie Burke[5], Nina Hallowell[6], Barbara A. Koenig[7] and Donald J. Willison[8,9]

Abstract

Discussion: Although health research conducted using these collections is broadly recognized as beneficent, secondary uses of these data and samples may be controversial. We examine both documented and hypothetical scenarios of secondary uses of health data and samples. In particular, we focus on the use of health data for purposes of:

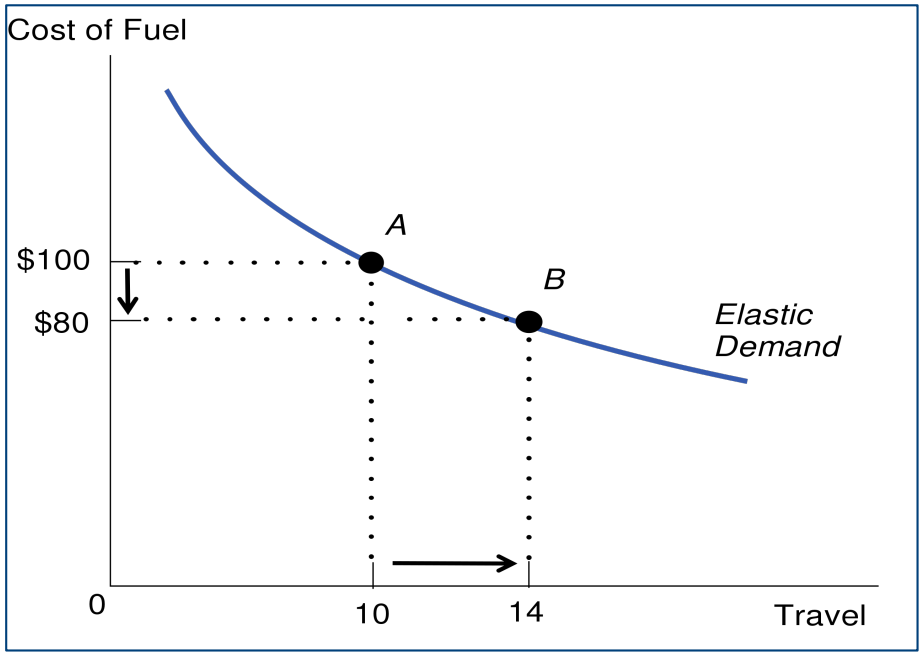
- Forensic investigations
- Civil lawsuits
- Identification of victims of mass casualty events
- Denial of entry for border security and immigration
- Making health resource rationing decisions
- Facilitating human rights abuses in autocratic regimes

(Continued on next page)

Economics of surveillance

- Jevons' paradox

- Video surveillance
  - Low marginal cost
- Facial recognition
  - Near zero marginal cost



- Without constraint, near infinite demand for surveillance

Why technology?

The picture of Dorian Gray

pidgeon
audio visual

5 St Anne's Close
London N6 6AR
England

pidgeon
audio visual

CEDRIC
PRICE

TECHNOLOGY
IS THE
ANSWER
BUT WHAT WAS THE
QUESTION?

Technology and humanism

Man by the Fall, fell at the same time from his state of innocence and from his dominion over creation. Both of these losses can in this life be in some part repaired; the former by religion and faith, the latter by arts and science.

— Francis Bacon, 1620

Technology and humanism

… by means of which, knowing the force and action of fire, water, air, the stars, the heavens, and all the other bodies that surround us, as distinctly as we know the various crafts of our artisans, we might also apply them in the same way to all the uses to which they are adapted, and thus render ourselves like lords and possessors of nature. And this is a result to be desired, not only in order to the invention of an infinity of arts, by which we might be enabled to enjoy without any trouble the fruits of the earth, and all its comforts, but also and especially for the preservation of health, which is without doubt, of all the blessings of this life, the first and fundamental one; for the mind is so intimately dependent upon the condition and relation of the organs of the body, that if any means can ever be found to render men wiser and more ingenious than hitherto, I believe that it is in Medicine they must be sought for.

— René Descartes, 1637


Human dignity
• Autonomy
• Rationality

Discussion

What about eugenics today?