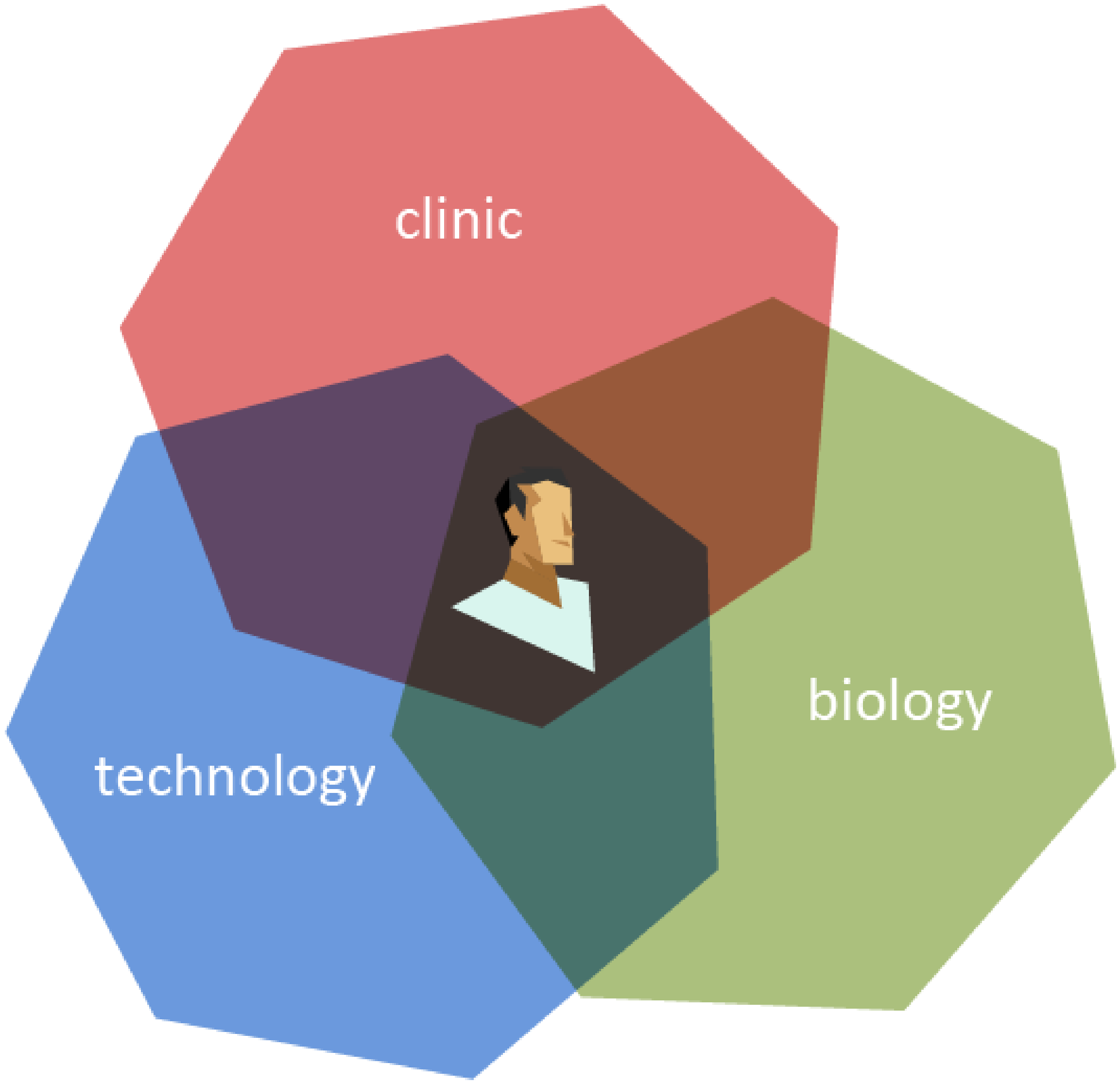
Healthcare challenges in the 21st Century
…and potential solutions

Professor dr. Philippe LAMBIN
The D-Lab & Dpt of Precision Medicine
Maastricht University

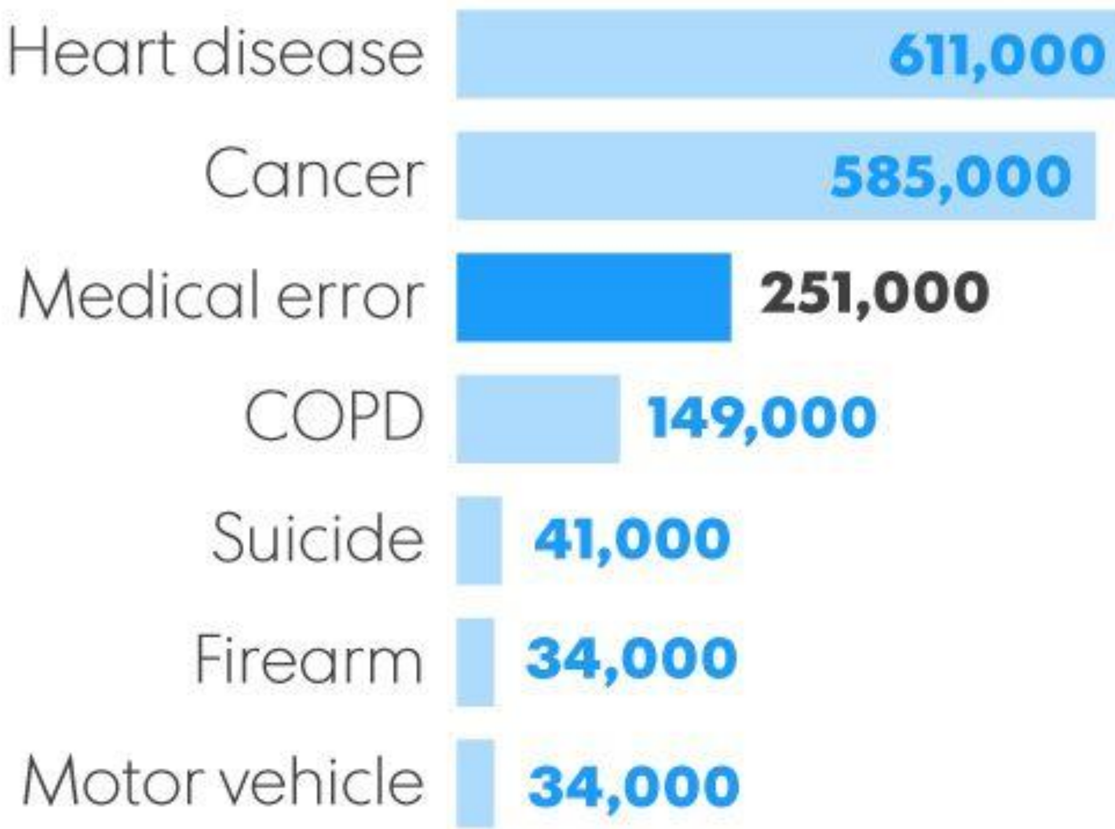
We believe in “Convergence Sciences”



Why?


Medical Errors & Hospital-Acquired Infections
kill up to 440,000
Americans
each year
That's more than two jumbo jets
full of passengers crashing every day

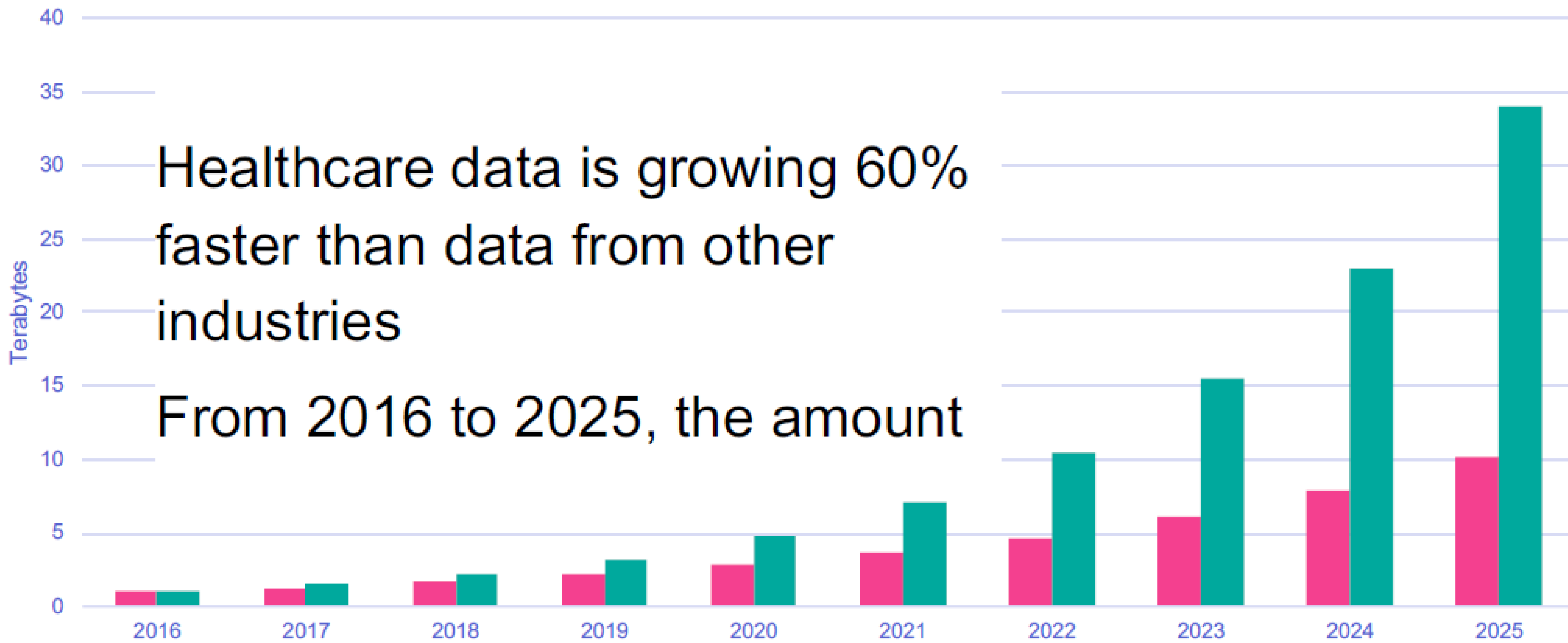
MEDICAL ERRORS NATION'S THIRD BIGGEST KILLER IN 2013



Source: Martin Makary, Michael Daniel study at Johns Hopkins University School of Medicine

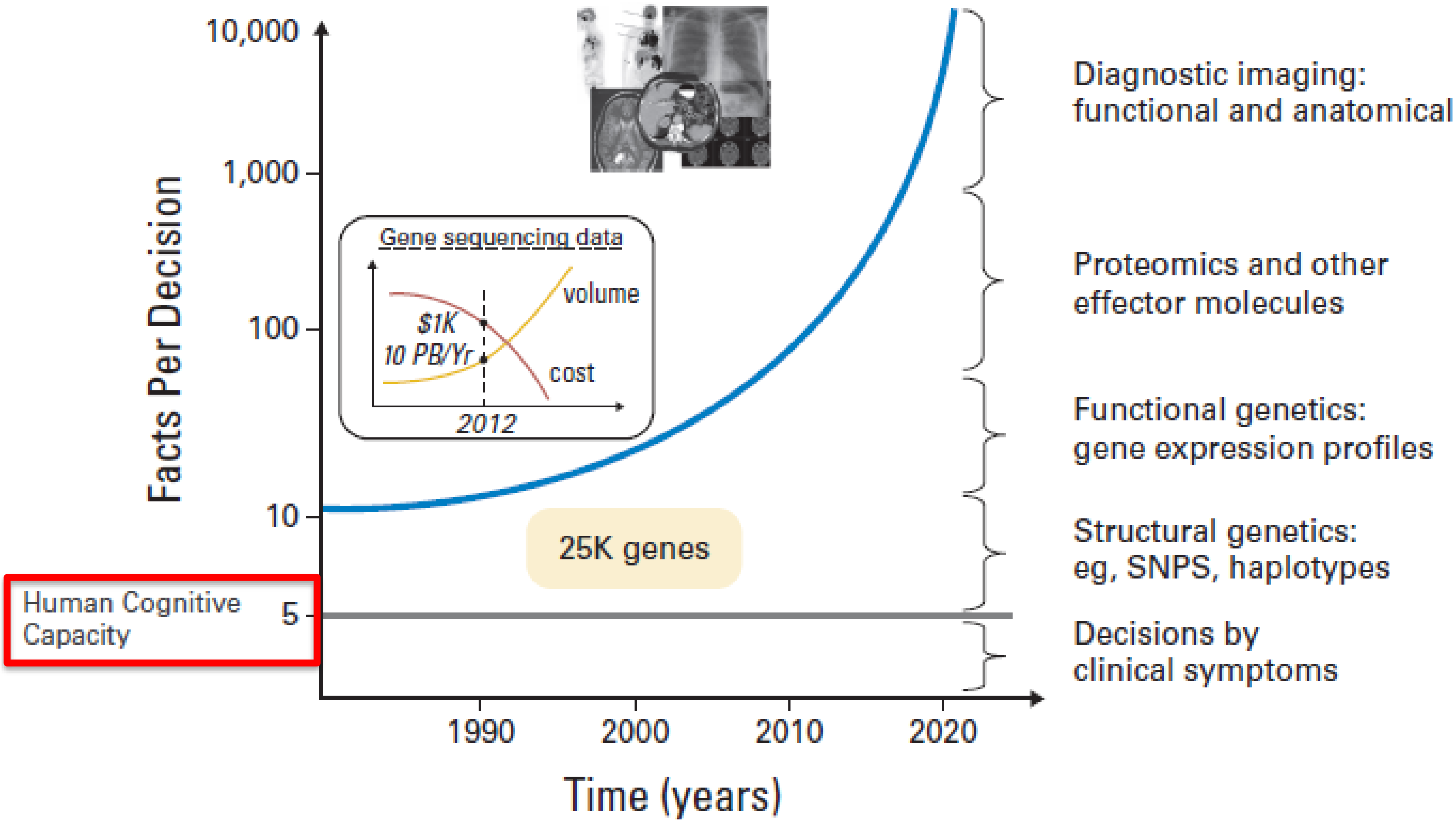
Healthcare data is growing 60% faster than data from other industries

From 2016 to 2025, the amount



1 TB of Data Over Time: All other Data

The problem of Big Data – The doctor (and administrator) is drowning



J Clin Oncol 2010;28:4268; JMI 2012 Friedman, Rigby; BMJ Clinical Evidence

Evidence based medicine

Conventional Clinical Research

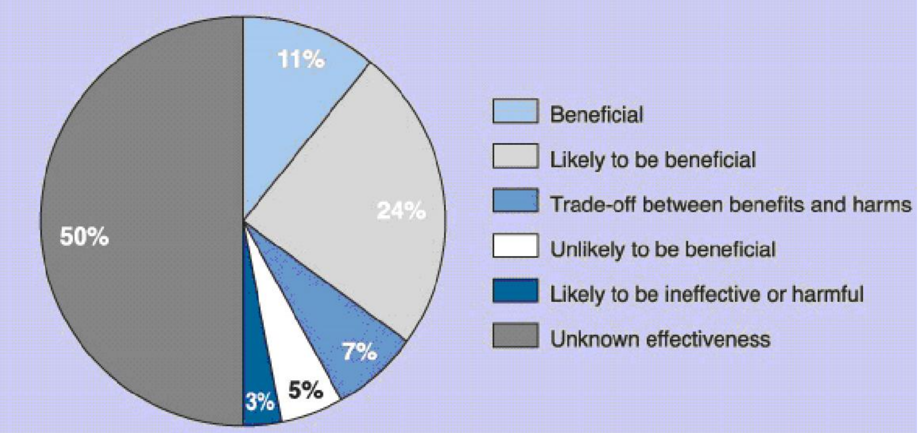
High data quality

Low data quantity

Controlled

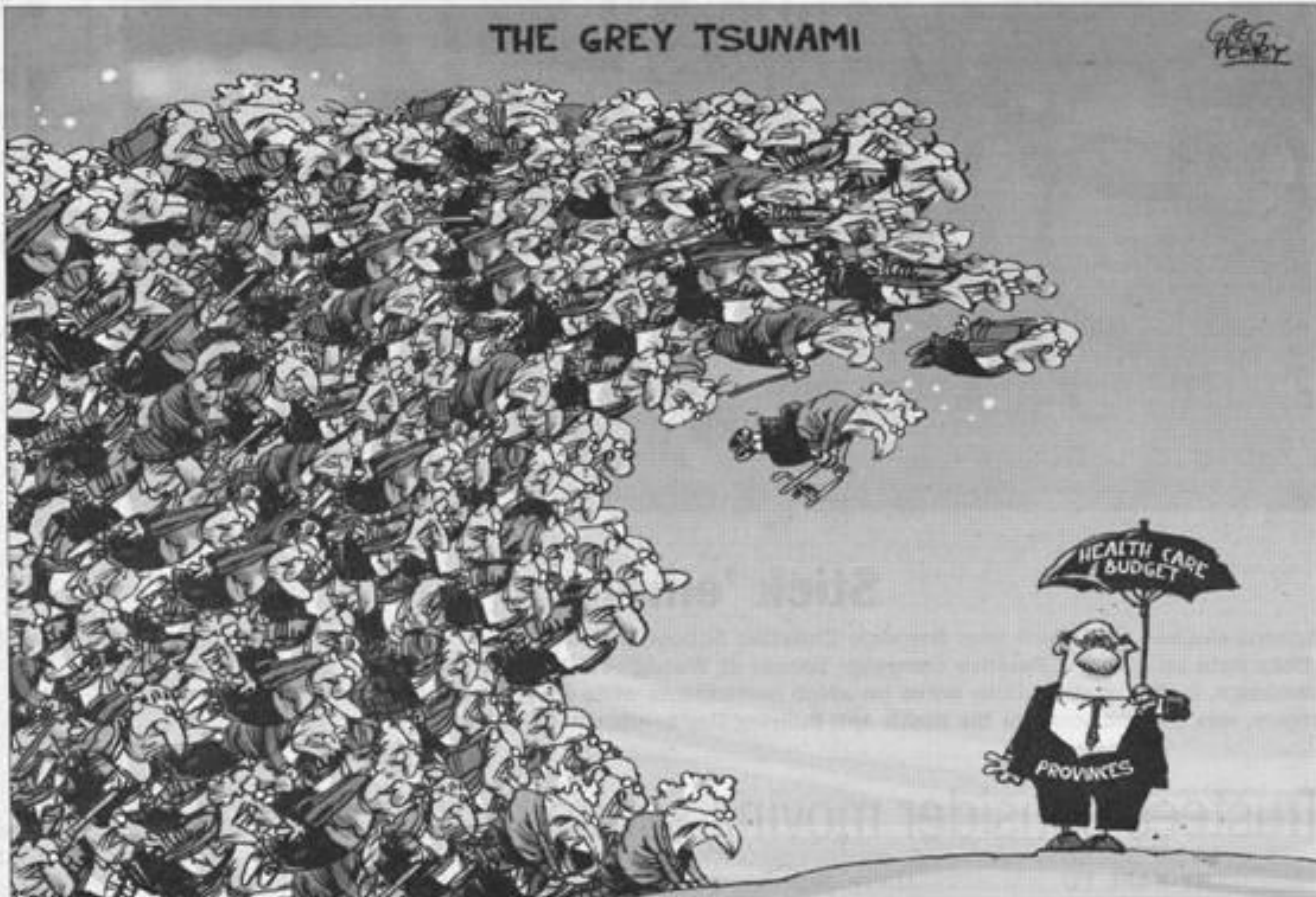
- Assigned patients
- “EORTC-RTOG grade” QA/Protocol
- Biobanking, translational research

- Less then 3% of the patients
- Highly biased population
- Randomized trials rarely done for new technologies

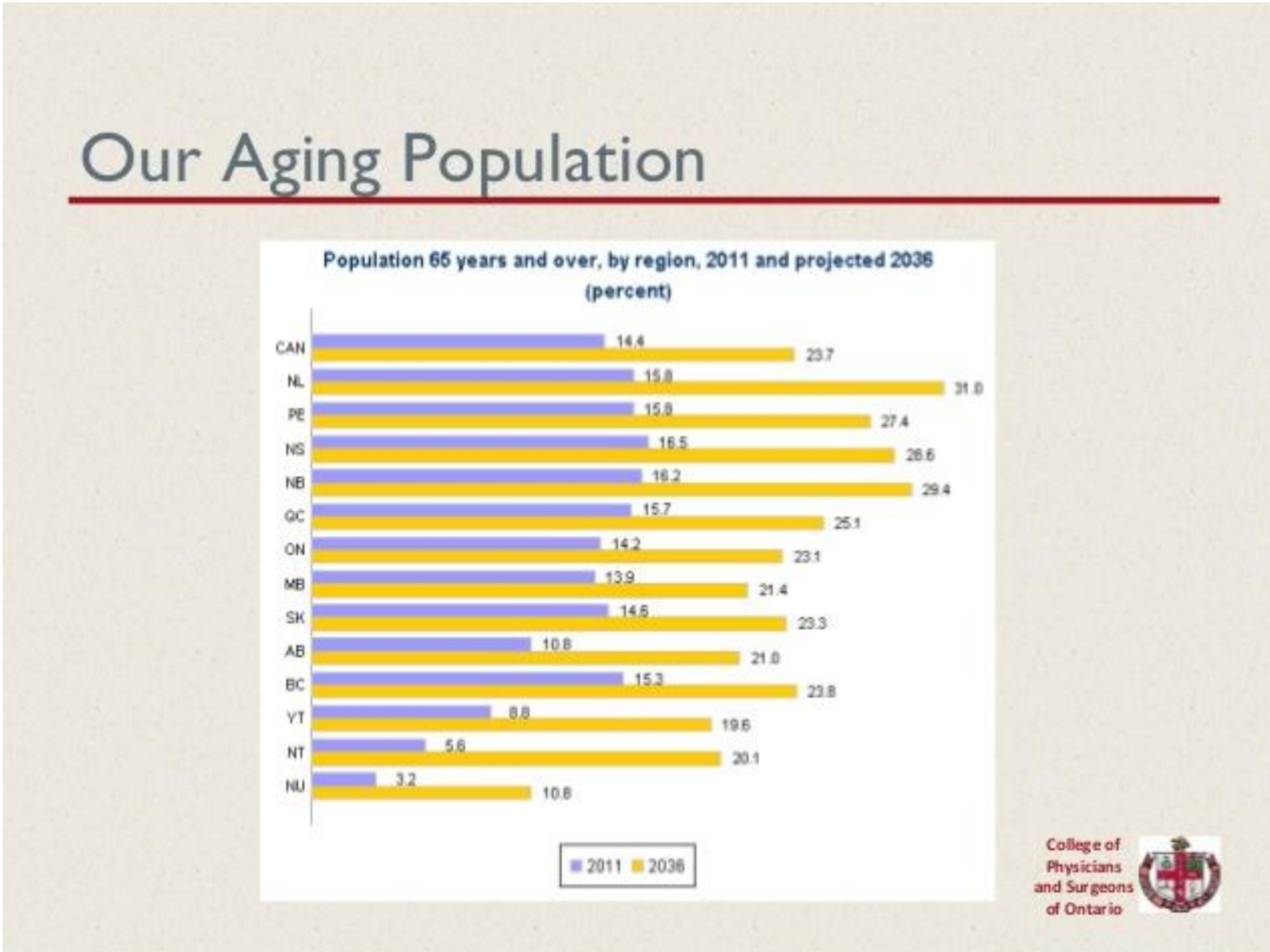


Effectiveness of 3000 treatments as reported in randomised controlled trials selected by Clinical Evidence. This does **not** indicate how oftentreatments are used in healthcare settings or their effectiveness in individual patients.

J Clin Oncol 2010;28:4268; JMI 2012 Friedman, Rigby; BMJ Clinical Evidence

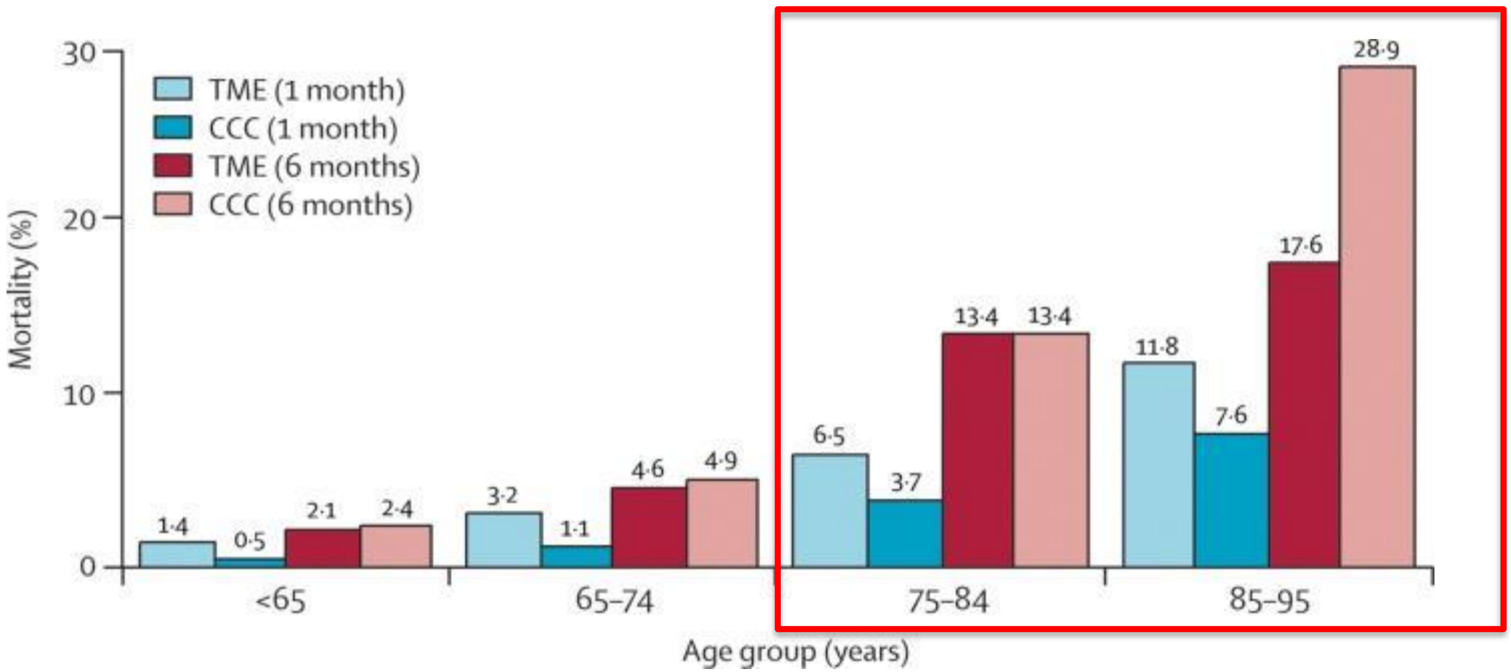

THE GREY TSUNAMI
HEALTH CARE BUDGET
PROVINCES

The grey tsunami

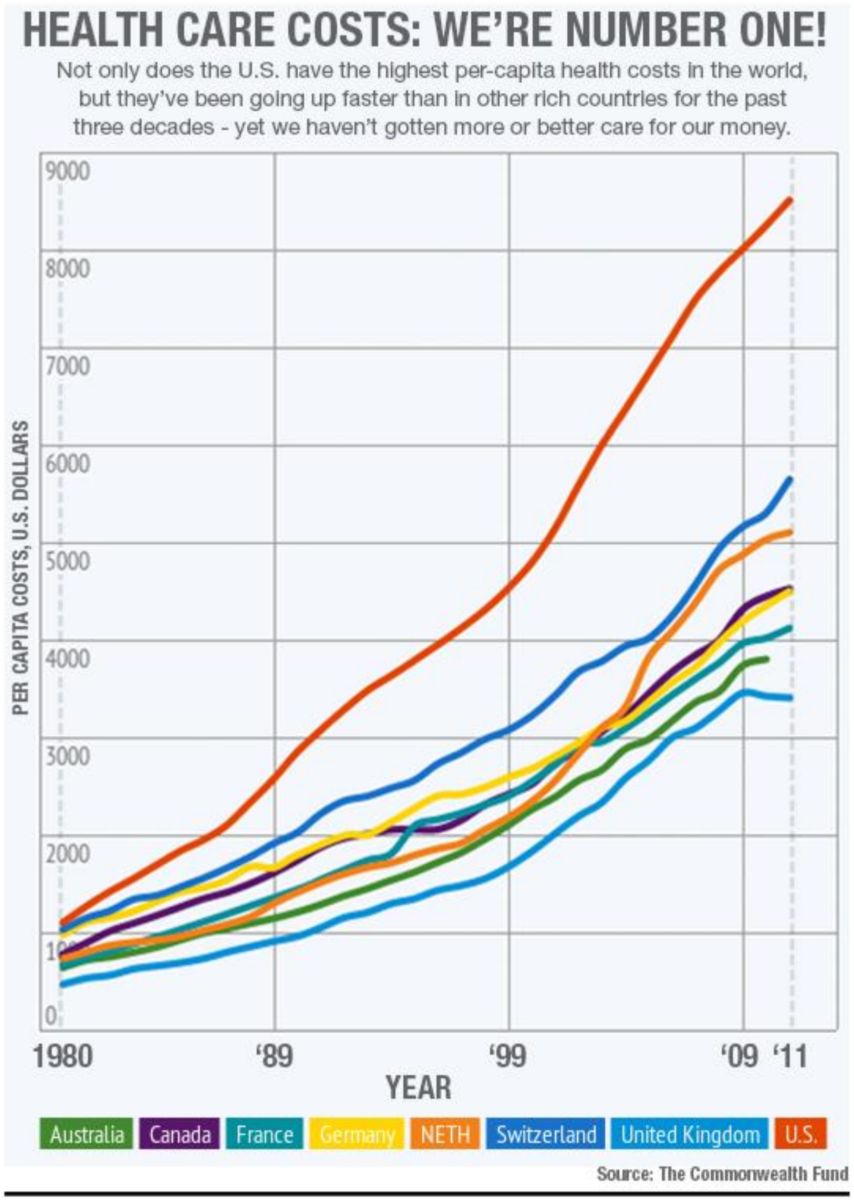


The Silver or Grey *Tsunami* is a metaphor used to describe population aging

Example: Elderly patient with rectal cancer - having *no evidence* can have dramatic consequences



Rutten et al. Lancet Oncology 2008; 9: 494

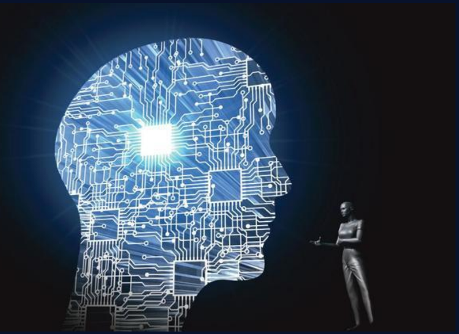


HEALTH CARE COSTS: WE'RE NUMBER ONE!
Not only does the U.S. have the highest per-capita health costs in the world, but they've been going up faster than in other rich countries for the past three decades - yet we haven't gotten more or better care for our money.
9000
8000
7000
6000
5000
4000
3000
2000
0
PER CAPITA COSTS, U.S. DOLLARS
1980
'89
'99
'09
'11
YEAR
Australia
Canada
France
Germany
NETH
Switzerland
United Kingdom
U.S.
Source: The Commonwealth Fund

The potential solutions?

The Fifth Revolution
Cognitive

Big Data creates more knowledge



2010

2018

Why? The 5 P's of Precision Medicine

« P » for Personalized

« P » for Preventive

« P » for Predictive

« P » for Participative

« P » for Pragmatic*

**New*: Value-based healthcare get paid based on outcomes that matter to patients.

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

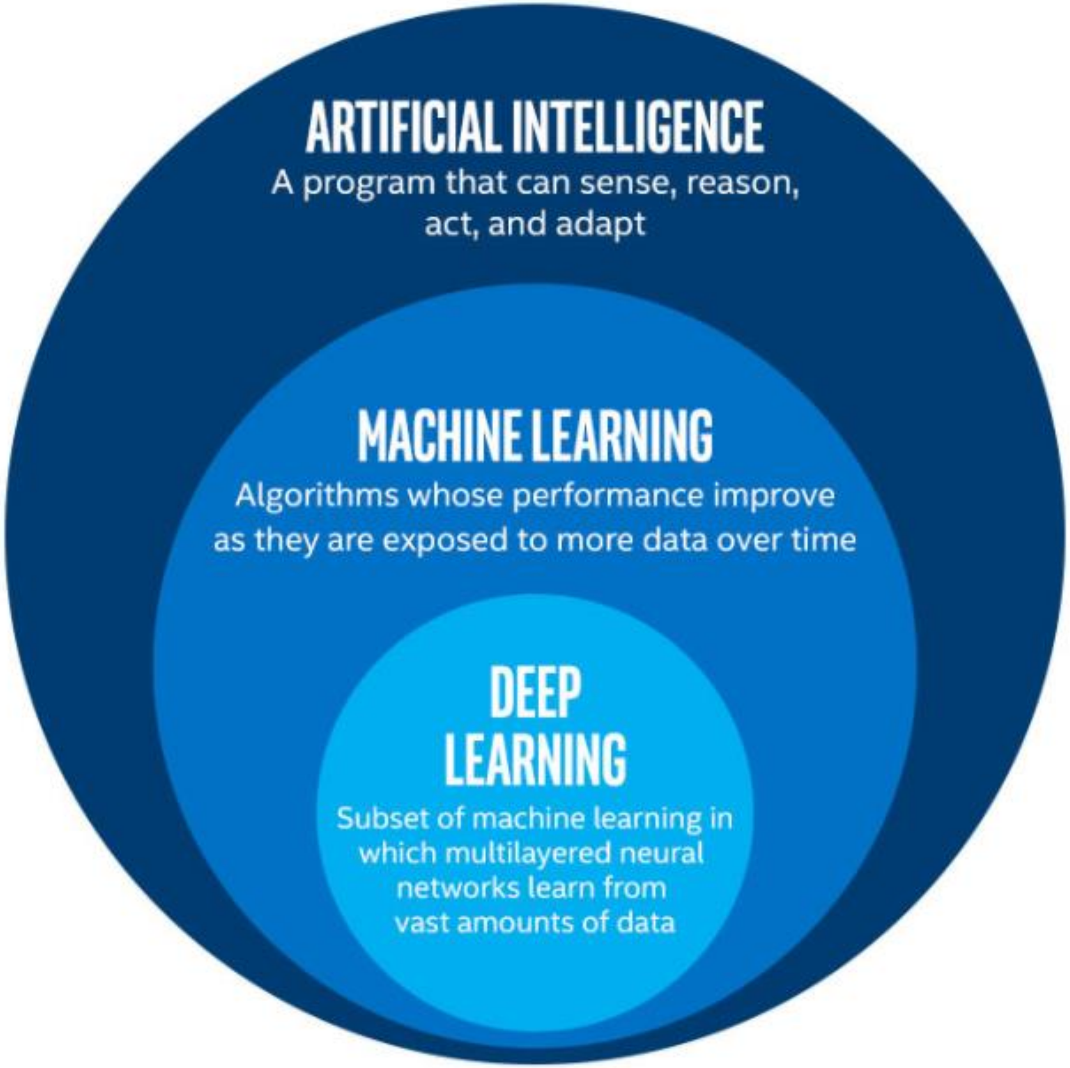
FRONTIERS IN MEDICINE

Machine Learning in Medicine

Alvin Rajkomar, M.D., Jeffrey Dean, Ph.D., and Isaac Kohane, M.D., Ph.D.

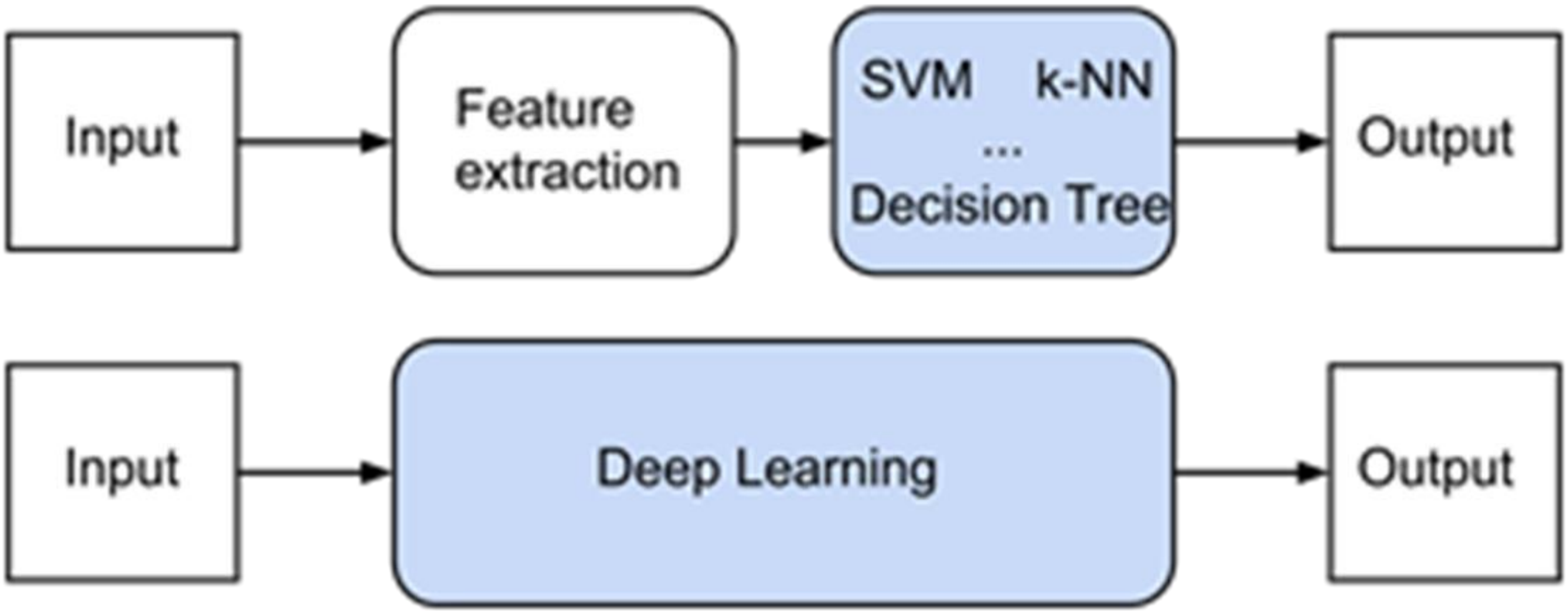
N ENGL J MED 380;14 NEJM.ORG APRIL 4, 2019

When we have large amount of data we need A.I.



Deist, Lambin et al. Med Phys Jul;45(7):3449-3459.2018

Glass box transparent and understandable >< the black box Deep Leaning like



BY TOM LIMONCELLI

Automation Should Be Like Iron Man, Not Ultron

Courtesy of Joe Deasy

http://queue.acm.org/detail.cfm?id=2841313

Iron Man's exoskeleton takes the abilities that Tony Stark has and *accentuates them*. By having his exoskeleton do this for him, he can focus on ***other things***. Of course, if he disagrees or wants to do something the program wasn't coded to do, he can *override* the trajectory.

Ultron, on the other hand, was intended to be *fully autonomous*. It did everything and was, basically, so complex that when it had to *be debugged* the only choice was (spoiler alert!) to destroy it.

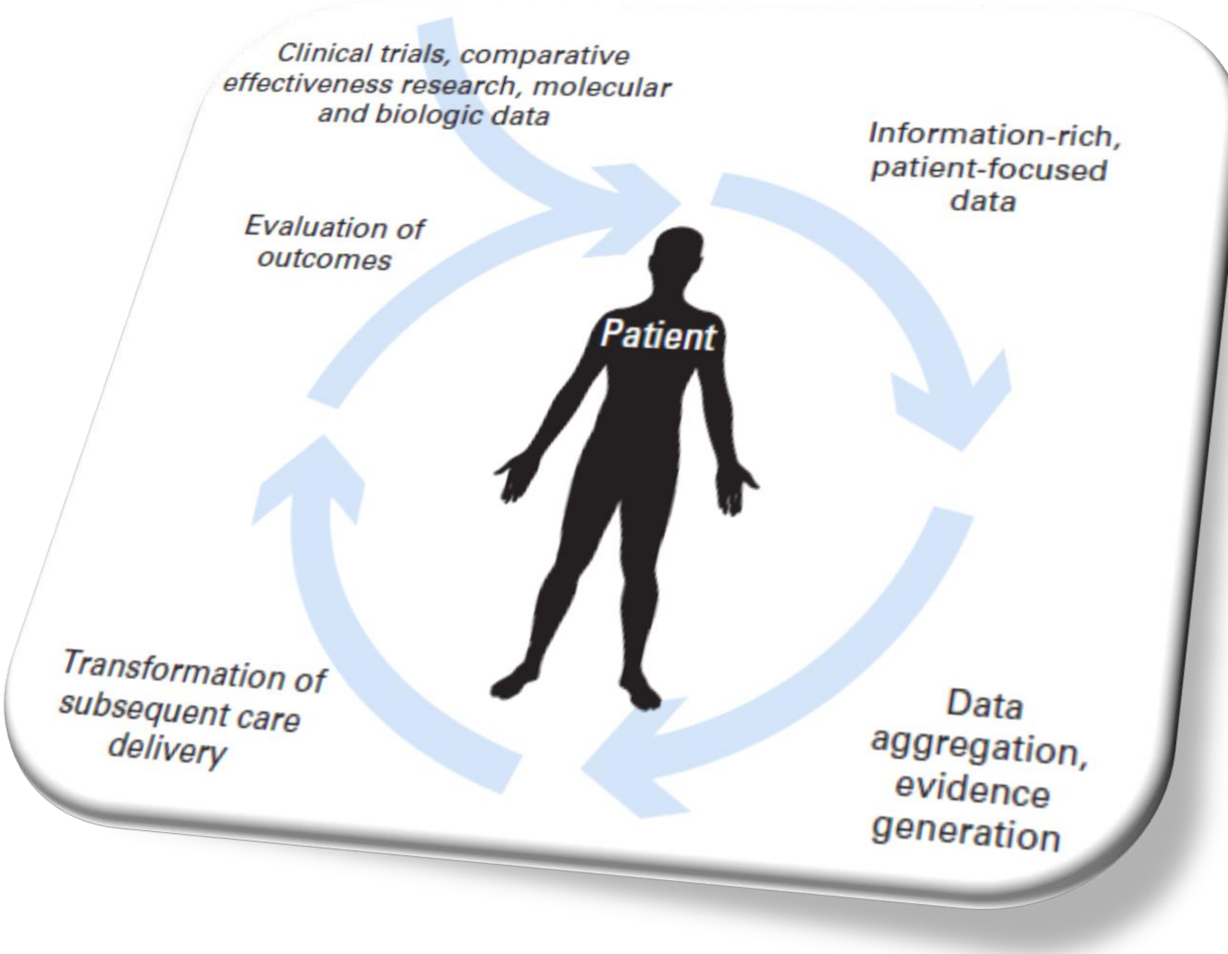
Proposal: Use the 97%: Rapid Learning Health Care or "Big data in health care"

[..] rapid learning [..] where we can **learn from each patient** to guide practice, is [..] crucial to guide rational health policy and to contain costs [..].

Lancet Oncol 2011;12:933

Examples:

1. *Radiotherapy CAT (www.eurocat.info)*
2. *ASCO's CancerLinQ*
3. *www.predictcancer.org*



Lambin *et al. Nat. Rev Clin Oncol 2012*, Adv. Drug Dev 2016

Conventional Clinical Research

High data quality

Low data quantity

Controlled

- Assigned patients
- “EORTC-RTOG grade” QA/Protocol
- Biobanking, translational research

Rapid Learning Health Care (“Big Data”)

Low data quality

High data quantity

Reality

- Unassigned patients
- “Clinical grade” QA/Protocol
- Ad hoc biobanking/translational research

Relton C et al. BMJ. 2010; Burbach et al. Trials 2015; Lambin et al. Acta Oncol 2015

Tension:

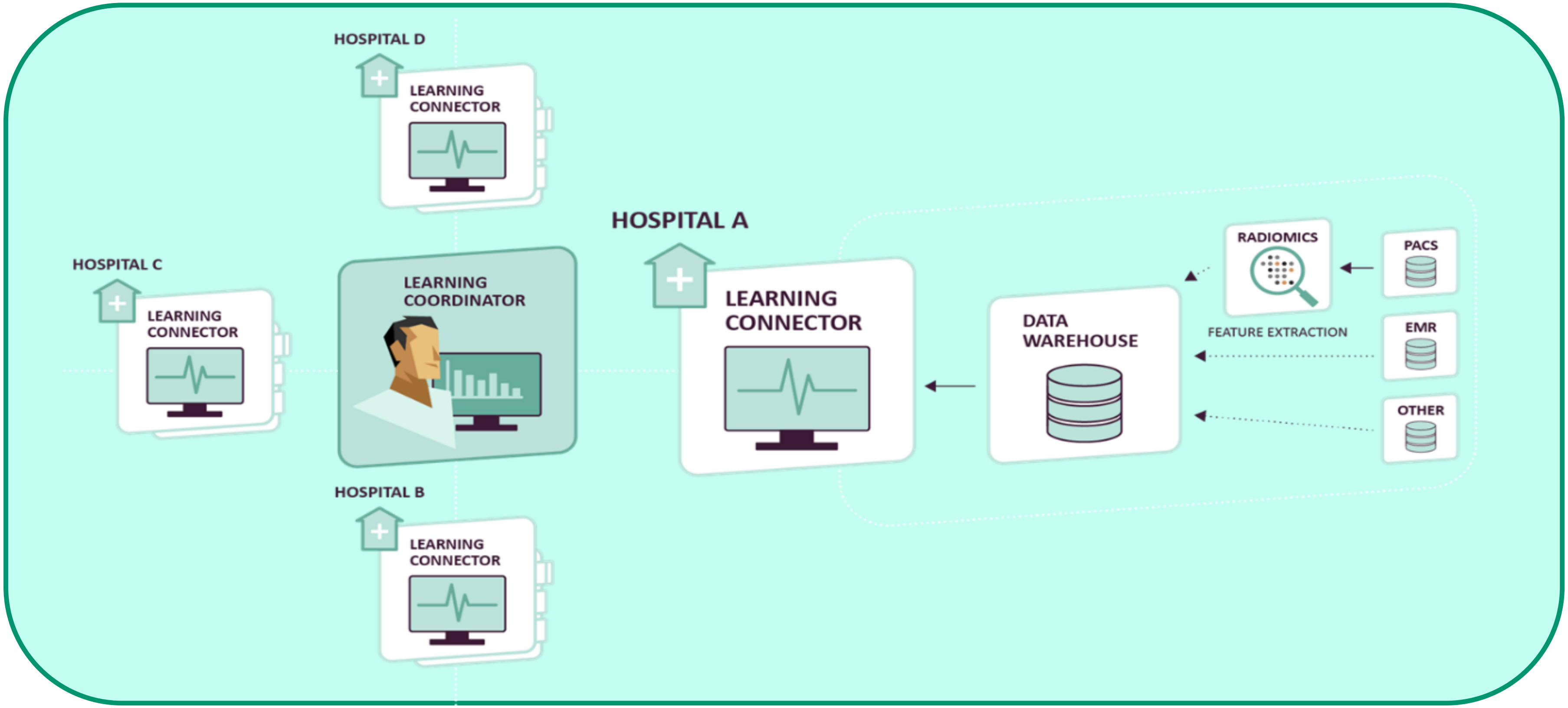
Big Data-based solidarity >< Privacy of individuals

Courtesy of David Townend

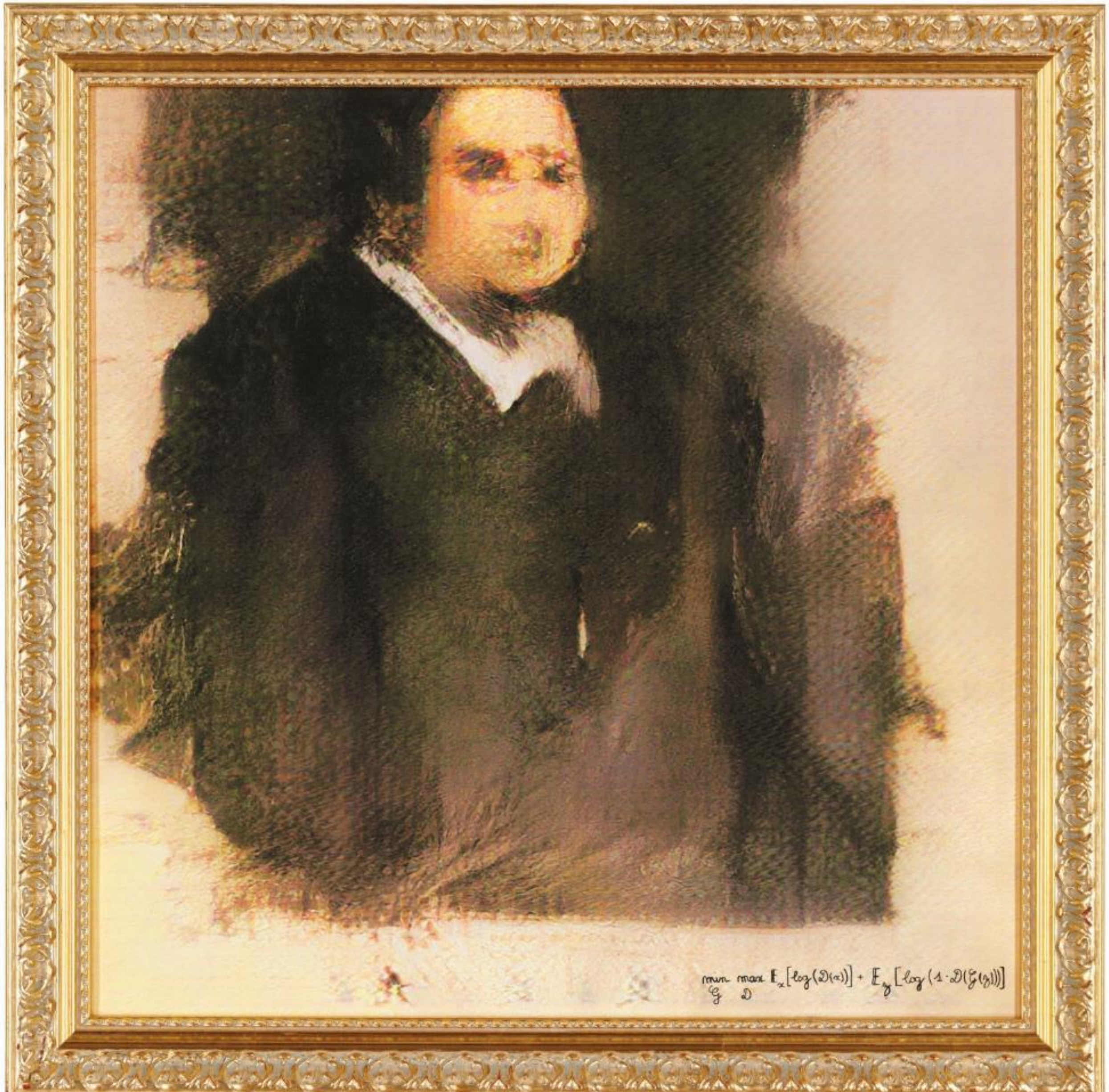
The technologies helping protecting privacy:

1. **distributed learning of federated databases,**
2. **synthetic data and**
3. **blockchain-like solutions**

Privacy preserving distributed learning



www.eurocat.info; Lambin et al. Radiother Oncol 2013, Deist et al 2017

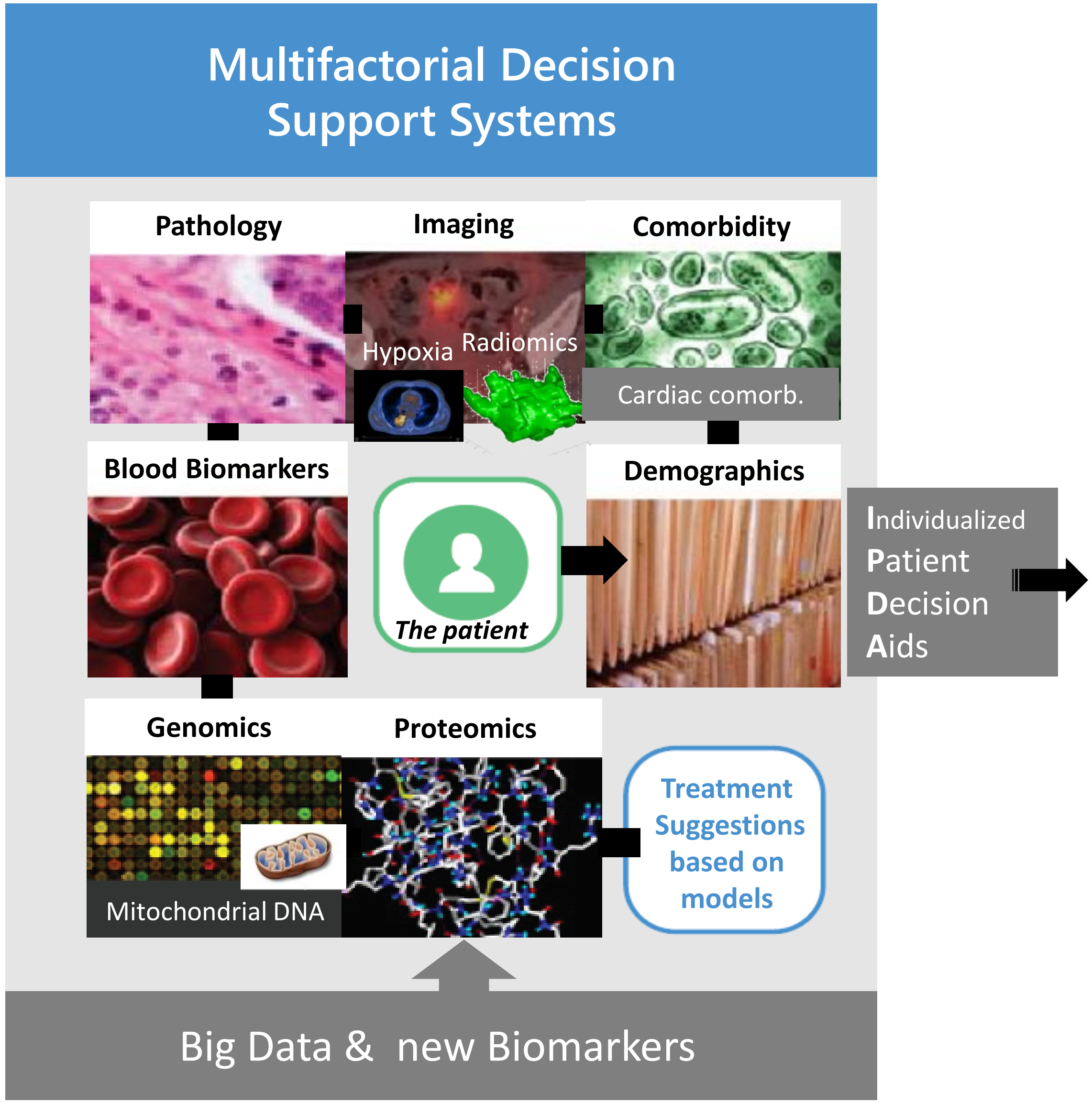


Edmond de Belamy is a generative adversarial network portrait painting constructed in 2018 by Paris-based arts-collective *Obvious, sold* for $432,500 at Christies.

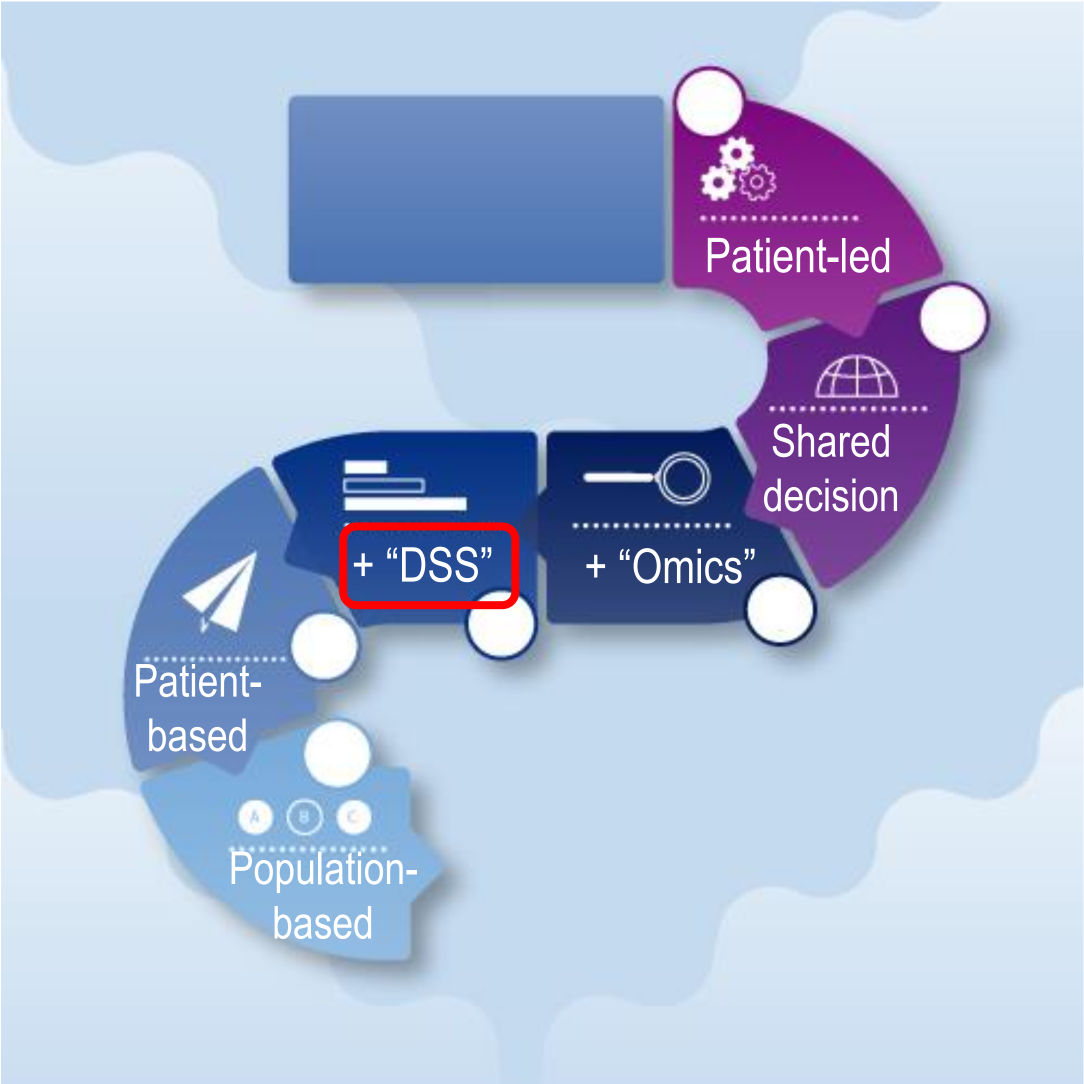
Precision medicine will only progress if the collection and integration of *multimodal* data - qualitative and quantitative - across time, and health status can be facilitated in a responsible manner.

Courtesy of Michel Dumontier

The solution = a virtual machine

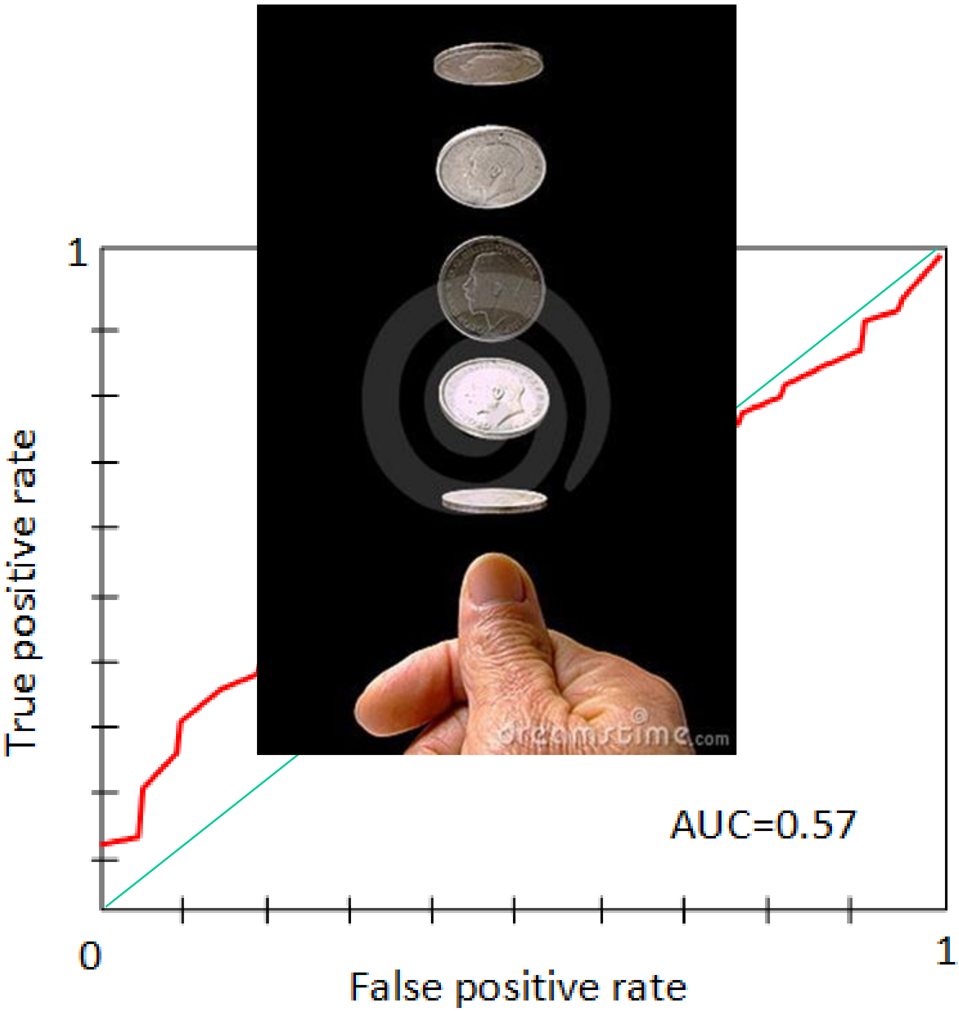


Lambin et al. Nature Rev. Clin. Oncol. 2013



Patient-led
Shared decision
+ “DSS”
+ “Omics”
Patient-based
Population-based

Prediction by RadOnc's? Two years survival of NSCLC



Non Small Cell Lung Cancer

2 year survival

30 patients

8 MDs

Retrospective

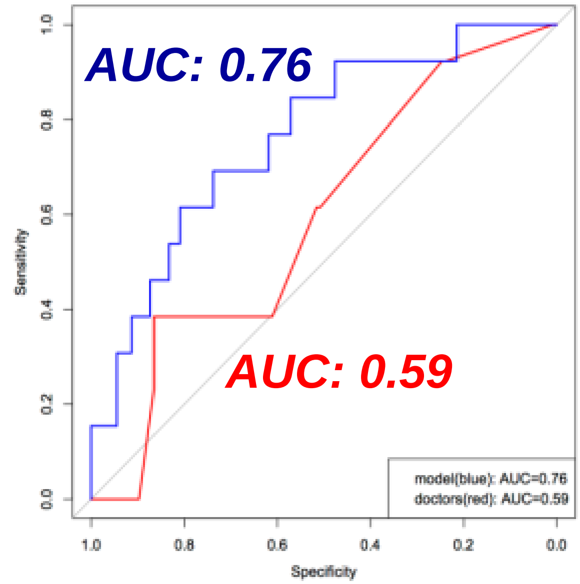
AUC: 0.57 (AUC 0.5 = random)

Cary Oberije *et al.* Radiother Oncol 2014

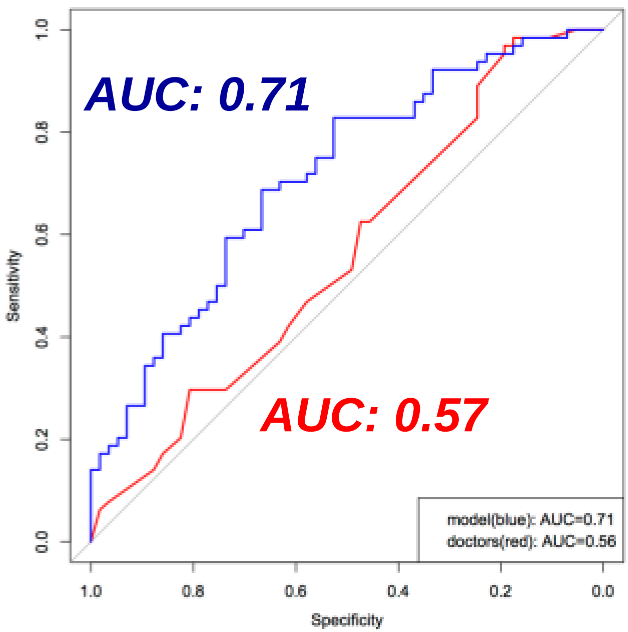
Prospective trial (n=154): Models (blue) always significantly better then Rad Onc (red) & TNM

RO’s
models

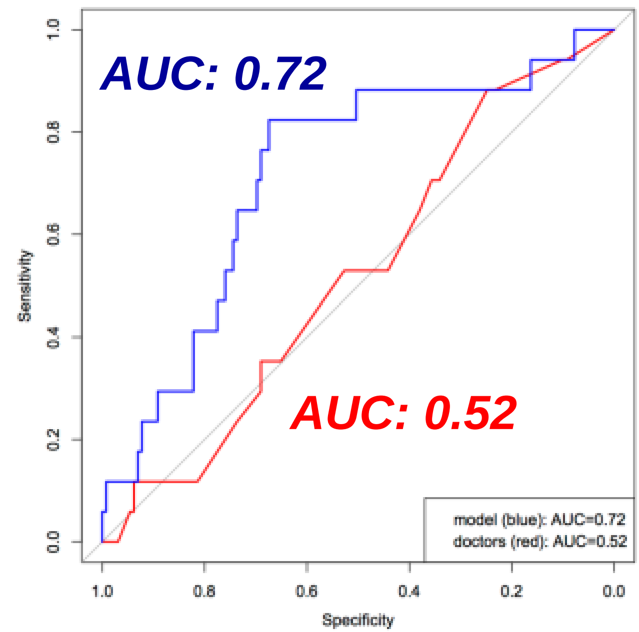
Dyspnea



Death at 2 years



Dysphagia



Cary Oberije et al RadiotherOncol 2014

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Vizury
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omputer models to help
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doctors
ors that affect prognosis
tment option
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Cancer patients could
rather than a doctor
ancer patients may soon have the
n a doctor after scientists devised
ans at predicting how sufferers w
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chemotherapy.
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a computer rather
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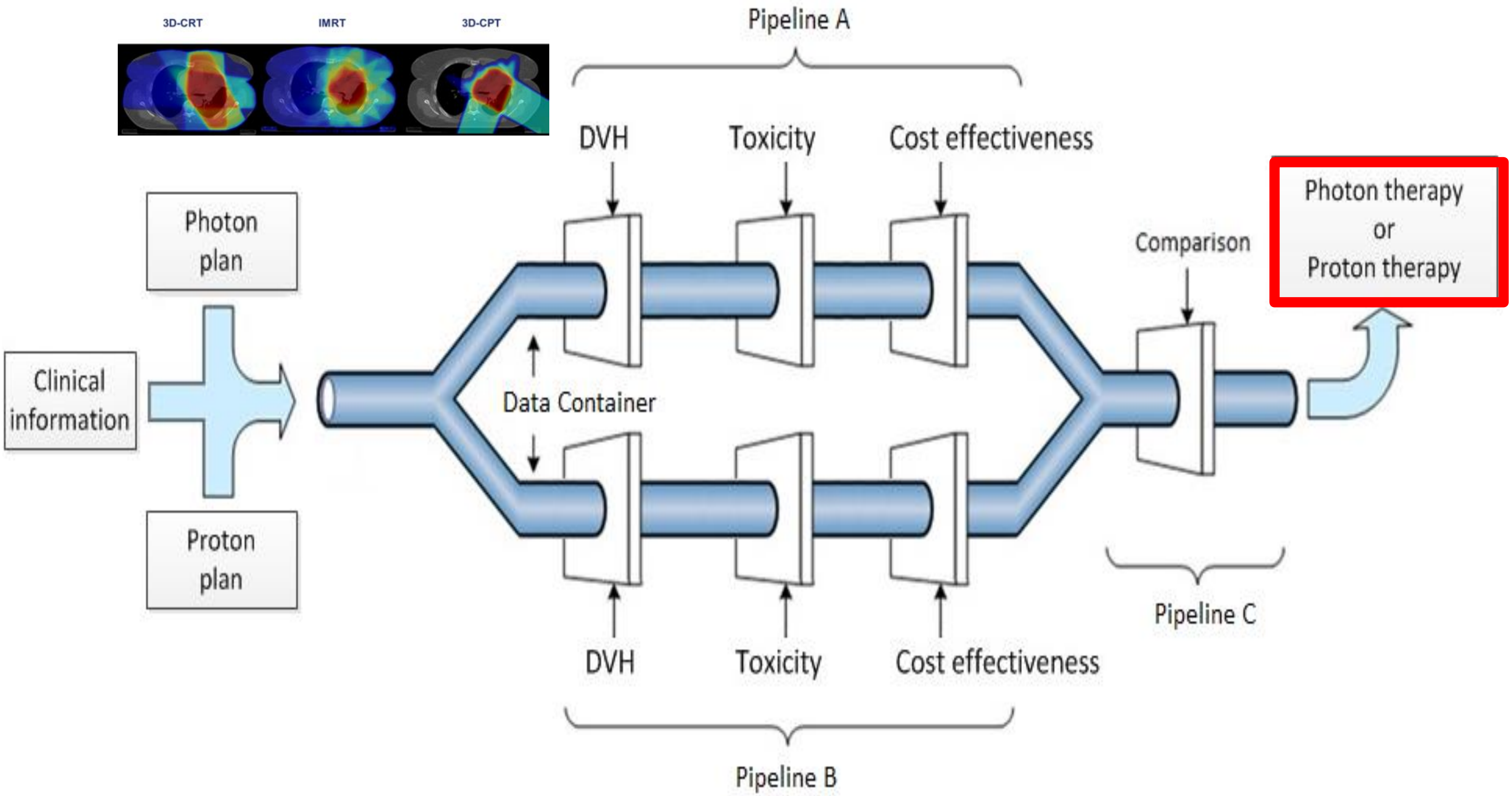
The INDEPENDENT
The computer will cancer prediction than a doctor
Mathematical formulas can outperform do
Steve Connor
22 April 2013
softw
Science
Your source for the latest researc
Mathematical Models Out-Perform Doctors in Predicting Cancer Patients' Responses to Treatment
20, 2013 — Mathematical prediction models are better than doctors at predicting the outcomes and responses of hu
to treatment, according to new research presented today (Saturday) at the 2nd Forum of the European
nd Oncology (ESTRO).

Decision Support System

example 1

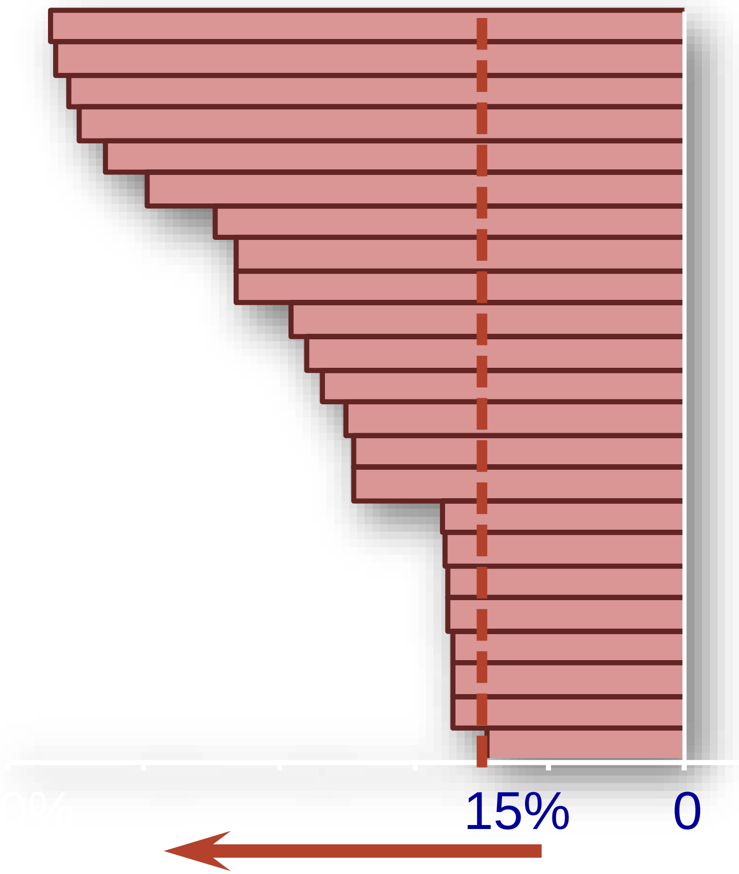
Protons versus photons

Proton therapy Decision Support System



Cheng Q, Roelofs E, Lambin P et al. Radiother Oncol 2016

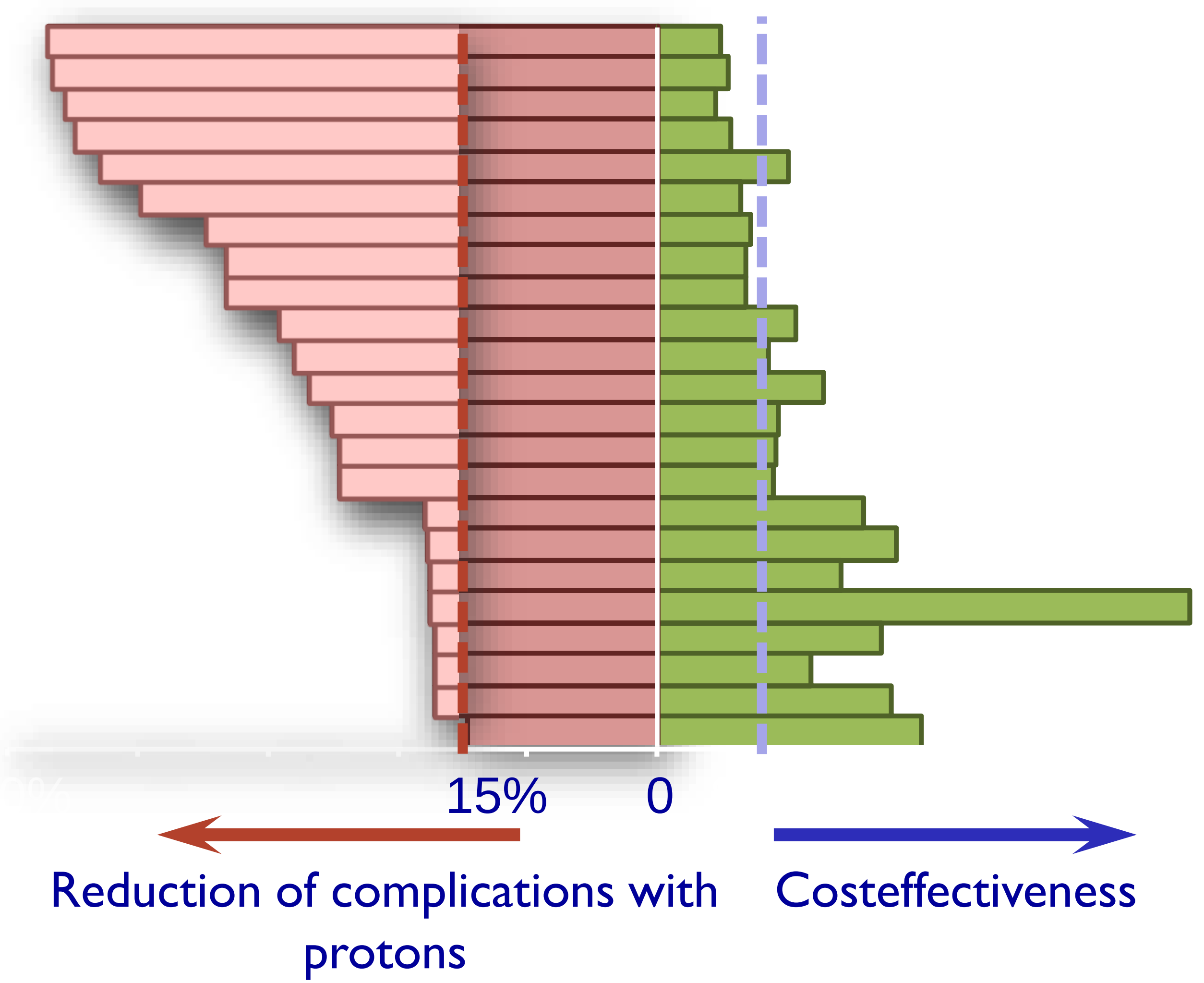
Proton Decision Support for H&N cancer



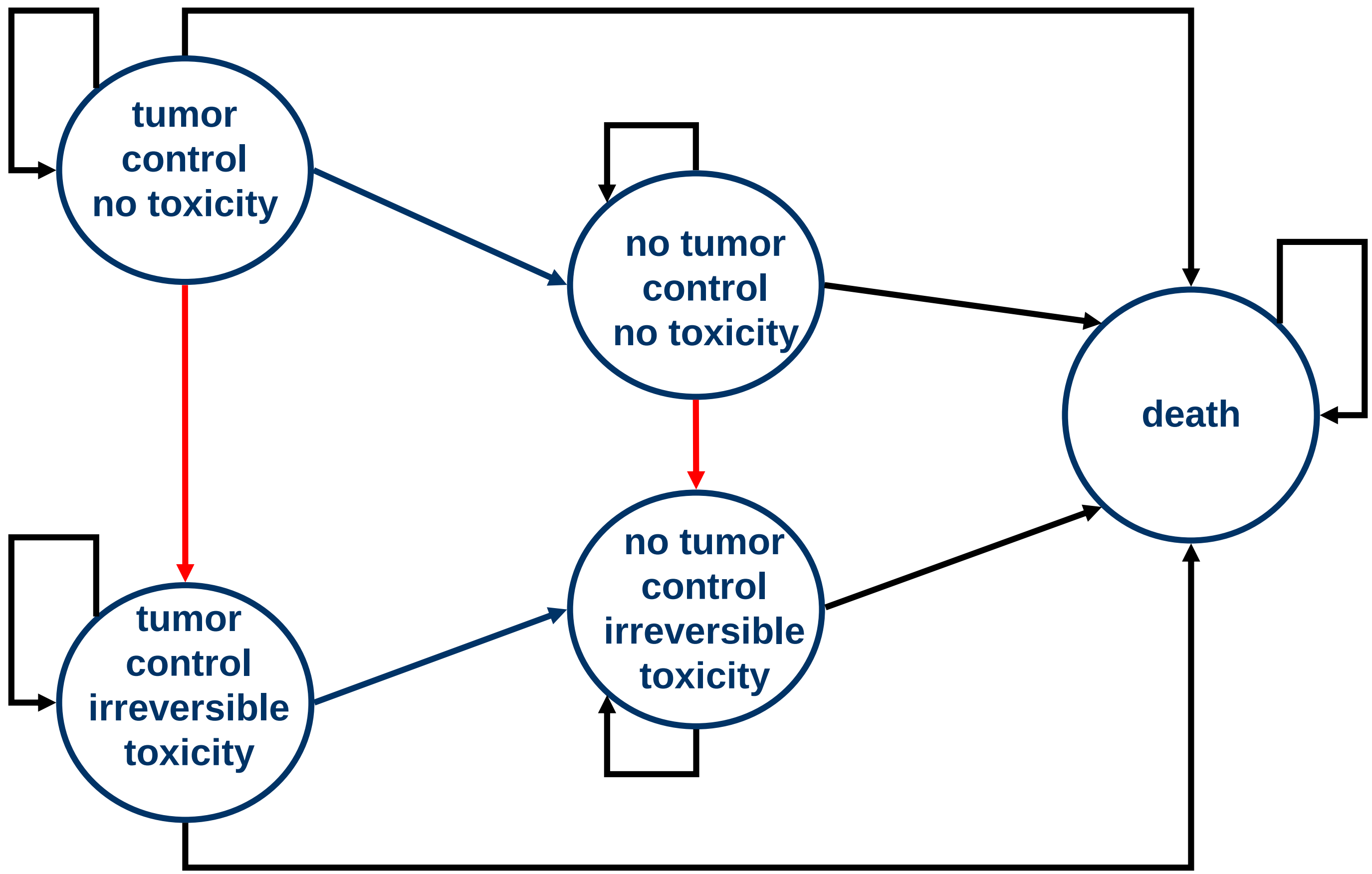
Reduction of complications with protons

Cheng Q, Roelofs E, Lambin P et al. Radiother Oncol 2016

Proton Decision Support for H&N cancer

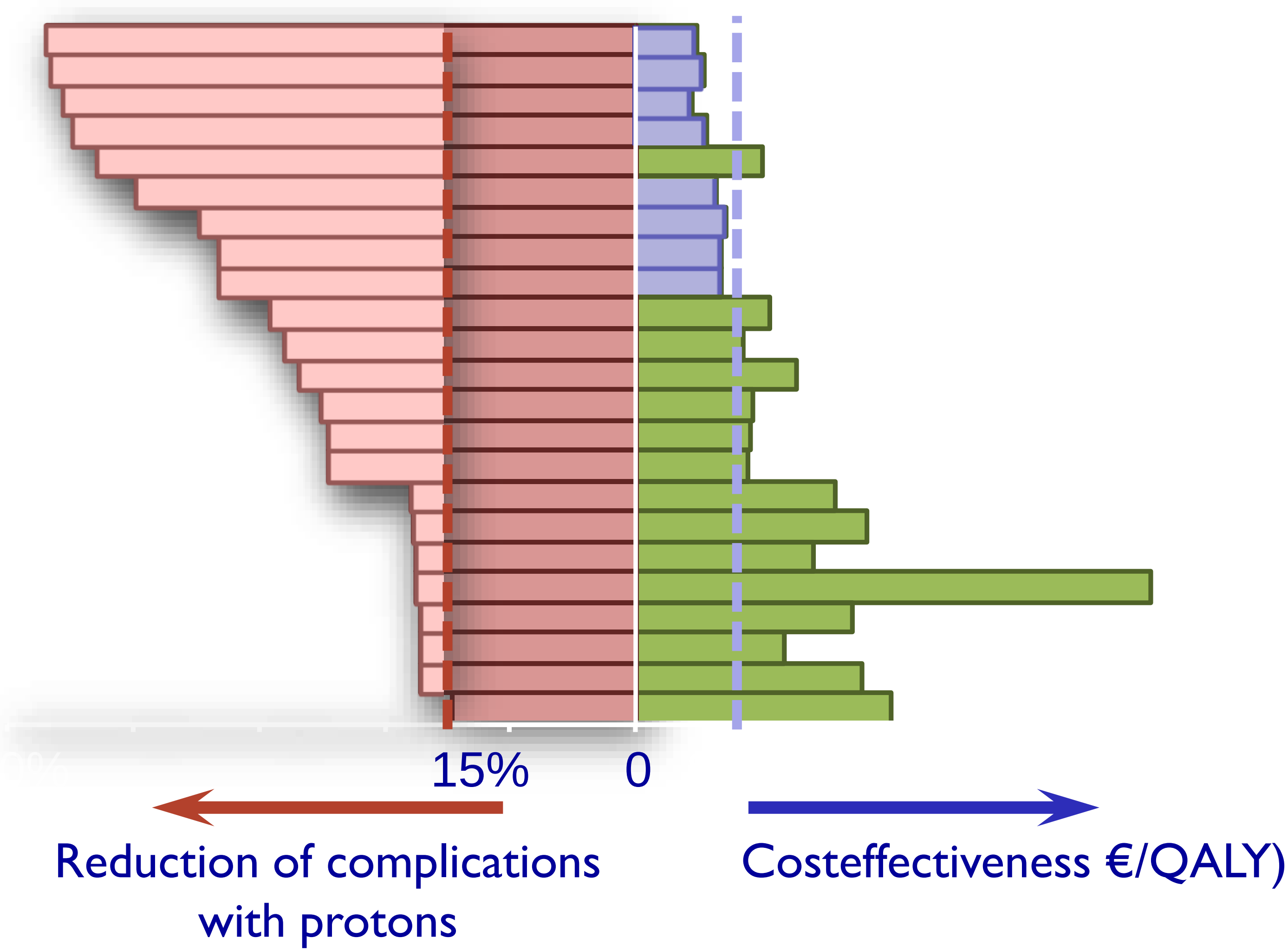


Markov model cost-effectiveness Lung cancer

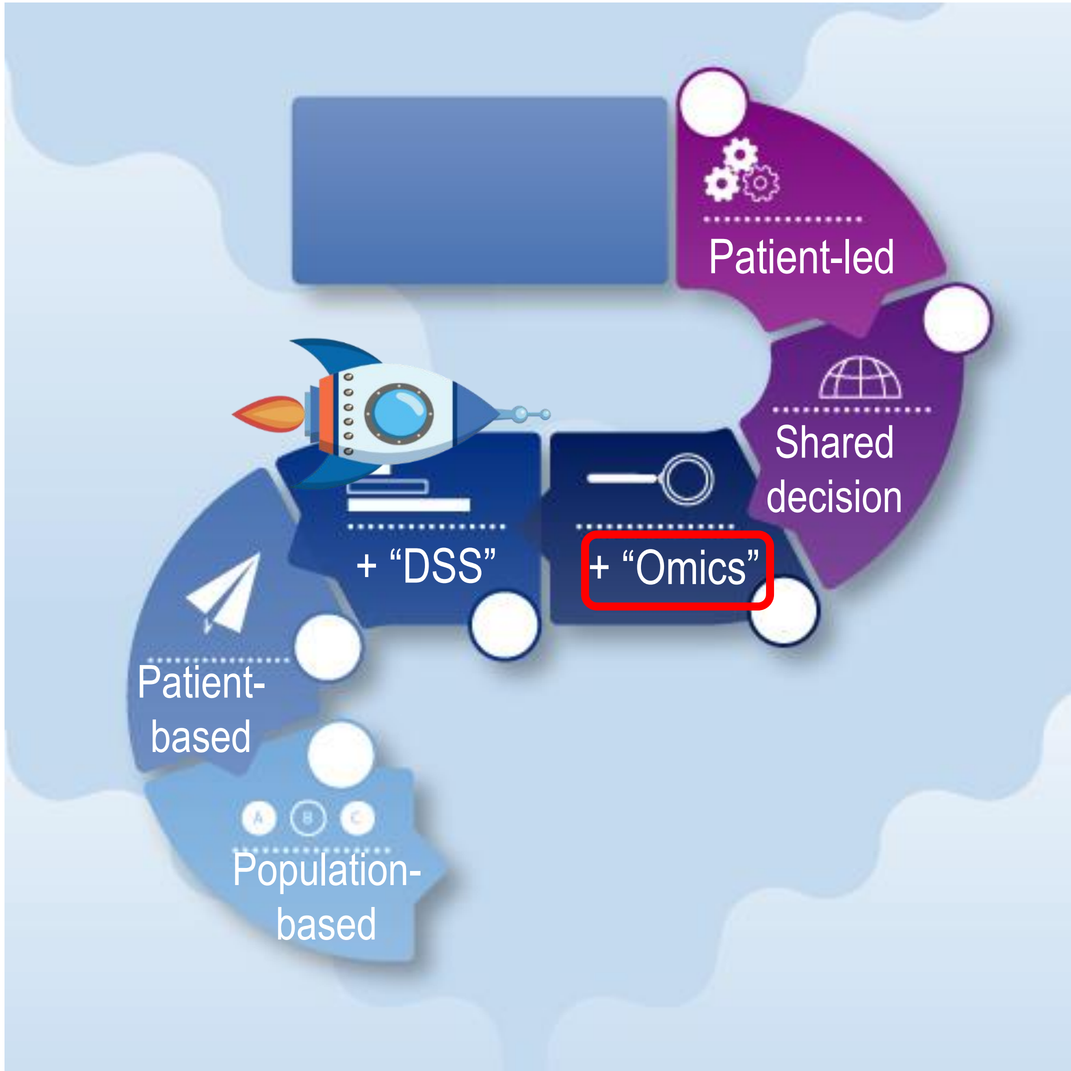


Cheng Q, Roelofs E, Lambin P et al. Radiother Oncol 2016

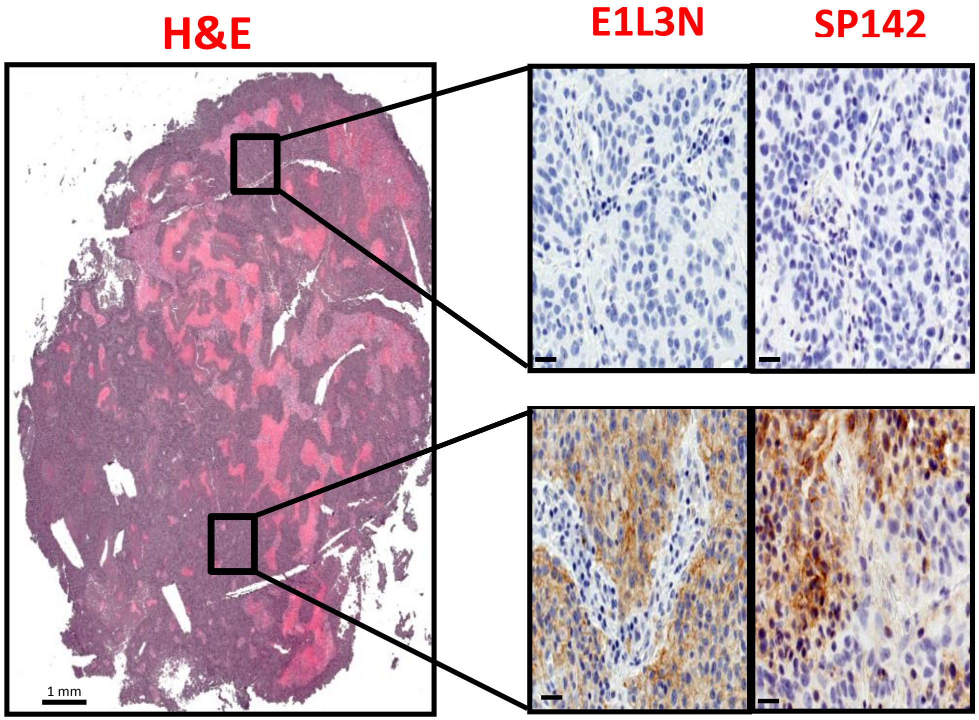
Proton Decision Support for H&N cancer



There are still unknown variables



Cancers are Heterogeneous (RCC)



Rizvi. et al. IASLC WCLC 2016

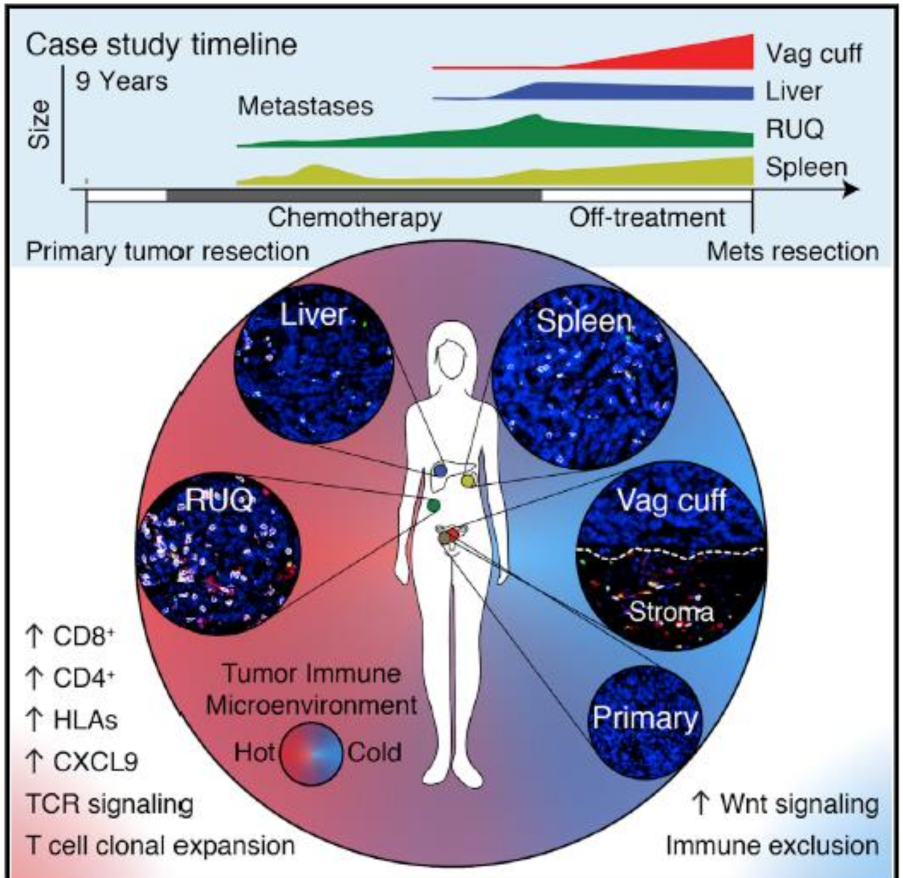
- PD-L1 alone is not an optimal biomarker
- Additional biomarkers are needed….

Article

Cell

Heterogeneous Tumor-Immune Microenvironments among Differentially Growing Metastases in an Ovarian Cancer Patient

Graphical Abstract



Authors

Alejandro Jiménez-Sánchez, Danish Memon, Stephane Pourpe, ..., Taha Merghoub, Alexandra Snyder, Martin L. Miller

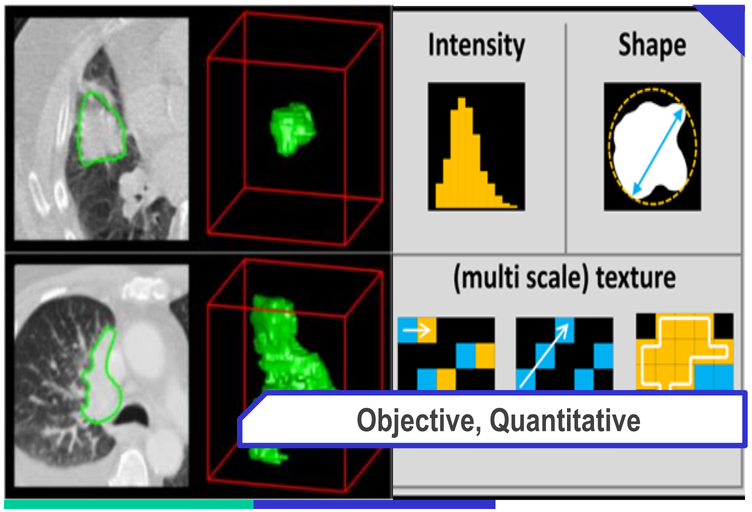
Correspondence

snyderca@mskcc.org (A.S.), martin.miller@cruk.cam.ac.uk (M.L.M.)

In Brief

Distinct tumor immune microenvironments co-exist within a single individual and may help to explain the heterogeneous fates of metastatic lesions often observed post-therapy.

The Radiomics hypothesis



Humans are apes

There is only so much information we can hold at the same time

Quantitative Image Analysis

Will disrupt current interpretative, subjective imaging

Lambin et al. EJC, 2012;; Lambin et al. Nat Rev Clin Oncol 2017

Future of Radiomics: combine information towards “Holomics”, “Panomics” or “Totalomics”

Defining the biological basis of radiomic phenotypes in lung cancer

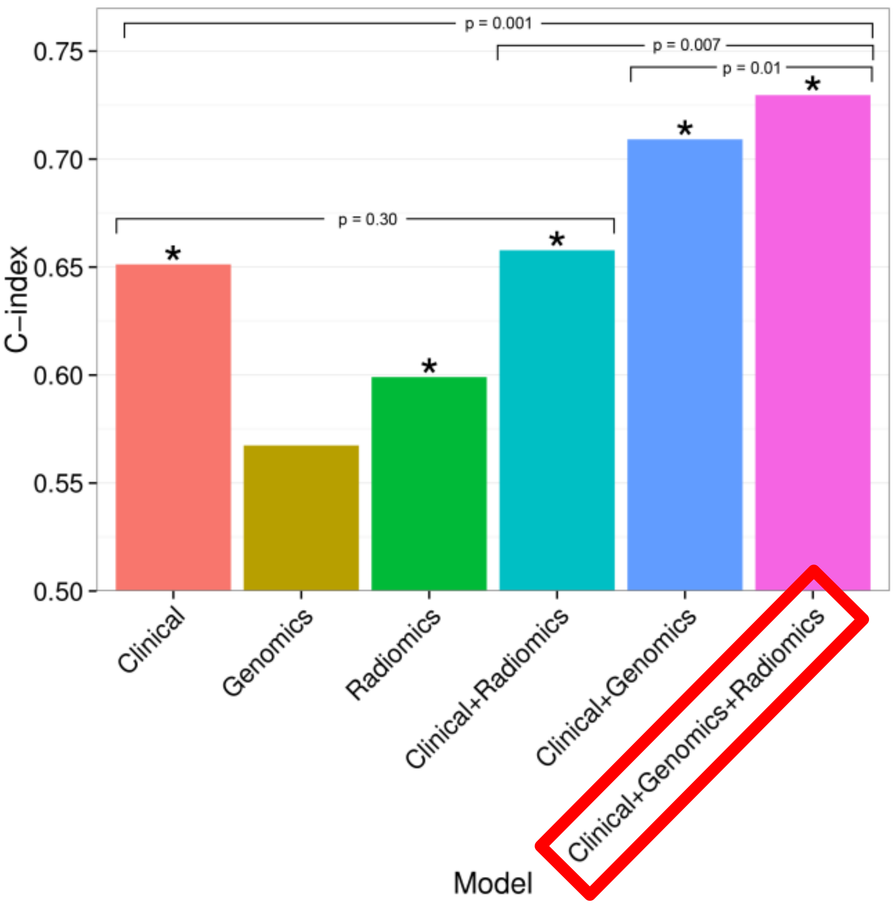
Patrick Grossmann[1,2], Olya Stringfield[3], Nehme El-Hachem[4], Marilyn M Bui[5], Emmanuel Rios Velazquez[1], Chintan Parmar[1,6], Ralph TH Leijenaar[6], Benjamin Haibe-Kains[7,8], Philippe Lambin[6], Robert J Gillies[3], Hugo JWL Aerts[1,2,9]*

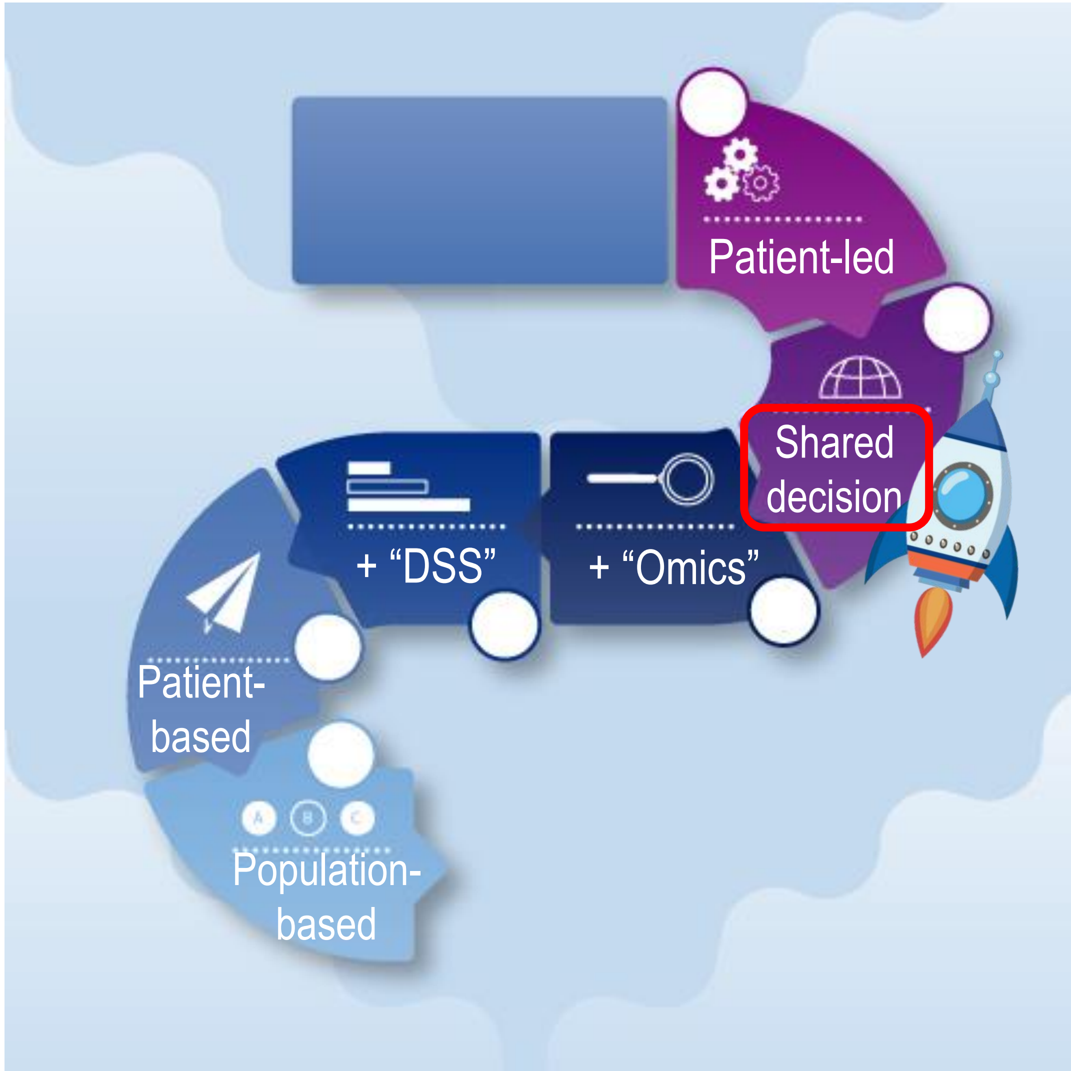
Combining different data types resulted in increased prognostic performances.

[18]F-fluorodeoxyglucose positron-emission tomography (FDG-PET)-Radiomics of metastatic lymph nodes and primary tumor in non-small cell lung cancer (NSCLC) – A prospective externally validated study

Sara Carvalho[1], Ralph T. H. Leijenaar[1], Esther G. C. Troost[1,2,3,4], Janna E. van Timmeren[1], Cary Oberije[1], Wouter van Elmpt[1], Lioe-Fee de Geus-Oei[5,6,7], Johan Bussink[8], Philippe Lambin[1]*

Combining imaging information based on FDG-PET-Radiomics features from tumors and LNs is desirable to achieve a higher prognostic discriminative power for NSCLC.

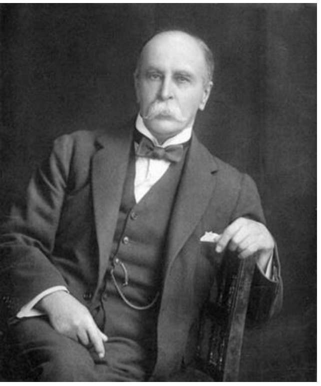



Patient-led
Shared decision
+ "DSS"
+ "Omics"
Patient-based
Population-based

About the 4th « P»: Participatory

"The good physician treats the disease;

the great physician treats the patient who has the disease".



Dr. William Osler, the father of modern medicine

Lambin P *et al.* Adv Drug Deliv Rev. 2017

…Nothing about me without me…

Valerie Billingham, Through the patients eyes. Salzburg seminar sessions 356, 1998.

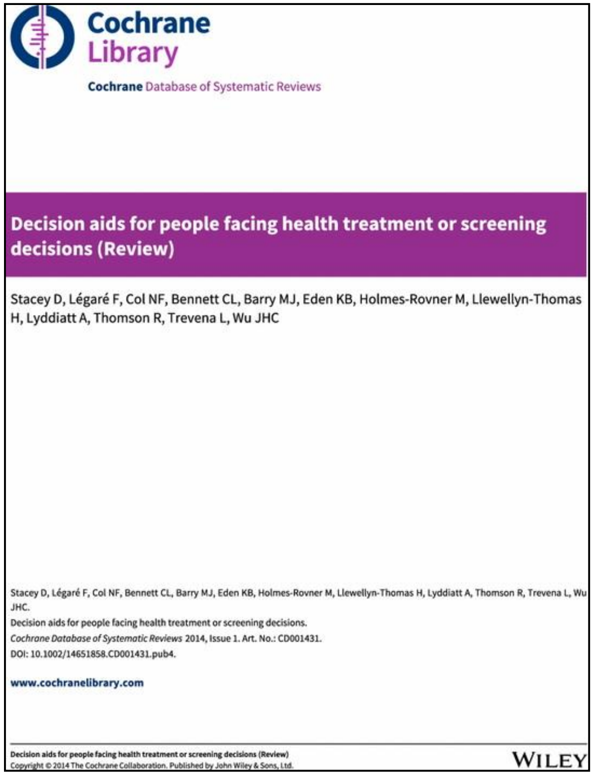
Healthcare in a land called People Power:
***nothing about me without me*.**

Tom Delbanco, MD, Donald M. Berwick, MD, Jo Ivey Boufford, MD, Edgman-Levitan, PA, 4, Gunter Ollenschager MD, Diane Plamping, PhD, and Richard G. Rockefeller, MD .

2001 *Health Expectations*, 4, pp. 144-150.

SDM: The current evidence

Cochrane database of systematic reviews 2017, issue 4. Art. No. C0001431



Cochrane Library

Cochrane Database of Systematic Reviews

Decision aids for people facing health treatment or screening decisions (Review)

Stacey D, Légaré F, Col NF, Bennett CL, Barry MJ, Eden KB, Holmes-Rovner M, Llewellyn-Thomas H, Lyddiatt A, Thomson R, Trevena L, Wu JHC

Stacey D, Légaré F, Col NF, Bennett CL, Barry MJ, Eden KB, Holmes-Rovner M, Llewellyn-Thomas H, Lyddiatt A, Thomson R, Trevena L, Wu JHC.
Decision aids for people facing health treatment or screening decisions.
Cochrane Database of Systematic Reviews 2014, Issue 1. Art. No.: CD001431.
DOI: 10.1002/14651858.CD001431.pub4.

www.cochranelibrary.com

Decision aids for people facing health treatment or screening decisions (Review)
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WILEY

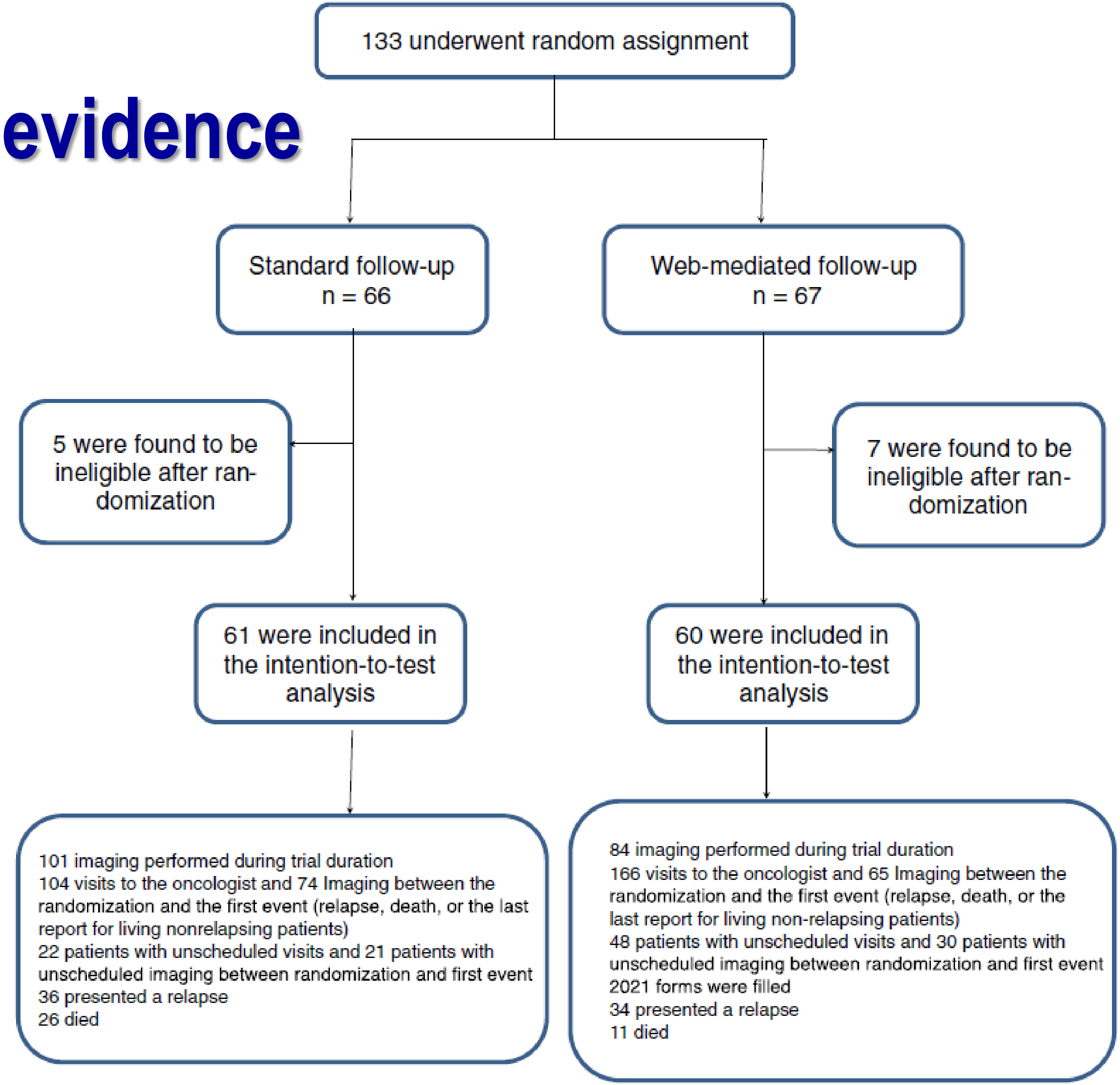
Increase in:

- **Participants' knowledge** (52 studies; N=13.316; ++++)
- **Accuracy** risk of perceptions (17 studies; N=5.096; +++)
- **Congruency** between informed values and care choices (10 studies; N=4.626; ++)

Decrease in:

- **Decisional conflict** (27 studies; N=5.707; +++)
- **Indecision** about personal values (23 studies; N=5.068; +++)
- **Proportion** of passive people in decision making (16 studies; N=3.180; ++)

Patient app: The current evidence



Denis et al. JNCI 2017

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<tr><td>Weight</td><td>65.7</td><td>65.8</td><td>66.4</td><td>66.8</td><td>67.4</td><td>66.8</td><td>66.8</td><td>66.6</td><td>66.6</td><td>67</td><td>67</td><td>66.7</td><td>65</td><td>65</td><td>66</td><td>66.3</td><td>[illegible]</td><td>66.3</td><td>67</td><td>66</td><td>66</td><td>66.5</td><td>[illegible]</td><td>64.6</td><td>[illegible]</td><td>[illegible]</td><td>63.2</td><td>[illegible]</td><td>[illegible]</td></tr>
<tr><td>Weight variation</td><td>-2.7</td><td>-2.8</td><td>-3.4</td><td>-3.8</td><td>-4.4</td><td>-3.8</td><td>-3.8</td><td>-3.6</td><td>-1.7</td><td>-3</td><td>-0.8</td><td>-0.9</td><td>0.7</td><td>0.8</td><td>0.4</td><td>0.5</td><td>[illegible]</td><td>0.5</td><td>-0.2</td><td>0.6</td><td>0.6</td><td>0.5</td><td>[illegible]</td><td>2.1</td><td>[illegible]</td><td>[illegible]</td><td>2.8</td><td>[illegible]</td><td>[illegible]</td></tr>
<tr><td>Appetite loss</td><td>1</td><td>0</td><td>0</td><td>0</td><td>0</td><td>1</td><td>1</td><td>0</td><td>1</td><td>0</td><td>1</td><td>2</td><td>2</td><td>1</td><td>0</td><td>0</td><td>0</td><td>2</td><td>2</td><td>1</td><td>1</td><td>3</td><td>2</td><td>2</td><td>2</td><td>2</td><td>1</td><td>1</td><td>1</td></tr>
<tr><td>Weakness</td><td>1</td><td>1</td><td>2</td><td>1</td><td>2</td><td>2</td><td>1</td><td>1</td><td>2</td><td>1</td><td>0</td><td>3</td><td>3</td><td>1</td><td>1</td><td>1</td><td>2</td><td>2</td><td>2</td><td>2</td><td>2</td><td>2</td><td>1</td><td>2</td><td>2</td><td>2</td><td>2</td><td>2</td><td>1</td></tr>
<tr><td>Pain</td><td>0</td><td>0</td><td>1</td><td>0</td><td>0</td><td>1</td><td>3</td><td>0</td><td>0</td><td>0</td><td>0</td><td>2</td><td>2</td><td>0</td><td>1</td><td>0</td><td>0</td><td>0</td><td>1</td><td>1</td><td>1</td><td>2</td><td>2</td><td>1</td><td>0</td><td>3</td><td>1</td><td>0</td><td>0</td></tr>
<tr><td>Cough</td><td>2</td><td>1</td><td>1</td><td>1</td><td>2</td><td>0</td><td>3</td><td>0</td><td>2</td><td>2</td><td>2</td><td>2</td><td>2</td><td>2</td><td>1</td><td>1</td><td>2</td><td>3</td><td>2</td><td>2</td><td>3</td><td>3</td><td>3</td><td>2</td><td>3</td><td>2</td><td>2</td><td>1</td><td>2</td></tr>
<tr><td>Breathlessness</td><td>1</td><td>1</td><td>2</td><td>1</td><td>2</td><td>1</td><td>2</td><td>1</td><td>2</td><td>2</td><td>2</td><td>0</td><td>2</td><td>1</td><td>1</td><td>0</td><td>1</td><td>2</td><td>2</td><td>2</td><td>2</td><td>2</td><td>2</td><td>2</td><td>2</td><td>2</td><td>2</td><td>1</td><td>1</td></tr>
<tr><td>Depression</td><td>1</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>Fiever</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>1</td><td>0</td><td>0</td><td>0</td><td>0</td><td>1</td><td>1</td><td>1</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>Face swelling</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>1</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>1</td><td>1</td><td>1</td><td>1</td><td>1</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>Lump under skin</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>Voice changing</td><td>0</td><td>0</td><td>1</td><td>0</td><td>0</td><td>1</td><td>1</td><td>1</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>1</td><td>1</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>Blood in sputum</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
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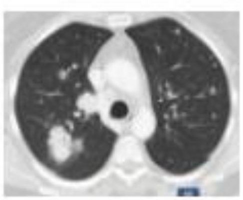
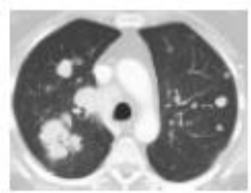
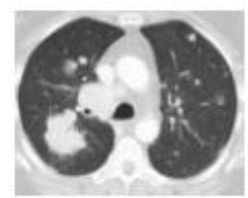
Objective response after induction chemotherapy: Maintenance



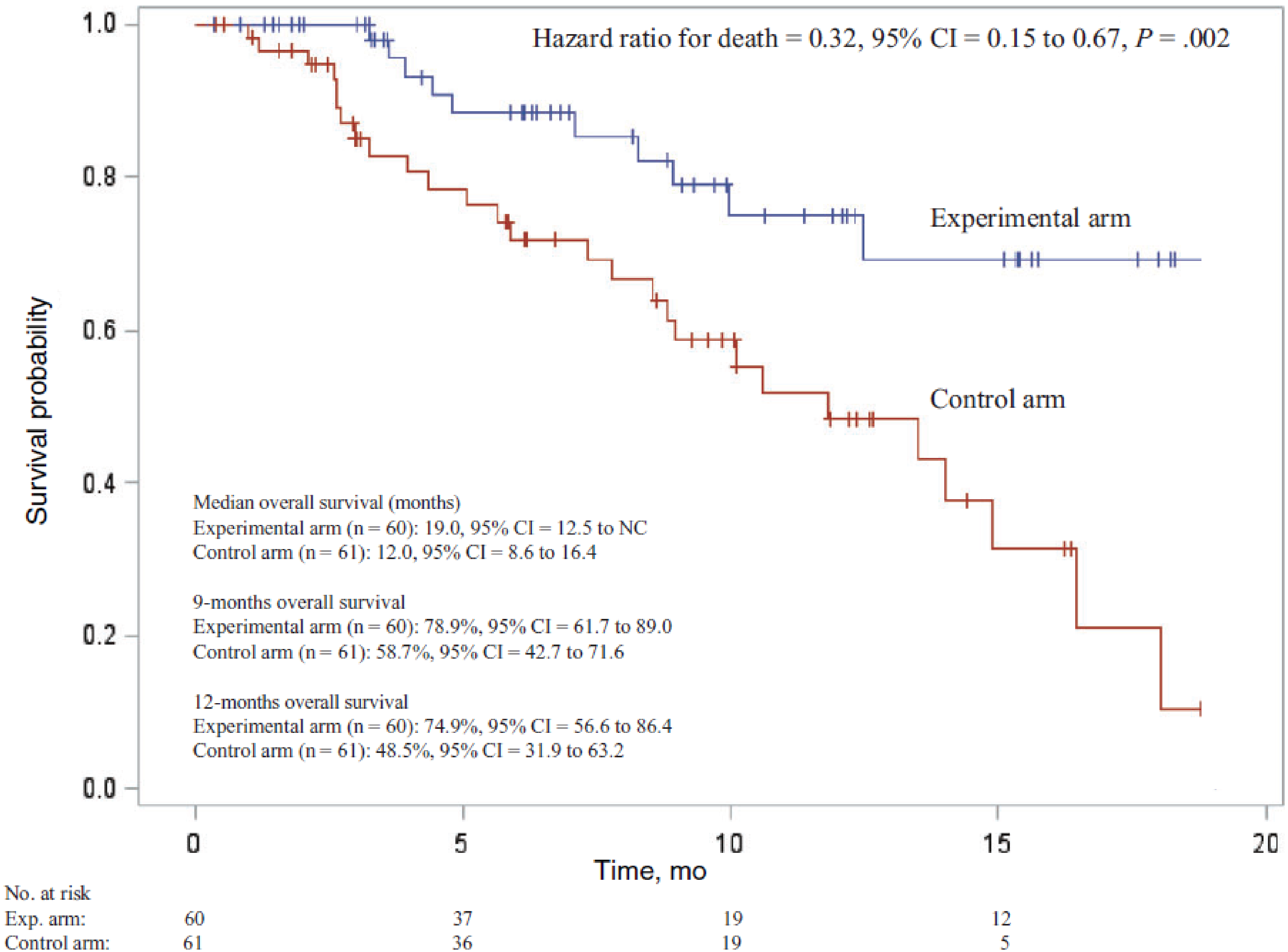
Progression:
➜ Docetaxel



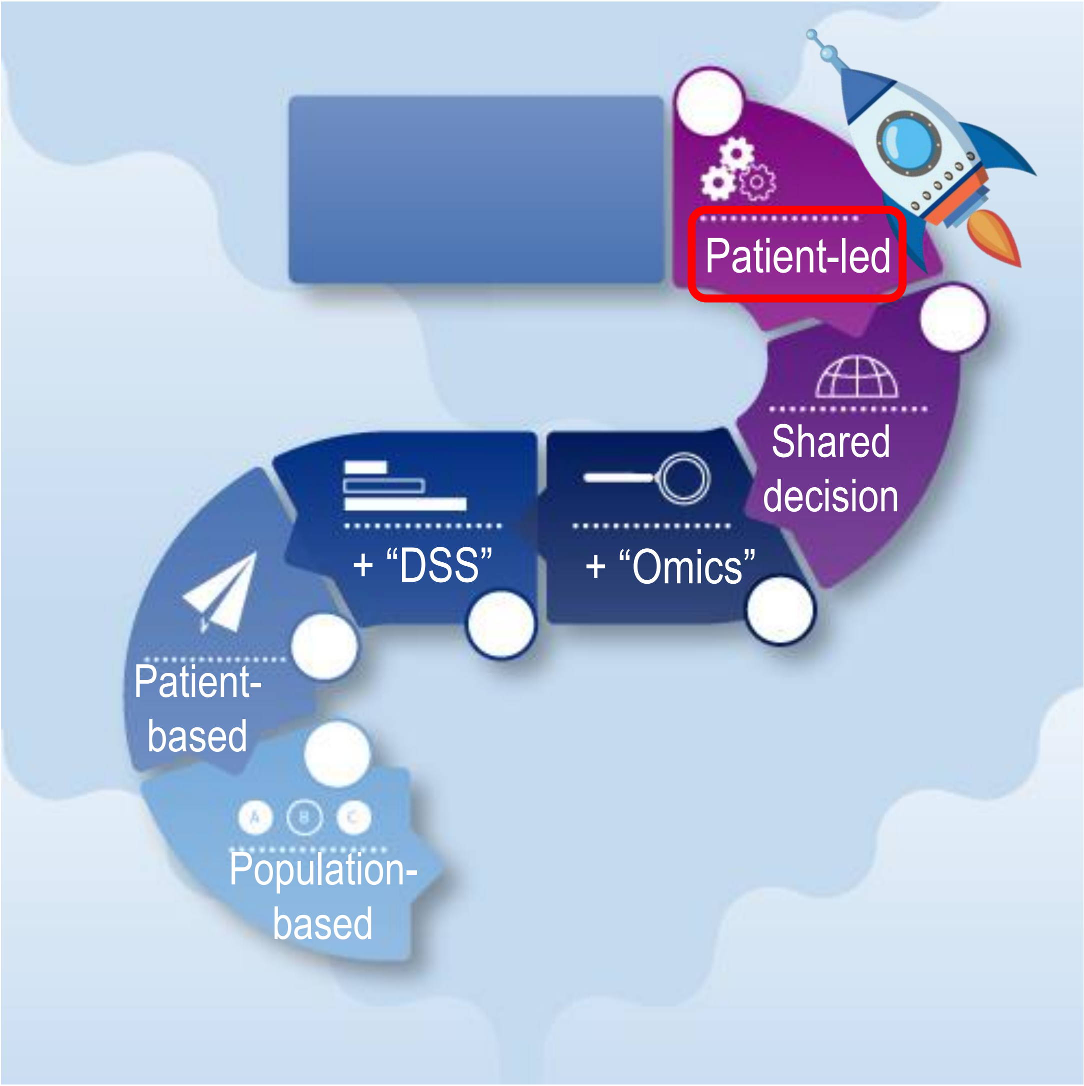
Progression:
➜ Nivolumab



Denis et al. JNCI 2017

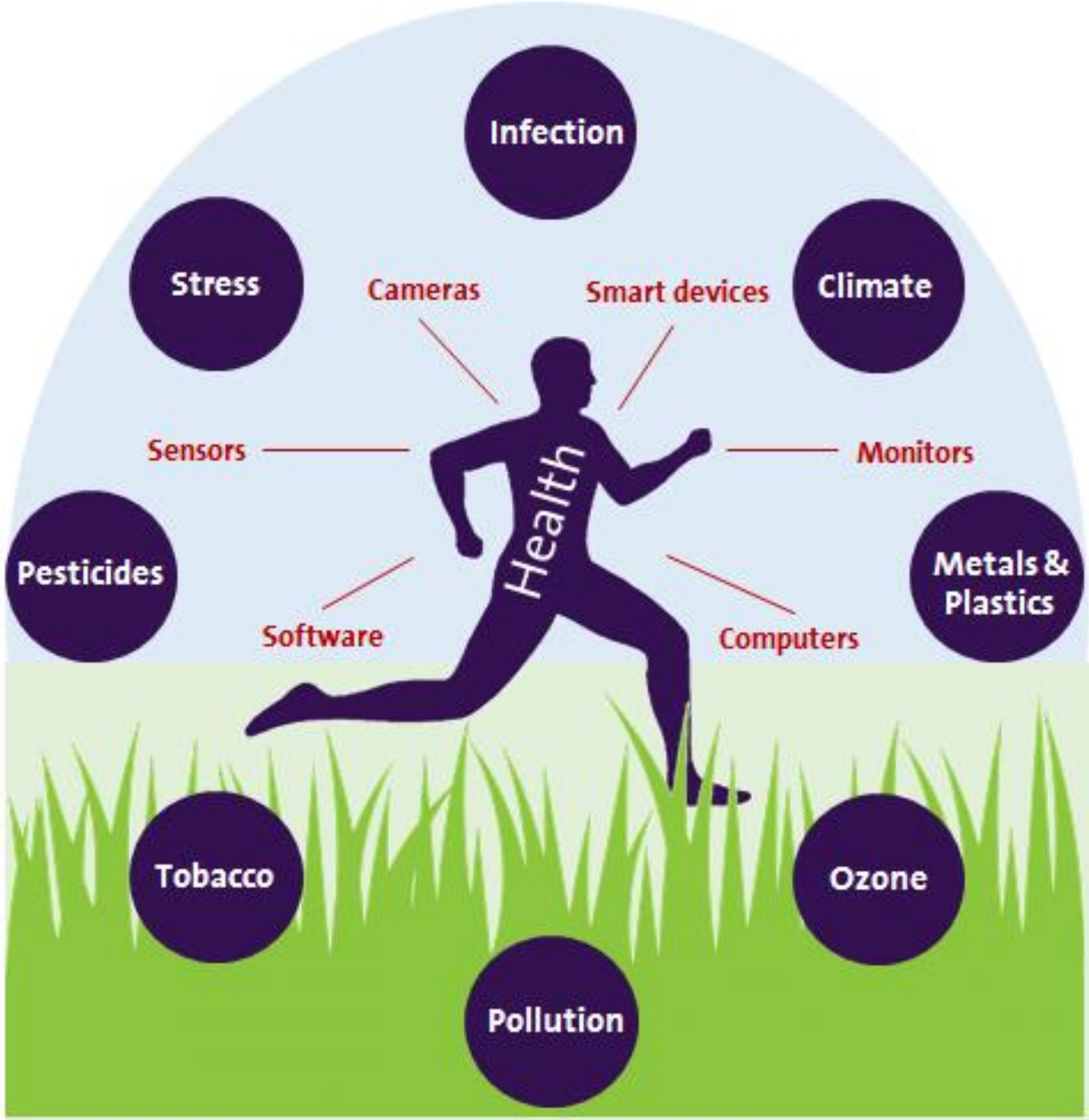


Denis et al. JNCI 2017



Patient-led
Shared decision
+ "Omics"
+ "DSS"
Patient-based
A B C
Population-based

The Exposome, adapted from NIH



What's next?

The patient managing its own data
= *Patient Electronic Health Record*

Data = 

Conclusions

- Healthcare challenges in the 21st Century
  - Too much information
  - Aging of the population “the silver tsunami”
  - Lack of evidence of treatment efficacy
  - Tension solidarity >< privacy
  - Increase costs
  - Request for more participative medicine

- There is evidence level 1 in favor of Shared Decision making (« Participatory Medicine »)

My Opinion

The clinicians who do not use A.I., will be replaced by the clinician who does.

Thank you for your attention

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Acknowledgments

"The D-Lab team"

visit: www.thedlab.info

"The M-Lab team"

website under construction

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erc

NWO

KWF
KANKER
BESTRIJDING

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