26th, september 2019, Institut Curie

Artificial intelligence for medecine: long on **promise**, short of **proof** ?

Dr Anne-Sophie HAMY-PETIT, MD, PhD

Residual Tumour and Response to Treatment
RT2Lab, INSERM U932, Immunity and Cancer
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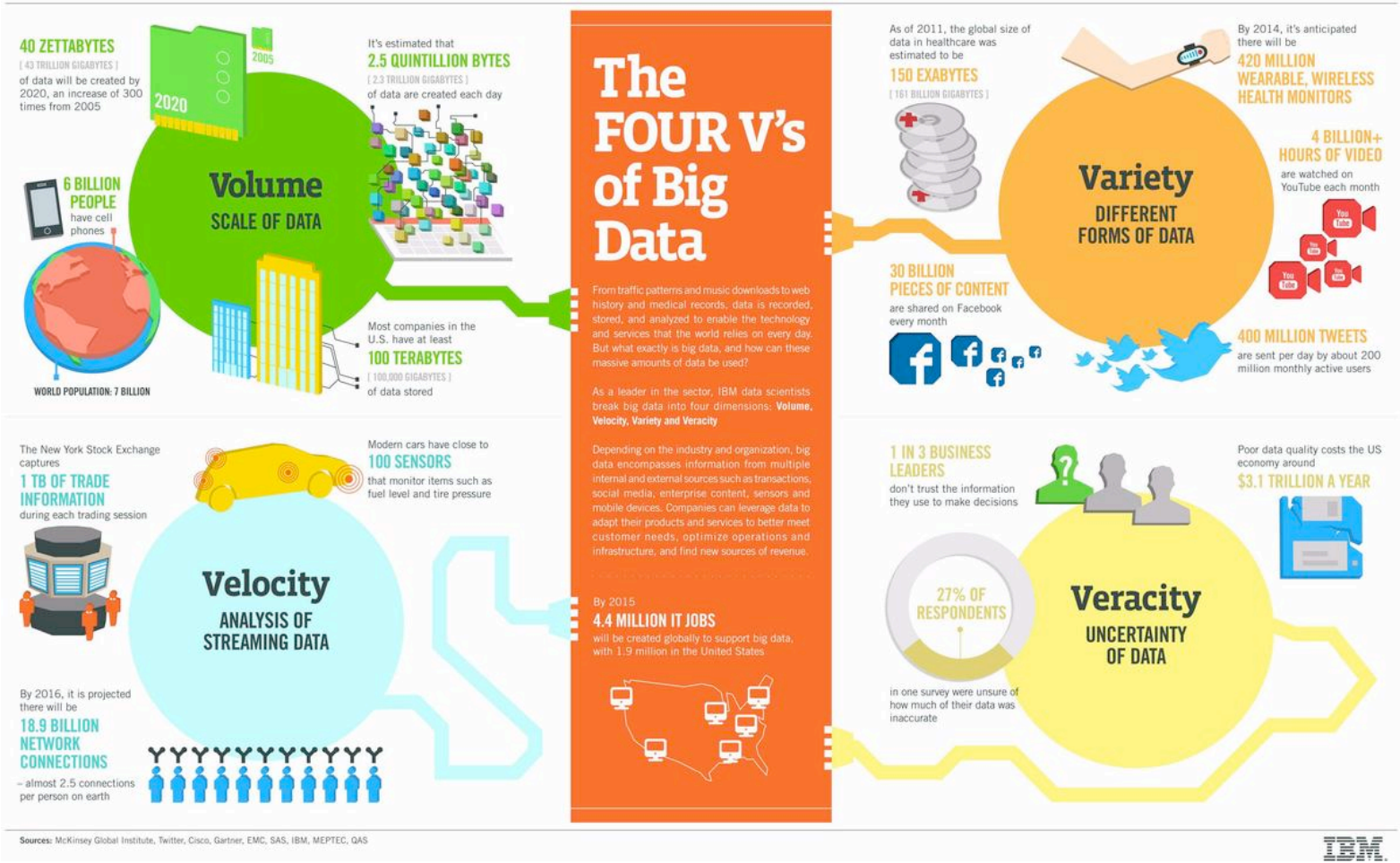
Previously, in the early 2010's, the **big data** era



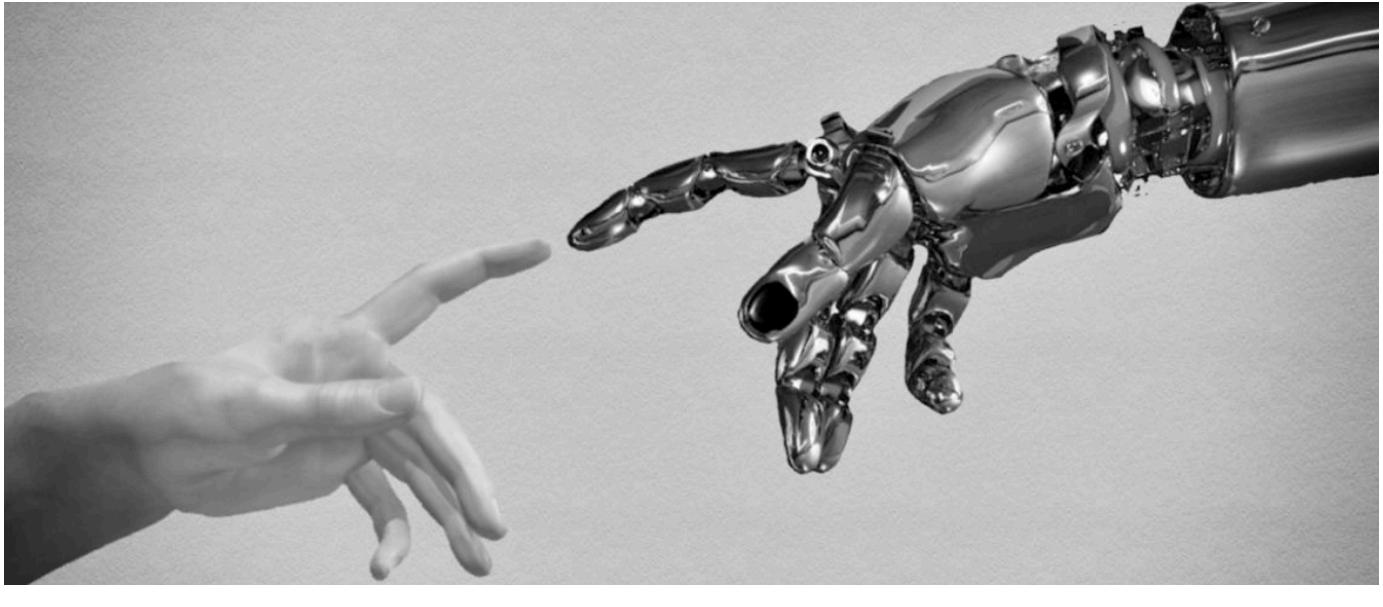
and the new buzzword is …… « **Artificial Intelligence** » !!!

artificial intelligence noun

Definition of *artificial intelligence*

1 : a branch of computer science dealing with the simulation of intelligent behavior in computers

2 : the capability of a machine to imitate intelligent human behavior



Machine learning - Deep learning

- Digitized **inputs**
- proceeding through **multiple layers** of **connected 'neurons'** that progressively detect features,
- Provides an **output**.
- **Autodidactic** quality; the neural network is not designed by humans, is determined by the **data itself**.
- **Supervised learning**, with training from known patterns and labeled input data

Deep neural network DDN / Réseaux de neurones

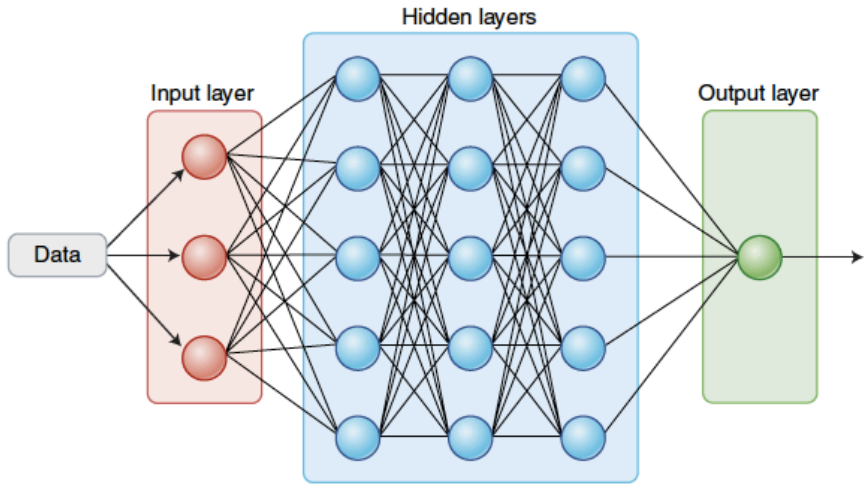


Fig. 1 | A deep neural network, simplified. Credit: Debbie Maizels/Springer Nature

*- Analytics are performed on previously **generated data in silico**, not prospectively in **real-world clinical conditions**.*
*- Lack of **large datasets of carefully annotated images** has been limiting across various disciplines in medicine.*

Radiology

Table 1 | Peer-reviewed publications of AI algorithms compared with doctors

Specialty	Images	Publication
Radiology/ neurology	CT head, acute neurological events	Titano et al. [27]
	CT head for brain hemorrhage	Arbabshirani et al.[19]
	CT head for trauma	Chilamkurthy et al.[20]
	CXR for metastatic lung nodules	Nam et al.[8]
	CXR for multiple findings	Singh et al.[7]
	Mammography for breast density	Lehman et al.[26]
	Wrist X-ray*	Lindsey et al.[9]

- **Increase efficiency** : per day, AI would process over 250 million images for the cost of about $1,000 !
- **AI-assisted** image interpretation and **clinician support**

⇒ Increase productivity and workflow gains

Pathology

Pathology	Breast cancer	Ehteshami Bejnordi et al.[41]
	Lung cancer (+driver mutation)	Coudray et al.[33]
	Brain tumors (+methylation)	Capper et al.[45]
	Breast cancer metastases*	Steiner et al.[35]
	Breast cancer metastases	Liu et al.[34]

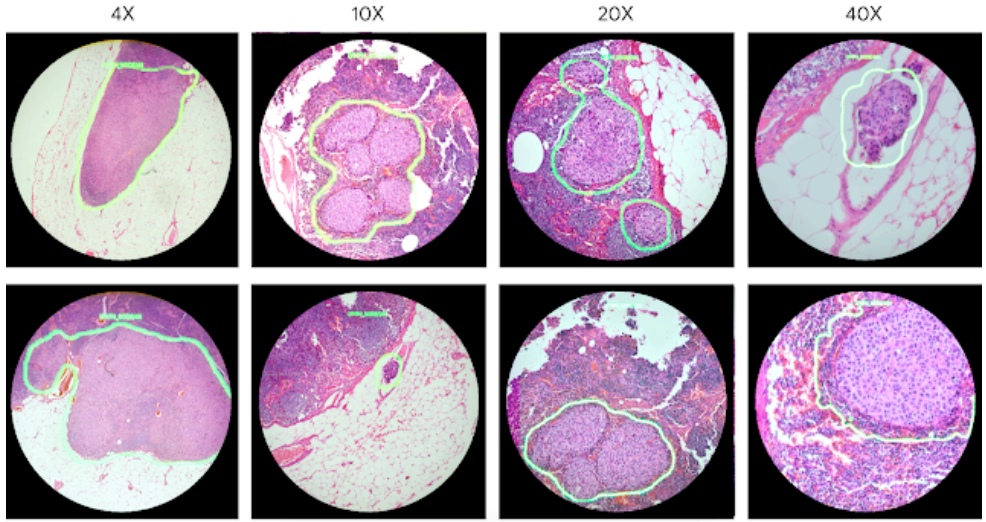
- Slower adoption of digitization of scans than radiologists
- Still not routinely converting glass slides to digital images and use **whole-slide imaging (WSI)**
- Marked heterogeneity and inconsistency among pathologists' interpretations of slides
- Some algorithms perform better than pathologists.
- Highly depending on the **time** given.

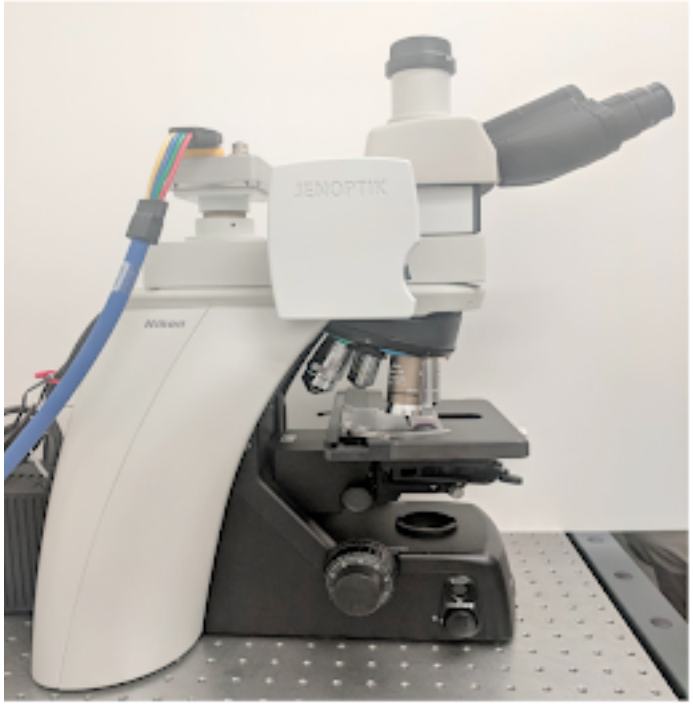
Breast **pathology**

nature medicine
TECHNICAL REPORT
https://doi.org/10.1038/s41591-019-0539-7

An augmented reality microscope with real-time artificial intelligence integration for cancer diagnosis

Po-Hsuan Cameron Chen[1,4], Krishna Gadepalli[1,4], Robert MacDonald[1,4], Yun Liu[1], Shiro Kadowaki[1], Kunal Nagpal[1], Timo Kohlberger[1], Jeffrey Dean[1], Greg S. Corrado[1], Jason D. Hipp[1,2], Craig H. Mermel[1*] and Martin C. Stumpe[1,3*]





https://ai.googleblog.com/2018/04/an-augmented-reality-microscope.html

Dermatology

AI system as good as experts at recognising skin cancers, say researchers

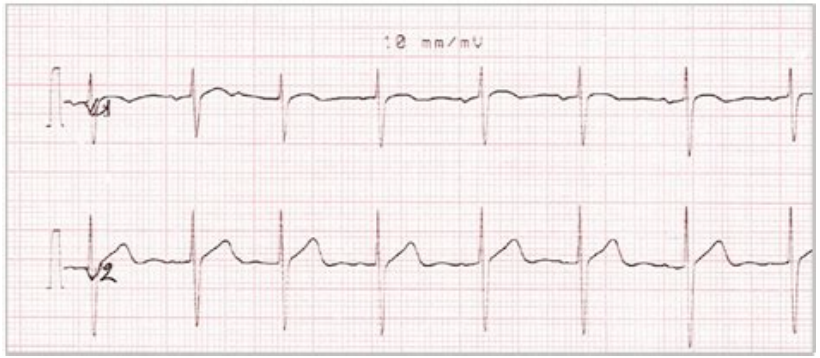
Deep learning-based system could be further developed for smartphones, increasing access to screening and aiding early detection of cancers

Search ⌄ The Guardian International e

Dermatology	Skin cancers	Esteva et al.[47]
	Melanoma	Haenssle et al.[48]
	Skin lesions	Han et al.[49]

Others

Cardiology



Cardiology	Echocardiography	Madani et al.[23]
	Echocardiography	Zhang et al.[24]

Ophtalmology

Ophthalmology	Diabetic retinopathy	Gulshan et al.[51]
	Diabetic retinopathy*	Abramoff et al.[31]
	Diabetic retinopathy*	Kanagasingam et al.[32]
	Congenital cataracts	Long et al.[38]
	Retinal diseases (OCT)	De Fauw et al.[56]
	Macular degeneration	Burlina et al.[52]
	Retinopathy of prematurity	Brown et al.[60]
	AMD and diabetic retinopathy	Kermany et al.[53]

AI and **health systems**

Table 3 | Selected reports of machine- and deep-learning algorithms to predict clinical outcomes and related parameters

Prediction	*n*	AUC	Publication (Reference number)
In-hospital mortality, unplanned readmission, prolonged LOS, final discharge diagnosis	216,221	0.93*0.75+0.85#	Rajkomar et al.[96]
All-cause 3-12 month mortality	221,284	0.93˜	Avati et al.[91]
Readmission	1,068	0.78	Shameer et al.[106]
Sepsis	230,936	0.67	Horng et al.[102]
Septic shock	16,234	0.83	Henry et al.[103]
Severe sepsis	203,000	0.85@	Culliton et al.[104]
Clostridium difficile infection	256,732	0.82++	Oh et al.[93]
Developing diseases	704,587	range	Miotto et al.[97]
Diagnosis	18,590	0.96	Yang et al.[90]
Dementia	76,367	0.91	Cleret de Langavant et al.[92]
Alzheimer's Disease (+ amyloid imaging)	273	0.91	Mathotaarachchi et al.[98]
Mortality after cancer chemotherapy	26,946	0.94	Elfiky et al.[95]
Disease onset for 133 conditions	298,000	range	Razavian et al.[105]
Suicide	5,543	0.84	Walsh et al.[86]
Delirium	18,223	0.68	Wong et al.[100]

LOS, length of stay; *n*, number of patients (training+validation datasets). For AUC values: *, in-hospital mortality; +, unplanned readmission; #, prolonged LOS; ˜, all patients; @, structured+unstructured data; ++, for University of Michigan site.

- Palliative care resources more efficient and precise.
- Very high **likelihood of short-term survival** => patient and doctor make decisions regarding resuscitation, mechanical ventilation,
- Determining **who is at risk** of developing **sepsis** or septic shock ….

- *Most models are essentially classifiers and are not capable of precise prediction at the individual level !!*

- Reduce the **workforce** : coding and billing, scheduling of operating rooms and clinic appointments…

Machine vision

Promoting ***safety*** by monitoring

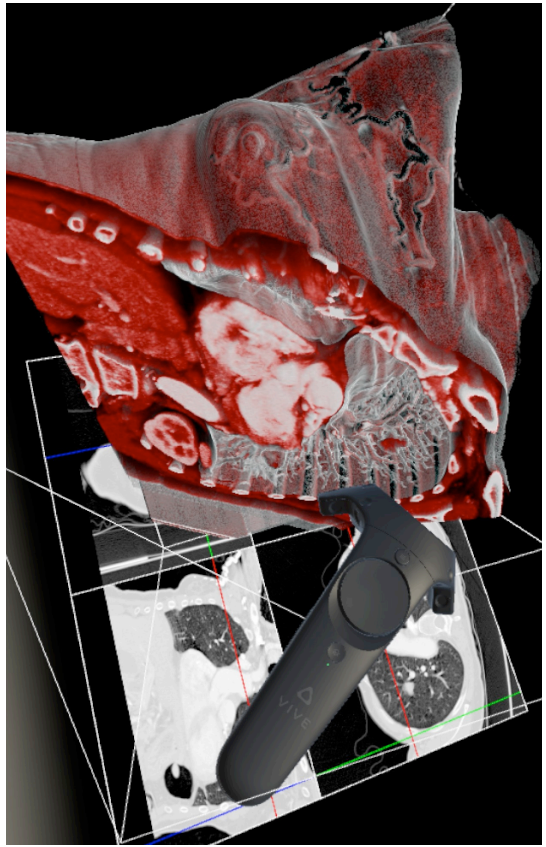
- proper clinician **handwashing**
- critically ill patients in the **intensive care unit**
- risk of **falling** for patients

Digitize ***surgery***

- Machine vision **observation** of the team and equipment in the operating room
- Increase performance of the surgeon; real-time, high-resolution, AI-processed **imaging** of the **relevant anatomy** of a patient;

Preparation for radiotherapy

- via the use of deep-learning algorithms for **image reconstruction**



El Beheiry M 2019 Mar 29;431(7):1315-1321

Wearables

- FDA-approved wearable **sensors** that can continuously monitor all vital signs
  - blood pressure,
  - heart rate and rhythm, blood
  - oxygen saturation,
  - respiratory rate,
  - temperature
- => **Potential** to **preempt** a large number of patients **being hospitalized** in the future.
  - Decreasing the **costs** of care
  - Increasing **comfort** for a patient and family
  - Reduction of **nosocomial** infections

There has not yet been algorithmic development and prospective testing for remote monitoring,

AI and **patients**

- 2017 : Smartwatch algorithm was FDA-cleared to detect **atrial fibrillation**
- In 2018 Apple received FDA approval for their algorithm used with the Apple Watch **Series 4**.
- **Smartphone exams with AI** for medical diagnostic purposes, (*skin lesions and rashes, ear infections, migraine headaches, and retinal diseases…)*.
- Apps are using AI to monitor **medical adherence**
- Continuous sensing of blood-glucose (for 2 weeks) + gut microbiome, physical activity, sleep, medications, all food and beverage intake,

=> ***Ability to predict the glycemic response to specific foods for an individual***

Towards a virtual medical coach?

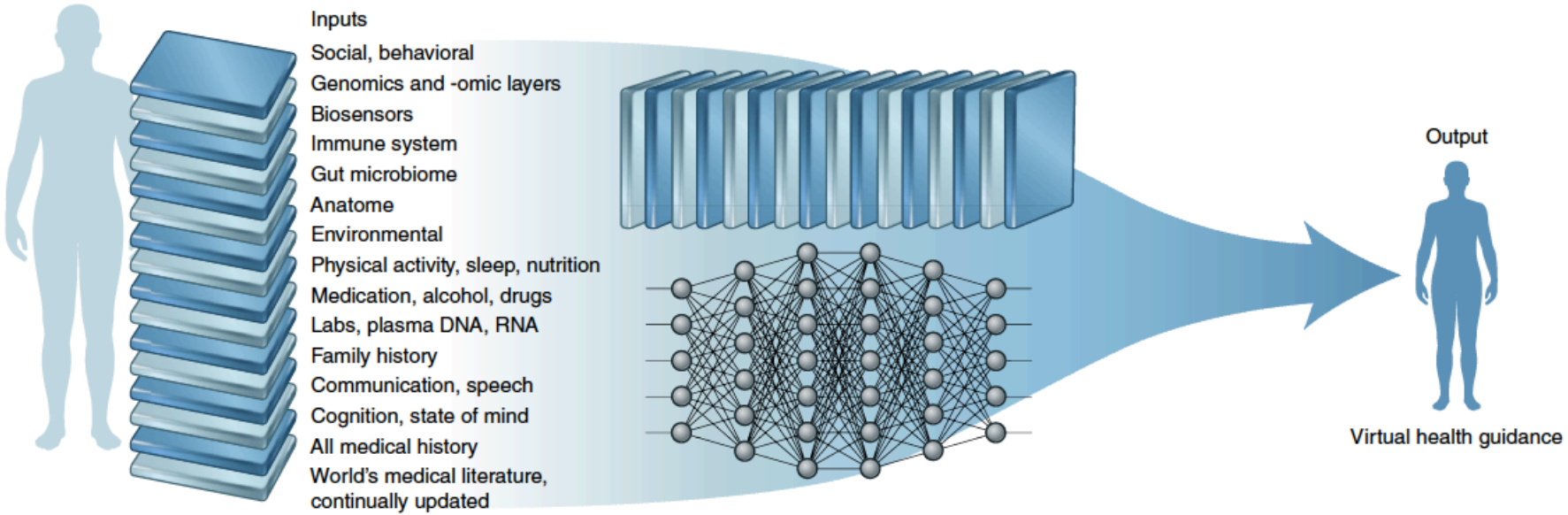


Fig. 3 | The virtual medical coach model with multi-modal data inputs and algorithms to provide individualized guidance. A virtual medical coach that uses comprehensive input from an individual that is deep learned to provide recommendations for preserving the person's health. Credit: Debbie Maizels/ Springer Nature

Promising fields of applications of AI

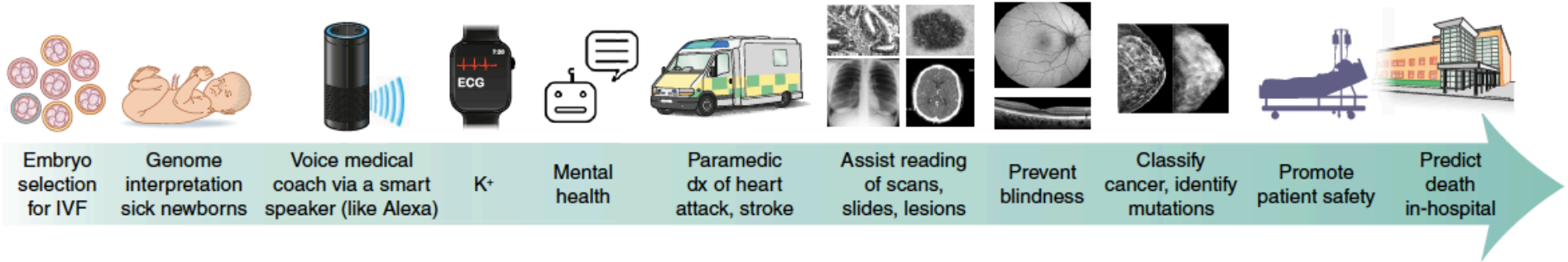
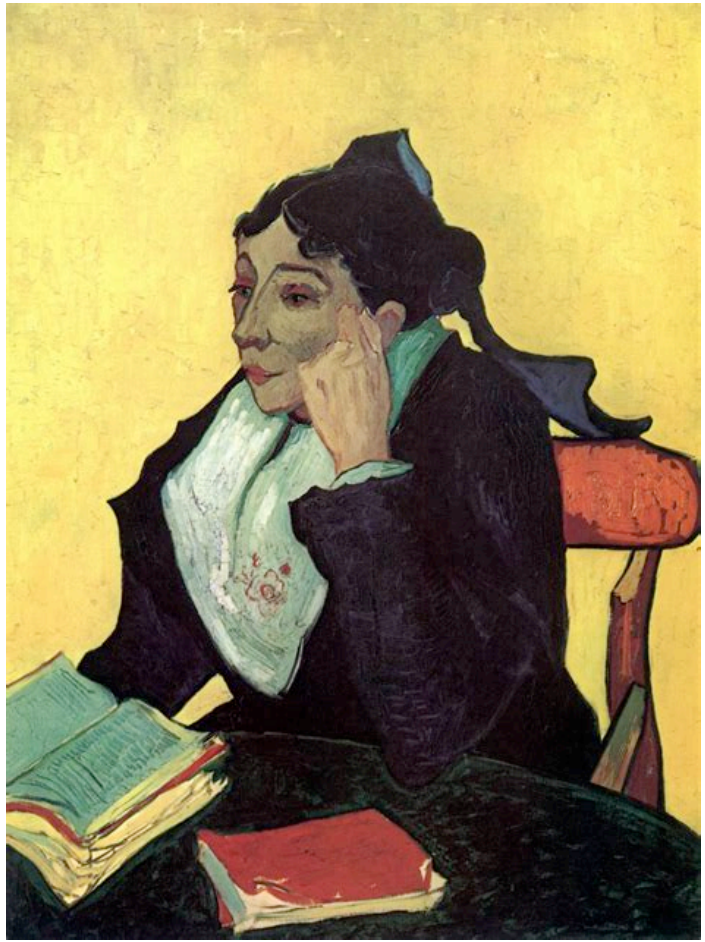


Fig. 2 | Examples of AI applications across the human lifespan. dx, diagnosis; IVF, in vitro fertilization K^+, potassium blood level. Credit: Debbie Maizels/ Springer Nature

AI in my **daily pratice** ?



« L'Arlesienne », Van Gogh, 1888

Watson *for oncology* is an example of AI failure

- Used by hundreds of hospitals around the world
- Recommending treatments for patients with cancer
- Algorithm based on a small number of synthetic, non- real cases with very limited input (real data) of oncologists.

EXCLUSIVE

STAT+

IBM's Watson supercomputer recommended 'unsafe and incorrect' cancer treatments, internal documents show

By CASEY ROSS @caseymross *and* IKE SWETLITZ / JULY 25, 2018

A STAT INVESTIGATION

IBM pitched its Watson supercomputer as a revolution in cancer care. It's nowhere close

By CASEY ROSS @caseymross *and* IKE SWETLITZ / SEPTEMBER 5, 2017

Is AI ***really*** changing medical practice ?

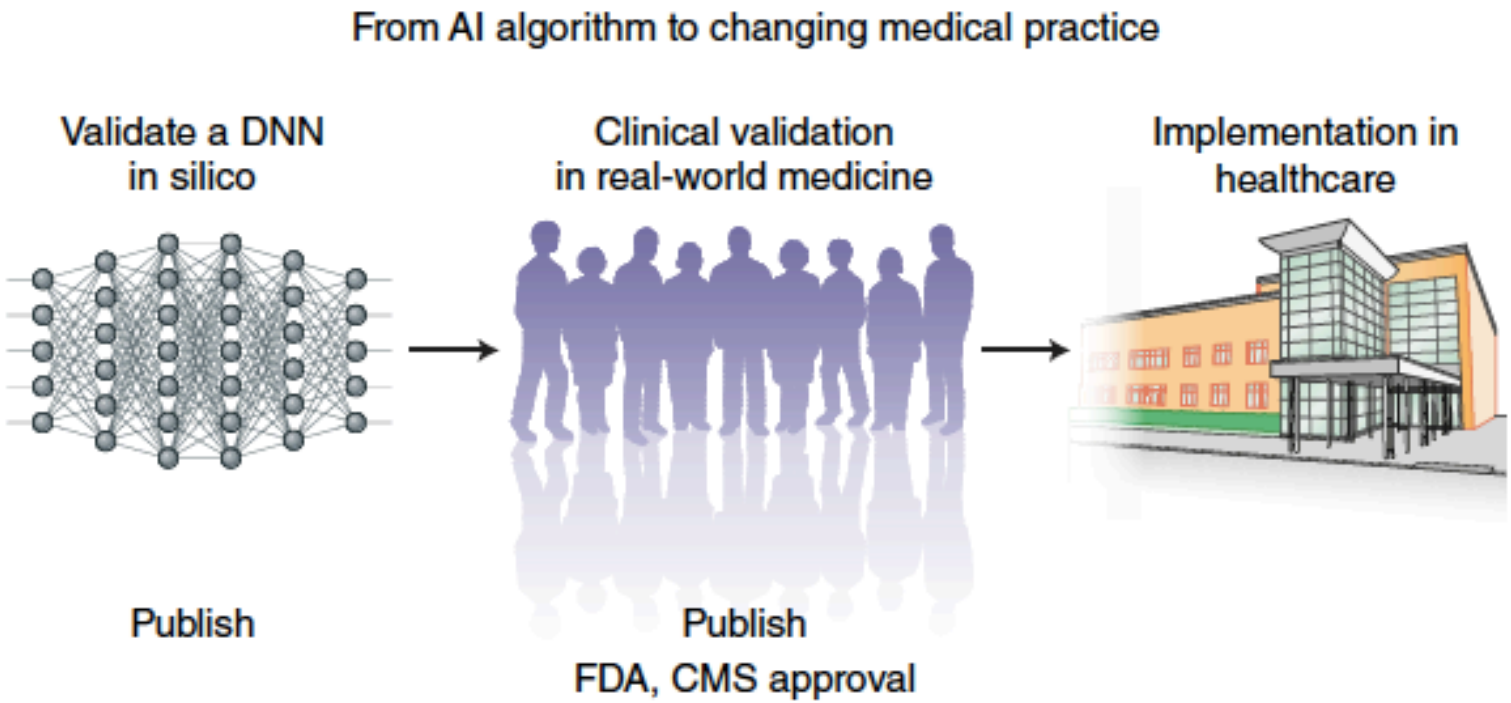
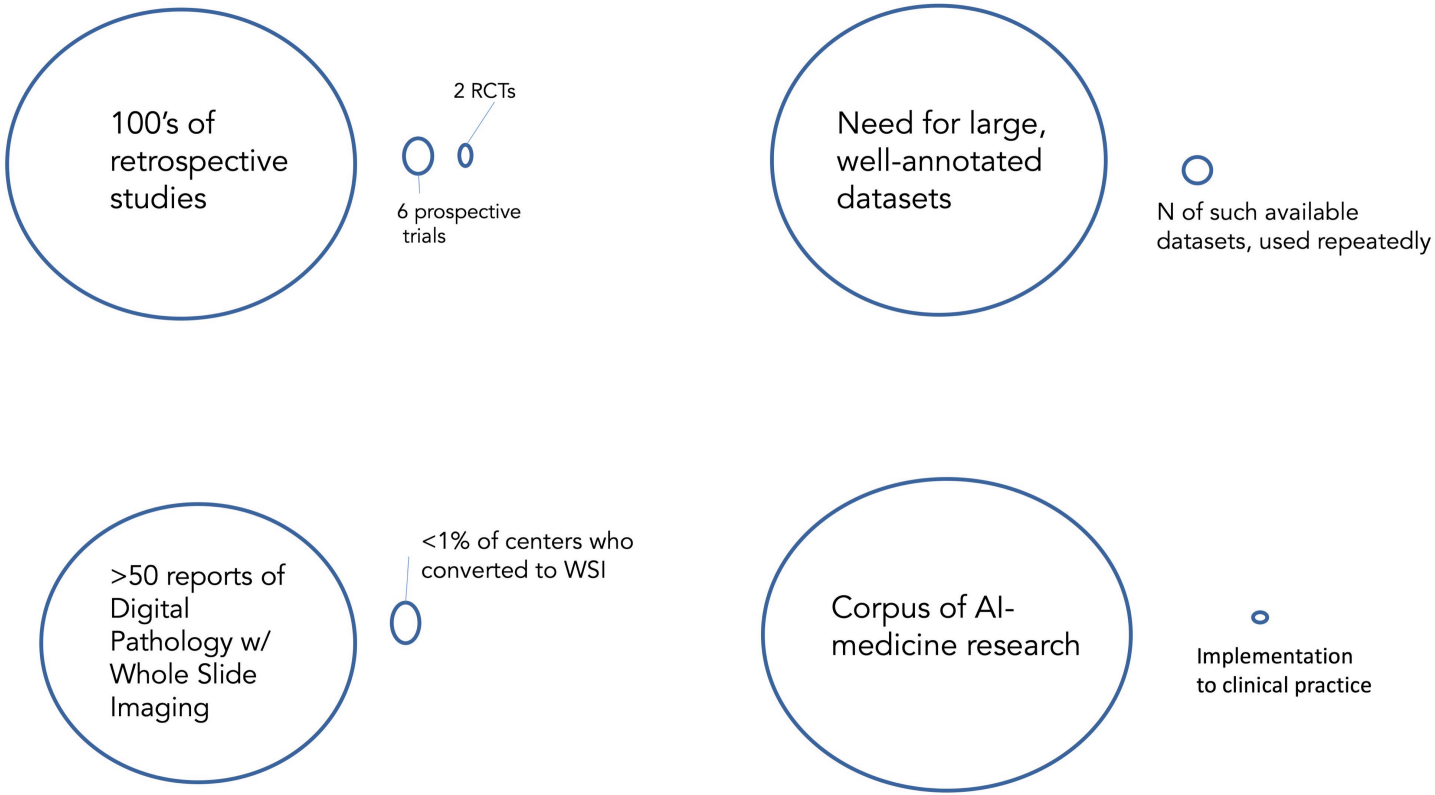


Fig. 4 | Call for due process of AI studies in medicine. The need to publish

Remarkable **lack** of prospective **validation** !



From Eric Topol

Is « **More data more informative** » ?

Digital medicine

Digital orthodoxy of human data collection

From Lancet aug 2019, Eric Topol

Is « **More data more informative** » ?

Digital medicine

Digital orthodoxy of human data collection

From Lancet aug 2019, Eric Topol

Limitations

Algorithms and data

- **Black box** and opaqueness
- **Inequity** : AI may widen the present gap in health outcomes
- Exacerbation inequity : many algorithms lack inclusion of **minorities** in datasets
- Single doctor's mistake hurting a patient # **vast potential** for a machine algorithm inducing **iatrogeny** !!

Privacy and security

- Problems of **hacking** and **data breaches**

- Risk of **deliberate hacking** of an algorithm to harm people at a large scale :

❖ *Overdosing insulin in diabetics*

❖ *Stimulating defibrillators !*

No health data **infrastructure** !

npj | Digital Medicine www.nature.com/npjdigitalmed

PERSPECTIVE OPEN

The "inconvenient truth" about AI in healthcare

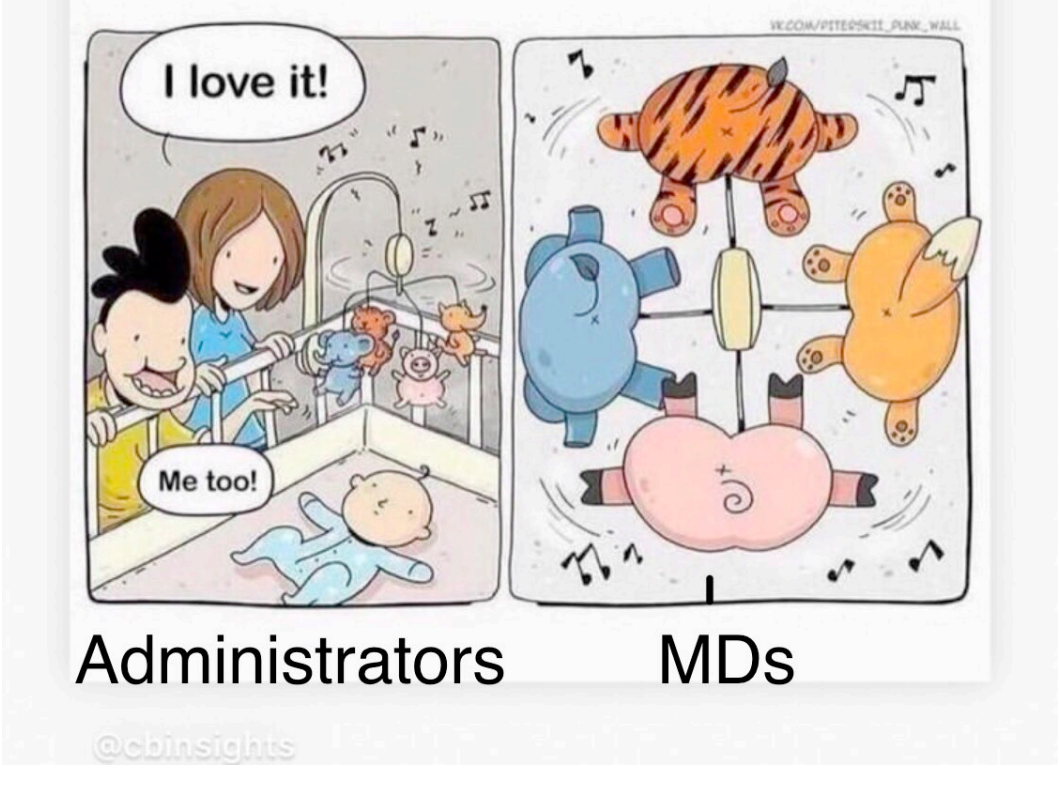
Trishan Panch[1,2], Heather Mattie[2,3] and Leo Anthony Celi[4,5]

npj Digital Medicine (2019)2:77 ; https://doi.org/10.1038/s41746-019-0155-4

- Each healthcare organization has built **its own data infrastructure**
- Most healthcare organizations **lack the data infrastructure** required to collect the data needed to train algorithms to :
  - Fit the **local** population / practices
  - Interrogate for **bias**
- Need for rigourous **evaluation** and **re-calibration** after implementation

⇒ Need to **agregate** data ! Simply adding AI applications to a **fragmented system** will not create substainable change.

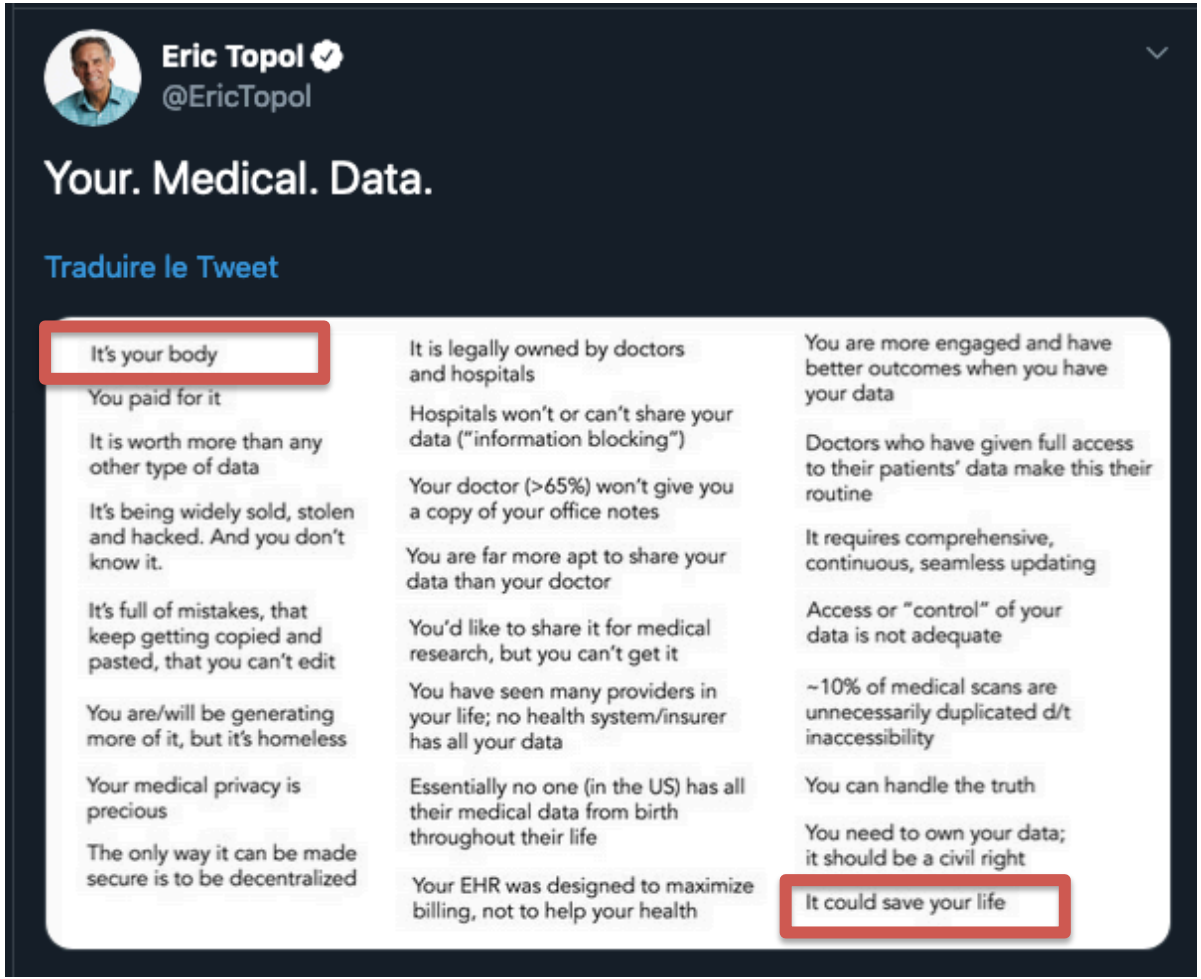
The largest and most valuable store of data in healthcare rests in **electronic medical records (EMRs)** !



clinician satisfaction with EMRs remains low, resulting in variable completeness and quality of data entry, and interoperability between different providers remains elusive.[11] The typical lament of a harried clinician is still "why does my EMR still suck and why don't all these systems just talk to each other?" Policy imperatives

From Bred Cox, MD

Who do health data **belong** to?



From Eric Topol

Who **owns** data? Who is **responsible** for it? Who can **use** it?

Many unanswered questions depending on :

- Degree of a social compact around healthcare itself as a **public good**,
- the tolerance to **public / private** partnership,
- the **public's trust** in both governments and the private sector to treat their healthcare data with due care and attention in the face of both **commercial and political** perverse incentives.

From Eric Topol

Should **Medical doctors** fear AI?

Should MD's fear AI?

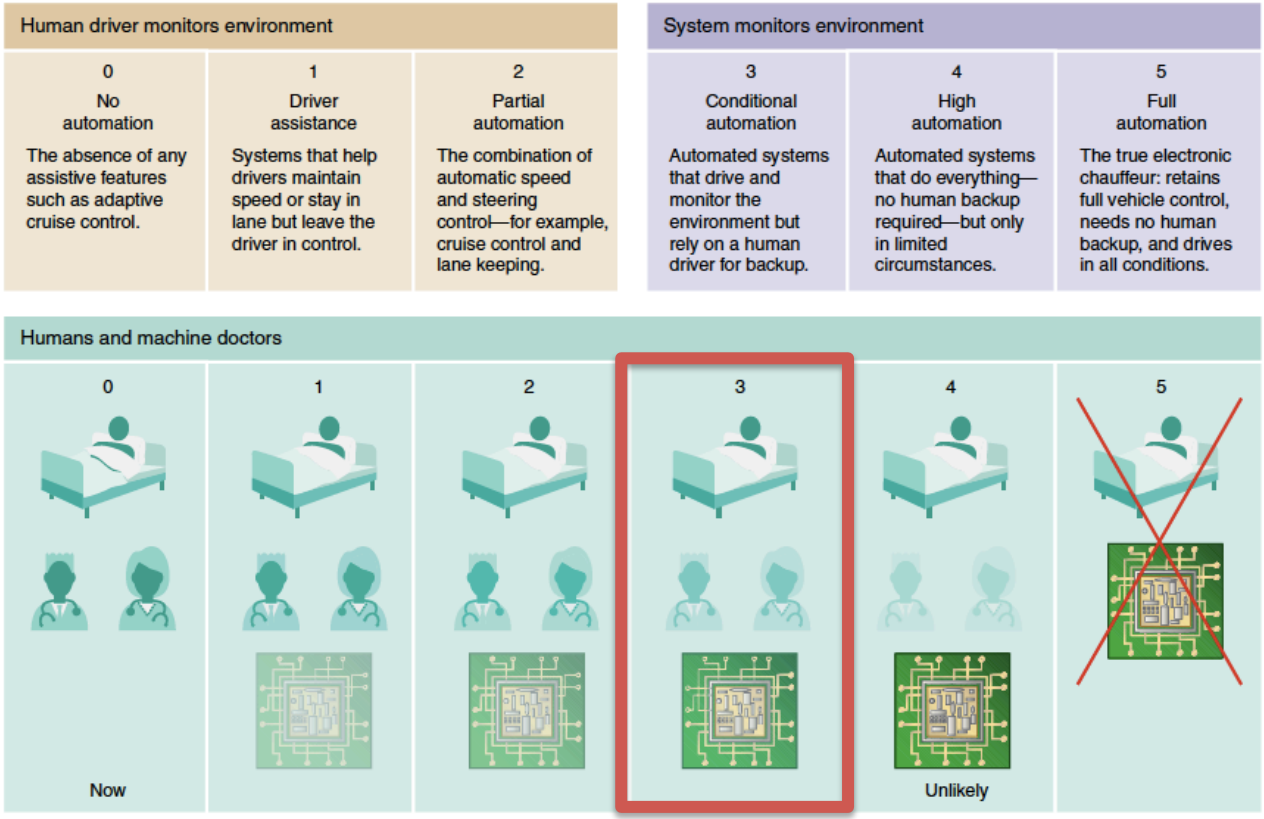


Fig. 5 | The analogy between self-driving cars and medicine. Level 5, full automation with no potential for human backup of clinicians, is not the objective. Nor is Level 4, with human backup in very limited conditions. The goal is for synergy, offsetting functions that machines do best combined with those that are best suited for clinicians. Credit: Debbie Maizels/Springer Nature

From Eric Topol

Should MD's fear AI?

Table 1 | Interdisciplinary teams may consist of stakeholders from different categories

Stakeholder categories	Examples
Knowledge experts	• Clinical experts • ML researchers • Health information and technology experts • Implementation experts
Decision-makers	• Hospital administrators • Institutional leadership • Regulatory agencies • State and federal government
Users	• Nurses • Physicians • Laboratory technicians • Patients • Friends and family (framily)

Wiens, Nature medecine, sept 2019

A **roadmap** for responsible machine learning for health care

Choosing the **right problems**

- A lack of intimate knowledge of the data often leads to misguided problem formulations and solutions.

Developping a **useful solution**

- Are the data appropriate? (ex: ICD for billing codes)
- Representative?

Considering **ethical implications**

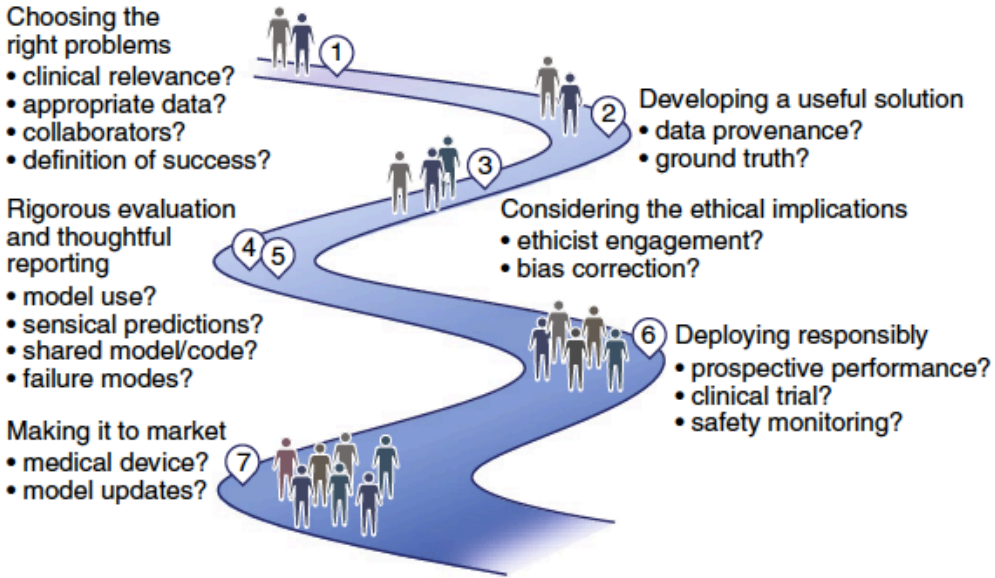
Rigourously **evaluate** the model

- Populations, metrics,

Thoughfully reporting **results**

- Sharing data source, outcomes, codes, packages…

Making it to the **market**



Wiens, Nature medecine, sept 2019

Thank you for your attention !!