

AI and Technological Innovations for Health

Regulatory Perspectives

M. Khair ElZarrad, PhD., M.P.H.

Deputy Director, Office of Medical Policy
Center for Drug Evaluation and Research
Food and Drug Administration

The views in this presentation do not
necessarily represent the policies of FDA

May 29, 2019

Disclosures: None

Evolving Paradigm for Evidence Generation



Technology is the cornerstone

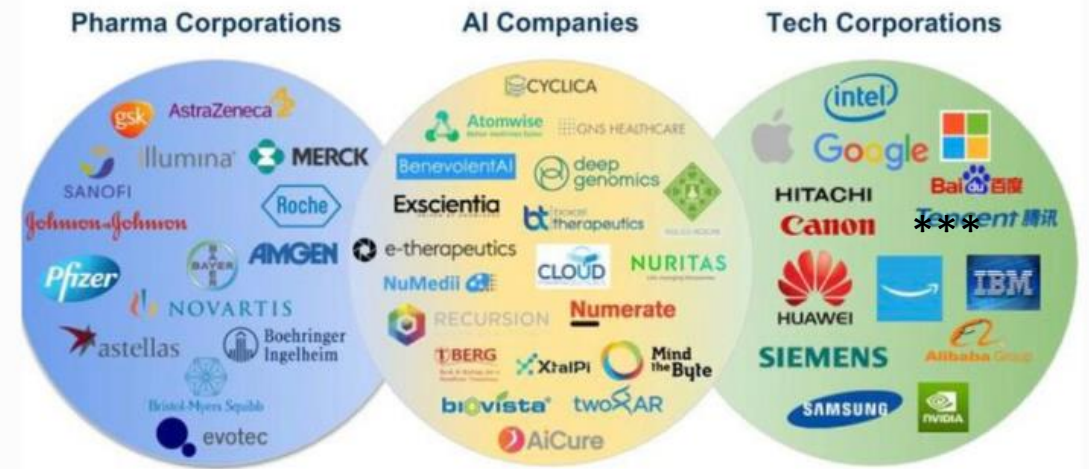
eye for pharma BARCELONA | 12TH-14TH MARCH 2019 #efpBarca

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Leading IT and Tech Corporations / AI Companies / Pharma Corporations Advanced AI in Healthcare and Drug Discovery

**



Different universes converge in the path of AI-based drug development DEEP KNOWLEDGE VENTURES

* From presentation by Paul Simms, Chairman, eyeforpharma

** From Forbes article by Yiannis Mouratidis: <https://www.forbes.com/sites/yiannismouratidis/2018/11/30/an-insight-of-ais-penetration-in-drug-development-market/#66bc8ce469dd>

Evolving Paradigm for Evidence Generation

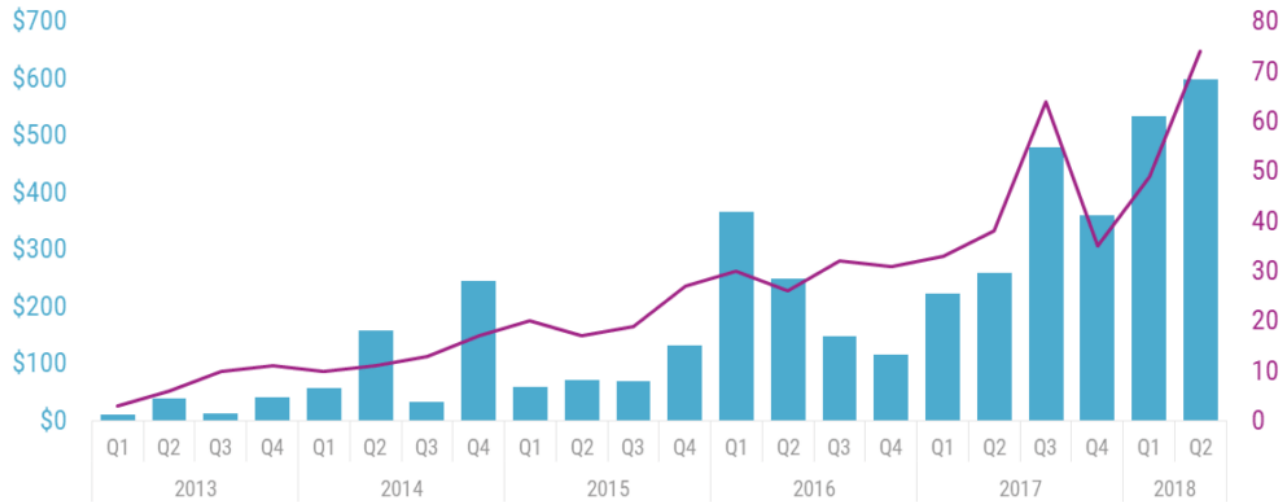


Technology is the cornerstone

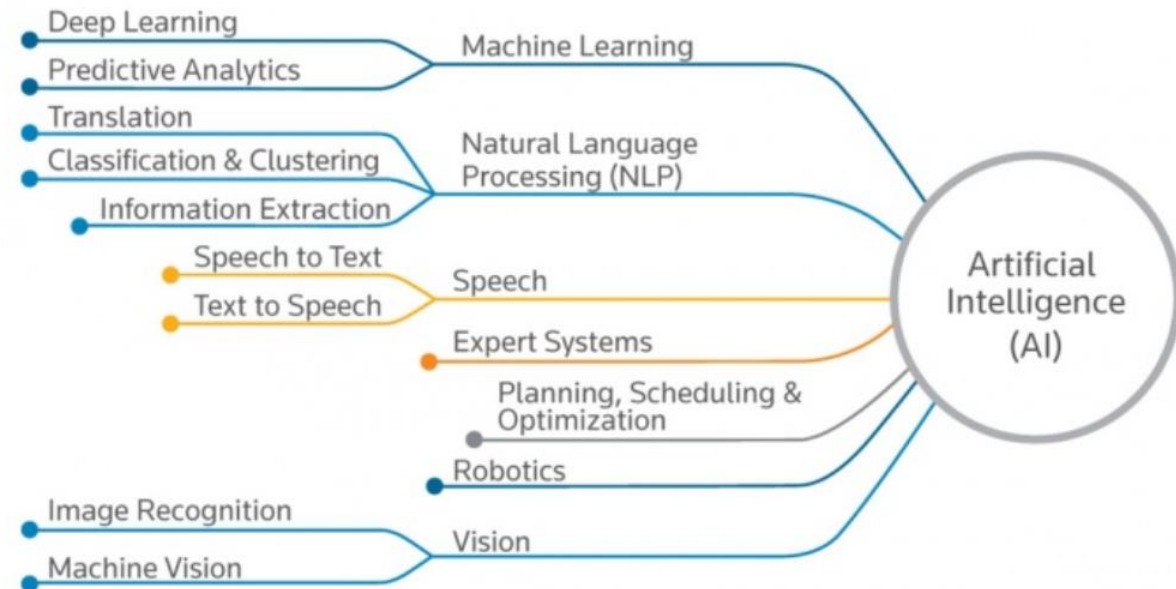
AI in healthcare funding hit a historic high in Q2'18

Disclosed equity funding, Q1'13 – Q2'18

Equity funding (\$M)

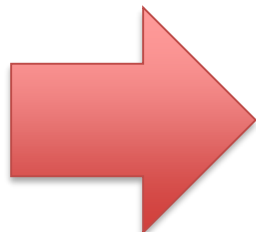
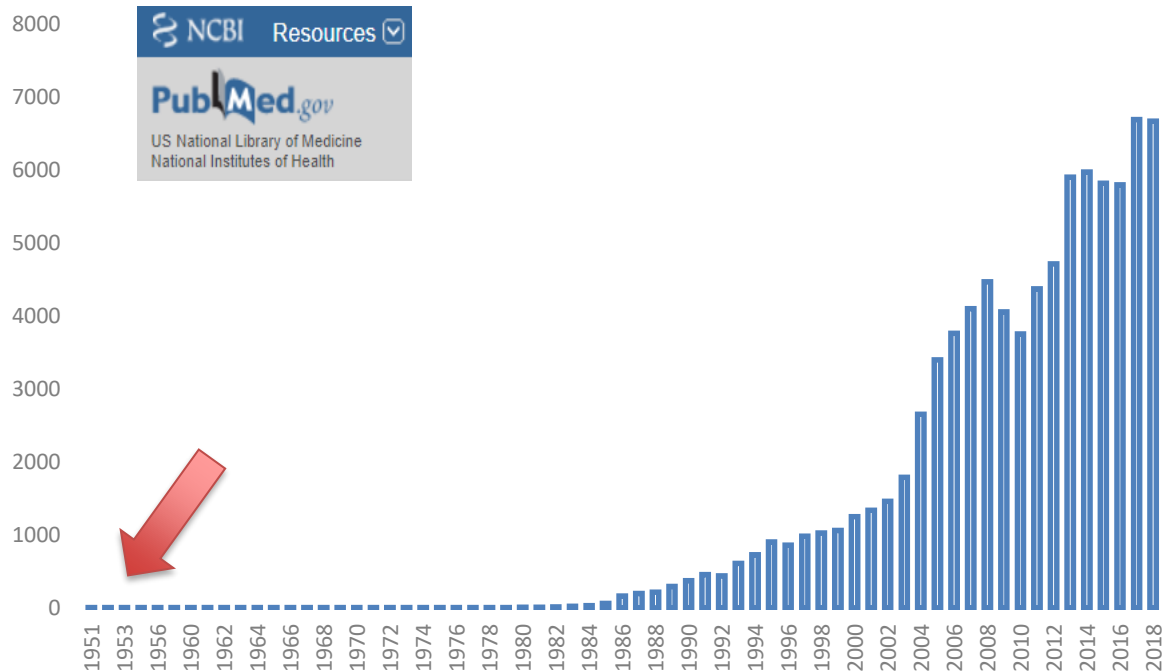


Source: cbinsights.com

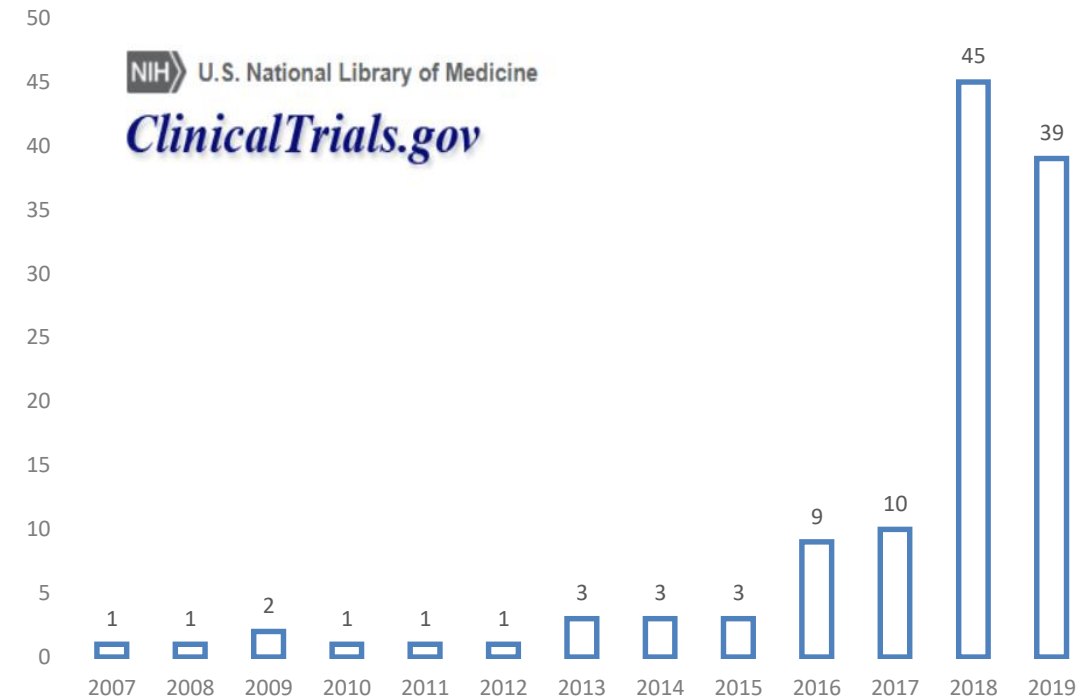


Beyond the Hype

Number of Scientific Papers with the Term Artificial Intelligence



Clinical Trials Incorporating AI



AI is not necessarily a new area....



NCBI Resources How To

PubMed.gov
US National Library of Medicine
National Institutes of Health

PubMed |

Advanced

Format: Abstract

Research. 1951 Jul;4(7):305-7.

Matter with a mind; a neurological research robot.

FLETCHER KH.

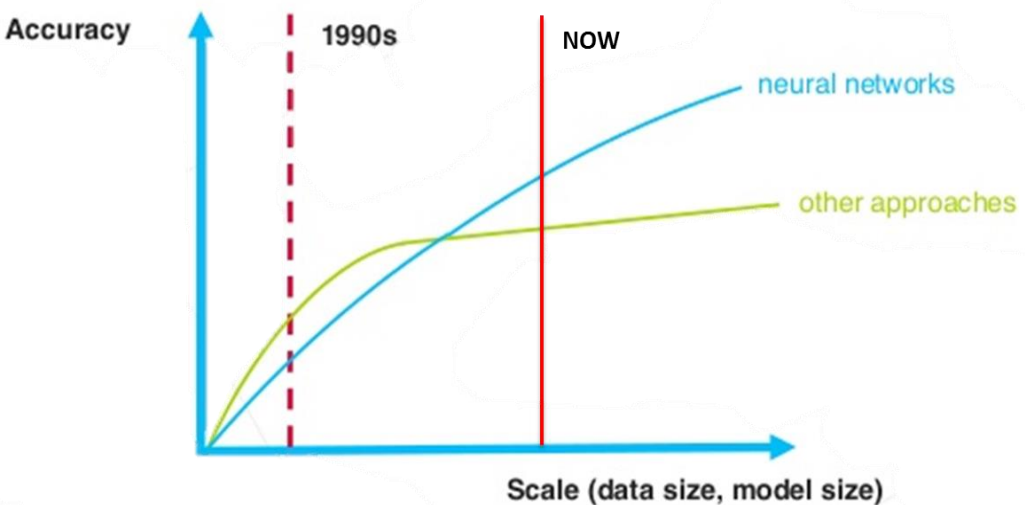
Dr. Grey Walter was a neurologist and robotics pioneer



<https://www.youtube.com/watch?v=ILULRImXkKo>

AI is not necessarily a new area. Why now?

More Data + Bigger Models



<https://www.scribd.com/document/355752799/Jeff-Dean-s-Lecture-for-YC-AI>

NCBI Resources How To

PubMed.gov
US National Library of Medicine
National Institutes of Health

PubMed [dropdown]
Advanced

Format: Abstract

Memo RM. 1963 Mar;86:1-35.

ARTIFICIAL INTELLIGENCE AND BRAIN MECHANISMS. MEM RM-3522-PR.

MARON ME.

PMID: 24547134

[Indexed for MEDLINE]



Missing Links in Computer Intelligence

The Imitation of Man by Machine

The view that machines will think as man does reveals misunderstanding of the nature of human thought.

Ulric Neisser

The paper by Ulric Neisser on "The imitation of man by machine" [*Science* 139, 193 (18 Jan. 1963)] describes three characteristics of human thought which are absent from machine programs. I would like to add a fourth characteristic which is, perhaps, the most important one. This is the property of "consciousness," the ability to be aware of the stimuli coming to us from our sense organs, and of the thoughts circulating in our own nerv-

Popular opinion about "artificial intelligence" has passed through two phases. A generation ago, very few people believed that any machine could ever think as a man does. Now, however, it is widely held that this goal will be reached quite soon, perhaps in our lifetimes. It is my thesis that the second of these attitudes is nearly as unsophisticated as the first. Yesterday's skepticism was based on ignorance of the capacities of machines; today's con-

fidence reflects a misunderstanding of the nature of thought.

There is no longer any doubt that computing machines can be programmed to behave in impressively intelligent ways. Marill (1) does not exaggerate in saying, "At present, we have, or are currently developing, machines that prove theorems, play games with sufficient skill to beat their inventors, recognize spoken words, translate text from one language to another,

Remarkable Progress in Image Recognition

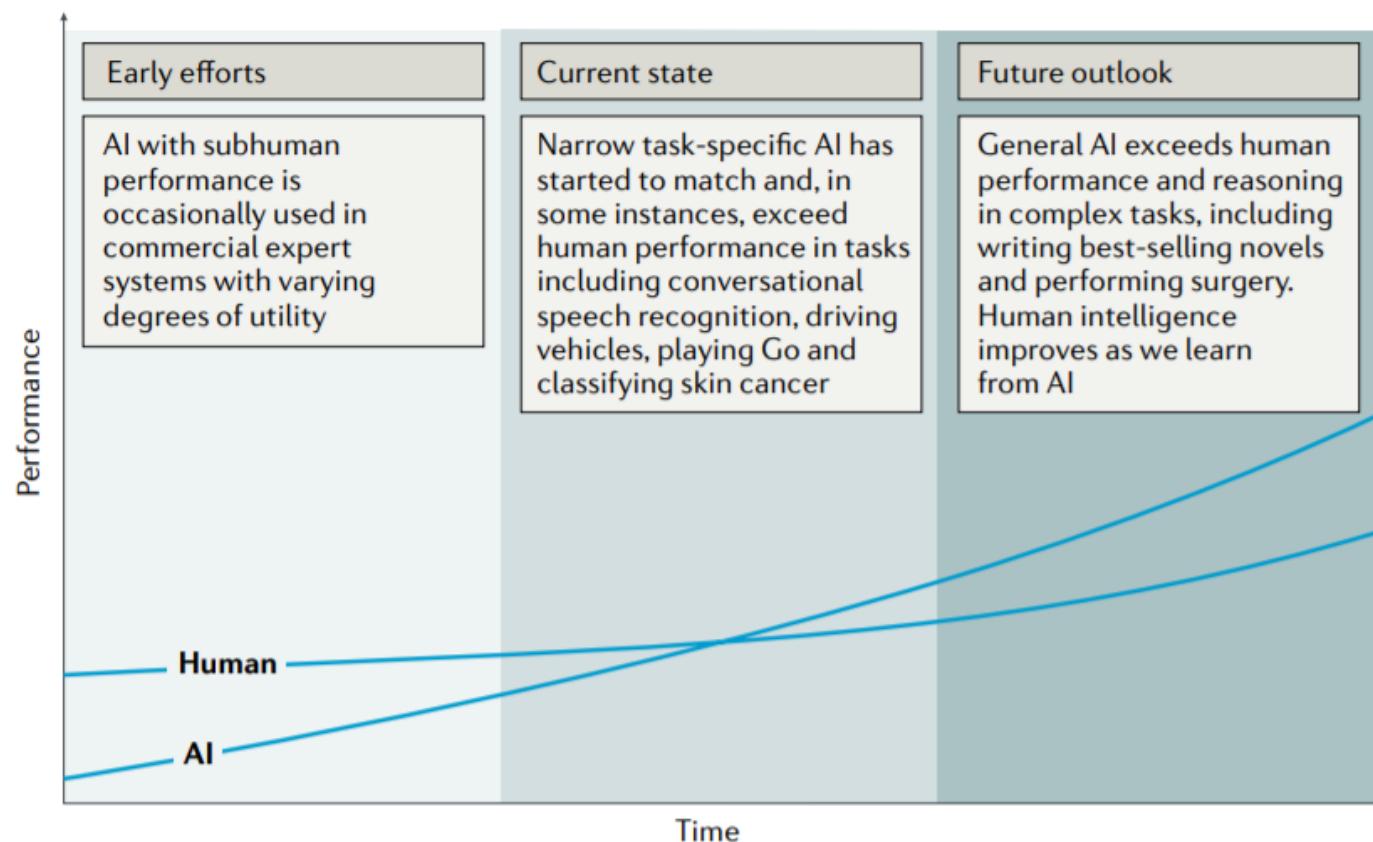


OPINION

Artificial intelligence in radiology

Ahmed Hosny^{ID}, Chintan Parmar, John Quackenbush^{ID}, Lawrence H. Schwartz and Hugo J. W. L. Aerts^{ID}

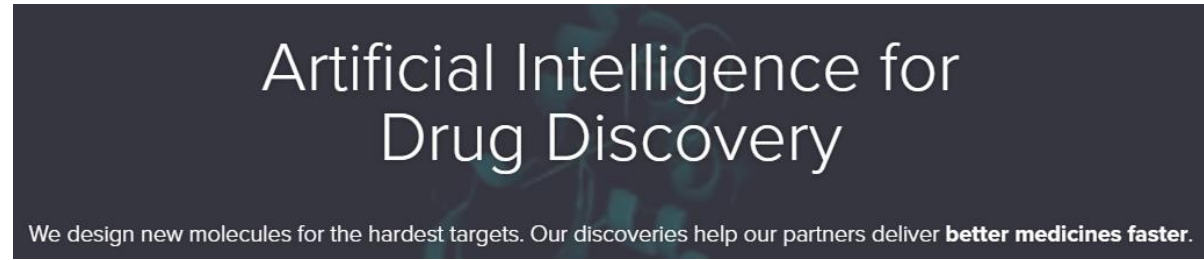
Abstract | Artificial intelligence (AI) algorithms, particularly deep learning, have demonstrated remarkable progress in image-recognition tasks. Methods ranging from convolutional neural networks to variational autoencoders have found myriad applications in the medical image analysis field, propelling it forward at a rapid pace. Historically, in radiology practice, trained physicians visually assessed medical images for the detection, characterization and monitoring of diseases. AI methods excel at automatically recognizing complex patterns in imaging data and providing quantitative, rather than qualitative, assessments of radiographic characteristics. In this Opinion article, we establish a general understanding of AI methods, particularly those pertaining to image-based tasks. We explore how these methods could impact multiple facets of radiology, with a general focus on applications in oncology, and demonstrate ways in which these methods are advancing the field. Finally, we discuss the challenges facing clinical implementation and provide our perspective on how the domain could be advanced.



Why does the FDA care?

1. Potential for every phase of drug development

- Discovery and target identification
- Preclinical
- Clinical
- Post-market



The future of real-world evidence

Biopharma companies focus on end-to-end, AI-driven, internal



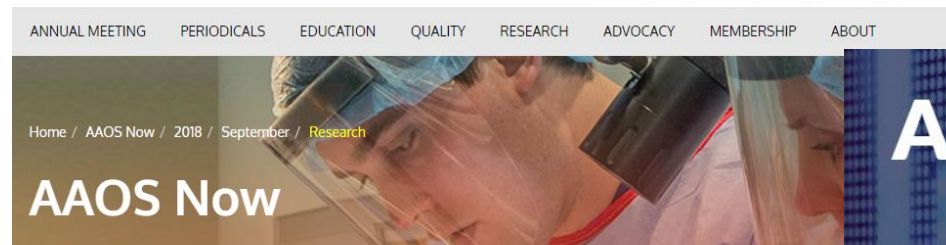
Brett Davis Jeff Morgan

2. Key to FDA's efforts on multiple fronts (RWE, Digital Health, etc.)

Classification and mutation prediction from non-small cell lung cancer histopathology images using deep learning

Nicolas Coudray^{1,2,9}, Paolo Santiago Ocampo^{3,9}, Theodore Sakellaropoulos⁴, Navneet Narula³, Matija Snuderl⁵, David Fenyo^{5,6}, Andre L. Moreira^{3,7}, Narges Razavian^{8*} and Aristotelis Tsirigos^{1,3*}

3. Capable of facilitating and refining clinical trials



DEVELOPMENT

Harnessing the Power of Real-World Evidence (RWE): A Checklist to Ensure Regulatory-Grade Data Quality

Rebecca A. Miksad¹ and Amy P. Abernethy¹

at Links

Low Home

t Issue

AAOS Now

Understanding the Impact of Artificial Intelligence on Orthopaedic Surgery

By: Alan M. Reznik, MD, MBA, FAAOS, and Kenneth Uri

AI & Machine Learning in Clinical Trials

How AI, Machine Learning and Analytics can Transform & Accelerate Clinical Trials

APRIL 12, 2018

PFIZER INNOVATION RESEARCH LAB - CAMBRIDGE, MA

AI algorithms are already being evaluated by FDA



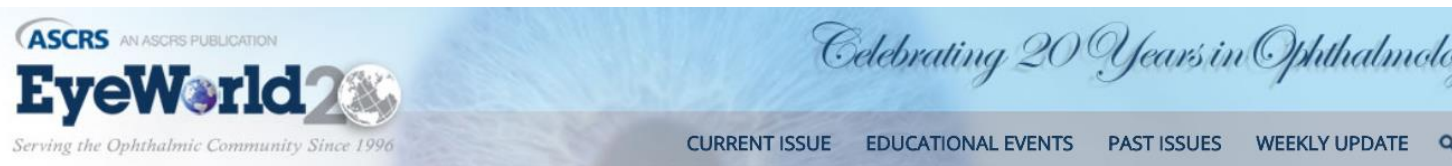
The screenshot shows the top portion of the FDA website. It features the FDA logo and the text "U.S. FOOD & DRUG ADMINISTRATION". Below this is a navigation menu with buttons for "Home", "Food", "Drugs", "Medical Devices", "Radiation-Emitting Products", "Vaccines, Blood & Biologics", and "Animal & Human Products". A "News & Events" section is also visible, with a breadcrumb trail: "Home > News & Events > Newsroom > Press Announcements".

FDA News Release

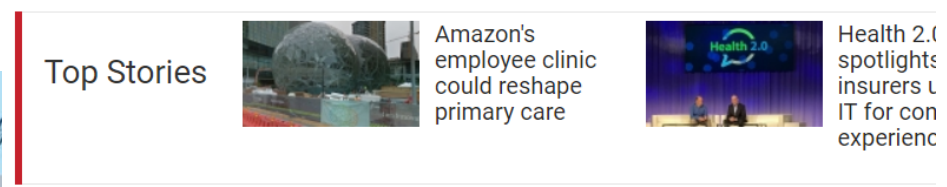
FDA permits marketing of artificial intelligence-based device to detect certain diabetes-related eye problems



FDA approves AI-powered diagnostic that doesn't need doctor's help



A banner for "EyeWorld 20" celebrating 20 years in ophthalmology. It features the ASCRS logo and the text "AN ASCRS PUBLICATION". The main text reads "EyeWorld 20" with a globe icon. Below this is the tagline "Celebrating 20 Years in Ophthalmology". At the bottom, there are navigation links for "CURRENT ISSUE", "EDUCATIONAL EVENTS", "PAST ISSUES", and "WEEKLY UPDATE".



A "Top Stories" section with three article thumbnails. The first is titled "Amazon's employee clinic could reshape primary care" with a photo of a modern building. The second is titled "Health 2.0 spotlights insurers' IT for consumer experience" with a photo of a stage event.

[Ophthalmology news - NEWS & OPINION](#) - First artificial intelligence system approved by the FDA to detect diabetic retinopathy

JUNE 2018

NEWS & OPINION

First artificial intelligence system approved by the FDA to detect diabetic retinopathy

APR 12 | MORE ON QUALITY AND SAFETY

FDA approves first AI tool for detecting retinopathy, NIH shows machine learning success in imaging

New technologies bring the promise of earlier detection and automation, both with an eye on lowering costs.

High-performance medicine: the convergence of human and artificial intelligence

Eric J. Topol

Table 2 | FDA AI approvals are accelerating

Company	FDA Approval	Indication
Apple	September 2018	Atrial fibrillation detection
Aidoc	August 2018	CT brain bleed diagnosis
iCAD	August 2018	Breast density via mammography
Zebra Medical	July 2018	Coronary calcium scoring
Bay Labs	June 2018	Echocardiogram EF determination
Neural Analytics	May 2018	Device for paramedic stroke diagnosis
IDx	April 2018	Diabetic retinopathy diagnosis
Icometrix	April 2018	MRI brain interpretation
Imagen	March 2018	X-ray wrist fracture diagnosis
Viz.ai	February 2018	CT stroke diagnosis
Arterys	February 2018	Liver and lung cancer (MRI, CT) diagnosis
MaxQ-AI	January 2018	CT brain bleed diagnosis
Alivecor	November 2017	Atrial fibrillation detection via Apple Watch
Arterys	January 2017	MRI heart interpretation

AI for Health – A fast evolving field with many opportunities and challenges

“DEEP MEDICINE SUMMARIZES HYPE AND THREAT, THEN TAKES US TO A PLACE WHERE NO ONE ELSE HAD GONE.”

Tom Insel, MD
nature

Eric Topol @EricTopol
physician-scientist, author, editor. My new book #DeepMedicine was just released deepmedicinebook.com

Tweets 19K | Following 461 | Followers 158K | Likes 15.9K

Tweets | Tweets & replies | Media

Eric Topol @EricTopol · 8 Oct 2017
Your. Medical. Data.

Who to follow · Refresh · View

- Rock Health @RockHealth
- Healthcare IT News @HealthcareITNews

Proposed Regulatory Framework for Modifications to Artificial Intelligence/Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD)

Discussion Paper and Request for Feedback



FDA's Proposed Approach to the Regulation of AI and ML-Based Software

RF Regulatory Focus™

Regulatory Focus™ > News Articles > 2019 > 4 > FDA Proposes Regulatory Framework for AI- and Machine Learning-Driven SaMD

FDA Proposes Regulatory Framework for AI- and Machine Learning-Driven SaMD

Posted 02 April 2019 | By Ana Mulero

The US Food and Drug Administration (FDA) requested feedback Tuesday on a new discussion paper that proposes applying a “focused review” approach to premarket assessments of software as a medical device (SaMD) technologies that are powered by artificial intelligence (AI) and machine learning (ML).

The agency said it may conduct a “focused review” in cases where proposed SaMD pre-specifications (SPS) and algorithm change protocols (ACP) “can be refined based on the real-world learning and training,” offering options for manufacturers to engage agency staff for such purposes. Options include contacting FDA review divisions to see if modifications fit under the approved or cleared model, and submitting pre-submissions for early discussions on modifications or premarket submissions or applications.



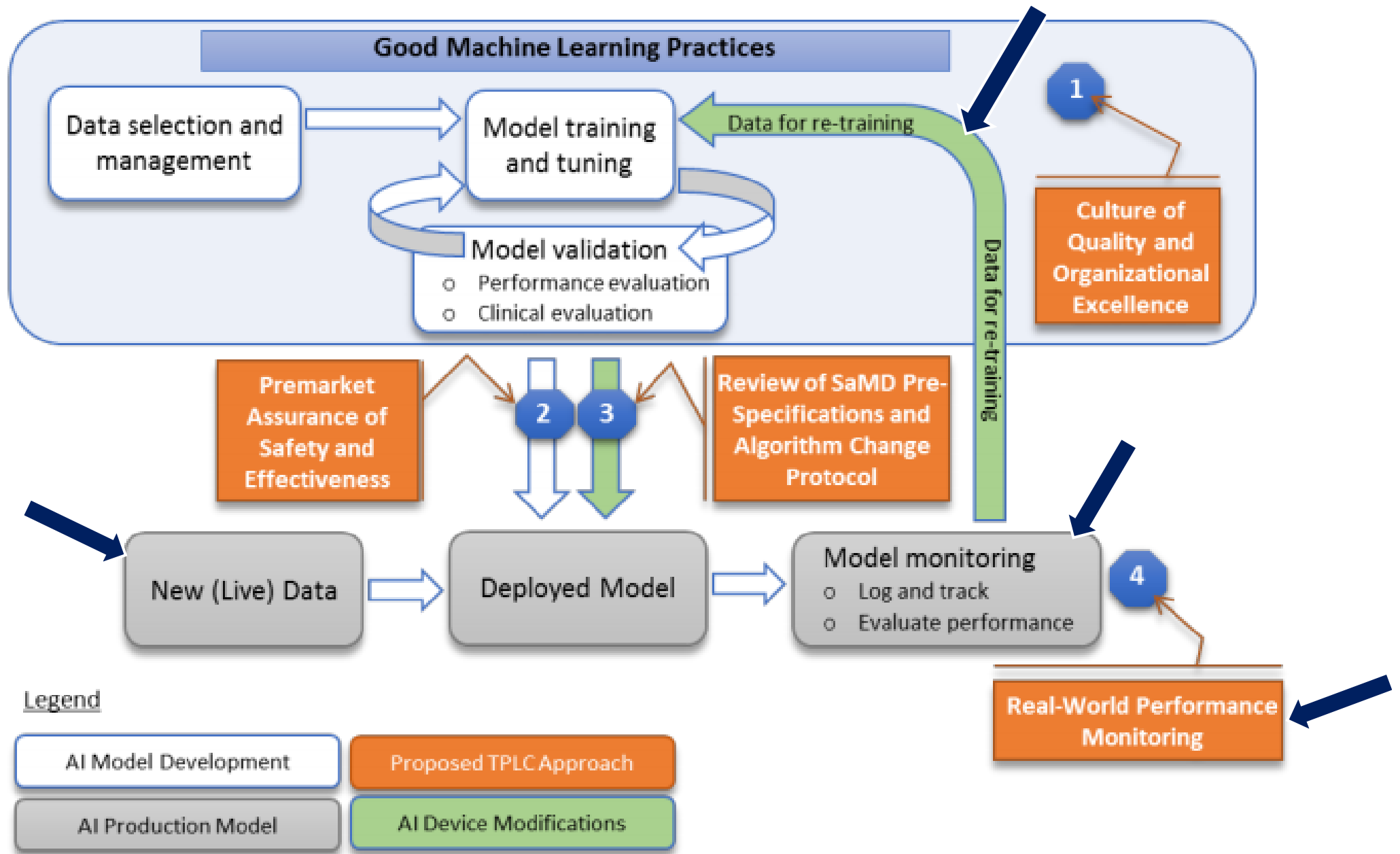


Figure 2: Overlay of FDA's TPLC approach on AI/ML workflow

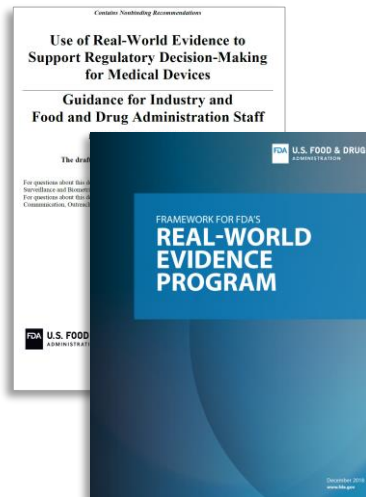
AI's potential is not limited to devices

FDA



The 21st Century Cures Act - Real-World Evidence

FDA shall establish a program to evaluate the potential use of real world evidence (RWE)



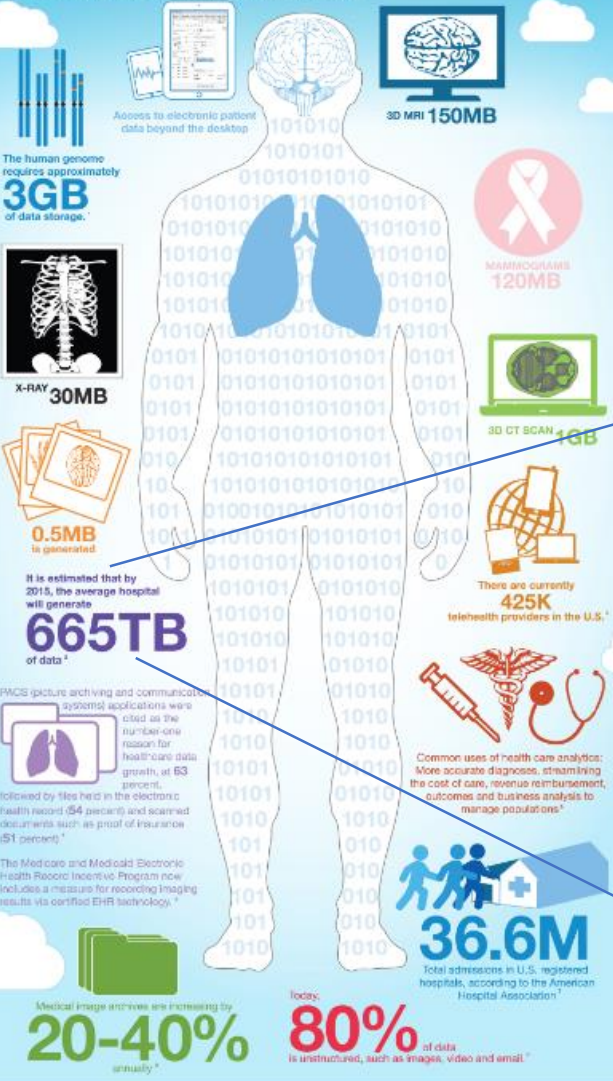
Real-World Data (RWD) are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources.

Real-World Evidence (RWE) is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD.

The Power of Healthcare Data

The Body as a Source of Big Data

Today data storage is essential for healthcare providers to see a patient's complete story of care, make the most informed decisions and enhance treatment and outcomes.

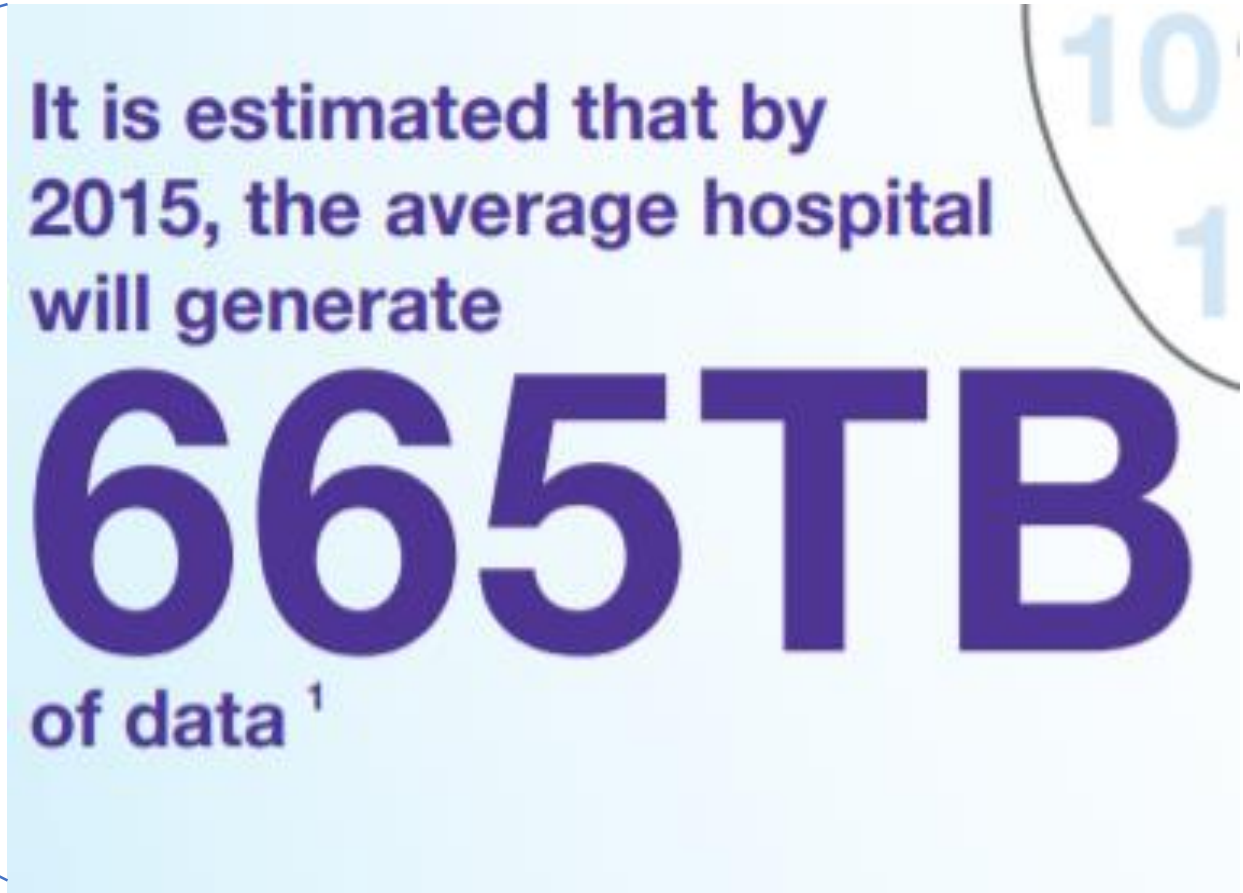


Health Data are Available

BUT Need

Structure, Organization, Verification, Cleaning

AI CAN HELP





What is needed?

- **Understanding the functions that lend themselves to AI adoption**
- **A convergence of multidisciplinary expertise**
 - Computer science alone will not produce breakthrough AI systems
 - We need **educational and training programs** that connect essential disciplines and targeted training
 - We need to understand the **ethical implications**
- **Pilots to explore the utility of AI systems - Evaluate successes and failures**
 - Failure here is not the standard concept we are used to— **failure is an integral part of machine learning/training. Data from failures in a learning AI system = better AI system.** Transparency is key.
- **Shared understanding of principles and approaches that are essential in designing and adopting AI systems (beyond the hype)**
 - The need for a **benchmarking** framework and approaches that ensure **quality continuum in the design of AI systems** (data and algorithms)
 - The need to understand that **AI is not necessarily the silver bullet for everything** - those designing algorithms (and teaching datasets) can't comprehend or impute all of the essential variables.

AI - A Part of the Digital Revolution

This is a continuum - Advances in digital technology, software, wearables, mHealth, and eHealth will further advance and inform the utility of AI in health (and vice versa).

Examples of current work streams

- The use of EHR and claims data
- Digital health tools
- Decentralized clinical trials
- Data standards

Use of Electronic Health Record Data in Clinical Investigations

Guidance for Industry



WHO W

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

Program: Mobile Clinical Trials (MCT)

July 2018
Procedural

Decentralized Clinical Trials

Novel Endpoints

Engaging Patients and Sites

Mobile Technologies

PROJECT:

Decentralized Clinical Trials

SHARE:



FEDERAL REGISTER

The Daily Journal of the United States Government



Notice

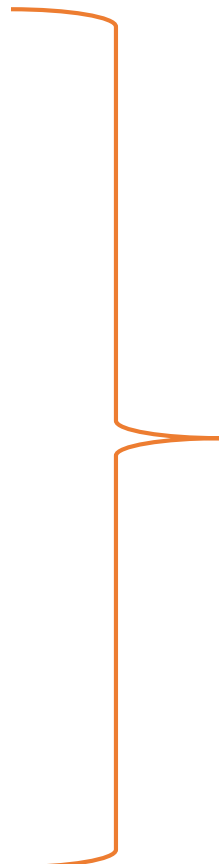
Prescription Drug-Use-Related Software; Establishment of a Public Docket; Request for Comments





Multifaceted Approach To Anticipate AI Innovations

- **Understanding the technology**
- **Benchmarking and validation**
- **Piloting and testing in real-world settings**
- **Ethical and privacy implications**
- **Ensuring quality continuum**
- **Audit trails and post-approval monitoring**
- **Transparency for AI (what would it look like? How would we work with the concept of Blackbox?, etc.)**



Simultaneous work and collaborations are needed on all fronts

Acknowledgements

- **Jacqueline Corrigan-Curay**
- **Leonard Sacks**
- **Elizabeth Kunkoski**
- **Dianne Paraoan**



U.S. Department of Health and Human Services
Food and Drug Administration