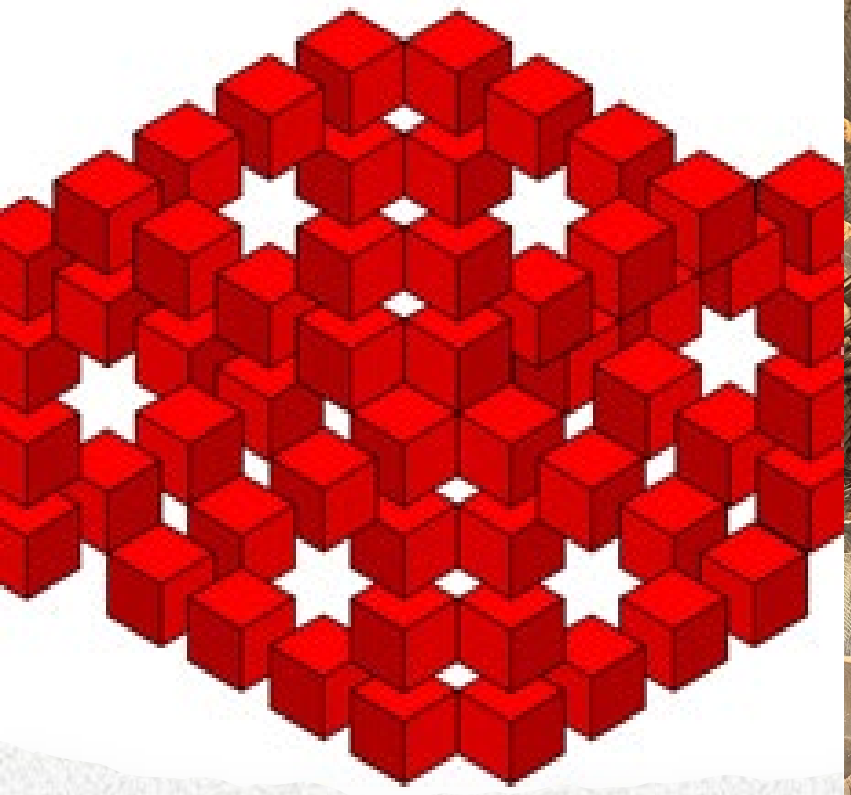

Health, Healthcare, Clinical-Medical Research, Remote Digital Health & Data-Informed Decision Systems in Healthcare Services

My 25+ year journey continues … with no end in sight except death.

by

Dr Shoumen Palit Austin Datta

Most of this material was presented on 10-11-2022 to the Digital Healthcare Sub-Committee members of the EU Political Action Committee (EUPAC) at a private meeting in Gif-sur-Yvette, France (organized by the “Science Valley” institutions in France). The author (no political affiliation) was invited to speak.

This document is “The Health of Nations – Part II”

“The Health of Nations” (Part I) – is in the MIT Library https://dspace.mit.edu/handle/1721.1/145774

“The Health of Nations” – Part 1 & Part 3 - MIT Library https://dspace.mit.edu/handle/1721.1/153283

Disclaimer:
This is not an original research R&D document.

This is an edited presentation composed of sections from my teaching slides at MIT and elsewhere. Part of this material was also used for my consulting engagements and may appear in various forms in other documents, lectures and white papers. Quite a few ideas are in documents and presentations related to talks at Massachusetts General Hospital MDPnP Lab events.

ACKNOWLEDGEMENTS

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Sheela Magge M.D., M.S.C.E., Professor of Pediatrics, Lawson Wilkins Endowed Chair of Pediatric Endocrinology and Director, Division of Pediatric Endocrinology
Johns Hopkins University School of Medicine
https://profiles.hopkinsmedicine.org/provider/Sheela+Magge/2700667
https://clinicalconnection.hopkinsmedicine.org/participant/sheela-natesh-magge-md-msce
www.niddk.nih.gov/-/media/Files/News/Meetings/Magge_Bio_508.pdf

Julian Goldman, M.D., F.A.S.A. Massachusetts General Hospital, Harvard Medical School
Anesthesia, Critical Care and Pain Medicine, MGH Research Institute
Director, Biomedical Engineering, Mass General Brigham (MGB) https://mdpnp.mgh.harvard.edu
https://researchers.mgh.harvard.edu/profile/14161732/Julian-Goldman

Sanjay Sarma, Ph.D., Vice-President, Massachusetts Institute of Technology (MIT)
Fred and Daniel Fort Flowers (1941) Professor of Mechanical Engineering, MIT
President, CEO and Dean, Asia School of Business (MIT Sloan, Kuala Lumpur, Malaysia)
https://meche.mit.edu/people/faculty/sesarma@mit.edu
https://asb.edu.my/about/leadership-team/sanjay-sarma/

Thomas H. McCoy, M.D., Assistant Prof of Medicine & Psychiatry, Harvard Medical School
CGM Psychiatry, Massachusetts General Hospital Research Institute; Psychiatrist, MGH
https://researchers.mgh.harvard.edu/profile/6264601/Thomas-McCoy

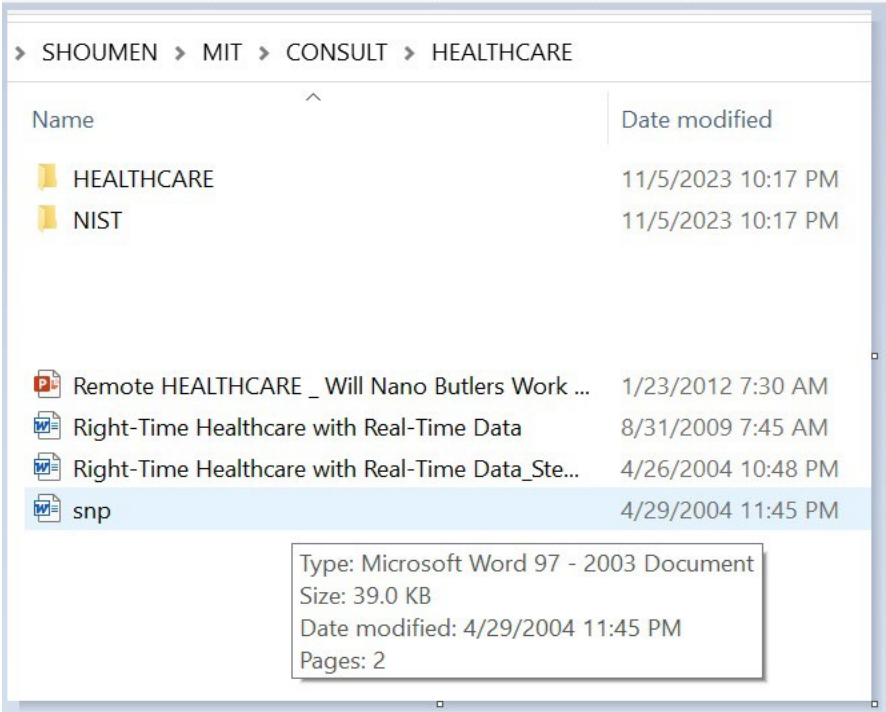
This presentation suggests “How to” create a $60 billion digital healthcare service business

Digital Healthcare Services:

Pursuit of Profitable Ideas ?

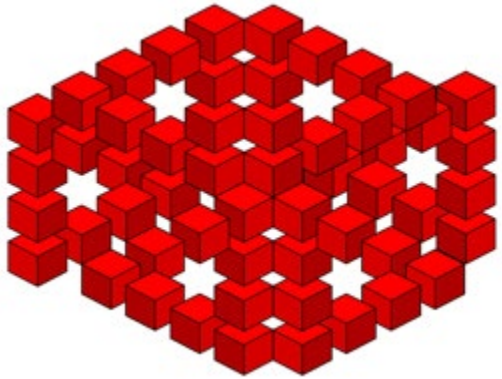
Proposed digital healthcare service business with $60 billion in annual revenues.

If limited to 1% profit, the healthcare service business will generate $600 million in annual profit.



Healthcare, Clinical Research, Digital Health

20+ years .. journey



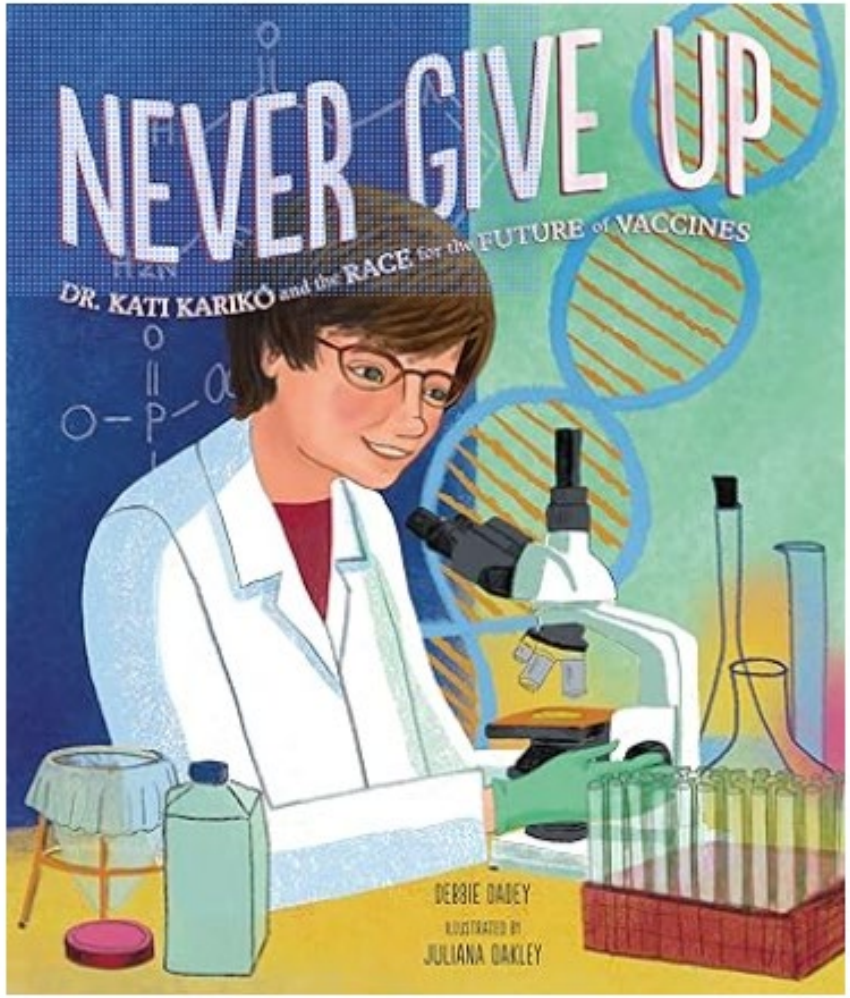
Dr Shoumen Palit Austin Datta

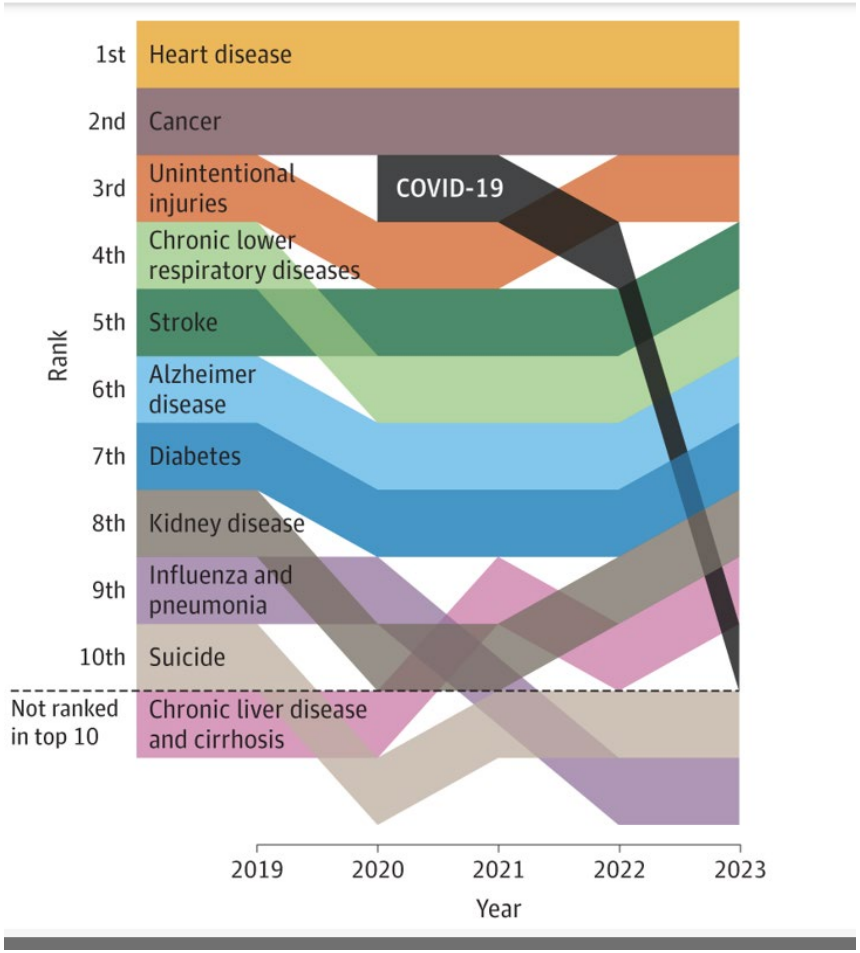
MIT Auto-ID Labs, Senior Member, Affiliate, Department of Mechanical Engineering, Massachusetts Institute of Technology ▪ shoumen@mit.edu

Senior Scientist, MDPnP Lab Medical Device Interoperability, Massachusetts General Hospital, Harvard Medical School ▪ sdatta8@mgh.harvard.edu

Context

Any long-term commitment to a purpose has a context, almost always. In my case, my interest in pursuing digital health is a 20+ year journey which still continues to grow because we haven't yet improved access to "care" in healthcare, sufficiently. We have the technology and the tools. Then, why is there such a deepening chasm between intent and implementation?





Ahmad FB, Cisewski JA, Anderson RN. Leading Causes of Death in the US, 2019-2023. JAMA. 2024 September 24;332(12): 957-8. doi: 10.1001/jama.2024.15563. PMID: 39116093.

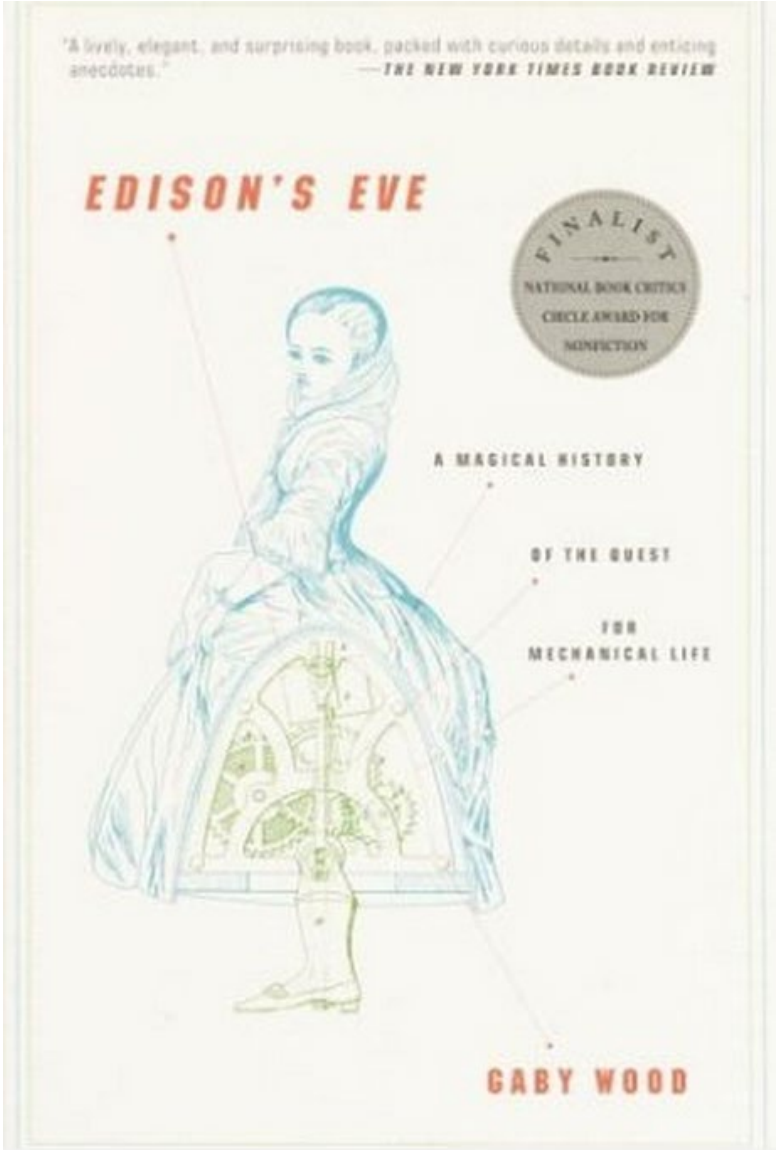
WHY DIGITAL

WHY DIGITAL HEALTH ?

“Digital” solutions (digital transformation) are a series of stepped ramps to semi-autonomous systems followed by the aspirational move toward autonomous and autonomy.

AUTOMATION

~3000 years of history



Wood, Gaby (2002) *Living Dolls: A Magical History of the Quest for Mechanical Life*. Paperback edition, Faber and Faber, 2003

Wood, Gaby (2003) *Edison's Eve : a magical history of the quest for mechanical life.* Anchor Books, NY.
https://archive.org/details/edisonsevemagica0000wood_n8o7

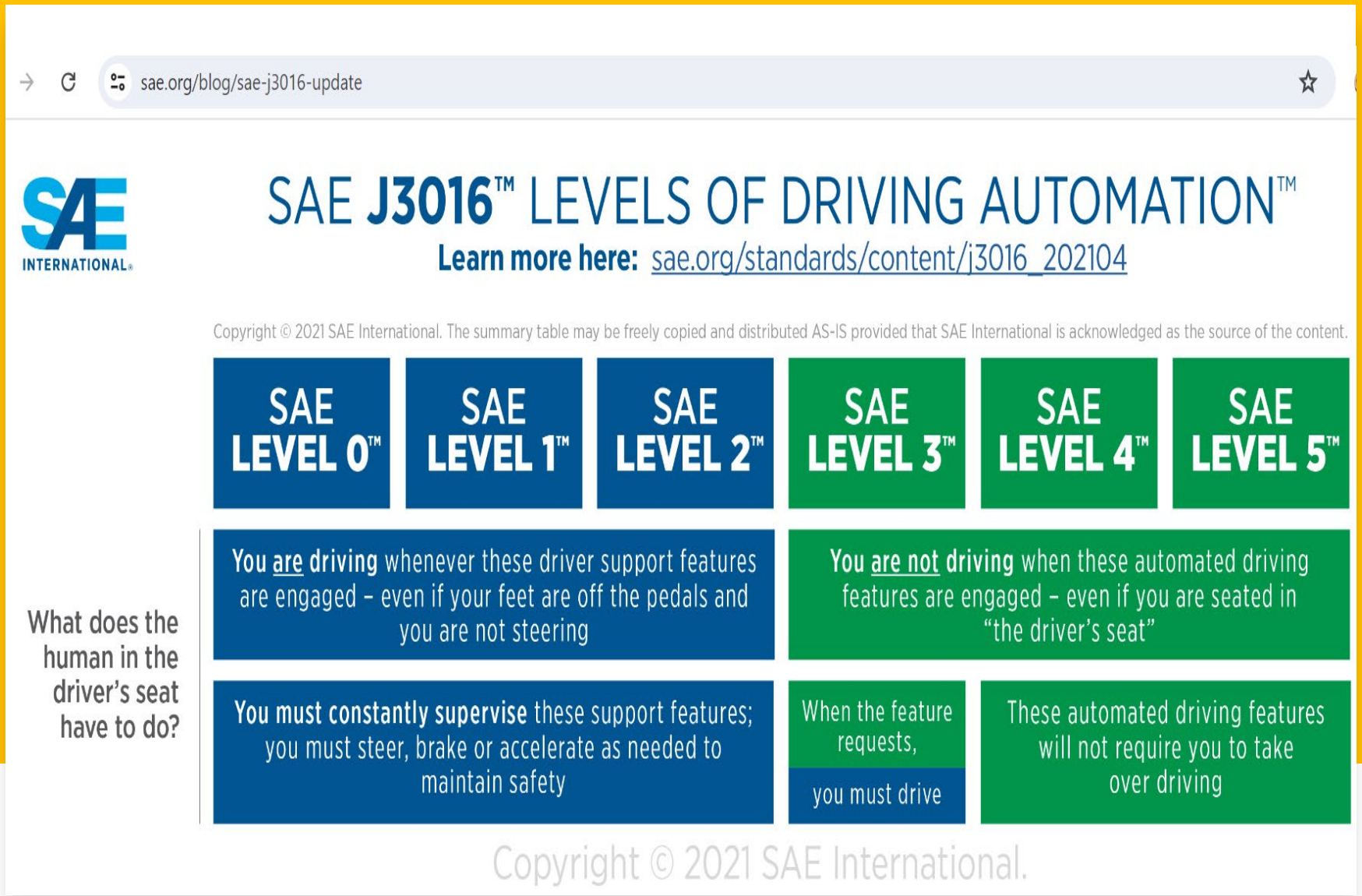
Source: Table V in DT-2024 available from the MIT Library https://dspace.mit.edu/handle/1721.1/140791

- **10th Century BC -** CHINA - Life-size, human-shaped figure created by engineer Yan Shi and presented to King Mu of Zhou (1023-957 BC)
- **8th Century BC -** GREECE - Athenian craftsman Daidalos created statues endowed with movement, e.g., The Bull of Pasiphae.
- **8th Century BC -** PERSIA (IRAQ) – Wind powered automata - statues that turned with the wind over the domes of the four gates and palace complex of Round City of Baghdad. Banū Mūsā brothers invented programmable automatic flute (documented in ref 861).
- **1st Century AD** - First programmable robot from Alexandria, Greece (circa 60 AD).
- **13th Century AD** - Al-Jazari described complex programmable humanoid automata amongst other machines he constructed (ref 861). Created the flushing toilet. Villard de Honnecourt (1230's) designed animal automata and an angel that perpetually turns to face the sun.
- **15th Century AD** - Leonardo da Vinci sketched a more complex automaton around the year 1495. The design of Leonardo's robot was not rediscovered until 1950's. The robot could, if built, move its arms, twist its head and sit up.
- **16th Century AD** - Smithsonian Institution has in its collection a clockwork monk, about 15 inches tall, created by Juanelo Turriano, mechanician to the Holy Roman Emperor Charles V (circa 1560).
- **18th Century AD** - Automaton Flute Player was constructed by Jacques de Vaucanson in 1737 (1709-1782) and first exhibited on February 11, 1738 in Paris, France. Vaucanson claims that the idea came to him in a dream. Later (1939) he created the digesting duck.

AUTOMATION

~3000 years of history

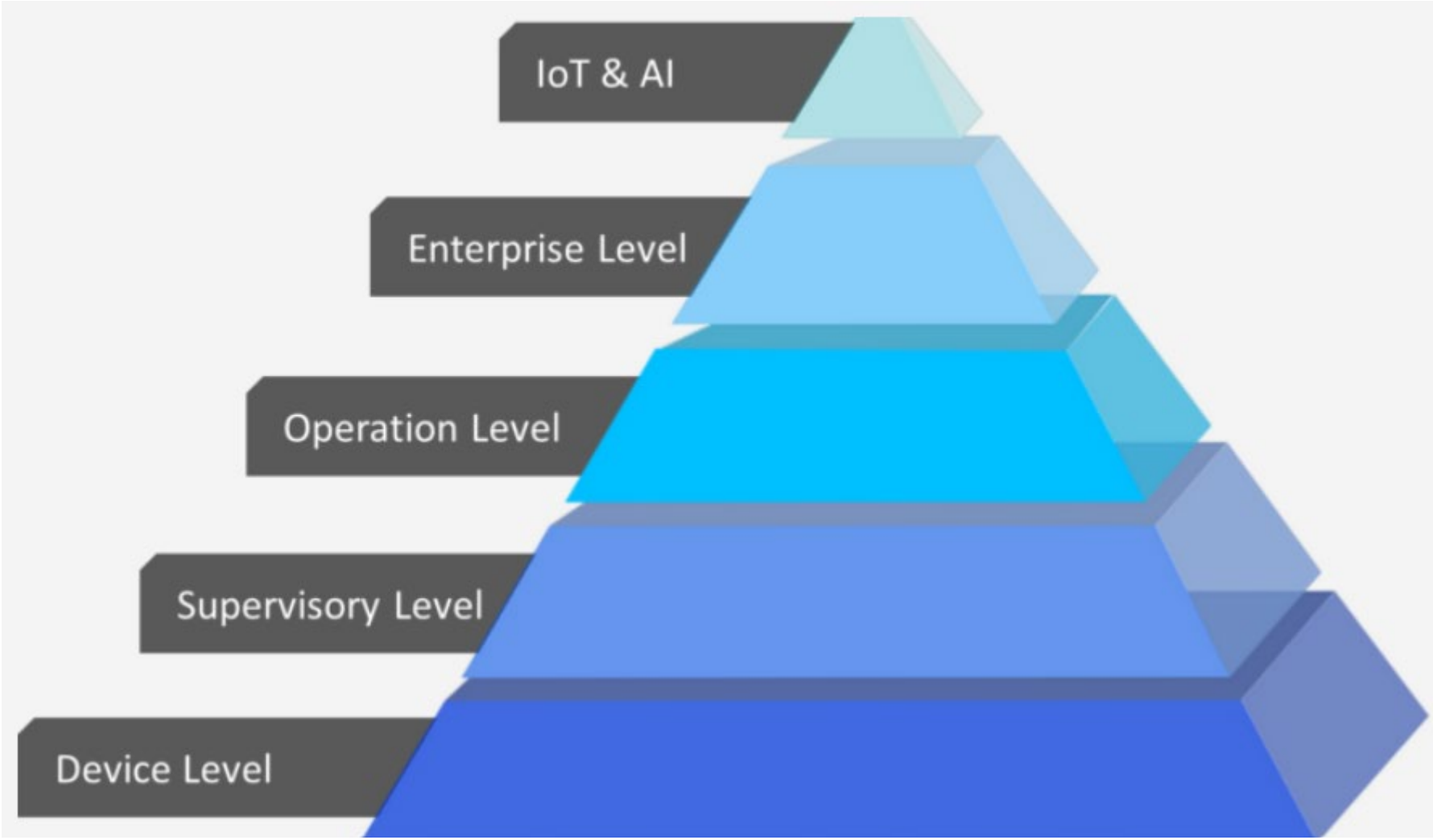
We think cars when we think of automation. Don't we?



Society of Automotive Engineers (SAE) ● https://www.sae.org/standards/content/j3016_202104/

https://ma.tt/2020/04/five-levels-of-autonomy/

AUTONOMY



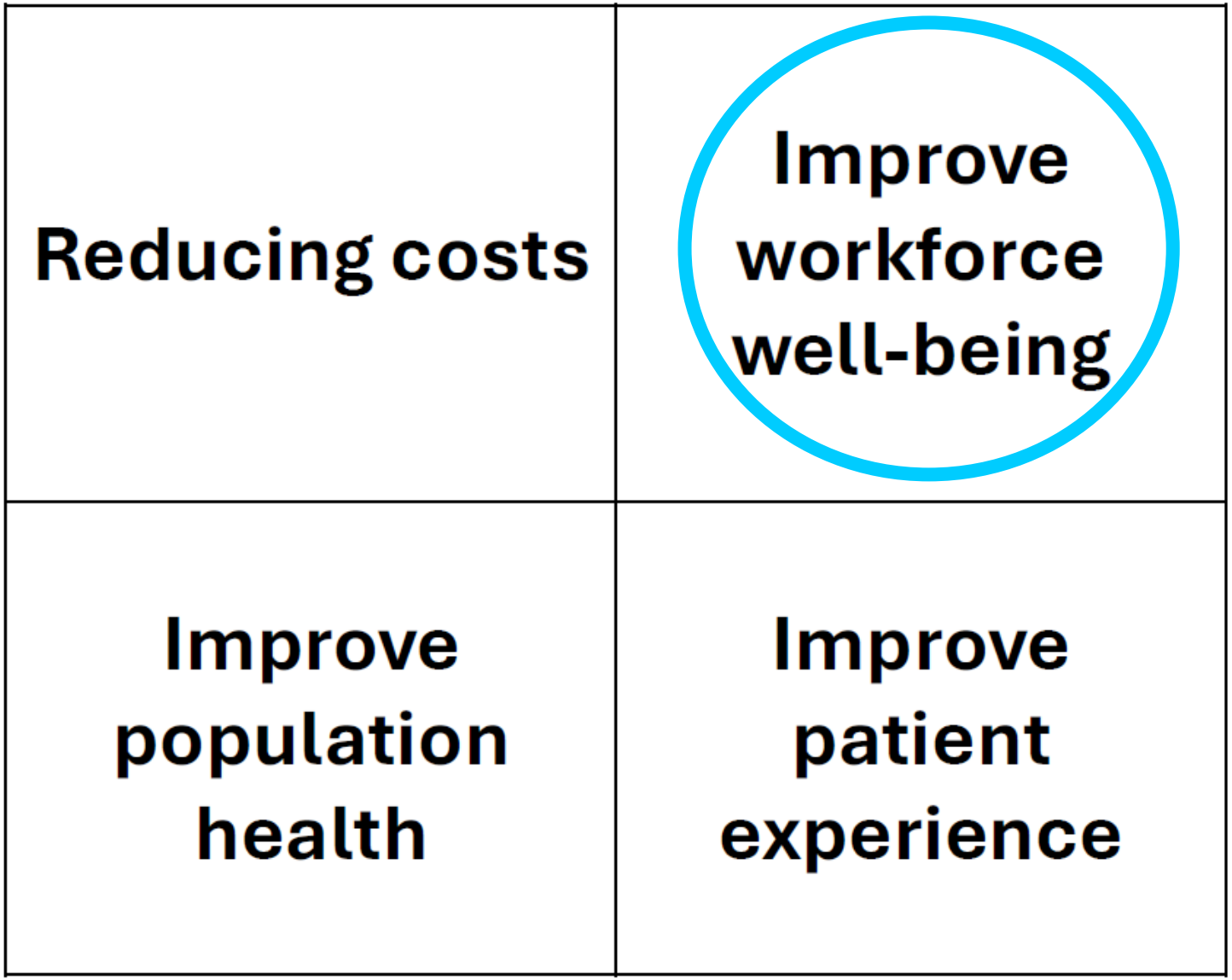
AUTONOMY

https://www.rnaautomation.com/insight/the-five-level-automation-pyramid-transforming-factories-of-the-future/

Why do we need autonomous medical systems in healthcare?

In the next few charts, we outline why some level of autonomy may become essential in healthcare of the future. However, risk in autonomous systems may be unacceptable. Alternative: semi-autonomous medical systems [SAMS] supervised and executed by humans-in-the-loop [SAMSHIL].

This article recommends that the Triple Aim be expanded to a Quadruple Aim



Bodenheimer T, Sinsky C. From triple to quadruple aim: care of the patient requires care of the provider. Ann Fam Med. 2014 Nov;12(6):573-576. doi: 10.1370/afm.1713. PMID: 25384822; PMCID: PMC4226781. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4226781/pdf/0120573.pdf

SHRINKING WORKFORCE

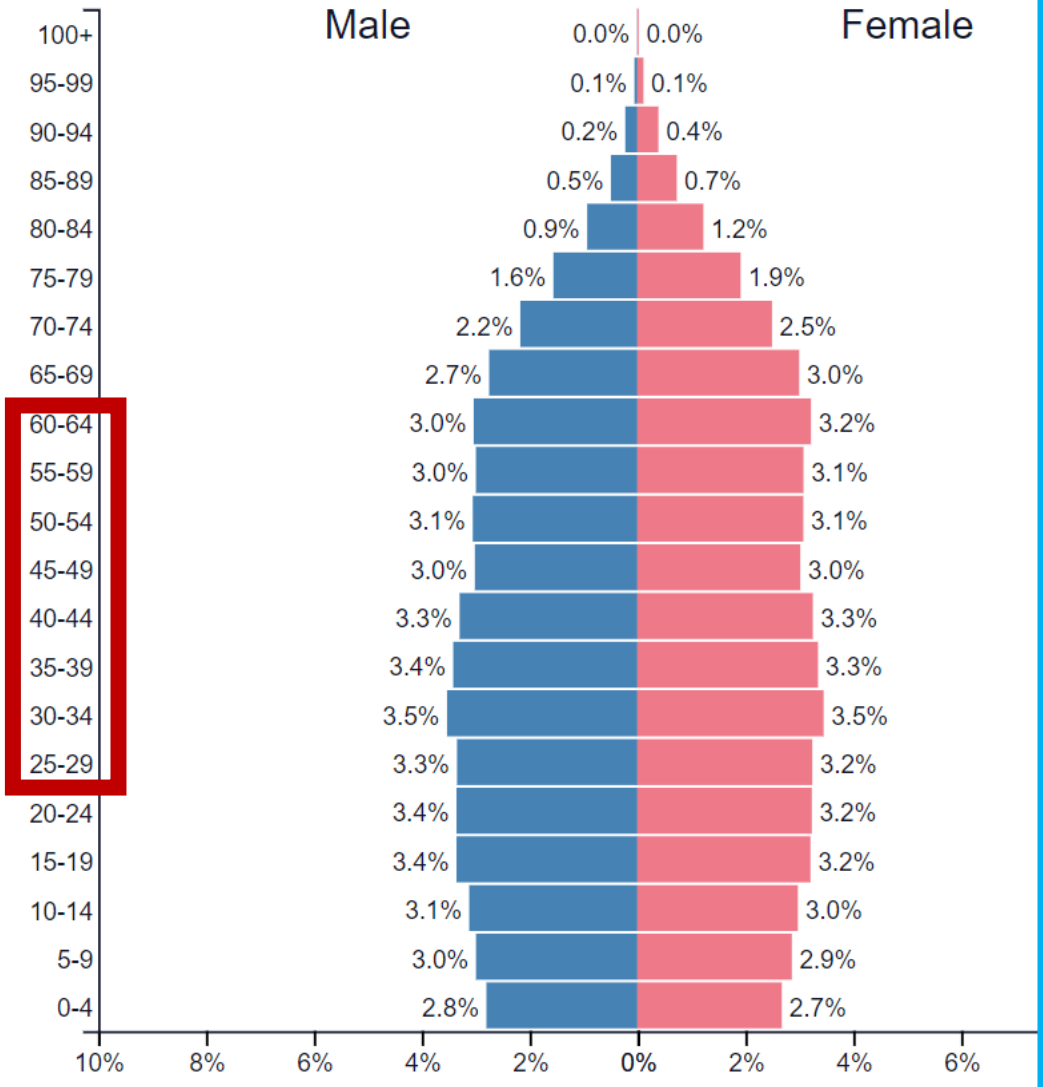
Changing (top-heavy) Demographics

Why some level of autonomy is an inescapable reality.

United States of America

2024

Population: 341,814,420

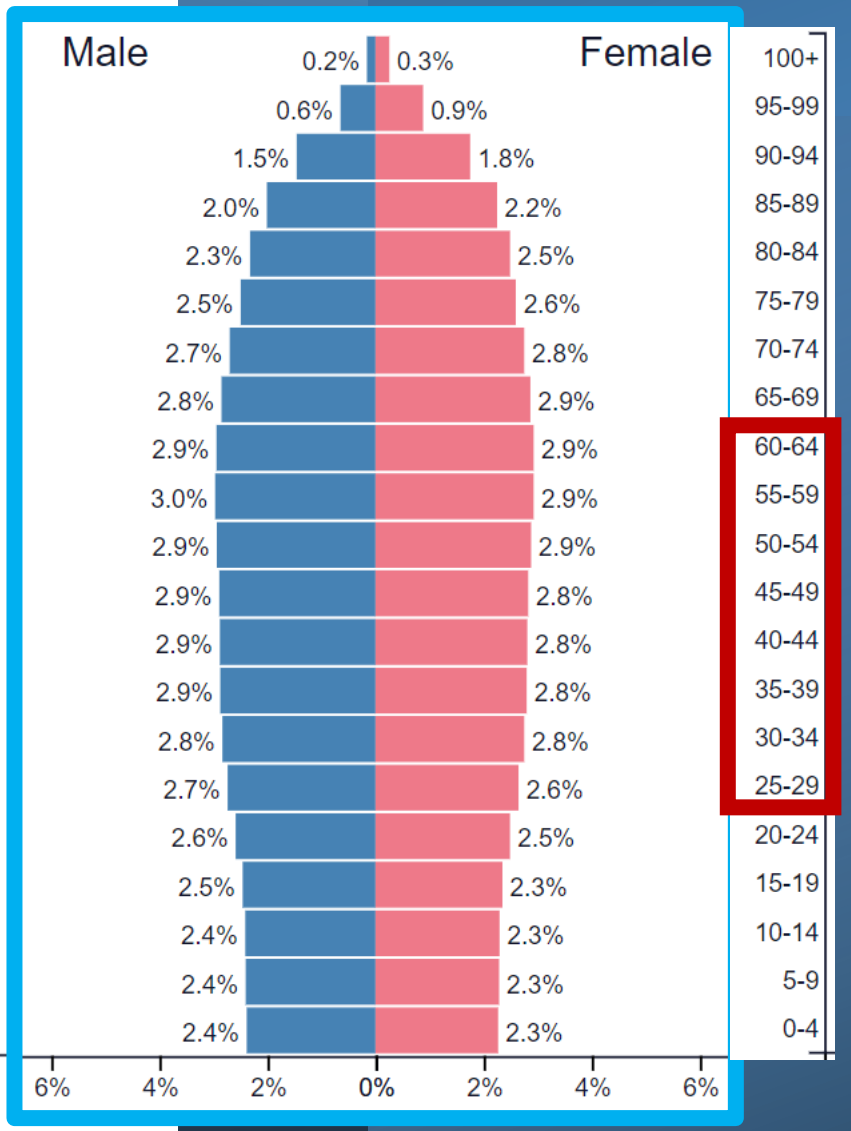


https://www.populationpyramid.net/united-states-of-america/2024/

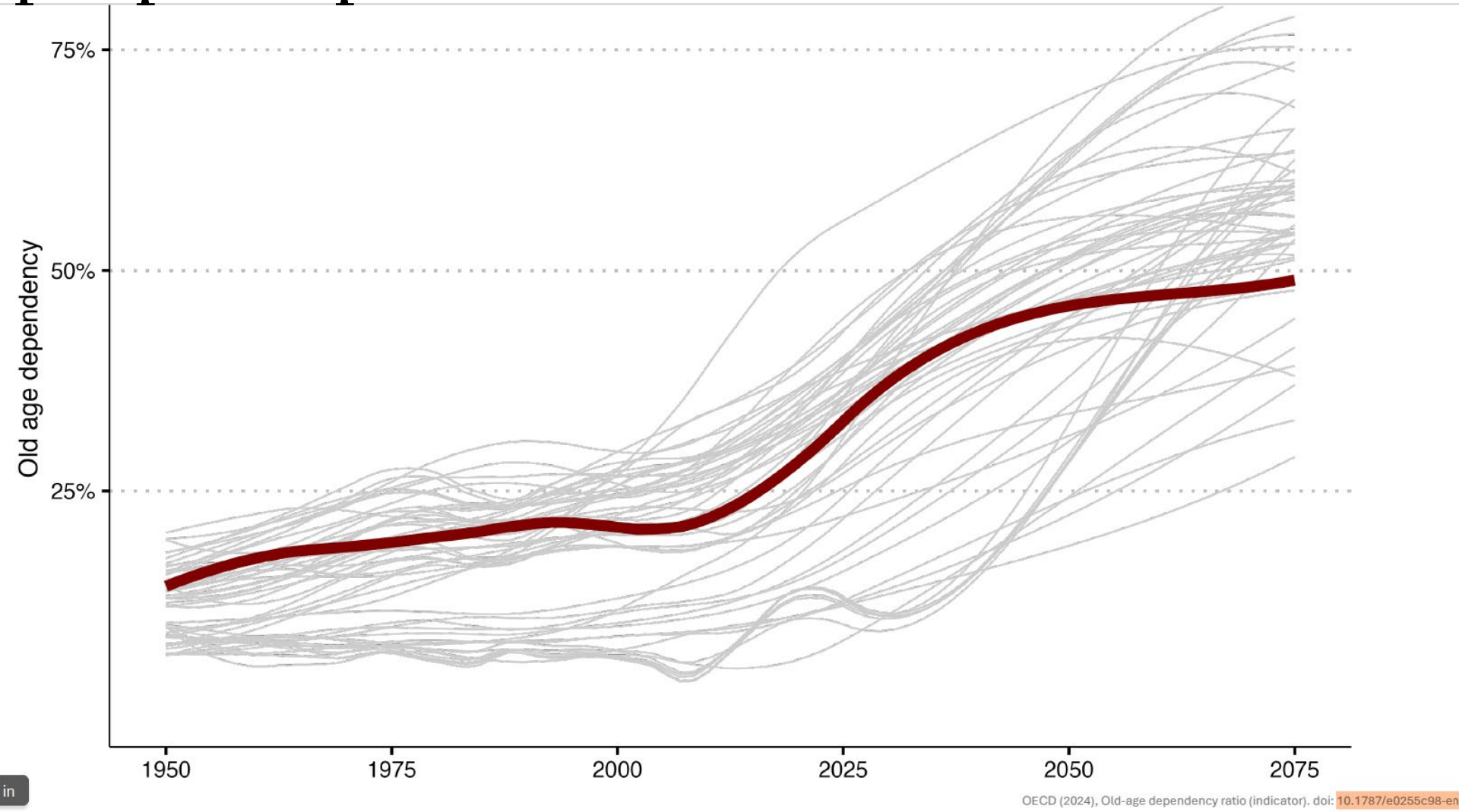
USA in 2100

394,041,155

https://www.populationpyramid.net/united-states-of-america/2100/



We are increasingly dependent on our older people to provide the healthcare services.



https://www.oecd.org/en/data/indicators/old-age-dependency-ratio.html
https://www.oecd-ilibrary.org/employment/oecd-labour-force-statistics-2022_dc0c92f0-en

Diagnosis By Radio

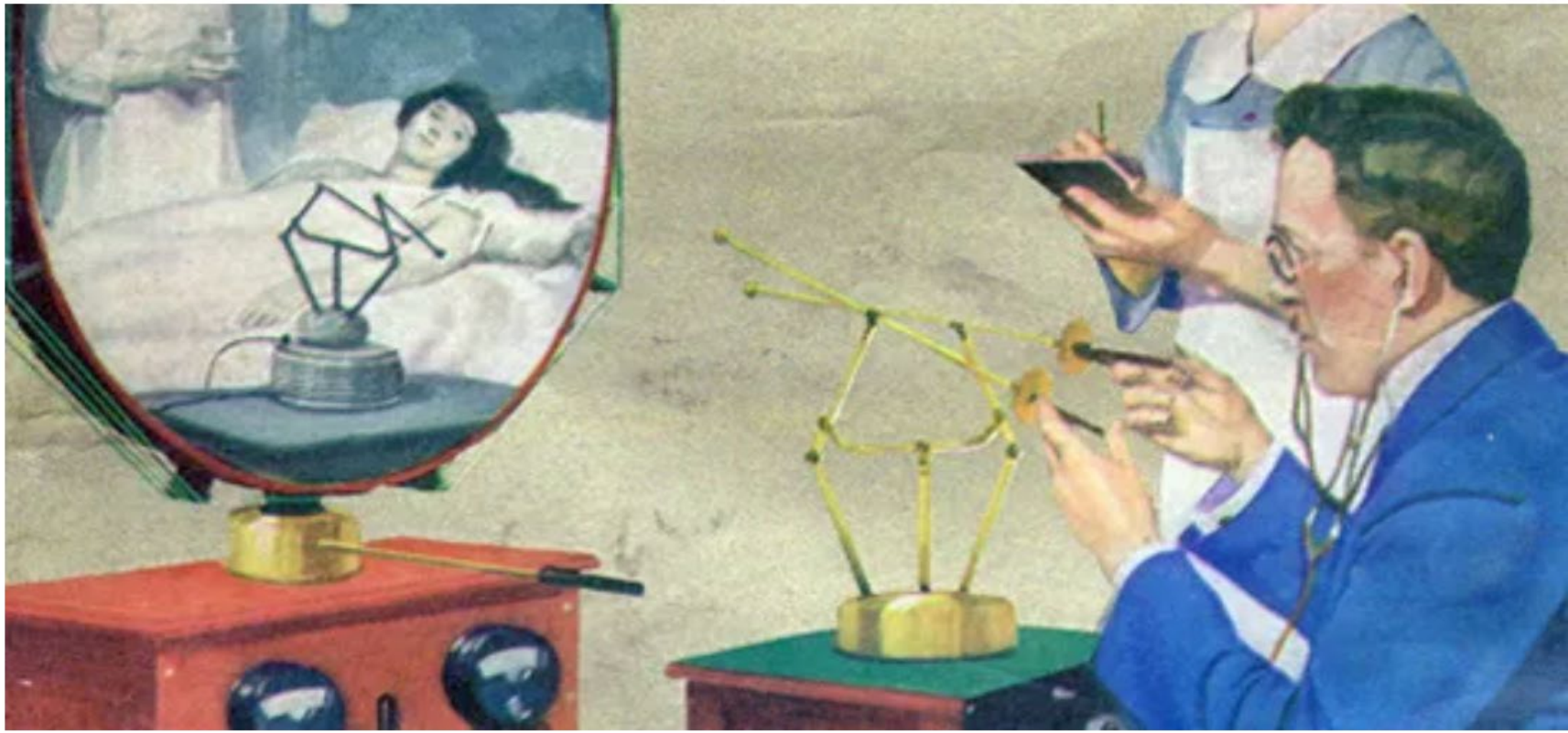
1925

https://isfdb.org/cgi-bin/pl.cgi?297302

Predicted ~100 years ago!

https://www.smithsonianmag.com/history/telemedicine-predicted-in-1925-124140942/

Smithsonian MAGAZINE



A doctor's diagnosis "by radio" on the cover of the February, 1925 issue of Science and Invention magazine

Science and Invention magazine

TeleHealth

TeleMedicine

www.tatrc.org/www/

https://mrdc.health.mil

LEFT – Col. Jeremy C. Pamplin, M.D., Commander of the Telemedicine and Advanced Technology Research Center (TATRC, US ARMY MRDC, DoD)

ABOUT TATRC

The Telemedicine and Advanced Technology Research Center (TATRC) is a Command under the U.S. Army Medical Research and Development Command (USAMRDC), located at Fort Detrick, Maryland. TATRC conducts and supports research through its four key divisions which include: Computational Biology, Digital Health, Medical Modeling & Simulation, and Medical Robotics and Autonomous Systems. Through the Advanced Medical Technology Initiative, TATRC sponsors clinicians across the military health systems to test new technologies and ideas in clinically relevant process improvement projects, during operational simulations, or with animal models. TATRC fosters research to address gaps in DoD medical programs and military healthcare. With an extensive network of partners, TATRC expertise is focused on the entire research spectrum, from early stage innovative research to technology demonstrations and implementation to benefit the Warfighter. TATRC Labs actively collaborate with commercial entities and academic institutions to address the requirements of our medical research programs through special funding and partnership opportunities.

https://www.tatrc.org/www/

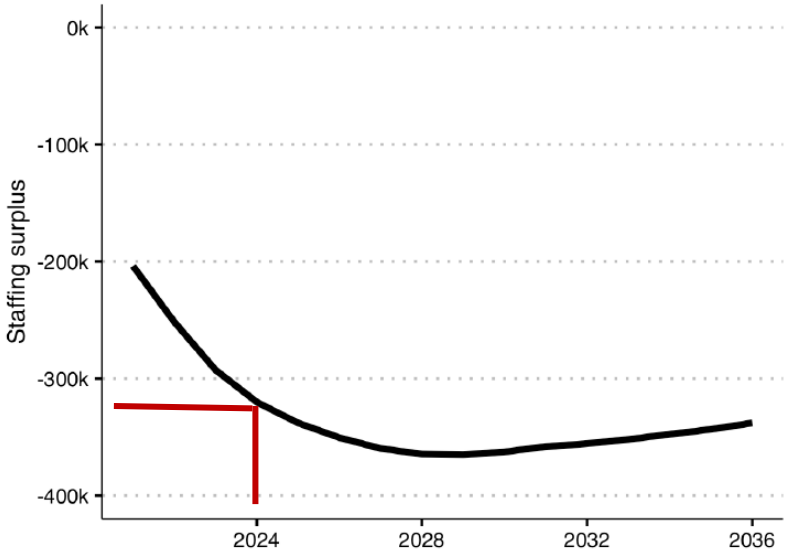
Automation

humans-in-the-loop

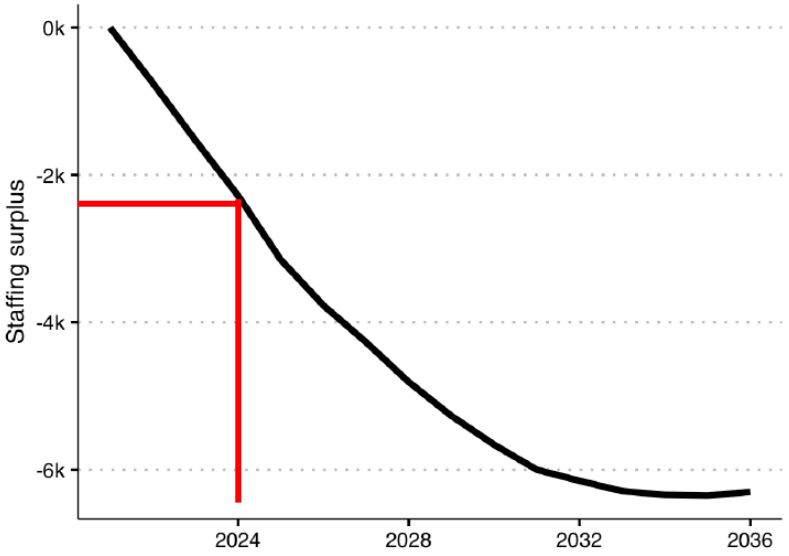
2024 shortfall >300,000 nurses and >2,000 anesthesiologists

Workforce gap *it will get worse because there aren't any "new" people*

Registered Nurses



Anesthesiologist



Department of Health and Human Services, Health Resources and Services Administration, Health Workforce

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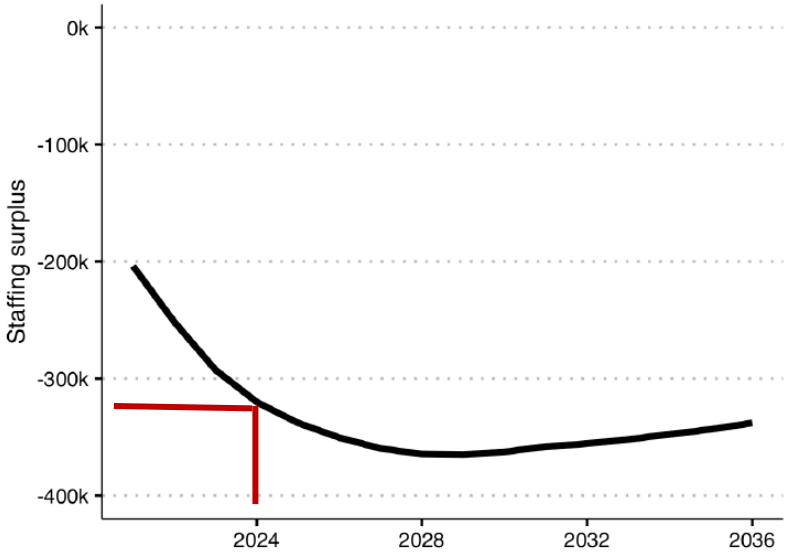
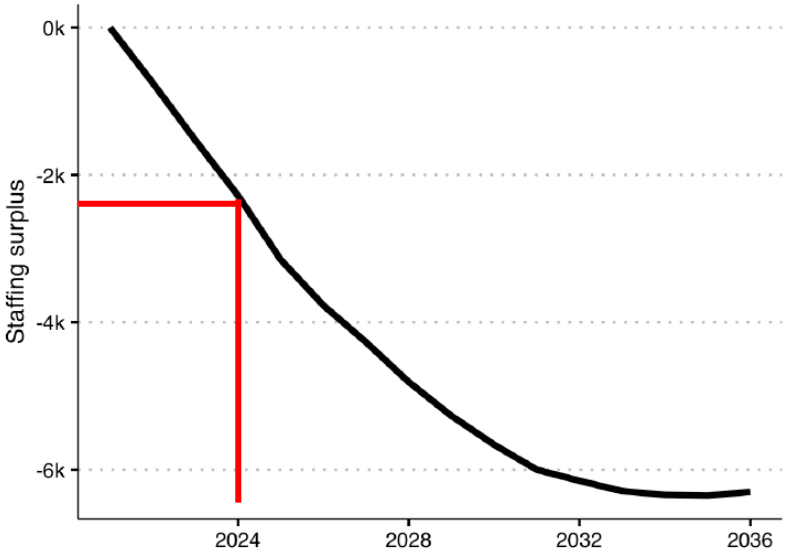


Anesthesiologist



Department of Health and Human Services, Health Resources and Services Administration, Health Workforce

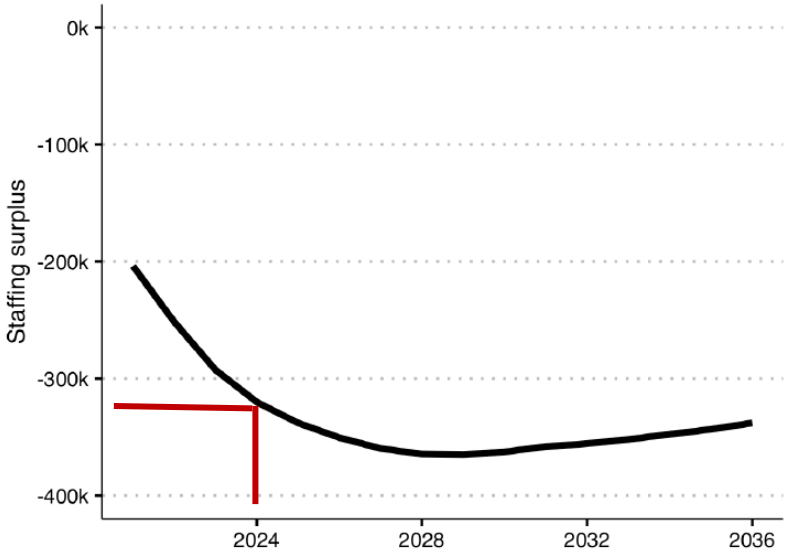
Automation HIL ?

Is the emergence of the SAMS-HIL era an inescapable reality ?

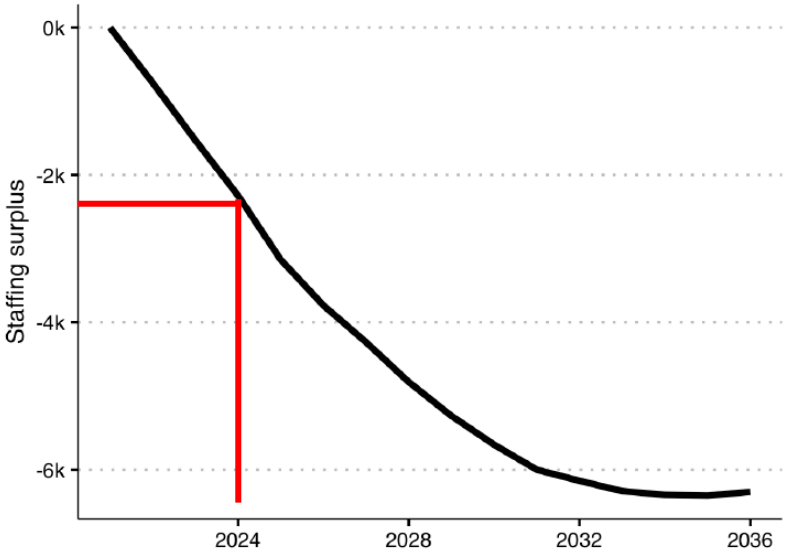
2024 shortfall >300,000 nurses and >2,000 anesthesiologists

Workforce gap *it will get worse because there aren't any "new" people*

Registered Nurses



Anesthesiologist



Department of Health and Human Services, Health Resources and Services Administration, Health Workforce

Semi-autonomous medical systems with humans-in-the-loop ?

Automated ?? Anesthesiologist

Potentially possible …

Abstract: Background: We previously developed an automated total intravenous anesthesia control system that uses new closed-loop system algorithms to administer propofol, remifentanil, and rocuronium based on the bispectral index and train-of-four data. We recently improved this automated control system by adding a safety mechanism and using a modified monitoring device.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10607889/pdf/jcm-12-06611.pdf

apicareonline.com/index.php/APIC/article/view/1178

pISSN: 1607-8322 , eISSN: 2220-5799

Anaesthesia,Pain & Intensive Care

A Bimonthly, International Journal of Anesthesiology, Pain Management, Intensive Care & Resuscitation

Comparison of propofol administration regulation by pharmacodynamic indicator esTEC (estimated target-effect-site concentration) versus BIS value

Yuka Matsuki
Department of Anesthesiology & Reanimatology, University of Fukui Hospital, Fukui, (Japan)

Osamu Nagata
Department of Anesthesiology, Center Hospital of the National Center for Global Health and Medicine, Tokyo, (Japan)

Yoshihiro Ogino
Ventilator & Anesthesia Device Business Operations, NIHON KOHDEN Corporation, Tokyo, (Japan)

Yuko Nakanishi
Department of Anesthesiology & Reanimatology, University of Fukui Hospital, Fukui, (Japan)

Kenji Shigemi
Department of Anesthesiology & Reanimatology, University of Fukui Hospital, Fukui, (Japan)

2019

https://doi.org/10.35975/apic.v23i4.1178

Comparison of propofol administration regulation by pharmacodynamic indicator esTEC (estimated target-effect-site concentration) versus BIS value

Yuka Matsuki[1], Osamu Nagata[2], Yoshihiro Ogino[3], Yuko Nakanishi[1], Kenji Shigemi[1]

[1]Department of Anesthesiology & Reanimatology, University of Fukui Hospital, Fukui, (Japan)

[2]Department of Anesthesiology, Center Hospital of the National Center for Global Health and Medicine, Tokyo, (Japan)

[3]Ventilator & Anesthesia Device Business Operations, NIHON KOHDEN Corporation, Tokyo, (Japan)

2019

Abstract: Background We previously developed an automated total intravenous anesthesia control system that uses new closed-loop system algorithms to administer propofol, remifentanil, and rocuronium based on the bispectral index and train-of-four data. We recently improved this automated control system by adding a safety mechanism and using a modified monitoring device. Methods:

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2023

Anesthesia Management via an Automated Control System for Propofol, Remifentanil, and Rocuronium Compared to Management by Anesthesiologists: An Investigator-Initiated Study

Osamu Nagata [1,†], Yuka Matsuki [1,*,†], Shuko Matsuda [1], Keita Hazama [2], Saiko Fukunaga [3], Hideki Nakatsuka [3], Fumiyo Yasuma [4], Yasuhiro Maehara [4], Shoko Fujioka [5], Karin Tajima [5], Ichiro Kondo [5], Itaru Ginoza [6], Misuzu Hayashi [6], Manabu Kakinohana [6] and Kenji Shigemi [1]

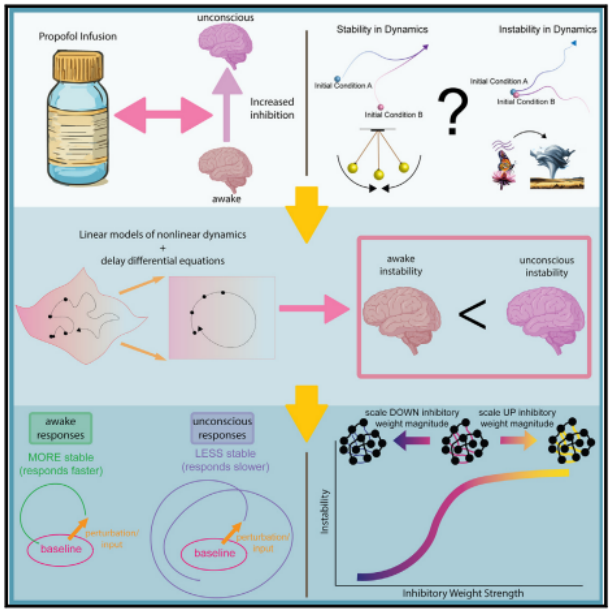
1 Department of Anesthesiology and Reanimatology, University of Fukui, Fukui 910-1193, Japan; o-nagata@fa2.so-net.ne.jp (O.N.)
2 Department of Anesthesiology and Intensive Care Medicine, Hiroshima City Hiroshima Citizens Hospital, Hiroshima 730-8518, Japan
3 Department of Anesthesiology and Intensive Care Medicine, Kawasaki Medical School, Kurashiki 701-0192, Japan
4 Department of Anesthesiology, Center Hospital of the National Center for Global Health and Medicine, Tokyo 162-8655, Japan
5 Departments of Anesthesiology, The Jikei University School of Medicine, Tokyo 105-8461, Japan
6 Department of Anesthesiology, University of the Ryukyu, Okinawa 903-0213, Japan
* Correspondence: ymatsuki@u-fukui.ac.jp; Tel.: +81-776-61-8391; Fax: +81-776-61-8116

Nagata O, Matsuki Y, Matsuda S, Hazama K, Fukunaga S, Nakatsuka H, Yasuma F, Maehara Y, Fujioka S, Tajima K, Kondo I, Ginoza I, Hayashi M, Kakinohana M, Shigemi K. Anesthesia Management via an Automated Control System for Propofol, Remifentanil, and Rocuronium Compared to Management by Anesthesiologists: An Investigator-Initiated Study. J Clin Med. 2023 Oct 19;12(20):6611. doi: 10.3390/jcm12206611. PMID: 37892749; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10607889/pdf/jcm-12-06611.pdf

Neuron

Propofol anesthesia destabilizes neural dynamics across cortex

Graphical abstract



Authors

Adam J. Eisen, Leo Kozachkov, André M. Bastos, ..., Emery N. Brown, Ila R. Fiete, Earl K. Miller

Correspondence

fiete@mit.edu (I.R.F.), ekmiller@mit.edu (E.K.M.)

In brief

Eisen and Kozachkov et al. develop a method to measure changes in neural stability. They find evidence that an anesthetic causes unconsciousness by destabilizing neural activity. It makes activity more susceptible to perturbation. This is due to excess inhibition in the brain.

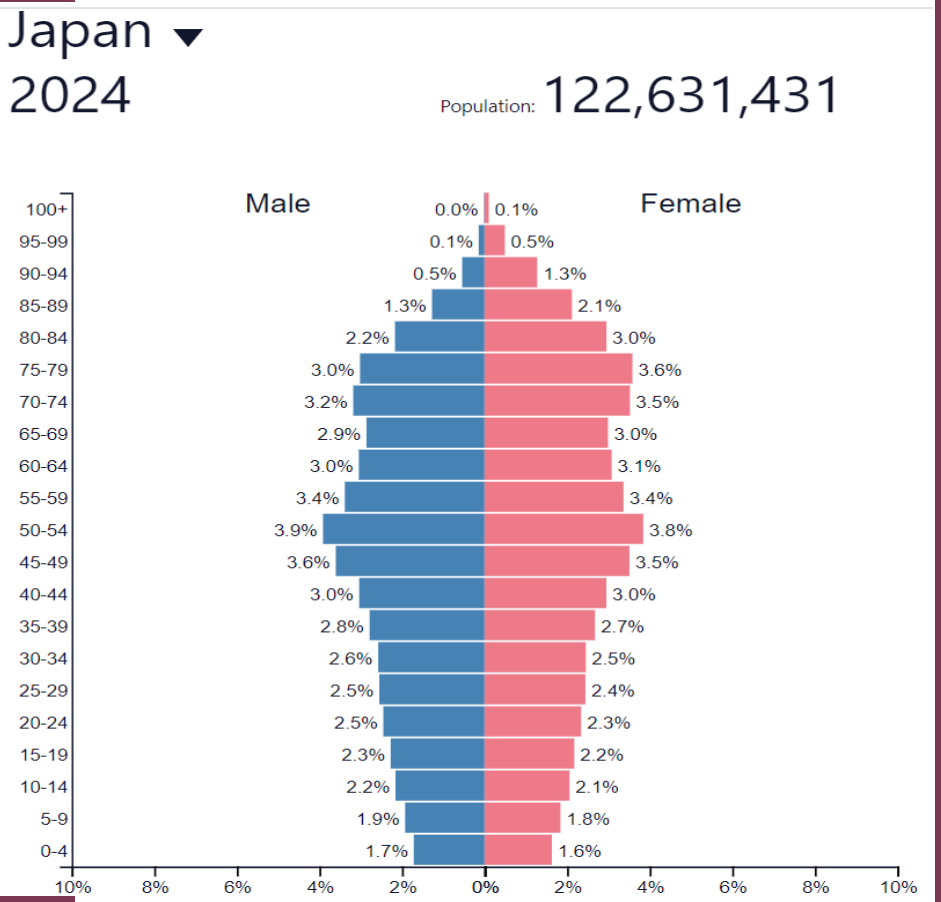
Highlights

- We developed DeLASE, a method for quantifying changes in neural stability
- During propofol-induced unconsciousness, neural activity was destabilized
- Destabilized artificial systems had similar dynamics to the destabilized brain
- Increasing inhibition, as propofol does, destabilized artificial network activity

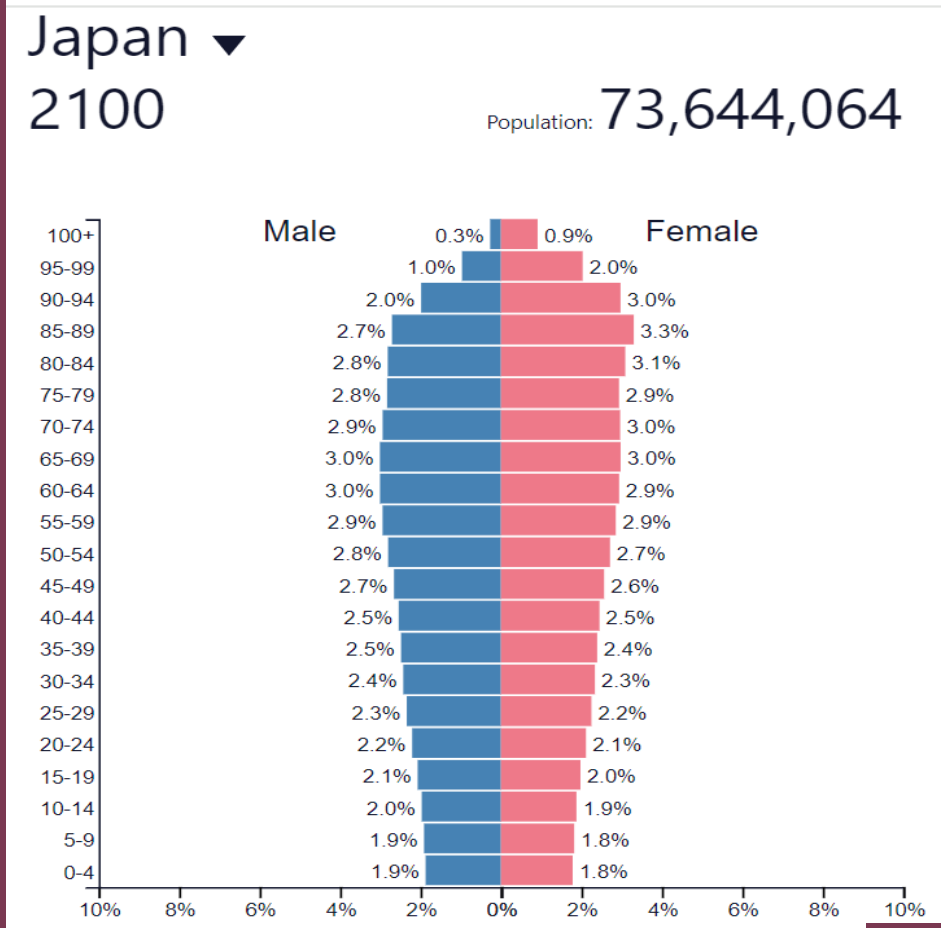
Eisen et al., 2024, Neuron 112, 1–15 (August 21, 2024)

https://doi.org/10.1016/j.neuron.2024.06.011

Is Japan desperate to automate?



https://www.populationpyramid.net/japan/2024/



https://www.populationpyramid.net/japan/2100/

technologyreview.com/2016/03/29/161269/automated-anesthesiologist-suffers-a-painful-defeat/

MIT Technology Review

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ARTIFICIAL INTELLIGENCE

Automated Anesthesiologist Suffers a Painful Defeat

A machine that makes anesthesiologists unnecessary for some medical procedures has failed amid poor sales and resistance from doctors and nurses.

By Tom Simonite

March 29, 2016

www.technologyreview.com/2016/03/29/161269/automated-anesthesiologist-suffers-a-painful-defeat/

PROC (BAYL UNIV MED CENT)
2018;31(1):117–119

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Anesthesiology, automation, and artificial intelligence

John C. Alexander, MD, MBA, and Girish P. Joshi, MBBS, MD

Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center, Dallas, Texas

ABSTRACT

There have been many attempts to incorporate automation into the practice of anesthesiology, though none have been successful. Fundamentally, these failures are due to the underlying complexity of anesthesia practice and the inability of rule-based feedback loops to fully master it. Recent innovations in artificial intelligence, especially machine learning, may usher in a new era of automation across many industries, including anesthesiology. It would be wise to consider the implications of such potential changes before they have been fully realized.

KEYWORDS Anesthesiology; automation; artificial intelligence; clinical decision support; machine learning

Alexander JC, Joshi GP. Anesthesiology, automation, and artificial intelligence. Proc (Bayl Univ Med Cent). 2017 Dec 5;31(1):117-119. doi: 10.1080/08998280.2017.1391036. PMID: 29686578; www.ncbi.nlm.nih.gov/pmc/articles/PMC5903534/pdf/ubmc-31-01-1391036.pdf

An example of automation collaboration

Massachusetts General Hospital

SaAMS

HARVARD
MEDICAL SCHOOL

The Need for a Collaborative Community to Advance the Development and Adoption of Smart and Autonomous Medical Systems (SaAMS)

Julian M. Goldman, M.D[1,2]., Yi Zhang, Ph.D.[1]

[1]Center for Smart and Autonomous Medical Systems / Medical Device Interoperability and Cybersecurity Program (MD PnP)
Department of Anesthesia, Critical Care and Pain Medicine. Massachusetts General Hospital; [2]Harvard Medical School, Boston, Massachusetts

Excerpt from STA 2020 Poster

STA 2020 Poster:
Verification of Interoperable Medical Devices for Closed-Loop Control of Anesthesia using Hardware-in-the-Loop Testing
J Goldman, Y Zhang, D Arney, S Weininger(FDA)

"The performance of medical devices (core medical functions and interface capabilities) must be characterized in detail to safely comprise the CLC system.

This poster documents the application of our research hardware-in-the-loop testbed for interoperable CLC devices."

What are Smart and Autonomous Medical Systems (SaAMS)?

SaAMS describe a wide range of medical systems designed from the ground up to enable smart apps to connect to medical devices to more safely and efficiently deliver transformative patient care solutions.

SaAMS may utilize sophisticated algorithms interacting with interoperable medical devices to perform tasks that improve patient safety or efficiency, make decisions, automate processes, enhance vigilance, personalize patient and user experiences, advance healthcare equity, and solve historically intractable problems. They may utilize artificial intelligence (AI) to adapt to new information, make predictions, and operate autonomously.

Excerpt rom STA 2020 Poster

The anesthesia technology community should collaborate to establish consensus safety, regulatory, and performance requirements that can be used as a baseline to characterize the capabilities of interoperable medical devices to enable and promote CLC anesthesia innovation.

To address that need, we are establishing a Smart and Autonomous Medical Systems (SaAMS) **initiative** to facilitate engagement by interested stakeholders (medical device manufacturers, health delivery organizations, funding entities, and regulators). We welcome your participation in the SaAMS initiative.

The SaAMS initiative progressed under TATRC NETCCN/TiDE and DoD FCT grant portfolios.

2024: SaAMS "Initiative" → Collaborative Community

A Collaborative Community can address challenging medical technology needs that no single manufacturer or other entity may be able to accomplish alone. This includes identifying and advancing key enabling device features and clinical system capabilities that address complex engineering and clinical challenges.

We are forming a Collaborative Community, as described by the FDA, "to achieve common outcomes, solve shared challenges, and leverage collective opportunities" to advance the maturity, adoption, and clinical use of SaAMS to improve patient care. [1]

Participants in the SaAMS Collaborative Community will comprise a wide range of experts including manufacturers, clinicians, engineers, researchers, government representatives, and the US FDA, to collaborate on the development of evidence to support safety. This safety framework is intended **to provide precompetitive evidence for use in the regulatory process to de-risk commercial development and increase the safety, effectiveness, and clinical usability of these systems**.

Examples of SaAMS applications

- Automated Closed Loop control of Intravenous Anesthesia (ACLIVA)
- Closed-loop vasopressor therapy
- Closed-Loop Fluid Administration
- Remote IV Infusion Pump Control and Remote Lung Ventilator Control
- Smart alarms that improve and specificity
- AI-based predictive clinical analytics

References

1. Collaborative Communities: Addressing Health Care Challenges Together, https://www.fda.gov/about-fda/cdrh-strategic-priorities-and-updates/collaborative-communities-addressing-health-care-challenges-together
2. MGH SaAMS Collaborative Community https://mdpnp.mgh.harvard.edu/saams-cc/
3. MD PnP Center for SaAMS https://mdpnp.mgh.harvard.edu/saams-center/

https://mdpnp.mgh.harvard.edu/saams-cc/

MD PnP™ → SaAMS

Acknowledgements

This research was supported in part under the Medical Technology Enterprise Consortium(MTEC) Research Project Number W81XWH-22-9-0004, funded by the Foreign Comparative Testing Program of the US Department of Defense (DoD). The views, opinions and/or findings contained in this poster are those of the authors and should not be construed as an official DoD position, policy or decision unless so designated by other documentation.

The Need for a Collaborative Community to Advance the Development and Adoption of Smart and Autonomous Medical Systems (SaAMS)

Julian M. Goldman, M.D[1,2]., Yi Zhang, Ph.D.[1]

[1]Center for Smart and Autonomous Medical Systems / Medical Device Interoperability and Cybersecurity Program (MD PnP)
Department of Anesthesia, Critical Care and Pain Medicine. Massachusetts General Hospital; [2]Harvard Medical School, Boston, Massachusetts

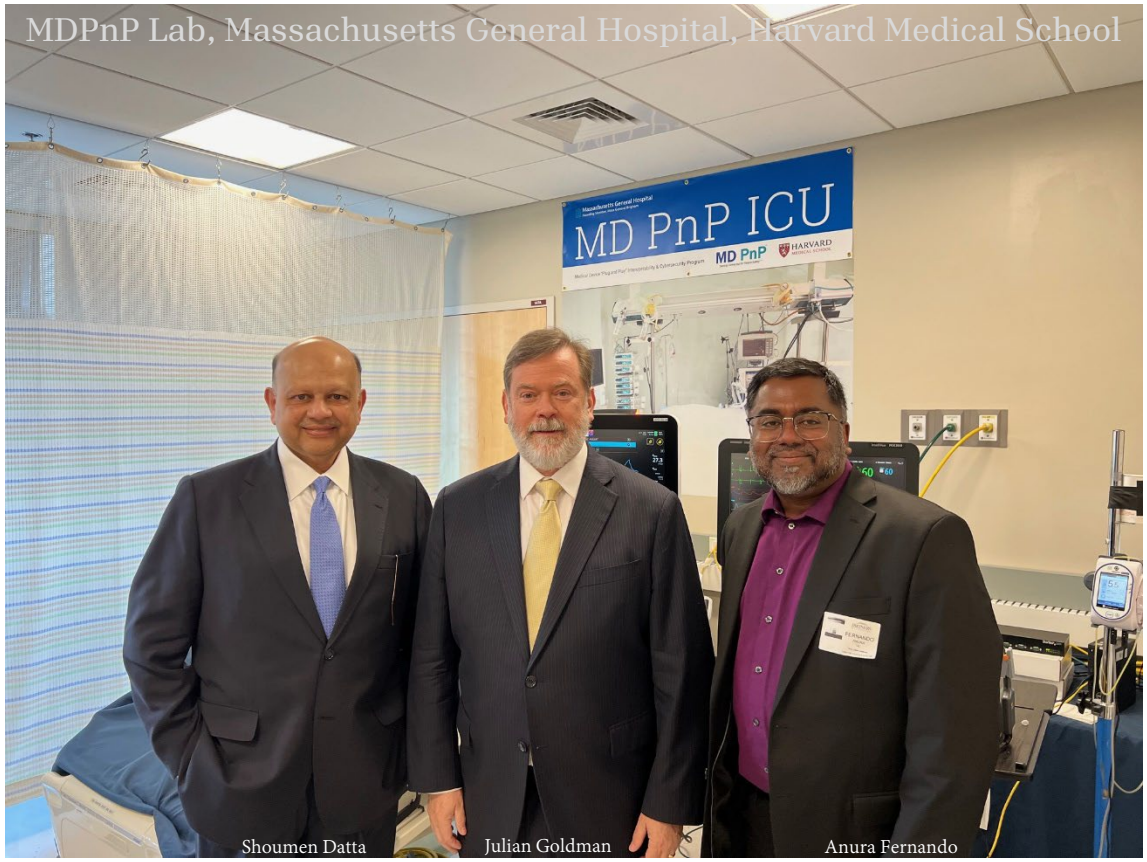
MD PnP™

SaAMS

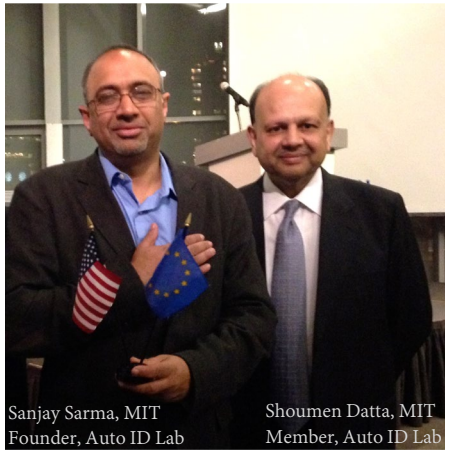
1989 ● (Department of Medicine) Massachusetts General Hospital, Harvard Medical School

Dr J Larry Jameson MD PhD Molecular Endocrinology / Neuro-Endocrinology Dr Anne Klibanski MD

Convergence



Multi-disciplinarity …



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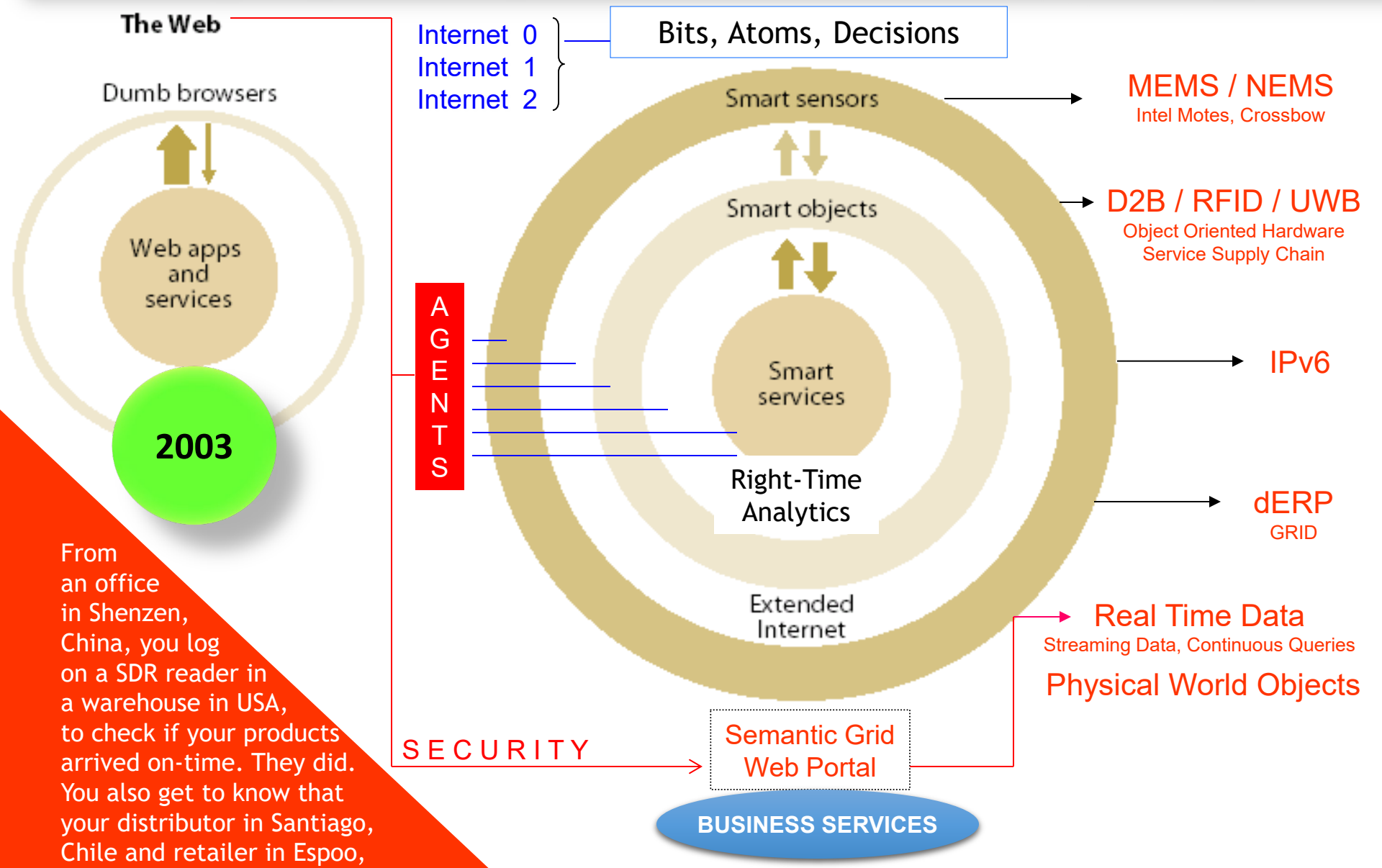
MIT AUTO-ID LABORATORY

The MIT AUTO-ID LABORATORY coined the term Internet of Things (IoT) and traces its roots back to 1999 with the founding of the Auto-ID Center, which laid much of the groundwork for the standardization of RFID technology and the introduction of the EPC. Now a member of the global Auto-ID Labs network, it continues to research the evolution and application of RFID systems, as well as other disruptive Internet of Things technologies.

Massachusetts Institute of Technology
Room 35-208, Cambridge, MA 02139-4307

1999

Connecting Ubiquitous Analytics in Real-Time with Data, Information, Application



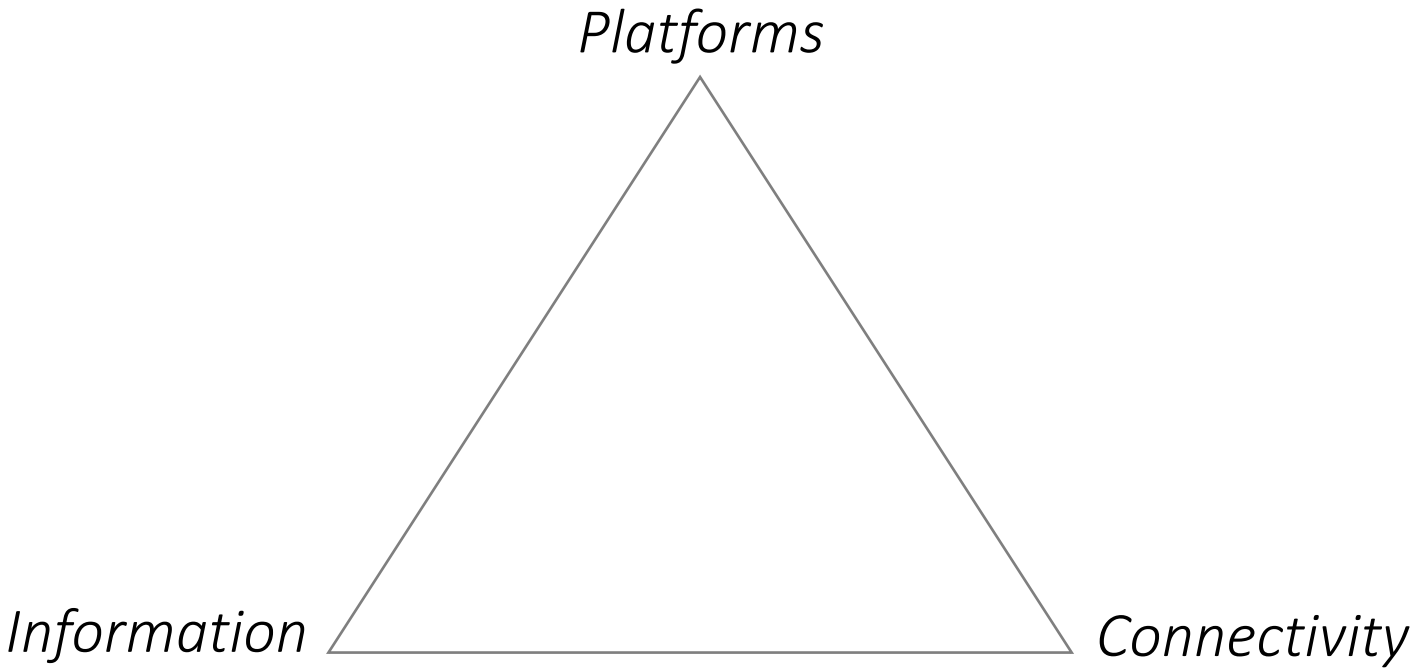
From an office in Shenzen, China, you log on a SDR reader in a warehouse in USA, to check if your products arrived on-time. They did. You also get to know that your distributor in Santiago, Chile and retailer in Espoo, Finland also checked the delivery status, moments before you logged on.

SDR Data Interrogators as Ubiquitous Internet Appliances in IoT (2003)

Platforms are indivisible but better understood if discussed as

Platform as a Principle = Information

Platform as a Practice = Connectivity



Platform as a Principle

Information

The Information Age is not over. It started with the Big Bang which created the Solar System and it may persist *ad infinitum* as long as the Solar System continues its physical existence. It is the mother of all platforms and the most fundamental fabric of connectivity. Our understanding of the difference between hydrogen and oxygen is based on information. The difference between bauxite and the material of the Coke can is information. Information is the differentiator between Apple Newton which died prematurely vs the almost identical Palm Pilot that once climbed the luminous summit. Information changes when the car you are driving is suddenly crushed in a collision with a truck. Think about the approximately 500 inhabitants of Mureybet, Syria in 8000BC and compare their information content to the approximately 1500 modern day inhabitants of Dingle village in County Kerry (Ireland) which boasts of at least 50 pubs in this miniscule hamlet near the Atlantic. Information has grown. Described by Claude Shannon in 1948 as informational entropy, it has been shown that the interpretation of entropy (formula) provided by Ludwig Boltzmann (the Boltzmann equation) becomes the Shannon equation, thus mathematically linking entropy and information.

Platform as a Practice

Connectivity

Is it a new theme? Isn't it fundamentally pervasive in every entity – physical, metaphysical and cyberphysical? Doesn't it transcend the sub-nano realm and the super-macro domain? Doesn't it define the astronomical universe, all biological systems and everything conceptual in between? The mobility of ancient civilizations to explore new worlds were physical connections between atoms. The bargain hunter's app to compare prices between various retailers is the new sense of value which connects bits with atoms. All things and processes are about connectivity. Invention and innovation was, is and will be about connecting the dots, real and/or virtual, perceived and/or imagined. Human thought, technological progress and the future of synaptic neuromorphic quantum dots are manifestations of connectivity, convergence and confluence of concepts. The sense of connectivity is germane to life and decision science. Its ubiquity makes us oblivious to its quintessential nature. To evoke the central theme of connectivity, therefore, is not an insight but rather recognizing the fabric of the future which is catalyzing every data-informed decision.

Convergence

~35 years is not enough

1989 ● Massachusetts General Hospital, Harvard Medical School

1999 ● MIT Auto ID Center ● RFID EPC Technology Board

2001 ● MIT Forum for Supply Chain Innovation

2003 ● MIT Data Center ● Semantics

2009 ● MIT Energy Initiative

Convergence

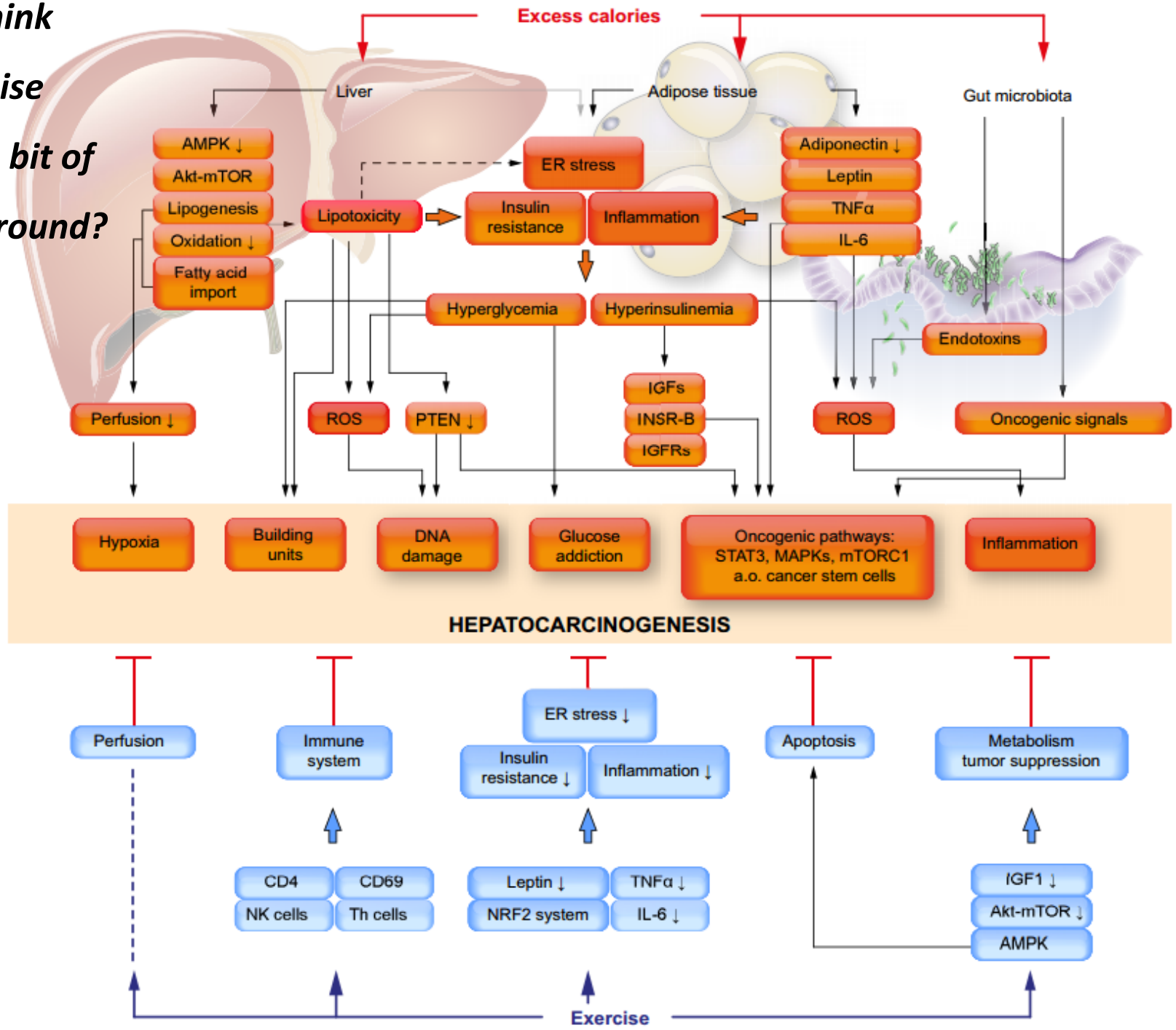
In my case, building bridges between research, medicine, engineering, business & data in decision science.

Ponte di Cecco, Ascoli Piceno

Health(care) *is connectivity*

There is no independent value. All data are interconnected and even dependent on other data. Isolating the value of an attribute is not impossible but ***assuming*** that we know or understand the ***cause*** of that value (causal analysis) is most likely to be incorrect.

Did you think that exercise was just a bit of running around?



Langston PK, Sun Y, Ryback BA, Mueller AL, Spiegelman BM, Benoist C, Mathis D. Regulatory T cells shield muscle mitochondria from interferon-γ-mediated damage to promote the beneficial effects of exercise. Sci Immunol. 2023 Nov 3; 8(89):eadi5377. doi: 10.1126/sciimmunol.adi5377. Epub 2023 Nov 3. PMID: 37922340.

ENTREPRENEURS 8/01/2015 @ 7:00AM | 1,215 views

The Leapfrog Opportunity In The World's Underserved Health Care Markets

President Uhuru Kenyatta of Kenya

+ Comment Now

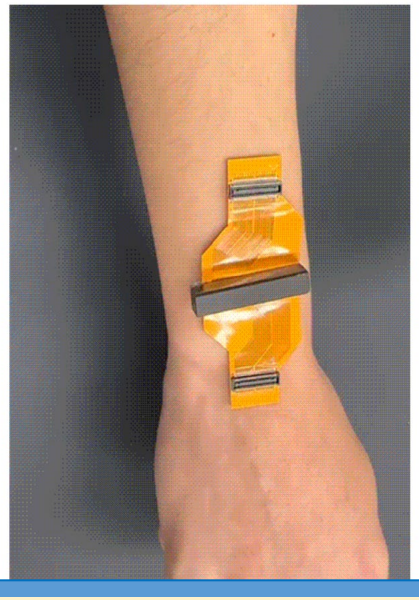
In Sub-Saharan Africa, traditional banking infrastructure has never quite gained a foothold. That's because instead of brick and mortar vaults, the region has seen sweeping use of mobile banking. Microfinancing and transfers, all from your cell phone, offered simplified, safer banking solutions for a fraction of the cost.

This is an example of "leapfrog" innovation and the same paradigm is beginning to emerge in health care in Africa, Asia and Latin America, creating a global opportunity for health innovators.

This past week President Obama was in Africa at the Global Entrepreneurship Summit calling on entrepreneurs and industry leaders to ignite growth on that continent and beyond. The question is will the leaders in today's largest health care markets seize the moment? Or will upstarts leap over them by bringing radically less expensive and more accessible healthcare options to the rest of the world?

http://onforb.es/1IQ1pSQ

MIT engineers have developed a small ultrasound sticker that can monitor the stiffness of organs deep inside the body. The sticker, about the size of a postage stamp, can be worn on the skin and is designed to pick up on signs of disease, such as liver and kidney failure and the progression of solid tumors.



Fulminant Hepatic Failure (*aka* acute liver failure, ALF)

https://news.mit.edu/2024/ultrasound-sticker-senses-changing-stiffness-deep-internal-organs-0209

Wearable bioadhesive ultrasound shear wave elastography

Hsiao-Chuan Liu[1,2]*†, Yushun Zeng[3]†, Chen Gong[3]†, Xiaoyu Chen[2], Piotr Kijanka[4], Junhang Zhang[3], Yuri Genyk[5], Hisham Tchelepi[6], Chonghe Wang[2], Qifa Zhou[1,3]*, Xuanhe Zhao[2,7]*

Acute liver failure (ALF) is a critical medical condition defined as the rapid development of hepatic dysfunction. Conventional ultrasound elastography cannot continuously monitor liver stiffness over the course of rapidly changing diseases for early detection due to the requirement of a handheld probe. In this study, we introduce wearable bioadhesive ultrasound elastography (BAUS-E), which can generate acoustic radiation force impulse (ARFI) to induce shear waves for the continuous monitoring of modulus changes. BAUS-E contains 128 channels with a compact design with only 24 mm in the azimuth direction for comfortable wearability. We further used BAUS-E to continuously monitor the stiffness of in vivo rat livers with ALF induced by D-galactosamine over 48 hours, and the stiffness change was observed within the first 6 hours. BAUS-E holds promise for clinical applications, particularly in patients after organ transplantation or postoperative care in the intensive care unit (ICU).

www.science.org/doi/epdf/10.1126/sciadv.adk8426

Fulminant hepatic failure, also known as acute liver failure (ALF), is defined as a severe liver injury resulting in the onset of hepatic encephalopathy within 8 weeks of the initial symptoms in patients without underlying liver disease (*1*). ALF has a high mortality rate of approximately 80% due to massive short-term cell death (*2*, *3*). This condition can occur as a result of various etiologies such as viral hepatitis (hepatitis A & E and hepatitis B), neoplastic infiltration, heart failure, mycotoxicosis, drug toxicity (*4*, *5*), or complications of liver transplantation (*1*, *6*). The survival rate of patients with ALF after 1 month is merely 23% if appropriate procedures such as liver transplantation or intensive care medicine are not immediately taken (*7*, *8*). Even after liver transplantation, postoperative complications may still lead to acute liver graft dysfunction (*6*, *9*) and high premature mortality (*10*). Therefore, prompt prognostic evaluation plays an important role in performing key & timely intensive care treatment of ALF, allowing graft salvage, and managing postoperative complications in the intensive care unit.

Electronic Nose for Diagnosis of Neurodegenerative Diseases

ClinicalTrials.gov ID NCT01291550

Sponsor Rambam Health Care Campus

Information provided by Rambam Health Care Campus

Last Update Posted 2011-02-08

Nanomedicine (Lond). 2013 Jan;8(1):43-56. doi: 10.2217/nnm.12.105. Epub 2012 Oct 15.

Detection of Alzheimer's and Parkinson's disease from exhaled breath using nanomaterial-based sensors

Ulrike Tisch [1], Ilana Schlesinger, Radu Ionescu, Maria Nassar, Noa Axelrod, Dorina Robertman, Yael Tessler, Faris Azar, Abraham Marmur, Judith Aharon-Peretz, Hossam Haick

Affiliations + expand

PMID: 23067372 DOI: 10.2217/nnm.12.105

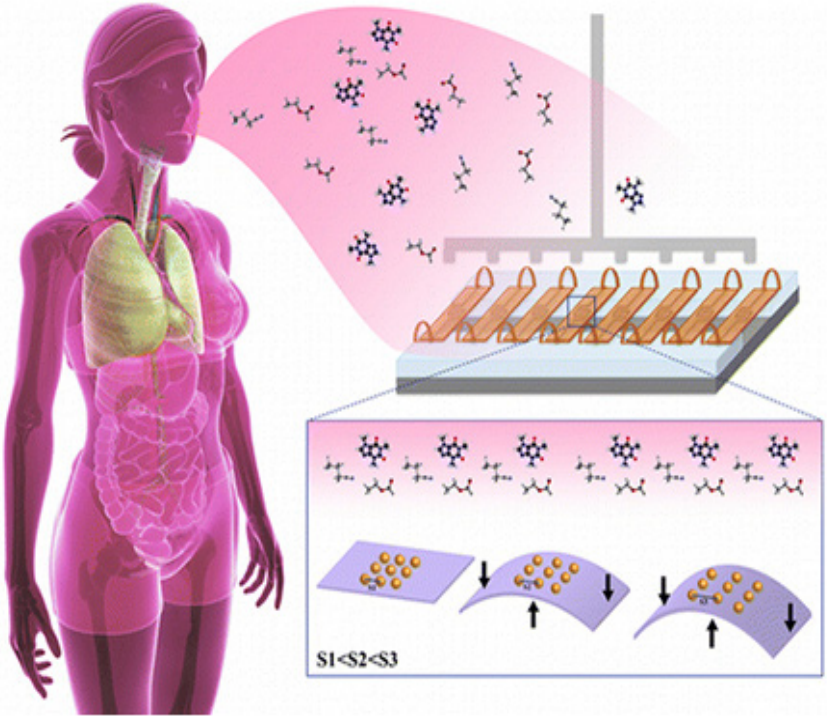
Tisch U, Schlesinger I, Ionescu R, Nassar M, Axelrod N, Robertman D, Tessler Y, Azar F, Marmur A, Aharon-Peretz J, Haick H. Detection of Alzheimer's and Parkinson's disease from exhaled breath using nanomaterial-based sensors. Nanomedicine (Lond). 2013 January;8(1):43-56. doi: 10.2217/nnm.12.105. Epub 2012 Oct 15. PMID: 23067372.

Electronic Nose Sniffs Out Ovarian Cancer in Exhaled Breath

OCTOBER 6TH, 2015 EDITORS NANOMEDICINE, ONCOLOGY

MIoT IoSH

We know that exhaled breath contains biomarkers that point to presence of existing disease, including cancer, but their detection is challenging without bulky and expensive equipment. Building specialized devices that detect volatile organic compounds linked to disease requires large sensor arrays, a limitation that has made them currently impractical. Now researchers at Technion –Israel Institute of Technology and Carmel Medical Center in Haifa, Israel have developed tiny flexible sensors that are each able to replicate the work of many. In a study testing the breath of 43 volunteers that included 17 ovarian cancer patients, their sensors achieved an 82% accuracy of detection.



The sensors are flexible and are made of gold nanoparticles that have molecules onto which volatile organic compounds (VOCs) attach to. When captured, the different VOCs bend the sensors at different angles depending on their nature and provide more information than simply whether they're there or not.

Dynamic Nanoparticle-Based Flexible Sensors: Diagnosis of Ovarian Carcinoma from Exhaled Breath

Nicole Kahn†, Ofer Lavie‡, Moran Paz‡, Yakir Segev‡, and Hossam Haick*†
† Department of Chemical Engineering and Russell Berrie Nanotechnology Institute, Technion–Israel Institute of Technology, Haifa 3200003, Israel
‡ Gynecological Oncology and Surgery Unit, Carmel Medical Center, Haifa 3436212, Israel

Nano Lett., Article ASAP
DOI: 10.1021/acs.nanolett.5b03052
Publication Date (Web): September 9, 2015

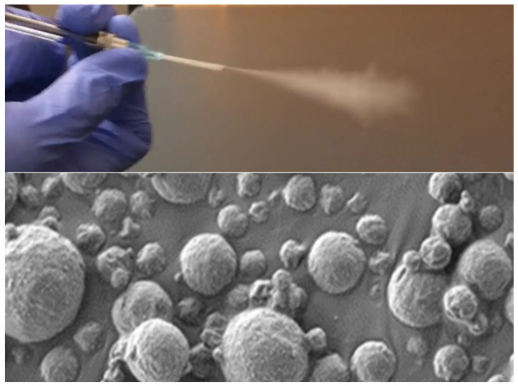
*E-mail: hhossam@technion.ac.il.

Warren AD, Kwong GA, Wood DK, Lin KY, Bhatia SN. (2014) ***Point-of-care diagnostics for noncommunicable diseases using synthetic urinary biomarkers and paper microfluidics.*** Proc Natl Acad Sci U S A. 2014 Mar 11;111(10):3671-6. doi: 10.1073/pnas.1314651111. Epub 2014 Feb 24.

Inhalable sensors could enable early lung cancer detection

The diagnostic, which requires only a simple urine test to read the results, could make lung cancer screening more accessible worldwide.

Anne Trafton | MIT News
January 5, 2024



SCIENCE ADVANCES | RESEARCH ARTICLE

HEALTH AND MEDICINE www.science.org/doi/epdf/10.1126/sciadv.adj9591

Inhalable point-of-care urinary diagnostic platform

Qian Zhong[1,2]†, Edward K. W. Tan[1,2]†, Carmen Martin-Alonso[1,3], Tiziana Parisi[1], Liangliang Hao[1,2,4], Jesse D. Kirkpatrick[1], Tarek Fadel[1,2], Heather E. Fleming[1], Tyler Jacks[1,5], Sangeeta N. Bhatia[1,2,3,4,6]*

Although low-dose computed tomography screening improves lung cancer survival in at-risk groups, inequality remains in lung cancer diagnosis due to limited access to and high costs of medical imaging infrastructure. We designed a needleless and imaging-free platform, termed PATROL (point-of-care aerosolizable nanosensors with tumor-responsive oligonucleotide barcodes), to reduce resource disparities for early detection of lung cancer. PATROL formulates a set of DNA-barcoded, activity-based nanosensors (ABNs) into an inhalable format. Lung cancer–associated proteases selectively cleave the ABNs, releasing synthetic DNA reporters that are eventually excreted via the urine. The urinary signatures of barcoded nanosensors are quantified within 20 min at room temperature using a multiplexable paper-based lateral flow assay. PATROL detects early-stage tumors in an autochthonous lung adenocarcinoma mouse model with high sensitivity and specificity. Tailoring the library of ABNs may enable not only the modular PATROL platform to lower the resource threshold for lung cancer early detection tools but also the rapid detection of chronic pulmonary disorders and infections.

biomedicines

MDPI

www.ncbi.nlm.nih.gov/pmc/articles/PMC10135468/pdf/biomedicines-11-01051.pdf

Review

Urinary Biomarkers and Point-of-Care Urinalysis Devices for Early Diagnosis and Management of Disease: A Review

Beatriz Sequeira-Antunes [1,2,*] and Hugo Alexandre Ferreira [1,2,*]

1 Institute of Biophysics and Biomedical Engineering, Faculty of Sciences, University of Lisbon, Campo Grande, 1749-016 Lisboa, Portugal
2 Exotictarget, 4900-378 Viana do Castelo, Portugal
* Correspondence: bsantunes@fc.ul.pt (B.S.-A.); hhferreira@fc.ul.pt (H.A.F.)

Malaria Diagnosis Using a Mobile Phone Polarized Microscope

Casey W. Pirnstill & Gerard L. Coté

Scientific Reports **5**, Article number: 13368 (2015)
doi:10.1038/srep13368

Received: 19 March 2015
Accepted: 14 July 2015
Published online: 25 August 2015

Poverty magnifies the need for health care while shrinking the capacity to finance it. Low-income countries face 56 percent of the global disease burden but account for only 2 percent of global health spending (World Bank 2005; Mathers, Lopez, and Murray, forthcoming). With spending levels of some $30 per capita on average, over half of it out of pocket, low-income countries face severe challenges

http://siteresources.worldbank.org/INTHSD/Resources/topics/Health-Financing/HFRChap7.pdf

But ….
US Abhors Low Cost Healthcare Alternatives

How the healthcare system discourages creating low-cost solutions

http://jama.jamanetwork.com/article.aspx?articleid=2429454

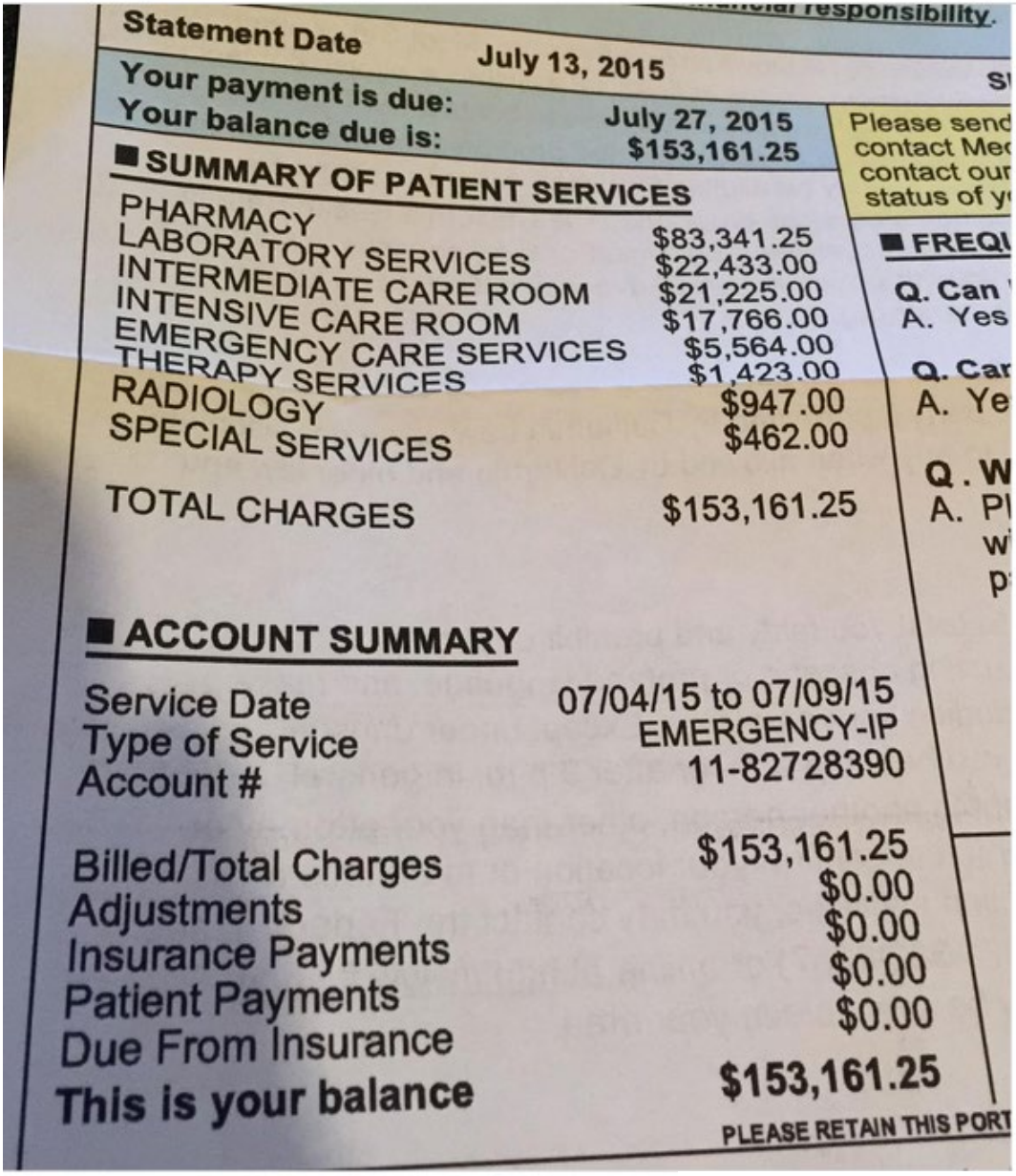
The U.S. leads the world in creating new drugs and healthcare tech, but the system discourages inventors from creating cost-lowering technologies in favor of ones with a healthy return on investment, according to an article at the *Journal of the American Medical Association*.

"In the United States, the surest way to generate a healthy return on investment is to increase health care spending, not reduce it," says the authors, from the Uniformed Services University of the Health Sciences and Yale School of Medicine.

They use as an example a low-cost, once-a-day pill to treat cardiovascular disease, with the estimated potential to reduce the incidence of myocardial infarction and stroke by more than 80 percent.

This $153,000 rattlesnake bite is everything wrong with American Healthcare

http://bit.ly/US-MEDICAL-WASTE



Statement Date July 13, 2015

Your payment is due: July 27, 2015
Your balance due is: $153,161.25

SUMMARY OF PATIENT SERVICES

PHARMACY	$83,341.25
LABORATORY SERVICES	$22,433.00
INTERMEDIATE CARE ROOM	$21,225.00
INTENSIVE CARE ROOM	$17,766.00
EMERGENCY CARE SERVICES	$5,564.00
THERAPY SERVICES	$1,423.00
RADIOLOGY	$947.00
SPECIAL SERVICES	$462.00
TOTAL CHARGES	$153,161.25

ACCOUNT SUMMARY

Service Date	07/04/15 to 07/09/15
Type of Service	EMERGENCY-IP
Account #	11-82728390
Billed/Total Charges	$153,161.25
Adjustments	$0.00
Insurance Payments	$0.00
Patient Payments	$0.00
Due From Insurance	$0.00
This is your balance	**$153,161.25**

PLEASE RETAIN THIS PORT

Dan Haggerty
@10NewsHaggerty

US AV PER CAPITA INCOME <$55,000

$153,161.25

US Hospital charges for

Treatment Of Snake Bite

80/20

US consumes 40% (approx) of the world's total financial resources for healthcare. The remaining OECD nations consume 40%.

Total global expenditure for health[1]	US$ 6.5 trillion
Total global expenditure for health per person per year	US$ 948
Country with highest total spending per person per year on health	United States (US$ 8362)
Country with lowest total spending per person per year on health	Eritrea (US$ 12)
Country with highest government spending per person per year on health	Luxembourg (US$ 6906)
Country with lowest government spending per person per year on health	Myanmar (US$ 2)
Country with highest annual out-of-pocket household spending on health	Switzerland (US$ 2412)
Country with lowest annual out-of-pocket household spending on health	Kiribati (US$ 0.2)
Average amount spent per person per year on health in countries belonging to the Organisation for Economic Co-operation and Development (OECD)	US$ 4380
Percentage of the world's population living in OECD countries	18% ← 20
Percentage of the world's total financial resources devoted to health currently spent	84% ← 80

www.who.int/mediacentre/factsheets/fs319/en/

$8,694

Median monthly cost in the US of eight cancer drugs

$2,587

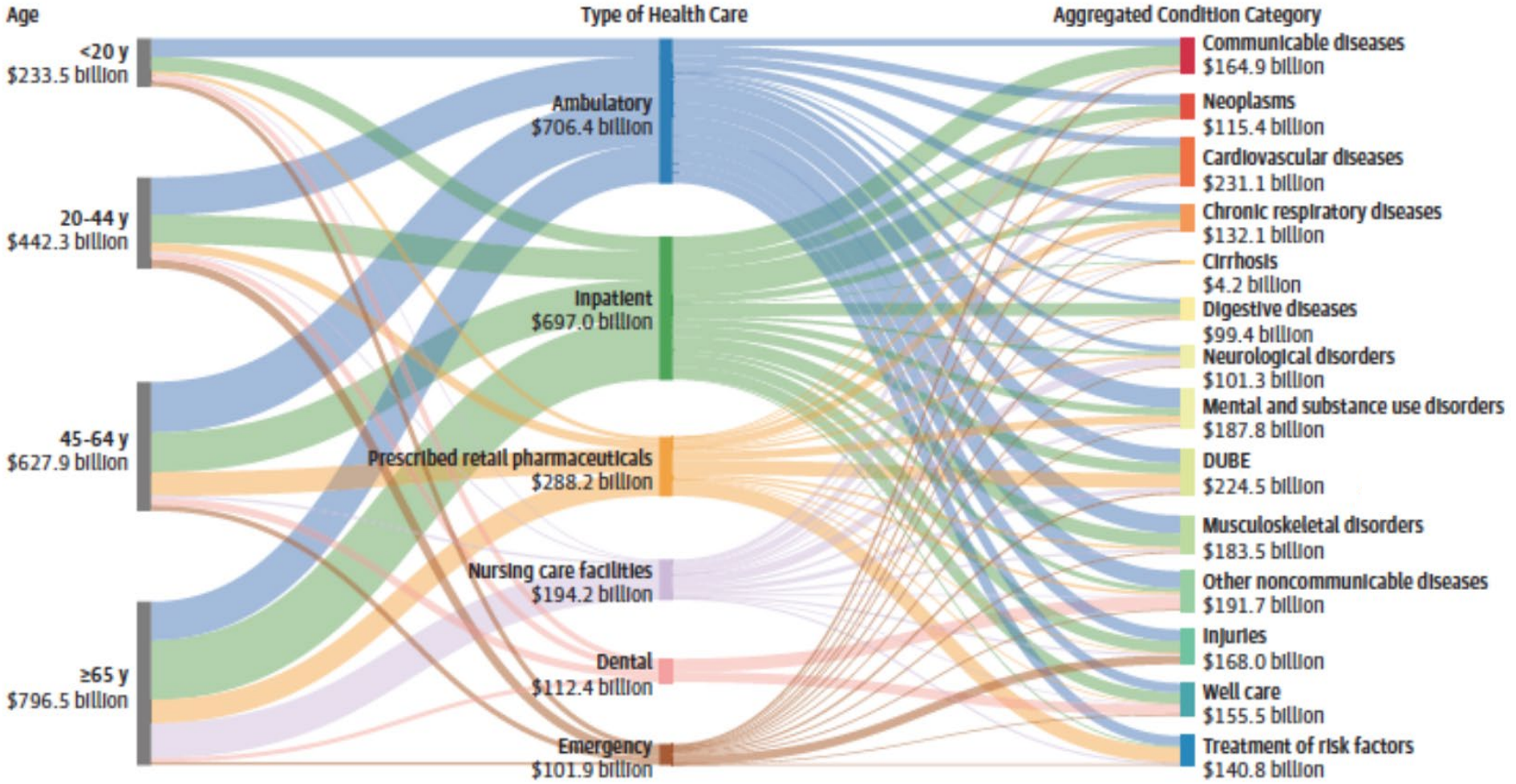
Median monthly cost in the UK of the same eight drugs

$2,741

Median monthly cost in Australia of the same drugs

FT

Personal Health Care Spending in the United States by Age Group, Aggregated Condition Category, and Type of Health Care, 2013



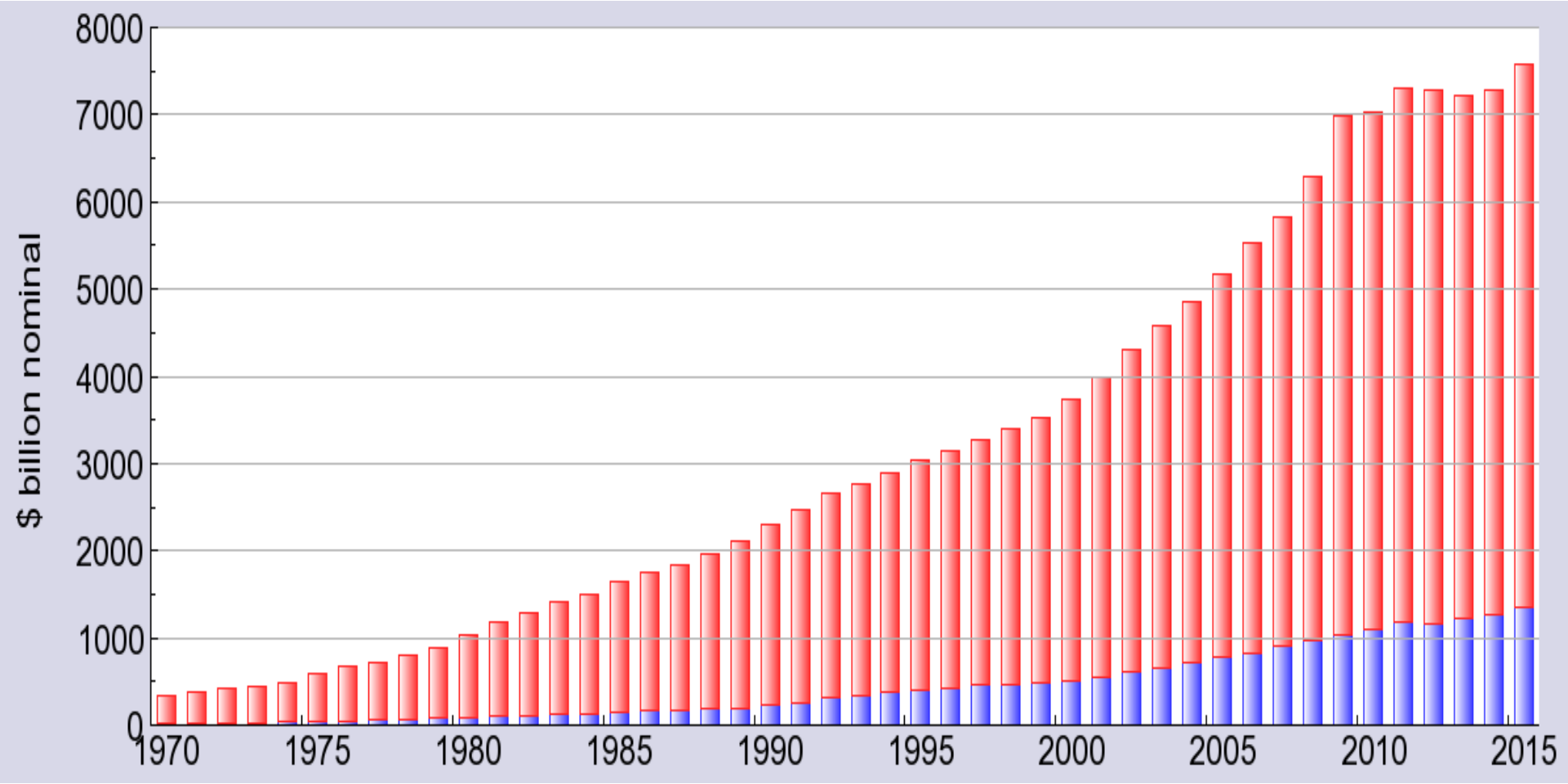
http://jamanetwork.com/journals/jama/fullarticle/2594716

https://image-store.slidesharecdn.com/8250a975-308d-40a7-a573-e4c1ab8d791b-original.png

DUBE indicates diabetes, urogenital, blood, and endocrine diseases. Reported in 2015 US dollars. Each of the 3 columns sums to the $2.1 trillion of 2013 spending disaggregated in this study. The length of each bar reflects the relative share of the $2.1 trillion attributed to that age group, condition category, or type of care. Communicable diseases included nutrition and maternal disorders. Table 3 lists the aggregated condition category in which each condition was classified.

Joseph L. Dieleman, PhD[1]; Ranju Baral, PhD[2]; Maxwell Birger,

TOTAL US HEALTHCARE SPENDING 1970-2015



www.usgovernmentspending.com/spending_chart_1970_2015USb_16s2li111mcn_00tF0t

US healthcare spending explained by **one** concept

TCE

Transaction Cost

The Sveriges Riksbank Prize in Economic Sciences in Memory of Alfred Nobel 1991

Ronald H. Coase

Ronald H. Coase
Facts

Photo from the Nobel Foundation archive.

Ronald H. Coase
The Sveriges Riksbank Prize in Economic Sciences in Memory of Alfred Nobel 1991

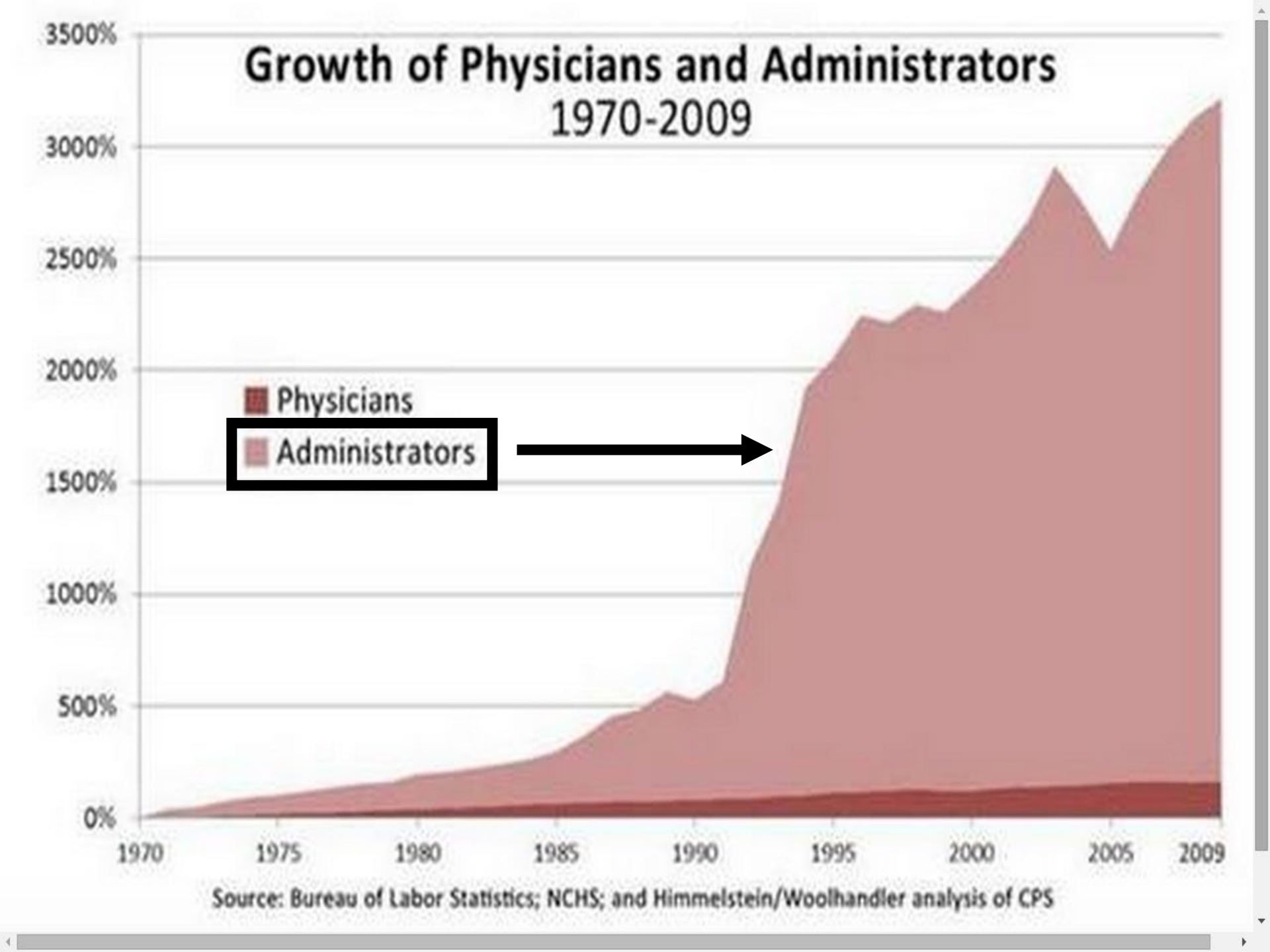
Born: 29 December 1910, Willesden, United Kingdom

Died: 2 September 2013, Chicago, IL, USA

Affiliation at the time of the award: University of Chicago, Chicago, IL, USA

Prize motivation: "for his discovery and clarification of the significance of transaction costs and property rights for the institutional structure and functioning of the economy"

https://www.nobelprize.org/prizes/economic-sciences/1991/coase/facts


Growth of Physicians and Administrators
1970-2009
3500%
3000%
2500%
2000%
1500%
1000%
500%
0%
Physicians
Administrators
1970
1975
1980
1985
1990
1995
2000
2005
2009
Source: Bureau of Labor Statistics; NCHS; and Himmelstein/Woolhandler analysis of CPS


English - detected
Japanese
the greatest good
最大の良いです
Saidai no yoidesu
Open in Google Translate


English - detected
Japanese
the greatest greed
最大の欲
Saidai no yoku
Open in Google Translate

Forbes

EPIC GREED

http://onforb.es/KWJHJF

BUSINESS 6/18/2012 @ 7:59AM | 98,482 views

The Staggering Cost Of An Epic Electronic Health Record Might Not Be Worth It

Judy Faulkner once walked into a roomful of hospital CIOs, tossed her macramé handbag on a table, and announced she came to decide who she wanted as customers. Faulkner doesn't do marketing. The formidable founder of electronic health records Epic Systems boasts an enviable roster of customers made up of prestigious hospitals and academic centers. She has quietly convinced them that her product is best: a single, seamless database—the fruit of a company that has grown organically, and shunned acquisitions. And, because it is no small task to deploy, she is there all the way to hand-hold jittery CIOs, and help them get millions of dollars in government subsidies by showing meaningful use of her EHR.

Her not-for-profit clientèle will need every penny of those taxpayers' dollars, but they won't cover anywhere near the staggering cost of an Epic EHR. Duke University Health System will shell out $700 million, so will Boston-based Partners HealthCare; University of California, San Francisco will pay $150 million.

$700 million

www.military.com/daily-news/2024/02/15/250000-va-patients-are-risk-of-receiving-wrong-medication-due-electronic-health-records-issue.html

Military.com News

› Military News

250,000 VA Patients Are at Risk of Receiving Wrong Medication Due to Electronic Health Records Issue

The faulty medication records are the latest problem to beset the rollout of the Oracle Cerner Millennium EHR (electronic health records) system. The VA has paused adapting/implementing software fixes. Military.com by Rebecca Kheel. 2-15-2024

https://www.fiercehealthcare.com/health-tech/va-renegotiates-10b-ehr-contract-stronger-performance-metrics-bigger-penalties

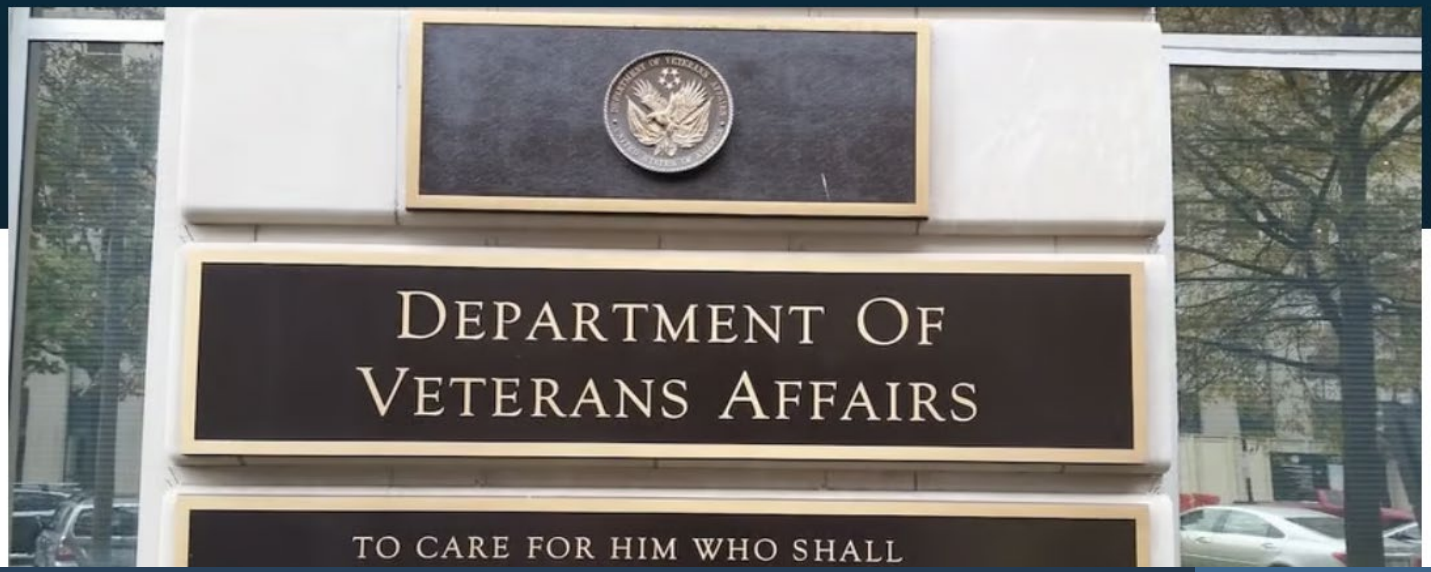
The VA has obligated $9.4 billion on the EHR program since fiscal 2018. The Oracle Cerner Millennium EHR system estimated to cost $10 billion was later revised to $16.1 billion and could increase to more than $50 billion in 28 years.

HEALTH TECH

GOP lawmakers ready to scrap Oracle Cerner's $16B VA contract unless 'deeply flawed' EHR fixed

By **Heather Landi** · Feb 1, 2023 8:00am

Department of Veterans Affairs (VA) | Oracle | Cerner | electronic health records (EHRs)



www.fiercehealthcare.com/health-tech/gop-lawmakers-ramp-pressure-va-and-oracle-cerner-fix-16b-ehr-project

But, is greed in the healthcare sector only limited to the United States

?

WHY DOCTORS OVERLOOK A USEFUL TREATMENT

Science Current Issue

What drives poor quality of care for child diarrhea? Experimental evidence from India

ZACHARY WAGNER, MANOJ MOHANAN, RUSHIL ZUTSHI, ARNAB MUKHERJI, AND NEERAJ SOOD Authors Info & Affiliations

SCIENCE · 9 Feb 2024 · Vol 383, Issue 6683 · DOI: 10.1126/science.adj9986

Editor's summary

Diarrhea is a leading cause of child mortality in India. It becomes deadly when excretions exacerbate severe dehydration and loss of electrolytes. Most health care providers in India know that oral rehydration salts (ORS) are an inexpensive, lifesaving treatment for child diarrhea, yet they are widely underused. Wagner *et al.* undertook randomized controlled trials involving standardized patients (actors trained to seek care for a child's diarrhea) who visited 2282 private health care providers in India. Trials were designed to identify three barriers driving underutilization: assuming patients lack interest in ORS, incentives to prescribe more lucrative (but inappropriate) medicines, and incentives to sell non-ORS medicines in stock when ORS are unavailable. The dominant barrier was assuming that patients were uninterested, showing that simple interventions could save many lives. — Ekeoma Uzogara

The study highlights "gap between knowing the right thing and doing the right thing."

https://www.science.org/doi/10.1126/science.adj9986
https://www.nature.com/articles/d41586-024-00351-x

Physicians often don't prescribe a cheap, lifesaving treatment for diarrhoea because they think their patients don't want it. That's the result of a large study looking at the use of oral rehydration solution in India. A survey showed that clinics, pharmacies and carers of sick children are mostly aware of the efficacy of the salty-sweet solution in preventing dehydration and reducing the risk of death in cases of diarrhoeal disease, but that it is often not prescribed. If an actor posing as the father of a sick child expressed a preference for the oral rehydration solution, they were twice as likely to get it as those who mentioned no treatment. The study highlights "the gap between knowing the right thing and doing the right thing," says health economist David Levine.

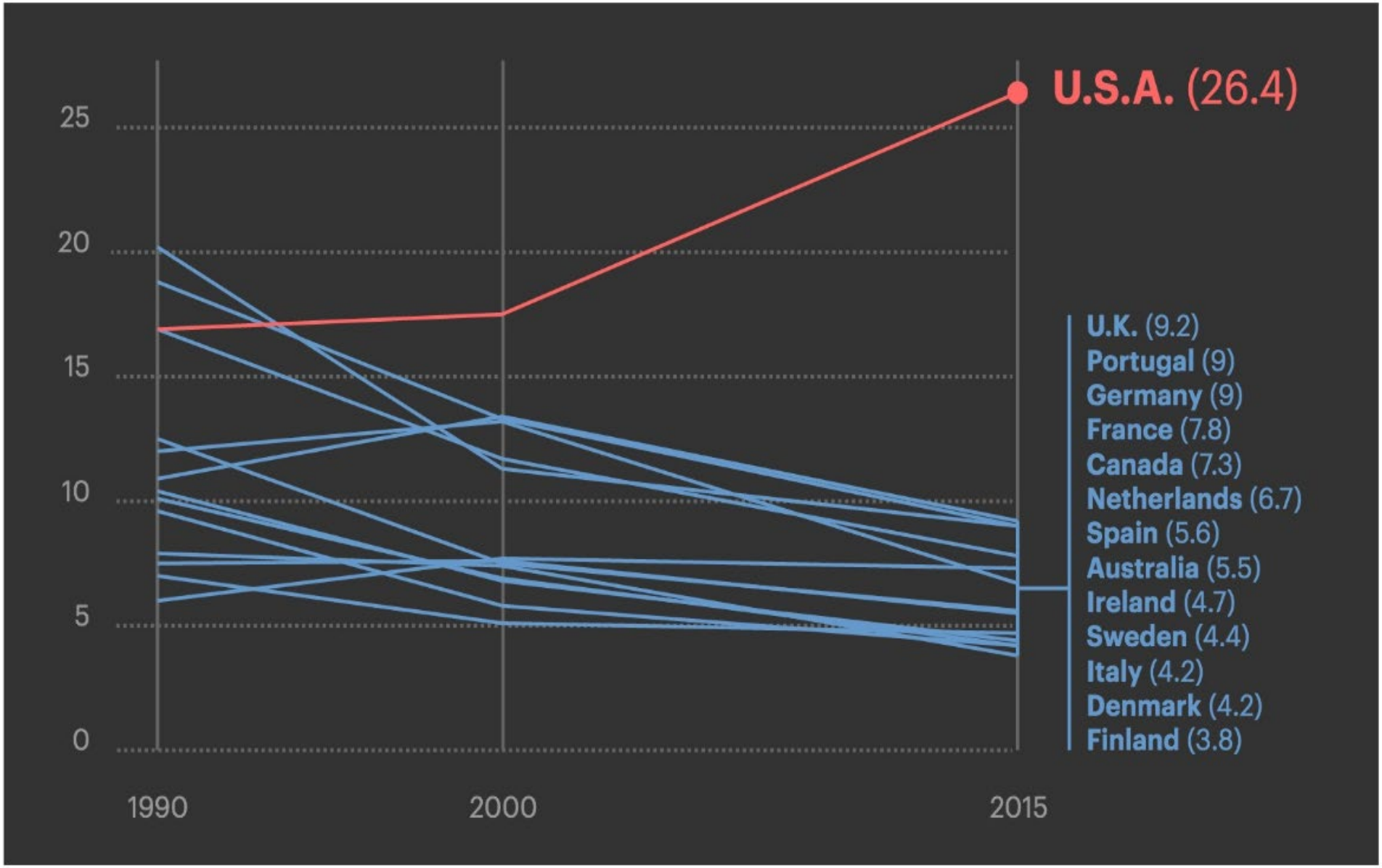
"Physicians often don't prescribe a cheap, lifesaving treatment for diarrhoea because they think their patients don't want it."

www.science.org/doi/10.1126/science.adj9986 ● www.nature.com/articles/d41586-024-00351-x

Healthcare

Let us review quality of care

Maternal Mortality Is Rising in the U.S. As It Declines Elsewhere



Per 100,000 live births. Source: "Global, regional, and national levels of maternal mortality, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015," The Lancet. Note: Only data for 1990, 2000 and 2015 was made available in the journal.

Leading causes of death in the USA

1. 597,689 Heart Disease
2. 574,743 Cancer
3. 138,080 Chronic lower respiratory diseases
4. 129,476 Stroke
5. 120,859 Accidents
6. 83,494 Alzheimer's disease
7. 69,071 Diabetes
8. 56,979 Influenza &Pneumonia
9. 47,112 Kidney diseases
10. 41,149 Suicide

www.cdc.gov/nchs/fastats/deaths.htm

Ahmad FB, Cisewski JA, Anderson RN. Leading Causes of Death in the US, 2019-2023. JAMA. 2024 September 24;332(12): 957-8. doi: 10.1001/jama.2024.15563. PMID: 39116093.

Table. Number of Deaths and Age-Adjusted Rate of Deaths for Leading Causes of Death—US, 2019-2023[a]

	No. of deaths (age-adjusted death rate per 100 000)[b]				
Underlying cause of death	2019	2020	2021	2022	2023
Total deaths	2 854 838 (715.2)	3 383 729 (835.4)	3 464 231 (879.7)	3 279 857 (798.8)	3 090 582 (750.4)
Heart disease	659 041 (161.5)	696 962 (168.2)	695 547 (173.8)	702 880 (167.2)	680 909 (162.1)
Cancer	599 601 (146.2)	602 350 (144.1)	605 213 (146.6)	608 371 (142.3)	613 331 (141.8)
Unintentional injuries	173 040 (49.3)	200 955 (57.6)	224 935 (64.7)	227 039 (64.0)	222 518 (62.3)
Stroke	150 005 (37.0)	160 264 (38.8)	162 890 (41.1)	165 393 (39.5)	162 639 (39.0)
Chronic lower respiratory diseases	156 979 (38.2)	152 657 (36.4)	142 342 (34.7)	147 382 (34.3)	145 350 (33.4)
Alzheimer disease	121 499 (29.8)	134 242 (32.4)	119 399 (31.0)	120 122 (28.9)	114 034 (27.8)
Diabetes	87 647 (21.6)	102 188 (24.8)	103 294 (25.4)	101 209 (24.1)	95 181 (22.4)
Kidney disease	51 565 (12.7)	52 547 (12.7)	54 358 (13.6)	57 937 (13.8)	55 250 (13.1)
Chronic liver disease and cirrhosis	44 358 (11.3)	51 642 (13.3)	56 585 (14.5)	54 803 (13.8)	52 220 (13.0)
COVID-19		350 831 (85.0)	416 893 (104.1)	186 552 (44.5)	49 928 (11.9)
Suicide	47 511 (13.9)	45 979 (13.5)	48 183 (14.1)	49 476 (14.2)	49 303 (14.1)
Influenza and pneumonia	49 783 (12.3)	53 544 (13.0)	41 917 (10.5)	47 052 (11.3)	45 182 (10.8)

VIEWPOINT

Leading Causes of Death in the US, 2019-2023

Farida B. Ahmad, MPH
National Center for Health Statistics, Mortality Statistics Branch, Division of Vital Statistics, Hyattsville, Maryland.

Jodi A. Cisewski, MPH
National Center for Health Statistics, Mortality Statistics Branch, Division of Vital Statistics, Hyattsville, Maryland.

Robert N. Anderson, PhD
National Center for Health Statistics, Mortality Statistics Branch, Division of Vital Statistics, Hyattsville, Maryland.

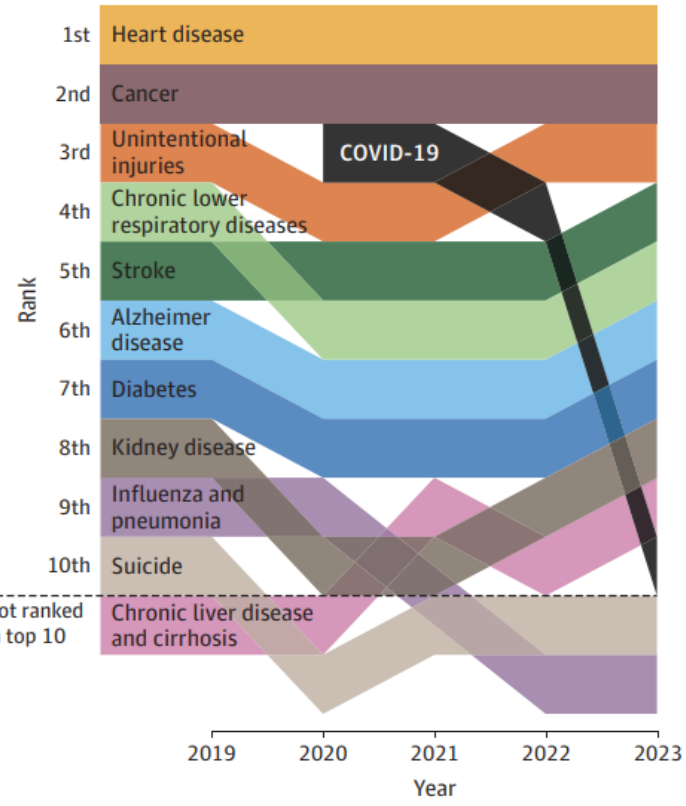
The annual mortality burden, the causes of mortality, and the changes over time are key indicators of population change. In the US, mortality statistics are derived from death certificate data from the National Center for Health Statistics National Vital Statistics System. These data provide both the annual mortality burden in numbers and by cause of death. Herein, we summarize the key findings from the newly released report from the National Center for Health Statistics on the leading causes of death in the US from 2019 to 2023.

Trends in the ranking of the leading causes of death in the US remained relatively stable until the COVID-19 pandemic. COVID-19 debuted as the third leading cause of death in 2020 and remained among the leading causes in subsequent years.[1] Provisional data from 2023 indicate a shift in the top causes of death, driven largely by a decrease in COVID-19 deaths.[2]

Mortality Data From the National Vital Statistics System

The National Vital Statistics System collects, processes, tabulates, and disseminates vital statistics based on death certificates filed in the 50 states and the District of Columbia.

Figure. Trends in the Ranking of Leading Causes of Death—US, 2019-2023



Source: National Center for Health Statistics.

Ahmad FB, Cisewski JA, Anderson RN. Leading Causes of Death in the US, 2019-2023. JAMA. 2024 September 24;332(12): 957-8. doi: 10.1001/jama.2024.15563. PMID: 39116093.

● 2010 ● OIG HHS bad hospital care deaths about 180,000 patients in Medicare alone in a year

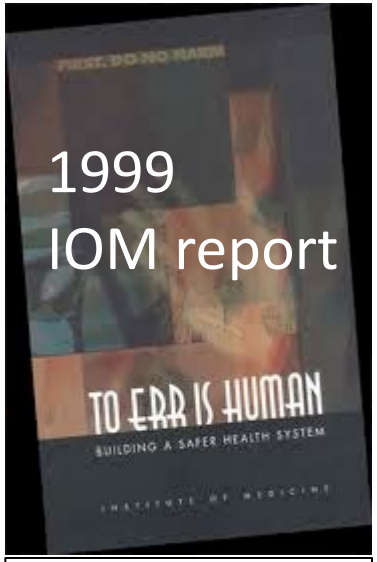
Patient Safety **2013**
Exploring Quality of Care in the U.S.

How Many Die From Medical Mistakes in U.S. Hospitals?

A New, Evidence-based Estimate of Patient Harms Associated with Hospital Care

John T. James, PhD

Dr Julian Goldman



98,000
deaths due to error

210,000 – 440,000 deaths

Even ~20 years after the 1999 IOM Report

REVIEWS

Rate of Preventable Mortality in Hospitalized Patients: a Systematic Review and Meta-analysis

Benjamin A. Rodwin, MD[1,2], Victor P. Bilan, MD[1,2], Naseema B. Merchant, MD[1,2], Catherine G. Steffens[2], Alyssa A. Grimshaw, MSLIS[3], Lori A. Bastian, MD, MPH[1,2], and Craig G. Gunderson, MD[1,2]

[1]Department of Medicine, Yale University School of Medicine, New Haven, CT, USA; [2]VA Connecticut Healthcare System, West Haven, CT, USA; [3]Harvey Cushing/John Hay Whitney Medical Library, Yale University School of Medicine, New Haven, CT, USA.

BACKGROUND: The number of preventable inpatient deaths in the USA is commonly estimated as between 44,000 and 98,000 deaths annually. Because many inpatient deaths are believed to be preventable, mortality rates are used for quality measures and reimbursement. We aimed to estimate the proportion of inpatient deaths that are preventable.

J Gen Intern Med 35(7):2099–106
DOI: 10.1007/s11606-019-05592-5

In conclusion, we found that 3.1% of inpatient deaths are judged by physician review to have been preventable. This rate is lower than previous estimates

Rodwin BA, Bilan VP, Merchant NB, Steffens CG, Grimshaw AA, Bastian LA, Gunderson CG. Rate of Preventable Mortality in Hospitalized Patients: a Systematic Review and Meta-analysis. J Gen Intern Med. 2020 July; 35(7):2099-2106. doi: 10.1007/s11606-019-05592-5. Epub 2020 January 21. PMID: 31965525; PMCID: PMC7351940. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7351940/pdf/11606_2019_Article_5592.pdf

400,000 deaths due to medical mistakes – shared with the US Senate

Deaths by medical mistakes hit records

Tejal Gandhi, MD, president of the National Patient Safety Foundation and associate professor of medicine, Harvard Medical School, spoke at the hearing.

The way IT is designed remains part of the problem

WASHINGTON | July 18, 2014

It's a chilling reality – one often overlooked in annual mortality statistics: Preventable medical errors persist as the No. 3 killer in the U.S. – third only to heart disease and cancer – claiming the lives of some 400,000 people each year. At a Senate hearing Thursday, patient safety officials put their best ideas forward on how to solve the crisis, with IT often at the center of discussions.

Hearing members, who spoke before the Subcommittee on Primary Health and Aging, not only underscored the devastating loss of human life – more than 1,000 people each day – but also called attention to the fact that these medical errors cost the nation a colossal $1 trillion each year.

"The tragedy that we're talking about here (is) deaths taking place that should not be taking place," said subcommittee Chair Sen. Bernie Sanders, I-Vt., in his opening remarks.

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

JANUARY 18, 2024

FUNDAMENTALS OF MEDICAL ETHICS

Responding to Medical Errors — Implementing the Modern Ethical Paradigm

Thomas H. Gallagher, M.D., and Allen Kachalia, M.D., J.D.

www.nejm.org/doi/full/10.1056/NEJMp2309554

Leading causes of death in the USA

1. 597,689 Heart Disease
2. 574,743 Cancer
3. 138,080 Chronic lower respiratory diseases
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5. 120,859 Accidents
6. 83,494 Alzheimer's disease
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8. 56,979 Influenza &Pneumonia
9. 47,112 Kidney diseases
10. 41,149 Suicide

www.cdc.gov/nchs/fastats/deaths.htm

BMJ 2016;353:i2139 doi: 10.1136/bmj.i2139 (Published 3 May 2016)

ANALYSIS

Medical error—the third leading cause of death in the US

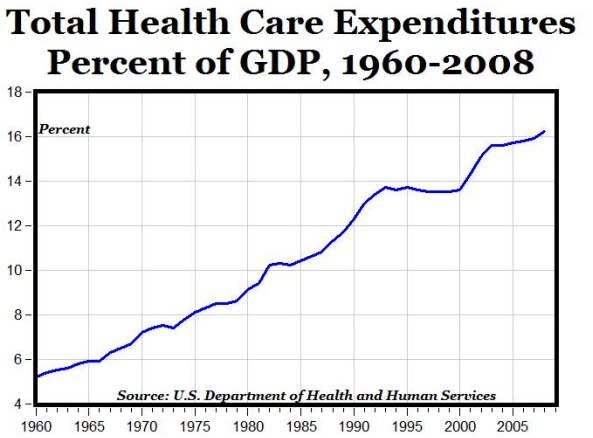
Medical error is not included on death certificates or in rankings of cause of death. **Martin Makary** and **Michael Daniel** assess its contribution to mortality and call for better reporting

Martin A Makary *professor*, Michael Daniel *research fellow*

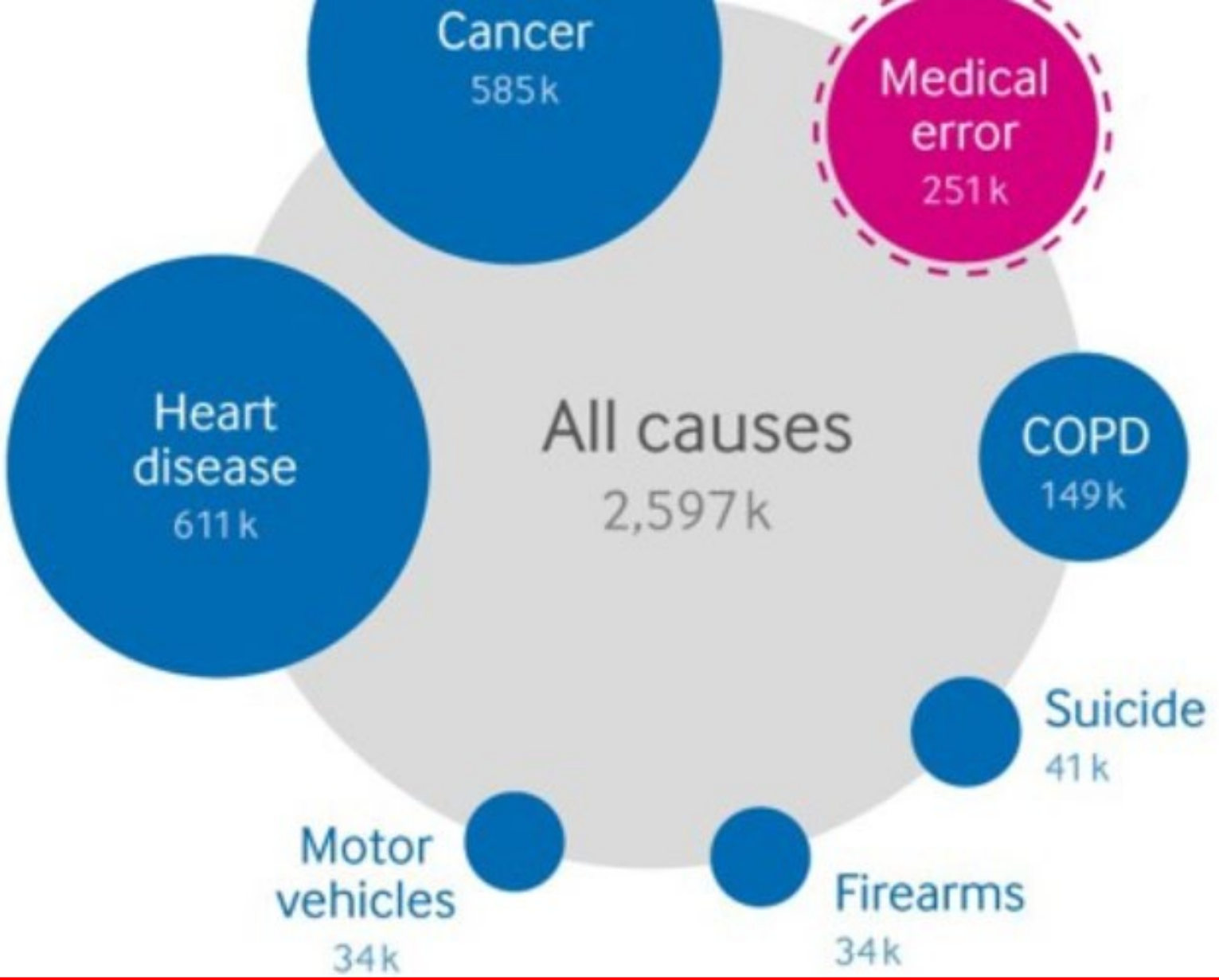
Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA

Third Leading cause of death in the USA ?

1. 597,689 Heart Disease
2. 574,743 Cancer
3. ***Deaths Due to Medical Errors (180,000 - 210,000 - 440,000)***
4. 138,080 Chronic lower respiratory diseases
5. 129,476 Stroke
6. 120,859 Accidents
7. 83,494 Alzheimer's disease
8. 69,071 Diabetes
9. 56,979 Influenza &Pneumonia
10. 47,112 Kidney diseases
11. 41,149 Suicide



Equivalent to at least one 747 airplane crash every day



Medical error - 3rd leading cause of death in US

BMJ 2016; 353 doi: https://doi.org/10.1136/bmj.i2139 (Published 03 May 2016)

Nurses blame interoperability woes for medical errors

$30B could be saved each year from better device coordination

March 16, 2015

Each year, a staggering 400,000 people are estimated to have died due to medical errors. What's more, each day there's also 10,000 serious complications resulting from medical mistakes. Part of the blame, nurses are saying, can be attributed to the lack of interoperability among medical devices.

MD PnP™

Getting Connected for Patient Safety™

Change Expectations > Change Technology > Change Healthcare

The Medical Device "Plug-and-Play" (MD PnP) Interoperability Program is promoting innovation in patient safety and clinical care by leading the adoption of patient-centric integration of medical devices and IT systems in clinical environments.

Search

HOME | ABOUT PROGRAM | PROJECTS | NEWS | EVENTS | PUBLICATIONS & TALKS | OUR LAB | Sitemap

Medical Device "Plug-and-Play" Interoperability Program working on "safe interoperability™" to improve patient safety

MD PnP MedTech Hackathon Open Medical Device and Data Integration Platforms to Support the Management of Ebola

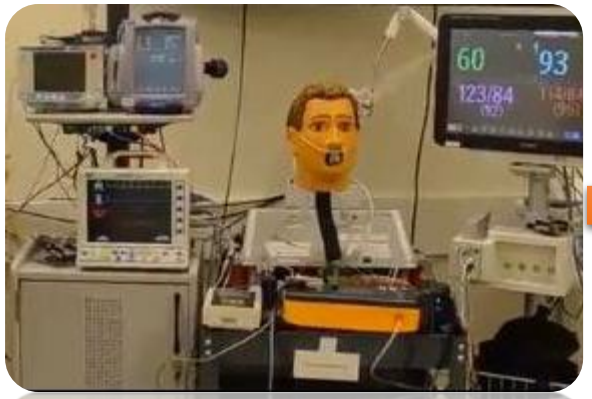
Autonomous Control of Morphine Infusion Pump – Medical Device and Data Integration

Infusion Pump

Capnometer

Patient Simulator
Ventilator

Intelligent Monitor



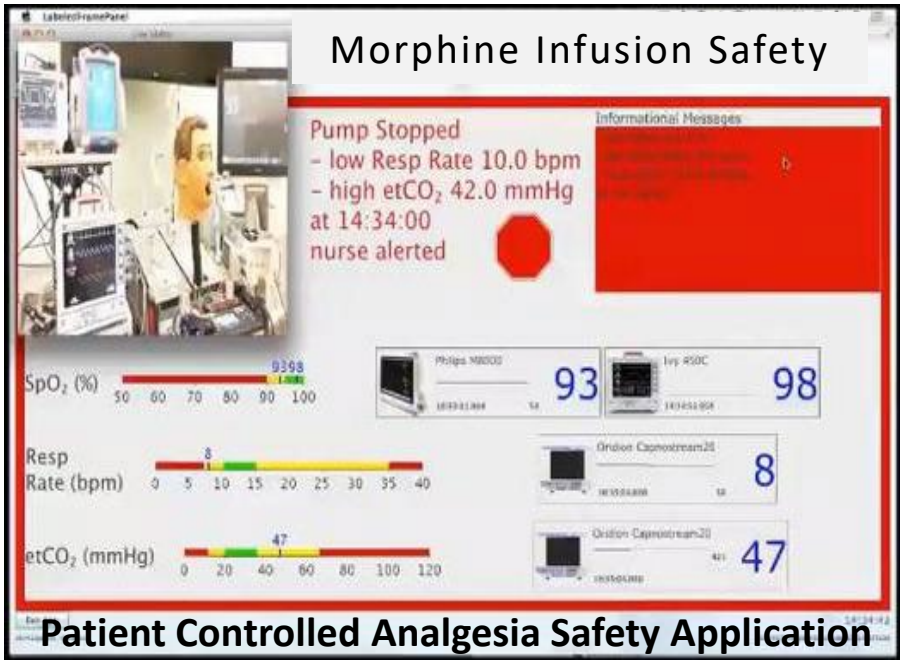
- ↓ O_2 Saturation
- ↓ Respiratory Rate
- ↑ end-tidal CO_2

Connected Data
Collective Analysis
Automated Response

Vital Signs Monitor

Simulator connected to vital signs monitor

Fluke ProSim 8 connected to intelligent monitor



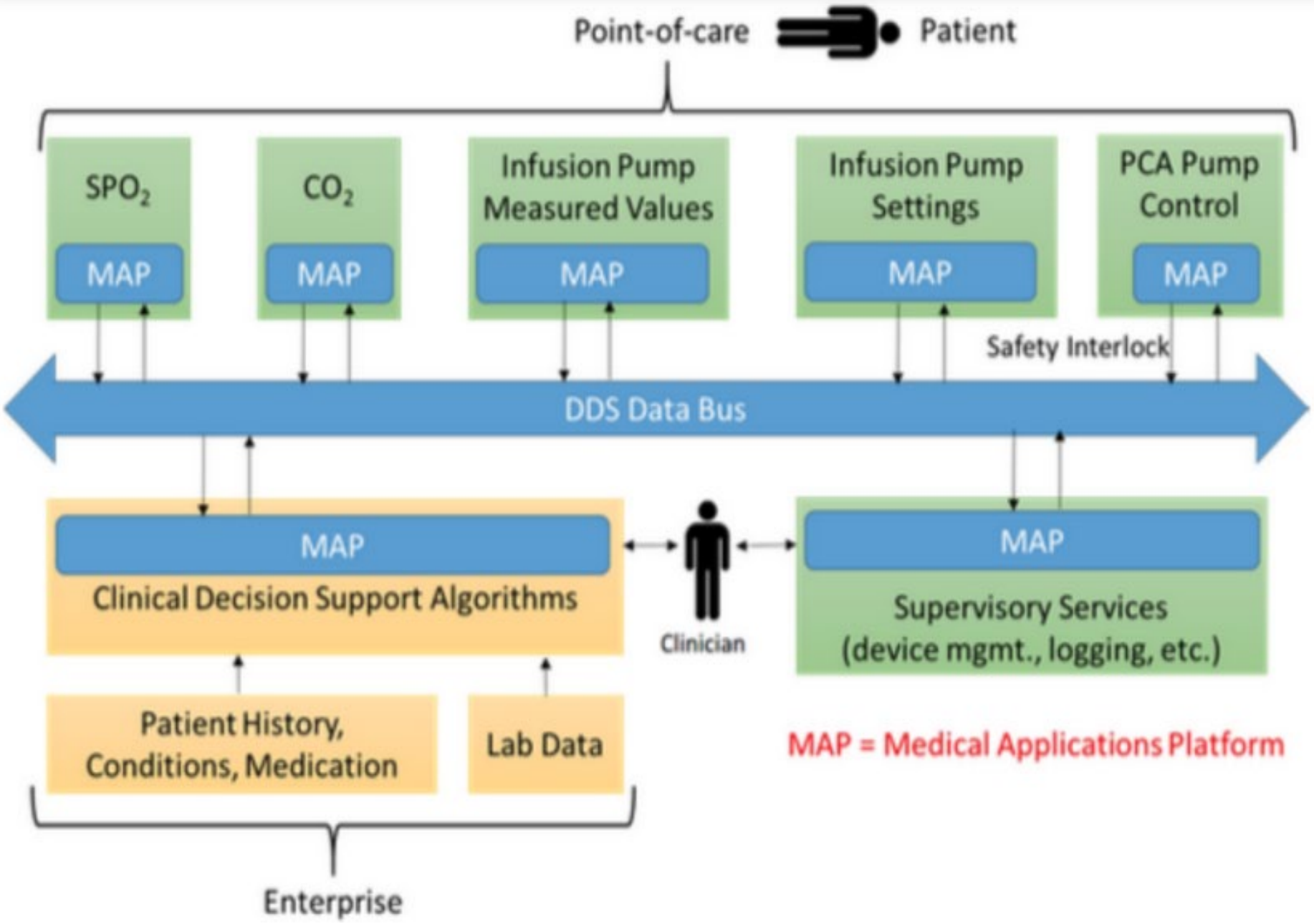
Patient Controlled Analgesia Safety Application

Julian Goldman MD (MDPnP.org and Partners.org)
Massachusetts General Hospital, Harvard Medical School
Harvard – MIT Center for Integrative Medicine and Information Technology

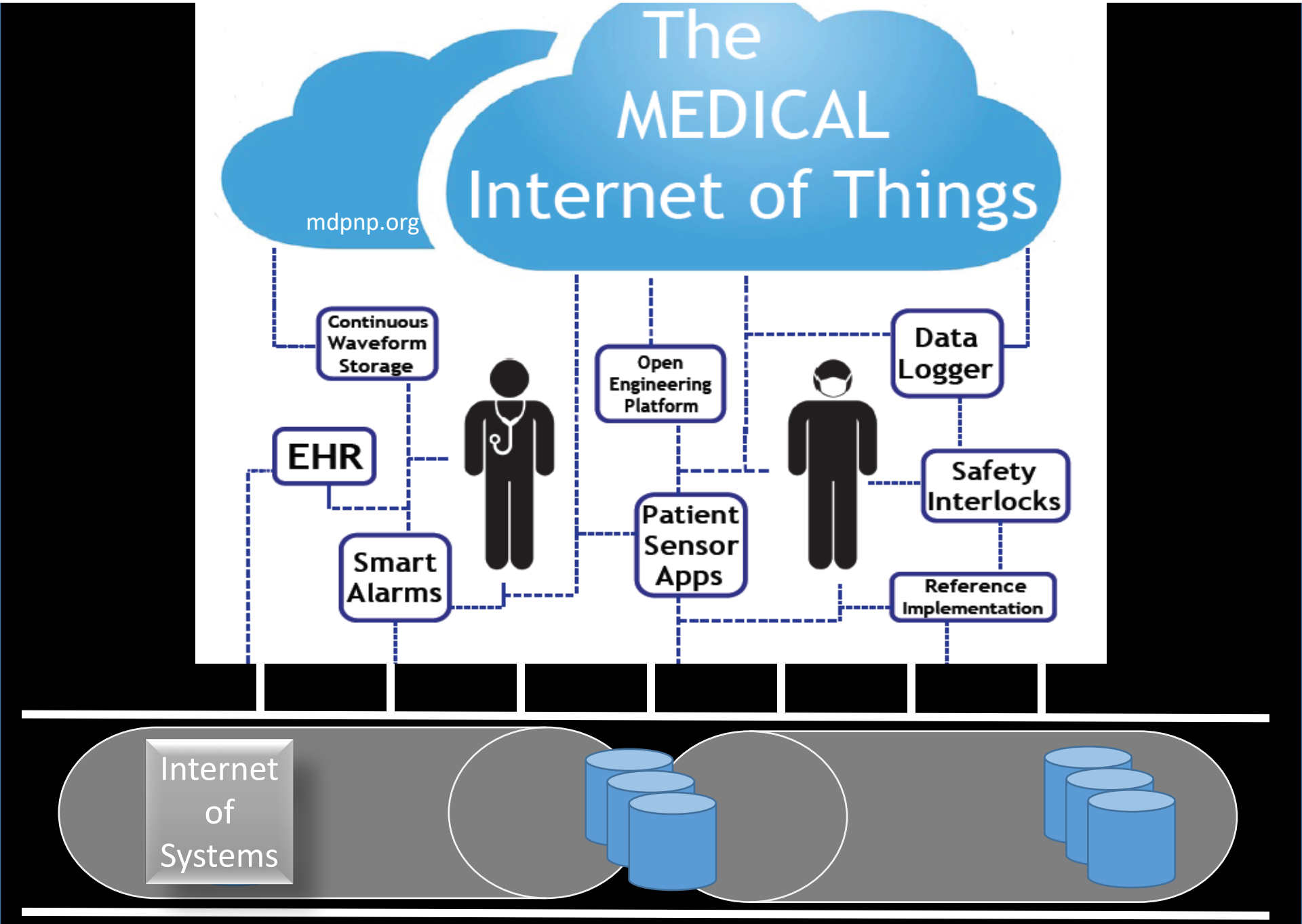
SOFTWARE APPROACH

Devices that can talk to each other and synthesize data to present an integrated physiological status that is patient centric and updates patient medical records

Autonomous Control of Morphine Infusion Pump – Medical Device and Data Integration



http://pulse.embs.org/november-2014/solving-interoperability-challenge/



KEY REQUIREMENT

Devices that can serve the masses and an open yet secure platform for interoperability and data fusion

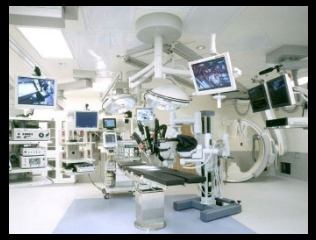
Healthcare Platforms – Integrated Clinical Environment
Data Logging & Access via Secure Interoperable Standard

Imaging

EHR-Admin

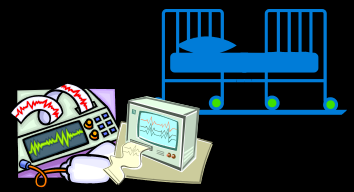
EMR-Physician

Clinical Devices



Medical History

Internet of Systems



Clinic - Ward

Pharmacy

Laboratory

Exchanges

Devices

Homecare

PROOF OF CONCEPT

Response to White House Call for Ebola Management

https://vimeo.com/111314176

Robotic Tools in Infectious Diseases Management
Need for Medical Device Interoperability Platform

www.gereports.com/post/104422691785/hospital-hack-a-thon-attacks-ebola-with-robots

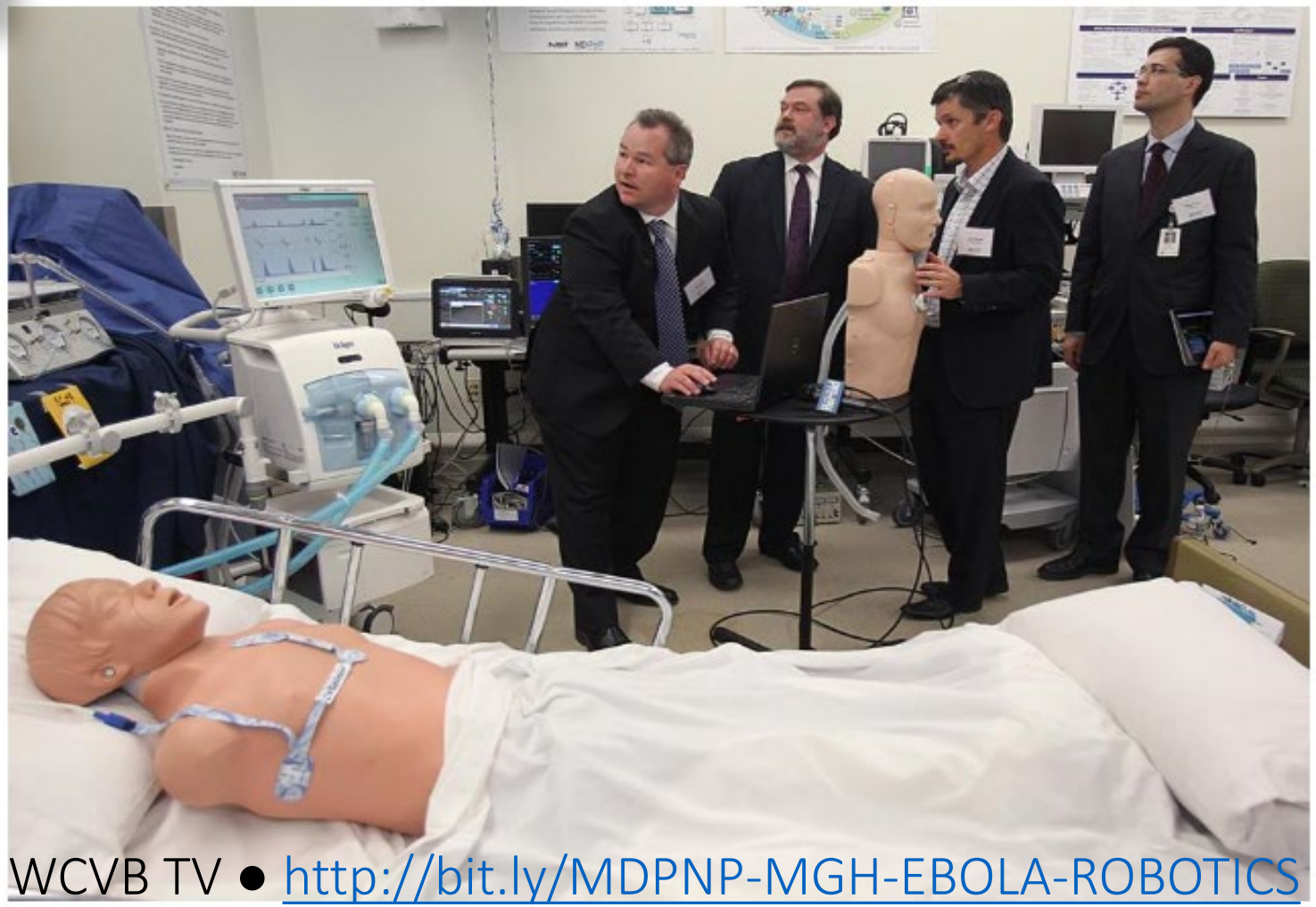
Need for Integrated Healthcare Platforms?

Ebola spurs rethinking of devices at MGH

By Carolyn Y. Johnson

| GLOBE STAFF NOVEMBER 07, 2014

You cannot buy a TV without a remote. You cannot buy a medical device with a remote. Dr Julian M Goldman (MGH/HMS) MD PnP



WCVB TV ● http://bit.ly/MDPNP-MGH-EBOLA-ROBOTICS

SUZANNE KREITER/GLOBE STAFF

Health officials demonstrated treating an Ebola patient remotely in a mock ICU. Pictured, left to right: Eric Lynn, Julian M. Goldman, Brian Russell, and Dave Arney.

EBOLA

COLLABORATORS

MD PnP MedTech Hackathon Open Medical Device and Data Integration Platforms to Support the Management of Ebola

Dr. Shuren received his B.S. and M.D. degrees from Northwestern University under its Honors Program in Medical Education. He completed his medical internship at Beth Israel Hospital in Boston, his neurology residency at Tufts New England Medical Center, and a fellowship in behavioral neurology and neuropsychology at the University of Florida. He received his J.D. from the University of Michigan.

Participation of the US FDA CDRH was a powerful incentive for medical device manufacturers to explore innovative medical technology solutions, especially those benefiting from interoperability between manufacturers

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
10903 New Hampshire Avenue
Room 5447, Building 66
Silver Spring, MD 20993-0002

November 3, 2014

Julian M. Goldman, MD
Director, Medical Device Interoperability Program
65 Landsdowne Street
Cambridge, MA 02139

Dear Dr. Goldman,

Thank you for reaching out to the Center for Devices and Radiological Health (CDRH) via our Emergency Preparedness/Operations and Medical Countermeasures (EMCM) Program.

We understand that The Medical Device "Plug-and-Play" (MD PnP) Interoperability Program, under your coordination, has been asked by the White House Office of Science and Technology Program to mobilize resources among medical device manufacturers and the clinical community, so as to design and demonstrate proof of concept for an interoperable platform that would enable critical care of Ebola-infected patients in an isolation environment with reduced exposure to health care workers.

FDA recognizes the importance of implementing strategies that minimize direct exposure of clinical personnel to patients infected with Ebola virus. We understand that MDPNP, along with its collaborators, are developing potential approaches that would include comprehensive data access and potential remote control of medical devices in the isolation environment, thereby reducing the risk of healthcare worker exposure to the virus.

CDRH recognizes the importance of these efforts and is ready and willing to collaborate with you, the clinical community and your industry partners to demonstrate the potential of this technology in serving this particular public health emergency. We are eager to observe the demonstration taking place Friday November 7th for OSTP, and we look forward to participating in the development of next steps with MDPNP and your medical device partners so as to do our part in enabling advancement of technology that can protect our healthcare workers who put themselves on the front line to promote the public health mission.

Sincerely,

Jeffrey Shuren, M.D., J.D.
Director
Center for Devices and
Radiological Health

Device, data, diagnostics

The Quest for Convergence of Platform and Interoperable Standards

US Federal HIT Goals from the ONC, US HHS

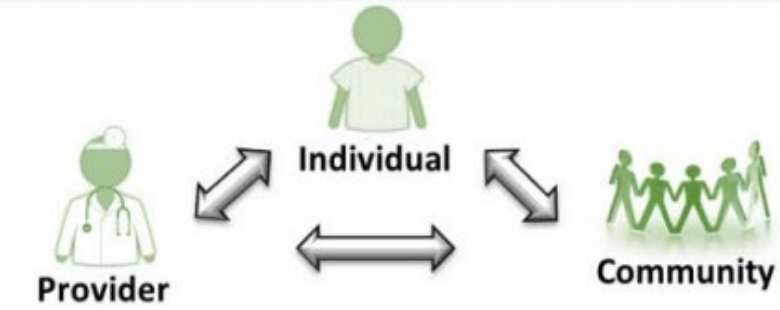
F
D
A

Collect

Goal 1: Expand Adoption of Health IT

Share

Goal 2: Advance Secure and Interoperable Health Information



Use

Goal 3: Strengthen Health Care Delivery

Goal 4: Advance the Health and Well-Being of Individuals and Communities

Goal 5: Advance Research, Scientific Knowledge, and Innovation

www.healthit.gov/sites/default/files/federal-healthIT-strategic-plan-2014.pdf

This is not a new problem. It has been recognized for a couple decades.

Healthcare tools may need an open platform to curate and catalyze data interoperability between devices to better treat the patient, in real-time.

www.cimit.org/services-engineering-resources.html

www.mdpnp.org/uploads/PSQH_Article.pdf

CIMIT®

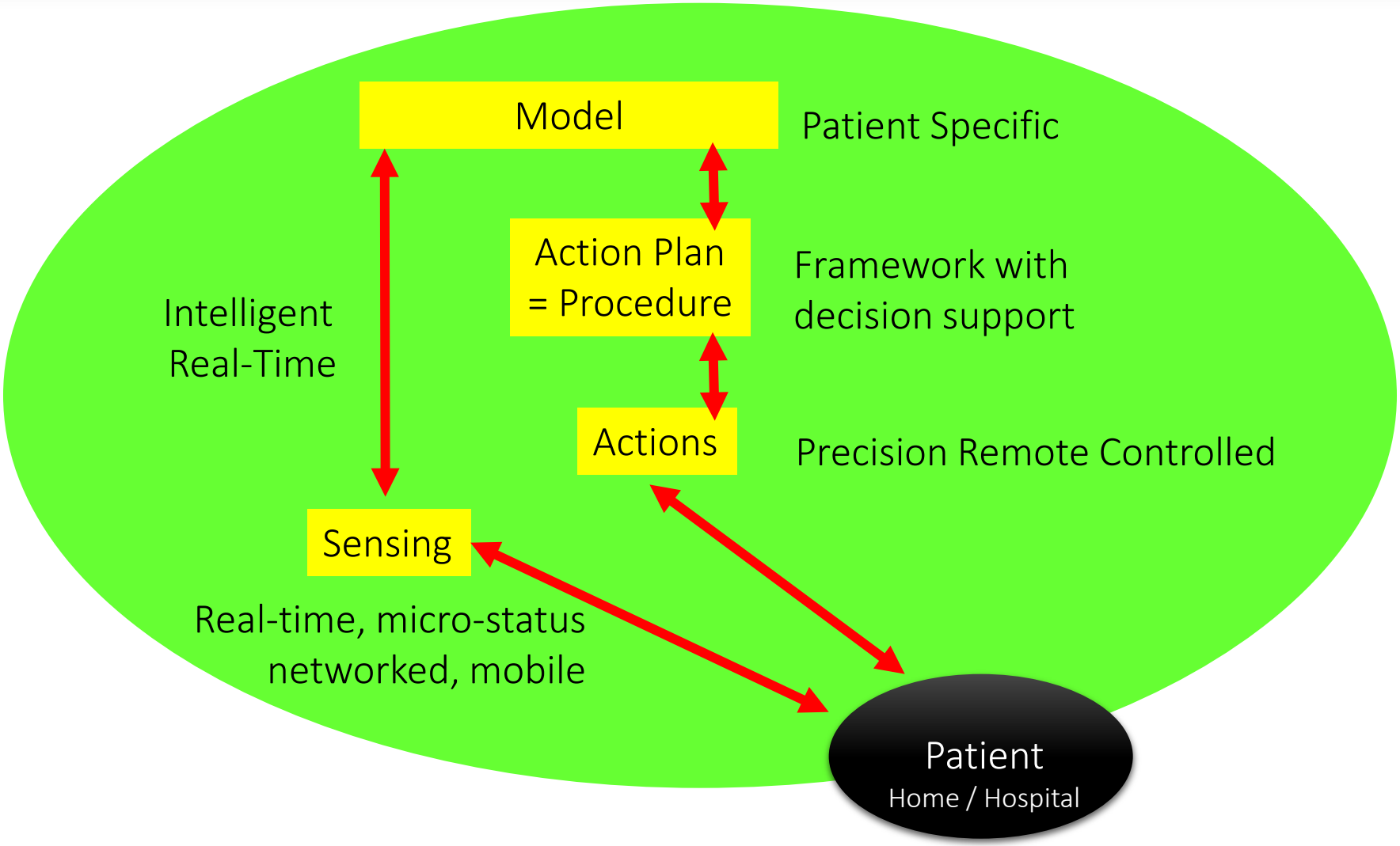
CIMIT Model

Clinical Impact

MIT is one of the four institutions that came together in 1998 to found CIMIT. In addition to the CIMIT-funded projects MIT researchers have pursued, CIMIT and MIT have been working together through guest faculty support of its Health Science and Technology Program to provide meaningful training in medical device development for graduate students.

The Medical Device "Plug-and-Play" (MD PnP) Interoperability Program was established in 2004 to lead the adoption of open standards and technology for medical device interoperability to support clinical innovation. The term "PnP" was adopted because the required technology infrastructure has many elements in common with the plug-and-play approach used in other computer-based systems. The program is affiliated with Massachusetts General Hospital (MGH), CIMIT (Center for Integration of Medicine and Innovative Technology), and Partners HealthCare Information Systems, with additional support from TATRC (U.S. Army Telemedicine & Advanced Technology Research Center). Having evolved from the OR of the Future program at MGH, the MD PnP program remains clinically grounded.

Early Remit of CIMIT – Sense, *then*, Respond – Future Integrated Healthcare Monitoring



The distinction between healthcare and other industry is in differentiation of scalability. Patient centricity as a service is not scalable but patient centric infrastructure (architecture) is scalable.

MD PnP™

Getting Connected for Patient Safety™

Medical Device "Plug-and-Play" Interoperability Program working on "safe interoperability™" to improve patient safety

The CIMIT MD PnP Lab opened in May 2006 to provide a vendor-neutral "sandbox" to evaluate the ability of candidate interoperability solutions to solve clinical problems, to model clinical use cases (in a simulation environment), to develop and test related network safety and security systems, and to support interoperability and standards conformance testing.

At the CIMIT Innovation Congress in November 2007, Dr. Julian Goldman demonstrated how patient safety could be improved by synchronization of the x-ray exposure with the ventilator during surgery.

OpenICE Test Bed

Now available to IIC Members

Integrated Clinical Environment

WWW.MDPNP.ORG

www.openice.info

Serial

OpenICE Device-Adapter

Any java-capable computer running OpenICE Device Adapter

Serial

OpenICE Device-Adapter

Ethernet Network

Any java-capable computer running OpenICE Supervisor

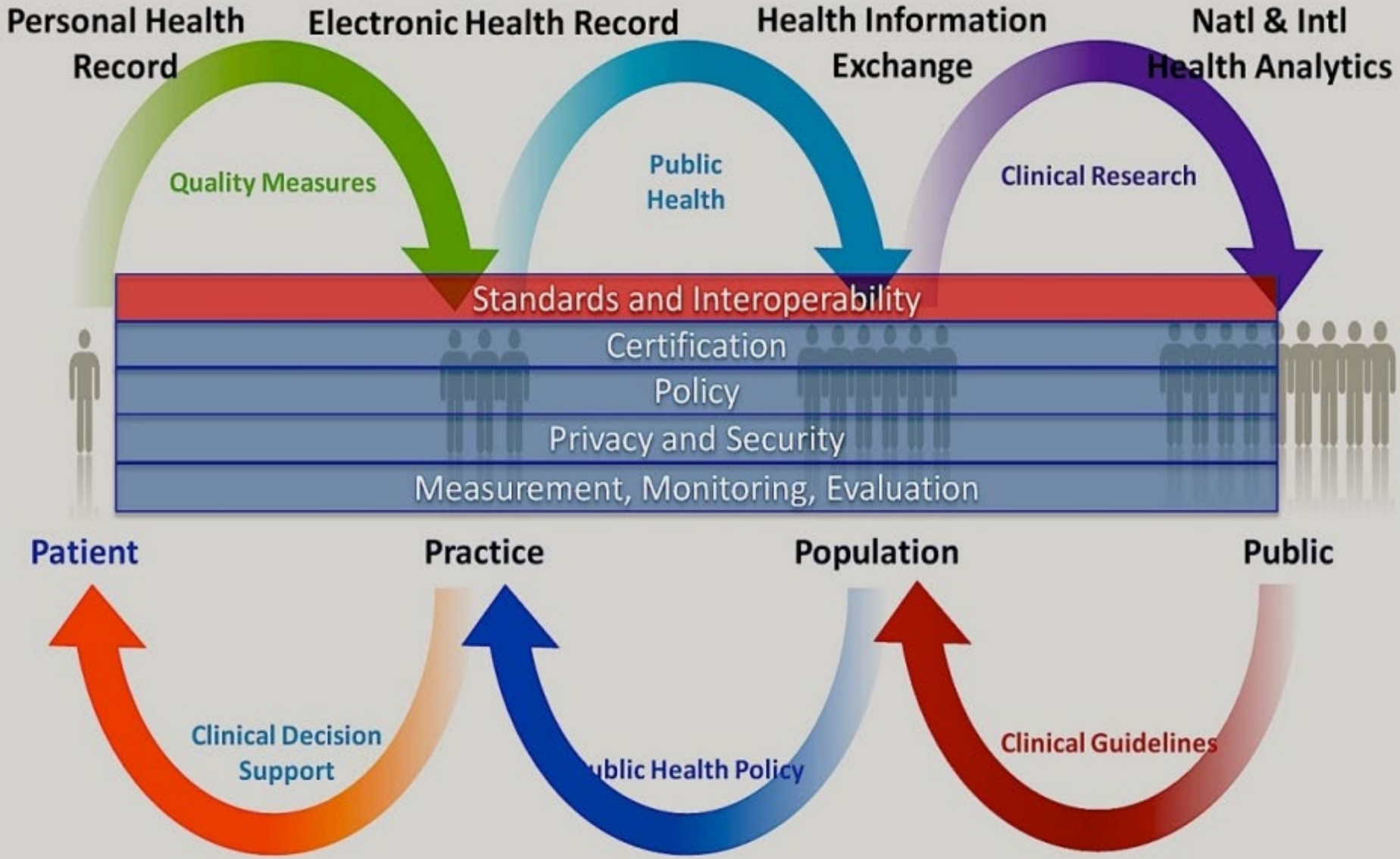
OpenICE Device Simulator

OpenICE Device Simulator running on any computer on the network

www.openice.info/demo.html

Shoumen Datta, Gary Gottlieb and Julian Goldman

Platform for Trusted Data Access via Secure Standards and Interoperability



Healthcare Data Interoperability & Standards

… semantics, data dictionaries, billing codes

- Terminology
  - SNOMED, LOINC
- Classification Systems
  - ICD10, CPT
- Devices
  - IEEE 11073
- EHR-Related
  - DICOM, HL7 (CDA)
- Interoperability
  - DICOM, HL7 Messaging, HIPAA Transactions, NCPDP
- Language Formats
  - XML, X12

Increase in computational time may be compensated by a relaxed priority queue which allows throughput scaling for large number of threads. Hence, parallelizing common algorithms to work on multicore chips: ***The SprayList*** www.mit.edu/~jerryzli/SprayList-CR.pdf

The Need for a Collaborative Community to Advance the Development and Adoption of Smart and Autonomous Medical Systems (SaAMS)

Julian M. Goldman, M.D[1,2]., Yi Zhang, Ph.D.[1]

[1]Center for Smart and Autonomous Medical Systems / Medical Device Interoperability and Cybersecurity Program (MD PnP)
Department of Anesthesia, Critical Care and Pain Medicine. Massachusetts General Hospital; [2]Harvard Medical School, Boston, Massachusetts

Excerpt from STA 2020 Poster

STA 2020 Poster:
Verification of Interoperable Medical Devices for Closed-Loop Control of Anesthesia using Hardware-in-the-Loop Testing
J Goldman, Y Zhang, D Arney, S Weininger(FDA)

"The performance of medical devices (core medical functions and interface capabilities) must be characterized in detail to safely comprise the CLC system.

This poster documents the application of our research hardware-in-the-loop testbed for interoperable CLC devices."

What are Smart and Autonomous Medical Systems (SaAMS)?

SaAMS describe a wide range of medical systems designed from the ground up to enable smart apps to connect to medical devices to more safely and efficiently deliver transformative patient care solutions.

SaAMS may utilize sophisticated algorithms interacting with interoperable medical devices to perform tasks that improve patient safety or efficiency, make decisions, automate processes, enhance vigilance, personalize patient and user experiences, advance healthcare equity, and solve historically intractable problems. They may utilize artificial intelligence (AI) to adapt to new information, make predictions, and operate autonomously.

Excerpt rom STA 2020 Poster

The anesthesia technology community should collaborate to establish consensus safety, regulatory, and performance requirements that can be used as a baseline to characterize the capabilities of interoperable medical devices to enable and promote CLC anesthesia innovation.

To address that need, we are establishing a Smart and Autonomous Medical Systems (SaAMS) **initiative** to facilitate engagement by interested stakeholders (medical device manufacturers, health delivery organizations, funding entities, and regulators). We welcome your participation in the SaAMS initiative.

The SaAMS initiative progressed under TATRC NETCCN/TiDE and DoD FCT grant portfolios.

2024: SaAMS "Initiative" → Collaborative Community

A Collaborative Community can address challenging medical technology needs that no single manufacturer or other entity may be able to accomplish alone. This includes identifying and advancing key enabling device features and clinical system capabilities that address complex engineering and clinical challenges.

We are forming a Collaborative Community, as described by the FDA, "to achieve common outcomes, solve shared challenges, and leverage collective opportunities" to advance the maturity, adoption, and clinical use of SaAMS to improve patient care. [1]

Participants in the SaAMS Collaborative Community will comprise a wide range of experts including manufacturers, clinicians, engineers, researchers, government representatives, and the US FDA, to collaborate on the development of evidence to support safety. This safety framework is intended **to provide precompetitive evidence for use in the regulatory process to de-risk commercial development and increase the safety, effectiveness, and clinical usability of these systems**.

Examples of SaAMS applications

- Automated Closed Loop control of Intravenous Anesthesia (ACLIVA)
- Closed-loop vasopressor therapy
- Closed-Loop Fluid Administration
- Remote IV Infusion Pump Control and Remote Lung Ventilator Control
- Smart alarms that improve and specificity
- AI-based predictive clinical analytics

References

1. Collaborative Communities: Addressing Health Care Challenges Together, https://www.fda.gov/about-fda/cdrh-strategic-priorities-and-updates/collaborative-communities-addressing-health-care-challenges-together
2. MGH SaAMS Collaborative Community https://mdpnp.mgh.harvard.edu/saams-cc/
3. MD PnP Center for SaAMS https://mdpnp.mgh.harvard.edu/saams-center/

https://mdpnp.mgh.harvard.edu/saams-cc/

MD PnP → SaAMS

Acknowledgements

This research was supported in part under the Medical Technology Enterprise Consortium(MTEC) Research Project Number W81XWH-22-9-0004, funded by the Foreign Comparative Testing Program of the US Department of Defense (DoD). The views, opinions and/or findings contained in this poster are those of the authors and should not be construed as an official DoD position, policy or decision unless so designated by other documentation.

What are Smart & Autonomous Medical Systems ?

Examples of SaAMS:

- **Automated closed loop control of intravenous anesthesia (ACLIVA)**
- **Closed-loop vasopressor (blood pressure) therapy**
- **Closed-loop IV fluid administration**
- **Remote (external data interface) control of Infusion Pumps, Lung Ventilators**
- **Real-time decision support system**
- **Integrated predictive clinical analytics**
- **Smart alarms that improve sensitivity to clinically significant events and enhance specificity to reduce non-actionable alarms and reduce alarm fatigue**

Integrating actuators, sensors, and smart clinical algorithms are key components of any decision support system, such as, SaAMS.

https://mdpnp.mgh.harvard.edu/saams-cc/

Other domains in demand

Diabetes Type II

Diabetes mellitus

Type 2 diabetes (T2D) is a multifactorial disease with substantial genetic risk, for which the underlying biological mechanisms are not fully understood. In this study, we identified multi-ancestry T2D genetic clusters by analyzing genetic data from diverse populations in 37 published T2D genome-wide association studies representing more than 1.4 million individuals. We implemented soft clustering with 650 T2D-associated genetic variants and 110 T2D-related traits, capturing known and novel T2D clusters with distinct cardiometabolic trait associations across two independent biobanks representing diverse genetic ancestral populations (African, n = 21,906; Admixed American, n = 14,410; East Asian, n =2,422; European, n = 90,093; and South Asian, n = 1,262). The 12 genetic clusters were enriched for specific single-cell regulatory regions. Several of the polygenic scores derived from the clusters differed in distribution among ancestry groups, including a significantly higher proportion of lipodystrophy-related polygenic risk in East Asian ancestry. T2D risk was equivalent at a body mass index (BMI) of 30 kg m^{-2} in the European subpopulation and 24.2 (22.9–25.5) kg m^{-2} in the East Asian subpopulation; after adjusting for cluster-specific genetic risk, the equivalent BMI threshold increased to 28.5 (27.1–30.0) kg m^{-2} in the East Asian group. Thus, these multi-ancestry T2D genetic clusters encompass a broader range of biological mechanisms and provide preliminary insights to explain ancestry-associated differences in T2D risk profiles.

https://doi.org/10.1038/s41591-024-02865-3 ◆ https://doi.org/10.1038/s41586-024-07019-6

World Sugar Trade (2010/2011)

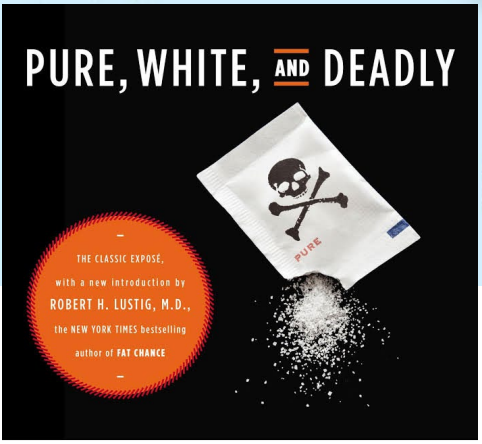
www.SAVEOURSUGAR.eu

SAVE OUR SUGAR

Support a Fair Deal for Cane Refiners

www.nytimes.com/2016/09/13/well/eat/how-the-sugar-industry-shifted-blame-to-fat.html?_r=0

www.npr.org/sections/thetwo-way/2016/09/13/493739074/50-years-ago-sugar-industry-quietly-paid-scientists-to-point-blame-at-fat



How Sugar Is Killing Us and What We Can Do to Stop It

John Yudkin

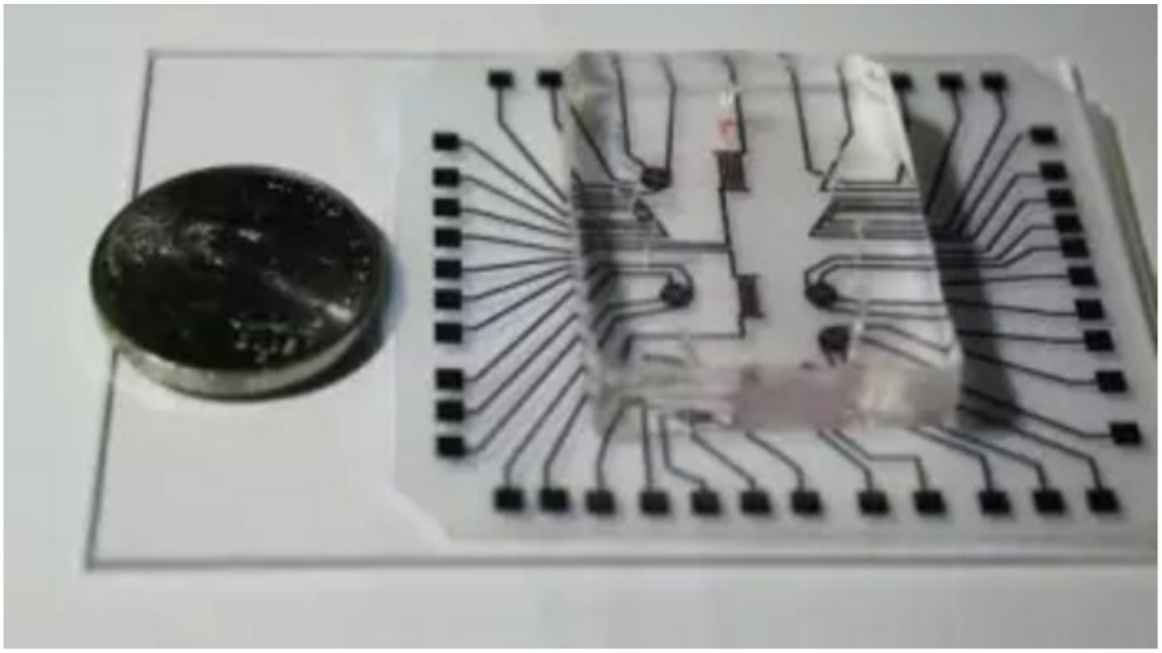
The sugar industry paid scientists in the 1960s to play down the link between sugar and heart disease and promote saturated fat as the culprit instead, newly released historical documents show.

http://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2548255

The documents show that a trade group called the Sugar Research Foundation, known today as the Sugar Association, paid three Harvard scientists the equivalent of about $50,000 in today's dollars to publish a 1967 review of research on sugar, fat and heart disease. The studies used in the review were handpicked by the sugar group, and the article, which was published in the prestigious New England Journal of Medicine, minimized the link between sugar and heart health and cast aspersions on the role of saturated fat.

www.ncbi.nlm.nih.gov/pubmed/5339699

IS HEALTHCARE A HUMAN RIGHT? IS IT FOR THE BILLIONS ?



This device costs one cent to make and could help deliver critical diagnostic care to remote, impoverished areas of the globe. (Image courtesy of Stanford.)

Multifunctional, inexpensive, and reusable nanoparticle-printed biochip for cell manipulation and diagnosis

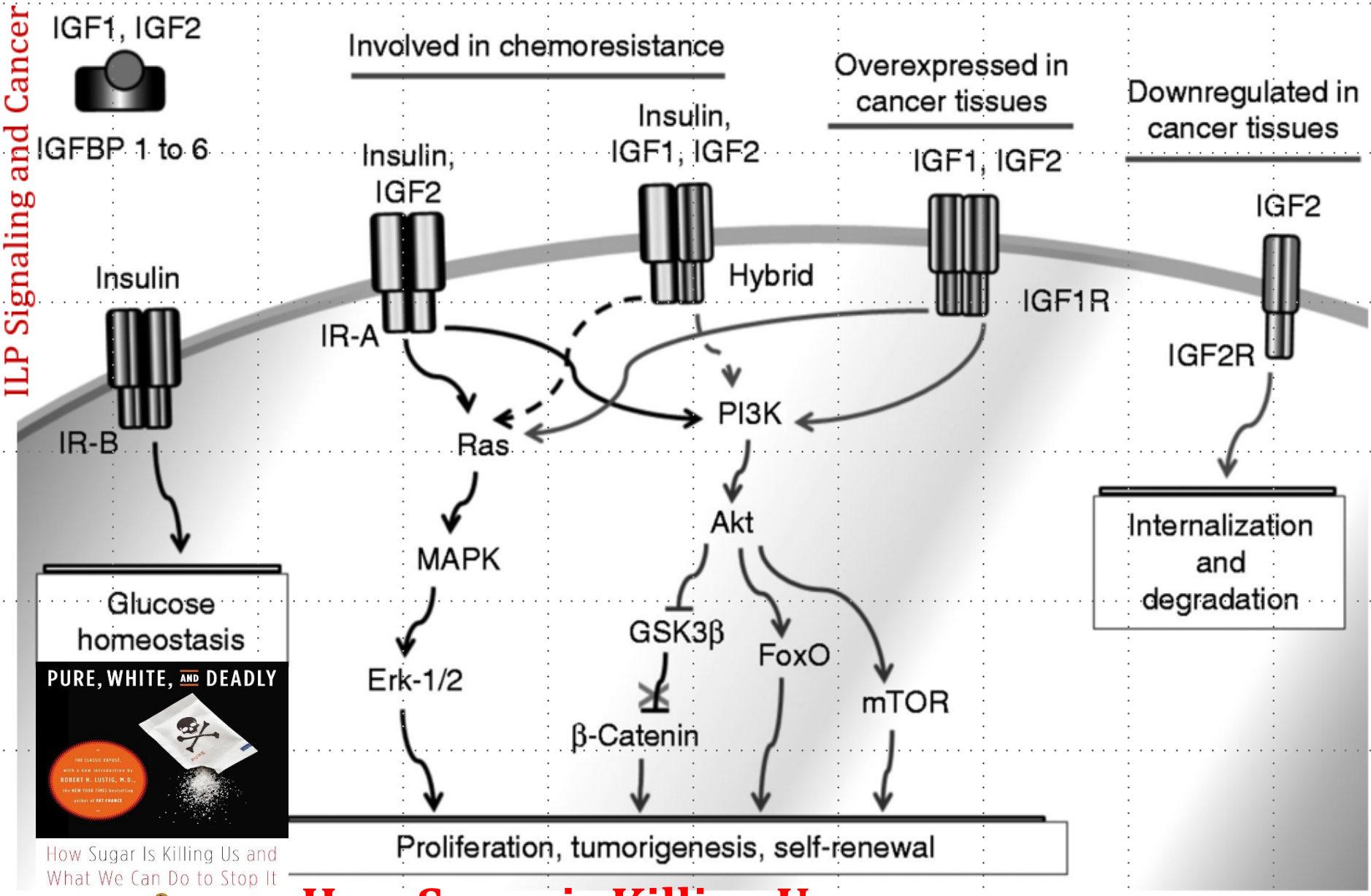
Rahim Esfandyarpour[a,b], Matthew J. DiDonato[c], Yuxin Yang[d], Naside Gozde Durmus[a,b], James S. Harris[d], and Ronald W. Davis[a,b,1]

http://www.pnas.org/content/114/8/E1306.abstract

Gozde Durmus

Insulin Resistance and Cancer

ILP Signaling and Cancer



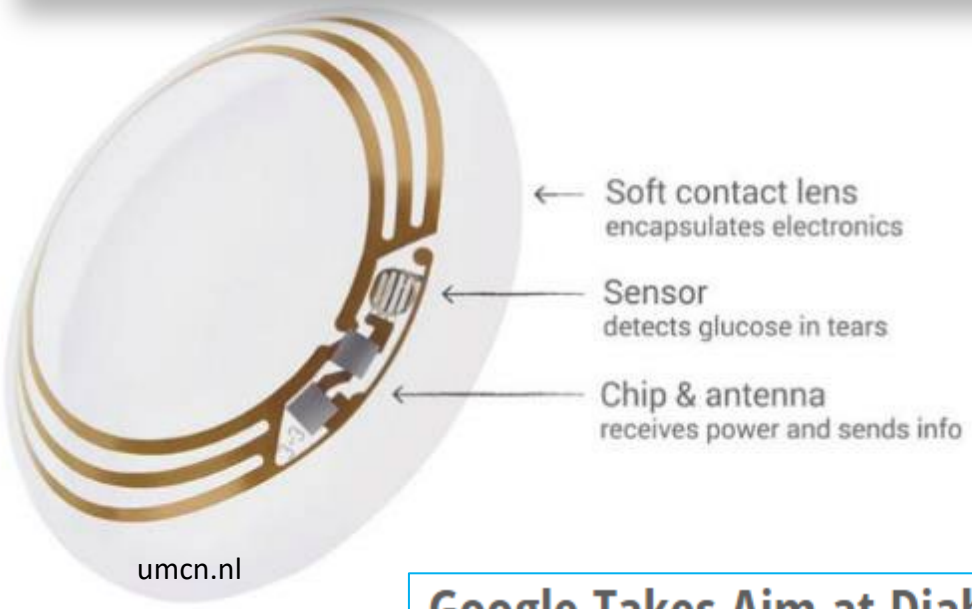
How Sugar Is Killing Us and What We Can Do to Stop It

John Yudkin

How Sugar is Killing Us

www.ncbi.nlm.nih.gov/pubmed/23207292

DIABETES – The next medical IoT Focus



umcn.nl

Google, DexCom to Make Glucose Monitoring Devices for Diabetes Patients

by Robin Sinha , 13 August 2015

Soon after the announcement of its new CEO Sundar Pichai and a holding company called Alphabet, the Google Life Sciences team has teamed up with a healthcare firm DexCom to build blood glucose monitoring devices for diabetes patients that are smaller and less expensive than current technologies.

Google Takes Aim at Diabetes with Big Data, Internet of Things

By **Jennifer Bresnick** on August 31, 2015

SANOFI

HARVARD MEDICAL SCHOOL

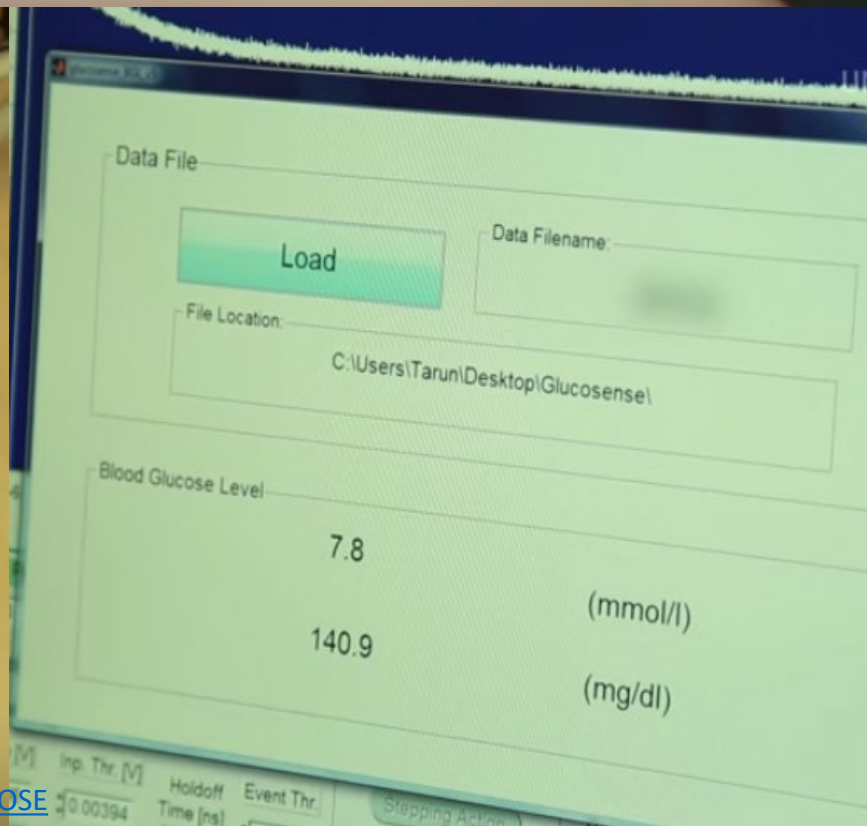
ABOUT HMS | EDUCATION

Joslin Diabetes Center

Freshly revitalized after Google's much-discussed reorganization under the **Alphabet** umbrella, the tech giant's life science team is once again **planning to tackle diabetes** with the help of big data analytics and innovative Internet of Things technologies.

With the formation of a new partnership that enlists the aid of the Joslin Diabetes Center and Sanofi, a multinational pharmaceutical developer, Google hopes to reduce the burden of Type 1 and Type 2 diabetes on both patients and providers.

BLOOD-FREE NON-INVASIVE BLOOD GLUCOSE

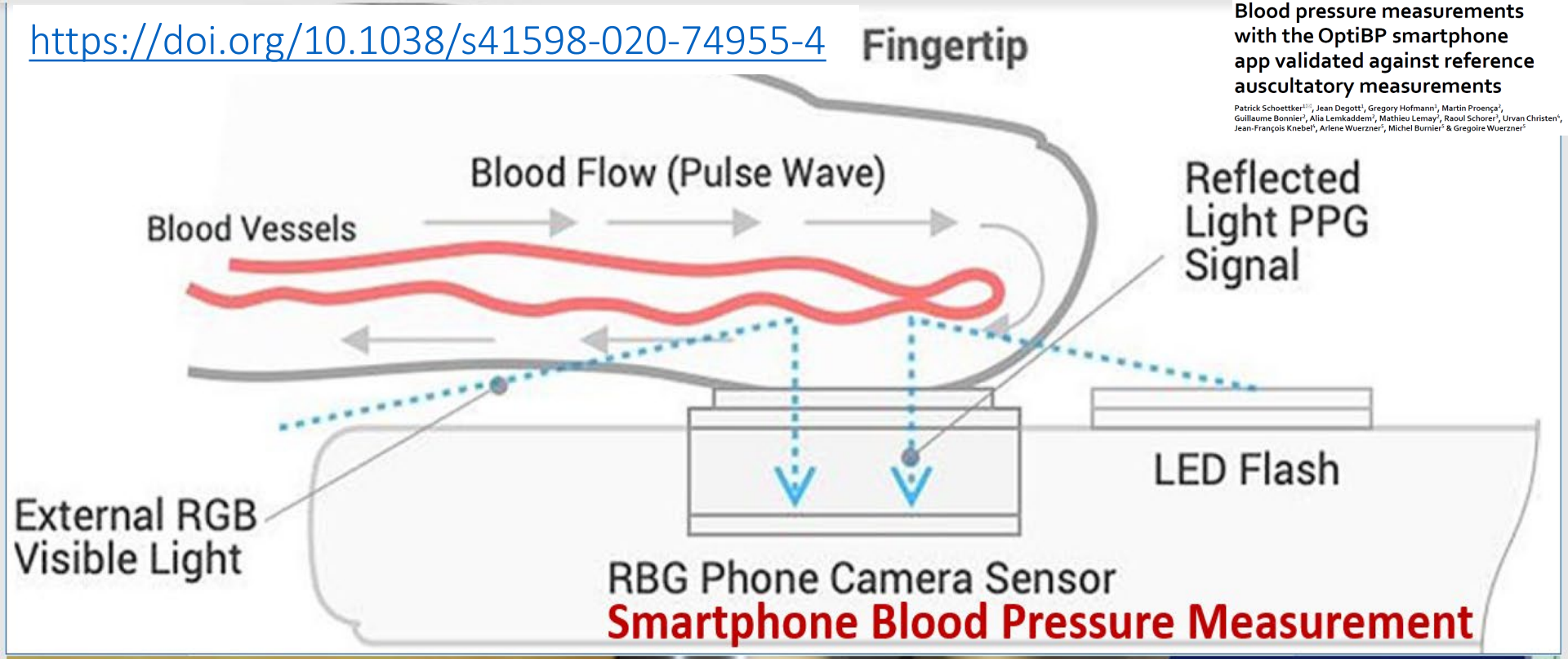


Professor Gin Jose, University of Leeds ● http://bit.ly/BLOOD-FREE-BLOOD-GLUCOSE

https://doi.org/10.1038/s41598-020-74955-4

Blood pressure measurements with the OptiBP smartphone app validated against reference auscultatory measurements

Patrick Schoettker[1,2], Jean Degott[1], Gregory Hofmann[1], Martin Proença[2], Guillaume Bonnier[2], Alia Lemkaddem[2], Mathieu Lemay[2], Raoul Schorer[1], Urvan Christen[1], Jean-François Knebel[1], Arlene Wuerzner[1], Michel Burnier[1] & Gregoire Wuerzner[1]



BLOOD-FREE NON-INVASIVE BLOOD HEMOGLOBIN ??

Laser excitation of oxy-hemoglobin generates highly specific resonance (Raman spectra) which could be exploited in the development of non-invasive tool to determine hemoglobin.

This statement is made by the author. It is merely a suggestion.

Wrig Nanosystems, a medical technology startup company which develops and markets a hemoglobin measurement device, has attracted financial interest from different investors in the product. The company has made an investment of up to 15 cr to commercialise and further develop the product and Avendus Wealth Management acted as the advisor to Wrig on this deal.

The list of investors includes Flipkart co-founders Sachin and Binny Bansal, Malvinder and Shivinder Singh (former Ranbaxy and Fortis promoters), Gurpreet Singh (Round Glass Partners) and others.

Diabetes Type I

First, a little bit (drop in an ocean) of a nice letter

Feidhmeannacht na Seirbhíse Sláinte,
Seirbhís Aisíocha Príomhchúraim
Bealach amach 5, M50, An Bóthar Thuaidh,
Fionnghlas, Baile Átha Cliath 11, D11 XKF3

Primary Care Reimbursement Service
Exit 5, M50, North Road, Finglas,
Dublin 11, D11 XKF3

www.pcrs.ie
t 01 8647100
e PCRS@hse.ie

25th October 2023

Circular 028/23

RE: Continuous Glucose Monitoring (CGM)

Dear Pharmacist,

The Health Information and Quality Authority (HIQA) published the rapid Health Technology Assessment of Continuous Glucose Monitoring (CGM) in Adults with Type 1 Diabetes Mellitus on 29th September 2023. The published document can be found at https://www.hiqa.ie/reports-and-publications/health-technology-assessment/rapid-health-technology-assessment-continuous.

In line with the advice from HIQA and due to the budget impact associated with CGM sensors, the HSE will establish a single managed access programme for all CGM systems for all individuals with Type I Diabetes Mellitus regardless of age. This online reimbursement application system will replace the current managed access system in place for FreeStyle Libre 1 and will apply to all CGM sensors on the Reimbursement List.

The reimbursement application system will continue to be confined to those hospital clinicians responsible for the initiation of CGM systems for individuals with Type 1 Diabetes Mellitus. It's intended that the online reimbursement application system will be in place by the end of the year and will be managed by the HSE Medicines Management Programme (MMP).

Reimbursement support for CGM sensors under Community Drug Schemes is for Type I Diabetes Mellitus only. Reimbursement of these products has not been extended to any other patient cohort.

To manage the growing expenditure in this area, the HSE Medicines Management Programme will be initiating work on a preferred CGM sensor(s) over the coming weeks.

Further information on the managed access system and the MMP preferred product initiative will be communicated in due course.

Yours faithfully,

Diabetes

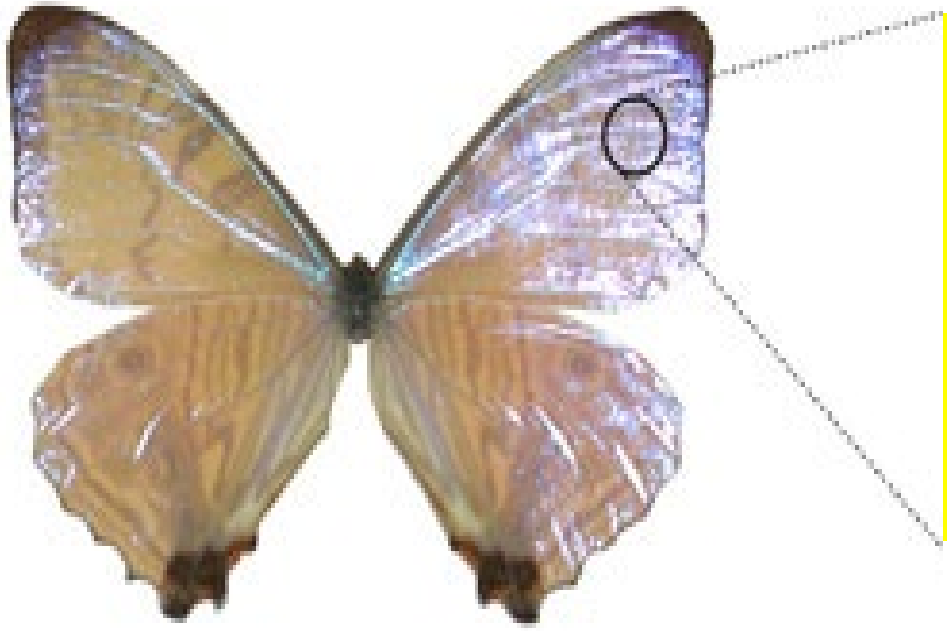
in general

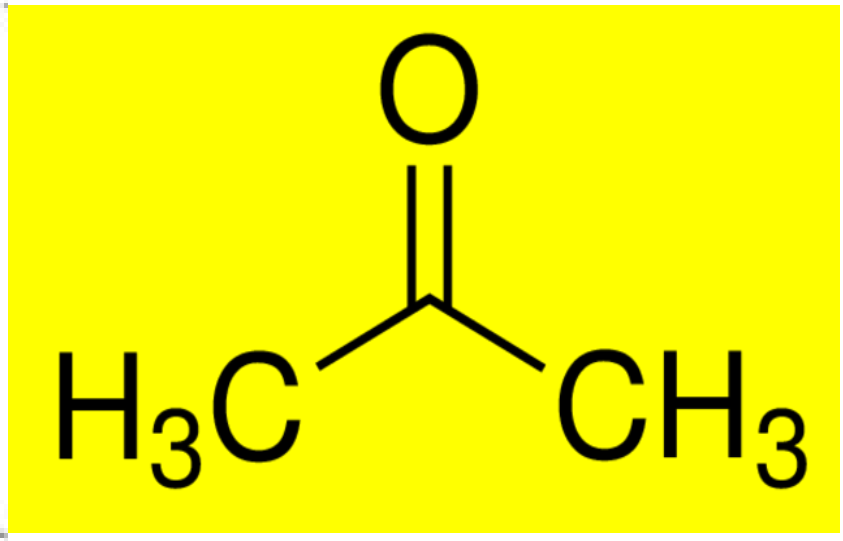
Diabetes Type I and Type II

20-year-old idea is still trying for lift off and trying to be useful

Can Butterflies Help Prevent Diabetes?

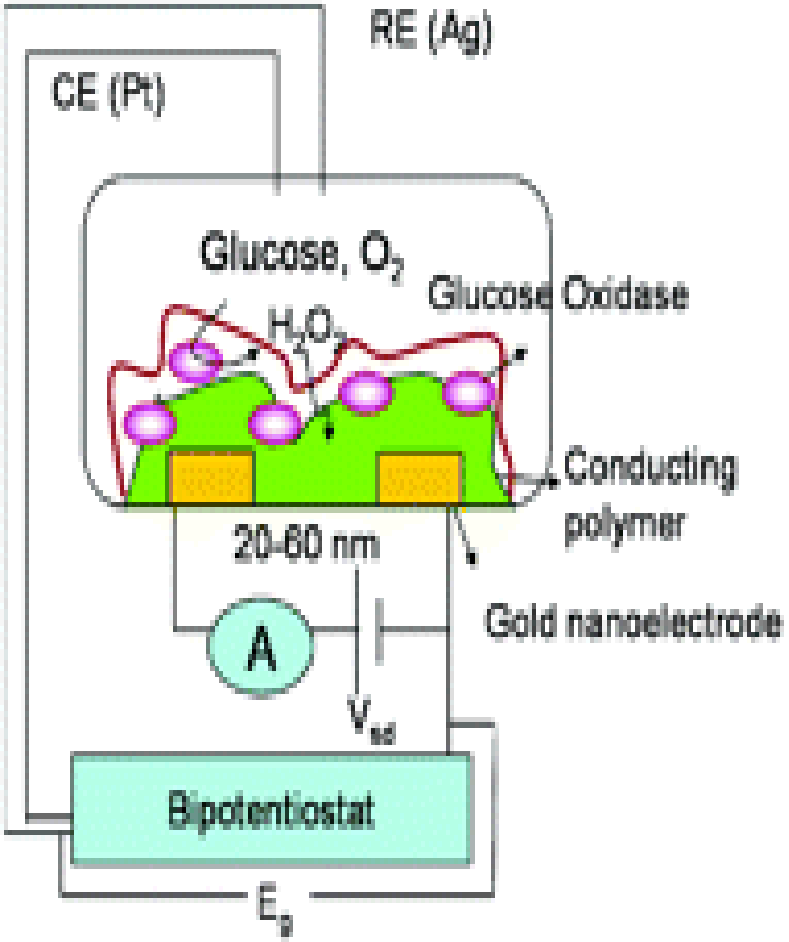
This is only a suggestion by the author and not a fact or system which is under investigation or is available at present.





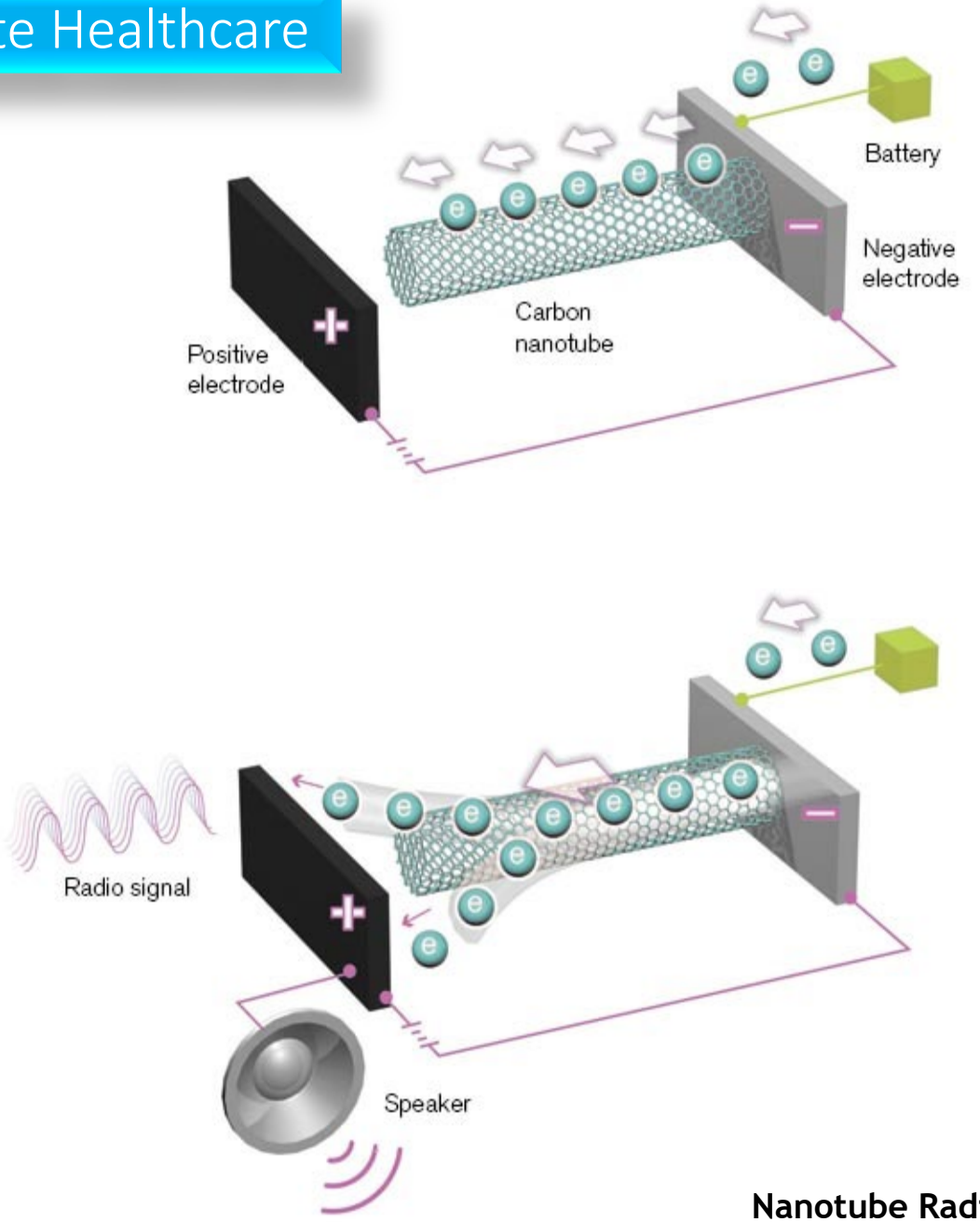
Dual Acetone Sensors on a single chip may differentiate between acetone in the environment vs acetone in the blood, breath or urine of diabetics. Subtractive analysis alerts to blood ketones. Occurs when body uses fat instead of glucose. It signals insulin dysfunction. If undiagnosed, it may lead to diabetic ketoacidosis (DKA) which may result in diabetic coma and may be fatal. The acetone (ketone bodies) sensors may be able to detect trace levels (nano milli moles eq) and may help preventive care to stem the clinical onset of type II diabetes mellitus (glucose >120 mg/dl).

Diabetes Diagnostics in Remote Healthcare



Blood Glucose Nano-sensor

NanoLetters (2004) 4 1785-1788

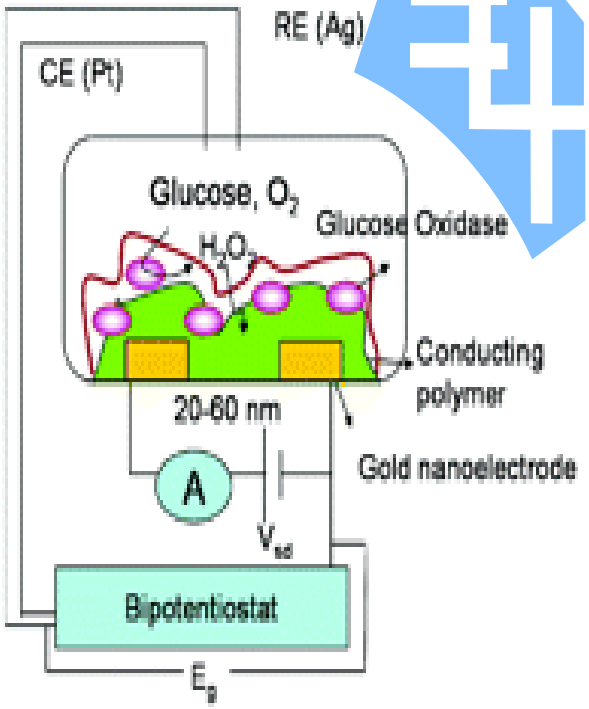


Nanotube Radio

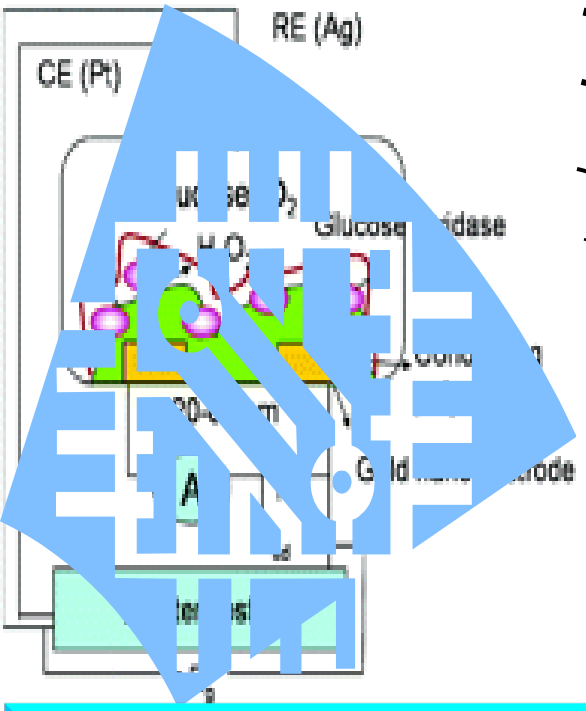
NanoLetters (2007) 7 3508-3511

Potential IoT Tool for Remote Heath Monitoring

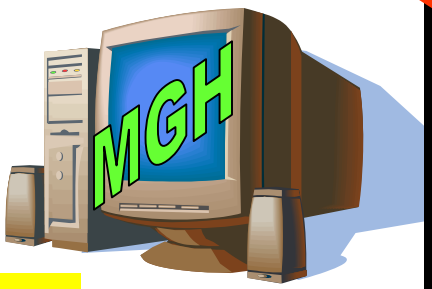
May I implant a glucose nano-sensor nano-radio chip on your shoulder? You are fat. You could become diabetic.



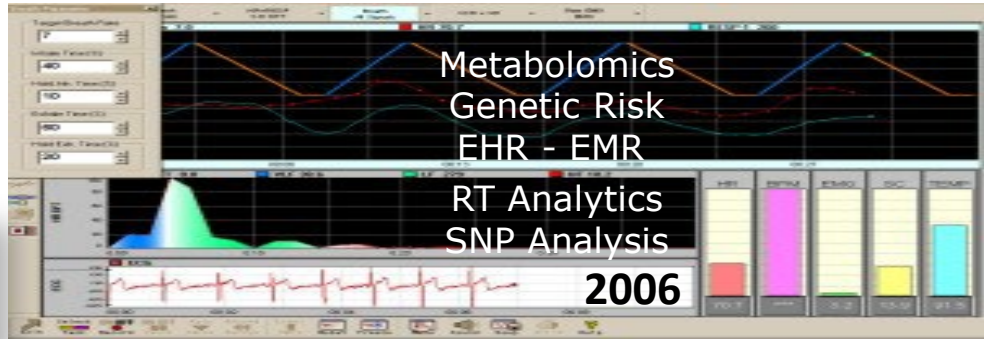
Prime Minister Bertie Ahern (Taoiseach) 2005 at TCD, IRL



802.11b
WiFi
802.11g



802.16a



Improved healthcare services, savings, create jobs from new products, new services and potential to create as well as capture new emerging markets of billions (BRICS)

TO DO

IoT is a digital by design metaphor

https://dspace.mit.edu/handle/1721.1/111021

IMPLEMENT

Blood Glucose home monitoring network, *n=100 (nodes)*

Blood Glucose home monitoring network, *n=100,000 (nodes)*

Cnoga's TensorTip device, CoG, allows an accurate and non-invasive monitoring of glucose levels in the blood.
https://www.timesofisrael.com/israeli-device-banishes-finger-pricking-for-sugar-levels-in-diabetes-patients/

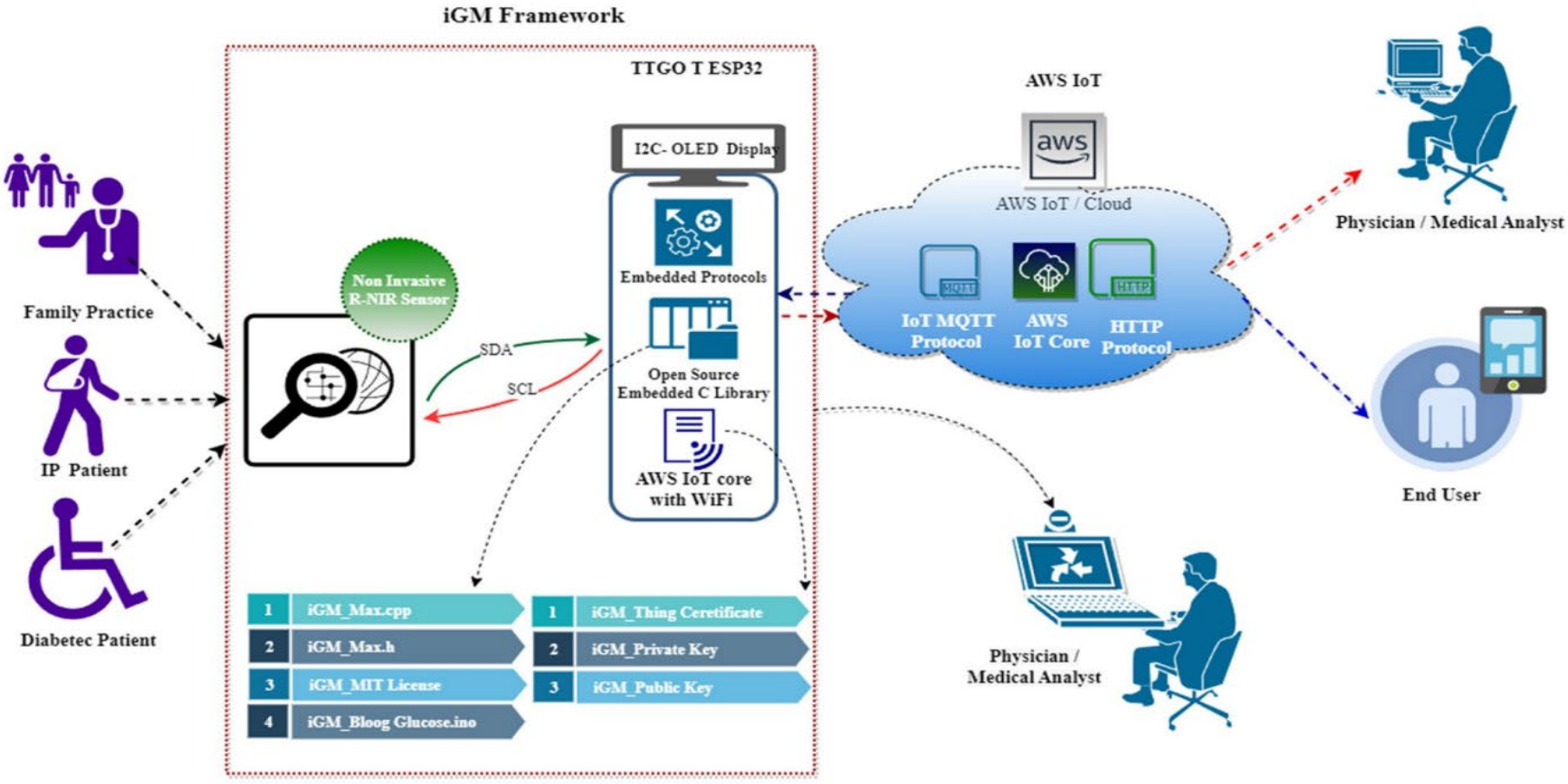
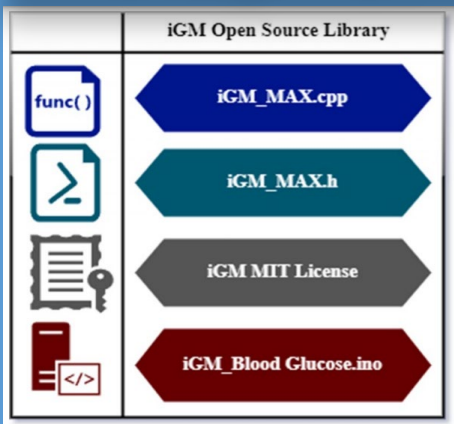


Figure 1. Proposed AWS assisted iGM framework for non-invasive blood glucose monitoring.

K. M, A., R, R., Krishnamoorthy, R. *et al.* "Internet of Things enabled open source assisted real-time blood glucose monitoring framework." *Science Rep* **14**, 6151 (2024). https://doi.org/10.1038/s41598-024-56677-z

IoT is a digital by design metaphor



https://doi.org/10.1038/s41598-024-56677-z

Figure 4. Structure of iGM open source library licensed by MIT.

Internet of Things enabled open source assisted real-time blood glucose monitoring framework

Abubeker K. M[1]✉, Ramani. R[2], Raja Krishnamoorthy[3], Sreenivasulu Gogula[4], Baskar. S[5], Sathish Muthu[6], Girinivasan Chellamuthu[7] & Kamalraj Subramaniam[8]

https://doi.org/10.1038/s41598-024-56677-z

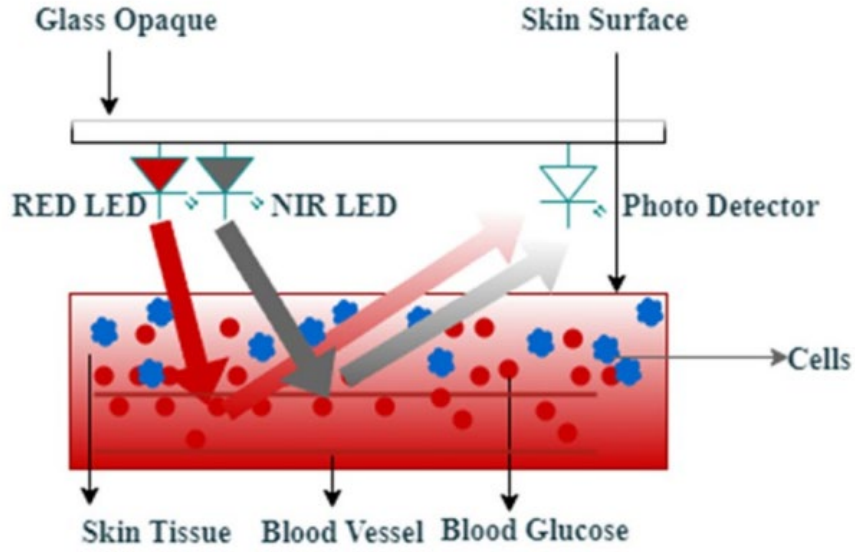


Figure 2. Red and near-infrared (R-NIR) signal absorption

Digital Transformation – IoT is a metaphor
https://dspace.mit.edu/handle/1721.1/111021

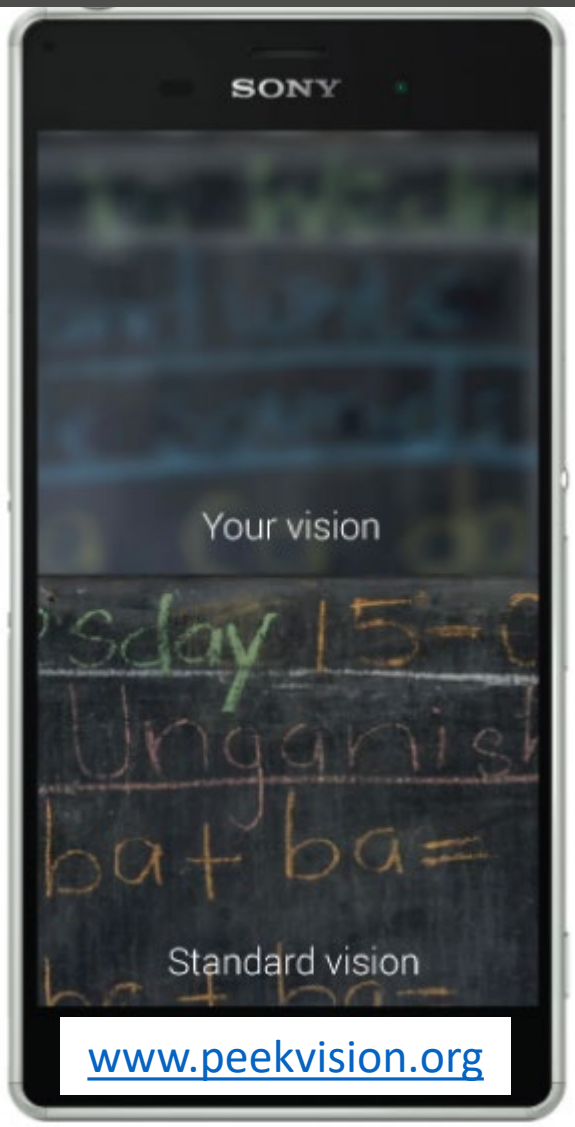
Farooq MS, Riaz S, Tehseen R, Farooq U, Saleem K. "Role of Internet of things in diabetes healthcare: Network infrastructure, taxonomy, challenges, and security model. Digit Health." 2023 June 6; 9:20552076231179056. doi: 10.1177/20552076231179056. PMID: 37312944; PMCID: PMC10259116.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10259116/pdf/10.1177_20552076231179056.pdf

Optics, Cardiovascular, …

Optics for the Masses

- View the retina with high quality imaging
- See cataracts clearly for classification
- Simulates a patient's eyesight on screen
- Visual acuity tests for eyesight
- Colour and contrast tests

The Peek Retina adapter is being developed through a collaboration between the University of Strathclyde, where Dr Mario Giardini heads the engineering design; the London School of Hygiene & Tropical Medicine; and the Glasgow Centre for Ophthalmic Research of NHS Greater Glasgow and Clyde.



www.peekvision.org

OPTICIAN'S CLINIC-IN-A-POCKET

A woman from Nakuru, Kenya, having a cataract scan with the Peek smartphone tool. This portable eye testing kit can diagnose eye problems in remote areas, where access to clinics is limited. ©Peek

What we hope is that it will provide eye care for those who are the poorest of the poor

Dr Andrew Bastawrous, London School of Hygiene and Tropical Medicine

www.bbc.com/news/health-22553730

What the phone app can do for eyes

Peek can diagnose a vast range of eye problems, blindness and vision impairments,

- Glaucoma
- Cataracts
- Macular degeneration
- Diabetic retinopathy
- Other retinal and optic nerve diseases.

Dr Leslie Saxon, University of Southern California

PHONE ECG DETECTS IRREGULAR HEARTBEAT

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

WEARABLE DIGITAL HEALTH TECHNOLOGIES IN MEDICINE

Stephen H. Friend, M.D., Ph.D., Geoffrey S. Ginsburg, M.D., Ph.D., Rosalind W. Picard, Sc.D., *Guest Editors*, and Jeffrey M. Drazen, M.D., *Editor*

Wearable Digital Health Technologies for Monitoring in Cardiovascular Medicine

Erica S. Spatz, M.D., M.H.S., Geoffrey S. Ginsburg, M.D., Ph.D., John S. Rumsfeld, M.D., Ph.D., and Mintu P. Turakhia, M.D., M.A.S.

From the Section of Cardiovascular Medicine, Yale School of Medicine, New Haven, CT (E.S.S.); the National Institutes of Health, Bethesda, MD (G.S.G.); the University of Colorado School of Medicine, Aurora (J.S.R.); and Meta Platforms, Menlo Park (J.S.R.), the Stanford Center for Digital Health, Stanford University School of Medicine, Stanford (M.P.T.), and iRhythm Technologies, San Francisco (M.P.T.) — all in California. Dr. Turakhia can be contacted at mintu@stanford.edu or at the Stanford Center for Digital Health, 300 Pasteur Dr. (H2146), Stanford, CA 94305.

N Engl J Med 2024;390:346-56.
DOI: 10.1056/NEJMra2301903

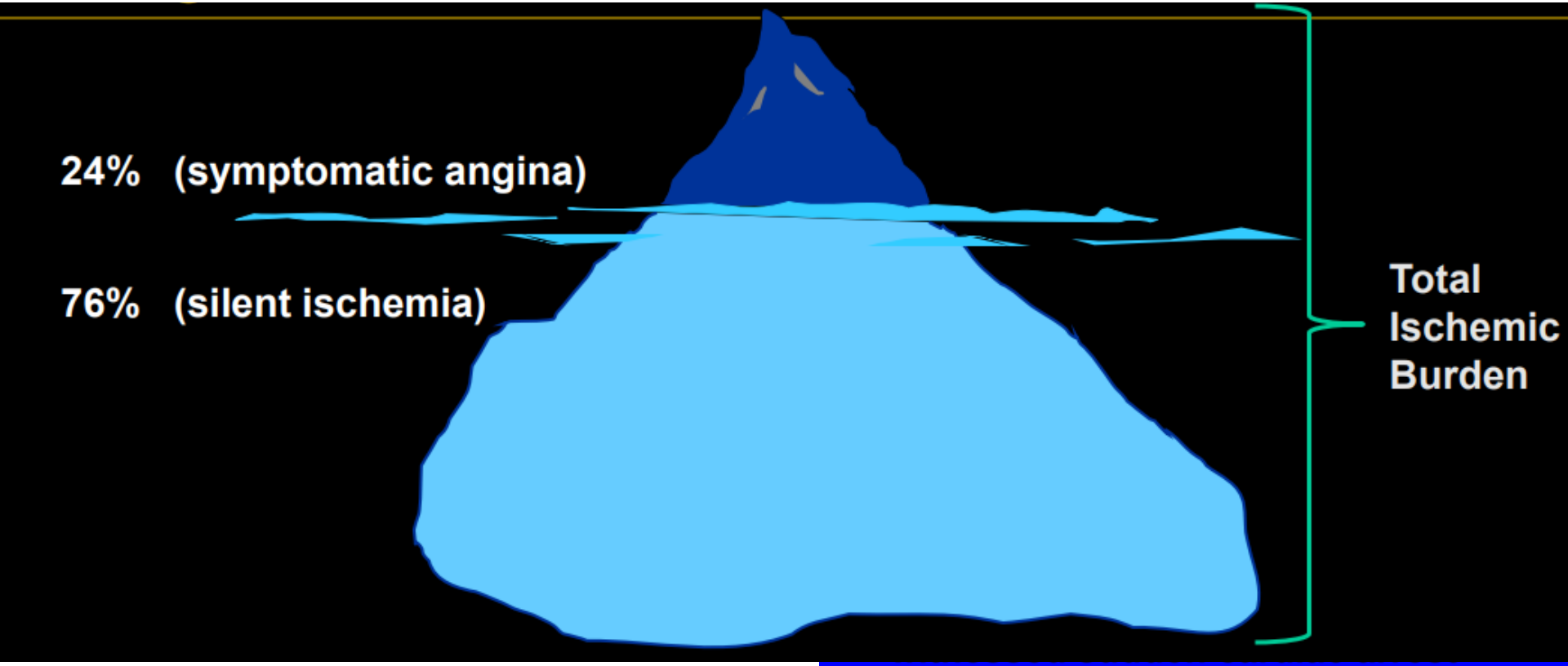
THIS REVIEW ARTICLE PRESENTS A THREE-PART TRUE-LIFE CLINICAL VIgnette that illustrates how digital health technology can aid providers caring for patients with cardiovascular disease. Specific information that would identify real patients has been removed or altered. Each vignette is followed by a discussion of how these methods were used in the care of the patient.

VIGNETTE, PART 1: REMOTE MONITORING OF CARDIOVASCULAR DISEASE

A 62-year-old woman with long-standing hypertension presents to the emergency department with decompensated heart failure and newly identified atrial fibrillation with rapid ventricular response. She is admitted for further evaluation and treatment and is found to have a left ventricular ejection fraction of 30%, which is thought to be tachycardia mediated from uncontrolled atrial fibrillation. After cardioversion and initiation of anticoagulation, antiarrhythmic drug therapy, and guideline-directed medical therapy for heart failure, she was enrolled in a remote patient monitoring program. Five days after discharge, she received a toolkit by mail that consisted of a blood-pressure cuff, a scale, a pulse oximeter, and a cellular hub that would transmit data to the remote care team.

Symptomatic Angina: The Tip of the Ischemic Iceberg

www.escardio.org/static_file/Escardio/education/live-events/courses/education-resource/Fri-11-SMI-Gutterman.pdf



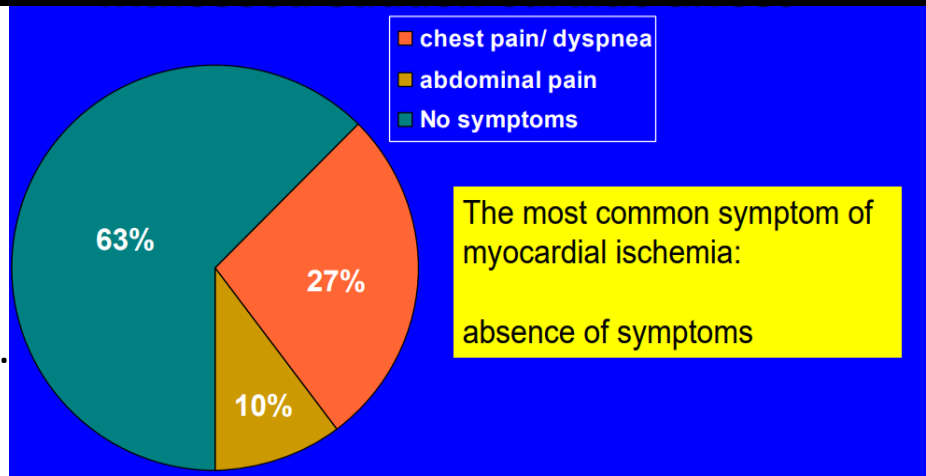
If you cannot sense, you cannot detect.

If you cannot predict, you cannot prevent.

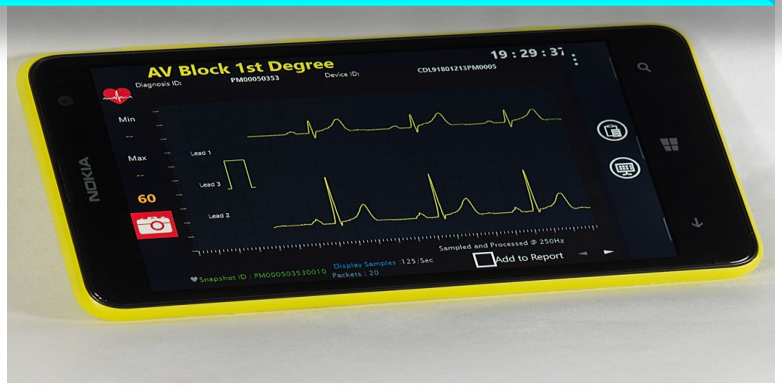
If you cannot measure, you do not have metrics.

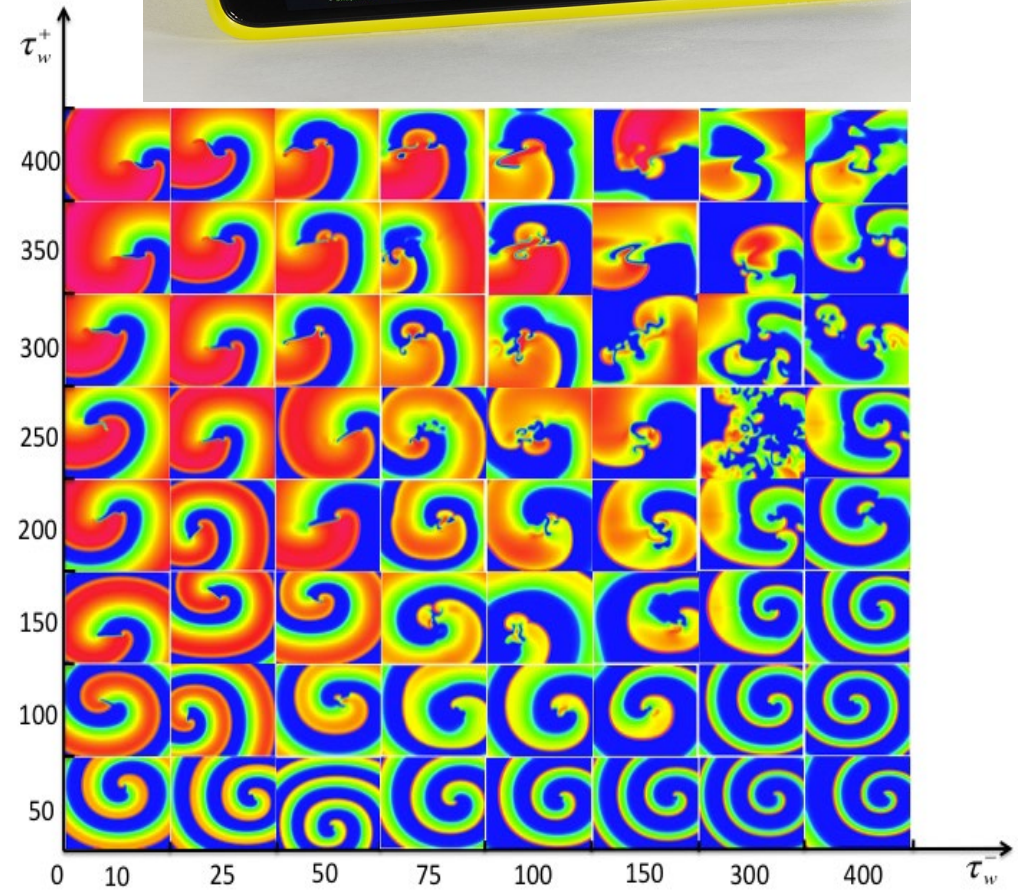
If you do not have data, you cannot take a decision.

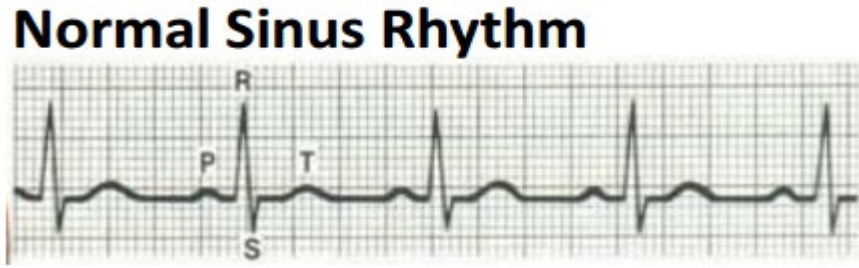
https://dspace.mit.edu/handle/1721.1/107893



CARDIAC ARRHYTHMIA DIAGNOSIS & REPORTING CARDIOLOGIST-in-a-POCKET

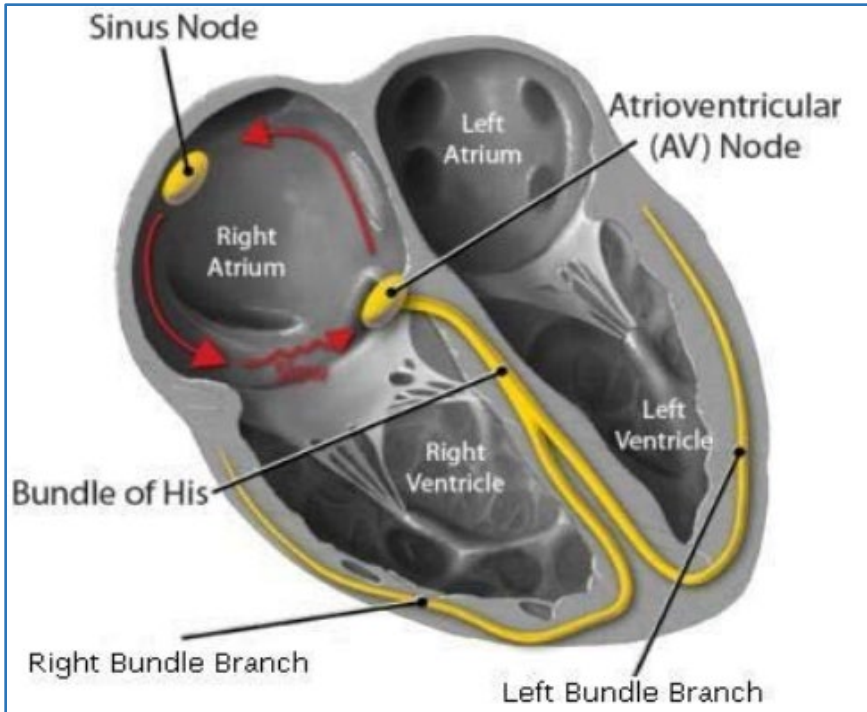




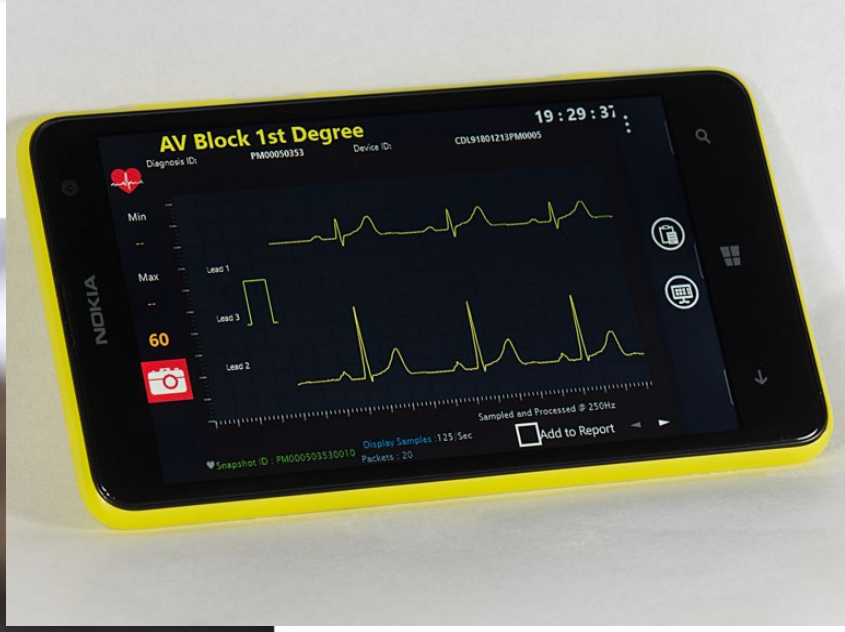


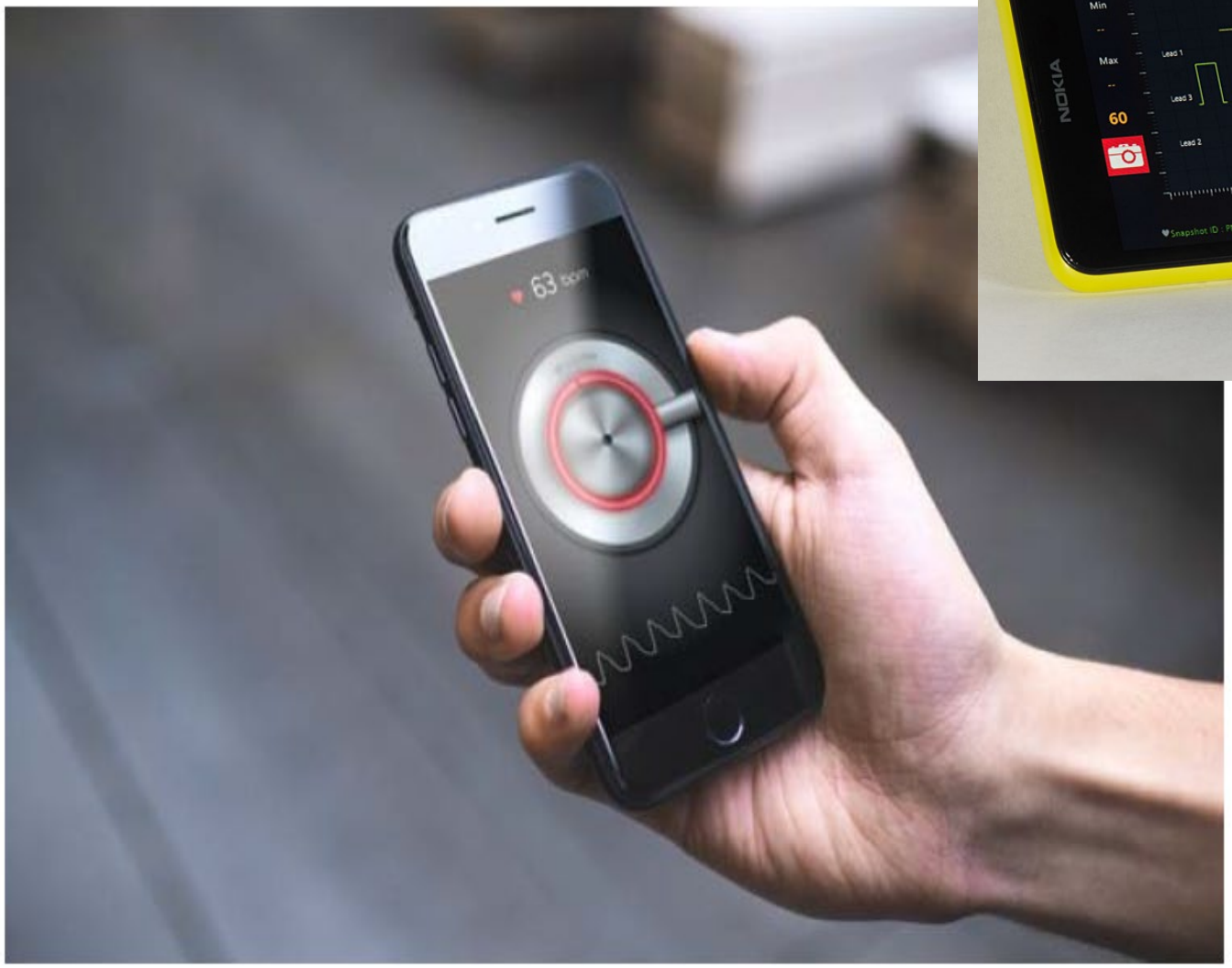
Circular pathways in the heart conduction system is a common cause of arrhythmias

www.seas.upenn.edu/sunfest/docs/slides/MALAMASPETER.pdf



MIT News
ON CAMPUS AND AROUND THE WORLD



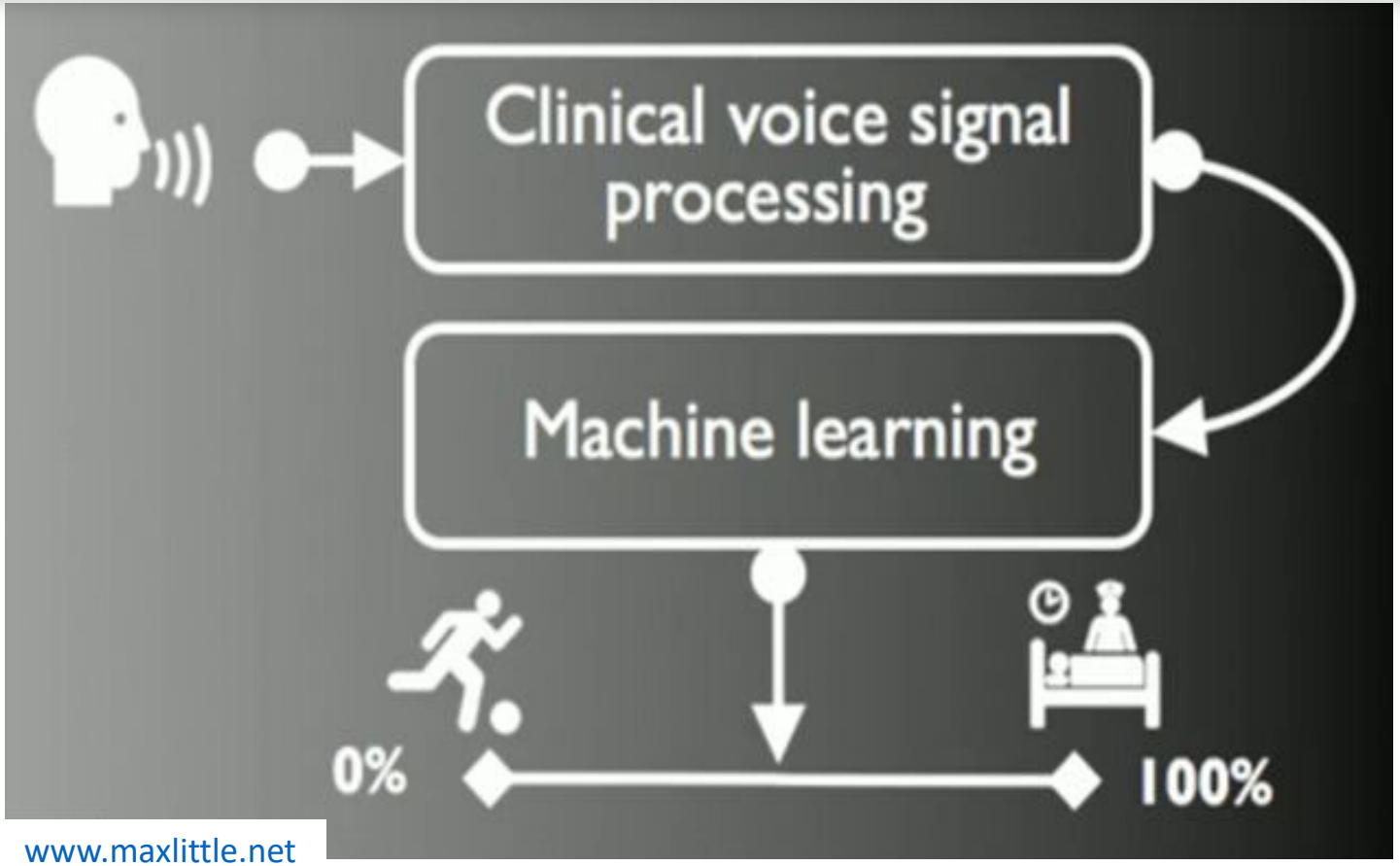


MIT Media Lab spinout Cardiio has developed a mobile app that uses a smartphone camera to detect facial signs of a heart arrhythmia associated with strokes.

Courtesy of Cardiio

App screens for arrhythmia using smartphone

Detection of Parkinson's Disease using a Smart Phone



www.maxlittle.net

Acoustic signal processing data may be used to detect Parkinson's Disease with a smartphone or predict torrential rainfall or used in hydrogeomorphology apps.

Falls
followed by
HIP & Knee Arthroplasty

Marsh M, Newman S. (2021) Trends and developments in hip and knee arthroplasty technology. J Rehabil Assist Technol Eng. 2021 Feb 8; 8:2055668320952043. doi: 10.1177/2055668320952043. PMID: 33614108

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7874345/pdf/10.1177_2055668320952043.pdf

Lucrative business (of hip & knee replacement)

Just compare the billing codes between ICD-09 and ICD-10

DIAGNOSIS CODES for SPRAINED & STRAINED ANKLES

ICD-9

845.00 Sprain and strain of ankle unspecied site
845.01 Sprain and strain of ankle, Deltoid ligament/ Internal collateral ligament
845.02 Sprain and strain of ankle, Calcaneobular (ligament)
845.03 Sprain and strain of ankle, Tibiobular (ligament) distal

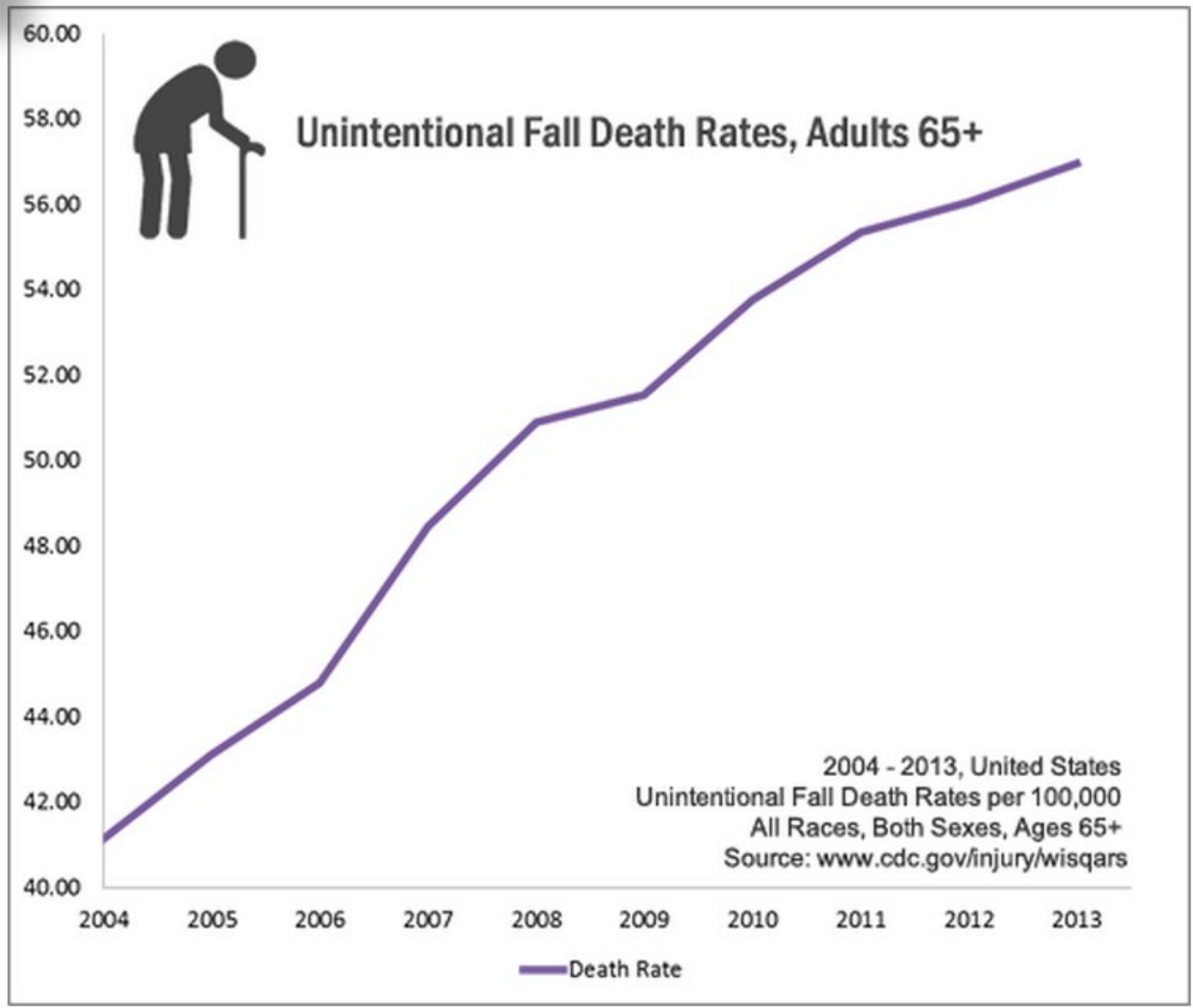
ICD-10

S93.401A Sprain of unspecied ligament of right ankle – initial encounter
S93.401D Sprain of unspecied ligament of right ankle – subsequent encounter
S93.401S Sprain of unspecied ligament of right ankle – sequela
S93.402A Sprain of unspecied ligament of left ankle – initial encounter
S93.402D Sprain of unspecied ligament of left ankle – subsequent encounter
S93.402S Sprain of unspecied ligament of left ankle – sequela
S93.409A Sprain of unspecied ligament of unspecied ankle – initial encounter
S93.409D Sprain of unspecied ligament of unspecied ankle - subsequent encounter
S93.409S Sprain of unspecied ligament of unspecied ankle – sequela
S93.412D Sprain of calcaneobular ligament of left ankle – subsequent encounter
S93.412S Sprain of calcaneobular ligament of left ankle – sequela
S93.419A Sprain of calcaneobular ligament of unspecied ankle – initial encounter
S93.419D Sprain of calcaneobular ligament of unspecied ankle – subsequent encounter
S93.419S Sprain of calcaneobular ligament of unspecied ankle
S93.431A Sprain of tibiobular ligament of right ankle – initial encounter
S93.431D Sprain of tibiobular ligament of right ankle – subsequent encounter
S93.431S Sprain of tibiobular ligament of right ankle – sequela
S93.432A Sprain of tibiobular ligament of left ankle – initial encounter
S93.432D Sprain of tibiobular ligament of left ankle – subsequent encounter
S93.432S Sprain of tibiobular ligament of left ankle – sequela
S93.439A Sprain of tibiobular ligament of unspecied ankle – initial encounter
S93.439D Sprain of tibiobular ligament of unspecied ankle – subsequent encounter
S93.439S Sprain of tibiobular ligament of unspecied ankle – sequela
S93.491A Sprain of other ligament of right ankle (Internal collateral/ talobular) initial encounter
S93.491D Sprain of other ligament of right ankle (Internal collateral/ talobular) subsequent encounter
S93.491S Sprain of other ligament of right ankle (Internal collateral/ talobular) sequela
S93.492A Sprain of other ligament of left ankle, initial encounter
S93.492D Sprain of other ligament of left ankle subsequent encounter
S93.492S Sprain of other ligament of left ankle sequela
S93.499A Sprain of other ligament of unspecied ankle initial encounter
S93.499D Sprain of other ligament of unspecied ankle subs encounter
S93.499S Sprain of other ligament of unspecied ankle (Internal collateral/talobular) sequela
S96.211A Strain of intrinsic muscle and tendon at right ankle and foot level initial encounter
S96.211D Strain of intrinsic muscle and tendon at right ankle and foot level subsequent encounter
S96.211S Strain of intrinsic muscle and tendon at right ankle and foot level sequela
S96.212A Strain of intrinsic muscle and tendon at left ankle and foot level initial encounter
S96.212D Strain of intrinsic muscle and tendon at left ankle and foot level subsequent encounter
S96.212S Strain of intrinsic muscle and tendon at left ankle and foot level sequela
S96.219A Strain of intrinsic muscle and tendon at ankle and foot level, unspecied side initial encounter
S96.219D Strain of intrinsic muscle and tendon at ankle and foot level, unspecied side subs encounter
S96.219S Strain of intrinsic muscle and tendon at ankle and foot level, unspecied side
S96.811A Strain of other muscles and tendons at right ankle and foot level initial encounter
S96.811D Strain of other muscles and tendons at right ankle and foot level subsequent encounter
S96.811S Strain of other muscles and tendons at right ankle and foot level sequela
S96.812A Strain of other muscles and tendons at left ankle and foot level initial encounter
S96.812D Strain of other muscles and tendons at left ankle and foot level subsequent encounter
S96.812S Strain of other muscles and tendons at left ankle and foot level sequela
S96.819A Strain of other muscles and tendons at ankle and foot level, unspecied side initial encounter
S96.819D Strain of other muscles and tendons at ankle and foot level, unspecied side subs encounter
S96.819S Strain of other muscles and tendons at ankle and foot level, unspecied side sequela
S96.911A Strain of unspecied muscle and tendon at right ankle and foot level initial encounter
S96.911D Strain of unspecied muscle and tendon at right ankle and foot level subs encounter
S96.911S Strain of unspecied muscle and tendon at right ankle and foot level sequela
S96.912A Strain of unspecied muscle and tendon at left ankle and foot level initial encounter
S96.912D Strain of unspecied muscle and tendon at left ankle and foot level subs encounter
S96.912S Strain of unspecied muscle and tendon at left ankle and foot level sequela
S96.919A Strain of unspecied muscle and tendon at ankle and foot level, unspec. side initial encounter
S96.919D Strain of unspecied muscle and tendon at ankle and foot level, unspec. side subs encounter
S96.919S Strain of unspecied muscle and tendon at ankle and foot level, unspec. side sequela

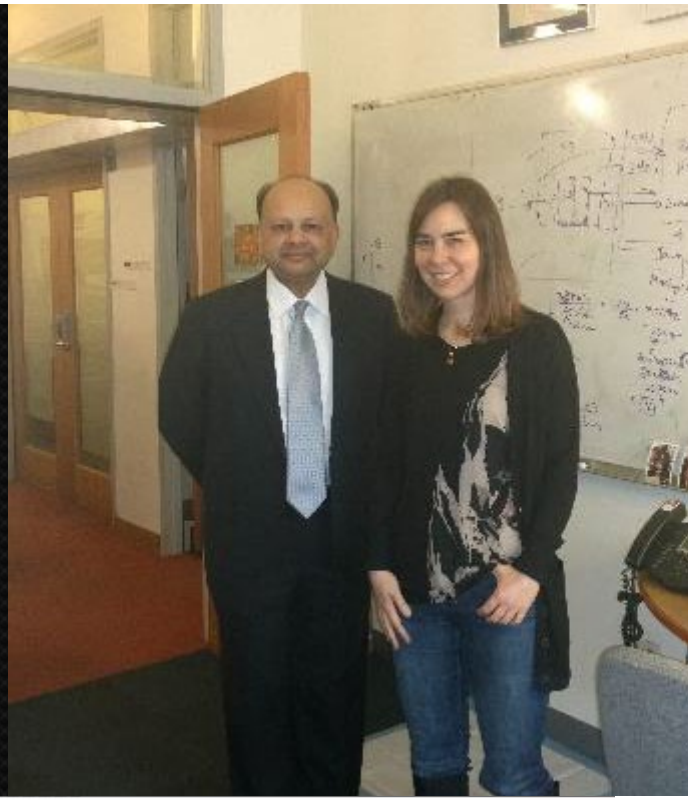
Lucrative business of hip and knee replacement ?

How To Prevent Falls …

2.5 million falls 2013
734,000 hospitalized
25,500 died from fall
$34 billion direct cost



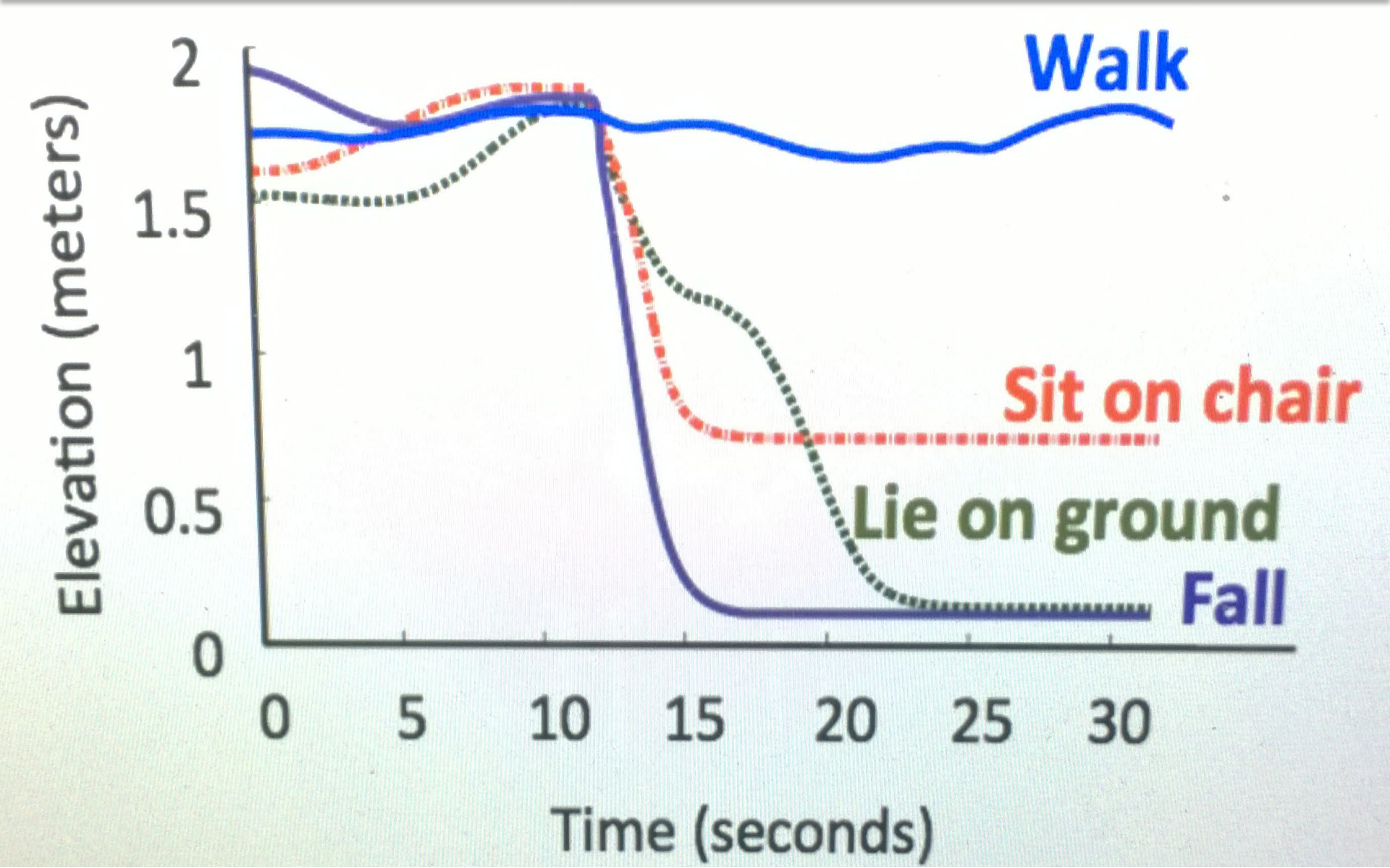
Professor Dina Katabi (MIT) presenting RF Reflection to President Obama (White House Demo, 4 August 2015)



President Obama invites MIT entrepreneurs to give demo at the White House http://bit.ly/President-Obama-with-Dina-Katabi

http://newsoffice.mit.edu/2015/president-obama-meets-mit-entrepreneurs-white-house-demo-day-0806

Fall Detection – Wire less, Sensor less, Without Wearables



RF Reflection Data - Professor Dina Katabi, Wireless Center, CSAIL, MIT ● IIC Member

https://mdpnp.mgh.harvard.edu/saams-cc/

Digital Health Frameworks

Must address security, data integration, diagnostic platforms and tools with health IT interoperability

The Agenda
INTERNET OF THINGS

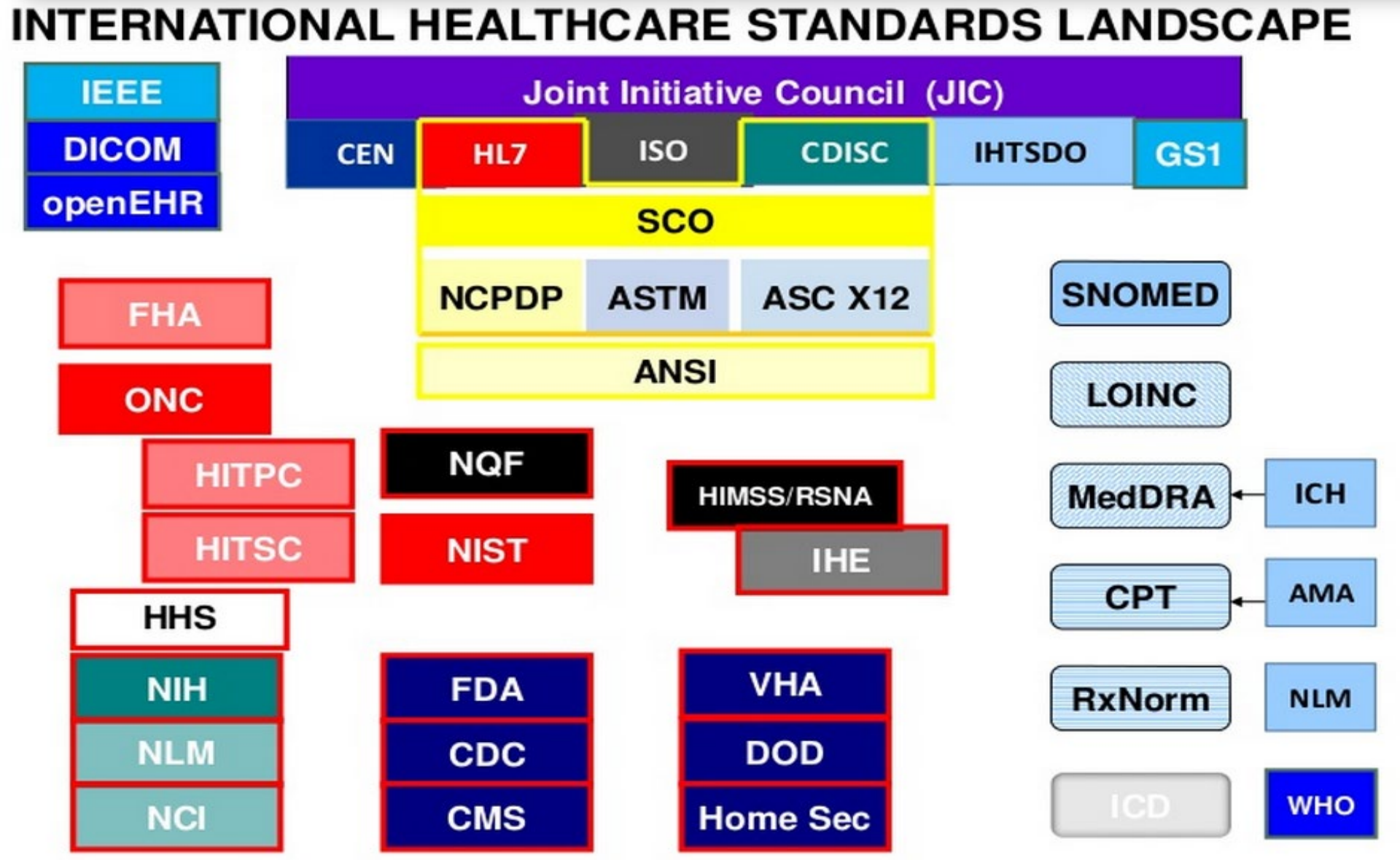
I helped invent the Internet of Things. Here's why I'm worried about how secure it is.

By SANJAY SARMA

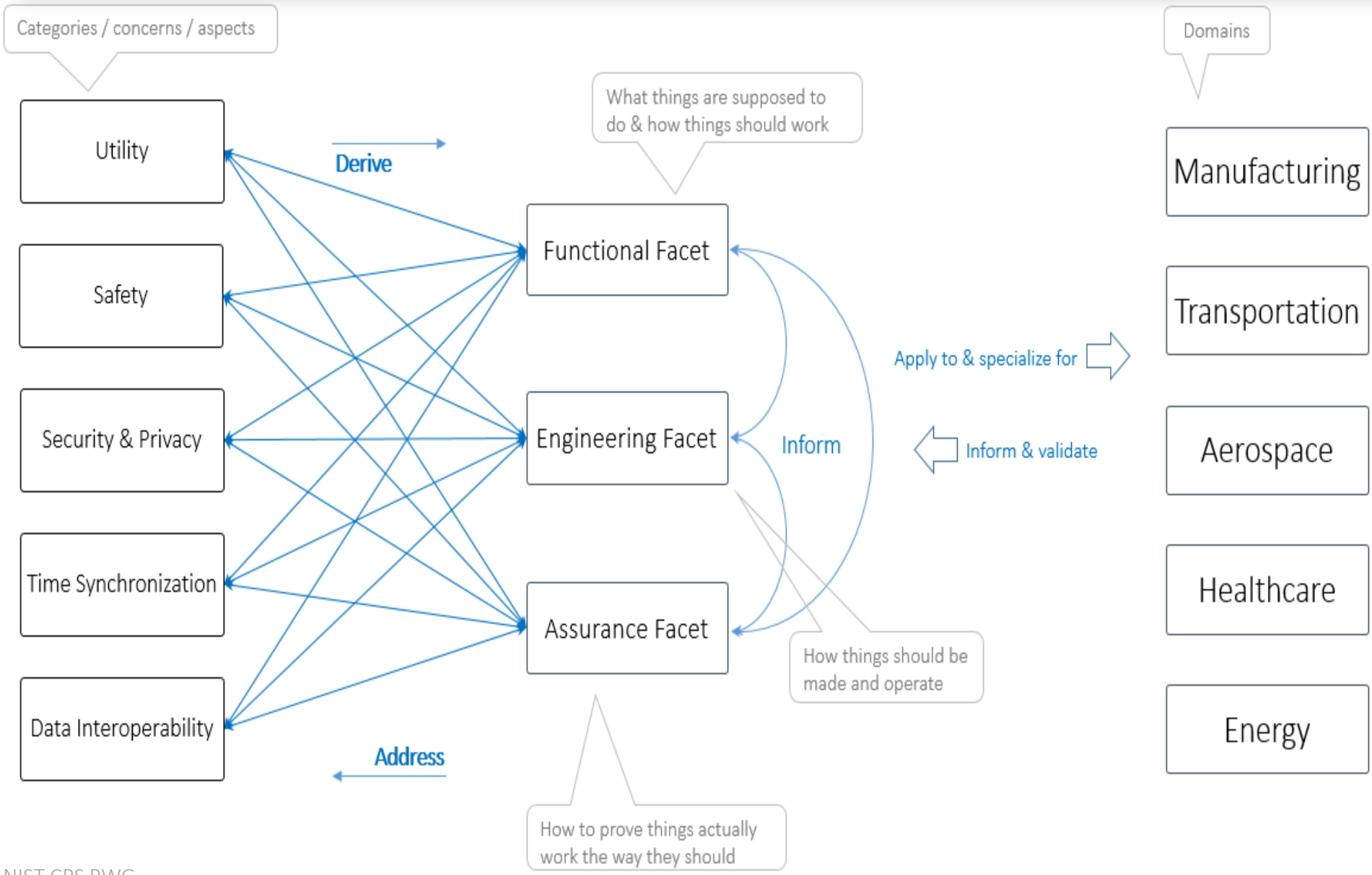
Peter Greenwood for POLITICO

I'm a mechanical engineering professor at MIT, and 17 years ago, with my colleagues David Brock, Kevin Ashton and Sunny Siu, I helped launch the research effort that laid some of the groundwork for the Internet of Things. As you might imagine, my life is pretty connected.

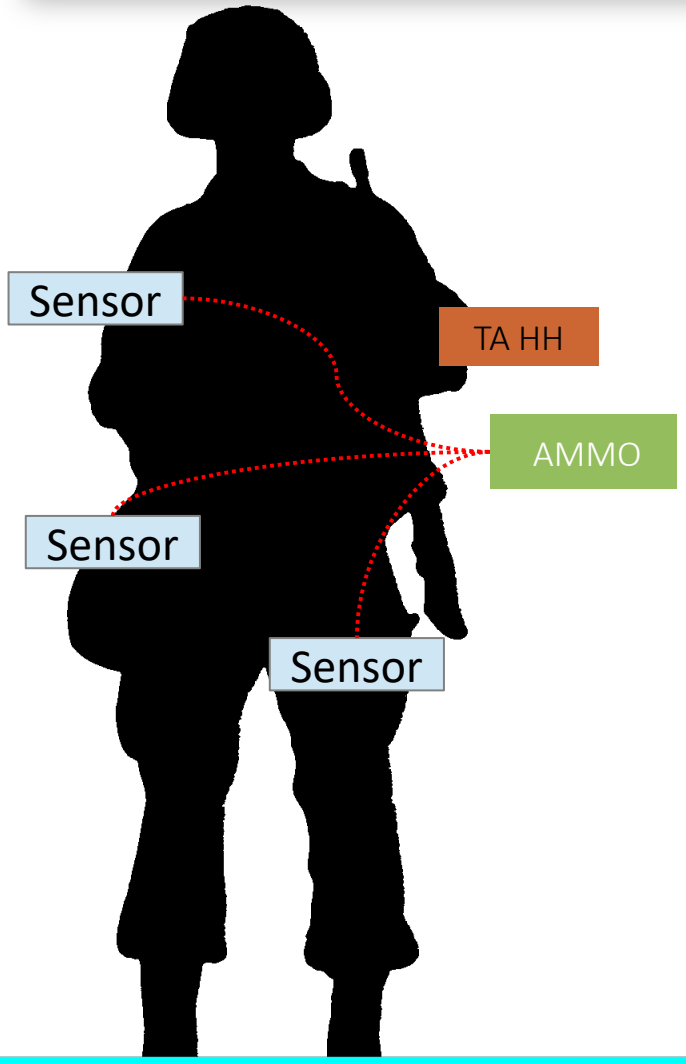
Barriers to Interoperability? Role of Ontology and Semantics in the Healthcare Standards Landscape



Apply Analytical Rigor of CPS to Health IT



BAN – Body Area Networks



- Bluetooth-enabled sensors / devices
- AMMO receives/uploads sensor data

- glucose
- heart rate
- pulse oximeter
- body temperature
- pedometer

- Soldier in desert (high temperature)
- Monitor health via sensor data / analytics
- Intervene before it is necessary / prevent A&E

POTENTIAL AMMO APPLICATIONS

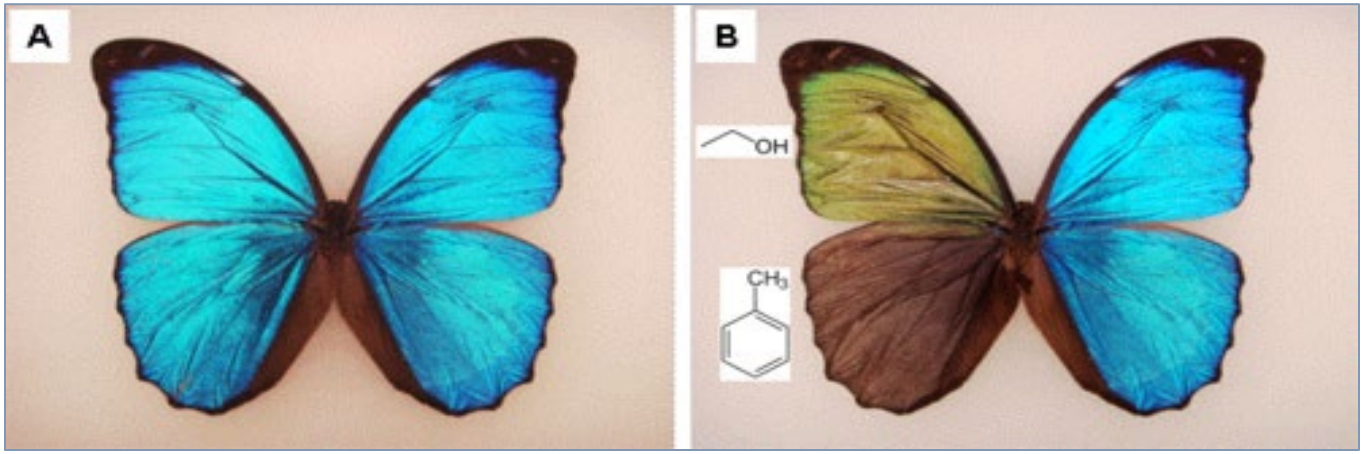
- Pre- and Post- surgery interactive care plan execution and monitoring
- Improved home-health & patient communication with social partners
- Remediate loss of HIV patients identified for anti-retro viral treatment
- Ebola Infection - patient, population and physician data / monitoring
- Adhoc mesh / zero configuration networking for search & rescue (A&E)
- Google Project Ara - integrated/on-platform tactical radio and SDR
- Novel nano-sensors with embedded sub-cutaneous radio/transmitters

Sandeep Neema

Android Mobile Middleware Objects

Internet of Preventive Medicine Era ● Wearable Diagnostic Devices
High Performance Ultra-Sensitive Nano-Sensors

Swiss engineer George de Mestro invented Velcro after his dog came home covered with thistle burrs, Speedo learned from sharkskin to make faster swimsuits, and chemical companies designed self-cleaning paint after studying lotus leaves.



These butterflies *(Morpho* wings) change their color when they come into contact with heat, gases and chemicals. The normal iridescent blue color of butterfly wings (A) changes when exposed to ethanol (panel B top) or toluene (panel B bottom). Acetone present in the breath of diabetic or pre-diabetic people can change the color of *Morpho* wings from brilliant blue to brilliant green (panel B top). Using nano-sensors, built on this principle of biomimicry, may help billions of people who are diabetic or pre-diabetic to better manage their health, diet and life.

New test can predict cancer up to 13 years before disease develops

http://genesdev.cshlp.org/content/19/18/2100.full.pdf+html

People who develop cancer have shorter telomeres, the caps at the end of chromosomes which protect the DNA

Target Specific Analytes in Detection, Monitoring & Treatment

Over the past 25 years of healthcare

- Good News

Great ideas, tools and "doing it" by powerpoint are in no short supply.

Calls for collaboration, standards, codes and platforms are echoing from almost everywhere.

- Bad News

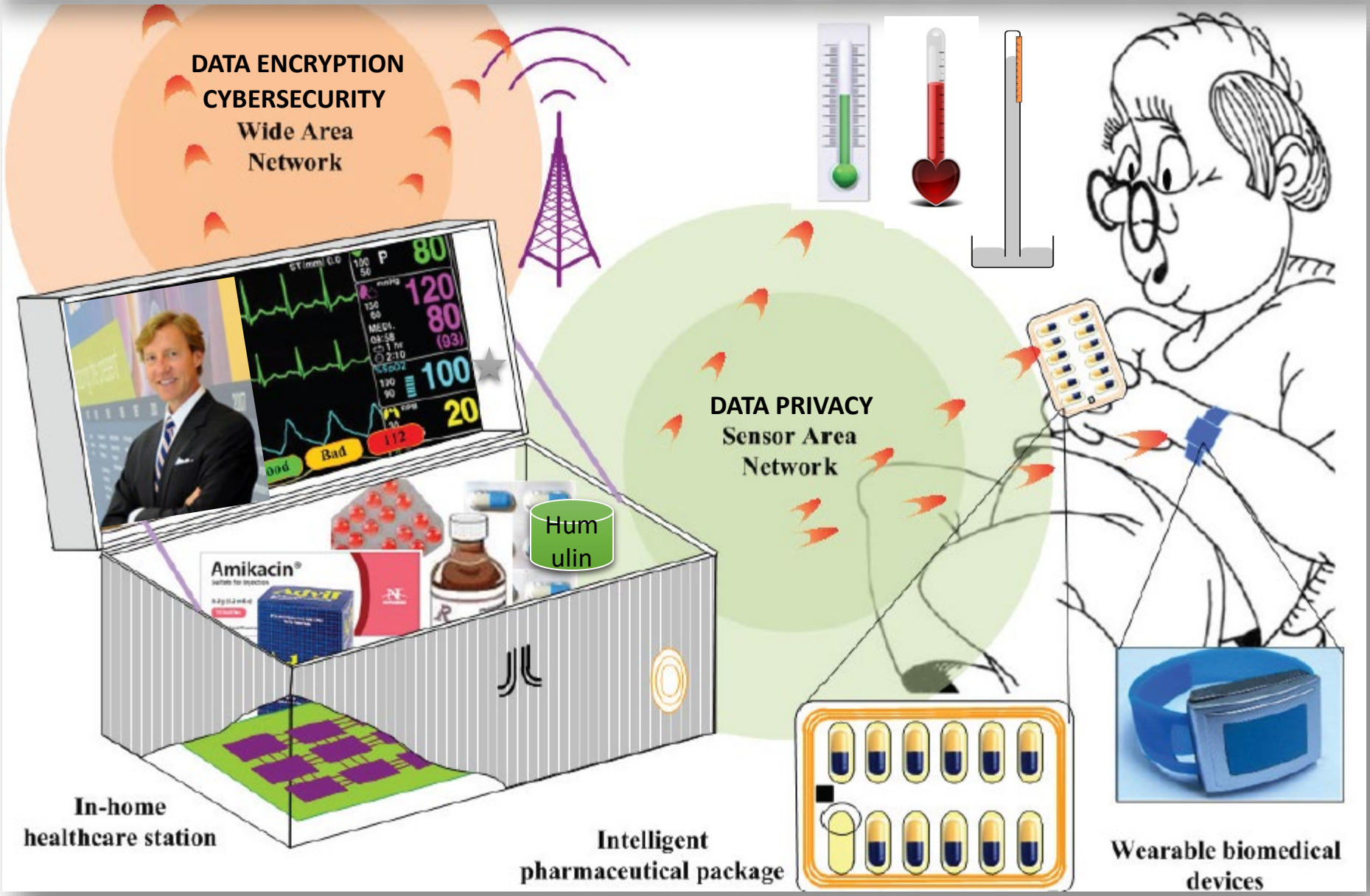
We haven't done even the basic diagnostics, e.g. blood glucose, for those who are non-affluent

We may not be "ready" if we wait for secure systems, standards and committee approved operating rules.

2 Great Grand Challenges

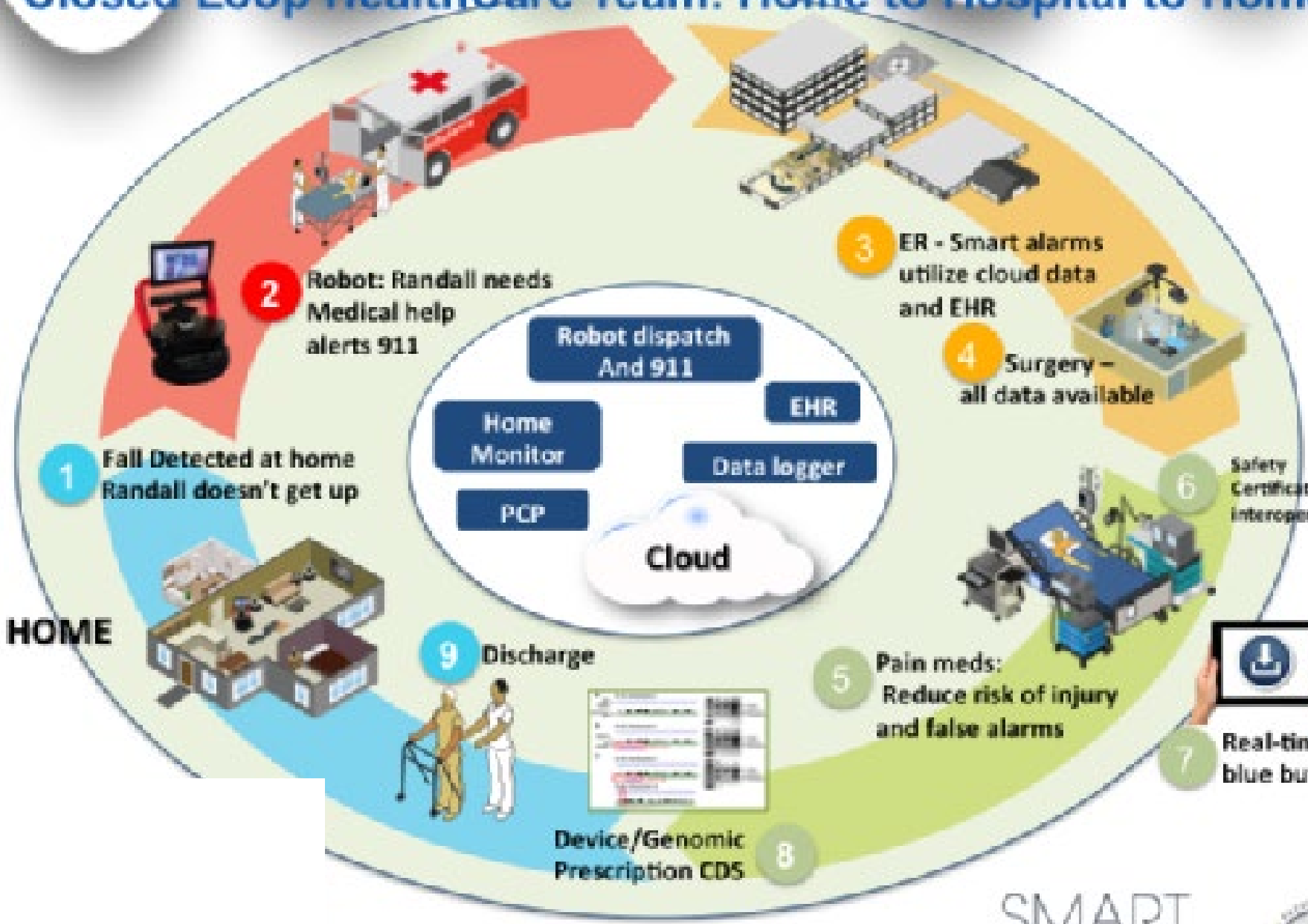
by CARTOON

Harry at home with hypercholesterolemia - Larry - Do I need Lipitor today?



Dr Jameson: Thanks for avoiding KFC. Your LDL-VLDL ratio looks good. No Lipitor today.

Closed Loop HealthCare Team: Home to Hospital to Home



Dr Julian Goldman MD
MDPnP – MGH – HMS

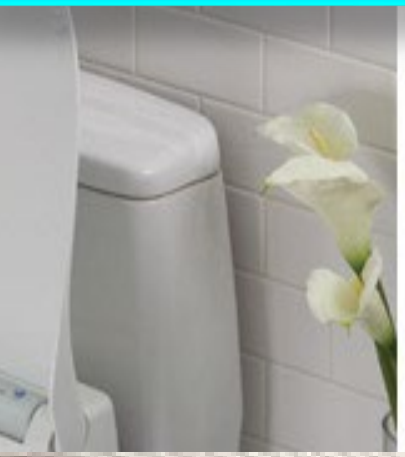
SMART AMERICA

5 Smaller (?) Challenges

sequential implementation

requires (strong) leadership

Pay-Per-Pee Home Health IoT Wireless Toilet Bowl Connected to Health IT



Weigh-scale, BMI, FOBT, urine analysis, sugar, ketone body analysis, blood pressure monitor, pulse oximeter, networked to phone via WiFi and/or Bluetooth with biometrics and face recognition for secure communication with physician and hospital or clinic, globally.

Walgreens Specials - $1.99 for 24-pack Diet Coke • $1.99 for Bone Density • $1.99 Mammogram

PDEXA SCAN
BONE MINERAL
DENSITY PROFILE

Value Network Ecosystem Testbed

Walgreens – Retail Healthcare
GE – Equipment
Cisco – IPv6 Routers
AT&T – Data Transmission
Intel – MIPS
IBM – Data Analytics
Samsung – Diagnostic Apps
Walmart – Grocery Supply Chain

CVS Special $0.99 for 1-quart Milk • $1.99 for Bone Density • $2.99 Mammogram

PDEXA SCAN
BONE MINERAL
DENSITY PROFILE

PDEXA SCAN
in every drug
store, petrol
pump, grocery

Osteoporosis

EU → 28 million in 2010 to 34 million in 2025 (increase of 23%)

US → 44 million (represents 55% of people aged 50+)

Brazil → 10 million (1 in every 17)

India → 36 million (2013)

China → 70 million (50+). Cost of treatment USD1.5 billion in 2006.
Estimated US$12.5 billion in 2020 and US$265 billion in 2050.

In 2008, Indonesia had 34 DXA machines, half of them in Jakarta (population 237 million) which translates to 0.001 machine per 10,000 population. The equivalent recommended number for Europe is 0.11 (per 10,000)

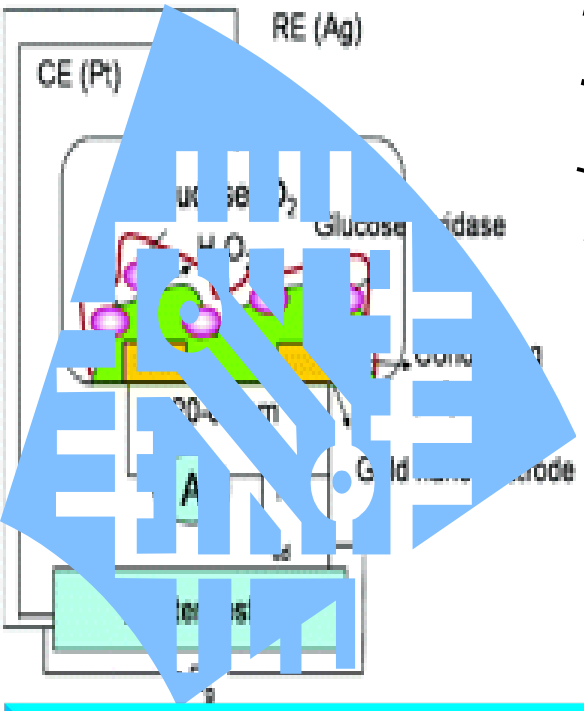
http://bit.ly/BONE-HEALTH

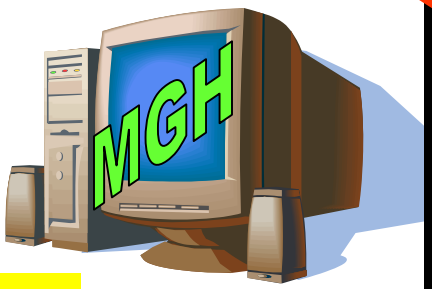
CONNECT

Health data

GROCERY STORE
PURCHASE LOG

Integrated system detects fall in bone density and correlates with reduced purchase of milk. Prevention for osteoporosis starts early. Avoids trauma and/or morbidity from broken bones. Connected healthcare data.





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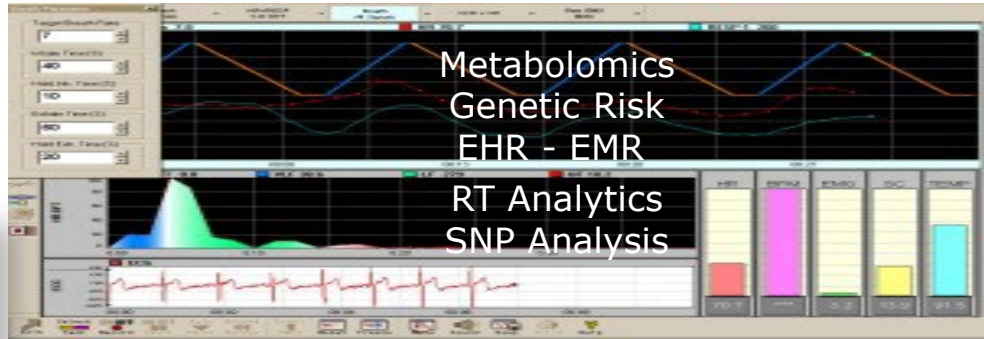


Improved healthcare services, savings, create jobs from new products, new services and potential to create as well as capture new emerging markets of billions (BRICS)

Pay 1c Per Analytics Apps, Data Distribution Service

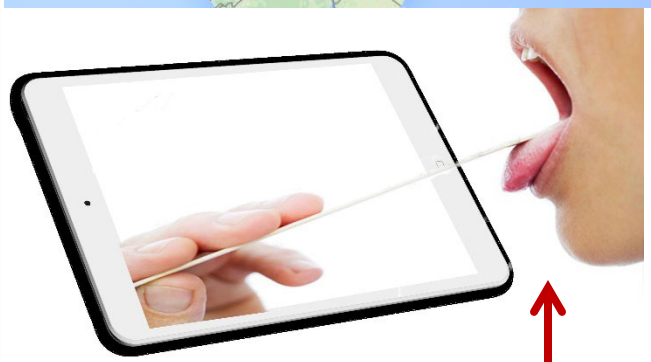
Glucose Sensor

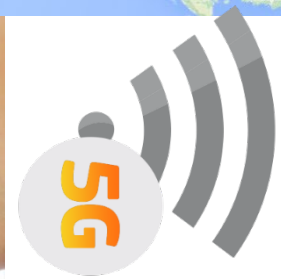
Cholesterol Sensor

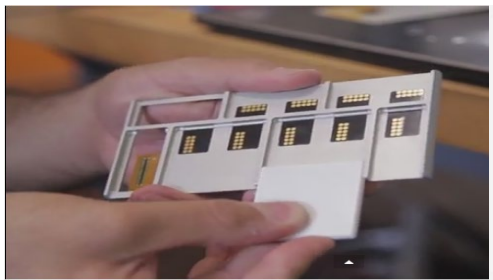
BNP Sensor

SARS-CoV-2 Sensor

What does the data suggest about my health?







Hot swappable, modular, smart

NK Labs
ARA Prototype

PAY A PENNY PER USE (PAPPU) – CENTRAL CONCEPT FOR SOCIAL BUSINESS PROFITABILITY

LET US PROFIT, GENTLY

PAPPU

The idea is to lower the barrier to market entry for products and services by eliminating initial capital cost (for example, you get a free phone if you pay a small charge per call). The concept of PAPPU suggests charging a very small fee (penny?) each time the customer uses the product and/or the service.

https://www.mdpi.com/2075-4418/10/1/22

PAPPU

Open Access Review

Peer-Review Record

Sensor-as-a-Service: Convergence of Sensor Analytic Point Solutions (SNAPS) and Pay-A-Penny-Per-Use (PAPPU) Paradigm as a Catalyst for Democratization of Healthcare in Underserved Communities

Diagnostics **2020**, *10*(1), 22; **https://doi.org/10.3390/diagnostics10010022**

by **Victoria Morgan** [1], **Lisseth Casso-Hartmann** [2,3], **David Bahamon-Pinzon** [4], **Kelli McCourt** [4], **Robert G. Hjort** [5], **Sahar Bahramzadeh** [6], **Irene Velez-Torres** [2,3], **Eric McLamore** [1], **Carmen Gomes** [5], **Evangelyn C. Alocilja** [7,8], **Nirajan Bhusal** [7,9,10], **Sunaina Shrestha** [10], **Nisha Pote** [10], **Ruben Kenny Briceno** [11,12,13,7], **Shoumen Palit Austin Datta** [1,14,15,16] and **Diana C. Vanegas** [3,4,*]

Reviewer 1: Anonymous

Reviewer 2: Anonymous

Diagnostics **2020**, *10*(1), 22; **https://doi.org/10.3390/diagnostics10010022**

Received: 18 December 2019 / Revised: 29 December 2019 / Accepted: 30 December 2019 / Published: 1 January 2020
(This article belongs to the Special Issue **Biosensors-Based Diagnostics**)

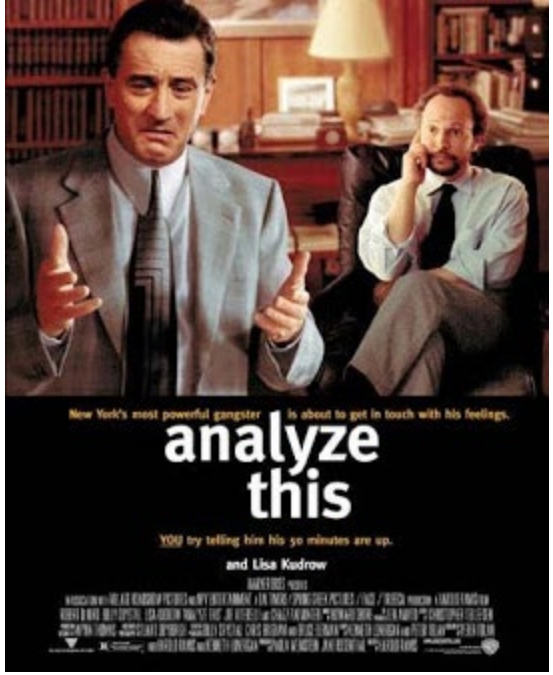
Round 1

Reviewer 1 Report

The manuscript is clearly written, well structured, I recommend this paper for publication in Diagnostics.

Another one bites the dust

Good intentions, 10 years later … here is one grand gesture …



UCSF

Samsung, UCSF Partner to Accelerate New Innovations in Preventive Health Technology

Pair Will Work to Validate Promising New Sensors and Analytics for Next-Generation Digital Health Solutions

By Kristen Bole on February 21, 2014 | Email | Print

The unbearable emptiness of action in healthcare ?

20 years later, bright ideas still hiding underneath a bushel ?

Healthcare Data Integration and Interoperability Platform is a Quintessential Global Infrastructure

Infrastructural technologies, in contrast, offer far more value when shared than when used in isolation. Imagine yourself in the early nineteenth century, and suppose that one manufacturing company held the rights to all the technology required to create a railroad. If it wanted to, that company could just build proprietary lines between its suppliers, its factories, and its distributors and run its own locomotives and railcars on the tracks. And it might well operate more efficiently as a result. But, for the broader economy, the value produced by such an arrangement would be trivial compared with the value that would be produced by building an open rail network connecting many companies and many buyers. The characteristics and economics of infrastructural technologies, whether railroads or telegraph lines or power generators, make it inevitable that they will be broadly shared—that they will become part of the general business infrastructure.

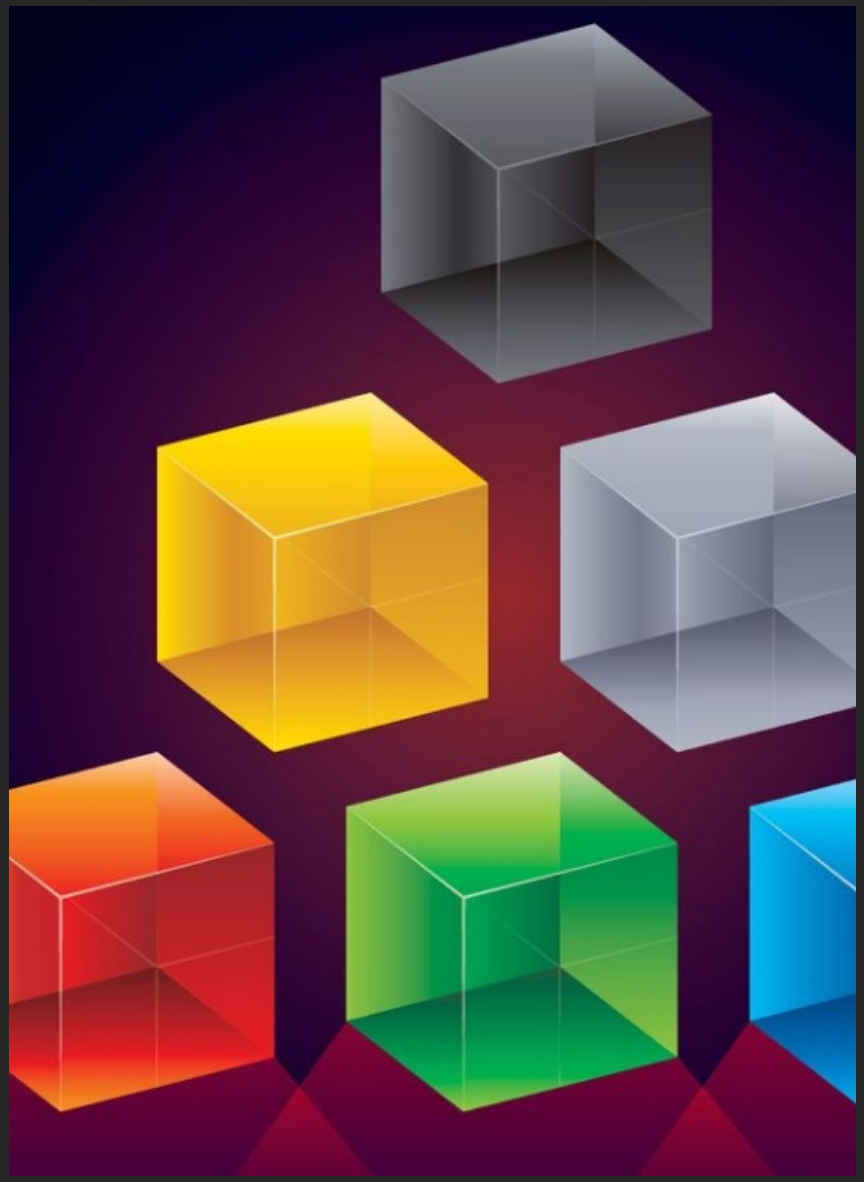
Nicholas Carr, Harvard Business Review, 2003 ● https://hbr.org/2003/05/it-doesnt-matter

Healthcare Platforms?

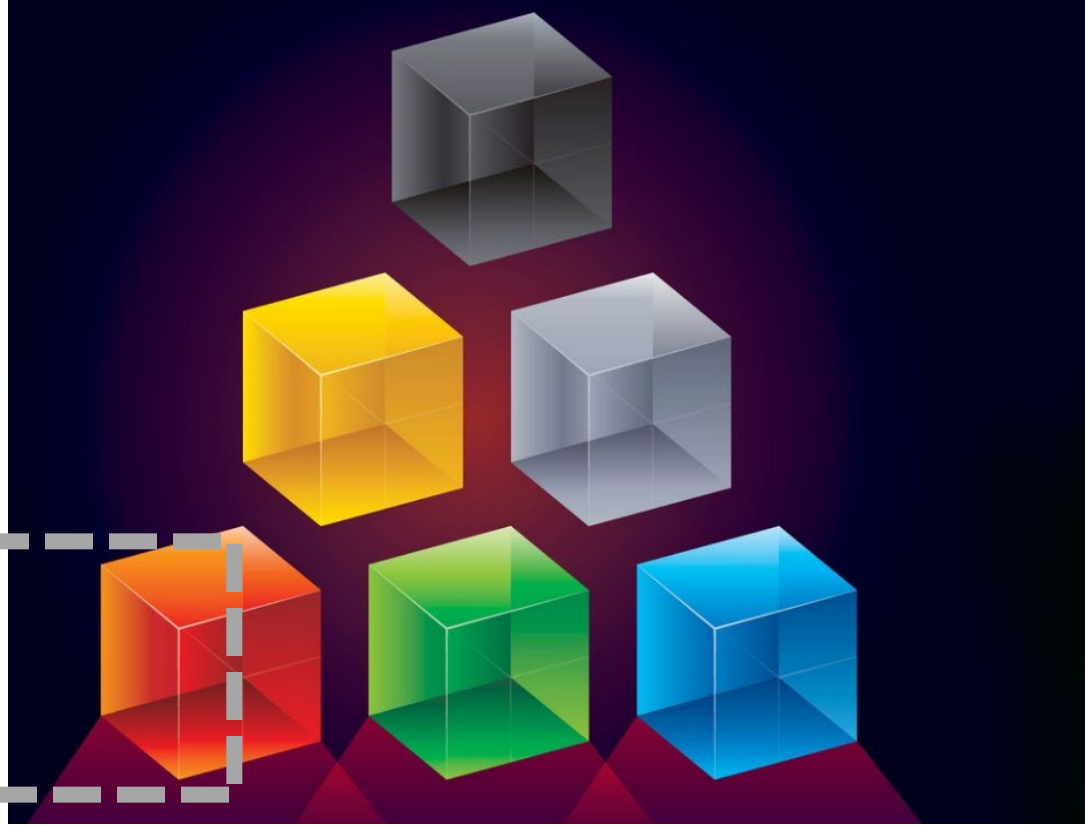
Perhaps not yet ready, for the next billion users

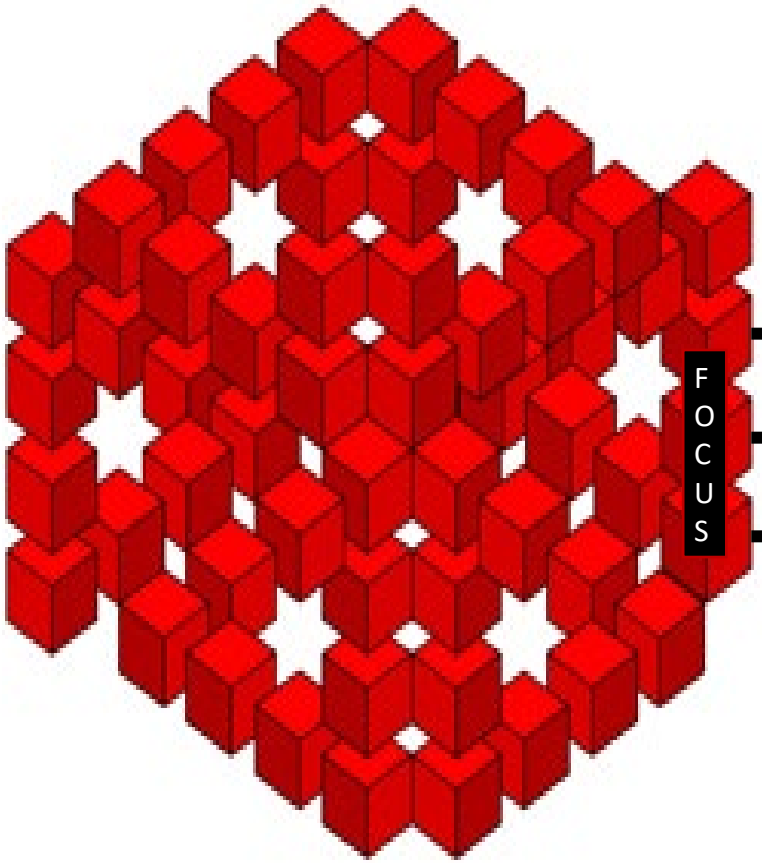
Let us focus on healthcare diagnostics, just a few solutions, for a few billion end users!

The “hare” approach to healthcare platforms are a grand vision which we should pursue.



Building system ‘blocks’ that can serve people sooner, rather than later, is the tortoise treatment.





Let us focus on healthcare diagnostics, just

a few solutions, for a few billion end users!

Please refer to "The Health of Nations" – Part I –

MIT Library

https://dspace.mit.edu/handle/1721.1/145774

WHY VACCINATION / IMMUNIZATION IS SO CRITICAL

VACCINATION AND IMMUNIZATION NOT ONLY REDUCES THE RISK FROM IMMEDIATE INFECTION AND TRANSMISSIBILITY OF THE INFECTION BUT ALSO REDUCES THE LONG TERM RISK OF OTHER (EVEN MORE SERIOUS) AFFLICTIONS WITH FAR GREATER SCOPE FOR MORBIDITY.

INFECTIOUS AGENTS, ESPECIALLY VIRUSES, INTERACTS WITH THE GENETIC MATERIAL OF CELLS, DIRECTLY OR INDIRECTLY. VIRUSES ARE KNOWN TO INFLICT CELLULAR DAMAGES. THE CUMULATIVE DETRIMENTAL EFFECT OF SUCH DAMAGES ARE UNCERTAIN. IT MAY MANIFEST IN THE FUTURE AS A DYSFUNCTION OR TRIGGER DORMANT CONDITIONS WHICH MAY BE UNTREATABLE AND AFFECT THE QUALITY OF LIFE.

MONKEY POX

nejm.org/doi/full/10.1056/NEJMicm2307920

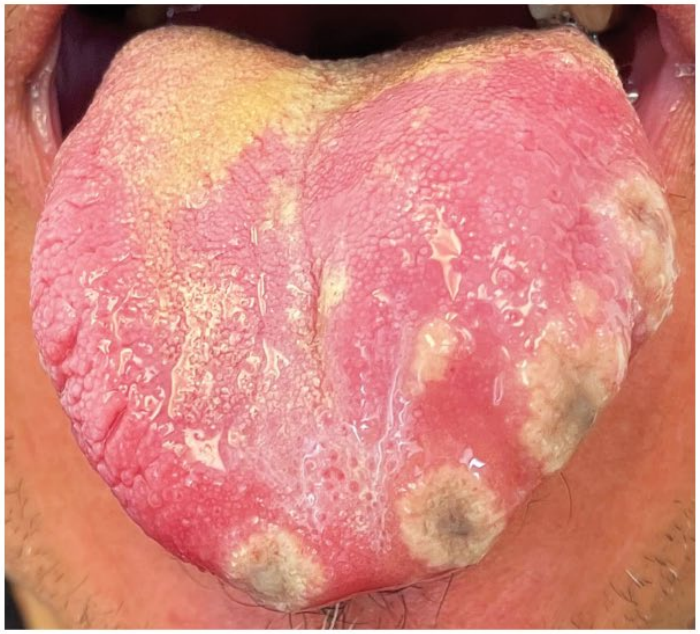
The NEW ENGLAND JOURNAL of MEDICINE

IMAGES IN CLINICAL MEDICINE

Mpox Tongue Lesions

David Dickson, M.D., Ph.D., and Angela Lai, M.D.

February 29, 2024
N Engl J Med 2024; 390:842
DOI: 10.1056/NEJMicm2307920
Metrics



A 49-year-old man with human immunodeficiency virus (HIV) infection presented to a primary care clinic with an 11-day history of painful tongue lesions and a 1-week history of sore throat and fevers. He had last been sexually active with his male partner 9 days before the onset of symptoms; his partner was asymptomatic. Five months before presentation, the patient's CD4 cell count had been 519 per microliter (reference range, 297 to 1551), and 1 month before presentation, the HIV viral load had been undetectable.

New England Journal of Medicine 2024; 390:842 DOI: 10.1056/NEJMicm2307920

February 29, 2024 ● https://www.nejm.org/doi/full/10.1056/NEJMicm2307920

A 49-year-old man with human immunodeficiency virus (HIV) infection presented to a primary care clinic with an 11-day history of painful tongue lesions and a 1-week history of sore throat and fevers. He had last been sexually active with his male partner 9 days before the onset of symptoms; his partner was asymptomatic. Five months before presentation, the patient's CD4 cell count had been 519 per microliter (reference range, 297 to 1551), and 1 month before presentation, the HIV viral load had been undetectable. On physical examination, four ulcers with central darkening and raised borders were seen on the tip and left lateral aspect of the tongue. Tender submandibular lymphadenopathy was also present on the left side. No other lesions were seen in the mouth or throat or on the skin. Testing of a tongue lesion with a polymerase-chain-reaction assay for the virus that causes mpox (formerly known as monkeypox) was positive. A diagnosis of mpox was made. During the eruptive phase of mpox, a rash is very common, but isolated oral mucosal lesions may be the only mucocutaneous manifestation — as occurred in this case. The patient was lost to follow-up with primary care after the diagnosis was made, so no antiviral treatment was given. During a telephone appointment with a different clinic 2 weeks later, he reported feeling in his usual health.

David Dickson, M.D., Ph.D.
University of California, Los Angeles,
ddickson@mednet.ucla.edu
Angela Lai, M.D.
VA Sepulveda Ambulatory Care Center and Nursing Home, North Hills, CA

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE BRIEF REPORT

Neurovascular Complications of Iatrogenic *Fusarium solani* Meningitis

Nora Strong, M.D., Grant Meeks, M.D., Sunil A. Sheth, M.D., Louise McCullough, M.D., Ph.D., Julian A. Villalba, M.D., Chunfeng Tan, M.D., Ph.D., Andrew Barreto, M.D., Audrey Wanger, Ph.D., Michelle McDonald, D.O., Peter Kan, M.D., M.P.H., Hashem Shaltoni, M.D., Jose Campo Maldonado, M.D., et al.

February 8, 2024
N Engl J Med 2024; 390:522-529
DOI: 10.1056/NEJMoa2308192

9 References

Summary

A multinational outbreak of nosocomial fusarium meningitis occurred among immunocompetent patients who had undergone surgery with epidural anesthesia in Mexico. The pathogen involved had a high predilection for the brain stem and vertebrobasilar arterial system and was associated with high mortality from vessel injury. Effective treatment options remain limited; in vitro susceptibility testing of the organism suggested that it is resistant to all currently approved antifungal medications in the United States. To highlight the severe complications associated with fusarium infection acquired in this manner, we report data, clinical courses, and outcomes from 13 patients in the outbreak who presented with symptoms after a median delay of 39 days.

There is little doubt that infection due to external agents, e.g., viruses, can trigger completely different types of diseases.

SCIENCE

13 January 2022

Vol 375, Issue 6578

pp. 296-301

DOI: 10.1126/science.abj8222

REPORT www.science.org/doi/epdf/10.1126/science.abj8222

MULTIPLE SCLEROSIS

Longitudinal analysis reveals high prevalence of Epstein-Barr virus associated with multiple sclerosis

Kjetil Bjornevik[1]†, Marianna Cortese[1]†, Brian C. Healy[2,3,4], Jens Kuhle[5], Michael J. Mina[6,7,8], Yumei Leng[6], Stephen J. Elledge[6], David W. Niebuhr[9], Ann I. Scher[9], Kassandra L. Munger[1]‡, Alberto Ascherio[1,10,11]*‡

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system of unknown etiology. We tested the hypothesis that MS is caused by Epstein-Barr virus (EBV) in a cohort comprising more than 10 million young adults on active duty in the US military, 955 of whom were diagnosed with MS during their period of service. Risk of MS increased 32-fold after infection with EBV but was not increased after infection with other viruses, including the similarly transmitted cytomegalovirus. Serum levels of neurofilament light chain, a biomarker of neuroaxonal degeneration, increased only after EBV seroconversion. These findings cannot be explained by any known risk factor for MS and suggest EBV as the leading cause of MS.

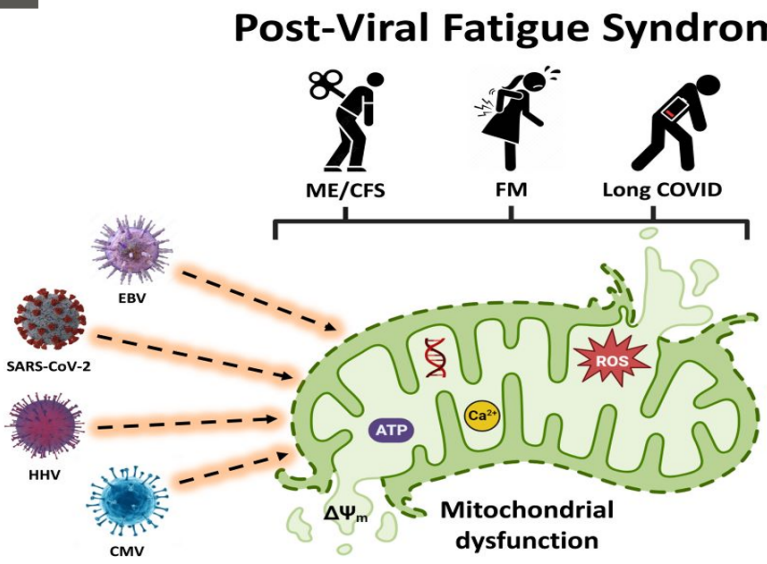
Expanded T lymphocytes in the cerebrospinal fluid of multiple sclerosis patients are specific for Epstein-Barr-virus-infected B cells

Assaf Gottlieb, H. Phuong T. Pham, Jerome G. Saltarrelli, and J. William Lindsey Authors Info & Affiliations

Edited by Lawrence Steinman, Stanford University, Stanford, CA; received September 12, 2023; accepted November 27, 2023

January 8, 2024 | 121 (3) e2315857121 | https://doi.org/10.1073/pnas.2315857121

https://doi.org/10.1073/pnas.2315857121



Article

https://doi.org/10.1038/s41467-023-44432-3

Muscle abnormalities worsen after post-exertional malaise in long COVID

Received: 21 March 2023

Accepted: 13 December 2023

Published online: 04 January 2024

Check for updates

Brent Appelman[1,2,15], Braeden T. Charlton[3,4,15], Richie P. Goulding[3,4], Tom J. Kerkhoff[3,4,5,6], Ellen A. Breedveld[3,4], Wendy Noort[3,4], Carla Offringa[3,4], Frank W. Bloemers[4,7], Michel van Weeghel[8], Bauke V. Schomakers[8], Pedro Coelho[9,10,11], Jelle J. Posthuma[7,12], Eleonora Aronica[11], W. Joost Wiersinga[1,2,13], Michèle van Vugt[2,14,15] & Rob C. I. Wüst[3,4,15]

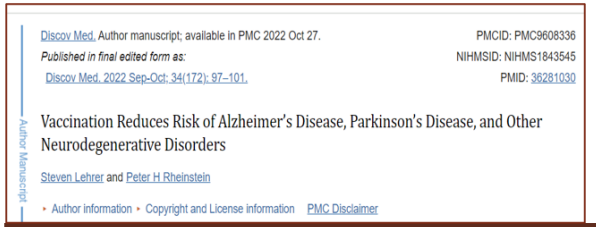
www.cell.com/action/showPdf?pii=S0896-6273%2822%2901147-3

Table 1 | Viral infections linked to neurodegenerative diseases

Disease	Infection
Alzheimer disease	Influenza and pneumonia
	Intestinal infections
	Meningitis
	Viral encephalitis
Amyotrophic lateral sclerosis	Human papilloma virus
Generalized dementia	Influenza and pneumonia
	Viral encephalitis
Multiple sclerosis	Epstein–Barr virus
	Herpes simplex virus
	Varicella zoster virus
Parkinson disease	Hepatitis C virus
	Influenza and pneumonia
Vascular dementia	Influenza and pneumonia
	Varicella zoster virus

Levine KS, Leonard HL, Blauwendraat C, Iwaki H, Johnson N, Bandres-Ciga S, Ferrucci L, Faghri F, Singleton AB, Nalls MA. Virus exposure & neurodegenerative disease risk across national biobanks. Neuron. 2023 Apr 5;111(7):1086-1093.e2. doi: 10.1016/j.neuron.2022.12.029. Epub 2023 January 19. PMID: 36669485

Data from national biobanks offer evidence that exposure to common viral pathogens increases the risk of Alzheimer's disease and other diseases (neurodegenerative diseases).



Discov Med. Author manuscript; available in PMC 2022 Oct 27.

PMCID: PMC9608336

Published in final edited form as:

NIHMSID: NIHMS1843545

Discov Med. 2022 Sep-Oct; 34(172): 97–101.

PMID: 36281030

Vaccination Reduces Risk of Alzheimer's Disease, Parkinson's Disease, and Other Neurodegenerative Disorders

Steven Lehrer and Peter H Rheinstein

Author information • Copyright and License information PMC Disclaimer

Author Manuscript

www.ncbi.nlm.nih.gov/pmc/articles/PMC9608336/pdf/nihms-1843545.pdf

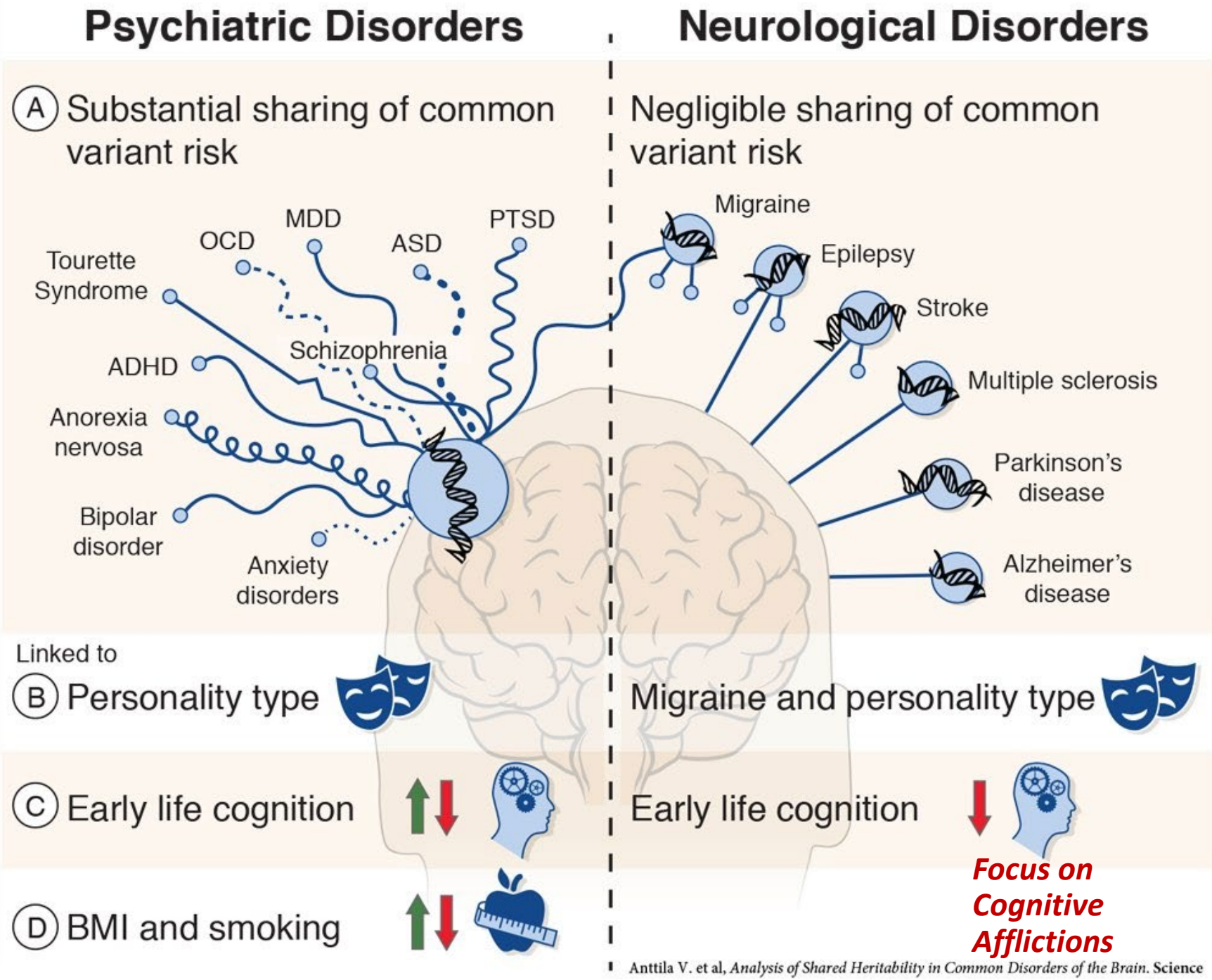
Neurodegenerative Diseases

Lack of cures in advanced stages makes it even more imperative that we find tools to **DETECT EARLY** and try to (at least) slow down the progression rather than the knee-jerk reaction to cry out for stem cell therapy.

Focus on Cognitive Afflictions

- Alzheimer's disease (ALZ)
- Attention deficit disorder (ADD)
- Dementia with Lewy bodies disease
- Early onset dementia
- Epilepsy-related cognitive dysfunction
- Fronto-temporal dementia
- Normal pressure hydrocephalus
- Parkinson related cognitive dysfunction
- Posterior cortical atrophy
- Primary progressive aphasia
- Stroke-related cognitive dysfunction
- Traumatic brain injury
- Other cognitive impairments (e.g., MS)
- Chemotherapy-related cognitive decline

Beware of the distinction between



WHY ?

Focus on Cognitive Afflictions

- Cognitive disorders often present early symptoms of motor neuron dysfunction (tremors, spasms) and minor speech defects (slurring, increase in recall time, occasional loss of short-term memory).

- Time series data (cumulative data) from individuals may reveal some of these changes and may even indicate ***rate*** of change (using analytical data tools).

- Clues to motion or speech changes can be detected (and data can be ***stored***) using common mobile devices (phones).

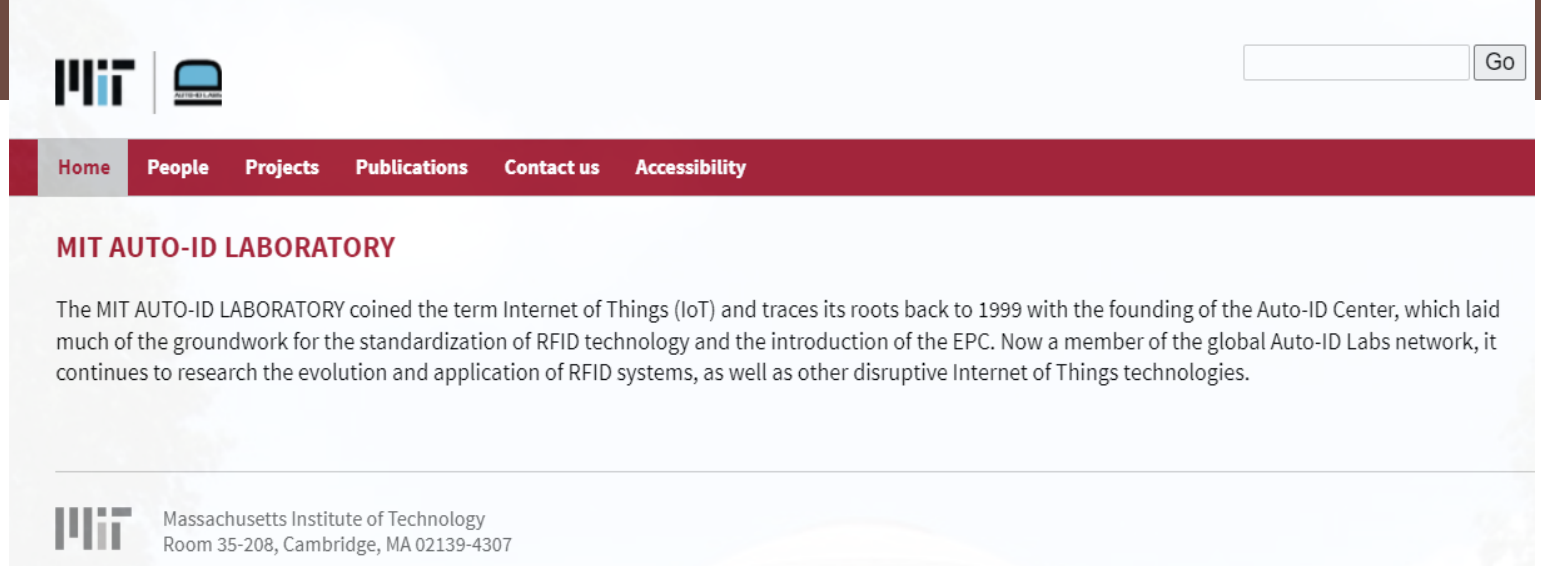
WHY ?

Focus on Cognitive Afflictions

- We have available mobile phone apps capable of running real-time analysis of hand “shake” functions while handling devices (movement sensors in phones).
- Data analysis of voice calls may reveal signals indicating speech impairment.
- Time series data (cumulative data) from individuals (with consent) can create “base line” functions. When compared, over time, we extract signals (e.g. PD related prodromal stage) indicative of potential future risk of morbidity.

We have known about these tools for 50 years

We have these detection tools operational (in some form) for more than a quarter century (> 25 years)



An Emerging Era in the Management of Parkinson's Disease: Wearable Technologies and the Internet of Things

Cristian F. Pasluosta, *Member, IEEE*, Heiko Gassner, Juergen Winkler, Jochen Klucken, and Bjoern M. Eskofier, *Member, IEEE*

Pasluosta CF, Gassner H, Winkler J, Klucken J, Eskofier BM. (2015) An Emerging Era in the Management of Parkinson's Disease: Wearable Technologies and the Internet of Things. IEEE J Biomed Health Inform. 2015 Nov; 19(6):1873-81. doi: 10.1109/JBHI.2015.2461555.

Solutions by PowerPoint are “at hand” for more than 20 years

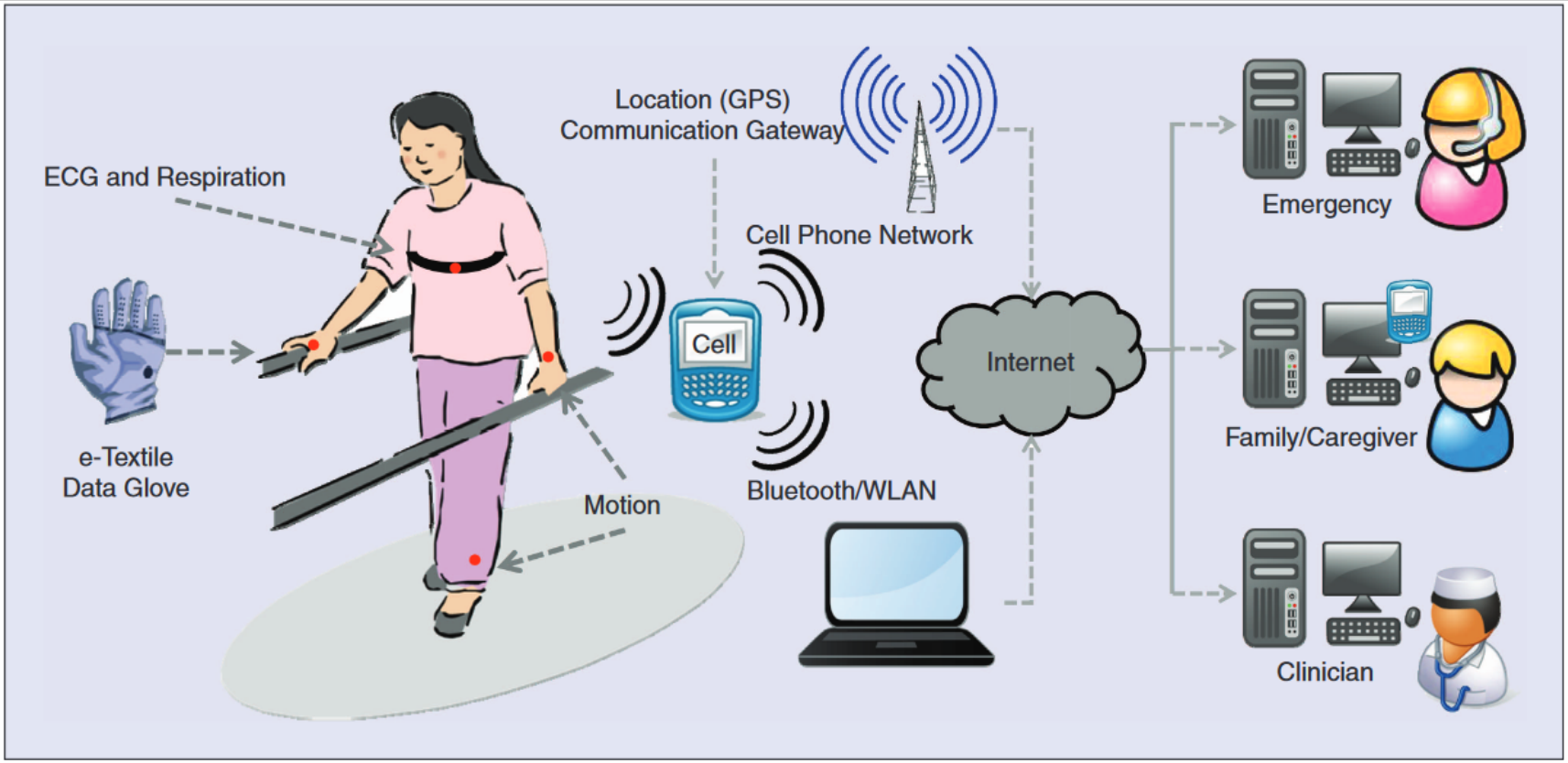


Fig. 1. Schematic representation of a system for patients' monitoring in the home and community settings. A subject is shown while exercising at the gym (e.g., undergoing balance therapy). Exercise compliance, exercise performance, and the associated physiological responses (i.e., heart rate and respiratory rate) are monitored via wearable sensors. A cell phone serves as a data logger and gateway for communication with a remote location via a cell phone network and/or the Internet.

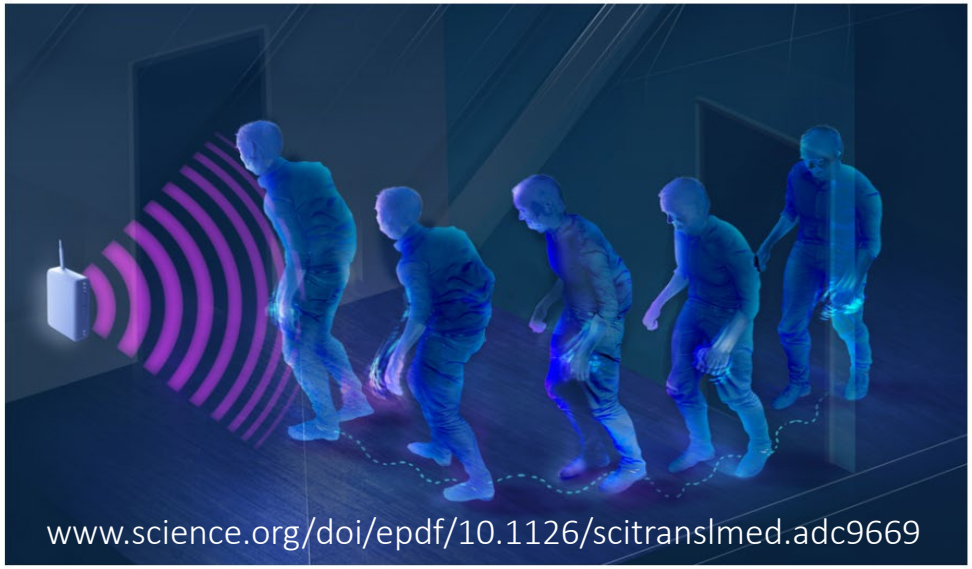
Paolo Bonato (2010) "Wearable Sensors and Systems," in *IEEE Engineering in Medicine and Biology Magazine*, vol. 29, no. 3, pp. 25-36, May-June 2010, doi: 10.1109/MEMB.2010.936554.

In-home wireless device tracks disease progression in Parkinson's patients

By continuously monitoring a patient's gait speed, the system can assess the condition's severity between visits to the doctor's office.

https://news.mit.edu/2022/home-wireless-parkinsons-progression-0921

Adam Zewe | MIT News Office
September 21, 2022



Parkinson's disease is the fastest-growing neurological disease, now affecting more than 10 million people worldwide, yet clinicians still face huge challenges in tracking its severity and progression.

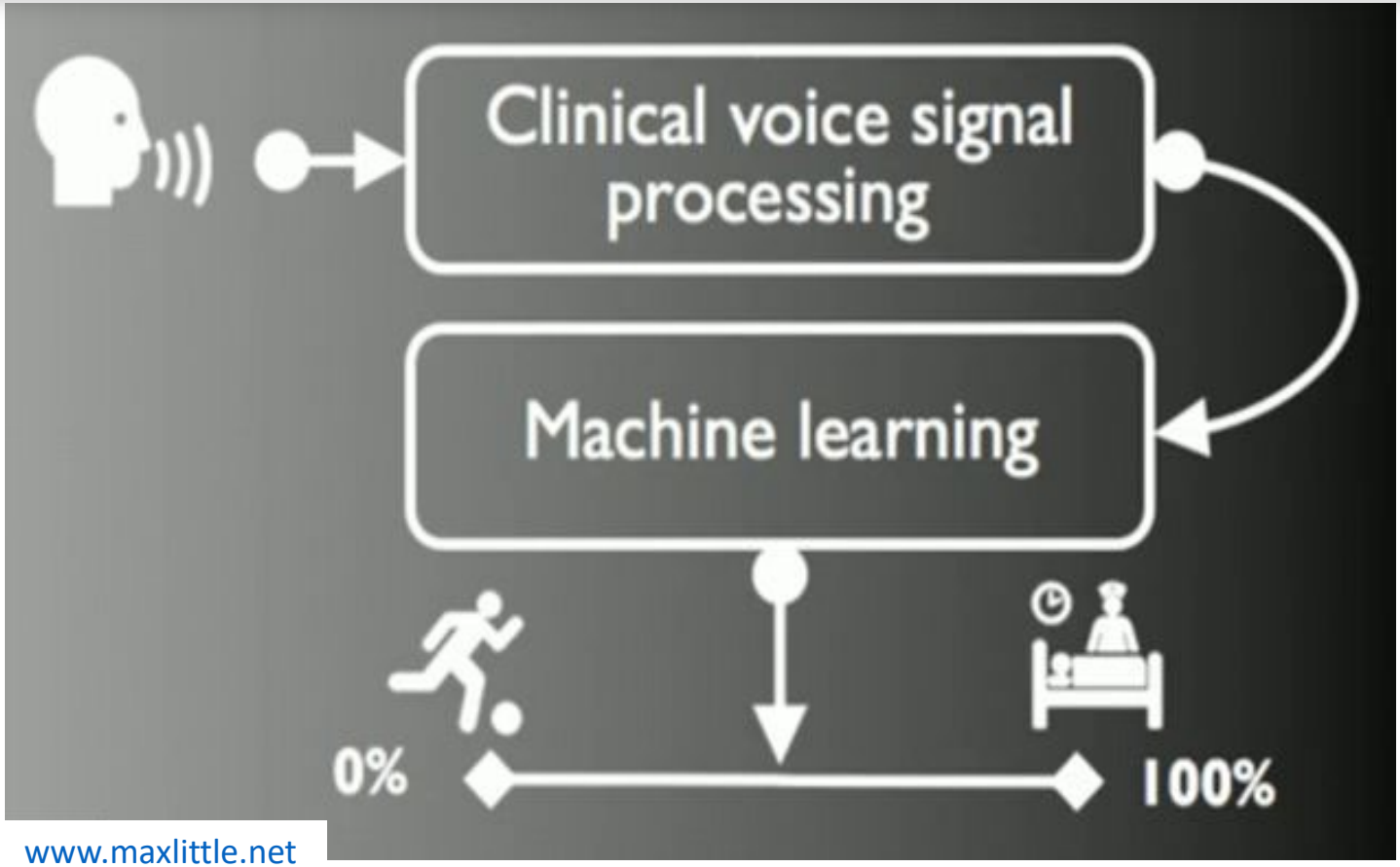
SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

PARKINSON'S DISEASE

Monitoring gait at home with radio waves in Parkinson's disease: A marker of severity, progression, and medication response

Yingcheng Liu[1]†*, Guo Zhang[1]†, Christopher G. Tarolli[2,3], Rumen Hristov[4], Stella Jensen-Roberts[2,3], Emma M. Waddell[2,3], Taylor L. Myers[2,3], Meghan E. Pawlik[2,3], Julia M. Soto[2,3], Renee M. Wilson[2,3], Yuzhe Yang[1], Timothy Nordahl[5], Karlo J. Lizarraga[2,3], Jamie L. Adams[2,3], Ruth B. Schneider[2,3], Karl Kieburtz[2,3], Terry Ellis[5], E. Ray Dorsey[2,3], Dina Katabi[1,4]

Detection of Parkinson's Disease using a Smart Phone - is so old news !!!



www.maxlittle.net

https://www.birmingham.ac.uk/staff/profiles/computer-science/academic-staff/little-max.aspx

Acoustic signal processing data may be used to detect Parkinson's Disease with a smartphone or predict torrential rainfall or used in hydrogeomorphology apps.

Smartphone Allows Capture of Speech Abnormalities Associated With High Risk of Developing Parkinson's Disease

Jan Rusz, Jan Hlavnička, Tereza Tykalová, Michal Novotný, Petr Dušek, Karel Šonka, and Evžen Růžička

nature medicine

Article

https://doi.org/10.1038/s41591-023-02440-2

Wearable movement-tracking data identify Parkinson's disease years before clinical diagnosis

Received: 5 December 2022

Accepted: 5 June 2023

Published online: 3 July 2023

Ann-Kathrin Schalkamp[1], Kathryn J. Peall[2], Neil A. Harrison[2,3] & Cynthia Sandor[1]

10 years later – nothing to report ??

Lakshminarayana *et al. Trials* 2014, **15**:374
http://www.trialsjournal.com/content/15/1/374

STUDY PROTOCOL Open Access

Smartphone- and internet-assisted self-management and adherence tools to manage Parkinson's disease (SMART-PD): study protocol for a randomised controlled trial (v7; 15 August 2014)

Rashmi Lakshminarayana[1*], Duolao Wang[2], David Burn[3], K Ray Chaudhuri[4], Gemma Cummins[5], Clare Galtrey[6], Bruce Hellman[1], Suvankar Pal[7], Jon Stamford[8], Malcolm Steiger[9], Adrian Williams[10] and The SMART-PD Investigators

Lakshminarayana, R., Wang, D., Burn, D. *et al.* Smartphone- and internet-assisted self-management and adherence tools to manage Parkinson's disease (SMART-PD): study protocol for a randomised controlled trial (v7; 15 August 2014). *Trials* **15**, 374 (2014). https://doi.org/10.1186/1745-6215-15-374

Where is the disconnect ??

We have smartphone-based mobile detection tools but even after 20 years we are still lacking coherent system of adoption by phone manufacturers to offer these motion/movement and speech sensors as a part of every phone just as we have built-in SMS app

THE DISCONNECT – mind the gap

The **bridge** between scientists, engineers and phone manufacturers (with a focus on tools for neuro-cognitive disorders) is still lacking active **leadership from science** and medicine.

THE DISCONNECT – mind the gap

Center for Integration of Medicine and Innovative Technology (CIMIT) https://news.mit.edu/1999/cimit-0512

CIMIT was pioneered by Professor John Parrish of Harvard Medical School and the Harvard-MIT Division of Health Sciences Technology, and is a consortium of MIT, the Massachusetts General Hospital, Brigham and Women's Hospital and Draper Labs.

ENTREPRENEURIAL INNOVATION IN PRACTICE OF MEDICINE
and
MANAGEMENT OF INTEGRATION (SECURITY) OF TECHNOLOGY

https://ecor.mgh.harvard.edu/Default.aspx?node_id=487

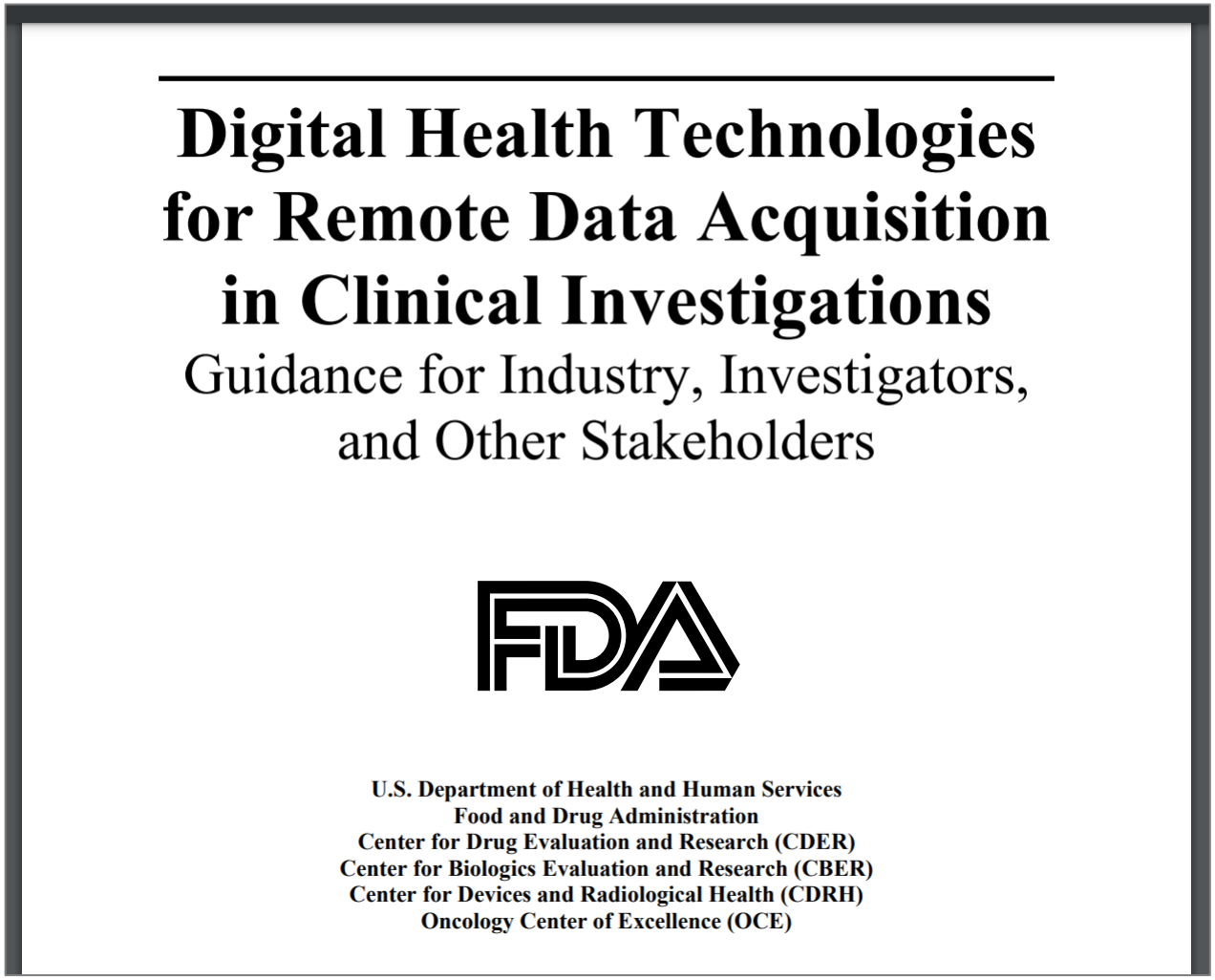
*We need a **leader** who is a scientist, understands neurology, semantics, cognition, data analytics, versed in principles of IoT, medical devices, devices for remote data collection, ground principles of cybersecurity and the business of innovation, technology, digital supply chain & management.*

https://www.fda.gov/media/155022/download

https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs

https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances

https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/guidance-documents-medical-devicesand-radiation-emitting-products



Digital Health Technologies for Remote Data Acquisition in Clinical Investigations

Guidance for Industry, Investigators, and Other Stakeholders

FDA

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)
Oncology Center of Excellence (OCE)

www.fda.gov/regulatory-information/search-fda-guidance-documents/digital-health-technologies-remote-data-acquisition-clinical-investigations

An even bigger picture

and a massive untapped entrepreneurial opportunity

Vital signs, including respiratory rate, oxygen saturation, blood pressure, pulse and temperature, are simplest, cheapest and probably most important information gathered on hospitalized patients [1]. However, despite being introduced into clinical practice more than a century ago, surprisingly few attempts have been made to quantify their clinical performance [2]. Changes in vital signs occur several hours prior to adverse events [3–7].

Brekke IJ, Puntervoll LH, Pedersen PB, Kellett J, Brabrand M. The value of vital sign trends in predicting and monitoring clinical deterioration: A systematic review. PLoS One. 2019 January 15; 14(1):e0210875. doi: 10.1371/journal.pone.0210875 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6333367/pdf/pone.0210875.pdf

10-Point Physiological PTSD

These 10 data points, over time (time series) may be able to predict and prevent 80% of healthcare events becoming an emergency. In 20% of individuals prevention can eliminate need for hospital care. In 80% of potential patients, it can reduce acuity of the condition.

Vital signs, including respiratory rate, oxygen saturation, blood pressure, pulse and temperature, are simplest, cheapest and probably most important information gathered on hospitalized patients [1]. However, despite being introduced into clinical practice more than a century ago, surprisingly few attempts have been made to quantify their clinical performance [2]. Changes in vital signs occur several hours prior to adverse events [3–7].

Brekke IJ, Puntervoll LH, Pedersen PB, Kellett J, Brabrand M. The value of vital sign trends in predicting and monitoring clinical deterioration: A systematic review. PLoS One. 2019 January 15; 14(1):e0210875. doi: 10.1371/journal.pone.0210875 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6333367/pdf/pone.0210875.pdf

10-Point Physiological PTSD

NON-INVASIVE Personal Time Series Data (PTSD in EHR/EMR)

- Blood Glucose
- Cholesterol (LDL)
- Urea (SUN)
- Hemoglobin
- Proteinuria

+

Non-Invasive Vital Signs (data)

- Respiratory Rate (RR)
- Oxygen Saturation (pOX)
- Blood Pressure (BP)
- Pulse
- Body Temperature

SUN - https://gh.bmj.com/content/bmjgh/5/5/e002312.full.pdf ● LDL - https://doi.org/10.1186/s12944-021-01571-0

We have most of the non-invasive tools and technologies to accomplish this task, now, without any new invention or innovation. Question: Who has the will and zeal to lead and implement the systemic integration of device and data which is key to generate healthcare analytics: predictive and prescriptive.

10-Point Physiological PTSD

NON-INVASIVE Personal Time Series Data (PTSD in EHR/EMR)

- Blood Glucose
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SUN - https://gh.bmj.com/content/bmjgh/5/5/e002312.full.pdf ● LDL - https://doi.org/10.1186/s12944-021-01571-0

☑ BUSINESS OF MAKING MONEY

10-Point Physiological PTSD

PAY A PENNY PER USE (PAPPU) – CENTRAL CONCEPT FOR SOCIAL BUSINESS PROFITABILITY

PAPPU

The idea is to lower the barrier to market entry for products and services by eliminating initial capital cost (for example, you get a free phone if you pay a small charge per call). The concept of PAPPU suggests charging a very small fee (penny?) each time the customer uses the product and/or the service.

☑ $60 billion / year

10-Point Physiological PTSD

USER PAYS ONE OR 10 PENNIES PER USE FOR EACH DATA POINT

- Blood Glucose
- Cholesterol (LDL)
- Urea (SUN)
- Hemoglobin
- Proteinuria

+

Non-Invasive Vital Signs (data)

- Respiratory Rate (RR)
- Oxygen Saturation (pOX)
- Blood Pressure (BP)
- Pulse
- Body Temperature

☑ **PAPPU model generates ~ US$60 billion in annual earnings**

☑ **10% of 1 billion affluent customers (100 million users pay 10 pennies per use = 100 pennies / day or ~US$36.5 billion p.a.)**

☑ **10% of 7 billion in rest-of-the-world (700 million users pay 10 pennies per day or ~US$25.5 billion per annum, in earnings)**

10-Point Physiological PTSD

USER PAYS 1 or 10 PENNIES PER USE FOR EACH DATA UPLOADED

- Blood Glucose
- Cholesterol (LDL)
- Urea (SUN)
- Hemoglobin
- Proteinuria

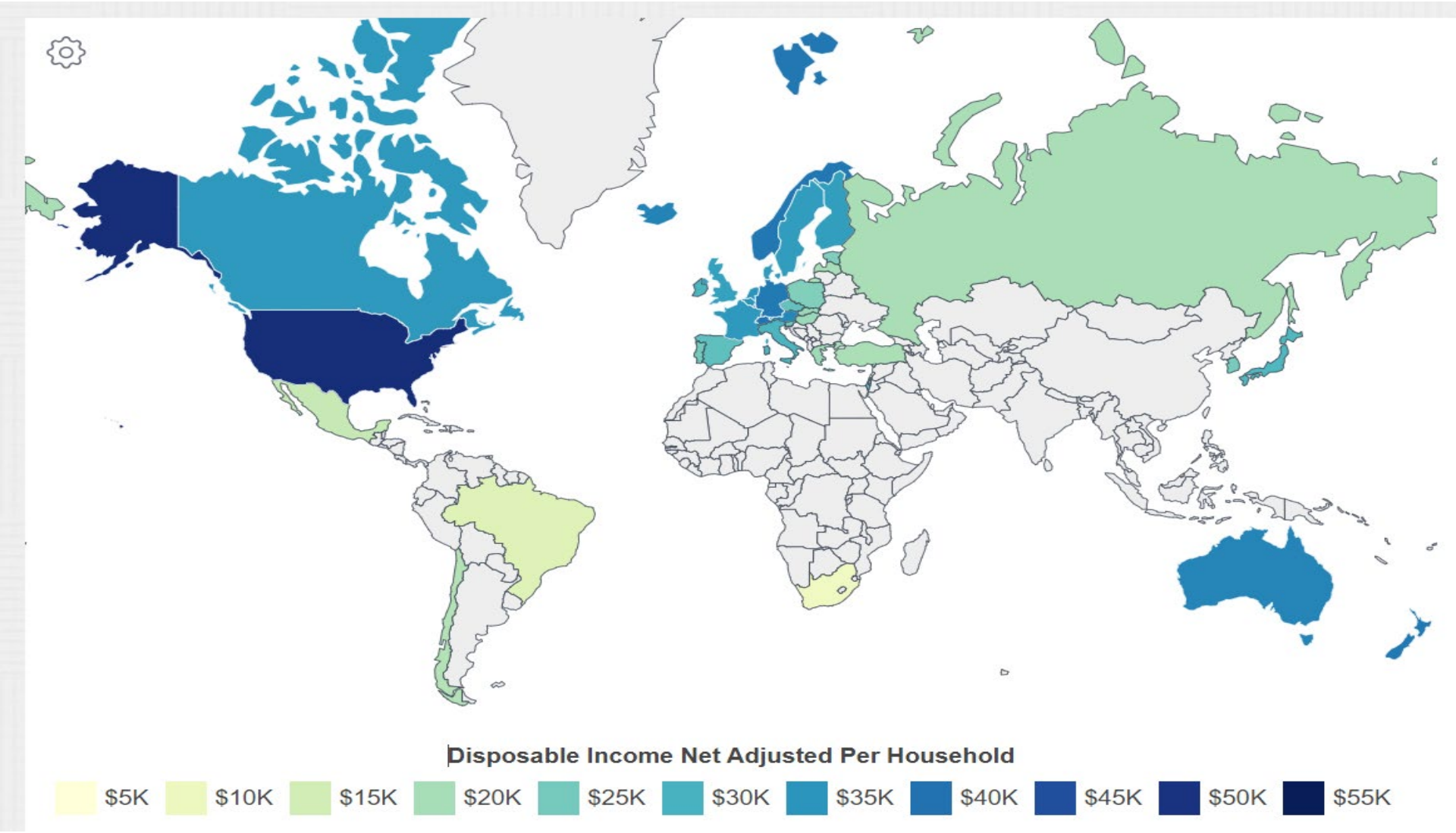
+

Non-Invasive Vital Signs (data)

- Respiratory Rate (RR)
- Oxygen Saturation (pOX)
- Blood Pressure (BP)
- Pulse
- Body Temperature

If the corporate implementation group is happy with potential $36.5 billion in annual earnings, then it can ignore 7 billion people and limit the healthcare service within the affluent markets.

Could PAPPU unleash the Immense Wealth of Nations?

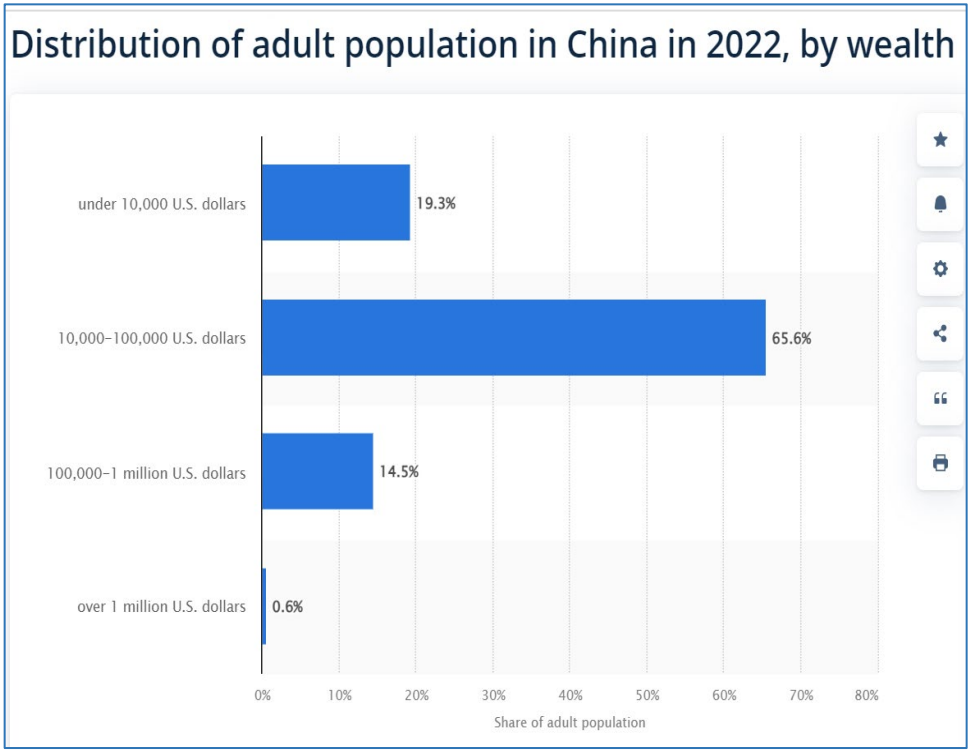


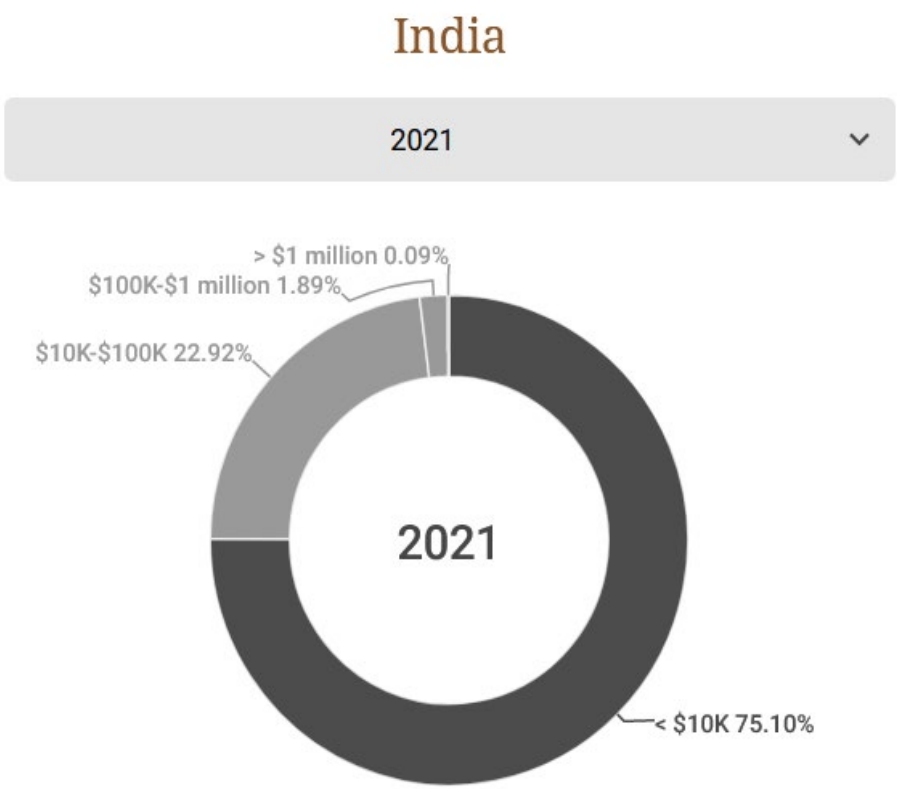
Can ~7 billion “poor people” spend US$36.50 per year?

https://worldpopulationreview.com/country-rankings/disposable-income-by-country

Fact Check (are the "numbers" credible?)

- Diagnostics does not equal to treatment. Without treatment, there is little value in diagnostics.
- Market of 700 million (non-affluent nations): Do they possess the purchasing power (treatment)?
- 432 million people are in the "middle class" category in India (FT *"have achieved economic security and able to indulge in discretionary consumption"*). 25% of 1.4 billion people (350 million) can afford to pay for treatment (post-diagnostics), according to wealth distribution in India.





https://www.themirrority.com/data/wealth-distribution
https://www.ft.com/content/be53790c-ea16-4e5c-9410-bac189fb2636
https://www.statista.com/statistics/960090/china-adult-population-distribution-by-wealth-group
https://www.business-standard.com/economy/news/indian-middle-class-will-nearly-double-to-61-by-2046-47-price-report-123070500864_1.html

$60 billion / year Healthcare Service

10-Point Physiological PTSD

USER PAYS ONE OR 10 PENNIES PER USE FOR EACH DATA POINT

- Blood Glucose
- Cholesterol (LDL)
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+

Non-Invasive Vital Signs (data)

- Respiratory Rate (RR)
- Oxygen Saturation (pOX)
- Blood Pressure (BP)
- Pulse
- Body Temperature

If limited to 1% profit, the healthcare service business will generate $600 million in annual profit.

Even if we assume that the PAPPU market for diagnostics exists (1.7 billion with the purchasing power for treatment followed by diagnostics). It will not be prudent to expect $60 billion in annual revenues, soon.

The nature of business investments & earnings

Healthcare service business with $60 billion in annual revenues.

If limited to 1% profit, the healthcare service business will generate $600 million in annual profit.

If limited to 1% profit, the healthcare service business will generate $600 million in annual profit.

The trap that executives often fall into, however, is assuming that opportunities for advantage will be available indefinitely. In actuality, the window for gaining advantage from infrastructural technology is open only briefly. When the technology's commercial potential begins to be broadly appreciated, huge amounts of cash are inevitably invested in it, and its build out proceeds with extreme speed. Railroad tracks, telegraph wires, power lines—all were laid or strung in a frenzy of activity. In the 30 years between 1846 and 1876, reports Eric Hobsbawm in *The Age of Capital*, the world's rail trackage increased from 17,424 km to 309,641 km. During this same period, total steamship tonnage also exploded, from 139,973 to 3,293,072 tons. The telegraph system spread even more swiftly. In Continental Europe, there were just 2,000 miles of telegraph wires in 1849; 20 years later, there were 110,000 miles. The pattern continued with electrical power. The number of central stations operated by utilities grew from 468 in 1889 to 4,364 in 1917, and the average capacity of each increased tenfold.

Nicholas Carr in Harvard Business Review, 2003 ● https://hbr.org/2003/05/it-doesnt-matter

Why governments may want to show their support for PTSD

10-Point Physiological PTSD

Anonymized PTSD may offer significant socio-spatial value for data-informed focus on public heath outreach, vastly improve allocation of limited resources and inform healthcare policies.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5023496/pdf/nihms811182.pdf and https://doi.org/10.1016/j.compenvurbsys.2020.101513

Data-Informed Personal Health and Analytics-Guided Personalized Healthcare

also helps

Anonymized Data-Informed Resource Allocation and Public Health Policy

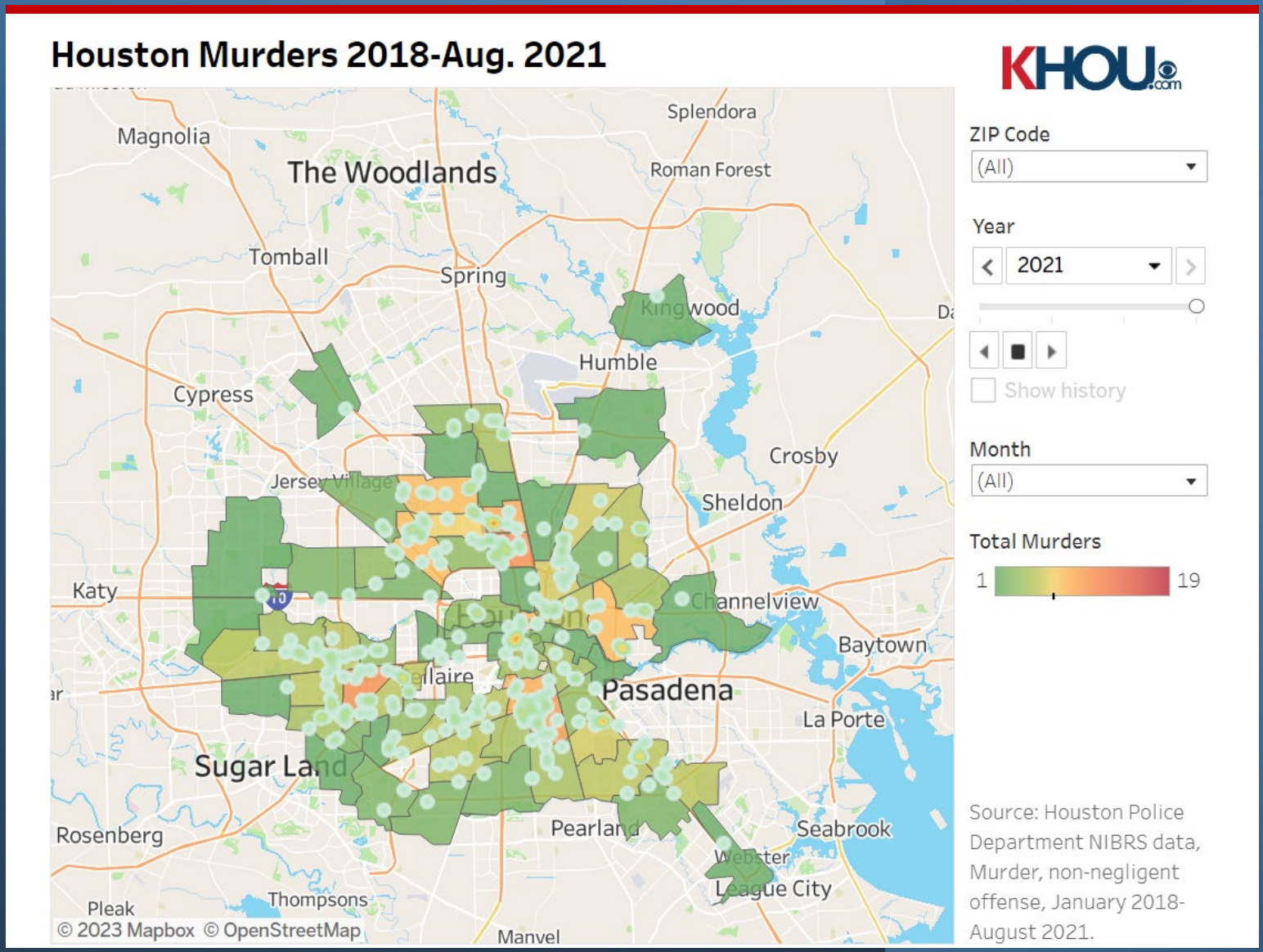
10-Point Physiological PTSD

Anonymized data (e.g., blood glucose), grouped by zip code, offers a snap-shot of areas in need of public health assistance to educate residents how to better deal with certain diseases, e.g., diabetes, cardiovascular (CV) risk, chronic obstructive pulmonary disease (COPD). Federal, state, local governments can focus resources to allocate services based on data & need, rather than health politics.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5023496/pdf/nihms811182.pdf and https://doi.org/10.1016/j.compenvurbsys.2020.101513

Instead of mapping TX murders by zip code, what if we map anonymized blood glucose data by zip code?

Houston murders by ZIP code
Search interactive map



SOURCE: www.khou.com/article/news/crime/khou11-investigates-houston-murders-by-zip-code/285-85665c91-9084-40f0-916b-16de9f842472

Ten-point PTSD, no matter how simple it may sound, still may not be feasible for resource constrained communities

Are there alternatives?

Alternatives to PTSD ??
Surrogate Metrics

Essentially, these quick metrics serve as surrogates that correlate with all kinds of factors that determine a person's overall health—which can otherwise be totally impractical, invasive, and expensive to measure directly. If we had to choose a single, simple, universal number to define health, any of these functional metrics might be a better contender than BMI.

The most common numbers are age and body weight. The U.S. health-care system places tremendous value on the latter, in the form of body-mass index, or BMI, a simple ratio of weight over height. BMI is used to define obesity and "overweight," and so to stratify risks in insurance and health-care industries. This number has come to be massively consequential in the lives of millions of people, and to influence the movement of billions of dollars.

Despite all this emphasis on body weight, the ability of BMI to predict mortality and disease has been called into question. Its inadequacy is famously evident in examples such as the human muscle-mound Dwayne "The Rock" Johnson qualifying as obese. BMI also ignores the health problems among the "skinny fat" (or "overfat" or "normal-weight obese").

Flegal KM, Kit BK, Orpana H, Graubard BI. (2013) Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. JAMA. 2013 January 2; 309(1):71-82 doi: 10.1001/jama.2012.113905. PMID: 23280227; PMCID: PMC4855514.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4855514/pdf/nihms754493.pdf
https://www.menshealth.com/weight-loss/a19537796/the-problem-with-bmi/
https://www.theatlantic.com/health/archive/2019/06/push-ups-body-weight-bmi/592834

Lesser Alternatives to PTSD Surrogate Metrics: Walking

The speed at which you walk, for example, can be eerily predictive of health status. In a study of nearly 35,000 people aged 65 years or older in the *Journal of the American Medical Association*, those who walked at about 2.6 feet per second over a short distance—which would amount to a mile in about 33 minutes—were likely to hit their average life expectancy. With every speed increase of around 4 inches per second, the chance of dying in the next decade fell by about 12 percent. (Whenever I think about this study, I start walking faster.)

Studenski S, Perera S, Patel K, Rosano C, Faulkner K, Inzitari M, Brach J, Chandler J, Cawthon P, Connor EB, Nevitt M, Visser M, Kritchevsky S, Badinelli S, Harris T, Newman AB, Cauley J, Ferrucci L, Guralnik J. "Gait speed and survival in older adults" JAMA. 2011 Jan 5; 305(1):50-8. doi: 10.1001/jama.2010.1923
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3080184/pdf/nihms268325.pdf
https://www.theatlantic.com/health/archive/2019/06/push-ups-body-weight-bmi/592834

In 2018, a study of half million middle-aged people found that lung cancer, heart disease, and all-cause mortality were well predicted by the strength of a person's grip.

Yes, how hard you can squeeze a grip meter. This was a better predictor of mortality than blood pressure or overall physical activity. A prior study found that grip strength among people in their 80s predicted the likelihood of making it past 100. Even more impressive, grip strength had good predictive ability in a study among 18-year-olds in the Swedish military on cardiovascular death 25 years later. **doi: 10.1136/bmj.e7279**

Celis-Morales CA, Welsh P, Lyall DM, Steell L, Petermann F, Anderson J, Iliodromiti S, Sillars A, Graham N, Mackay DF, Pell JP, Gill JMR, Sattar N, Gray SR. Associations of grip strength with cardiovascular, respiratory, and cancer outcomes and all cause mortality: prospective cohort study of half a million UK Biobank participants. BMJ. 2018 May 8; 361:k1651. doi: 10.1136/bmj.k1651. PMID: 29739772; PMCID: PMC5939721.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5939721/?report=printable
https://www.theatlantic.com/health/archive/2019/06/push-ups-body-weight-bmi/592834

The Power of One Push-Up

Several simple ways of measuring a person's health might matter more than body weight.

By James Hamblin

Cristina Quicler / AFP / Getty

https://www.theatlantic.com/health/archive/2019/06/push-ups-body-weight-bmi/592834

Alternatives to PTSD
Surrogate Metrics: Walking, Grip, Push-up

Another study made headlines earlier this year for declaring that push-up abilities could predict heart disease. Stefanos Kales, a professor at Harvard Medical School, noticed that the leading cause of death of firefighters on duty was not smoke inhalation, burns, or trauma, but sudden cardiac death. This is usually caused by coronary-artery disease. Even in this high-risk profession, people are most likely to die of the same thing as everyone else.

Still, the profession needed effective screening tests to define fitness for duty. Because firefighters are generally physically fit people, Kales's lab looked at push-ups. He found that they were an even better predictor of cardiovascular disease than a submaximal treadmill test.

Yang J, Christophi CA, Farioli A, Baur DM, Moffatt S, Zollinger TW, Kales SN. "Association Between Push-up Exercise Capacity and Future Cardiovascular Events Among Active Adult Men" JAMA Netw Open. 2019 Feb 1; 2(2):e188341. doi: 10.1001/jamanetworkopen.2018.8341.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6484614/?report=printable
https://www.theatlantic.com/health/archive/2019/06/push-ups-body-weight-bmi/592834

Alternatives to PTSD in less affluent nations

Surrogate Metrics: Walking, Grip, Push-up

It may be rational to think that these metrics could be helpful to resource constrained communities in Africa.

Alternatives to PTSD in less affluent nations

Surrogate Metrics: Walking, Grip, Push-up

But charlatans have other plans

How the HYPE has infected Africa

"What do you guys think? We're really excited about reimagining the global healthcare system for good!"

Fred Swaniker

https://en.wikipedia.org/wiki/Fred_Swaniker

The “AI” CANCER INFECTS RWANDA ?

A project driven by Sand Technologies is the ‘Health Intelligence Center’. It's set to revolutionize rural healthcare in areas worldwide facing a shortage of medical personnel and general resource constraints. We've built the first one in Rwanda, and the results have been really impressive. The standout feature of the Health Intelligence Center (nicknamed The Blue Room because of its blue lights) is its ability to analyze massive amounts of health data, recognize disease patterns, assist with system-level decisions, enable more efficient resource allocation, etc. With all this data, we can begin building AI models to identify causes of chronic illnesses and even possibly cancer, so we can focus more on preventative care versus our current model of reactive (and expensive) care when it’s too late. It can also identify early signs of a pandemic, helping to prevent its rapid spread. Listen to what our Program Lead, Nancy Umutoni (who is an alumna of The African Leadership University), and her colleague Marie Christelle Ishimwe have to say. What do you have to say Fred Swaniker? Is this big show going to save Rwanda?

The negativity towards AI

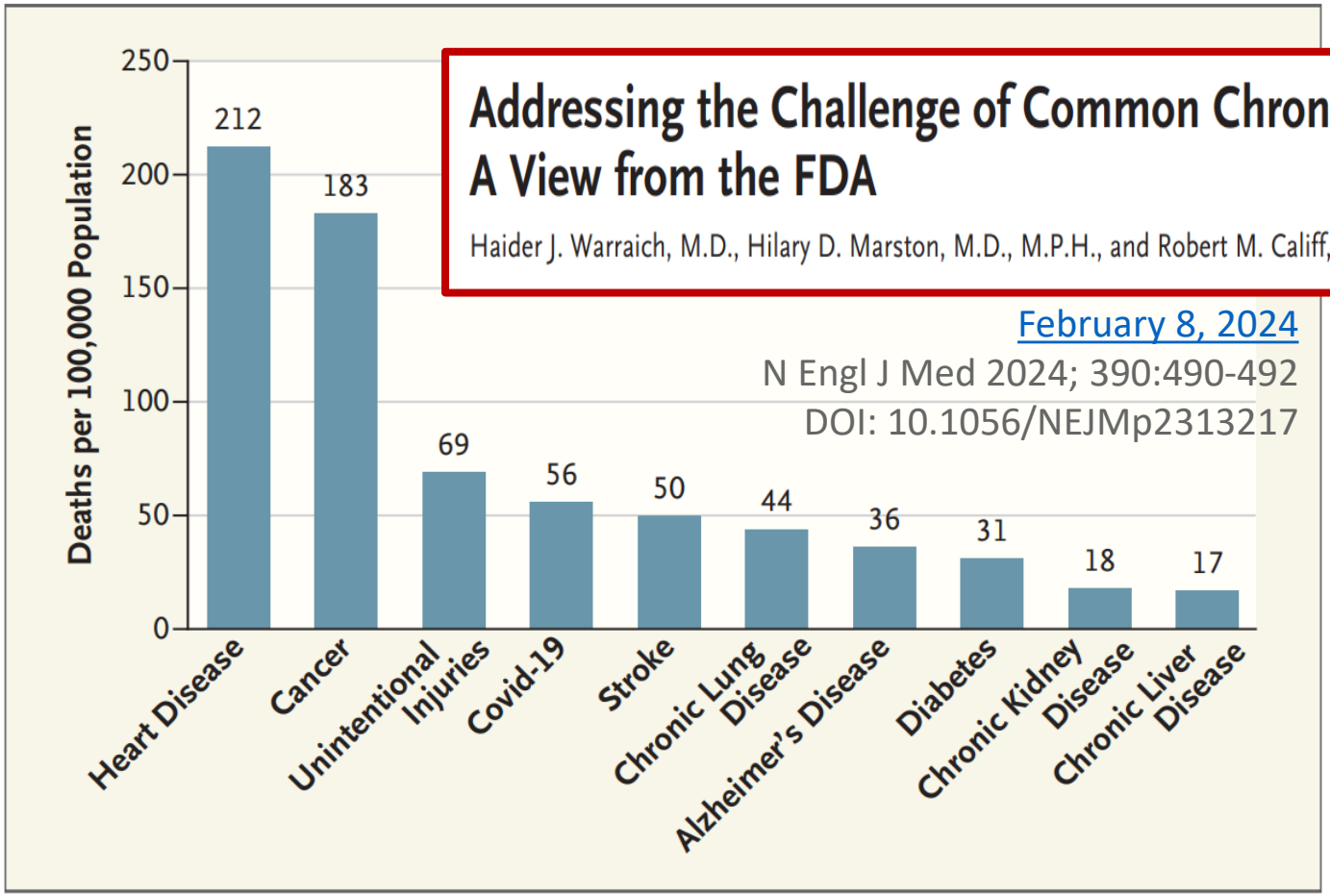
justified for unscientific, unhinged, blasphemous statements like

“AI models to identify causes of chronic illnesses”

"AI models to identify causes of chronic illnesses"

claims Fred Swaniker "Blue Room with blue lights"

Warraich HJ, Marston HD, Califf RM. **Addressing the Challenge of Common Chronic Diseases - A View from the FDA**. N Engl J Med. 2024 February 8; 390(6):490-492. doi: 10.1056/NEJMp2313217 PMID: 38314843.

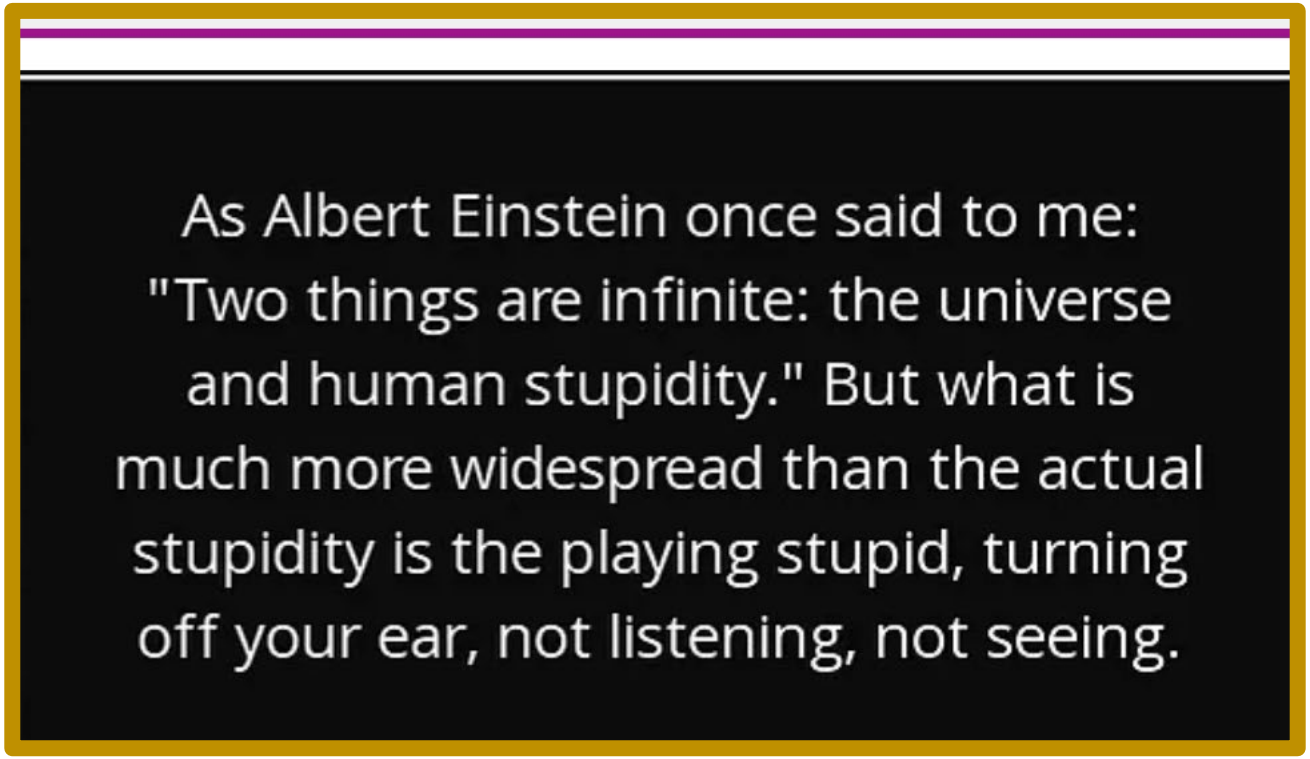


Crude Mortality for the 10 Leading Causes of Death in the United States, 2022.

Preliminary data are from the Centers for Disease Control and Prevention's WONDER database.

“AI models to identify causes of chronic illnesses”

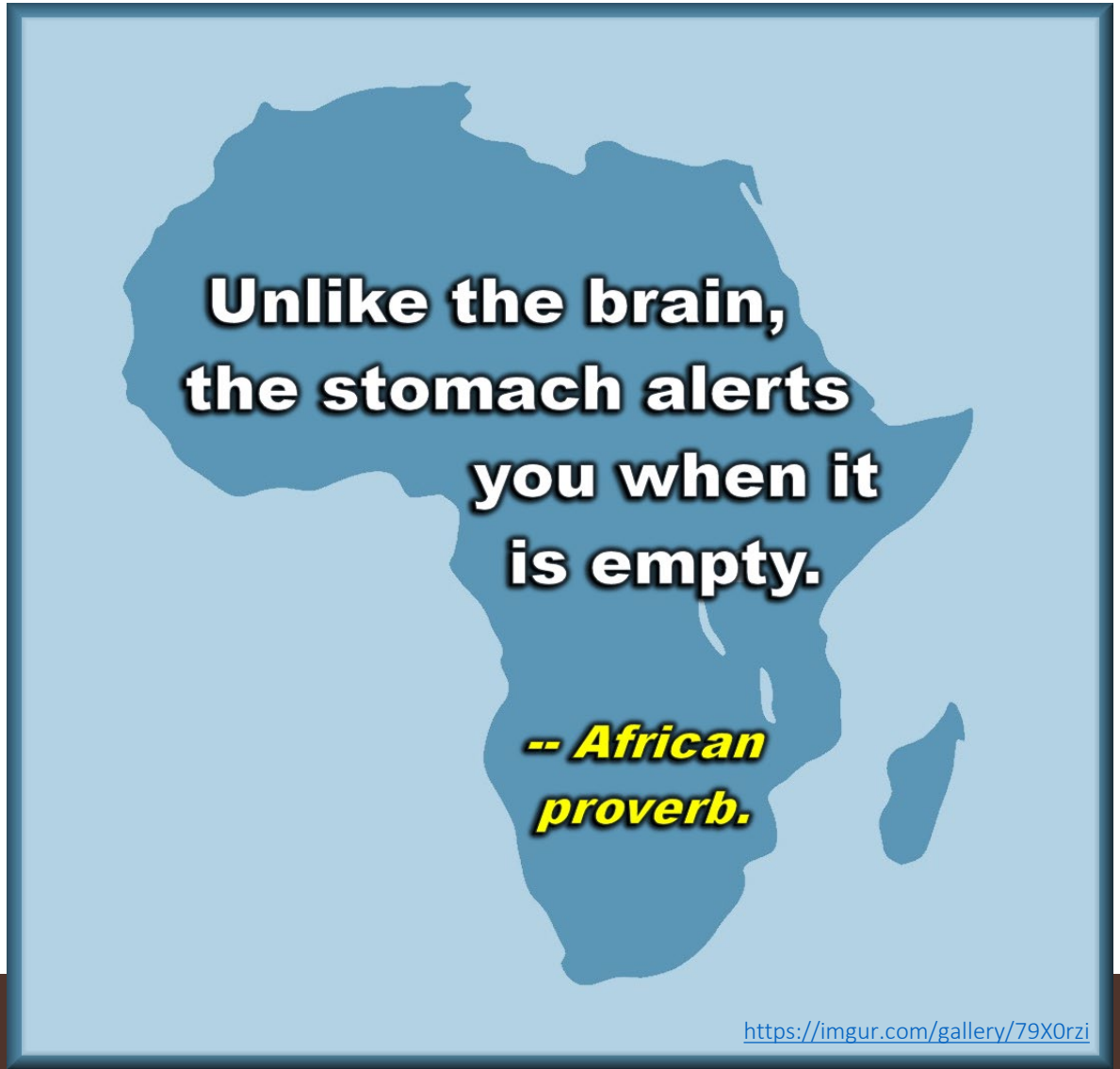
claims Fred Swaniker “Blue Room with blue lights”



https://myreachingout.wixsite.com/myblog/single-post/2019/07/15/human-stupidity-no-limits-on-height-width-or-depth-as-albert-einstein-rightly-said

“AI models to identify causes of chronic illnesses”

“Ghanian” Fred Swaniker “Blue Room with blue lights”

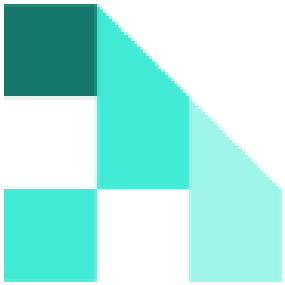


www.technologyreview.com/2024/03/04/1089403/large-language-models-amazing-but-nobody-knows-why

MIT Technology Review

Don't fall into the tech sector's marketing trap by believing that these models are omniscient or factual, or even near ready for the jobs we are expecting them to do. Because of their unpredictability, out-of-control biases, security vulnerabilities, and propensity to make things up, their usefulness is extremely limited. They can help humans brainstorm, and they can entertain us. But, knowing how glitchy and prone to failure these models are, it's probably not a good idea to trust them with your credit card details, your sensitive information, or any critical use cases.

As the scientists in Will's piece say, it's still early days in the field of AI research. According to Boaz Barak, a computer scientist at Harvard University who is currently on secondment to OpenAI's superalignment team, many people in the field compare it to physics at the beginning of the 20th century, when Einstein came up with the theory of relativity.



The Algorithm

By Melissa Heikkilä • 3.4.24

https://mailchi.mp/technologyreview/nobody-knows-how-ai-works?e=a99fe08ed2

All facets of healthcare are based on rigor of science and basic science research.

Healthcare treatment is not a toy for technology pranks although technology is often an useful tool.

“That experience convinced me that if I want to make big discoveries, I have to focus on basic science,” he says. “It also gave me the confidence that if I can succeed at MIT, I can succeed just about anywhere and in any field of biology.”

Healthcare operations aren’t about research but connecting the dots of knowledge to benefit the diagnosis and treatment of disease. Tools are useful. But, the gross puffery about AI models to “identify causes of illnesses” are glib, smug, smarmy, slick and sycophantic marketing efforts peddled by pseudo-scientists.

What can super-healing species teach us about regeneration?

Albert Almada PhD ’13 studies the mechanics of how stem cells rebuild tissues. “Digging deep into the science is what MIT taught me,” he says.

Lillian Eden | Department of Biology
February 21, 2024

https://www.technologyreview.com/2017/10/06/241837/the-seven-deadly-sins-of-ai-predictions/

MIT Technology Review

https://people.csail.mit.edu/brooks

The Seven Deadly Sins of AI Predictions

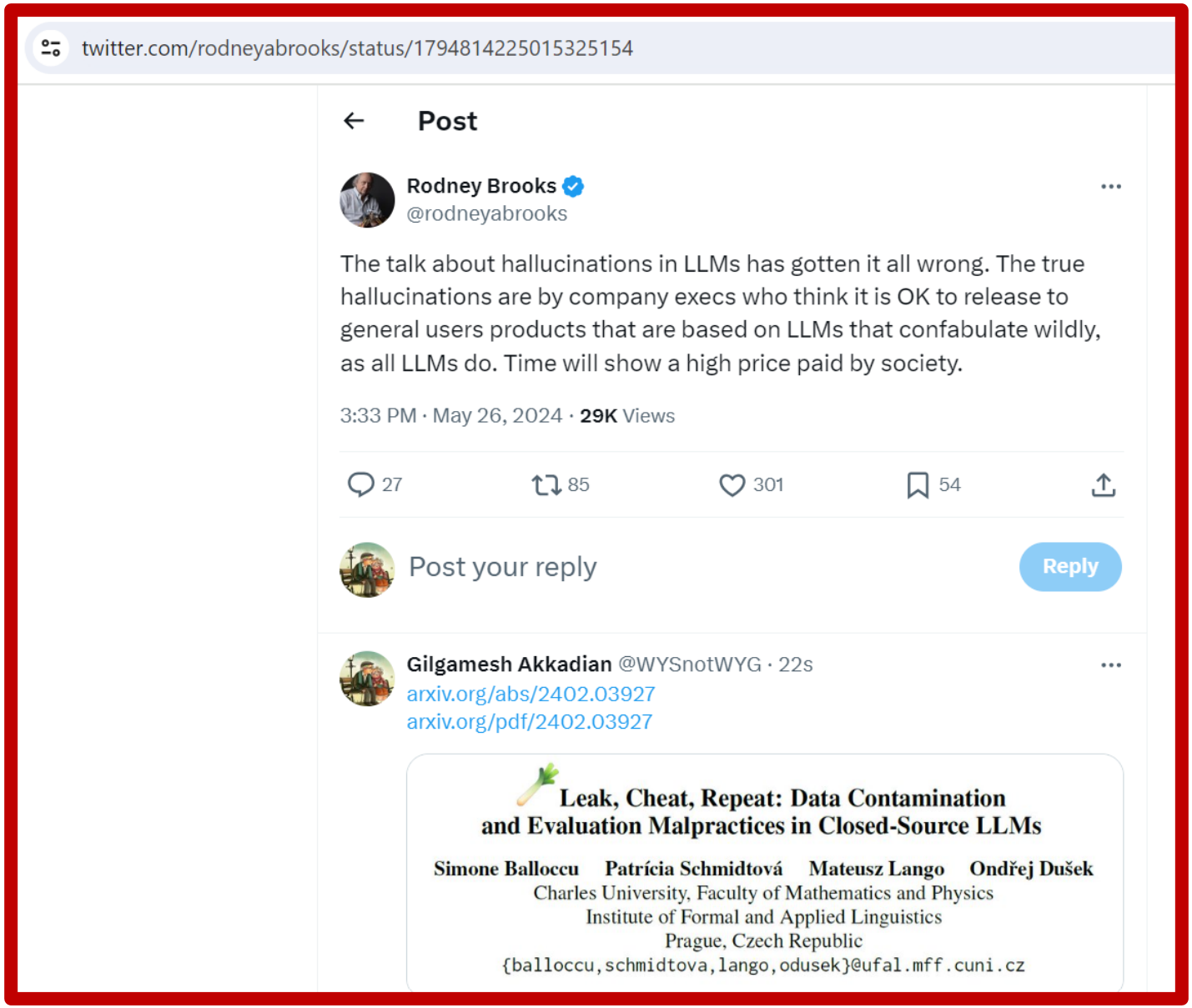
Mistaken extrapolations, limited imagination, and other common mistakes that distract us from thinking more productively about the future.

By Rodney Brooks

October 6, 2017

Rodney Brooks is the Panasonic Professor of Robotics (emeritus) at MIT. He is a robotics entrepreneur. Dr. Brooks is the former Director (1997 - 2007) of the MIT Artificial Intelligence Laboratory and then the MIT Computer Science & Artificial Intelligence Laboratory (CSAIL). He received a Ph.D. in Computer Science from Stanford University in 1981. He held research positions at Carnegie Mellon University and MIT, and a faculty position at Stanford before joining the faculty of MIT in 1984. From June 2014 until May 2020 he was a member of the Visiting Committee on Advanced Technology, VCAT, at the National Institute of Standards and Technology, NIST. Since June 2015 he has been an external member of GE's Robotics Advisory Council. From January 2016 until mid 2019 he was Deputy Chairman of the Advisory Board of Toyota Research Institute. From February 2019 until January 2021 he was "Luminary" at Bell Labs. Dr. Brooks is a Member of the National Academy of Engineering (NAE), a Founding Fellow of the Association for the Advancement of Artificial Intelligence (AAAI), a Fellow of the American Academy of Arts & Sciences (AAAS), a Fellow of the American Association for the Advancement of Science (the other AAAS), a Fellow of the Association for Computing Machinery (ACM), a Fellow of the Institute of Electrical and Electronics Engineers (IEEE), a Member of the Australian Academy of Science (AAS) and a Fellow of the Australian Academy of Technological Sciences and Engineering (ATSE).

Don’t subject your data to hallucinations



Who is Rodney Brooks? ● https://people.csail.mit.edu/brooks

www.nature.com/articles/d41586-024-02420-7

www.nature.com/articles/s41586-024-07566-y

nature.com/articles/d41586-024-02420-7

nature

AI ... naturally nonsensical

NEWS | 24 July 2024

AI models fed AI-generated data quickly spew nonsense

Researchers gave successive versions of a large language model information produced by previous generations of the AI – and observed rapid collapse.

By Elizabeth Gibney

Article

AI models collapse when trained on recursively generated data

https://doi.org/10.1038/s41586-024-07566-y

Received: 20 October 2023

Accepted: 14 May 2024

Published online: 24 July 2024

Open access

Check for updates

Ilia Shumailov[1,8]✉, Zakhar Shumaylov[2,8]✉, Yiren Zhao[3], Nicolas Papernot[4,5], Ross Anderson[6,7,9] & Yarin Gal[1]✉

Stable diffusion revolutionized image creation from descriptive text. GPT-2 (ref. 1), GPT-3(.5) (ref. 2) and GPT-4 (ref. 3) demonstrated high performance across a variety of language tasks. ChatGPT introduced such language models to the public. It is now clear that generative artificial intelligence (AI) such as large language models (LLMs) is here to stay and will substantially change the ecosystem of online text and images. Here we consider what may happen to GPT-{*n*} once LLMs contribute much of the text found online. We find that indiscriminate use of model-generated content in training causes irreversible defects in the resulting models, in which tails of the original content distribution disappear. We refer to this effect as 'model collapse' and show that it can occur in LLMs as well as in variational autoencoders (VAEs) and Gaussian mixture models (GMMs). We build theoretical intuition behind the phenomenon and portray its ubiquity among all learned generative models. We demonstrate that it must be taken seriously if we are to sustain the benefits of training from large-scale data scraped from the web. Indeed, the value of data collected about genuine human interactions with systems will be increasingly valuable in the presence of LLM-generated content in data crawled from the Internet.

Does not need

"The Blue Room because of its blue lights"

and such unctuous displays represent the wheedling use of technology only fit for very stupid movies (e.g., https://www.imdb.com/title/tt13603966/) using pedestrian actors (e.g., Matthias Schweighöfer)

Why the continent of Africa needs more time to tune the engine and does not need to polish the chrome such as Fred Swaniker's puffery (the Blue Room because of its blue lights)

hls.harvard.edu/today/using-her-voice-to-address-gender-based-violence-in-the-african-context/

Teaching & Learning

Lifting women up

First Lady of Sierra Leone Fatima Maada Bio is working to end gender-based violence, and empower women

Mar 18, 2024 By Colleen Walsh

Credit: Lorin Granger

https://hls.harvard.edu/today/using-her-voice-to-address-gender-based-violence-in-the-african-context/

According to the 2019 Sierra Leone Demographic and Health Survey, 61% of women and girls between the ages of 15-49 have experienced physical violence since the age 15, and 7% have experienced sexual violence. The non-governmental organization Human Rights Watch has said sexual violence during the nation's civil war from 1991 to 2002, "affected thousands of girls and women of all ages," and was rooted in "the persistent human rights violations that push women into a lower status with limited rights in all spheres of their lives." For more information go to https://dhsprogram.com/pubs/pdf/FR365/FR365.pdf


Blood Bank
Digital
IDEAS

What is next after PTSD

LIQUID BIOPSIES

SCALE POPULATION HEALTH USING LIQUID BIOPSIES VIA COMMUNITY BLOOD BANKS?

How to transform SOFT ideas into HARD reality

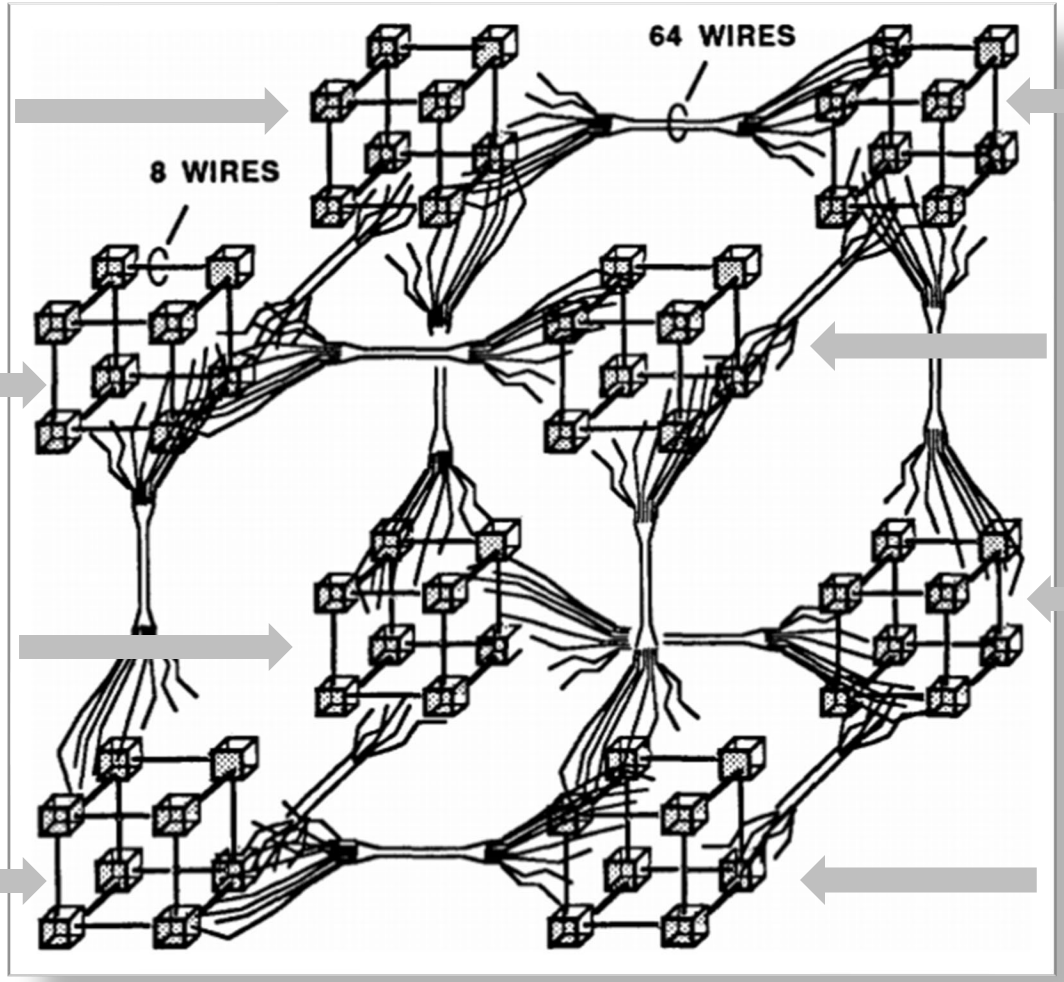
CONVERGENCE OF A SPECTRUM OF NODES TO INFORM AND INFLUENCE KEY PERFORMANCE INDICATORS (KPI)

SCIENCE & SCIENTISTS

GRANTS & DONORS

WORKFORCE DEVELOPMENT

RESEARCH & CREDIBILITY



EQUIPMENT & REPOSITORIES

BUSINESS DEVELOPMENT

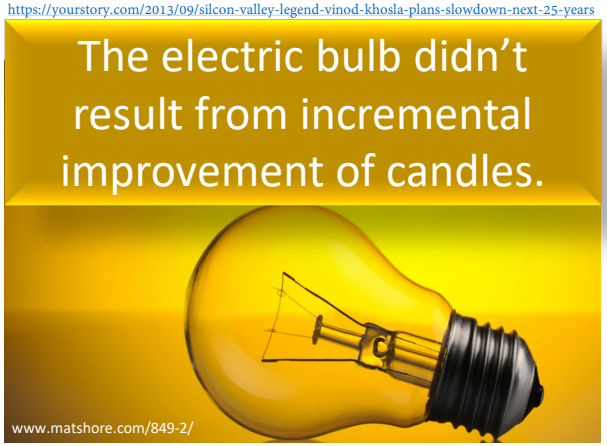
PRODUCTS & MARKETING

GOVERNMENT LIAISON & PR

Explore Parts 3, 2 and 1 – here - https://dspace.mit.edu/handle/1721.1/153283

Outsiders innovate ??

https://yourstory.com/2013/09/silcon-valley-legend-vinod-khosla-plans-slowdown-next-25-years



NBC didn't change media. YouTube did. NASA didn't reinvent space exploration. SpaceX did. GM didn't innovate electric car. Tesla did. AT&T didn't create smart phones. Apple did. Walmart could not innovate retail. Amazon did.

SENSE OF FUTURE THINKING

SOFT

for

HARD

Healthcare-Associated Research & Development

Outsiders innovate ??

Blood Bank Digital

https://hbr.org/2011/08/henry-ford-never-said-the-fast

Harvard Business Review

"If I had asked people what they wanted, they would have said faster horses."

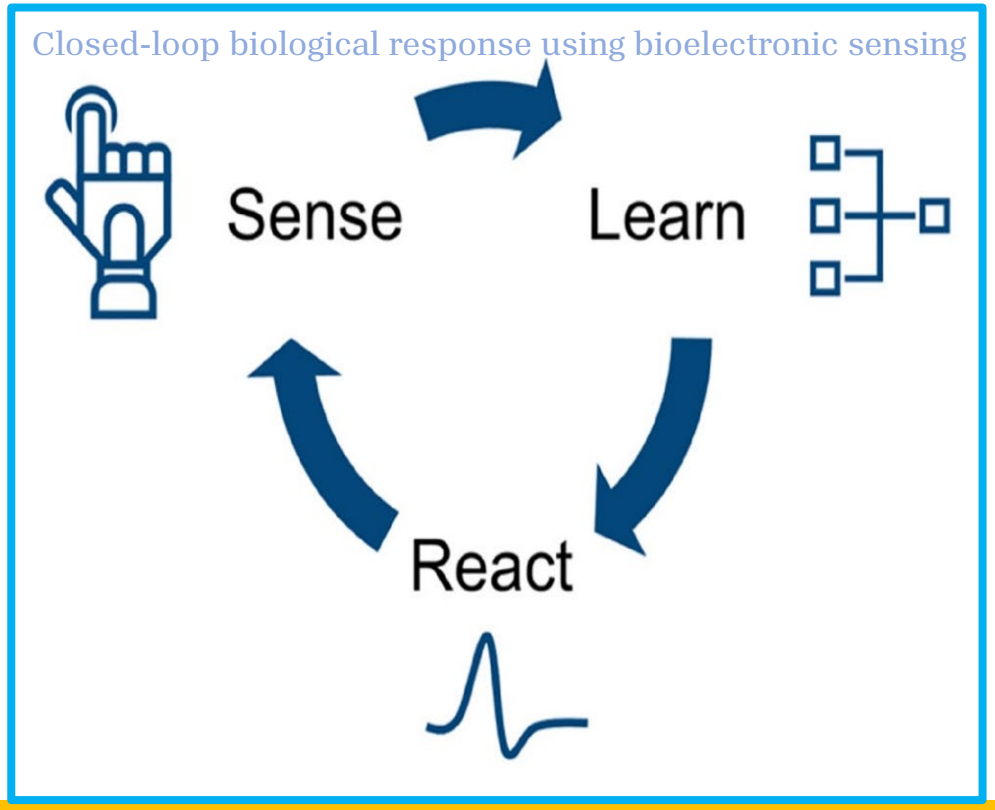
Digital Health Hematology Services (DHHS)

Dr Shoumen Palit Austin Datta

MIT Auto-ID Labs, Senior Member, Research Affiliate, Department of Mechanical Engineering, Massachusetts Institute of Technology ▪ shoumen@mit.edu

Senior Scientist, MDPnP Lab, Cybersecurity Program and SaAMS, Massachusetts General Hospital, Harvard Medical School ▪ sdatta8@mgh.harvard.edu

Digital Convergence of Biological Transactions



Data-Informed Decision Support (DIDS) Systems

Distributed Secure Near Real-time Mobile Digital Health Services

But, at a cost ...

Transaction Cost

The Sveriges Riksbank Prize in Economic Sciences in Memory of Alfred Nobel 1991

Ronald H. Coase

Ronald H. Coase
Facts

Photo from the Nobel Foundation archive.

Ronald H. Coase
The Sveriges Riksbank Prize in Economic Sciences in Memory of Alfred Nobel 1991

Born: 29 December 1910, Willesden, United Kingdom

Died: 2 September 2013, Chicago, IL, USA

Affiliation at the time of the award: University of Chicago, Chicago, IL, USA

Prize motivation: "for his discovery and clarification of the significance of transaction costs and property rights for the institutional structure and functioning of the economy"

https://www.nobelprize.org/prizes/economic-sciences/1991/coase/facts

BIOBANKS

Been there, done that?

UK Biobank is an intensively characterised prospective cohort of 500,000 adults aged 40–69 years, recruited between 2006 and 2010. The study was established to enable researchers worldwide to undertake health-related research in the public interest.

ELSEVIER

Health Policy and Technology

Volume 1, Issue 3, September 2012, Pages 123-126

UK Biobank: Current status and what it means for epidemiology

Naomi Allen [a b], Cathie Sudlow [a c], Paul Downey [a], Tim Peakman [a], John Danesh [d], Paul Elliott [e], John Gallacher [f], Jane Green [g], Paul Matthews [h], Jill Pell [i], Tim Sprosen [j], Rory Collins [a b], on behalf of UK Biobank [1]

Cambridge Prisms: Precision Medicine

www.cambridge.org/pcm

UK biobank: Enhanced assessment of the epidemiology and long-term impact of coronavirus disease-2019

Qi Feng[1,2], Ben Lacey[1,2], Jelena Bešević[1,2], Wemimo Omiyale[1,2], Megan Conroy[1,2], Fenella Starkey[1,2], Catherine Calvin[1,2], Howard Callen[1,2], Laura Bramley[1,2], Samantha Welsh[2], Allen Young[1,2], Mark Effingham[2], Alan Young[1,2], Rory Collins[1,2], Jo Holliday[1,2] and Naomi Allen[1,2]

[1]Oxford Population Health, Clinical Trial Service Unit and Epidemiological Studies Unit (CTSU), Nuffield Department of Population Health, University of Oxford, Oxford, UK and [2]UK Biobank, Stockport, Greater Manchester, UK

Review

Cite this article: Feng Q, Lacey B, Bešević J, Omiyale W, Conroy M, Starkey F, Calvin C, Callen H, Bramley L, Welsh S, Young A, Effingham M, Young A, Collins R, Holliday J and Allen N (2023). UK biobank: Enhanced assessment of the epidemiology and long-term impact of coronavirus disease-2019. *Cambridge Prisms: Precision Medicine*, **1**, e30, 1–9
https://doi.org/10.1017/pcm.2023.18

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Revised: 08 July 2023
Accepted: 18 July 2023

The Evolution of a Large Biobank at Mass General Brigham

Natalie T. Boutin [1], Samantha B. Schecter [1], Emma F. Perez [2], Natasha S. Tchamitchian [1], Xander R. Cerretani [1], Vivian S. Gainer [3], Matthew S. Lebo [1,2], Lisa M. Mahanta [1], Elizabeth W. Karlson [1,2,*] and Jordan W. Smoller [1,4]

[1] Mass General Brigham Personalized Medicine, Boston, MA 02115, USA
[2] Brigham and Women's Hospital, Boston, MA 02115, USA
[3] Mass General Brigham Research Information Science & Computing, Boston, MA 02115, USA
[4] Massachusetts General Hospital, Boston, MA 02114, USA
* Correspondence: ekarlson@bwh.harvard.edu; Tel.: +1-617-732-5078; Fax: +1-617-713-3030

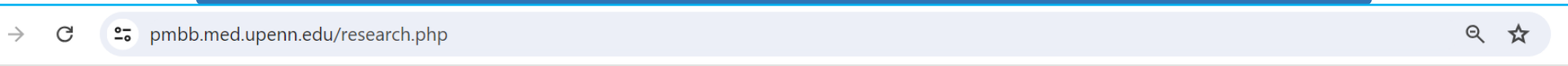
Abstract: The Mass General Brigham Biobank (formerly Partners HealthCare Biobank) is a large repository of biospecimens and data linked to extensive electronic health record data and survey data. Its objective is to support and enable translational research focused on genomic, environmental, biomarker and family history associations with disease phenotypes. The Biobank has enrolled more than 135,000 participants, generated genomic data on more than 65,000 of its participants, distributed approximately 153,000 biospecimens, and served close to 450 institutional studies with biospecimens or data. Although the Biobank has been successful, based on some measures of output, this has required substantial institutional investment. In addition, several challenges are ongoing, including: (1) developing a sustainable cost model that doesn't rely as heavily on institutional funding; (2) integrating Biobank operations into clinical workflows; and (3) building a research resource that is diverse and promotes equity in research. Here, we describe the evolution of the Biobank and highlight key lessons learned

Boutin NT, Schecter SB, Perez EF, Tchamitchian NS, Cerretani XR, Gainer VS, Lebo MS, Mahanta LM, Karlson EW, Smoller JW. Evolution of a Large Biobank at Mass General Brigham. J Personaized Medicine. 2022 August 17;12(8):1323. doi: 10.3390/jpm12081323. PMID: 36013271; PMCID: PMC9410531. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9410531/pdf/jpm-12-01323.pdf

MGB Biobank at MGH

The state-of-the-art Biobank at MGH provides researchers with access to high-quality samples to help foster research and advance the practice of medicine and our understanding of the causes of common diseases.

- Website: https://www.massgeneralbrigham.org/en/research-and-innovation/participate-in-research/biobank/for-researchers
- Mass General Brigham personalized medicine for information on how to obtain samples and how to collaborate with the Partners Biobank.



Penn Medicine BioBank Research

Revolutionizing Medicine: How Biobanks Are a Valuable Resource for Advancing Healthcare

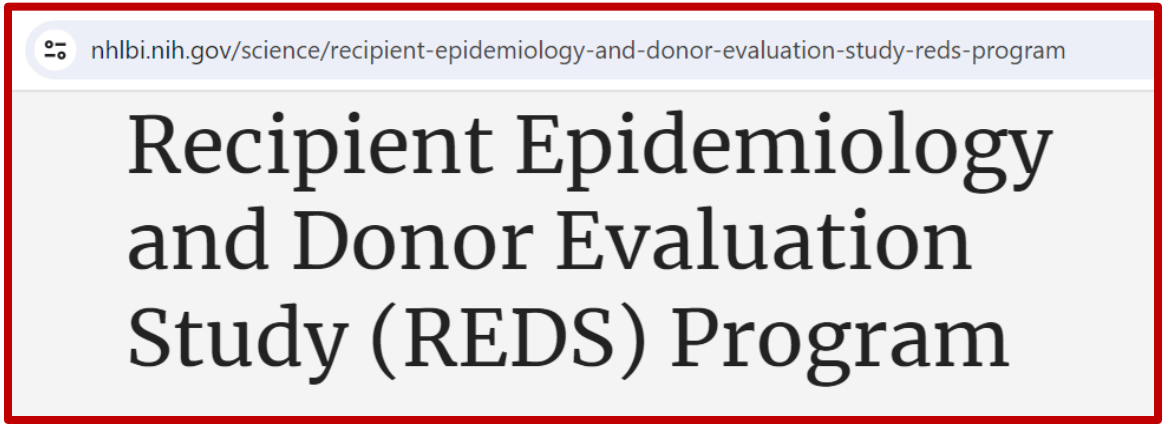
Biobanks play a pivotal role in modern healthcare. Biobanks are a warehouse of invaluable biological and genetic information that drive medical research, innovation, and personalized patient care. The Penn Medicine BioBank (PMBB) is a resource that collects and combines various health-related data, including medical records, genetic information, and lifestyle details from surveys, to aid in scientific studies and medical advancements. The PMBB is also part of a global initiative, the Global Biobank Meta-Analysis Initiative that merges genetic data from 23 biobanks worldwide, enhancing our understanding of disease and promoting drug discovery. Researchers and clinicians have developed tools to integrate genetic data and clinical data for precision medicine.

These tools have allowed researchers to:

- identify specific genes that are associated with different diseases
- identify shared genetic factors that may influence unrelated conditions, like cardiovascular disease and mental health disorders
- understand how genes impact how patients respond to certain medications
- study genes to predict the risk of developing diseases like urinary tract stones, different cancers, psychiatric disorders

What about blood bank and cord blood bank epidemiology?

Not much, yet.



What is the goal of the REDS program?

The goal of the REDS program is to evaluate and improve the safety and availability of the blood supply, as well as the safety and effectiveness of transfusion therapies. The program also works to proactively address potential emerging threats to the nation's blood supply and serves as a resource for ongoing work in transfusion research. Now in its fourth phase, the Recipient Epidemiology and Donor Evaluation Study-IV-Pediatric (REDS-IV-P) program aims primarily at improving the benefits of transfusion while reducing its risks; the REDS program also has a new focus on previously understudied populations.

Over the past 30 years, REDS has been the premier research program in blood collection and transfusion safety in the United States. **www.nhlbi.nih.gov**

Blood Bank

and

Cord Blood Bank

Epidemiology ??

www.brighamandwomens.org/obgyn/cord-blood-donation

www.dana-farber.org/how-you-can-help/get-involved/donate-bone-marrow-stem-cells

An element of DHHS ?

Blood Bank

and

Cord Blood Bank

Epidemiology

Foundation of DHHS ?

LIQUID BIOPSIES

SCALE POPULATION HEALTH USING LIQUID BIOPSIES VIA COMMUNITY BLOOD BANKS?

Angioni D, Delrieu J, Hansson O, Fillit H, Aisen P, Cummings J, Sims JR, Braunstein JB, Sabbagh M, Bittner T, Pontecorvo M, Bozeat S, Dage JL, Largent E, Mattke S, Correa O, Gutierrez Robledo LM, Baldivieso V, Willis DR, Atri A, Bateman RJ, Ousset PJ, Vellas B, Weiner M. ***Blood Biomarkers from Research Use to Clinical Practice: What Must Be Done? A Report from the EU/US CTAD Task Force.*** J Prev Alzheimers Dis. 2022; 9(4):569-579. doi: 10.14283/jpad.2022.85. PMID: 36281661; PMCID: PMC9683846. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9683846/pdf/nihms-1846920.pdf

Castro-Giner F, Gkountela S, Donato C, Alborelli I, Quagliata L, Ng CKY, Piscuoglio S, Aceto N. ***Cancer Diagnosis Using a Liquid Biopsy: Challenges and Expectations***. Diagnostics (Basel). 2018 May 9 ;8(2):31. doi: 10.3390/diagnostics8020031. PMID: 29747380; PMCID: PMC6023445. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6023445/pdf/diagnostics-08-00031.pdf

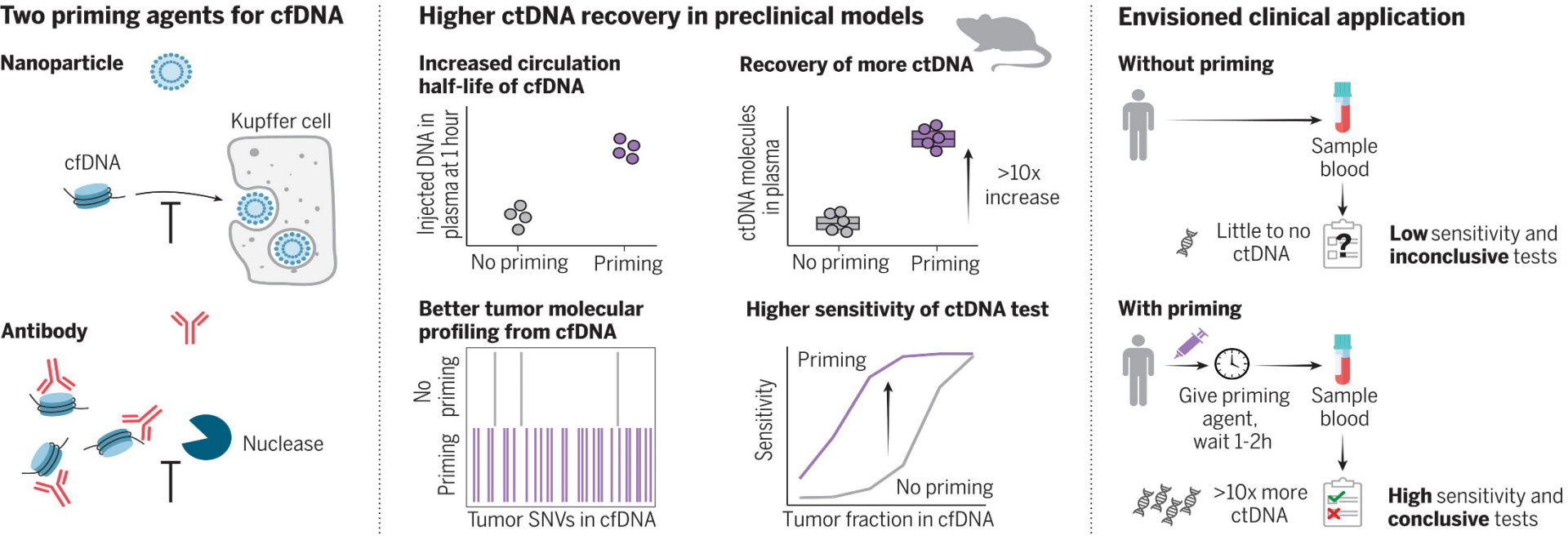
LIQUID BIOPSY (LB)

why it can scale

Liquid biopsies (LB) using blood can scale to reveal **personal** as well as **population health** signals (predictive) because blood draw in clinics and blood donation in community blood banks can be accomplished with relative ease and at a low cost even for resource constrained communities.

Key performance indicators (KPI) for liquid biopsies are sensitivity, predictive outcome (precision and accuracy). Key performance driver (KPD) is cost.

LIQUID BIOPSY - surpassing sensitivity limits by transiently augmenting the level of circulating tumor DNA (ctDNA) in blood (using nanoparticle priming agents) to attenuate clearance of cell-free DNA (cfDNA) in vivo.



https://www.science.org/doi/10.1126/science.adf2341

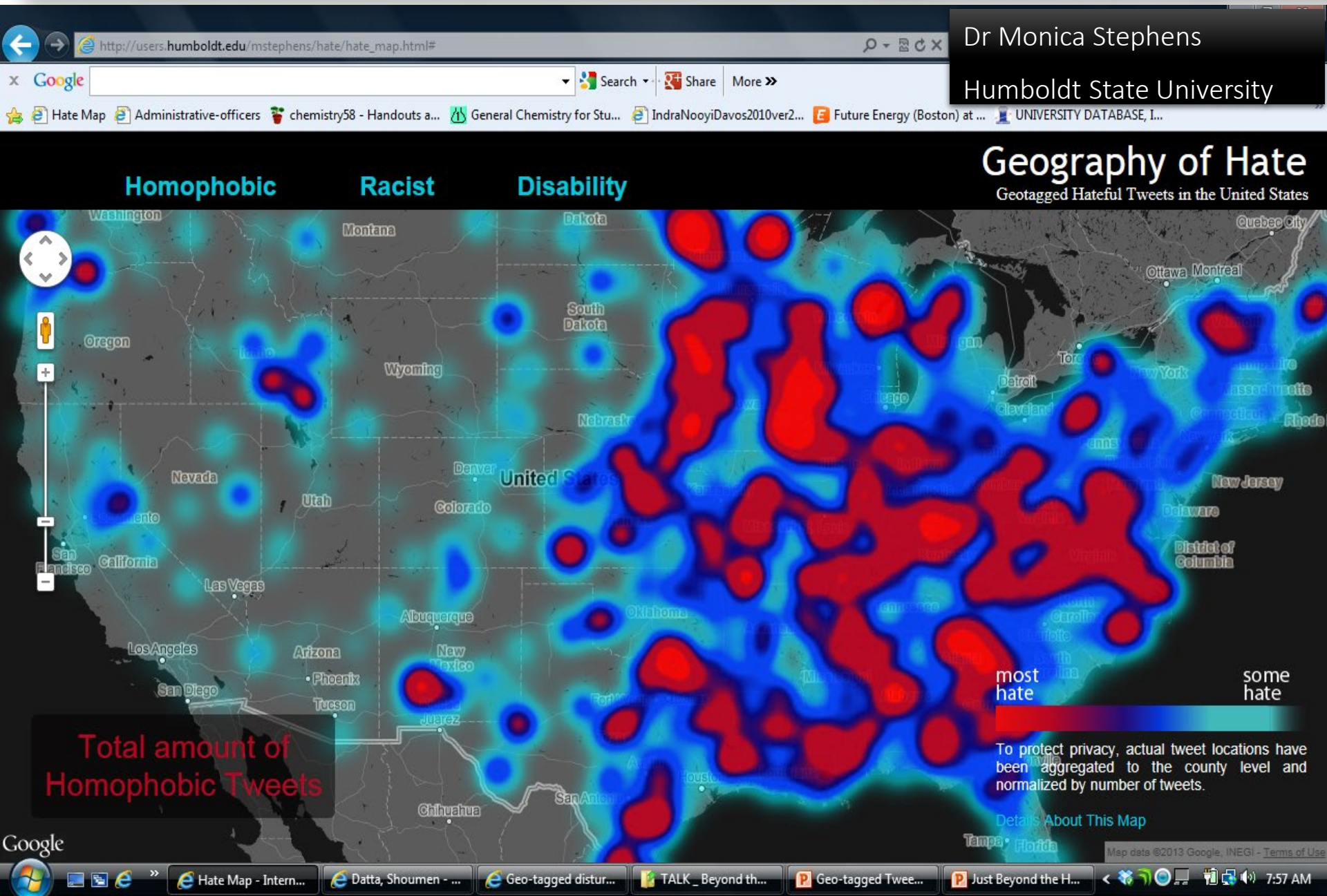
Priming agents (PA) reduce the clearance of cell-free (cf) DNA and enhance the sensitivity of liquid biopsies.

Priming agents transiently attenuate natural clearance mechanisms for cfDNA and consist of nanoparticles that act on the cells responsible for cfDNA clearance (top left) or DNA-binding antibodies that protect cfDNA from cellular uptake and enzymatic digestion (bottom left). In preclinical models, priming agents increased the half-life of cfDNA, enhanced recovery of circulating tumor (ct) DNA, and improved tumor molecular profiling from ctDNA and sensitivity of ctDNA testing (middle). PA's administered 1 to 2 hours prior to a blood draw, improves recovery of ctDNA and may boost the sensitivity of many types of liquid biopsy tests (right).

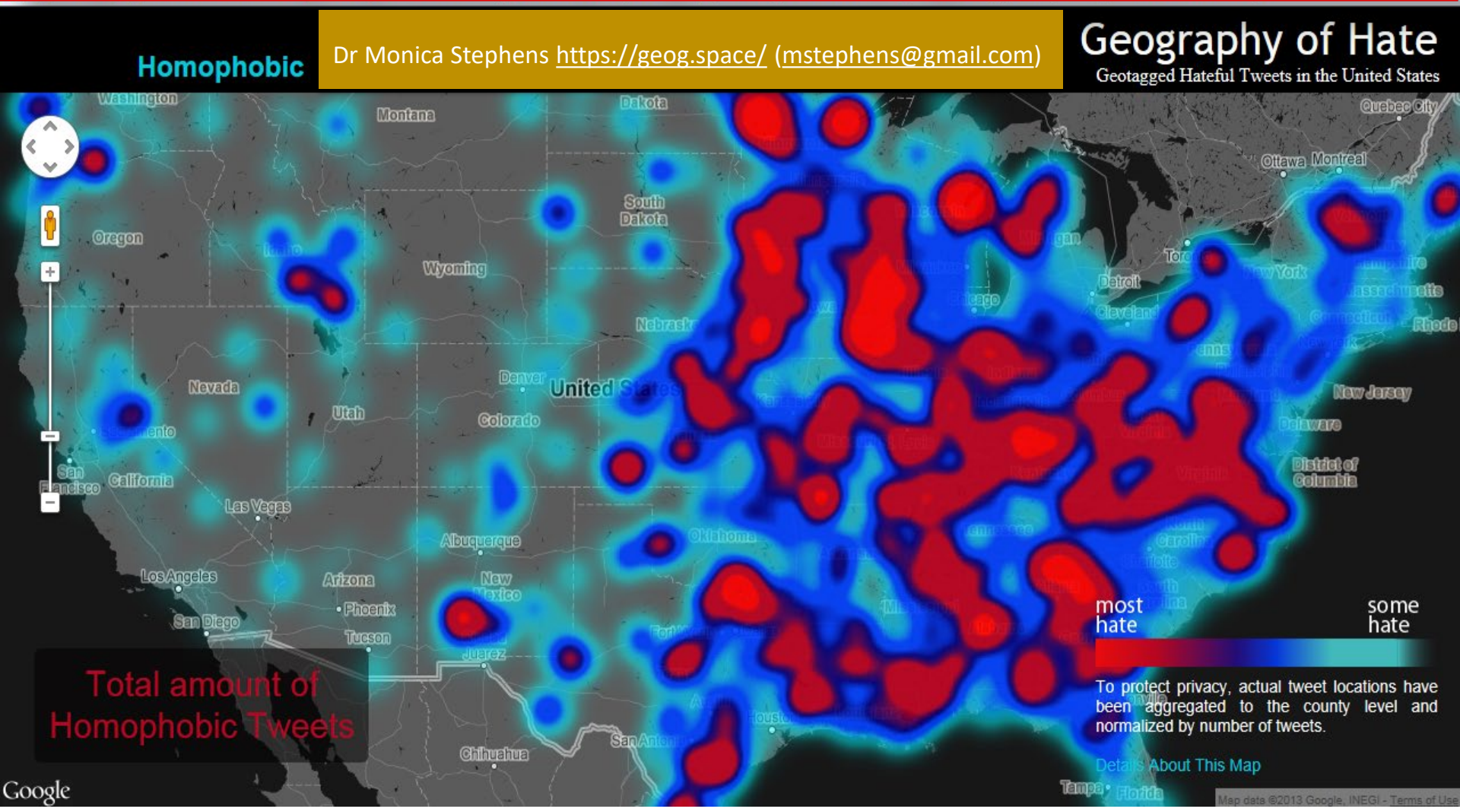
Twitter Data Analytics from Geo Tagged Social Signals

Dr Monica Stephens

Humboldt State University



Instead of mapping hate, let us map anonymized liquid biopsy data by zip code (e.g., cancer clusters?)



LIQUID BIOPSY (population genetics?) from BLOOD BANKS ?

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 14, 2024 VOL. 390 NO. 11

A Cell-free DNA Blood-Based Test for Colorectal Cancer Screening

Daniel C. Chung, M.D., Darrell M. Gray II, M.D., M.P.H., Harminder Singh, M.D., Rachel B. Issaka, M.D., M.A.S., Victoria M. Raymond, M.S., Craig Eagle, M.D., Sylvia Hu, Ph.D., Darya I. Chudova, Ph.D., AmirAli Talasaz, Ph.D., Joel K. Greenson, M.D., Frank A. Sinicrope, M.D., Samir Gupta, M.D., M.S.C.S., and William M. Grady, M.D.

Published March 13, 2024 ▪ N Engl J Med 2024;390:973-983 ▪ DOI: 10.1056/NEJMoa2304714

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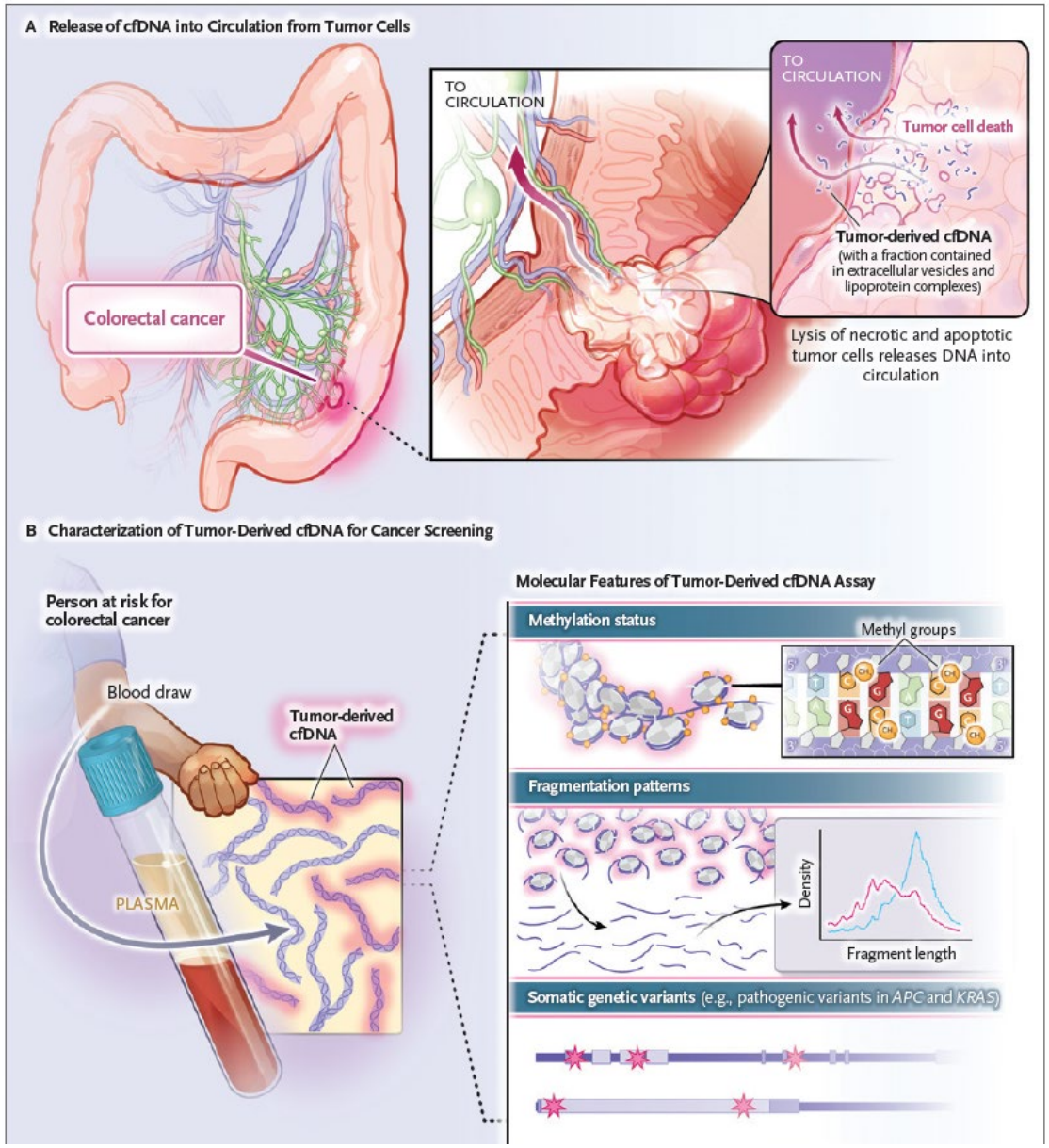


Chung DC, Gray DM 2nd, Singh H, Issaka RB, Raymond VM, Eagle C, Hu S, Chudova DI, Talasaz A, Greenson JK, Sinicrope FA, Gupta S, Grady WM. **A Cell-free DNA Blood-Based Test for Colorectal Cancer Screening.** N Engl J Med. 2024 March 14; 390(11):973-983. doi: 10.1056/NEJMoa2304714. PMID: 38477985.

LIQUID BIOPSY using samples from cord BLOOD BANKS

There is an **immense** (yet cryptic) potential for multi-generational epidemiologic studies to analyze bio-markers and specific precision changes in personal profiles over time and/or before/after any metabolic event (e.g., CoVID-19, CVD, COPD, PKD). The molecular metabolic signatures may be analyzed from stored blood in blood banks and pathology labs.

Proof is in the Pudding ?

FRAMINGHAM HEART STUDY

https://www.nhlbi.nih.gov/science/framingham-heart-study-fhs

FHS began in 1948. This is what was reported in 2024

Li C, Stražar M, Mohamed AMT, Pacheco JA, Walker RL, Lebar T, Zhao S, Lockart J, Dame A, Thurimella K, Jeanfavre S, Brown EM, Ang QY, Berdy B, Sergio D, Invernizzi R, Tinoco A, Pishchany G, Vasan RS, Balskus E, Huttenhower C, Vlamakis H, Clish C, Shaw SY, Plichta DR, Xavier RJ. ***Gut microbiome and metabolome profiling in Framingham heart study reveals cholesterol-metabolizing bacteria.*** Cell. 2024 March 21: S0092-8674(24)00305-2. doi: 10.1016/j.cell.2024.03.014 https://pubmed.ncbi.nlm.nih.gov/38569543/

FRAMINGHAM HEART STUDY

https://www.nhlbi.nih.gov/science/framingham-heart-study-fhs

Stool metagenomics and metabolomics from **1,429 Framingham Heart Study** participants revealed microbiome and metabolome composition. Specifically, the study found bacterial species from the *Oscillibacter* genus were associated with decreased fecal and plasma cholesterol levels. A bacterial enzyme called ismA can metabolize cholesterol into coprostanol, a lipid excreted, instead of absorbed by the body. Gut bacteria, including several *Oscillibacter* species, correlate with lower cholesterol levels in people. These bacteria could also metabolize cholesterol in lab experiments. Whether these bacteria can directly influence blood cholesterol in people needs to be confirmed. If delivered to the right place in the gut, it might lead to new treatments using bacteria to transform artery-clogging cholesterol into a more harmless form. How about direct enzyme (ismA) delivery using mRNA?

FRAMINGHAM HEART STUDY - *started in 1948 and still helpful*

Li C, Stražar M, Mohamed AMT, Pacheco JA, Walker RL, Lebar T, Zhao S, Lockart J, Dame A, Thurimella K, Jeanfavre S, Brown EM, Ang QY, Berdy B, Sergio D, Invernizzi R, Tinoco A, Pishchany G, Vasan RS, Balskus E, Huttenhower C, Vlamakis H, Clish C, Shaw SY, Plichta DR, Xavier RJ. ***Gut microbiome and metabolome profiling in Framingham heart study reveals cholesterol-metabolizing bacteria.*** Cell. 2024 March 21: S0092-8674(24)00305-2. doi: 10.1016/j.cell.2024.03.014 https://pubmed.ncbi.nlm.nih.gov/38569543/

https://www.nhlbi.nih.gov/science/framingham-heart-study-fhs

What is the goal of the FHS?

The NHLBI has a long history of supporting large population and epidemiology studies that have transformed the way the public approaches heart disease. These studies involve studying the health of various populations to uncover patterns, trends, and outcomes that may be applicable to the general population. When it launched in 1948 the original goal of the Framingham Heart Study (FHS) was to identify common factors or characteristics that contribute to cardiovascular disease. Over the years, the FHS has become a successful, multigenerational study that analyzes family patterns of cardiovascular and other diseases, while gathering more genetic information from the two generations that followed the original study participants. The FHS also has expanded to include diverse populations so that risk factors in these different groups can be understood.

NIH National Heart, Lung, and Blood Institute

75 YEARS Bringing Research to Life

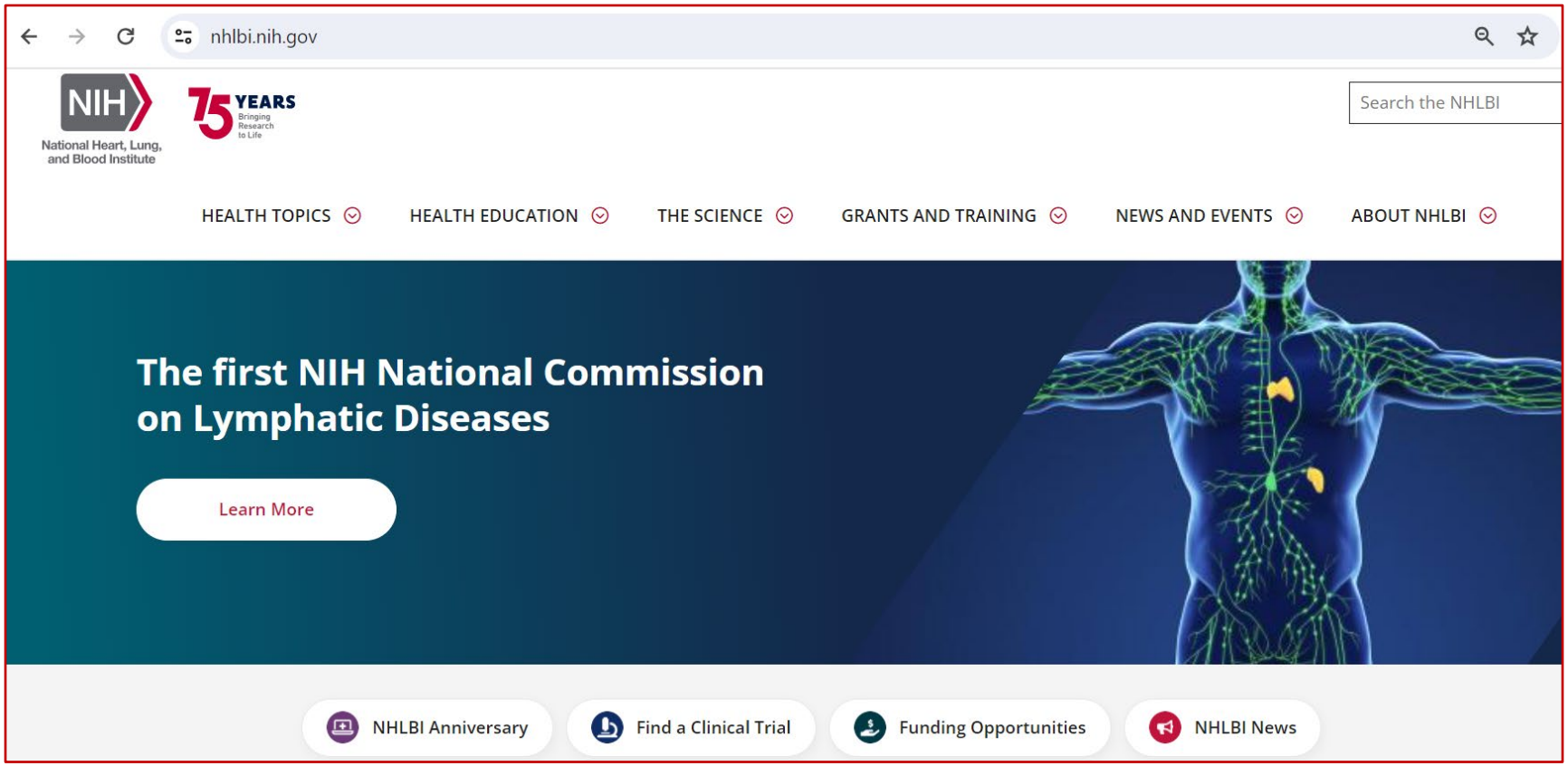
> FHS is a longitudinal study

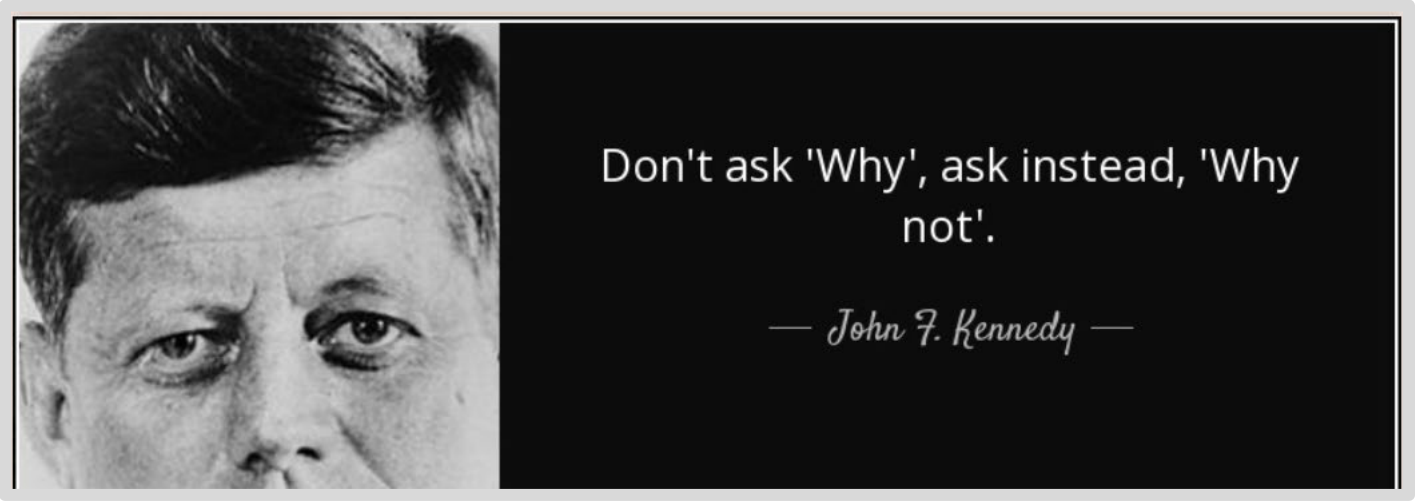
- *The FHS had over 15,000 people from three generations, including the original participants, their children, and their grandchildren at the start of each cohort.*
- *FHS findings have informed the understanding of how cardiovascular health affects the rest of the body.*
- *The study found high blood pressure and high blood cholesterol to be major risk factors for cardiovascular disease.*
- *In the past half century, the study has produced approximately 6,000 articles in leading medical journals.*
- *Data and biologic resources from the study are available for researchers to use, which continue to spur new scientific discoveries.*

What is possible using data from research on stored blood bank samples (cord blood)?

Molecular metabolomics, proteomics & genetics of diseases?

this is happening …





nhlbi.nih.gov

NIH National Heart, Lung, and Blood Institute

75 YEARS Bringing Research to Life

Search the NHLBI

HEALTH TOPICS | HEALTH EDUCATION | THE SCIENCE | GRANTS AND TRAINING | NEWS AND EVENTS | ABOUT NHLBI

The first NIH National Commission

Blood Bank Repositories for Research

NHLBI Anniversary | Find a Clinical Trial | Funding Opportunities | NHLBI News

Tsunami

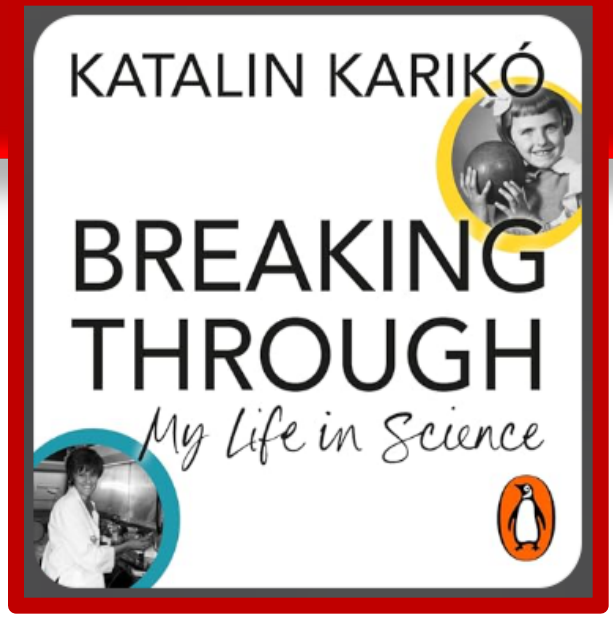
of research findings, waiting to happen!

Blood Bank Repositories for Research

Tsunami

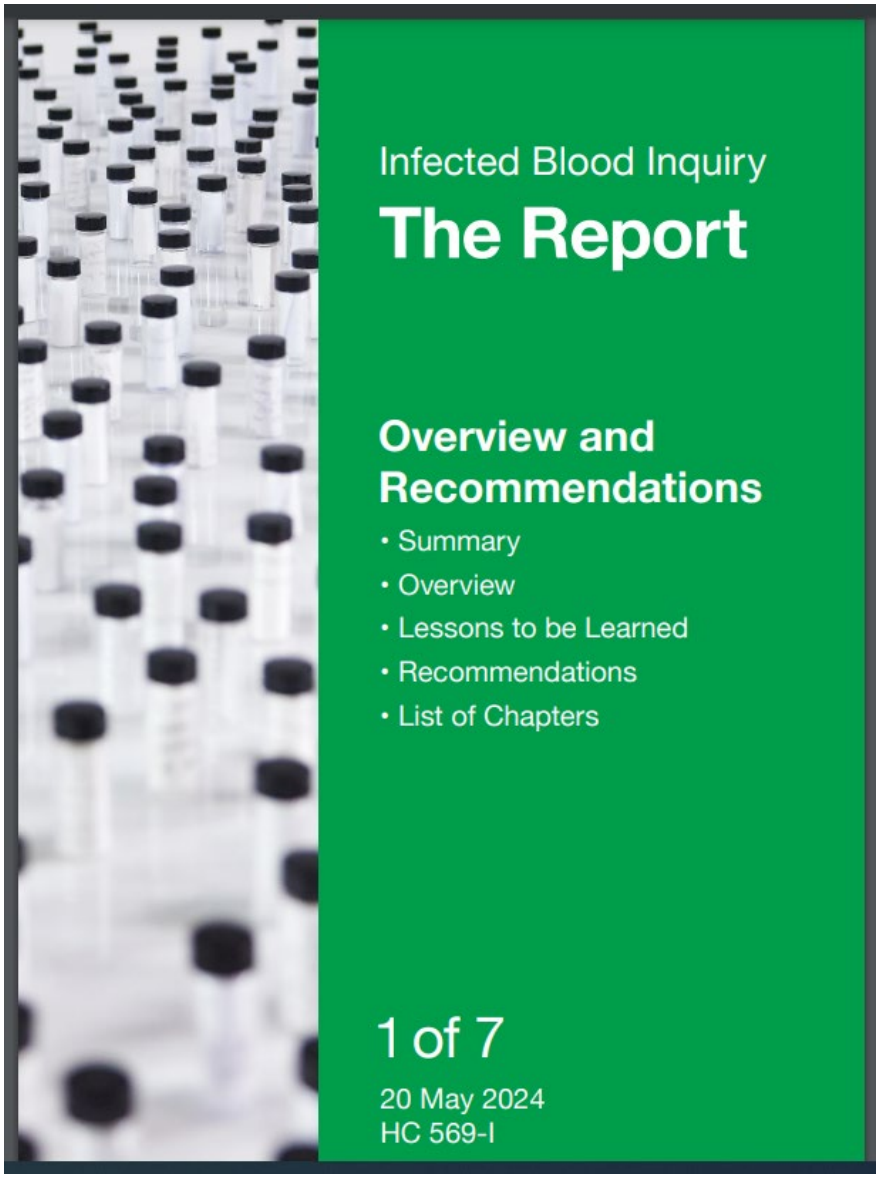
of research findings, waiting to happen!

Tsunami needs to be triggered
Research needs leader to breakthrough



www.nobelprize.org/prizes/medicine/2023/kariko/facts

https://www.infectedbloodinquiry.org.uk/reports/inquiry-report



Volume 1
https://www.infectedbloodinquiry.org.uk/sites/default/files/Volume_1.pdf

Volume 2
https://www.infectedbloodinquiry.org.uk/sites/default/files/Volume_2.pdf

Volume 3
https://www.infectedbloodinquiry.org.uk/sites/default/files/Volume_3.pdf

Volume 4
https://www.infectedbloodinquiry.org.uk/sites/default/files/Volume_4.pdf

Volume 5
https://www.infectedbloodinquiry.org.uk/sites/default/files/Volume_5.pdf

Volume 6
https://www.infectedbloodinquiry.org.uk/sites/default/files/Volume_6.pdf

Volume 7
https://www.infectedbloodinquiry.org.uk/sites/default/files/Volume_7.pdf

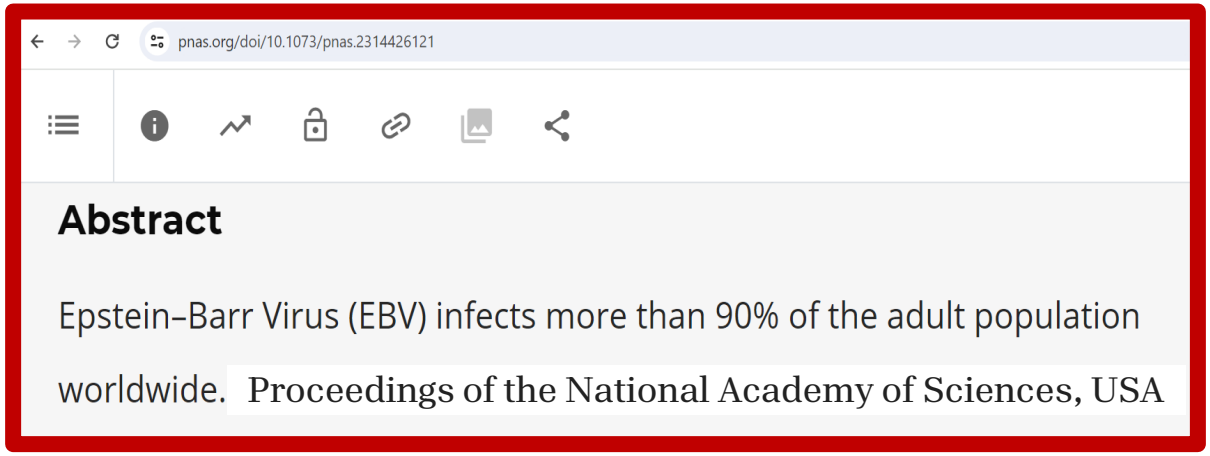
https://www.infectedbloodinquiry.org.uk/reports/final-report-volume-1.html

Tsunami

of research findings, waiting to happen!

Just think of one example ➔

EBV



90% of the adult population is infected with Epstein-Barr Virus (EBV), worldwide.

Maroui MA, Odongo GA, Mundo L, Manara F, Mure F, Fusil F, Jay A, Gheit T, Michailidis TM, Ferrara D, Leoncini L, Murray P, Manet E, Ohlmann T, De Boevre M, De Saeger S, Cosset FL, Lazzi S, Accardi R, Herceg Z, Gruffat H, Khoueiry R. (2024) ***Aflatoxin B1 and Epstein-Barr virus-induced CCL22 expression stimulates B cell infection.*** Proceedings of the National Academy of Sciences U S A. 2024 April 16; 121(16):e2314426121. doi: 10.1073/pnas.2314426121. Epub 2024 April 4. PMID: 38574017 https://pubmed.ncbi.nlm.nih.gov/38574017/

Data

from cross-sectional research, still chained in blood banks and labs?

Can we detect EBV in stored blood samples?

Yes

?

Gulley ML. ***Molecular diagnosis of Epstein-Barr virus-related diseases.*** J Mol Diagn. 2001 Feb; 3(1):1-10. doi: 10.1016/S1525-1578(10)60642-3. PMID: 11227065; PMCID: PMC1907346.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1907346/pdf/0043.pdf

Ayee R, Ofori MEO, Wright E, Quaye O. (2020) ***Epstein Barr Virus Associated Lymphomas and Epithelia Cancers in Humans.*** J Cancer 2020; 11(7):1737-1750. doi:10.7150/jca.37282. https://www.jcancer.org/v11p1737.htm

Establishment of latent infection by EBV has been implicated in several malignancies [30] due to the expression of limited sets of latent proteins, shown to play various biological roles discussed in Table 1.

Table 1

Biological activities of Epstein Barr virus latency stage gene products and associated cancers

EBV associated cancers

EBV latency protein	Type of latency	Biological activity	Associated cancers[d]
EBNA-1[a]	Latency I, II, III	Segregation of viral genome in progenies, DNA replication, inhibition of MHC class I, enhances p53 degradation	Burkitt lymphoma, Gastric cancer, Breast cancer
EBNA-2	Latency III	Upregulation of host and viral proteins (transactivation), facilitate B cell immortalization	Posttransplant lymphoproliferative disorder
EBNA-3	Latency III	Transcription transactivation of both host and viral proteins, immortalization of B cell	Posttransplant lymphoproliferative disorder
EBNA-LP[b]	Latency III	Transactivation of EBNA-2 to inactivate tumor suppressors, essential for immortalization of B cells	Posttransplant lymphoproliferative disorder
LMP-1/2[c]	Latency II/III	B cell survival, upregulation of antiapoptotic proteins, mimics CD 40 ligand associated signaling, constitutively activate growth and cell survival promoting signaling pathways	Hodgkin lymphoma, Nasopharyngeal cancer, Posttransplant lymphoproliferative disorder, T/NK cell lymphoma, Breast cancer
EBV-Micro RNAs	Latency I, II, III	Target host mRNAs involved in apoptosis, proliferation and transformation. Suppress antigen presentation and activation of immune cells	Gastric cancer, T/NK cell lymphoma, nasopharyngeal cancer

[a] EBNA-1 is expressed and detected in all EBV associated malignancies. [b] EBNA-LP is also known as EBNA-5. [c] LMP-1/2 are both involved in epithelia and B cell tumors, however, LMP 2 is frequently detected in a majority of all tumors as compared to LMP-1. [d] The associated tumors are not only limited to the ones discussed in this review.

Transmission of EBV through transplantation and blood transfusion has been reported. EBV establishes latent infection in B lymphocytes where it expresses limited sets of proteins (ETPs, EBNAs, LMP) and EBER. Hematopoietic cell derived tumors include but not limited to Burkitt's lymphoma, Hodgkin lymphoma, post-transplant lymphoproliferative disorders, and natural killer (NK)/T cell lymphoma. EBV also causes epithelia derived malignancies such as nasopharyngeal cancer, gastric cancer, and breast cancer.

Information

from research findings just from one virus may save millions of lives.

If we can't detect, we can't treat, we can't cure

Blood Banks ?

Real potential for cross-sectional data to feed and morph into longitudinal epidemiologic study.

Lancet. 1964 Mar 28;1(7335):702-3. doi: 10.1016/s0140-6736(64)91524-7.

VIRUS PARTICLES IN CULTURED LYMPHOBLASTS FROM BURKITT'S LYMPHOMA

M A EPSTEIN, B G ACHONG, Y M BARR

PMID: 14107961 DOI: 10.1016/s0140-6736(64)91524-7

That's why it is called Epstein-Barr Virus.

90% of 8 billion people are infected with EBV

Sir Michael Anthony Epstein (1921–2024)

Codiscoverer of the Epstein-Barr virus

RICHARD F. AMBINDER AND RENA R. XIAN Authors Info & Affiliations

SCIENCE · 18 Apr 2024 · Vol 384, Issue 6693 · p. 274 · DOI: 10.1126/science.adp2961

Lancet. 1964 Mar 28;1(7335):702-3. doi: 10.1016/s0140-6736(64)91524-7.

VIRUS PARTICLES IN CULTURED LYMPHOBLASTS FROM BURKITT'S LYMPHOMA

M A EPSTEIN, B G ACHONG, Y M BARR

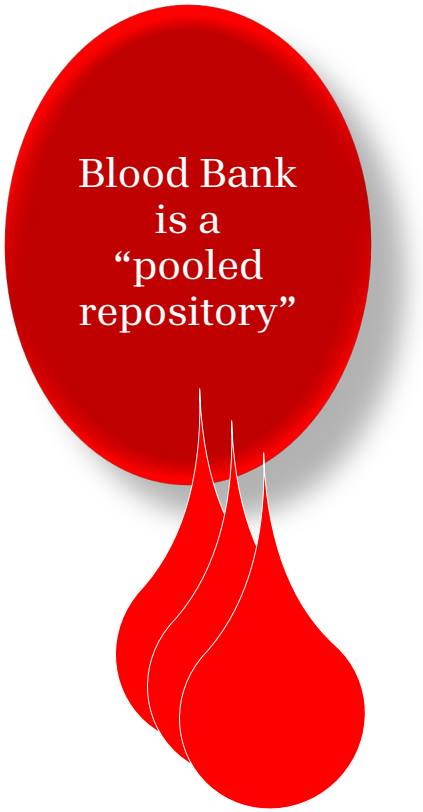
PMID: 14107961 DOI: 10.1016/s0140-6736(64)91524-7

Sir Michael Anthony Epstein, pathologist who identified the first known human cancer–causing virus, died on **6 February 2024** at the age of 102. His team's pioneering work investigating primary tumor tissue and cultured tumor specimens from Ugandan children with jaw tumors identified the virus that now bears his name: the Epstein-Barr virus (EBV). EBV is associated with the tumor Epstein was studying, now known as Burkitt lymphoma, as well as a variety of other cancers and illnesses, including infectious mononucleosis and multiple sclerosis.

https://doi.org/10.1126/science.adp2961

Born in London, England, on 18 May 1921, Epstein studied medicine at Trinity College at the University of Cambridge and Middlesex Hospital Medical School in London. After national service with the Royal Army Medical Corps in India, he returned to the Middlesex Hospital, where there was interest in, as he wrote in his chapter of *Epstein Barr Virus Volume 1*, "the then deeply unfashionable chicken cancer viruses." In 1911, Peyton Rous had characterized a virus in chickens that led to cancer, but there had been little interest in the implications. In 1956, Epstein spent a year studying electron microscopy with George Palade at the Rockefeller Institute in New York City. Palade convinced Epstein that viruses could be categorized on the basis of how they looked. Epstein again returned to the Middlesex Hospital, where he investigated the morphology of Rous sarcoma virus with electron microscopy and showed that it was an RNA virus.

Epstein was thus familiar with both cancer-causing viruses and electron microscopy when he happened to attend a lunchtime lecture by Denis Burkitt on a cancer prevalent in African children. Burkitt was a British Colonial Service medical officer based in Uganda, on leave in the UK. He described a tumor that typically arose in the jaw and quickly led to death, but what most interested Epstein was Burkitt's data showing that the geographical distribution of the tumor in Africa depended on temperature and rainfall. This suggested to Epstein that, as he wrote later, "a biological agent must play a part in causation," and he immediately "postulated a climate-dependent arthropod vector spreading a cancer-causing virus." Epstein decided to halt his current work and look for a virus in the lymphoma. He obtained funding from the British Empire Cancer Campaign (later Cancer Research UK) to travel to Uganda to, as he wrote, "work out how a regular supply of lymphoma samples" could be flown to his laboratory in London for testing.



ncbi.nlm.nih.gov/pmc/articles/PMC5618724/

Journal Article

T1-mapping using the Shortened Modified Look-Locker Inversion Recovery (ShMOLLI) technique has been validated in single- and multi-center clinical studies for a variety of cardiovascular diseases [17–28, 30–41]. It is also used in the UK Biobank (over 10,000 datasets acquired; projected total: 100’000, [42, 43]), and the ongoing multi-centre Hypertrophic Cardiomyopathy Registry study (HCMR; 2750 patients, [42–44]). We have a large resource of clinical and research scans with T1-mapping accumulated from pooled evidence from the past 7 years [18, 19, 23, 24, 26, 28, 30, 31, 34, 35, 39, 45]. In this study of 1291 subjects, we characterized commonly encountered clinical myocardial conditions using T1-mapping, derived native T1 ranges, and produced sample-size calculations to guide future clinical studies and trials.

Liu *et al. Journal of Cardiovascular Magnetic Resonance* (2017) 19:74
DOI 10.1186/s12968-017-0386-y

Journal of Cardiovascular Magnetic Resonance

RESEARCH Open Access

Measurement of myocardial native T1 in cardiovascular diseases and norm in 1291 subjects

Joanna M. Liu[1], Alexander Liu[1], Joana Leal[1], Fiona McMillan[1], Jane Francis[1], Andreas Greiser[2], Oliver J. Rider[1], Saul Myerson[1], Stefan Neubauer[1], Vanessa M. Ferreira[1] and Stefan K. Piechnik[1*]

Liu JM, Liu A, Leal J, McMillan F, Francis J, Greiser A, Rider OJ, Myerson S, Neubauer S, Ferreira VM, Piechnik SK. ***Measurement of myocardial native T1 in cardiovascular diseases and norm in 1291 subjects.*** J Cardiovasc Magn Reson. 2017 September 28;19(1):74. doi: 10.1186/s12968-017-0386-y https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5618724/pdf/12968_2017_Article_386.pdf

ncbi.nlm.nih.gov/pmc/articles/PMC6861460/table/T1/?report=objectonly

https://doi.org/10.1182/blood-2016-06-721688

Table I

Delobel J, Rubin O, Prudent M, Crettaz D, Tissot JD, Lion N. (2010) ***Biomarker analysis of stored blood products: emphasis on pre-analytical issues.*** Int J Mol Sci. 2010 November 17;11(11):4601-4617. doi: 10.3390/ijms11114601. www.ncbi.nlm.nih.gov/pmc/articles/PMC3000103/pdf/ijms-11-04601.pdf

Parameters	Day 0	Day 3	Day 7	Day 14	Day 28	P value
Sodium	152.8 ± 4.01	150.1 ± 2.89	147.9 ± 1.41	143.1 ± 1.97	141.9± 3.99	<0.001
Potassium	4.33±1.29	6.73±2.43	9.93±2.97	14.16±4.56	19.89±4.01	<0.001
Chloride	86.32±1.96	89.55±2.05	93.91±2.44	96.83±2.19	91.34±1.09	<0.001
Calcium	0.06+0.007	0.062±0.005	0.063±0.004	0.0067±0.001	0.0066±0.021	NS
Urea	27.71±3.99	25.19±2.70	26.11±3.18	24.32±2.45	24.17±2.56	NS
Creatinine	0.99±0.04	1.02±0.02	1.07±0.04	1.01±0.06	1.02±0.01	NS
AST (mg/dl)	21.95 ± 4.91	23.54±6.32	28.43±3.22	38.26±9.90	44.31±8.55	<0.001
ALT (mg/dl)	40.65±13.65	40.43±18.89	39.54±23.66	44.87±13.76	46.32±10.87	0.487
LDH (mg/dl)	202.54±17.87	289.21±23.98	487.91±97.93	523.65±113.54	643.32±187.8	<0.001
Proteins (g/dl)	6.76±0.77	6.43±0.76	5.99±0.11	6.87±0.3	6.7±0.88	NS
PH	7.22±0.18	7.01±0.33	6.91±0.44	6.89±0.23	6.77±0.54	<0.001

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6861460/pdf/PJMS-35-1697.pdf

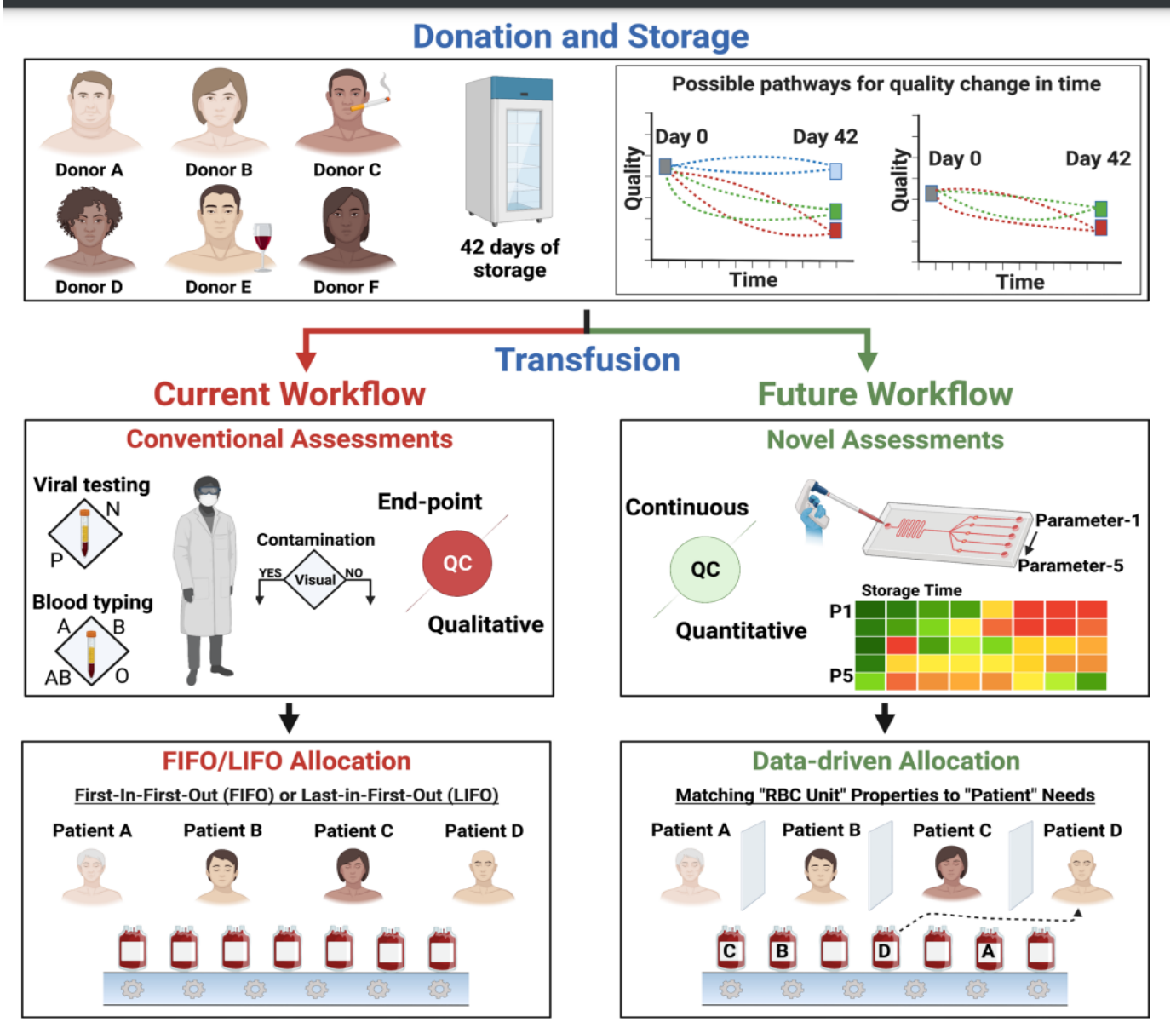


Fig. 1. The current and proposed future workflow for RBC storage and transfusion medicine.

Isiksacan Z, D'Alessandro A, Wolf SM, McKenna DH, Tessier SN, Kucukal E, Gokaltun AA, William N, Sandlin RD, Bischof J, Mohandas N, Busch MP, Elbuken C, Gurkan UA, Toner M, Acker JP, Yarmush ML, Usta OB. *Assessment of stored red blood cells through lab-on-a-chip technologies for precision transfusion medicine.* Proc Natl Acad Sci U S A. 2023 August 8; 120(32):e2115616120. doi: 10.1073/pnas.2115616120 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10410732/pdf/pnas.202115616.pdf

blood®

Volume 143, Issue 5, 1 February 2024, Pages 456-472

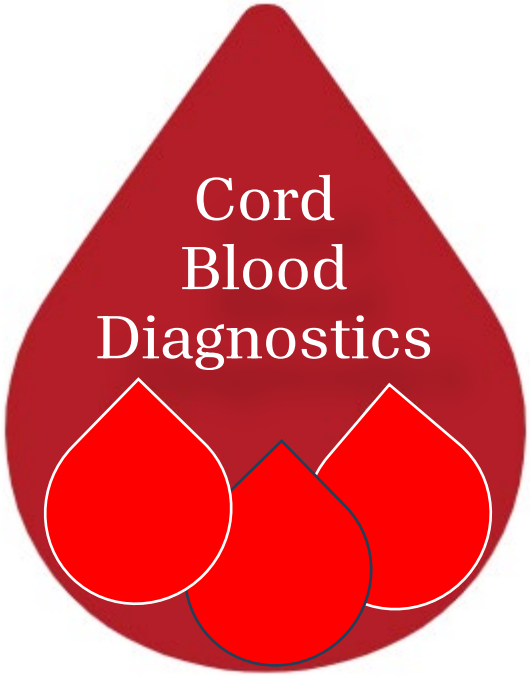
TRANSFUSION MEDICINE

Regulation of kynurenine metabolism by blood donor genetics and biology impacts red cell hemolysis invitro and invivo

Travis Nemkov [*1,2], Daniel Stephenson [*1], Christopher Erickson [1], Monika Dzieciatkowska [1], Alicia Key [1], Amy Moore [3], Eric J. Earley [3], Grier P. Page [3], Ian S. Lacroix [1], Mars Stone [4,5], Xutao Deng [4,5], Thomas Raife [6], Steven Kleinman [7], James C. Zimring [8], Nareg Roubinian [4,5,9], Kirk C. Hansen [1], Michael P. Busch [4,5], Philip J. Norris [4,5], Angelo D'Alessandro [1,2], Recipient Epidemiology and Donor Evaluation Study-IV-P

Kynurenine is a marker of osmotic fragility, and its levels are reproducible within a donor across donations. Polymorphisms in SLC7A5, ATXN2 are associated with kynurenine levels in stored RBCs, Hgb increments, and in vivo hemolysis upon transfusion. https://doi.org/10.1182/blood.2023022052

Data analyses from cord blood are a cross-sectional study with potential for longitudinal research.



Bio-markers on-a-chip may lead to predictive/prognostic clues for personalized risk mitigation clinical strategies.

Guibert N, Pradines A, Favre G, Mazieres J. ***Current and future applications of liquid biopsy in non-small cell lung cancer from early to advanced stages.*** Eur Respir Rev. 2020 February 12; 29(155):190052. doi: 10.1183/16000617.0052-2019. PMID: 32051167; PMCID: PMC9488537. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9488537/pdf/ERR-0052-2019.pdf

Šutić M, Vukić A, Baranašić J, Försti A, Džubur F, Samaržija M, Jakopović M, Brčić L, Knežević J. (2021) ***Diagnostic, Predictive, and Prognostic Biomarkers in Non-Small Cell Lung Cancer (NSCLC) Management.*** J Pers Med. 2021 October 27;11(11):1102. doi: 10.3390/jpm11111102. PMID: 34834454; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8624402/pdf/jpm-11-01102.pdf

The Minimal Dataset for Cancer of the 1+Million Genomes Initiative www.biorxiv.org/content/10.1101/2023.10.07.561259v1.full.pdf+html

Imagine the treasure trove of data hiding in stored blood samples in blood banks

What epidemiology of blood donors can reveal about population public health

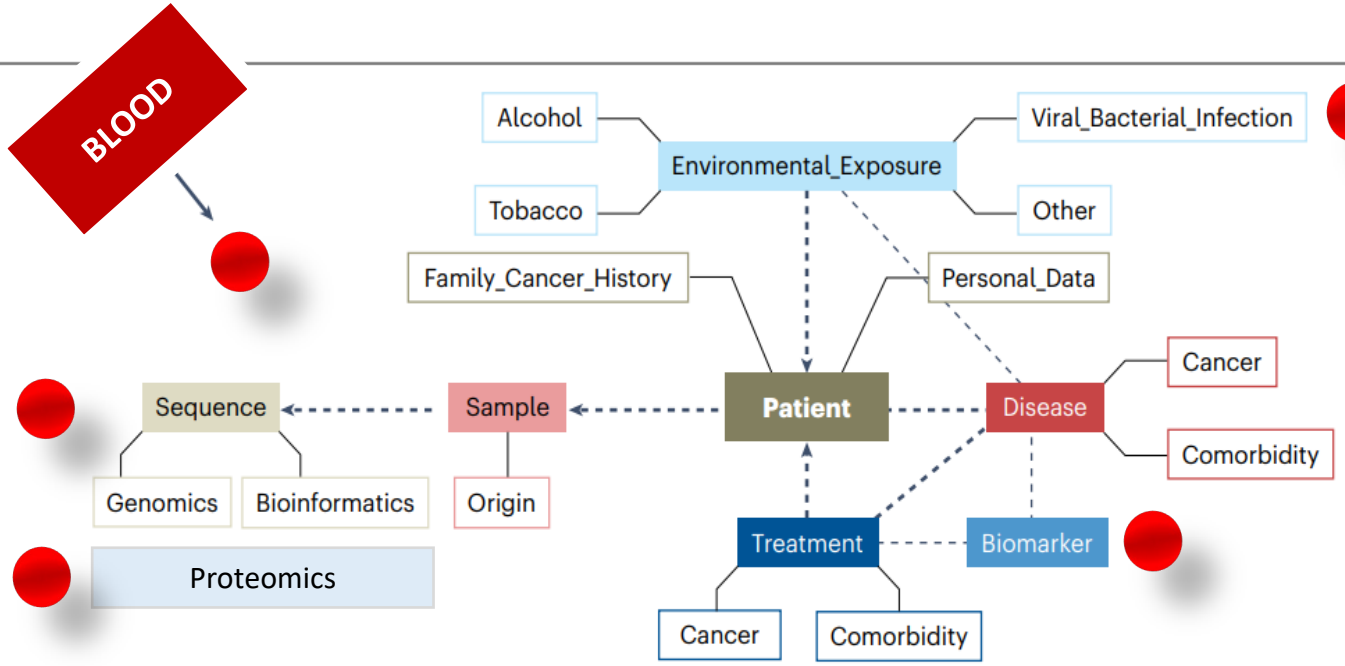


Fig. 1 | The 1+MG-MDC structure. Illustration of the 1+MG-MDC structure, comprising eight conceptual domains and related subdomains. Thick dotted lines indicate connections between domains, in some instances an additional arrowhead denotes directionality. Thin dotted lines indicate potential relationships between domains. Adapted from ref. 6.

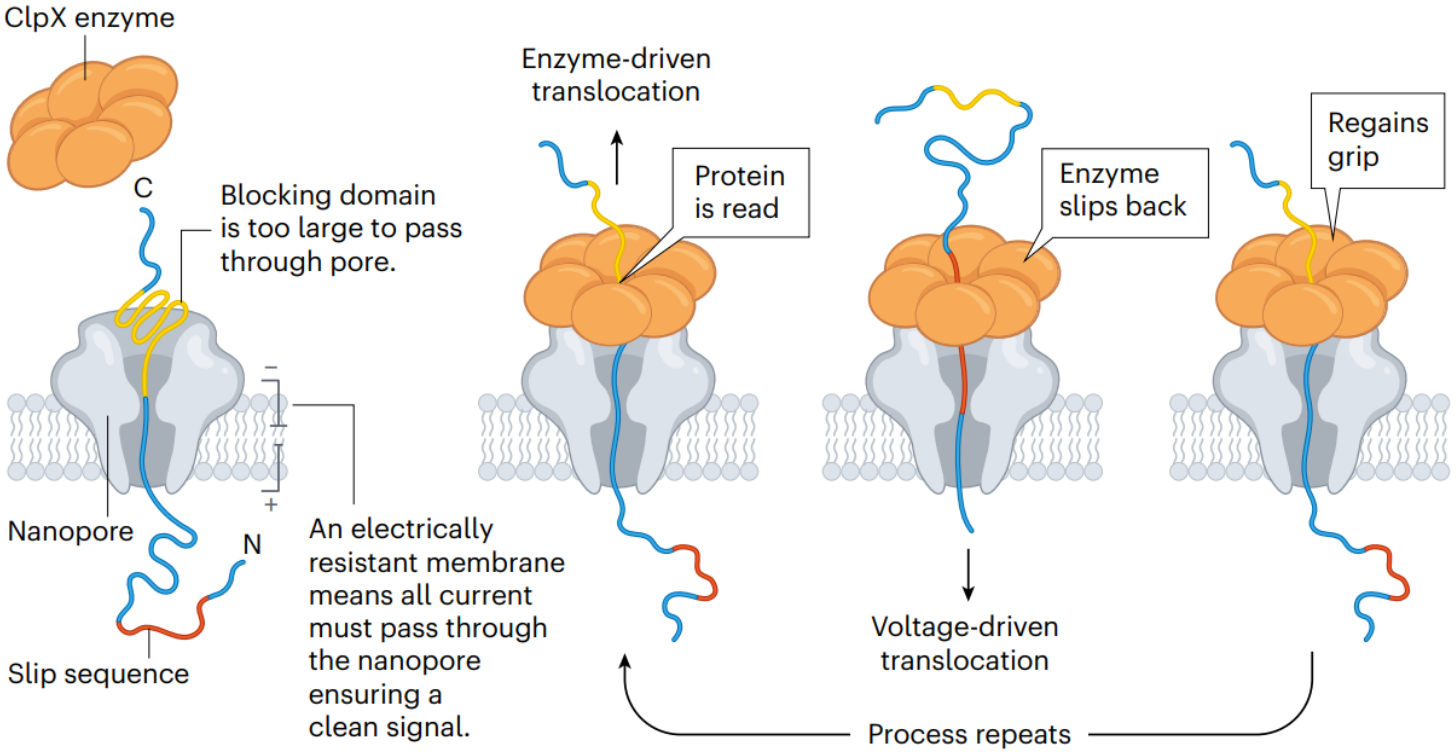
https://www.nature.com/articles/s41588-024-01721-x.pdf

Riba M, Sala C, Culhane AC, Flobak Å, Patocs A, Boye K, Plevova K, Pospíšilová Š, Gandolfi G, Morelli MJ, Bucci G, Edsjö A, Lassen U, Al-Shahrour F, Lopez-Bigas N, Hovland R, Cuppen E, Valencia A, Poirel HA, Rosenquist R, Scollen S, Arenas Marquez J, Belien J, De Nicolo A, De Maria R, Torrents D, Tonon G. **The 1+Million Genomes Minimal Dataset for Cancer.** Nat Genet. 2024 May 3. doi: 10.1038/s41588-024-01721-x

https://media.nature.com/original/magazine-assets/d41586-024-01280-5/d41586-024-01280-5.pdf

READ AND REPEAT

One nanopore-based protein-sequencing strategy uses the push and pull of an electric field, the ClpX enzyme (orange) and a 'slip sequence' to move a protein back and forth across a membrane, providing multiple views of the protein sequence and increasing accuracy.



A nanopore sequencing device is typically used for sequencing DNA and RNA.

NANOPORE SEQUENCING COMES FOR PROTEINS

l'humanité a besoin de rêveurs

Will there be bumps on the road to success? Undoubtedly.

Humanity needs dreamers

https://pccm.princeton.edu/events/humanity-needs-dreamers-visit-marie-curie-1

https://www.cambridgema.gov/cpl/calendarofevents/2018/04/19/humanityneedsdreamersavisitwithmariecurie

www.colorado.edu/cuwizards/2020/11/14/december-5-2020-humanity-needs-dreamers-visit-marie-curie-susan-marie-frontczak

Article | **Separation Sample Preparation** 26 November 2012

Blood bank bias: Protein biomarkers of stored red blood cells

Overview

Several biomarkers of degradation in stored red blood cells have been identified in a proteomics study, providing an opportunity to estimate deterioration during storage as well as blood doping in sports.

Storage-induced changes of the cytosolic red blood cell proteome analyzed by 2D DIGE and high-resolution/high-accuracy MS.

Walpurgis K [1], Kohler M , Thomas A , Wenzel F , Geyer H , Schänzer W , Thevis M

Author information

Proteomics, 09 Oct 2012, 12(21):3263-3272
https://doi.org/10.1002/pmic.201200280 PMID: 22965759

BUT

If only 1% of the global population (~8 billion people) use diagnostics & treatment, imagine the business potential of research results!

If ethical profitability of social businesses can help improve healthcare for even 10% of the global population, then we helped ~800 million more!

Leukapheresis to enrich for T (CAR-T) lymphocytes for non-affluent nations?

CUTTING-EDGE CANCER THERAPY IS MADE IN INDIA — AT ONE-TENTH THE COST

The treatment, called NexCAR19, raises hopes that a transformative class of medicine will become more readily available in low- and middle-income countries.

By Smriti Mallapaty

A small Indian biotechnology company is producing a home-grown version of a cutting-edge cancer treatment known as chimeric antigen receptor (CAR) T-cell therapy that was pioneered in the United States. CAR-T therapies are used mainly to treat blood cancers and have burgeoned in the past few years. The Indian CAR-T therapy costs one-tenth that of comparable commercial products available globally.

A single treatment of NexCAR19, manufactured by Mumbai-based ImmunoACT, costs between US$30,000 and $40,000. The first CAR-T therapy was approved in the United States in 2017, and commercial CAR-T therapies currently cost between $370,000 and $530,000, not including hospital fees and drugs to treat side effects. These treatments have also shown promise in treating autoimmune diseases and brain cancer.

India's drug regulator approved NexCAR19 for therapeutic use in India in October. By December, ImmunoACT was administering the therapy to paying patients, and it is now treating some two-dozen people a month in hospitals across the country.

"It's a dream come true," says Alka Dwivedi, an immunologist who helped to develop NexCAR19 and is now at the US National Cancer Institute (NCI) in Bethesda, Maryland. Her voice becomes tender as she describes seeing the first patient's cancer go into remission. These are people for whom all other treatments have failed, says Dwivedi.

https://www.nature.com/articles/d41586-024-00809-y.pdf

The social business of medicine guided by ethical profitability for for-profit ventures? **Model for non-affluent non-OECD nations?**

COST IN USA

$530,000

NEWS | 21 March 2024 https://www.nature.com/articles/d41586-024-00809-y

Cutting-edge CAR-T cancer therapy is now made in India — at one-tenth the cost

The treatment, called NexCAR19, raises hopes that this transformative class of medicine will become more readily available in low- and middle-income countries.

COST IN INDIA

$30,000

A single treatment of NexCAR19, manufactured by Mumbai-based ImmunoACT, costs between US$30,000 and $40,000. The first CAR-T therapy was approved in the United States in 2017, and commercial CAR-T therapies in the US cost between $370,000 and $530,000, not including hospital fees and drugs to treat side effects. These treatments have also shown promise in treating autoimmune diseases and brain cancer. "It's a dream come true," says Alka Dwivedi, an immunologist who helped to develop NexCAR19 and is now at the US National Cancer Institute (NCI, NIH) in Bethesda, MD. These are people for whom all other treatments have failed, says Dwivedi. There is a "tremendous patient need", says Nirali Shah, a paediatric oncologist at NCI, NIH who is also an academic collaborator of the researchers at ImmunoACT. "It's positive news," says Renato Cunha, a haematologist at the Grupo Oncoclínicas in São Paulo, Brazil. He says the Indian product could pave the way for making advanced cellular therapies accessible to other low- and middle-income countries. "Hope is the word that comes to mind."

The potential for blood banks and blood donors as a source for CAR-T cells?

nature.com/articles/d41586-024-00470-5

NEWS | 22 February 2024 | Correction 22 February 2024

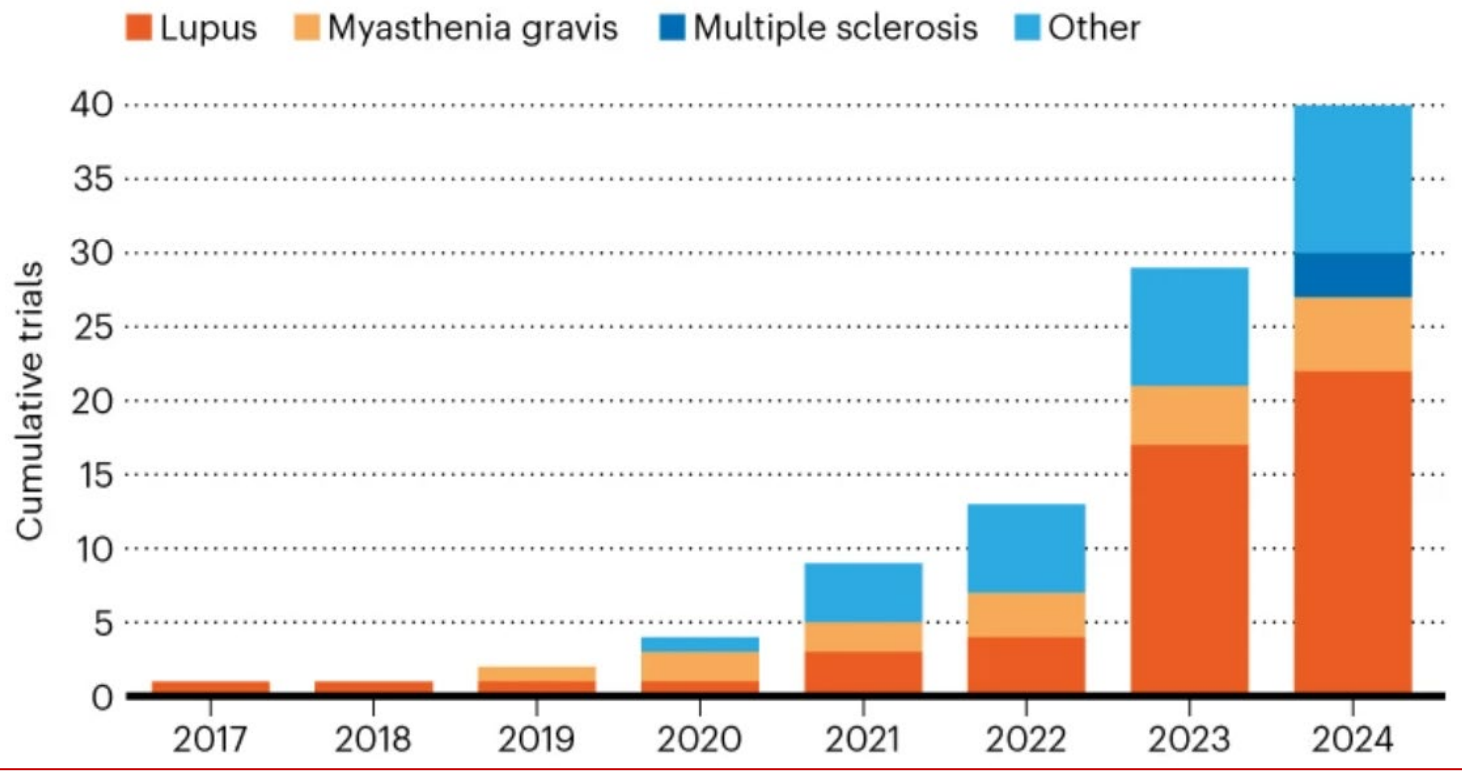
CAR-T therapy for multiple sclerosis enters US trials for first time

Hopes are high that engineered immune cells, which are already in use to treat blood cancer, will halt the progression of a degenerative autoimmune disorder.

nature.com/articles/d41586-024-00470-5 www.nature.com/articles/d41586-024-00470-5

ENLISTING IMMUNE CELLS TO TREAT AUTOIMMUNE DISEASE

The number of clinical trials of CAR T cells — engineered immune cells — used to treat autoimmune disorders has grown rapidly over the past seven years. Testing of CAR-T therapy for the autoimmune disorder lupus accounts for the bulk of the trials.



Biol Blood Marrow Transplant 21 (2015) 1188–1194

Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

Review

Cord Blood Banking in the Arab World: Current Status and Future Developments

Monica M. Matsumoto [1], Rana Dajani [2], Kirstin R.W. Matthews [1,*]

[1] James A. Baker III Institute for Public Policy, Science and Technology Policy Program, Rice University, Houston, Texas
[2] Department of Biology and Biotechnology, Hashemite University of Jordan, Zarqa, Jordan

http://dx.doi.org/10.1016/j.bbmt.2015.01.012 1083-8791/

Table 3
Timeline of Major CB Banking Developments in the Arab World

Year	Development
1998	First CB transplant is performed in Arab world
2003	SA: KFSH-RC begins performing CB transplants (from imported units)
	Muslim World League's Jurisprudential Council issues a *fatwa* approving CB for research and therapy
2006	UAE: DCRC opens first CB bank in the region, as a public–private hybrid model
	SA: KFSH-RC opens the Kingdom's first public CB bank
	UAE: Cryo-Save Arabia, the largest private CB storage facility in the region, opens in Dubai Healthcare City
2007	EG: National Blood Policy is approved with procedural guidelines for CB collection and storage
2009	QA: Virgin Health Bank moves its headquarters from London to Doha
	EG: CellSafe opens as the country's first private CB bank
2011	QA: Virgin Health Bank is granted the first (and only, to date) license for CB procurement, processing, and storage
	SA: KAIMRC opens the country's second public CB bank and creates the Saudi Donor Registry
	QA: Virgin Health Bank opens storage and processing facility at Qatar Science & Technology Park
	EG: National Stem Cell Committee is created and tasked with establishing regulations for stem cell research and therapy as well as a public CB bank
2012	EG: Stem cell research center opens at Sheikh Zayed Hospital
	QA: Stem cell research policy is enacted into legislation, allowing research using CB stem cells
2013	EG: Center for Stem Cell Research and Regenerative Medicine opens in Zewail City of Science & Technology
2014	JO: New stem cell research law is passed, including regulations for CB banking
2015	JO: Projected opening of the first in-country private CB storage facility by the company, BabyCord Jordan
	EG: Projected opening of the country's first public CB bank, located at Assiut University, in partnership with Zewail City of Science & Technology
2016	JO: Projected opening of the country's first public CB bank, located at KHCC

The potential for cord blood banks as an autologous source for CAR-T cells?

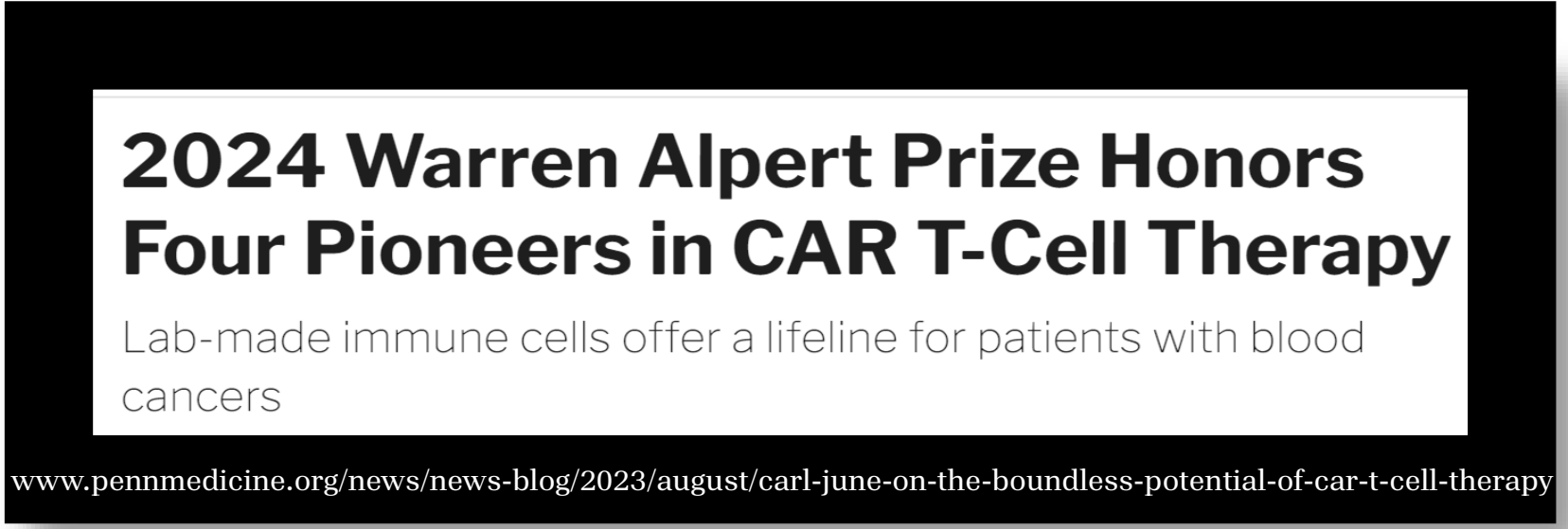
Table 1
Relevant Demographic, Health, and Economic Indicators of 5 Arab Countries Studied: Jordan, Saudi Arabia, UAE, Egypt, and Qatar

Country	Population	Arab	Fert	GNI	Health $	Hosp Beds	Leukemia	Lymphoma
Jordan	7.93M	98%	3.16	$4.95k	8.4%	1.8	6.1	8.2
Saudi Arabia	27.3M	90%	2.17	$26.2k	3.7%	2.2	3.8	7.9
UAE	5.63M	13%‖	2.36	$38.6k	3.3%	1.9	3.7	6.7
Egypt	86.9M	99%	2.87	$3.16k	4.9%	1.7	5.9	9.3
Qatar	2.12M	40%	1.92	$85.5k	1.9%	1.2	4.9	7.7

Table 2
Current CB Banking Options in the Arab World

CB Bank	Type	Storage Location	Collection Office Location(s)
BabyCord	Priv	USA (Boston), Jordan (Amman)*	Jordan
Biovault Family	Priv	UK (Plymouth)	Lebanon, UAE
CellSafe	Priv	Egypt (Cairo)	Egypt
Cells4Life	Priv	UK (Burgess Hill, Essex)	Bahrain, Egypt, Jordan, Kuwait, Lebanon, Qatar, Saudi Arabia, UAE
Center for Stem Cell Research & Regenerative Medicine	Publ	Egypt (Assiut)*	Egypt
Cryo-Save	Priv	UAE (Dubai), Belgium (Niel)	Egypt, Kuwait, Oman, Saudi Arabia, UAE
DCRC†	Hybr	UAE (Dubai)	UAE
Future Health Biobank	Priv	UK (Nottingham), Switzerland (Châtel-St-Denis)	Bahrain, Egypt, Jordan, Kuwait, Lebanon, Morocco, Qatar, Saudi Arabia, Syria, UAE
KAIMRC	Publ	Saudi Arabia (Riyadh)	Saudi Arabia
KFSH-RC†	Publ	Saudi Arabia (Riyadh)	Saudi Arabia
KHCC	Publ	Jordan (Amman)*	Jordan
Precious Cells	Priv	UK (Middlesex)	Jordan, Lebanon, UAE
Smart Cells	Priv	UK (West Drayton)	Egypt, Jordan, Kuwait, Lebanon, Syria, UAE
Sultan Qaboos Univ. Hospital	Publ	Oman (Muscat)	Oman
Virgin Health Bank	Priv, Hybr	Qatar (Doha)	Qatar

Matsumoto MM, Dajani R, Matthews KR. **Cord Blood Banking in the Arab World: Current Status and Future Developments. Biol Blood Marrow Transplant.** 2015 July; 21(7):1188-94. doi: 10.1016/j.bbmt.2015.01.012. Epub 2015 Feb 14. PMID: 25687797.

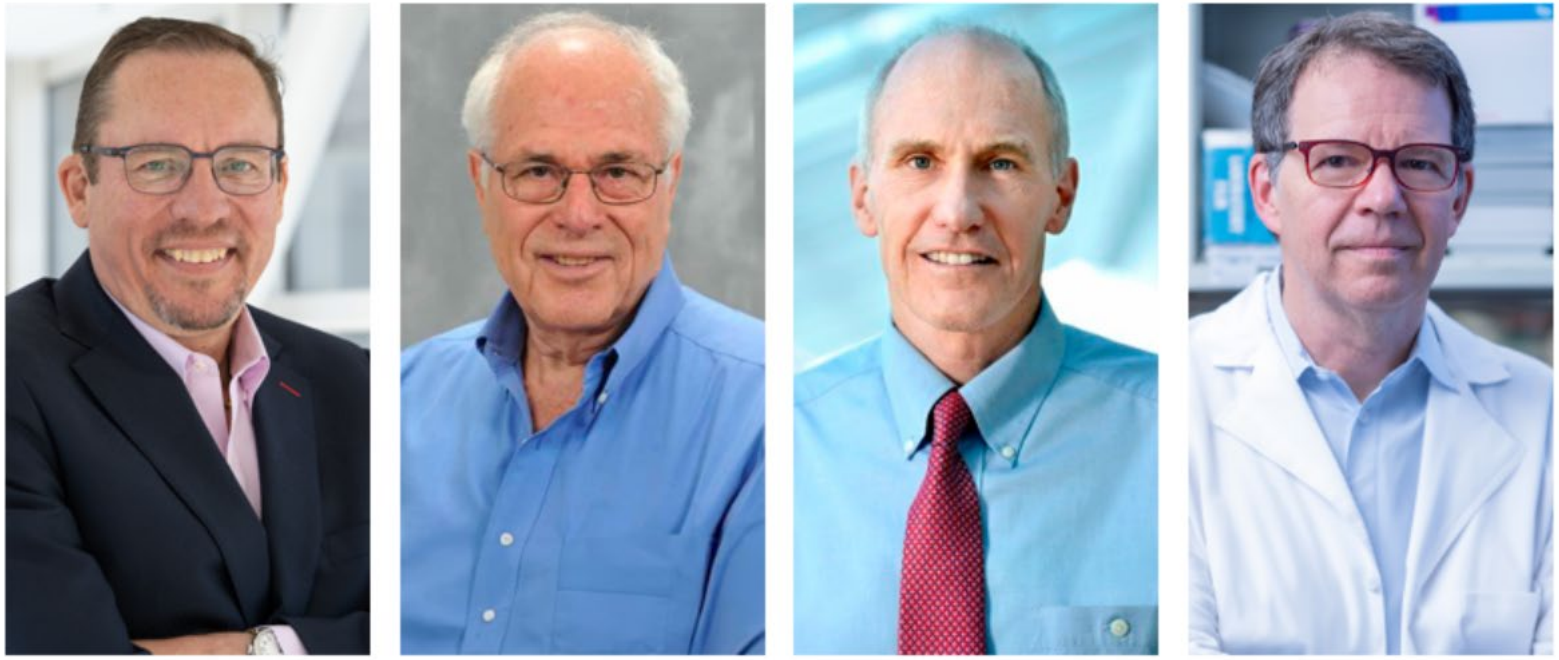


Kalos M, Levine BL, Porter DL, Katz S, Grupp SA, Bagg A, June CH. **T cells with chimeric antigen receptors have potent antitumor effects and can establish memory in patients with advanced leukemia.** Sci Transl Med. 2011 August 10; 3(95):95ra73. doi: 10.1126/scitranslmed.3002842
www.ncbi.nlm.nih.gov/pmc/articles/PMC3393096/pdf/nihms384661.pdf

Porter DL, Levine BL, Kalos M, Bagg A, June CH. **Chimeric antigen receptor-modified T cells in chronic lymphoid leukemia.** N Engl J Med. 2011 Aug 25;365(8):725-33. doi: 10.1056/NEJMoa1103849. Epub 2011 Aug 10. Erratum in: N Engl J Med. 2016 Mar 10;374(10):998. doi: 10.1056/NEJMx160005
www.ncbi.nlm.nih.gov/pmc/articles/PMC3387277/pdf/nihms-320786.pdf

2024 Warren Alpert Prize Honors Four Pioneers in CAR T-Cell Therapy

Lab-made immune cells offer a lifeline for patients with blood cancers



•Renier Brentjens, Katherine Anne Gioia Endowed Chair of Medicine and deputy director of Roswell Park Comprehensive Cancer Center

•Zelig Eshhar, professor emeritus, the Weizmann Institute of Science, chair of Immunology, Division of R&D, Sourasky Medical Center, Israel

•Carl June, Richard W. Vague Professor in Immunotherapy, University of Pennsylvania Perelman School of Medicine

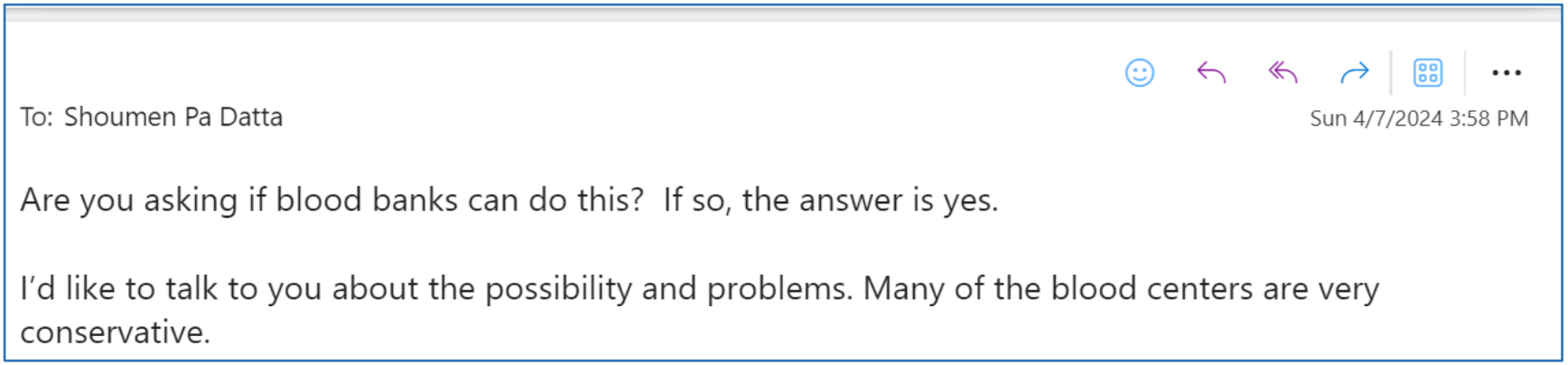
•Michel Sadelain, Stephen and Barbara Friedman Chair, founding director of the Center for Cell Engineering at Memorial Sloan Kettering Cancer Center

https://hms.harvard.edu/news/2024-warren-alpert-prize-honors-four-pioneers-car-t-cell-therapy

Potential for blood banks / cord blood banks in cellular & molecular therapy

FUTURE FORWARD RESEARCH – THINK VERY FAR BEYOND THE HORIZON

- Take any blood and transform HLA gene expression to match recipient (HLA typing) for transfusion medicine
- Apheresis of donor blood to enrich for desired cell types (e.g., CAR-T) and induce HLA gene expression for immune match
- Use CD34+ cord blood cells and induce (iPSC) to make immuno-compatible tissue (any tissue, organoid) for transplantation



To: Shoumen Pa Datta

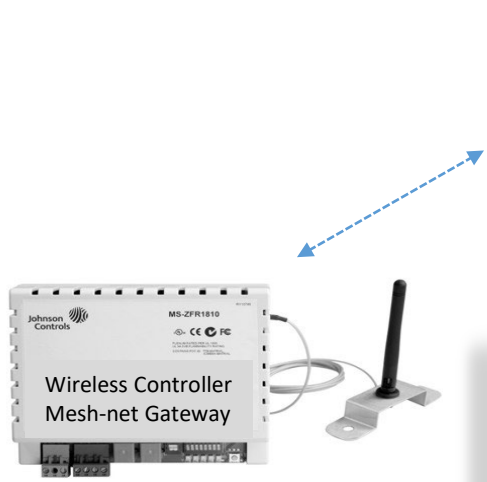
Sun 4/7/2024 3:58 PM

Are you asking if blood banks can do this? If so, the answer is yes.

I'd like to talk to you about the possibility and problems. Many of the blood centers are very conservative.

Former CEO of a Blood Bank

Digital Health Hematology Services (DHHS is far closer at hand)



Local Wireless Sensor Mesh Network

DHHS IN THE NEAR-FUTURE OF BLOOD BANKS ?

Data-Informed Decision Support (DIDS) Systems
Distributed Secure Near Real-time Mobile Digital Health Services

RESEARCH FEATURE

Future of medicine: Lab-on-a-chip devices starting to make an impact

September 27, 2021

Izadifar, Z., Cotton, J., Chen, S. *et al.* Mucus production, host-microbiome interactions, hormone sensitivity, and innate immune responses modeled in human cervix chips. *Nat Commun* **15**, 4578 (2024). https://doi.org/10.1038/s41467-024-48910-0

Article

https://doi.org/10.1038/s41467-024-48910-0

Mucus production, host-microbiome interactions, hormone sensitivity, and innate immune responses modeled in human cervix chips

Received: 22 April 2023

Accepted: 22 March 2024

Published online: 29 May 2024

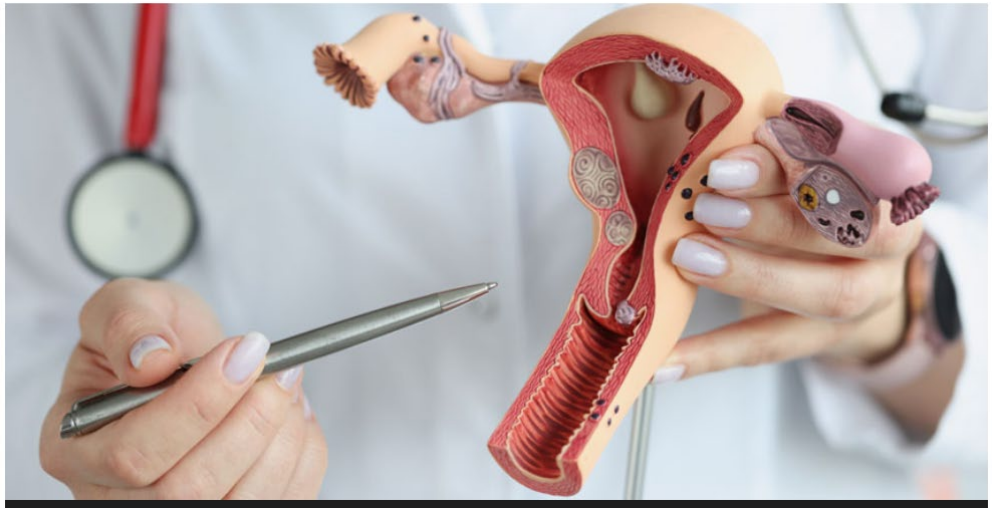
Zohreh Izadifar[1,5], Justin Cotton[1], Siyu Chen[2], Viktor Horvath[1], Anna Stejskalova[1], Aakanksha Gulati[1], Nina T. LoGrande[1], Bogdan Budnik[1], Sanjid Shahriar[1], Erin R. Doherty[1], Yixuan Xie[2], Tania To[1], Sarah E. Gilpin[1], Adama M. Sesay[1], Girija Goyal[1], Carlito B. Lebrilla[2] & Donald E. Ingber[1,3,4]

HARVARD MEDICAL SCHOOL

Cervix-on-a-Chip to Accelerate Research on Women's Health

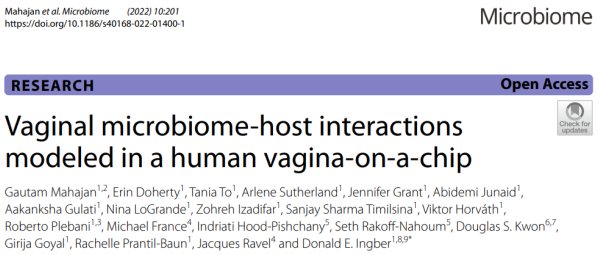
New model could lead to better understanding of, treatments for diseases of female reproductive tract

June 6, 2024 | Research



https://hms.harvard.edu/news/cervix-chip-accelerate-research-womens-health

Mahajan G, Doherty E, To T, Sutherland A, Grant J, Junaid A, Gulati A, LoGrande N, Izadifar Z, Timilsina SS, Horváth V, Plebani R, France M, Hood-Pishchany I, Rakoff-Nahoum S, Kwon DS, Goyal G, Prantil-Baun R, Ravel J, Ingber DE. **Vaginal microbiome-host interactions modeled in a human vagina-on-a-chip.** Microbiome. 2022 Nov 26; 10(1):201. doi: 10.1186/s40168-022-01400-1



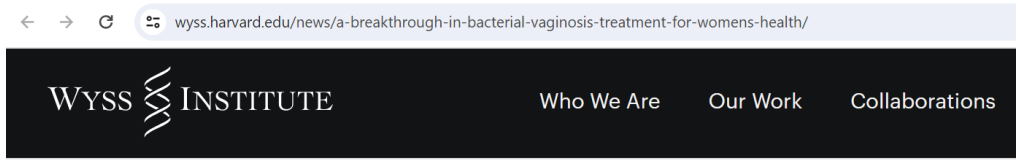
Mahajan *et al. Microbiome* (2022) 10:201
https://doi.org/10.1186/s40168-022-01400-1

Microbiome

RESEARCH Open Access

Vaginal microbiome-host interactions modeled in a human vagina-on-a-chip

Gautam Mahajan[1,2], Erin Doherty[1], Tania To[1], Arlene Sutherland[1], Jennifer Grant[1], Abidemi Junaid[1], Aakanksha Gulati[1], Nina LoGrande[1], Zohreh Izadifar[1], Sanjay Sharma Timilsina[1], Viktor Horváth[1], Roberto Plebani[1,3], Michael France[4], Indriati Hood-Pishchany[5], Seth Rakoff-Nahoum[5], Douglas S. Kwon[6,7], Girija Goyal[1], Rachelle Prantil-Baun[1], Jacques Ravel[4] and Donald E. Ingber[1,8,9*]



wyss.harvard.edu/news/a-breakthrough-in-bacterial-vaginosis-treatment-for-womens-health/

WYSS INSTITUTE Who We Are Our Work Collaborations

A breakthrough in bacterial vaginosis treatment for women's health

November 28, 2022

Human Organ Chip allows researchers to study effects of microbiome on vaginal health

HARVARD MEDICAL SCHOOL

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9701078/pdf/40168_2022_Article_1400.pdf
https://wyss.harvard.edu/news/a-breakthrough-in-bacterial-vaginosis-treatment-for-womens-health/

A digital microfluidic analyzer stands behind a disposable lab-on-a-chip cartridge (forefront), where blood samples are collected to screen for the presence of rare diseases.

nhlbi.nih.gov/news/2021/future-medicine-lab-chip-devices-starting-make-impact

Researchers supported by the NHLBI are playing a key role in the development of this technology — and for good reason. The chips not only are capable of quickly diagnosing diseases, but they can also do so at a lower cost, faster speed, and with higher accuracy than their bulkier counterparts, researchers say. Some may be coming to a hospital or medicine cabinet near you.

"Watching discoveries move from the lab to the clinic is incredibly exciting," said Stephanie M. Davis, Ph.D., NHLBI's Small Business Program Coordinator. "The NHLBI Small Business Program is thrilled to see lab-on-a-chip technologies finally move toward the marketplace."

https://www.nhlbi.nih.gov/news/2021/future-medicine-lab-chip-devices-starting-make-impact

Is it in practice? Yes! Massachusetts General Hospital, Harvard Medical School

Published in final edited form as:
Annu Rev Biomed Eng. 2005 ; 7: 77–103. doi:10.1146/annurev.bioeng.7.011205.135108.

BLOOD-ON-A-CHIP

Mehmet Toner and **Daniel Irimia**
BioMEMS Resource Center, Center for Engineering in Medicine and Surgical Services, Massachusetts General Hospital, Shriners Hospital for Children, and Harvard Medical School, Boston, Massachusetts 02114

Mehmet Toner: mtoner@hms.harvard.edu; Daniel Irimia: dirimia@hms.harvard.edu

Abstract

Accurate, fast, and affordable analysis of the cellular component of blood is of prime interest for medicine and research. Yet, most often sample preparation procedures for blood analysis involve handling steps prone to introducing artifacts, whereas analysis methods commonly require skilled technicians and well-equipped, expensive laboratories. Developing more gentle protocols and affordable instruments for specific blood analysis tasks is becoming possible through the recent progress in the area of microfluidics and lab-on-a-chip-type devices. Precise control over the cell microenvironment during separation procedures and the ability to scale down the analysis to very small volumes of blood are among the most attractive capabilities of the new approaches. Here we review some of the emerging principles for manipulating blood cells at microscale and promising high-throughput approaches to blood cell separation using microdevices. Examples of specific single-purpose devices are described together with integration strategies for blood cell separation and analysis modules.

Keywords

lab-on-a-chip; point-of-care diagnostic; cell separation; sample preparation; microfluidic

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3779643/pdf/nihms506695.pdf

https://doi.org/10.1038/s41467-022-28499-y OPEN

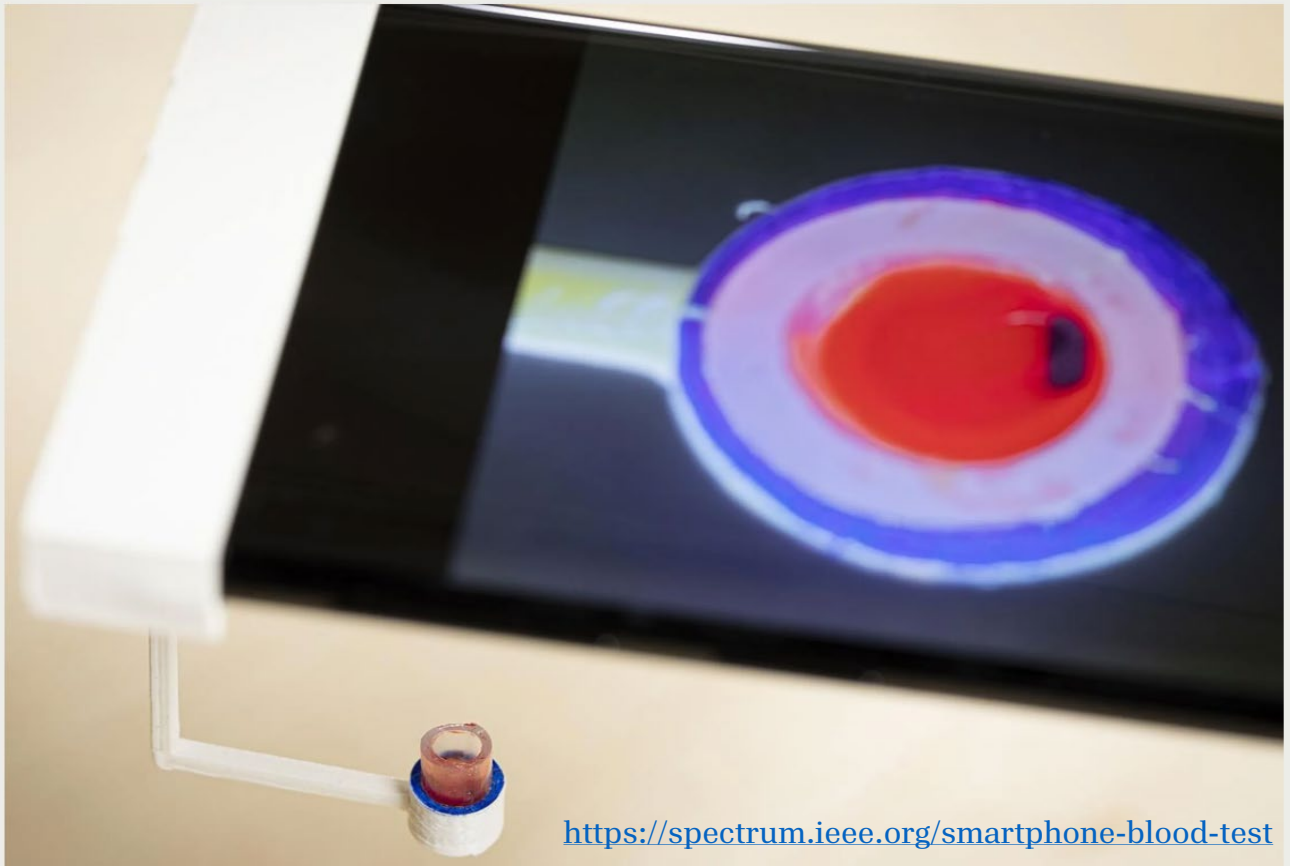
Micro-mechanical blood clot testing using smartphones

Justin Chan [1✉], Kelly Michaelsen [2✉], Joanne K. Estergreen[3], Daniel E. Sabath [3] & Shyamnath Gollakota [1✉]

University of Washington researchers have developed a new blood-clotting test that uses only a single drop of blood and a smartphone with a plastic attachment that holds a tiny cup [shown here] beneath the phone's camera.

Blood Test Only Needs a Drop and a Smartphone for Results › The tech shows promise, although user-friendly "single drop of blood" platforms are still a few years away

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8837659/pdf/41467_2022_Article_28499.pdf



https://spectrum.ieee.org/smartphone-blood-test

Chan J, Michaelsen K, Estergreen JK, Sabath DE, Gollakota S. ***Micro-mechanical blood clot testing using smartphones.*** Nature Commun. 2022 Feb 11; 13(1):831. doi: 10.1038/s41467-022-28499-y. PMID: 35149711; PMCID: PMC8837659.

DE GRUYTER

Clin Chem Lab Med 2024; aop

Théo Willeman*, Justine Grunwald, Marc Manceau, Frédéric Lapierre, Lila Krebs-Drouot, Coralie Boudin, Virginie Scolan, Hélène Eysseric-Guerin, Françoise Stanke-Labesque and Bruno Revol

Smartphone swabs as an emerging tool for toxicology testing: a proof-of-concept study in a nightclub

https://doi.org/10.1515/cclm-2024-0242
Received February 22, 2024; accepted March 27, 2024;
published online April 5, 2024

From the journal Clinical Chemistry and Laboratory Medicine (CCLM)
https://doi.org/10.1515/cclm-2024-0242

RESEARCH ARTICLE

Resistivity detection of perfluoroalkyl substances with fluorous polyaniline in an electrical lateral flow sensor

Sohyun Park, Collette T. Gordon, and Timothy M. Swager | Authors Info & Affiliations

Contributed by Timothy M. Swager; received October 5, 2023; accepted February 6, 2024; reviewed by William R. Dichtel, Howard E. Katz, and John Reynolds

March 12, 2024 | 121 (12) e2317300121 | https://doi.org/10.1073/pnas.2317300121

OPEN

Check for updates

Per- and polyfluoroalkyl substances (PFAS) and thyroid hormone measurements in dried blood spots and neonatal characteristics: a pilot study

Ana K. Rosen Vollmar[1], Elizabeth Z. Lin[1], Sara L. Nason[2], Katerina Santiago[3], Caroline H. Johnson[1], Xiaomei Ma[3], Krystal J. Godri Pollitt[1] and Nicole C. Deziel[1]

Is a PFAS smartphone sensor in the works?

BACKGROUND: Pediatric thyroid diseases have been increasing in recent years. Environmental risk factors such as exposures to chemical contaminants may play a role but are largely unexplored. Archived neonatal dried blood spots (DBS) offer an innovative approach to investigate environmental exposures and effects.

OBJECTIVE: In this pilot study, we applied a new method for quantifying per- and polyfluoroalkyl substances (PFAS) to 18 archived DBS from babies born in California from 1985–2018 and acquired thyroid hormone measurements from newborn screening tests. Leveraging these novel data, we evaluated (1) changes in the concentrations of eight PFAS over time and (2) the relationship between PFAS concentrations, thyroid hormone concentrations, and neonatal characteristics to inform future research.

METHODS: PFAS concentrations in DBS were measured using ultra-high-performance liquid chromatography-mass spectrometry. Summary statistics and non-parametric Wilcoxon rank-sum and Kruskal–Wallis tests were used to evaluate temporal changes in PFAS concentrations and relationships between PFAS concentrations, thyroid hormone concentrations, and neonatal characteristics.

RESULTS: The concentration and detection frequencies of several PFAS (PFOA, PFOS, and PFOSA) declined over the assessment period. We observed that the timing of specimen collection in hours after birth was related to thyroid hormone but not PFAS concentrations, and that thyroid hormones were related to some PFAS concentrations (PFOA and PFOS).

IMPACT STATEMENT: This pilot study examines the relationship between concentrations of eight per- and polyfluoroalkyl substances (PFAS), thyroid hormone levels, and neonatal characteristics in newborn dried blood spots (DBS) collected over a period of 33 years. To our knowledge, 6 of the 22 PFAS we attempted to measure have not been quantified previously in neonatal DBS, and this is the first study to examine both PFAS and thyroid hormone concentrations using DBS. This research demonstrates the feasibility of using newborn DBS for quantifying PFAS exposures in population-based studies, highlights methodological considerations in the use of thyroid hormone data for future studies using newborn DBS, and indicates potential relationships between PFAS concentrations and thyroid hormones for follow-up in future research.

Keywords: PFAS; Per- and polyfluoroalkyl substances; Dried blood spot; Thyroid hormone; Newborn; Environmental exposure

Journal of Exposure Science & Environmental Epidemiology (2023) 33:737–747; https://doi.org/10.1038/s41370-023-00603-4

https://www.niehs.nih.gov/health/topics/agents/pfc

Rosen Vollmar AK, Lin EZ, Nason SL, Santiago K, Johnson CH, Ma X, Godri Pollitt KJ, Deziel NC. ***Per- and polyfluoroalkyl substances (PFAS) and thyroid hormone measurements in dried blood spots and neonatal characteristics: a pilot study.*** J Expo Sci Environ Epidemiol. 2023 September; 33(5): 737-747. doi: 10.1038/s41370-023-00603-4. Epub 2023 Sep 20. PMID: 37730931; PMCID: PMC10541328. https://www.nature.com/articles/s41370-023-00603-4.pdf

Business strategy of low usage fees lowers the barrier to market entry.

Don't think market of millions. Think about creating markets for the

NEXT BILLION USERS with mobile phones!

◆ Think cable TV

Remember **PAY PER VIEW ?**

◆ Think plain old telephone system (POTS)

Remember **PAY PER CALL ?**

◆ Think purchasing power parity (PPP) of the next billion users

Remember PAPPU (**PAY A PENNY PER USE**)

Victoria Morgan, Lisseth Casso-Hartman, David Bahamon-Pinzon, Kelli McCourt, Robert G. Hjort, Sahar Bahramzadeh, Irene Velez-Torres, Eric McLamore, Carmen Gomes, Evangelyn C. Alocilja, Shoumen Palit Austin Datta and Diana C. Vanegas (2019) ***Sensor-as-a-Service: Convergence of Sensor Analytic Point Solutions (SNAPS) and Pay-A-Penny-Per-Use (PAPPU) Paradigm as a Catalyst for Democratization of Healthcare in Underserved Communities.*** Diagnostics *2020*, 10 *(1), 22* https://doi.org/10.3390/diagnostics10010022 and download from the MIT Library https://dspace.mit.edu/handle/1721.1/123983

PAY PER USE ◦ Analytics-Lab-on-a-Chip-on-a-Flash Drive

BLOOD BANK TEST SENSOR

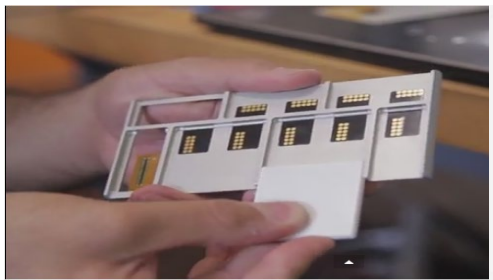
EBV Sensor

Glucose Sensor

Cholesterol Sensor

SARS-CoV-2 Sensor

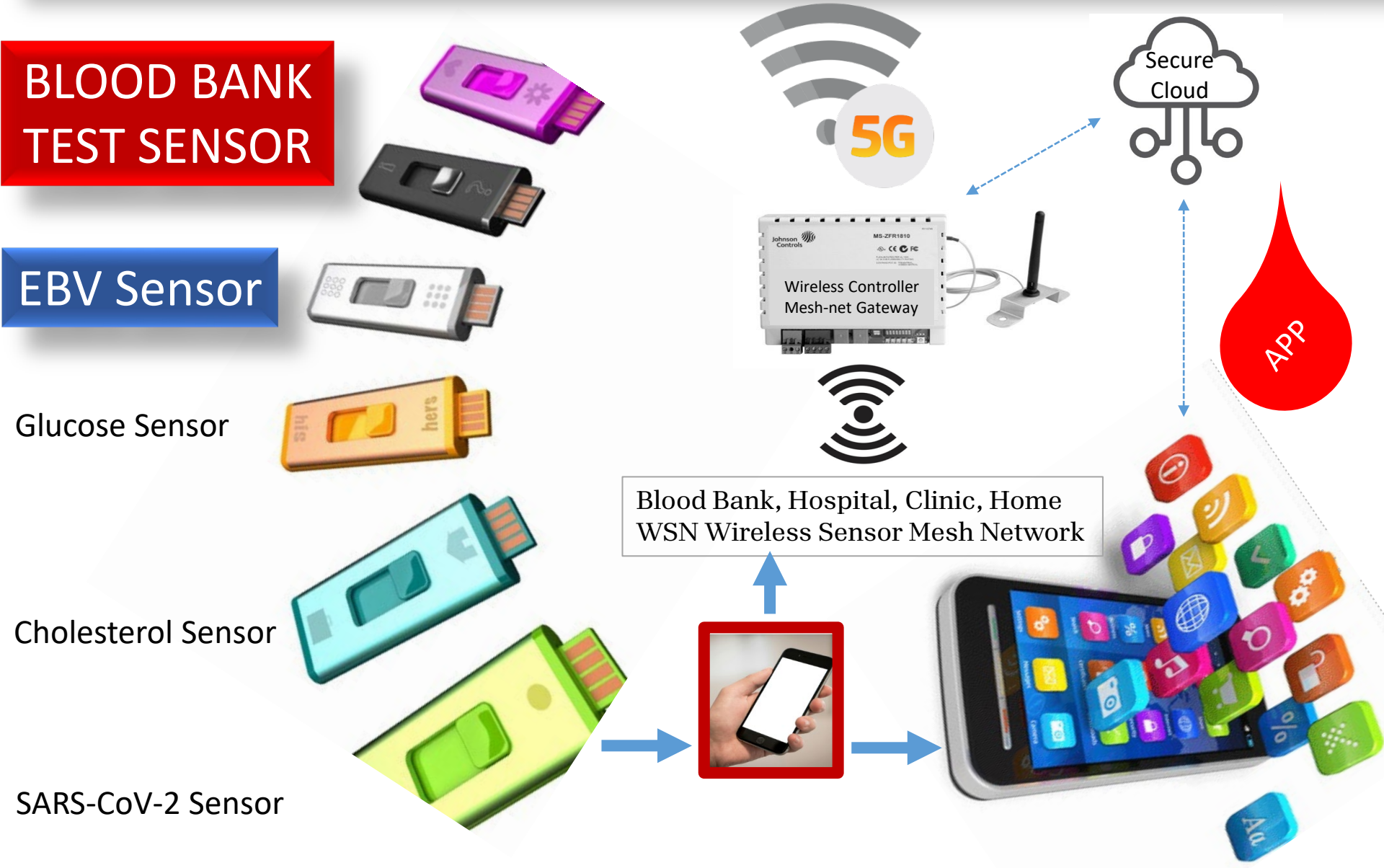
There's an app for that



Hot swappable, modular, smart

NK Labs
ARA Prototype

Digital Health: Analytics-Lab-on-a-Chip-on-a-FlashDrive



Nanotechnology for Hematology, Blood Transfusion, and Artificial Blood

Micro and Nano Technologies

2022, Pages 265-283

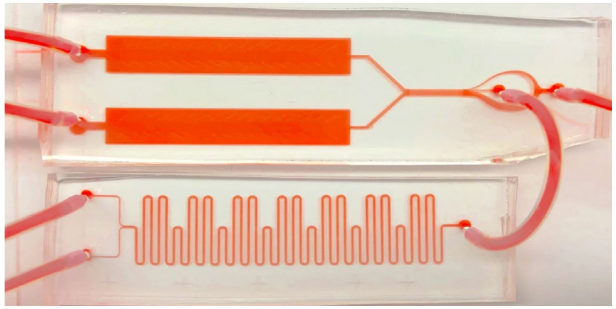
Chapter 12 - Lab-on-a-chip for analysis of blood

Hayder A. Abdulbari

https://doi.org/10.1016/B978-0-12-823971-1.00013-1

Abstract

With the growing popularity of microfluidics devices, medical science is also progressing its way through fast and efficient microfabricated diagnosis devices. Blood testing and analysis are primary and necessary steps in medical diagnosis; hence smart and fast microdiagnostic devices are considered essential. Blood is the most vital fluid, containing all the essential minerals and vitamins, and it can be a carrier for other biological pathogens such as a bacterium, virus, or other microorganism, making it the perfect subject for analysis for an accurate diagnosis. This chapter introduces and discusses microfluidics technology's influence on the diagnosis of blood diseases. The chapter starts with a comprehensive introduction of the rapid development of microfluidics technology and its applications followed by sections that detail the microfluidics science fundamentals, lab-on-chip, and microfabrication techniques. It then explains specifically the influence of microfluidics technology in the development of different blood testing techniques and methods with a more comprehensive focus on its applications in sexually transmitted diseases.



A protoype of the RT-ELISA, essentially an entire lab within a chip with tiny pipes and valves no wider than a human hair | Photo by Caitlin Maikawa

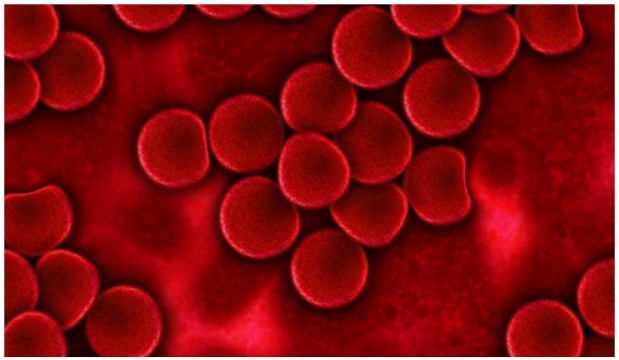
For even the most routine of medical checkups, a blood test is often the first order of business.

https://medicalxpress.com/news/2024-01-biomarker-quality-blood-donations.html

JANUARY 31, 2024 Editors' notes

Researchers identify new biomarker in quality of blood donations

by Kelsea Pieters, CU Anschutz Medical Campus



engineering.stanford.edu/magazine/article/new-lab-chip-turns-blood-test-snapshots-continuous-movies

Stanford University

Stanford | ENGINEERING

Computation & Data, Electronics & Networking, Health

A new lab-on-a-chip turns blood test snapshots into continuous movies

The device can sense levels of virtually any protein or molecule in the blood, and could be transformative for disease detection, patient monitoring and biomedical research.

Poudineh M, Maikawa CL, Ma EY, Pan J, Mamerow D, Hang Y, Baker SW, Beirami A, Yoshikawa A, Eisenstein M, Kim S, Vučković J, Appel EA, Soh HT. (2021) ***A fluorescence sandwich immunoassay for the real-time continuous detection of glucose and insulin in live animals.*** Nat Biomed Eng. 2021 Jan; 5(1):53-63. doi: 10.1038/s41551-020-00661-1. Epub 2020 December 21. PMID: 33349659; PMCID: PMC7856282. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7856282/pdf/nihms-1646031.pdf

To: Shoumen Pa Datta

Sun 4/7/2024 3:58 PM

Are you asking if blood banks can do this? If so, the answer is yes.

I'd like to talk to you about the possibility and problems.

Former CEO of a Blood Bank

Digital Health Hematology Services (DHHS)

Local Wireless Sensor Mesh Network

Wireless Sensors

Blood Bank Digital

Data-Informed Decision Support (DIDS) Systems
Distributed Secure Near Real-time Mobile Digital Health Services

Proof of Concept – Principles & Practice of DIDS

Datta, 2018 / Datta, 2023

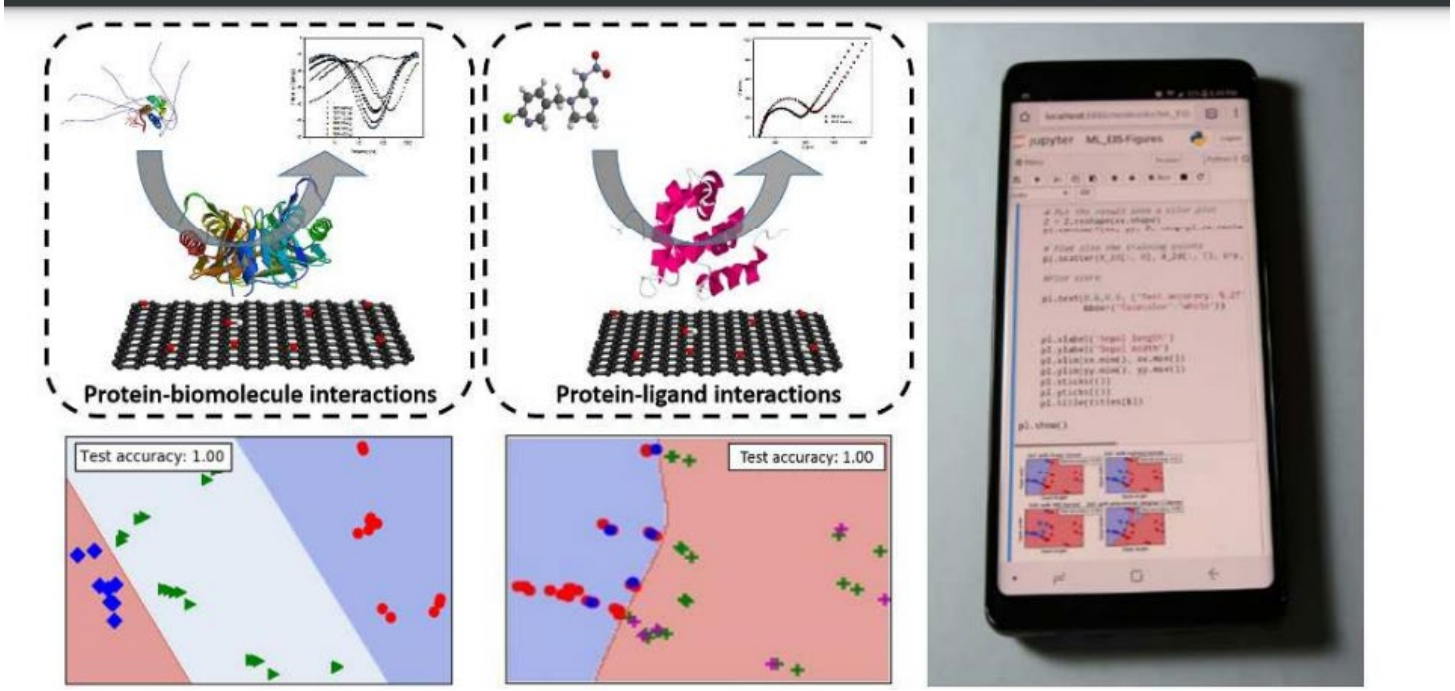
Data-Informed Decision Support (DIDS) Systems

Distributed Near◆ Real-time Mobile Detection Services

Rong Y , Padron AV , Hagerty KJ , Nelson N , Chi S , Keyhani NO , Katz J , **Datta** SPA , Gomes C , McLamore ES (2018) ***Post hoc support vector machine learning for impedimetric biosensors based on weak protein-ligand interactions.*** Analyst. 2018 April 30;143(9):2066-75 doi: 10.1039/c8an00065d

Near◆ Real-time depends on material science (sensor engineering), biochemical & physical chemistry** of molecular interactions (binding kinetics, affinity, equilibrium), timing in software systems (Δt) and network engineering infrastructure with respect to telecommunications (latency, bandwidth and jitter).

** McLamore, Eric S. and **Datta,** Shoumen P.A. (2023) ***A Connected World: System-Level Support through Biosensors*** Annual Review of Analytical Chemistry (Palo Alto, CA) 2023 June 14; 16(1):285-309. doi: 10.1146/annurev-anchem-100322-040914. Epub 2023 April 5. PMID: 37018797.
https://doi.org/10.1146/annurev-anchem-100322-040914
MIT Library https://dspace.mit.edu/handle/1721.1/123983



Proof of Concept: Data-Informed Decision Support (DIDS)

Figure 1. An open source support vector machine learning algorithm was developed for analyzing impedimetric biosensor data. Interactions. We tested the tool for analyzing weak/transient interactions including protein-DNA, protein-protein, and protein-small molecule. The cloud-based tool can be used for point of need applications with a mobile phone or tablet.

Rong Y , Padron AV , Hagerty KJ , Nelson N , Chi S , Keyhani NO , Katz J , Datta SPA , Gomes C , McLamore ES . ***Post hoc support vector machine learning for impedimetric biosensors based on weak protein-ligand interactions.*** Analyst. 2018 Apr 30;143(9):2066-75 doi: 10.1039/c8an00065d PMID: 29629449.

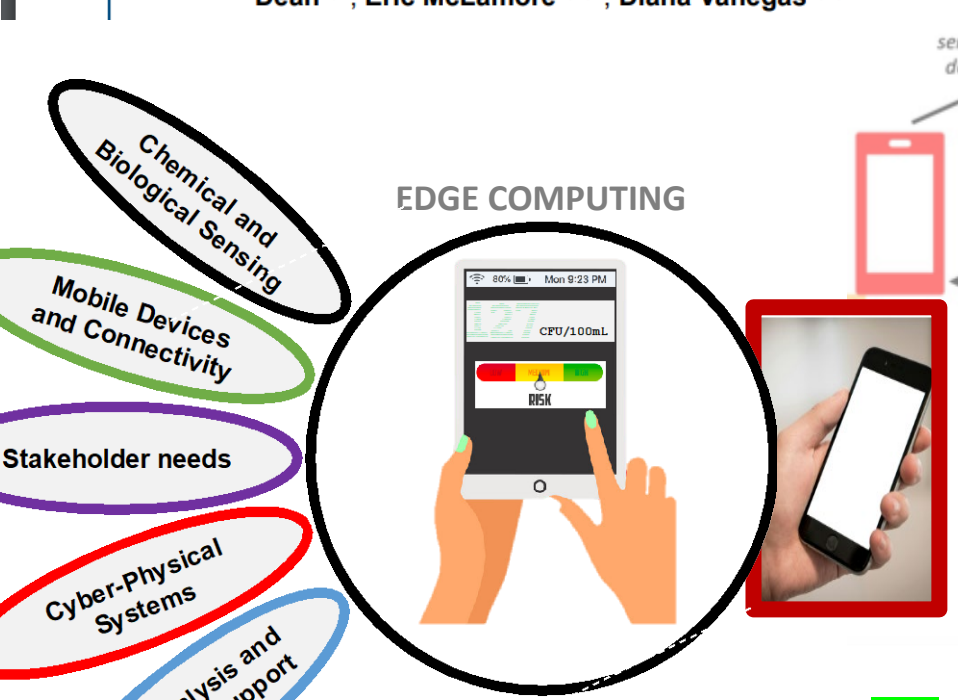
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9386735/pdf/nihms-1827456.pdf

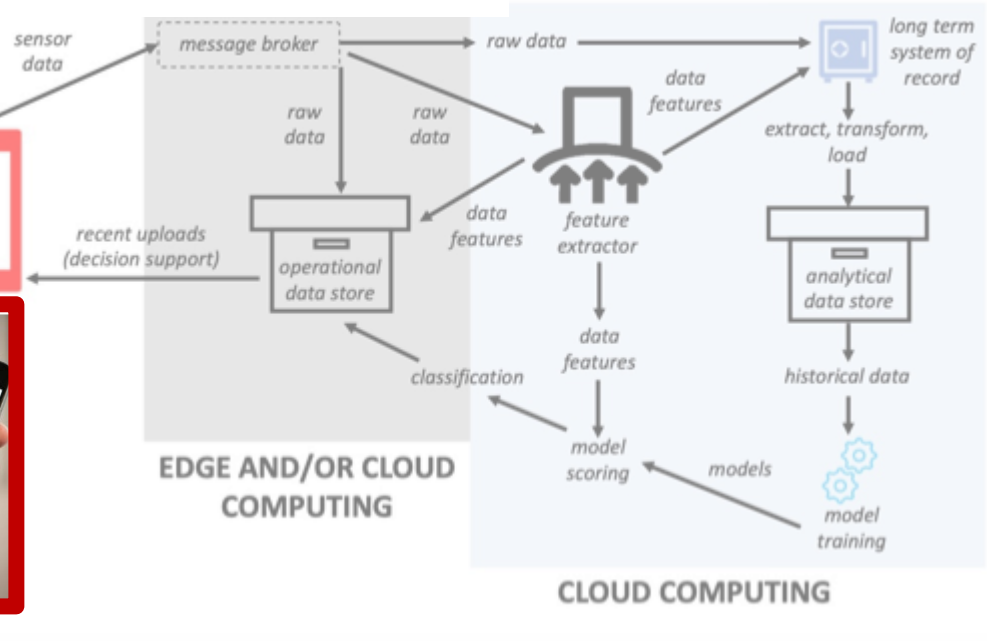
Published in final edited form as:

Front Sens (Lausanne). 2022 ; 3: . doi:10.3389/fsens.2022.917380.

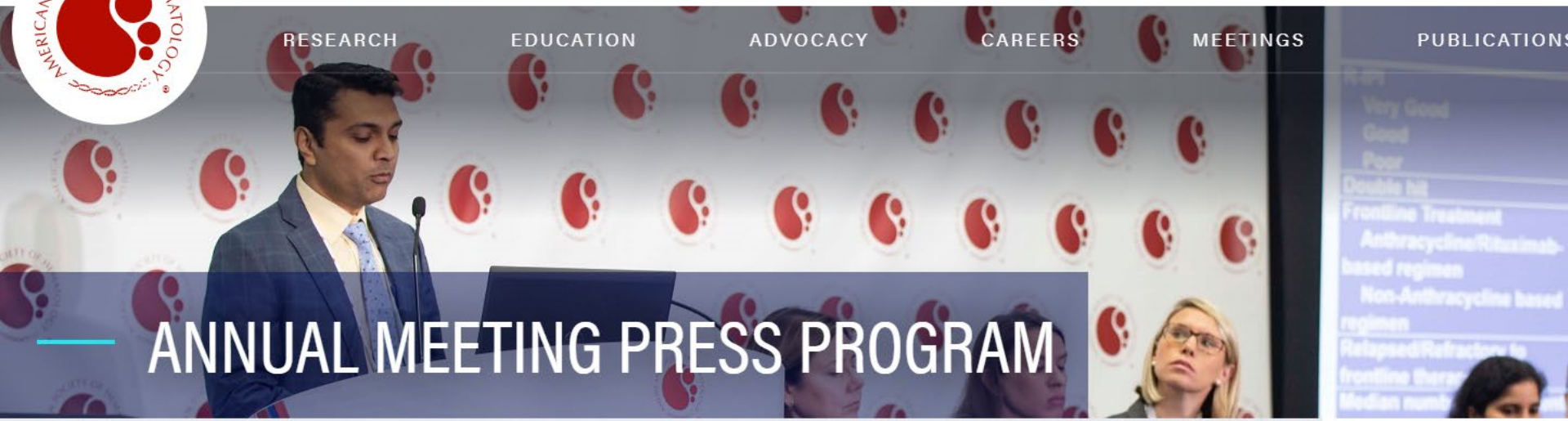
Development of a Biosensor Based on Angiotensin-Converting Enzyme II for Severe Acute Respiratory Syndrome Coronavirus 2 Detection in Human Saliva

Geisianny Moreira[1,2], **Lisseth Casso-Hartmann**[1], **Shoumen Palit Austin Datta**[3,4], **Delphine Dean**[5,6], **Eric McLamore**[1,2,7], **Diana Vanegas**[1,2,*]





McLamore ES, Palit Austin **Datta** S, Morgan V, Cavallaro N, Kiker G, Jenkins DM, Rong Y, Gomes C, Claussen J, Vanegas D, Alocilja EC. ***SNAPS: Sensor Analytics Point Solutions for Detection & Decision Support Systems***. Sensors (Basel). 2019 November 13; 19(22):4935. doi: 10.3390/s19224935. PMID: 31766116
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6891700/pdf/sensors-19-04935.pdf



Studies Highlight Impacts of Applying New Technologies in Everyday Care

CITATION

PUBLISHED ON:

DEC 09 2023

Digital Health Hematology Services (DHHS)

not if, but when

Data-Informed Decision Support (DIDS) Systems
Distributed Secure Near Real-time Mobile Digital Health Services

Digital Health : The new BMI ??

Body-Machine Interface (BMI)

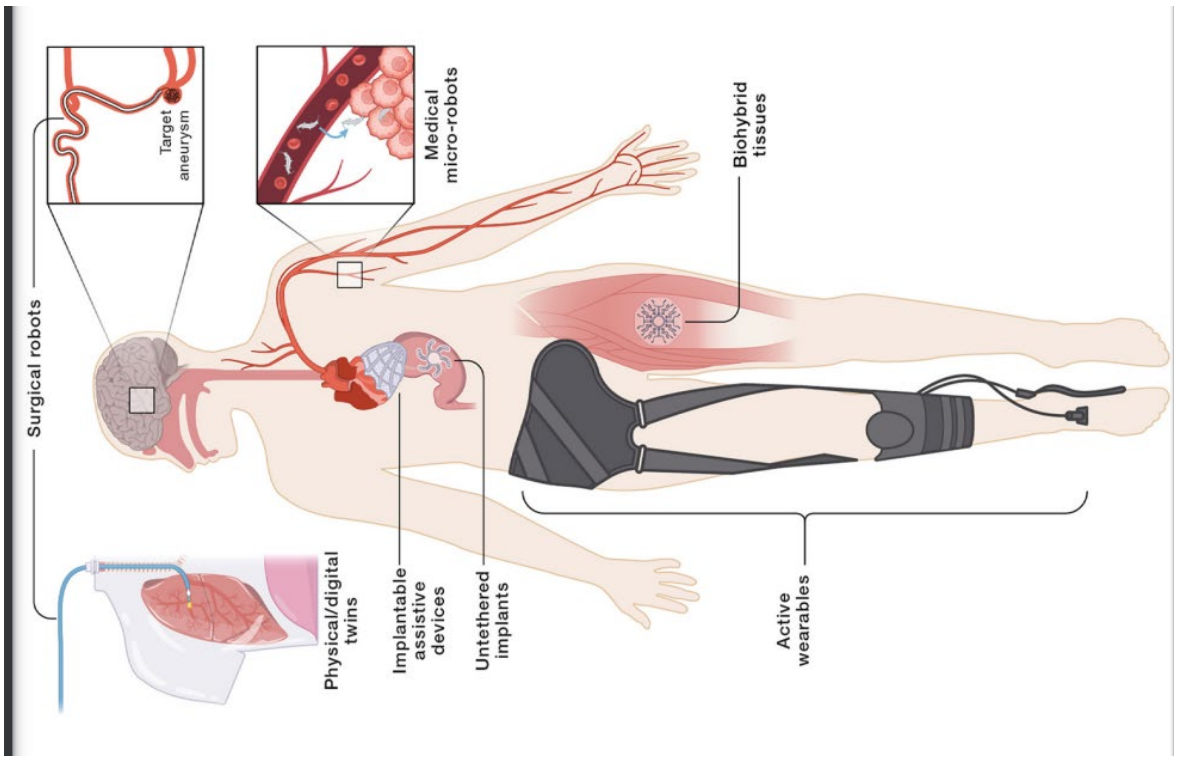
not if, but when

Data-Informed Decision Support (DIDS) Systems
Distributed Secure Near Real-time Mobile Digital Health Services

SOFT

Soft robotics for human health

Ritu Raman[1,*] **and Cecilia Laschi**[2,*]
[1]Department of Mechanical Engineering, Massachusetts Institute of Technology, Cambridge, MA, USA
[2]Department of Mechanical Engineering, National University of Singapore, Singapore, Singapore
*Correspondence: ritur@mit.edu (R.R.), mpeclc@nus.edu.sg (C.L.)
https://doi.org/10.1016/j.device.2024.100432



Therapeutic interventions *in vivo* to provide longitudinal health monitoring & modulation

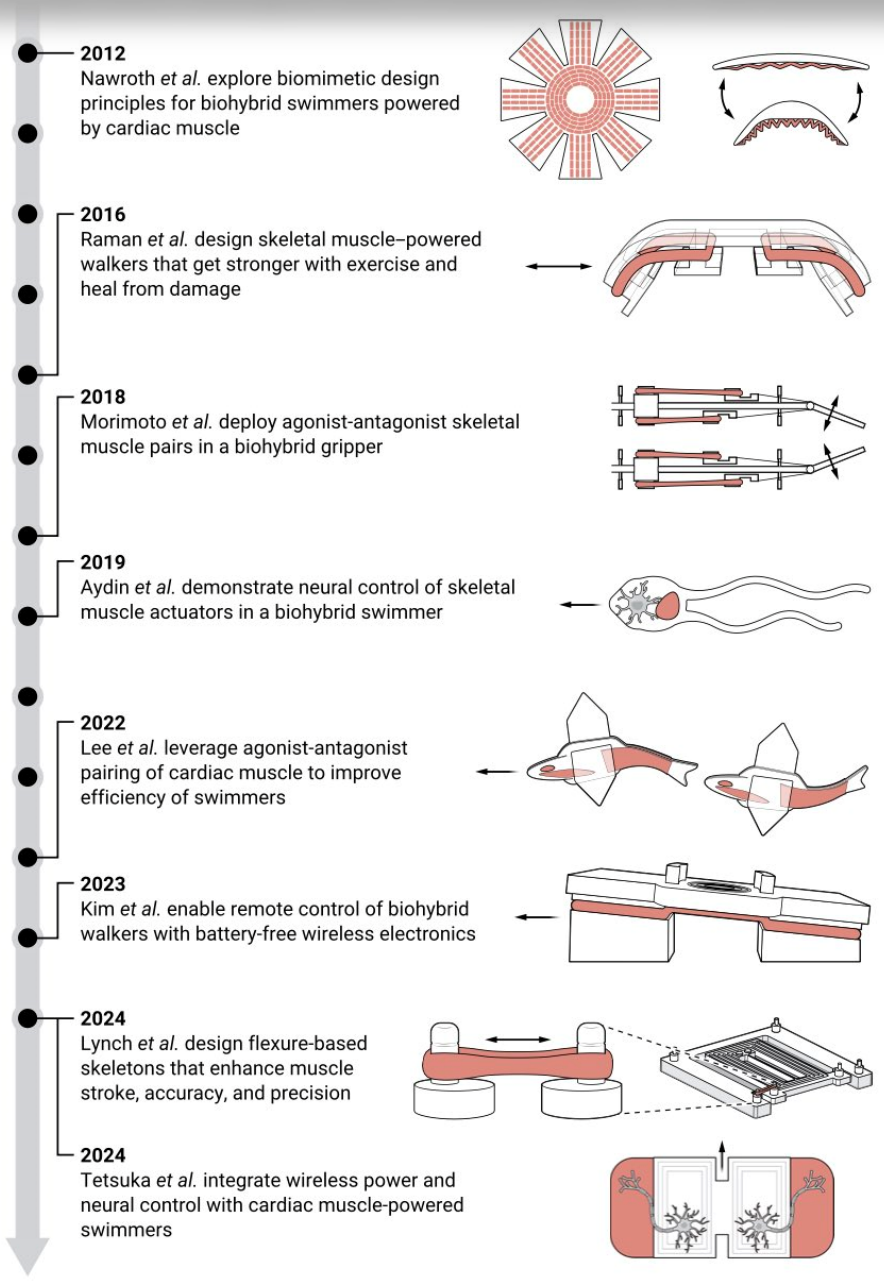
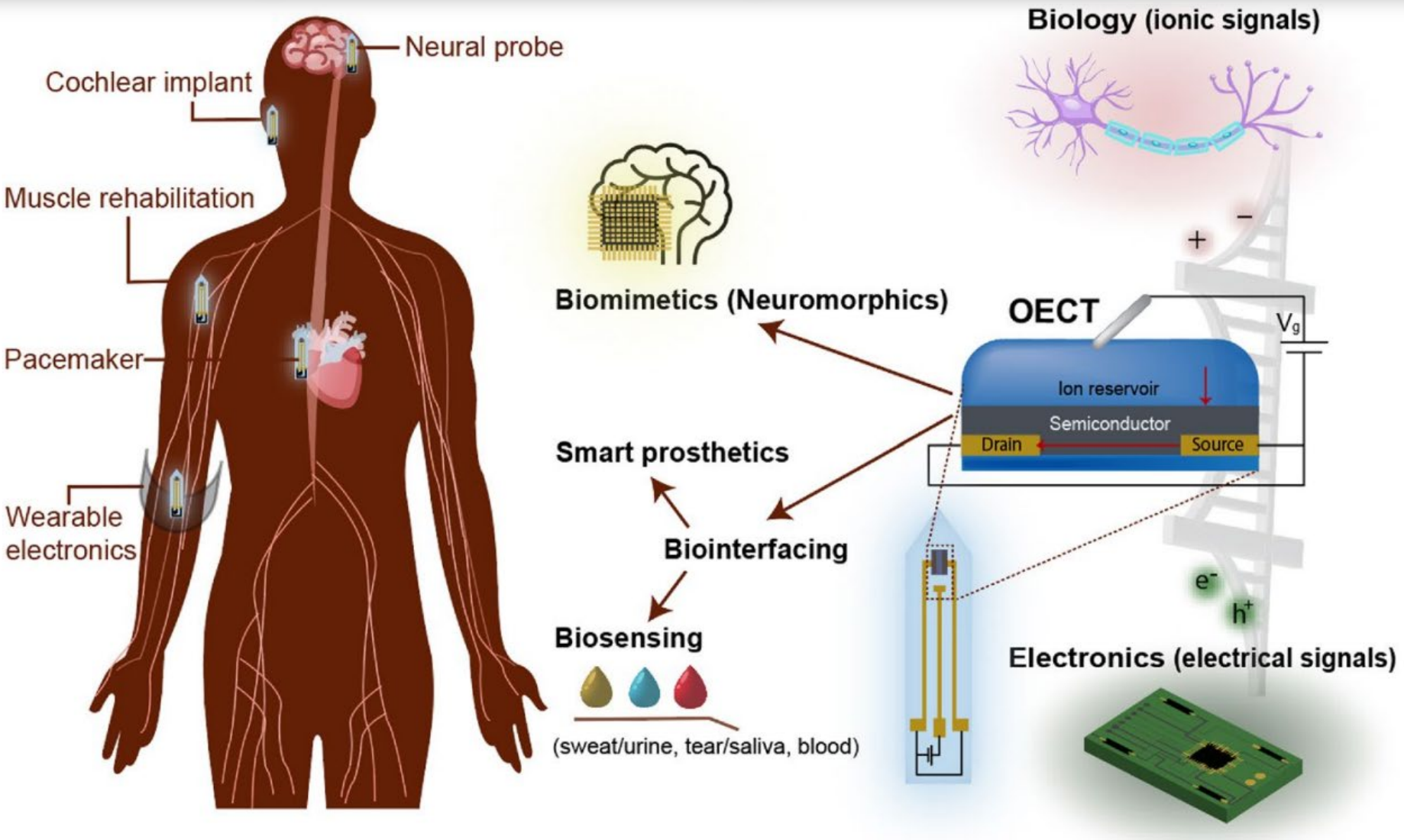


Fig. 1. An incomplete history of biohybrid robotics, showcasing recent efforts to enhance the efficiency, reproducibility, and complexity of cardiac and skeletal muscle–powered machines.

SOFT

Body-Machine Interface (in a material world)

https://dmse.mit.edu/faculty/aristide-gumyusenge



Roh, H., Cunin, C., Samal, S. *et al.* **Towards organic electronics that learn at the body-machine interface: A materials journey.** *MRS Communications* **12**, 565–577 (2022). https://doi.org/10.1557/s43579-022-00269-3

Is this the soul of BMI (body-machine interface) ?
Bio-sensing using organic electrochemical transistors

https://dmse.mit.edu/faculty/aristide-gumyusenge https://www.aristide.mit.edu

https://docs.google.com/document/d/e/2PACX-1vSJplrGJdAe40FKzeA_pb85Haumn0ZNh-oIKHbb-QRPnUeJMt_fHulub89ZzP-jug/pub

What is the question? Only good questions will unlock the potential of convergence.

CONVERGE ?

Population genetics (local, global)
from metabolomic data acquired
from blood bank (blood donors)
and blood (cord) bank samples

with

BMI (body-machine interface) data

Cellular senescence is a stress response that elicits a permanent cell cycle arrest and triggers phenotypic changes, e.g., production of a bioactive secretome, referred to as the senescence-associated secretory phenotype (**SASP**). Acute senescence induction protects against cancer and limits fibrosis, but lingering senescent cells drive age-related disorders. Targeting senescent cells to delay aging and limit dysfunction, known as “senotherapy,” could be a fool’s errand. Yet, drugs that selectively kill senescent cells, termed “senolytics” are gaining momentum. SASP-centered molecules are targets for senescence-associated diseases. Should we target these molecules, too?

What type of metabolome ?

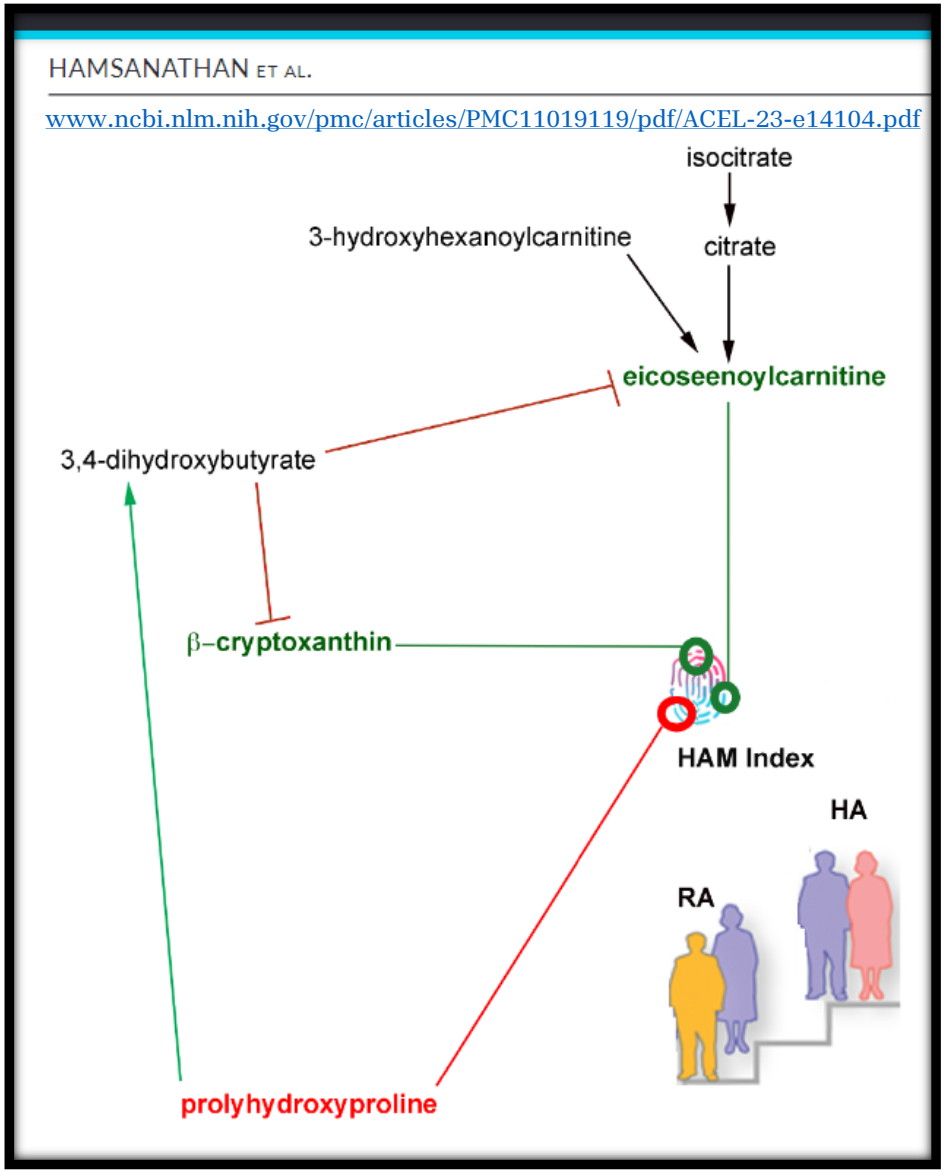
Clues for target molecules ?

Molecular fingerprint from senescence-associated

secretome phenotype (SASP) / inflammation markers

Birch J, Gil J. (2020) **Senescence and the SASP: many therapeutic avenues.** Genes Dev. 2020 Dec 1; 34(23-24):1565-1576. doi: 10.1101/gad.343129.120. PMID: 33262144
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7706700/pdf/1565.pdf

Hamsanathan S, Anthonymuthu T, Prosser D, Lokshin A, Greenspan SL, Resnick NM, Perera S, Okawa S, Narasimhan G, Gurkar AU. **A molecular index for biological age identified from the metabolome and senescence-associated secretome in humans.** Aging Cell. 2024 April; 23(4):e14104. doi: 10.1111/acel.14104. Epub 2024 March 7. PMID: 38454639; PMCID: PMC11019119.



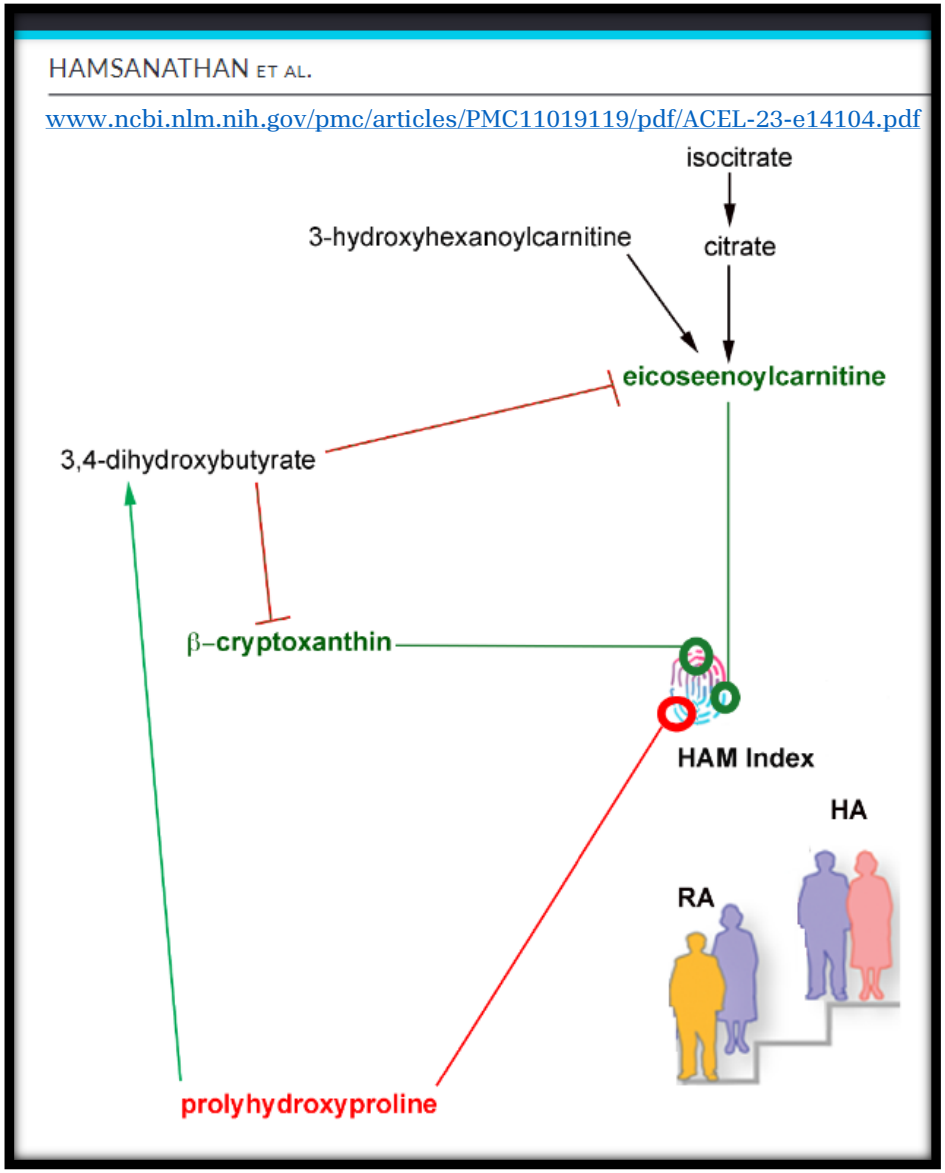
CAUSAL (??) METABOLITES FOR BIOLOGICAL AGING ?

Eicosenoylcarnitine and β-cryptoxanthin were positively causal to the healthy aging metabolic (HAM) index (HAMI) whereas prolyhydroxyproline had a negative impact on HAMI. Other metabolites, for example, 3,4 dihydroxybutyrate were seen to negatively impact β-cryptoxanthin and eicosenoylcarnitine. Prolyhydroxyproline was identified to positively influence 3,4 dihydroxybutyrate, suggesting cross talk between these group of metabolites (implicated in HAM and biological aging).

Could these molecules also serve as targets for testing donor blood samples?

https://onlinelibrary.wiley.com/doi/epdf/10.1111/acel.14104

Hamsanathan S, Anthonymuthu T, Prosser D, Lokshin A, Greenspan SL, Resnick NM, Perera S, Okawa S, Narasimhan G, Gurkar AU. **A molecular index for biological age identified from the metabolome and senescence-associated secretome in humans.** Aging Cell. 2024 April; 23(4):e14104. doi: 10.1111/acel.14104. Epub 2024 March 7. PMID: 38454639; PMCID: PMC11019119.



CAUSAL (??) METABOLITES FOR BIOLOGICAL AGING ?

Could these molecules also serve as targets for testing donor blood samples?

Can we envision a longitudinal epidemiological study where we test for these metabolites in stored blood samples from repeat blood donors in blood banks, locally and globally?

Will such analyses provide time series metabolomic data on the dynamics of these metabolites?

Can such data reveal target molecules for future cellular and molecular therapies?

https://onlinelibrary.wiley.com/doi/epdf/10.1111/acel.14104

It bears to be reiterated

CONVERGE

Population genetics (local, global) from metabolomic data acquired from blood bank (blood donors) and blood (cord) bank samples

with

BMI (body-machine interface) data

Invention?
Innovation??

*connecting **“spaces unrelated”** to catalyze discovery*

NEW BLOOD

www.science.org/content/article/ultimate-blood-substitute-us-military-betting-46-million

THERE WILL BE BLOOD

Is mimicking the cells that carry hemoglobin the key to a blood substitute?

Better than nature?

doi: 10.1126/science.za6bz9o

Decades of efforts have failed to develop a good substitute for oxygen-carrying red blood cells. A new candidate, ErythroMer, is still in preclinical testing but could be more durable and versatile than the real thing.

	Red blood cells	ErythroMer
SHELF LIFE	42 days	2 years
SIZE	7–8 μm	~0.2 μm
COMPATIBILITY	By blood type	Universal

A. FISHER/*SCIENCE*

For now, no human blood substitute is commercially available in the U.S. "There's a real gap here where we don't have access to blood for people bleeding to death outside of the hospital," says Doctor, who co-founded and is chief science officer of KaloCyte, a company hoping to develop ErythroMer into a commercial product.

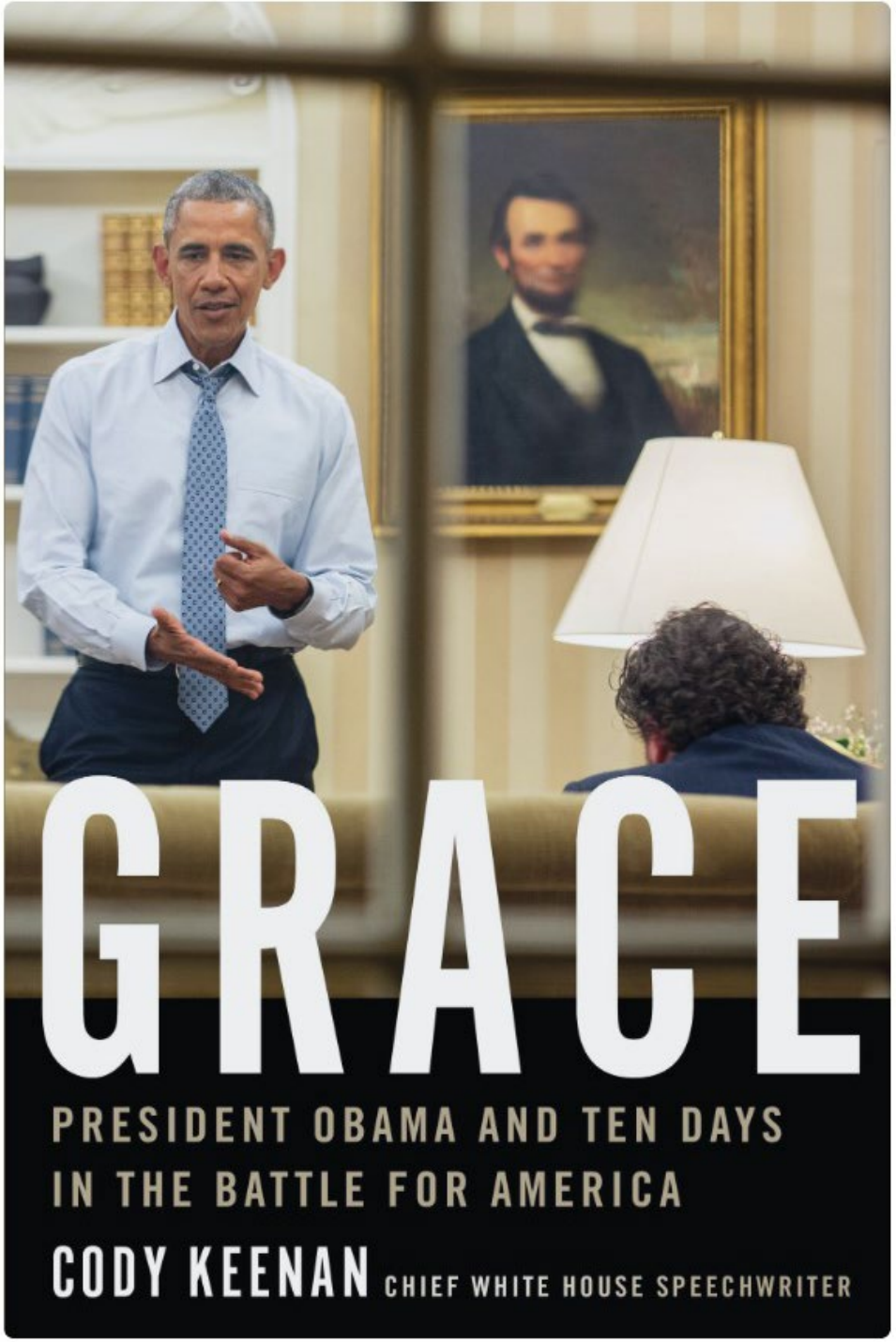
Universal Medium of Health, Healing, Humanity

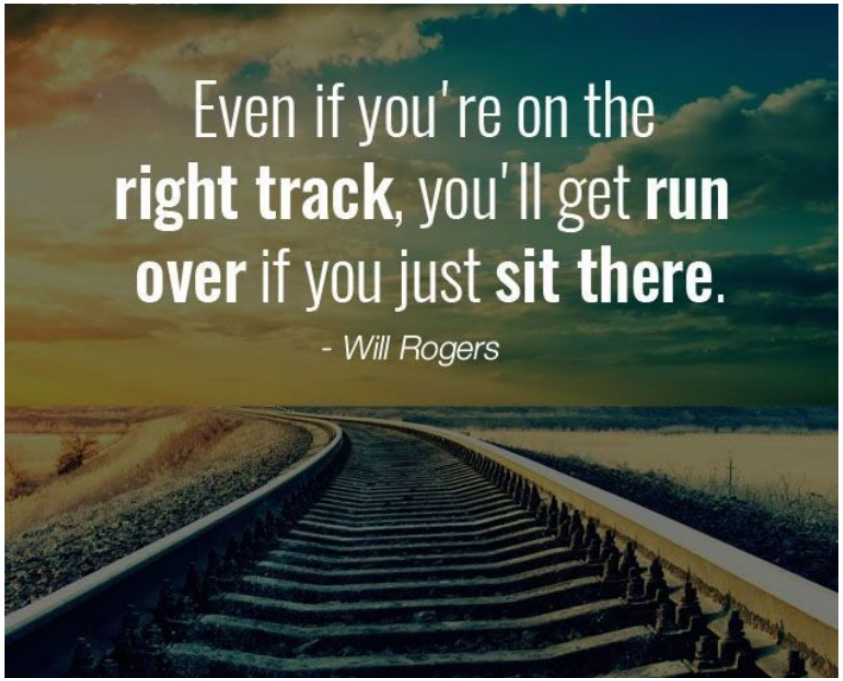
~ 5 million Americans will need a blood transfusion each year. Someone needs blood every 2 seconds. 1 in 7 people entering a hospital need blood. ~ 22,000 liters of donated blood used each day, i.e., almost ~ 1,000 liters of blood transfused every hour, every day, every year, to save lives.

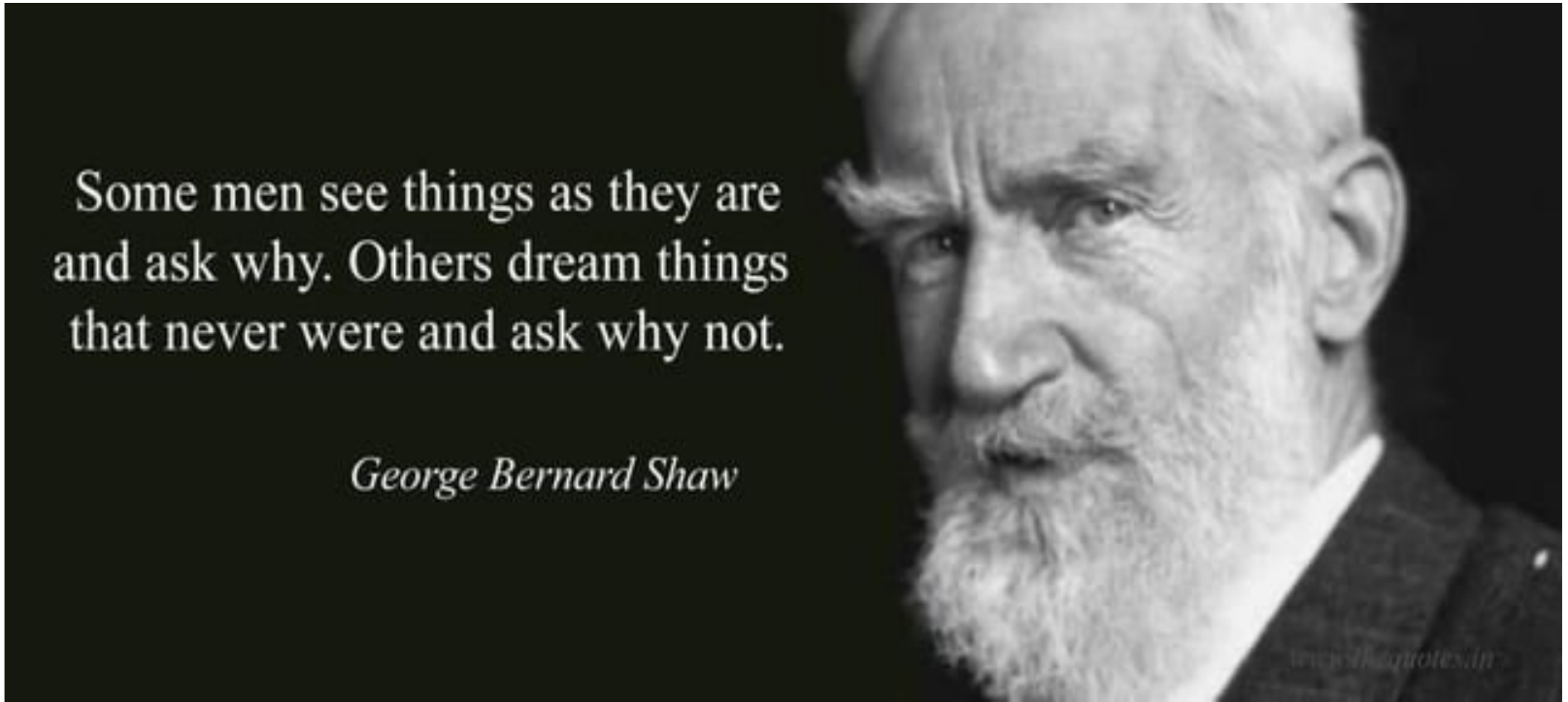
www.aha.org/news/headline/2024-01-29-groups-release-updated-statistics-us-blood-donation-use ◆ www.bloodbankofalaska.org/blood-facts

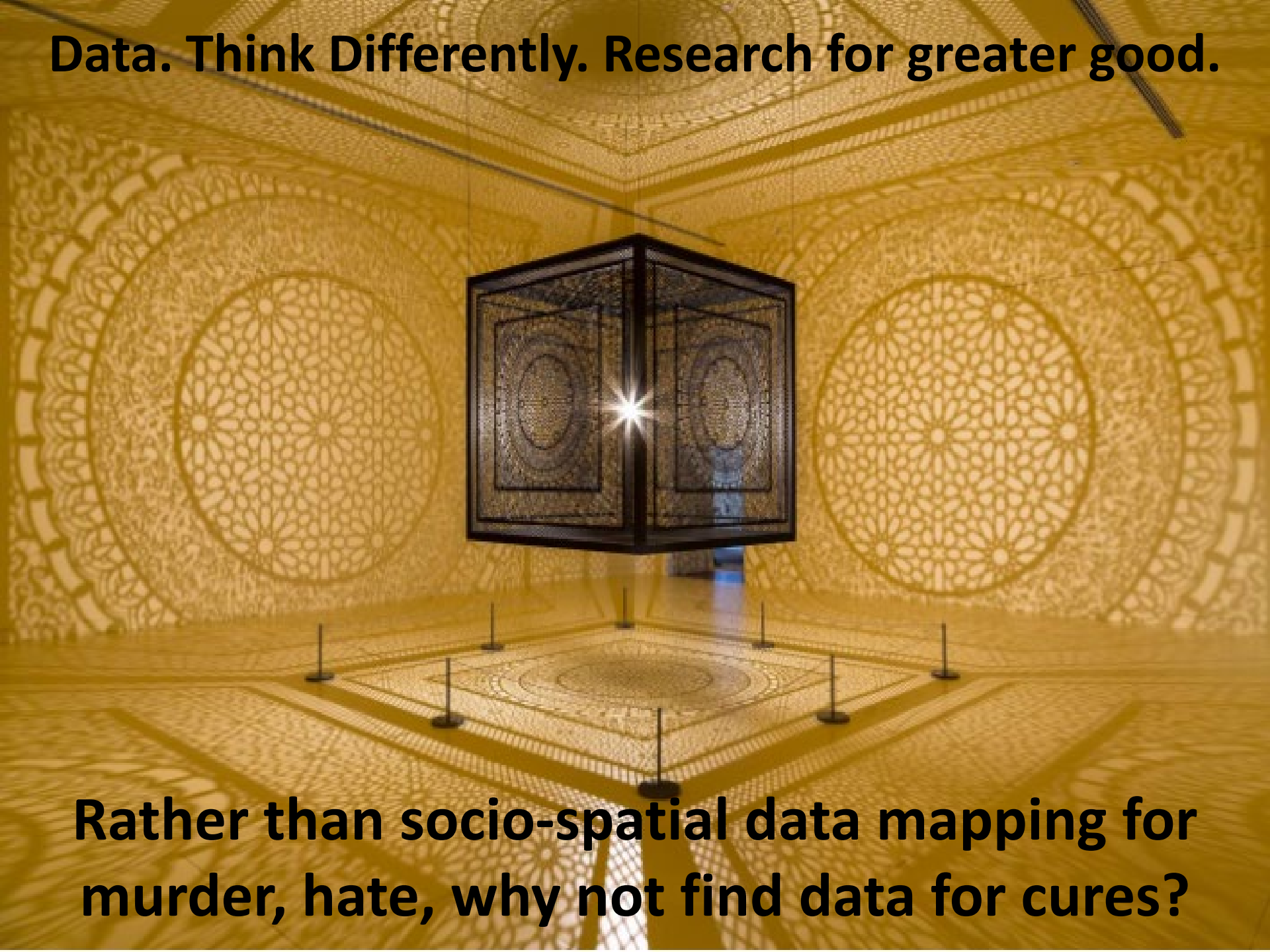
“FOCUS ON PURPOSE, NOT YOUR TITLE.”

“Worry less about what you want to be and think more about what you want to do.” Focus on purpose, for example, helping save lives and you’ll always have an impact, even if it is a drop in the ocean of need.




Even if you're on the
right track, you'll get run
over if you just sit there.
- Will Rogers


Some men see things as they are
and ask why. Others dream things
that never were and ask why not.
George Bernard Shaw


Data. Think Differently. Research for greater good.
Rather than socio-spatial data mapping for murder, hate, why not find data for cures?

DON’T MAKE THIS MISTAKE WITH DATA

PLEASE DON’T LET

AI

CORRUPT AND RUIN YOUR DATA ANALYTICS

https://www.technologyreview.com/2017/10/06/241837/the-seven-deadly-sins-of-ai-predictions/

MIT Technology Review

https://people.csail.mit.edu/brooks

The Seven Deadly Sins of AI Predictions

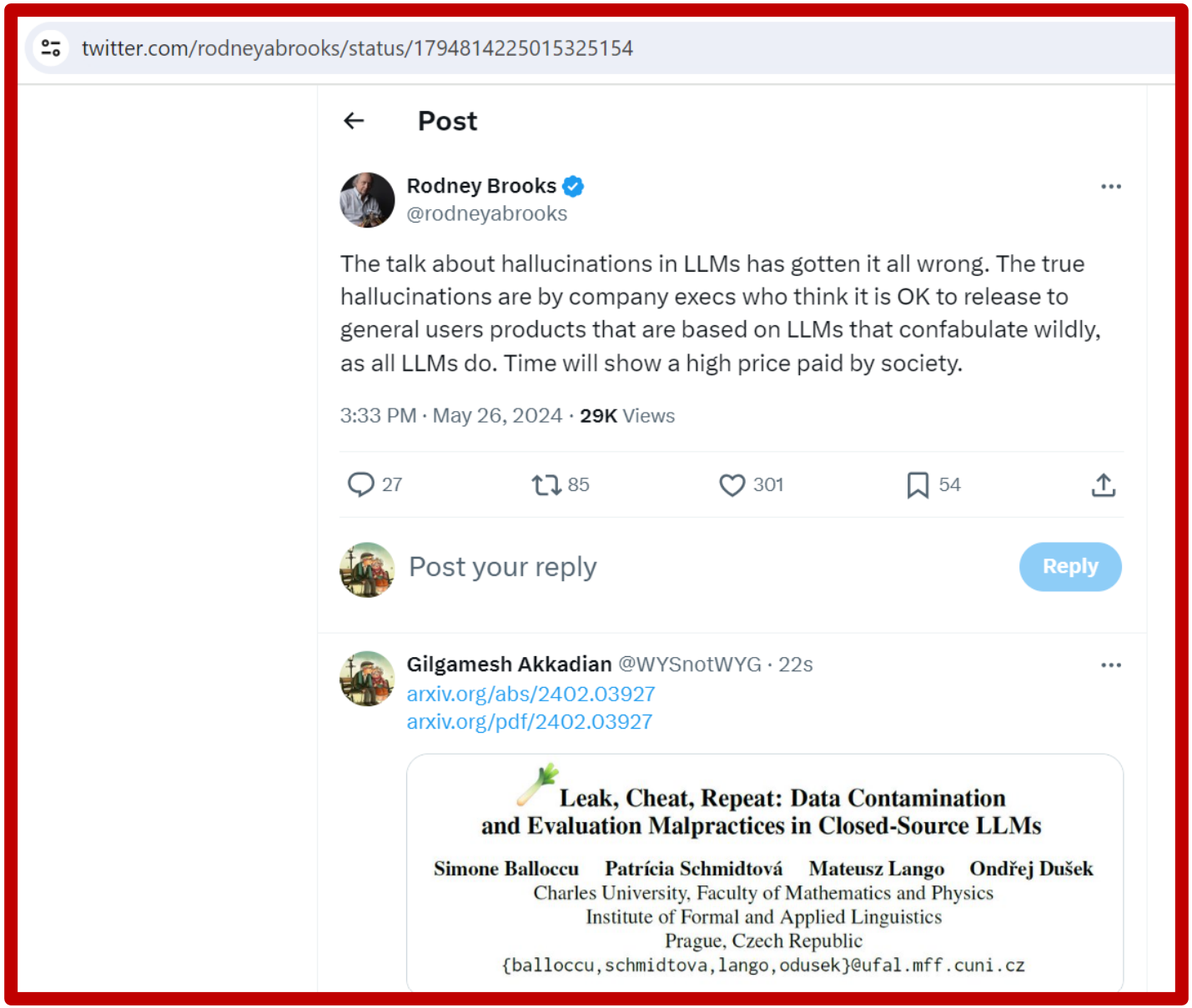
Mistaken extrapolations, limited imagination, and other common mistakes that distract us from thinking more productively about the future.

By Rodney Brooks

October 6, 2017

Rodney Brooks is the Panasonic Professor of Robotics (emeritus) at MIT. He is a robotics entrepreneur. Dr. Brooks is the former Director (1997 - 2007) of the MIT Artificial Intelligence Laboratory and then the MIT Computer Science & Artificial Intelligence Laboratory (CSAIL). He received a Ph.D. in Computer Science from Stanford University in 1981. He held research positions at Carnegie Mellon University and MIT, and a faculty position at Stanford before joining the faculty of MIT in 1984. From June 2014 until May 2020 he was a member of the Visiting Committee on Advanced Technology, VCAT, at the National Institute of Standards and Technology, NIST. Since June 2015 he has been an external member of GE's Robotics Advisory Council. From January 2016 until mid 2019 he was Deputy Chairman of the Advisory Board of Toyota Research Institute. From February 2019 until January 2021 he was "Luminary" at Bell Labs. Dr. Brooks is a Member of the National Academy of Engineering (NAE), a Founding Fellow of the Association for the Advancement of Artificial Intelligence (AAAI), a Fellow of the American Academy of Arts & Sciences (AAAS), a Fellow of the American Association for the Advancement of Science (the other AAAS), a Fellow of the Association for Computing Machinery (ACM), a Fellow of the Institute of Electrical and Electronics Engineers (IEEE), a Member of the Australian Academy of Science (AAS) and a Fellow of the Australian Academy of Technological Sciences and Engineering (ATSE).

Don’t subject your data to hallucinations



Who is Rodney Brooks? ● https://people.csail.mit.edu/brooks

www.nature.com/articles/d41586-024-02420-7

www.nature.com/articles/s41586-024-07566-y

nature.com/articles/d41586-024-02420-7

nature

AI ... naturally nonsensical

NEWS | 24 July 2024

AI models fed AI-generated data quickly spew nonsense

Researchers gave successive versions of a large language model information produced by previous generations of the AI – and observed rapid collapse.

By Elizabeth Gibney

Article

AI models collapse when trained on recursively generated data

https://doi.org/10.1038/s41586-024-07566-y

Received: 20 October 2023

Accepted: 14 May 2024

Published online: 24 July 2024

Open access

Check for updates

Ilia Shumailov[1,8]✉, Zakhar Shumaylov[2,8]✉, Yiren Zhao[3], Nicolas Papernot[4,5], Ross Anderson[6,7,9] & Yarin Gal[1]✉

Stable diffusion revolutionized image creation from descriptive text. GPT-2 (ref. 1), GPT-3(.5) (ref. 2) and GPT-4 (ref. 3) demonstrated high performance across a variety of language tasks. ChatGPT introduced such language models to the public. It is now clear that generative artificial intelligence (AI) such as large language models (LLMs) is here to stay and will substantially change the ecosystem of online text and images. Here we consider what may happen to GPT-{*n*} once LLMs contribute much of the text found online. We find that indiscriminate use of model-generated content in training causes irreversible defects in the resulting models, in which tails of the original content distribution disappear. We refer to this effect as 'model collapse' and show that it can occur in LLMs as well as in variational autoencoders (VAEs) and Gaussian mixture models (GMMs). We build theoretical intuition behind the phenomenon and portray its ubiquity among all learned generative models. We demonstrate that it must be taken seriously if we are to sustain the benefits of training from large-scale data scraped from the web. Indeed, the value of data collected about genuine human interactions with systems will be increasingly valuable in the presence of LLM-generated content in data crawled from the Internet.

What to do with ideas & uncorrupted data from research outcomes?

Here's one option, perhaps …

techcrunch.com/2024/04/06/when-it-comes-to-building-startups-in-boston-success-begets-success/

When it comes to building startups in Boston, success begets success

And from HubSpot to Klaviyo, it's had its share of successful exits

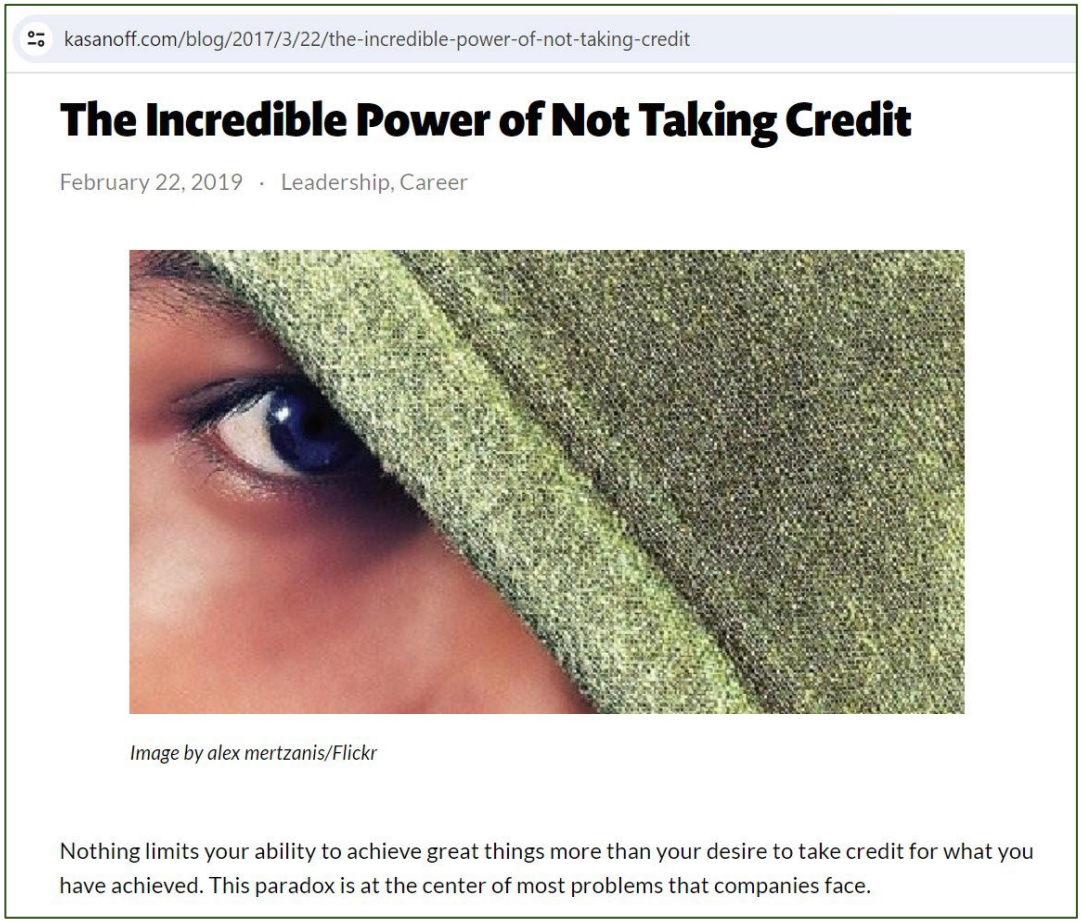
Ron Miller @ron_miller / 1:07 PM EDT • April 6, 2024

Comment

INNOVATE

https://techcrunch.com/2024/04/06/when-it-comes-to-building-startups-in-boston-success-begets-success

Collaborate Globally
Create Partnerships
Foster Key Alliances
Aspire to Inspire
Be Exemplary
Credibility
Dignity
Ethics
Teach
Learn
STEM
R&D



Happiness is key to success. Success is not the key to happiness.

STEM is a quite smart and fetching (catchy) moniker for marketing due to its global semantic cognitive imprint (aka “buzz”), but in education, it ought to become

STEEMM

Science ∘ Technology ∘ Engineering ∘ Economics ∘ Medicine ∘ Mathematics

*Utopians will be euphoric with STEEMM**MAHH** with the addition of Music, Arts, Humanities and History, as well.*

This document is “The Health of Nations – Part II”

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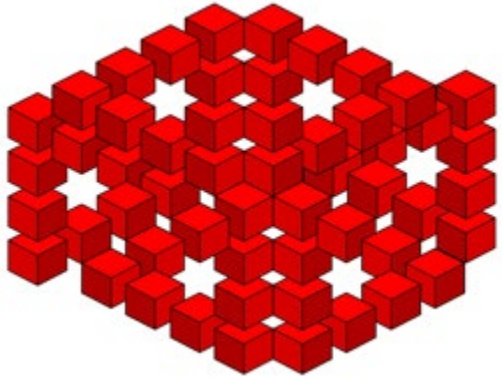

I have created nothing new

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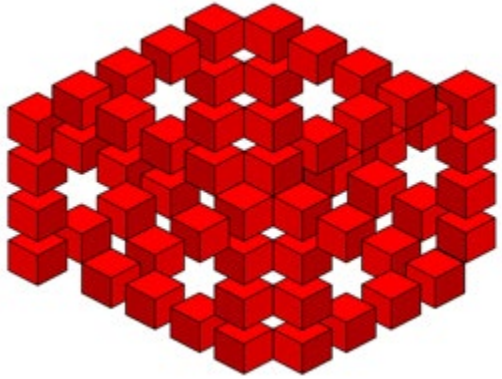
https://dspace.mit.edu/handle/1721.1/107893

Review "Healthcare" PDF for more cartoons

Forward looking statements and projections in this presentation are neither easy to accomplish nor instantaneous but are possible and credible.



Dr Shoumen Palit Austin Datta

MIT Auto-ID Labs, Senior Member, Affiliate, Department of Mechanical Engineering, Massachusetts Institute of Technology ▪ shoumen@mit.edu

Senior Scientist, MDPnP Lab Medical Device Interoperability, Massachusetts General Hospital, Harvard Medical School ▪ sdatta8@mgh.harvard.edu

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Anahita Dua, M.D., M.B.A., M.S.C., F.A.C.S., Vascular Surgeon, Associate Professor of Surgery, HMS Director, Vascular Lab; Co-Director, PADC/LEAPP; Assoc Director, Wound Care Center, Massachusetts General Hospital, Harvard Medical School www.massgeneral.org/doctors/20714/anahita-dua https://vascular.org/news-advocacy/articles-press-releases/dr-anahita-dua-named-presidential-leadership-scholar

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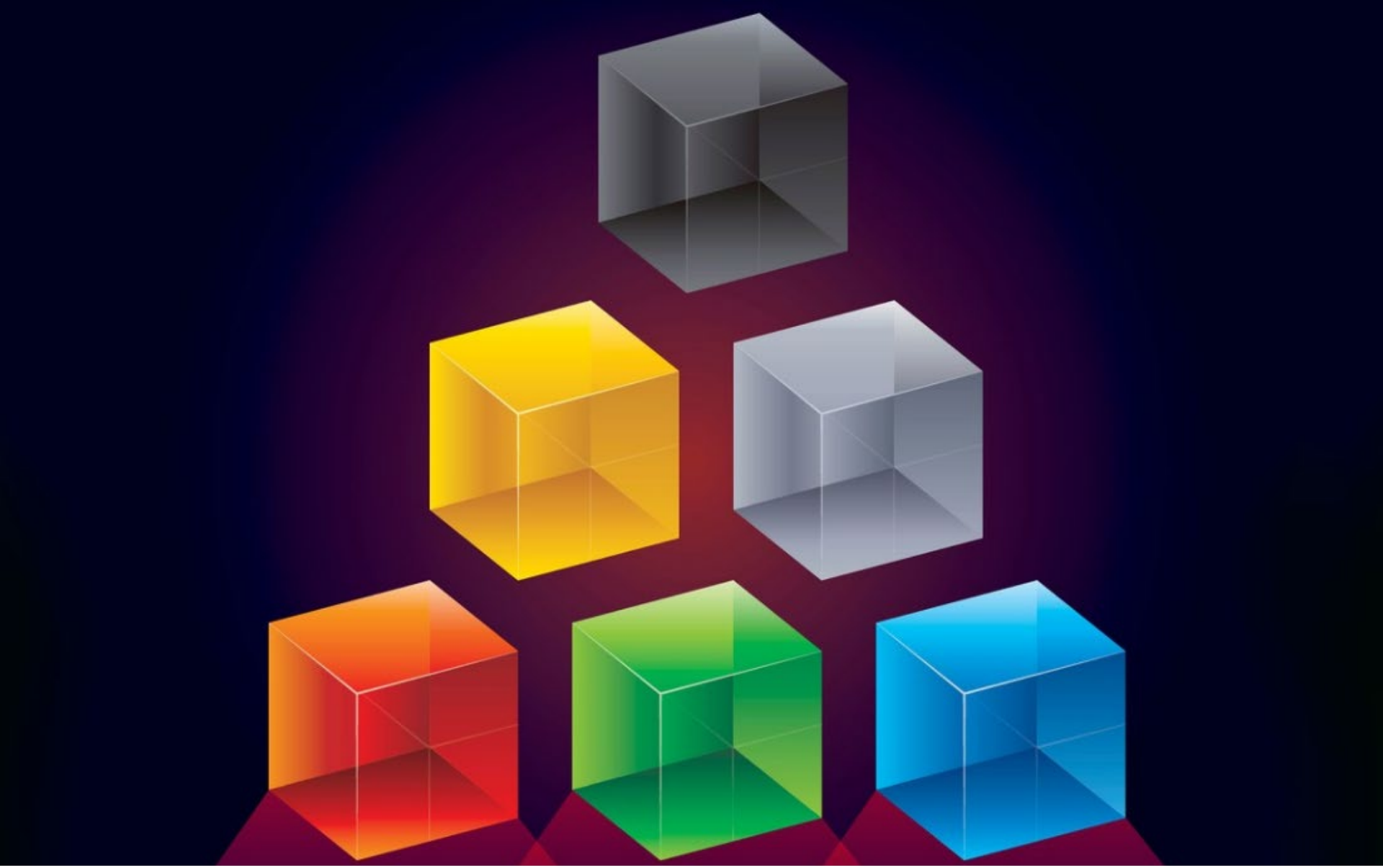
Julian Goldman, M.D., F.A.S.A. Massachusetts General Hospital, Harvard Medical School
Anesthesia, Critical Care and Pain Medicine, MGH Research Institute
Director, Biomedical Engineering, Mass General Brigham (MGB) https://mdpnp.mgh.harvard.edu
https://researchers.mgh.harvard.edu/profile/14161732/Julian-Goldman

Sanjay Sarma, Ph.D., Vice-President, Massachusetts Institute of Technology (MIT)
Fred and Daniel Fort Flowers (1941) Professor of Mechanical Engineering, MIT
President, CEO and Dean, Asia School of Business (MIT Sloan, Kuala Lumpur, Malaysia)
https://meche.mit.edu/people/faculty/sesarma@mit.edu
https://asb.edu.my/about/leadership-team/sanjay-sarma/

Thomas H. McCoy, M.D., Assistant Prof of Medicine & Psychiatry, Harvard Medical School
CGM Psychiatry, Massachusetts General Hospital Research Institute; Psychiatrist, MGH
https://researchers.mgh.harvard.edu/profile/6264601/Thomas-McCoy



http://bit.ly/HEALTHCARE-RESOURCE-01

MIT Auto-ID Labs, Senior Member, Affiliate, Department of Mechanical Engineering, Massachusetts Institute of Technology ▪ shoumen@mit.edu

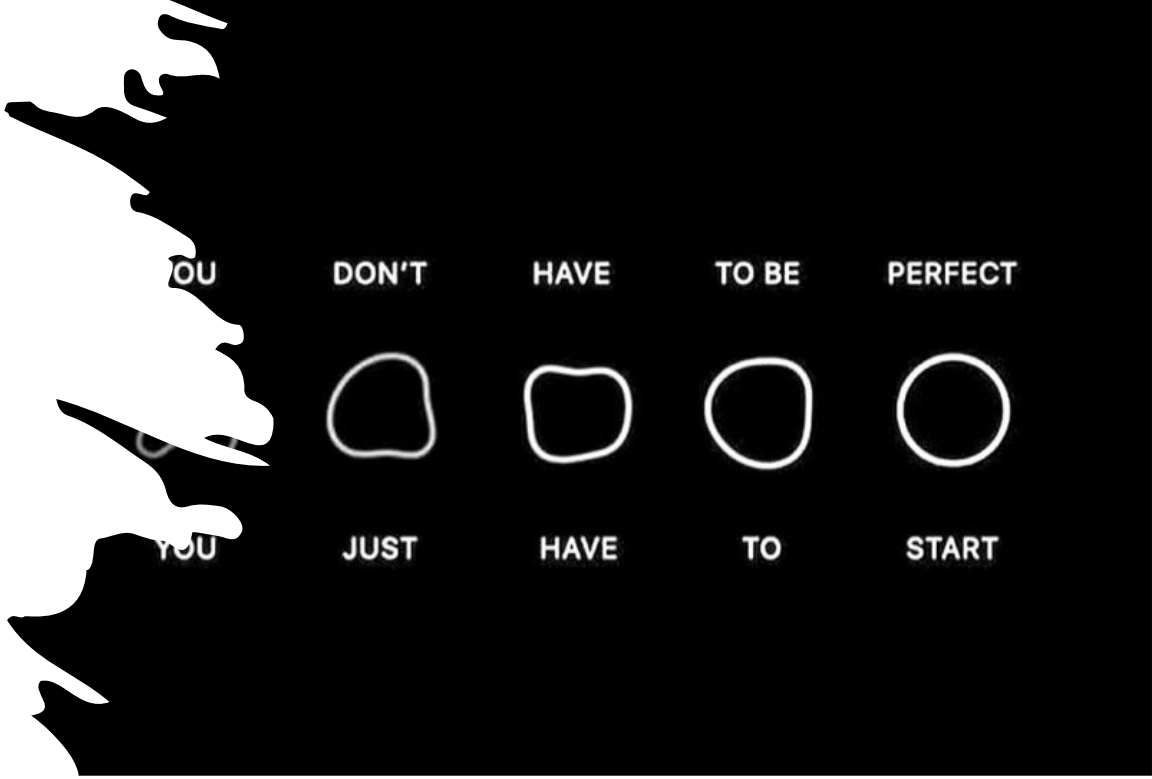
Senior Scientist, MDPnP Lab Medical Device Interoperability, Massachusetts General Hospital, Harvard Medical School ▪ sdatta8@mgh.harvard.edu

Most of this material was presented on 10-11-2022 to the Digital Healthcare Sub-Committee members of the EU Political Action Committee (EUPAC) at a private meeting in Gif-sur-Yvette, France (organized by the “Science Valley” institutions in France). The author (no political affiliation) was invited to speak.

How to

This section was added after 10-11-2022. It was edited in 2023 & updated in 2024 during talks/presentations to biotech and medtech entrepreneurs, VCs, companies and “digital healthcare / digital transformation” executive education sessions in US, EU and SK (remote).

- Change is not accompanied by a formula.



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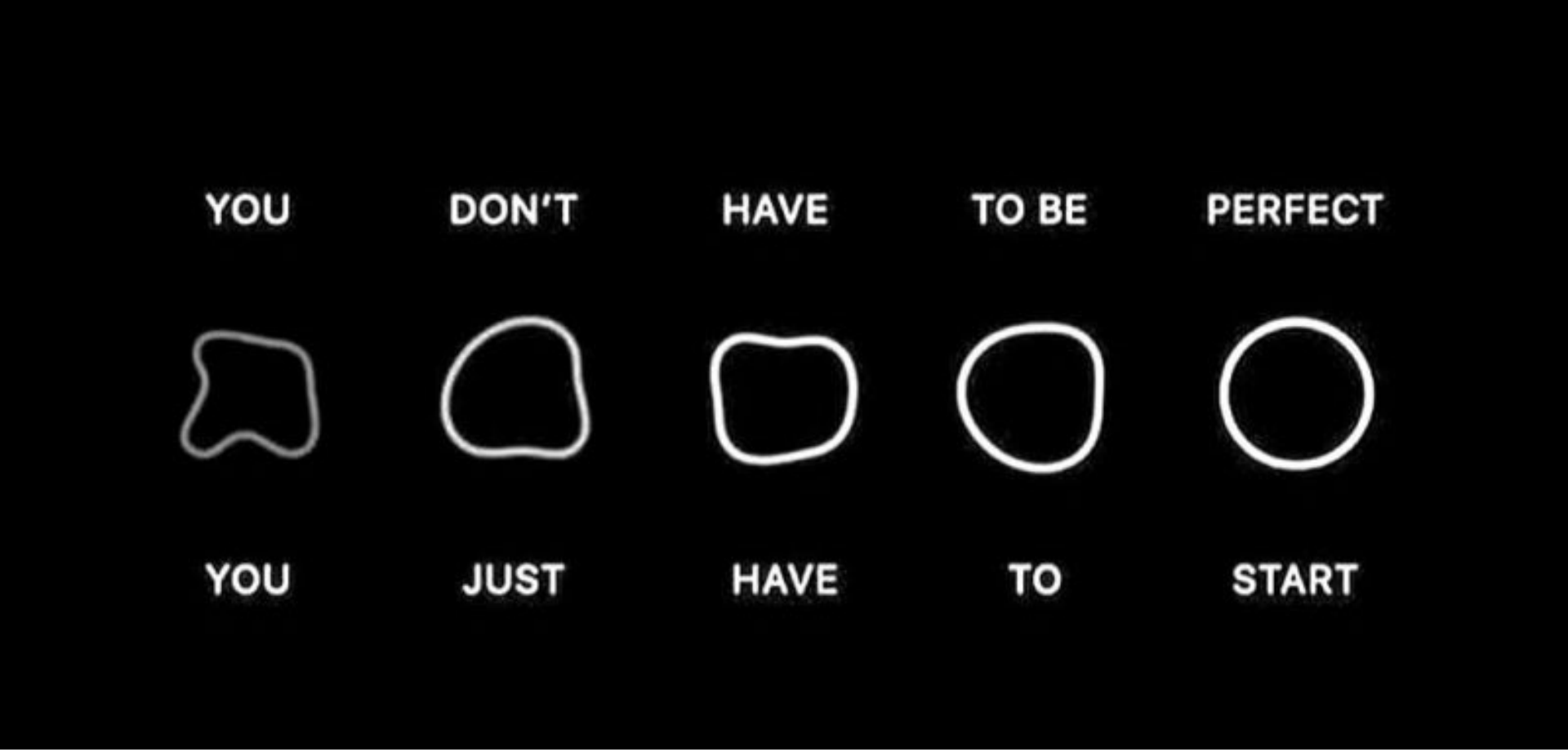
https://sloanreview.mit.edu › article › first-to-market-fir...

First to Market, First to Fail? Real Causes of Enduring Market ...

by GJ Tellis · 1996 · Cited by 584 — Using a historical method, the authors try to determine why pioneeers **fail** and **early** leaders succeed.

https://sloanreview.mit.edu/article/first-to-market-first-to-fail-real-causes-of-enduring-market-leadership



Digital transformation of healthcare and adoption of digital solutions in medicine will favor the bold and the unconventional approach as long as the science and engineering of the digital device or medical system can withstand the most rigorous evaluation by experts.

Healthcare Digital Solutions are not business as usual

Then why should we treat it as a widget? Why use the conventional product marketing approach? Why assume that the highly educated customers (MDs/MD-PhDs) will trust the device, its data,its operation and the outcome? Why should you forget that medical digital solutions can spell life/death?

Healthcare Digital Solutions

sales, marketing, and profitability

must be based on

TRUSTED COLLABORATION

TRUSTED COLLABORATION

TRUSTED COLLABORATION

IN RESPONSE TO THE EBOLA CRISIS, 2014

C O L L A B O R A T E

to transform the world

Dr. Shuren received his B.S. and M.D. degrees from Northwestern University under its Honors Program in Medical Education. He completed his medical internship at Beth Israel Hospital in Boston, his neurology residency at Tufts New England Medical Center, and a fellowship in behavioral neurology and neuropsychology at the University of Florida. He received his J.D. from the University of Michigan.

Participation of the US FDA CDRH was a powerful incentive for medical device manufacturers to explore innovative medical technology solutions, especially those benefiting from interoperability between manufacturers

JEFF SHUREN
DIRECTOR
FDA
CDRH

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
10903 New Hampshire Avenue
Room 5447, Building 66
Silver Spring, MD 20993-0002

November 3, 2014

Julian M. Goldman, MD
Director, Medical Device Interoperability Program
65 Landsdowne Street
Cambridge, MA 02139

Dear Dr. Goldman,

Thank you for reaching out to the Center for Devices and Radiological Health (CDRH) via our Emergency Preparedness/Operations and Medical Countermeasures (EMCM) Program.

We understand that The Medical Device "Plug-and-Play" (MD PnP) Interoperability Program, under your coordination, has been asked by the White House Office of Science and Technology Program to mobilize resources among medical device manufacturers and the clinical community, so as to design and demonstrate proof of concept for an interoperable platform that would enable critical care of Ebola-infected patients in an isolation environment with reduced exposure to health care workers.

FDA recognizes the importance of implementing strategies that minimize direct exposure of clinical personnel to patients infected with Ebola virus. We understand that MDPNP, along with its collaborators, are developing potential approaches that would include comprehensive data access and potential remote control of medical devices in the isolation environment, thereby reducing the risk of healthcare worker exposure to the virus.

CDRH recognizes the importance of these efforts and is ready and willing to collaborate with you, the clinical community and your industry partners to demonstrate the potential of this technology in serving this particular public health emergency. We are eager to observe the demonstration taking place Friday November 7th for OSTP, and we look forward to participating in the development of next steps with MDPNP and your medical device partners so as to do our part in enabling advancement of technology that can protect our healthcare workers who put themselves on the front line to promote the public health mission.

Sincerely,

Jeffrey Shuren, M.D., J.D.
Director
Center for Devices and
Radiological Health

ACTIVE PARTICIPATION OF FDA & MDPnP

EBOLA

COLLABORATORS

MD PnP MedTech Hackathon Open Medical Device and Data Integration Platforms to Support the Management of Ebola

TRUST DEPENDS ON

CREDIBILITY

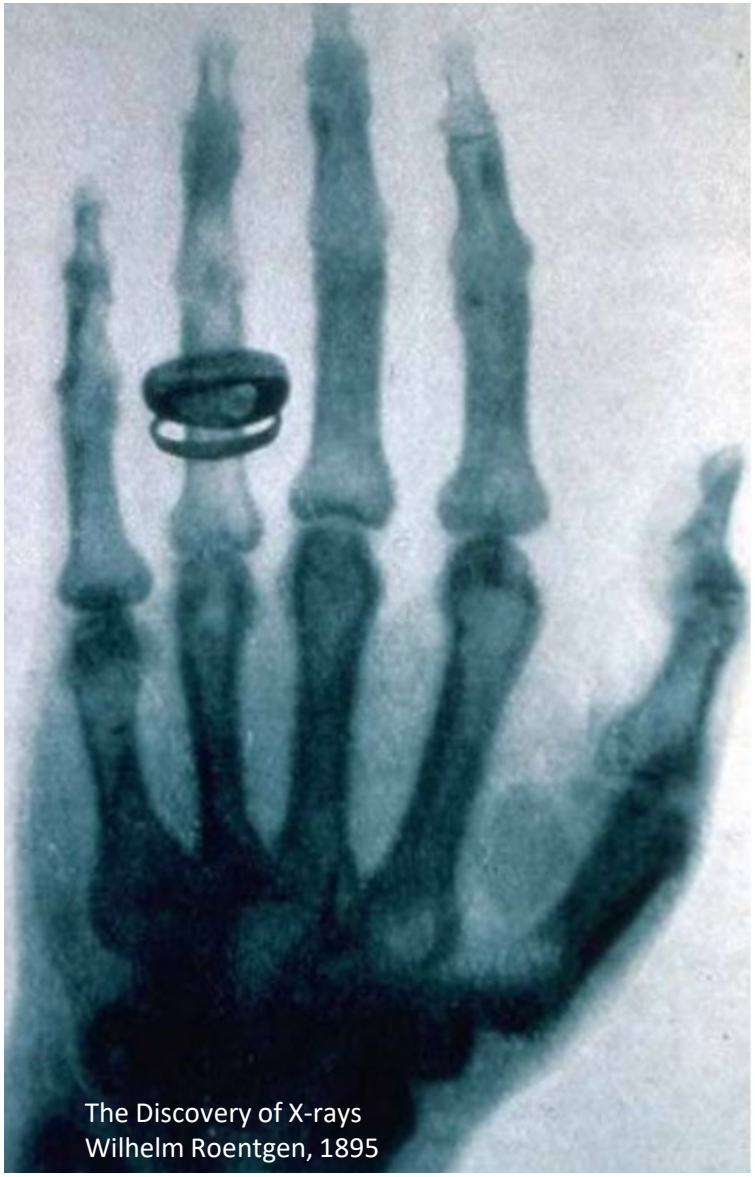
Communicate

Collaborate

Cooperate

CoCreate

Credible



The Discovery of X-rays
Wilhelm Roentgen, 1895

Communicate

Collaborate

Cooperate

CoCreate

Credible

CLINICAL RESEARCH PARTNERSHIPS

Customer is exposed to products you have

Company is exposed to customer's need (present, future)

Understand case-specific functional requirement for cSESI

(cyber) Security, Efficiency, Scalability, Interoperability

Communicate

Collaborate

Cooperate

CoCreate

Credible

CLINICAL RESEARCH PARTNERSHIPS

Be a trusted advisor, innovation partner and creative provider

NOT

just a vendor, supplier, contractor

Communicate

Collaborate

Cooperate

CoCreate

Credible

CLINICAL RESEARCH PARTNERSHIPS

initiate, catalyze, lead

new product development

enhance existing products/systems

integrate hardware/software dependent network of functions

co-create purpose-specific network of devices and incorporate cSESI

Communicate

Collaborate

Cooperate

CoCreate

Credible

CLINICAL RESEARCH PARTNERSHIPS

initiate, catalyze, lead

joint federal grants for

funding

research, development, innovation

Communicate

Collaborate

Cooperate

CoCreate

Credible

CLINICAL RESEARCH PARTNERSHIPS

Proof of Excellence

Co-creation of Testbed

New Customer Pre-sales Site Visit

Amplification of Business Development

Communicate

Collaborate

Cooperate

CoCreate

Credible

CLINICAL RESEARCH PARTNERSHIPS

Proof of Excellence

Co-creation of Testbed

Create Testbeds in hospitals with global recognition

Market pre-sales (biz dev) by leveraging brand value

University and University Hospital R&D Alliances

Idea generation

Evolution of device hardware/software

Predict what tools/devices future may need

Create the Future

Build, Test, Evaluate

Partner to Implement

Communicate
Collaborate
Cooperate
CoCreate
Credible

ACADEMIC R&D

CREDIBILITY

KEY TO BRAND

RECOGNITION

Academic-Industry Forum

under the umbrella of

CASTE

Council of Advisors for Science, Technology and Engineering

Academic platform for inviting competitors

Medium for name / brand recognition

Networking for future partners

Inviting funding agencies

Building Relationships

Exploring Unknowns

Decision Makers

Invite “Stars”

CASTE is inspired by PCAST as in https://www.whitehouse.gov/pcast/

Academic-Industry Forum

under the umbrella of

CASTE

Council of Advisors for Science, Technology and Engineering

CREDIBILITY

OF INVITED MEMBERS

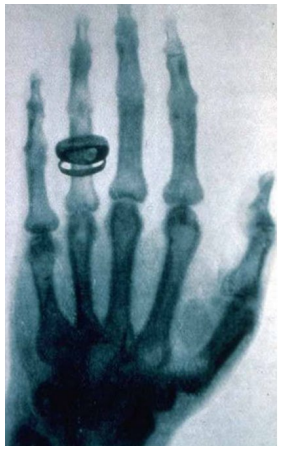
OFFERS MOMENTUM

“HOW TO” promote Digital Solutions for Healthcare, usher Digital Transformation in Medicine, catalyze Digital System of Systems

SUMMARY

- Build relationships with high credibility individuals.
- Build clinical research partnerships through specific nodes of credible decision makers, in the system, with the skills to accelerate implementation.
- Build university and university teaching hospital affiliated R&D “lablets” to extract a sense of the future through collaboration and personnel (future employees).
- Create an academic-industry forum using CASTE to bring together high performing credibility brands.

NOTES:



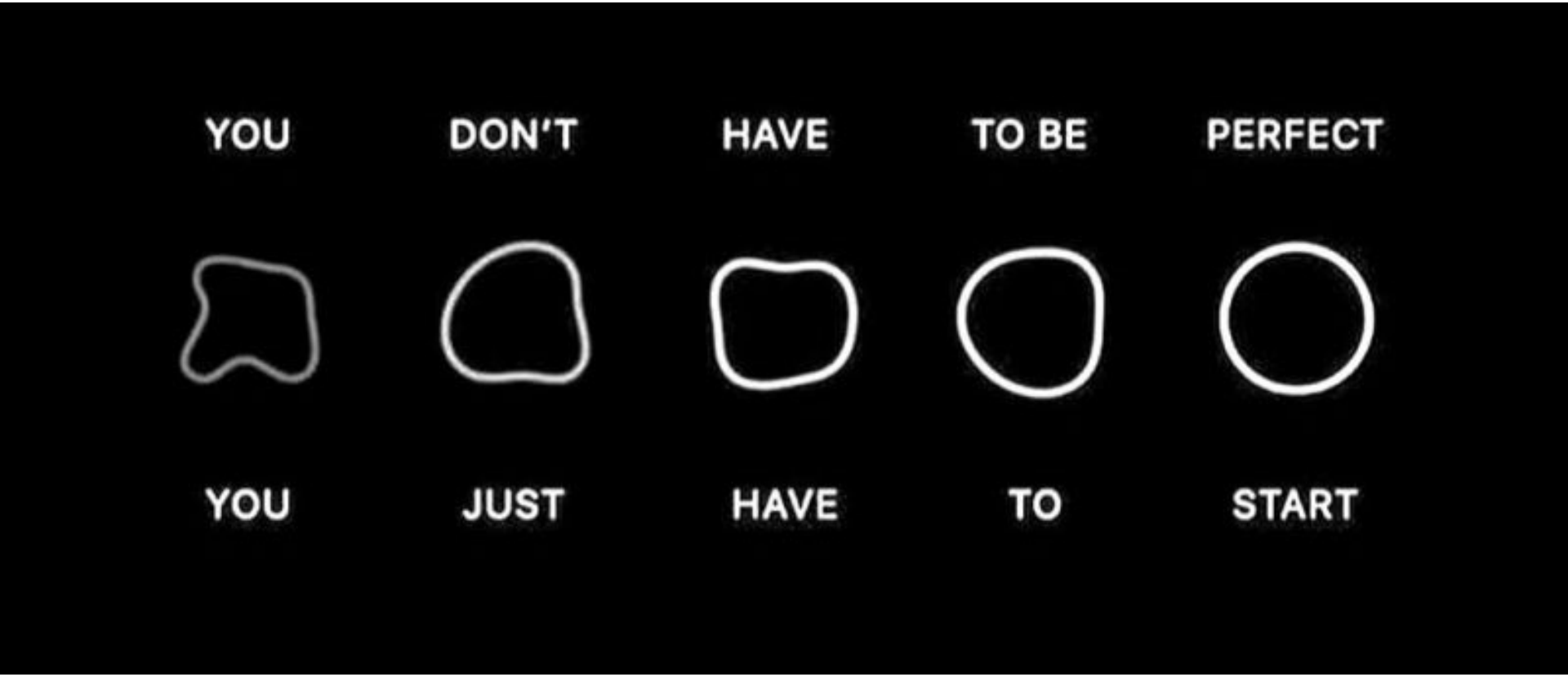
- Building relationships are key but not difficult. But, nurturing the relationship is far more significant for long term value/credibility (strategic continuity infuses trust).
- Companies tend to focus on relationships to amplify profitability. It is not a prudent approach because long term credibility outshines short term potential for profit. Nodes of influencers are more effective in catalyzing change, if influence is based on credibility, even in a different field.
- Partnerships without trust are brittle with limited potential for ROI. Financial investment in the partnership is critical but it is also important to consider human investment (company scientist as a visiting research fellow working with practitioners). Creative balance of investment/individuals, when combined, yields more than the sum of the parts.
- University alliances are good sources of ideas, supply chain of talent, potential for grant funding for collaborative R&D.
- CASTE could be a powerful platform for profitability as long as the focus is on credibility, rigor, optimizing performance.

https://www.blackrock.com/corporate/literature/whitepaper/lifting-global-growth-by-investing-in-women.pdf

WISE

Women in Science and Engineering

About the author – please visit https://dspace.mit.edu/handle/1721.1/146158



Shoumen Palit Austin Datta

MDPnP Lab and Cybersecurity Program, Department of Anesthesiology, Massachusetts General Hospital, Harvard Medical School, Partners Research Building, 65 Landsdowne Street, Cambridge, MA 02139, USA (sdatta8@mgh.harvard.edu) https://mdpnp.mgh.harvard.edu

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MIT Auto-ID Labs, 35-208, Department of Mechanical Engineering, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, MA 02139, USA (shoumen@mit.edu) https://autoid.mit.edu/shoumen-datta▪http://autoid.mit.edu/people-2