

2019 Underwriting Issues & Innovation Seminar
July 28-30, 2019
Rosemont, IL

Medical/Technological Advances

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2019 Underwriting Issues & Innovation Seminar

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Session #4, It's All About Wellbeing – Not Healthcare

7/29/2019



SOCIETY OF ACTUARIES

Antitrust Compliance Guidelines

Active participation in the Society of Actuaries is an important aspect of membership. While the positive contributions of professional societies and associations are well-recognized and encouraged, association activities are vulnerable to close antitrust scrutiny. By their very nature, associations bring together industry competitors and other market participants.

The United States antitrust laws aim to protect consumers by preserving the free economy and prohibiting anti-competitive business practices; they promote competition. There are both state and federal antitrust laws, although state antitrust laws closely follow federal law. The Sherman Act, is the primary U.S. antitrust law pertaining to association activities. The Sherman Act prohibits every contract, combination or conspiracy that places an unreasonable restraint on trade. There are, however, some activities that are illegal under all circumstances, such as price fixing, market allocation and collusive bidding.

There is no safe harbor under the antitrust law for professional association activities. Therefore, association meeting participants should refrain from discussing any activity that could potentially be construed as having an anti-competitive effect. Discussions relating to product or service pricing, market allocations, membership restrictions, product standardization or other conditions on trade could arguably be perceived as a restraint on trade and may expose the SOA and its members to antitrust enforcement procedures.

While participating in all SOA in person meetings, webinars, teleconferences or side discussions, you should avoid discussing competitively sensitive information with competitors and follow these guidelines:

- **Do not** discuss prices for services or products or anything else that might affect prices
- **Do not** discuss what you or other entities plan to do in a particular geographic or product markets or with particular customers.
- **Do not** speak on behalf of the SOA or any of its committees unless specifically authorized to do so.
- **Do** leave a meeting where any anticompetitive pricing or market allocation discussion occurs.
- **Do** alert SOA staff and/or legal counsel to any concerning discussions
- **Do** consult with legal counsel before raising any matter or making a statement that may involve competitively sensitive information.

Adherence to these guidelines involves not only avoidance of antitrust violations, but avoidance of behavior which might be so construed. These guidelines only provide an overview of prohibited activities. SOA legal counsel reviews meeting agenda and materials as deemed appropriate and any discussion that departs from the formal agenda should be scrutinized carefully. Antitrust compliance is everyone's responsibility; however, please seek legal counsel if you have any questions or concerns.

Presentation Disclaimer

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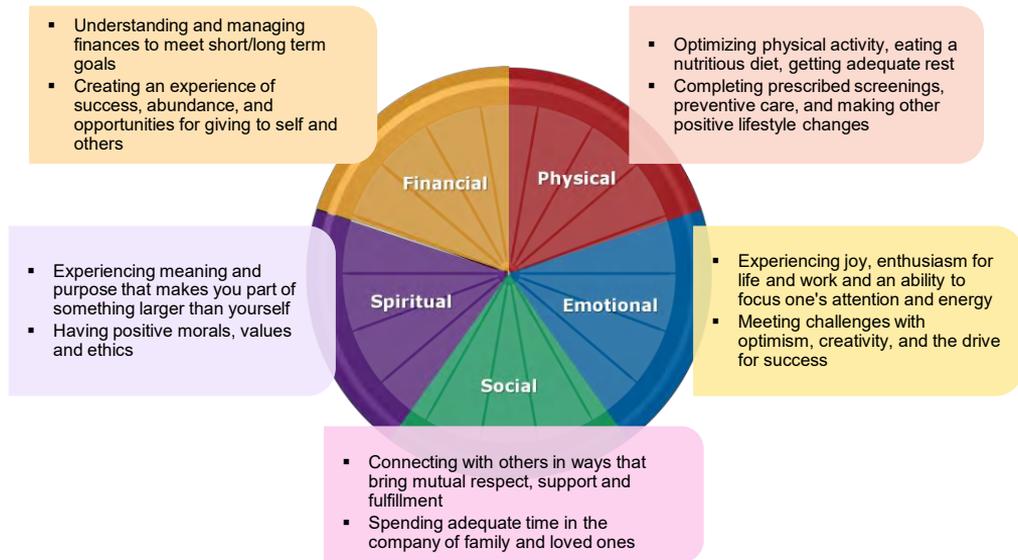
Atul Gawande, MD

“We’ve been wrong about what our job is in medicine. We think our job is to ensure health and survival. But really it is larger than that. It is to enable well-being”

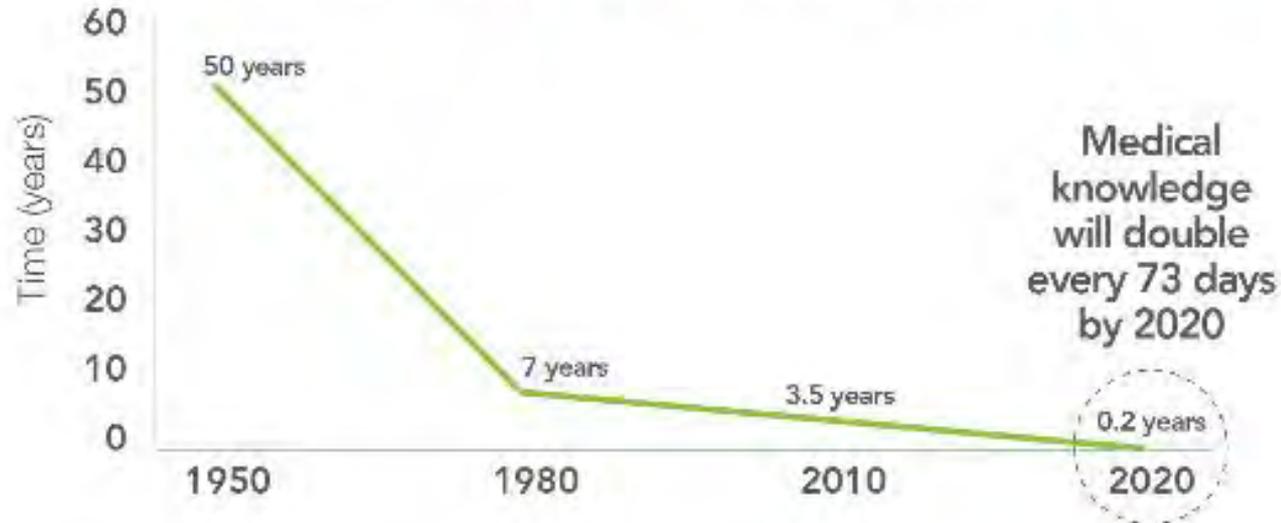
As an insurance company we
are in a unique position to
Impact multidimensional well-being



Prudential Global Health - 5 Dimensions of Health



Time To Double Medical Knowledge Is Decreasing



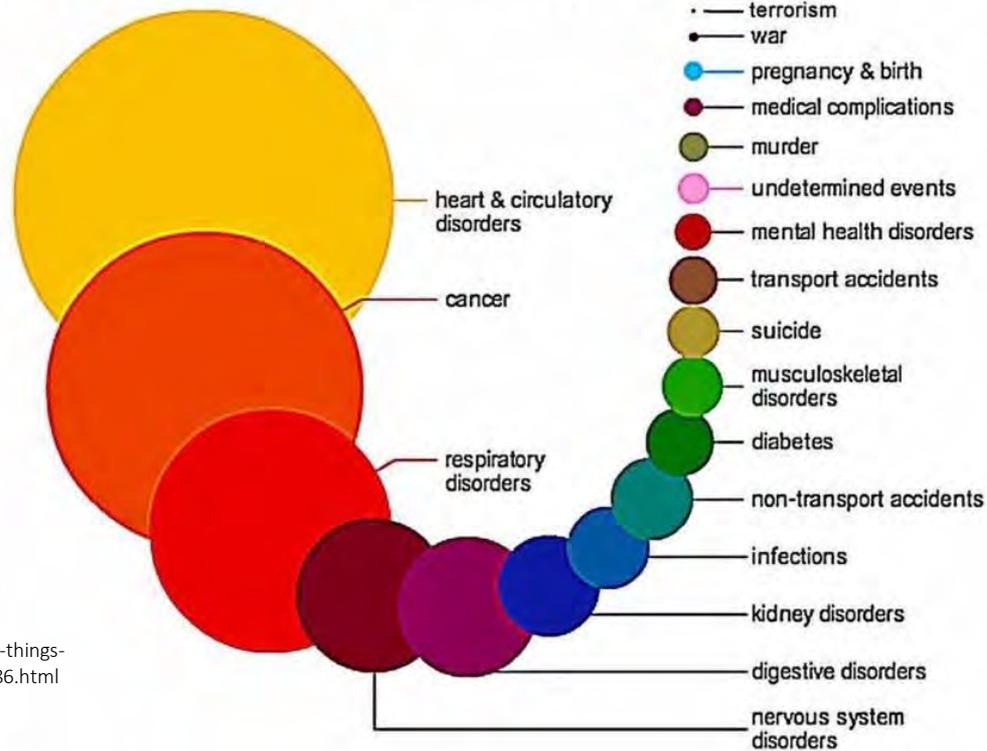
Graphic source, NCBI, "CHALLENGES AND OPPORTUNITIES FACING MEDICAL EDUCATION"
Peter Densen, MD, 2011

<https://econvue.com/pulse/goodbye-%E2%80%9Cknow-it-all%E2%80%9D-medicine%E2%80%99s-liberating-knowledge-explosion>

Our current healthcare system – the good, the bad and the ugly



Leading causes of death in perspective

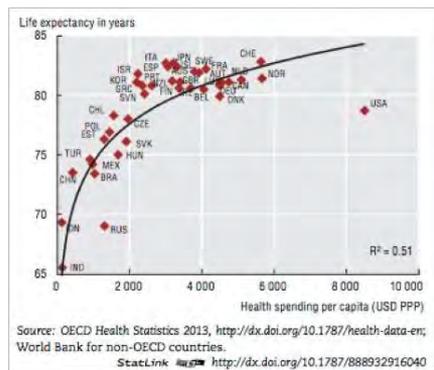


<https://www.independent.co.uk/news/health/the-things-most-likely-to-kill-you-in-one-infographic-a7747386.html>

NHS

Healthcare in the United States and Longevity

- Cost – Highest healthcare cost of ANY country 17.1% of GDP (next highest is France with 11.6% GDP)
- Quality Metrics – U.S. is marginal at best!
 - Infant Mortality – 36 countries beat the United States in infant survival
 - Life Expectancy – United States is 42nd in the world *
- Where do the dollars go if not to improve health through lower infant mortality and longevity?
 - Safety? – No – Over 250,000 patients die each year from accidental injuries, medication errors, adverse drug reactions in hospitals and outpatient centers – 3rd leading cause of death behind heart disease and cancer; Millions more are injured.
 - Dollars go to administrative costs – 1/3 of all money spent
- Medical Regulation Heaviest regulations of any healthcare system; many agencies in oversight
 - Laws and regulations covering doctors, hospitals and the healthcare system account for 1/2 of the language of the entire body of law.
- Lower numbers of physicians and fewer physician visits per capita and fewer hospitalizations
- Higher use of diagnostic imaging and prescription medications, higher costs of care



Squires, David, and Chloe Anderson. "U.S. Health Care from a Global Perspective." *The Commonwealth Fund*, 8 Oct. 2015, www.commonwealthfund.org/publications/issue-briefs/2015/oct/us-health-care-from-a-global-perspective.

Social Predictors - The Sake of All Study (Delmar Blvd St. Louis)

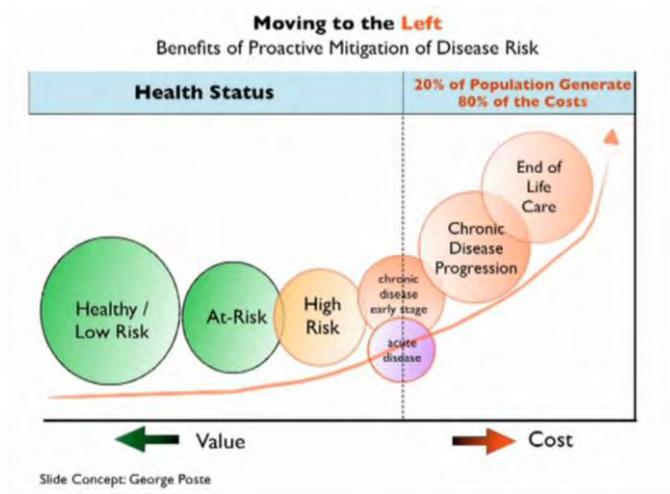


- Differences –
 - Healthy food access – 91%:71%
 - Inadequate Prenatal Care - 5%:27%
 - Infant Death Rate (per 1000) - 5:15
 - Average Life Expectancy - 85:67

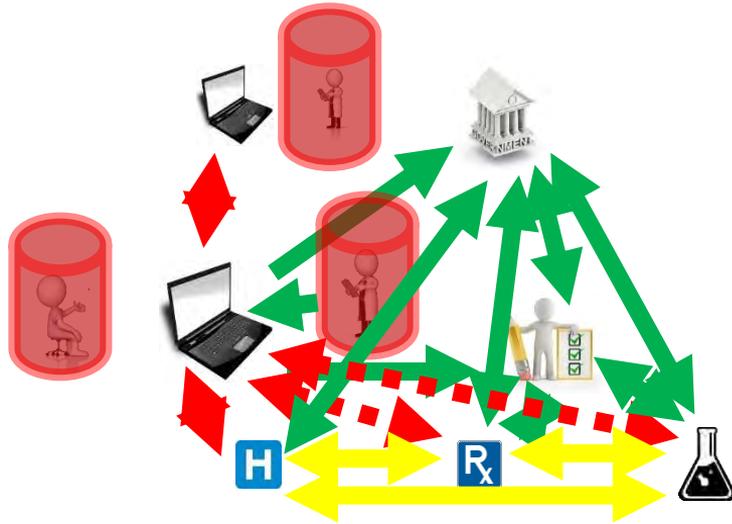
<http://www.welivehere.show/posts/2016/3/28/segregation-is-literally-killing-us-health-researcher-says>

More Explanations to Poorer Outcomes

- Absence of Universal Health – even Affordable Care Act hasn't changed access for all
 - Poor access – people in the US go without needed care because of cost
 - Rapid access to specialized care/urgent care
 - Less likely to report to primary care
 - Proponents of the US system say lower wait times for care - is it appropriate care? Other countries like UK and France tend to have higher acuity in outpatient setting and even higher acuity in the ER
 - Treatment selection
 - Generic drug utilization, cheaper branded drugs (Sofosbuvir for Hep C costs \$84,000-\$168,000 per course in the US compared to \$900 in Egypt – it costs \$136 per course to make – 100,000% profit in the US)
 - Care cost allocation



The Data Exchange Conundrum – key data players are in isolated and noncollaborative silos



Rationale for more seamless interoperability:

- Medical knowledge doubling time 2-3 months by 2020
- Medical errors the 3rd leading cause of mortality; even more impressive numbers of needless morbid complications
- Physicians argue that EMRs have not improved health outcomes for their patients, but have consumed 1/3 of their working hours on documentation
- US – highest healthcare cost as percent of GDP - 1/3 of \$ go towards administration
- Reactive care forces us to spend 80% of our medical costs on 20% of the population
- Less than half of hospitals and about a quarter of physicians can fully interoperate to reduce duplication and eliminate errors and costs.

The failure of electronic medical records to interoperate has completely removed the human element out of healthcare and funneled critical data in the direction of Government and Payors and away from Providers and Patients. This data exchange incurs huge administrative costs without a return in the form of personalized quality care.

Cost to consumer of current healthcare system

Adults in the US polled:

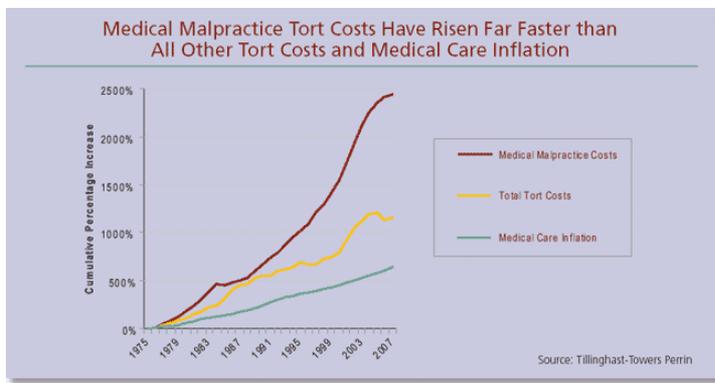
- 25% say current healthcare delivery directly hurts the individual; 15% say it helps
- While benefits remained about the same in 70% of those polled – 35% say they pay more in Co-pays and deductibles and 45% say they pay more in premiums
- Families and seniors say they pay increasingly more since 2013

Hinderaker, John. "NPR and Harvard Say: Obamacare Is a Complete Failure." *Power Line*. Power Line, 09 Mar. 2016. Web. 17 Jan. 2017.

"What Is the Conservative Argument against Obamacare and What Solution to the Problems with Our Healthcare System Would They Offer Instead?" *Quora*. Quora, n.d. Web. 17 Jan. 2017.

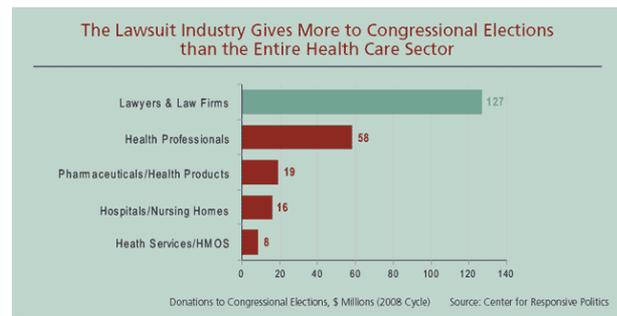
Moffit, Robert E., and Alyene Senger. "The Obama Medicare Agenda: Why Seniors Will Fare Worse." *Heritage*. The Heritage Foundation, 23 May 2013. Web. 17 Jan. 2017.

Lawsuits



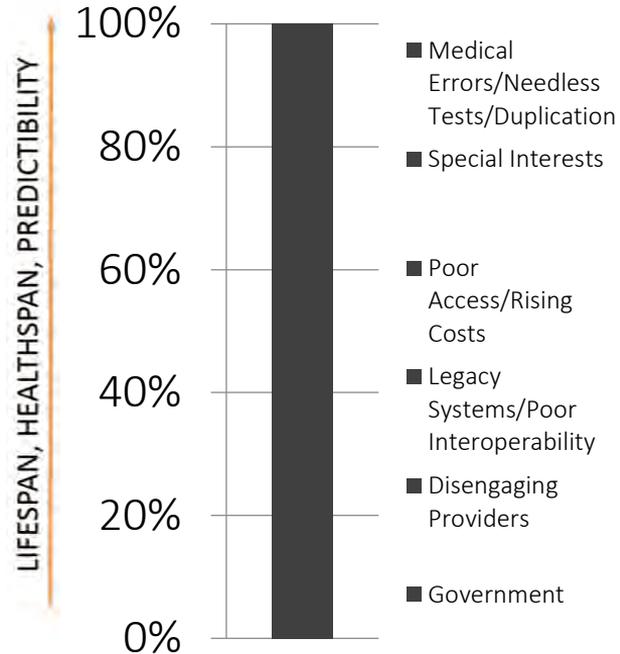
- 72% of Americans think lawsuits compromise doctor decisions
- 83% think there should be tort reform in healthcare reform
- Tort adds direct and indirect costs, defensive medicine with expensive tests, and doctors shying away from making life altering and lifesaving decisions

- High C-section rate – 5 fold rise affected by doctors’ and hospitals’ fear of delivering children with CP
- Awards for CP - \$5 million - \$100 million for a single case in New York
- Lawsuits have not improved health outcomes – the rate of cerebral palsy has not changed



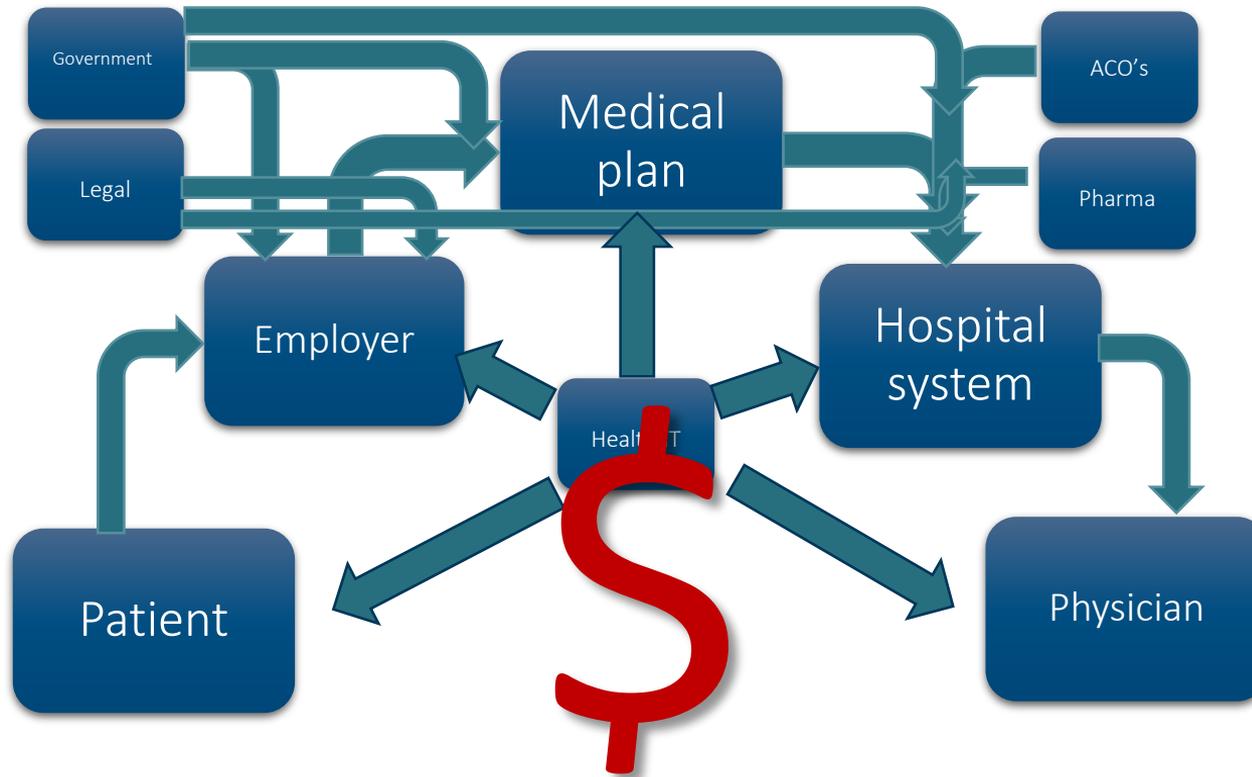
"Health Hazard." *Trial Lawyers Inc. Health Care Update*, Oct. 2009. *Trial Lawyers, Inc.*, www.triallawyersinc.com/pdfs/tli_update_8.pdf.

The Total Patient

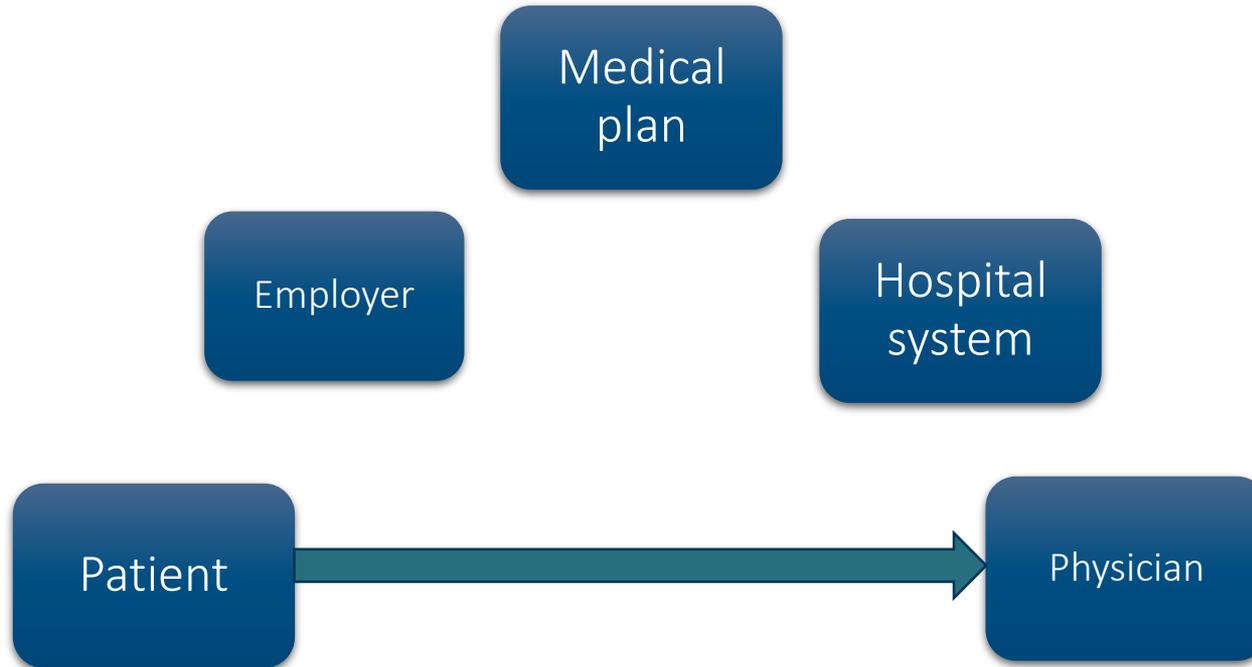


HealthCatalyst. "Predicting the Future of Predictive Analytics in Healthcare - HAS Session 23." *YouTube*. YouTube, 20 Oct. 2014. Web. 17 Jan. 2017.

Current Physician-Patient Relationship



Physician-Patient Relationship of the Future



The value in an unadulterated Physician-Patient Relationship – we talk about personalization, but have become depersonalized

- “. . .we have found that independent primary-care doctors are able to change their care models in weeks and rapidly learn how to use data to drive savings and quality. For small practices, it does not take years to root out waste, rewire referrals to providers who charge less but deliver more, and redesign schedules so patients can see their doctors more often to avert emergency-room visits and readmissions. . .
- Large health systems deliver “personalized” care in the same way that GM can sell you a car with the desired options. Yet personal relationships of the kind often found in smaller practices are the key to the practice of medicine. They are the relationships that doctors want to forge with patients, and vice versa. It may sound old-fashioned, but what I have learned is that we do not need to sacrifice this unique feature of our health-care system as we move forward in adapting new value-based payment models and improving the health of patients.” – Kocher, Bob. Obamacare Architect - *The Wall Street Journal*. Dow Jones & Company, 31 July 2016. Web. 11 Jan. 2017.

So what are some of the technologies that are helping to shape the future



The present and future of medicine

	Healthcare Professionals	Patients
Prepare & Prevent	Digital Literacy in Medical Education	Gamification Based Wellness
	Virtual Dissection	Curated Online Information
	Full Physiological Simulation	Microchips Modelling Clinical Trials
		DIY Biotechnology
Data Inputs & Diagnostics	Holographic Data Input	Home Diagnostics
	Medical Tricorder	Robotic Nurse Assistant
	Smartwatch	Semantic Health Records
	Augmented Reality	Wearable E-Skins
	Real-Time Diagnostics In the OR	Embedded Sensors
		Digestible Sensors
Therapy & Follow Up	Personalized Genomics	
	Multi-functional Radiology	Evidence-based Mobile Health
	Artificial Organs	
	Remote Touch	3D Printed Biomaterials & Drugs
	Adherence Control	
	Robotic Interventions	Optogenetics
	Telemedicine	Humanoid Robots
	Inter-disciplinary Therapies	Virtual Trials
Augmenting Human Capabilities		
Outcome & Consequences	Customized Mobile Apps	Meaningful Use of Social Media
	Nanorobots In Blood	
	Virtual Reality Applications	Redesigned Hospital Experience
	Artificial Intelligence in Medical Decision Support	Recreational Cyborgs
	Virtual-Digital Brains	

Mesko, Bertalam. "The Guide to the Future of Medicine." (n.d.): n. pag. Creative Commons Attribution. Web. 17 Jan. 2017.

Already Available
In Progress
Still Needs Time

Medscape listed 10 Tech Advances that Can Change Medicine

1. Artificial Intelligence – Accurately interpret pathology slides, x-rays, skin lesions and retinas
2. Advanced Wearable Sensors -flexible, stretchable, printable, battery-less and able to track physiologic metrics, chemistries and environmental changes like UV light.
3. Liquid Biopsy for Cancer – cell-free plasma tumor DNA (tDNA) – can be detected in large cohorts of people using tDNA or tDNA methylation
4. Virtual Medical Center for Remote Monitoring (“Bedless Hospital” Mercy Virtual in St. Louis) and Increase in Telemedicine.
5. CRISPR Genome Editing – for cancer, sickle cell, etc.
6. Smartphone Echocardiography
7. Lab in Your Pocket – HIV, HPV, Influenza, Group A strep
8. Cancer prediction/Whole Genome Sequencing
9. Microfluidics Chips for Labs via a Droplet of Blood
10. Virtual Reality for Pain, Phobias and Prevention of Falls

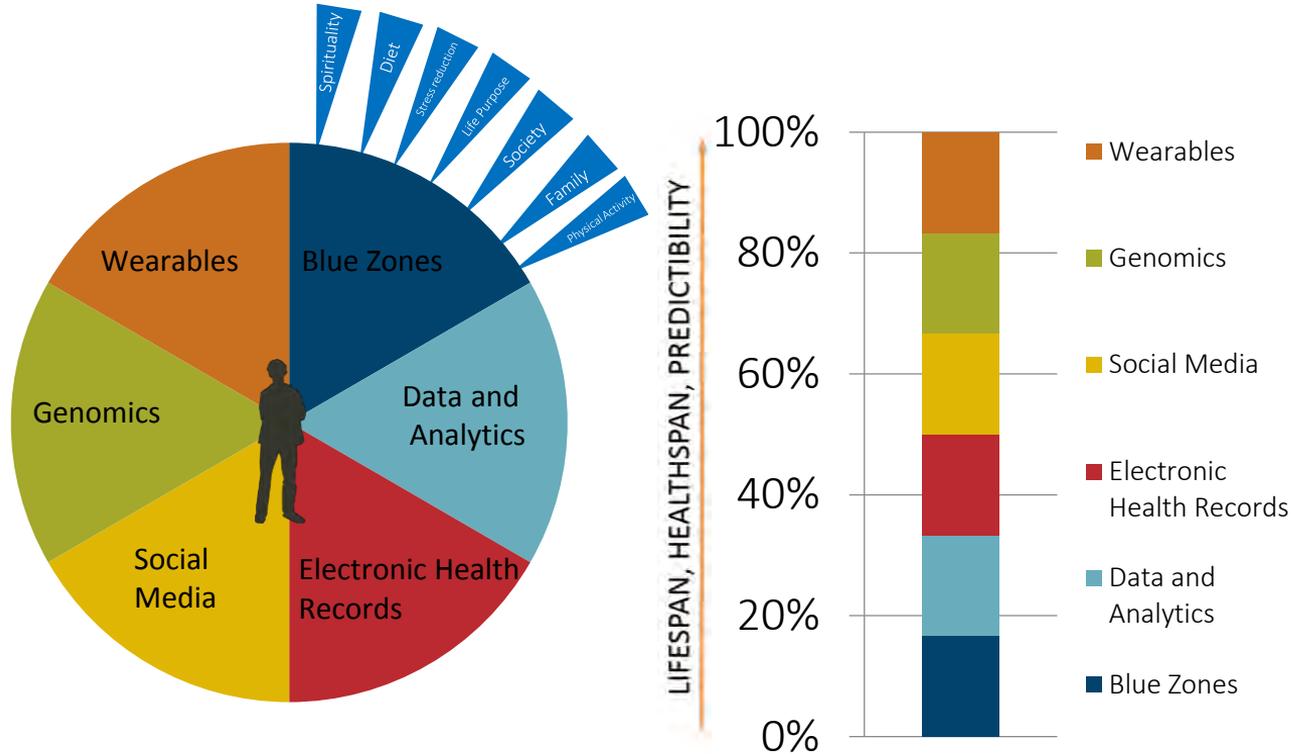
•We will go over these advances in more over the course of this presentation

Topol, Eric J. "10 Tech Advances That Can Change Medicine." *Medscape*. WebMD LLC, 16 Dec. 2016. Web. 17 Jan. 2017.

Some of the low hanging fruits aren't technological – but technology proves they work

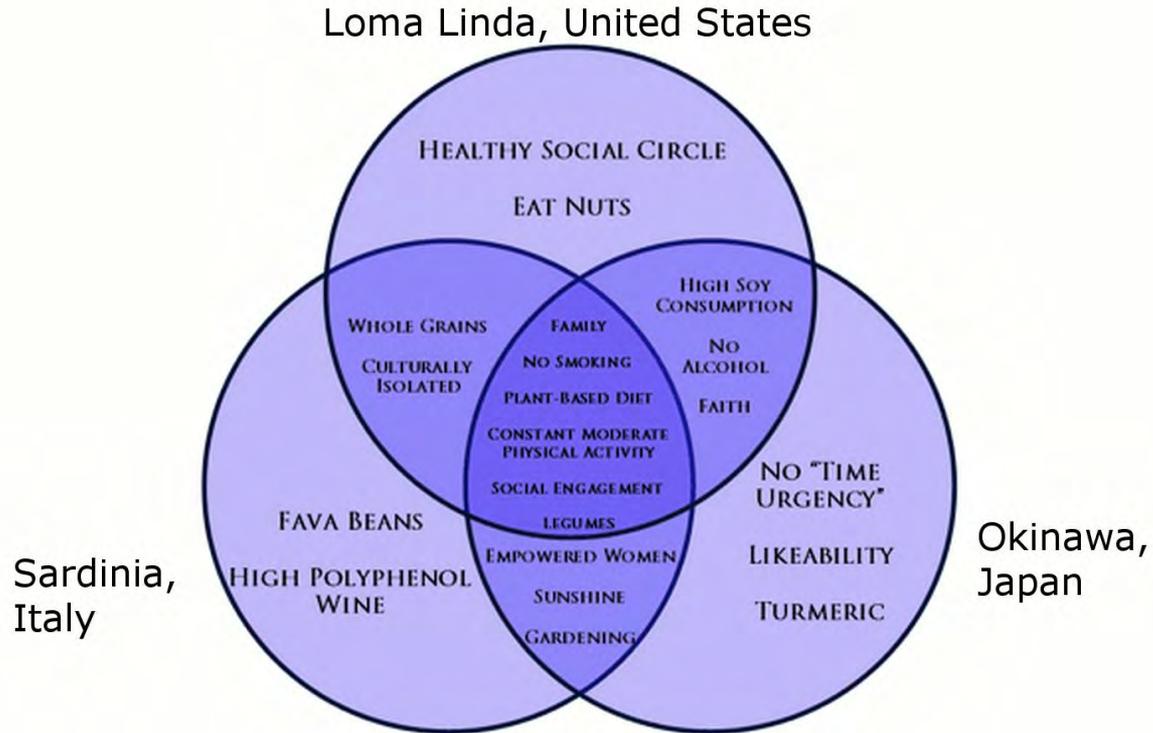


The Total Patient improved by Health



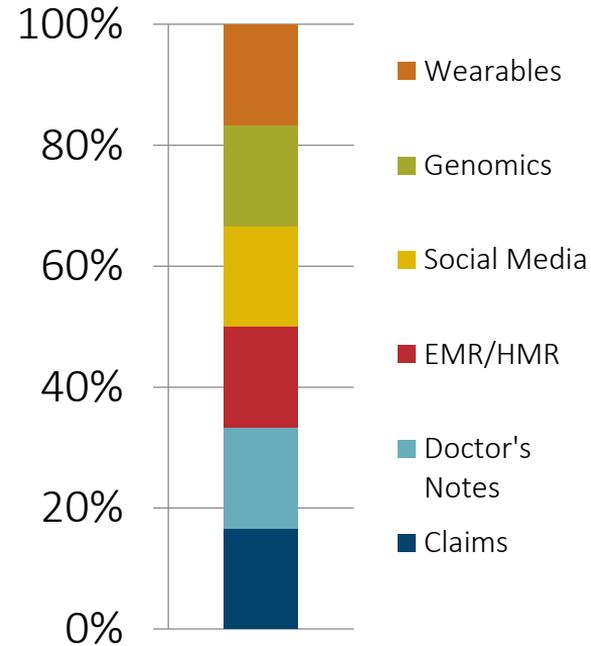
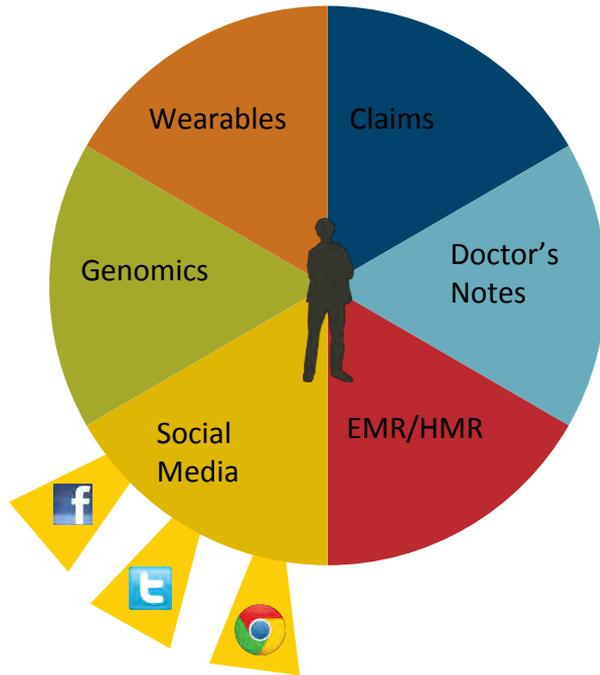
HealthCatalyst. "Predicting the Future of Predictive Analytics in Healthcare - HAS Session 23." *YouTube*. YouTube, 20 Oct. 2014. Web. 17 Jan. 2017.

What leads to longevity in the Blue Zones



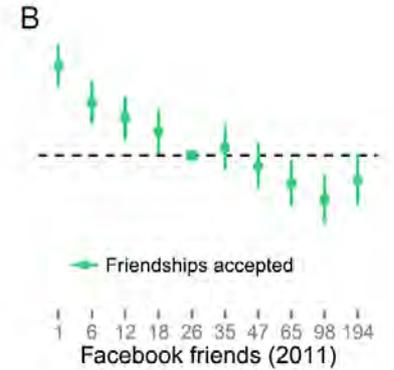
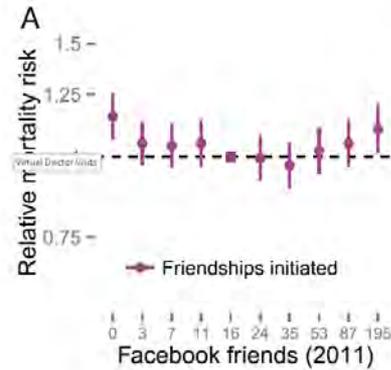
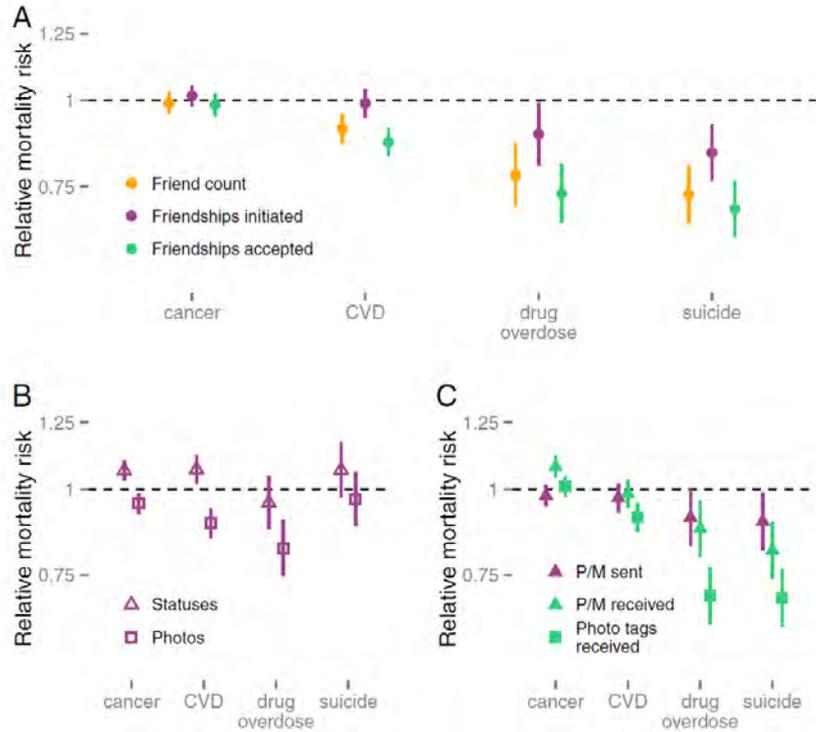
(Public Domain, <https://en.wikipedia.org/w/index.php?curid=9630319>)

The Total Patient improved by Health



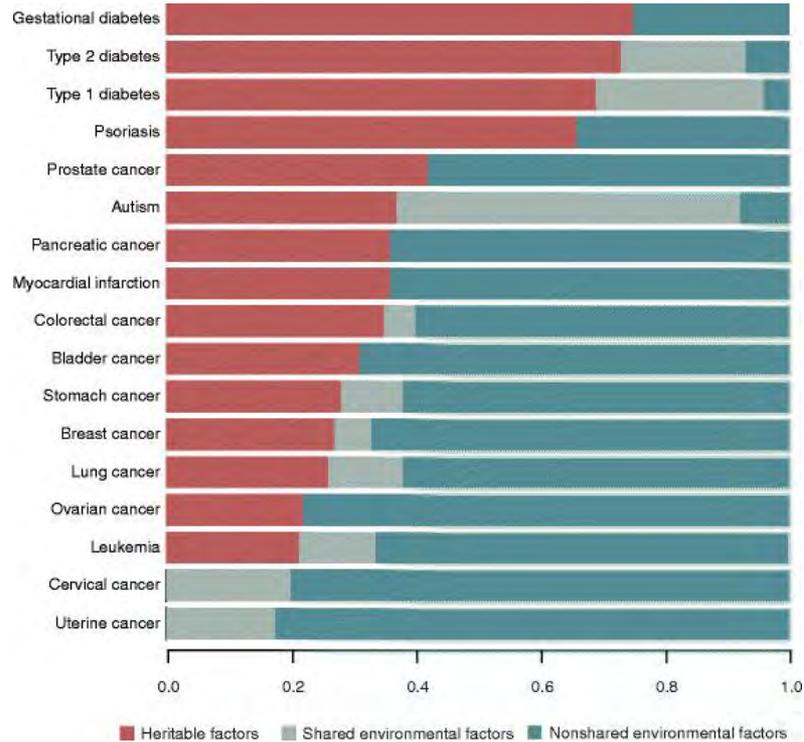
HealthCatalyst. "Predicting the Future of Predictive Analytics in Healthcare - HAS Session 23." *YouTube*. YouTube, 20 Oct. 2014. Web. 17 Jan. 2017.

Social media and mortality



Obstetrics, William R., Moira Burke, Nicholas A. Christakis, and James H. Fowler. "Online Social Integration Is Associated with Reduced Mortality Risk." *Proceedings of the National Academy of Sciences*. National Academy of Sciences, 15 Sept. 2016. Web. 11 Jan. 2017.

The impact of Environment/Epigenetics – Monozygotic twin study



Any cool new technologies primed for disrupting healthspan and lifespan?



3D Printing

Prosthetics

Magnetic Resonance-guided Focused Ultrasound (MRg-FUS)

Robots

Nanotechnology

Microfluidics

Genomics and Molecular Biology

Virtual Doctor Visits

3D Printing – Clinical Applications

•Case Study – First Full Skull Reconstruction

- 3 year old Chinese girl with congenital hydrocephalus
 - Excessive cerebrospinal fluid in brain → head swells to 4x normal size
 - Would not have survived without treatment
 - Child bedridden, could not lift head
- Used three 3D printed titanium mesh skull implants
- 17 hour surgery – drained fluid, replaced skull



Borrelli, Lizette. "Chinese Girl Becomes World's First To Receive Full Reconstruction Via 3D Printing." *Medical Daily*. N.p., 16 July 2015. Web. 11 Nov. 2016.

3D Printing – Clinical Applications

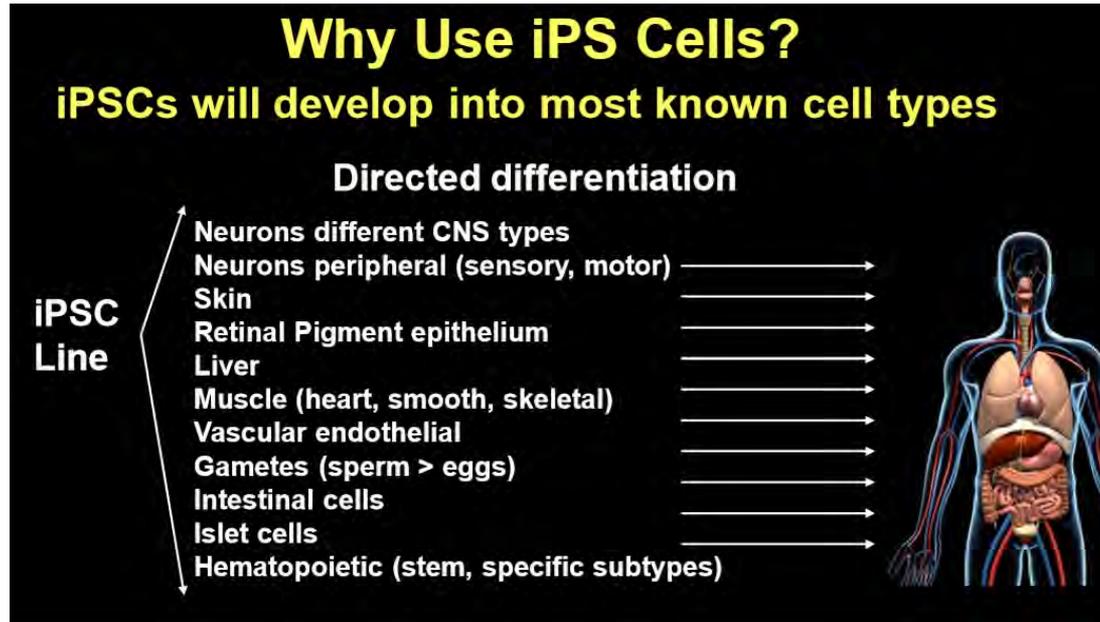


•Examples of UNYQ sleeves



UNYQ. UNYQ, n.d. Web. 11 Jan. 2017.

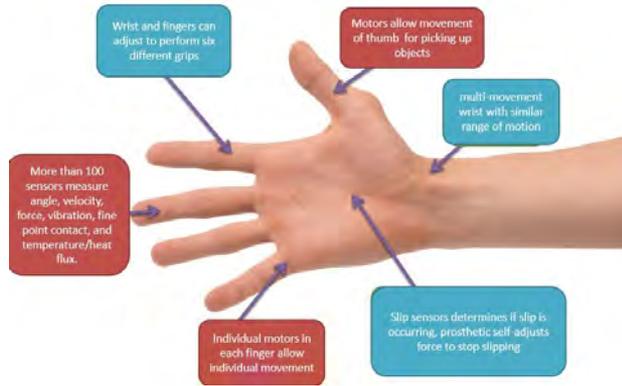
Wadhwa, Tarun. "Using 3D Printing And Design To Change The Way We Look At Disability." *Forbes*. Forbes Magazine, 26 July 2014. Web. 1 Nov. 2016.



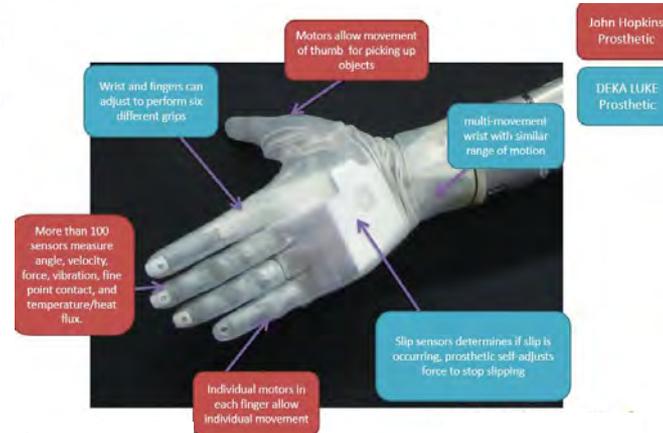
Induced Pluripotent Stem Cell is harvested and directed to become an organoid

Credits to Bruce R. Conklin, MD – Gladstone Institute and UCSF – Innovative Genomics Institute

Prosthetics



Myoelectric Prostheses

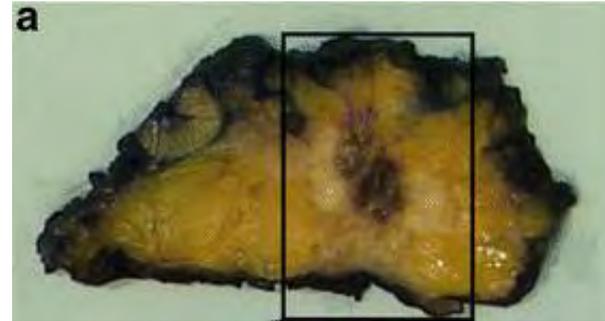
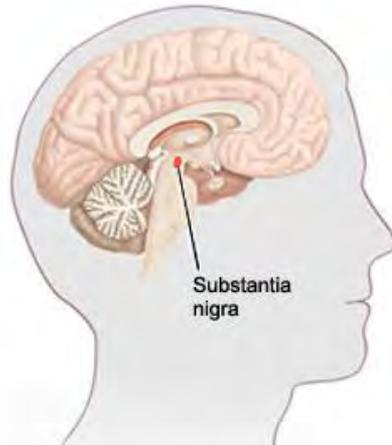


Guizzo, Erico. "Dean Kamen's "Luke Arm" Prosthesis Receives FDA Approval." *IEEE SPECTRUM: Technology, Engineering, and Science News*. n.p., 13 May 2014. Web. 4 Nov. 2016.

News, CBS. "Bionic DEKA Arm, Mind-controlled Prosthetic, Approved by FDA." *CBS News*. CBS Interactive, 12 May 2014. Web. 4 Nov. 2016.

"Prosthetic Limbs, Controlled by Thought." *The New York Times*. The New York Times, 20 May 2015. Web. 4 Nov. 2016.

MRg-FUS – Case Studies – Parkinson's and Breast Cancer



<https://www.youtube.com/watch?v=VbDZzBcMd5E>

Merckel, Laura G., et al. "First clinical experience with a dedicated MRI-guided high-intensity focused ultrasound system for breast cancer ablation." *European Radiology*, no. 26, 2016, pp. 4037-46. *Springer*, doi:10.1007/s00330-016-4222-9.

Robots



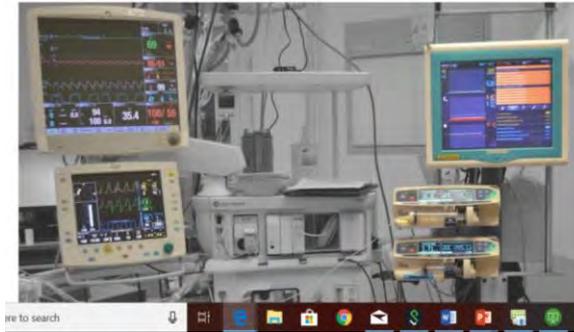
Da Vinci Surgery System



Veebot

'We are convinced the machine can do human anesthesiologists'

By Todd C. Frankel
May 15, 2015



Icontrol RP

"Stryker Mako Robotic-Arm Assisted Surgery." *Stryker*. N.p., n.d. Web. 11 Nov. 2016.

"Da Vinci® Surgery: Minimally Invasive Surgery." *Da Vinci Surgery | Robotic-Assisted Surgery. Intuitive Surgical*, n.d. Web. 4 Nov. 2016.

Dorrier, Jason. "Catherine Mohr: The Da Vinci Surgical Robot and Beyond." *Singularity Hub*. Singularity University, 22 Feb. 2013. Web. 4 Nov. 2016.

Nanotechnology – Clinical Applications

•Heart Disease

- Testing two nanobots to break up clogged arteries
 - 1st nanobot – chain of 3 or more iron oxide beads that loosen plaque; delivers anti-coagulant medication after plaque removed
 - 2nd nanobot- drill like, pushes all the plaque out
- MRI used to power and steer nanobots
- Testing on mice
- Human trials by 2019

•Cancer

- DNA origami method
 - Robot only unfolds to give medicine when certain molecules bind to it
 - Very accurate → only attacks cancer cells, unlike current cancer treatment
- Leukemia bot – unfolds when leukemia antigen binds
- Beginning human trials with leukemia

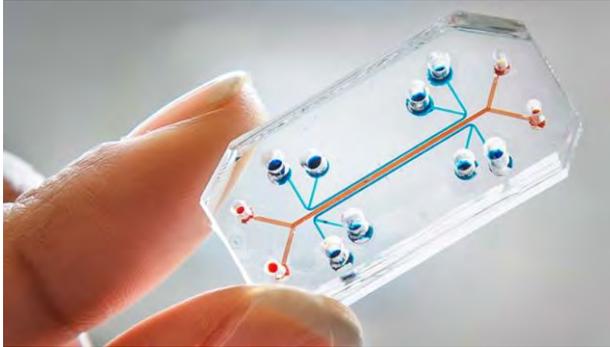
Dorrier, Jason. "Can DNA Nanobots Successfully Treat Cancer Patients? First Human Trial Soon." *Singularity Hub*. Singularity University, 8 Jan. 2015. Web. 4 Nov. 2016.

Douglas, S. M., I. Bachelet, and G. M. Church. "A Logic-Gated Nanorobot for Targeted Transport of Molecular Payloads." *Science* 335.6070 (2012): 831-34. Web. 5 Nov. 2016.

Faulstick, Britt. "Drexel's Microscale 'Transformer' Robots Are Joining Forces to Break Through Blocked Arteries." *DrexelNow*. Drexel University, 24 June 2015. Web. 11 Nov. 2016.

Grunberg, Alexandra. "Nanobots Could Be the Future of the Medical Industry." *Outer Places*. N.p., 1 June 2015. Web. 5 Nov. 2016.

Microfluidics – Clinical Applications

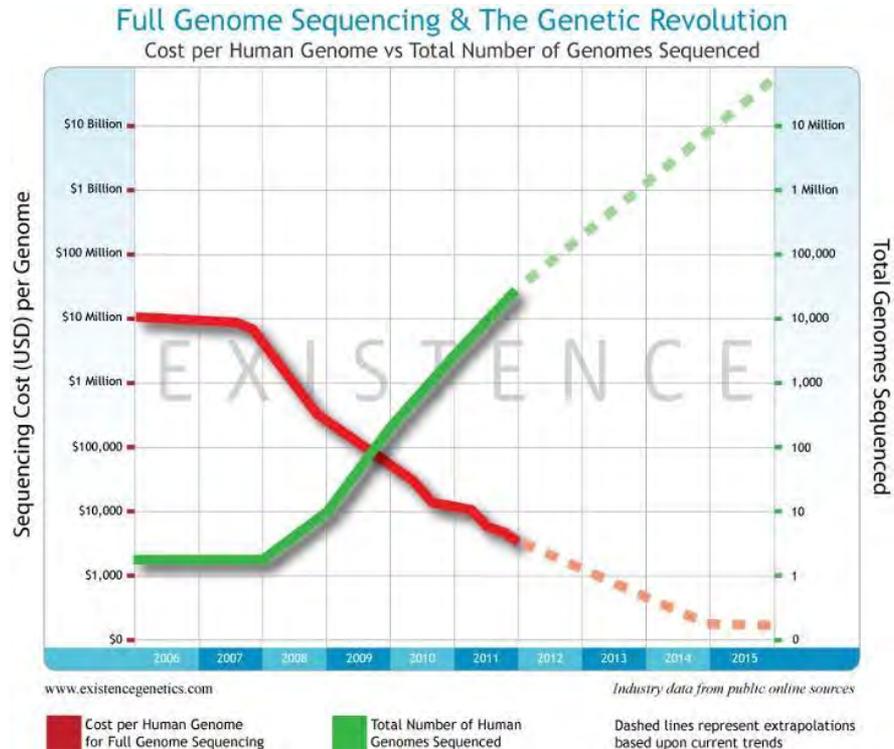


- Organ-on-a-chip
 - Mimic organ physiology and function on a microfluidic chip
 - Study certain behaviors and functions
 - Link chips together to study effect on organ system
 - Wide application for drug testing
 - Determine correct dose of medicine
 - Understand how the medication will effect organs
 - Eventually move away from animal testing
- Cancer-on-a-chip
 - Study the progression of different cancers
 - Test efficiency of drug on disease
 - Practical for understanding diseases that progress in a short period of time

Bhatia, Sangeeta N., and Donald E. Ingber. "Microfluidic Organs-on-chips." *Nature Biotechnology* 32.8 (2014): 760-72. Web. 15 Nov. 2016.

Reardon, Sara. "'Organs-on-chips' Go Mainstream." *Nature.com*. Macmillan Publishers, 15 July 2015. Web. 15 Nov. 2016.

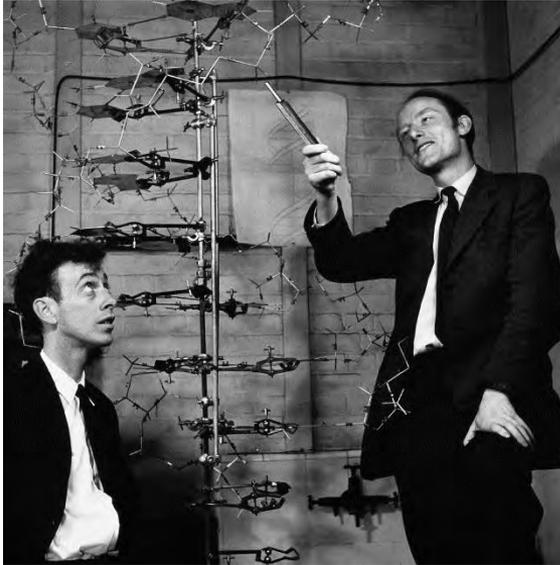
Genomics - Where Are We? – Current State of the Art shows Worldwide progress



So for the diseases that matter to underwriting today:

- Multiple genes are involved in most inheritance – 80-90% of chronic diseases are coded by 40-50 genes apiece which need to be turned on in a correct sequence for disease to be established
- Despite this, there are ongoing studies that will solve the genetic code, even for diseases that have multiple gene inheritance
 - The technology is there to “crack the code for how the major causes of morbidity and mortality are determined”
 - And to determine lifespan, but also importantly health span
- THE SCIENCE HAS NOT CAUGHT UP
- THERE ARE TOO MANY BARRIERS TO MASS POPULATION ENGAGEMENT
- WHO IS GOING INTERPRET AND ACT ON RESULTS OBTAINED ON GENETIC TESTING IN OUR HEALTHCARE ECOSYSTEMS THAT ARE ALREADY SATURATED

James Watson (1953) becomes the second human to have his entire genome sequenced (he's 84 and largely healthy)



- Son with Schizophrenia – no predictive gene was sequenced
- Grandmother with Alzheimer's disease (died at 84) – he didn't want to know his Apo E4 gene status
- He carried a version of the BRCA1 gene – his sister had breast cancer, he had no daughters
- He has a cancer promoting genetic variant – no cancers except basal cell carcinoma - largely underwritten at +0
- According to genetics, he should have:
 - Cockayne syndrome – accelerated aging, small head, stunted growth, mental handicap and photophobia –
 - Usher syndrome – the disease Helen Keller had
- Human Genome is useful for rare single mutation diseases (which don't impact aggregate mortality) – but if **“he brought that map to his doctor that the doctor would know only 1- 3% more about his health than from a good physical exam”**
- 3 years after sequencing his genome had changed by 3%

<http://www.bio-itworld.com/newsitems/2007/may/05-31-07-watson-genome/>

http://www.slate.com/articles/health_and_science/science/2017/05/science_is_broken_how_much_should_we_fix_it.html

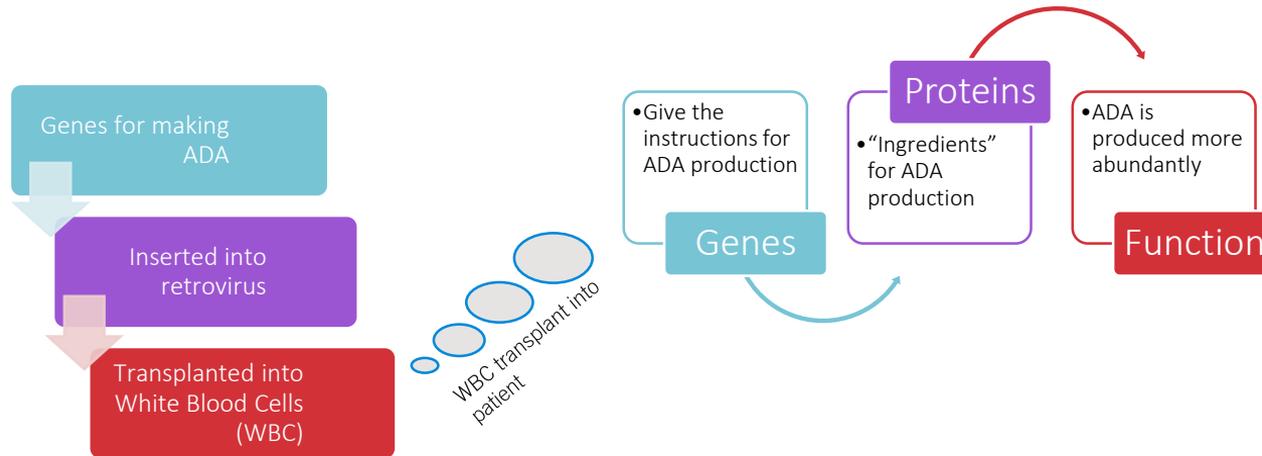
Understanding genomics allows society to invest in and be aware of technologies that ~~treat~~ . . . Cure disease

- With longer life – clearer predictability
- With longer life and disease free survival – the possibility of offering novel policies
- With longer life and disease free survival that is predictable . . . Our consumer deliverable becomes personalized . . . An clear success of companies in today's marketplaces is about personalization . . . Insurance, like life, is not one size fits all.
- Think of Amazon, Alibaba and Apple

Genomic Clinical Applications – Genome Correction

• Gene therapy – greater understanding → opportunity to stop in the earliest stages

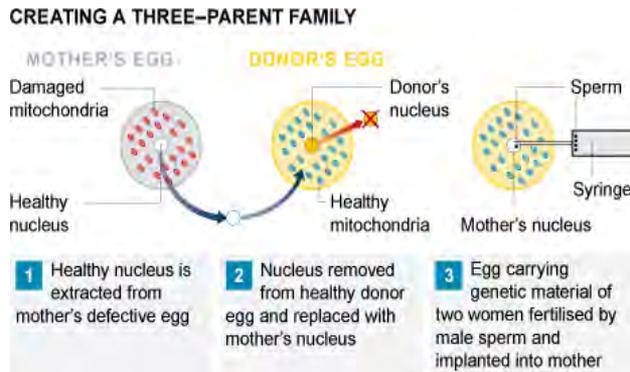
- 1st Case of Successful Gene Therapy
 - September 1990 – NIH Clinical Center; young female patients (4 y.o. & 9 y.o.) with adenosine deaminase (ADA) deficiency
 - **ADA deficiency** – genetic disease that causes severe combined immunodeficiency (improper function of white blood cells); babies typically do not live past age 2 without treatment
 - **Successful; girls showed steady increase in ADA concentration in WBC following therapy**



"Revolution in Progress: Human Genetics and Medical Research - History - Gene Therapy." *National Institute of Health*, history.nih.gov/exhibits/genetics/sect4.htm.

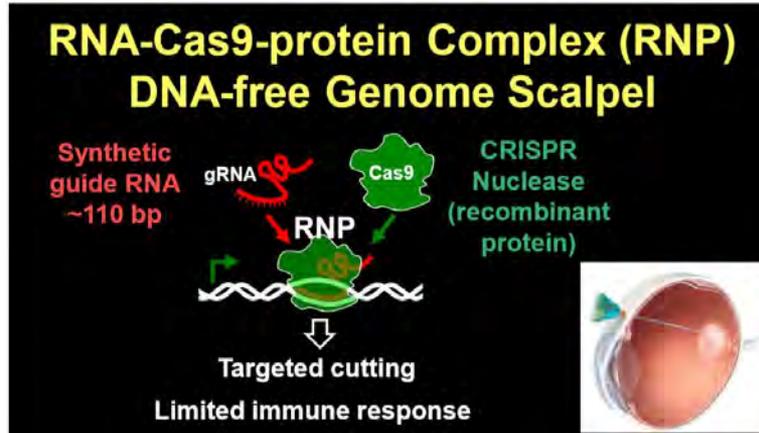
Clinical Applications – Genetic Engineering

- Genetic engineering - deliberate modification of the characteristics of an organism by manipulating its genetic material
- Baby boy & “three parents” in Mexico
 - Mother was carrier of mitochondrial DNA for Leigh’s disease
 - 2 children previously died from Leigh’s disease (6 y.o. & 8 mo.)
 - **Leigh’s disease** – progressive loss of mental & movement abilities, children typically die within 2-3 yrs.
 - Severe respiratory problems, weakness/paralysis of eye muscles, degeneration of nerves, lactate build-up in body
 - Rarely survive to teen years/adulthood
 - Boy was born healthy without complications
 - Increased life expectancy of child from 2-3 yrs. old → ≈72.5 yrs. old
- Procedure done in Mexico due to regulation in US & other countries



"'Three-parent baby' claim raises hopes — and ethical concerns." *Nature*, www.nature.com/news/three-parent-baby-claim-raises-hopes-and-ethical-concerns-1.20698

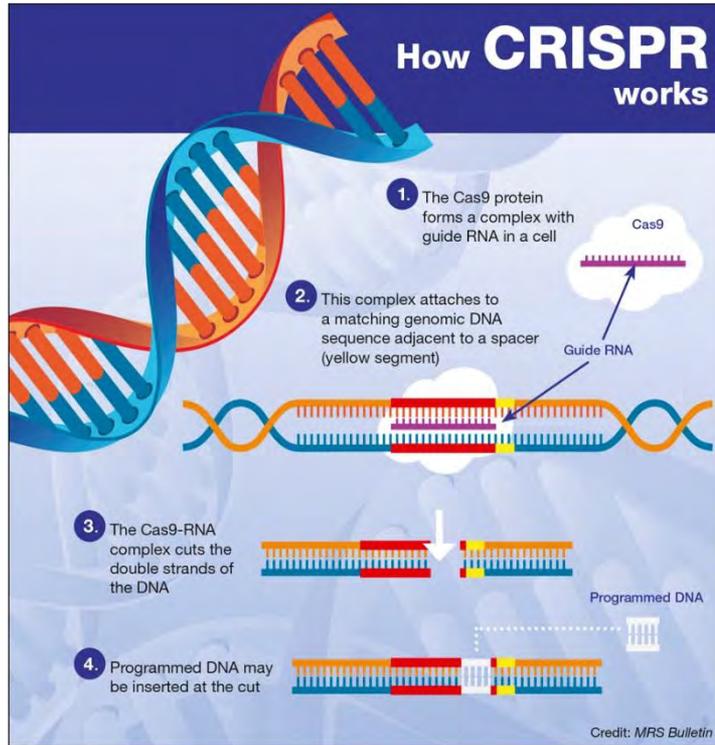
Clinical Applications – Genome Correction – CRISPR/Cas9



UCSF Currently focused on blindness and motor neuron disease like Charcot Marie Tooth – results of tissue growth and are already doing patient selection

Credits to Bruce R. Conklin, MD – Gladstone Institute and UCSF – Innovative Genomics Institute

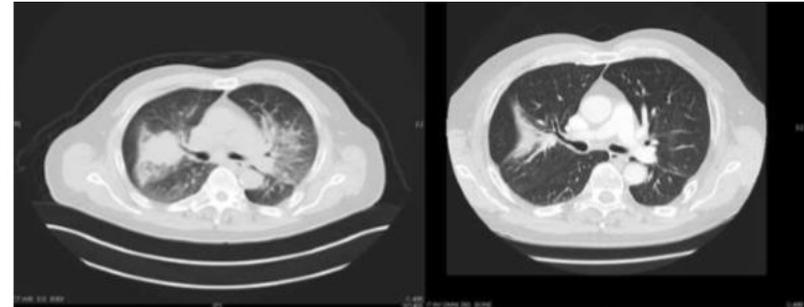
CRISPR



<https://www.cambridge.org/core/journals/mrs-bulletin/news/crispr-implications-for-materials-science>

What about targeted “medicines”

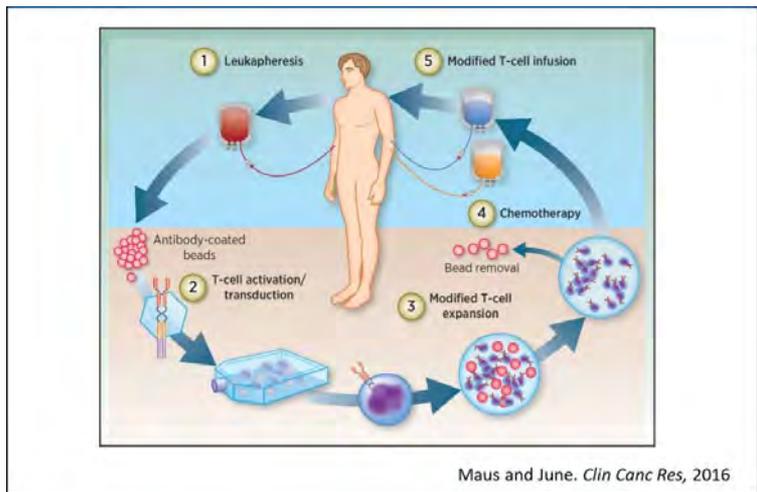
- Best case example is that of Lung Cancer
 - In 2018, 250,000 new cases and 150,000 deaths
 - 25% of all cancer deaths and more than colon, breast and prostate combined
 - In nonsmokers and considered as a separate disease – 6th leading cause of death
 - Until recently (2010) median survival with therapy was 8 months
 - Identification of driver mutations which stimulate cancer growth
 - In US, FDA has approved HER-2, KIT, RET, BRAF for non-lung cancer
 - Lung Cancer – FDA has approved EGFR, ALK, ROS-1, BRAF
 - Curing cancer – not just lung cancer
 - Side effects
 - Today – Median survival > 3 years if patient has EGFR, ALK, ROS-1 mutations (about 15% of non small cell lung cancers)
 - So what’s the downside?



The Work of Renato Martins, MD – Oncology, University of Washington

CAR T Cell Manufacturing

- Chimeric Antigen Receptor – synthetic T cell receptor.
- Has Immunoglobulin as well as a T cell receptor complex. They are not restricted to require a certain cell
- CD19 Immunotherapy target – it is a protein on all B cell and therefore B-cell malignancies – removing B cells has consequences, but ultimately patients live without significant implications on immunity.
- Side effects - Prolonged cytopenias – cytokine release syndrome – infection risk does not seem to be a big issue. Rate of death is 2% and correlates with tumor burden. Coma, cerebral edema, it is reversible. They get B cell aplasias. If infections happen – they can get IVIG.
- Pediatric ALL – complete response rate of 90% - relapses do occur – main cause of relapse is loss of CD19 in the tumor through mutations. Common in ALL. Consideration of CD22 CAR-T to improve sustained remission
- Cant use for other tumors, no common antigen
- NHL, MM, Adult ALL



Clinical Applications – Personalized Medicine

•Pharmacogenomics

- Determine reaction to medicine before taking it
 - Some people cannot metabolize certain medicine, altering its effectiveness
 - Genetic variants can cause worse side effects
 - Plavix
 - Medicine to prevent heart attack and stroke
 - 15% cannot metabolize
 - Variant in genome known
 - \$9.3 billion market in 2011 → save \$1.4 billion
 - Abacavir
 - Antiviral drug for HIV
 - Specific allele variants cause a higher risk of hypersensitivity
 - Symptoms of hypersensitivity → fever, rash, gastrointestinal problems, respiratory problems, death caused by organ failure.



- Eliminate trial and error through QEEG and Pharmacogenomics
- Find the drug with the best efficacy for mental health with least side effects

"Abacavir: Indications, Side Effects, Warnings." *Drugs.com*. Drugs.com, n.d. Web. 11 Jan. 2017.

Leach, Rick, and TEDxTalks. "The Rise of Genomic Medicine." *YouTube*. YouTube, 25 June 2013. Web. 11 Jan. 2017.

Genetic Counseling

Stay at the forefront
of precision medicine.

InformedDNA is the authority on the
appropriate use of genetic tests.

We're the largest and most experienced nationwide
full-time staff of independent genetics specialists.



- Not everyone needs cancer gene testing
- We could deploy cancer testing that is for an appropriate population
- Take the example of BRCA gene testing
 - Only 1/3 of people with familial breast cancer require BRCA testing
 - Of those that get genetically noted to require BRCA testing only 10% of the tests are positive
 - If you take high risk individuals who are identified and don't report to us results and you prescribe appropriate screening, their morbidity and mortality is less than those with average risk

Virtual Doctor Visits

- Connects patients and doctors using video chat
- Interact with doctors hundreds of miles away
- More affordable and accessible
 - Cheaper than going to the ER
 - Rural areas can have better healthcare without moving
 - Specialists can reach more people
- Addresses issue of shortage of medical professionals → need fewer doctors because one doctor can reach a wider group of people
- Issue of who pays
 - Some insurance companies cover → varying amounts covered



Bailey, Melissa. "As Virtual Doctor Visits Take Off, Debate over Who Should Pay Heats up." *STAT*. N.p., 22 Mar. 2016. Web. 15 Nov. 2016.

Miller, Claire Cain. "The Doctor Will See You Now - Online." *The New York Times*. The New York Times, 19 Nov. 2008. Web. 11 Nov. 2016.

Welcome, Mr. Jones, to your Annual
Checkup

ID
check/Fac
e scan

Vision
Testing

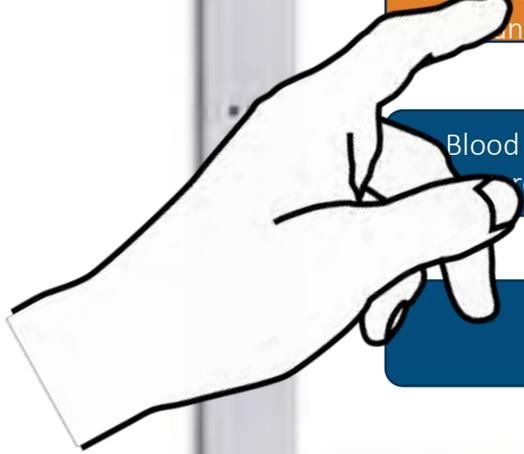
Body Scan

Blood
Pressure

Auscultation

Blood
Testing

Medical Consult



And then . . . There's the power of data



Flight Path

- When flying a plane, we can use data to change flight path
 - Have an initial plan → adjust with real time updates from weather
 - Accurately predict the safest flight, avoiding dangerous weather
 - Creates 500 GB per 6 hour flight
- Healthcare has all the information that creates the total patient
 - Could predict an individual's trajectory for a year
 - 1 human creates 100 MG of data per year



If flights create more data, why can't we create flight paths for humans?

HealthCatalyst. "Predicting the Future of Predictive Analytics in Healthcare - HAS Session 23." *YouTube*. YouTube, 20 Oct. 2014. Web. 17 Jan. 2017.

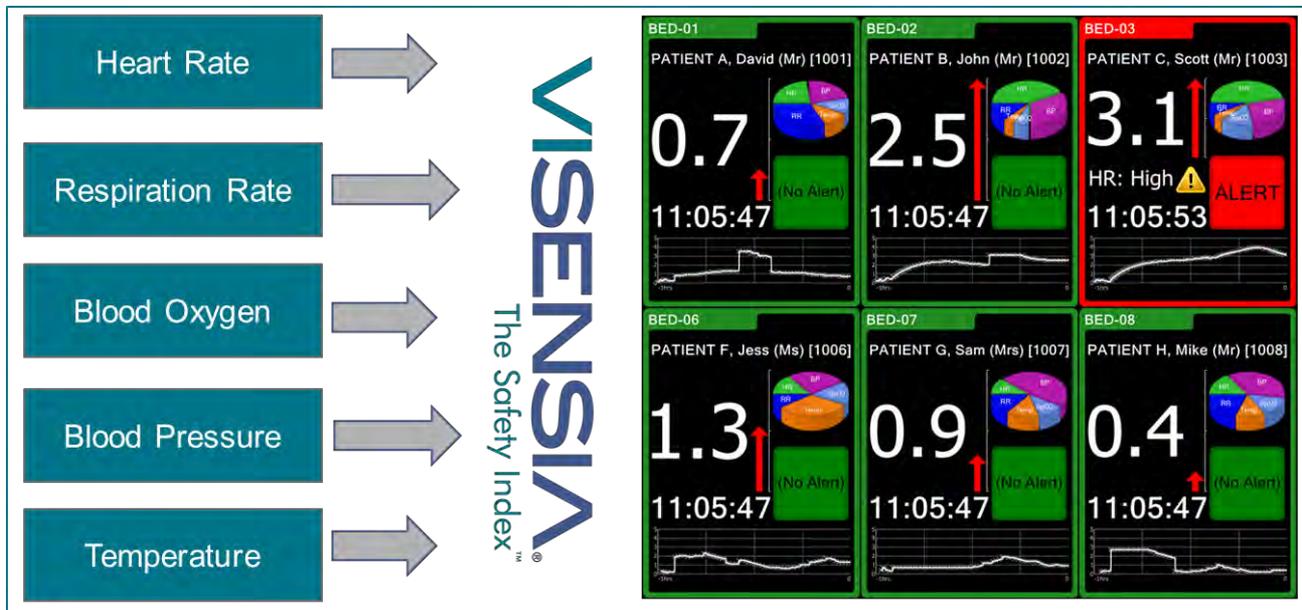
Qualcomm Tricorder XPrize

- Currently a competition to develop a portable, wireless, palm based device that monitors health conditions for unprecedented access to personal health metrics. It will diagnose 13 health conditions (12 disease states and wellness). Will evaluate 5 vital signs. All of the data analysis and assessment will be independent of healthcare worker.



"Qualcomm Tricorder XPRIZE." XPRIZE. XPRIZE Foundation, n.d. Web. 17 Jan. 2017.

Longevity Case Study - Visensia (The Safety Index)



"Visensia." OBS Medical. OBS Medical Ltd, n.d. Web. 17 Jan. 2017.

Impacts of Social Media on Antibiotic Resistance, Suicidality, Insomnia, Medication side effects . . . The lists go on and on

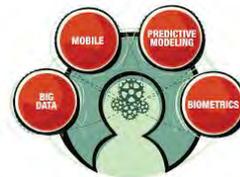
Results: User data such as number of tweets, friends, followers, and location were collected, as well as the time and date of tweets. Additionally, the sentiment of each tweet and average sentiment of each user were determined to investigate differences between non-sleep and sleep groups. It was found that sleep group users were significantly less active on Twitter ($P= .04$), had fewer friends ($P< .001$), and fewer followers ($P< .001$) compared to others, after adjusting for the length of time each user's account has been active. Sleep group users were more active during typical sleeping hours than others, which may suggest they were having difficulty sleeping. Sleep group users also had significantly lower sentiment in their tweets ($P< .001$), indicating a possible relationship between sleep and psychosocial issues.

In 2009, the Centers for Disease Control and Prevention (CDC) took advantage of social media posts made by users ranging from possible symptoms to claims of possible outbreak of the H1N1 virus. In addition to traditional avenues, the CDC used social media to directly engage the public. The general public quickly acquired information to benefit from this approach. The government intelligently mobilized resources and prevented mass panic. A 24-hour informational hotline was created in addition to press briefings for media and health alert networks, daily postings to reach additional audiences [2]. The CDC, in the wake of the pandemic, created the "Predict the Influenza Season Challenge" competition. The participants were encouraged to develop modeling tools that predicted seasonal flu activity based solely on information gathered from social media networks [3].

Depression, if left untreated, leads to multiple mental and physical health problems. Suicide is one risk factor for depressed patients. Researchers have been studying how to predict suicide by identifying content in social media networks that serve as 'red flags' to suicidal tendencies [7]. These methods would contribute to a more rigorous suicide screening and prevention programs that would greatly benefit counselors and patients.

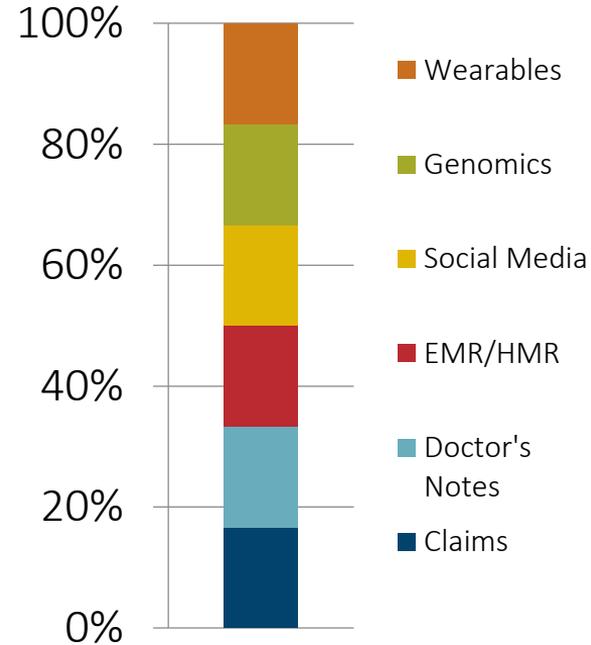
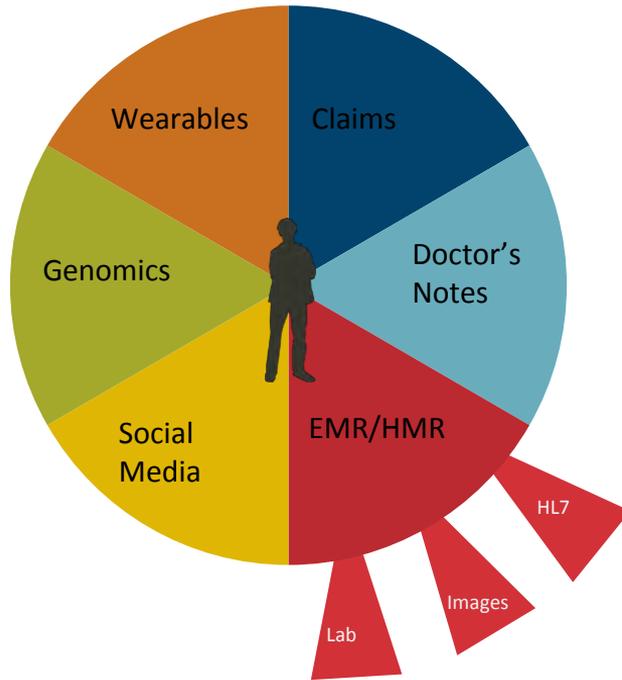
Jool

- Users create Jool accounts, do a health assessment and then begin the process of change through commitment to new direction
- After two days of use, Jool begins to send tailored messages based on HRA
- In 1 week each user's model can offer insights into factors that impact energy and willpower
- At 15 days, the tool gives accurate energy and willpower predictions and tailored tips to maximizing both.
- Some of the tools are
 - A purpose composer – crafting purpose in personal, home, work and community settings
 - Assess and align behaviors to core values such as reputation, spirituality, etc.
 - Capture and monitor health assessment data – BMI, stress, pain, smoking, etc.
 - Track health based on sleep, presence, willpower
 - Tool to optimize energy and willpower and 2 user defined outcomes (could be mood or headache cycles or even their golf game)
 - Follows trends over time



Jool Health. www.joolhealth.com.

The Total Patient improved by Health



HealthCatalyst. "Predicting the Future of Predictive Analytics in Healthcare - HAS Session 23." *YouTube*. YouTube, 20 Oct. 2014. Web. 17 Jan. 2017.

Cardiogram & UCSF



eHeart study –

- Heart disease affects 1/3 of Americans - #1 killer in the country
- Using this mobile health app worldwide coupled with “big data” to determine what causes heart disease
 - Prevention
 - Treatment
- Proven 95+% sensitivity and specificity for atrial fibrillation through assessment of heart rate variabilities
- Occult hypertension, diabetes, sleep apnea, tobacco use show predictable variabilities

Benefits to medicine

- Disease outcomes changed by early detection and treatment.

Benefits to our business

- Better predictability of mortality from one of top industry causes of mortality
- An opportunity to enhance the consumer experience for continuous touch

Wearables – OM clothing

The image shows a website banner for Signal's wearables. At the top left is the Signal logo, consisting of a black circle with a white 'M' shape inside, followed by the word 'signal' in a lowercase sans-serif font. To the right of the logo is a navigation menu with four items: 'Our Collection', 'Our Technology', 'What's New', and 'Whitepapers'. The 'Work With Us' item is highlighted with a blue background. The main banner features a photograph of a woman and a man in athletic wear. Overlaid on the photo is the text 'Personalized medical-grade biometric data to achieve optimal health.' Below this text is a button that says 'Discover our technology' with a downward-pointing arrow below it. At the bottom of the banner, there are three statistics, each with an icon above it: a heart icon for '1.8 billion+ heartbeats recorded', a lung icon for '500 million+ breaths recorded', and a clock icon for '330 thousand+ hours of data collected'.

●M signal

Our Collection Our Technology What's New Whitepapers [Work With Us](#)

Personalized medical-grade biometric data to achieve optimal health.

[Discover our technology](#)

↓

-  **1.8 billion+**
heartbeats recorded
-  **500 million+**
breaths recorded
-  **330 thousand+**
hours of data collected

Genomic Data



Informed**DNA**
Genetics, Decoded.



Data doesn't need to come from traditional sources or traditional disruptors



6
SEP

The Frightening Science of Prediction: How Target & 10 Others Make Money Predicting Your Next Life Event



<https://scienceofrevenue.com/2012/09/06/the-frightening-science-of-prediction-how-target-10-other-companies-make-money-by-predicting-by-your-next-life-event/>

10. Predicting Your Future Health (All Health Insurers): All major health insurers now use predictive analytics to predict your future health problems and likely treatment costs. According to the [American Journal of Managed Care](#), “statistical tools might detect the diabetic patients with the highest probability of hospitalization in the following year based on age, coexisting chronic illnesses, medication adherence, and past patterns of care.” Health care providers use past claim data, known health issues, and even surveys and electronic medical records.

11. Predicting Death (The Life Insurance Industry): This may be the oldest and most established use of predictive analytics. The actuarial industry was partially built on the science of predicting an individual’s life expectancy based on known facts. While highly regulated, every life insurance company uses as much data as it can legally touch to build models predicting how long individual policyholders are likely to live.

QUESTIONS



SOCIETY OF
ACTUARIES®



Prudential
Bring Your Challenges

Appendix

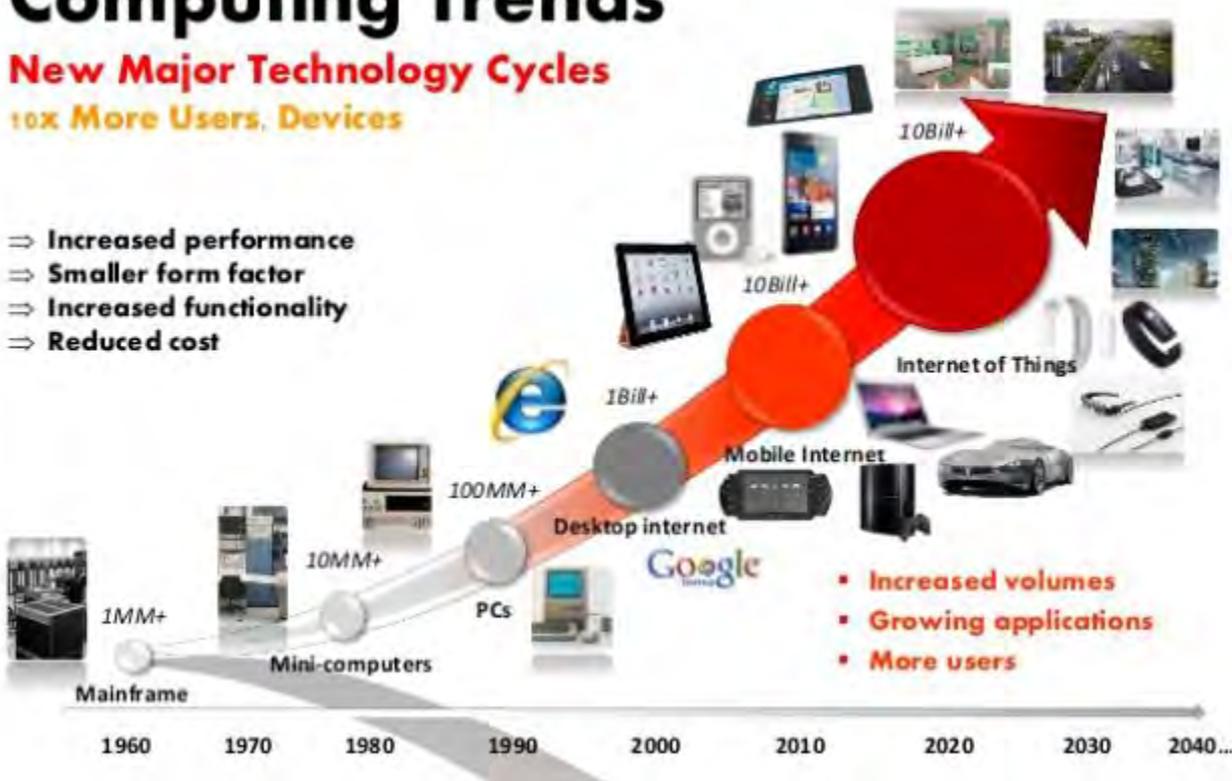


Computing Trends

New Major Technology Cycles

10X More Users, Devices

- ⇒ Increased performance
- ⇒ Smaller form factor
- ⇒ Increased functionality
- ⇒ Reduced cost



MOORE'S LAW

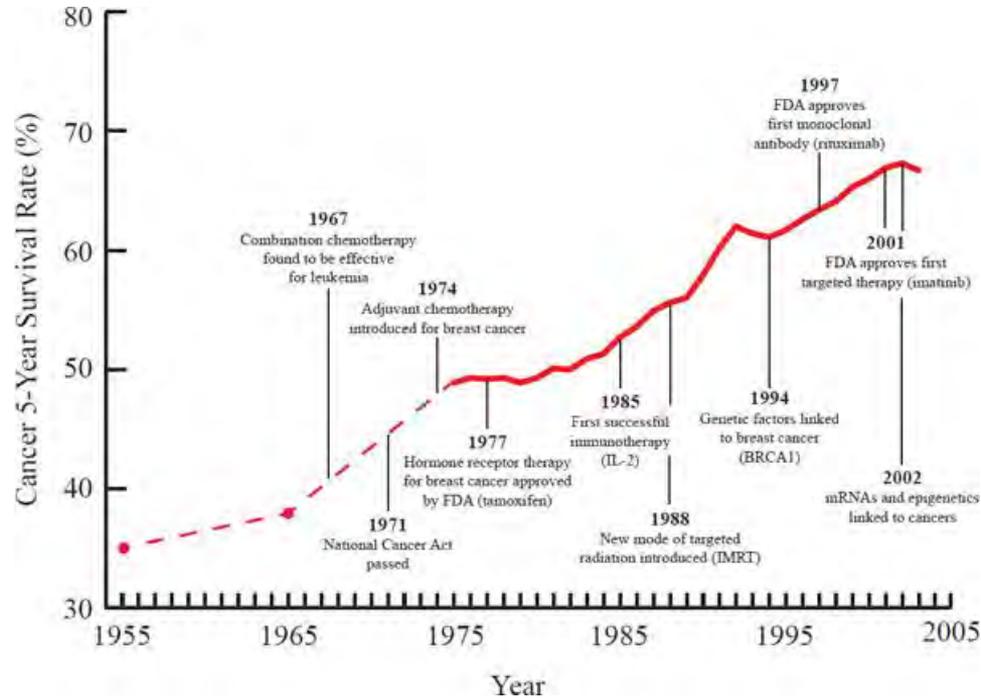
In 1965 Intel's co-founder Gordon Moore said:

“ The number of transistors incorporated in a chip will approximately double every 24 months. ”

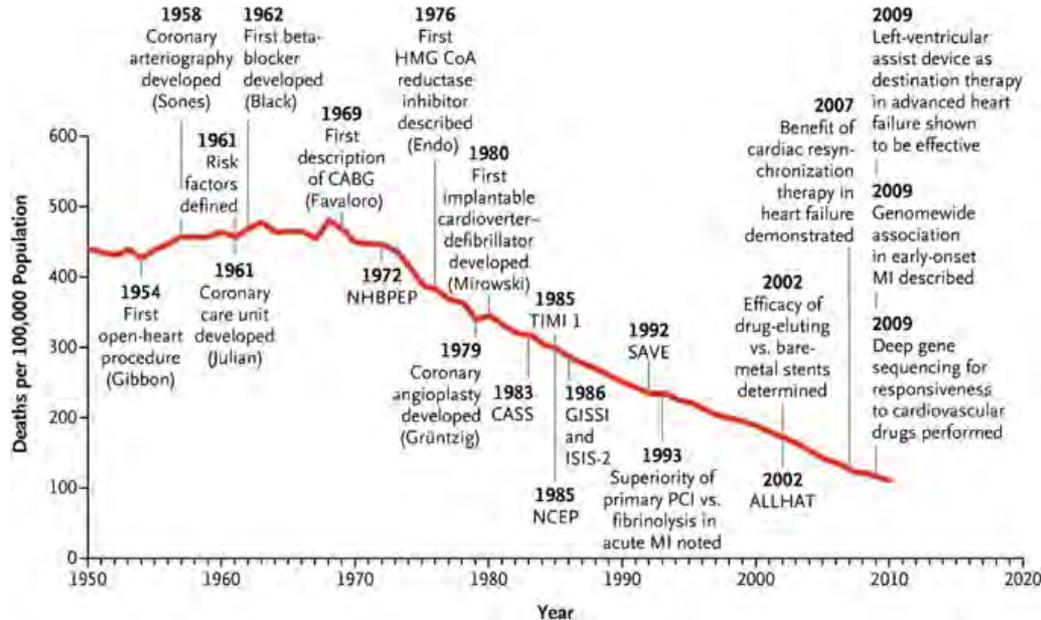
<https://disruptionhub.com/moores-law-infographic/>

https://www.slideshare.net/Yole_Developpement/advanced-packaging-role-after-moores-law-transition-from-technology-node-era-to-functionality-era-2016-presentation-by-rozalia-beica-of-yole-developpement-at-xxx-conference

Technology, Time and Cancer 5 year survival rate



Technology, Time and CV disease mortality



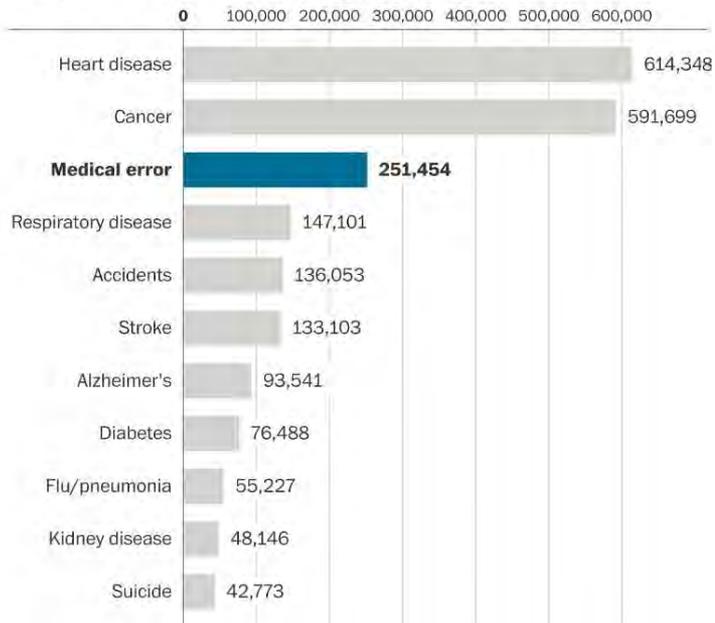
For Context –

- 1983 – CASS was surgery vs. nonsurgery in CAD
- 1985 – NCEP - Set National Cholesterol Guideline
- 1985 – TIMI – Thrombolysis in Myocardial infarctions
- 1986 – GISSI and ISIS-2 deal with thrombolysis
- 2002 – ALLHAT - Hypertension

Healthcare impact on longevity

Death in the United States

Johns Hopkins University researchers estimate that medical error is now the third leading cause of death. Here's a ranking by yearly deaths.



Source: National Center for Health Statistics, BMJ

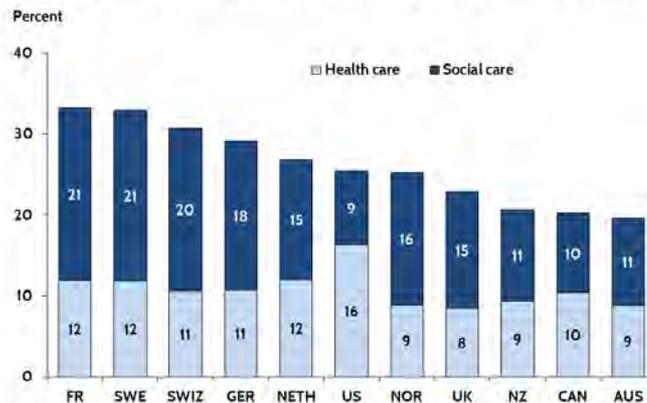
THE WASHINGTON POST

Cha, Ariana Eunjung. "Researchers: Medical errors now third leading cause of death in United States." *The Washington Post*, 3 May 2016, www.washingtonpost.com/news/to-your-health/wp/2016/05/03/researchers-medical-errors-now-third-leading-cause-of-death-in-united-states/?utm_term=.2bf5c4ef566c.

Healthcare in the United States and Social Predictors

- Also social services (retirement, housing, etc. lower than healthcare spending – social services play an important role in shaping health trajectories and mitigating health disparities.)
- Study in Health Affairs December 2015 – Socioeconomic differences in life expectancy have risen in recent decades, whether measured by education or earnings – impacts on an aging population as a whole

Exhibit 8. Health and Social Care Spending as a Percentage of GDP

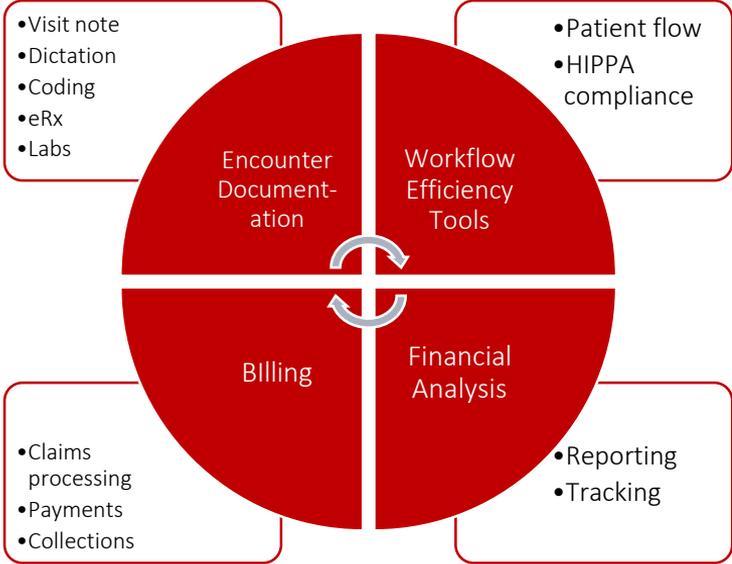


Notes: GDP refers to gross domestic product
Source: E. H. Bradley and L. A. Taylor, *The American Health Care Paradox: Why Spending More is Getting Us Less*. Public Affairs, 2013.

Jones, Henry. "How Medical Boards Nationalized Health Care." *Mises Institute*, 25 Feb. 2005, mises.org/library/how-medical-boards-nationalized-health-care.

Squires, David, and Chloe Anderson. "U.S. Health Care from a Global Perspective." *The Commonwealth Fund*, 8 Oct. 2015, www.commonwealthfund.org/publications/issue-briefs/2015/oct/us-health-care-from-a-global-perspective.

What EMR provides



But EMR is a Necessity

"We will make sure that every doctor's office and hospital in this country is using cutting edge technology and electronic medical records so that we can cut red tape, prevent medical mistakes, and help save billions of dollars each year,"

- President Obama



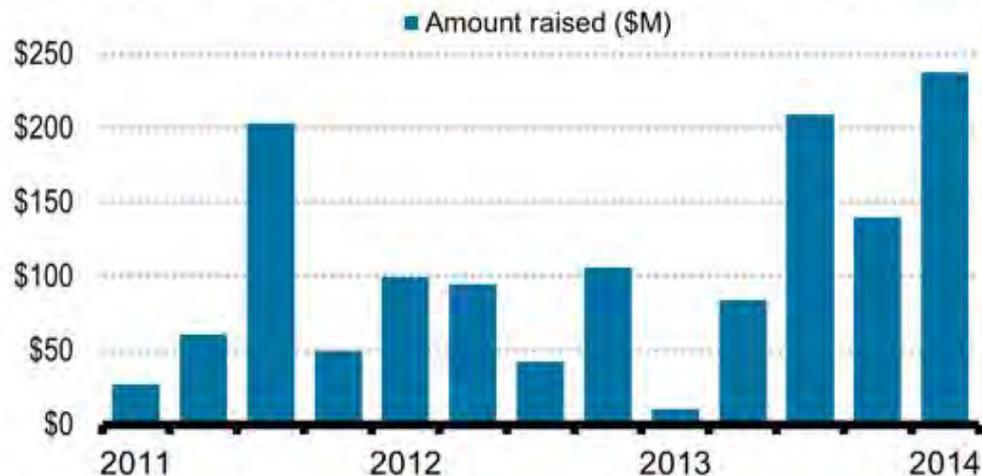
“Other countries have led in the adoption of modern health information systems, but U.S. physicians and hospitals are catching up as they respond to significant financial incentives to adopt and make meaningful use of health information technology systems.” This business mindset is incorrect as only about 1/5 the base cost of a comprehensive EMR is covered with physician incentive and the penalties are far too small for physicians to change behaviors. Moreover, only a small percentage of physicians in some circles are meaningfully embracing EMR

Source: “Stimulating the Adoption of Health Information Technology” (NEJM Apr09), President Obama Dec 6, 2008 radio address

Early Affordable Care outcomes

Health-Care Administration Software

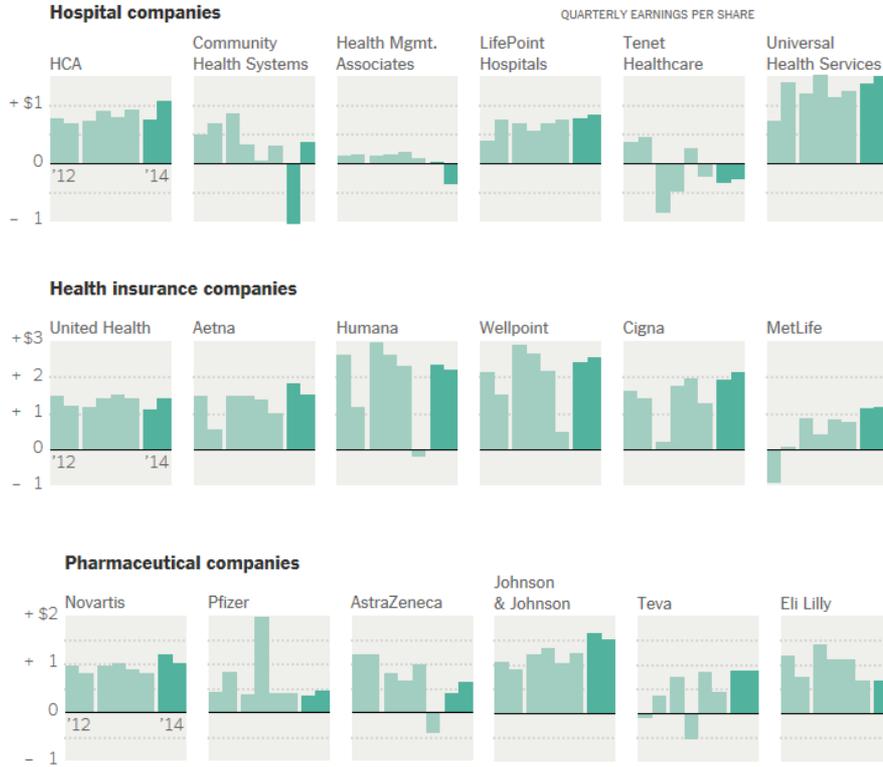
Companies developing software to bring the health-care industry into the modern era raised \$237.5M in 1Q.



Source: Dow Jones VentureSource | WSJ.com

Griggs, Troy, Haeyoun Park, Alicia Parlapiano, Sona Patel, Karl Russell, and R. Smith. "Is the Affordable Care Act Working?" *The New York Times*. The New York Times Company, 26 Oct. 2014. Web. 17 Jan. 2017.

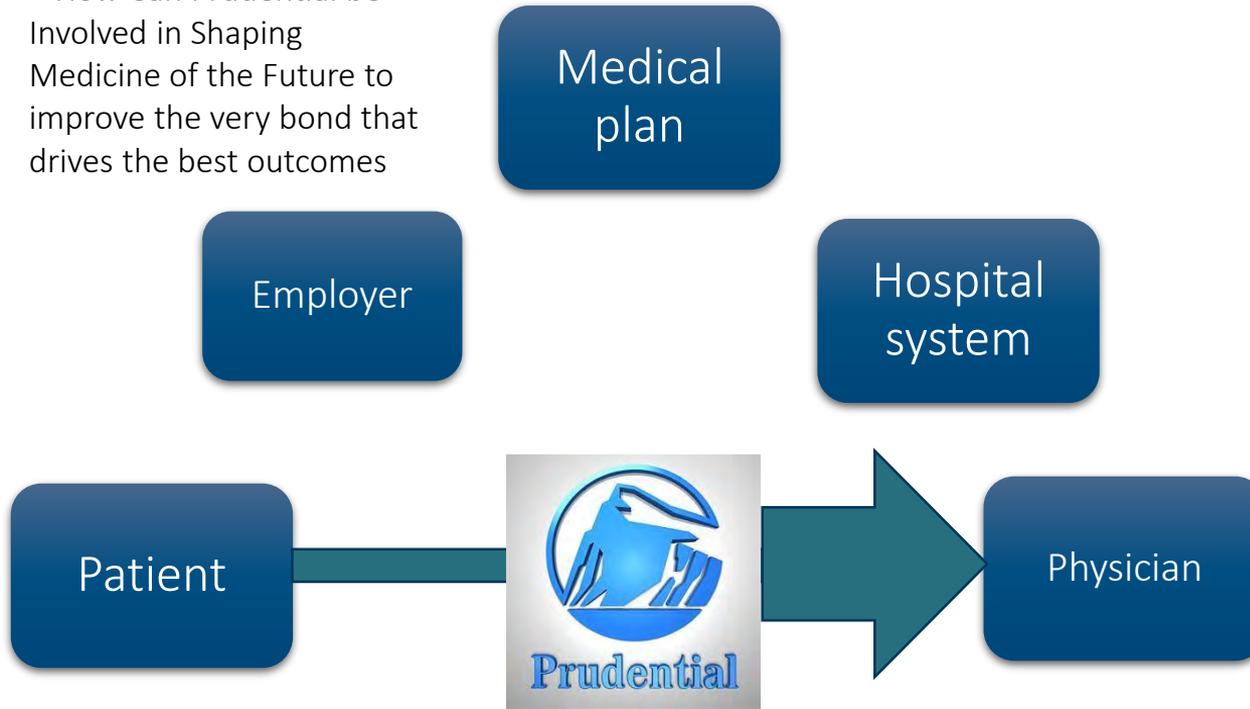
Early Affordable Care outcomes



Griggs, Troy, Haeyoun Park, Alicia Parlapiano, Sona Patel, Karl Russell, and R. Smith. "Is the Affordable Care Act Working?" *The New York Times*. The New York Times Company, 26 Oct. 2014. Web. 17 Jan. 2017.

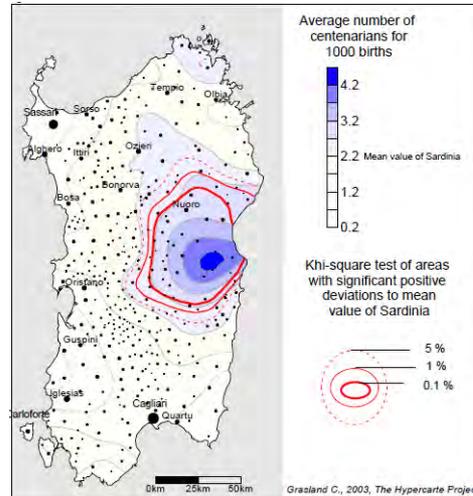
Physician-Patient Relationship of the Future

– How Can Prudential be Involved in Shaping Medicine of the Future to improve the very bond that drives the best outcomes



The AKEA Study

- 2004 epidemiologic study on centenarians living in Sardinia
 - Prevalence of centenarians is higher there than in other European countries (16.6/100,000 inhabitants)
 - Lower female to male ratio of centenarians of 2:1
 - Most notable in the Nuoro province (1:1) which is the most remote and mountainous of the provinces – This is the blue zone – area of greatest concentration within a larger area of overall increased longevity
 - Genetic isolation with minimal immigration
 - Little to no access to healthcare
 - Not only lifespan but healthspan
 - Consistent living habits, culture and traditions



Experimental Gerontology, Elsevier, 2004, 39 (9), pp.1423-1429. laude Grasland, Michel Poulain. Identification of a geographic area characterized by extreme longevity in the Sardinia island: the AKEA study.

Blue Zones

- Dan Buettner identified longevity hot spots in his book Blue Zones in 2009
 - Sardinia – men live the longest here as compared to anywhere else in the world – multigenerational family
 - Okinawa Japan – oldest female, longest disability-free life expectancy; 1/5 rate of colon and breast cancer; 1/6 rate of cardiovascular disease – social purpose
 - Loma Linda, California – Seventh Day Adventists – volunteerism and spirituality
 - Nicoya Peninsula, Costa Rica
 - Icaria, Greece – highest percentage of 90 year olds (1 in 3 people make it to 90, 20% lower cancer, 50% lower CAD and no dementia)
 - Oland, Smaland, Skane in Sweden



Impact – Longevity (Extreme Cases of Longevity)

Progeria 101/FAQ." *Progeria Research Foundation*,
www.progeriaresearch.org/progeria_101.html.

Progeria - Accelerated aging syndrome

"prematurely old" – growth failure, aged looking skin

Children may acquire osteoporosis, cardiovascular disease and can be susceptible to stroke

Most children with Progeria die of a heart attack or stroke at about 14 years old

Many Genetic Causes:

Sebastiani, Paola, et al. "Genetic Signatures of Exceptional Longevity in Humans." *PLoS ONE*, 2012. *PubMed*, doi:10.1371/journal.pone.0029848.

Centenarians – the world's oldest people (100+)

Genetics plays a role in extreme longevity

Case Study – "Genetic Signatures of Exceptional Longevity"

90% of centenarians can be clustered based on "genetic signatures" of predictive factors for longevity

Telomere Length

Centenarians:

Healthy centenarians & offspring show better maintenance of telomere length (due to genetics + health), showing connection to telomeres and aging

Progeria:

Telomere shortening and dysfunction has proven to induce production of progerin, a protein that encourages age-related cell damage

Terry, Dellara F., et al. "Association of Longer Telomeres With Better Health in Centenarians." *The Journals of Gerontology*, a ser., vol. 63, no. 8, 2008, pp. 809-12, biomedgerontology.oxfordjournals.org/content/63/8/809.short.

Impact – Longevity- Invest in Companies that provide lifestyle modification to these goals

- Telomeres and Lifestyle Factors: Roles in Cellular Aging
 - Examined link between **stress and telomere length**
 - Shortened telomere – 3x mortality risk
 - Studied care givers because stressful position
 - Directly related to individual’s sense of stress
 - Perceived as stressed, telomere will be shorter
 - **Meditation Training (mindfulness and purpose), Immune Cell Telomerase Activity, and Psychological Mediators**
 - Link between meditation and telomerase, which regenerates telomeres
 - Greater telomerase activity after 3 months at meditation retreat
 - Even in disease states – Prostate Cancer
- Purpose** in Life is Associated with Mortality Among Community-Dwelling Older Persons
 - Studied link between **purpose in life and mortality**
 - Purpose in life associated with longer life → not affected by gender, age, race, or education
 - Hazard risk for someone with high purpose was 57% of the risk for person with low purpose
 - Telomerase increase, telomere length increase

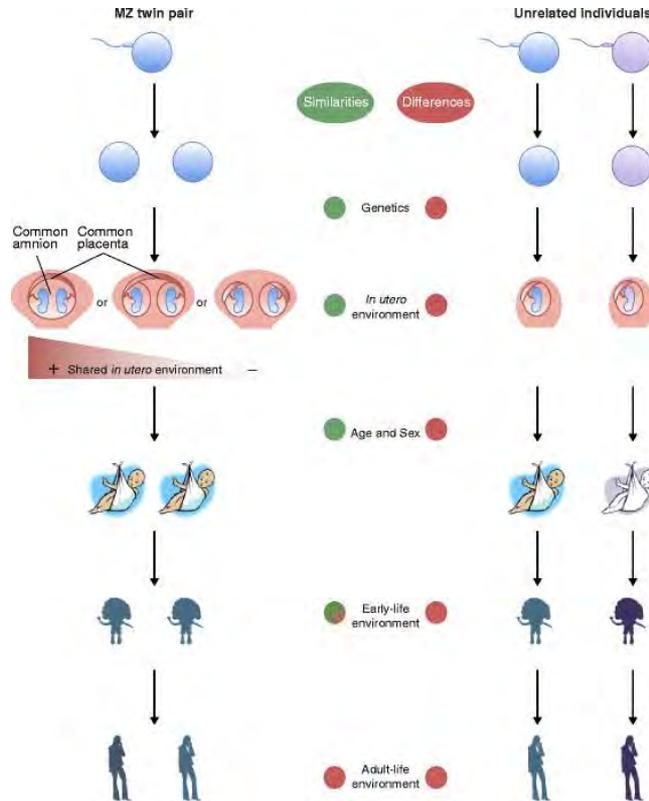
Boyle, Patricia A., Lisa L. Barnes, Aron S. Buchman, and David A. Bennett. "Purpose in Life Is Associated With Mortality Among Community-Dwelling Older Persons." *Psychosomatic Medicine* 71.5 (2009): 574-79. Web. 28 Oct. 2016.

Epel, E. S., et al. "Meditation and vacation effects have an impact on disease-associated molecular phenotypes." *Translational Psychiatry*, vol. 6, 30 Aug. 2016, doi:10.1038/tp.2016.164.

Lin, Jue, Elissa Epel, and Elizabeth Blackburn. "Telomeres and Lifestyle Factors: Roles in Cellular Aging." *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis* 730.1-2 (2012): 85-89. Web. 7 Oct. 2016.

Jacobs, Tonya L., et al. "Intensive Meditation Training, Immune Cell Telomerase Activity, and Psychological Mediators." *Psychoneuroendocrinology* 36.5 (2011): 664-81. 17 Sept. 2010. Web. 7 Oct. 2016.

Environment – the why!



3D Printing

- What is 3D printing?
 - Print layer by layer of a material with precise positioning
 - Cost effective way to create devices and materials
 - Many clinical applications
 - Surgical planning – Use detailed image of organ to determine anomaly and how to approach surgery, less complications
 - Surgical training – surgeons can practice on 3D models, especially with specific issues
 - Food – 3D print a variety of foods, make diet healthier by using better ingredients
 - Medicine
 - Biomaterial printing for tissues and organs
 - Prosthetics

3D Printing – Clinical Applications

•Medicine

- Use 3D printer and chemical inks to print medicine
- Could create personalized medicine
- Print medicine in different shapes so they release drugs at different rates
- Lee Cronin's Vision
 - Consumer would be able to buy 3D printer, chemical inks, and drug blueprints
 - Print medicine from the comfort of home
 - Use own stem cells to make custom drugs

•Case Study

- Spritam
 - Medicine for epilepsy
 - First FDA approved 3D printed medicine
 - Design – highly porous formulation
 - Allows the medicine to dissolve faster than the average pill
 - Medicine is able to begin working quicker → less likely to have consequences from seizure

Basulto, Dominic. "Why It Matters That the FDA Just Approved the First 3D-printed Drug." *The Washington Post*. WP Company, 11 Aug. 2015. Web. 3 Nov. 2016.

Cronin, Lee. "Print Your Own Medicine." *Lee Cronin: Print Your Own Medicine | TED Talk | TED.com*. TED, June 2012. Web. 28 Oct. 2016.

Spritam. Aprexia Pharmaceuticals Company, n.d. Web. 11 Jan. 2017.

ENABLING NEW CAPABILITIES IN PATIENT-CENTRIC THERAPY

Using an aqueous fluid to bind together multiple layers of powder, our unique, patent-protected 3DP technology platform can be used to solve some of your toughest therapeutic challenges across multiple therapeutic areas.



HIGHER DOSE LOADS

Support dose loading up to 1,000 mg



FAST-DISSOLVING

Rapidly disintegrates on contact with liquid by breaking the bonds created during the 3DP process



TASTE MASKING

Allows the application of enhanced taste-masking techniques

3D Printing – Clinical Applications

•Organs

- Able to use biocompatible materials to print simple organs
 - Currently only organs with a maximum of two types of cells i.e. cartilage, skin, hollow organs
- Wake Forest Institute working on 3D printer that directly prints skin onto wound

•Case Studies

- Organovo
 - Successfully printed functional liver that can live up to 28 days
 - Currently working on printing kidney
 - Partnered with Merck to use 3D liver for drug testing → eventually could have no clinical trials
- 3D printed retinas
 - Inkjet printer used to print living retina cells of adult rats
 - Used cells from adult nervous center
 - Able to print multiple levels for a fully functioning retina

"Merck Inks Multi-year Collaboration Deal with Organovo to Use 3D Printed Liver System for Drug Testing." *3ders.org*. N.p., 24 Apr. 2015. Web. 3 Nov. 2016.
Noonan, Jessica. "Lab-Grown 'Custom' Organs May Be Future of Medicine." *ABC News*. ABC News Network, 25 June 2012. Web. 1 Nov. 2016.
Organovo. Organovo Holdings, n.d. Web. 11 Jan. 2017.

Radenkovic, Dina, Atefeh Solouk, and Alexander Seifalian. "Personalized Development of Human Organs Using 3D Printing Technology." *Medical Hypotheses* 87 (2016): 30-33. Web. 3 Nov. 2016.

Prosthetics



"Introducing Jesse Sullivan, the World's First "Bionic Man"" *Jesse Sullivan, First "Bio"* Rehabilitation Institute of Chicago, n.d. Web. 4 Nov. 2016

Sofge, Erik. "Brain-Controlled Bionic Legs Are Finally Here." *Popular Science*. N.p., 20 May 2015. Web. 4 Nov. 2016.

"SYMBIONIC® LEG 3." *Össur*. Össur Corporate, n.d. Web. 11 Jan. 2017.

Palermo, Elizabeth. "New Robotic Exoskeleton Is Controlled by Human Thoughts." *LiveScience*. Purch, 21 Aug. 2015. Web. 4 Nov. 2016.

Borison, Rebecca. "The Human Exoskeleton Got The FDA Go-Ahead To Help Paraplegics Walk." *Business Insider*. Business Insider, 27 June 2014. Web. 4 Nov. 2016.

Brewster, Signe. "This \$40,000 Robotic Exoskeleton Lets the Paralyzed Walk." *MIT Technology Review*. MIT Technology Review, 1 Feb. 2016. Web. 4 Nov. 2016.

Yeates, Ed. "Quadriplegic Teen Walks Again Thanks to Exoskeleton." *DeseretNews.com*. Deseret Digital Media, 03 Apr. 2015. Web. 4 Nov. 2016.

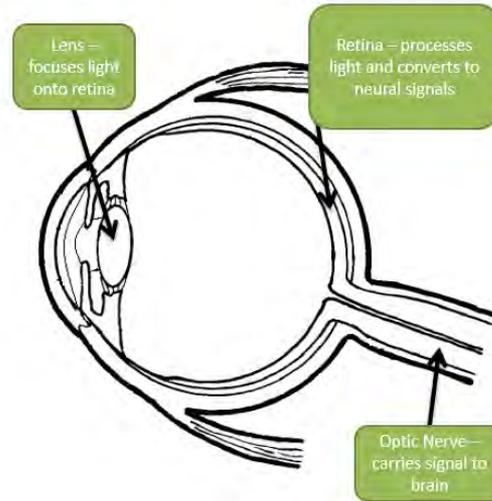


- Rewalk Suit

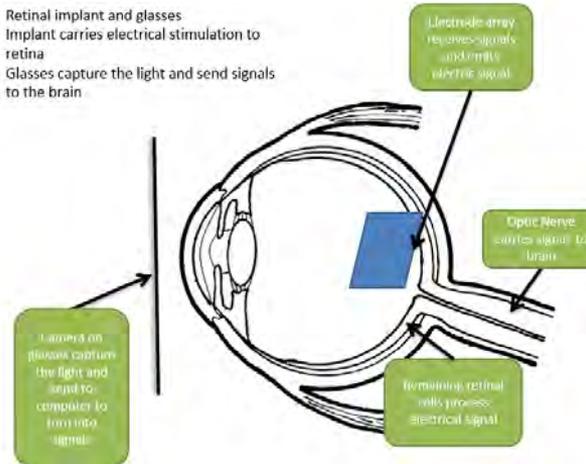


- Brain Powered Exoskeleton

Prosthetics – Argus II



- Retinal implant and glasses
- Implant carries electrical stimulation to retina
- Glasses capture the light and send signals to the brain



"Argus® II Retinal Prosthesis System." *Second Sight Argus® II Retinal Prosthesis System*. Second Sight, n.d. Web. 4 Nov. 2016.

Magnetic Resonance-guided Focused Ultrasound (MRg-FUS)

- What is MRg-FUS?
 - Non-invasive therapy → involves MRI thermal imaging coupled with focused ultrasound on affected area
 - Pinpoints and guides the treatment by measuring temperature changes inside the body
 - Essentially “zaps” away problem area
 - Precise treatment minimizes effect on surrounding areas of the body
 - Currently in clinical use for fibroids, bone metastases pain management, essential tremor

Magnetic Resonance-guided Focused Ultrasound (MRg-FUS)

Type	Procedure		
Neurological	Essential Tremors	Neuropathic Pain	Parkinson's Disease
Oncological	Kidney Cancer	Liver Cancer	Pancreatic Cancer
	Breast Cancer	Soft Tissue Tumors	Bone Metastases
Musculoskeletal	Back Pain		Osteoid Osteoma
Women's Health	Breast Fibroadenomas		Uterine Fibroids
Urological	Benign Prostatic Hyperplasia		Uterine Adenomyosis
Endocrine Disorders	Thyroid Nodules		
	Outside US Approval	Inside and FDA Approval	https://www.youtube.com/watch?v=VbDZzBcMd5E

Bariatric Surgery to Cure Diabetes – University of Washington - Saurabh Khandelwal, M.D.

SURGERY VERSUS MEDICAL THERAPY

Bariatric Surgery versus Intensive Medical Therapy for Diabetes – 3 year outcomes. Schauer P, et al. NEJM 2014.

- **Prospective RCT: STAMPEDE TRIAL** (*Surgical Treatment and Medications Potentially Eradicate Diabetes Efficiently*)
- 150pts with uncontrolled T2DM randomized to: 1) intensive medical therapy alone, versus intensive medical therapy with 2) RYGB or 3) LSG.
- Intensive therapy: adjustment of medical therapy every 3mo. X2 years and then every 6mo thereafter.
- Primary endpoint: A1C \leq 6.0% with/without use of diabetes medications
- Secondary outcomes: weight loss, BP, lipid levels, renal function, ophthalmologic outcomes, medication use, adverse events, QOL

UW Medicine

MECHANISMS

- Reduced ghrelin
 - Modulates dopaminergic reward pathways
- Upregulation of GLP-1, PYY, Neurotensin
 - Anorexia, decreased gastric emptying
- Increased taste/olfactory function, meal-size aversion, reduced hunger
- Neuroplastic structural recovery
 - restoration of functional connectivity, normalization of brain response to food

UW Medicine

- Patients who were insulin requiring prior to sleeve gastrectomy went home on no basal insulin, despite not having lost weight
- Even those who regained weight, just by virtue of weight loss, there was a reduction in morbidity and mortality by having lost weight in the first place.

STAMPEDE TRIAL, 3YR OUTCOMES

- Mean age 48 \pm 8 years
- 68% women
- Mean baseline A1c 9.3 \pm 1.5%
- Mean BMI 36.0 \pm 3.5
- 91% completed 36 months of follow up
- Endpoints: A1C \leq 6.0%

	Medical therapy	Gastric Bypass	Sleeve Gastrectomy
A1c \leq 6.0%	5%	38%	24%
% weight lost	4.2% \pm 8.3%	24.5% \pm 9.1%	21.1% \pm 8.9%

UW Medicine

Robots – Clinical Application

- Robotic Pharmacist
 - Fills prescriptions, stocks medicine → drug vending machine
 - Frees up pharmacists time for more patient interaction
 - Variety of systems being used
 - Fills medication with 99.9% accuracy
 - Medical error is one of the leading causes of death → 54% of medical error comes from medical dispensing error
- Case Study
 - PillPack
 - Prescriptions delivered monthly in packages with day and time
 - Use robots in packing
 - One robot dispenses pills into package → second robot double checks → pharmacist triple checks
 - UCSF Hospital
 - Prepares oral and injectable medicine
 - No error in first 350,000 medications filled
 - Minimize errors – doctors input prescription into computer, barcodes on medication and patient to ensure correct delivery

"New UCSF Robotic Pharmacy Aims to Improve Patient Safety." *University of California San Francisco*. The Regents of The University of California, 7 Mar. 2011. Web. 21 Nov. 2016.

Murray, Peter. "Meet ROBOT-Rx, The Robot Pharmacist Doling Out 350 Million Doses Per Year." *Singularity Hub*. Singularity Education Group, 3 June 2012. Web. 11 Nov. 2016.

PillPack. PillPack, n.d. Web. 11 Jan. 2017.

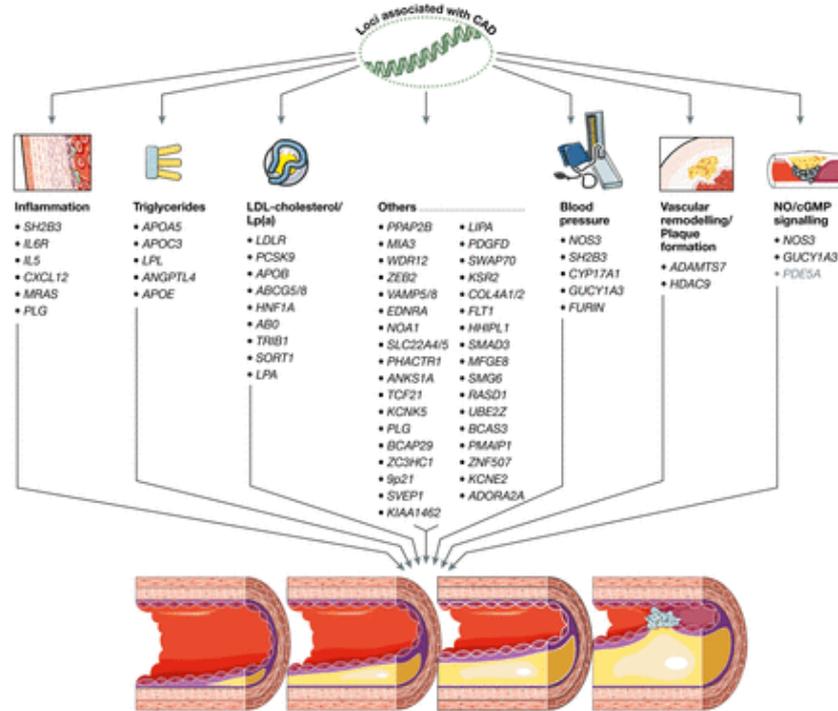
The genes involved in sudden death in athletes

A

Phenotypes	Protein	Gene symbol	Frequency in mutated patients	Ref.
Hypertrophic Cardiomyopathy 	Beta Myosin heavy chain	<i>MYH7</i>	25-35%	16, 63
	Myosin binding protein C, cardiac	<i>MYBPC3</i>	30-50%	16, 63
	Cardiac troponin T	<i>TNNI2</i>	5-7%	16, 63
	Cardiac troponin I	<i>TNNI3</i>	3-5%	16, 63
	Myosin, light chain 2, regulatory	<i>MYL2</i>	~3-5%	16
	Myosin, light chain 3, essential	<i>MYL3</i>	~2%	16
	Alpha Tropomyosin, Alpha Myosin heavy chain, Titin, Cardiac Actin, Telethonin, Myozenin	<i>TPM1, MYH6, TTN, ACTC1, TCAP, MYOZ2</i>	rare	
Dilated Cardiomyopathy 	Lamin A/C	<i>LMNA</i>	5- 10%	27-63
	Beta Myosin heavy chain (β MHC)	<i>MYH7</i>	~7%	27
	Cardiac troponin T (cTNT)	<i>TNNI2</i>	~4%	27
	Myosin binding protein C, cardiac (cMyBPC3)	<i>MYBPC3</i>	~1%	27
	Sodium channel, type V, α subunit	<i>SCN5A</i>	5-10%	63
	Cardiac troponin I (cTNI)	<i>TNNI3</i>	~1%	27
	Myosin, light chain 2, regulatory	<i>MYL2</i>	~1%	
	Myosin, light chain 3, essential	<i>MYL3</i>	~1%	
	Desmin	<i>DES</i>	~3%	
	BCL2-associated athanogene 3	<i>BAG-3</i>	~3%	
Alpha Tropomyosin, Titin, Cardiac Actin, Telethonin, Myozenin,	<i>TPM1, TTN, ACTC1, TCAP, MYOZ2</i>	~2%		
Arrhythmogenic right ventricular cardiomyopathy (ARVC) 	Plakophilin 2	<i>PKP2</i>	11-43%	20-59
	Desmoglein 2	<i>DSG2</i>	12-40%	20-59
	Desmoplakin	<i>DSP</i>	6-16%	20-59
	Desmocollin 2	<i>DSC2</i>	rare	20-59
	Junction plakoglobin	<i>JUP</i>	rare	20-59
	Ryanodine receptor 2	<i>RYR2</i>	rare	20-59
	Transmembrane protein 43	<i>TMEM43</i>	rare	20-59
Syndromic Cardiomyopathy	Protein	Gene symbol	Inheritance	
	HCM+WPW (Wolff Parkinson White)	Protein kinase, AMP-activated, γ 2	<i>PRKAG2</i>	Autosomal Dominant
	Danon disease	Lysosomal-associated membrane protein 2	<i>LAMP2</i>	X linked
	Pompe disease	alpha Glucosidase	<i>GAA</i>	Recessive
	Fabry disease	alpha Galactosidase	<i>GLA</i>	X Linked
	Friedreich syndrome	Fratxin	<i>FXN</i>	Recessive
	Marfan Syndrome	Fibrillin 1	<i>FBN1</i>	Dominant

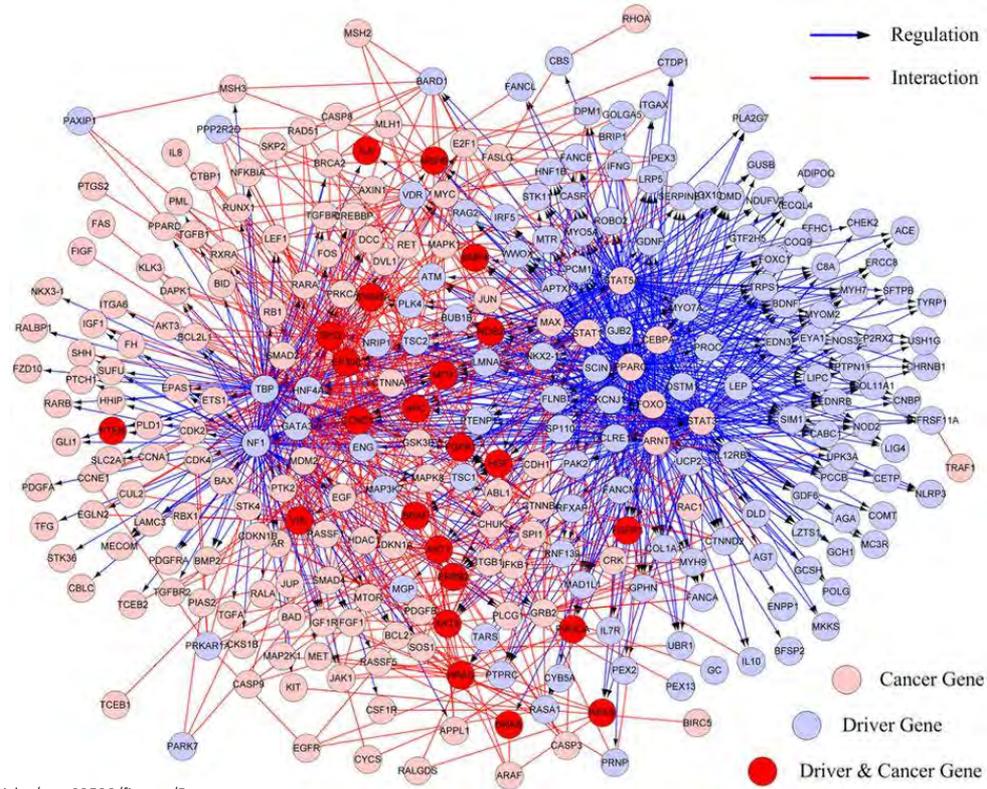
https://bjsm.bmj.com/content/46/Suppl_1/i59

Genetics of Atherosclerosis



<http://embomolmed.embopress.org/content/8/7/688>

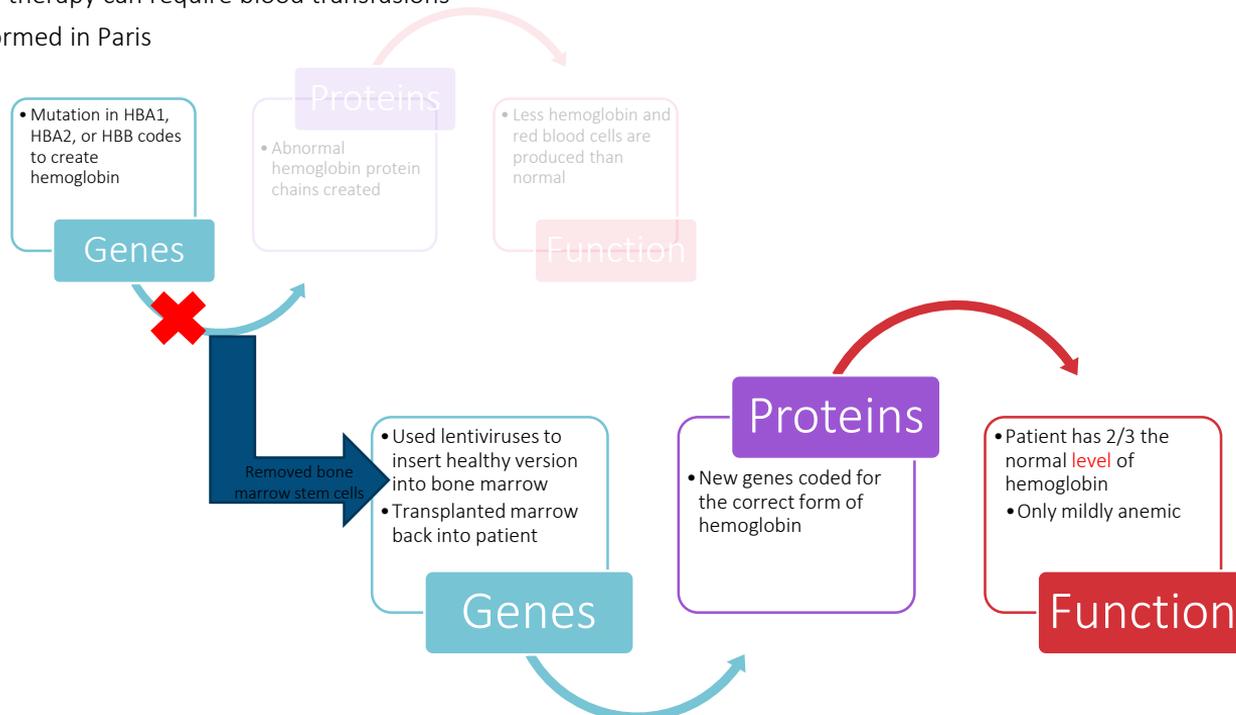
Cancer genes



<https://www.nature.com/articles/srep03538/figures/5>

Clinical Applications – Genome Correction

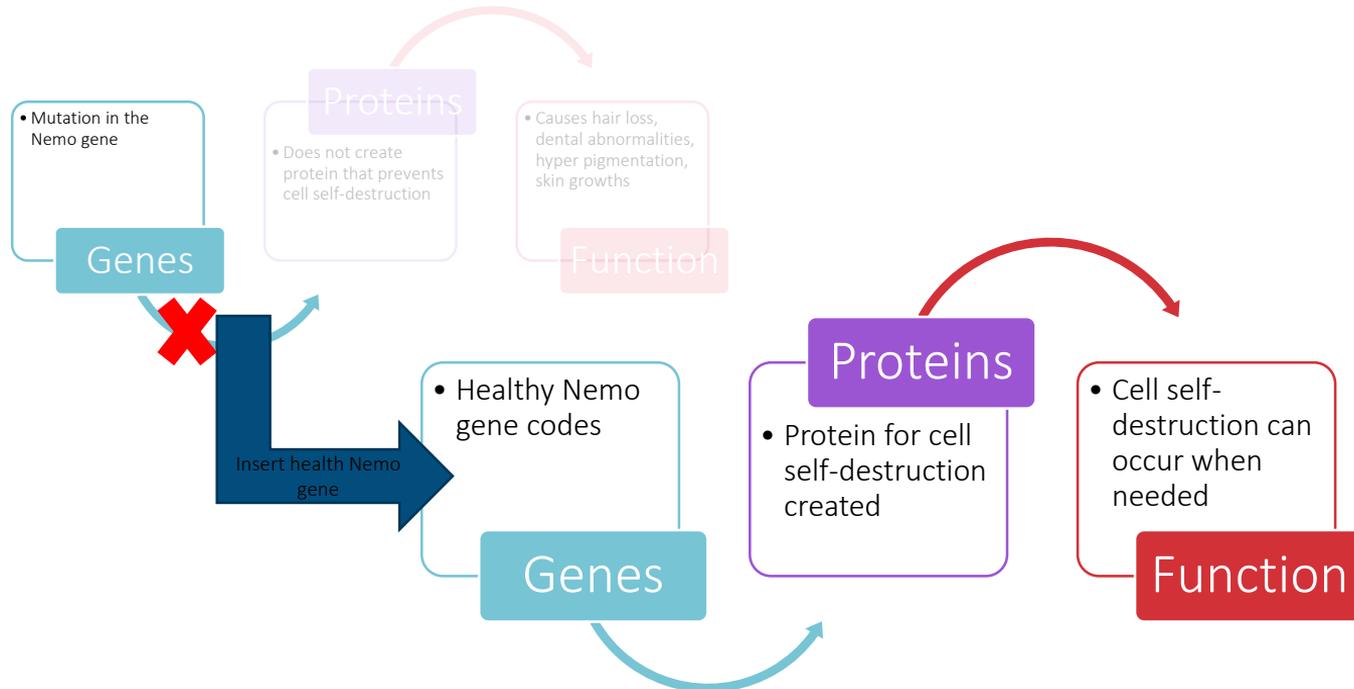
- Hereditary Blood Disease
- Treat thalassemia
 - Without gene therapy can require blood transfusions
- Treatment performed in Paris



Gravitz, Lauren. "Gene Therapy Combats Hereditary Blood Disease." *MIT Technology Review*. MIT Technology Review, 16 Sept. 2010. Web. 14 Oct. 2016.

Clinical Applications – Genome Correction

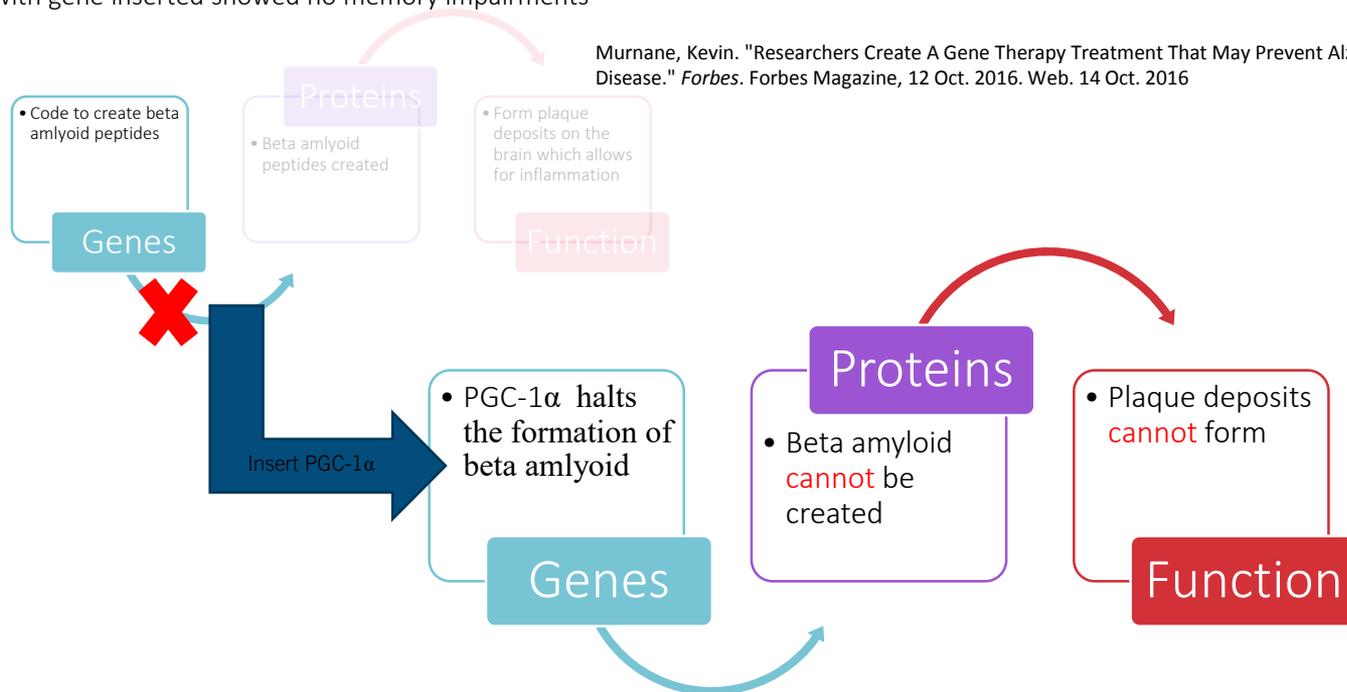
- Neurovascular disorder gene therapy
- Incontinentia Pigmenti – rare X linked disease
- Adeno-associated virus (AAV) engineered to deliver *Nemo* gene to mouse with Incontinentia Pigmenti (IP) → reversed abnormalities



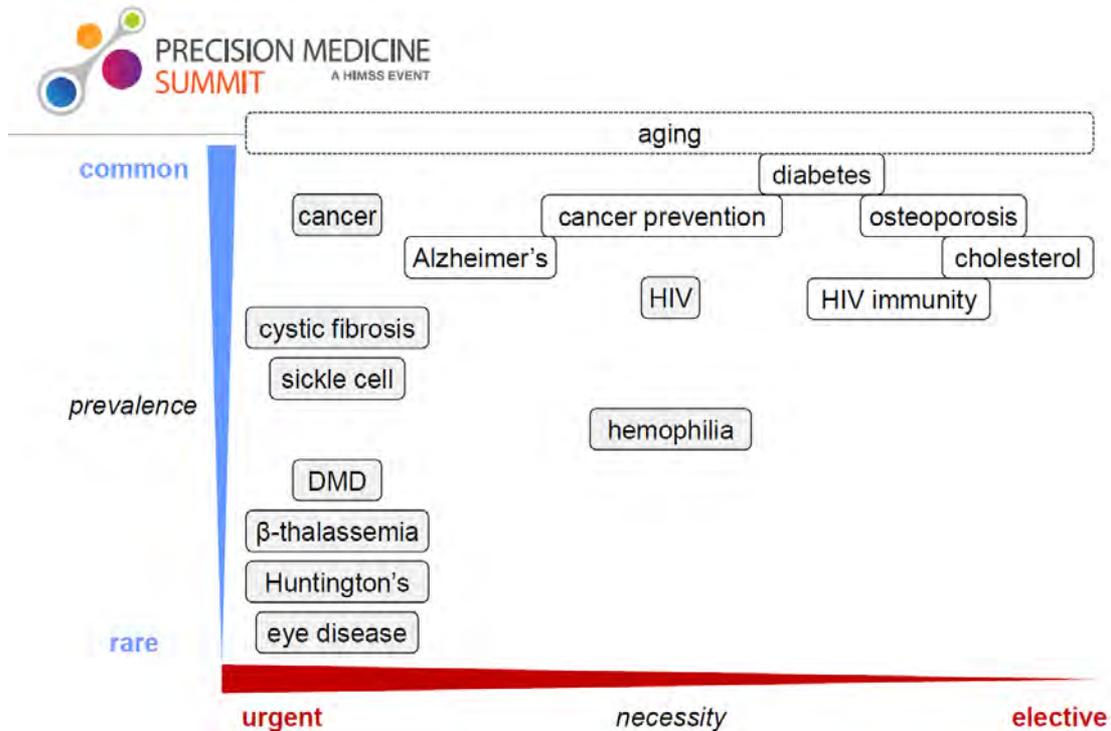
Marchiò, S., Sidman, R. L., Arap, W., & Pasqualini, R. (2016). Brain endothelial cell-targeted gene therapy of neurovascular disorders. *EMBO Molecular Medicine*, 8(6), 592-594. doi:10.15252/emmm.201606407

Clinical Applications – Genome Correction

- Preventative treatment for Alzheimer's
- Current worldwide cost of coping with Alzheimer's → \$818 billion
- Gene therapy tested on mice was able to halt the start of Alzheimer's
 - Mice with gene inserted showed no memory impairments

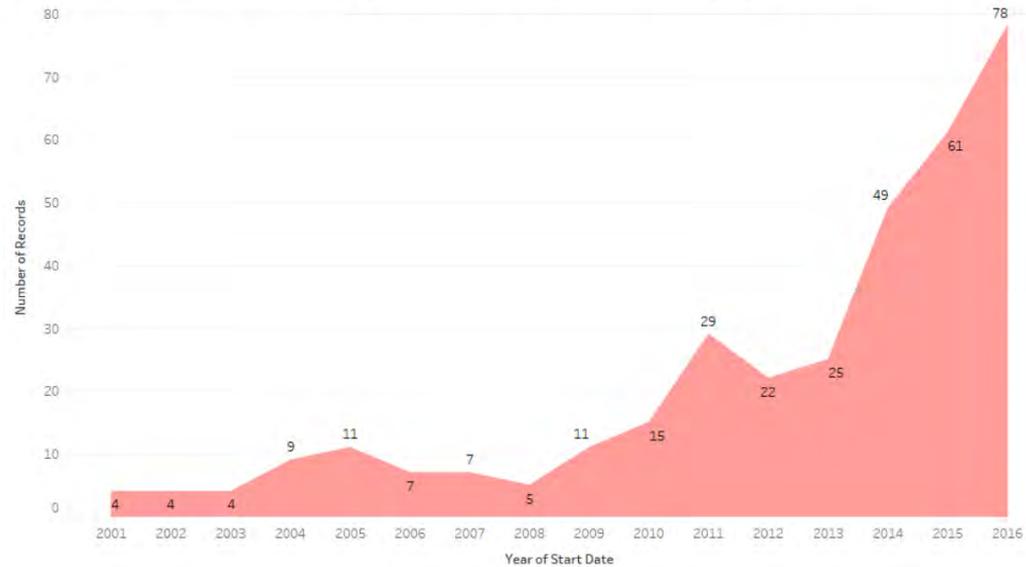


Opportunities to cure disease - Ross Wilson, UC Berkley



Momentum

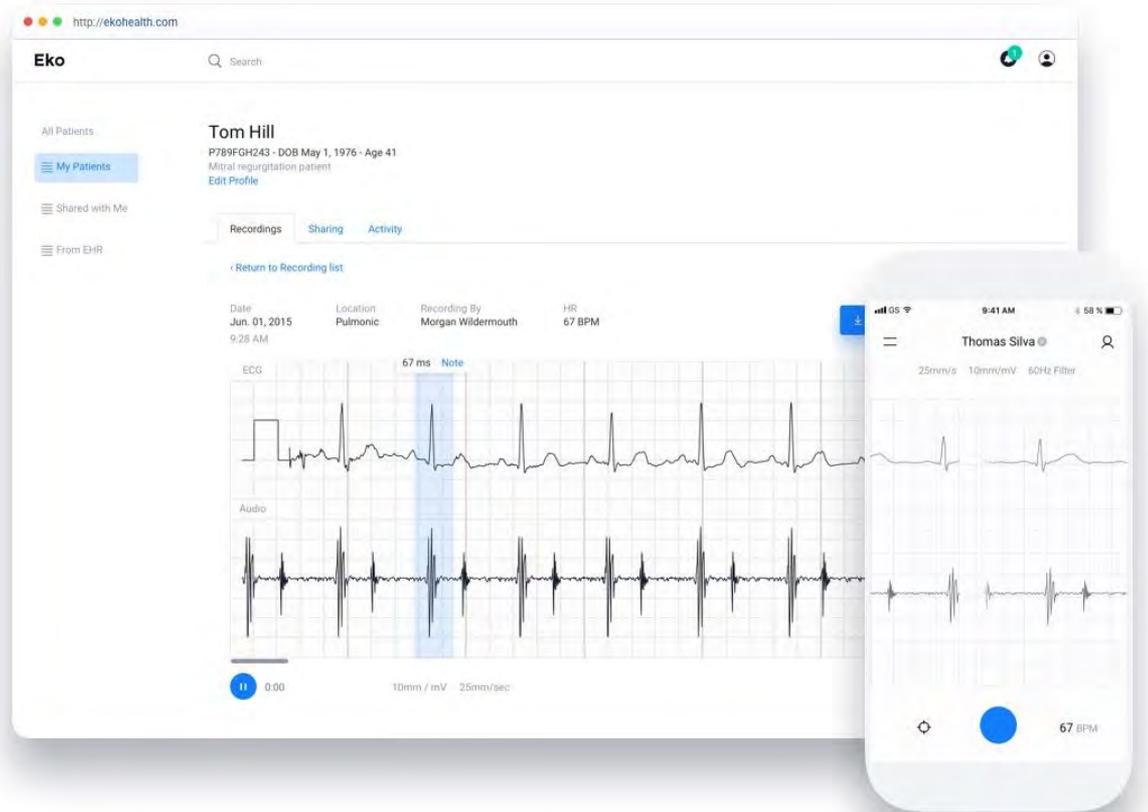
Number of Gene Therapy Clinical Trial Initiations Per Year



Virtual Doctor Visits

- Companies that offer service:
 - Teladoc
 - American Well
 - Carena
 - Zipnosis
 - Ringadoc
 - PlushCare
 - MeVisit
 - Stat Health
 - MDLive
 - Virtuwell
- Study shows poor accuracy
- Tested 8 popular companies with 599 visits
 - $\frac{1}{4}$ received wrong diagnosis
 - Only 54% followed protocols
- More regulation in order for correct diagnosis

AI driven auscultation



Blood collection



**VENIPUNCTURE:
PAINFUL AND UNCOMFORTABLE**



**FINGERSTICK:
PAINFUL**



**TAP:
PAINLESS**

NEW BLOOD COLLECTION EXPERIENCE

At some point, we have all experienced having blood drawn directly from a vein, usually in the crook of the elbow. There is nothing worse than watching someone insert a needle into your vein, often more than once, and then seeing your blood fill several tubes. TAP, the world's first push-button blood collection device, eliminates all of this and makes blood collection simple, convenient, and virtually painless.

Gone are the days of tourniquets, large needles, lancets, tubes, and bandages. No more sitting in a waiting room waiting anxiously to have your blood drawn. Instead, the small device is positioned on a patient's upper arm and with just a 'tap', blood is collected. Future versions of TAP will enable patients to collect their own blood anywhere. No more sitting in a

<http://www.7sbio.com/tap/>

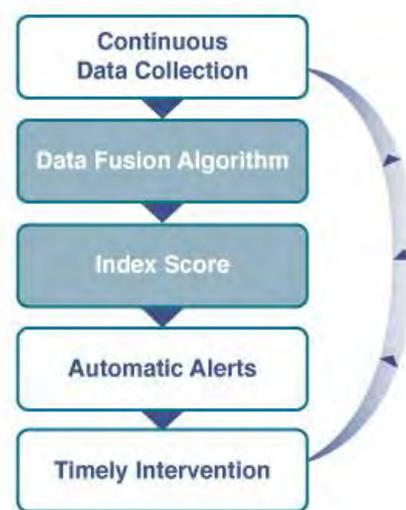
Internally traveling sensors

- Given Imaging (www.givenimaging.com) – GI imaging through capsules
 - Capsule endoscopies – PillCam SB, Colon, Eso, Patency – evaluate different parts of the gut looking for areas of bleeding, disease (ie. Cancer)
 - Reflux - Bravo pH monitoring system; Digitrapper pH-Z system
 - Motility monitoring – Mano Scan Manometry, SmartPill
- Benefits – these visualize lesions in patients who cannot tolerate anesthesia or a longer procedure
- Limitations – fail to detect small anomalies
- Foresight Institute– robot that travels in patient’s blood to detect and treat
 - Tumors
 - Arteriosclerosis
 - Blood clots
 - Accumulation of scar tissue
 - Pockets of infection



Benefits of Visensia

- Analysis and interpretation of up to 5 vital signs (heart rate, respiration rate, oxygen saturation, temperature, blood pressure) collected from bedside monitors and ambulatory devices or manually during routine observations leads to the Safety Index
 - Indications of wellness
 - Improvement of clinical outcomes
 - Optimization of scarce medical resources
 - HL7 interface from existent device both periodic and continuous
 - Numerical index is generated 0-5 representing patient's wellness (5 critical)
 - Alerts when a single parameter deviates by +/- 3 SD or when two parameters alter by less
 - Simple unambiguous call to action
 - Improved clinical outcomes
- Benefits
 - Identify crises earlier and accelerate response times
 - 6.33 hours prior to human detection of crisis
 - 3 fold reduction in number of crises
 - 50% reduction in crisis duration
 - 37.5% reduction in code-blues
 - Improve communication
 - High sensitivity
 - Identifies cardio-pulmonary events (10x better than human process)
 - High specificity
 - 95% of alerts are "true positives"
 - Fewer ICU transfers; 34.5% reduction in mortality; ½ day reduction in hospital stay



"Visensia." *OBS Medical*. OBS Medical Ltd, n.d. Web. 17 Jan. 2017.

Jool Vibe and how companies can impact organizational change to impact productivity



Predictive and Prescriptive Analytics

- Cases with practical use
 - High cost patients
 - 5% of patients account for 50% of healthcare costs
 - Better management of these patients → decreased costs
 - Make predictions of who will be a high cost patient → determine the correct care needed
 - Readmissions
 - 30% of pediatric readmissions are preventable
 - Use algorithm to determine who should be readmitted → make sure that patients are doing the prescribed treatment
 - Decompensation
 - Monitor all patients at risk for decompensation → period of time before it happens when data can determine the risk
 - If patient begins to show signs of decompensation, prescribe the correct next steps
 - Adverse drug reaction
 - Can predict if a patient will benefit from treatment, be harmed, or have no reaction
 - Determine if they should prescribe medication
 - Treatment optimization for diseases affecting multi-organs
 - Predict trajectory of the diseases → figure out who would benefit the most from certain therapies

Bates, David W., Suchi Sari, Lucila Ohno-Machado³, Anand Shah, and Gabriel Escobar. "Big Data In Health Care: Using Analytics To Identify And Manage High-Risk And High-Cost Patients." *HealthAffairs*. Project HOPE, 01 July 2014. Web. 29 Nov. 2016.

CrowdMed – Case Study

- Patients waste time and \$ traveling between specialists → no diagnosis
 - One doctor opinion is not always accurate/best answer
- **Solution: combine crowdsourcing & telemedicine to produce diagnoses**
- Patients submit cases & medical info (can be anonymous)
 - “Medical Detectives” submit solutions to various cases
 - Typically doctors/medical students
 - “Prediction Market Technology” filters and collects suggestions
 - Separate valid suggestions from off-base
 - Produce report with suggestions for treatment
- >60% reported success
- Estimated decrease in medical bills

Select a case

Which case do you feel best qualified to solve?

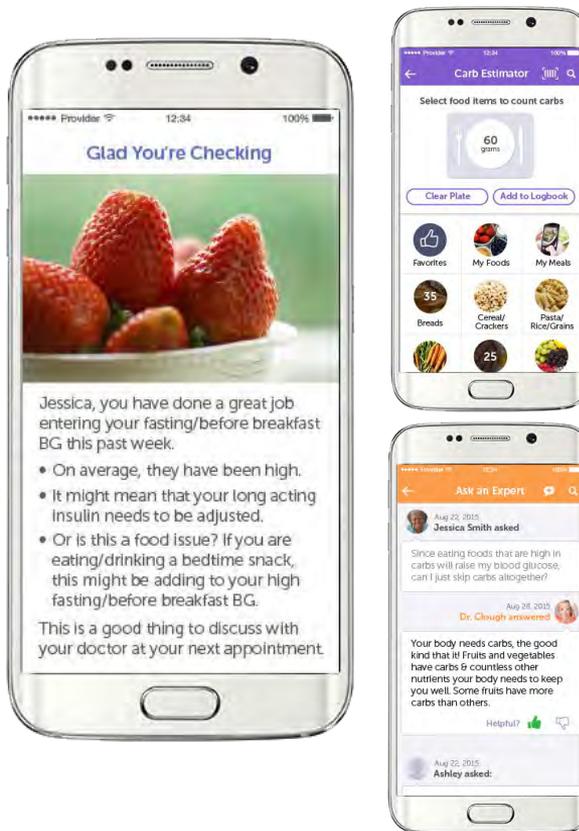
Case #	Name	Age	Symptoms	Max Reward
Case #5123	Cassidy	62	occasional pain in several areas of the body like stomach joints, hips, etc but not headache. but 2 years ago the upper	9,000
Case #8005	Veronique	51	connective tissue disorder, likely Ehlers-Danlos, but not specified- do not fit into typical types, hypermobility, spinal degeneration, extreme	16,000
Case #4105	Merrill	57	Very low count on white blood cells, Leucocytes 1,96 Giga/L, Polynucleaires 449 mm3, blood sedimentation 1st hour 44, second hour 85.	16,000

"CrowdMed." *CrowdMed*, crowdmed.com.

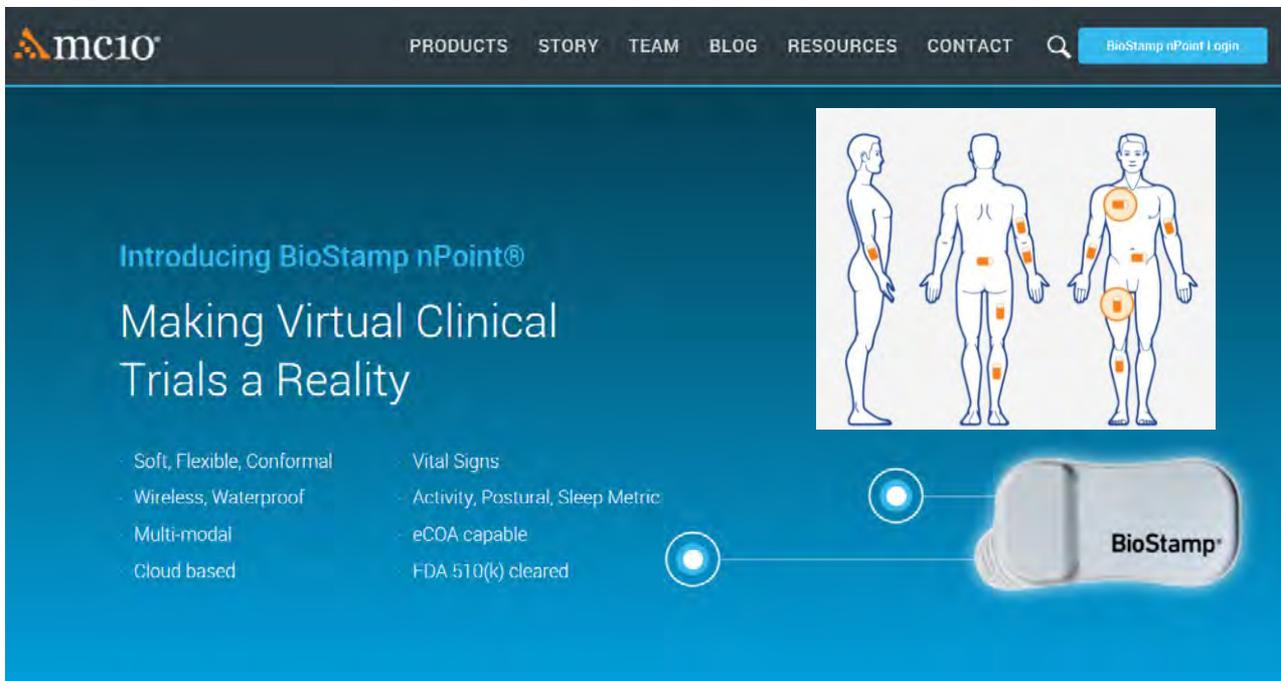
WellDoc BlueStar – Case Study

- 1st mobile prescription technology
- Requires doctor prescription to use service → FDA approved
 - App-based self-management health plan for Type 2 Diabetes
- Analyzes patient-inserted data (blood glucose, medications, etc.)
- Past data trends & analytics → guidance & improve efficacy of the patient's healthcare team
- Progress is sent to doctor before every visit
- Special Features
 - Restaurant locator, videos, carb counting, “ask an expert”, motivating messages
- Clinical study – decreased amount of A1C in patients, decrease in hospital & ER visits

"WellDoc BlueStar." *WellDoc*, www.welldoc.com/product/bluestar.



Biostamps and Digital Tattoos



The screenshot shows the mc10 website interface. At the top, there is a navigation bar with links for PRODUCTS, STORY, TEAM, BLOG, RESOURCES, and CONTACT, along with a search icon and a "BioStamp nPoint Login" button. The main content area features the following text and graphics:

Introducing BioStamp nPoint®

Making Virtual Clinical Trials a Reality

- Soft, Flexible, Conformal
- Wireless, Waterproof
- Multi-modal
- Cloud based
- Vital Signs
- Activity, Postural, Sleep Metric
- eCOA capable
- FDA 510(k) cleared

Three human figures illustrate the placement of BioStamp sensors on the back, arm, and leg. A close-up image of the BioStamp device is shown on the right, with two callout circles highlighting its features.

Continuous Glucose Monitoring

MINIMED™ 670G INSULIN PUMP SYSTEM



MiniMed™ 670G Insulin Pump and CGM system

An insulin pump combined with a CGM can enable your pump to automatically adjust your basal (background) insulin every five minutes based on your CGM readings*.

MiniMed™ 670G system includes our newest and most advanced CGM, the Guardian™ Sensor 3 and the Guardian™ Link 3 transmitter. It is the first and only system that constantly self-adjusts* to automatically keep your sugar levels in range.

The MiniMed™ 670G system helps stabilize glucose levels with fewer highs and lows, so you can focus less on your diabetes and more on whatever the day brings.

[LEARN MORE](#)

[▶ HOW IT WORKS](#)

GUARDIAN™ CONNECT SMART CGM



For people using insulin injections

The Guardian™ Connect CGM monitors your glucose levels day and night and alerts you of highs or lows before they happen. You can set alerts anywhere from 10 to 60 minutes, getting notified exactly when you want. The system includes a small sensor worn up to seven days and a slim, discreet Bluetooth® transmitter. They work together to send precise glucose readings automatically to your phone every five minutes. The Smart CGM system comes with exclusive access to the Sugar IQ diabetes assistant, that helps you understand your daily glucose patterns and identify activities affecting them—for a full picture of your diabetes.¹

Guardian™ Connect CGM has you covered — and looks ahead — so you can focus on living your life, instead of watching your glucose levels.

[LEARN MORE](#)

[▶ HOW IT WORKS](#)

IPRO™ 2 PROFESSIONAL CGM



A simple way to better control your diabetes.

The iPro™ 2 Professional CGM system records your glucose levels 24 hours a day for up to six days. Used intermittently, the iPro™ 2 system provides your physician with insights into how the nutrition plan, medication regimen and daily activities affect your glucose levels, enabling them to make more informed decisions regarding your diabetes management.

[LEARN MORE](#)

[▶ HOW IT WORKS](#)

Medtronic

Express Scripts

- Size of data set

- Collects 160 quadrillion bits of data
- 1.4 billion prescriptions each year
- Claims from 100 million Americans
- 100 million life years

- Speed of data

- 22 milliseconds checks for 3200 drug rules, interactions, overdosing and duplications; 2203 medical rules, contraindications, allergies
- 40 predictive models to detect
- Likelihood of patient drug discontinuation
- Best method of communication for each patient
- Active fraud at a given pharmacy

- Specific Suite of Solutions

- ScreenRx – predictive models which consider 400 variables to determine who is likely to stop taking meds and intervene. 98% accuracy in predicting noncompliance 1 year in advance – 9 times more accurate than patient self-reporting

Express Scripts. www.express-scripts.com/index.htm.

Other potential strategic partners to navigate care – improve lives and improve our risk



