THE FUTURE OF MEDICINE

Solving the Puzzle

Western New York may seem an unlikely place to invent the future of medicine. But in fact, Western New York–and the many communities like us around the country–are where the real battle over the future will take place.

While we are not home to the biggest pharmaceutical companies, nor are we the home of famous biotech and healthcare unicorns, we are where their creations are inevitably headed. Silicon Valley may be their pilot market, but places like Western New York are their proving ground. As you'll see in Trickle-Up Innovation (p. 28), breakthroughs can—and, increasingly, will—happen everywhere. But no matter where an innovation originates, until it works on Main Street, under our constraints, the future of medicine hasn't really arrived.

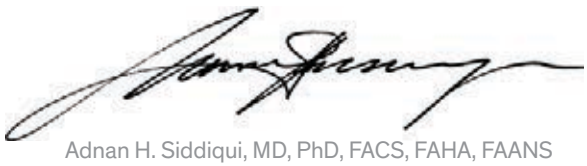
Our challenges in Western New York are typical of so many other places around the country. With 2 million people, we are plenty big—so we're no small challenge. Few in our community have the wealth reserves to pay for super-premium care; the vast majority have to accept what their insurance alone can cover. The health of our population shows the wear and tear of long winters, lives spent working on our feet and a steady diet of hearty but not heart-healthy comfort food. We're aging, and presenting the typical signs that go hand in hand with aging—higher rates of stroke, cancer, Alzheimer's and heart disease.

Those of us who take care of this community feel deeply invested. We care not just for our patients, but for the greater community and the healthcare system itself, across all providers. **We've built the Jacobs Institute on the premise that fostering innovation is the most important thing we can do to ensure improved quality of care for current and future generations. We commissioned this report to rally and prepare local medical communities for the impending future. Our hope is that this report brings the stakeholders in our community and yours to the table to form long-term strategic innovation plans.**

The report accurately describes the current state of affairs in major cities, and it applies here. Providers are swamped with new mandated reporting requirements and are competing at too many levels, from primary care through specializations, rather than focusing on what they do best in the market, and getting ever better and more efficient at it. Our brands lack clarity, so patients feel confused and uninformed. All this accomplishes is slowly leaking market share to outsiders. Today, it's patients choosing to get care down in Pittsburgh—or at Walmart. Soon, as the report warns, it'll be national and global health brands reaching out to our patient population with virtual care. The same way Amazon has run roughshod over retailers' business models, it—or Google, or Apple—could suddenly turn healthcare on its head by digitizing medicine at scale.

As mighty a challenge as it was to gaze into the years ahead and envision medicine's future, the even harder work will be done here, locally. It's somewhat like solving a Rubik's Cube—you understand what it's supposed to get to, but it's a puzzle to get there, one twist at a time. As you read this report, we encourage you to ponder how the future depicted creates new opportunities and might shape our strategic development plans for the years ahead.

L. Nelson "Nick" Hopkins, MD, FACS
Founder & Chief Scientific Officer
The Jacobs Institute



Adnan H. Siddiqui, MD, PhD, FACS, FAHA, FAANS
Chief Medical Officer
The Jacobs Institute

Contents

→ http://futureof.org

Chairman's Letter

The Jacobs Institute was created in memory of my brother, Lawrence D. Jacobs, MD. Larry was a born innovator with a passion for taking care of people and a knack for forging new paths through roadblocks previously thought insurmountable.

As chair of Neurology at the University at Buffalo, Larry was collaborating with researchers at Roswell Park Cancer Institute to explore the cancer treatment potential of interferons. He followed a hunch that the proteins could also slow down the ravages of multiple sclerosis, which affects a disproportionate number of Western New York residents. That hunch led to a new treatment that has improved and extended the lives of millions of MS sufferers around the world.

Larry's discovery would not have been possible without the proximity—both geographically and intellectually—of the institutions on the Buffalo Niagara Medical Campus, which will soon include the university's state-of-the-art Jacobs School of Medicine and Biomedical Sciences. The "collisions" that take place among Western New York's medical community allow researchers, like my late brother, to set out with one intention and end up with a wholly unexpected, but life-saving, outcome.

The Jacobs Institute, at the heart of the campus, is the organizational embodiment of Larry's approach to medicine. It provides a lasting home for innovation and collaboration across medical disciplines as well as between industry and academia. The JI does more than encourage collisions; it facilitates them. With interactions between the world's leading vascular clinicians across several sub-specialties, the JI generates a steady flow of new, out-of-the-box methodologies and medical device innovation.

This report is inspired by the JI's futuristic approach to medicine. While it may contain some unsettling projections, readers should ultimately feel great optimism: treatments of all kinds are becoming vastly more affordable and available around the globe; artificial intelligence is helping our medical practitioners be more precise in diagnosing and treating maladies; and powered by bioinformatics, digital interventions are poised to replace invasive and drug-based measures in many areas.

The Western New York medical community is elevating medical discovery and delivery at every level. With this expertise, we are leading the local, national and global conversation with the hope that it sparks debate and inspires innovation among practitioners, administrators, academicians and policymakers. We look forward to hearing your thoughts.

Jeremy M. Jacobs
Chairman, Jacobs Institute Board of Directors
Chairman, Delaware North

FORCES OF CHANGE

In this report, we don't shy away from making specific predictions on just how the dominoes fall. To make those forecasts, we picked the 26 most powerful forces in the world that will shape medicine. Eleven of these forces are new medical technologies. Seven of the forces are computing technologies, and eight are global sociodemographic forces. Our panel of futurists and consulted experts each ranked the 26 forces on a scale of 1 to 10. The average across all futurists resulted in a force strength score.

Using the same methodology, we ranked all the stakeholders in healthcare on a motility scale. A higher motility score meant that stakeholder was more likely to break away, or switch. Stakeholders who have demonstrated previous switching behavior, for instance, would likely switch again. For example, in the last decade we've seen physicians take buyouts en masse to be employed by hospital networks, and we've seen a major migration to self-funding among large employers.

Envisioning the far-out future of medicine is easy. The hard part is seeing the path between today and that future. Many promising trends in medicine fizzle out simply because healthcare mainstays like Big Pharma, Medicaid, the FDA and insurance companies carry too much inertia. Innovation can only enter the picture from the edges.

Factoring force by motility led to a model that identified where change would happen first. As those first movers began to break away, or adapt, the inertia of the whole system was destabilized, step by step. Over time, yet other pieces broke away. By this method, we arrived at market predictions over time, and we forecast adoption curves for the new technologies over 25 years. That calculus roots our stories, sector by sector.

What happens when exponential forces meet intractable objects?

COMPUTING

MOORE'S LAW
Reports of a slowing in Moore's Law are inaccurate. Graphical processing units, used for artificial intelligence, have kept it on track.

SENSORS
Not only is the cost of sensors going down 15% per year, but their quality and sensitivity is simultaneously going up at the same rate. Ultra-low-field sensors that ping the network less frequently reduce the cost 10×.

DIGITAL MANUFACTURING
Already, we can print 3-D devices and stents that are a precise fit for any patient. Bioprinting tissues, even organs, will be necessary for every hospital.

MIXED REALITY
Imagine hospice pods where the dying are virtually transported to sunny beaches. Imagine replacing medical charts with visualizations of a patient's different systems.

SMARTPHONE CANOPY
By 2020, 7 billion people will be connected to the internet. 5G wireless will increase data transfer speed by 100× over 4G. Phone plug-ins turn a phone into a medical device that can read scans, connect to sensors, process lab tests and offer telemedicine.

BLOCKCHAIN
The future of security is splintering data into infinite fragments stored all over the world. Each fragment is meaningless on its own. The index is kept in unhackable blockchains.

QUANTUM COMPUTING
Massively more powerful than classical computers, quantum computers will let us create tomorrow's drugs in a fraction of the current R&D cycle—and easily break the military-grade cryptography protecting today's medical records.

SOCIAL

INTERNATIONAL MIDDLE-CLASS EXPLOSION
Just in the last seven years, half a billion people in China have become able to afford first-world diets. The first world's medical conditions will follow—an avalanche of diabetes and vascular diseases.

OPEN FORCE MOVEMENT
Consumer activism that demands full transparency of every product's origins, in banking and healthcare, will lead to consumer control of their own data. In drug development, connected consumers will put pressure on pharma like never before.

BIRTH RATE & AGING OF POPULATION
Worldwide infant mortality has been cut in half since the new century began. Subsequently, birth rates fell—and continue to fall.

URBANIZATION & GLOBALIZATION
The density and mobility of people mean much greater risk for epidemics and the spread of disease. Global health brands will emerge; health deliveries that are confined to national borders will be long-term losers to organizations that can operate as global corporations.

ONLINE EDUCATION
Today, people Google their symptoms. Soon, patients will be able to take an entire class on their condition, taught by a doctor. Patients will be as informed as medical professionals. We will retrain doctors and train nurses online, too.

JOB DISPLACEMENT FROM AUTOMATION
Over the next few decades, large segments of the population are likely to become unemployed due to automation, significantly changing our economic structure and presenting new lifestyle diseases.

WEALTH GAP
Historically, health was the great equalizer. Even the wealthy got diseases, in some cases at higher rates. In 1977, if you were lucky enough to live to 65 in the US, you were (on average) going to live to 80 years old, rich or poor. No longer is that true—wealth extends life by 6 years.

RELIGIOUS BELIEFS
The US is the most religious of all industrialized countries; it's also the epicenter of medical research. Religious beliefs slow the adoption of assisted reproductive technology (ART), and will repel the adoption of epigenetic editing, though it was in stem cell research that religious beliefs hit the brakes the hardest. The outlier here is end-of-life care; surprisingly, the more religious patients are, the more likely their families are to choose very expensive end-of-life procedures. Hospice care is the preferred option for less religious and nonreligious people.

Healthcare will not just be altered by the proliferation of new medical technologies coming up from research labs. Change will also be driven by exponential growth in computing technologies, as well as long-term sociodemographic trends.

THE NEW MEDICAL TECHNOLOGIES

IMMUNOTHERAPY
Cancer cells avoid detection by our immune systems by camouflaging themselves. Immunotherapy unmasks the cancer cells so that our body can naturally attack them.

OPTOGENETICS
Literally shining a light into the brain, to alter the neural oscillation of brainwaves or take control of neuronal firing. This will be used on Alzheimer's, where it upregulates microglia cells that clean up plaques. It also will be used to take control of pain, and in mental health applications.

BIOELECTRONIC MEDICINE
Implanting microchips that stimulate the nervous system with current, whether to bypass failed motor neurons or to trigger the natural drugs the body needs to heal itself.

NANOMEDICINE
Bottom-up assembly of machines that can perform actions at the cellular level. For instance, delivering chemotherapy payloads directly into cancer cells (and only to cancer cells).

ARTIFICIAL INTELLIGENCE
Computational learning of hidden patterns over vast datasets of genetic libraries, patient records and medical images. AI is already being used to find biomarkers, diagnose diseases and monitor patients' vital signs to send them alerts before symptoms appear.

ROBOTICS
Miniaturization of robotic instruments will aid in highly complicated or repetitive surgeries, while replacing humans in data-driven procedures like radiology and anesthesiology. Robots will not lead to massive layoffs, but we will need fewer people in healthcare over time, as is the case in almost every industry. At hospitals, robots can clean rooms, transport patients, pick up laundry and deliver medicine.

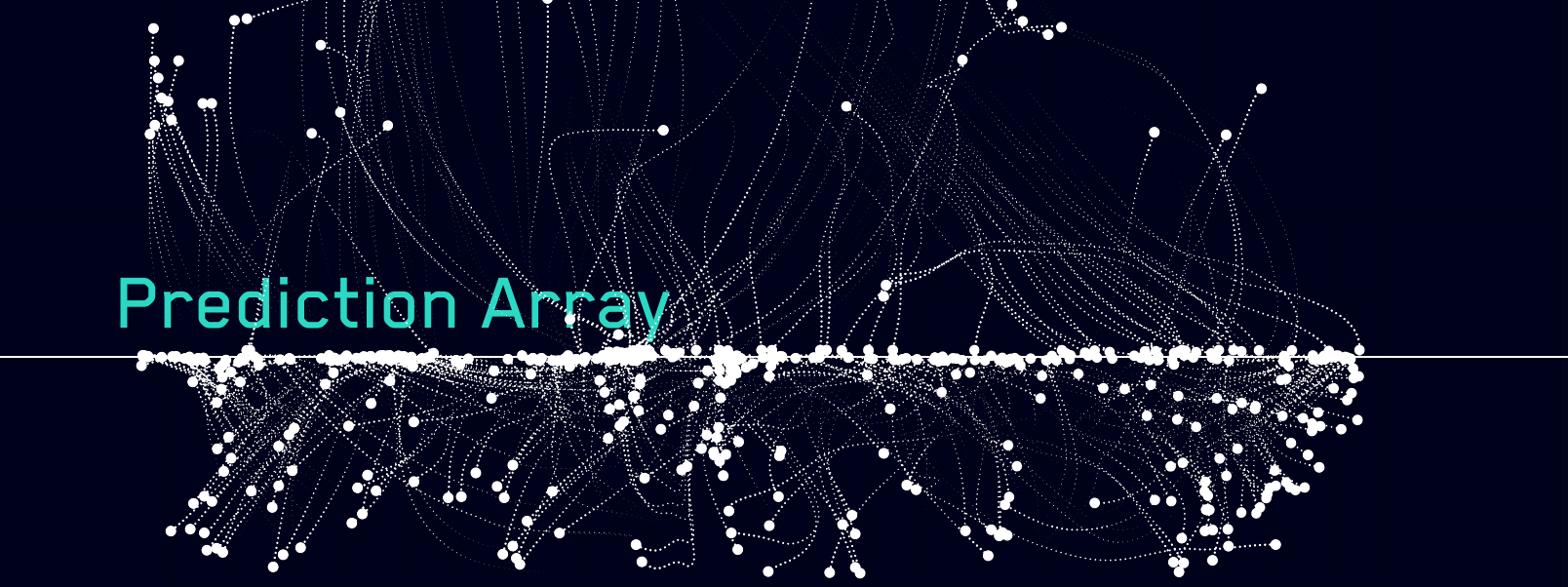
CRISPR
A gene editing tool that's cheap ($75), precise and fast becoming universal, CRISPR adopts the mechanism that bacteria use to recognize and attack viruses. It can be used on any organism, any species, plant or animal.

EPIGENETIC ENHANCEMENT
Gene-expression editing doesn't change the underlying genetic code, and doesn't introduce code from other organisms. Rather, it just tweaks how a gene gets expressed. Because of this difference, epigenetics is likely to be the vector by which gene editing for enhancement reasons (not medical necessity) becomes socially acceptable.

STEM CELL REACTIVATION
Rather than injecting new stem cells, these methods hack the signaling that causes our existing stem cells to slow down with age. The effect is to wake up our aged stem cells to function like young stem cells, repairing and regenerating the body.

TRIAL-IN-A-DISH
You can grow your own brain in a dish. You can grow 100 of them, in fact, and test out medicines to see which works best. Individual drugs can be tried against a patient's own neurons or heart muscle cells to look for efficacy before prescribing. This could drastically reduce side effects and the guessing game that doctors must play when prescribing chemotherapy and antipsychotics.

PAIN BLOCKERS
One in five adults lives with chronic pain. Pain signals travel along nerves' Nav 1.7 sodium channel. No less than nine channel blockers are in development, with three already in clinical trials. The potential to decrease pain more radically, without the side effects of opioids, could rescue a huge portion of the population from debilitation.



Prediction Array

THE FUTURE IS NOW

01

100,000 Parkinson's patients have **deep-brain stimulators** implanted in the chest and wired to the brain to manage symptoms.

02

Hospitals' first experience with **AI** is not on the clinical side—it's AI that helps you run your hospital better, through resource management and labor optimization.

03

"**Previvors**," those with high-risk genetics for serious medical conditions, are organizing into powerful consumer advocate groups.

04

Clinical trials using **CRISPR** to release the brakes on the immune response have begun in China for aggressive lung and esophageal cancers.

05

Kaiser has already started its own **school of medicine**, rather than outsourcing physician development to universities.

06

Value-based care is already here through the Shared Savings incentives. In Buffalo, the Catholic Health ACO saved $28 million, receiving a reward of $14 million—the third largest amount among all first-year programs.

5 YEARS

01

Full genomic testing of IVF embryos will allow parents to select the embryo with the lowest risk factors for future disease.

02

The FDA will consider a **drug's price** in its approval process, allowing drug competition and price competition.

03

Hospital networks will have huge, centralized command centers for **remote monitoring of patients**, whether those patients are in a network hospital or at home.

04

Checkpoint inhibitor immunotherapies will **replace chemotherapy** as the first-line intervention for half of cancers.

05

Over one-third of all surgeries will be performed with robotic assistance. Fully autonomous **robotic surgical platforms** prove their effectiveness and are (slowly) adopted.

06

AR headsets and screens will replace medical charts, which will be too thick with data to be scanned linearly. **Automated medical records** using natural language processing will cut data entry time 4×.

07

Driverless cars will reduce accident rates by 90%, eliminating over 2.25 million visits to emergency rooms each year.

10 YEARS

01

Virtual reality headsets for Alzheimer's patients will be used daily to stave off the disease. Light therapy at gamma rhythm reawakens the brain's natural immune cells that attack and clear amyloid beta.

02

Parabiosis injections of blood plasma taken from healthy young people will prolong the period of our lives where most of us stay fairly disease free. For those who can afford it, 80 will be the new 50.

03

Computational pre-optimization of patient **biomarkers** will improve the odds of a new drug's approval by 3× and reduce development cost 10×.

04

By clearing the body of **senescent cells** and their toxic signals, stem cells in 40-year-old knees will again grow cartilage.

05

Back surgery—currently driving 7% of operating room budgets—will be far less common, replaced by everything from powered exoskeletons to stem cell activation to reverse osteoporosis.

20 YEARS

01

Programmable flu "shot" will mean an end to the yearly needle, using robotic nanospheres which can change shape and prime the host immune system.

02

Nanoparticle swimmers guided by magnets will clear arterial plaques.

03

Open-source Electronic Health Records (EHRs) will reach 90% market share, displacing closed systems. But it won't be a single open-source system; there will be many of them.

04

Transplants of organs from anybody will be possible by using CRISPR to tweak the immune receptors that identify transplanted organs as foreign.

05

Medicine looks more like construction, with general contractors (doctors) managing different teams (subcontractors) with the help of checklists, protocols, AI, etc.

Editors' Letter

WITH MORE THAN A CENTURY of combined experience at the frontiers of technology, business and science, our team of researchers, editors, doctors and designers set out to explore future scenarios in what we consider the most fascinating, important, complex and, ultimately, personal topic there is: medicine.

Our goal for this project is more practical than simply unveiling startling scenarios from the next twenty years. By highlighting the emergent forces that will precipitate the changes illustrated here, we hope to give our readers a framework and a set of tools that will help them team up with one another to build bridges—bridges connecting today's dynamic and uncertain reality to some of the massively beneficial future states laid out here. But first, and just as importantly, we hope the report will serve as the catalyst to spark the initial conversations that give rise to those bridge-building collaborations.

One of the initial mysteries we encountered: with so many of the world's best minds hard at work developing technologies and practices to improve healthcare, why should the industry lag behind others in taking advantage of the breakthroughs currently fueling progress in so many other industries? The answer, as most healthcare practitioners and entrepreneurs can attest, is that regulatory policy, insurance economics and many other unique factors make innovation more difficult in medicine than in any other field.

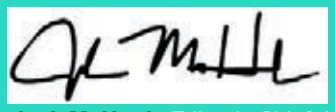
As we compared notes over months of interviews, conferences and research, the surprises came frequently. The common theme was speed: how quickly ordinary people are embracing the concept of genetic engineering; the acceleration of machine learning's role in diagnostics; the rapidly changing job outlook for the medical practitioner workforce; the speed and diversity of medical innovation happening in developing areas around the world.

Among the most profound realizations that occurred to our team: at the same time as advanced imaging technology gives us an increasingly clear picture of our present physiological status, the convergent trio of genomics, big data and predictive analytics gives us an increasingly clear line of sight into both our biological past and future. When coupled with advanced technology, DNA turns out to be that most elusive of science fiction plot devices: a working time-travel mechanism.

HOW TO USE THIS REPORT

We've designed the Future of Medicine report to be useful and challenging whether you're dipping into it for quick insights or taking a deep dive. However, we'd recommend starting with the Forces of Change (p. 4), which lays out the technological and social currents we see shaping the future landscape. Then, to get an idea of our methodology, read on to Prediction Array (p. 8) for a set of example scenarios and a description of how our team goes about probing the future. After that, dive into the main sections of the report, letting your curiosity be your guide.

The final step: share and discuss the report. Our hope is that the ensuing conversation and debate will serve to help the industry's leaders navigate past the obstacles presented by our rapidly changing environment and create a future that improves lives around the world.



Josh McHugh, Editor in Chief, Attention Span FWD Group

Po Bronson, Senior Editor, Attention Span FWD Group

Chris Cowart, Executive Editor, Attention Span FWD Group

ATTENTION SPAN
FWD GROUP

JOSH McHUGH
EDITOR IN CHIEF

Josh's career began at **Forbes**, where he opened the magazine's Silicon Valley bureau. Next stop: contributing editor at **Wired**, with assignments for **Vanity Fair**, **Outside** and others. His journalistic work includes first-person accounts of stints as a test subject in a NASA hyper-gravity experiment and in a clinical paleolithic diet study, and a six-month attempt to dunk a basketball. The CEO of Attention Span, Josh holds a BA in English from Yale.

PO BRONSON
SENIOR EDITOR

Po is the author of seven books, most recently **The New York Times** bestseller **Top Dog: The Science of Winning and Losing**, which has become mandatory reading at many professional sports franchises and USA Olympics programs. His science journalism has won nine national awards, and he has been cited in over 100 academic journals and over 300 books.

CHRIS COWART
EXECUTIVE EDITOR

Chris Cowart is a futurist, designer and business innovator, and an investor at Montage Ventures. While at IDEO for 14 years, he won numerous design awards and patents, and led the Health & Wellness practice and the Palo Alto location. One project highlight was the image-guided neurosurgical platform he developed with Medtronic. He serves as design and innovation faculty at Singularity University in Silicon Valley.

The Future of Medicine Team

ETHAN WATTERS
CONTRIBUTING EDITOR

Ethan is a journalist who has spent the last two decades writing about culture and psychology. He is the author of **Crazy Like Us: The Globalization of the American Psyche** and **Urban Tribes: A Generation Redefines Friendship, Family, and Commitment**. His writing has appeared in **The New York Times Magazine**, **Outside**, **Discover**, **Men's Journal** and **Wired**, among other national publications.

PATRICK HOUSE, PhD
SCIENCE EDITOR

Patrick has a PhD in neuroscience from Stanford University and writes on science, technology and culture for publications such as **The New Yorker** online and **Slate**. His scientific research has been featured by **The New York Times**, **National Geographic** and **Radiolab**, among other outlets. He is working on a book on the role of elegance in neuroscience, to be published in 2019. He lives in San Francisco.

JOSHUA SPANOGLE, MD
CONTRIBUTING EDITOR

Joshua is a practicing dermatologic surgeon and author. His bestselling thrillers (**Isolation Ward** and **Flawless**) have earned comparisons to Michael Crichton and Scott Turow. He holds degrees from Yale and Stanford Medical School.

NATALIE JONES
RESEARCH EDITOR

Natalie is a reporter based in Oakland, California. She loves to work with sound, write prose and dig up facts. When not doing those things, she consumes a lot of media and spends loads of time outside. Some favorite topics to cover are health, agriculture, food and the environment. She has reported for NPR, KQED, KALW, **Grist** and **Civil Eats**.

TYSON LAW
CREATIVE DIRECTOR

Tyson is the design director for Attention Span's FWD Group. He received his master's in Architecture from the University of Pennsylvania School of Design, where he studied design, fabrication and visualization. Ty specializes in user experience design and architectural environments. He received his BS in Electronic Arts from Rensselaer Polytechnic Institute.

SHAWN ROBERTSON
SENIOR ART DIRECTOR

Shawn is a San Francisco Bay Area–based senior art director and designer. She studied at California College of the Arts, San Diego State University and UCLA, and her background is in design, art, textiles, theater and women's studies. She has worked for world-class advertising agencies and design clients on accounts that range from cars to food, and fashion to tech.

LARRY HABEGGER
EDITORIAL PRODUCER

Larry Habegger is cofounder and executive editor of Travelers' Tales, where he has worked on all of the company's 140-plus books and helps oversee their publishing program. He writes mainly about world travel, and is cofounder of The Prose Doctors, an editors consortium. He holds a BA in English from Dartmouth.

SUZEE BARRABEE
PRINT PRODUCER

Suzee Barrabee is an art and print producer who has spent most of her career working in advertising on a range of accounts such as Nike, Chevrolet, Facebook, Comcast and the NBA. She has had the pleasure of working with such diverse talent as Britney Spears and an alligator.

ETHAN FLETCHER
DESIGNER

Ethan is an interdisciplinary designer and programmer at Attention Span who specializes in web, graphic and game design. He received his BS in Emerging Media from Ithaca College, where he also minored in and studied game development, web development and computer science. Ethan also spent a number of years studying and developing informal foreign language acquisition tools and techniques in the form of a purposeful video game.

ALLI STREETER
DESIGNER

Alli is a graphic designer for Attention Span. She studied Interior Design at Syracuse University College of Visual and Performing Arts before receiving a Graphic Design BFA from Massachusetts College of Art and Design. Alli specializes in typographic/layout design, but also enjoys pattern design and constructing unique products by hand.

LONG ELLIS II
PROJECT MANAGER

Long leads business development for Attention Span's FWD Group, which specializes in research, content creation and consulting to propel organizations to the forefront of innovation. Long started his career in entertainment in Los Angeles, first at the agency International Creative Management, followed by the production company Good Universe in Beverly Hills. He received his BA in History from Princeton.

SPECIAL THANKS

Jeremy M. Jacobs; Bruce K. Moskowitz, MD; Satish Tripathi, PhD; Kenneth Snyder, MD; Jody Lomeo; Candace Johnson, PhD; Thomas Lombardo, MD; Matt Enstice; Joe McDonald; Kenneth Pearsen, MD; James Kelly; Dan Zimmer; Todd Merry; Katie Gorman; Bill Gresser; Bill Maggio; Will Kushner; Kenneth Trauner, MD; Sandeep Giri; Jim Robinson and Raju Rishi; Luke Bonney and Niko Skievaski; Sean Lane; Jessica Mega, MD; Karen Horgan; Daniel Burnett, MD; Joon Yun, MD; Arvind Gupta; Mudit Garg; David Maltz; Sumbul Desai, MD; Eliot Lazar, MD; Arthur Reingold, MD; Julie Parsonnet, MD; Andrea Cheville, MD; Malay Gandhi; Bradley Thomas; Christopher Zachary, MBBS; Andrew Blau; Jonathan Mindes; FutureDeluxe; Scripps Translational Science Institute; San Francisco Writers' Grotto.

The healthcare industry is vastly underestimating the ripple effects of virtual medicine. Remember record stores?

Virtual Destruction

Just as ATMs, then online banking, drastically reduced the need to walk into banks, online health means far fewer people need to come to doctors in person to be cared for by them. The extent of structural disruption this will bring is being vastly underestimated.

When you're sick, the last thing you want to have to do is wait for an appointment, then wait for your labs, then wait for your results, only to wait for another appointment. The imminent future of hospital systems is already here.

» State line regulations on telemedicine are being obliterated. **18 states have agreed to the Interstate Medical Licensure Compact**, and a dozen more are in the process of approving.

» The Johns Hopkins Hospital monitors patients in its network through a **22-screen command center**.

» Montefiore Health System opened a **12-story ambulatory surgical center—with no hospital beds**.

» **Virtual consultations** at Kaiser—whether by phone, email or video—**are fully half of all interactions** between a health professional and a patient.

» The CDC's free **Text4baby—an advice-giving app for expectant and new mothers—has been used by over a million subscribers**.

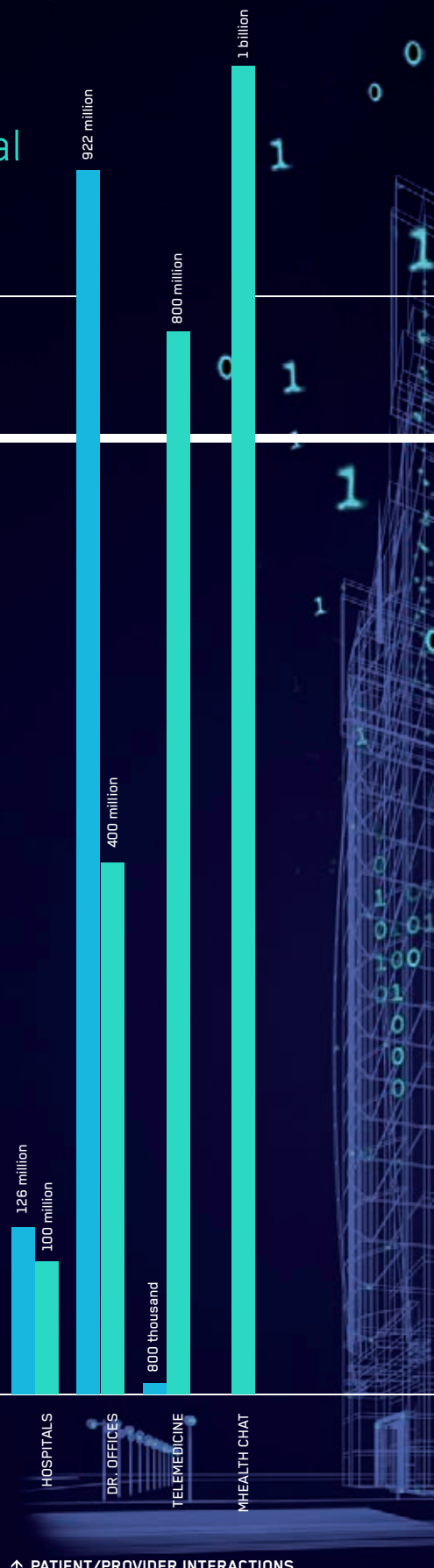
» At Kaiser's Oakland medical center, **algorithms ping nurses' phones when a baby is showing abnormal biometrics**.

» In Japan, Amazon is already doing **same-day drug delivery** to your home or office.

TODAY
88% of doctor consultations are **not** at a hospital.

IN 7 YEARS
We'll see a 1000× increase in telemedicine, but even that phenomenon will be surpassed by health chat.

	TODAY	IN 7 YEARS
Number one reason to visit a doctor in person:	COUGH	PRENATAL EXAM
Most common diagnosis:	HYPERTENSION/BLOOD PRESSURE	PRE-DIABETES
PREVENTIVE CARE	20%	20%
NEW PROBLEM	33%	15%
CHRONIC PROBLEM	31%	56%
FLARE-UP	8%	5%
PRE- OR POST-SURGERY	7%	4%
LAB TESTS DONE	13 BILLION	30 BILLION



INSTANT-ACCESS MEDICINE WILL HELP WIN THE WAR OF TRUST

Getting healthcare will be radically faster. Whether by online chat or telemedicine, you'll be able to consult with physicians in minutes, not days. Faster lab testing, and even home lab testing with lab-on-a-chip technology, can lead to a diagnosis in under an hour. In some cases, constant-monitoring sensors will detect you're getting ill—even before you feel any symptoms. Together, these create Instant-Access Medicine, eliminating the pervasive waiting game that drives costs up and allows ailments to go untreated.

WHAT PATIENTS WAIT FOR

01

WAIT to see if it goes away on its own.

02

If it doesn't, **WAIT** for an appointment.

03

WAIT for lab test results.

04

WAIT for referral to specialist.

05

WAIT for appointment with specialist.

06

WAIT for more test or scan results.

07

Once treatment begins, **WAIT** to heal.

Every time patients have to wait, they feel powerless and lack agency. Frustrated, they take to the internet to Google their symptoms and remedies. Quickly, they're directed to a $51 billion netherworld where they read that medical science is corrupt, the pharmaceutical industry spreads propaganda and the FDA suppresses the truth about alternative herbal remedies. Why wait, the internet beckons, when you can order online now? Or visit your local naturopathy shop, no prescription needed. Desperate for a remedy, patients think, Well, it's natural, I might as well try it. The worst part is that 70% of patients who use herbal medicines don't tell their physician they're doing so, largely because the patients fear being told to stop. Systematically, this breeds a lack of faith in scientific medicine.

Instant-Access Medicine will help restore trust in the system, simply by eliminating these vulnerable waiting phases. Patients will feel more empowered to get consultations and results and interventions at a pace they control.

"We won't be having patients come into offices. A layer of healthcare will emerge that's a lot like interacting with Amazon. Whether or not a human is on the other side won't matter. Drugs will be shipped to you by Uber." **—Josh Makower, New Enterprise Associates**

← RECENT HISTORY

Two big trends have altered the healthcare landscape over the last decade:

HOSPITALS BUYING PRIVATE PRACTICES

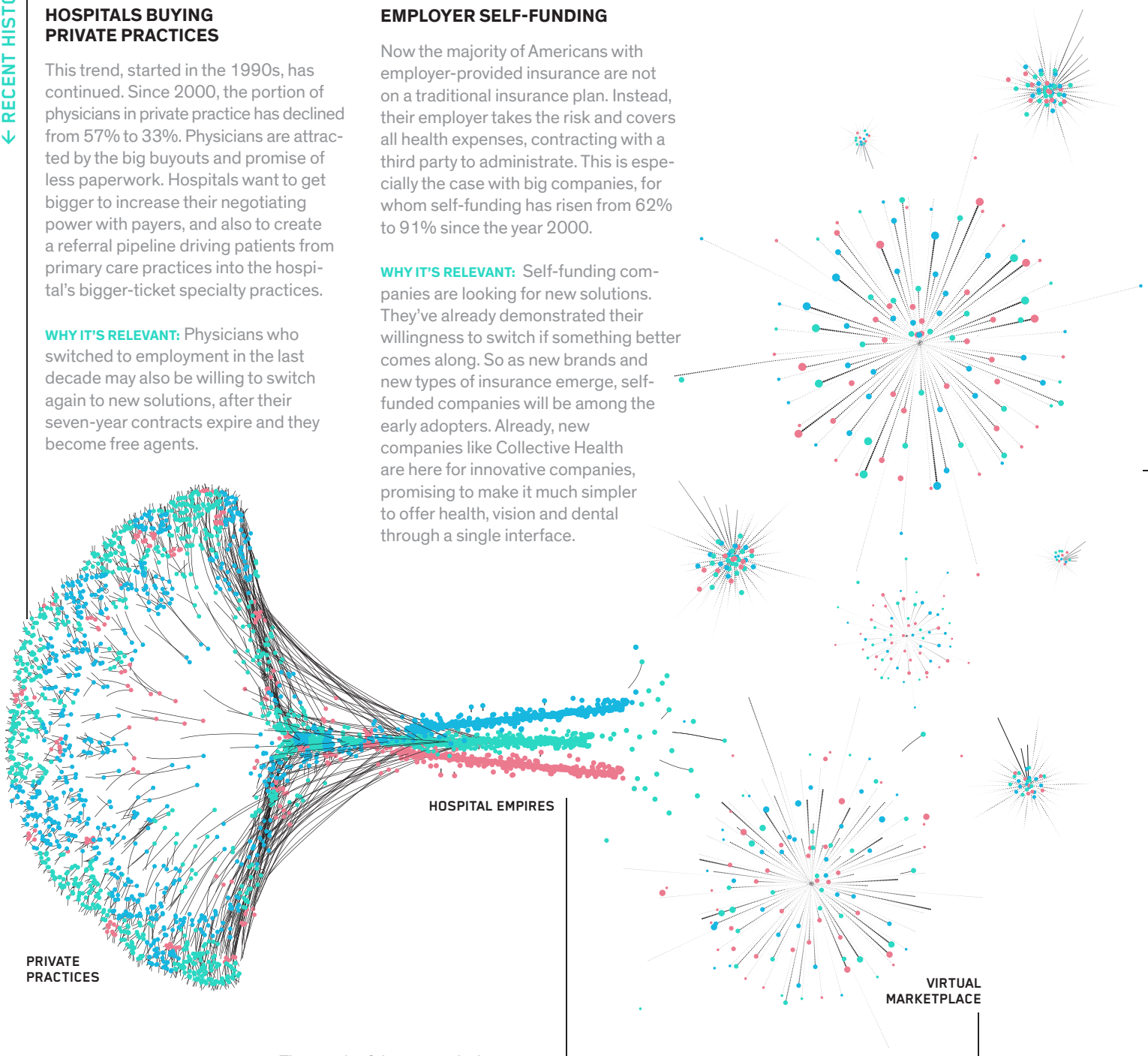
This trend, started in the 1990s, has continued. Since 2000, the portion of physicians in private practice has declined from 57% to 33%. Physicians are attracted by the big buyouts and promise of less paperwork. Hospitals want to get bigger to increase their negotiating power with payers, and also to create a referral pipeline driving patients from primary care practices into the hospital's bigger-ticket specialty practices.

WHY IT'S RELEVANT: Physicians who switched to employment in the last decade may also be willing to switch again to new solutions, after their seven-year contracts expire and they become free agents.

EMPLOYER SELF-FUNDING

Now the majority of Americans with employer-provided insurance are not on a traditional insurance plan. Instead, their employer takes the risk and covers all health expenses, contracting with a third party to administrate. This is especially the case with big companies, for whom self-funding has risen from 62% to 91% since the year 2000.

WHY IT'S RELEVANT: Self-funding companies are looking for new solutions. They've already demonstrated their willingness to switch if something better comes along. So as new brands and new types of insurance emerge, self-funded companies will be among the early adopters. Already, new companies like Collective Health are here for innovative companies, promising to make it much simpler to offer health, vision and dental through a single interface.



TODAY →

The result of these trends, however, is that in most major cities, there are four to eight vertically integrated empires that are essentially doing the same thing: competing with each other at every level, from primary care through specializations. The differences between them are not clear to consumers. They all promise similar services and features. They all claim to be the best place to be if you have a stroke, have cancer or have a baby.

THE NEXT TEN YEARS →

The next decade will see this orderly vertical integration disrupted as healthcare migrates to **virtual medicine**.

There will be two main strategies to capitalize on the drastic change—get bigger, or get more agile.

The Benefit of Being Bigger

Once you have virtual medicine practices and patient flows figured out, it's very easy to scale up, because that front end of the business is highly digital. While it's not quite Netflix, which could go live in 130 new countries on the same day, or Uber, which could launch in 22 countries in the same year, the scalability of digital systems is remarkable. So if your virtual medicine practice works for 500,000 patients, it'll work for 5 million.

The organizations that get a leg up on virtual medicine will be in a great position to acquire the laggards. M&A activity will increase significantly, and then skyrocket as interoperability improves. Right now, consolidation continues despite the fact that the lack of interoperability creates enormous friction for acquisitions. Similarly, the health networks that get significant efficiencies out of their artificial intelligence, whether it's their own system or that of an AI specialist like Qventus, will be buyers.

NONPROFITS IN PERIL

The traditional advantages of a nonprofit—borrowing at a lower rate, not having to pay taxes—will deteriorate as credit agencies continue to downgrade the outlook on community health nonprofits in the face of so much change. Around the country, the trend of taking on private equity partners will pick up steam. Ten years from now, when these equity partners can cash out, a wave of hospital exits will pronounce the verdict on who really added value and who has to conduct a fire sale.

"I think we will have a few mega-brands, like Johns Hopkins and Mayo, across many states and internationally. Other brands will be successful by focusing on their specialty expertise, such as cancer care. It will be a mistake to confine any healthcare organization to just the US market." **—Geoffrey Clapp, healthcare entrepreneur and advisor**

The Benefit of Being Agile

Agile organizations gain an advantage with every policy change or technological change, because they can respond faster and more fully. Some vertically integrated organizations will decide to pivot, selling their primary care networks and some specialist practices to focus on a specialty market and really deliver superior care. But the majority of agile organizations will be new entrants with digital-age DNA. Soon the landscape will be populated with all manner of hybrids:

01

DISEASE-MONITORING CARE MANAGEMENT COMPANIES

Already, new companies like Virta Health promise to reverse diabetes and insulin dependency. Using biomonitoring and constant feedback, supplemented by virtual medicine, these disease-specific companies could prove to be payers' best recommendation to many patients—a win-win for everyone except the hospital networks that no longer regularly treat those patients.

02

CONSUMER SHOPPING ENGINES

New companies like Stride Health inform consumers in new ways, bringing clarity to the look-alike brands in insurance and healthcare. They run forecasts for patients over the long term to help them make more personal decisions.

03

INSURANCE × PROVIDER MASHUPS

Oscar Health targets millennials, offering not just insurance, but some front-end services: fitness trackers, unlimited telemedicine and generic drugs without referral—all with a friendly new face that feels very different from the Blues.

04

DISINTERMEDIATORS

While the back end of care delivery may be the same, the customer-facing front end will have many different "skins," each of which is optimally designed for a specific customer segment. Once in the system, their pathways of usage can be tailored. They'll send a patient to one hospital for this condition, but to another hospital for a different condition.

Don't be surprised if companies that succeed get bought by Silicon Valley giants. **The EHR industry lives in fear of a future where Amazon Web Services becomes the dominant hosting service.** But that may just be a first step. According to recent international surveys, one-third of people would bank with Facebook, Amazon and Google if those services were offered. They likely feel the same about their health services. While Google has invested in clinical data diagnosis and longevity research, Amazon is already hiring to deliver healthcare programs—incubating the project for Amazon employees, then opening parts up to the world. **Apple is also making a big push into healthcare with its HealthKit, ResearchKit and CareKit software frameworks, and recently hired telemedicine superstar Sumbul Desai away from Stanford.**

"You've gotta be able to hunt. You should eat what you kill. Train your own workforce to do it your way. I have to compete with Walmart, where even Medicaid patients are happy to pay $30 in cash out of pocket." **—Dr. Raul Vazquez, Greater Buffalo United Accountable Healthcare Network, New York State's first ACO for Medicaid patients**

Once we know what diseases we're likely to get, what can we do about it? Band together into previvor communities—and push for cures.

Previvors

In the past, disease was a crapshoot. Few of us knew with a high degree of certainty that a specific serious medical condition was in our future, much less when the disease would strike. This will soon change. Thanks to the artificial intelligence and machine learning revolution, most of us will become "previvors"—that is, **we will know which of the 10,000 known human diseases are in our future long before we develop symptoms**. Over the next decade those predictions will become both more accurate and more foresighted—increasing the time we have to effect change and seek professional help.

The impact of previvors on the medical field can already be seen in the communities of those with the BRCA1 and BRCA2 mutations and among healthy individuals carrying the HIV virus. Both of these groups coalesced into large consumer-activist organizations advocating for novel treatments and compelling regulatory agencies to speed adoption of promising drugs and interventions. Unfortunately, medicine's ability to forecast diseases often outpaces breakthroughs for effective interventions and cures. Facilitated by social media, connected groups of previvors will band together to share peer-to-peer information—some valuable, some junk science.

As future research illuminates clear genetic connections between certain genes and illnesses, an increasing number of people will become previvors. For the first time, the FDA recently approved direct-to-consumer genetic test kits that will reveal risk markers for different diseases. As such consumer test kits become popular and increasingly accurate, the medical world should expect a flood of new patients worried about diseases they don't yet have.

Testing for specific disease-related genes is only the beginning.

Machine learning and artificial intelligence are already making remarkable new advances in disease forecasting. Much of the data needed for advanced AI disease forecasting already exists. Researchers are harvesting petabytes of patient records and medical images. Adding to that mountain of data are the thousands of clinical trials and the tens of thousands of human genomes that have been partially or fully sequenced.

Researchers at Mount Sinai Hospital in New York recently used machine learning on a collection of 700,000 patient records and found they could outperform traditional ways of forecasting disease for a wide variety of conditions, including diabetes, schizophrenia and various cancers.

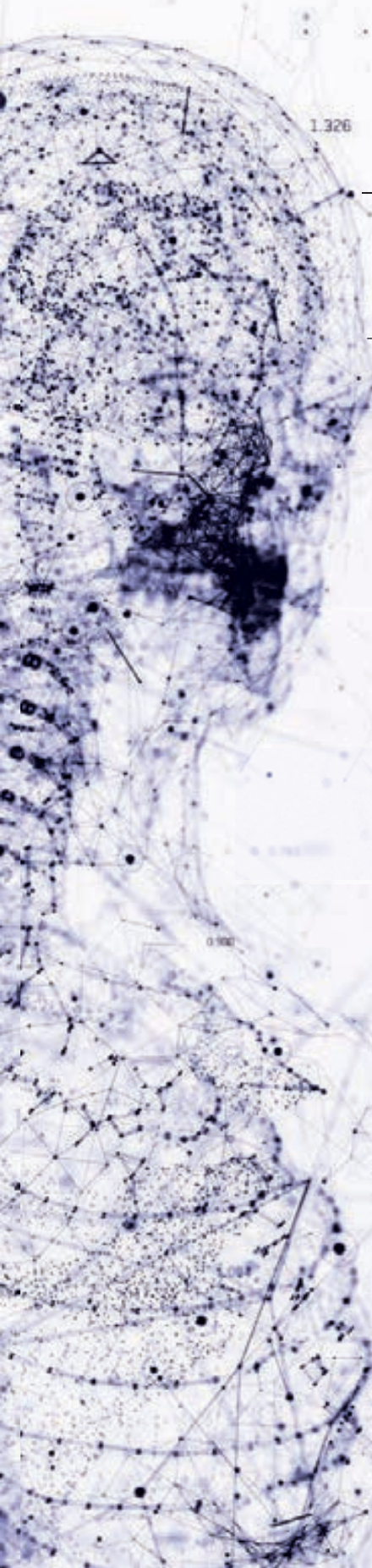
Currently half of men and two-thirds of women who die suddenly of coronary heart disease have no previous warning signs.

Using 200,000 patient records and new machine learning tools, researchers at Sutter Health in California were able to predict heart failure 9 months earlier than doctors using traditional methods.

University of California medical centers are currently using AI to harvest insights from over 13 million patient records.

ADVANTAGE: AI

50%	**MEN** Patients who die suddenly of coronary heart disease with no previous warning
66%	**WOMEN**
9 MONTHS	Machine learning edge over doctors in heart failure prediction



100%

Patient population that will present with 1+ previvor conditions within 20 years

CONDITION	CURRENT DIAGNOSIS AND TREATMENT	KEY PREVIVOR FUTURE MOMENTS	POSSIBLE PREVIVOR PREVENTIVE TREATMENTS
Breast cancer	BRCA1 and BRCA2 mutation. Breast removal.	AI algorithms will allow women to know with more certainty when or if breast removal is necessary.	Gene therapy using CRISPR will remove health threats encoded in BRCA genes and keep them from being passed to future generations.
Parkinson's disease	Disease diagnosed at onset of symptoms. Family history increases likelihood.	Our interactions with touch screens will pick up early signs of the condition.	Early deep-brain stimulation—either through wearable or implantable devices—will be employed at earliest signs of the condition.
Alzheimer's disease	No specific test exists to diagnose Alzheimer's. Family history increases likelihood. Low efficacy drug treatments.	AI algorithms analyzing polygenic risks and brain imaging will predict the disease in early adulthood.	Optogenetic stimulation of interneurons through implantable devices may decrease amyloid-beta production before symptoms appear.
Celiac disease	A blood test and intestinal biopsy can provide a diagnosis. Dietary changes.	Sensors in toothbrushes and toilets will monitor and predict all gut-related conditions.	A sensor and drug delivery device placed into the digestive tract meters out pneumococcal vaccine for ongoing treatment.
Type 2 diabetes	Prediabetes blood testing can give type 2 previvors a decade to make behavior changes.	Lifestyle, diet and blood monitoring through sensors and the internet of things will provide new data for doctors and patients.	Personalized diet designed for individual genome. Constant blood and metabolism monitoring.
Cardio-vascular disease	Diagnosis is attained through blood tests, X-rays and electrocardiograms—often after a dramatic heart event.	Implanted vascular flow bots and heart rhythm monitors warn of coming danger.	Patients check into hospitals before life-threatening cardiovascular events.

THE FUTURE IS NOW Previvors with high-risk genetics for serious medical conditions self-organize into powerful consumer advocacy groups

3–5 YEARS

80%

of most common conditions will have insurance-company mandated genetic screening

10 YEARS

95%

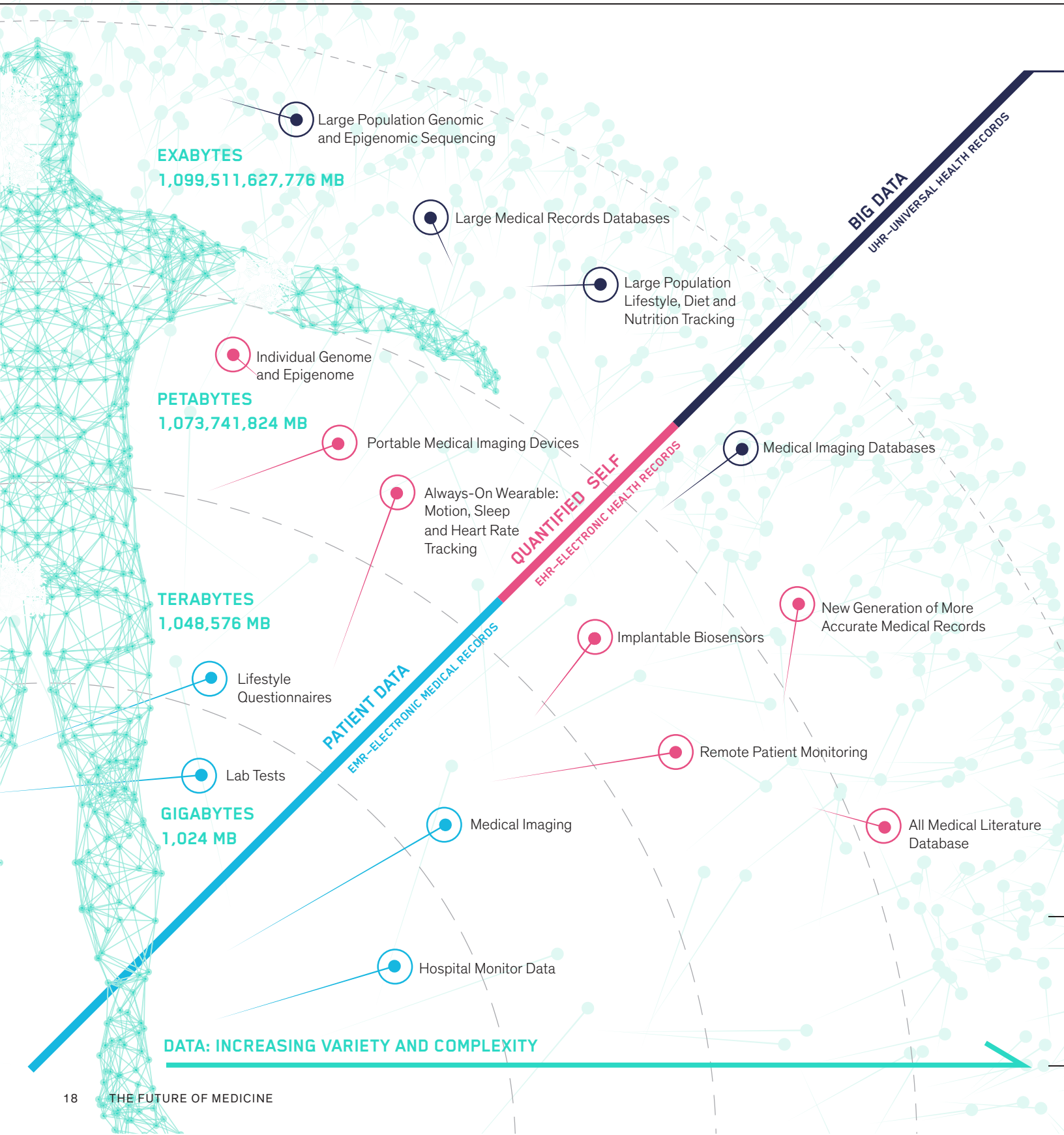
of conditions will be predictable from birth

20 YEARS

100%

We will detect and edit genes for adverse health conditions, then cure those conditions before birth

Forecasting Disease with Data



"Lots of diseases are preventable, but they happen so slowly that people get worse without realizing it. If we can use deep learning as a powerful tool to give patients a wake-up call, we'd be able to prevent diseases when there's still time."

—Professor Narges Razavian, New York University Langone School of Medicine

THE SOURCES OF DATA PUT TO USE BY AI WILL BOTH WIDEN AND DEEPEN OVER THE NEXT DECADE

The amount of data created by the human body is potentially limitless, and the collection of that data has already moved outside hospitals and doctors' offices.

Fitbits and watches that collect health information on sleep, activity and heart rate are just the beginning. Sophisticated mobile cardiac monitoring devices and implantable blood chemistry sensors will produce always-on patient data. Such devices will first be deployed on patients with serious illnesses, but eventually they will become so small, noninvasive and inexpensive that they will be used by everyone. Information will be instantly sent through our mobile devices to the cloud to be monitored on health dashboards at lifestyle-disease companies that send alerts to your doctor when diseases are forecast in your future.

As real-time data collection becomes widespread, new groups of previvors will emerge. Eventually, AI will be able to combine lifestyle and environmental data, genetic propensities and biometric tracking to forecast most major diseases sometimes years in advance.

These predictive diagnostics, real-time data and genomic analysis will combine to form a new data standard: the **Universal Health Record**.

BY THE TIME PATIENTS BEGIN SHOWING UP AT DOCTORS' OFFICES IN DRIVERLESS CARS (ANOTHER AI ADVANCE), MANY OF THEM WILL BE EXPECTING TREATMENTS FOR DISEASES THEY DON'T YET HAVE

This will likely lower healthcare costs, as fewer patients will present in acute condition, but will require a rethinking of treatment offerings. The promise of AI disease forecasting—particularly when it comes to diseases affected by lifestyle—is that the longer the patients have to change their behavior, the more chance they have of avoiding or deferring the illness.

As effective preventive interventions come online, more and more people will want to know their previvor status. Early detection will become an obsession. To avoid costly acute illnesses, wearing sensors and having blood labs done monthly won't just be covered by your insurance provider—it'll be mandatory.

Soon sensors—some just outside the body, some inside—won't just monitor the body, they'll actually intervene. Many people will be wearing some equivalent of an automatic insulin pump for their previvor condition. Already, over 100,000 Parkinson's patients have pulse generators implanted in their chests that are wired up to their brains to control tremors. In this way, medicine will be mimicking the body's own homeostatic systems, ever shortening the loop between imbalance, diagnosis and treatment.

BLACK BOX DIAGNOSIS

The long-term outlook for AI and previvorship is a little spooky. As AI machines mine more data, patients will learn that they are headed for certain diseases without any clear understanding of how the AI algorithm made that determination. This opacity is what technologists refer to as the "dark secret" of AI: the way it looks for patterns in data becomes so complicated that not even the computer scientists who design the algorithms can reverse engineer the patterns it ultimately recognizes.

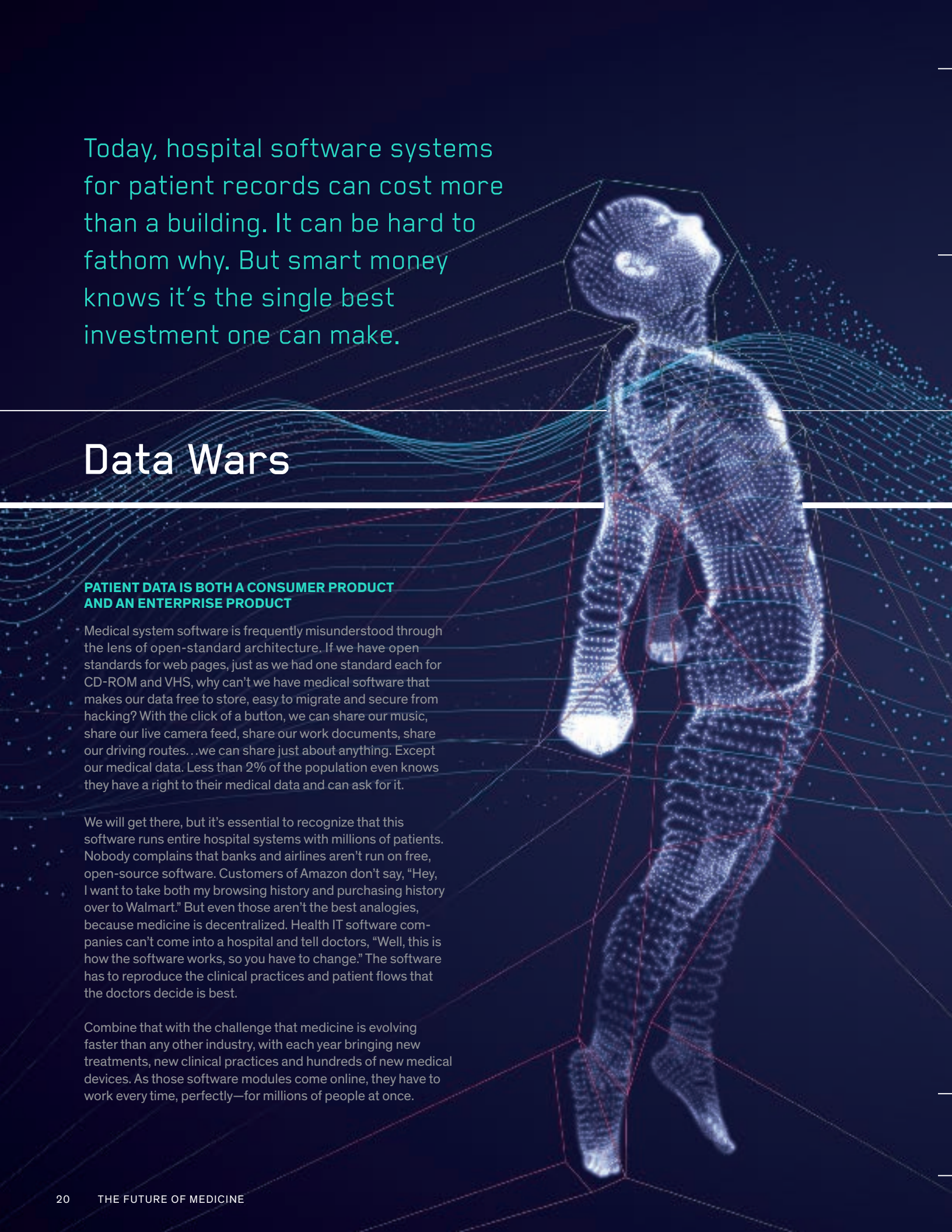
With life-and-death stakes, accuracy will outweigh our desire for human comprehension. A computer may one day tell us to expect a heart attack within the next year but not be able to tell us exactly how or why that prediction was made. "We can build these models," one researcher said, "but we don't know how they work."

"Whether it's an investment decision, a medical decision or maybe a military decision, you don't want to just rely on a 'black box' method. It is a problem that is already relevant, and it's going to be much more relevant in the future."

—Tommi Jaakkola, professor at MIT specializing in machine learning

Today, hospital software systems for patient records can cost more than a building. It can be hard to fathom why. But smart money knows it's the single best investment one can make.

Data Wars



PATIENT DATA IS BOTH A CONSUMER PRODUCT AND AN ENTERPRISE PRODUCT

Medical system software is frequently misunderstood through the lens of open-standard architecture. If we have open standards for web pages, just as we had one standard each for CD-ROM and VHS, why can't we have medical software that makes our data free to store, easy to migrate and secure from hacking? With the click of a button, we can share our music, share our live camera feed, share our work documents, share our driving routes. . .we can share just about anything. Except our medical data. Less than 2% of the population even knows they have a right to their medical data and can ask for it.

We will get there, but it's essential to recognize that this software runs entire hospital systems with millions of patients. Nobody complains that banks and airlines aren't run on free, open-source software. Customers of Amazon don't say, "Hey, I want to take both my browsing history and purchasing history over to Walmart." But even those aren't the best analogies, because medicine is decentralized. Health IT software companies can't come into a hospital and tell doctors, "Well, this is how the software works, so you have to change." The software has to reproduce the clinical practices and patient flows that the doctors decide is best.

Combine that with the challenge that medicine is evolving faster than any other industry, with each year bringing new treatments, new clinical practices and hundreds of new medical devices. As those software modules come online, they have to work every time, perfectly—for millions of people at once.

"I am a doctor. I have posted a sign over our fax machine that reads 'THE SOURCE OF ALL EVIL.' We're freakin' busy. My office struggles to get through a day not killing someone and getting everyone home at a reasonable hour. We respond to a lot of forms that must be filled out, signed and faxed back. Yes, we could do this electronically, but there exists no clear standard as to what constitutes a verifiable, secure, traceable signature that everyone recognizes." **—Posting to a physician message board**

HOW WE GOT HERE

Since 2009, the federal government has disbursed $30 billion in incentive payments to foster the transition to electronic medical records, but no open standard has been in place. 456,000 physicians received some sort of incentive payment. This incentive money inflated the value of contracts, allowing hospital systems to prioritize control of their data over the cost of the system.

Over 80% of the country moved to electronic records, but the data ended up in silos. HIPAA laws and anti-kick-back statutes also continue to prevent information exchanges.

During the same period, hospital consolidation continued. Mergers and buy-out deal flow never slowed, as hospitals felt they had to get bigger to survive. But this led to a Frankenstein of Electronic Health Record systems on the back end.

JUST HOW BAD IS IT?

01

245 different EHR systems are in use.

02

Doctors in community hospitals spend 44% of their time in front of a computer, compared to only 28% in direct patient care.

03

Stage 2 "Meaningful Use" data sharing requirements are so complex that only about 11% of physicians have been able to comply.

04

Even when different hospitals use the same EHR system, their versions are often so customized that only bare-bones data can be shared.

05

Faxing medical records from one medical office to another is still all too common. Ironically, it's easier.

MAKING IT EVEN MORE COMPLICATED...

Today's EHR for a single patient can be dozens of pages long, including everything from the times of nurse check-ins to lab results to scan images. **But tomorrow's EHR will be exponentially larger and the system infinitely more complex.**

245 different EHR systems is nothing compared to the 165,000 health apps for the smartphone that want to integrate sensor data into the medical record. There are over 7,000 medical device companies, and many of the gadgets they make now have sensors ready to communicate to the network.

These apps and devices provide continuous monitoring, so rather than lab results being taken once a year, they capture data minute by minute—even up to 100 times per second. Even if one could share this data stream, the tsunami of raw data would be effectively meaningless without the relevant number crunching and visualization tools.

THE AI FACTOR

Great examples of the power of machine learning on medical data are easy to find today. Dr. Atul Butte, director of the Institute for Computational Health Sciences at UCSF, employed AI on big public datasets to isolate a molecular treatment for small-cell lung cancer; Butte predicts computational optimization can bring drug development down from $1 billion to a mere $100,000, and from 10 years to 2 years. Many public datasets are being created: Harvard's Personal Genome Project, MHealth, Chicago Health Atlas and HealthData.gov are just a few among dozens of accessible libraries.

However, most live medical data in EHRs is decisively not AI-ready. It has to be extracted and standardized, which is laborious work. Machine learning can then scour the data to discover "hidden layers," i.e., patterns never seen before. But that intelligence can't then just turn around and run on the live EHR data, especially when it's looking for something extremely complex, such as a constellation of genes interacting with lifestyle factors. Even when EHRs do comply to a standard, that EHR architecture typically was not built from the ground up for AI optimization.

Anyone and everyone will promise artificial intelligence insight from data. But it's those who are already doing it, across millions of patients, on live data, who have the distinct advantage.

"Interoperability is the holy grail. The problem is that people have to get paid for it."
—Geoffrey Clapp, healthcare entrepreneur and advisor

"The danger is a foreign hack into an academic medical center which is a research site for a big pharmaceutical company. The hackers could make off not just with patient data, but with the pharma company's intellectual property. Pharma companies need to lean on hospitals to get their data into more secure cloud computing." **—John Hallock, Change Healthcare**

Security Problems

HACKER TYPOLOGY

HACKTIVISTS
Motivated by political or ideological revenge

SCRIPT KIDDIES
Unskilled programmers using malware tools like CryptoLocker they can buy online

CYBERCRIMINAL NETWORKS
Often put lots of script kiddies to work

NATION-STATES
Sometimes the stolen data never gets used, and never reappears. One prevailing theory is they're using the stolen data to model their own health systems.

- **2.3 million** Americans every year are victimized by medical identity theft, most often by someone using their identity to get prescription drugs or medical services
- **43%** of all identity thefts in the US were for fraudulent medical services
- On the darknet, stolen medical data fetches **10× the price** of stolen credit card data
- **81% of healthcare CIOs** admit their organization has been compromised by cyberattacks
- **Average % of budget** devoted to cybersecurity:
  – finance & banking: 12%
  – healthcare: 6%

ANATOMY OF A RANSOMWARE ATTACK

A cybercriminal network called Shadow Brokers steals hacking tools from the NSA, and releases them on the darknet to waves of script kiddies.

The NSA warns Microsoft that their operating system is at risk.

Microsoft releases a free patch to fix it in March of 2017—except those running old XP have to pay an expensive price.

The National Health Service in Britain, which uses XP and serves 50 million people, can't afford Microsoft's price.

May 2017: The "WannaCry" ransomware attack hits 104 countries, most notably the NHS of Britain. 48 health organizations have no access to testing equipment or patient information. Patients are sent home and surgeries postponed.

IS THE CLOUD SAFER?

Cloud systems are generally more secure, using redundancy and partitioning to limit the scale of any intrusions. However, cloud systems have been hacked, too. The weakest point of any data network is the human access. Even though data is encrypted, the decryption keys pass through a computer's RAM, and at that point they can be accessed.

The vulnerability of devices is so problematic, we will see a new branch of the FDA, responsible not for determining the effectiveness of a device, but for approving its security architecture.

ANONYMITY? UNLIKELY

Consumer data companies like LexisNexis Risk Solutions and Acxiom already have compiled thousands of data points on a majority of Americans. This data has been sold repeatedly, making it highly likely that medical data has been integrated with consumer behavior data.

SO WHAT'S THE ANSWER?

No system is entirely impenetrable. One solution: don't make data safe—make it not worth stealing. New security systems based on the blockchain are so hard to crack that it would take supercomputers years to unlock the stolen data. They use tumblers to disperse data into fragments, so a patient's medical record is not in one place. Companies like Blockchain Health and partnerships like MedRec (at MIT) are using blockchain on market segments like clinical research and pharmaceutical prescriptions to perfect their systems.

HAS THE BLOCKCHAIN BEEN HACKED?

Yes, Bitcoin cryptocurrency exchanges have been hacked. Twice. $118 million has been stolen. **If you're scared, you should be.**

How It Changes:
The Road from EHR to UHR—Universal Health Records

EHR companies are in a race to adapt to these new forces. Consolidation is inevitable around the EHRs that can deliver on these criteria:

01

WINNER-TAKE-ALL AI

The migration to value-based care will only make the software system more critical. Whichever EHR standard can deliver the greatest AI benefits, both by improving care and reducing costs, will gain market share rapidly. Current clinical practices and patient flows—meticulously coded into each hospital's custom EHRs—will suddenly be obsolete. Cloud technology and artificial intelligence will also drastically reduce switching costs. Laborious implementations won't be necessary: AI translators will learn and migrate data for you, with no staff involvement.

02

MIDDLEWARE BECOMES THE IOT ACCESS POINT

Most devices and health apps read and write to EHRs via middleware systems, which serve like translators. The better these translation methods become, the more they'll be favored as the standard to be built on for devices—because they can talk to different systems. Interoperability standards and medical device registries are essential for safety and security. It's bad to have your EHR hacked—but it's worse to have your pacemaker hacked.

03

OPEN ALLIANCES

Initiatives like CommonWell Alliance and the Sequoia Project are pushing EHRs to standardize. Open source systems exist but are not nearly as robust as Android and Linux. But don't expect a single standard to emerge. Smartphones can exchange texts and photos, but there are competing ecosystems, not one. Apple, by maintaining strict control, gets everything to work seamlessly. Even Google has taken more control of Android.

04

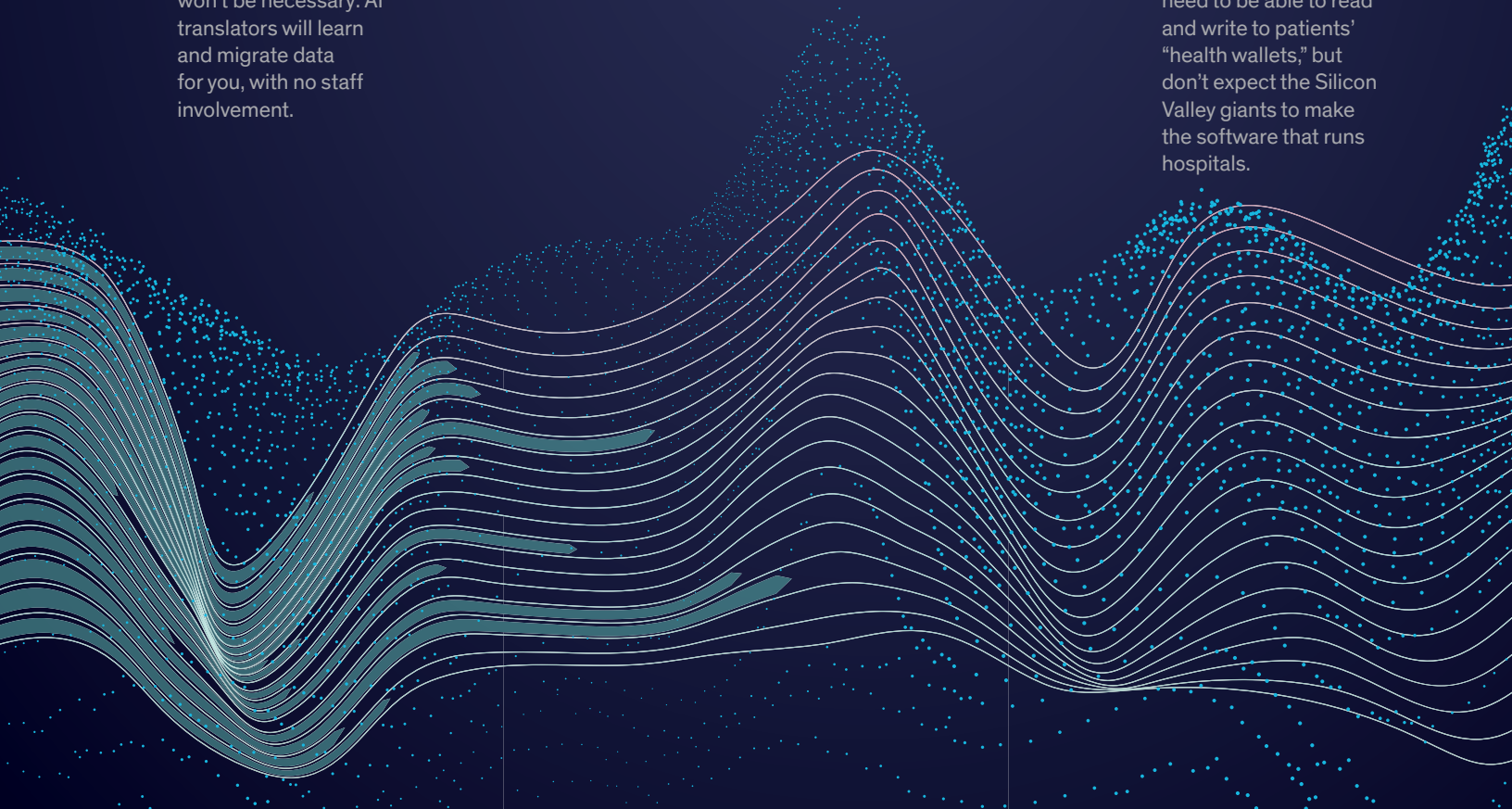
GLOBAL SCALABILITY

The fight to conquer the nation will inevitably shift to conquering the globe. Global scalability requires a system that can be rolled out successfully at drastically lower price points. Epic Systems' two lower-cost versions, Utility and Sonnet, are examples of how every EHR standard will need to make itself adaptable.

05

THE SILICON VALLEY GIANTS

Amazon, Google and Apple are all invading the healthcare space, and will continue to make acquisitions that help patients gradually take control of their own data and understand their own health choices. Upstarts who provide a path toward true interoperability, like CrossChx, makers of universal patient-ID software, will be likely targets. But these giants will be very careful not to make a misstep in the high-stakes healthcare arena that could potentially destroy their reputation. EHRs will need to be able to read and write to patients' "health wallets," but don't expect the Silicon Valley giants to make the software that runs hospitals.



When will the next pandemic hit? How will we monitor it and contain its spread? Will epidemics become more frequent and less deadly—or less frequent and more deadly?

The Pandemic Arms Race

By 2040, a combination of mega-cities, climate change, an increasing global population and high rates of travel will result in the first influenza-based major pandemic of the 21st century. This will galvanize political will and spur development of technology to accelerate vaccine production and distribution.

As the world's population lives longer, latent disease and disease of the aged or infirm will increase dramatically.

Globally, lifestyle diseases will reach pandemic levels.

NATO-LIKE FIRST RESPONDERS

As global epidemic response shifts away from policy and toward technological innovation and rapid, coordinated first response and delivery, the WHO will become increasingly irrelevant in the initial response stages. During recent global epidemics, for example, NGOs have taken more and more of a role in the first weeks and months because of their legal and social flexibility.

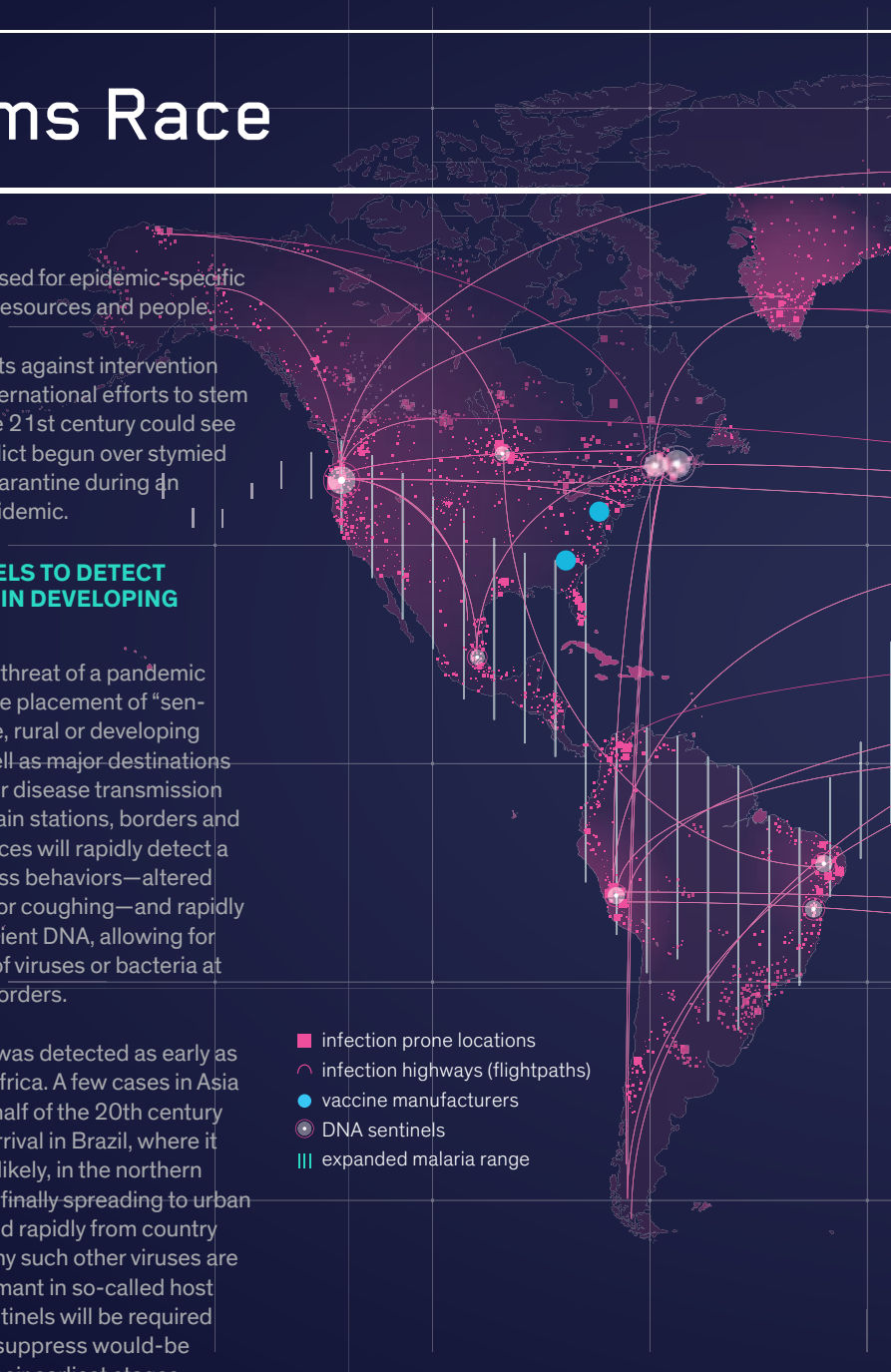
Eventually, a NATO-like organization for global health will need to be created, capable of coordinating basic prophylactic and anticipatory measures. Preparatory drills, coordination of supply chains and rapid intervention agreements could ensure readiness. Aging military or naval equipment, likely from the US or other developed countries, will be repurposed for epidemic-specific stockpiling of resources and people.

Sovereign rights against intervention will muddle international efforts to stem epidemics. The 21st century could see an armed conflict begun over stymied attempts at quarantine during an early-stage epidemic.

DNA SENTINELS TO DETECT OUTBREAKS IN DEVELOPING COUNTRIES

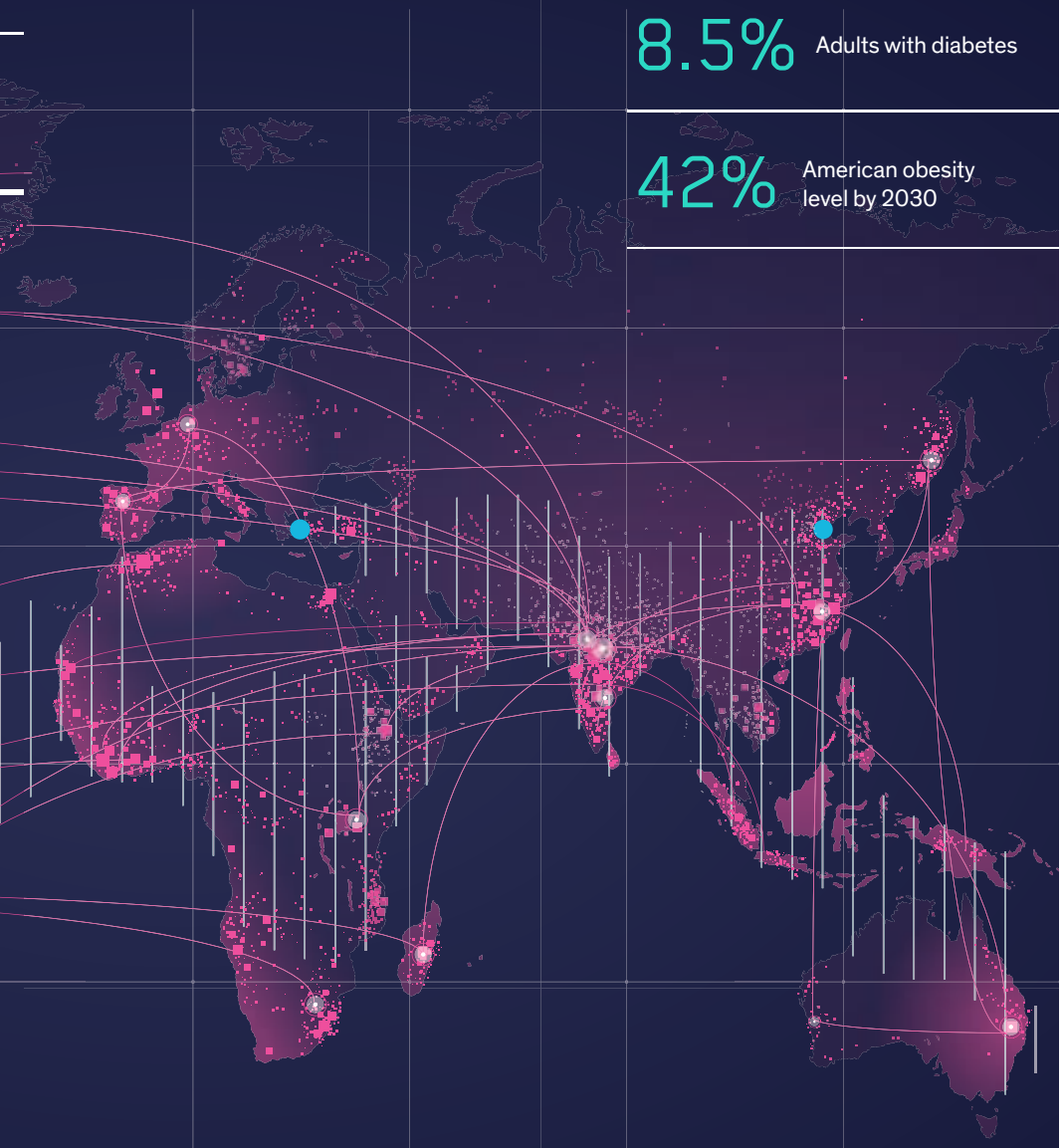
A pandemic or threat of a pandemic will mobilize the placement of "sentinels" in jungle, rural or developing hotspots as well as major destinations and settings for disease transmission like airports, train stations, borders and hospitals. Devices will rapidly detect a fever or sickness behaviors—altered gait, sneezing or coughing—and rapidly sequence ambient DNA, allowing for the detection of viruses or bacteria at international borders.

The Zika virus was detected as early as the 1940s in Africa. A few cases in Asia in the second half of the 20th century preceded its arrival in Brazil, where it then mutated, likely, in the northern jungles before finally spreading to urban populations and rapidly from country to country. Many such other viruses are likely lying dormant in so-called host reservoirs. Sentinels will be required to detect and suppress would-be epidemics in their earliest stages.



"We can do the job, if we have the resources." **—Dr. Margaret Chan, former director-general, World Health Organization**

"An epidemic is one of the few catastrophes that could set the world back drastically in the next few decades. By building a global warning and response system, we can prepare for it and prevent millions of deaths." **—Bill Gates**



8.5% Adults with diabetes

42% American obesity level by 2030

CLIMATE CHANGE WILL EXPAND DISEASE HOST RANGES

Based on climate change predictions, the host range of many disease-carrying mosquitoes and insects could extend to the US, afflicting poor, rural parts of many Southern and Gulf Coast states.

Changes in local ecologies, water temperature and host and vector availability, upon which many diseases depend, could imbalance microorganism competition, leading to unexpected blooms of disease. Species of Salmonella, for example, increase reproduction as temperatures rise within a range of 7°C–37°C. Increased temperatures may also have unintended benefits—the malaria parasite ceases development above 33°C.

LIFESTYLE DISEASE AVALANCHE

10 million people die of communicable diseases per year, 18% of total worldwide deaths. According to the WHO, diseases linked to lifestyle choices lead to the early deaths of an additional 16 million people per year.

8.5% of adults have diabetes.

Lifestyle diseases like diabetes, which kills 1.5 million per year and contributes to the deaths of another 2 million per year, and obesity, which contributes to the deaths of 2.8 million per year, will reach pandemic status.

By 2030, the CDC predicts that 42% of Americans will be obese and that 11% will be severely obese. Based on 2010 levels, such an increase would add an estimated $549.5 billion to total medical expenses.

Major grocers could begin targeting consumer diets personalized to genomes or offer disincentivization pricing for at-risk individuals, effectively taxing lifestyle disease.

Portable food scanners will allow people to test the composition of their food and track their diet using apps. With a concerted effort, the food industry could work with health technology companies to make poor diet the new smoking: inconvenient, costly and socially unacceptable. The alternative: obesity becomes the new normal, stalling or reversing the overall increase in life expectancy.

The FDA recently approved the first artificial pancreas, and closed-loop (fully automated) versions are in development. Combined with gamification of diet and health, digital contact lenses and implantable or biometric tattoos will help manage chronic conditions like diabetes.

Influenza Isn't Going Anywhere

"We simply need a better vaccine against influenza, one that works better and lasts longer."
—Dr. Thomas Frieden, former director, CDC

SEASONAL FLU

Only 43% of people get a seasonal flu shot. In a recent year, the CDC reported that only 56% of people who received the vaccine were protected.

Influenza kills half a million people and seriously sickens five million more every year. **Influenza was the leading cause of death in the US in 1900 and will be again by 2050 due to an aging population and vaccine ineffectiveness among the elderly.**

By 2050, because of an increasingly susceptible and longer-living elderly population, the economic impact of dealing with seasonal flu alone will grow from $87 billion (2016) to $500 billion per year.

A MUTATING ENEMY

Mutations in individual nucleotides accumulate in an influenza virus and lead to seasonal vaccine ineffectiveness. Influenza pandemics like those seen in 1957, 1968 and 2009—and like those to come—are due not to small, pointed mutations but instead to reassortments of the viral genome when two or more viruses combine to create a new subtype. This commonly occurs after passing from animal to animal or animal to human.

VACCINE DEVELOPMENT

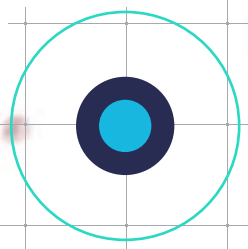
The pace of vaccine development will increase steadily as rapid sequencing technology interacts with the printing and on-demand and decentralized manufacturing of proteins. No longer will a few private companies manufacture and distribute vaccines. Instead, federal agencies will develop and send protein "blueprints" to global pharmacies for printing. This will greatly increase the pipeline speed from detection to inoculation and effectively eliminate the infrastructure problem of vaccine distribution. The problem of an individual's choice to not vaccinate will still remain.

One day, bioelectronic, immune-like cells will be able to hunt, cut up or otherwise target viruses. They will also be programmable. Vaccines will be simple software updates. No shots needed. Today, many major disease-causing viruses are either preventable, treatable or can be managed with chronic care. Vaccine technology is less than half the battle. Access to care remains the biggest hurdle for global treatment.

THE "PENICILLIN MOMENT" IN ANTIVIRAL RESEARCH

There were almost 100 million virus-associated deaths in the 20th century. More than half of all virus-related deaths in the 20th century were due to influenza and its variants.

For a few years, penicillin was a singular "silver bullet" against bacterial diseases. **In the future, a combination of surveillance and early outbreak detection, rapid vaccine development and immune system engineering could result in a post-virus world.** By the end of the 21st century, viruses will still exist, and people will still die from them, but not in nearly the numbers they did in the 20th century.



Bacteria Fight Back

"[The greatest risk] to human health comes in the form of antibiotic-resistant bacteria. We live in a bacterial world where we will never be able to stay ahead of the mutation curve. A test of our resilience is how far behind the curve we allow ourselves to fall." **—World Economic Forum**

HUMAN STRAIN
+
HIGHLY PATHOGENIC
NON-HUMAN STRAIN
=
HIGHLY PATHOGENIC
HUMAN STRAIN

DISEASE LATENCY

Up to one-third of the world lives with latent tuberculosis infection.

Tuberculosis (TB) is responsible for 1.8 million deaths per year, and both multi-drug resistant (MDR) and extensively drug resistant (XTR) TB are on the rise.

India has the highest burden of TB, a ticking time bomb. Any number of relatively likely immunological challenges—a new HIV-like virus, a low-level radiation event on the Pakistan border—could cause a reoccurrence of TB and multiplicative effect of MDR and XTR TB, which could then spread from India.

MANAGING ANTIBIOTIC RESISTANCE

Antibiotic resistance is projected by some to kill 50 million per year by 2050—about the same as the total number of deaths in 2016 from all causes combined. **This could come at a total economic cost of $100 trillion.**

Despite this, there is an almost total collapse of the antibacterial R&D pipeline.

In response to major crises, many dozens of novel antibiotic technologies will be developed, like designer bacteriophages or nano-spike surface coatings.

As of 2016, 40 new antibiotics were in clinical development. However, novel antibiotic development is poorly incentivized—only one in five drugs admitted to Phase 1 trials make it to patients, and in some cases the drugs can be obsolete by the time they finish trials. As market incentives decrease even further for the development of antibiotic drugs, a federal agency will be put in charge of antibiotic technology, stockpiling and development.

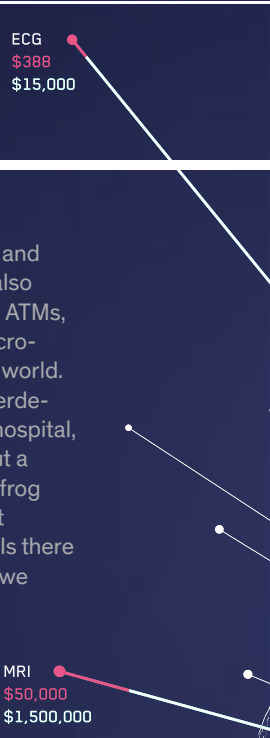
TUBERCULOSIS
WORLD POPULATION
33% – LIVING WITH
LATENT TB

"Gentlemen, it is the microbes who will have the last word."
— Louis Pasteur

Central exploding virus illustration by PixelBuddha.net

Medical care in the developing world is being vastly improved with a new generation of ultra-low-cost medical technology—often invented at universities and accelerators in the US. Here's how this leapfrog med tech could end up disrupting first-world healthcare systems.

Trickle-Up Innovation



For a century, the leading edge of medicine was always invented for rich countries, and slowly trickled down to poor countries. The developing world got the hand-me-downs—everything from medical school training to diagnostic equipment to clinical practices lagged some number of years behind the newest innovations. Modeled on our system, developing-world systems were always playing catch-up, perpetually forced to compromise by the lack of money.

BUT THAT STORY IS CHANGING

Fired up by grants from the Gates Foundation and other NGOs, first-world inventors are now designing new ultra-low-cost products aimed straight for the developing world. Hackathon projects are turning into startups with solutions for third-world medical needs such as malaria, HIV and cervical cancer prevention. At the same time, local innovators in the developing world have been energized to invent their own solutions for low-resource settings. The benefits have been astounding:

01

Maternal mortality has been cut in half, partly due to widespread distribution of 40-cent medical kits to prevent infections.

02

Infant mortality has been cut in half.

03

Cervical cancer can be cut by a third with a simple test using common vinegar to check for lesions.

Much of Africa skipped landlines and went straight to wireless. Africa also leapfrogged branch banking and ATMs, adopting mobile banking and micro-credit earlier than the developed world. In a similar way, much of the underdeveloped world has never seen a hospital, and barely ever seen a doctor. But a radically different, low-cost, leapfrog medical system is emerging. As it improves, we will inevitably ask, "Is there anything they've figured out that we should learn from?"

OUTFITTING DISTRIBUTED MEDICAL CENTERS ACROSS THE DEVELOPING WORLD IS ABOUT TO BECOME 10× MORE AFFORDABLE

Though considered inferior now, these low-cost technologies will evolve rapidly and improve in quality.

FIRST-WORLD STANDARD OF CARE	10x AFFORDABILITY (OR MORE)
Charge for anesthesia **$2,000**	**$200** Per procedure with anesthesia robot
Blue light phototherapy machine for jaundiced babies **$3,000**	**$350** Machine from D-Rev which uses LEDs that last 10 times longer than CFL bulbs
Ventilators **$3,000–$40,000**	**$300** OneBreath ventilator that runs on a 12-volt battery
Vacuum pressure wound therapy kit to speed healing **$1,100**	**$3** Hand pump developed for disaster relief teams
GE MAC 5500 HD ECG machine **$15,000**	**$388** GE MAC i ECG machine
Premature infant incubator **$20,000**	**$25** Embrace infant warmer that's "recharged" by submerging in hot water
Molecular microscope **$50,000**	**$500** Smartphone attachment
4-D ultrasound systems **$115,000**	**$3,500** Mobile ultrasound system for midwives, or **$300** Butterfly's ultrasound-on-a-chip smartphone attachment
MRI machines that rely on huge superconducting magnets, so have to be housed in special suites **$1,500,000**	**$50,000** Ultra-low-field MRIs, operating at 6.5 millitesla, which use 450× less power
The network for a new hospital today is built with 192 strands of fiber and 29,000 Cat 6 drops; TIA-1179 shielded network cable to every workstation.	Mesh wifi connected to urban hubs via 5G

INCUBATOR
$25
$20,000

VENTILATOR
$300
$3,000 - $40,000

MICROSCOPE
$500
$50,000

10x ↓

Cost of outfitting distributed medical centers across the developing world

"Rich countries can learn a great deal about health and human services from poorer ones… Combining the learning from rich and poor countries can give us new insight on how to improve health." **—Lord Nigel Crisp, former CEO, UK National Health Service**

LAB-ON-A-CHIP DIAGNOSTICS

In many countries, clinics have the drugs to treat a disease but lack the diagnostic tools to screen patients for treatment. For instance, the survival rate of breast cancer patients in low-income countries is half what it is here, due to lack of affordable early diagnostics.

Recent advances in microfabrication and nanofabrication have powered the invention of single-use chip tests that replace traditional laboratory synthesis and chemical analysis. These chips, which can be printed in high volume, come packed with micro-scale pumps, capillary channels and reagents for less than a few dollars per chip. They produce results at the point of care rapidly, and can be used in physicians' offices, in the field or even at home.

- 274 companies are contributing to the market with their expertise.
- Inkjet printers using nanoparticle ink can produce tests for 1 cent each.
- Dr. Aydogan Ozcan at UCLA has invented a lab-on-a-chip cytometer for $5 to help the 90% of people with HIV who have never been tested for the disease.

CAPABILITIES THUS FAR

YEAST CELL VIABILITY
METASTATIC CELL DETECTION
GOUT DIAGNOSIS
ENZYME ASSAYS
TARGETED DNA SEQUENCING
ANTIMICROBIAL RESISTANCE
EBOLA
DENGUE AND YELLOW FEVER

REVERSE INNOVATION

Popularized by Dartmouth professors Vijay Govindarajan and Chris Trimble, the concept of reverse innovation refers to products and methods adopted and perfected first in the developing world before they are spread to the industrialized world. Mobile banking and microfinance were the first noted examples, but now there's a deluge of innovations: biomass gasification power plants, small steam turbines, battery-powered home refrigerators, infotainment systems for motorbikes, etc. Doctors in Alabama running an AIDS clinic turned to Zambia to learn how to make sure patients attend follow-up appointments.

CLASSIC DISRUPTION THEORY

Clayton Christensen's disruption theory describes how market leaders are knocked off their pedestals not by innovation at the high end, but from underneath. Entrants gain a foothold by delivering to low-end markets overlooked by incumbents. They are considered inferior by most of the market, but with constant improvement reach quality standards that serve the middle market.

LEARNING FROM INDIA

In India, the average patient pays 65% of their costs out of pocket, on extremely limited resources. Hospitals there have learned to treat problems of the eyes, heart and kidneys, provide maternity care and orthopedic medicine, and treat cancer for less than 10% of US costs.

Microinsurance

With premiums as low as $5 a year, microinsurance pulls rural communities into health networks, offering telemedicine, catastrophic coverage for birthing complications and immunizations. Cellular service providers even offer free health microinsurance for customers who buy monthly minutes.

50-cent E-Consultations

Max Healthcare in India extends its hub-and-spoke network into 400 Punjab villages by setting up telemedicine kiosks at safe drinking water access hubs.

$1,500 Cardiac Bypass Surgery

Cost in US: $144,000
Cost in India: $1,500*

How they do it:

- High-volume specialization allows a grafting surgeon to operate on 5–6 patients per hour. Chest opening, vein harvesting and suturing are performed by junior doctors.
- Sterilization and reuse of surgical tools
- Manufacturing of stents for 1/10th the cost

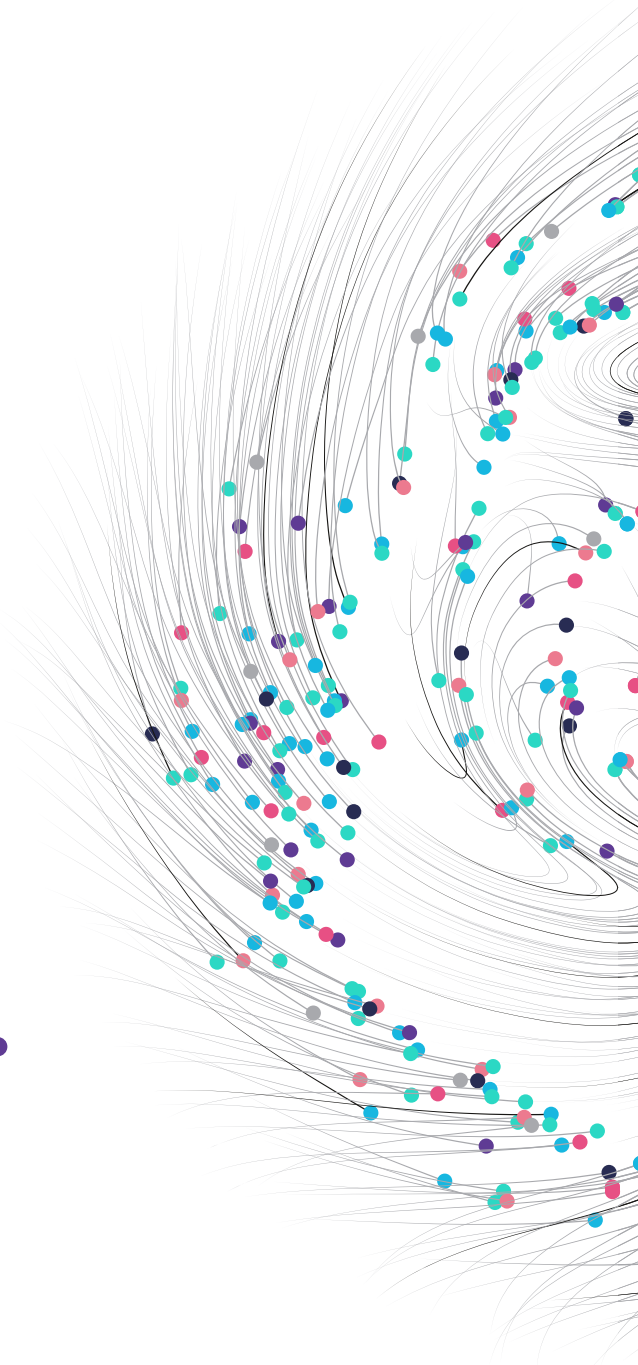
*Mortality and infection rates are comparable to good American hospitals.

$41 Cataract Surgery

Aravind Eye Care, inspired by McDonald's high-volume service, has performed 4 million operations. Paying patients, who are charged $41 to $125 depending on the surgery, subsidize free surgery for the poor. All surgeons rotate between paying and free wards. Intraocular lenses are manufactured for only $2.

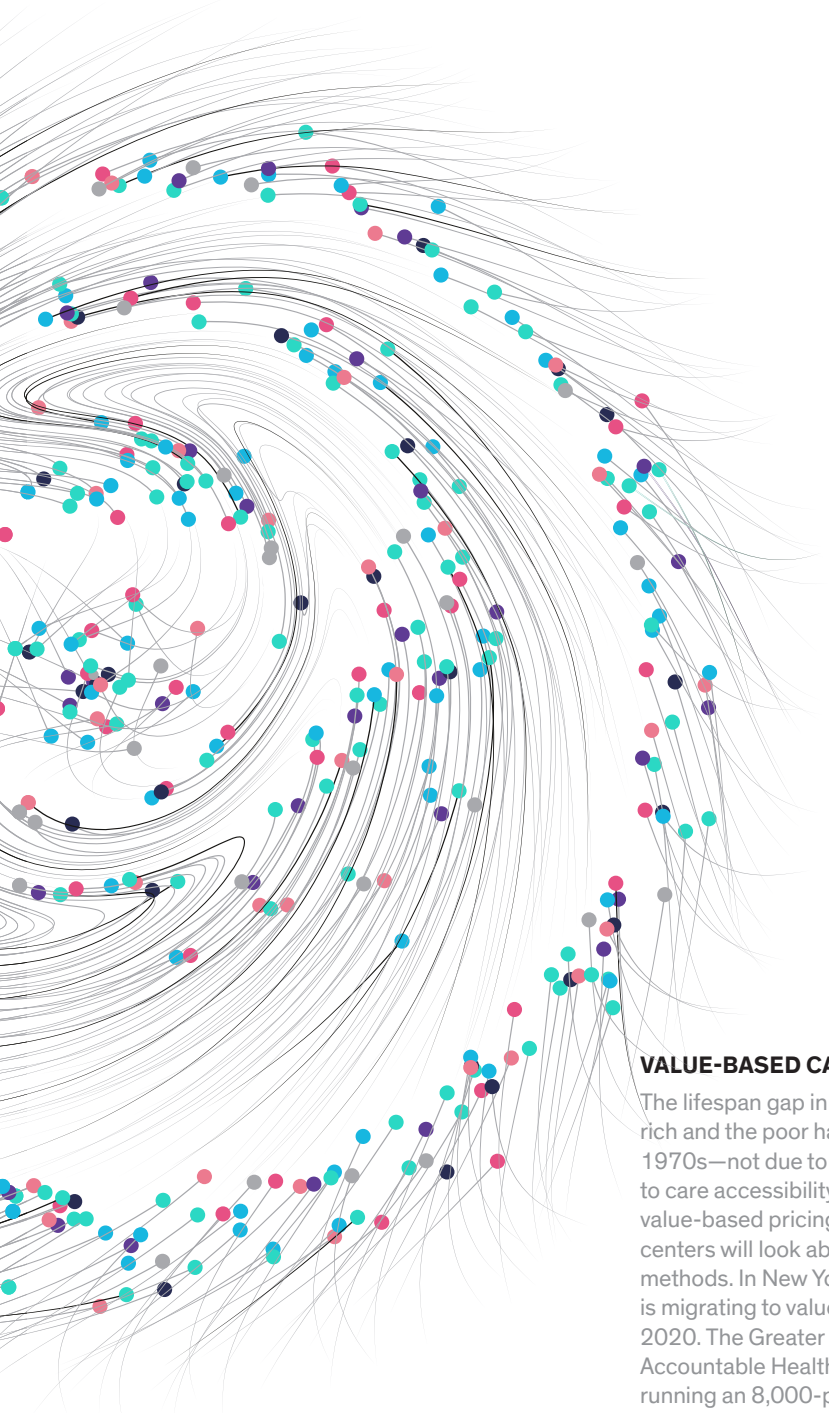
THE GLOBAL MIDDLE CLASS

In a decade, the booming Asian middle class will be 6× the size of the American middle class. While the wealthy will buy Western medical care, the new middle class will get its medical care through systems imported from the developing world, including microinsurance, e-consultation services, assembly-line surgery and birthing care.



Medical Innovation Will Flow in Both Directions

"Life science is easier to model on a computer than in wet form. The more medicine gets digitized and becomes an information product, the more it will follow Moore's law."
—Steve Jurvetson, venture capitalist



MEDICAL TOURISM

Medical tourism started with patients coming to America to get the best treatment. In the last decade, far more patients have been going the other direction, for everything from heart valve replacements to fertility treatments to addiction recovery. More than 1 million Americans a year cross borders for treatment. These patients return as de facto ambassadors testifying to the quality of low-cost care.

HOW MUCH CAN YOU SAVE?
INDIA: 65–90%
MALAYSIA: 65–80%
COSTA RICA: 45–65%
MEXICO: 40–65%

Health City Cayman Islands, founded by renowned Bangalore heart surgeon Devi Shetty, offers heart surgery, hip replacement and neurosurgery for 40% of US prices, just a two-hour flight from the Atlantic coast.

CUBA EXPORTS

Isolated from the rest of the world, Cuba invested heavily in biotechnology and public health, developing the capacity to cheaply produce 70% of their pharmaceuticals. 30,000 Cuban medical staff are working in over 60 countries around the world. High rates of lung cancer led to the invention of CIMAvax, a vaccine used for both prevention and post-radiation maintenance. The Roswell Park Cancer Institute is bringing CIMAvax to the American market.

VALUE-BASED CARE

The lifespan gap in the US between the rich and the poor has doubled since the 1970s—not due to quality of care, but to care accessibility. Rewarded by new value-based pricing, community health centers will look abroad for wisdom and methods. In New York State, Medicaid is migrating to value-based care by 2020. The Greater Buffalo United Accountable Healthcare Network is running an 8,000-patient pilot program through a network of community-based private practices. Community health workers call and visit chronic-care patients in their homes. Adopting the customer-service methodologies of retail, a new holistic clinic offers a gym and nutrition kitchen on the first floor, primary care on the second floor and specialists on the third floor.

Facing such a furious rate of innovation, and so much medical data being collected outside formal clinical trials, is the regulatory system capable of keeping pace? Will the future of medicine be ungoverned?

Can the FDA Keep Up?

BIG PHARMA IS CLEARLY AT A CROSSROADS

For two decades, healthcare has relied on Big Pharma to crank out wonder drugs to control our disease symptoms and risk factors. But progress has slowed—in some cases stalled.

- 7 of the 13 historic pharmaceutical companies had no new molecular entities (NMEs) approved in 2016.
- Even as the cost of developing a drug is rising, the odds of getting a drug from Phase 1 all the way to FDA approval have fallen below 10%.
- Those odds in oncology are only 5.1%, in cardiovascular only 6.6% and in neurology only 8.4%.
- As a result, financial returns across Big Pharma have steadily fallen over the current decade from 11% to 3.7%.

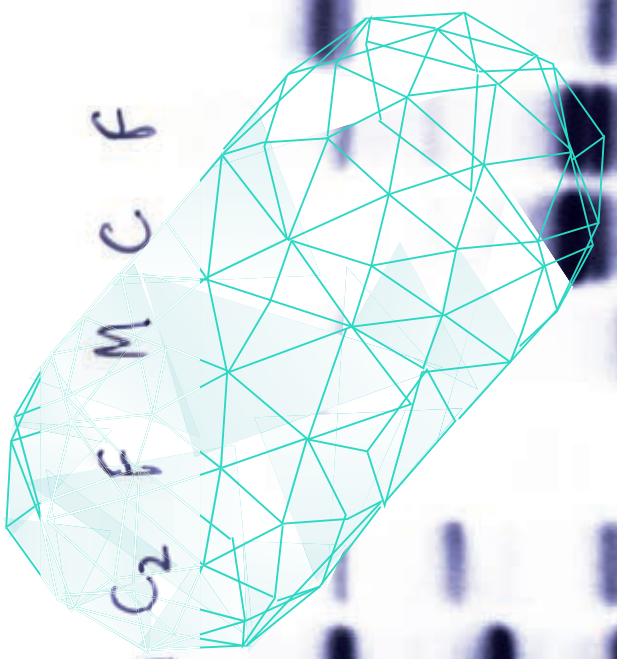
$154 billion is spent every year on drug research. That annual investment is in jeopardy if it doesn't pay out. Already the R&D investment into antibiotics and vaccines has slowed to a trickle because of the lack of financial return.

BIOMARKER DRUGS WILL END THE ERA OF BLOCKBUSTER DRUG ECONOMICS

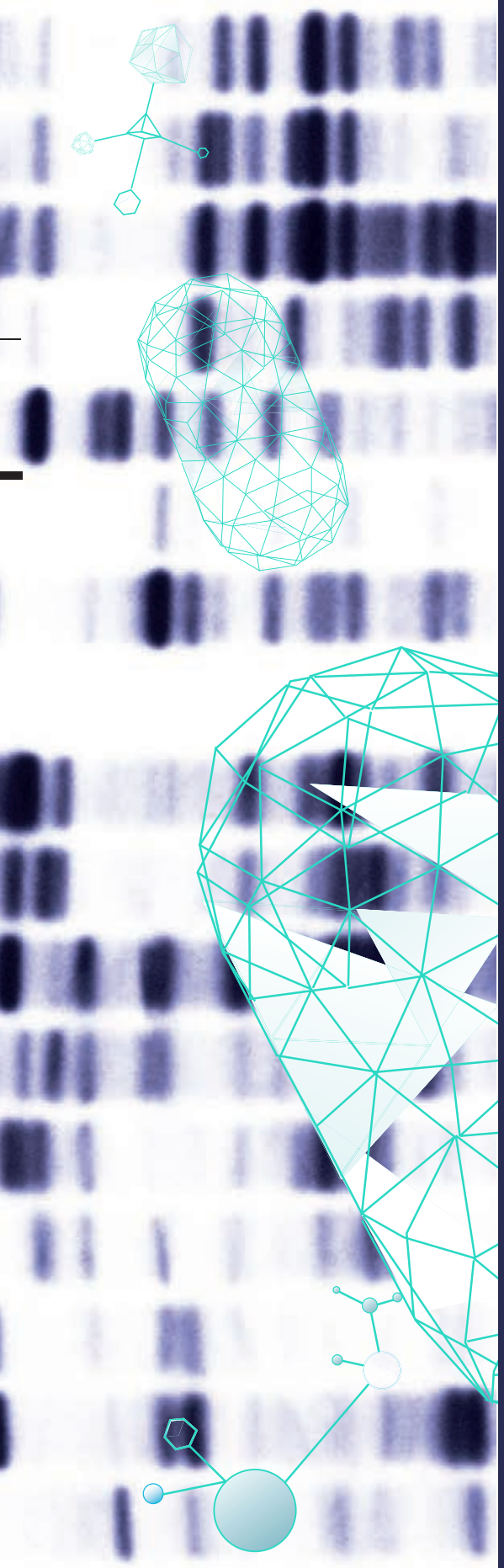
Research into genetic biomarkers has dramatically helped figure out why drugs work in some patients and not in others. There are already 62 cancer treatments approved for specific genetic subpopulations, and 238 overall. When they work, they tend to work far better. This raises the odds of approval considerably. Clinical trials that use genetic selection criteria have a 3× better chance of negotiating the full approval pathway. Critically, given that Phase 3 trials are so expensive, those odds of approval double.

All of this reduces development risk, but the tradeoff is clear: the genetic screening means the market size for any of these drugs is much smaller.

There is a bright spot, however: Pharma companies' libraries of previously failed compounds can now be reanalyzed by biomarker interactions. They might have worked for certain genetic profiles. Potentially, many of those compounds can be brought back to market with low R&D investment.



3x Better chance that trials using genetic selection criteria will clear the approval process



39% American patients who have delayed a drug regimen due to its price

PRICE PUSHBACK

39% of American patients have delayed a drug regimen due to its price.

The FDA is forbidden by law from considering a drug's price in the evaluation process, and only approves drugs that prove they're better than existing treatments. Most other countries do consider a drug's cost, and often approve drugs that don't work quite as well if they cost less. The result is per capita spending on drugs in the US is twice the international average.

THE RISING PRICES OF DRUGS ARE PROVOKING CONSUMER ACTIVISM AND POLITICAL SCRUTINY

Some shocking examples:

Emflaza: This muscular dystrophy steroid was available outside the US for decades. American families were able to import it, paying $1,600 or less per year. When Marathon Pharmaceuticals licensed it for the US market, they wanted to charge $89,000 a year, arguing the market size was so small (12,000 American patients), they needed to charge that price to get a return. Marathon took so much heat they had to sell Emflaza to PTC Therapeutics.

Daraprim: Nowadays, when a drug comes off patent, sometimes the price for the generic version goes up, not down. This happens when the FDA licenses only one manufacturer to make it, creating an artificial monopoly—or even granting an exclusive marketing license to drugs that had been available for decades. When Turing Pharmaceuticals got licensed to make Daraprim, they raised the price from $13.50 a pill to $750. Successful activism led to a near boycott: monthly sales fell from 22,500 pills to only 600 pills.

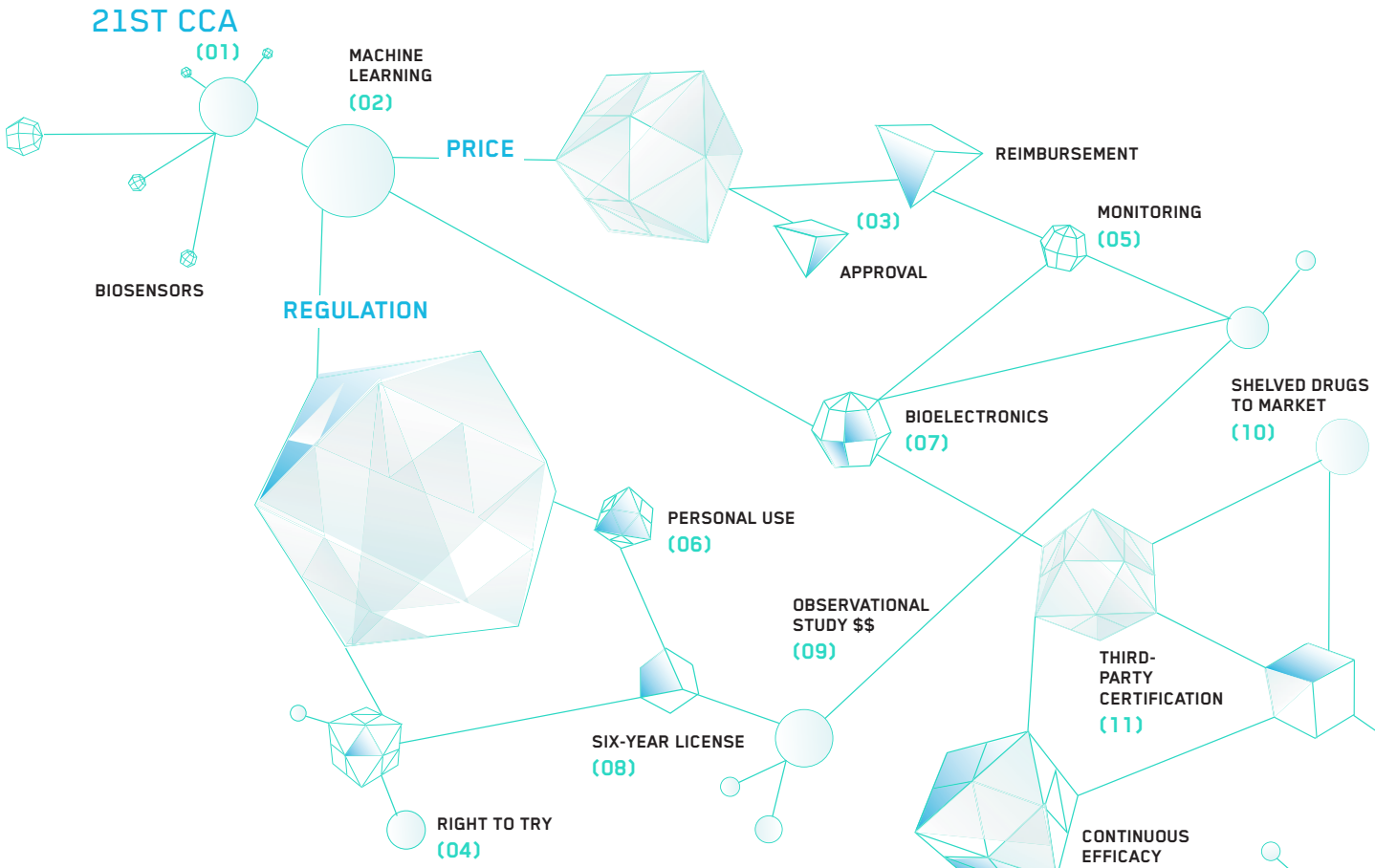
INSURERS ARE PUSHING BACK, TOO, WANTING MORE EVIDENCE THAN WAS SUBMITTED TO THE FDA BEFORE THEY'LL COVER A DRUG

Amgen's cardiovascular drug, Repatha, was expected to be a game-changer. Insurers, however, restricted coverage to only those with extremely high cholesterol, saying Repatha's efficacy wasn't worth the $14,000 price when the prevailing treatment only cost $150 a year.

DESPERATELY SEEKING AFFORDABILITY, PATIENTS TURN TO ONLINE PHARMACIES THAT PROMISE TO SEND THREE-MONTH SUPPLIES FROM OVERSEAS

Of the 30,000 prescription drug websites, 96% are operating illegally with no pharmacy license at all. The drugs may or may not be what's advertised.

Where does this all lead? It won't change wholesale, with a sweeping act of Congress. Instead, it will change piece by piece—a chain reaction.



Critical Insight

It seems like a simple question. "How do we know if a drug works?" But in the future this question will be answered differently. Bayesian statistics are surpassing frequentist statistics in the age of the internet and machine learning. Historically, the scientific gold standard has always been group-based evidence. A drug might work on some patients, but if it doesn't work well enough across the group it's considered a failed trial—and it's not even made available to those who were benefiting. But biosensors and continuous monitoring can change the math. Genetic biomarkers have prepared us for this conceptual leap. "Efficacy" can be personalized. We can prove a drug's benefits patient by patient, and stop the drug's use whenever the benefits disappear.

01

Last year's **21st Century Cures Act** (often overlooked because of ACA reform) already forced the FDA to consider data from outside clinical trials, such as observational studies, insurance data and patient input. For the first time, the FDA will have to confront data collected via biosensors during continuous monitoring—rather than just before/after endpoints.

02

The FDA has scoffed at surrogate endpoints in trials. They won't be able to once **machine learning** on large datasets kicks out hidden layers, concretely tying constellations of surrogates to long-term outcomes.

03

Because of the high prices, insurers will force a stark **decoupling of approval and reimbursement**.

04

The **"Right to Try"** movement will force the FDA to allow terminal patients the opportunity to try drugs approved in other countries.

05

Insurers will start to require **biosensor monitoring** of surrogate endpoints, to be sure some drugs are actually effective on each individual patient. Diabetes or heart conditions will go first.

06

"Personal use" purchasing will be tolerated. Alarmed by more people buying drugs online that might be harmful and counterfeit, the FDA won't intervene when patients buy from licensed pharmacies abroad that get real drugs from approved manufacturers.

07

Bioelectronic devices will begin to **replace some drugs**. Their manufacturers, as well as disease management companies, will preach to the public an ideal of going off medications.

08

More countries will follow Japan, allowing drugs in emerging research areas a **six-year license** after only Phase 2. During those six years, evidence of real-world efficacy can be accumulated. Pressure on the US to follow will mount.

09

While it still may be illegal to pay your way into an official clinical trial, it will be legal to pay your way into an **observational study**. Pharma will learn to use this to defray costs.

10

Pharma will partner with the FDA to consider drug price, not just drug efficacy, in its review. Price competition will open the door for shelved drugs to enter the market.

11

To handle the sheer volume of authorizations, drug regulation will become like financial regulation—reliant on **third-party certification** companies, akin to credit rating agencies.

12

Having long wanted post-market studies on drugs, the FDA will grant some drugs a **temporary license** after Phase 2 if continuous efficacy can be monitored. Patients who don't get benefits will have to go off the drug immediately. Those who get verifiable benefits will stay on.

13

A new era of drug development will begin.

"The pace of innovation is amazingly fast, but regulatory issues and authorities cannot keep up. Though the FDA has made some great steps forward, they will face major dangers in the coming years." **—Bertalan Mesko, the Medical Futurist**

The FDA's Global Safety Net

Those who predict the FDA will be radically weakened in this future are dead wrong. Quite the opposite. **The FDA's global safety net plan will become the reality. The American FDA and its partner agencies will play the same role in medicine as the American military does in patrolling the world's seas and skies.**

Many people believe the FDA can't possibly regulate rogue medicine around the world. They are overlooking the way the FDA is already building a fairly effective global trust network.

» Pharma companies desperately want a single international regulatory standard, predicting it could reduce development costs by 20%.

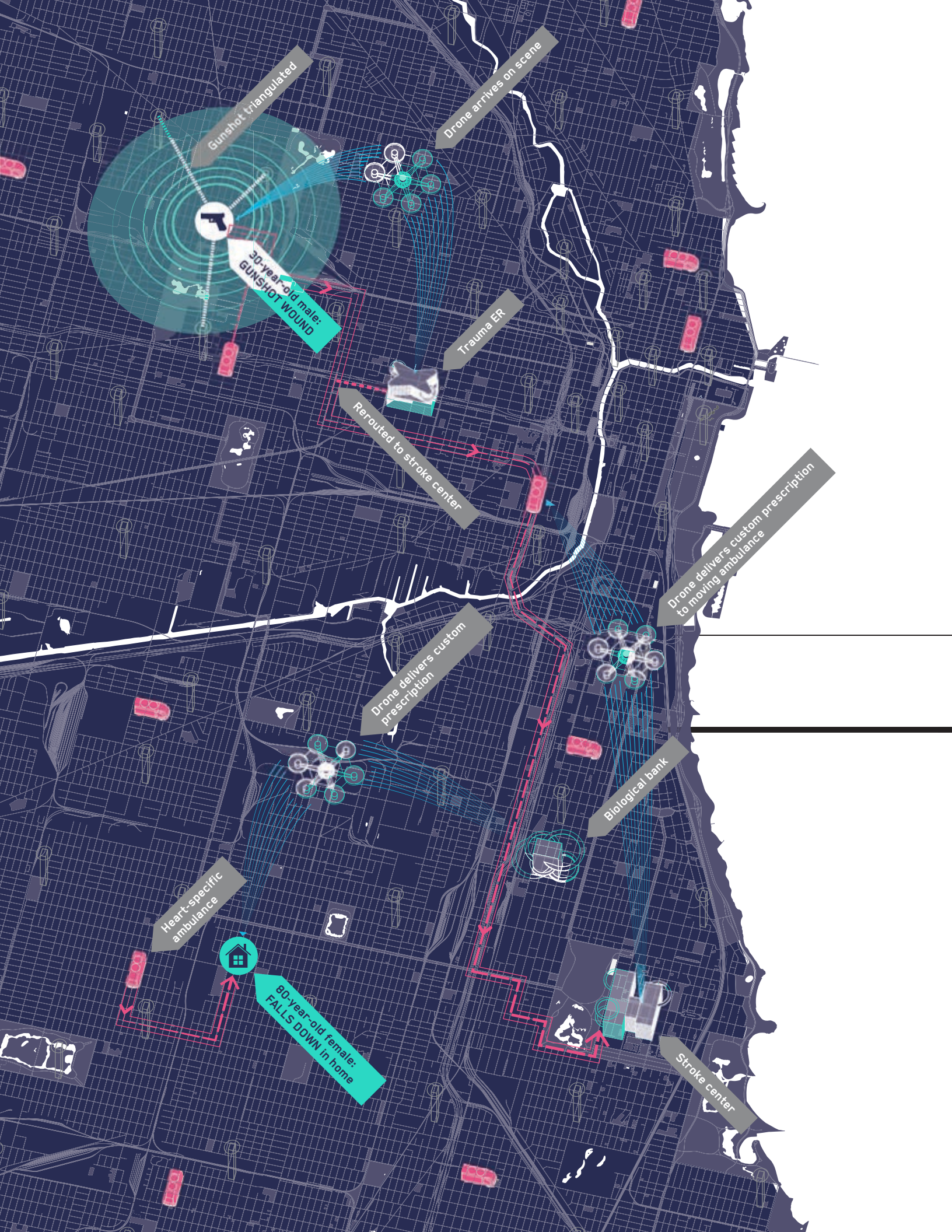
» Clinical trials are now distributed to sites internationally. More than half of all clinical sites are outside the US. This forces regulatory agencies to coordinate. Rather than being "rogue" incubators of fringe science, these international hospitals and universities all conform to American standards of good clinical practice to be eligible for inclusion in the trials.

» No trials are conducted without some US sites, and all the trial sites comply with the same standard as inside the US, and go through inspection and investigation.

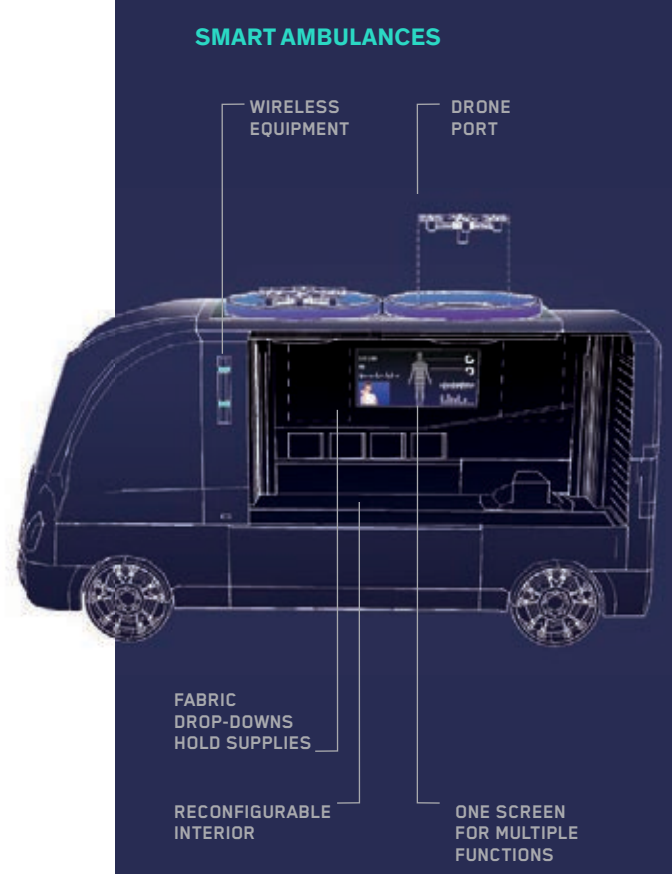
» Through pacts, treaties and licensing deals, the US is bringing the world together. 143 international agreements are already in place among 43 nations.

» The FDA already asserts authority over 300,000 foreign facilities that ship to the US, and last year alone it inspected over 3,500 of them.

» The FDA already has to govern all the food products imported to the US. That's some 37 million shipments a year. Their expertise in food will translate increasingly to drugs.


Gunshot triangulated
Drone arrives on scene
30-year-old male: GUNSHOT WOUND
Trauma ER
Rerouted to stroke center
Drone delivers custom prescription to moving ambulance
Drone delivers custom prescription
Biological bank
Heart-specific ambulance
80-year-old female: FALLS DOWN in home
Stroke center

Medical calls make up 73.3% of 911 calls. National "gold standard" ambulance response time is to arrive within eight minutes 90% of the time. However, the complexity of first response means that many cities fall short of this standard today.



Trauma: 30 Minutes

Though national data is difficult to compile, a recent auto insurance report put the national emergency response time to fatal accidents at 15 minutes and 19 seconds. In Chicago, **it sometimes takes up to 33 minutes** for an ambulance to arrive at a scene.

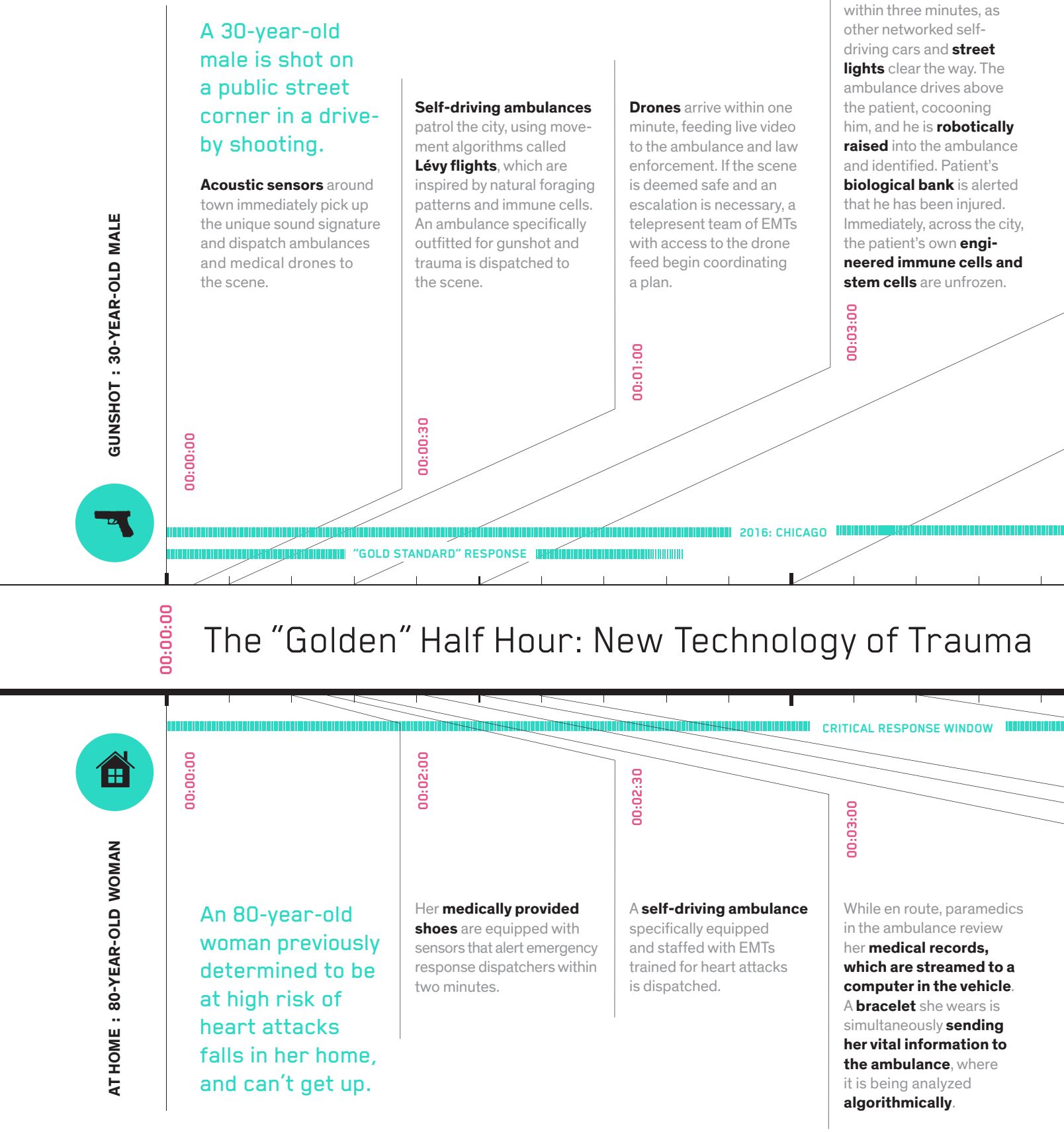
Anyone presenting with a suspected heart attack should be evaluated and treated in less than 20 minutes. **A recent study found that average wait time for women is 25.5 minutes and 18.5 minutes for men in the ER.**

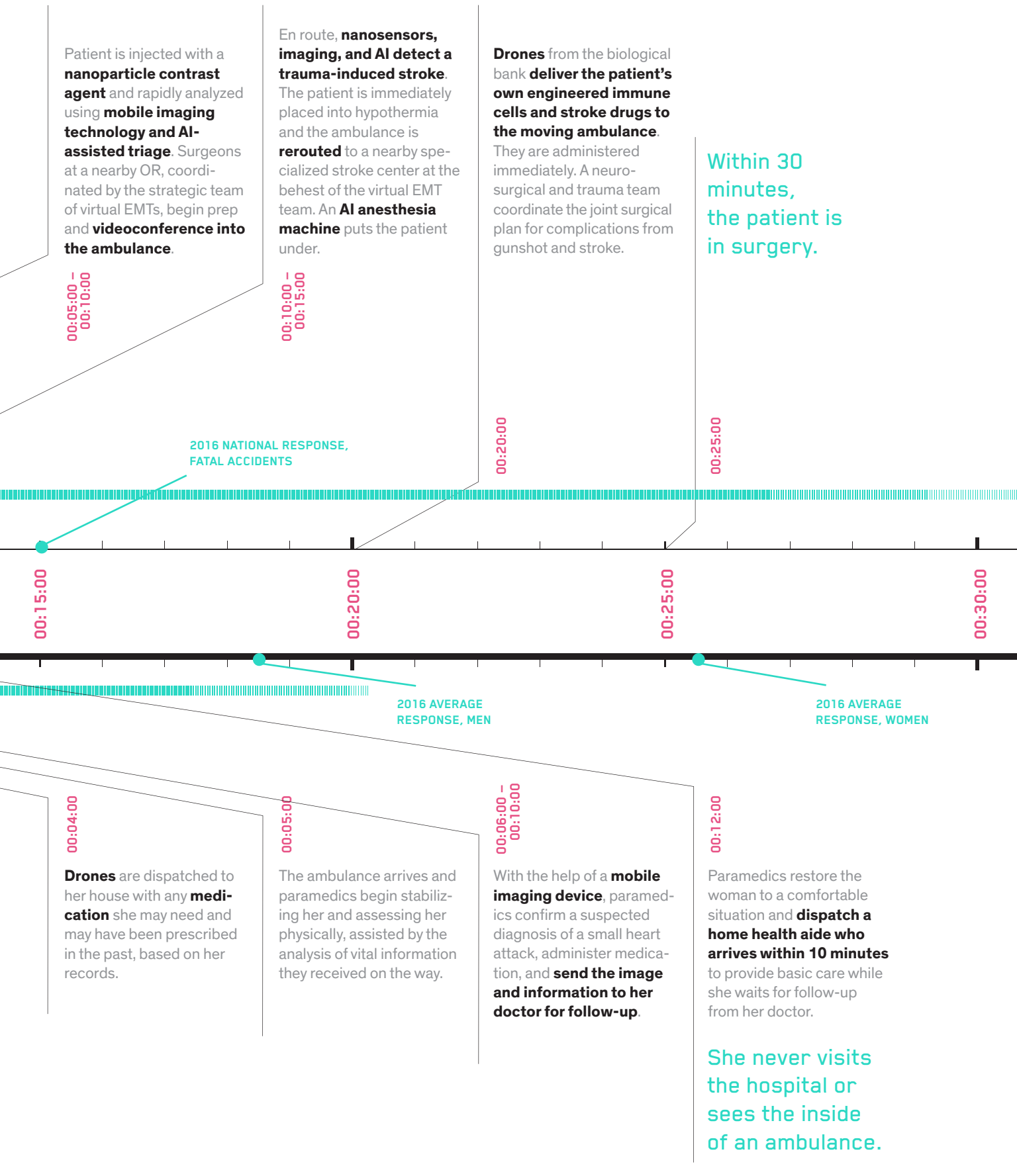
Chicago, a city of 3 million, is currently served by only 250 pieces of first-response equipment, including fire engines, fire trucks, ambulances, squads and helicopters. **Fire calls made up only 3.7% of Chicago Fire Department calls. That's 20 times more medical calls than fire calls**.

Ambulances of the future will be telepresent command centers, highly networked to local hospitals and cloud computing centers. Specialized ambulances for different trauma types will always be in motion and coordinate their responses, like a citywide immune system.

Physical redesigns for driverless ambulances and the miniaturization of imaging technologies will allow for rapid in-ambulance diagnoses. **Triage will move out of the hospital.** Blood can be taken and analyzed or sent by an ambulance-based drone to a lab anywhere in the city, within minutes. Specialized trauma teams on a local or national level can be patched into the ambulance to craft a surgical plan before the patient even arrives at the hospital.

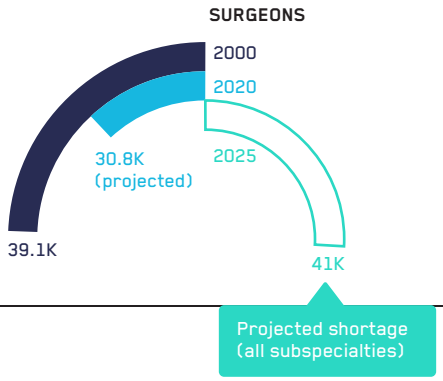
The "Golden" Half Hour: New Technology of Trauma




Patient is injected with a **nanoparticle contrast agent** and rapidly analyzed using **mobile imaging technology and AI-assisted triage**. Surgeons at a nearby OR, coordinated by the strategic team of virtual EMTs, begin prep and **videoconference into the ambulance**.
00:05:00 – 00:10:00
En route, **nanosensors, imaging, and AI detect a trauma-induced stroke**. The patient is immediately placed into hypothermia and the ambulance is **rerouted** to a nearby specialized stroke center at the behest of the virtual EMT team. An **AI anesthesia machine** puts the patient under.
00:10:00 – 00:15:00
Drones from the biological bank **deliver the patient's own engineered immune cells and stroke drugs to the moving ambulance**. They are administered immediately. A neurosurgical and trauma team coordinate the joint surgical plan for complications from gunshot and stroke.
Within 30 minutes, the patient is in surgery.
00:20:00
00:25:00
2016 NATIONAL RESPONSE, FATAL ACCIDENTS
00:15:00
00:20:00
00:25:00
00:30:00
2016 AVERAGE RESPONSE, MEN
2016 AVERAGE RESPONSE, WOMEN
00:04:00
Drones are dispatched to her house with any **medication** she may need and may have been prescribed in the past, based on her records.
00:05:00
The ambulance arrives and paramedics begin stabilizing her and assessing her physically, assisted by the analysis of vital information they received on the way.
00:06:00 – 00:10:00
With the help of a **mobile imaging device**, paramedics confirm a suspected diagnosis of a small heart attack, administer medication, and **send the image and information to her doctor for follow-up**.
00:12:00
Paramedics restore the woman to a comfortable situation and **dispatch a home health aide who arrives within 10 minutes** to provide basic care while she waits for follow-up from her doctor.
She never visits the hospital or sees the inside of an ambulance.

Think self-driving cars are impressive? Steel yourself: robots will perform more surgeries than human surgeons—and most surgeries will happen outside of hospitals.

A growing, aging population means a greater need for surgery. Increased life expectancy will be the primary driver behind increased surgical volume, and there are not enough surgeons to meet the demand.



The Future of Surgery

THE ROBOTS ARE COMING. THE ROBOTS ARE HERE.

WHAT ROBOTS ARE DOING NOW

Autonomously suturing soft tissue (pig intestine) as well or better than human surgeons in an experimental system.

Milling bone with submillimeter accuracy prior to placing joint implants.

Semi-autonomously harvesting and implanting individual follicles for hair transplantation.

Assisting neurosurgeons treating epilepsy. Robots place electrodes into the brain instead of on the brain surface and need 2–3 mm holes in the cranium instead of a 4×4 cm craniotomy. Robots can reduce operative time by half.

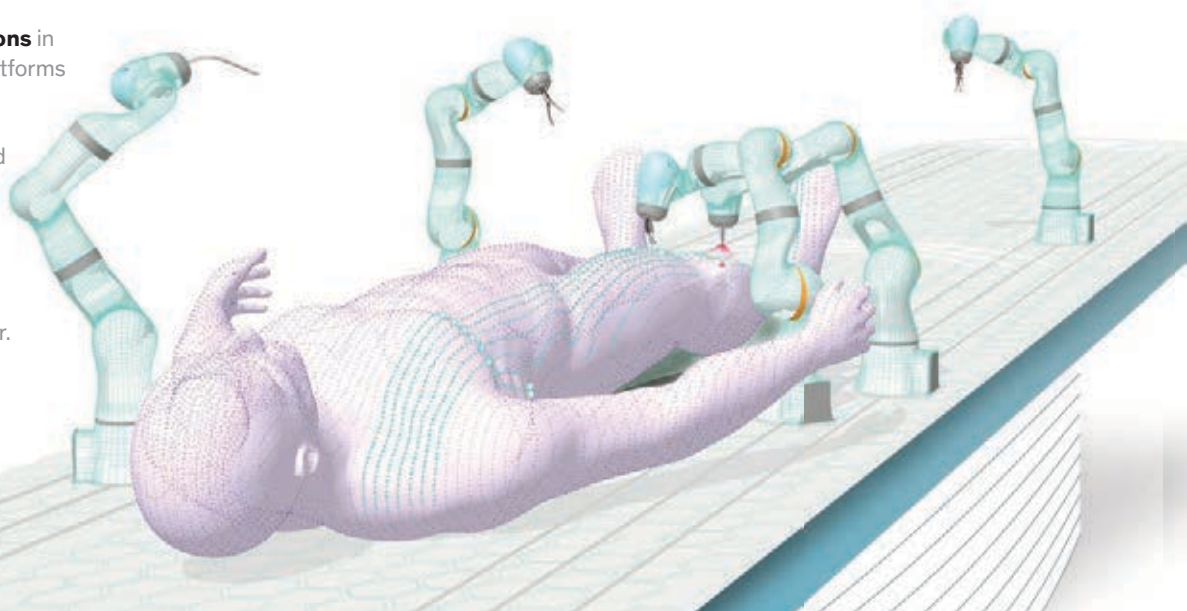
Assisting orthopedic surgeons in knee and hip replacement. Platforms offer real-time virtual imaging and robotic-arm guidance for cutting and removing diseased tissue and placing implants.

Assisting gynecologic, general, ENT and urologic surgeons in over 700,000 soft tissue procedures per year.

PLATFORMS IN HUMAN TRIAL PHASE OR APPROVED BY FDA OR CE MARK

DOMAIN	COMPANY
CARDIOVASCULAR	Intuitive Surgical
ORTHOPEDICS	Stryker
	OMNI
	Smith & Nephew
	THINK Surgical
NEUROSURGERY	Renishaw
	Zimmer Biomet
SPINE	Mazor Robotics
	Zimmer Biomet
	Globus Medical
ENDOVASCULAR	Hansen Medical
	Corindus
	Stereotaxis

DOMAIN	COMPANY
LAPAROSCOPIC/ SOFT TISSUE	Smart Tissue
	Anastomosis Robot (STAR)
	Intuitive Surgical
	TransEnterix
	Titan Medical
	Medrobotics
	Virtual Incision
ENDOSCOPY	Medrobotics
	Auris
HAIR TRANSPLANTATION	Restoration Robotics



"In 20 years, people will think it's crazy that a doctor still does surgery." **—Evan Anderson, Luma Therapeutics**

"In 100 years, we will think it was crazy that we used to cut the body open." **—Arvind Gupta, IndieBio**

SEPARATING HYPE FROM REALITY

Today, we are still in the very early stages of the robotic surgery revolution.

Robotic surgery (or robotic-assisted surgery) promises to alleviate some of the anticipated surgeon shortage, but, for now, the technology doesn't necessarily mean better health outcomes, decreased cost or across-the-board efficiencies.

Current data on the clinical benefit of robotic surgery is equivocal. For soft tissue, most studies show (at best) parity between robotic surgery and established methods of minimally invasive surgery. Though robotic surgery often cuts down on post-op recovery time, actual operative time is increased for many procedures (decreased for fewer), due in part to surgeons' learning curve with the technology. Except in certain situations (prostate cancer, for example) there has been little ironclad evidence for robotic surgery's improvement in morbidity or mortality.

For orthopedics, the data show that operative variables (implant positioning, soft tissue balancing) are better controlled with robotic surgery than with manual surgery. However, there have been few high-quality studies on patient functional outcomes and survivorship.

48M+ Inpatient procedures (2009)

44.5M Soft tissue surgeries

ROBOTIC SURGICAL SYSTEMS COST A LOT UP FRONT AND HAVE HIGH RECURRING COSTS

A da Vinci laparoscopic robotics system (Intuitive Surgical) will set you back $1.5–$2 million. Annual service contracts run between $100,000 and $170,000, not including the cost of consumables—single use tools and supplies. It's estimated that a facility needs to perform 100 robotic surgeries per year to produce a viable financial return within six years. Per case, da Vinci costs $3,000 more than traditional laparoscopic surgery for removal of an ovarian cyst, and up to 3× more for gallbladder removal.

Orthopedic robots can cost about $1 million up front. Knee joint replacement costs $2,700 more with a robot.

However, in a value-based reimbursement environment, costs will eventually be outweighed by improved outcomes and consequent savings.

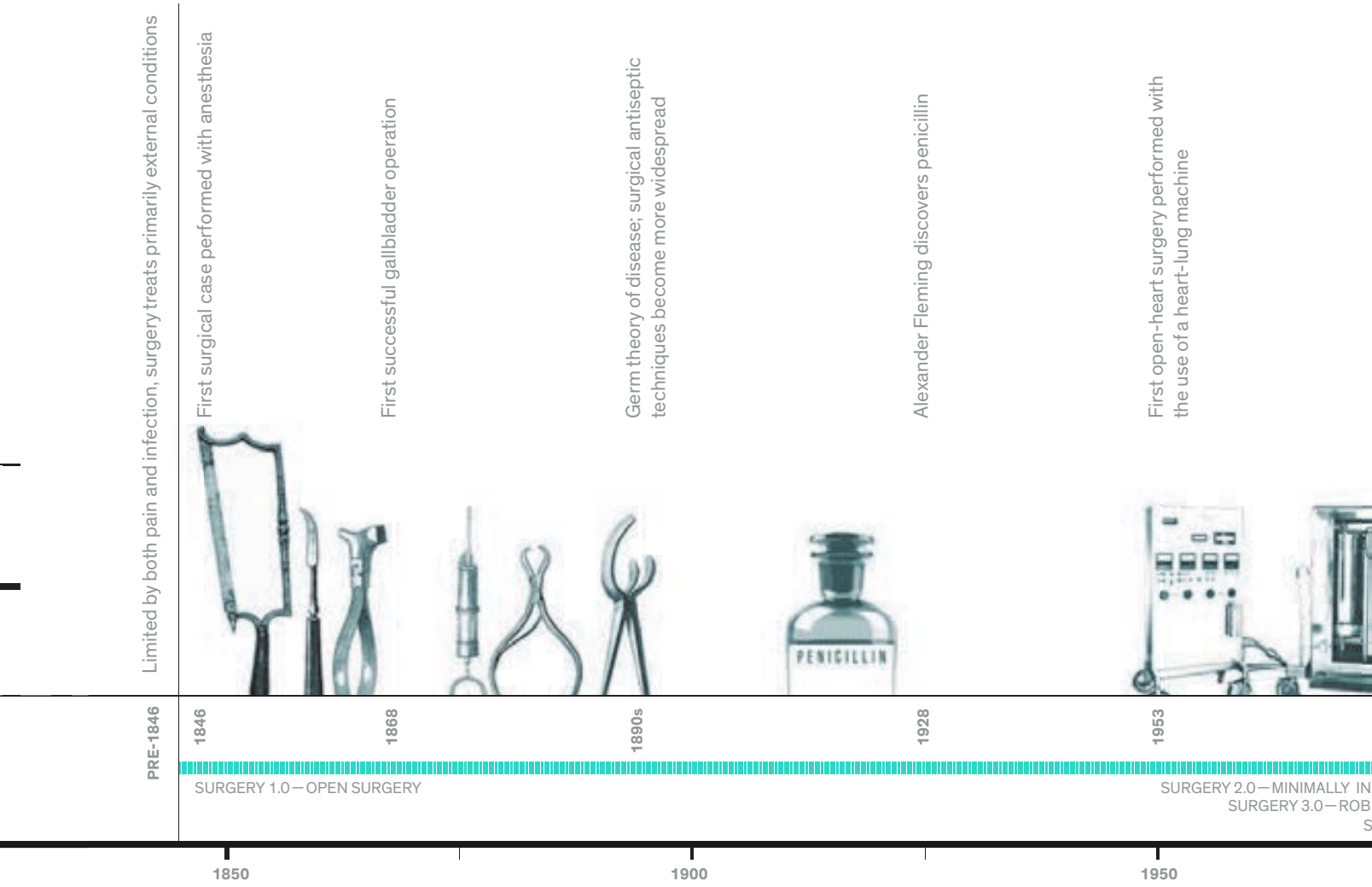
» **The economics** of robotic surgery will win out. As the financial sophistication of healthcare organizations increases, and as value-based medicine takes hold, there will be more rigorous evaluation of major purchasing decisions, i.e., for surgical robots and robot assistants. Joint replacement, for example, costs more when performed with a robot. But with the advent of new bundled cost containment models (CMS's Comprehensive Care for Joint Replacement Model), improved outcomes (fewer hospital admissions and joint revisions) will result in increased institutional revenue. If robots improve outcomes, thereby lowering overall costs, institutions will buy them. Goldman Sachs estimates that the number of robotic surgeries will double in the next two years.

» **Efficacy data will improve.** Robotic platforms that can demonstrate improved clinical outcomes and greater efficiency will dominate the market. In the next 20 years, premier robotics companies will lock in their customer base, and continue to make money off recurrent revenue streams (service contracts and consumables).

» **Efficiency will improve** as surgeons become more familiar and comfortable with robotic platforms.

» **New models of financing robot utilization** (e.g., OMNIBotics' pay-per-procedure) will lower the barrier to entry for healthcare organizations.

» **The calculus** behind whether to purchase a robot will change. Currently, the decision to purchase a surgical robot is often not based on cost considerations or improved patient outcomes, but rather on marketing and recruiting objectives: patients want the newest technology, conflating technology with quality; new surgeons, trained in robotics, want to employ those skills. Smaller hospitals in particular feel they are in an "arms race" for patients and talent against larger institutions, but their surgical volumes can be low. With increased hospital consolidation and the move toward providing surgical care at high-volume centers, smaller, lower volume institutions will evaluate hard cost-benefit metrics against softer ones like marketing and recruiting.



THE PACE OF TECHNOLOGICAL DEVELOPMENT WILL BE FAST

Autonomous driving is a difficult machine learning problem. It relies on multiple inputs, constant surveillance of the environment, constant adjustment. Autonomous vehicles will likely be fully functioning within three years. Having cracked the code that allows for control in high-risk situations like driving, the machine-learning workforce that gave us autonomous cars will turn its attention to a new challenge: surgery.

Because soft tissue is deformable and moves easily, robotic manipulation of it presents a more challenging machine learning problem (more movement = more data inputs) than operating on fixed or rigid targets.

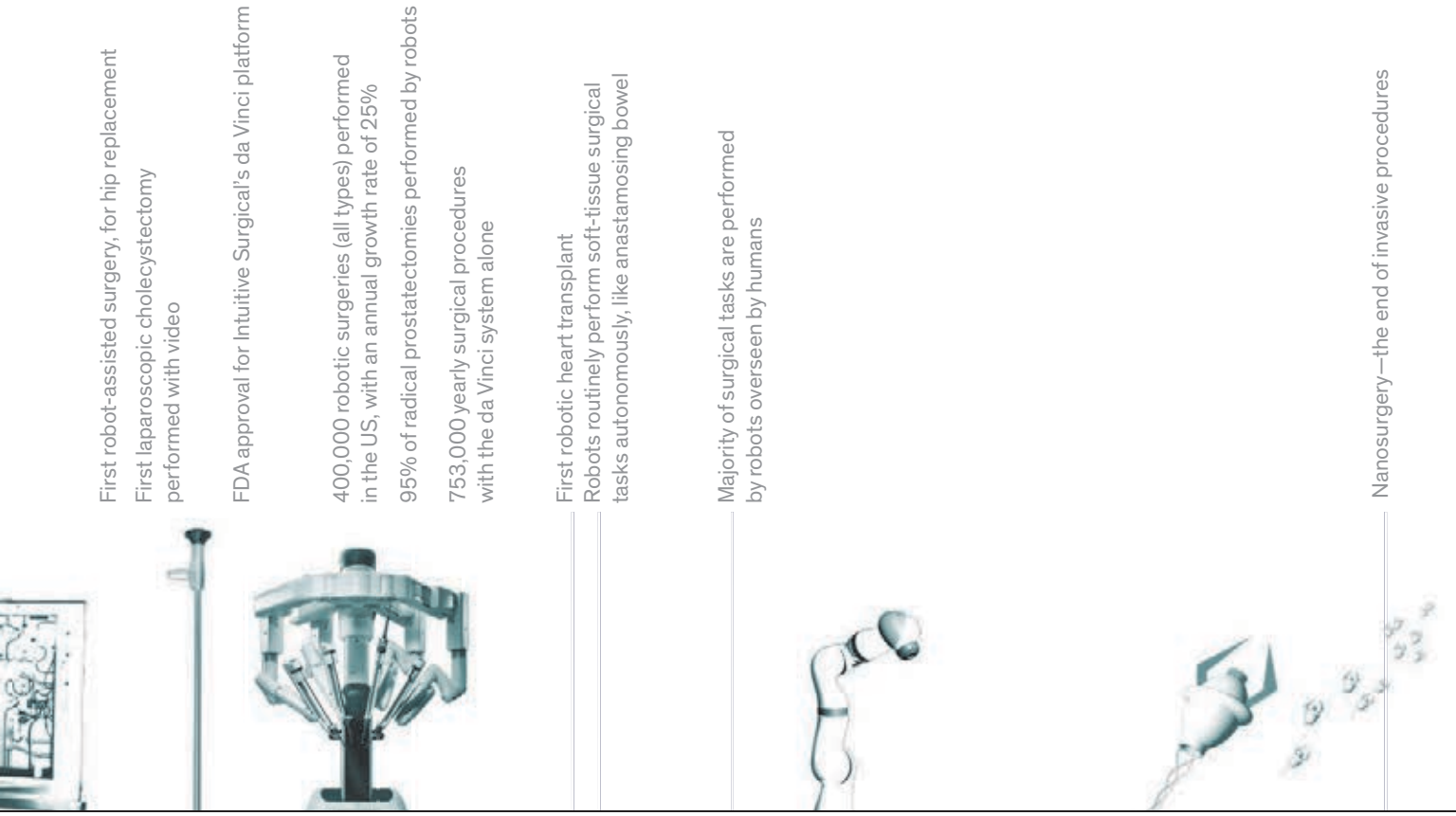
The majority of robotic surgery platforms focus on fixed targets:

- ELECTRODE PLACEMENT IN THE BRAIN TO TARGET EPILEPTIC FOCI
- ABLATION (FOR CARDIAC ARRHYTHMIAS)
- STENT PLACEMENT
- SPINE SURGERY
- JOINT REPLACEMENT & OTHER ORTHOPEDIC
- HAIR TRANSPLANTS

Currently, robot assistants help plan surgery and/or aid the surgeon in performing it by enhancing dexterity or removing the surgeon from dangerous environments (radiation in endovascular procedures, for example). As haptic feedback, visualization and device dexterity improve, robots will increasingly take over more tasks for any given procedure.

The incorporation of AI into surgical platforms will have profound effects in dynamic surgical environments, like soft tissue. The da Vinci platform essentially enhances the surgeon (better dexterity, better visualization, better access). In the next 10 years, we will see robots start to autonomously perform discrete (but complicated) surgical tasks like the anastomosis of bowel. Once AI is built into platforms, robots will not just assist in key components of surgery, they will perform entire surgeries themselves, allowing a single surgeon to oversee multiple operations.

Robots will get smaller, allowing for more flexibility (to use in a broad range of procedures) and better access to difficult sites.



GAME CHANGERS

Surgery will move into a new phase, incorporating AI, enhanced instrumentation and enhanced visualization. At the same time, some conditions previously treated with surgery will be treated with non-invasive methodologies.

Surgery 4.0 Verb Surgical, a joint venture between Johnson & Johnson and Verily (formerly Google Life Sciences) proposes a new paradigm: digital surgery.

Platform, not robot Flexible digital surgery platforms will allow for a la carte selection of appropriate technology.

Advanced imaging and machine learning algorithms, but not robots, may be required for one procedure; robots may be added for another.

An App Store for surgery? Open platforms allow for plug and play of different functionality (instrumentation, visualization, robotics), giving the surgeon unmatched flexibility. Currently, a surgeon is "locked into" using a particular robot's instrumentation and visualization and software. In 10 years, a surgeon will be able to choose visualization from one company, instrumentation from another.

Standardization and improvement of surgeons' performance As in manufacturing, digital surgery platforms will use information and standardized processes to reduce variability, optimizing surgeons' outcomes across the board.

PILLARS OF DIGITAL SURGERY

01 ROBOTICS

02 ADVANCED IMAGING

03 MACHINE LEARNING

04 ADVANCED INSTRUMENTATION

05 BIG DATA

ASCs: Surgery Moves Out of the Hospital

Low-acuity surgeries and procedures (joint replacement, cataract surgery, endoscopy) are performed in various settings: **ambulatory surgery centers** (ASCs), hospitals or hospital outpatient departments. Though the explosive growth of ASCs has leveled off since the mid-2000s, the number of centers and surgeries performed there continues to increase. Hospitals, which formerly opposed the formation of ASCs, are now opening new ASCs on their own or in joint ventures with physicians.

ASC ATTRIBUTES:

01

Ownership Any number of parties: physicians, management companies, hospitals.

02

Location Anywhere, subject to certificate of need (CON) programs currently active in 34 states. CON programs regulate the opening of new healthcare facilities in a given location.

03

Reimbursement Approximately 60% of what hospitals are paid for any given procedure (due to different payment schedules for ASC- versus hospital-based procedures).

04

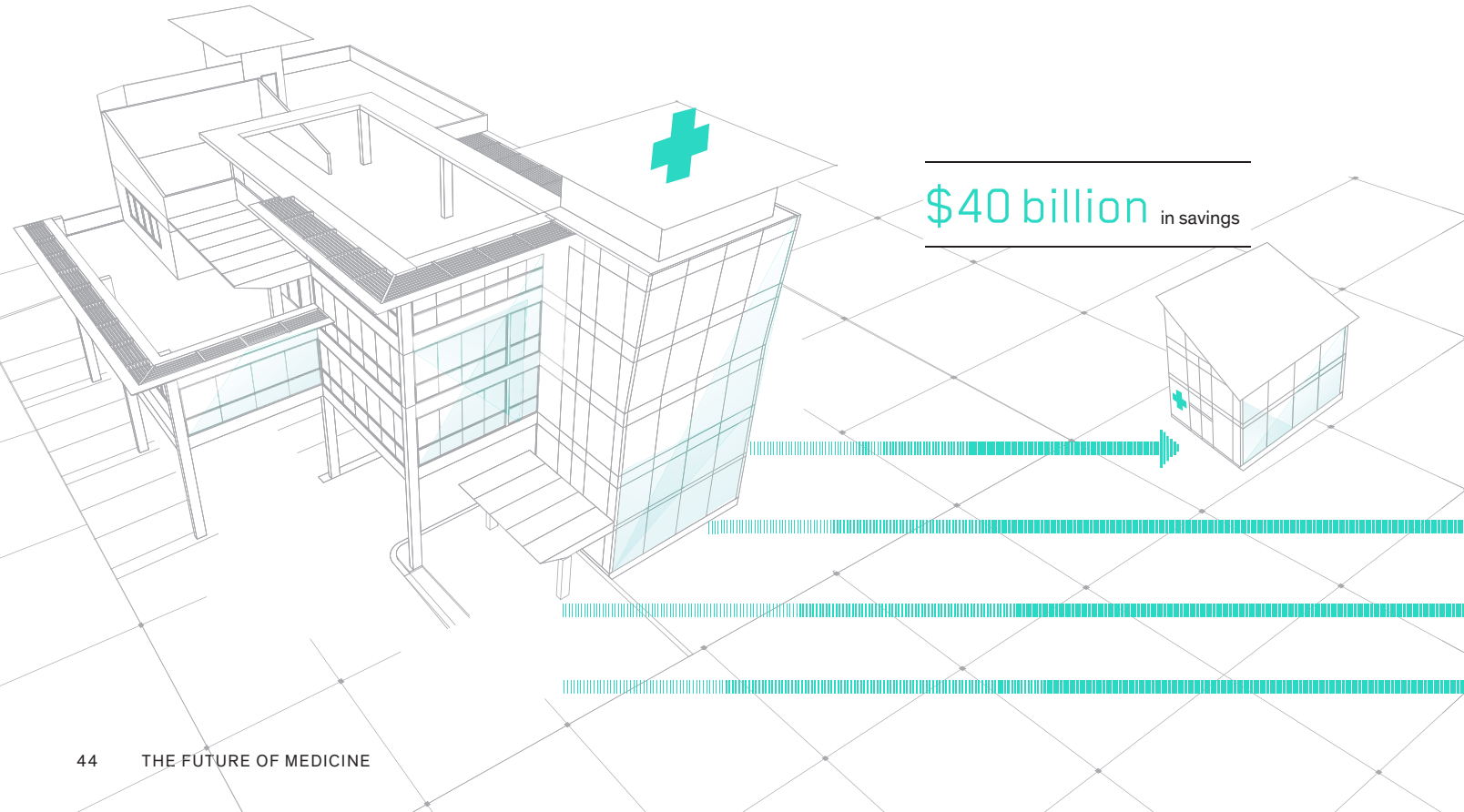
Cost of care Savings of more than $40 billion for procedures in ASCs versus a hospital. For example, in 2014, cataract surgery cost $2,932 in an ASC, $5,672 in a hospital. Savings would also accrue to patients themselves; it's estimated that a family of four would save $525–$874 a year if all outpatient surgery was reimbursed at ASC rates.

05

Efficiency 25% increased efficiency in ASCs over hospitals.

06

Quality Similar or superior to hospital-based care.



$40 billion in savings

THOUGH THE TOTAL NUMBER OF SURGERIES will increase, the conditions for which surgery is needed will **decrease**.

COMMON SURGERIES (PER YEAR)	NONINVASIVE, EMERGING ALTERNATIVES
CATARACTS 3.6 million	**COMPOUND DROPS** that prevent oxidative damage and abnormal protein aggregation will prevent cataracts from developing
JOINT REPLACEMENT	**STEM CELL REACTIVATION** or implantation for cartilage regeneration
KNEE 700,000 (2030 estimate: 3.48 million)	
HIP 300,000	
SHOULDER 73,000	
ROTATOR CUFF REPAIR 250,000	**STEM CELL REACTIVATION** or implantation for tendon and muscle regeneration
SPINE PROCEDURES 1.4 million	**STEM CELL REACTIVATION** or implantation for degenerative disk disease
ANGIOPLASTY 600,000	**NANOPARTICLE "SWIMMERS"** that clear atherosclerotic plaques
CANCER TUMOR REMOVAL 200,000	**TARGETED THERAPIES** signal transduction inhibitors, apoptosis inducers, immunotherapy

07

Patient satisfaction Often higher in ASCs secondary to a number of factors (ease of parking, ease of navigating smaller buildings, care team focus on specific types of procedures).

Value-based models will push more low-acuity surgical care to ASCs, which deliver reduced cost, increased efficiency and patient satisfaction, and equal or better quality. Despite political opposition from hospitals that wish to preserve their higher reimbursement, the numbers are too compelling. Hospitals will still be the location for emergency/trauma/high-complexity surgeries. The number of ASCs will increase steadily (as will the number of ASCs with hospital partners) unless there is a closing of the gap in reimbursement between care in ASCs versus hospitals, in which case ASC-based care will accelerate dramatically.

CATARACT SURGERY COST 2014

$2,932 at an ACS

$5,672 at a hospital

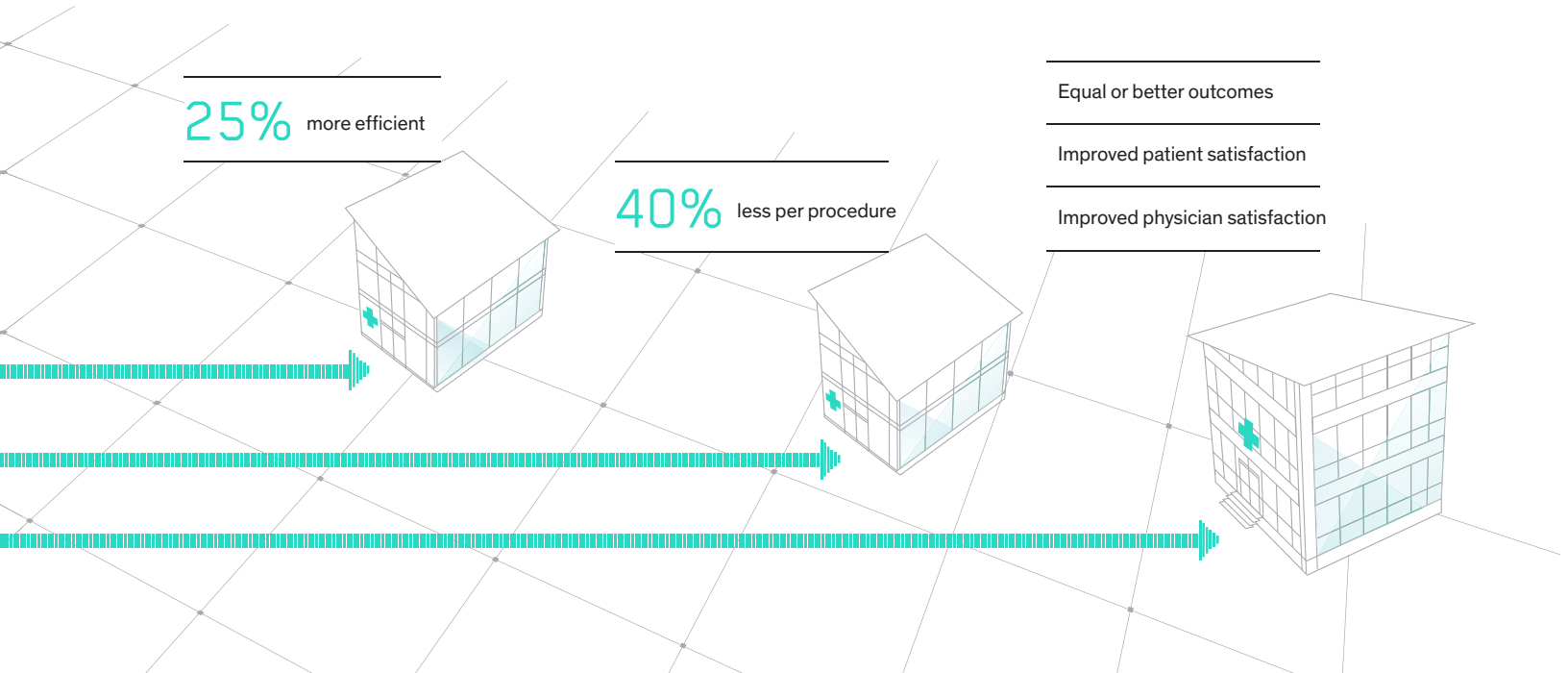
25% more efficient

40% less per procedure

Equal or better outcomes

Improved patient satisfaction

Improved physician satisfaction



The hierarchy of healthcare providers, with doctors at the apex of a pyramid, is flattening and broadening. Physician training will change radically as AI takes over diagnostics, VR/AR and robotics revolutionize surgery, and non-MDs take a larger role in delivering care.

The Provider Workforce

BACK TO SCHOOL: TRAINING DOCTORS

Until recently, medical school curricula had been largely unchanged since Abraham Flexner outlined the Structure/Process format of medical education in 1910. For most of the past century, students were trained in a binary system: two years of the basic sciences (anatomy and physiology, pathology and biochemistry) followed by two years of clinical training. That was fine for a world in which doctors learned, essentially, a trade that was:

01

hyper-rational

02

focused on sickness and acute care

03

targeted at individuals as opposed to communities

04

practiced (more or less unchanged) for decades.

But with the explosion of information and technology, the repositioning of the doctor from kingpin to team member, and the recognition that doctors are integral players in an enormously complex system, medical schools are being forced to adapt.

With input from organized medicine (the American Medical Association, the Association of American Medical Colleges, others) curricula have begun to change. Some schools have responded to the call for doctors to be more familiar with the rapidly evolving healthcare environment by adding courses in health systems science, medical economics and quality/safety measures. Competency-based education is gaining momentum. Recognizing that the information learned in medical school becomes rapidly out-of-date, some institutions have incorporated adaptive learning (learning how to learn) into their core training.

EVOLVING MEDICAL EDUCATION

We are in the middle of a paradigm shift in medical education. While there is yet no dominant, overarching philosophy like Flexner's, competency-based education may well crystallize into its replacement. Medical schools will be labs for experimentation. Gradually, new

best practices will emerge. In the meantime, look for the following changes to play out over the next ten years.

COMPETENCY-BASED EDUCATION

COMPONENTS
Identifying outcomes
Defining performance levels
Creating a framework for evaluation
Continually assessing programs

DOMAINS
Patient care
Knowledge for practice
Practice-based learning
Interpersonal/communication skills
Professionalism
Systems-based practice
Interprofessional collaboration
Personal & professional development

MORE COMPETENCY-BASED CURRICULA, MORE ADAPTIVE LEARNING ELEMENTS

One early example: Stanford and Khan Academy are piloting a program for self-directed medical coursework.

MIXED REALITY

Virtual reality and augmented reality will continue to make inroads into medical education. VR systems allow students to experience surgery more intimately (and at scale) than trying to see over a surgeon's shoulder, and the addition of haptic feedback to surgical VR training modules will enable students to train in hands-on simulated environments. VR is already being used to enhance empathy, for example, by letting students experience life as an 80-year-old man with hearing and vision problems. **VR/AR anatomy will take students inside the body and give them exposure to the dynamics of disease progression, physiological changes and the effects of interventions.**

VR currently used in medical education:

01

CPR training for medical providers and patients (Next Galaxy and Miami Children's Health System developing modules to teach CPR)

02

Surgery instruction from a first-person point of view (The Virtual Surgeon by Medical Realities)

03

Trauma simulations (Royal College of Surgeons in Ireland)

04

Empathy training (Embodied Labs and the University of Illinois, Chicago)

05

Anatomy (Unimersiv)

The impact of VR and AR will be felt beyond medical education as they become more integrated into practice. For example, surgeons already use VR to plan and practice surgery before ever cutting the patient.

MD + IT

Technology won't just change how doctors learn, but what they learn. In addition to EHRs, 70% of physicians used electronic resources during patient consultation hours in 2016, up from 47% in 2014. Medical school curricula and postgraduate training will need to prepare doctors to be more effective using digital tools like messaging, video chat, AR and VR. More students will be offered classes in interpreting AI-generated data and making individual treatment recommendations for specific patients (like a course currently being offered by Harvard-MIT).

MORE THREE-YEAR MEDICAL DEGREES

Currently, there are nine medical schools that offer three-year degrees. More are planned. Though some programs track students into primary care, others offer access to specialty training. First-mover schools will have a competitive advantage for applicants who know the specialty they'll pursue, want to open time for additional training and/or want to reduce their debt burden.

By compressing core medical curricula (basic science, organ system, core clinical rotations) into 2.5–3 years, medical schools will allow students to gain additional training in nonclinical disciplines—innovation and translational medicine, healthcare policy and organizational science, data science and genomics. For example, Mayo Clinic School of Medicine in Arizona will enroll its first class in 2017, and all students will be awarded a certificate in science of healthcare delivery in addition to their MD. USC offers an accelerated four-year MD-MPH degree.

MORE COMBINED DEGREES, MD + OTHER

MD-MS, MD-MPH and MD-MBA programs will proliferate. There are currently 65 MD-MBA joint-degree programs, more than double the number in 2000. Such ancillary training will also move into post-graduate (residency) training, where elective time may be dedicated to more formal education (graduate degrees, for example).

TEAM PLAYERS, NOT SOLOISTS

Recognizing that medical care delivery is becoming more team-based, schools will shift their focus in the types of applicants they admit. There will be less emphasis on individuality, more on collaborative potential. Tools to evaluate candidates' soft skills (like the McMaster Multiple Mini Interview) have been adopted by many schools internationally and will gain traction in the United States.

MED SCHOOL 2.0: BALANCED AND FLEXIBLE

Medical school applicants' attitudes toward the profession will be "push-pull," both responding to changes in the job market and forcing changes. Expectations of autonomy will adjust downward, both structurally (working as an employee instead of as a practice owner, for example) and in practice (following protocols and AI-generated diagnoses and treatment plans). Conversely, the demand for work-life balance will intensify. More schools will train students for practice in their own systems, e.g., Kaiser's new school of medicine, opening in 2019.

INTEREST IN PURSUING A MEDICAL DEGREE WILL REMAIN HIGH

Currently, less than 40% of medical school applicants actually gain admission to medical school. Even a significant falloff in applications will still result in most (if not all) medical schools filling their classes.

Disrupting the Doctor

By 2025, the Association of American Medical Colleges predicts that there will be a shortage of up to 95,900 doctors (35,600 primary care MDs and 60,300 specialists) despite a 25% increase in the number of graduating medical students 2002–2016. The major drivers are an aging population and the Affordable Care Act, which brought millions of new patients into the healthcare system.

However, the rise of nonphysician providers and the influence of technology will be profound, and we predict that the perceived doctor shortage will become a doctor glut for some specialties.

"Aspects of endocrinology, anesthesia, intensive care and radiology are primarily data driven, therefore they would be some of the early areas ripe for the use of AI, ML and automation." **—Sumbul Desai, Apple and Stanford University**

RADIOLOGY IS THE CANARY IN THE COAL MINE

A radiologist's job is to analyze data and look for patterns and deviations from patterns, things that computers and AI do well (and computers don't need to sleep). AI will pre-read images—highlighting areas of concern and offering possible diagnoses, noting incidental findings—cutting down on read times and, despite an overall increase in medical imaging, reduce the total amount of work for radiologists. Technological dislocation and imbalanced labor supply-demand mean that the disruption of radiology is in full swing:

01

Enlitic's deep learning radiology platform performed 50% better than human radiologists in classifying malignancies and had a false-negative rate of 0%.

02

IBM's acquisition of Merge Healthcare gave Watson a 30-billion-image dataset from which to learn radiology.

03

Radiology as a specialty is becoming less attractive:

- 10% drop in residency slots 2013–2017
- 30% of radiology residency programs unfilled in 2016
- Starting salary decrease from $450,000 to $300,000.
- Competition for radiology residencies—one of the most in demand as recently as 2009—was by 2014 less than that for pediatrics, historically one of the less competitive.

"I think if you work as a radiologist, you're like the coyote that's already over the edge of the cliff but hasn't looked down...People should stop training radiologists now."
—Geoffrey Hinton, Creative Destruction Lab's Machine Learning and the Market for Intelligence conference, October 2016

"It is inevitable that, in the future, the majority of physicians' diagnosis, prescription and monitoring, which over time may approach 80% of total doctors'/internists' time spent on medicine, will be replaced by smart hardware, software and testing."
—Vinod Khosla, September 2016

PATHOLOGY HAS A SIMILAR PAST TO RADIOLOGY, SIMILAR FUTURE

Like radiology, pathology relies on image analysis, pattern recognition and identifying deviations from the pattern—elements amenable to AI. Now, clinical pathology relies largely on glass slides and light microscopy, but anything that can be digitized will be digitized. Though FDA clearance for digital pathology has been slow, certain uses have been approved (e.g., immunohistochemistry image analysis). A "whole slide" imaging platform from Philips has just been approved. The trend toward digital pathology will continue, and the US will follow the EU, where CE-IVD mark has allowed clinical platforms since 2014. We anticipate that pathology, like radiology, will move closer to clinical medicine.

RADIOLOGY AND PATHOLOGY MAY COMBINE INTO A NEW SPECIALTY, INFORMATION SPECIALIST

As suggested by Saurabh Jha and Eric Topol, information specialists won't focus on extracting information from histology and images, but rather manage AI-extracted information and place it in the clinical context of the patient.

COGNITIVE SPECIALTIES WILL CEDE GROUND TO ALGORITHMS

Hematology, endocrinology, nephrology and cardiology all rely on collecting, analyzing and synthesizing data. AI anticipates sepsis before there are observable symptoms, allowing for early and more effective interventions. In hematology, an AI algorithm predicted outcomes for certain treatments in chronic myeloid leukemia. Heart disease, kidney failure and diabetic crises move at a slower pace than sepsis, but likewise rely on data inputs.

PRIMARY CARE DOCTORS' RESPONSIBILITIES WILL MOVE UPSTREAM

Much of day-to-day primary care is algorithmic and driven by protocols, and can be off-loaded to AI and midlevel providers. Increasingly, primary care physicians will lead midlevel teams, focus on complex cases, and manage triage. However, as triage itself becomes more protocol based, AI will begin to make triage decisions. For all cognitive specialties, including primary care, technological inroads will allow doctors (and midlevels) to concentrate on challenging cases and the human aspects of medicine: effective communication, empathy and ethics.

ANESTHESIOLOGY WILL EXPAND OUTSIDE THE OR

Even as increases in surgical volume mean greater need for anesthesia services, the need will be met with more nurse anesthetists and other midlevels (with and without MD supervision) and with technology. (Johnson & Johnson's robot anesthetist, Sedasys, delivered high quality care at a fraction of the cost of an MD anesthesiologist, but was pulled from the market largely because of political opposition from anesthesiologists. We anticipate that this is a temporary setback for robotics in anesthesiology.) Anesthesiologists will be forced to prove their value as the need for MDs in the OR decreases. MD anesthesiologists' scope of practice will broaden to include more perioperative care and care coordination, with the anesthesiologist "quarterbacking" care teams.

2016: Sedasys system proven effective, but pulled from market because of anesthesiologist pushback

MANY ASPECTS OF PROCEDURAL MEDICINE WILL BE PROTECTED FROM AUTOMATION

Technology will assist, rather than replace, surgeons and proceduralists. For some specialties, components of p ractice will change. Dermatologists, for example, may not evaluate a lesion's malignancy—which will be done remotely with cell phone pictures fed through AI—but will still perform the biopsy.

2016: An AI algorithm performed as well as dermatologists in assessing common malignant lesions

INTEREST IN CLINICAL INFORMATICS WILL INTENSIFY

The Clinical Informatics subspecialty was officially recognized by the American Board of Medical Specialties in 2011. Formal fellowship programs began in 2014 and have grown from one (at Stanford) to 26. The deluge of collected health data, the increasing use of AI and analytics to make sense of the data, and the challenges of applying it to clinical situations (both individually and to a population) mean that the demand for MDs formally trained in clinical informatics will explode. Certification for nonphysicians in clinical informatics will also increase.

400 surgeries

Successful use of a closed-loop autonomous robot anesthetist, 2016 clinical trial

The Doctor's Assistants Will See You Now

THE GEOGRAPHIC MALDISTRIBUTION OF DOCTORS WILL MATTER LESS

As some policy experts suggest, maybe there's not an overall shortage of doctors, just a shortage in some places (and an oversupply in others). Washington, DC, has 103 doctors per 100,000 people; Mesa, AZ, has 50. Telehealth, telemedicine and remote monitoring mean that many cognitive physicians will be able to live anywhere. In other words, a doctor living in DC will be able to treat and coordinate care (delivered on the ground by nonphysicians) for a patient in Mesa. However, the regulations governing telehealth—for both reimbursement and licensure—are complex, confusing and often set at the state level. Though political will to advance telehealth appears to be building, the lack of standard policies continues to hinder large-scale adoption.

- 48 states have some form of reimbursement for telehealth in public (Medicaid) programs.
- 31 states and Washington, DC, have private-payer parity laws for telemedicine, up from 18 in 2013.

PROGRESS IN STATE TELEMEDICINE REGULATION

STATE POLICY	NUMBER OF STATES 2014	2016
Pay for **STORE-AND-FORWARD*** (in addition to real-time) services	9	13
Pay for **REMOTE MONITORING**	16	22
Confer **LICENSE/CERTIFICATE IN TELEHEALTH SERVICES**	8	9
Participate in the **INTERSTATE MEDICAL LICENSURE COMPACT**, allowing cross-state licensing	11	18

*Store-and-forward: asynchronous communication in which a patient sends data and a picture, for example, to a physician who will review later.

NONPHYSICIAN PROVIDERS WILL GROW IN NUMBER AND IN SCOPE OF PRACTICE, ALLEVIATING ANTICIPATED PHYSICIAN SHORTAGES

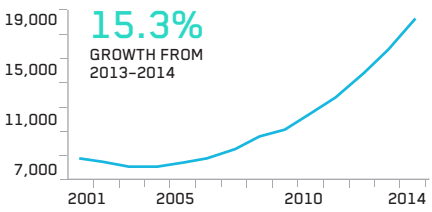
In primary care, nurse practitioners (NPs) and physician assistants (PAs) have been shown to deliver care equal to that of MDs and cost much less. Nurse practitioners have full practice autonomy in 23 states and Washington, DC, up from 20 in 2014. Nurse anesthetists can operate independently (without the supervision of an MD) in 27 states, including Washington, DC, up from 17 in 2014.

Even pharmacists are pivoting to clinical care. In California, pharmacists won the authority to prescribe certain medications, such as nicotine replacement and hormonal birth control.

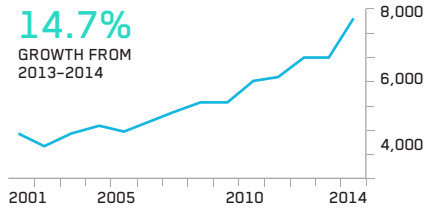
NUMBER OF NPs AND PAs, 2010–2016

	2010	2016
NURSE PRACTITIONER	106,000	150,200
PHYSICIAN ASSISTANT	80,000	115,500

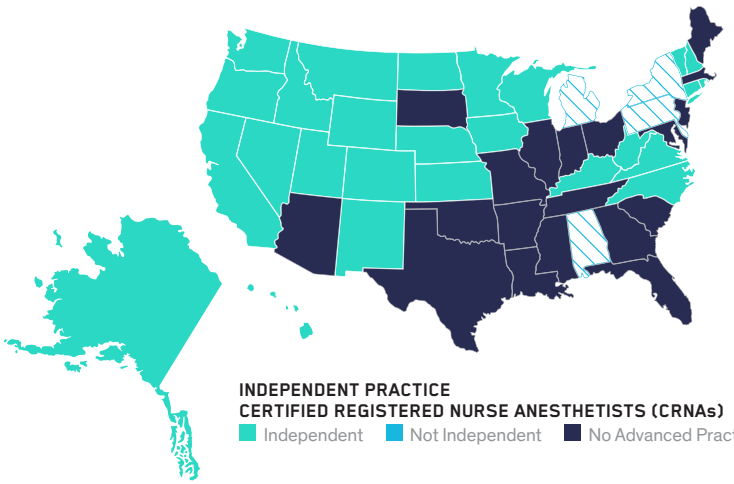
GROWTH IN NURSE PRACTITIONER GRADUATES, 2001–2014



PHYSICIAN ASSISTANT PIPELINE GROWTH, 2001–2014 (NEWLY LICENSED PAs)



No study has found a difference in the quality of care delivered by nurse anesthetists versus MD anesthetists.



"Using midlevels [NPs and PAs] for primary care is very effective [and is] a way forward to tackle the primary care shortage." **—Fredric Meyer, dean of Mayo Clinic School of Medicine**

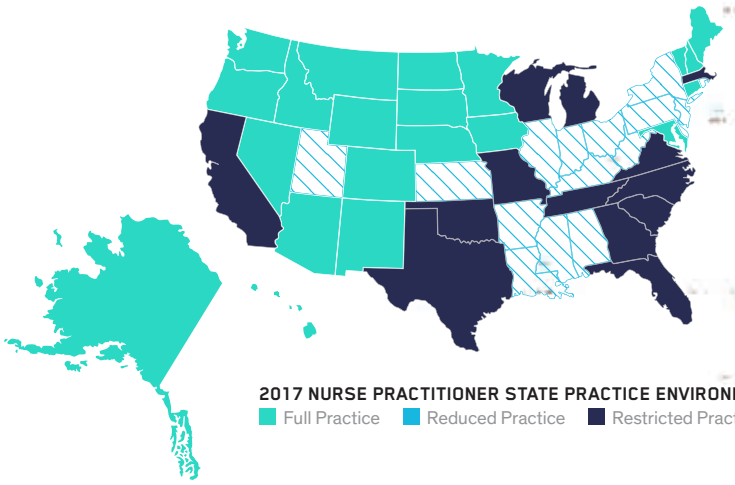
THE RELIANCE ON UNLICENSED ASSISTIVE PERSONNEL (UAP) WILL INCREASE

UAP are the nation's nursing assistants, home health workers and others who provide bedside care and help with patients' daily activities. Already in hypergrowth, the market for UAP will intensify, driven primarily by demographic trends, e.g., the aging population. Active remote patient monitoring and AI-assisted predictive analytics (engaging the patient before she gets sick) mean that healthcare will move further downstream, from doctor to nonphysician provider to UAP and (finally) to the patient. MOOCs and Khan Academy–type open courses will allow UAP to acquire specific skills for semi-skilled duties.

THOUGH THE RANKS OF UAP WILL SWELL, SOME NONPHYSICIAN HEALTHCARE WORKERS WILL SEE THEIR JOBS CHANGE (OR DISAPPEAR)

At medical centers such as UCSF, Geisinger Health and the University of Pittsburgh, **robots** perform orderly duties (delivering lab specimens,surgical supplies, meals, linens, etc.). At UCSF, a robot pharmacist has delivered more than a million prescriptions over five years with 100% accuracy, replacing five pharmacy technicians.

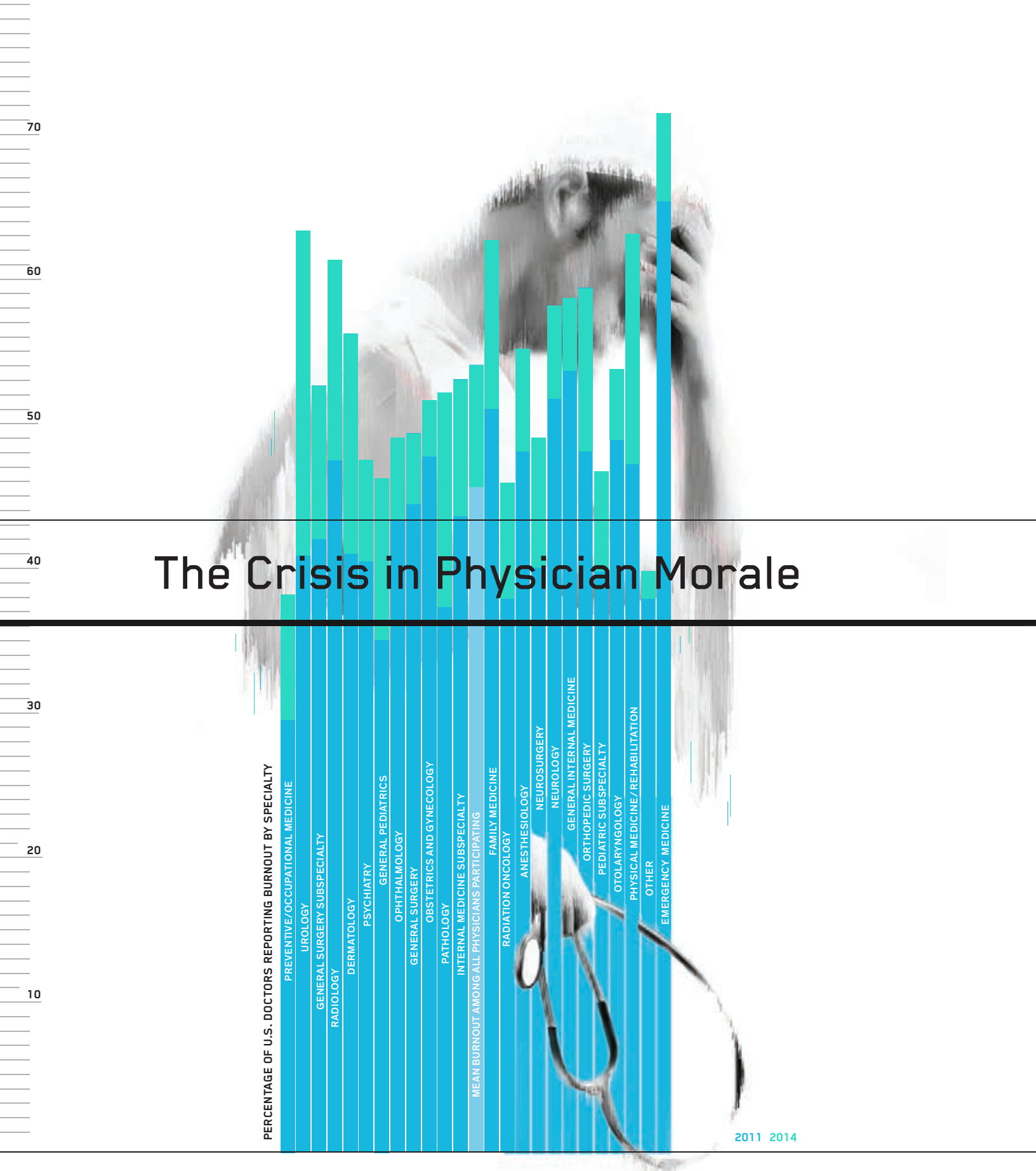
In primary care, nurse practitioners deliver as high quality care and produce as good health outcomes as MDs.



2017 NURSE PRACTITIONER STATE PRACTICE ENVIRONMENT

Full Practice | Reduced Practice | Restricted Practice

The Crisis in Physician Morale



"It's hard for anyone outside the profession to understand just how rotten the job has become."
—Daniela Drake, MD

Buried in paperwork, snarled in endless technology turnover, hemmed in by increased performance monitoring and challenged by a new breed of empowered (and often ill-informed) patients, morale among doctors is at the lowest levels ever recorded.

Over half of physicians are burned out and/or dissatisfied with their work-life balance, which compares unfavorably to the general employed population. More than 60% of doctors are somewhat or very pessimistic about the future of medicine, and over half of doctors would not recommend a career in medicine to a young person, with some surveys going as high as 90%. A survey of doctors and nurse practitioners showed that both groups were more likely to recommend that students become nurse practitioners rather than primary care physicians.

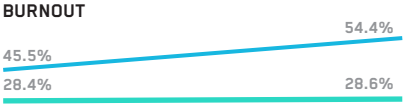
One major academic medical center saw burnout rates increase from 24% to 36% from 2013 to 2016. During the same time frame, reported "high professional fulfillment" fell from 24% to 14%.

THE TOP 5 MOST BURNED OUT SPECIALTIES

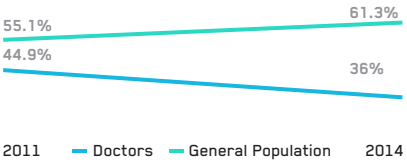
- EMERGENCY MEDICINE (>70%)
- UROLOGY (63.6%)
- PHYSICAL MEDICINE AND REHABILITATION (63.3%)
- FAMILY MEDICINE (63%)
- RADIOLOGY (61.4%)

Nine specialties showed a **>10% increase** in burnout 2014 over 2011.

BURNOUT



SATISFACTION WITH WORK-LIFE BALANCE



Our physicians are burning out en masse. Will improved industry policies and assistive technology arrive in time to turn the tide?

CAUSES OF BURNOUT

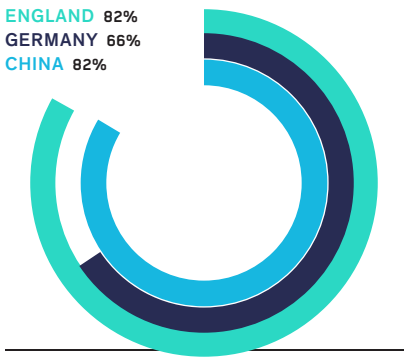
- Loss of autonomy and control over work
  - Too many bureaucratic tasks
  - Too many patients
  - Feeling like "a cog in a wheel"
- Increased performance measures (quality, cost, patient satisfaction)
- Increased complexity of medical care
- Technological fatigue, especially EHRs
- Changes in the doctor-patient relationship (shift from "patient" to "healthcare consumer"), i.e., difficult patients

Maintenance of certification (MOC) is also a driver of physician dissatisfaction. MOC is a recertification program that allows doctors to maintain specialty board status and consists of completing training and evaluative modules, and taking an exam. Doctors complain that it is too burdensome: expensive and time consuming. Internists will spend an average of $23,607 each in MOC costs over 10 years. The cumulative cost of MOC to the healthcare system is estimated to be $5.7 billion over 10 years.

SYMPTOMS OF BURNOUT

- Emotional exhaustion
- Increased depersonalization
- Decreased sense of personal accomplishment
- Depression
- Suicidal ideation

INTERNATIONAL PHYSICIAN BURNOUT



$250K–$1M

Cost to replace one physician

CONSEQUENCES OF BURNOUT

- Early retirement, scaling back clinical duties
- Decreased patient safety
- Decreased quality of care
- Increased healthcare costs
  - More testing and referrals
  - Greater malpractice risk

Physician burnout doesn't just affect doctors. It affects all of us. Burned out doctors make more mistakes and appear to deliver lower quality of care. Beyond patient care and doctor well-being, burnout impacts the bottom line. Replacing a physician who retires early or leaves medicine to pursue other career opportunities costs **between $250K and $1M**.

AND PHYSICIAN BURNOUT ISN'T JUST A US PHENOMENON

82% of physicians in England experience mental illness. In Germany, 66% of physicians report some degree of burnout. In China, it's 82%.

"If I wanted to work on an assembly line, I didn't need to go to medical school."
"Nothing will change because we are completely expendable."

—Physician comments to "Physician Burnout Is a Public Health Crisis: A Message to Our Fellow Health Care CEOs," in *Health Affairs*, 2017

Doctor Suicide

Physician suicide is estimated to be 400 annually, one of the highest rates among all professions. Advocates maintain that physician suicide is under-reported, hushed up, masked. Physician deaths from "accidental overdoses" may actually be suicide, since doctors are unlikely to overdose on medications.

40% of US physicians screened positive for depression. 7.2% had thoughts of killing themselves in the previous 12 months, compared with 4.0% for the general population. And doctors don't just think about suicide more than the general public—they actually do it more. They're better at suicide. Greater knowledge and access to lethal methods mean physician completion of suicide is higher than that of the general public, 1.4–2.3×. Female completion is even higher: 2.5–4× that of the general public.

400/year

Estimated physician suicides

American Doctors Are Killing Themselves and No One Is Talking About It
The Daily Beast, March 2015

Why Doctors Are Sick of Their Profession
The Wall Street Journal, May 2016

The Hidden Epidemic of Doctor Suicides
Fast Company, February 2016

The Story Behind Epidemic Doctor Burnout and Suicide Statistics
Forbes, January 2016

The Way Forward

A 2016 AMA summit described burnout as a matter of "absolute urgency." Healthcare leaders have publicly pledged to systematically track and measure physician well-being. The AMA, Stanford and the Mayo Clinic are developing a national consortium on physician wellness.

WAYS TO IMPROVE PHYSICIAN MORALE

- [ ] Optimize **physician support** in the practice environment
- [ ] Train healthcare leaders to **foster physician engagement**
- [ ] Improve physician **career fit**
- [ ] Foster a sense of **community and flexibility**, thereby giving physicians more control
- [ ] Create **programs** for physician well-being

ZERO PAPERWORK, EFFORTLESS DATA CAPTURE

Making doctors' lives easier is a booming business. The healthcare AI sector is growing 50% a year, and is expected to top $10 billion in 2023. Some early standouts:

AUGMEDIX uses AR headsets to stream doctor-patient interactions to remote scribes, reducing documentation time by 80% and saving doctors up to three hours a day.

HEALTHTENSOR reviews data in patients' medical records to help doctors instantly pick the correct ICD codes for diagnoses and procedures—out of 68,000 possible choices.

CLOUDMEDX combs through patients' medical histories and clinical databases to give doctors real-time risk assessment and decision support during patient visits.

Improvement will accelerate as physician wellness is tied to existing metrics: patient satisfaction, quality of care, productivity. In addition to more traditional cost centers (supplies, capital equipment), healthcare organizations will account for the true price of physician burnout. Standout organizations will highlight physician satisfaction to boost recruiting.

Complicated EHR systems are the bane of physicians' workdays. Most doctors spend almost twice as much time wrestling with EHRs and other desk work as they spend with patients. In order to retain physicians, hospital systems will pressure existing EHR vendors to improve user interfaces—or they will upgrade to new, improved EHR systems.

In the near term, hospitals and practices will unburden physicians of clerical/administrative duties via medical scribes, who follow doctors through their clinical rounds, taking notes and completing data-entry tasks. Studies show that scribes have a positive impact on both physician satisfaction and productivity. By 2020, the number of medical scribes helping doctors is projected to jump to 100,000, a 5× increase from 2014.

Doctors' experience in the workplace will improve even more dramatically through the 2020s, as automated data collection and AI-powered decision support unburden them from routine tasks, streamline complex processes and reduce the stress of sifting through patient data to find needles in medical-record haystacks.

Today, mental health care is a combination of social support and pharmaceutical intervention. This approach has failed to stem the rising tide of mental illness in the US. Will major advances in genetics, brain imaging and technology inside and outside the body supplement, alter or replace these standards?

THE COMING MENTAL ILLNESS PANDEMIC

Rapid urbanization will spark a significant rise in a wide range of neuropsychiatric illnesses, including depression, anorexia, anxiety, post-traumatic stress disorder, psychosis and schizophrenia. All of these disorders have been linked to the stresses of living in megacities.

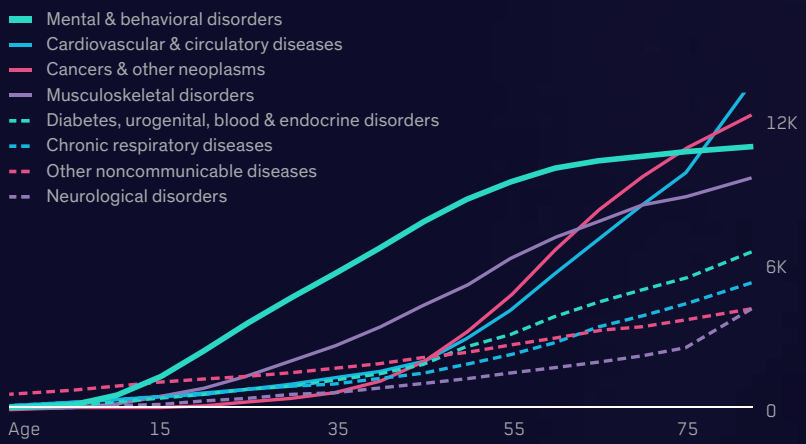
Children growing up in cities, for example, have twice the odds of developing schizophrenia in adulthood than children living in rural settings. By 2025 more than 60% of the world's population will live in large, sprawling cities.

The biological and psychosocial triggers for this impact on mental health have yet to be fully identified.

Redefining Mental Health Care

As research and volumetric imaging reveal a more detailed account of the causes of mental conditions, and digital diagnostic tools and interventions take over from pharmaceuticals, psychiatry will move back into the hospital.

Bioelectronics companies will replace pharmaceutical companies, as sensors, chips and telemetry data become essential to diagnosis, treatment and tracking patient data.



MENTAL ILLNESS LEADS ALL DEBILITATING FACTORS BETWEEN AGES 15–70
Cumulative years lost to disease/disorders by age

Poverty, higher crime rates and lower social cohesion are likely factors. Urbanization and migration lead to the breakdown of families, kin networks and communities. That loss of social capital increases stress on individuals.

Although the rise in mental illnesses in urban environments likely has social causes, drug companies have been actively trying to convince foreign populations to adopt a Western "brain disease" narrative. To date, Western drug treatments, including antipsychotics and antidepressants, have become popular in cultures across industrialized Asia and Africa. The diagnosis of "depression" was rarely used in Japan, for instance, until drug companies effectively marketed antidepressants there in the early 1990s. Now the condition is commonplace.

"The care provided for the mentally ill in the US is a disaster that shames our country."
—Dr. Allen Frances, chair of the DSM-IV Task Force

50% Nearly half of people with a mental disorder meet criteria for two or more disorders

9M Almost 9 million people have both a mental and a substance abuse disorder

REDEFINING DISEASE

The borders of mental illness categories are dynamic, culturally influenced and focus almost exclusively on groupings of symptoms. **In recent years, "not otherwise specified" has been used as often as any of the specific diagnostic categories of the Diagnostic and Statistical Manual for Mental Disorders (DSM).** Diagnostic categories are created by consensus but show high levels of comorbidities and common symptoms. For example, mood and anxiety disorders are themselves comorbid with substance abuse and personality and eating disorders. **This conceptual muddle argues strongly for a reclassification of mental illnesses based on causes, not symptoms.**

Some research institutions have already abandoned the DSM—the "bible" of the mental health field—and have pioneered diagnostic systems based on measurable scientific indicators.

Machine learning algorithms will sift through mountains of data—from smartphones, metabolic biosensors, in-home sleep trackers, speech processors and body language monitors—to identify mental health "signatures."

Within the next decade, mental diseases will be defined, diagnosed and treated by AI.

The Digital Revolution in Mental Health

"Psychiatrists remain the only medical specialists that rarely look at the organ they treat."
—Dr. Daniel Amen, brain disorder specialist and director of the Amen Clinics

REINTEGRATION OF PSYCHIATRY INTO THE HOSPITAL

Successes in off-label use of implantable brain devices for sleep, arousal and attention will spur an elective brain enhancement industry. Robot-guided anesthesia, biological computer chips and AI-guided surgery will increase safety and cut surgical time drastically. Inevitably, these devices will be installed endoscopically, greatly enhancing their general adoption and elective appeal.

Advanced neuroimaging will become de facto in the diagnosis and treatment of many mental diseases, bringing psychiatric patients back into the hospital. Of course, someone will have to pay, given that NIMH data indicate that one in five Americans experiences a mental illness in a given year.

A dry central nervous system (CNS) drug pipeline and the hit-or-miss effectiveness of current CNS drugs will accelerate imaging-based drug efficacy studies. In combination with genomic data and stem cell–based in vitro drug screenings, these technologies will precede a revolution in personalized, patient-directed drug treatment. No longer will psychiatrists pull their first medications for a patient out of a hat. It might not even be psychiatrists doing the prescribing—psychiatry could become a radiological science.

A form of reinstitutionalization will become increasingly popular, modeled after addiction clinics. **Private addiction centers available today will be bought up or expand into psychotic and depressive treatment centers, all of which offer short-term treatment and care.** The balance between reinstitutionalization and personal autonomy will reemerge as a major social and political debate.

MENTAL HEALTH IS THE NEW DIABETES

Major neurodegenerative diseases and those often associated with aging will become "diabetes-like," requiring a lifetime of early detection, care and intervention. At a point when options to intervene match disease detection (via genomics, behavior tracking, imaging and/or biopsy), those neurodegenerative diseases found to be largely preventable will create a new class of "previvor" patients—up to 25% of the US—that need chronic treatment on a recurring basis. **Today's companies focusing on "brain training" will pivot to absorb this massive source of revenue, and private clinics will pop up everywhere offering regular treatments.**

Bioelectronic implants in the blood or CNS will monitor and one day intervene. As implanted, home and interventional sensors begin to allow homeostatic or metabolic feedback models for maintenance of many illnesses, "pacemakers" will find their way into the CNS.

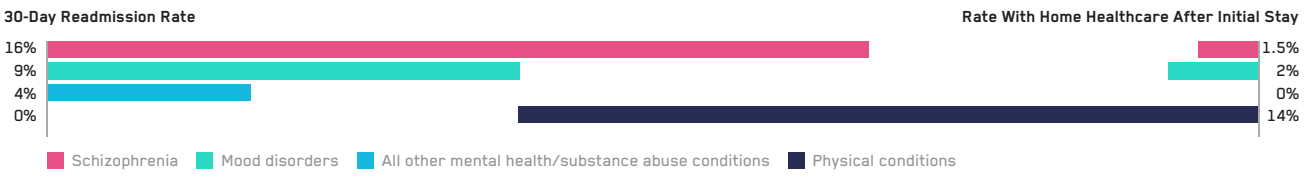
Depending on the adoption rates of embryonic prescreening, genetic intervention or assisted reproduction, genomic risk factors and accelerants for many age-related diseases will be removed from the general population in only a few generations. **Such genomic vaccinations will outpace research into a cure for such diseases.** Alzheimer's may never be cured, but simply removed from Western populations.

THE PSYCHOACTIVE COMEBACK

Today, drugs for mental disease are by and large variations of those deemed effective decades ago. These have failed to stem the rising tide of mental illness in the US. Succumbing to mounting social pressures, the FDA will reschedule the psychoactive components of many recreational drugs—MDMA, psilocybin, ketamine, ibogaine—and their derivatives.

Patentable derivatives will reawaken the dry CNS clinical pipeline and outmaneuver the social and legal complexities of adoption.

HOME HEALTHCARE IMPACT ON HOSPITAL READMISSION



"Recent data suggest that ketamine, given intravenously, might be the most important breakthrough in antidepressant treatment in decades." **—Dr. Tom Insel, former head of the NIMH**

SLEEP

One in three adults does not get enough sleep, despite its prominence in basic health. Apnea affects 18 million in the US, with a market of $4 billion per year in medical devices.

4% of US adults over age 20 use a prescription sleep aid.

It is thought that sleep disturbance is a core component in many psychotic and mood disorders, often exacerbating or causing some symptoms. As non-pharmacological sleep aid treatments become effective, diagnoses of sleep disorders will increase drastically. The major driver of bio-electronic, elective brain implants will be maintenance of sleep and wakefulness. The NIH will declare the 2020s the "Decade of Sleep."

Smart mattresses will record sleep patterns, light, temperature and pressure to personalize sleep. A combination of **AI and wearable sensors** will allow for precisely timed waking during the optimal sleep phase.

Active brainwave monitoring in combination with basic brain implants will be able to prevent or interrupt the memory and subjective experience of nightmares, relieving sufferers of trauma-related mental disease.

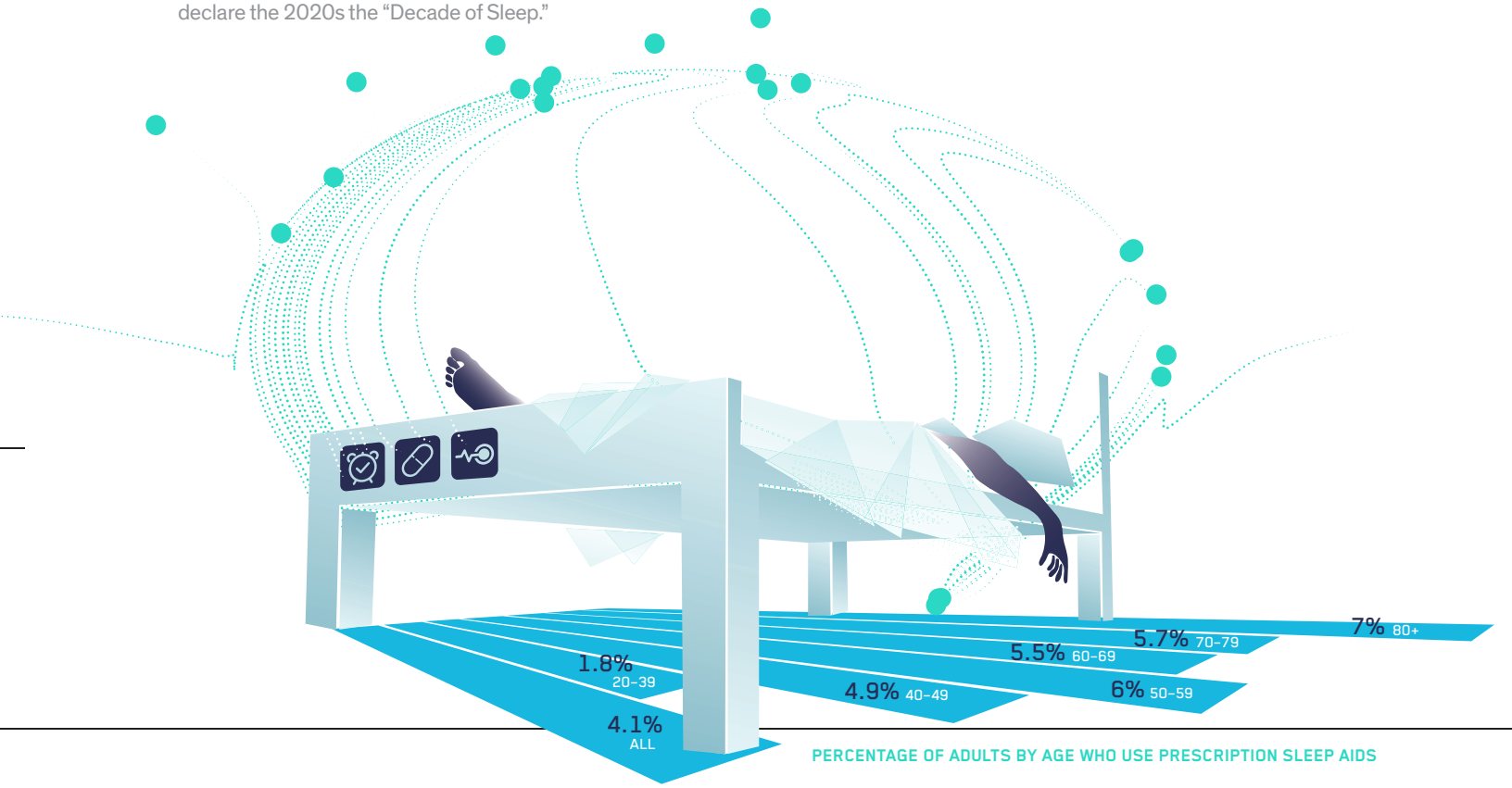
TECHNOLOGY SUPPLEMENTATION

On-demand therapy and cognitive training via smartphones, VR or telepresence will replace all but acute crises in psychiatry.

"Nudging" apps will subtly prompt beneficial behavior, and stress-reduction algorithms in navigation systems will route drivers with hypertension or anxiety around high-traffic areas.

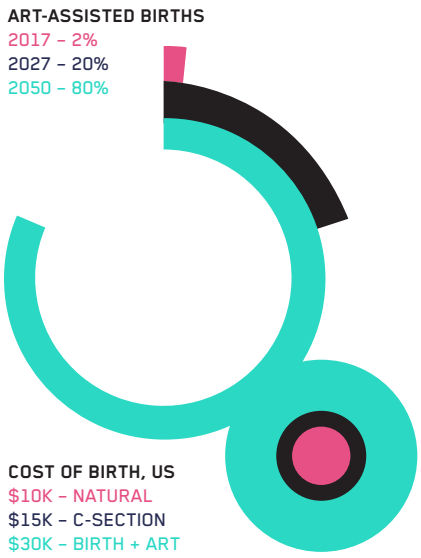
2,800 Sleep labs in the US

$7B Annual billings for sleep disorder diagnoses



PERCENTAGE OF ADULTS BY AGE WHO USE PRESCRIPTION SLEEP AIDS

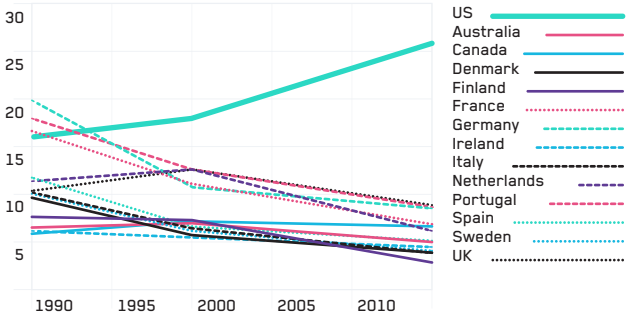
For the babies of the future and their parents, the potential benefits of assisted reproductive technology (ART) like germline editing and artificial wombs are undeniable. Which breakthroughs will prompt society to overcome traditional aversions to prenatal interventions? Safety first. Enhancement later.



The ART of Making a Baby

21st Century Pregnancy

26 WOMEN DIE PER 100,000 LIVE BIRTHS IN THE US, THE HIGHEST RATE IN THE DEVELOPED WORLD



MATERNAL SAFETY

More women die of pregnancy complications in the US than in any other developed nation. The US is the only developed country where maternal mortality is going up, not down. Our mortality rate is almost 400% higher than it is in Canada, 700% higher than in Italy. **Maternal safety concerns will drive initial willingness to use ART in the US.**

Infant health concerns will also accelerate use of ART. Despite a general squeamishness toward gene editing and human enhancement, 57% of Americans say they would use monogenetic germline editing to prevent severe disease in their own child.

The total average cost per birth in the US—including preterm, postpartum and standard obstetric care—is the most expensive in the world, 2–3 times higher than in Switzerland, the second most expensive of developed countries.

Today, there are 4 million births in the US at a cost of at least $50 billion per year. As interventional options increase, each with a cost, the whole process of reproduction and birth will become at least 2–3 times more expensive. **Total revenue in the US for birth-related care through 2050 will be at least $1.5 trillion.**

Today, ART contributes to around 64,000 births, 1%–2% of the total.

For the first time in human history, there are dozens of ways to make a baby. Soon, there will be many more. IVF and artificial insemination will be revolutionized by the ability to derive sperm and egg cells—gametes—from stem cells.

This technology will fundamentally alter the process of human reproduction from dating to mate selection to the legal and social understanding of parenthood. Marriage will become less common as it decouples from reproduction. Biologically, a baby will become more than the sum of its two parents.

THE RISE OF FERTILITY CLINICS AND BIRTH CENTERS

Stem cell–derived gametes may be labeled by the FDA as drugs or biological products and therefore be subject to approval. As a response, fertility clinics will segregate into non–disease altering (superficial-only traits, non–FDA regulated) and disease altering (FDA regulated).

These genomics companies will patent processes of removing individual diseases from genomes, rather than developing drugs to treat or cure them. Fertility clinics offering ART will pay license fees to—or, more likely, be owned by—genomics companies.

Today there are 500 for-profit fertility clinics, about 1 for every 11 hospitals in the US. As fertilization moves out of the hospital, thousands of birth centers will pop up by 2050, at least one per hospital in the US.

At first, prospective US parents will travel abroad for embryonic implantation and germline editing for basic disease traits but will return to the US to deliver the baby.

FERTILITY CLINIC EXPANSION

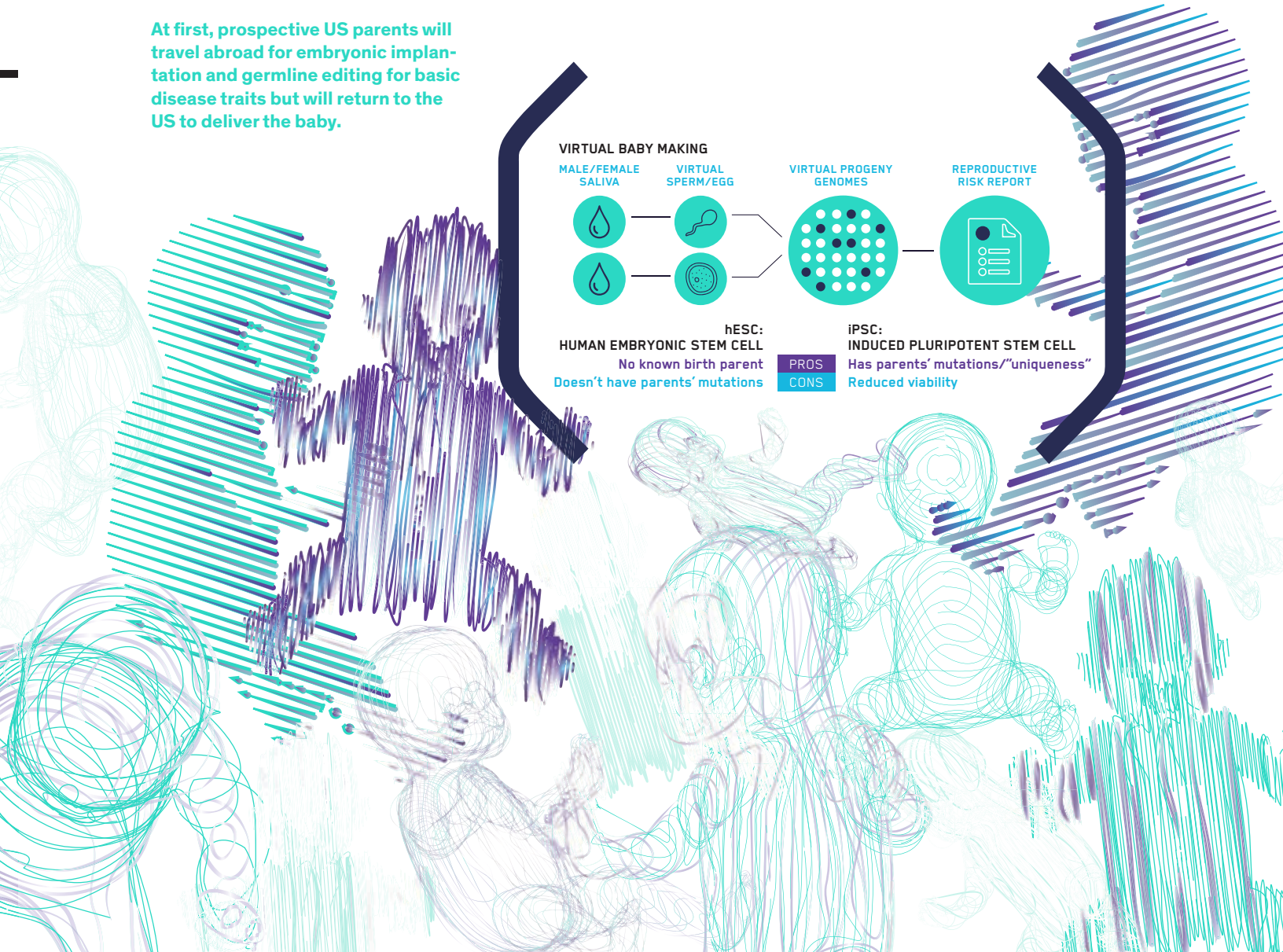
Fertility clinics in Europe, Asia and Mexico will offer germline editing at high cost based on less stringent regulations. Those children will be born in the US as full citizens. This will become a social and political issue as groups try to stop the practice by moving to deny "enhanced" children US citizenship.

Clinics could offer a range of technologies before fertilization to predict likely embryonic outcomes. Before having a child, couples may submit blood tests to AI companies like GenePeeks to learn their future children's genetic probabilities—and whether a union should even happen.

BIOLOGICAL BANKING

Today, there are around 500 cord blood storage banks. These will evolve to store many types of patient cells, including marrow and enhanced, modified immune cells, ready to be reinserted as medically needed. **As patients gain control of their medical records and gain at-will choice for medical service, their loyalty will tend to follow wherever their cells are banked.**

Genomic data from almost every ART baby will be stored, eventually finding its way into the hands of law enforcement and hackers. A dramatic reduction in certain types of crime will cause a societal upheaval as forensics teams gain access to genomic databases and more sensitive methods of DNA sequencing.



THE ARTIFICIAL WOMB WILL CHANGE EVERYTHING

Micro-term birth will become increasingly more common as synthetic blood and artificial womb technology makes early-term delivery viable. Pregnancies could be one to two terms shorter and much safer.

A fetus, for example, could be removed via C-section during the second trimester and placed into an artificial womb. A natural nine-month course will only be used for dangerous or natural births or for those who cannot afford early-term birth. **As a result, C-section will become the number one surgical procedure in the US.**

This will lead to a dramatic rise in both international and domestic surrogacy. Today, surrogacy costs an average of $100,000 to $150,000. Its popularity will increase as gestation cycles, cost and the risk of complications decrease, allowing a fertile woman to birth up to two children per year.

More than eight in ten women start breastfeeding their children after birth, but only 30% are still breastfeeding one year out. Smart breast pumps that track flow, quality and composition of milk will become a standard postpartum analysis service and revenue stream for hospitals. AI-based at-home crib tracking will alert the parent and hospital to any abnormalities in infant sleep or behavior.

THE NEW NORMAL

Worldwide there will be at least 3 billion births between now and 2050.

Technologies to generate sperm and egg from either sex and screen them for known genetic risks will allow up to 1 million people per year who cannot otherwise reproduce to have children "of their own," including infertile and gay couples. These are likely to be the early adopters of stem cell–dependent ART.

Uni-parenting—a single woman using induced pluripotent stem cells to fertilize her own egg with stem cell–derived sperm—will become increasingly common. **It will no longer take two humans to create a child.**

Legal custody and the concept of parenthood will become much more about rearing as so-called "multiplex parenting" allows a combination of up to 32 or more parental genomes.

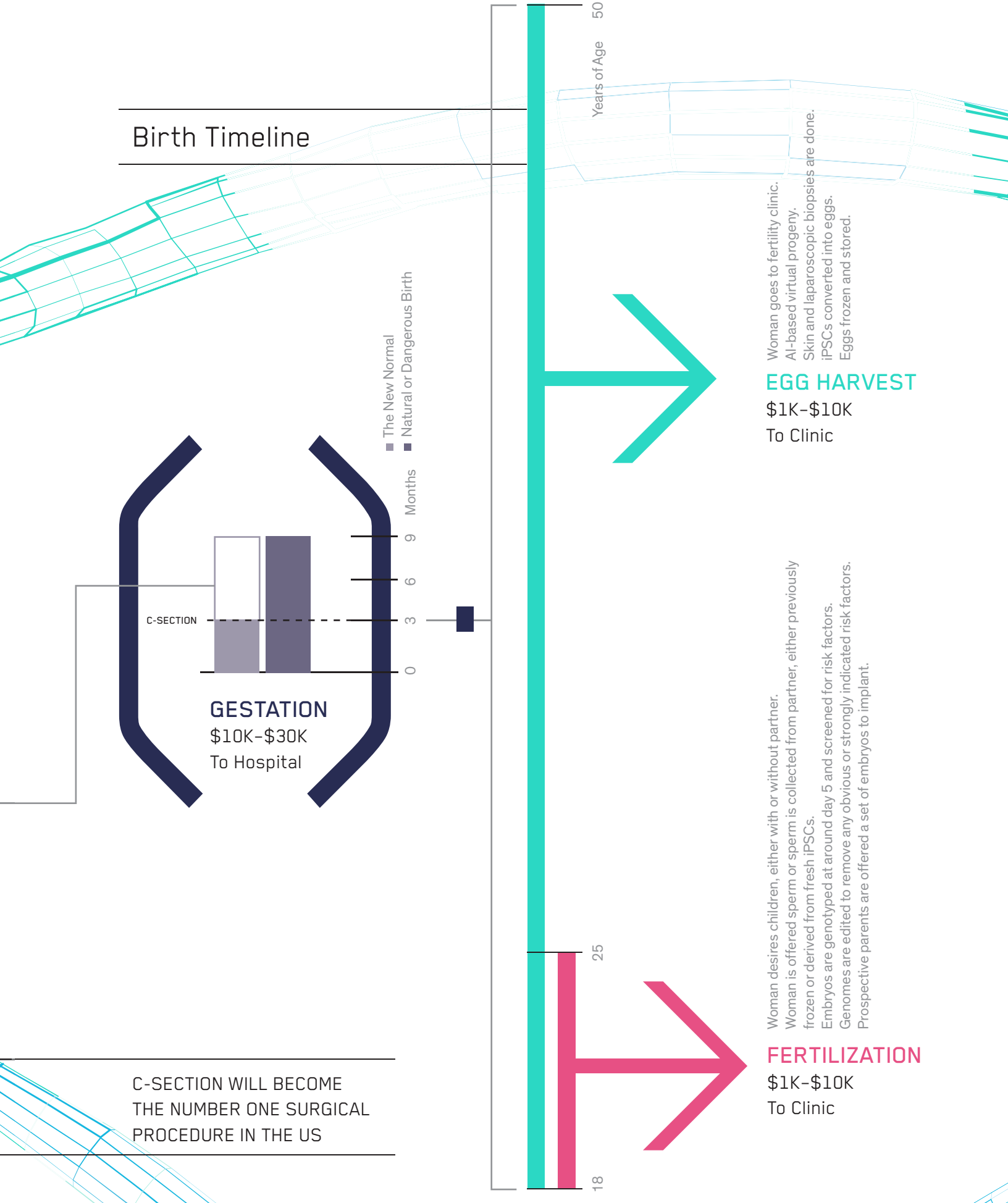
When ART becomes safe, cheap, reliable and preferable, permanent sterilization for both men and women at young adulthood will become near universal, drastically reducing or eliminating accidental pregnancies.

ARTIFICIAL WOMB

3 Billion Births

Between Now and 2050

Birth Timeline



Woman goes to fertility clinic.
AI-based virtual progeny.
Skin and laparoscopic biopsies are done.
iPSCs converted into eggs.
Eggs frozen and stored.

EGG HARVEST

$1K–$10K

To Clinic

GESTATION

$10K–$30K

To Hospital

Woman desires children, either with or without partner.
Woman is offered sperm or sperm is collected from partner, either previously frozen or derived from fresh iPSCs.
Embryos are genotyped at around day 5 and screened for risk factors.
Genomes are edited to remove any obvious or strongly indicated risk factors.
Prospective parents are offered a set of embryos to implant.

FERTILIZATION

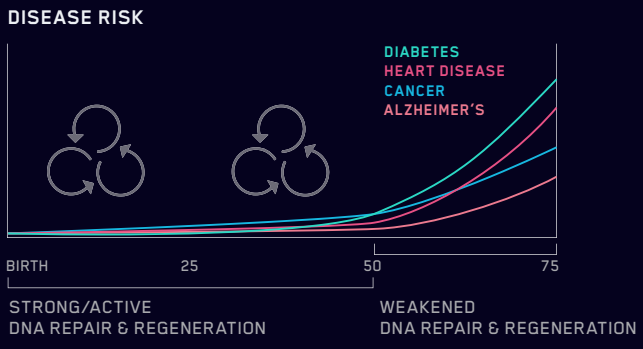
$1K–$10K

To Clinic

C-SECTION WILL BECOME THE NUMBER ONE SURGICAL PROCEDURE IN THE US

Regeneration

The greatest healthcare technology in the world is already here. It's in the bodies of young people, whose natural capacity to repair DNA and replace tissue keeps them well. What if we could hack those repair systems so their effectiveness did not decline with age? Instead of going after diseases one at a time, science is tackling them all at once by targeting the underlying susceptibility.



Early Inspirations

CALORIE RESTRICTION

Scientists have recognized since the 1930s that mice on calorie-restricted diets can live 2× longer. It's shown to work in every species studied. We just didn't know why it worked or how to safely take advantage of it. Gradually, science has drilled down on the metabolic and cellular mechanisms. A rhesus monkey at the University of Wisconsin is living to the human equivalent of 130 years old on a calorie-restricted diet.

PARABIOSIS

Old people have just as many stem cells as young people—so why don't they work just as well? In search of the answer, in 2005, Thomas Rando at Stanford connected two mice together, an old mouse and a young one, to share a circulatory system. Quite simply, the old mouse grew younger—because **compounds in the young blood reactivated the stem cells** of the old mouse, **triggering tissue genesis**. A race began to find exactly which compounds in young blood are at work.

TELOMERASE

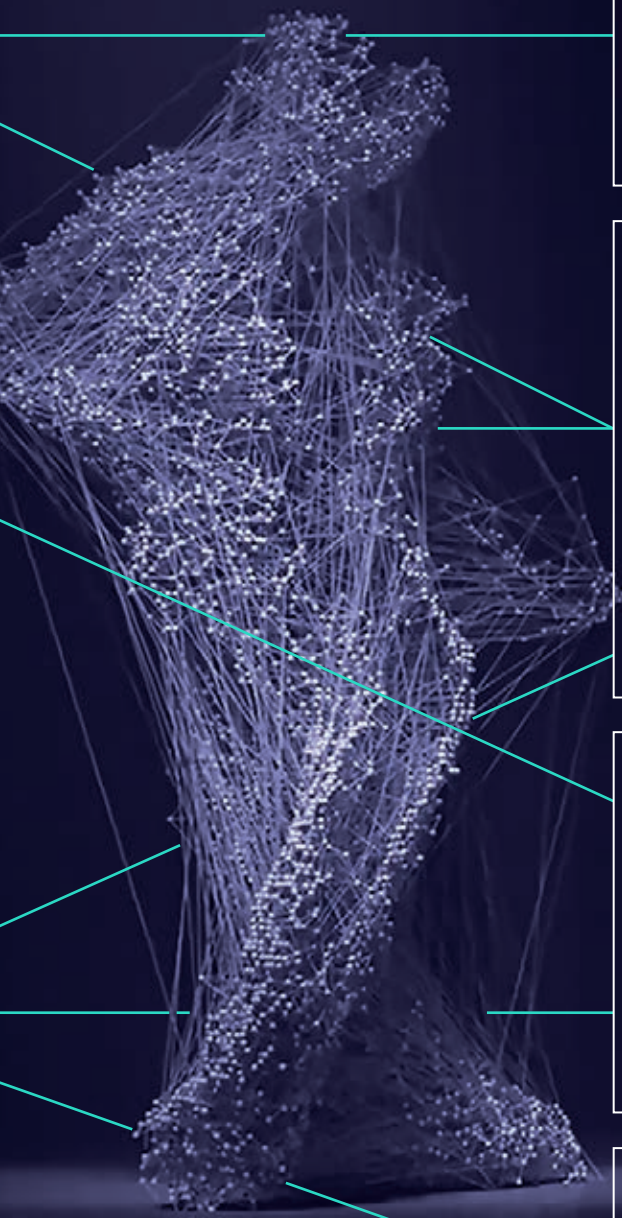
Telomeres are the caps on the end of our chromosomes. Every time a cell divides, the cap shortens. After 50 to 70 divisions, the cell will die because there's no telomere left. However, the enzyme **telomerase works to replace and repair the caps, allowing the cell to divide without limit**. For their work on the discovery of telomerase, Elizabeth Blackburn and Carol Greider were awarded the Nobel Prize in 2009.

"Sperm and eggs from older people still have the power to create a brand new baby. The genetic capacity for youth is in us all. Learning from that, we can trick our cells into thinking they're younger than they are." **—Elizabeth Blackburn, Nobel Prize winner**

"Age is by far the biggest risk factor for heart disease. It's seven times more important than high cholesterol." **—Eric Verdin, CEO of the Buck Institute**

A Decade Later

These scientific investigations into the biochemical pathways of aging have moved incredibly fast from the lab to commercialization.



The research on how **calorie restriction** slows aging has drilled down to the metabolism coenzyme NAD+, which regulates the sirtuin class of cellular mechanism proteins, critical to DNA repair. NAD+ is a coenzyme found in all living cells, but it declines with age. **Just putting drops of NAD+ into mice's drinking water led to obvious age reversal within a week.** The muscle tissue of 2-year-old mice soon had qualities identical to that of 3-month-old pups. Trials in humans are in the recruiting stage, and will focus at first on brain repair after a mild concussion.

When a cell's chromosomal telomeres shorten to the point it can't divide anymore, it enters a stage called **senescence**. It's kind of a zombie cell. Non-functional but not dead, it sends out poisonous signals to nearby cells—signals that both promote cancer and tell stem cells to stop their magic. Senescent cells are typically cleared by our immune system, but as we age, our immune system falters and the cells accumulate. They can comprise 10% to 15% of an older person's body.

Unity Biotechnology in San Francisco has developed a drug that causes zombie senescent cells to die. **In lab tests of their drug, human knee stem cells regain their ability to regrow cartilage. Clinical trials have begun.**

Meanwhile, the compound rapamycin is already FDA approved. It's used to temporarily suppress the immune system after organ transplants, but it also blocks senescent cell signaling. By loading nanoparticles of rapamycin into molecules that bind only to senescent cells, we can silence them—without suppressing immune cells.

Several studies involving mouse-to-mouse **blood transfusions** have demonstrated confirmed antiaging effects. To make the jump to humans, researchers started by injecting mice with young human plasma (from teenagers or from umbilical cords of newborns). The infusion doesn't just boost the recipients physically, it also improves their cognition and memory. This brain boosting has been connected to the TIMP2 protein present in plasma.

Now human-to-human plasma transfusions have begun. A trial is under way at a hospital in South Korea to test whether injections of human umbilical cord plasma have antiaging effects in older healthy people. The Silicon Valley startup Alkahest has found no safety concerns using teen blood plasma in Alzheimer's patients, and is now looking at its efficacy.

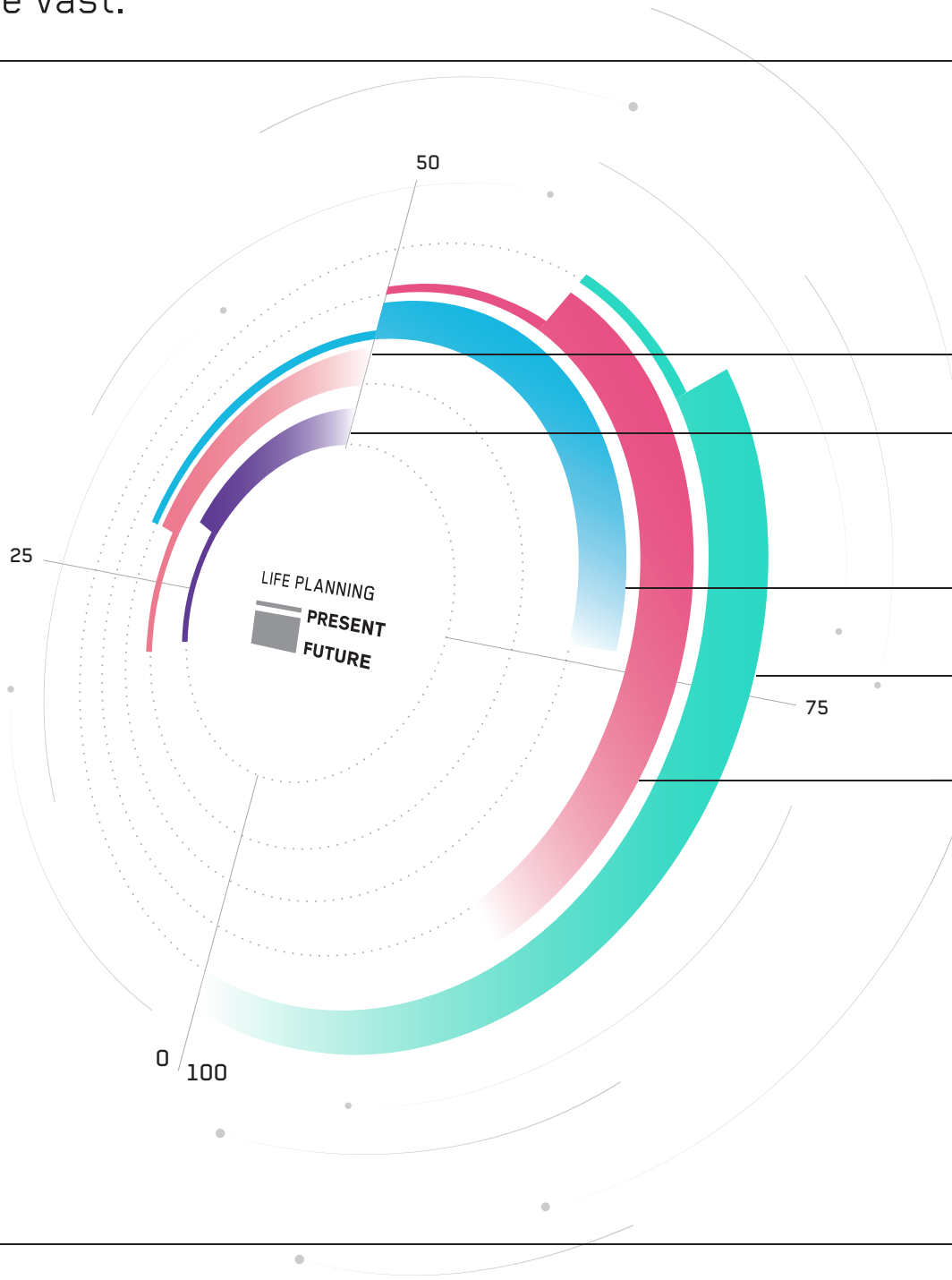
Gene therapy that targets telomerase is yet a fourth approach. Essentially it gives the renewal power of stem cells to other cells. While not yet tested in humans, it's had a remarkable effect on aging mice, delaying or reversing osteoporosis and insulin sensitivity, and improving muscle strength and coordination. This approach had been considered dangerous because, presumably, it might make cancer cells immortal, too. However, scientists have successfully found a way for this gene therapy only to target slowly dividing cells, **opening the door to a permanent solution to prevent cellular senescence**.

How will society be shaped by this field of science? The ramifications are vast.

Because the FDA does not currently consider aging itself a disease, the approved uses in the next 10 years will be restricted to very specific conditions. Nevertheless, the word will get out that these interventions might have a universal benefit. **Their off-label use will produce a highly charged debate as patient advocacy groups clamor for their "right to try."** As always is the case, the supplement industry will cash in, touting their precursor or building block's miracle effects.

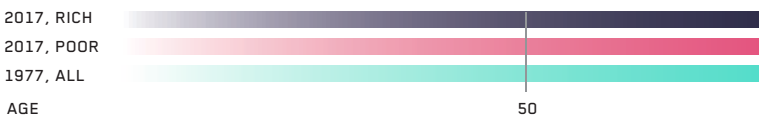
In the meantime, **the benefits of plasma transfusion will mean "blood vacations" at medical spas will be popular**. It could also lead to "blood farms," where young people in poor countries get their blood harvested for use abroad. But the likelihood for corruption in that kind of system is huge. The research to create synthetic blood will accelerate—scientists have already figured out how to make red blood stem cells fly past their normal 50,000 production limit.

If the FDA removes black box warnings on any treatments, such as TIMP2 or NAD+, **we will see an explosion of clinics offering antiaging solutions**. Their use will be elective and not covered by insurance, exacerbating the gap between rich and poor that has already widened considerably since the 1970s.



LIFE EXPECTANCY

In 1977, if you were lucky enough to live to 65, you were (on average) going to live to 80 years old, rich or poor. Today, a poor person who makes it to 65 is only likely to live to 81. **A rich person, to 87**.



CHILDREN

Young working couples will no longer feel like they are in a race against time, trying to advance their careers and bear children before they are too old. Parents will be confident they can use assisted reproductive technology to have children later. Orthopedic stem cell technology will mean they can coach the kids' little league soccer teams as 60-somethings. Knowing they can keep working longer and afford more children, the birth rate for high-income families will go up, while the birth rate for low-income families will go down.

ATHLETICS

Older professional athletes are certain. Golf and tennis more so than other sports, because cognitive control under pressure is most critical in those contests. Triggering the ability to regrow cartilage or heal muscle damage faster won't be considered "doping." Better fitness regimens have already put us on this path. In 1990, half the women tennis players in the year-end Top 10 were teenagers during that season. Currently, there are only three teenagers in the Top 100.

CAREER

Rather than retiring, **waves of people will consider a full career change at midlife**—including going back to school—because they know they'll live far longer. Many colleges will create branches in urban centers focused on adult reeducation degrees. And because the aged often face age discrimination, we will celebrate start-ups that are committed to hiring these self-remade graduates.

HOUSEHOLDS

Three- and four-generation households will become far more common, because we won't need to send the grandparents to assisted living centers where medical treatment is on site. They'll be healthy enough far longer. Real estate developers will need to take this into account. Grandparents will become an even more common solution to childcare for working couples, and "grandparent quality" will become a bigger factor in choosing a marital partner. Reducing the stress of marriage will lower the divorce rate when children are still at home.

LIVING LONGER

It will bankrupt Social Security, but not Medicare. When Social Security was created, in 1935, life expectancy was only 62. The number of people over age 65 will balloon. But this won't hurt Medicare, and in fact it will help it—because people over 65 will have a lot less heart disease, diabetes, cancer and Alzheimer's.

It's critical to see the future of medicine as an opportunity, not a threat. There is always opportunity in change. Huge bets of global capital are being made by those who believe they can get ahead of those changes and gain market share as the changes unfold. This same approach is available to any stakeholder who dares to think this way: don't just stem the tide as the industry gets disrupted—take advantage.

DOUBLE DOWN ON STRENGTHS

Wherever you already are an innovator and market leader, double down. Specialization leads to excellence. The reward for innovation is extremely high: you can leverage your strength, not just gaining market share locally, but potentially licensing your process or your technology around the country or the world.

DIVEST WEAKER OFFERINGS

Where you are not strong, divest and replace with partnerships. Create clarity around your brand. If you aren't known for doing something really well, you're likely to be disrupted there anyway by others who nail it. No single healthcare organization can be best in class at everything. Get ahead of this change.

EVALUATE NEW TECH AGGRESSIVELY

Invest in your tech-scouting personnel. Evaluate new technologies relentlessly. Be discriminating in where you need the most precise (and expensive) equipment, and if it's not your area of strength, consider using new ultra-low-cost devices instead to improve margins.

Opportunities

In other words, to get ahead of the market, you don't have to invent the future of medicine (though this can happen anywhere). You just have to adopt it earlier.

TEAM UP

Establish a strategic task force in your community among healthcare stakeholders.

LEAD WITH RESEARCH

Medical schools should be the leading face of change in their local communities. Even competing industry stakeholders can find commonality in guiding their local medical school to best prepare physicians for the future. Build up the best local medical center into a clinical trial site and research organization—and then have the medical school be a resource and partner to seed new initiatives.

BROADEN THE CURRICULUM

Medical schools should compress the traditional curriculum to allow time for students to study policy, health science, economics and technology.

INCUBATE INNOVATION

If you don't have a med-tech incubator, start one. If there's already one in town, start another. Fill them not just with medical students, but also with computing and mechanical engineers, designers and business students. Give them access to your internal processes to get familiar with your pain points. Whenever they see a problem, they just might invent a solution.

ACCELERATE THE QUEUE

Where you can't adopt virtual care, make wait time your KPI. Long wait times erode patients' confidence and rob them of their autonomy. In turn, this leads them to look elsewhere for answers—be that the internet, alternative medicine or another physician. Shorter waits will rebuild trust and bolster the bottom lines of organizations that value patients' time.

EMBRACE AI

The easiest path to getting familiar with artificial intelligence is to use it to more efficiently run your hospital, on non-clinical data.

GET OUTSIDE

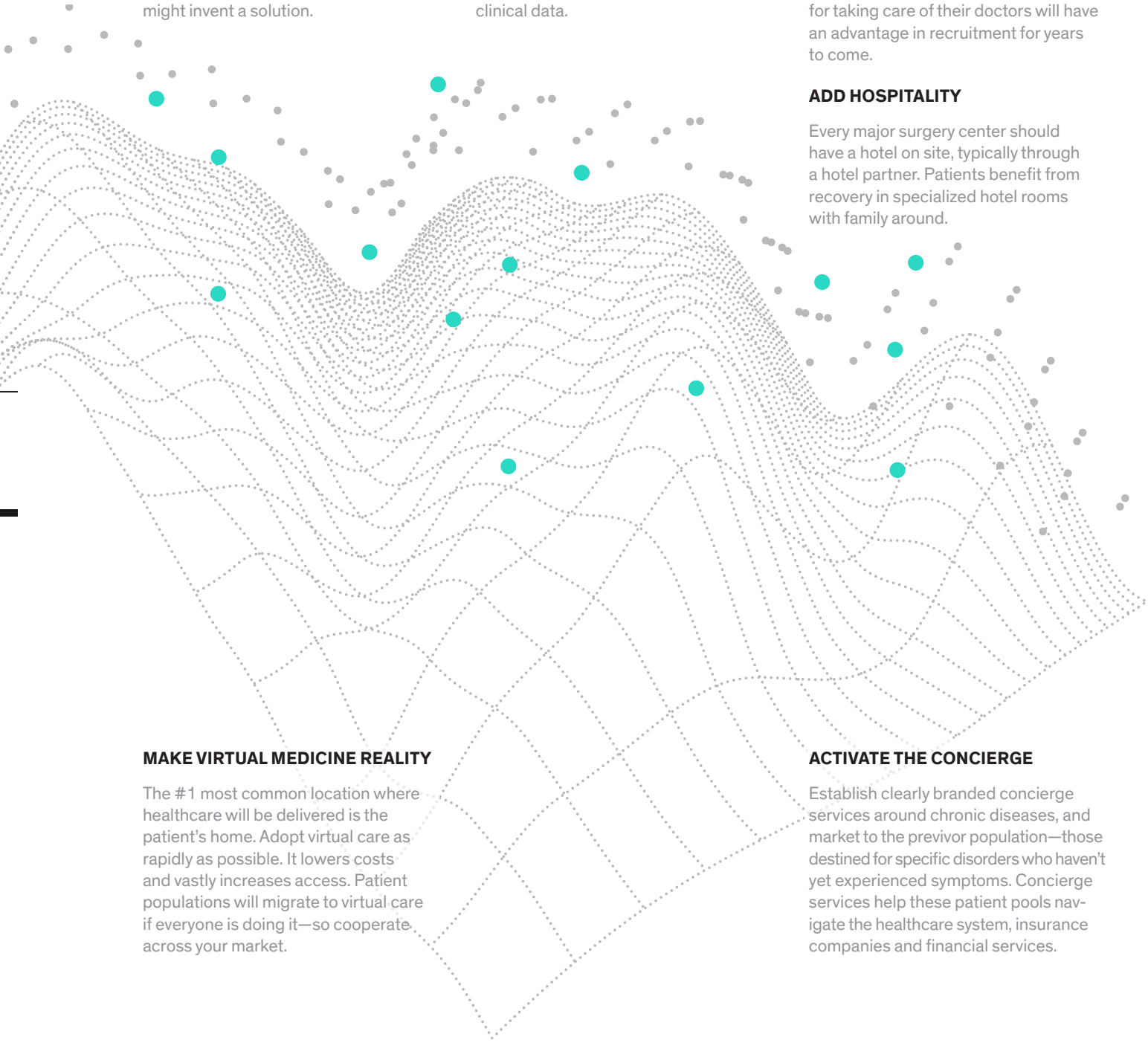
Be proactive about establishing ASCs. Though the reimbursement advantage of performing low-acuity surgeries in hospitals is attractive, value-based care models (which are here to stay) will likely increasingly favor ASCs. Patient and provider satisfaction will also be enhanced.

MAKE DOCTORS HAPPY

The time for institutions to establish a reputation as "physician friendly" is now. The crisis in physician morale is starting to draw the attention it warrants, and organizations that become known for taking care of their doctors will have an advantage in recruitment for years to come.

ADD HOSPITALITY

Every major surgery center should have a hotel on site, typically through a hotel partner. Patients benefit from recovery in specialized hotel rooms with family around.



MAKE VIRTUAL MEDICINE REALITY

The #1 most common location where healthcare will be delivered is the patient's home. Adopt virtual care as rapidly as possible. It lowers costs and vastly increases access. Patient populations will migrate to virtual care if everyone is doing it—so cooperate across your market.

ACTIVATE THE CONCIERGE

Establish clearly branded concierge services around chronic diseases, and market to the previvor population—those destined for specific disorders who haven't yet experienced symptoms. Concierge services help these patient pools navigate the healthcare system, insurance companies and financial services.

Policy Relaunch

WE CAN SOLVE HEALTHCARE REFORM

But to get there, we need to reframe the debate. Thus far, it's been an argument predicated on what healthcare is and has been. The real solution lies in what healthcare will be, and what it will take to get there.

At its crux, the healthcare debate is about cost versus quality. The conventional wisdom is that these are tradeoffs: offer the best healthcare in the world for those who can afford it, or insure everybody with mediocre care. The voice declaring that both are possible isn't at the table. But that's what innovation delivers, everywhere it's turned loose.

For instance, one of the core policy arguments is over preexisting conditions, typically defined by a patient's having shown symptoms and sought medical treatment. This definition and concept will be laughed at in the future, in which an ever-increasing portion of society will know their condition long before they ever show traditional symptoms. We'll be diagnosed early enough, and either treated or prescribed a change in lifestyle, such that it's both far cheaper and more effective. In other words, having been previously diagnosed and treated means **a lower future cost burden, not greater**. Providers and insurers may even want patients to have been previously treated, rather than decline them, if they're confident their methodology of managing the condition is better.

The social definition of quality of care is in the midst of a transformation. High quality was once defined as being able to have a regular doctor—someone who knew your history and whom you saw consistently. Being able to choose your doctor became the next dividing line: the haves got to choose, while the have-nots had to see whoever was on duty. They didn't know you—except by reading your charts and labs. Today, there's a recognition that those lab tests and images are better than ever, and may be vastly more important than knowing you personally, or having seen you before, or even seeing you in person at all. Your charts—your Universal Health Record—are the "real" you, medically. The new definition of quality is the physician who does not miss some little detail, some unusual pattern. Quality is spotting it early.

The central question the medical community must confront is whether seeing patients in person must be the dominant modality of diagnosis. We can make drastic cost reductions by migrating rapidly to virtual healthcare. By tracking patients with wearables and mobile devices, and communicating with them by text message or chat, society will get more accessibility for less expense. Artificial intelligence has the advantage of learning simultaneously from millions of patients, rather than one at a time. No human doctor will be able to have as much "experience" as an artificial one.

Data interoperability presents another paradigm shift. Electronic Health Records are about to explode with wearable and device data; a doctor might measure heart rate variability once per visit, but a common wearable measures it 100 times per second. The value is not so much in the data as in the artificial intelligence that observes the data and sees hidden patterns to make predictions.

The right way to reform the US medical malpractice system is not to impose damage caps, but to change the basis for finding a doctor liable for malpractice in the first place. Doctors should have a safe harbor from malpractice suits if they follow evidence-based protocols published by a professional medical association, rather than being evaluated by the standard of "customary practice," defined as what doctors typically do. This leads to defensive medicine and excessive costs.

We need to incentivize innovation in every domain and at every level. We need to make profits by providing care, not by denying people care. We need price competition among drug makers and a shift to continuous efficacy monitoring in exchange for quicker access to market. We need bold experiments in insurance markets. We need to create more clarity in healthcare brands by truly offering different experiences for patients. We need to rely more on disease-management companies for chronic care. The resources our society is committing to healthcare can stretch much farther than they do now.

The future of medicine is incredibly bright for every stakeholder. Healthcare policy is perhaps the greatest single factor in whether the future painted here arrives in ten years, or is delayed for ten more. Scientific discovery from academia will not slow down, nor will technology innovation from startups. But how fast medical innovators' work migrates from lab to market, and on to widespread adoption, is very much in the hands of policymakers. Policy can be an accelerant or a brake. We hope the future of medicine portrayed in this report assures policymakers that the sooner we get there, the better.