Healthcare Reimagined

Introduction

While progress in medicine continues to astound us, it hides a modus operandi that hasn't changed for decades – a bricks and mortar model of delivering healthcare reactively to treat illness and disease. Although highly lucrative for healthcare providers and Big Pharma, it is archaic, capital intensive and, in many ways, broken.

Thanks to broad adoption of mobile computing and advances in technologies such as wearables and artificial intelligence (AI), we are now witnessing the beginnings of a revolution in healthcare that will vastly improve disease detection and the management of chronic illness, address spiralling costs and make services accessible to another billion people.

At Mangrove, we believe digital health represents one of the very largest opportunities for value creation. This report will explore the rise of mHealth and the convergence of medicine with AI and Big Data. It will also explain the value of clinically-proven software interventions, while dispelling the myth that doctors are better placed to build digital health businesses.

"The idea that you need to be a clinician to build a successful digital health business is a complete fallacy. In fact, it is more likely a hindrance than a help. Only outsiders, who come entirely unconditioned by industry experience and cultural thinking, are able to radically reimagine the solution to a problem."

—Mark Tluszcz, CEO at Mangrove Capital Partners

God-like powers but fundamental shortcomings

From 3D printing of body organs and the development of bionic eyes to the reprogramming of immune cells to fight cancer, it is difficult not to be impressed by the constant advance of medicine. Likewise, the daily achievements of healthcare institutions such as the UK's National Health Service (NHS) in providing care and treating patients are nothing short of remarkable.
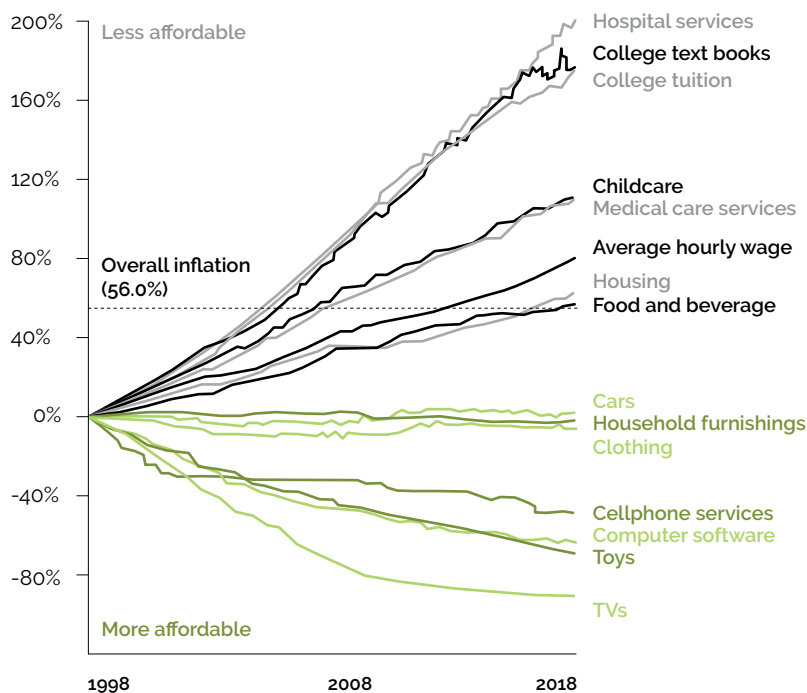
And yet there are fundamental problems with healthcare that need solving, the most obvious being its ever-rising cost. After many years of steady increases, healthcare spend in the United States reached $3.65 trillion in 2018 – equating to $11,212 per person. According to a recent analysis by U.S. federal government actuaries, healthcare spend will continue to rise at an annual

growth rate of 5.5% from 2018 to 2027, reaching 19.4% of the country's entire GDP by 2027.

With the delivery of healthcare becoming increasingly sophisticated and capital intensive, it is perhaps unsurprising that the cost of treatment continues to rise. While the contributions of historical technological progress to improvement in health outcomes are substantial, examples of cost-cutting effects are few and far between. On the contrary, technological advances such as magnetic resonance imaging (MRI) are widely seen as the most important driver of the rise in health-care spending. However, it is the long-entrenched dependence of healthcare on a corrective rather than preventative approach that makes the path of ever-rising costs seemingly inescapable.

Price changes (January 1998 – December 2018)
Selected US consumer goods, and services, wages

Source: American Enterprise Institute (AEI)

It doesn't help that private healthcare providers and pharmaceutical companies have little incentive to reduce the incidence of illness and disease. Like any other business, they are driven by profit. And like any other industry, these incumbents are focused on preserving the status quo.

The issue is amplified by extreme information asymmetry. A market is deemed efficient when all pertinent information is available to all participants at the same time. Human health is highly complex and it is extremely difficult for patients to make well informed decisions given limited access to information on drug trials, alternative medications and patient outcomes. Instead they must entrust decision-making to doctors, whatever the cost.

Growing pains and disjointed experiences

An ageing population and changes in societal behaviour are also contributing to a steady increase in common long-term health problems. For example, the number of people diagnosed with diabetes in the UK has more than doubled from 1.4 million to almost 3.5 million since 1996 (Diabetes Society).

Chronic illness and disease place an enormous strain on healthcare services. The Centers for Disease Control and Prevention estimates that chronic diseases account for 70% of U.S. deaths and 75% of U.S. health care spending. In the UK, diabetes alone accounts for 10% of the NHS budget for England and Wales, equating to over £25,000 being spent on diabetes every minute.

The patient population as a whole is also becoming more complex thanks to increasing awareness of health conditions and the rise of 'cyberchondria'. In the UK, the average member of the public now sees a GP six times a year; double the number of visits from a decade ago[1].

Only Human

Research has also shown that doctors are prone to error. An analysis of three large observational studies involving US adult populations found a rate of outpatient diagnostic errors of 5.08%, or approximately 12 million US adults every year (Singh H; Meyer AND; Thomas EJ; 2014). The study
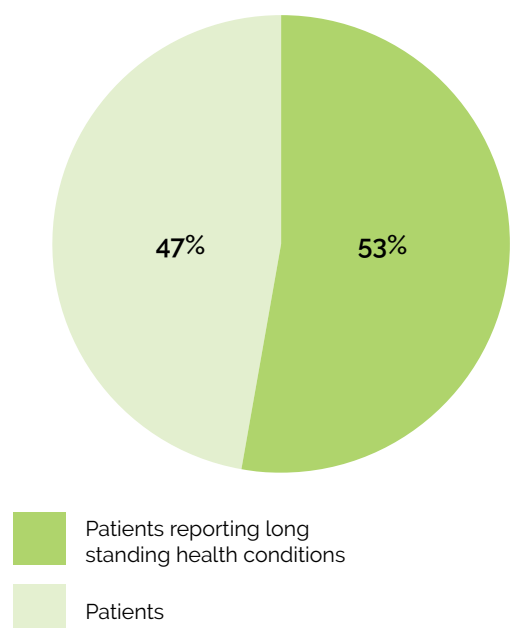
also concluded that about half of these errors could potentially be harmful. Meanwhile a study by researchers from the Universities of York, Manchester and Sheffield revealed that an estimated 237 million medication errors occur in the NHS in England every year and that avoidable adverse drug reactions (ADRs) cause hundreds of deaths.

The patient experience

With most consumer-facing industries evolving at a rapid pace, the sleepy advance of healthcare is becoming ever more apparent. Part of the problem is the complex and fragmented nature of the healthcare industry, which has led to an array of disconnected systems and siloed data. As a result, interactions with healthcare providers are often painfully disjointed.

Patients increasingly expect the kind of proactive service, personalised interactions and connected experiences that they encounter in other industries. And with the healthcare industry failing to adapt, they are looking for alternatives.

Around 53 per cent of all patients in England report having long standing health conditions (BMA 2017)

47%   53%

■ Patients reporting long standing health conditions

▢ Patients

1. NHS Digital - Trends in Consultation Rates in General Practice (1995-2009)

The promise of Mobile Health (mHealth)

The concept of digital health continues to evolve and is becoming increasingly broad, covering everything from mobile applications and wearables to genomics, disease diagnostics and AI tools for drug discovery. Essentially, it is about applying digital transformation, through disruptive technologies and cultural change, to the healthcare sector.

Crucially, the use of mobile devices at the point-of-care is driving a profound shift in the healthcare delivery model: from one that is health-system generated to one that is remote and patient-generated. Since the launch of the App Store, health and fitness has been one of the largest categories of apps and one of the most popular in terms of consumer spend. Offering anytime, anywhere care, the access on-demand model of mHealth presents an unparalleled opportunity to increase patient engagement, reduce healthcare costs and improve outcomes.

The benefits of mHealth are also compelling for managing chronic conditions, such as diabetes and hypertension, where the effectiveness of the prescribed treatment is largely dependent on the will of the patient and the choices that are made day-to-day outside of the formal healthcare system. mHealth can help by engaging with patients on a daily basis and making progress tracking tools available to both patient and physician.
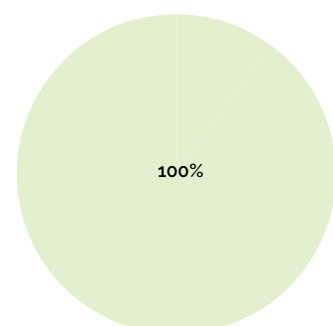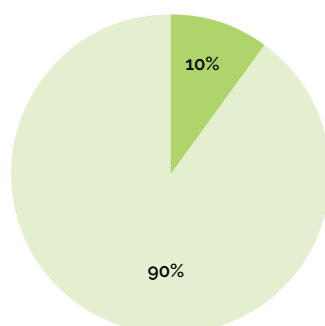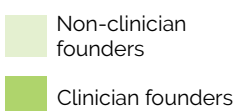
By pushing personal health data back to the patient, mHealth companies are helping users make better decisions and promoting more proactive behaviours. And with a deluge of new health data emerging from mobile apps, wearables and sensors, there is an opportunity to learn much more about the causes of illnesses and diseases. mHealth, therefore, offers a profound opportunity to move from a corrective health paradigm to a preventative one.

It is a common misconception that clinicians are best placed to build digital health startups. The basis for this assumption is that only clinicians fully understand the unique complexities of the sector – an industry in which mistakes can make the difference between life and death. However, history has shown that industries are not reinvented by incumbents. Just like any other industry, healthcare is best revolutionized from the outside and not from within. Those outside of the industry bring fresh perspective and are more readily able to conceive patient-centric solutions. And while some mHealth companies need to be tested and deployed by traditional healthcare providers, many are able to circumvent these antiquated organisations entirely.

This is supported by our analysis. Of the top 50 medical apps by revenue, only five (10%) were founded by doctors. Meanwhile of the top 50 medical apps by monthly active users (MAU), none were conceived and built by doctors[2].

Clinician vs non-clinician founders of the top 50 medical apps by revenue.

Clinician vs non-clinician founders of the top 50 medical apps by MAU.

Non-clinician founders

Clinician founders
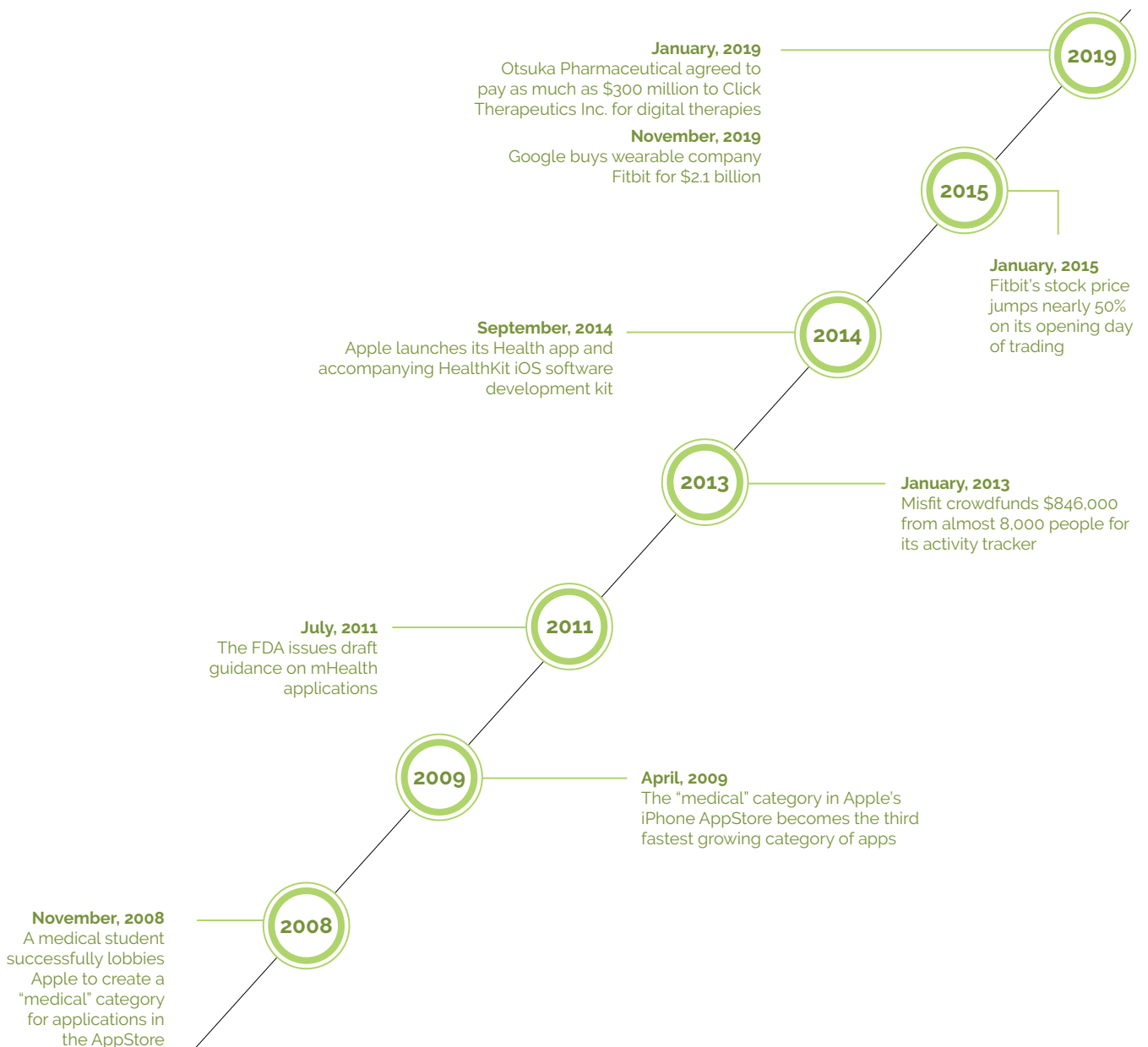

10%

90%

100%

2. Mangrove internal research based on SensorTower medical app data

Evolution of Mobile Health

"The single most unused person in health care is the patient."

— David Cutler, Otto Eckstein Professor of Applied Economics in the Department of Economics at Harvard

January, 2019
Otsuka Pharmaceutical agreed to pay as much as $300 million to Click Therapeutics Inc. for digital therapies

2019

November, 2019
Google buys wearable company Fitbit for $2.1 billion

2015

January, 2015
Fitbit's stock price jumps nearly 50% on its opening day of trading

September, 2014
Apple launches its Health app and accompanying HealthKit iOS software development kit

2014

2013

January, 2013
Misfit crowdfunds $846,000 from almost 8,000 people for its activity tracker

July, 2011
The FDA issues draft guidance on mHealth applications

2011

2009

April, 2009
The "medical" category in Apple's iPhone AppStore becomes the third fastest growing category of apps

November, 2008
A medical student successfully lobbies Apple to create a "medical" category for applications in the AppStore

2008

Biology, AI and Big data: A powerful combination

While mHealth is profoundly changing the healthcare delivery model, AI and Big Data are revolutionising our approach to medicine and care.

"Evidence-based medicine" is the backbone of modern medicine, integrating clinical experience and patient values with the best available research information. The gold standard is the double-blind, prospective study, where an adequate sample of patients is selected, some are given a particular treatment while others are given either a different treatment or a placebo and then a measurable endpoint is analysed based on the response.

While it forms the basis of a scientific approach in medicine, it limits our understanding of health to the hypotheses which we choose to test. Furthermore, it is open to significant cognitive bias as the questions that are asked and the tests that are carried out are subject to prejudice.

Thanks to the rise of AI and Big Data, we are now moving beyond the hypothesis-testing-conclusions methodology. Rather than drawing and testing specific hypotheses, we can simply analyse the data that already exists and make predictions from the patterns that are unearthed.

By collecting and connecting anonymized data on human health, from inside and outside the healthcare environment, we can analyze the relationships between different prevention or treatment techniques and patient outcomes. Furthermore, data can be used to assess *all* the variables that pertain to a specific individual and make precise, personalized recommendations that could not come from sample-based studies.

AI, if developed and used appropriately, offers the potential for decision-making that is not only speedier and more accurate than that of humans, but also less biased and more rational.

"AI/Big Data has significant potential to change healthcare. But healthcare is one of the slowest industries to take on new technology -- and physicians/healthcare providers are reluctant to change. Cost and implementation time will be additional barriers -- along with fear of losing autonomy to 'machines'. I anticipate it will be slow-going for hospitals/ medical centers to take on such new technologies -- but, ultimately I think it is inevitable."

—Tarun Jain MD, Associate Professor of Obstetrics and Gynecology at Northwestern University Feinberg School of Medicine

Reinventing primary care

While some digital health startups have focused on incremental changes, others are taking a much bolder approach. K Health is a company with an ambitious goal: free primary healthcare for the world.

K Health is building the world's first accurate and trusted AI-driven medical information layer. The K Health team has translated 400 million medical charts including diagnostics and treatments into a smart mobile app, in essence creating the world's first automated doctor. This translation required building a complex parsing and medical ontology system and resulted in a database of 2 billion individual data points which the app can leverage based on user interactions.

How it works:

1. On the company's free mobile app, users spend three-to-four minutes answering an average of 21 questions about their background and the symptoms they're experiencing.

2. K Health then provides an accurate, personalized and data-driven assessment, explaining how doctors diagnosed and treated people with similar symptoms.

3. If necessary (and for a small fee), users can talk to an expert doctor who can diagnose, prescribe medicine, and order lab tests.

Within a year of launch, K Health processed more than 3 million free virtual "doctor visits", illustrating the enthusiasm among consumers for an automated health service as well as the opportunity to relieve pressure on primary care providers. With more accurate at-home diagnostic information, users can make better preventative health decisions and avoid unnecessary trips to in-person care. Of course, the impact of K Health in emerging markets could be even more transformational given that at least half of the world's population cannot obtain essential health services.

K Health – Over 3 million free virtual "doctor visits" within a year of launch.

Importantly, this is not a product that would have been conceived by a physician. After all, the Hippocratic Oath, held sacred by physicians, states that 'warmth, sympathy, and understanding may outweigh the surgeon's knife or the chemist's drug'. K Health co-founder and CEO Allon Bloch previously founded Vroom, an online marketplace for used cars.

AI-driven detection and prevention

The American Cancer Society expects that the worldwide burden of cancer will rise to 21.7 million cases by 2030 and according to the IMS Institute for Healthcare Informatics the worldwide market for cancer treatments is expected to reach $150 billion by 2020. As well as vastly improving survival rates, early detection greatly reduces cancer's financial impact. There's now an opportunity for dramatically increasing cancer screening thanks to companies such as Kheiron Medical, which uses AI to help doctors find malignancies in mammograms.

Big Data and AI also offer an opportunity to advance prevention by revealing unexpected relationships and pathways that would otherwise remain hidden. AI is already being used to identify patients at risk of developing diseases. For example, IBM recently announced an AI-powered screening tool that could potentially identify Type 1 diabetes antibodies in people's blood. The program pinpointed similarities among people with specific antibodies for the disease and the timeline of their Type 1 diabetes progression.

Indeed, AI has now been used in an intriguing array of studies, from predicting cardiovascular risk factors by analysing retinal scans to spotting mental health conditions by examining an individual's choice of words, tone of voice and facial expressions.

Similarly, consumer health apps are now moving beyond health tracking to detecting and predicting potential health issues. Flo Health, the most popular women's health app, recently worked with medical experts to develop a pre-diagnostic tool that evaluates a woman's risk for the hormonal imbalance known as polycystic ovary syndrome. The condition is a prevalent health problem among women of childbearing age and can make conceiving without fertility treatments more difficult for some women.

In just one month, more than 636,000 women completed Flo's health assessment – to put this into perspective, the sample size for traditional medical research is rarely more than 200. The app then recommended to those at risk that they ask their doctors about the hormonal disorder. By encouraging women at risk to consult their doctor, the app is helping its users to understand and identify potential barriers to conception. These women may never have learnt about polycystic ovary syndrome had they relied solely upon traditional health providers.

"Women's sexual and reproductive health has got little attention from the pharmaceutical industry. The focus is on cardiovascular and malignant diseases."

— Professor Emeritus Johannes Bitzer, Universitätsspital Basel, Switzerland

"Women are 50% of the world population, and a healthy woman plays an essential part of the survival of the human race. If we do not understand the issues and problems of women's health, I think that the human race is in danger."

— Dr. Tahir Mahmood, Chair of Standards of Care European Board and College of Obstetrics and Gynaecology

The value of clinically-proven software interventions

With hundreds of thousands of digital health apps now available, part of the challenge is finding solutions that provide real value. The digital health space is characterized by players able to rapidly iterate technology, but often at the expense of traditional medical product design, safety testing and clinical efficacy trials. A 2018 analysis of published randomized control trials (RCTs) found just 23 RCTs of currently available apps had been conducted, and less than half of those showed a positive health effect from the app in question.

Digital therapeutics (DTx) are software-based interventions that are proven to have a direct impact on an illness or disease. It is very early days for this type of software, but pharmaceutical companies are showing significant interest in DTx. As well as making treatment far more accessible for patients, DTx create new revenue streams for pharmaceutical companies at a much lower cost than their traditional products (as software can be distributed much more efficiently than medicines).

DTx will also give pharmaceutical companies access to data they've never had before. Importantly, this goes far beyond data from a randomized controlled trial. DTx will give pharmaceutical companies and physicians real-time results from millions of patients and, through accurate and normalized Big Data, will continue to provide powerful insights over time that can be used to improve treatment or even create entirely new products. This data influx could impact side-effect management, drive better R&D and improve patient adherence to treatment (e.g. by tracking usage and providing the necessary reminders). With the FDA now considering DTx as medical devices and granting market exclusivity extensions, DTx companies can also help traditional drug companies to enhance their existing drug-based treatments in order to secure market exclusivity extensions.

The DTx market is still in its infancy but is expected to be worth more than $32bn by 2024 according to Juniper Research.

Most digital therapeutics companies are currently focusing on mental health and cognitive behaviour conditions, including substance abuse, depression and anxiety — often employing strategies rooted in cognitive behavioural therapy. Of course, obtaining FDA approval is not trivial for a young, mobile app startup. The need for scientific based theories, clinical tests, and standards-based operations are often not in the DNA of many digital health companies.

Having built a team which incorporates medical expertise, Happify Health was able to develop a condition agnostic digital treatment program capable of reducing anxiety and depression symptoms by 25%, according to a 2018 study. Its experience as a successful direct-to-consumer application with millions of users, combined with deep technology expertise and clinically-proven digital therapeutics, has put it on the radar of pharmaceutical companies. It is now one of a handful of companies globally that has struck deals with Big Pharma, having partnered with Sanofi to develop a prescription software intervention for treating depression among people living with multiple sclerosis (MS).

"Happify Health's ability to address mental health issues so effectively in a digital environment provides an ideal complement to Sanofi's traditional therapies."

— Ameet Nathwani, Sanofi's chief medical officer and chief digital officer.

Privacy concerns

While the explosion of health data – from patient lifestyle and family history data to genetic data - presents enormous potential for improving our understanding of illness and disease, it also amplifies privacy concerns. For publicly-funded institutions such as the NHS, the tension between utility and privacy is particularly acute.

However we must not lose sight of the benefits. The data generated by commercial wearables and apps has the potential to alter how we study human behaviour and how we intervene to improve health. These datasets are orders of magnitude larger than those in traditional research studies and can be accessed by researchers at relatively low cost. While recent security breaches and cases of unauthorised transfer of health data have shown there are privacy issues that need resolving, it is entirely possible to create a privacy framework that fosters innovation while protecting the privacy of patients.

Regulatory hurdles

With the quantity and variety of digital health products growing daily, regulators are increasingly swamped with requests for regulatory approval. As digital health products differ from traditional medical devices, the process of testing and analyse these products also requires different skills and expertise. As a result, digital health startups can face paralysing delays in getting their products approved.

Many developers are also being exposed to medical device regulation for the first time and without the expertise and benefits of scale that traditional manufacturers possess. And with the emergence of machine learning models, the line between what is and is not a medical device is increasingly blurred.

This can make it difficult to know the scope of the regulatory burden, which may also differ depending on the country or region.

According to our analysis, the most successful consumer health apps are side-lining regulatory approvals and focusing on growth. Only 2.6% of the leading medical apps (by monthly active users and revenue) have FDA certification. Of course, FDA certification is easier to obtain following mass adoption thanks to the availability of data. It can then be used to build further credibility and partnerships with traditional healthcare providers and Big Pharma.

Only 2.6% of the leading medical apps (by monthly active users and revenue) have FDA certification

Conclusions

The power of AI to extend life is already abundantly clear. With very considerable investment now flowing into AI-driven health businesses and healthcare transforming from an analogue sector into a digital one, the space has advanced dramatically over the last three years. The industry is now moving from a structure that treats sick people to one which, through AI, is predicting and preventing illness and disease.

mHealth will unlock the cheapest and most efficient healthcare and make it available to billions of people via their smartphones. For those areas that lack physical resources or where healthcare is prohibitively expensive, mHealth may prove to be the internet's most valued legacy.

Interestingly, the future of DTx may lie in cooperation rather than in competition with Big Pharma and drug development. By partnering with Big Pharma in bringing combination therapies to market, DTx companies can help to unlock new revenue streams for both parties. Similarly, rather than entirely disrupt traditional healthcare, mHealth will augment existing capabilities to prevent, detect and treat illnesses and disease.

There is, of course, a considerable change in mindset required to leverage the full potential of AI and Big Data. And there are very significant differences between the 'move fast, break things' culture of the technology sector and that of the traditional healthcare industry. The leading medical apps are first and foremost technology companies founded by strong operators, but the winners of tomorrow will be those businesses that successfully marry technology expertise and product skills with solid medical experience.

About Mangrove Capital Partners

Mangrove Capital Partners (www.mangrove.vc) is Europe's leading early stage venture capital firm. It works with top entrepreneurial talent at the earliest stages of innovation, with the aim of being the first institutional investor: the firm has co- created projects and regularly injects funds prior to product launch, often in unproven, unusual or unfavoured technologies. Mangrove manages more than $1 billion in assets and is headquartered in Luxembourg with offices in Berlin and Tel Aviv.

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