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SILICON VALLEY COMES TO THE UK

REFILLING THE INNOVATOR'S PRESCRIPTION

The new wave of medtech

CONCLUSIONS FROM SILICON VALLEY COMES TO THE UK 2013

Jessica Bland

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The Silicon Valley Comes to the UK (SVC2UK) programme is a series of events that bring together early stage investors, successful serial entrepreneurs, students and alumni with leading Silicon Valley serial entrepreneurs and investors to discuss and debate how and why they have come to create and fund today's most disruptive technologies that aim to change our world.

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FOREWORD

Bringing the techniques of data science to healthcare offers business opportunities for new entrants that will fundamentally improve outcomes not only for patients, but also for doctors and the healthcare system in the next ten years. We debated at Silicon Valley comes to the UK 2013 if this kind of medtech would result in the first trillion pound company valuation and consensus suggested that it would. The question is whether or not this company will be headquartered in the UK, US, or indeed elsewhere.

Technology has started radically changing the lives of those in and dedicated to healthcare, but the transformation has only just begun.

This paper explores and explains what the future is likely to look like for patients and doctors, and examines the implications for institutions currently involved in the industry. The good news is that there will be massive improvement in the lives of patients and doctors and the entire healthcare system.

The bad news is that people in the institutions that have shaped this industry historically will be left behind if they do not help their organisations adapt. There are new entrants waiting in the wings with products that are fundamentally better at serving the interests of the customers. A revolution awaits.

We examine this revolution by building a detailed theoretical foundation, and supplement this with an engaging set of case studies of new entrants that have delivered amazing outcomes at a fraction of the cost of previous services.

In the modern healthcare landscape, emphasis is often on decreasing the cost of delivering care, but ensuring excellent quality of patient care is just as important. This is where medtech has a substantial impact – not only does it greatly improve interactivity between clinicians and patients, and the quality of patient outcomes, but it also decreases costs. These are two targets which policymakers in government have historically attacked independently, as they have previously involved very different approaches. Medtech can improve them both simultaneously. Smashing the worlds of medicine and 'tech' or data together combines these approaches, and has greatly improved the future trajectory of patient care.

It is an exciting time to be involved in the medtech sector, regardless of your role. The revolution in patient care does not just affect the way in which patients are healed. This particular paradigm shift reverberates significantly deeper than that. It affects the way patients and doctors interact, the way the healthcare system is structured, and eliminates the barriers between patient and physician. The future of mankind in these modern, changing times is uncertain, unstable, and dynamic. In order for future generations to adapt to such uncertainty, and create sustainability, it is vital that the way we deliver healthcare can adapt with equal dynamism. Through better understanding of powerful new revelations in technology, we can prepare future generations for whatever may lie ahead. By ensuring that the avenues through which patient care is delivered are open to new innovations, we ensure that future generations can launch themselves along the road to better healthcare.

This paper provides useful policy insights, in addition to examining various powerful examples of medtech developments as case studies. Please join us in the goal of trying to advance patient care; an extraordinarily good cause which will change the future of mankind in wholly positive ways. This report is one of many important steps which must be taken.

Sherry Coutu, Co-Chair of Silicon Valley Comes to the UK

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EXECUTIVE SUMMARY

A new wave of medical technologies offers novel business opportunities for investors and entrepreneurs. Silicon Valley Comes to the UK (SVC2UK) and Nesta present a snapshot of the early breakers, and how they will play into changes in the broader healthcare sector.

These technologies are not on the whole specialist medical devices and diagnostic tools like surgical equipment or genetic sequencing technology. This wave comes from the same advances that have driven massive disruption in other sectors – from telecoms and publishing to music and entertainment. Portable hardware, abundant data and consumer–facing digital platforms have led to a new kind of medtech, which some are calling digital health.

Silicon Valley Comes to the UK is a series of industry supported events with business leaders, investors and serial entrepreneurs and run by students. In 2013, big data was the headline theme with medtech as a key areas of focus. The 2013 SVC2UK event in Cambridge was an opportunity to interview entrepreneurs at the intersection between consumer technology, data–driven innovation and healthcare. As well as consulting other experts in the field, and with the benefit of recent Nesta research on innovation in healthcare, these interviews form the basis of this report.

This report begins with (Box 1) a global taxonomy of medical devices. We've highlighted where the new wave of medtech is concentrated in this broader range of medical technologies. Chapter 1 sets this up in more detail, looking at US and UK investment in medtech and how these compare to the new arrivals in digital health.

Chapter 2 looks in more detail at areas where this new wave promises to change medical practice. We first look at changes already underway, particularly the effects of technologies that monitor daily activities. There is a new user–driven marketplace, where medical devices are available direct to consumers. This opportunity extends beyond empowering individuals to be proactive about their health – it is creating a culture of preventative care. Second, this chapter looks towards a future where large–scale data analysis and new kinds of hardware will be available for more sophisticated forms of prevention, diagnosis and treatment: often in combination with more traditional medical technologies like prosthetics or genomics.

As the new wave of medtech embeds itself in more sophisticated products and services, innovation must increasingly respond to the unique features of the healthcare sector: from the burden of chronic disease to navigating the complex relationships between doctors, researchers and government policy. Chapter 3 looks at the potential points of tension this could create. Chapter 4 identifies differences in how this might play out in the US and UK.

Chapter 5 returns to implications for the nearer term. We illustrate our vision for portable personal healthcare using technologies already under development, many of which featured at SVC2UK 2013. This is intended as a provocation for investors, policymakers and entrepreneurs thinking about catching this new medtech wave.

INTRODUCTION

> *In the 21st century we need to complement the sick care system we have already. We need a system built from today's signature technologies – not the signature technologies of the 20th century. Buildings that provide electricity and people with knowledge will become software and computational power with intelligence in the cloud. And products become services tailored to you, your genes and your behaviour... Things are changing from buildings, people and products to software, services and mobile devices.*
>
> **Andrew Thompson,**
> **Proteus Digital Health**

Healthcare technology evokes images of MRI scanners, paramedics' defibrillators and intricate surgical kits. More recently, there are promises of medicines, based on the next generation of genetic technologies that will read, reconstruct and rewrite our genomes. These are examples of hard-to-reach technologies that require highly skilled technicians and years of training to use. But there is another group of medical technologies arriving on the scene. Often more like games or toys, there is a growing group of accessible and portable consumer medical technologies – a new wave of medtech.

The early breakers tell the beginning of a story familiar from other sectors.

Having developed the theory of an Innovator's Dilemma to describe disruptive innovation in other sectors, in *The Innovator's Prescription* Clayton Christenson and his co-authors turn their attention to healthcare. They use two growth compasses to understand changes to the medical diagnostics and devices market. In common with the history of personal computing or telecoms industries, medical devices are undergoing a process of centralisation-decentralisation, at the same times as the commoditisation of expertise.[1]

Decentralised care

The development of specialist, often large equipment and the availability of electricity moved healthcare into hospitals a century ago. This process of centralisation is now in reverse. Portable devices are decentralising healthcare in the same way that the printing press moved from central warehouses into the office, the home and now remote printing via smart phones. With each stage or wave of decentralisation, technologies become more ubiquitous, affordable and convenient.

However, different types of medtech device are at different stages of this process. Human genome sequencing is still highly centralised, whereas diabetics now manage their own care with home testing kits. The new wave of highly portable technologies, operated by users rather than professionals, has only just started.

Doctors as commodities

While there is already evidence of decentralisation, the idea that medical expertise will be deployed only in a few highly specialist contexts of care is much more controversial. Silicon Valley leaders, who see healthcare as simply catching up with other digital sectors, argue it's only a matter of time before doctors are pushed aside by computers. Serial investor, Vinod Khosla, said in 2012:[2]

> *"Computers are much better than people at organizing and recalling information… Contrary to popular opinion, they're also better at integrating and balancing considerations of patient symptoms, history, demeanour, environmental factors, and population management guidelines than the average physician."*

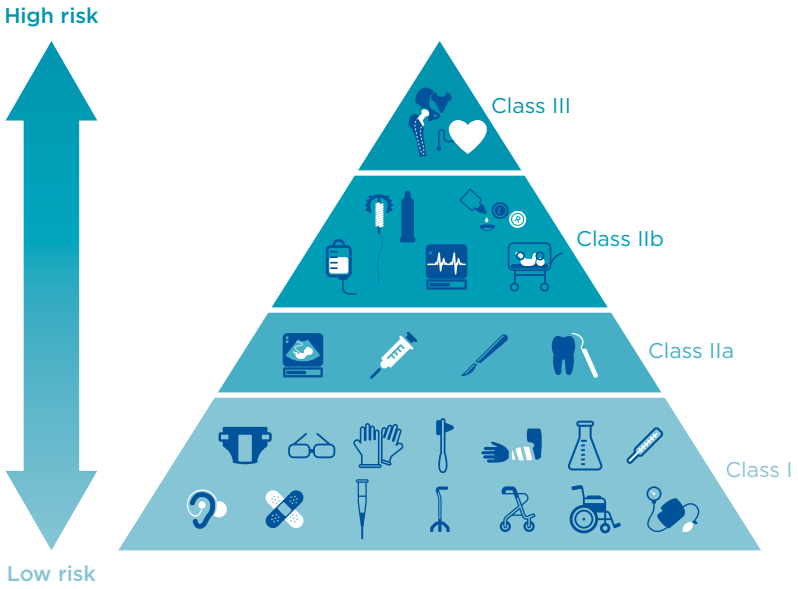
Pharmaceuticals expert and ex–doctor, David Shaywitz replied:

> *"I disagree with Khosla's perspective, or more accurately, I bring a different set of experiences and biases. Trained as a physician, and working in the medical products industry, it's perhaps not surprising I view deep experience in healthcare and the complexity of the healthcare system as enormously enabling."*

As the wave of medtech innovation continues, this tension is unlikely to disappear. Christensen's prognosis is that specialists will not be needed for some procedures. For example, radiologists will guide surgery using imaging techniques, removing the role of a surgeon. Highly skilled clinicians, he predicts, will solve only the most complex problems that have come to them through a web of automated analysis and non–medical expertise.

This report takes Christensen's predictions seriously. Digital health products populate what were mainly imagined innovations in his 2009 book. By examining these products from the point of view of their creators, this report adds some detail to Christensen's template for a new wave of medtech.

Box 1: **Taxonomy of medical devices**[3]



The global nomenclature for medical devices has 16 categories, holding a total of 20,000 generic products. In this diagram those categories intersect with the four risk classes for medical devices in European legislation. So far the new wave of medtech is mainly made up from low-risk consumer facing products. For example mobile apps or Neurosky's brainwave monitoring headsets are in Class I. Others, such as Cambridge Cognition's diagnostic test for cognitive ability move higher up the pyramid. Some of the most exciting, take Proteus Digital Health's technology based on ingestible sensing, are classed as even higher risk. As the new wave of medtech continues – and as digital health products integrate with existing medical technologies – more and more will come under risk classes IIB and III. Devices will have increasing power over diagnosis and more frequently be embedded in the body.

Code	Classification	Example
01	Active implantable technology	Cardiac pacemakers, neurostimulators
02	Anaesthetic and respiratory technology	Oxygen mask, gas delivery unit, anaesthesia breathing circuit
03	Dental technology	Dentistry tools, alloys, resins, floss, brushes
04	Electromechanical medical technology	X-ray machine, laser, scanner
05	Hospital hardware	Hospital bed
06	In vitro diagnostic technology	Pregnancy test, genetic test, glucose strip
07	Non-active implantable technology	Hip or knee joint replacement, cardiac stent
08	Ophthalmic and optical technology	Spectacles, contact lenses, intraocular lenses, ophthalmoscope
09	Reusable instruments	Surgical instruments, rigid endoscopes, blood pressure cuffs, stethoscopes, skin electrodes
10	Single use technology	Syringes, needles, latex gloves, balloon catheters
11	Technical aids for disabled	Wheelchairs, walking frames, hearing aids
12	Diagnostic and therapeutic radiation technology	Radiotherapy units
13	Complementary therapy devices	Acupuncture needles/devices, bio-energy mapping systems/software, magnets, moxibustion devices, suction cups
14	Biological-derived devices	Biological heart valves
15	Healthcare facility products and adaptations	Gas delivery systems
16	Laboratory equipment	Most in vitro diagnostic which are not reagents

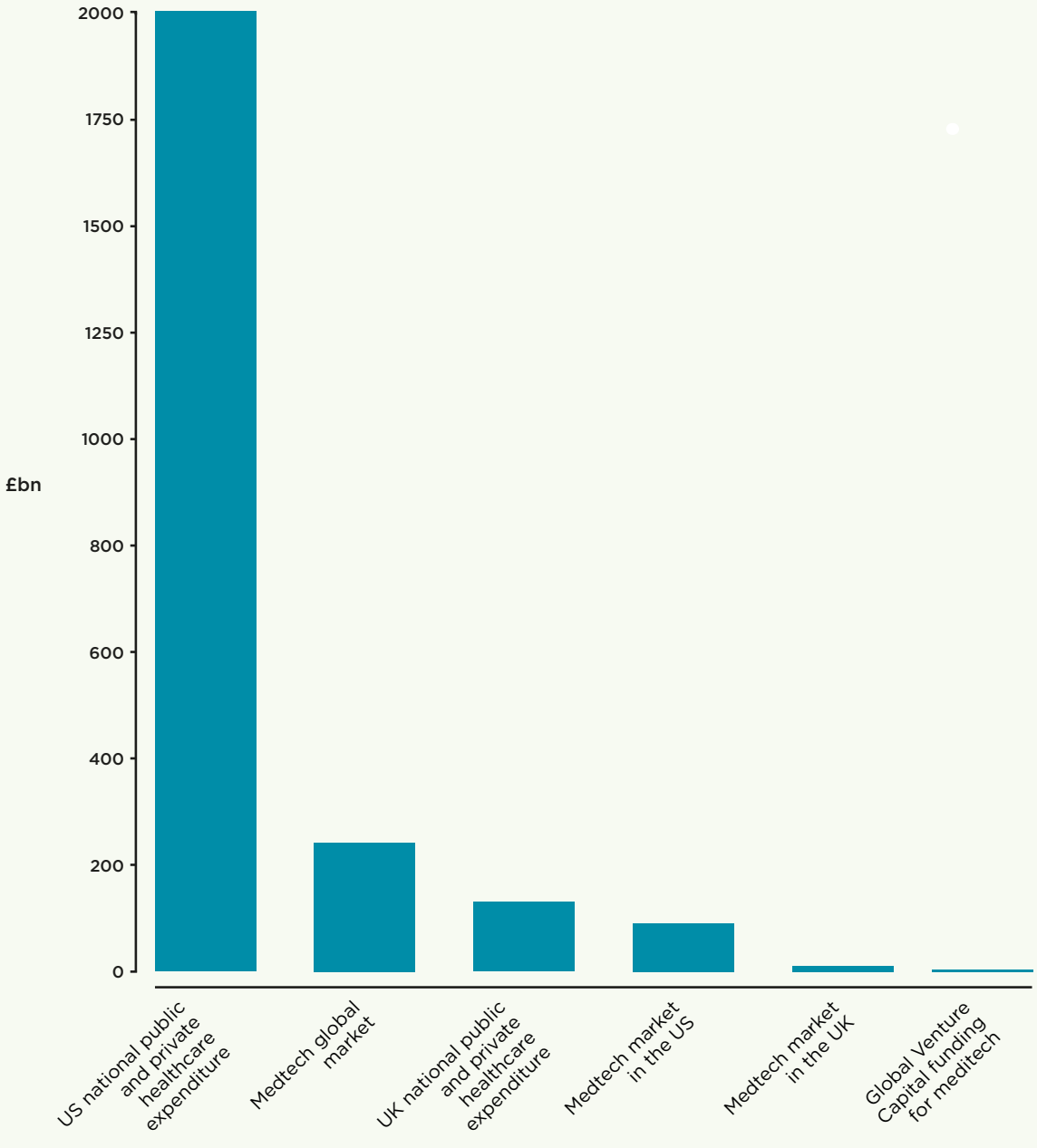
Chapter 1:

MEDTECH INVESTMENT TODAY AND THE POTENTIAL FOR A NEW WAVE OF DIGITAL TECHNOLOGIES

1.1 The established medtech sector

The global medical technology market is worth about £250 billion according to one estimate based on 2012 manufacturers' prices, with £100 billion in the US and £9 billion in the UK.[4] Box 2 gives a sense of the relative magnitude of this investment.

Box 2: **A question of scale: annual figures for medical technology investment**

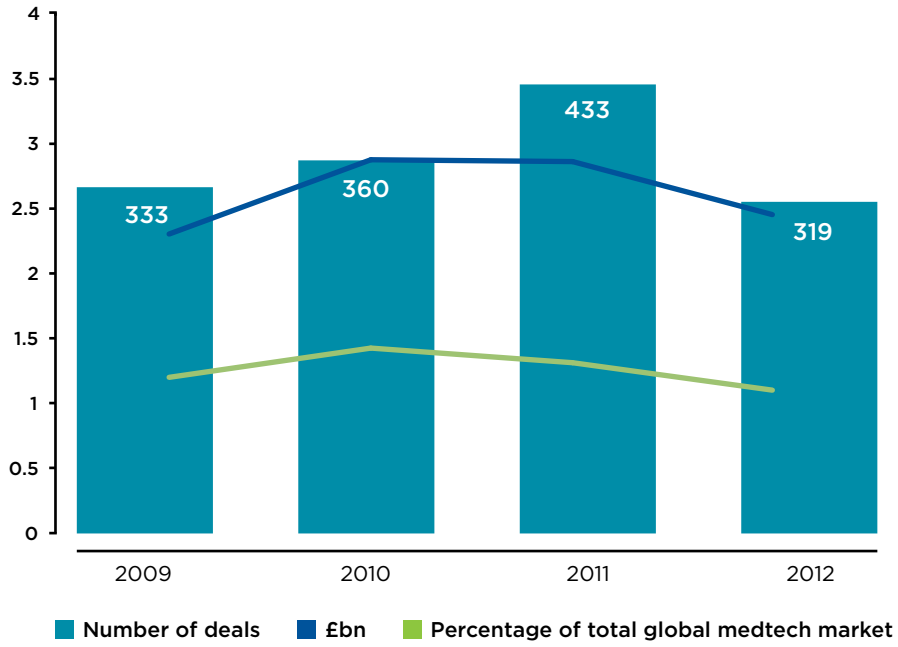


This established medtech sector is mainly SMES – 99 per cent of this sector in the UK. Figure 1a illustrates the reasonable returns in the sector.[5]

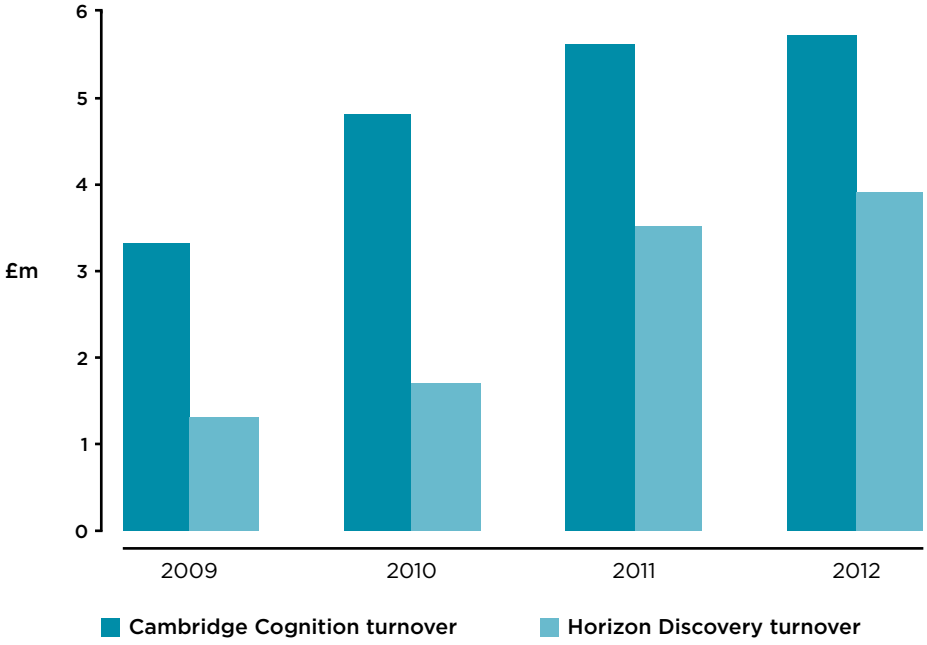
Large biomedical companies are beginning to build capacity in this area. Johnson & Johnson is forecast to be the world's number one medtech company, with a predicted $33.4 billion global sales in 2018 up from $27.4 billion in 2012. The imaging company, Siemens, lead in terms of R&D expenditure and are likely to continue to lead over the next five years.[6]

Figure 1: **A stable medtech market**[7]

a: **Global venture capital medtech investment**



b: **UK medtech company turnover**

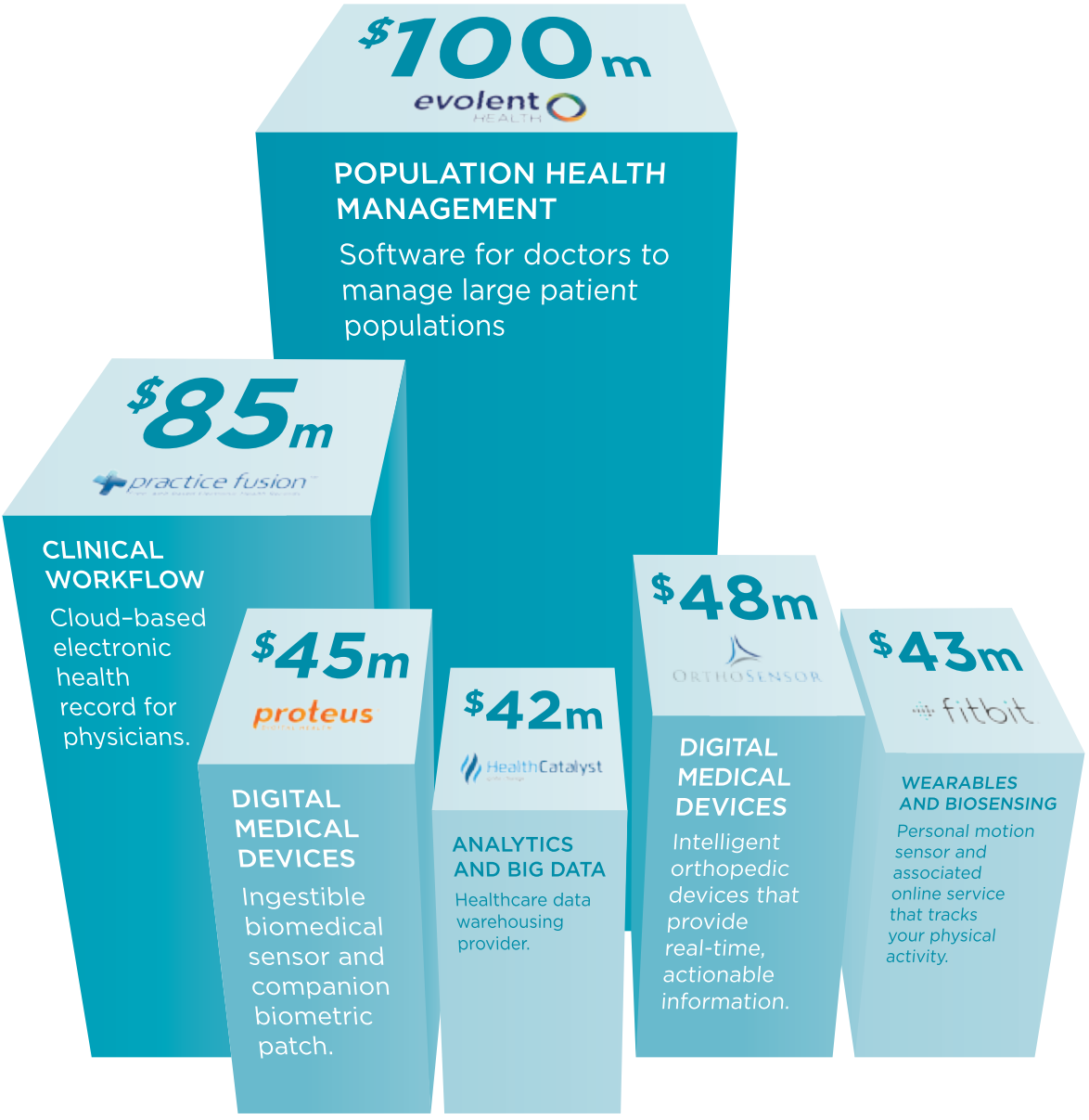


1.2 Digital health: A few early breakers

The UK medical technology sector – including larger companies – has grown over the last four years, with the combined turnover of UK medical technology companies increasing by 50 per cent between 2009 and 2012. The number of companies has increased by 12 per cent in the same period.[8] Figure 1b shows increasing turnover for two companies featured at SVC2UK 2013.

This growth is dwarfed by the level of investment in a small number of firms in the US. Proteus Digital Health won $25.4 million in venture funding in 2009, $62.5m in 2013 and $31.6 million debt funding in January 2014. Figure 2 shows the headline, single investment in Proteus and five other US digital health companies in 2013. Castlight Health provides a digital platform for US company employees to choose their own healthcare options. They raised over $100 million in 2013 and are rumoured to be seeking a $2 billion initial public offering in 2014.[10]

Figure 2: **In 2013 20 per cent of US Venture Capital funding for digital health went to six firms**[11]



Silicon Valley startup incubator Rock Health reports digital health investments growing from under $1 billion in 2011 to almost £2 billion in 2013.[12] This is much higher percentage growth than for medical technology in general, which grew from £217 billion in 2011 to £223 billion in 2012.[13]

Some of these digital health technologies fall under the mainstream medtech definition, but others do not. Mobile Health Apps or M–Health has been a growing market since it took the headlines at the agenda–setting Consumer Electronics Show 2012. It accounts for $564 million of the $2.2 billion venture investment in digital health last year.

As Siemens' increasing investment in R&D suggests, it is not just the incumbent healthcare companies that are building their capacity in this area. Both Apple and Google researchers visited the US Food and Drug Administration about medical device regulation in early 2014.

Apple's 2014 iPhone iOS 8 software update is likely to feature a marquee application codenamed Healthbook. The software will act as a single store for statistics about activity levels that the GPS and accelerometer on a smart phone can measure, like walking distance and speed. Using the camera there are now apps that can track physiological signals like blood pressure and heart rate. The new software is also likely to allow users to enter details about their medications so that they could be reminded to take pills at scheduled times.

Digital health looks ready to provide some early breakers in a new medtech wave that has piqued the interest of large healthcare and life sciences companies, as well as technology giants.

1.3 The promise of a new wave of technologies

The new shape of medtech is taken from a template left by the digital transformation of more consumer–facing sectors.

In 2003, Andrew Thompson and his business partner sat back from a series of entrepreneurial healthcare ventures, from surgical devices to cancer treatments. They set about building a ten year view of the sector, partly because their experience taught them that building a healthcare company takes a decade. They looked at how digital technologies are revolutionising other sectors and asked how healthcare could be transformed as well.

Proteus Digital Health aims to transform healthcare by combining three key trends in digital technology – miniaturisation, cloud–based data sharing and mobile. Proteus is contributing to the digital revolution in healthcare through ingestible and wearable sensing. The process involves placing a tiny ingestible sensor, the size of a poppy seed, inside a tablet or medicine. It is powered by contact with stomach fluid and sends a unique signal to a patch worn on the torso marking the precise time the medication is ingested. The patch transmits the ingestion data, along with other information about the patient's physiology such as rest and activity patterns to a secure smart phone or tablet app. The patient elects whether they want to share the data with doctors, family or friends via the app.

Two years later, Stanley Yang – after leaving his consumer electronics business – was introduced to a group of professors who showed him a headset that detects changes in brain waves in order to drive a toy car. The electroencephalogram (EEG) headset measures beta waves associated with human emotional response and concentration. Historically medical professionals, including neurologists, behaviour therapists and psychiatrists used EEGs as a diagnostic tool. But these devices were falling out of fashion in academic medical research. Yang saw something in this new portable version that could make it successful in the consumer technology market:

> *When you have a brand new technology it is very difficult to convince the consumers to drop all their habits and learn a brand new skill. I need a way to introduce technology to the public with something they are familiar with. When I say you can use your brainwaves to control a car, people think that's kind of strange. But when I say here is the Star Wars Jedi Force Trainer, everyone goes 'Ok, I know what that is!'.*

This led Yang to found Neurosky, which provides affordable EEG headsets to the mass market. (See Box 3 in Chapter 2.) Dan Edwards, MD at HealthTech Advisory (a division of Sagentia Group) agreed that Yang brings something new to medtech.

> *As healthcare becomes more consumer-led we'll see the market entry of companies which are consumer and service savvy. Traditional medtech companies are really struggling to adapt their approach to business to fit with the emerging connected healthcare opportunity and the field is ripe for new entrants to steal a lead in this booming market.*

The re-appropriation of consumer digital technology for healthcare defines the new wave of medtech. But as the wave progresses it will start to interact with previous waves of healthcare technologies. These waves have also brought techniques from adjacent sectors to bear on healthcare practices. Cambridge-based Abcam used novel biotechnologies in the late 1990s to mass produce antibodies used for medical research and for treatment. Abcam is now valued at £1 billion, and has 25 per cent of the world market for antibodies. Section 2.4 looks forward to a time when genomic medicine becomes more widely available, looking at some of the ways it will influence the wave of digital health technologies. Box 5 in Chapter 3 imagines a data sharing system that is more appropriate for an era when personal health, including genetic, information is available in abundance.

Chapter 2:

THE EFFECTS OF NEW MEDTECH ON MEDICAL PRACTICE

Digital services have enabled consumer–driven innovation and customisation in other sectors. Local supermarket offers are based on the buying patterns of reward point customers. Customised toys or trainers are made possible through online design services and intelligent manufacturing software.

Consumer–driven innovation is happening in medtech as well. There is a move from mass produced pharmaceuticals to highly personalised medical treatment. Increasingly people have power over their own health data so they can decide what to do with it. Medical treatment is moving away from large companies and centralised healthcare services. Andrew Thompson called this the beginning of an era of 'mass personalisation'.

This chapter first looks in more details at digital health devices already available, particularly those available direct to consumers. This opportunity extends beyond empowering individuals to be proactive about their health – it is creating a culture of preventative care outside of hospital.

The last two sections look towards a future where large–scale data analysis and new kinds of hardware will be available for more sophisticated forms of prevention, diagnosis and treatment. Section 2.3 describes new ways of integrating patient data, devices and research: 'algorithmic medicine'.[14] Section 2.4 examines the decade–old promise of medicines specific to patients' genetics, which is still to be realised. A legacy of research investment means that genetically–precise treatment will follow close on the heels of today's digital health technologies.

2.1 Monitoring technologies – creating a culture of preventative care

Wearable technology could catalyse the distribution of medtech and the way we use it. A 2011 market assessment, estimated that there will be 80 million sports, fitness and 'wellness' wearable devices by 2016.[15] Imagine a future when someone goes to a hospital and uploads their data. There is no need to tell a doctor how they feel, the data does it for them. This future might become reality very soon. Stanley Yang:

> *"It is very important not just to treat diseases, but to have something that all of us can walk around with. (And I would argue this is a bigger market.) So I don't have to think about my health. But if I run into a problem I want to know before I run into that problem."*

Yang imagined a near future where people will receive a notification that their blood pressure dropped this morning and that an appointment has been made for them in an emergency medical centre. When they arrive at the clinic all of the detailed data about them will have already been analysed ready to help diagnose them. Don Jones from Qualcomm Life recently compared mobile health to the dashboard, gauges and alarm signals in a car, making it easier for patients and their doctors to track what is happening with their bodies.[16] Dan Edwards from HealthTech Advisory called for the realisation of Yang's vision. He urged those innovating in healthcare to consider the whole continuum of care, from predicting a disease, through diagnosis and treatment, and argued that the 35:65 ratio of preventative care to treatment needs to switch to 65:35 to address unsustainable cost of healthcare.

Technologies that monitor lifestyle factors, and prompt users to change their everyday habits, will play an important role in the prevention and management of chronic disease (see Section 3.1).

Other technologies function more like early–warning systems. Proteus Digital Health may one day monitors bipolar and schizophrenia sufferers' social activity on their phone or tablet as well as whether they are taking their medication. Increases in activity may be attributed to the beginning of a manic period. Doctors and family members can then decide to intervene based on these behavioural signals, as well as real time physiological data.

2.2 Diagnostics and treatment at home – increasing convenience

There are also moves to integrate non–invasive medical intervention into daily routine. As Stanley Yang put it, we are moving *"from humans conforming to machines to machines conforming to humans".* Some devices have moved hospital treatments or examinations into patients' homes.

Cambridge Temperature Concepts DuoFertility device can improve chances of pregnancy without invasive procedures. A stick–on patch containing a coin–sized chip records body temperature every few minutes overnight. A hand–held device is then used to read out the temperature data collected via a wireless connection. Data is analysed remotely by the Cambridge Temperature Concepts team and the woman is given a likelihood that she ovulated in the last two days and whether she will in the next six. Early data demonstrates a pregnancy rate after six months similar to that of a cycle of IVF for couples with unexplained infertility or moderate factors affecting their ability to conceive.

EEG kits, like Neurosky's, have been used identify children with concentration disorders, including ADD and ADHD by tracking brain waves associated with mental concentration. More recently, EEGs have also been used in biofeedback therapy, a non–invasive complementary tool used as an alternative to commonplace medications such as Ritalin. Neurosky's wizard–training game Focus Pocus improves a player's cognitive abilities including memory recall, impulse control, and the ability to concentrate. Some US medical practitioners are now prescribing Focus Pocus. This makes biofeedback therapy for ADHD patients available at home – replacing two to three hospital visits a week.

Andiamo, supported by Nesta through Bethnal Green Ventures' acceleration programme, is developing disabled children's orthotics like back supports. They use handheld scanners and 3D printers to produce these at home, potentially reducing the waiting time from 13 weeks to 48 hours. They improve the accuracy of orthotics: a perennial issue for patients, especially for children while they are growing.

2.3 Algorithmic medicine – new forms of integrating treatment and research

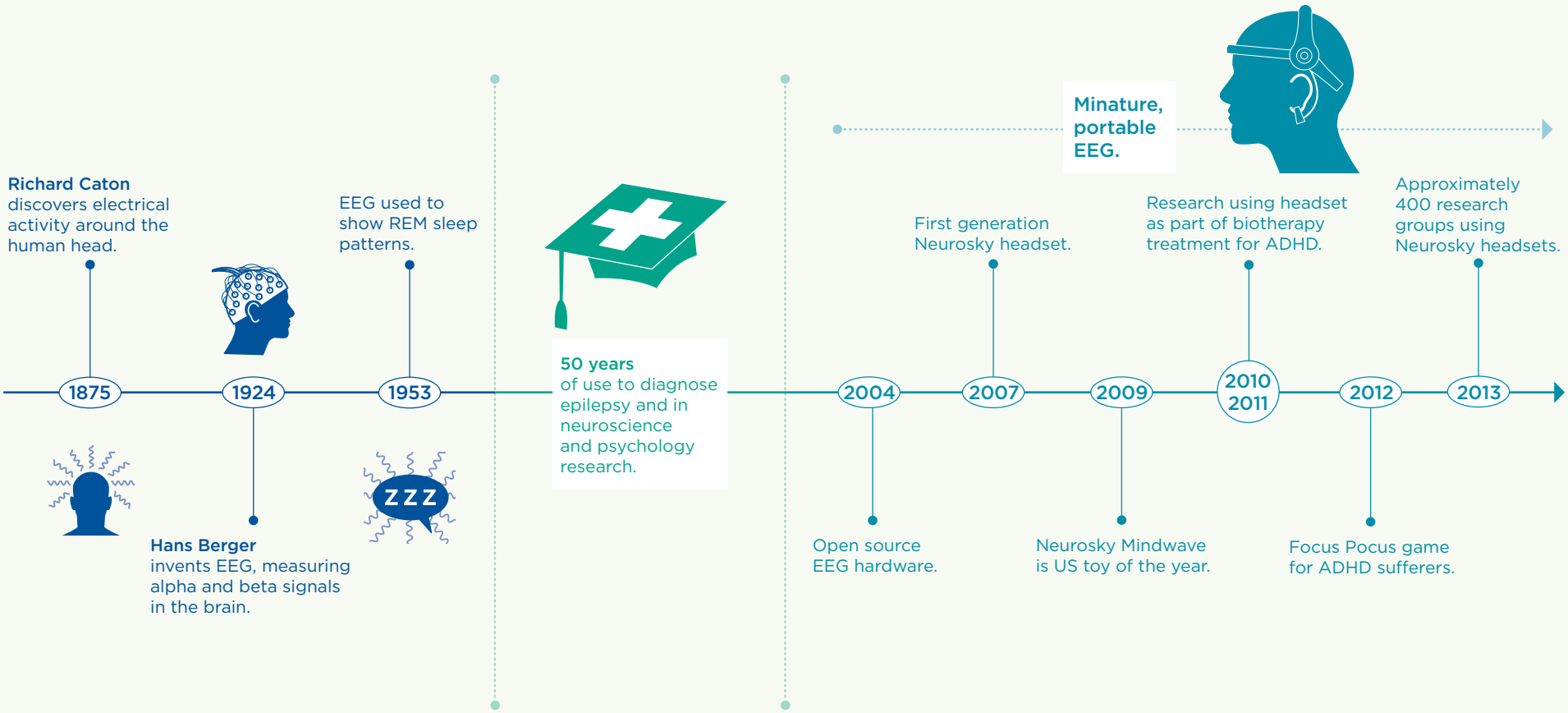
Real time patient data is a new resource for optimising medical care. Increased connectivity is fundamentally changing how and how quickly we can all access new data, and so changing what we can do with that data. In *Doctor Know: a Health Knowledge Commons,* Nesta, The Young Foundation and the Institute for Digital Healthcare at Warwick University argued that there is an emerging system of health knowledge that clinicians, patients, their families and communities all access in real time. The close feedback loops between these communities is speeding up improvements in medtech products and developing new kinds of treatment. Box 3 tells Neurosky's unique version of this story.

Cambridge Cognition's technology is used in several hundred clinical research sites in 50 countries, testing patients' cognitive function for diagnosis and for use in clinical trials. Connectivity has enabled real–time data streaming and visualisation. This means they can check patient responses against expectations, measure, monitor and recommended procedural modifications (e.g. to accelerate patient enrolment) for research and clinical institutions even as the trial is progressing – reducing costs and improving data quality Their research team use this information to test the underlying software, providing phased update of reference standards for assessing patients. Cambridge Temperature Concepts do much the same in order to increase the accuracy of DuoFertility's predictions of ovulation.

In the future, Proteus Digital Health may be able to aggregate behavioural and activity data to uncover new insights into existing pharmaceutical therapies.This could give early signs of the effectiveness of particular drugs. Clinical trials with schizophrenics and bipolar sufferers have already begun this process. Proteus are working with clinicians to better understand the disorders, and how the platform can be modified to help manage them.

Box 3: **The EEG – medical device to toy and back again**

Neurosky took large, expensive medical equipment, miniaturised it and turned it into consumer electronics. The customer base this created became a fertile test bed for medical research. It has taken their devices back into the clinical setting, treating ADHD.



2.4 Genomic medicine – the promise of precision treatment

In 2000 new genetic sequencing techniques and massive data storage capabilities came together in the Human Genome Project, sequencing the first human genome. There were headlines at the time ushering in the new era of personalised medicine. Darrin Disley from Horizon Discovery started in SVC2UK presentation saying *"the reality is that genome was one person, at one point in time and at one fixed state of health".* Now thousands of people have had their genetic code interpreted. But diagnosis based on a patient's genetic profile is still difficult. Few diseases have been traced back to a specific genetic cause.

In 2014 there are new kinds of promise for these techniques. Former Chair of the UK Medical Research Council, and Nesta's Chairman, Sir John Chisholm argued in his prediction for this year that:

> *"Given the phenomenal complexity that billions of years of evolution have buried in the genome we need much larger datasets to give big data analytics the chance to start unpicking the insights which lie within. At some point the innovative and entrepreneurial drive of the new sequencing companies, coupled with the increasing digitisation of health records, will lead to vast opportunities, allowing the world wide analytics community to unearth hidden secrets."*[17]

His hope is that the 100,000 Genome Project in the UK will provide a new rich dataset for this kind of analysis. This new company was set up by the Department of Health to sequence the DNA of up to 100,000 patients over the next five years. It will concentrate on improving understanding of the genetic basis for cancer, rare diseases and infectious diseases. The companies that will do this analysis are already here. Eagle Genomics was founded in 2008 by Cambridge MBA graduate Abel Ureta-Vidal. The company provides large-scale data analysis techniques for life sciences companies across several sectors. Located near the European Bioinformatics Institute outside Cambridge, Eagle is part of an emerging centre of excellence.

In March 2014 Craig Venter, whose private company competed with the publicly-funded Human Genome Project, launched a new US company called Human Longevity, co-founded with Peter Diamandis. Venter aims to set up the world's largest human DNA sequencing operation, capable of processing 40,000 human genomes a year. The company will analyse the data itself, with a focus on improving understanding of age-related illnesses like cancer and heart disease.

Drugs based on genetic profile will improve the accuracy of medicines. Stratifying medicine by patients' genetic makeup reduces trial and error in medical treatment, and will reduce the cost of care. At the moment, approximately of 60 per cent drugs are effective. This number is only 25 per cent for cancer treatments. Sometimes the success of a drug depends on the genetic profile of the patient. Until 2004 the drug Iressa had a 10 per cent success rate treating lung cancer. Those that responded to it often lived for months or years longer than their diagnosis. Then researchers discovered that Iressa attacked cancers that came from a specific genetic mutation – and was effective only in those cases. European legislation now indicates this drug for all lung cancer patients with the mutation.

Some predict that genetically-precise medicines will help the pharmaceutical industry to bounce back. One forecast shows growth in the prescription drug market increasing to the same levels as medtech growth from 2015 onwards.[18] The pharmaceutical business model requires reconstruction to develop drugs aimed at specific genetic populations rather than reaching for the decreasing number of drugs with a mass market.

Darrin Disley argued that the real opportunity comes from more direct genetic interventions – gene therapy. Horizon Discovery develops technologies that allow scientists to edit genomes, usually by replacing a mutated gene with a functional one. These techniques have had a chequered history. In the 1980s some patients in gene therapy trials lost their ability to fight off an infection; their immune systems failed. High hopes for these techniques have returned recently. In January 2014, researchers improved the sight of six people suffering from an inherited genetic eye disease, Choroideremia, which left sufferers blind. Researchers introduced a virus that attached itself to cells in the patient's eye, replacing the faulty gene that causes blindness with a functional copy. Within two years all six patients had improved their sight. The tools to make this kind of gene replacement are improving all the time. Disley imagines a future where we can edit the human genome on demand.

Developments in genetic analysis promise a new generation of personalised medicine. But they sit in a more traditional nexus between life science research and specialist medical care. They are not yet as visible as the scalable digital health products that most people see.

Chapter 3:

WHAT MAKES THE HEALTHCARE SECTOR DIFFERENT

As the new wave of medtech embeds itself in more sophisticated products and services, innovation will increasingly rely on the unique features of the healthcare sector: from responding to the burden of chronic disease to navigating the complex relationships between doctors, researchers and government policy. This chapter looks at these one by one. It starts with an example that brings them all together.

Box 4: **Understanding product development in the healthcare sector through a single example**

Andy Blackwell from Cambridge Cognition, framed the long journey from idea to successful product product introduction to the NHS in terms of a single health problem: the need for better tools to diagnose dementia. Specifically, he wanted to develop objective understanding a patient's mental state at the point of care, using a standardised tool. The team behind the product developed tests for cognitive function as part of their academic research in the neurosciences. Spinning the technology out of Cambridge University, the team originally saw a market for selling their test to other researchers, and set up Cambridge Cognition in order to do so. Marketing the product to the academic community – the products are now used in over 700 research institutions – resulted in a global network of advocates for the technology and a continual stream of independent research data validating the effectiveness of the tool. It was then adopted by large pharmaceutical companies, who saw the value in the software for evaluating the safety and efficacy of investigational drugs. Enabled by the arrival of ubiquitous mobile computing, the tool finally made it into GP surgeries when it could demonstrate the time and money it saved and the improvements in diagnosis over conventional, highly subjective tests.

The development of Cambridge Cognition's software was motivated by the need to treat chronic disease (3.1). It was successful because of three factors: responsible management of new kind of data about patients (3.2 and 3.3); the cost–savings it offered a health service (3.4); and a sustained relationship between academics, doctors, patients and industry (3.5).

3.1 The burden of chronic disease

In the 20th century, we built a healthcare system to manage acute problems like pneumonia. It was based on what Andrew Thompson calls *"the signature tech of that time: sophisticated buildings, educated people and high–tech products that were tested in everybody and worked in some bodies".* The demands on the healthcare system have changed.

Globally, the death rate from chronic disease is double the death rate from the combination of all infectious diseases (including HIV, tuberculosis, and malaria), maternal and perinatal conditions and nutritional deficiencies. In 2009, UN Secretary Ban Ki–Moon called the burden of chronic disease *"a public health emergency in slow motion".*[19]

Nearly half of all Americans and approximately a quarter of people in England live with a chronic condition such as high blood pressure, diabetes or asthma.[20]

Increased preventative care (Section 2.1) would improve treatment of chronic disease. The risk of dementia increases with lifestyle factors such as diet, exercise and smoking. The risk is built up over a lifetime.[21]

3.2 Privacy concerns about sharing personal data

Medtech products and services with the greatest potential are those that balance legitimate privacy concerns, commercial value and the value to society that comes from sharing health information.

Digital privacy has been a central theme of public debate in the last five years. At the core of the discussion, there is a tension between the right to a private life and legitimate public interest. The subject of debate has moved from details of MPs' expenses and the Leveson enquiry into phone hacking by journalists through to Wikileaks' publication of diplomatic telegrams and Edward Snowden's revelations about the US Government eavesdropping on civilian communication. The headlines have been about leaked documents, freedom of the press and the proper limits of government power. None are simple cases of security breaches, where improvements in security would have removed controversy. Current debate about privacy embodies a tension between individuals' rights and value for society. It will not be solved with a technological fix.

Everyone has a legitimate legal interest in safeguarding their privacy if data could be used to exploit, stigmatise, or discriminate against them, or if it infringes on personal autonomy.[22] This is not the same as an absolute right to all data about ourselves. For instance, European legislation around personal data allows that data is shared when it is in the public interest, including for academic health research. New legislation is likely to standardise researchers' rights to access personal data across European states.[23] This will make it easier for researchers to apply for data outside their nation state. The NHS is taking steps to make patient health records available to researchers via care.data.

The move to electronic health records in the US (Section 4.2) brings with it a series of companies changing the relationship between the patients and centralised health service providers. Hello Health offer medical practices a fee for each patient that signs up for the Hello Health patient record database. Patients pay to sign up to Hello Health, which improves the convenience of booking appointments, allows them to email doctors directly and shares their information amongst their different specialist physicians. Nat Findlay, CEO of Hello Health, reiterated that *"we do not sell the data in our system or use it for commercial purposes"* in a blog post to the company's website in 2014. The data is, however, fed back into the healthcare system in aggregate form, in order to help improve quality of care. And the US Government financially rewards companies adding to the network of electronic health records.

The Finnish Government has invested in Taltioni, a single database and service platform containing health information about Finnish citizens. Everyone can store, collect, produce and share electronic information related to their own health. Data is shared with health and care providers, but only if and when people grant access to that organisation. Information can also be shared with another user or healthcare professional. Information shared by family members makes it possible to participate in their care. The rationale behind this system is to encourage more proactive healthcare.

UK citizens have long had worries about reuse of health information. A 2006 UK survey showed that only 69 per cent of the UK population were willing to share their personal health records for medical research purposes.[24] The NHS has been accused of failing to communicate exactly how much care.data will share and with whom.[25] They have also failed to address the much more obvious issue that this kind of survey result reveals; almost a quarter of the population are not convinced by the argument that the value to society gained from sharing their medical records is great enough to mitigate against the potential loss of privacy. It's important to build systems that take into account the significant group of people who would not be happy sharing their official records.

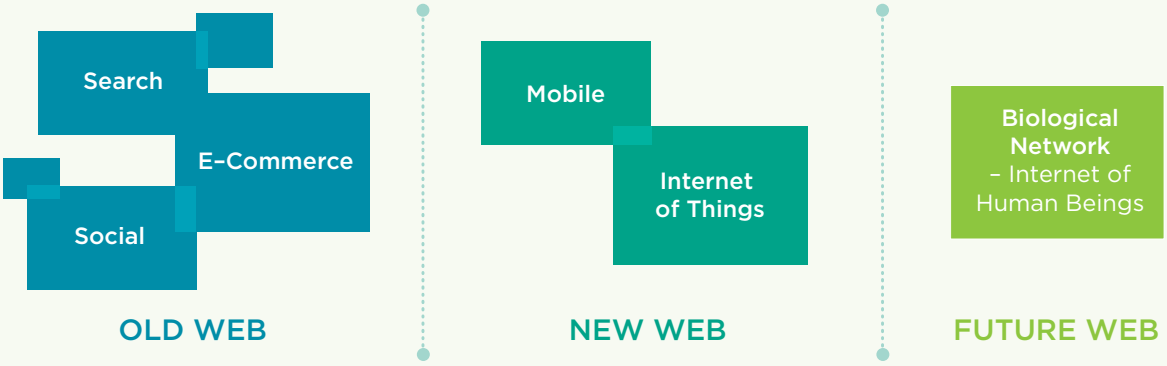
The picture might be different for sharing specific physiological data. A recent survey showed 84 per cent of people in Brazil, China, France, India, Indonesia, Italy, Japan and the US would share their vital statistics like blood pressure, and 75 per cent would share information from a special monitor that's been swallowed to track internal organ health.[26] But that still leaves 16 per cent or 25 per cent, depending on the device, that would not be comfortable with a service sharing their data.

There are new companies formed to help people create personal data banks to retain or regain privacy. Qiy in the Netherlands, Mydex in the UK and Personal in the US store and protect personal data, loaning it to companies (potentially including healthcare providers) that the user trusts. These services are sold on empowering citizens to take back control over their private information. HealthBank is a patient co-operative based in Switzerland, aiming to build a global secure depository for patient data.

Other services are emerging that help users sell their data. Our Health Data Co-operative in the US is built on the premise that patients should benefit economically from access by third parties to their health information. A New York based startup, DataCoup offer people $8 a month to sell transaction information from a credit card and the data from their social media accounts. In the future, they may also allow people to sell information from apps devices that collect information about their health, and possibly more formal health records too.[27] Last year, Appcelerator – an app development platform with over 200 million users – acquired a tool called Singly that allows individuals to collect API feeds from several of health apps at once. Singly was created to simplify health data collection into a single database, but it could also be used as an easy access point for buyers. Handshake is a UK-based personal data marketplace (in closed beta at the moment) that allows you to negotiate a price for your personal data directly with the companies that want to buy it. Andre Boorsma in the Netherland has developed the idea of a digital currency that trades health data for Healthcoins that could be used to pay for healthcare or for healthy food.[28]

These are repositories that create a layer over the current consent systems available online. DNA Guide's Alice Rathjen started her talk at SVC2UK by outlining how genetic data and biometrics may cause the web to evolve into an 'Internet of Human Beings'. She advocates that the UK consider converting health record into biological domains, so that patient ownership of the data is clear.

Box 5: **Old web, new web, future web**



Alice Rathjen described the first generation of the internet or The Old Web as centred on search functions, social networking and e-commerce. The New Web has shifted to mobile access and networks of sensors systems like smart electricity meters or GPS watches. This web spreads data about individual humans across different nodes on a network. The Future Web consists of a network of digital human beings that are emerging out of the oceans of big data.

Rathjen argued that: *"we need to start discussing, and becoming conscious of, the evolution of our digital humanity".* She thinks that the proliferation of health data, particularly genetic data, should be used to build an internet of human beings. Instead of worrying about loss of privacy, *"we take these biometrics which are combined with big data, and rather than being fearful, we turn this tech on its head"* to create personal domains that re-introduce human autonomy to the web.

Her vision is a future where individuals hold their own portable personal health records, including traditional health records. But it would also include three other types of information: genetic, physiological and lifestyle. Everyone could choose where they register this information: *"human beings would become top level domains on the web, with the ability to take themselves offline."* Examples of registrar domains for the UK could be: www.patient_ID.nhs.uk.bio, www.patient_ID.sanger.ac.uk.bio or www.patient_ID.ncri.org.uk.bio. These domains would send out information to individuals in an RSS feed, regularly updating them with how their data is used, allowing them to operate real time consent.

Researchers could begin converting their human genetic datasets into biological domains and serve as temporary guardians until the data was returned to the patients' control. Those researchers who move from open and 'de-identified' data to real time 'consented' data will end up with better data, and more of it. Scientists will have access to more detailed information about individuals, and more people would share their data if it is clear what they are consenting to share and with whom.

DNA Guide is developing technical systems to enable people to give highly specific consent – deciding which part of a genome is shared. It also lets researchers annotate a genome, giving detail on the quality of sequencing and analysis. The DNA Guide system could produce better quality control and more dynamic updates and consent.

Behind Alice's vision of a .bio domain owned by each individual – with a variety of domain registrars for genetic data – is a desire to avoid creating a Facebook for health data. The technologies for managing large populations of genetic data are so powerful that human autonomy must be built into these systems by design.

3.3 The ethics of patients engaging directly with the healthcare system

The promise of algorithmic medicine (Section 2.3) points to a future when not just our records but our devices are intimately connected with the healthcare system. Neurosky were approached during SVC2UK by a Cambridge academic asking how he could use their EEG kit for patient trials. Stanley Yang's response was to ask why doesn't the researcher bypass the official trial and send out a request for data from the 100,000 EU citizens who have already bought a Neurosky headset for themselves. Neurosky work closely with the research community, and they know one of the reasons users buy the kit is to take part in research.

New monitoring technologies bring with them new ethical implications, particularly for how and when a patient is told about their diagnosis. This is a particularly acute concern when the disorder has no known cure. In the 1960s, a survey of doctors revealed that 90 per cent did not reveal diagnosis of cancer. The same survey 20 years later showed that 98 per cent of doctors reported the diagnosis to patients. This is partly due to a shift in medical training. But it is also because cancer treatment has improved, and doctors could give their patients treatment options.[29] Genetic sequencing technologies like 23andMe and diagnostics like Cambridge Cognition's software provides early signals of unmodifiable diseases or conditions underserved by currently available treatments. They bring back to the fore questions over whether it's ethical to pass on that information to a patient. Some of these concerns are partly addressed by EU moves to mandate gene counselling (Section 4.33).

Taking Stanley Yang's imagined near future for monitoring technology (Section 2.1), it's not clear what the guidelines should be for a clinician that sees signals on a remote monitoring device that point to an imminent fatal heart attack. Should the patient be warned and brought into hospital even if they have a 98 per cent chance of death? As the breadth of data available for preventative care increases, other novel forms of support for patients and doctors will need to be considered.

Patient groups have become a new kind of intermediary in the healthcare system. Inspired by Stephen Heywood's frustrations when he was diagnosed with the rare condition, amyotrophic lateral sclerosis (ALS), PatientsLikeMe was founded a decade ago to answer questions about treatment options, and about what to expect for those diagnosed with long–term medical conditions. The online platform now provides support groups and data sharing for patients with dozens of conditions including MS, Parkinson's disease, HIV, epilepsy and people with transplanted organs. Participants note what hurts, where and for how long. They list their drugs and dosages and score how well they alleviate their symptoms. The site then compiles the information into graphics available for anyone to see.

PatientsLikeMe provides information about patient experience that has long been missing from research that often drops off after a drug is approved. But this proactive approach falls outside the usual checks and balances of the healthcare sector, including safeguards on reuse of patient information. There needs to be more support for developing guidelines for patient groups – encouraging them to be more involved with patient care, but with clear consent mechanisms and reuse criteria.

There are opportunities for individuals to take a more active role in research. Trialreach is a portal for patients to access information about clinical trials near them. It was born from the founder's frustration with the fragmentation of clinical trials in the UK. People could only apply for trials in their own NHS Trust. The platform offers free access to clinical trial information, and is free for public sector trials to advertise. Trialreach sells the service to large pharmaceutical clients looking for patients. The majority of their business is currently with commercial clients in the US, but there is discussion of bringing the platform inside the UK NHS system.

Trialreach's founder, Pablo Gravier, hopes that his platform is the beginning of a more general change in the way that patients engage with health research. There are some examples of people leading healthcare research themselves. Maria Gjerpe, an ME patient from Norway, raised $1.2 million for a clinical trial using crowdfunding. Gravier wants to see more people challenging what trials are done and how they are designed. The advantage of this kind of engagement is that it is embedded in the healthcare system: it does not rely on self-described symptoms, the data has a known origin and it can be more readily used to develop new medicines.

3.4 Providing cost-effective treatment

Nesta predicted that the NHS could save £4.4 billion a year if it adopted innovations that involve patients, their families and communities more directly in the management of long-term health conditions.[30] This saving is based on better collaboration between communities, social care and the NHS, and reductions in unplanned admissions and the requirements for expensive, acute care. Workplace healthcare programmes can reduce health risks including high cholesterol levels, cigarette smoking and high blood pressure. One large multinational US company estimated that it saved $4.7 for every dollar invested in its programme.[31]

Medical technology can also play a part in these reductions, often by commoditising doctors – i.e. deploying them at one step removed from treatment or diagnosis.

The causes and effects of many mental health conditions, including those associated with long-term physical health conditions, can be treated by Cognitive Behavioural Therapy (CBT): depression, drug and alcohol abuse and pain management for instance. PsychologyOnline offers live CBT accessed via the internet. Therapy is delivered via an instant-messaging conversation with a qualified therapist. The instant-messaging approach removes stigma and inhibition from what are often difficult and embarrassing conversations, leading to improved outcomes (60–70 per cent recovery vs. the national average of less than 50 per cent) and quicker recovery – on average 40 per cent fewer sessions are required than with traditional face-to-face therapy. In addition neither the therapist nor the service user needs to travel to attend appointments, which are usually conducted out of office hours. PsychologyOnline was founded by two NHS psychologists in 2011, keen to use the techniques validated by a clinical trial published in *The Lancet* in 2009 to make more effective use of resources and improve outcomes.[32] High demand for CBT in the UK has created long waiting lists. PsychologyOnline has been used to remove waiting lists altogether for patients referred for CBT by GPs in Surrey, where PsychologyOnline has been commissioned by five NHS Clinical Commissioning Groups (CCGs) covering 141 GP surgeries.

There are other similar technologies taking significant steps to make treatment much more accessible. Sleepio is a six week programme of therapy developed by CBT expert Colin Espie. The service monitors patients' sleep patterns, using these to suggest a daily schedules including activity levels and relaxation tapes. This system takes a different approach from online therapy; it removes the therapist altogether, using a computer algorithm and peer support to treat insomnia. Cambridge Temperature Concepts' DuoFertility system costs £495, much cheaper than the IVF treatment it is as successful as. Genomic medicine promises to provide new kinds of gains in cost efficiencies because it can provide genetically personalised care (see Section 2.4).

These systems and others like them could eventually automate some of the services currently provided by doctors. But there are risks in devolving too much to computer-based services. Automated self-help for depression and anxiety has had mixed results as it requires significant patient motivation, which is often lacking in such conditions. Sleepio is different because insomnia sufferers are often more motivated. Cost-savings delivered by disintermediation of medical services are not always successful. Sometimes they miss vital factors in treating a complex condition. This echoes David Shaywitz' warning (in the introduction) about the complexities of healthcare, and the need for professional input to create realistic limits on the role of new products.

3.5 Sustained relationships between patients, doctors and researchers

Previous Nesta research has set out the argument for collaboration in the UK biomedical industry,[33] recommending more coordination between universities, the NHS and businesses. Algorithmic medicine (Section 2.3) is creating new relationships between the groups, as well as more directly with patients. These new means of collaboration could accelerate research and treatment is many areas. Medtech has a significant part to play in this reformed knowledge creation and sharing system.

Cambridge Cognition's success was built on building a successful product for use in biomedical research before it reached the mass market. Without that test bed, they would not have produced the software platform, nor had the validation required for selling back into the healthcare system.

Many of the participants at SVC2UK see their companies as part of an active community of researchers. Andy Blackwell characterised Cambridge Cognition as a central part of a burgeoning applied neuroscience and technology community in the UK, acting as a partner in a number of large-scale academic-industry translational research programmes. Horizon Discovery is currently involved in several major European translational research initiatives including clinical trials that use biomarkers to improve cancer therapy outcomes. Eagle Genomics provides tools that are primarily used for bioinformatics analysis by scientists.

Neurosky does this differently. They open up their data platform to researchers, and have over 400 universities using it, but purposefully stay away from taking part in research themselves. This keeps regulatory overheads to a minimum. As the consumer-led medtech sector grows, and legislation gets tougher, there are likely to be more platforms like this that choose to sit firmly outside the medical research landscape.

Embedding innovation in clinical practice is not easy. Doctors are concerned with managing their workflow and costs, and a new product or service must show that it is valuable in these terms. Recent Nesta research shows that a small group of GPs are consistent early adopters of innovations.[34] A follow-up project will look in more detail at the adoption of new innovations in secondary care and public services more generally. Andy Blackwell made the point that these early adopters are often also innovators themselves, and often want to customise a product:

> *"There is a community of enthusiasts familiar with the technology applied in the context of clinical research that already understand the potential value if applied in a healthcare setting. The early adopters just need some awareness that the healthcare product exists and then they come to you. Although this will always depend on the policy drivers: for example underdiagnosis of dementia or lack of access to psychological therapy because of waiting lists."*

Successful integration with doctors comes from understanding how they assess potential new products and services. If a product can be integrated into their workflow or respond to a national policy, then it is likely to gain more traction.

Chapter 4:

DIFFERENCES IN US AND UK SUPPORT FOR MEDTECH STARTUPS

Chapter 1 describes how large incumbent healthcare firms are watching the startup market closely (1.1) and how Silicon Valley experience in consumer technology platforms has provided an easy segue into digital health investment (1.2). At the same time, pockets of life sciences expertise in Europe may be important in fundamental disruptions yet to come (2.4).

Chapter 3 outlines key features of the healthcare sector – the non-technology factors that will give the new wave of medtech a distinctive shape. As the new wave of medtech embeds itself in more sophisticated products and services, innovation will increasingly respond to the unique characteristics of the healthcare sector.

The medtech startup environment also is also affected by specific factors related to national investment culture and regulation. This chapter looks at how differences between the UK and the US affect the potential for SME medtech growth.

In both countries there are powerful service providers and strong legislation, with large firms that know how to navigate both. David Cleevely illustrated the direct affect this has on startup funding decisions in his introduction to the SVC2UK 2013 health summit debate:

> *"There are some very significant barriers with medtech because there are hundreds of years of established protocols, processes and procedures in medicine. And no matter how clever the idea, you have so many hurdles to get across... So when we at Cambridge Angels get a pitch about medical technology, one where you would have to deal with the NHS in the UK, we often have to say sorry we're not really interested."*

And there are good reasons that many of these barriers will not go away. Personalised medicine, unlike personalised manufacturing (3D printing), still requires a high degree of interpretation and expert analysis. Pacemakers need to be verified for accuracy and safety to much higher standards than sensors than monitor household electricity use.

But there is also a fundamental skew to investment in medtech. It is a market is built on more than entertainment; it's built on improving human wellbeing. *"If you want to make a bet, I would say its health. If we're willing to spend so much on tech, how much will we spend on our health?"* said Herman Hauser introducing a session speculating on the first $1 trillion company at SVC2UK 2013.

Cleevely went on to illustrate the force of the social, rather than economic, value on investment decisions in medtech:

> *"But sometimes the trouble is the passion, the vision for what this could do, the fact that you are saving lives and making quality of life much better. This means that against our better judgement sometimes we invest because we also believe this stuff is really important."*

The opportunity of digital technology is greater, but the barriers to entry are higher than for other sectors that have digitised many of their products and services. These barriers differ from nation to nation.

4.1 Investment opportunities

Early-stage investment in the UK has traditionally had a bad reputation compared to the US. In 2012, UK venture investment was 6 per cent of that in the US, despite having 20 per cent of the population and 16 per cent of the GDP. The story for the health sector is even tougher; 12 per cent of UK venture investment between 2008 and 2012 was in biotechnology and health; 20 per cent of US investment was in this sector. Recent Nesta research concluded that this gap is in part due to the environment for entrepreneurs – differences in culture, talent pool and regulation. The research also pointed to poor exit performance as a contributing factor.[35]

Interviews with entrepreneurs at the SVC2UK event provided an overview of the transatlantic investment environment as well as medtech specifically. Some participants made a familiar argument about what had led them to set up medtech companies on the West Coast. Andrew Thompson said *"Silicon Valley works because it is the biggest high-risk capital market in the world. It works because a 27 year old with a good idea can go to someone on Sand Hill Road and within 48 hours get five million bucks".* The expansion of US East Coast venture markets in recent years has not recreated the same investment culture found on the West Coast. Several interviewees for Nesta's recent research suggested that West Coast investors place a premium on high growth rates rather than current revenues or margins. On the East Coast this tendency is less, and for UK and European investors, revenue and margin have much greater importance in establishing a valuation. The legacy of fast turnaround financing, and an emphasis on potential customer numbers rather than the profits, keeps some entrepreneurs in Silicon Valley.

Other speakers argued that the UK has turned itself into an attractive destination for small companies. Corporation tax will drop to 20 per cent from April 2015, reducing to 10 per cent for R&D arising from UK registered patents (the patent box). Tax credits are available for R&D spending. Darrin Disley said: *"I am advising American startups in Silicon Valley to move to the UK to take advantage of the tax credits, and the low corporation rates if you look at the patent box."*

4.2 Integration with national health services and policies

Recent US policies have created indirect incentives for healthcare startups. Povl Verder, digital health advisor and CEO, SIME Diagnostics, said that in the US *"healthcare technology used to be where startups went to die".* The 2009 The Health Information Technology for Economic and Clinical Health (HITECH) Act changed this, providing $25.9 billion for health information technologies. This led to a new network of population-level health information. Followed by the 2010 Affordable Care Act, the US startup scene has had some strong policies turning its focus towards healthcare.

Jeremy Hunt, the UK Secretary of State for Health, set himself the self-confessed 'brave' target of providing researchers with online access to NHS patient records via care.data by 2015. When George Freeman was made Government Life Sciences Adviser in 2011, he helped create a Biomedical Catalyst Fund that offers proof-of-concept funding for small companies to work in the NHS. This supportive environment for new genetic sequencing and analysis companies is expanding in London. The flagship Francis Crick Institute for medical research in King's Cross is under construction. There are plans for a £1 million MedCity set up to rival the 15,000 new companies attributed to East London's TechCity initiative.[36]

At SVC2UK 2013 there remained echoes of an old story about UK weaknesses in turning inventions into companies and scaling those companies. Although Darrin Disley advises startups to move to the UK, he also bemoans the country's lack of entrepreneurial culture: *"it needs ambition from entrepreneurs to want to drive and grow great companies and not just to make millions of dollars."* He challenged the SVC2UK audience to change that.

Opinions at SVC2UK differed on whether having a national healthcare system made it easier to scale innovation or not. Andrew Thompson argued that each NHS Trust is different, while selling to care providers like Kaiser Permanente in the US offers great gains; they have nine million customers. Historically the national system in the UK has been heralded as a great platform for innovation, improved by the addition of the National Institute for Health Research in 2006. New intermediaries – such as Academic Health Science Networks and Clinical Commissioning Groups – will have an important role to play in bringing innovation to bear on the UK healthcare system.

Dan Edwards argued that better integration of new technologies will come from more proactive clinicians: *"we need to unplug doctors from their immediate treatment scenarios and get them to go upstream".* He pointed to the Medical Futures Awards judged by NHS leaders as an example of a move in that direction. There could also be initiatives that use the recognised pool of early adopter GPs to help companies much earlier in their design process. To encourage more institutional entrepreneurship and early adoption in the NHS, the UK's National Institute for Clinical Excellence (NICE), has started Medtech Innovation Briefings for healthcare staff considering using new medical devices.[37]

In the US, particularly in Silicon Valley, there are many doctors–turned–entrepreneurs. Some have come through programmes like Stanford's StartX Med. This intensive course helps medical students accelerate the development of their ideas for new healthcare technologies including consumer IT and hardware. The 100 companies formed in the programme's first two years raised an average of $1.8 million each from investors. Healthbox, another accelerator programme, has recently added London to the list of US cities they operate in. Black Forrest has recently set up as Europe's first accelerator programme dedicated to the health and fitness sector. It follows a successful health technology Startupbootcamp Dublin in 2013. However, the European programmes are not integrated into medical training in the same way that Stanford's is.

4.3 **Regulation**

A new wave of medical technologies comes with a particularly difficult regulatory problem. The speed of digital technology innovation has outpaced regulators in the last decade. Medtech comes with much more immediate public concerns than other sectors. Misdiagnosis, the leaking of highly sensitive personal data, and what some are calling iPodchondria – hypochondria caused by excessive monitoring of personal activity – are already making headlines.[38]

Andy Blackwell warned that *"the ultra–fast product iteration that we see in consumer apps is very unlikely to be matched for digital healthcare products that are rightly subject to stringent regulation".* The bar for a minimal viable product when that product is an app is different when the new version of that product has to go back through regulatory approval. Although, Blackwell added, this needs to be seen in proportion to other barriers to innovation; the ability of the healthcare system to adopt and engage with new medical technologies is a much more significant impediment to progress than the due process of medical device regulation, at least in the EU.

Even companies coming to medtech from other, less highly regulated sectors are approaching with caution. The meetings between Apple and Google specialists and regulators mentioned in Section 1.2 are far upstream of product development.

Medtech regulation depends on two things – the novelty of the device and its potential risk.

There are four categories of risk for medical devices in Europe (see Box 1). Low–risk (Class I) devices like hearing aids and wheelchairs can be self–certified; the manufacturer must declare the product meets the requirements of European Commission directives, receiving a conformity marking or CE mark in return. High–risk (Class III) items like pacemakers are tested by national

bodies in each EU state. In the US there are three classes with similar distinctions. But in the US there is no self-certification, or equivalent of the CE mark in the lowest risk category. Instead, submissions must be made under each class or for a 501(k) exemption when an item is similar to pre-existing products.

4.31 The FDA is the Gold Standard

In November 2013 23andMe – a Google-backed venture offering human genome sequencing – was asked by the US Food and Drug Administration (FDA) to stop providing health-related advice with customers' genome information.[39] 23andMe had failed to pursue their application for FDA clearance to provide this kind of advice for over a year. The company's Personal Genome Service had up to that point provided individual reports on hundreds of diseases and conditions. The service marketed itself as a first step toward mitigating serious diseases. The FDA was concerned about the public health consequences of inaccurate results. 23andMe have now suspended health advice services. One of details missing from the public account of the 23andMe case is why they failed to receive the 501(k) exemption from the FDA when they applied for it in 2012. Ninety-nine per cent of medical devices in the US receive regulatory clearance using this exemption offered to items that are similar to pre-existing products. This greatly reduces the costs of bringing a product to market. By leading the way among commercial genome sequencing companies in the US, 23andMe were subject to a first-mover disadvantage.

Proteus Digital Health knew that developing and certifying a new kind of sensor to monitor the body from the inside would be a long process. They were the first company to provide this kind of sensor, adding not just a new product to the market but a new category in the class of high-risk medical devices. This process took five years and hundreds of millions of dollars.

Andrew Thompson acknowledges that it would have been quicker and cheaper to carry out their product assurance in the EU, where a firm applies to a national notified body, the Medicines and Healthcare Products Regulatory Agency in the UK. But, Thompson argued, it is easier to scale medtech through the FDA process. The FDA's 'Gold standard' is also a global standard: *"so once you are through that process there is access to other markets outside Europe."* Proteus's system is particularly attractive to the Chinese market. They can monitor adherence for those on long-term medication, responding to a major global medical issue – 50 per cent of patients with a chronic disease fail to take their medicine correctly.[40] China also has a large market of counterfeit medicines. Proteus's ingestible sensor gives each pill a unique identifier, making counterfeits more difficult. Having pushed through the FDA process, Proteus may find it easier to move into other markets like China.

4.32 The European CE mark offers a way into the market

The story is quite different for medtech devices that are more like consumer technology, those in the low-risk class in Box 1. Stanley Yang:

> *"It is easier to deploy these kinds of technology, if they do need FDA-like approval, in the UK rather than the US. This is because of the medical CE grade for products that are not providing medical advice. Silicon Valley is usually the first place you deploy new technologies. But in medical realm I think because of the Government regulation, this [Europe] will become the fertile ground."*

Yang went on to compare Neurosky's devices to vitamin pills. When devices are more like vitamins than prescription drugs, he argued that the European regulator system was more attractive. Other interviewees felt this is the case even for more tightly regulated technologies.

Povl Verder described pharmaceutical companies' pipelines of ideas: from Europe, where they can try things out without negotiating the tough FDA process, across to the US once they show potential for financial return.

Responding to any regulatory regime in medtech is a significant undertaking. UK interviewees emphasised the paperwork required for CE mark. The researcher that led Cambridge Temperature Concepts CE mark application was proud that it took them only five months. Often it can take years.

Yang's comparison of medical technology to vitamin pills brings to mind ethical issues in the health supplement sector. iPodchondria for digital health apps may be just the start. As more and more information is provided direct to consumers, what measures are in place to help people interpret it? There was a hint of this problem in the later paragraphs of the FDA's letter to 23andMe. The letter mentions *"the risk that a direct-to-consumer test result may be used by a patient to self-manage"* and states that *"serious concerns are raised if test results are not adequately understood by patients".* In other areas – like vitamins and supplements – people are free to take health-related risks. It's not clear that it is part of the FDA's jurisdiction to ask 23andMe to manage how people use the information they provide. But there has been little public debate about the role of regulators in responsibly governing this expanding digital health sector.

4.33 European and US legislation has started to respond in principle if not in practice

In 2013 the European Parliament voted to amend the definition of a medical device so that a product providing information concerning direct or indirect impact on health would be considered a medical device. The proposal also makes genetic counselling mandatory and reiterates the need for explicit informed consent for genetic testing. After a series of scandals including breast implants and metal-on-metal hip replacement, the proposed changes will also increase the level of reporting and testing for devices that fall under Class II and III. The European Parliament wants to tighten CE mark rules, raising the level of expertise a manufacturer must have in order to apply for one. Previous proposals from one of the Parliamentary Committees, to bring in US-style approval for high-risk devices rather than continuing with the CE mark, did not make it into the current draft.[41]

In the US, the FDA is considering bringing laboratory-developed tests, currently sold without requiring direct regulatory oversight, under its control. The agency's requirements have been getting stricter overall as well. The FDA gave almost half as many approvals for high-risk devices in in 2013 compared to 2012.[42]

Chapter 5:

MEDTECH BY DESIGN: WHAT CAN BE DONE NOW TO DELIVER A THRIVING, RESPONSIBLE SECTOR?

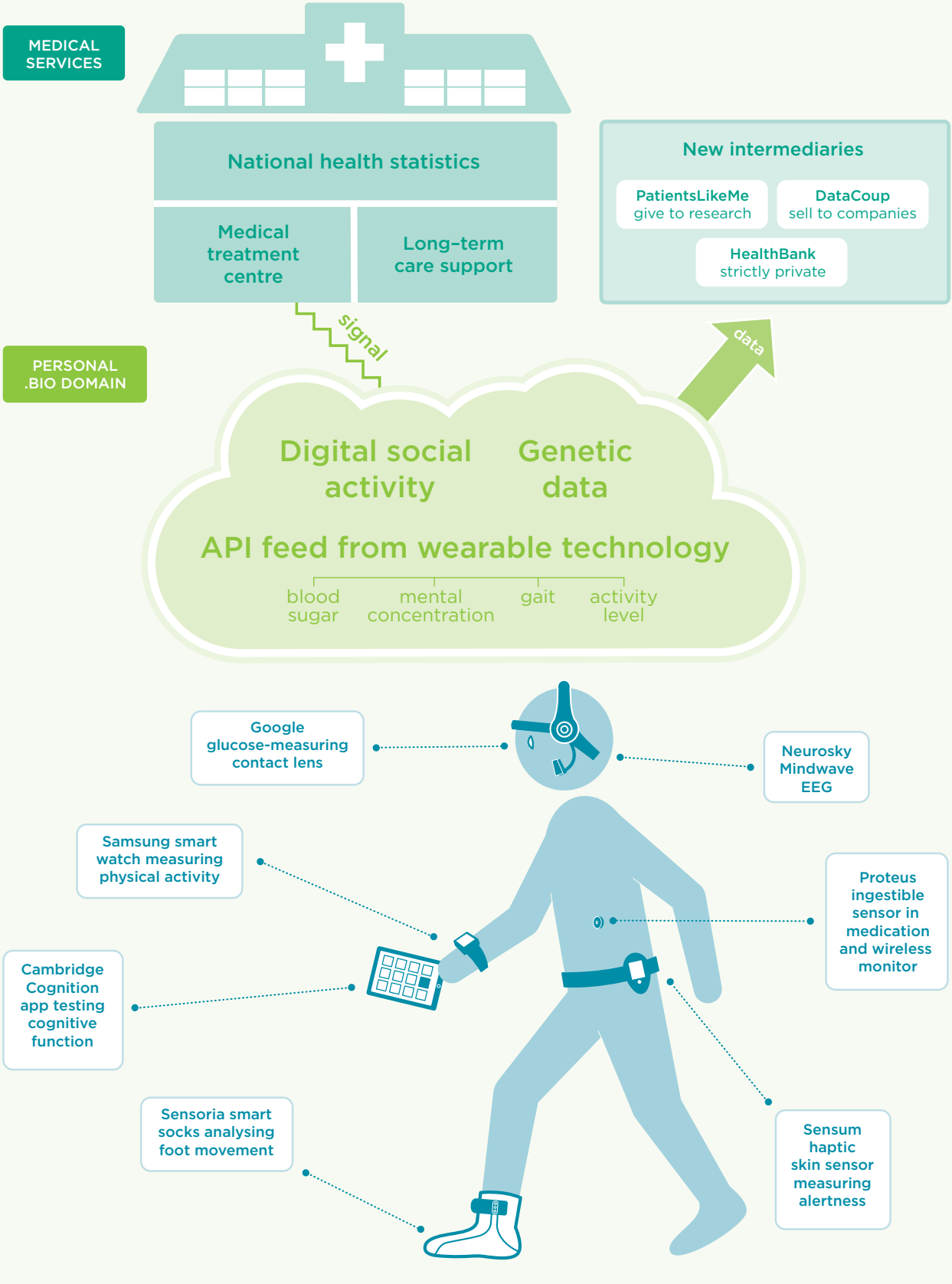
Having described the factors shaping the healthcare sector in the long run, and which will determine where and how new digital technologies develop, we return now to implications for the nearer term. We present a vision for portable personal healthcare using technologies already under development, many of which featured at SVC2UK 2013. This is intended as a provocation for investors, policymakers and entrepreneurs thinking about catching this new medtech wave.

This is not a new idea. Nesta's previous proposal for a Health Knowledge Commons centred on the individual not the hospital; the People Powered Health programme funded community-based initiatives to support these changes. This chapter adds to this idea from the medtech community's perspective.

Christensen's predictions of decentralised control of medical devices may cause regulatory havoc. The idea of medical expertise as a commodity has already aggravated the clinical profession. But it is precisely Christensen's vision that excited the SVC2UK 2013 participants. The extended version of Andrew Thompson's quote that introduced this report:

> *"In the 21st century we need to complement the sick care system we have already. We need a system built from today's signature technologies – not the signature technologies of the 20th century. Buildings that provide electricity and people with knowledge will become software and computational power with intelligence in the cloud. And products become services tailored to you, your genes and your behaviour... Things are changing from buildings, people and products to software, services and mobile devices. There will be a confluence of semiconductors, medicines and medical devices all coming together as software – all being fused together into a single product system where the identity of the product is essentially a software platform. That's a big change. That's the future."*

Box 6: **Portable personal health: a vision for the future**



CONCLUSION

When it comes to leading a new wave of medtech innovation, the volume of early-stage capital and experience with consumer technology give Silicon Valley a perennial advantage. However, the UK has favourable regulation for medical devices, a legacy of life sciences research and new mechanisms for embedding cutting-edge knowledge in a national health system.

But it is urgent need that kicks disruptive innovation into gear. The fear of an extra 30 million more patients under the Affordable Care Act could be enough to push the US out in front. The sheer scale of the problem will always be a factor. In 2015, US spending on healthcare could hit $4 trillion.[43]

Digital platforms – whether to check on medication adherence or providing biosensor data about our daily lives – are exciting because they scale quickly. Mobile health applications made up $564 million of the $2.2 billion venture investments in digital health last year.[44]

But it will be a new generation of biosensors and genetically-precise medicines that monitor our every move that will transform our healthcare systems. Real-time feedback from patients and rich genetic data sets will help companies and researchers connect with all stages of the care continuum, from prevention to diagnosis and treatment. This is vital at a time when most healthcare spending is on managing long-term conditions, which require close monitoring. These will also be helpful in the transition to more disease prevention than treatment.

The strongest vision of a new wave of medtech comes from those integrating new products and services into existing healthcare practices. These products avoid sidelining clinicians to the point that they lose the trust necessary for successful treatment. Instead, doctors have more knowledge to help them make decisions. And there are new tools that fit medical care around the demands of daily life. Portable – both physically and in terms of data – personal healthcare is the promise of the next decade.

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Nesta

1 Plough Place
London EC4A 1DE

research@nesta.org.uk
www.twitter.com/nesta_uk
www.facebook.com/nesta.uk

www.nesta.org.uk

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