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FUTURE OF HEALTHCARE

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TECHNOLOGY

Opportunities and obstacles with next-level tech

There is some way to go before game-changing technologies are deployed to revolutionise patient care and the working practices of healthcare professionals, but there are encouraging signs of progress

Oliver Pickup


Hero Images/Getty Images

The future is already here; it's just not evenly distributed. So said American-Canadian writer William Gibson, father of the cyberpunk sub-genre of science fiction, who has had his finger on the pulse of breakthrough innovations for decades. His perceptive comment is extremely apt when assessing healthcare technology in 2019.

Next-level tech innovations, unimaginable a decade ago, are beginning to upgrade how patients, practitioners and medical systems interact with one another; they are just not evenly distributed, yet.

Cruelly, we are afforded only fleeting glimpses of what the complete healthcare picture of the future might look like: nanotechnology for the treatment of cancer, for example, or genome research and manipulation or artificial intelligence (AI) used for genome sequencing.

Progress has been slowed, especially in the UK where regulation is tight, through a lack of mainstream adoption, wariness of under-tested technology, as well as the exorbitant cost and time to develop market-ready healthcare products.

There are, though, plenty of encouraging signs. "Smartwatches, activity sensors, biometrics, monitoring devices and healthcare software applications are already widespread," says Panos Constantinides, associate professor of digital innovation at Warwick Business School.

"These new digital technologies all enhance interactions between patients, practitioners and healthcare systems, and generate huge amounts of useful data. They also benefit patients by improving waiting times and their overall patient pathways, all the way to prevention medicine and better diagnoses and treatment options."

When it comes to new intelligent technologies, such as robots powered by deep neural networks, machine-learning algorithms used for image processing, big data analysis and others, innovators need to build public confidence and trust, says Professor Constantinides. This takes considerable time, money and lobbying.

Jake Freivald, vice president of marketing at New York-headquartered software company Information Builders, posits that technology in general and data in particular have always played a part in healthcare improvements.

Indeed, Florence Nightingale, the founder of modern nursing who died 119 years ago, originally trained as a statistician. "Using data-based evidence, she recorded the numbers of deaths in military hospitals and showed that, after introducing sanitation and better nutrition, the mortality rate fell from 42 per cent to 2 per cent," notes Mr Freivald.

The potential of healthcare technology is enormous, says Barbara Harpham, chair of the Medical Technology Group (MTG), a not-for-profit group working to improve patient access to effective healthcare technologies. She cites a 2017 MTG study that calculated some £500 million could be generated in reduced long-term health costs and benefit payments through the use of just eight technologies, including sepsis diagnosis, wound care and coronary angioplasty.

"Despite the vast benefits, uptake of healthcare technology is often hampered by short-term approaches and a myopic view on healthcare budgets," she says. "These fail to recognise the long-term benefits of reduced hospitalisations, improved quality of life for patients and their families, as well as the potential to return people of working age to employment."

Professor Christopher Eden, one of the UK's top-ranked prostate cancer surgeons and an advocate of robotic surgery, argues: "Most doctors have a jaded view of digital health solutions, having seen over the years so many attempts at National Health Service IT integration fail expensively. We work daily with technology, but the NHS's hardware changes slowly and the software tends to run on Windows XP."

The consultant urological surgeon at Santis, a private London cancer clinic specialising in robotic prostatectomy, continues: "For digital health solutions to be embraced, they have to offer something to the doctor: a more efficient way of working, improved diagnostics, AI, and something to the patient, notably better access to information and to healthcare."

Professor Eden says that while the general attitude towards healthcare technology has changed for the better over the last decade, there is still some way to go to unlock its full potential. "Doctors and patients now all have smartphones and use apps, but not the same apps working on the same platform; that's the future," he adds. "It's possible because we have the hardware. What is standing in the way is a lack of multidisciplinary buy-in and integration."

Niamh McKenna, health lead at Accenture, is more optimistic. "There have been some exciting developments in the evolution of the smartphone as a diagnostic tool," she says. "This is a natural progression given how easy it now is to connect internet of things devices to smartphones, like those that monitor blood pressure or glucose levels, for instance.

"As such, diagnosis can now be run in a similar way to how it would be run in a hospital, just from a portable device. This is an easy step for clinical diagnosis on the move and has great potential for application in remote areas, like developing countries, mobile medical staff and self-care."

Ms McKenna believes the step beyond this is leveraging functions in the smartphone to turn it into a medical device. This would be a game-changer, she enthuses, particularly in areas where it is hard to access clinicians.

Neil Mesher, chief executive of Philips UK and Ireland, is equally upbeat about the future of healthcare technology and welcomes the establishment, in February, of NHSX. "This specialist joint unit to drive technology in the NHS is one way that health technology innovators and industry leaders can engage more directly with both clinicians and the government to create a culture of innovation," he says.

"NHSX will accelerate the adoption of proven, safe, tested existing healthcare technology across the system, breaking down some of the silos that have delayed progress."

When NHSX was unveiled, health secretary Matthew Hancock heralded "the beginning of the tech revolution". Patients and practitioners alike will be hoping it provides a much-needed shot in the arm for the UK healthcare system, and opens the theatre door to bigger and better innovations.

56%
of physicians in the UK believe it is likely that artificial intelligence technologies will be commonly used in the next decade for diagnosis, medical imaging analysis and medication management

45%
of consumers in the UK would be very or completely willing to be treated virtually for common acute symptoms instead of in-person visits

44%
would consider using an in-home diagnostic test and sending the information to a doctor

EY 2019

WOMEN'S HEALTHCARE

Roots of inequality go deep across healthcare

How unbalanced participation in clinical trials and a basic misunderstanding of women's health needs have resulted in unequal levels of public care

Nichi Hodgson

For decades women have been perceived to pay closer attention than men to their own wellbeing and that of their families. Women, for instance, attend more primary care appointments than men. Yet in 2017, statistics from Public Health England showed the average man spends 20 per cent of his life in poor health compared with 25 per cent for the average woman. Why is this?

Look beyond that more frequent access to primary care, driven mainly by female reproductive needs, and it is clear that there is an inherent bias in the healthcare system that begins before women have even received a diagnosis.

Women do not take part in clinical trials at anywhere near the rate that men do. "There has been a systematic imbalance in research data generated during the last 30 years, which in turn affects the optimal use of therapies in women," says Annalisa Jenkins, a medic-turned-biopharmaceutical executive who now focuses on finding biotech solutions to healthcare.

"We see this all over the world. Women balancing the care of family members and partners all too frequently gets in the way of them volunteering for a clinical trial; it's just easier for men to volunteer."

But it's not as simple as women being too busy to contribute to research that's the problem. It was only in 1993 that the US National Institutes of Health stipulated that women had to be included in research trials.

"There is this perception that men provide a cleaner 'base' because they don't take birth control and don't have to go through the experiences of pregnancy and childbirth. This has meant, accordingly, that fewer women are used to deliver data and so we end up with results and insights which reflect the needs of men alone."

In many cases, a care solution worked out for men doesn't translate for women. HIV medication, for example, was first developed for the treatment of gay men.

"When these medications were taken to Africa, where the predominant population affected was young women, there just wasn't the data available to help the women," says Dr Jenkins. "Essentially, we are developing medicines for only half the world."

In the case of diseases that are considered "male", but also affect women, women's health can fall by the wayside, for example with heart disease.

"Traditionally people have perceived heart disease to be a disease of men," says Dr Jenkins. "As a result of the implantation of prevention, and new medicines and lifestyle interventions, the rate of disease has now fallen in men. Conversely, in some parts of the world, women's rate has increased."

And then there's the perception that women experience pain altogether differently. As psychologist Becky Spellman puts it: "More generally, women with chronic pain conditions are much more likely than men to be diagnosed as having a condition that is psychological or psychosomatic in origin.

"While some conditions certainly do have a psychological element, this assumption has often led to women being misdiagnosed or not receiving a diagnosis for many years. This can mean they are not being treated appropriately or even that a treatable condition can become a chronic one."

> **[Unequal research] means women are not being treated appropriately or that a treatable condition can become a chronic one**

Given that women in England and Wales are currently twice as likely to experience a chronic health condition, according to the British Medical Association, addressing the bias is clearly a pressing issue.

At the same time, women evidently have specific healthcare needs surrounding fertility, pregnancy and menopause which require different and unique solutions altogether. Again, bias can affect every element of female healthcare. Currently, it takes an average of seven years for a woman to be diagnosed with endometriosis, a common condition that affects around 170 million women globally. Why? "Many of them are told that their pain is psychological or all in the mind," says Dr Spellman.

Thankfully, attitudes to female healthcare are transforming, led by a wave of female medics, technologists and campaigners who simply won't allow female health to be taken less seriously. The US Food and Drug Administration has finally approved the first drug for endometriosis, while the femtech, or female technology, market is forecast to grow to £50 billion by 2025, according to research and consulting firm Frost & Sullivan.

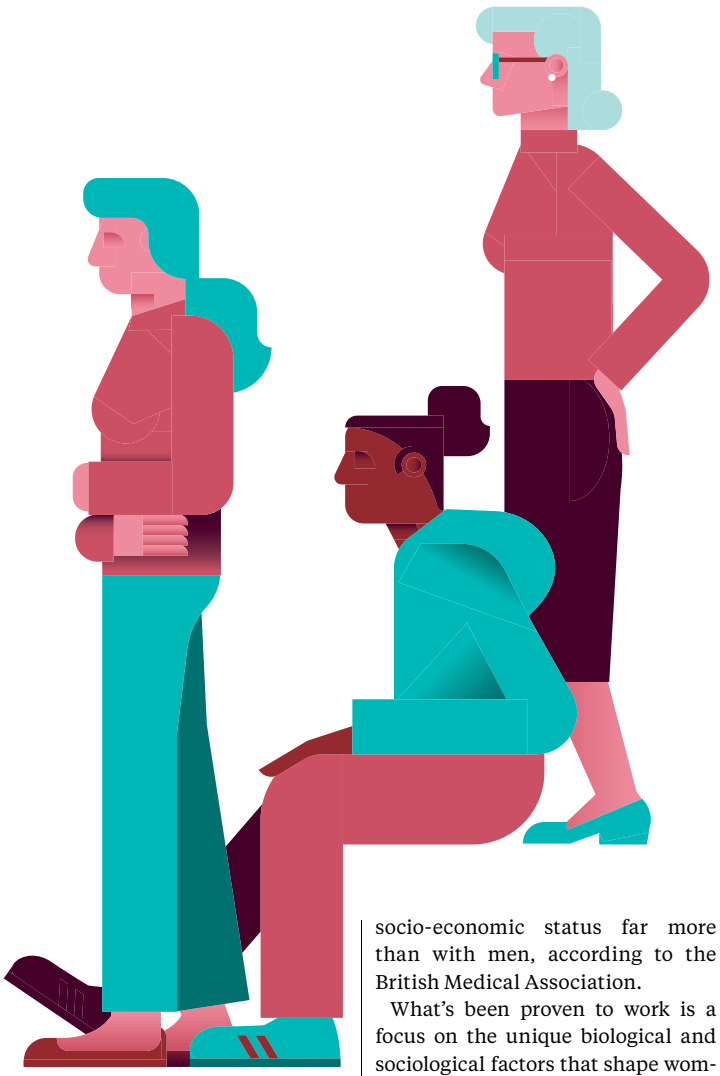
With women's increased legal, social and economic power comes a refusal to accept sub-par treatment. While legislators and investors are finally coming to the conclusion that such areas are no longer optional healthcare, the next step is to secure appropriate investment.

"Take menopause, something that every woman who lives to a certain age will experience during her lifetime," says Dr Jenkins. "Yet if you look at the amount of capital flowing into this space and look at the companies, and drugs and pipeline, you'll find it's an empty pipeline. It simply hasn't been seriously considered a commercial opportunity. And that's what we are trying to change."

GENDER INEQUALITIES IN HEALTHCARE

	M	F
Difference between male and female attitudes to public healthcare from the EU's most recent Gender Equality Index		
Percentage who perceive their own health to be good or very good	69.6%	64.4%
Life expectancy at birth (years)	77.9	83.3
Healthy life at birth (years)	62.6	63.3
Percentage without self-reported unmet needs for medical examination	95.4%	94.5%

Eurostat, 2017



While women make up some 70 per cent of the healthcare workforce, they make up only 30 per cent of C-level executives and just 13 per cent of chief executives. And while the most innovative solutions to female healthcare problems, everything from IVF treatment to the redesign of the speculum, are coming from women-led operations, only 9 per cent of healthtech businesses are currently founded by females.

Still, huge funding rounds for femtech businesses are becoming more common. Take Ava, the fertility bracelet startup which received $30 million to expand into contraception and other female healthcare last year. Or Elvie, creators of the first silent breast pump, that received $42 million to develop tech-based solutions to female health needs at every stage of life.

Femtech can also give patients greater information about their bodies that they can use to navigate interactions with medical professionals more confidently, which helps to offset the historical bias issue. With the NHS currently cutting fertility services budgets, IVF app Salve, for example, focuses on providing users with information about the process so they can ask the right questions of clinical providers and take a more dynamic role in their treatment.

But while consumer technology may be closing the gap between wealthier women and men, it isn't touching the needs of the poorest women, whose health issues, including everything from abortion to mental health care and domestic abuse to Alzheimer's, are disproportionately affected by their socio-economic status far more than with men, according to the British Medical Association.

What's been proven to work is a focus on the unique biological and sociological factors that shape women's health needs. Take the recent move in Scotland and Wales to end "period poverty" by making sanitary products freely available to girls and women in education and on low incomes. Or the cervical cancer screening programme in England and Wales, which has reduced deaths by 70 per cent since it began in 1988, although screening numbers are now starting to fall again.

Public health can transform female healthcare says Dr Jenkins, but only when it is prioritised. "Take cervical cancer; we now have a very effective vaccine which could wipe it out in a generation," she says. "But because public health has not yet articulated that we care enough about women's healthcare, we are vacillating. Comparably, if we had found a cure for testicular cancer, would we not have solved it by now?"

When it comes to direct action on the issues nobody seems to be taking seriously, it's dedicated lobbyists who make all the difference. Female genital mutilation (FGM) is an issue which currently affects some 200 million globally, with 1,005 new cases registered in England and Wales between April and June 2018 alone.

It's thanks to campaigners, such as Nimco Ali, Somali social activist, co-founder and director of the Daughters of Eve non-profit organisation, who have dedicated years to lobbying MPs that the UK has finally made its first prosecution for FGM, tightened laws to help children at risk of the procedure, and allocated national funding to help health services and schools identify and support victims.

For Ms Ali, the issue is believing women when they tell us they have a problem. "Language is key. We need to listen to women and accept they know their body," she says. ●

INTERVIEW

Integrated care is the future, says NHS England chair

Chair of NHS England **Lord Prior** tells of his determination to transform the health service as a power for good in an increasingly ailing society

Interview by Magda Ibrahim
Portrait by Matt Grayson

When he became chair of NHS England just weeks before publication of the *NHS Long-Term Plan*, Lord Prior was under no illusion about the task ahead.

The former health minister and Conservative MP David Prior inherited a health service that had changed little in its 70-year history, facing successive winter crises and with the fear of an already stretched workforce potentially taking a Brexit body blow.

For the UK's largest employer, developing a long-term plan that operated on a schedule outside the political cycle was essential. Yet it is fundamentally driven by unlocking the £20.5-billion settlement, promised to the NHS by the government, over the next five years.

The ambitious blueprint, unveiled in January, to overhaul the health service during the coming decade "is not a Soviet, top-down plan where we state how many tractors will be produced in the next ten years", says Lord Prior.

"This is very much a bottom-up exercise," he says. "We spoke to all the major charities and third sector, and with the main patient groups and politicians, to develop the *NHS Long-Term Plan*.

"In the past, the NHS has been bedevilled by political changes, so it is important we have built consensus about the direction of travel. It provides an insurance policy against political change over the period of the plan."

Priorities in the plan are clear: improvements in treatments for cancer, cardiovascular disease, maternity and neonatal health, mental health, stroke, diabetes, respiratory care, and children and young people's health.

While many of these priorities are aligned with measurable targets – to increase the proportion of cancers diagnosed at stages 1 and 2 from around half to three quarters by 2028 and to halve stillbirth, maternal and neonatal mortality by 2025, for example – there is still uncertainty over some issues.

Lack of clarity over hospital waiting times was addressed in the latest clinical review of NHS access standards, published in March, but a proposed move from the previous four-hour A&E waiting time standard to measuring average waiting time has yet to be fully defined.

"Quite a few targets have become totemic in their significance and we have sometimes taken our eye off the ball in terms of clinical outcomes, which is what really matters," Lord Prior points out.

One of the most well-documented priorities is a focus on mental health services. Lord Prior highlights his own experience – his wife and son both have bipolar disorder – while prime minister Theresa May has been an advocate of mental health services following her niece's suicide.

These personal stories align with a broader public demand for mental health services to be given equal importance with physical health.

The long-term plan commits extra funding to mental health with an additional £2.3 billion a year for services by 2023-4 and the goal of ensuring 100 per cent of children and young people, who need specialist care, can access it over the coming decade.

Annual physical health checks will be given to 110,000 more people living with severe mental health problems, bringing the total to 390,000 annual checks by 2023-4.

"The separation of mental health from physical health created a false dichotomy," says Lord Prior. "But we are getting closer to parity where people recognise poor mental health can be as debilitating and painful as bad physical health, and so many people suffer with both.

"More resources will go on mental health because there was so much unmet demand before. My personal passion is coincident with the needs of the population as a whole and I hope we can see improvement in five years' time."

While Lord Prior points to the dramatically reducing cost of genome sequencing and digital technological advances cutting the cost of clinical trials as major innovations in improving disease diagnosis and prevention in the future, there is no escaping the immediate challenge of multimorbidity, where patients have two or more chronic conditions, especially in the rapidly aging population.

"Multimorbidity is the single most important shaper of the plan," he emphasises. "We all accept the existing structure of the NHS was set up for a completely different population to the one we have now.

"Most of our hospital beds are occupied by elderly people with multiple conditions, yet most of those people could be better treated outside a hospital, which is why we are putting so much more emphasis on prevention and digital techniques to enable people to remain in their homes for longer."

The new integrated care systems, which currently exist in some areas, but will be rolled out across England by 2021, are set to be pivotal in providing "much more holistic care closer to the home", says Lord Prior.

"This is the really fundamental change in the long-term plan and aims to get rid of silos," he says. "If we carry on seeing demand in acute services rising as it has, we will need thousands more acute beds by the mid-2020s. That is not going to happen."

Patients will have an online care plan which can be monitored by all healthcare professionals, from a GP to a mental health nurse or social prescriber.

Meanwhile, tech advances mean a proliferation of wearable and home-based devices that can be used to monitor people remotely, so they can stay at home for longer.

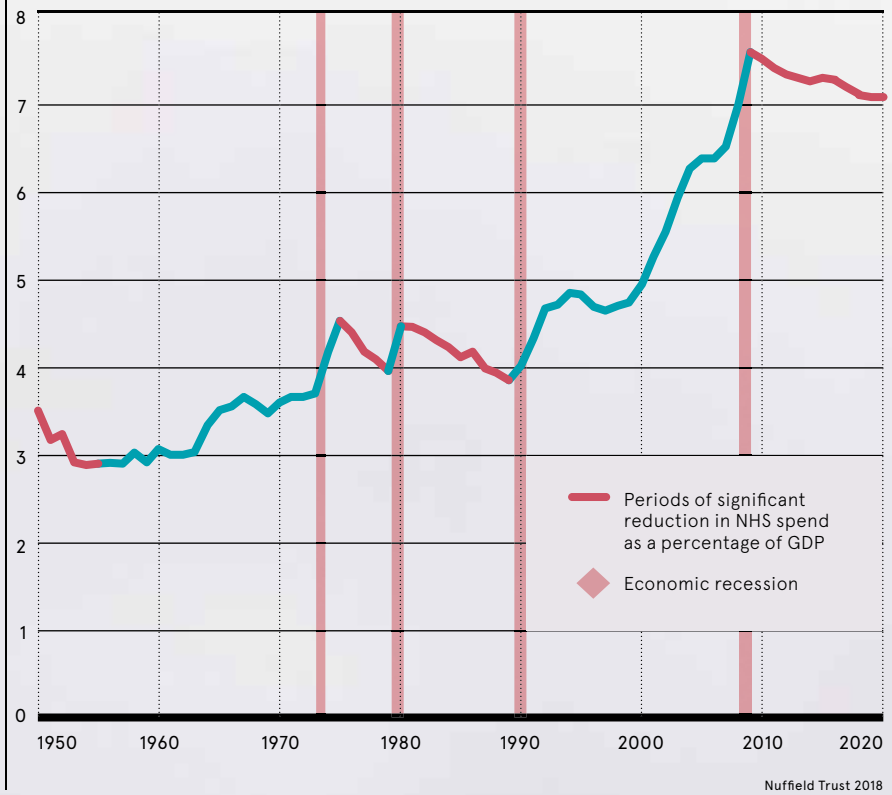
"But you cannot replace caring people with robots," warns Lord Prior. "The human interaction is very important and that human relationship will remain very important, while tech will assist."

With the NHS experiencing a workforce shortage of more than 30,000 nurses and 3,000 GPs, maintaining the human interaction and meeting the clinical need is a tough challenge.

"We have been trying for the past 20 years to get more out of the system and have put huge pressure on those who work in the NHS," Lord Prior concedes.

NHS SPENDING OVER 70 YEARS

Spending as a percentage of GDP; future estimated based on NHS England plans scaled to UK



Nuffield Trust 2018

With no silver bullet for the staffing crisis, the *NHS Long-Term Plan* supports increasing medical school places by 25 per cent, from 6,000 to 7,500, and aims to cut nursing vacancies from 11.6 per cent to 5 per cent by 2028 through introducing online nursing degrees and funding clinical nursing placements. "Investing in the caring professions has to be the right thing to do," says Lord Prior.

At the same time, he backs the government drive to get more people working with artificial intelligence and machine-learning within the healthcare system. "I would like to see, within the doctors' training programme, more room for some of this newer technology as well as anatomy and diseases," he says.

Outside of the long-term plan, Lord Prior raises the challenges posed by Brexit and immigration policy in plugging the ongoing workforce gap.

"When you look at the care delivered in the NHS, much of it is delivered by people on relatively low incomes working in residential or domiciliary care, earning less than £15,000 a year," he says. "It is not just about having an immigration policy favourable to high earners, but also to those who are not that well paid."

Meanwhile, improving diversity among the workforce, especially in senior leadership, will pay dividends in health outcomes long term, he says.

"All the evidence shows that greater diversity is equated with better outcomes and greater success," he explains. "We know there is a lot of improvement we need to make and we are transparent about that. We would like the senior management to broadly reflect the wider population."

Grappling with the challenges, yet buoyed by the opportunities of 2019, the NHS could be operating in a very different form in 2029.

"In an increasingly fragile, fragmented and disconnected society, the NHS has a huge moral and social purpose that goes beyond just healthcare," Lord Prior concludes. "Tax-funded healthcare from the day everyone is born is hugely important. Whatever your means or genomic inheritance, we are all in this together."

In an increasingly fragile, fragmented and disconnected society, the NHS has a huge moral and social purpose that goes beyond just healthcare

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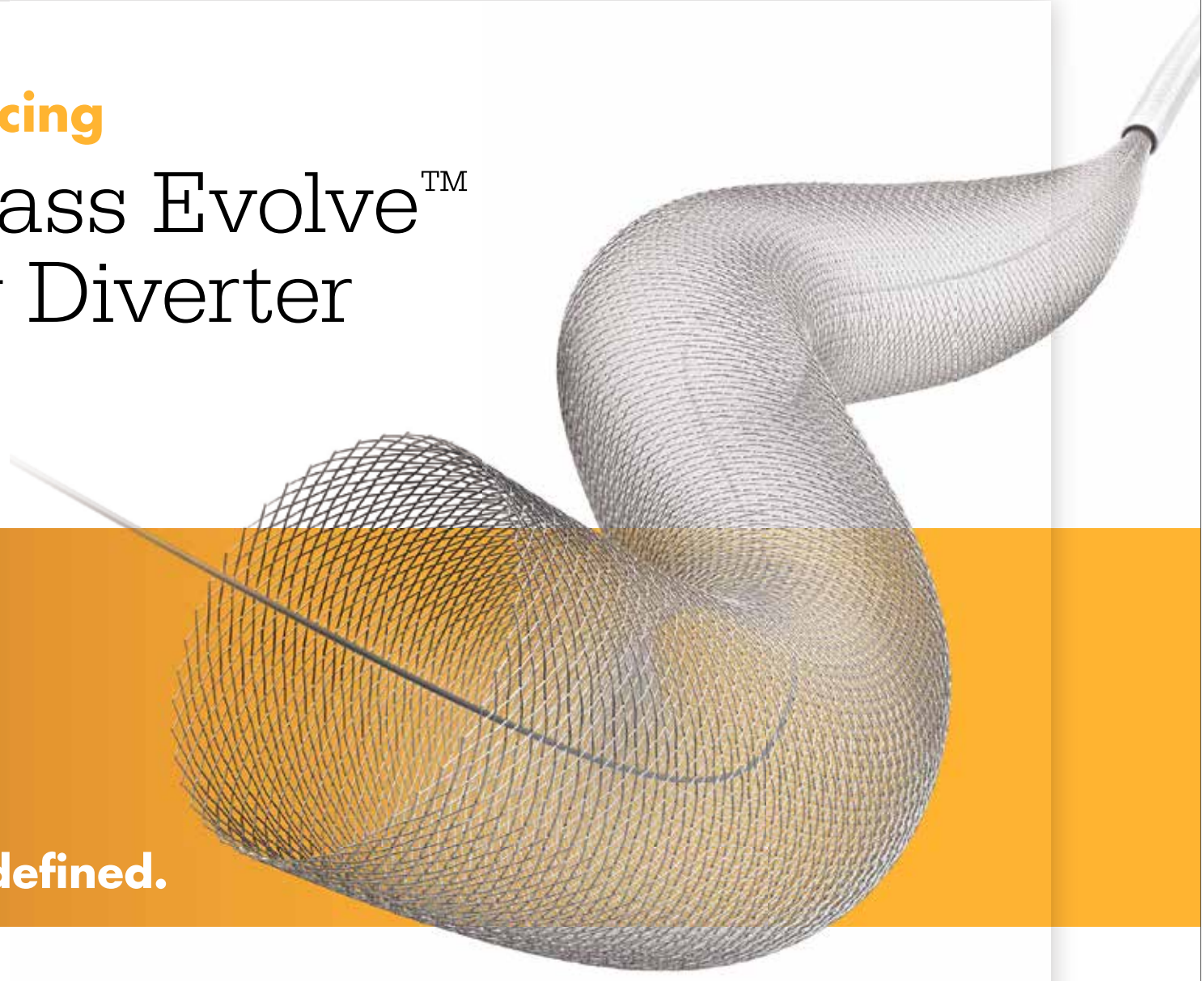

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PATIENT COMPLIANCE

The fight to end non-adherence

Digital medicine could provide the answer to the costly problems of patient compliance and failure to follow medical advice correctly

John Illman

The so-called rule of thirds highlights one of medicine's biggest challenges: patient compliance. It states that a third of patients take medical advice to a degree that it is effective; a third follow advice, but not enough for it to work; and a third just do not bother.

It is widely estimated that medicines are not taken as prescribed 50 per cent of the time; which should not be sniffed at given the NHS spends £16 billion on drugs each year.

It is hard to estimate the precise cost of poor patient compliance; £300 million is widely quoted, but this may be a vast underestimate because of a sinister domino effect.

For example, one in four patients reportedly do not take blood pressure medication as prescribed, according to a University of Leicester study on hypertensive patients. Many are symptom-free and assume they do not need treatment, but high blood pressure is a silent killer, and implicated in tens of thousands of heart attacks and strokes that strike without warning.

The British Heart Foundation reported in 2018 that the total annual cost of treating heart and circulatory diseases in the UK was £9 billion.

Theories abound in ignorance about how to improve patient compliance. Experts have recommended, among many other things, adjusting the timing and frequency of medication, alarm systems, and sending reminders by post, email or telephone.

The answer may lie in digital medicine and technologies and products that directly impact diagnosis, prevention and treatment. These include artificial intelligence, machine learning, robotics, telemedicine and wearables.

Wearables such as the Apple Watch not only help to enhance patient compliance by issuing pill reminders, but also save lives. For instance, a 62-year-old builder felt terrible after lunch. When his watch revealed an abnormally high pulse rate, he called an ambulance. Doctors told him that he might have died if he had gone straight home.

Wearables and smartphones can also track other vital signs such as abnormal heart rhythms, blood glucose and blood pressure. Instant access to such critical information may make us more health conscious and, it is hoped, medicine compliant.

Digital interventions are also helping patients handle complex and potentially confusing medicine regimes. For example, Andrew had to take 32 pills in the morning and 32 at night after his second kidney transplant. The smartphone app MyMedSchedule successfully sent him pill alerts via text messages.

The need for so many pills may seem extraordinary, but kidney transplant patients routinely take immunosuppressants, anti-inflammatory agents, blood-pressure tablets, aspirin, cholesterol-lowering statins and phosphate binders to restrict phosphorus absorption from food.

They are not the only patients with large pill schedules. More than a third of over-75s in the UK reportedly take four or more medicines a day; the greater the number, the greater the possible scope for errors and confusion.

Concern over patient compliance is not restricted to pills and tablets. In March, Asthma UK warned that more than a million people in the UK could be at risk from potentially life-threatening asthma attacks because of inhaler misuse. They use inhalers to get medicines into their lungs, but poor technique can leave the medicine in the mouth or back of the throat, where it can cause side effects such as oral thrush or a sore throat.

Asthma UK says: "Every day, the lives of three families are devastated by the death of a loved one to an asthma attack and tragically two thirds of these deaths are preventable."

The charity's warning followed a US study involving 7,558 patients. An innovative digital sensor attached to their inhalers showed that 84 per cent of them had faulty techniques, according to a report in the *Journal of Allergy and Clinical Immunology in Practice*. The study was carried out by digital health company Propeller Health in partnership with the University of Colorado School of Medicine and Children's Hospital Colorado.

Linked to the patient's mobile phone or computer, the sensor can alert the patient and provide medication reminders, air quality forecasts, symptom advice and self-management tips.

In theory most patients need only a few tweaks to their inhaler technique to get it right, but who is going to advise them? Asthma UK says: "According to national guidelines, everyone with asthma should get their inhaler technique checked as part of their yearly asthma review with their GP or asthma nurse. But with dozens of types of inhalers that need to be taken in different ways, it can be difficult for doctors and nurses to know how they all work."

This is a strong argument for a switch to digital health, an argument supported by the *NHS Long-Term Plan*. Published in January, the plan states: "People will be empowered, and their experience of health and care will be transformed by the ability to access, manage and contribute to digital tools, information and services. We will ensure these technologies work for everyone, from the most digitally literate to the most technology averse."

But independent think tank the King's Fund warns: "Like many others, we have been deeply concerned about the state of the NHS workforce and its ability to deliver existing commitments, let alone any new ones."

There is another reason for caution. The government has snatched back money previously allocated to digital projects. This may have been a false economy in view of the vast cost of poor patient compliance, among many other things.

50%

of all medicines are not taken as precribed on average

US Centres for Disease Control and Preventio

> **Digital interventions are helping patients handle complex and potentially confusing medicine regimes**

Five types of pharmaceutical waste

NHS England

1. **Non-compliance** Patient does not take medicines as prescribed. May take incorrect doses or at irregular intervals
2. **Intentional non-adherence** Patient stops taking medication due to adverse side effects or personal beliefs
3. **Unintentional non-adherence** Patient stops taking medicine, or fails to take at correct intervals, due to forgetfulness
4. **Non-preventable waste** Patient dies and unused medicines are wasted, or a change in treatment means current dispensed medicines are no longer required
5. **Preventable waste** Patient stockpiles medicines `just in case'. All items from repeat prescriptions are dispensed even if patient no longer takes the medicine

Peace of mind for chest-pain patients

Cardiac care is on the verge of a giant step-change thanks to a great British success story which has fused innovation, scientific engineering and clinical intelligence

A new medical technology, which has the potential to revolutionise the chest-pain pathways in hospitals around the world, is about to go live, backed by a major clinical study and successful private funding rounds.

Creavo Medical Technologies is at the pivotal moment in a five-year journey to develop its award-winning Corsens® system, which is intended to act as an aid for physicians to give an early all-clear to a number of people who attend hospitals with chest pain and are currently forced to complete a lengthy and anxious testing pathway.

The technology, which applies principles of physics to measure the heart's magnetic signals, means that some of these chest-pain patients can be reassured they are not having a heart attack and can return home rather than spending up to eight hours in a hospital.

"The target audience are people who have been completely well one moment then they suffer chest pain which they assume is a heart attack. They are rushed into hospital and are naturally fearful," says Creavo chief executive Steve Parker, who had more than 40 years' experience in giant US medical technology companies before launching the startup, a spin-out from Leeds University, in 2014.

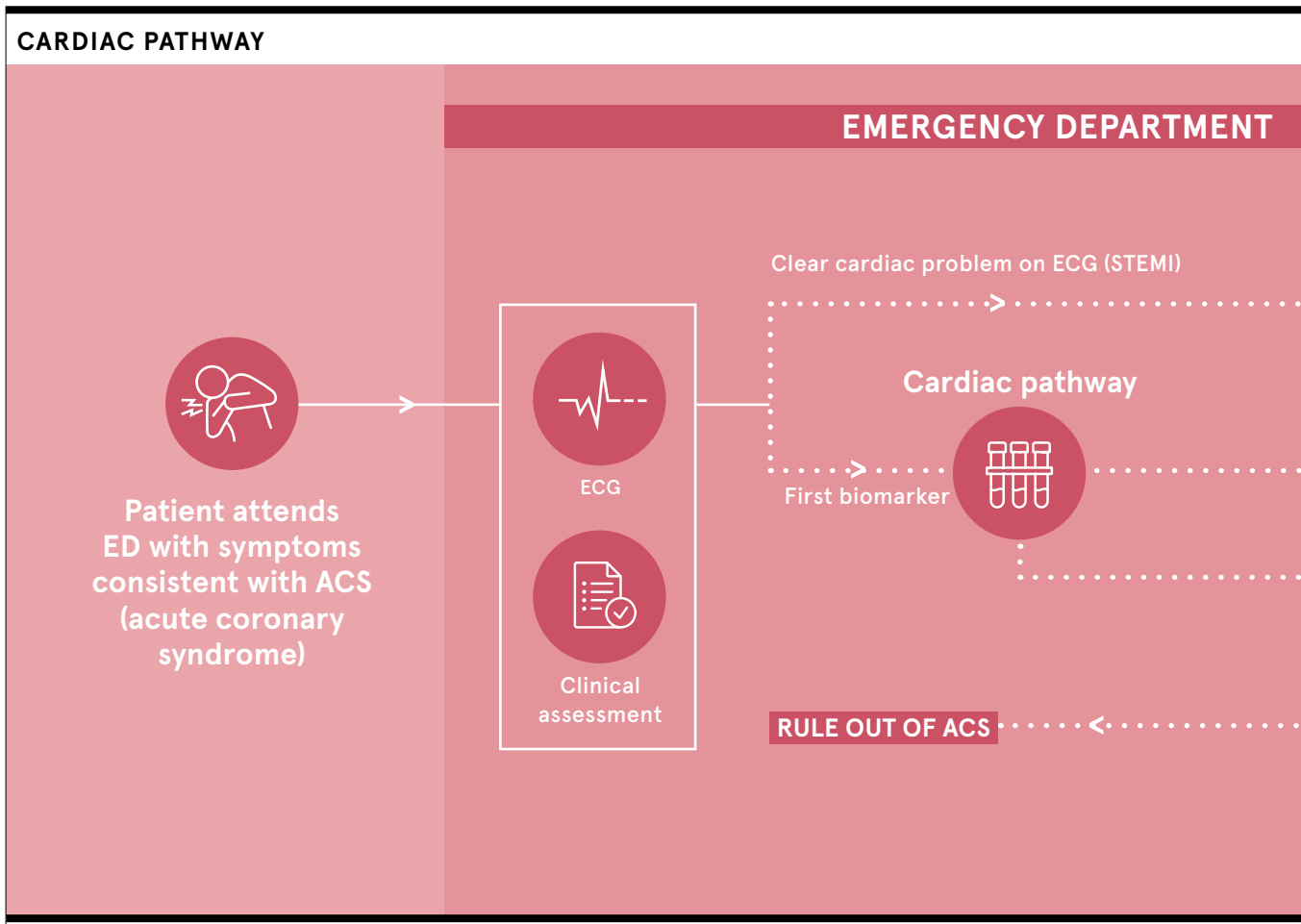
"If we can identify those not at risk at an early stage, we put both their minds at rest and free up resources in the emergency department for the people who really do need them. This is a patient, economic and technology story that comes together to make a very effective business model."

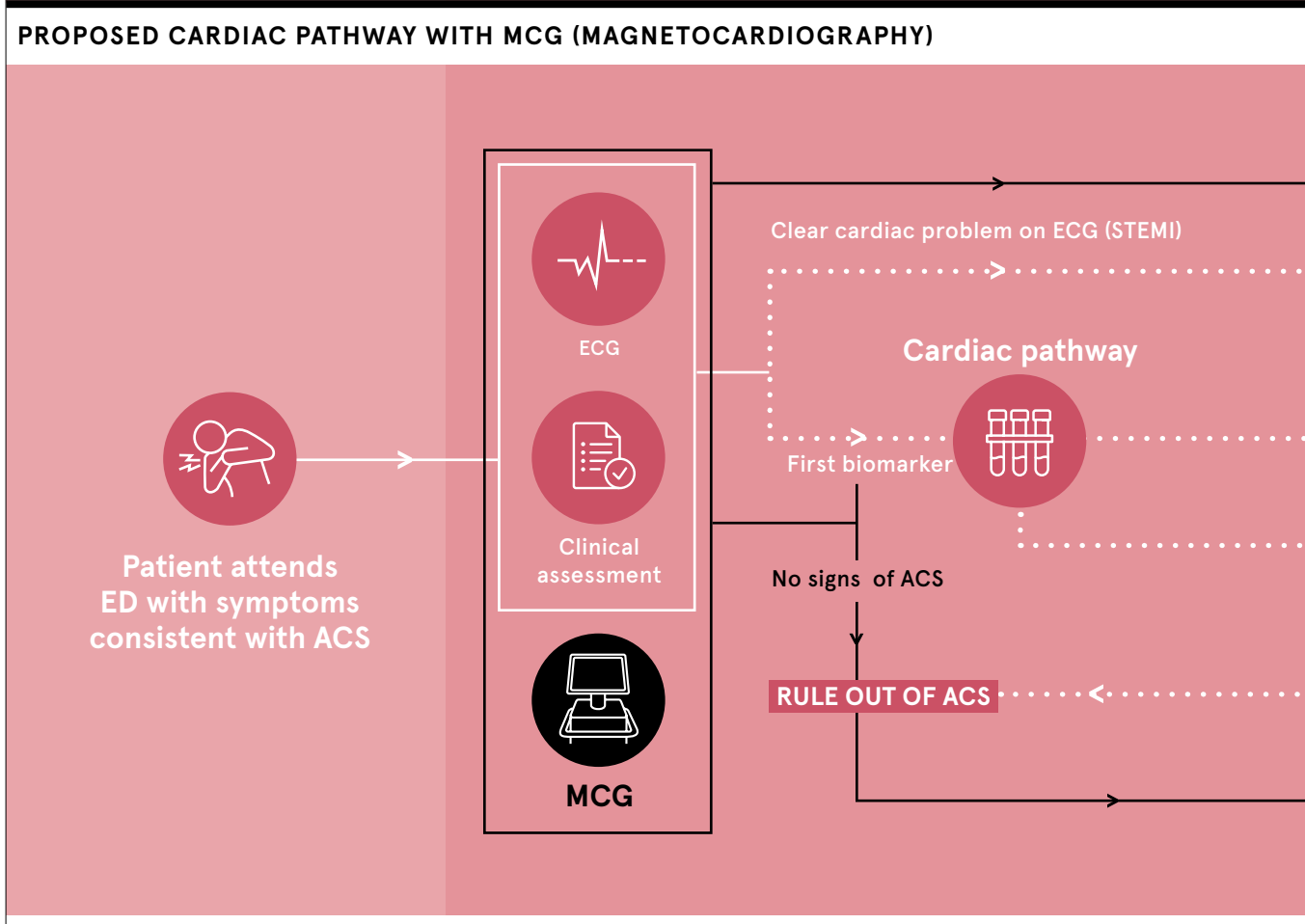
The technology, which Creavo has packed into a portable unit, can assess the heart's condition within minutes by a non-invasive scan, delivered encouraging results in early studies and is about to receive the results of a large study at five busy UK hospital emergency departments.

There is a large amount of interest in the technology with many saying it has the potential to be a game-changer.

The company is just embarking on its latest funding round with continued support from its existing private healthcare investors, including the IP Group. It has just moved into a new base in Coventry and is gearing up for production of the compact device, which can be wheeled to a patient's bedside and operated by healthcare professionals.

Creavo has an impressive medical advisory board. "We have great support from our medical advisory board. They are positively engaged and that is a great indication of the excitement it is generating," says Mr Parker. "We have not been short of investment and support because we have the right people and have a very engaging story; most people will know someone who has been through that hospital process. We have been supported very strongly by our investors, which has enabled us to grow the UK study very quickly. They are committed to our future."



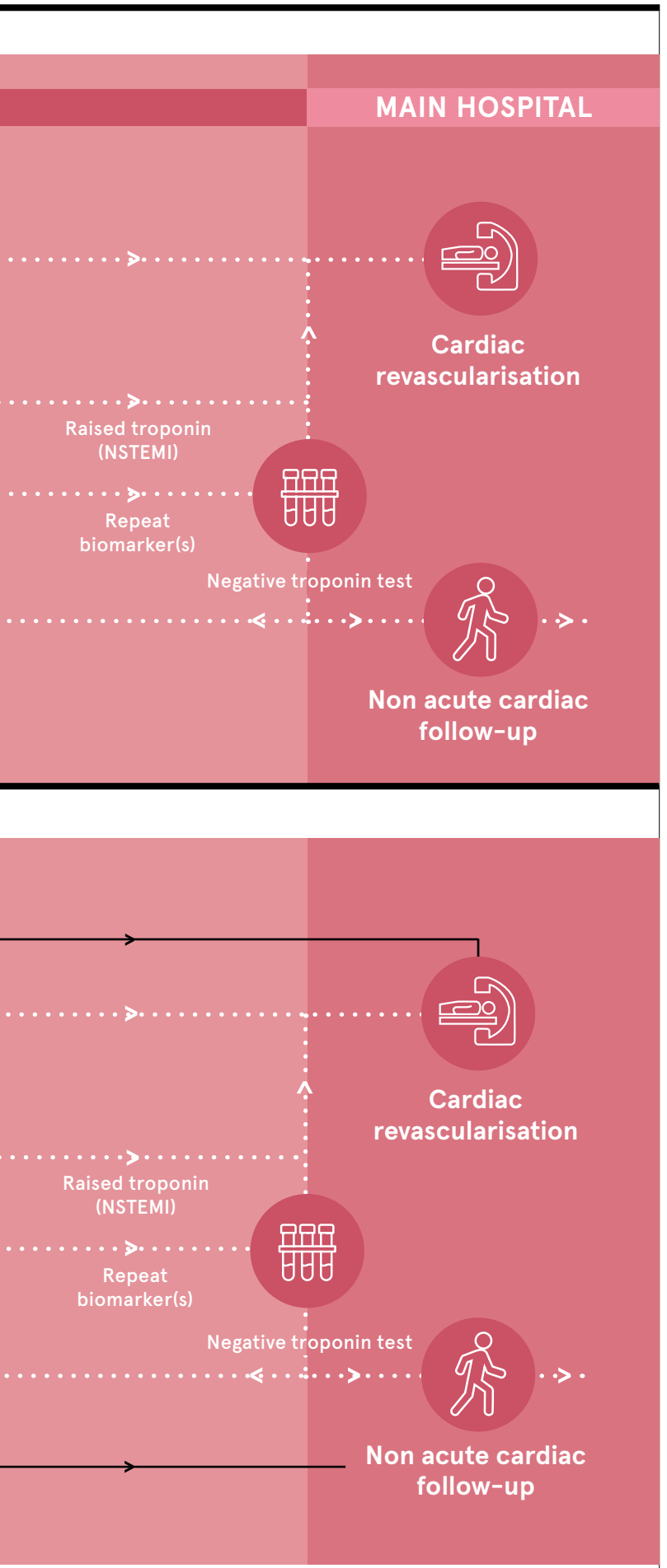


> **This is a patient, economic and technology story that comes together to make a very effective business model**

The UK study results are expected towards the end of the year and will coincide with a planned European market launch, followed by further studies and a US launch towards the end of 2020.

"The pure business model is that patients who go through the pathway, but don't have a problem, are expensive to hospitals," Mr Parker adds. "Even using conservative numbers, we expect to have a huge impact. A major cost is incurred assessing people at low risk of heart attack by putting them through the current chest-pain pathway.

"The really exciting element is that this is a platform technology with multiple applications and £20 billion of business opportunities, but we are resolutely focused on getting Corsens to market. We have planned to achieve regulatory clearance on our device in the second half of this year to coincide with publication of clinical trial data, which will really start our commercial journey



How it works

The world's stressed emergency departments are struggling to cope with rising levels of patients, including those reporting with chest pain who need to go through a lengthy assessment pathway before they can be discharged.

The Corsens® technology utilises a dinner plate-sized sensor passed over the patient's chest that picks up subtle variations in the heart's magnetic field which is designed to rapidly identify if it is functioning normally.

In combination with a clinical examination and an electrocardiogram, it is intended to act as an aid to help clinicians send a number of patients home before the current standard of care chest-pain pathway, which can be up to eight hours.

"The technology reassures patients and relatives, and has the potential for major logistical improvements to the number of people staying too long in emergency departments," says Dr Richard Charles, former consultant cardiologist and medical director at the Liverpool Heart and Chest Hospital.

"A major cost is incurred assessing people at low risk of heart attack by putting them through the current chest pain pathway, so this development could certainly add to our ability to reduce those costs to medical care."

Dr Charles, chair of Creavo's medical advisory board, adds: "Incorporated into a well-honed system, this could result in patients being sent home reassured within 30 minutes or directed on to a more appropriate pathway for their chest pain."

Professor Richard Body, consultant in emergency medicine at Manchester University NHS Foundation Trust, has welcomed the potential of Creavo's device in the face of increasingly crowded A&E departments.

"We have to think disruptively and innovatively," he says. "We don't necessarily need incremental improvements in the technologies we are using; we need new technologies that might enable us to deliver care in other environments."

Pending regulatory approval

in Europe. We will also be closing recruitment in a US study around the third quarter of 2019, which starts us on the road to a US launch by the end of 2020."

IP Group has been involved with the device since its inception and is the company's longest-running and biggest shareholder. Dr Simon Graindorge, a partner in its life sciences and healthcare division, says: "I have been investing in early-stage technologies for 15 years and have never been involved in a technology that has such a widespread need as this, and is universally understood and endorsed by clinicians who understand the problem.

"Every clinician you talk to cuts you off at about the second sentence because they understand exactly what the problem is; they deal with it daily and understand how this has the potential to change what they do. The clinical support has been powerful and they have a strong management team that is doing a great job."

IP Group came on board after Dr Graindorge met Professor Ben Varcoe of the University of Leeds School of Physics and Astronomy, who suffered heart trouble and was told by his cardiologist at the end of a busy clinic: "At last, someone with a genuine problem."

The burden of pushing a procession of patients through cardiac testing and then follow-up clinic appointments was explained, and Professor Varcoe began applying his knowledge of quantum electrodynamics to map the electrical signals of a healthy heart.

Professor Varcoe, who is Creavo's chief scientific officer, discovered abnormal patterns in the magnetic fields reflect a loss of oxygen to the heart muscle (ischaemia), indicating the need for further tests and treatment, while a heart free from ischaemic issues emits a different set of signals that are picked up by the device.

"We specialise in investing in early-stage projects deriving from university research," adds Dr Graindorge. "This is a genuine platform that can be used in different areas, aside from its first application in the emergency setting. If the company can achieve its goals over the next two to three years, it will be in a fantastic place."

Creavo has just celebrated its fifth anniversary with a move to new premises future-proofed for its expansion and the commercialisation of the Corsens device for which it has already secured European and Middle-East distribution partners.

The company and its staff have won industry accolades at the Institute of Engineering and Technology Innovation Awards, which celebrate the very best in new innovations in science, engineering and technology, showcasing entries from around the world. It followed up with the Institute of Physics' Start Up Award in 2018.

"The awards are great recognition for the work we have achieved as a young company with a great business idea with huge potential that is founded on a physics invention," says Mr Parker. "We are driven by a desire to get these products to the frontline of healthcare where they can make a significant difference to patients, doctors and national health systems.

"This is a British invention, funded predominantly by British investors and we have created 50 high-calibre jobs. It talks to the levels of innovation in the UK, the investment, the tax credits and all the elements that have helped us, and demonstrates the UK market is very strong in supporting the medtech business. It is a great British success story."

For more information please visit creavomedtech.com

CREAVO
MEDICAL TECHNOLOGIES

AGEING

We're living much longer, but are we healthier?

Increases in life expectancy will put unprecedented pressure on our healthcare systems. Exploring the science of ageing and our understanding of co-morbidities will be crucial in tackling this 'longevity trap'

Danny Buckland

The statistics of an ageing population are a klaxon call of distress for policymakers and financial modellers desperate to balance the equation of supporting a demographic with voracious healthcare needs.

Life expectancy in the UK has increased by around 30 years during a century garlanded with astonishing medical and public health advances. The over-65 cohort is expected to rise from its current level of one in six of the population to almost one in four by 2035, with people aged 85-plus reaching 4.6 per cent of the population, according to projections from the Office for National Statistics.

A triumph, no doubt, but one which needs to be tempered by the fact that the number of older people diagnosed with four or more diseases will double between 2015 and 2035. We are living longer but, for many, those extra years are blighted by ill health.

The fiscal elastic holding the straining NHS in place is unlikely to cope with the elderly bulge, but a wave of research and innovation is offering scientific hope to challenges that will define both the health and wealth of future generations.

Factoring and finessing social policy will play a crucial role to ensure health and social care budgets resist the pressure-cooker forces brought by an ageing population, but scientific discovery is gearing up to declaw the ravages of ageing.

Mapping the human genome has supercharged biological understanding and this is being fed through prisms of technology and population data analytics to reveal disease trends and how to combat them.

Work, lifestyle and built environments have to improve to help society make the most of its extra years, but the transformative challenges and answers lie deep in our molecular and cellular structure.

"I refer to it as the longevity trap," says Thomas von Zglinicki, professor of cellular gerontology and scientific director of the Institute of Ageing at Newcastle University. "You have a long life, but it can be pretty miserable on the personal side and on the societal side it becomes pretty expensive.

"Research says that we are expanding the lifespan, but we are not expanding healthy lifespan; people live longer, but they have more diseases for longer."

The Institute studied a cohort of 85 year olds and found all had multiple diseases; women averaging five and men four.

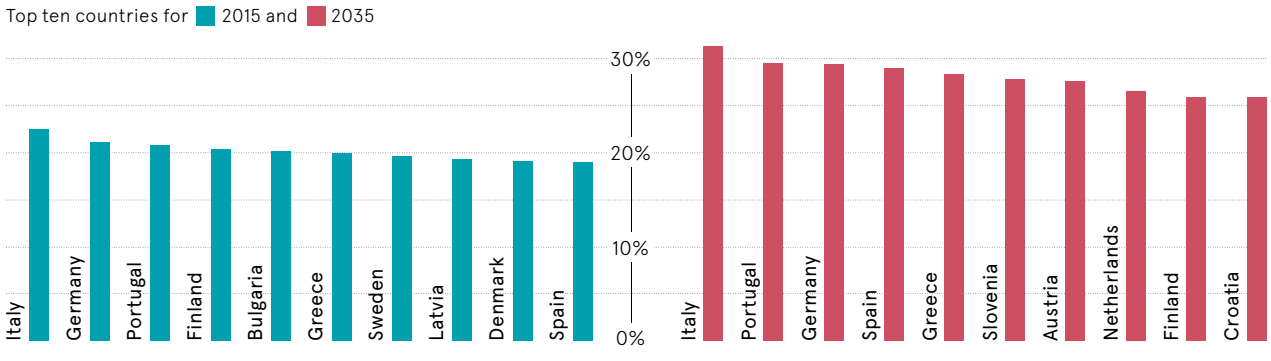
"None of them had no disease and this was quite shocking," says Professor von Zglinicki, who has published more than 200 papers on the cell and molecular biology of ageing. "The long-standing medical approach of treating one disease at a time is at the end of its potential in that respect. Even if you could heal all the people with cardiovascular disease (CVD), they would have four or five diseases that are all related to the ageing process."

Science is unpicking the corrosive influence of senescence, where cells stop dividing and lose their purpose which was once considered an irreversible factor of ageing. But work at Newcastle, and other centres around the world, has illuminated the destructive nature of these rogue performers that destabilise neighbouring cells and promote low-level inflammation, which has been identified as a trigger for many aspects of ageing.

"Working with the Mayo Clinic in the United States, we have shown that if you selectively kill senescent

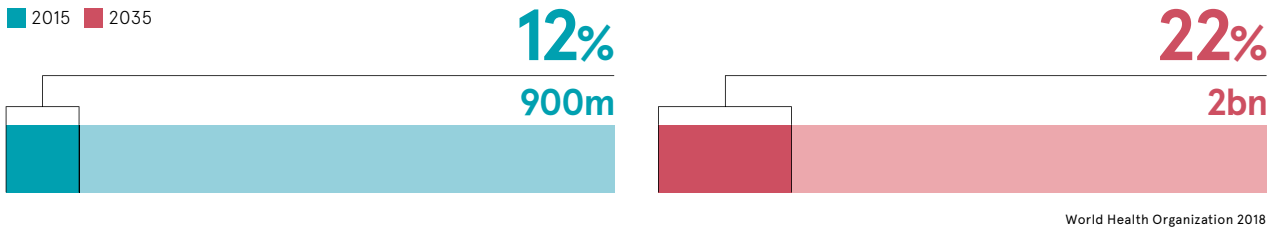
> **The long-standing medical approach of treating one disease at a time is at the end of its potential**

PROPORTION OF EUROPEAN POPULATIONS AGED 65 AND OLDER



United Nations 2017

GLOBAL POPULATION AGED 60 AND OLDER



World Health Organization 2018

Science of ageing

Ageing has become a magnetic field for researchers, innovators and regulators with the government pledging £300 million to ensure the UK leads the way in healthy ageing.

A generation ago, life expectancy was plugged at around 70 while there are now ten million people alive who can expect to celebrate their centenaries, compared with the 1,500 today.

The field has gone from scientific backwater to cutting edge with a raft of vibrant research projects that challenge the fundamentals of how the body deals with decline.

Early trials of senolytic drugs, which target damaged cells that interfere with physical function, found they could clear a model of the chronic and irreversible lung condition idiopathic pulmonary fibrosis.

A discovery at the University of Virginia School of Medicine identified that wrinkles in cell nuclei, which contain our DNA, prevent genes from working and accelerate the ageing process. The US scientists are now modifying viruses to deliver the protein lamin to smooth the surfaces and regenerate cell function.

New Jersey-based firm Celularity is developing stem cell therapies to augment longevity by targeting organ and tissue repair to improve health span.

The pace is feverish and discoveries open new vistas of understanding, but it is a race against time. An ageing population that cannot work and needs elevated levels of healthcare is a disastrous prospect.

The Japanese government is in a virtual state of national emergency as its people age and the workforce shrinks. It is acknowledged as the most ageing of developed countries and saw its care home population tripling from 1.49 million to 4.45 million between 2000 and 2012.

It is now straining every technological, scientific and societal sinew to find ways of keeping its people healthy and productive.

The UK hopes its strong backing of science will make the nation fit to face the looming problems of an ageing population and, ultimately, prosper from their extended good health.

cells then you can postpone multiple age-related disabilities and disease," he says. "We have not yet translated this into humans and, although that is a big step, the data is immensely encouraging.

"The first data from the US clinical trials will tell us whether we have a realistic chance of translating what we know from mice into humans and I think, optimistically, interventions that kill senescent cells will be beneficial. The earliest application will be in people who age faster than they should, those people who have had chemotherapy and radiotherapy treatment who get muscle wasting and cognitive, CVD and metabolic decline earlier than the normal population. To help these people is a realistic goal over the next ten years."

This cautious confidence is shared across healthcare investment with venture capital heavily backing bioscience companies such as Life Biosciences, a US startup, which swiftly completed a $50-million funding round in January to investigate eight pathways of age-related decline. Juvenescence, a UK biotech, drew in $50 million in funding last year to pursue artificial intelligence-generated programmes to support ageing populations.

But a sticking point in the headlong rush comes from a lack of clinical trials on elderly people with co-morbidities. They are a difficult group to corral for long-running tests and pharmaceutical companies focus on patients with one condition to give them "clean" results.

"There is a disconnect between scientific research and discovery, and getting that into a form that benefits patients," says Miles Witham, professor of trials for older people at the National Institute for Health Research Newcastle Biomedical Research Centre.

> **Older people are the biggest consumers of healthcare yet we don't do nearly enough research with them**

"Older people are the biggest consumers of healthcare yet we don't do nearly enough research with them. Our aim is to take what we learn in the laboratories and translate it into things that might make a difference to older people in their lives. It is not about extending life and making people live for ever, it is about improving quality of life and keeping people healthier for longer."

Designing clinical trials that have logistical flex and address the real-life healthcare needs of an older group with multiple diseases will, Professor Witham believes, transform science from the aspirational to the applicable.

The impact of ageing on the individual, society and the NHS is writ large in the almost emblematic old-age conditions of osteoporosis – three million sufferers in the UK with 500,000 receiving treatment for fragility fractures – and hip fractures that hit 65,958 in 2017, according to NHS figures.

But a five-year programme funded by the Medical Research Council (MRC) is identifying a whole-life approach to combat ageing and research conducted by Professor Cyrus Cooper, director of the MRC Lifecourse Epidemiology Unit at Southampton University, is already tackling the worst outcomes of musculoskeletal decline.

"The chilling facts are that 25 per cent of patients are dead within six months of a hip fracture and 50 per cent of those surviving cannot walk unaided, while one third of them has to go into a nursing home at a cost of £4.2 billion a year," says Professor Cooper.

By developing a risk assessment tool combined with a bone-density scan, he was able to reduce hip fracture rates by 28 per cent in a trial of 12,500 women aged 70 to 85. The unit has also proved that supplementing vitamin D intake in maternal mothers boosts bone density in their children, potentially making them less susceptible to osteoporosis and fracture in the future.

"This tackles a once inevitable consequence of ageing with interventions at two time points, not just at the later stages of life," he adds. "There is also a huge amount of evidence about the influence of diet and exercise in between, so it is important to look at ageing from a lifecourse perspective."

A fusion of science, innovation and pragmatism is needed to open up a fresh landscape of healthier later years and, although eternal youth remains a fantastical concept, reducing the crippling impacts of ill health on an ageing population is a clear reality.

IMPLICATIONS OF AGEING

The proportion of elderly people across the c
continue to swell as life expectancies rise, but
will have on health services will be unprecede
the following data, healthcare spending per ca
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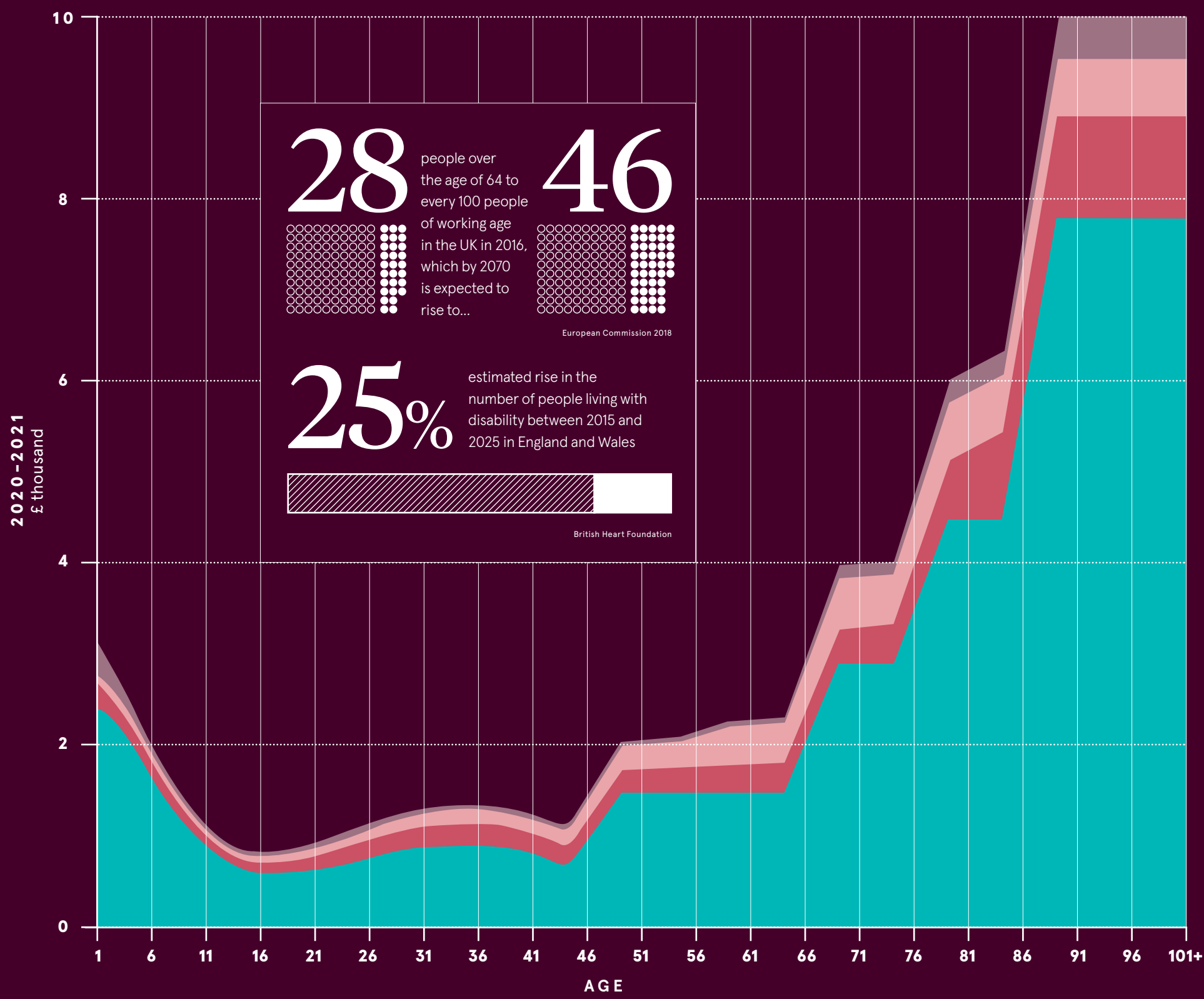
HEALTH SPENDING RISES SHARPLY IN OLD AGE

Representative profile for annual health spending per capita, based estimated 2020-21 prices



28 people over the age of 64 to every 100 people of working age in the UK in 2016, which by 2070 is expected to rise to... **46**

European Commission 2018

25% estimated rise in the number of people living with disability between 2015 and 2025 in England and Wales

British Heart Foundation

Office for Budget Responsibility 2017

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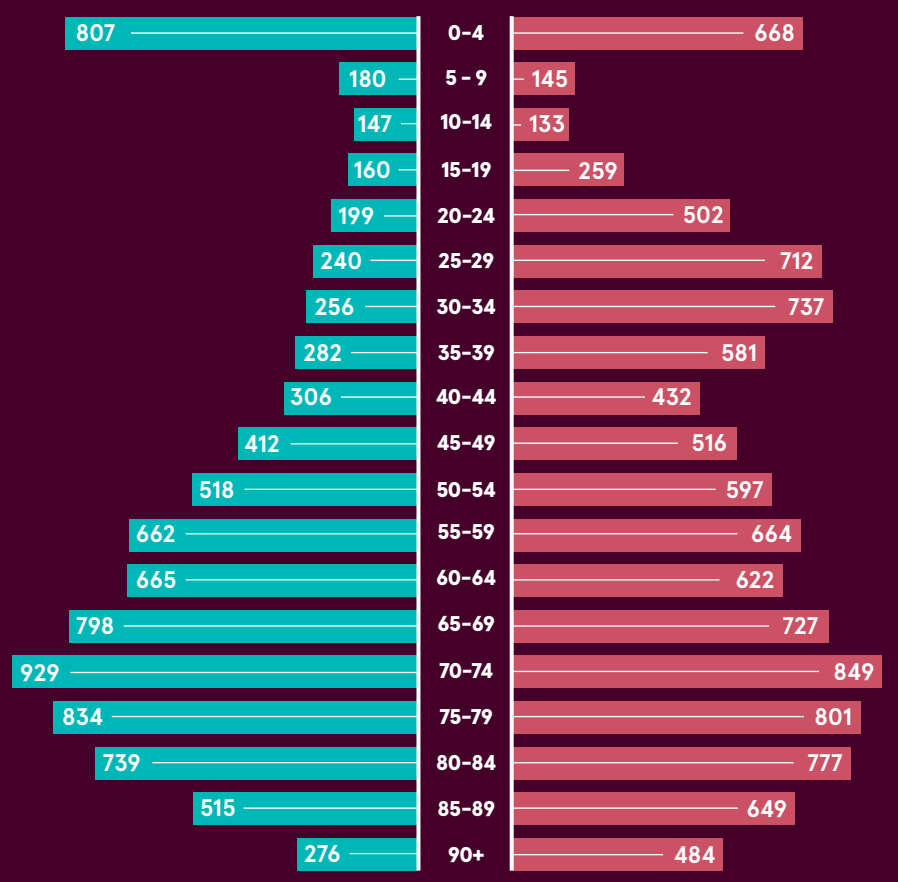
HOSPITAL EPISODES BY AGE

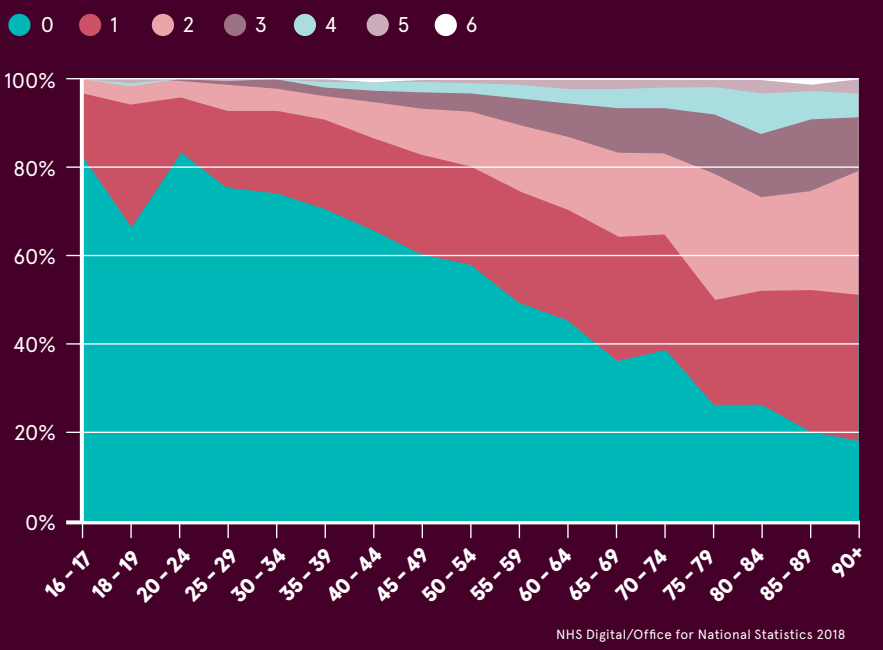
Finished consultant episodes or FCEs in England by age band in 2017-18 (thousands)



NHS Digital 2019

NUMBER OF HEALTH CONDITIONS BY AGE

Percentage of population in England with the following number of health conditions



NHS Digital/Office for National Statistics 2018

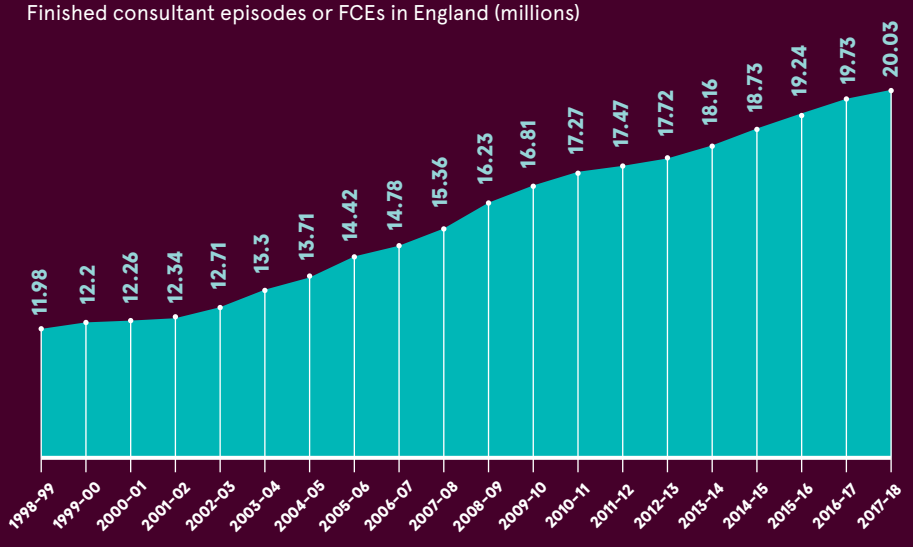
NUMBER OF PEOPLE AGED 90 YEARS AND OVER

Population by age range over 90 (thousands)

Office for National Statistics 2018

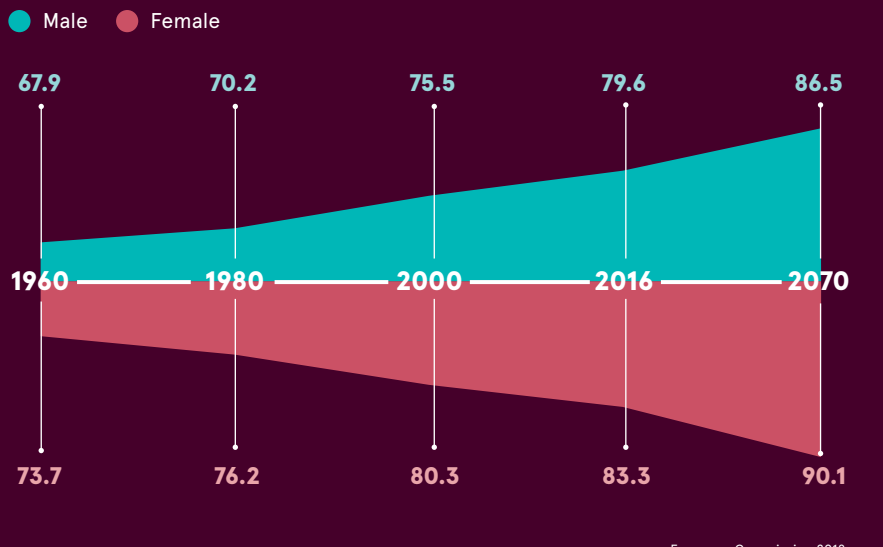
HOSPITAL EPISODES BY YEAR

Finished consultant episodes or FCEs in England (millions)



NHS Digital 2019

LIFE EXPECTANCY AT BIRTH



European Commission 2018

RESEARCH

The true cost of white-washed research

Genetics and medical studies have largely over-represented people of white, European descent, which could have huge ramifications for the advancement of health research

Nick Easen


Shutterstock

If all humanity was wiped out tomorrow and we had to reconstruct mankind from genetic data and research found on computers across the globe, our avatar would look mostly white and Caucasian. You would be hard pushed to rebuild Asian and African populations with their resplendent genetic variety. This has huge implications for our health, globally.

In an age when the burning injustices of diversity and inclusion are being codified into law, society and in businesses worldwide, it is only now being fully realised in genetics and medical studies.

"The lack of diversity may be one of the biggest challenges that we face in the potential advancement in health research," explains Dara Richardson-Heron, chief engagement officer at the All of Us Research Program in the United States.

Genome-wide association studies show that more than three quarters of published research is derived from volunteers with European ancestry, whereas Asians represent 10 per cent and Africans 2 per cent. In mental health, 96 per cent of people studied are from Westernised, educated, industrial and rich democracies. Minorities are currently poorly represented in the UK Biobank, which aims to genotype 500,000 people. So the big picture is hardly one of inclusion.

The problem of healthcare inequalities also existed before we sequenced the human genome, but as our knowledge of genetics and links to disease increases, promising new tailored treatments, the lack of diversity matters more.

"This a major issue and one that researchers and funders must address. We're starting to see changes, but many challenges remain," says Mary De Silva, head of population health at Wellcome.

Diversity matters in medical research and clinical trials because diseases vary greatly depending on the community you study. "In complex problems such as Alzheimer's, cardiovascular disease, diabetes and multiple sclerosis, we know that manifestations vary across populations," says Giorgio Sirugo, associate professor at the University of Pennsylvania School of Medicine. "Transferring findings from one population to another is a major problem."

For instance, South Asians have higher levels of heart disease and diabetes, while South Americans have more asthma and a poor response to certain inhalers. "The common criticism is that research findings found by using white individuals will benefit mostly white individuals," says Doug Speed, assistant professor at the Aarhus Institute of Advanced Studies in Denmark.

Doctors may also diagnose conditions or prescribe medicine that will work for those with European genes, but for other racial backgrounds, it can be less effective.

"In my opinion, all medicine is impacted when there's no diversity in the system," says Emmanuel Peprah, assistant professor at New York University College of Global Public Health.

"Medical studies start from basic discoveries to research, which then focuses on how to bring to scale, at a population level, evidence-based discovery. In each of those significant steps, if populations of diverse background are omitted, the implications for the findings and those that could potentially benefit from the research decreases."

All areas, from medicine to surgery, from diagnoses to treatments, from drug discovery to organ transplantation, could be impacted. The good thing is the medical profession is now working hard to redress this imbalance.

"We are aware of the dangers of extrapolating from research in Western populations. We are also very much aware of the importance of understanding the influence of ethnic diversity on health," says Dr Joe McNamara, head of population health at the Medical Research Council.

> **Transferring findings from one population to another is a major problem**

A number of projects have been funded. There's the Human Heredity and Health in Africa initiative, the All of Us Research Program in America, which will gather data from more than a million people including minorities, the Born in Bradford birth cohort, with a high representation of people of South-Asian origin, and the China Kadoorie Biobank, made up of data from 500,000 people across China.

"However, the structures and incentives in the research ecosystem make this work the exception rather than the rule," says Ms De Silva. "A concerted effort by funders, including national governments, is needed to change the incentive structure, and to fund and value research in more diverse populations."

Professor David van Heel, who leads the East London Genes & Health project, is recruiting 100,000 British-Bangladeshis and British-Pakistanis with the aim of linking genes with health records. He realises recruitment is a big issue.

"Trust is so important," he says. "Different communities react to different enrolment techniques. Face-to-face recruitment in a trusted setting works for South-Asian people here in east London; via post, smartphone or online recruitment doesn't work. People are also willing to get involved if they've experienced ill health among family or friends."

Some groups have been sceptical or hesitant to participate in research. Studies have been described as exploitative or unethical, while results and discoveries haven't been shared with those who took part.

"It's important that individuals know how they may benefit when they choose to participate in research," says Dr Richardson-Heron. "We're offering an opportunity for under-represented communities to have a seat at the table, from the start, in building a research programme that may have a significant impact on the health of their communities and for future generations."

Yet there's still a defence for homogeneity in genetic studies. "It can be more efficient and a better way to spend money focusing on one ethnic group. A study of 10,000 individuals from one population will likely be more successful than a study of 20,000 individuals from 20 populations," explains Dr Speed. "The problem is the majority of studies are all white and very few non-white." The promising thing is that diversity is now a buzzword in the healthcare community too.

3/4+
of published research is derived from volunteers with European ancestry

1/10
uses people with Asian descent

1/50
uses people with African descent

Giorgio Sirugo/University of Pennsylvania School of Medicine 2019

Tech empowers people to take more control of their wellbeing

Private healthcare insurance providers are tapping into the latest technology innovations, giving individuals, business owners and their teams excellent ways to manage their health

Any individual's experience of looking after their own wellbeing could typically involve factors such as good eating, exercise and treatments from medical specialists when needed. But a wealth of new technologies are now being made available to empower people in addressing their own health issues more consistently and help companies support employees in this area.

"Technology is putting control of a medical condition or a wellness desire in the hands of the consumer, and enabling them to be much more proactive in terms of health management and getting a better quality of life," explains Richard Cooper, head of digital and ecommerce at private healthcare firm AXA PPP healthcare.

Innovations already having a notable impact include a shoe attachment with a laser pointer that provides visual cues to people with an unsteady gait, enabling them to walk much more quickly and easily. This remarkable innovation, called Path Finder, has proven to be enormously helpful to people suffering from Parkinson's disease.

The creator of Path Finder is among the winners of AXA PPP healthcare's Health Tech & You Awards, which support innovation among health technology pioneers. As with many other entrants to that competition, the inspiration for Path Finder came from a source close to home with the creator's father suffering from Parkinson's.

Lise Pape, chief executive of the company behind Path Finder, Walk With Path, used her design and engineering background to create a solution that helps people walk much more confidently and experience a significantly enhanced quality of life.

For AXA PPP healthcare, the goal in engaging with and encouraging the creation of new health and wellbeing technologies is to play a more all-round role in supporting its customers to stay healthy. With the Health Tech & You Awards, the company discovers useful innovations in the health technology field, and also provides vital promotion and support for innovators.

AXA PPP healthcare focuses on supporting innovators' smart ideas. "By taking this approach we're engaging with creators and pioneers, who are single minded in their focus on enhancing people's health and wellbeing," says Mr Cooper. "As a part of this, we're helping them to realise their ideas and bring them to fruition."

In turn, the innovators support business owners and their employees by creating the technologies that help workforces manage their health and wellbeing. One of the solutions discovered at the Health Tech & You Awards is Emoquo, a personalised digital coaching app that helps employees deal with everyday workplace challenges quickly and in confidence. The app is based on advice for employees from more than 25 coaches and therapists, and it also anonymously highlights common challenges to managers so they can improve workplace culture. Concerning employee health, AXA PPP healthcare has been working particularly closely with LiveSmart, which offers personalised digital health assessments to help business owners build a happier, healthier workforce. It gives their teams the chance to take a blood test at home and send it off for assessment. Employees receive an in-depth report based on their blood test results, giving them an analysis of a number of physiological factors they could consider as part of an effort to improve their all-round mental, physical and nutritional health.

> **For AXA PPP healthcare, the goal in engaging with and encouraging the creation of new health and wellbeing technologies is to play a more all-round role in supporting its customers to stay healthy**

Technology is also helping business owners provide their employees with fast access to health support. AXA PPP healthcare has implemented a service called Doctor@Hand, which enables employees to book online GP appointments and have consultations at a time and place that suits them best. The service covers everything from diagnostics to referrals, and enables business owners and their teams to talk to a GP, often within a matter of hours, either by phone or via video chat. Doctor@Hand is provided by Doctor Care Anywhere.

Dr Arup Paul, deputy chief medical officer at AXA PPP healthcare, says emerging health tech innovations offer real value in areas ranging from telehealth and wellbeing tracking to health professionals' training. It is essential, he says, that there is a framework for testing new technologies, accepted by clinicians and regulators. He adds there is a growing swell of opinion among doctors and scientists that the rigour in studies using apps and artificial intelligence follows best practice and strong results are often visible, as already promoted by the World Health Organization.

From AXA PPP healthcare's perspective, work is advancing to help people learn how to access and use their own health and wellbeing information more consistently and harness technology that improves their lives.

Mr Cooper concludes: "In the past, companies like ours would have been branded simply as insurance providers, but now we're able to offer a much broader range of health and wellbeing products and services of which insurance is just one aspect. We're able to have a relationship with a customer throughout their lifespan, and provide support with their health and wellbeing needs."

HEALTH TECH SURVEY

31%

agree that technology will play a significant role in their health, wellbeing and fitness in 5 years' time

41%

of those who have had a face-to-face GP appointment in the last year would be interested in having a virtual appointment with a GP

37%

think that using health technology would positively impact their health

43%

think that technology can help manage a long-term health condition

41%

would be interested in having an 'at home' health test that would include an ongoing coaching program to help them achieve their health and wellbeing goals

Health Tech Survey conducted by YouGov on behalf of AXA PPP healthcare, 20th-21st November 2017. Sample size: 2057. The survey was carried out online. The figures have been weighted and are representative of all GB adults (aged 18+).

Commercial feature

01

Breakthrough cell therapies treating blood cancers

A major research project has put the UK at the forefront of revolutionary cell therapy treatments for blood cancer patients

Early results from the COBALT trial and other studies show that aggressive cancers can be tamed with CAR-T therapies which re-engineer the body's immune system to seek out and neutralise abnormal and malignant cells.

The process, which takes T cells from a patient's body and genetically modifies them to recognise specific cancer cells, has been proven to put some cases of lymphoma and leukaemia into retreat, and has now become available on the NHS.

The COBALT trial, conducted by University College London, was designed to look at the safety of using CAR-T therapy for people with an aggressive type of non-Hodgkin lymphoma called diffuse large B-cell lymphoma (DLBCL). The therapy targets a protein called CD19 found on the surface of some lymphoma cells with the aim of controlling the cancer before proceeding to a bone marrow transplant.

Parallel commercial advances reached a significant milestone last year with the European approval of a CAR-T therapy for both B-cell acute lymphoblastic leukemia and DLBCL. Manufacturing processes are still being refined and, while research continues into potential side effects and toxicity, CAR-T is seen as a dynamic therapy with the power to combat blood cancers and in the future may have the same effect on solid organ cancers.

Bloodwise, the blood cancer charity, is funding COBALT and research on several CAR-T initiatives. Dr Alasdair Rankin, its director of research, policy and support, says: "The big excitement is that these cellular therapies are coming to blood cancers first and they have the potential to make transformative change.

"We are just at the beginning of the wave and in ten years' time we will be looking back on these innovative treatments, saying they are not very sophisticated because we will have progressed to mark three or four."

The research underpins the potency of CAR-T in patients with advanced disease and, importantly, has allowed the UK to build experience with both manufacturing and delivery of these therapies, so treatments can be prepared and delivered safely and more cost effectively. The work, which started with a laborious processing line approach, has been shaped into an industry-leading automated template.

"Our early process was very

Blood cancer in numbers

1 in 19
people will get blood cancer at some point in their lives

15k
people in the UK die from blood cancer each year, more than breast cancer or prostate cancer

240k
people currently living with blood cancer in the UK

4.7k
people currently on clinical trials funded by Bloodwise

3 in 10
blood cancer cases in England are diagnosed after presenting to the NHS as an emergency

02

03

01
A vial of blood in the laboratory

02
Preparing intravenous drugs in a hospital laboratory

03
Professor Karl Peggs

transplantation at University College London Hospitals. "Bloodwise has been hugely supportive of cell therapy research, not just CAR-T, over the past decade. This has been a high-risk area, but they have always been there when others haven't. They have been prepared to support trials involving these extremely complex therapies associated with higher technical risk.

"Bloodwise was forward looking and supportive of cellular therapy and because of that we have been able to make CAR-T a reality."

He believes that more licensed products will soon become available across a spectrum of blood cancers, while translating those discoveries to solid cancers is a longer-term goal.

NHS England has made CAR-T therapies available to eligible patients through the Cancer Drugs Fund, for the treatment of children and young adults with acute lymphoblastic leukaemia, and adults with DLBCL. Other Bloodwise-funded CAR-T research projects are examining cell structures for new targets in other blood cancers, as well as trying to discover new delivery techniques that will keep costs down.

It is still not clear if a patient will remain in remission because CAR-T hasn't been around long enough to know. But Bloodwise is confident that every step will contribute to finessed treatments that can have a transformative impact and pave the way for more discovery across all blood cancers and into solid organ cancers.

"We are committed to saving more lives by investing in the most exciting research into CAR-T therapy," says Dr Rankin. "We are at the dawn of an exciting era and it is evident that CAR-T has the potential to be an effective treatment for an awful lot of people.

"One of the challenges is going to be about the NHS being ready and able to deliver this. It is building capacity as fast as it can and has responded really positively."

University College London Hospitals recently announced a partnership with the Exilarch's Foundation to develop Europe's first unit dedicated to delivering these therapies, the Sir Naim Dangoor Centre for Cellular Therapy.

"How we make these treatments more affordable and more effective, as well as moving them into other cancers, is going to be a challenge, but we are going to see lots and lots of improvements through research over the coming years," Dr Rankin concludes.

For further information please visit bloodwise.org.uk

Bloodwise
The **blood cancer** charity

HOW CAR-T THERAPY IS GIVEN

1 T cells are taken from the patient's blood

During a visit to hospital, blood is taken from the patient. The T cells (a type of white blood cell) are removed. The remaining blood is given back to the patient.

2 T cells are turned into CAR-T cells

In the laboratory, the T cells are genetically modified so they can recognise and kill specific cancer cells. They are now called CAR-T cells. The CAR-T cells are multiplied to make enough for the treatment.

3 CAR-T cells are given to the patient

The patient has chemotherapy, which reduces the number of normal T cells in the blood. This makes room for the CAR-T cells. After chemotherapy, the CAR-T cells are put back into the patient's blood through a drip.

4 CAR-T cells attack cancer cells

The CAR-T cells continue to multiply in the bloodstream, finding and killing cancer cells. CAR-T cells may remain in the bloodstream for some time to help prevent cancer from coming back.

> **One of the challenges is going to be about the NHS being ready and able to deliver this**

labour intensive with lots of people gowned up and working one step at a time, which meant we could not make many products and that it was costly," says Professor Karl Peggs, project leader and scientific director of the National Institute for Health Research Blood and Transplant Research Unit in Stem Cells and Immunotherapies.

"We realised that we needed to create an automated process that could be performed in closed systems without manufacturing in such a high-dependency and high-cost manufacturing environment.

"Our work has enabled us to reduce cost and complexity significantly, with multiple machines in a single room each capable of manufacturing a dose of cells. Our early trials taught us an awful lot and established important infrastructure. With that knowledge and processes in place, we can look at fresh ideas and new patient groups that might benefit.

"Thanks to our funders, we are now in a very good position to take other academic programmes forward, while industry partners are much keener to work with us to run big international trials and this means we get more access to new therapies for UK patients through commercial studies.

"The knock-on effect of our research is that manufacturing is cheaper and more efficient with far lower failure rates. Rather than treating one patient per month, we can now make multiple products and treat a lot more patients. The ability to be able to offer therapies patients cannot get elsewhere is hugely important."

The COBALT trial was launched before CAR-T had gained scientific traction, so funding was an issue.

"It was not as easy to get funding then as it is now, but Bloodwise provided the bulk of what we needed," says Professor Peggs, who is also honorary consultant in haematology and

About Bloodwise

Bloodwise is at the forefront of scientific advances that have dramatically improved survival rates and treatment outcomes for patients with blood cancer, the third biggest cancer killer.

The charity's world-class research programme funds more than 400 scientists working across 160 projects, which are decoding a destructive condition with over 100 identified types, and providing hope to the 15,000 people diagnosed with blood cancer every year.

The work covers patients of all ages and ranges across 40 clinical trials into every treatment potential, including complex signalling mechanisms involved in the body's immune response and the behaviour of malignant cancer cells.

"The big excitement is CAR-T therapies and it is likely that we are only beginning to see the benefits they can bring," says Dr Alasdair Rankin, director of research, policy and support. "Bloodwise research is part of the greater effort to push forward improvements in this incredibly exciting treatment.

"CAR-T is effectively a fifth arm to cancer treatment. At this stage only a few people with blood cancer will receive it so, in all the excitement, it is important people with blood cancer know that existing treatments, such as surgery, radiotherapy, chemotherapy, and targeted drugs and biologicals, are working well and improving all the time. So no one should think they are being given sub-standard treatment if they are not offered CAR-T.

"We are investing in all areas of research. Blood cancer is now a well-defined disease area and there is a bright future ahead with more targeted, kinder treatments and that is good news for the 40,000 people diagnosed every year.

"There are scientific and logistical challenges ahead, but there is no lack of good ideas and initiatives, so one of the challenges is to pick the right elements that will be most effective and getting them to the patients as fast as possible."

Bloodwise research has also helped to improve survival rates for childhood leukaemia dramatically through the minimal residual disease test, which was developed by Bloodwise researchers and adopted by the NHS. It is used to spare children from the harshest treatments if they do not need them and identify those children most at risk of relapse.

"Our research programme is comprehensive and involves dedicated scientists, doctors and researchers all driving towards better treatments for patients," adds Dr Rankin. "The funds we receive go a long way to the vital research that saves lives and gives people better lives."

Dr Alasdair Rankin
Director of research, policy and support
Bloodwise

Commercial feature

Stopping the revolving door of mental health care

The best way to end a revolving-door approach to mental health is to put the person first, not the condition, and provide necessary care without delay

The recently published ten-year plan for the NHS made a welcome commitment to increase spending on mental health by some £1.9 billion. This urgently needed funding will help to improve the care of people with mental illness, an area of healthcare that has always suffered from significant underinvestment compared with physical healthcare.

Currently, the UK has a revolving door of mental healthcare, whereby patients who are discharged from hospital are later readmitted due to a lack of available care in the community. This is failing patients and their families, the NHS and healthcare providers.

At Cygnet Health Care we take a considered, long-term approach to addressing mental illness and have pioneered a range of new services to treat our service users, though we recognise that all providers in the sector need to do more to ensure the best outcomes for patients.

Patients currently face long waiting lists

Currently patients with serious mental health issues, leading them to self-harm or attempt suicide, are being left to wait as long as two years for specialist support. GPs and community health professionals do what they can to support mental health patients on waiting lists, but many patients come to harm and need emergency treatment in A&E.

When patients are finally admitted to an appropriate care facility, the demand for beds, limited budgets and an NHS target-driven culture means they are often discharged long before treatment has been effective and they are ready to go home.

Consequently, patients find themselves virtually abandoned in their communities, struggling to survive before eventually being readmitted to hospital. So, it continues, and each time the patient becomes more vulnerable and the prospect of recovery more distant.

Lack of community-based support is a serious issue

Patients are at increased risk after they have been discharged from hospital, yet the support available to them is poor. A report by the mental health charity Mind confirms what we know from our own experience that NHS mental health teams do not check up on vulnerable people after their discharge, as required by the National Institute for Health and Care Excellence, within one week.

Patients should only be discharged from specialist mental health services when there are ongoing care arrangements in place for them. Failure to do so can put the patient at risk of harm, their condition can relapse and it can mean they are more likely to go back into hospital.

This revolving-door approach is failing patients and their loved ones. It also comes at huge, avoidable cost to taxpayers, at a time when the NHS is under intense pressure to make best use of every pound spent to ensure its long-term sustainability.

We need to treat the underlying causes

At Cygnet Health Care we know that the most effective response to mental illness is to treat the underlying causes and this takes time. There is no quick fix for patients with acute mental illness. We have developed an array of services for patients with mental health needs, and have built a reputation for delivering pioneering services and outstanding outcomes for the people in our care.

We have more than 150 centres across the UK, with over 1,000 beds. Our national network of services provides treatment, care and rehabilitation for men and women, including specialist services that provide low or medium security for individuals with personality disorder, autistic spectrum disorder or who are deaf.

We are very proud that the Care Quality Commission (CQC) has just rated the care provided by three of our hospitals; Cygnet Cedars and Sherwood Lodge – Cygnet's specialist learning disability hospitals, and Sherwood House, Cygnet's specialist rehabilitation mental health hospital – as 'outstanding'.

Cygnet Sherwood Lodge achieved the extraordinary accolade of being rated as outstanding across all five of the CQC's assessment categories for caring, safe, effective, responsive and well-led services, and it joins Cygnet Elms as the second of only two learning disability hospitals in the country to have achieved this extremely rare honour.

We provide safe and comfortable mental health rehabilitation environments to help people rebuild their life and vocational skills, ready to regain their place in the community. Our low and medium-secure services are focused on therapy and recovery, with the aim to progress service users into the least restrictive environment possible.

> **We provide safe and comfortable mental health rehabilitation environments to help people rebuild their life and vocational skills, ready to regain their place in the community**

Our range of emergency and rapid access services for adults include hospitals that can provide psychiatric intensive care units, acute wards, older adult-specific services and those for people with a learning disability. We offer a national network of more than 200 beds to meet the acute needs of people requiring a rapid admission to mental health services, including those who may need an intensive care environment.

We work closely with NHS England, NHS Wales, clinical commissioning groups, NHS provider trusts, other NHS authorities, local authorities, and individuals and their families to create and provide packages of treatment, rehabilitation and care that give the best possible chance of positive outcomes.

Driving quality healthcare is our priority

Cygnet continually works to improve the quality of treatment for those who use our services. We aim always to have people at the centre of their care and to keep our standards high.

We support these commitments with high standards of staffing, including a continuous programme of learning and development for all employees, evidence-based training and regular staff appraisals, alongside a high staff-to-service-user ratio enabling individual care. We make sure there is always an appropriately qualified consultant doctor available.

Service users are encouraged and supported to be involved in the day-to-day running of each service, which helps us ensure the correct high standards of accommodation, catering, therapy and activities are provided. There is a comprehensive daily therapy and activity programme created by specialist staff and available to all patients.

We are committed to maintaining national good practice standards and are members of quality review forums such as QNIC (Quality Network for Inpatient CAMHS or child and adolescent mental health services) and The Quality Network, and are monitored by the Care Quality Commission.

By monitoring policies and procedures regularly, we make sure they are in line with up-to-date professional guidelines and proven good practice. We also arrange independent audits of our clinical care and management systems, and make the reports available to all relevant bodies.

At Cygnet we share society's aspiration for all people with mental health issues to live their lives in the community as fully as possible. We believe that to end the revolving-door approach to mental health, the best way is to put the person first, not the condition, and ensure the fullest range of options for care is available to all.

75%

of people referred to the Improving Access to Psychology Therapies (IAPT) programme should begin treatment within six weeks of referral and...

95%

of people referred to the IAPT programme should begin treatment within 18 weeks of referral

More than...

53%

of people experiencing a first episode of psychosis currently will start treatment within a NICE-recommended package of care with a specialist early intervention in psychosis service within two weeks of referral. This is due to rise to...

60%

by the end of 2020/21

Clinically-led Review of NHS Access Standards - Interim Report from the NHS National Medical Director

For more information please visit www.cygnethealth.co.uk

Cygnet Health Care

OPINION

‘Superbugs don’t respect borders, and neither should we in looking for solutions’


William West / Getty Images

It’s become a well-worn story: doctors and health experts warning of a dystopian future when the drugs won’t work; when drug-resistant superbugs are so widespread, that routine procedures such as childbirth and hip replacements become deadly.

Alexander Fleming’s serendipitous discovery of penicillin in 1928 gave the world its first antibiotic. Penicillin and the other antibiotics that followed revolutionised modern medicine. The ability of doctors to treat infections was transformed, and these wonder drugs became the foundation for countless medical advances. But their power is being compromised by the rise of superbugs.

If the problem is not successfully addressed ten million people each year could be dying by 2050 due to antibiotic resistance. The warnings are no overstatement, but while they continue to make headlines, the topic has become the basis of political handwringing rather than practical action.

The crisis is already upon us, affecting everyone, rich or poor, home or abroad. In India, the most recent estimates suggest that 58,000 newborns die every year because of hard-to-treat infections that do not respond to even ‘last-line’ antibiotics.

Here in the UK, headlines recently shared news of a young girl saved by extraordinary measures from a drug-resistant infection that her cystic fibrosis made her hugely susceptible too. She was lucky enough to have access to first-class medical facilities – most do not.

Public Health England has warned that three million common procedures such as hip replacements and caesareans would become hazardous due to antibiotic resistance, even in first-rate hospitals. They warn that infections acquired from surgery could double, utterly changing the risk profile of ‘routine’ procedures.

This problem threatens health and global development. According to the World Bank, by 2030, 24 million people in lower and middle-income countries will be pushed into poverty if we cannot stop the spread of superbugs. This issue was set at the top of the global political agenda with a high-level meeting at the 2016 UN General Assembly. But despite warm words and promises since, widespread and ambitious action remains elusive.

Scientists, health leaders and clinicians have made clear what must be done to ensure we do not sleepwalk into the end of modern medicine. We must improve incentives for novel antibiotic development; ensure proper antibiotic stewardship across the globe; accelerate innovation and implementation of diagnostics, especially for low-resources settings; and we must prevent and protect against infection by improving hygiene and sanitation especially in countries where the burden of drug resistance is highest.

New antibiotics are an important part of the solution, but decades of disinvestment and hugely unfavourable economic conditions have left the incredibly important responsibility of developing novel treatments to just a handful of startups, while larger pharmaceutical companies have left the space due to the lack of long-term profitability. We have seen promising early development from startups supported through government and philanthropic funding initiatives such as CARB-X. However, we urgently need to fix how we incentivise bringing antibiotics from basic research to treatments for patients, or the innovations will be futile.

The UK government is leading efforts to address the problems facing the ailing antibiotic market and recently announced a limited new ‘Netflix’ pricing model pilot. This would see the NHS pay developers a fixed fee for antibiotics, based on the value of the drugs to the service rather than by quantity in a hope to provide better incentives for drug developers. But there will be a two-year delay before it is implemented and possibly no fresh funding from the Treasury for the NHS to make the pilot happen – a huge shortfall of the otherwise ambitious proposal. We need real change now, that is well funded, and it needs to be global, not just in high-income settings.

Low and middle-income settings face both the highest burden and often the least infrastructure to respond to the threat. However, it is in these countries that we often see the most pioneering action to combat drug resistance. For example, in India, startup Bugworks is the first company in Asia to secure funding from the global antibiotic accelerator, CARB-X. Bugworks is aiming to create the first novel class of antibiotics since the 1960s.

In Tanzania, a national network of accredited community shops called *duka la dawas* has been set up to address the misuse of antibiotics and inappropriate over-the-counter sales that are commonplace in many countries. There are now 12,000 trained drug dispensers in Tanzanian community shops and the scheme is rolling out across other African nations and beyond. The dispensing of antibiotics for common health conditions that usually do not require them has decreased from 37 per cent to 12 per cent.

While projects like these show that lower-income countries can be the source of pioneering solutions rather than simply being part of the superbug ‘problem’, they cannot be expected to take on this huge challenge alone.

A report last year from the OECD suggests that interventions costing a mere $2 per person per year in a country could cut superbug-related deaths significantly. In high-income countries, such figures seem trifling: less than a cup of coffee.

But in lower-income settings, intervention on this scale these would require funding and infrastructure which is unrealistic. Governments around the world must look beyond national borders and support countries to scale local solutions that have proven to be effective.

Since the end of the second world war, we’ve relied on antibiotics as if they would never fail us. But through this overuse we are not just risking lives; we risk the entirety of modern medicine. Superbugs don’t respect borders, and neither should we in looking for solutions. ●

Dr Tim Jinks
Head of drug-resistant infections
Wellcome

UNCONTROLLED ANTIMICROBIAL RESISTANCE (AMR)

700k
people worldwide currently die each year due to AMR

2.4m
could die in high-income countries between 2015 and 2050 without a sustained effort to contain AMR

10m
could die each year by 2050 due to AMR, based on the most alarming scenario if not action is taken

£
Economic damage of uncontrolled AMR could be comparable to the shocks experienced during the 2008-09 financial crisis

United Nations 2019


Matteo Vistocco on Unsplash

CHRONIC PAIN

Why we still don't understand chronic pain

Chronic pain is on the rise, and yet there is still no silver bullet to treat this little-understood area of healthcare

Martin Barrow

Chronic pain is the 21st-century curse. It blights the lives of millions and imposes a huge burden on health and care systems.

Despite advances in medical science, we are often at a loss to understand what causes chronic pain or how it should be treated. What's more, the opioid drugs which had become the default option to help people manage chronic pain are under intense scrutiny because of their high risk of dependency and harmful side effects.

Incidence of chronic pain is increasing. This is partly down to an ageing population, with older people more likely to suffer with back or nerve pain and long-term conditions such as arthritis and rheumatism. Our sedentary lifestyles and an increase in obesity are also to blame.

Economic cost is difficult to quantify, but back pain alone accounts for around £10 billion a year in sickness absence.

The definition of chronic pain is itself fairly arbitrary, usually taken to mean pain that lasts for more than 12 weeks. According to the British Pain Society, more than two fifths of the UK population live with chronic pain. That's around 28 million people who face a daily struggle to live their lives as they would wish.

At a fundamental level, chronic pain is a matter of biology. Nerve impulses alert the brain about tissue damage that no longer exists, if it ever did. But complex social and psychological factors are also at play, and they seem to help determine why some people cope better than others with chronic pain.

Sometimes the causes of chronic pain are obvious, such as a physical injury or an illness. But there may also be no clear cause. Pain is a very personal and subjective experience.

There is no test that can measure and locate pain with precision. Chronic pain may occur in a variety of locations in the body and for many different reasons. So health professionals rely on the patient's own description of the type, timing and location of pain. This makes diagnosis difficult and complicates the process of identifying effective treatment.

Despite decades of research, chronic pain remains notoriously hard to control and there is an over-reliance on opioid painkillers. A survey by the American Academy of Pain Medicine found that even comprehensive treatment with painkilling prescription drugs helps, on average, only about 58 per cent of people with chronic pain.

> **It blights the lives of millions and imposes a huge burden on health and care systems**

Even though doubts exist about their effectiveness in helping to manage chronic pain over long periods, there has been a steep increase in prescriptions of opioid drugs in England and Wales. The number of prescriptions for opioids, such as morphine and fentanyl, has risen from 14 million in 2008 to 23 million last year.

The Department of Health and Social Care has ordered manufacturers to provide warnings on their labels, saying the drugs can cause addiction. This also includes over-the-counter codeine-based painkillers which, although weaker in strength, can also cause dependency.

It is worth bearing in mind that until the late-1990s, opioids were usually restricted in the UK to cancer patients and for those in acute pain following surgery, but subsequently they were increasingly prescribed for chronic pain.

But if access to opioids is to be restricted, what are the alternatives? More and more, health professionals are being trained to take a holistic approach, addressing a patient's mental health and emotional wellbeing as well as their physical health.

Negative emotions, including sadness and anxiety, seem to aggravate chronic pain. For example, people who dwell on their discomfort tend to be more disabled by chronic pain than those who try to take pain in their stride. And among people with chronic pain stemming from a work-related injury, those who report poor job satisfaction fare worse than those who say they like their jobs. However, negative emotions can be a result of chronic pain as well as a cause.

There are pharmacological alternatives to opioids. These include non-steroidal anti-inflammatories which help to reduce swelling that is the cause of much chronic pain. Tricyclic antidepressants can be effective in treating nerve pain. A class of medication called gabapentinoids, originally used as anti-seizure drugs, is useful in calming over-firing nerves.

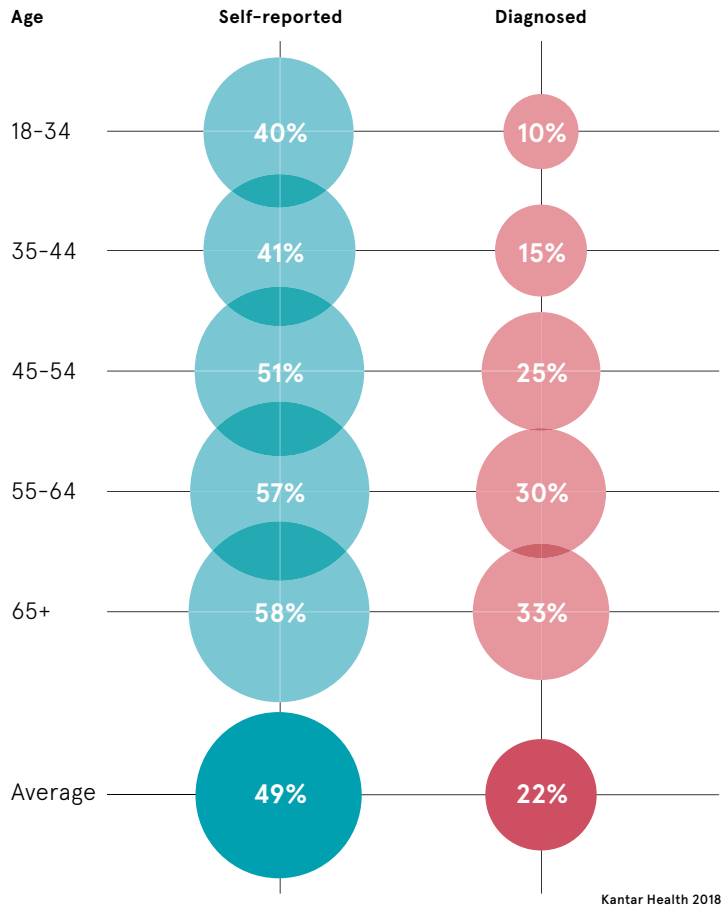
Localised numbing of problem areas can also help. For example, patients undergoing shoulder surgery receive an injection of anaesthetic in the lower neck that numbs the area for 18 hours. Meanwhile, non-drug treatments, such as ice, massages, acupuncture and relaxation training, can be especially useful in treating chronic pain.

A short course of physical therapy by a physio or occupational therapist can help patients to move better, relieve pain and make daily tasks, such as walking, climbing stairs and getting out of bed, easier. Treatment involves stretching exercises and manipulation to improve movement.

Although significant gaps remain in our understanding of chronic pain, we have come a long way since the days when doctors recommended bed rest for weeks or months on end. We now know that this is the worst possible approach. Exercise and work are key to recovery. The goal of modern treatment is to reduce pain and improve function, so patients can resume day-to-day activities.

Patients and their healthcare providers have a number of options for the treatment of pain. Some are more effective than others. Whatever the treatment plan, it is important to remember that chronic pain usually cannot be cured, but it can be managed.

SHARE OF UK ADULTS WITH A PAIN CONDITION



Kantar Health 2018

Neik Crick/Smart Ideas Photography

INTERVIEW

Learning to live with pain

Martin Barrow

Charlotte Walker has lived with chronic pain for almost ten years. On the worst days she wished she were dead. "You mourn the loss of the person you used to be," she says. Coping with the constant pain is exhausting. "The pain in my right shoulder was like my arm being cut off with a blunt saw."

Charlotte, who lives in Dorset, was diagnosed with osteoarthritis at the age of 34, and was subsequently diagnosed with fibromyalgia and joint hypermobility.

"I'm not sure what caused my arthritis but I know that genetically, arthritis runs in my family. So does fibromyalgia," says Charlotte. "When I was first diagnosed, it was strangely a relief because I had a name for my condition, so I could go away and research it. However, reading material can be quite depressing because arthritis is a long-term condition that has no cure.

"When the pain and fatigue associated with arthritis was at its height, it was very depressing and very hard to feel like you will have to live with the condition long-term without getting help."

When Charlotte was first diagnosed a rheumatologist, she was prescribed medication that triggered an allergic reaction. "I looked for alternative routes such as getting a massage, Reiki treatments, lymphatic drainage and acupuncture. I also tried alternative medication like magnesium to help with the condition. All these alternative routes are what I call 'my maintenance' of my condition."

Charlotte feels that society does not appreciate the impact of chronic pain on people's lives. "Unless you have gone through it you don't understand," she says.

"The fatigue is actually missed quite a lot because a lot of people talk about pain which you can somewhat deal with using pain medication. But I don't think you can deal with the fatigue, the fatigue is like literally being run over by a bus or a truck and then being asked to get up again, so it's tough."

Charlotte is a member of the charity Arthritis Action, whose support has helped her to self-manage her condition. She has also received good support from her GP and NHS occupational therapist. With their help her pain has become more manageable and she is able to do things which a year ago would have been impossible.

> **The fatigue is like being run over by a bus or a truck and then being asked to get up again**

Charlotte now runs her own business, Animal Health & Healing, helping animals to recover from serious illness. "Relationships you have with animals can also really help and I am lucky I had my dog and cat in those hard times," she says. "They are non-judgmental and give unconditional love which is what you need when you are at your lowest point."

CHRONIC PAIN

Exploring the future of pain management

Searching for new ways to help people manage chronic pain has become the Holy Grail for the pharmaceutical industry. Demand is rising inexorably while concerns are growing about the effectiveness and long-term impact of established treatments, such as opioid drugs. Here are four exciting developments which could improve the lives of millions of people

Martin Barrow

BSIP/Getty Images

Neurostimulation

A stimulator is placed under the skin, generating an electronic impulse which passes to the spine. This scrambles the pain messages being sent via the nerves, interrupting them before they reach the brain, so they are no longer recognised as being anything other than comfortable. Pain can move and intensify as the patient changes positions so they can adjust the strength and location of stimulation to address these changes in pain with a handheld programmer. Early results are positive, particularly with patients who have lost limbs and suffer from phantom-limb pain.

Stem cells

Stem cell therapy is an emerging treatment option for chronic pain. It uses a person's own stem cells to repair damaged tissue and regenerate healthy tissue, to help repair and heal damage and degeneration. Stem cell treatments have reduced the need for prescription medication and surgery, proving to be a helpful tool towards managing and potentially eliminating pain in the body. When it comes to pain management, the stem cells gathered from bone marrow seem to be the most effective at treating painful conditions and injuries.

Platelet-rich plasma

Commonly referred to as PRP, this is a process that leverages the body's natural healing process to provide a non-operative, permanent solution for conditions such as arthritis and ligament or tendon sprains and tears. PRP therapy is a concentration of platelets injected into the damaged ligaments, tendons and joints to promote tissue repair and accelerate healing. Platelets are rich in growth and healing factors which means, on average, an injured individual can get back to a pain-free life in four to six weeks. PRP is used by professional athletes to treat end-of-season symptoms including swelling, stiffness, inflammation, tenderness and pain.

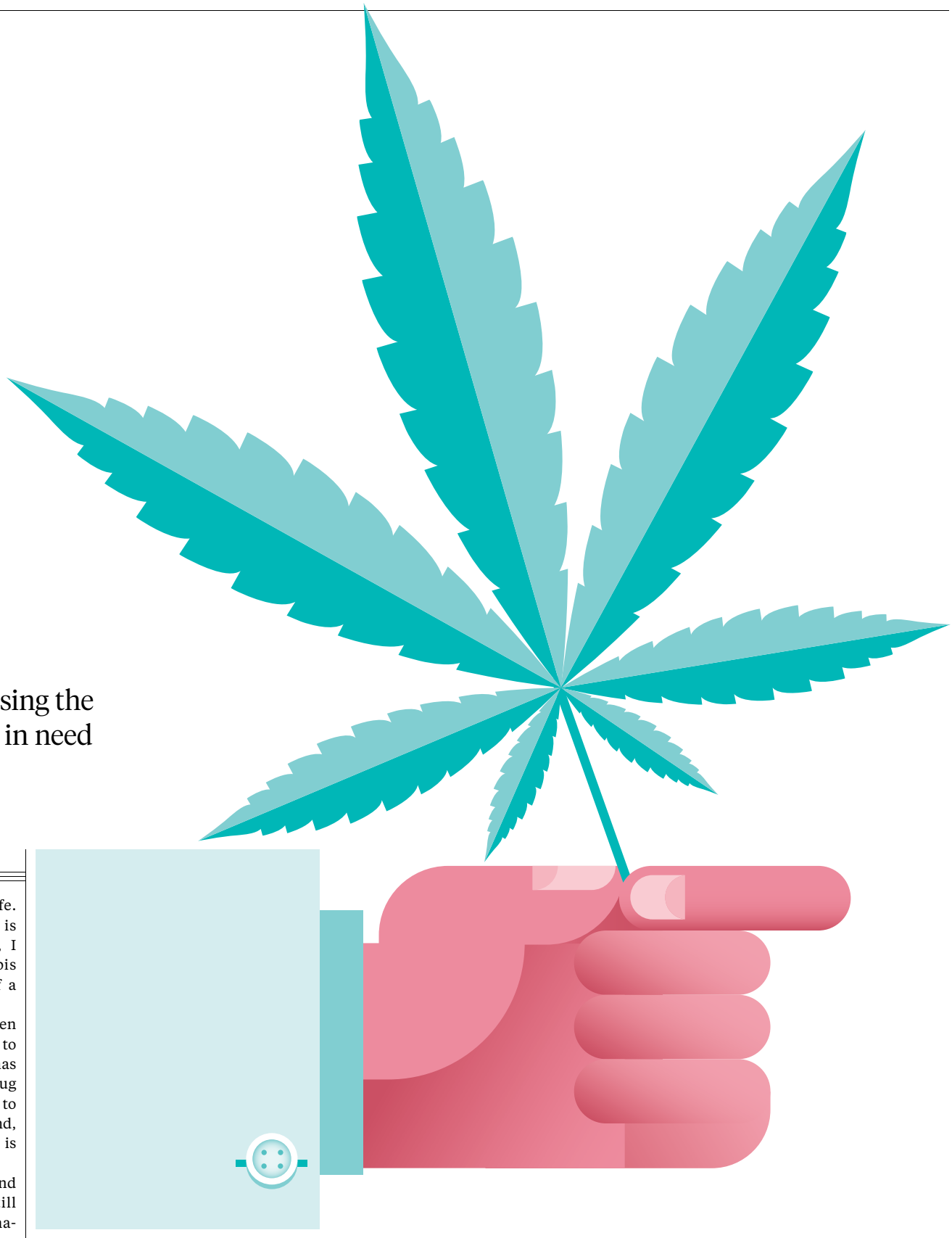
Nanotechnology

Advances in nanotechnology, which manipulates particles that are 100,000 times smaller than the width of a human hair, have the potential to transform pain management. The technology supports minimally invasive surgery, which reduces peripheral damage and speeds up recovery, and makes it possible to deliver medication in the smallest doses where it is needed most, reducing potentially harmful side effects.

MEDICAL CANNABIS

Medical cannabis: legalised but unprescribed

Despite last year's change in the law legalising the supply of medical cannabis, NHS patients in need are still being refused prescriptions



James Gordon

Stephen can't work. In fact, he can barely walk. He describes the pain he feels as persistent torture. "It started in my shoulder four weeks after the birth of my first child," he says. "I didn't know what was causing it, just that the pain was excruciating."

After a battery of tests, Stephen was diagnosed with facioscapulohumeral muscular dystrophy, a muscle-wasting condition which affects between 2,000 and 2,500 people in the UK.

Stephen, who also suffers from fibromyalgia, which affects his right arm, both hands, lower back, hips, legs and both feet, was given a range of strong pain-killing drugs, including co-codamol, pregabalin and tramadol. But he stopped taking them after being unable to cope with terrible side effects, which put him in a zombie-like state and left him with suicidal thoughts.

It was then that Stephen turned to cannabis. He has been using it for nearly five years to treat all his symptoms. He calls it a miracle drug: "It saved my life. I can sleep, eat; my mobility is better and, most importantly, I can feel like and be me. Cannabis gives me hope of some sort of a normal life."

But there's a problem. Stephen uses one gram of cannabis a day to treat his condition and says he has no choice but to buy it from a drug dealer. "I hate the fact that I have to break the law to get my supply and, because this is unregulated, it is very costly," he says.

However, why are Stephen and thousands of others in the UK still risking their liberty to buy cannabis? Last October, the Home Office changed the law, giving specialist doctors the go-ahead to prescribe cannabis-based medicines legally. Yet, curiously, seven months on, despite there being 80,000 UK doctors who are legally certified to prescribe medical cannabis, not a single NHS prescription has been given out, according to Jon Liebling, chief researcher at the Centre for Medicinal Cannabis.

Mr Liebling, who is also co-founder and director of Cannabis Patient Advocacy and Support Services, says apparent intransigence by the NHS and local authorities has only served to stigmatise and alienate patients.

"We've seen doctors being very strongly encouraged not to write prescriptions," he says. "Patients have been banned from trust hospitals and we know of at least two doctors who have been threatened with being reported to the General Medical Council, or getting into severe difficulty, should they even submit a prescription."

So why do doctors, who have been licensed to do so, still feel unable to prescribe medicinal cannabis?

Mr Liebling explains: "Firstly, a lack of clinical evidence and a paucity of medical professional knowledge of cannabis and cannabis-based medicinal products (CBMPs) has had a paralysing effect on

> **"I can sleep, eat; my mobility is better and I can feel like and be me. Cannabis gives me hope of some sort of a normal life**

The NHS stance on medical cannabis

From October 2018, doctors on the Specialist Register of the General Medical Council have been able to prescribe cannabis-based medicinal products. However, the NHS says these products should not be considered a "first-line treatment"

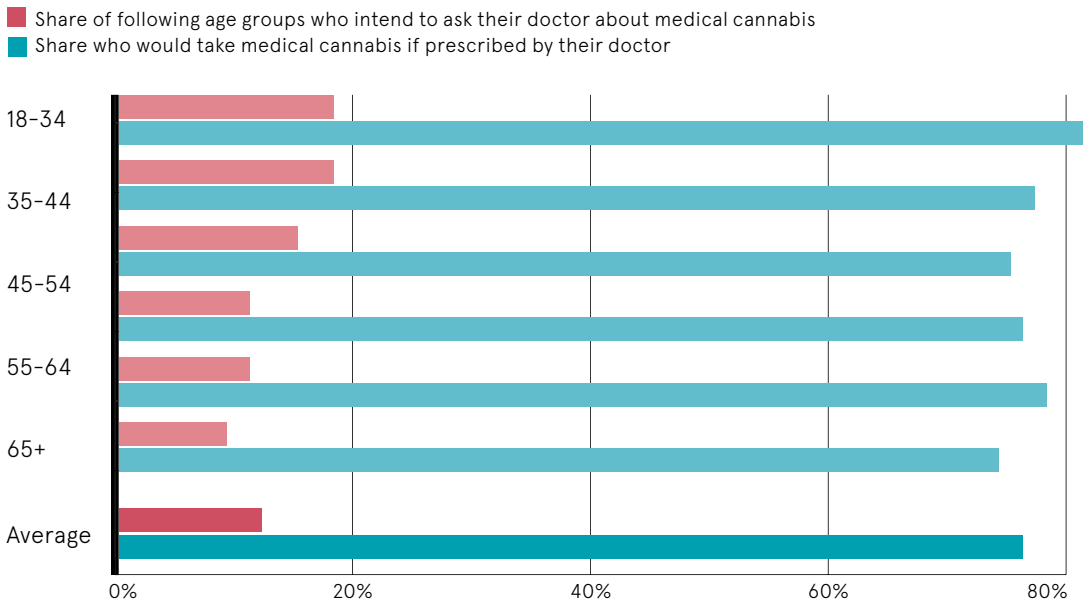
A recent review by the UK's chief medical officer found "conclusive evidence of the therapeutic benefit of some cannabis-based products for certain medical conditions"

According to the NHS website, "very few people" in England are likely to get a prescription, as it is only used to treat severe forms of epilepsy and vomiting or nausea caused by chemotherapy

One cannabis-based medicine is licensed for people with MS-related muscle spasticity, though availability on the NHS is limited, and NICE doesn't recommend doctors to prescribe it "as it is not cost effective"

On the topic of long-term pain, the NHS says there is some evidence to support its treatment, but this evidence is "not yet strong enough to recommend it for pain relief"

MAJORITY OF ADULTS WHO ARE OPEN TO MEDICAL CANNABIS



Populus 2018

the NHS. Secondly, because all CBMPs, with the exception of Sativex, which is a fully licensed drug, doctors are not insured to prescribe them, meaning if a patient were to have an adverse reaction, that doctor or the trust, where he or she works, could be deemed culpable."

However, Royal College of Physicians' president Professor Andrew Goddard says doctors may be reluctant to prescribe cannabidiol (CBD), with or without tetrahydrocannabinol (THC), for adults with chronic pain because of the weakness of the evidence for benefit as opposed to harm.

"Recent studies show that only 29 per cent of adults with chronic pain would experience a 30 per cent improvement in pain or, put another way, you would need to treat twenty four people to see benefit in one person. When it comes to the harms of those drugs, you only need to treat six people to see significant harms," he says. "Furthermore, none of the studies has shown whether or not quality of life has been improved."

Mr Liebling disagrees, doubting current randomised controlled trials which, he says, only test one strain of medical cannabis against a placebo. "If a more varied and nuanced cycle of trials was conducted, which tested varying of levels of THC and CBD together, we would probably see a much larger proportion of adults benefiting; maybe as many as 80 per cent," he claims.

Another limiting factor is cost. According to the Royal College of Physicians, figures presented to MPs on the Health Select Committee range from £500 a month to £25,000 a year. However, Mr Liebling says there are cheaper, and effective, CBMPs available.

The National Institute for Health and Care Excellence is due to publish guidelines in the autumn, which it is hoped will give doctors the information they require to consider prescribing medical cannabis.

Also the University of Birmingham is working with the NHS to produce an education programme, while the University of Bath and University College London have written a review for *The BMJ*, which provides advice for doctors who may wish to prescribe medicinal cannabis products to treat their patients in the interim.

Tom Freeman of the University of Bath's Addiction and Mental Health Group says: "In the review, we looked at a range of studies which revealed how cancer patients, and those suffering from MS, epilepsy and chronic pain responded to cannabis-based medicines. The studies demonstrate that medicines based on cannabis and cannabinoids are diverse.

"One of the key takeaway messages is that different cannabinoids have different uses. Take THC and CBD. Several studies have shown that used in combination, THC and CBD can alleviate chronic pain. Others reveal CBD on its own can be used to treat epilepsy, while THC could prove to be an effective drug to treat vomiting brought on by chemotherapy."

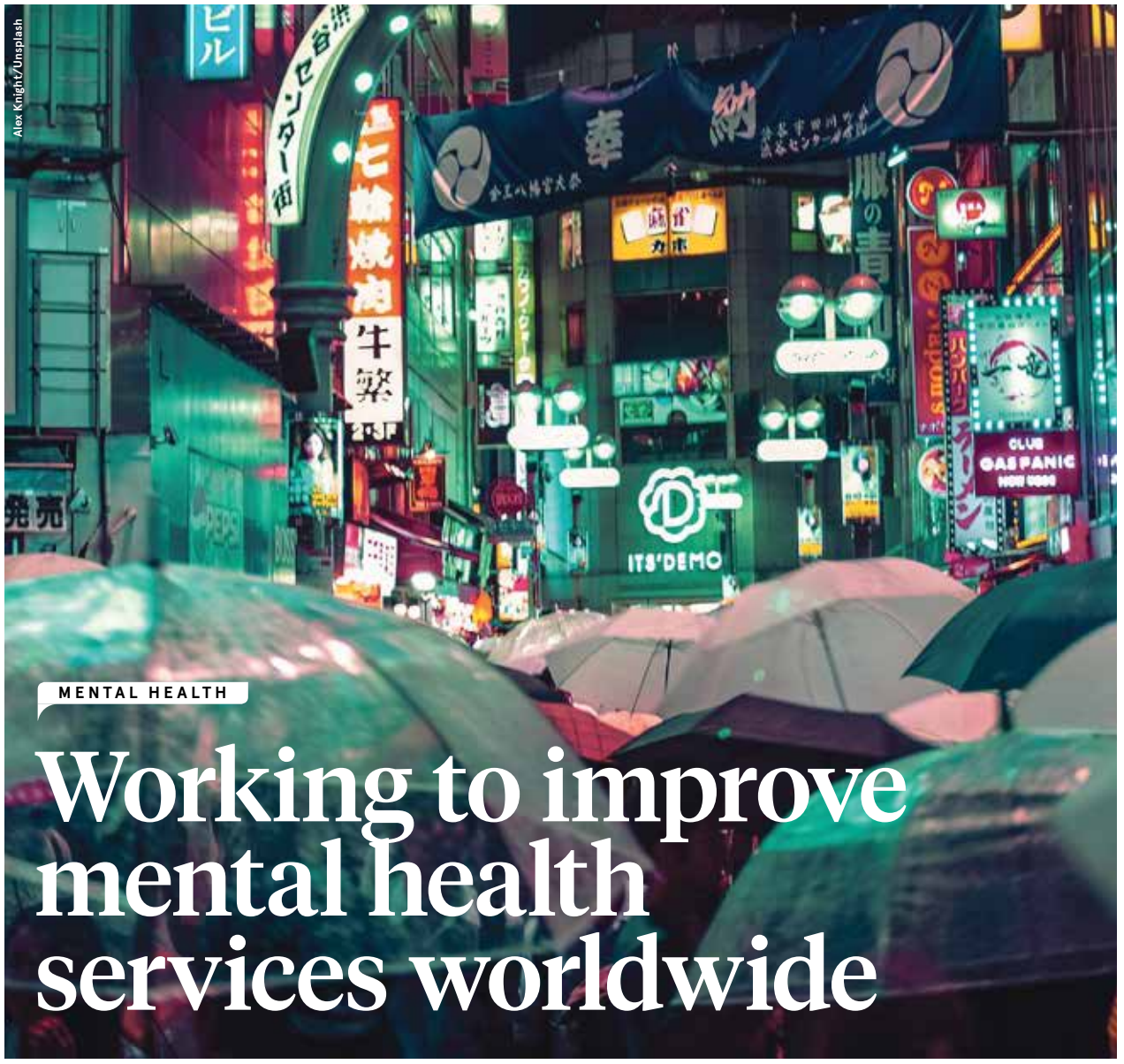
So how long before the stigma attached to medical cannabis disappears and doctors feel confident to prescribe it?

Dr Freeman says: "Now medical cannabis is no longer categorised as a schedule 1 drug, the National Institute for Health Research has announced a specific funding call dedicated to cannabis-based medicines. While research takes time, as a result of these changes in legislation, more funding will be released, the results of which will shed new light on possible future use-cases."

Mr Liebling agrees that trials are the only way to resolve the impasse and thinks one comprehensive, randomised controlled trial could be enough.

"I believe that if the trial is robust, fully randomised and stakeholders agree it could end early, should results prove conclusive in favour of medical cannabis at an early stage, we could see changes within 18 months, rather than three to five years," he says.

For Stephen, just one of many hundreds of thousands in the UK who suffer from chronic pain, it's a change that can't come soon enough.



Alex Knight/Unsplash

MENTAL HEALTH

Working to improve mental health services worldwide

There are large disparities in how governments around the world address mental health services, but a number of initiatives are prompting conversations and raising public awareness

Eleanor Morgan

Mental health is a vital part of our constitution as human beings, yet anyone, anywhere, can experience mental distress at some point in their lives, irrespective of colour, creed or culture.

From symptoms of anxiety and depression to debilitating conditions such as bipolar disorder or schizophrenia, poor mental health is one of the main causes of the overall disease burden worldwide. Responsibility for helping to improve people's wellbeing lies with governments and it is a bleak reality that some countries have no mental health policy or legislation at all.

Lack of knowledge, discrimination and stigma are the biggest obstacles to seeking, or providing, care and the World Health Organization (WHO) has been systemically addressing the problem with its *Mental Health Action Plan* since 2013, striving to bolster productive leadership for global mental health, improve information systems and provide comprehensive mental health services in community settings.

This is particularly important in developing countries where the combination of poverty, myth and ritual often mean so many people suffer in silence without accessing treatment. Up to 85 per cent of people with severe mental health issues receive no treatment in low and middle-income countries, according to WHO.

Since 2007, the anti-stigma campaign Time to Change has contributed to a marked change in attitudes towards mental health in England and Wales. The campaign has now joined forces with international development and disability organisation CBM, which is already providing psychological support to those affected by humanitarian crises, to address global mental health stigma.

This year, pilot programmes will be launched in low-income Commonwealth countries, including India, Kenya, Nigeria, Ghana and Uganda, working with local organisations and individuals with experience of mental health problems to challenge prejudice, open up conversation and offer psychological intervention.

However, if our governing bodies are not discussing mental health openly, how do we find the language to discuss it with ourselves, let alone others? Wider change only happens when those in power set a precedent.

In Japan, which had experienced one of the highest suicide rates in the developed world for a long time, suicide was a socially taboo topic that was rarely addressed publicly, contributing to a culture of secrecy and repression.

However, a number of initiatives over the past decade and a half have been set up to encourage conversations and raise public awareness, particularly during the month of March, when suicide rates were known to increase.

The suicide rate has now fallen by more than a third since peaking in 2009, following the country's worst recession since the Second World War, and now stands at 16.5 per 100,000 inhabitants, according to government statistics.

Reaching those that need help is a priority in addressing global mental health. Remote counselling is growing in the UK, with services such as TalkSpace and BetterHelp pairing individuals with counsellors who can offer guidance and support over text message.

But, while the anonymity of these services is appealing, particularly if distress pertains to socially taboo issues such as addiction or sexual abuse, there is significant scepticism among mental health professionals over replacing face-to-face psychological support.

In some sparsely populated countries, where isolation can be a powerful contributor to a person's mental health, remote therapy services have been implemented to good effect.

In Finland, an online therapy service called Mental Health Hub was set up ten years ago in light of how hard it was for patients in rural areas to get help. The service, which offers computer-assisted cognitive behavioural therapy for depression, anxiety and substance abuse, is now used by every hospital district in the country.

Advances in brain science have been steadily expanding our understanding of the biology of mental illness. As robust evidence shows how environmental factors, such as poverty, influence global mental health, it is simplistic and wholly inaccurate to position mental health issues as purely biological.

However, identifying genetic markers may influence treatment options in the future. In 2013, a landmark study showed that autism, attention deficit hyperactivity disorder, depression, bipolar disorder and schizophrenia were genetically linked.

In a quest to make mental health treatment more individualised, there are major trials taking place in the United States, UK and elsewhere in Europe to see whether technological advances enable patients' DNA to be screened to identify biomarkers that predict how they will respond to different medications. Antidepressants are commonly used to treat depression and anxiety. But many people do not respond to the first medication prescribed and improvement in symptoms is often not seen for four to six weeks.

Tel Aviv-based startup Taliaz are developing an artificial intelligence-driven tool called Predictix, based on algorithms developed by analysing the largest clinical trial on depression to date, the Sequenced Treatment Alternatives to Relieve Depression Study.

By combining genetic, neurological and environmental data with a simple DNA test and a clinical history taken by a psychiatrist, the algorithms are said to have predicted effectiveness and negative effects of current antidepressant medications with nearly 75 per cent accuracy.

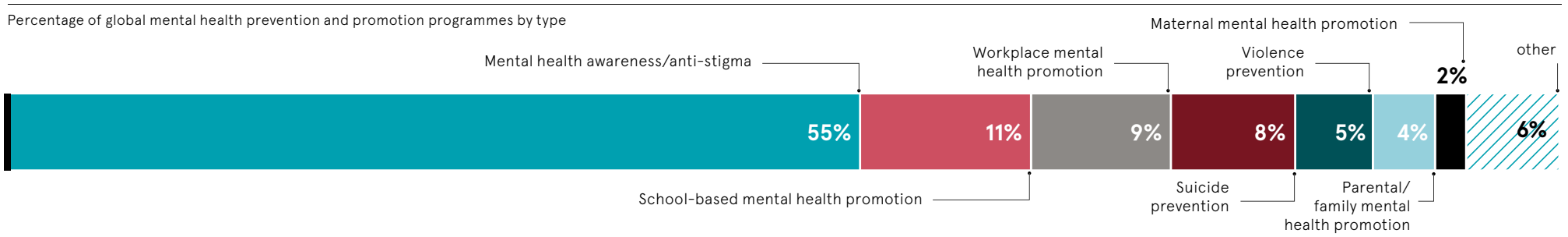
> **Lack of knowledge, discrimination and stigma are the biggest obstacles**

Meanwhile, virtual reality technology has been harnessed by researchers in the treatment of anxiety disorders, such as post-traumatic stress disorder, phobias and obsessive-compulsive disorder over the past 15 years. This year, however, a groundbreaking revelation was made by British startup Oxford VR's co-founder Daniel Freeman, who said he believes that VR technology is applicable to almost all mental health conditions. At the University of Amsterdam, the ability for VR to bring real-life experiences into clinicians' offices – rather than relying on patient testimony – is also being researched as a promising diagnostic tool.

Clearly, technological advances mean the future of global mental health treatment may look very different. However, if innovations to date are anything to go by, some interaction with a professional is still key. After all, as a species literally wired to connect with one another, we cannot heal without human interaction.

PROMOTION AND PREVENTION

Percentage of global mental health prevention and promotion programmes by type



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Intended use/indications for use

The AXS Catalyst Distal Access Catheter is indicated for use in facilitating the insertion and guidance of appropriately sized interventional devices into a selected blood vessel in the peripheral and neurovascular systems. It is also indicated for the removal/aspiration of soft emboli and thrombi from vessels in the peripheral and neurovasculature.

AXS Infinity LS Long Sheath

See package insert for complete indications, contraindications, warnings and instructions for use.

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The AXS Infinity LS Long Sheath is indicated for the introduction of interventional devices into the peripheral, coronary, and neuro vasculature.

Excelsior XT-27 Microcatheter

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Intended use / indications for use

Stryker Neurovascular Excelsior XT-27 Microcatheter is intended to assist in the delivery of diagnostic agents (such as contrast media), therapeutic agents, and non-liquid interventional devices (such as stents) that are indicated for use in the neurovasculature and with a catheter of 0.027 inches in inner diameter.

Surpass Evolve Flow Diverter System

See package insert for complete indications, contraindications, warnings and instructions for use.

Intended use/indications for use

The Surpass Evolve Flow Diverter System is indicated for use for the treatment of saccular or fusiform intracranial aneurysms arising from a parent vessel with a diameter ≥2.0mm and ≤5.0mm.

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