

FUTURE HEALTH, CARE AND WELLBEING

About the Author	3
Personalised Medicine	5
Stem-cell Medicine	11
Nano-scale Medicine	13
Gene-therapy and Gene-editing	15
Digital Health	17
Impacts	24

About the Author

Ray Hammond has been researching, writing and speaking about future trends and developments for almost 40 years.

He is the author of 14 books on the future and he has written, consulted and lectured for the world's great corporations, for governments and for many universities in Europe, the USA and in Asia. He is a regular broadcaster on both national and international radio and TV channels.



In 2010, Michal Gorbachev presented him with a medal for his services to futurology which was issued by the Italian Chamber of Deputies on behalf of the United Nations. In the citation, President Gorbachev wrote:

"We are delighted to honour Ray Hammond for his constant commitment to research and for his stunning speculations about the future, enlightened by scientific knowledge and an evident concern for humankind."

Author's Note

This report represents my own opinions about likely future developments. It does not represent the views of Allianz Partners. When I was asked to research and write this report, I was provided with guidance about the topic areas to research, but I was given a free hand to develop all editorial matter independently. Any errors and omissions are my own responsibility.

Future Health, Care and Wellbeing

Medical science and healthcare delivery are conservative, slow-moving sectors that are highly resistant to change. Witness the tento fifteen-year development cycles in pharmaceuticals, the immense difficulty of pushing reform through politically sensitive health systems and the cautious nature of regulators. But over the next 20 years five major revolutions will transform how medicine is practised and how healthcare is delivered. These revolutions are:

- Personalised medicine based on personal DNA analysis and electronic health data collected from individual patients
- 2. Stem-cell medicine the use of stem cells to repair/regrow tissue and organs
- 3. Nano-scale medicine drug delivery and development at sub-microscopic levels
- Gene therapy and gene-editing altering human DNA to improve health
- Digital health using artificial intelligence (AI) and digital technology to diagnose and to monitor patient health

Each of these five revolutions would individually transform the prospects for human health and longevity. But taken together they will produce an entirely new paradigm for healthcare; one in which consumers will collect their own health data, geneticists will remove hereditary diseases from the population, artificial intelligence systems will routinely aid diagnosis and treatments will be tailored and personalised for individual patients.

Like so many other industries and sectors, healthcare is being seriously disrupted by digital technology and the scale of disruption will be all the greater because of the vast size of the healthcare market.

Health provision is one of the world's largest and fastest-growing markets, consuming over 10 per cent of gross domestic product in all developed nations. The annual global market is estimated to be worth around \$8.1 trillion and it is currently growing at 4.3 per cent each year. Annual global spending on healthcare is forecast to rise to \$18.28 trillion by 2040.

Given its economic cost and its importance to all citizens, the healthcare sector is highly politicised, tightly regulated and hotly debated in almost all rich countries. For that reason, the future will be distributed unevenly in healthcare and some nations will be earlier to authorise and deploy new health technologies and treatments than others. For the sake of your future health it very much matters where you live.

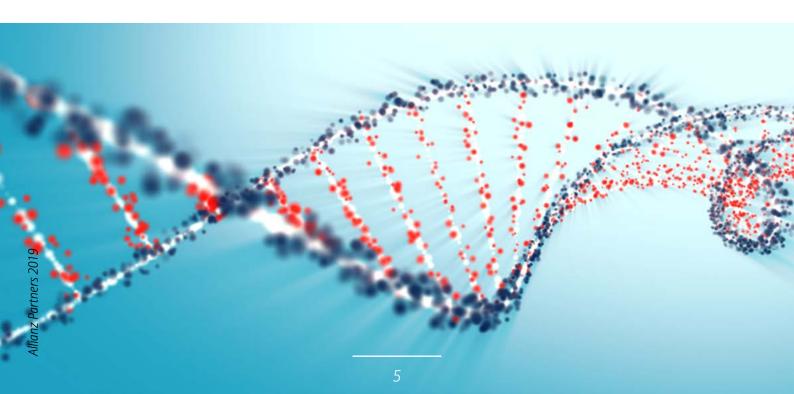
Trend 1: DNA-Based Personalised Medicine

Science-based medicine has only been practised for a little over a century and during that time family physicians have taken a 'one size fits all' approach to treating patients. This bold statement is a little unfair to doctors who have, of course, varied drua doses, drua selection and treatment recommendations on a patient-by-patient basis. But, until very recently, the most common drugs available to doctors have themselves been designed to be all-purpose treatments. In the West, the pervading approach to prescribing drugs is almost unbelievably 'scatter gun' and wasteful in its approach. A number of studies suggest that up to 80 per cent of patients do not respond to the ten most often prescribed drugs for common maladies.

But now DNA analysis of individual human genomes is starting to enable doctors to treat patients with drugs best suited to their personal DNA. This is the start of what is called 'Personalised Medicine', sometimes also described as 'Precision Medicine'.

All three billion base pairs in the human genome (the DNA 'map' which describes a human's biology) were first sequenced by the USA's <u>Human Genome Project</u> in 2001. At that time, it was an incredibly computer-intensive and time-intensive task and it cost approximately \$2.7 billion.

Eight years later the cost of a full genome sequence was about \$100,000, a few years later the sequencing was available for \$10,000 and currently it is on offer for \$399. Little demonstrates better the falling cost and rapidly growing power of computer processing.



DNA Sequencing For Cancer Treatment

Oncologists are pioneering the use of DNA analysis to deliver truly personalised medicine. Each patient's cancer has a unique combination of genetic changes, and tumour DNA sequencing is widely used to identify these cancer-specific DNA changes.

In some cases, a knowledge of the genetic alterations in a cancer can help oncologists determine a treatment plan. Some treatments particularly, some targeted therapies - are effective only for people whose cancer cells have specific genetic

alterations that cause the cells to grow out of control (these are sometimes called 'driver' mutations).

For example, <u>mutations</u> in the <u>EGFR</u> gene that make cells divide rapidly are found in some patients' lung cancer cells. A patient whose lung cancer cells harbour an EGFR mutation may respond best to treatment

with drugs called EGFR inhibitors. Clinical tumour DNA sequencing can reveal whether a patient's lung tumour has an EGFR mutation.

Tumour DNA sequencing in oncology has already extended tens of thousands of lives and <u>new drugs are</u> now being approved to treat cancers according to their DNA type, rather than their location in the body. This is a new way of looking at cancer and it provides a clear indication of just how central DNA sequencing will become to all medicine in the future.

DNA Sequencing In General Medicine

Today, family doctors do not routinely offer patients DNA sequencing as part of the diagnostic process (although at least one nation is planning to offer healthy patients individual **DNA** testing for a small charge).

But if a doctor suspects that a patient's symptoms point towards a disease that is known to be linked to a particular gene, or set of genes, they will frequently order a DNA test to see if that particular gene sequence is present.

> The use of DNA sequencing to detect rare diseases linked to specific genes is particularly useful in diagnosing about 7,000 so-called Mendelian diseases and disorders.

But by 2040 medical science will have collected DNA sequencing data from tens of millions of patients and analysis

of this vast data pool will enable far more accurate associations and correlations to be made between diseases and gene sequences.

By 2040 medical

science will have

collected DNA

sequencing data

from tens of

millions

of patients

Consumer DNA Sequencing

Many companies now offer consumers their own personal DNA sequencing services. These include <u>23andMe</u>, <u>Dante Labs</u>, <u>HomeDNA</u> and <u>24Genetics</u>. But do today's personal, direct-to-consumer DNA analysis services have any medical value for consumers, or for doctors? Well, for a start, DNA testing can suggest which diseases and conditions a patient is most, and least, susceptible to. It can also suggest which prescription drugs are most likely to be effective for a particular individual.

Many doctors and geneticists have reacted to direct-to-consumer DNA sequencing with alarm. The medical reports supplied as part of consumer genetic testing over the last decade have NOT been precise predictors of what illnesses individuals are going to contract and which they are likely to avoid. They have been, at best, a rough guide.

As we are now learning, most conditions and diseases are the result of multiple sets of genes (polygenic causes) and environmental factors and the type of results that have been delivered to consumers over the last decade should be read with caution.

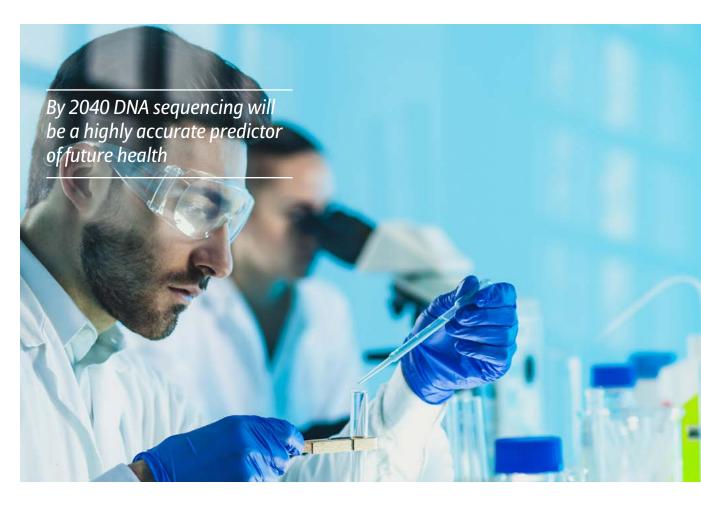
But every year we learn more about which genes and gene sets are involved in specific illnesses and conditions and direct-to-consumer DNA sequencing is now far more accurate than it was a decade ago.

In that time, geneticists and data scientists have been improving their ability to convert genetic data into useful insights – forecasting which people are at triple the average risk for heart attack or identifying women who are at high risk for breast cancer even if they don't have a family history or a BRCA gene mutation. Parallel advances have dramatically changed the way we search for and make sense of volumes of data, while smartphones continue their unrelenting march toward becoming the de facto portal through which we access data and make informed decisions.

By the end of 2018, 26 million people – consumers, not patients – had paid commercial companies to sequence their DNA Today there are new DNA sequencing and interpretation apps such as MyGeneRank which consider the polygenic implications of individual DNA tests – looking for gene groups likely to cause future health problems – and these point to a future in which consumer DNA testing will provide accurate and

comprehensive guides to likely future health.

By the end of 2018, <u>26 million people</u> – consumers, not patients – had paid commercial companies to sequence their DNA. Instead of getting tests done reactively, on a doctor's orders, many of these people will be using the data proactively to help them make decisions about their own health.



DNA And Drug Response

The second benefit offered by personal DNA analysis is that a patient – and his or her doctor – can start to discover which prescription drugs are likely to be most effective in treating a condition. This is a field known as pharmacogenomics.

But while these indications are useful, they cannot yet be said to provide a blueprint for medical treatment. Today's medical-risk interpretations of over-the-counter DNA tests are only just becoming accurate enough to be of value to doctors, but they indicate that as we learn more about the role of specific genes in disease such tests will become increasingly useful. By 2040 DNA sequencing will be a highly accurate predictor of future health and I think it likely that every patient will have his or her DNA decoded and available to healthcare professionals as part of their medical records.

Collecting Genomic Data

The UK leads the world in the race to gather mass DNA information and, as a result, to better understand the implications of genetic data. In 2012 the UK government announced the 100,000 Genome Project, the world's first National Genome Data Bank.

This project aimed to sequence 100,000 genomes from around 70,000 people. Participants are NHS patients with a rare disease, plus their families, and patients with cancer.

The idea is to create a new genomic medicine service for the UK's National Health Service – transforming the way people are cared for. Patients may be offered a diagnosis where there wasn't one before. In time, there is also the potential for new and more effective treatments.

While this report was in preparation, the UK government announced that it had reached its initial target of sequencing 100,000 full genomes and stated that one in four participants with rare diseases had received a diagnosis for the first time, while potentially actionable findings were provided for up to half of cancer patients who now had been given the opportunity to take part in a clinical trial or to receive a targeted therapy.

As the project extends it will also enable new medical research.

Combining genomic sequence data with medical records is a ground-breaking resource. Researchers will study how best to use genomics in healthcare and how best to interpret the data to help patients. The causes, diagnosis and treatment of disease will also be investigated.

The UK government also aims to kickstart a British genomics industry. The 100,000 Genome Project was already the largest national sequencing project of its kind in the world when, in late 2018, UK Health Minister Matt Hancock announced that he was extending the project to collect an additional five million human genomes over the following five years.

By 2040 this project will have become a rich and widely used source of genomic data which will almost certainly have yielded up information about the genomic causation for thousands of conditions and diseases.

Other nations have also embarked on large-scale genome gathering including <u>France</u>, <u>The Netherlands</u> and Iceland.

The Icelandic genome project is particularly advanced, and it has thrown up legal, moral and ethical questions which will have to be answered in all nations as the gathering of genomic data increases.

The principal question is whether contributors to DNA gene banks should be warned when their DNA sequence shows they are carriers of a gene that makes them liable to contract a serious illness – for example, mutations of the BRCA1 and BRCA2 genes which suggests women will be far more likely to get breast cancer. The Icelandic government is refusing to warn DNA contributors of such findings on the grounds that the contributors did not give their specific consent to be informed of such findings when they provided their DNA samples. This has led to much debate in the nation, a debate that will rage in all other nations as the practice of building population gene banks spreads.

Allianz Partners 2019

By 2040 Every Newborn Baby Will Be DNA Sequenced

In Boston, newly-born babies are routinely having their DNA sequenced. This is part of a clinical trial to see how useful the genomic information will prove as the children grow up and as some of them inevitably require medical treatment.

Families of newborns are enrolled from Boston Children's Hospital and Brigham and Women's Hospital nurseries, and half are randomised to receive genomic sequencing and a report on their child's DNA that includes monogenic disease variants (disorders caused by a single gene), recessive carrier variants for childhood onset or actionable disorders (children who may carry a gene that can cause disease in future generations), and pharmacogenomic variants (genes that indicate the potential for any unusual reaction to specific drugs).

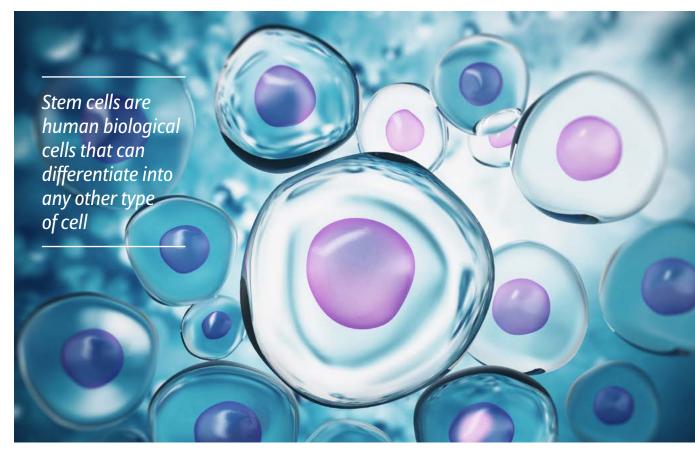
The results of the trial will take decades to be fully revealed but early indications have been encouraging. Overall, DNA sequencing of 51 babies turned up pathogenic or likely pathogenic gene variants in four of the babies. All were dominant, requiring only one copy of the gene to cause disease. Three of the variants have been linked to heart conditions, though the infants have not yet shown symptoms; two of the children are now being followed at Boston Children's Hospital. The fourth variant was linked to an enzyme defect not picked up by standard non-DNA new-born screening. This variant hasn't yet caused symptoms, but the infant will likely be treated with nutritional supplements as a precaution.



Another 47 infants were found to be carriers of recessive variant genes but were apparently unaffected themselves. Two infants had pharmacogenomic variants that could alter their metabolisation of certain drugs. Another infant had a variant in BRCA2, a gene linked to breast cancer.

Since breast cancer is an adult disease, the team decided to get special permission from the study's ethics board to disclose the result to the family since the newborn's mother could also be at risk.

These early results are already unambiguous and by 2040 it is likely that all health services will be offering DNA sequencing of newly-born babies as a matter of routine.



Trend 2: The Promise Of Stem-Cell Medicine

The development of treatments and cures based on stem cells seems so promising that this science has been described as 'the penicillin of the 21st century'.

Stem cells are human biological cells that can differentiate into any other type of cell and which can then divide to produce more of the same type of stem cells. In short, stem cells can be coaxed to grow any sort of human tissue and can even grow entire replacement organs.

There are two general categories of medical <u>applications for stem cells</u>: first, as an actual therapy, and second, as a way to grow tissue in order to model diseases to help researchers develop treatments.

At present, there are several types of conditions that either are being treated with stem cell-based therapies or that hold out the prospect for such therapies in the future.

These include autoimmune diseases, neurological disorders, cancers and infertility. Specific diseases for which stem cell therapies are being tested include multiple sclerosis, rheumatoid arthritis, juvenile idiopathic arthritis, Crohn's disease, type 1 diabetes mellitus, autoimmune cytopenias, systemic lupus erythematosus and systemic sclerosis.

Furthermore, stem cells are already being used in regenerative medicine to replace or repair tissues and organs damaged by disease or injury. The significant advantage of this type of stem cell tissue regeneration is that if the donor stem cells are harvested from the patient, new techniques now under development mean that by 2040 there should be no problem with autoimmune rejection of the new cells.

And stem cells are being trialled with significant success in the treatment of strokes, coronary disease, brain damage and macular degeneration (age-related loss of sight).

One of the most therapeutically promising prospects of stem cell research has been the possibility of repairing or replacing damaged organs and tissues — that is, of replicating the generative process that normally takes place only within the body. While embryonic stem cells

have shown a great deal of potential in this area, owing to their pluripotency — their ability to develop into a wide variety of tissue types — there have been some successes in using adult stem cells as well.

For example, in 2008, adult stem cells were used to create a <u>new</u> trachea for a woman in

her early thirties and adult stem cell treatments have been used for many years to successfully treat <u>leukaemia</u> and related bone/blood cancers through bone marrow transplants.

Additionally, doctors have recently used hematopoietic stem cells (stem cells in blood) to successfully culture human red blood cells in the lab, which are used in blood transfusions. The cultured red blood cells are able to survive and mature into fully functioning cells in the patients' bloodstreams, demonstrating the potential of these cells to serve as an alternative to conventional blood donation (patients are able to generate their own blood transfusions within their body).

In order to cultivate these cells, researchers needed to find the right mix of growth factors that would coax the hematopoietic stem cells to successfully differentiate.

While this represents a major breakthrough in stem cell therapy that will surely be beneficial to many patients in need of blood transfusions, the fact that researchers have only recently been able to use stem cells to regenerate red blood cells is indicative of the challenges facing the

> development of labgrown tissue and organ regeneration.

stem cell therapies are still in the development stage and many more trials will be needed before their use becomes widespread and routine. Worryingly, many stemcell treatment clinics have been set up in poorlyregulated territories (e.g.

Mexico, India and China) which are offering unproven stem-cell therapies to seriously ill patients desperate for a cure. And unregulated stem-cell clinics are offering treatments of dubious value in some states of the USA. Often these expensive treatments are useless and sometimes they are dangerous.

But it is clear that stem-cell medicine will become an important and powerful tool in mainstream medicine by 2040.

Despite their promise,

Stem cells

are already

being used in

regererative

medicine to

replace or repair

tissues and

organs

Allianz Partners 2019

Trend 3: Nano-Scale Medicine

'Nanotechnology' is the term used to describe science, engineering and technology conducted at the nanoscale, which is about 1 to 100 nanometres. One nanometre is one billionth of a metre.

Nano-scale medicine applies the knowledge and tools of nanotechnology to the prevention and treatment of disease. This involves the use of nanoscale materials, such as biocompatible nanoparticles and, in time, it is hoped that nanorobots can be created for diagnosis, drug delivery, sensing or actuation purposes in a living organism. (A nanorobot is a device ranging in size from 0.1-10 micrometres and constructed of nanoscale or molecular components to carry out a particular task within the body).

We are still at the very early stages of developing medical treatments at this sub-microscopic scale, but already the field is showing enormous promise.

The tiny size of nanomaterials is similar to that of most biological molecules and structures; therefore, nanomaterials can be useful for both treatments in living patients and in laboratory biomedical research and applications. Thus far, the integration of nanomaterials with biology has led to the development of diagnostic devices, contrast agents, analytical tools and physical therapy applications.



The most widely used application of nanotechnology in medicine currently being developed involves employing nanoparticles to deliver drugs, heat, light or other substances to specific types of cells (such as cancer cells). Particles are engineered so that they are attracted to diseased cells, which allows direct treatment of those cells. This technique reduces damage to healthy cells in the body and allows for earlier detection of disease. A patient's overall drug consumption (and the potential for side-effects) can be significantly reduced by depositing the active agent of the drug in the diseased region only, and in a dose no higher than needed.



For example, nanoparticles that deliver chemotherapy drugs directly to cancer cells are under development.

Tests are in progress for targeted delivery of chemotherapy drugs and their final approval for their use with cancer patients is pending.

Today, nanomedicines are being used to improve the treatment and the lives of patients suffering from a variety of disorders including ovarian and breast cancer, kidney disease, fungal infections, elevated cholesterol, menopausal symptoms, multiple sclerosis, chronic pain, asthma and emphysema.

While most of today's research in nanomedicine involves altering molecules to make drug delivery more accurate, some scientists are discovering other uses for molecular manipulation.

Researchers at Georgia State
University are using nanoparticles in an influenza vaccine that targets a portion of the virus that is present in all influenza viruses. Their intent is to develop a vaccine that will work on all influenza viruses

And researchers at the Wyss Institute are testing nanoparticles that release drugs when subjected to <u>sheer force</u>, such as occurs when passing through a section of artery that has been partially blocked by a blood clot. Lab tests on animals have shown that this method is effective in delivering drugs used to dissolve clots.

Nanomedicine is still in its infancy but eventually this field may outperform all other branches of medical science. As scientists learn how to manipulate cells at the molecular level they will be able to create 'designer drugs' (personalised pharmaceuticals) that are far more powerful than today's pharmaceuticals.

Allianz Partners 2019

Trend 4: Gene Editing

We are all the product of our genes and the idea that we could edit DNA in either embryos or in adult humans is one of the most powerful ideas in medicine. It is also one of the most controversial.

Concerns about the ethics of gene editing have accelerated in the past decade as a new technique for editing DNA has been developed. Called CRISPR-Cas9, this form of gene editing has been compared to 'cut and paste' word-processing techniques and has greatly simplified the process of gene editing.

Instead of rearranging words, CRISPR gene editing rewrites DNA, the biological code that makes up the instruction manuals of living organisms. With gene editing, researchers can disable target genes, correct harmful mutations,

and change the activity of specific genes in plants and animals, including humans.

Gene editing has already been used to modify people's immune cells to fight cancer or be resistant to HIV infection. But it could also be used to fix defective genes in human embryos and so prevent babies from inheriting serious diseases. This is controversial because the genetic changes would affect their sperm or egg cells, meaning the genetic edits and any bad side effects could be passed on to future generations.

Currently, <u>most research</u> into genome editing is carried out to understand diseases using cells in laboratories and animal models. Scientists are still working to determine whether this approach is safe and effective for use in humans.

It is being explored in research on a wide variety of diseases, including single-gene disorders such as cystic fibrosis, haemophilia, and sickle cell disease. It also holds promise for the treatment and prevention of more complex diseases, such as cancer, heart disease, mental illness and human immunodeficiency virus (HIV) infection.

Trials of gene
editing in living
humans have
already been
carried out

But trials of gene editing in living humans have already been carried out. In 2017 researchers infused a patient's blood with gene-editing tools, aiming to treat his severe inherited disease. The 44-year-old patient had a rare metabolic disorder

called <u>Hunter syndrome</u>. A year later the researchers declared the trial a <u>success</u> and they have now received approval to carry out more trials in living patients.

In April 2018 a clinical trial of gene editing to treat beta-thalassemia in humans was approved in Europe. The clinical trial is one of over a dozen that have been initiated since the advent of the CRISPR-Cas9 gene editing technique. Most of these trials are in China, working on the use of CRISPR in cancer, but there are also several underway in the U.S.

Allianz Partners 2019

Globally there are around 60,000 people born each year who have beta-thalassemia, a rare blood condition where there is an abnormal haemoglobin which can result in anaemia and low oxygen levels in the blood.

The trial in Europe uses CRISPR techniques to turn off the gene that causes this disorder, and instead helps red blood cells manufacture a form of haemoglobin produced in new-borns that isn't impacted by the mutation.

In the longer term, gene editing holds enormous promise for <u>eradicating</u> inherited disease and improving human longevity. But ethicists <u>worry</u> that gene editing could be used to produce 'designer babies' or to accidentally create long-term threats to the <u>human germline</u>. There also remains the high risk of unintended consequences that also applies to editing the genes of other life forms, from mice and mosquitos to microbes.

And as this report was in the final stages of compilation, surprising news came from China that the first gene editing of human embryos has already occurred. Geneticist He Jiankui announced at a conference that he had edited two embryos which were implanted into their mother's womb. The result was the birth of two apparently healthy babies.

The unidentified twin girls, the products of IVF treatment, had a single gene, called CCR5, altered to make them less susceptible to HIV infection. The edit was performed when the embryos were just a day old — early enough to become incorporated in the germline, meaning it can be passed down the generations.



Such far-reaching changes are widely prohibited, including, for example, by the Council of Europe's 1997 Convention on Human Rights and Biomedicine. Scientific protocol demands that any genetically altered embryos be destroyed before developing, and never implanted.

Academic uproar followed Dr He's announcements and the Chinese government has closed his laboratory prior to mounting an investigation into his work. One comment posted below a YouTube video in which Dr He explains the gene editing process reads, "You just opened Pandora's box on behalf of the entire human race."



Trend 5: Medicine Goes Digital

As in so many other areas, we are in the process of rapidly applying digital technology to medicine, healthcare and to our own bodies. We are harnessing artificial intelligence (AI) to improve medical diagnoses and treatment, we are using robots to look after the old and vulnerable, we are using computer power to decode our individual DNA and we are using the genomic data collected to personalise medical treatments for those who are seriously ill.

Today, fit and well consumers are strapping fashionable <u>wearable</u> <u>sensors</u> to their wrists and their bodies to count their steps, to measure their fitness, to monitor their hearts, their breathing, their stress, their blood oxygen levels and their sleep patterns.

Soon healthy 'informed patients' will also be monitoring their <u>blood</u> <u>pressure</u>, <u>blood glucose</u> levels, <u>potassium levels</u> and other key health indicators with the same fashionable wearable devices (without the need for cumbersome equipment or invasive blood testing).

Electrocardiogram machines (ECG units) are now appearing as inexpensive, ultra-portable accessories for smartphones allowing heart patients to monitor their own cardiac rhythms during their daily lives and, when necessary, to instantly send the results to their heart specialist for interpretation (and, with the help of artificial intelligence, basic interpretation can now be done by the patients themselves). And Apple's latest iteration of its smart watch provides simple ECG measurements at the wearer's wrist.

Low cost, hand-held <u>ultrasound scanners</u> are also available as accessories for smartphones and pregnant women can gain the reassurance of watching their babies' movements in real-time in the comfort of their own homes. Sports medics, trainers and coaches can make preliminary checks on injuries incurred at the sports field, track gymnasium or pool.

Robots have long been used in operating theatres to carry out precision surgery, but as the cost of robots falls dramatically and their functionality increases, more and more operations are now being carried out by machines working under human supervision. Crucially, human surgeons are able to control surgical robots remotely ('robotic

telesurgery') and this means that rare surgical expertise is now becoming available anywhere in the world. By 2040 the capability of robotic surgical assistants and the speed and reliability of network communications will have reached the point that human surgical specialists – e.g. an eye surgeon – will spend much of their time operating on patients who physically are in a different country or on another continent.

This prospect of increasing robotassisted surgery will be a much-needed boost to overstretched healthcare systems. When robots are used as aids to surgery, operations are usually completed with precision, miniaturization, smaller incisions, decreased blood loss, less pain, and quicker healing time. Crucially for hospitals, <u>in-patient stays are reduced</u>.

During surgery, some patients may opt to immerse themselves in virtual reality worlds rather than receive a

conventional anaesthetic.

VR systems are already

being used successfully for
this purpose and following

this purpose and following an operation patients report feeling no pain.

Digitally-controlled
3-D printers are now
manufacturing custommade replacement bones,
body parts and prosthetics
– manufacturing those
parts in locations close to

patient-recipients (e.g. in

hospitals) – and providing these rapidly and at far lower cost than traditional medical manufacturing techniques.

And an <u>Israeli technology start-up</u> is now able to 3D-print scaffoldings for lungs which allow stem cells to be used to grow new lungs for human transplantation.

Everything about medicine and healthcare is being transformed by digital technology.

This prospect of

Allianz Partners 2019

The Informed Patient

For more than 20 years patients have been scouring the internet for clues to diagnose ailments, for information about known conditions and for general medical advice. And for over a decade, patients have been connecting with other patients on social media to discuss their conditions, to compare treatments, to review and rate doctors, surgeons and hospitals and to receive invaluable support from their peers. Patients now belong to support networks.

Consumers who need instant medical advice can now consult doctors virtually using an app on their smartphones. For a small monthly fee, or for a one-off payment, patients can talk via video apps with qualified doctors who are able to issue prescriptions and make referrals. Traditional health service structures and formalities are being bypassed.

More controversially, smartphone apps have been produced in which AI is used to substitute for a human doctor. Ada offers an app which includes an AI-powered 'chatbot' that will respond to patients' queries about their symptoms and health issues. The app also provides virtual connections to human doctors when required but critics of the app suggest there should be regulation of AI-doctor technologies that interact directly with members of the public.

Medicine Personalised By Data

Pharmaceutical companies are using digital technology to monitor patients and to record data on drug performance in real world conditions. The new insights such data offers allows drug researchers to improve drugs and to invent new treatments – and to test them more effectively, under more realistic conditions, than has ever been possible before.

The data that is collected from wearable health technology will also allow doctors to further personalise their treatment of individual patients. Coupled with the information gleaned by the sequencing of patients' DNA this will allow doctors to tailor treatments for their patients with extreme precision.

For example, the <u>Kardia</u> ECG smartphone app and sensor pad allows users to record their heart's sinewave in order to monitor for unusual heart rhythms that might suggest a coronary condition called <u>atrial fibrillation</u> (where there is an irregular and sometimes abnormally fast heart rate).

A patient with atrial fibrillation is able to record his or her heart rhythm sinewave on their smartphone at times when they are experiencing symptoms and when they're not. The patient is also able to dictate details of any symptoms being felt whilst the ECG recording is being made.



Over time, regular ECG readings taken at home will provide a cardiologist with a detailed history of how the patient's heart is performing over a period of weeks or months, at different times of day and night and at the time when different symptoms were being experienced. This information will provide insight into the severity of the condition and will allow the cardiologist to precisely tailor the medical intervention required.

In years to come, <u>data collected</u> from wearables, from smartphone apps and from sensors, will provide the monitoring and recording of metabolic, cardiovascular and gastrointestinal conditions.

Other functions that will be monitored will include sleep, neurological functions, movement disorders and mental health, maternal, pre- and neo-natal care and pulmonary health and environmental exposures.

Such historical ambulatory data has never before been available to doctors, drug company researchers or the designers of artificial intelligence algorithms. The insights gained will allow doctors to further personalise treatments for individual patients and, in addition, it will play a major role in shaping new medical knowledge and public health policy.

Allianz Partners 2019

Changing the Doctor-Patient Relationship

Because of the internet and digital technology, the knowledge that was once the sole property of doctors and other medical professionals is becoming democratised and from now on patients will be much better equipped to monitor their daily health and to work to actively preserve and cherish their most precious and important asset: 'wellness'.

The arrival of digital health technology does not suggest doctors are no longer necessary – quite the

opposite. But the healthmonitoring technology, communications infrastructure and rich store of medical knowledge and support now becoming available to consumers will, in time, redefine the role of both patients and doctors. This process will free up medical professionals from some of their basic

body-monitoring, history taking and repetitive treatment duties to become more personal, more investigative and more creative in their healing and care-giving.

To be clear, the role of doctors and surgeons in dealing with patient care remains paramount. There is no replacement for the relationships created between medic and patient. There is only a partial replacement for a small part of the knowledge that medical training provides.

Above all, there is no substitute for the experience that comes with years of reaching diagnoses and dealing with specific conditions. It is important that access to medical information is not confused or conflated with the allimportant practical experience that doctors gain as they treat thousands of patients over many years. However, some of the technology this report describes is intended to keep patients out of the doctor's surgery. Once consumers get the bug for monitoring their own fitness and health many wonder how they ever lived with such uncommunicative bodies.

The arrival of digital health technology does not suggest doctors are no longer necessary

their pulse and pressure reading any time) will to seem as structure as getting into dashboard or screen. Not know their blood-su

Not being able to see their pulse and blood pressure readings (at any time) will come to seem as strange to many health consumers as getting into a car that does not have a dashboard or display screen. Not knowing their blood-sugar level, cholesterol reading or blood oxygen level

(if relevant to your state of health) will be like embarking on a journey without a smartphone, Sat-Nav system or a map. It will become simply unthinkable. People will look back with amazement at the time when our bodies were not 'smart', and we were forced to wander the world oblivious and blind to our physical health and unaware of the ever-changing state of our bodies.

At a broader level, the network is becoming the doctor. As smartphones and AI learn to diagnose illnesses by 'listening' to a cough and to detect the early onset of Parkinson's disease by monitoring its user's gait, we will start to turn to our smart devices and their supporting networks as our primary care resource – the first stop when we need non-emergency medical advice.

As the sensors and health-monitoring abilities of portable and wearable devices rapidly improve, and as the capabilities of internet-based artificial intelligence health diagnosis improves exponentially, a large proportion of the population will rely to an increasing extent on computeraided self-monitoring, self-diagnosing and self-treatment for its primary healthcare needs.

Digital technology will also change the way patients interact with doctors. Doctors are already reporting that patients are requesting the right to record consultations on their smartphones and this is a practice that will increase over the years until it becomes routine.

Gone are the days when patients desperately try to remember what the doctor has said during an examination or consultation and as 'life logging' the practice of routinely recording all of life's events – becomes more and more accepted in society, so doctors should come to accept and welcome that just as all police interactions with the public will be recorded in the future, so all contact between doctors and patients will be similarly logged. These recordings will become part of patients' digital health files and misunderstandings and errors will be reduced as a result.



The Impact Of Artificial Intelligence

Artificial Intelligence (AI) systems are already proving to be <u>as capable as human doctors</u> in diagnosing some limited and specific diseases and conditions but, as the technology improves in speed and capability, the number and range of maladies AI can diagnose will rapidly increase.

One of the greatest benefits of using AI systems in medicine is that it has the potential to unlock clinically relevant information hidden in massive amounts of data which, in turn, can assist in clinical decision making. A second form of AI known as machine learning can learn from this data to improve the accuracy of its own decision making.

Today, AI is being used to read medical scans to detect cancers, to diagnose Alzheimer's disease, to sift through millions of pages of medical evidence to suggest diagnosis, to provide virtual nursing services and to aid drug development in pharmaceutical companies.

Al is also providing algorithms to improve and accelerate MRI scanning and even to create 3-D moving pictures of a beating heart (while also showing in real time how much blood is pumped with each contraction).

Al-powered automation has the potential to increase healthcare productivity by relieving doctors and nurses of routine activities. In the future Al 'chatbots' equipped with deep learning algorithms could relieve emergency room personnel of tending to large numbers of walk-in patients with non-emergencies like sore throats and urinary tract infections.



predicted that AI-enabled operational efficiencies could represent sizable savings in the healthcare budget in developed countries. Estimates for the United States range from 1 to 2 per cent of GDP. In other rich countries, estimated savings would be 0.5 to 1 per cent of GDP. Full AI adoption could raise the productivity of registered nurses by 40 to 50 per cent. McKinsey research has found that this could allow hospitals to cut staffing costs in half while still significantly reducing patient waiting time.



Change Won't Come Easily To The Medical Profession

However, any change to the way formal healthcare is provided will not come easily. For reasons of patient safety, the medical profession is ultra- conservative: after all, the primary Hippocratic mantra is primum non nocere – 'First, do no harm'

But despite the resistance of the conservative medical profession, it is now becoming clear that access to medical information and health monitoring data is the right of every human. Medical power and knowledge are being transferred from the high priesthood of doctors to the general public. Dr Eric Topol, a distinguished U.S. cardiologist and champion of digital health, recently summed up this concept in the title of his influential book, 'The Patient Will See You Now'.

Dr Topol is a rare, but not unique, example of a medical professional who understands the implications of digital health. He and a few others realise that the medical profession faces huge disruption, but he has already identified the myriad benefits that will flow to both patients and doctors as our bodies become smart.

In time, many of the tests and checks that were once available only in a doctor's surgery or in a pathology lab will be available instantly via your smartphone and other add-on devices. And the collection of sensors on and around your body will, very quickly, develop and evolve to become an onbody health and fitness network which will work 24 hours a day to help keep you as well informed and as healthy as possible. Some of these sensors may be incorporated into everyday items of clothing and, eventually, into our skin and blood.

Our bodies are natural walking 'data generators' and all that is needed to tap into this resource are inexpensive biosensors to capture the data and some clever algorithms to interpret it. A glance at the historical records of, for example, your daily activity levels, the calories you've burned each day, your sleep patterns, your long-term resting heart rate and your average blood pressure, will tell you (and your doctor) far more about your real state of health or illness than any single-visit "snapshot" check-up carried out in a doctor's surgery ever could.

Until now, it has been very difficult for a doctor to see how patients' bodies behave over time (other than when a patient is confined to a hospital bed) and this new type of low-cost ambulatory data will lead to better, faster and more accurate detection of problems, diagnosis and appropriate treatment. It will improve

the health of millions and today's annual physical check-up or 'exam' will be replaced by a continuous stream of real-life, real-time information from your body. (In fact, the value of the annual physical exam has now been shown to be <u>far less than once thought</u> and many medical professionals regard this well-established procedure as worthless).

The medical profession has long understood the huge value of ambulatory data. However, until very recently medical equipment for capturing ambulatory recordings has been bulky and expensive.

Doctors have been cautious in prescribing the use of such equipment and patients have been reluctant to wear uncomfortable systems.

Yet real-world historical ambulatory data of your blood pressure, lungfunction, heart rhythm, potassium levels, blood oxygen content or glucose levels (just to mention a few of the measurements now possible) is the most valuable information available to our physicians. Doctors can experiment with treatments – changing doses, changing drugs or withdrawing a particular medication

> - and get rapid, realtime feedback of how to the change (as will you). This is how your data will help doctors further personalise your treatment – over and above selecting treatments based on your DNA profile.

For example, a diabetic with a real-time read-

out of his or her <u>blood-sugar level on</u> a smartphone can see instantly how a meal, or a certain item of food or drink, affects body glucose. This has a powerful and instant modifying effect on diet and behaviour and, first the first time, provides the patient with the feedback necessary to take momentto-moment control and manage the condition. If you know that eating a fully ripe banana increases your blood-sugar (glucose) reading 30 minutes later by an unwelcome 0.25 mmol/L (millimoles per litre), you might either avoid that fruit or pick a less ripe banana in future.

your body responds

Our bodies are

natural walking

'data generators',

all that is needed

to tap into this

are inexpensive

biosensors

Devices that monitor our sleep – wristbands, smartphones, underblanket sensors, etc. – are already providing insights into conditions and diseases that could be gained in no other way. One tagging device that was originally designed to keep tabs on offenders has shown that patients with Parkinson's disease suffer episodes that occur during sleep – something that was completely unknown previously.

Instead of being difficult to interrogate, our bodies will soon become 'smart' and transparent recorders and reporters of physiological data. This is a most profound change in medicine and in human healthcare.

Soon our physicians will be able to have real-time reports on the condition of all their many patients as they go about their daily lives. This data will stream wirelessly into the cloud (accessible from doctors' surgeries) 24 hours a day and, even though our doctors will not have the time to monitor such individual information streams personally, their own AI-monitoring systems will alert them to any change in their patients' data that requires their urgent attention.

It may seem fanciful today, but it will not be long before most informed patients over 50 (and many younger patients) will have smart bodies which are permanently connected and continuously streaming data to their doctors' offices (and to their own cloud-based storage systems).

The key phrase in the last paragraph is 'informed patients' because it is clear that there are a large number of patients in the general population who simply don't want to take any responsibility for their own wellbeing.



In fact, the members of this group have little interest in their own health, other than when they are suddenly debilitated and need immediate assistance. Health professionals estimate this group to be as large as a third of the overall population with the other two thirds showing varying degrees of interest in health which range from minimal to deeply engaged. Whether the disinterested 33 per cent will become more interested in their own health when monitoring devices are very cheap or even provided free of charge – is doubtful. But the potential impact of digital health on healthcare and social economics on the more interested majority still remains profound.

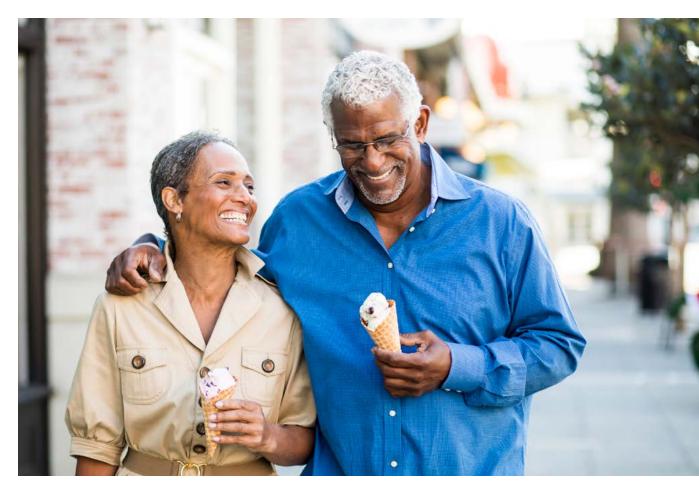


Health data collected from patients as they go about their daily lives ('ambulatory data collection' – ADC) is an entirely new phenomenon. The volume of data streaming from health wearables worn continuously by tens of millions of people will be vast, but 'Big Data' analytic data-mining tools have now been developed which will help researchers make sense of these huge pools of biometric information.

A completely new field of "predictive medical data mining" will develop as researchers identify data sets that provide early warning of physiological trouble ahead or indications of disease as it develops. We have never previously had long-term cardiac data from humans as they pursue their daily occupations (and as they sleep) and it is highly likely that researchers will develop new algorithms to automatically identify the first signs of impending cardio-vascular problems.

Similarly, medical researchers have never had long-term logs of sleep patterns, breathing rates, blood pressure, blood-glucose levels, stress levels, etc. A whole new horizon of predictive medicine is coming into sight. This will turn the low-cost sensors that we will wear on our bodies, that will be incorporated into clothing and that will inhabit our bathroom scales and other devices around our home, car, school and workplace, into massively powerful early warning systems for human health.

Another super-valuable by-product of widespread ambulatory population monitoring will be that this ADC data becomes available to pharmaceutical companies.



At present, drug companies test new drugs in what are supposedly rigorous clinical trials and then have to wait a long time for real-world semi-anecdotal feedback (usually provided by doctors in secondhand descriptions of their patients' experiences) as the drug enters use in the general population. If the drug companies were able to directly access ambulatory data from those using their drug in the real world, imagine the improvements that might be possible to guidelines for use and even to the drug itself.

It may be said that whilst change in traditional healthcare proceeds at a rate similar to the speed of continental drift, digital and internet developments occur at a speed which seems to be closer to the speed of light. The two do not appear to be compatible, and something will have to give.

However, these formerly separate sectors (medicine and information technology) are now converging rapidly and a number of very powerful outside factors will ensure that it is medical tradition that has to give way.

The super-powerful external factors that will shake and reshape medical practice include:

1. The rapidly ageing population in the developed world

The Baby Boomer generation is now close to, or already in, early retirement and in some developed nations those over 65 will, for the first time, outnumber all other generations.

With more old people come more long-lasting, chronic diseases (now re-branded less pejoratively as LTCs -'Long Term Conditions') and, therefore, higher healthcare costs. Around 33 per cent of the UK adult population now has a chronic disease whilst <u>60 per</u> cent of adult Americans are similarly afflicted.

The apparent difference between the two nations may be real, it may be as a result of different medical definitions in use or it may reflect the

more aggressive approach to treatment typical of the profit-driven US health system.

All this will be good business for privately funded healthcare systems - provided patients can find the money necessary for treatment or to pay their health insurance premiums.

But for taxpayer-funded healthcare systems (national public health schemes are standard in the majority of developed societies outside of the USA) the increasing number of elderly patients and the increasing cost of healthcare technology is certain to mean more rationing of care and greater pressure on the price of drugs, and on limited medical resources.

Huge numbers of old people with chronic illnesses – those ailments that never get cured, only managed (arthritis, diabetes, hypertension, COPD, etc.) – have never existed in any society before; previously most of our older people have died before they reached the point of needing continuous healthcare. This huge elderly group of chronically ill patients will be a vast and unprecedented drain on our taxpayer-funded health systems.

2. Most countries suffer from a serious mismatch: the demand for healthcare is rising faster than the supply of doctors.

In the USA the Association of American Medical Colleges predicts a shortage of 45,000 primary-care doctors by 2020, precisely the type of doctor who might manage the chronic conditions of the elderly.

There's a similar shortage of doctors in Germany and it is estimated that by 2020 in Europe as a whole, <u>230,000</u>

> doctors' roles and 590,000 nursing positions will need to be filled. In less than a decade, there will be a professional shortfall of 1 million jobs in the European health sector

(including all roles).

In the UK, hospitals are facing a shortage of 20,000 doctors and 64,000 nurses. During

2017 the UK had 2.8 practising doctors for every 1,000 people – fewer than all other European countries including Bulgaria, Estonia and Latvia.

3. The rapidly escalating cost of healthcare treatment

Dedicated, high-end medical technology is tremendously expensive and drug development is becoming ever lengthier and costlier (resulting in ever more expensive drugs).

It may seem strange that whilst other areas of technology development such as computers and televisions produce better products at lower costs, this axiom does not hold true in healthcare.

The UK annual

budget for

the NHS is

\$153 billion.

In the USA, it's

\$3.5 trillion

The main reason for the extra costs is the expense of carrying out more complex clinical trials and the investment involved in clearing multiple regulatory hurdles. Health equipment and drugs have to be proved to be reasonably safe before they can be used on the public (which doesn't necessarily mean they are also effective).

In the UK the annual budget for the NHS is \$153 billion. In the USA, the annual healthcare budget is \$3.5 trillion.

The vast disparity in these figures is not explained by the fact that America's population is five times larger than the UK's. If population numbers alone made the different the US healthcare budget would be \$581 billion not \$3.5 trillion. As US surgeon Dr Atul Gawande explains in his book 'Being Mortal' on the US healthcare system, "If terminal patients - rather than insurance companies or the government – had to pay the added costs for the treatments they choose instead of hospice, they would take the trade-offs (between the cost and the extension of life) into account more. Terminal cancer patients wouldn't pay \$80,000 for drugs, and end-stage heart failure patients wouldn't pay \$50,000 for defibrillators, offering at best a few months extra survival."

4. The method of funding used by most public and semi-public healthcare systems

Most national public healthcare services are funded directly by the taxes paid into the scheme by the working population. There is no historical 'pot of money' saved up over time – each year the costs of the health service are paid directly from the taxes received from the population.



This would appear to be a giant 'pyramid scheme' as it relies on more and more people joining the programme and paying tax contributions for the system to provide more and more services to those who need it. But as joining is mandatory under law for working people, there would be nothing wrong or illegal with such a government-mandated scheme if the tax-paying population was still growing. The problem in most developed nations is that the working population is shrinking even as the retired population is growing. Fewer people are paying into the scheme whilst more and more people are requiring ever more expensive treatment. The potential for collapse is clear.

As the world knows, the American healthcare system faces significant challenges, despite Barack Obama's heroic attempts at marginal reform (and the failed attempts at reform made during the Clinton Administration of the 1990s). Accordingly, Americans pay significantly more for prescription drugs and medical devices than patients in the rest of the world and the American private insurance-based system rewards doctors for carrying out unnecessary procedures.

As things stand, Dr Atul Gawande has summed it up: "The soaring cost of healthcare has become the greatest threat to the long-term solvency of most advanced nations, and the incurable (chronic elderly) account for a lot of it."

So, it is clear that there are four major reasons

that will force healthcare professionals in the developed world to embrace patient empowerment: the ageing population, a shortage of medical professionals, the rapidly escalating cost of specialist medical-treatment technology and the method by which health systems are funded (by quasi-pyramid/Ponzi schemes).

5. Are the Five Revolutions Occurring In Healthcare A Solution To The Health-Care Crisis?

All five of the medical-science revolutions described earlier are likely to make medical science and healthcare provision more effective at maintaining a healthy population.

But, at the same time, the first four of the new medical methodologies – DNA-personalised medicine, stemcell treatments, nano-scale medicine and gene editing – are likely to dramatically increase the number of different conditions that can be treated successfully. Some of these treatments may mean that patients require no further healthcare for that particular condition but, inevitably, the treatments and cures that flow as a result of these successes will increase longevity and increase population

demands on the health service. At present, I am inclined to think that health services in the developed world will continue to see increasing demand as people live longer and more and more diseases succumb to science-based medicine. As a result, healthcare costs will continue to increase.

The soaring cost of healthcare has become the greatest threat to the long-term solvency of most advanced nations

But the fifth revolution I describe – Digital Health – is likely to improve the overall wellness of populations. Patient empowerment through the use of the internet, digital technology, low-cost bio-sensors and direct-to-consumer DNA analysis will help to ease the burden on national health systems.

Even if only 20 per cent of patients used new technologies to take more responsibility for their wellbeing over the next ten years, the burden on doctors' offices and hospitals would be substantially reduced.

Additionally, these technologies can serve as a key ingredient in fuelling a prevention revolution by helping ignite a culture of health awareness worldwide.

31

But beyond personal health technologies, the answer to the myriad problems facing our national healthcare systems, almost everyone in healthcare agrees, must be constant innovation within the management of health systems. From improved drug development and disease diagnosis to the way care is provided, new and better ways of managing public health services must continue to emerge.

One of the best ways to ensure that innovation in healthcare delivery maintains its momentum is for management to keep a close eye on new techniques that are being delivered in healthcare systems in other nations.

For example, India's physicians are forced to provide innovative and entrepreneurial approaches to delivering healthcare because the population is so large and poverty so widespread. Western healthcare management can learn from such examples. And there also needs to be more attention given to the results of international best outcomes studies if healthcare services around the world are going to provide the best possible care for the patients of 2040.

