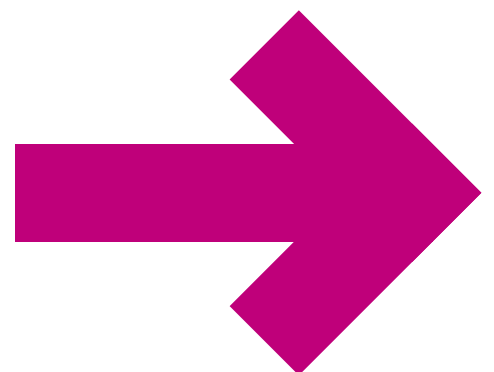


IMPROVING OUTCOMES THROUGH PERSONALISED MEDICINE

Working at the cutting edge of science to improve patients' lives



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Description A vision for Personalised Medicine in the NHS
It sets out, in layman's terms, the personalised medicine "story" using some of the material that supported Board discussions in September 2015 and in May 2016, and which is already in the public domain. It still needs some final drafting and design tweaks but the messages will not change in any substantial way. It contains no new policy announcements or commitments.

Cross Reference

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Contents

Contents	3
Foreword	4
1. Introduction	5
2. A new era of medicine	6
2.1 What is personalised medicine?	6
2.2 The changing way medicine will be delivered	6
2.3 A new targeted treatment approach	7
2.4 Enabled by integrated informatics	7
2.5 Building on the 100,000 Genomes Project	9
3. Why adopt a personalised medicine approach?	11
3.1 The four 'P's of personalised medicine	11
3.2 Wider benefits of personalised medicine	13
4. Making personalised medicine a reality in the NHS	14
4.1 Embracing the future	14
4.2 The building blocks are already in place	16
4.3 How to get involved	17

Foreword

“The NHS belongs to the people.

It is there to improve our health and wellbeing, supporting us to keep mentally and physically well, to get better when we are ill and, when we cannot fully recover, to stay as well as we can until the end of our lives. It works at the limit of science – bringing the highest levels of human knowledge and skill to save lives and improve health. It touches our lives at times of basic human need, when care and compassion are what matters most.”

NHS Constitution

As Nye Bevan said at the time of the creation of the NHS, “the eyes of the world are turning to Great Britain”. This is no less true today as we stand on the brink of a new era of medicine. Across the world, we are witnessing a healthcare revolution driven by scientific and technological advances – in genomics, informatics and bio nanotechnology to name but a few – which are enhancing our ability to more precisely diagnose illnesses and target treatment of disease.

These advances are happening now and they are an intrinsic part of delivering the NHS Five Year Forward View and closing the finance and efficiency, the care and quality, and the health and wellbeing gaps.

Britain has the opportunity to be at the forefront of this new era of medicine, delivering 21st century healthcare. As the single biggest integrated healthcare system, combined with our world leading science base and global reputation for innovation, we have the opportunity and capability to transform the way we deliver healthcare to secure benefits for our patients, our society and our economy.

If we get our approach right, the NHS will become the first health service in the world to truly embrace personalised medicine. We will create a healthcare system focused on improving health, not just treating illness, able to accurately predict disease and tailor treatments, with shared decision making at its heart.

It will only be possible to achieve this if we continue to work with people across the entire health and care system. At a local level with providers, commissioners, patients and the public, and with our national partners including the Department of Health, NHS Improvement, Health Education England, Public Health England, NHS Digital, and Genomics England. Everyone, from patients to clinicians, commissioners to academics, has a part to play as we continue our journey to make this vision a reality across the NHS in England.



Sir Malcolm Grant,
Chair of NHS England



Prof Sue Hill OBE,
NHS Chief Scientific
Officer for England

1. Introduction

The NHS has a long and internationally renowned track record of innovation and creativity: in vitro fertilisation; the development of MRI and CT scanning; the portable defibrillator; the disposable syringe; the world's first antibiotic; and mapping the structure of DNA. These are just a few of the breakthroughs that have been made by British clinicians and scientists for the benefit of patients. These advances have also benefitted the UK economy, with new ideas and technology in this sector kick-starting businesses, creating jobs and supporting exports across the world.

The NHS continues to operate at the limit of science. Through the 100,000 Genomes Project, a ground breaking and world leading initiative, the NHS is building partnerships with academia and industry to decode the human genome, in people with rare diseases and cancer. Clinical teams in the 13 NHS Genomic Medicine Centres are enabling the NHS to become the first health service to collect and use whole genome sequencing alongside routine collection of clinical and diagnostic data on a large scale.

Whole Genome Sequencing provides a huge step forward in the diagnostic information available. It involves looking at an individual's entire DNA, rather than looking at specific genes or groups of genes. When analysed with other information about our health and the way people live their lives, it provides much richer information about the complex interactions within a person, and between them and their environment. It offers a greater understanding of the underlying causes, triggers and drivers of disease as well as the likely success or failure of drugs and interventions.

The concept of personalised medicine is not new. Clinicians have been working to personalise care, tailored to people's individual health needs, throughout the history of medicine. But never before has it been possible to predict how each of our bodies will respond to specific interventions, or identify which of us is at risk of developing an illness. New possibilities are now emerging as we bring together novel approaches, such as whole genome sequencing, data and informatics, and wearable technology. It is the interconnections between these innovations that make it possible to move to truly personalised care.

Technological and scientific advances are already here and will continue to develop and improve medical practice; change is inevitable. For the NHS, we must consider not whether we should go down the route of personalised medicine, but instead how we can best respond and adapt so that those who could benefit have the opportunity – regardless of where they live, the illnesses they have, or where their care is provided. Personalised medicine is important not only for the 1 in 17 people who have a rare disease, or for those living with cancer, but also for the many others who have or are at risk of developing other common diseases.¹

We are on a journey towards embedding a personalised medicine approach into mainstream healthcare. This document sets out what we mean by personalised medicine, and the approach we will take, working with our partners, so that we can embrace the future, whilst ensuring the ethical, equality and economic implications are fully recognised and addressed.

¹ <http://www.rare-disease.org.uk/what-is-a-rare-disease>

2. A new era of medicine

2.1 What is personalised medicine?

Personalised medicine:

Personalised medicine: a move away from a 'one size fits all' approach to the treatment and care of patients with a particular condition, to one which uses new approaches to better manage patients' health and target therapies to achieve the best outcomes in the management of a patient's disease or predisposition to disease.

We are all unique. Our health is determined by our inherited genetic differences combined with our lifestyles and other environmental factors. By combining and analysing information about our genome, with clinical and diagnostic information and then comparing that with data from others, patterns can be identified.

Together this information can help to determine our individual risk of developing disease, detect illness earlier, provide an accurate diagnosis, and determine the most effective interventions to help improve our health, be they medicines, lifestyle choices, or even simple changes in diet.

In the early 20th century we saw the first connection between genetic inheritance and susceptibility to disease.² In 2000, the first draft of the human genome sequence was announced, which gave clues about what individual differences might mean for our health. But it was at a cost of over £2 billion for a single sequence.³ Today, because of new sequencing technology, there has been a dramatic drop in the cost which, coupled with the availability of high speed computing needed for analysis, means it is possible to consider this technology as part of routine healthcare.

2.2 The changing way medicine will be delivered

Traditionally, medicine has been built around clinical teams specialising in a particular organ system working back from a patient's symptoms to arrive at a diagnosis.

Personalised medicine turns this approach on its head. It recognises that complex diseases should no longer be considered as a single entity. One disease may have many different forms, or 'subtypes', resulting from the complex interaction of our biological make-up and the diverse pathological and physiological processes in our bodies. These will not only vary between patients who have the same disease but also within an individual patient as they get older and their body changes.

As we integrate and analyse genomic and other data, we can find common factors and causes of variation, resulting in the discovery of new pathways of disease, changing how diseases are thought of and treated. It enables us to recognise that the same underlying change in our DNA or genome can lead to problems in very different parts of the body, which would not have been previously identified with a more traditional care approach.

² Garrod AE. Incidence of alkaptonuria: a study in chemical individuality. *Lancet*. 1902; 2:653–6.

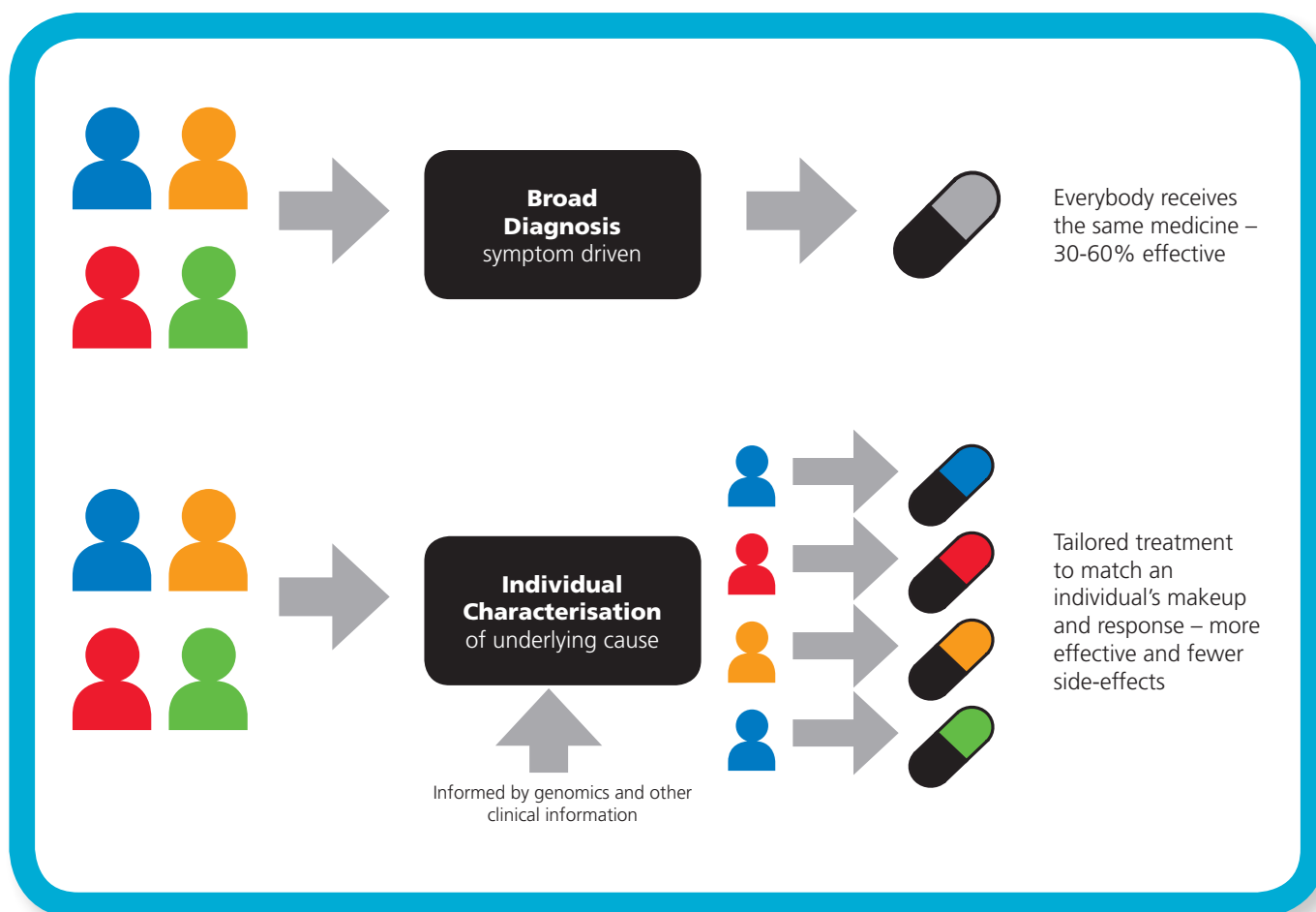
³ <https://www.genomicsengland.co.uk/from-one-to-one-hundred-thousand>

2.3 A new targeted treatment approach

The current blockbuster approach to drug development assumes that all patients with a particular condition respond similarly to a given drug. All patients with the same condition receive the same first line treatment even though it may be only 30 to 60% effective.

Personalised medicine will provide opportunities to improve how we treat disease. Based on comprehensive genomic and diagnostic characterisation, different subtypes of patients within a given condition can be identified, and treatment can be tailored to the underlying cause, as illustrated in Figure 1.

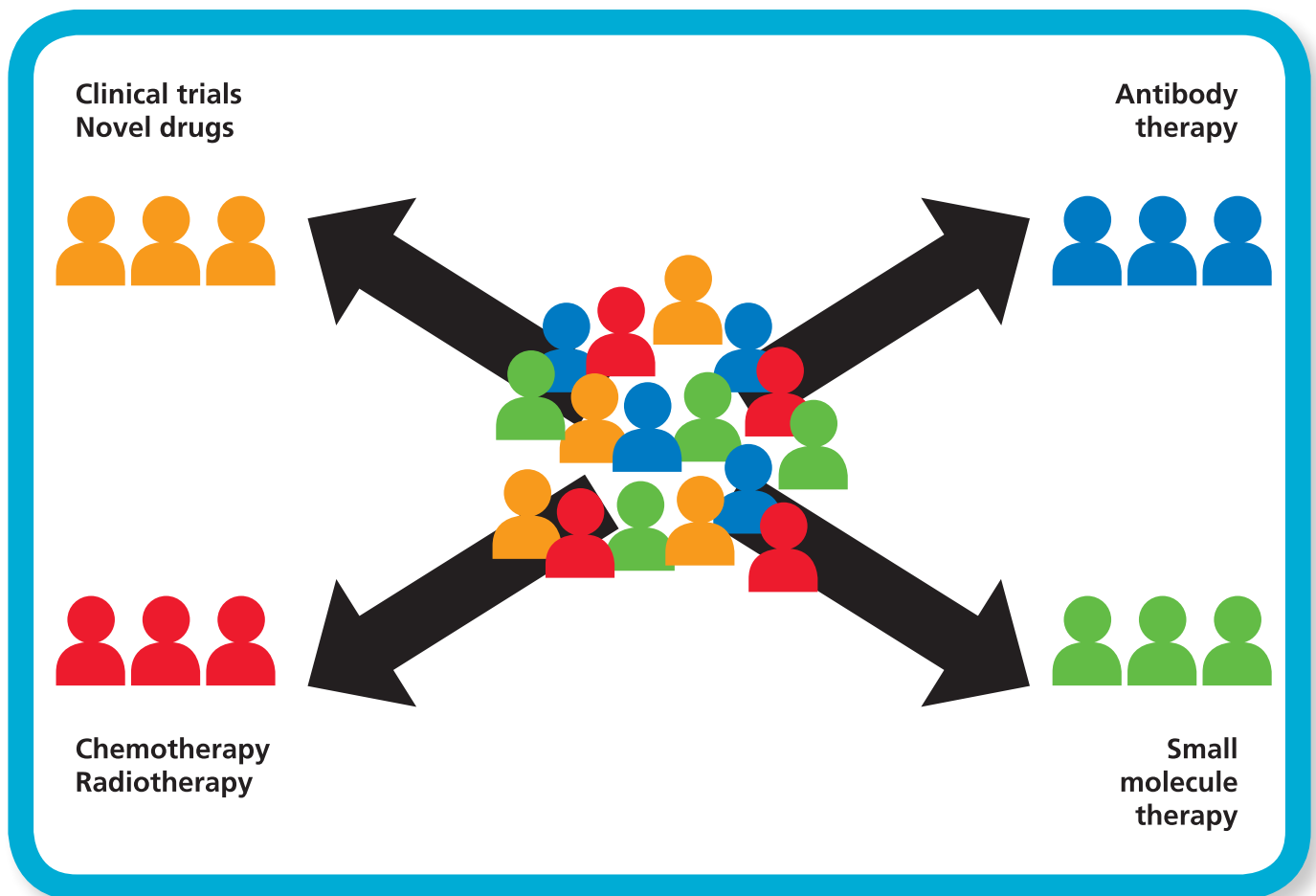
Figure 1



Cancer is one condition where this approach is already more common place, following major biological insights and medical advances. All cancer has a genetic base. Today, we can offer a genomic, or 'molecular' diagnosis, which means that we better understand the genetic base and can use this information to help select the most effective treatment, greatly improving chances of survival. This can be used for a wide range of cancers such as melanoma (skin cancer), leukaemia, colon, brain and breast cancers.

This understanding means that cancer patients can be stratified according to what will be most effective for their condition, illustrated in Figure 2. It may also mean that patients with different types of cancer may, on the basis of the genomic diagnosis, receive similar treatments.

Figure 2



Molecular diagnosis and treatment stratification for lung cancer

Following molecular stratification a patient's tumour can now be classified as either EGFR positive (responsive to antibody therapy) or ALK positive (responsive to small molecule therapy), enabling them to start treatment on the therapy regime that will have the most benefit to respond to their specific genomic variant.

Personalised medicine will help to maximise the value we can secure from the £15 billion that the NHS currently spends on drugs each year. It will create the opportunity to find new purposes for, and better use of, existing medicines including generics and biosimilars. It will also help us to use other non-pharmacological treatments, and even, in some patients, simple dietary or lifestyle interventions.

The NHS will work closely with research and industry colleagues to ensure, as far as is possible, existing and new treatments are available in an evidenced based and affordable way, giving best value to patients. Within Specialised Services for example, personalised medicine will be a key aspect of the strategic approach to meeting the health and wellbeing challenge, bringing a more preventative approach to these vital, but often rare and expensive treatments.

2.4 Enabled by integrated informatics

We have more data about people, their habits and their health than we have ever had before - 90% of all recorded human data has been captured in the last two years.⁴ To maximise the true value of the information available about our health, we need to bring together genomic, clinical and diagnostic, medicines, and lifestyle data. It is the integration and analysis of this information that forms the powerhouse for personalised medicine.

Building an integrated informatics system across a healthcare system is difficult: we've tried in the past and struggled, but the challenges are not insurmountable. Work is already taking place through NHS Digital to deliver the NHS Paperless 2020 programme, an ambitious plan to create fully interoperable electronic health records, supported by information sharing and data linkage.

The scale of the interdependency between integrated informatics and delivering personalised medicine cannot be overstated. Nor should the challenges. The information that comes from a single human genome produces enough information to fill a stack of paperback books over 60 meters high, so the data storage requirements are vast.⁵ And the security of data, and consent/privacy arrangements for patients are paramount. The NHS, with its NHS number for each individual, is almost alone in the world in being able to put together health information across a person's entire life. This potentially gives UK citizens a unique health advantage and health informatics are the key enabler. The foundations for this step change in health care are already being put in place.

2.5 Building on the 100,000 Genomes Project

The 100,000 Genomes Project is an ambitious programme that focuses on sequencing the whole genome of families with rare diseases and patients with common cancers, together with detailed clinical and diagnostic data to enable the clinical significance of variation in the genome to be assessed. The Project is both a clinical care project designed to transform NHS practice, and a research project creating anonymised repositories of samples and related data for research purposes.⁶

The Project aims to:

- increase discovery of pathogenic variants leading to new treatments, devices and diagnostics;
- accelerate uptake with advanced genomic medicine practice integrated into the NHS;
- increase public understanding and support for genomic medicine; and
- stimulate and advance UK life sciences industry and commercial activity in genomics.

⁴ Science Museum, who currently have a Big Data exhibition <http://www.sciencemuseum.org.uk/about-us/press/april-2016/our-lives-in-data>.

⁵ <http://www.yourgenome.org/facts/what-is-a-genome>

⁶ The Project received ethics approval on this basis

NHS England has established a national network of 13 Genomic Medicine Centres delivering genomic services across the country. Each of the Genomic Medicine Centres is working in partnership with local providers, across populations of 3 to 5 million, to enable:

- patients and family members, with their informed consent, to participate in the project;
- greater patient and public involvement in the dialogue about genomic medicine;
- clinical and diagnostic data to be captured and collated in new datasets that inform the overall interpretation of the genome sequence and its expression;
- new tracking, collection and handling processes for samples, including the introduction of fresh frozen cancer samples for optimal DNA extraction;
- the creation of genomic medicine multi-disciplinary teams for rare diseases and cancer to help analyse what their genetic information means for that patient; and
- shared risk and decision making through new governance and partnership arrangements across the NHS, with active support from the Academic Health Science Networks.

The Project is coordinated by Genomics England, who have procured whole genome sequencing services and analytical providers. They have created a unique database that enables approved researchers, clinicians, and industry to work on de-identified data to enhance clinical interpretation and answer arising research questions.

Knowledge from the Project will enable clinical teams to better characterise an individual's condition, learn from others with the same disease and connect seemingly different conditions with the same underlying genomic cause.

Through the project we are laying the foundations for a personalised medicine approach across the NHS. This is not light years away; it is already changing people's lives.

Jessica has a **rare condition** that doctors struggled to identify precisely. Her family participated in the **100,000 Genomes Project** via Great Ormond Street Hospital (GOSH) to try and find a diagnosis for Jessica. Whole Genomes Sequencing returned a molecular diagnosis, setting them free to make decisions about the treatment options for their child.



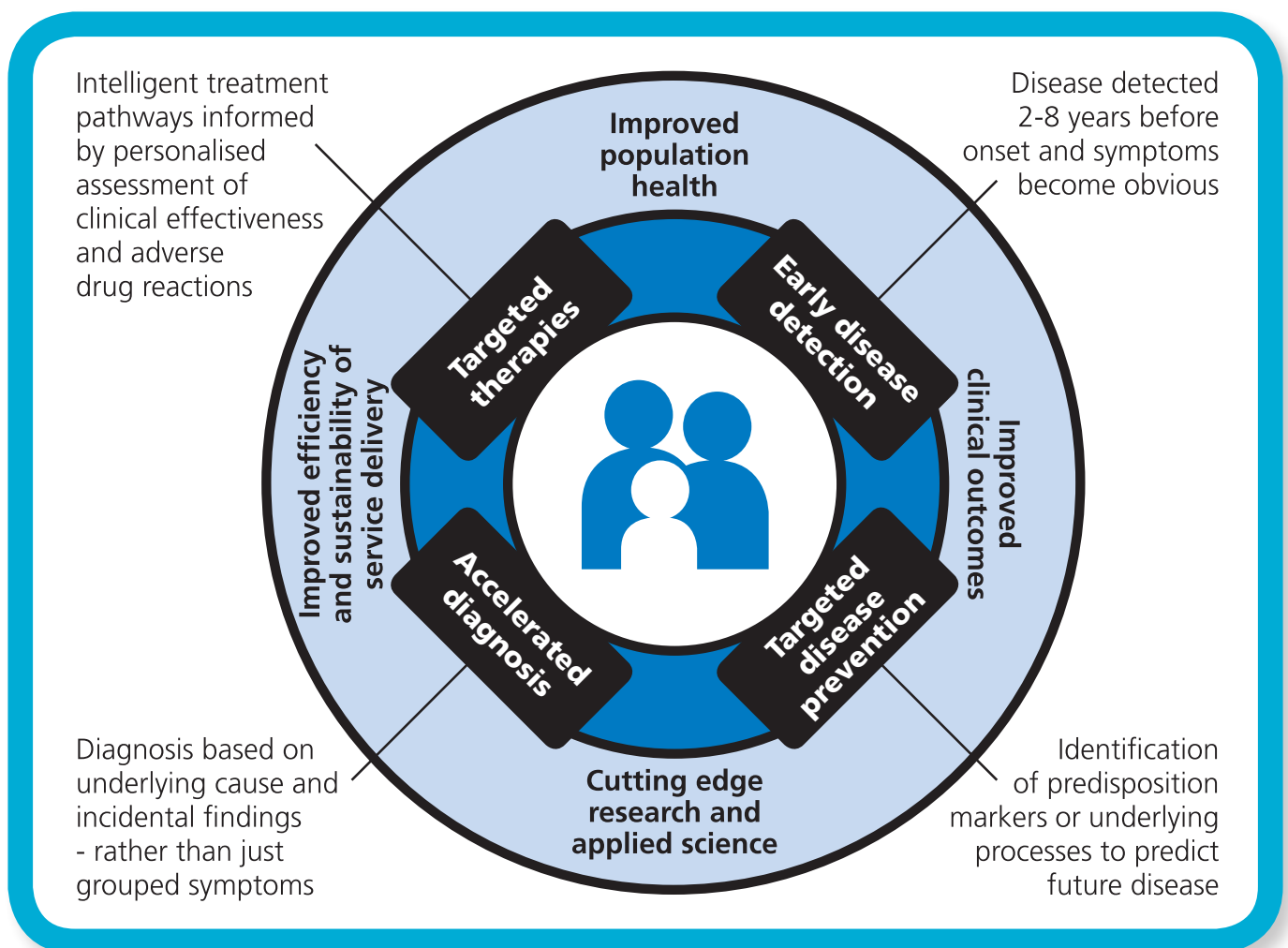
“The outcome has taken the uncertainty out for us and the worry of not knowing what was wrong. Now that we have this diagnosis there are things we can do differently straight away. A special diet means her medication can decrease and her epilepsy be more easily controlled.”

3 Why adopt a personalised medicine approach?

There is global recognition of the potential benefits of personalised medicine. Health systems including the US, Germany, France, Canada, Australia, China and India are formulating policy and research programmes to support the adoption of more personalised approaches to healthcare.

Personalised medicine has advantages for individual patients, for populations, for the NHS, for science and for the wider economy, as described in Figure 3.

Figure 3



3.1 The four 'P's of personalised medicine

Prediction and prevention of disease

Using genomic technologies and other diagnostics we will be able to identify people most at risk of disease even before the onset of their symptoms. Earlier detection will open up the prospect of new treatment options and support people to make informed lifestyle choices. This will create the potential to reduce the growing burden of disease, particularly for long term conditions such as cardiovascular diseases, cancer, chronic respiratory diseases and diabetes.

Familial Hypercholesterolemia (FH)

FH causes raised cholesterol and a significant risk of heart attack and other cardiac events in the under 50s. It affects 1 in 250 people – but only 1 in 6 of these are diagnosed. By systematically using both genetic and biochemical testing, FH can be identified and affected people can receive inexpensive medicines to protect them from future problems.

More precise diagnoses

Currently a diagnosis is made based on tests and investigations of a patient's symptoms. But whilst two patients might share the same symptoms, the cause of them could be different. Knowledge of each individual's complex molecular and cellular processes, informed by other clinical and diagnostic information, will enable us to fully understand the abnormal function and determine the true cause of the symptoms.

This ability to diagnose more precisely can be optimised when coupled with new and improved technologies such as those that provide rapid and real time results and those that can be used at the point of care. Patients and health professionals can make shared decisions about medicines and adjust dosing in real time.

Targeted and personalised interventions

Personalised medicine offers the opportunity to move away from 'trial-and-error' prescribing to optimal therapy first time round.

Currently key pharmaceutical interventions are effective in only 30-60% of patients due to differences in the way an individual responds to and metabolises medicines. Knowledge of the genetic variants responsible for individual drug response can be used to create an individual's 'pharmacogenomic' profile, identifying optimal treatment.

We are already beginning to see the development of simple point of care tests, based on genomic knowledge, which enable clinicians in a wide variety of settings to identify the best therapy. This marks the beginning of an end to the frustrating and costly practice of 'trial-and-error' prescribing. The development and regulatory approval of so called companion diagnostics - a diagnostic test, device or imaging tool used as a companion to a therapeutic drug - is already making this a reality.

Warfarin

Warfarin is a common and effective treatment to prevent blood clots, but patients show a 40-fold difference in dose needed. The current 'trial and error' approach to discover the right dose for an individual means some suffer significant problems as their treatment is worked out. Appropriate testing can be used so people get the right dose sooner – cutting side-effects and improving outcomes.

Variants in our genetic code can also be used to predict the potential for adverse drug reactions. 1 in 15 hospital admissions in the UK are linked to adverse drug reactions. The ability to predict and prevent their occurrence has significant potential to reduce burden on accident and emergency units and to significantly improve a patient's experience.

Preventing dangerous side effects

Abacavir is the first-line treatment for HIV in the NHS. However about 1 in 17 people have a bad reaction to the drug – which, at worst, can be fatal – due to a variation in their immune system. All patients now have a specific genomic test before they start taking Abacavir, which identifies those who would have an allergic reaction. This has significantly reduced the pressure on NHS services that previously had to deal with people who only found out they were allergic after they started taking the drug.

A more participatory role for patients

The ability for a clinician to discuss with their patients information about individual genomic characteristics, lifestyle and environmental factors, and interpret personal data from wearable technology will drive a new type of conversation. They can consider lifestyle changes, and when treatments might not be necessary. It might also lead patients to consider preventative measures when there is high likelihood of a disease developing.

This is a new era of medicine and it requires new knowledge amongst professionals, patients and the public to have confidence in using the information available to them.

Diabetes – when less can be more

The standard approach to newly-diagnosed Type 1 diabetes is to treat it with regular insulin injections. However there are other forms of diabetes that can appear clinically like Type 1 diabetes, but have different underlying causes and can be treated much more simply. A simple genetic test can identify some patients who can be better treated using tablets or even some patients who are best managed by no treatment at all. This prevents the health risks of poorly-managed diabetes, saves these individuals the inconvenience and discomfort of a lifetime of unnecessary injections, and stops the NHS using resources on treatments that they don't need.

3.2 Wider benefits of personalised medicine

In addition to improving outcomes for individuals, personalised medicine has a number of wider benefits.

We can strengthen our ability to design appropriate health and care for our local populations through a more sophisticated understanding of the impact of age, gender and ethnicity or lifestyle factors that influence the onset of disease.

This will enable us to be far smarter in the way that we manage and leverage the limited resources that we have.

New partnerships will be central in driving forward a personalised medicine approach – bringing together clinical practice, academic rigour, industry skills and the active involvement of patients and patient groups. These new relationships will also create opportunities to strengthen the UK's research base, helping to bolster the UK economy through growth in the life science sector.

4 Making personalised medicine a reality in the NHS

We are facing a challenging time in the NHS. Demand continues to rise, placing our services and our staff under huge pressure. Despite this, the NHS continues to ensure that the millions of people who use health services every day receive excellent care.

But it is clear, when funding is so tight, that the pressures on the NHS cannot be relieved by continuing with business as usual. In the NHS Five Year Forward View, the NHS leadership set out a compelling vision for the future. A vision for how the NHS can close the finance and efficiency, care and quality and health and wellbeing gaps by becoming a system informed and shaped by research and innovation, focused on prevention and earlier detection of disease, and able to deliver improvements in outcomes through new models of care. Personalised medicine with science and innovation at its core is integral to making the vision a reality.

The potential benefits of personalised medicine are significant, and the changes are inevitable, but we must rise to the challenge in a considered and proactive way. We will need to embed systematically the approach into mainstream healthcare whilst ensuring the ethical, equality and economic implications are fully recognised and addressed. We must ensure that patients and the public are confident in the use of these technologies and that we can mitigate any potential concerns, particularly in the area of data security and confidentiality.

The approach the NHS takes to commissioning personalised medicine will need to align with activity across the health and care system to ensure it is delivered in an affordable way. We will need to ensure that the system develops appropriate education and training, effective digital and informatics, with deepening patient involvement and empowerment. The potential is significant, and there are real and tangible developments that will take place over the coming decade.

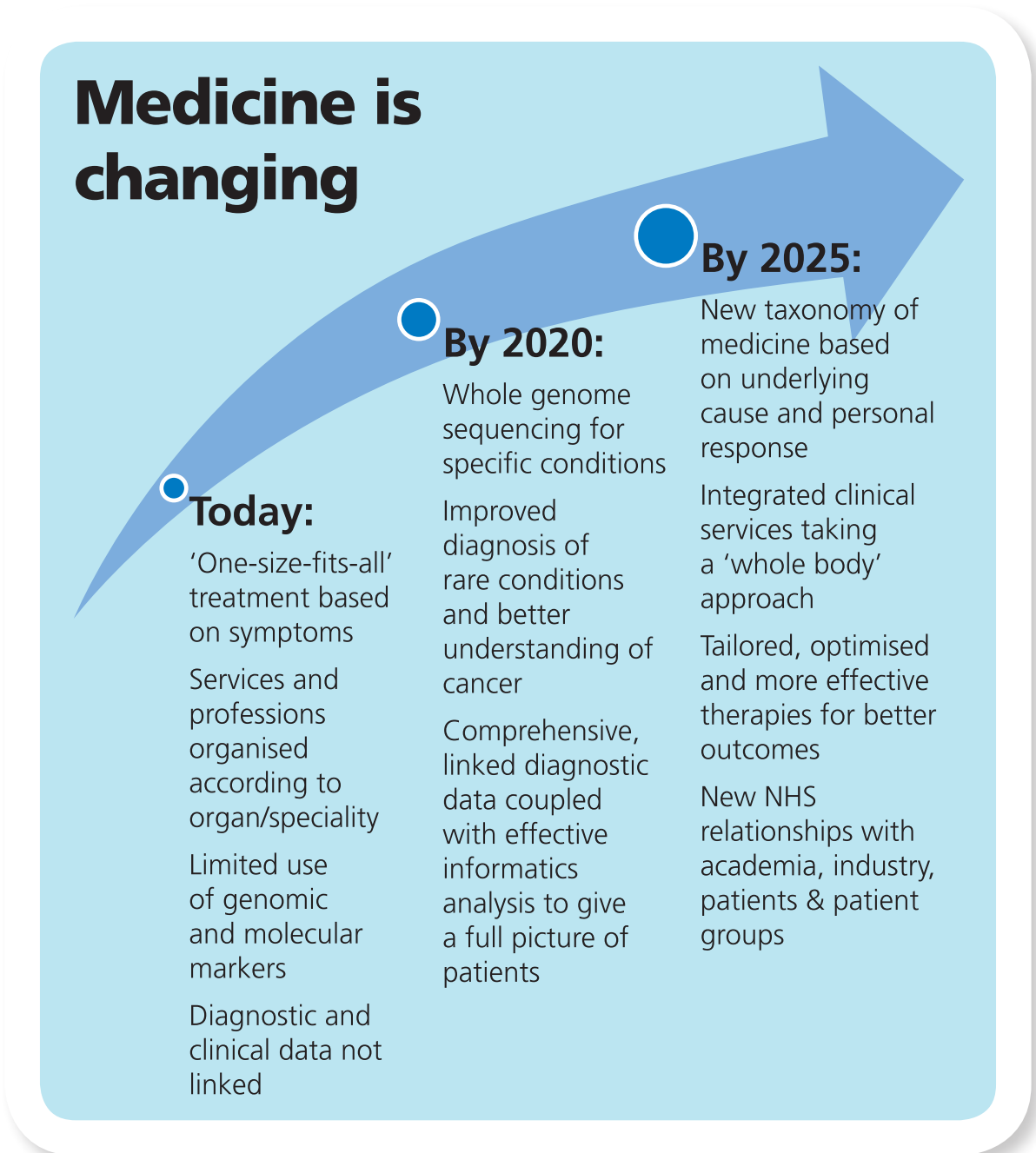
4.1 Embracing the future

Technological developments across a range of areas are coming together to provide the necessary ingredients to spread a personalised medicine approach across healthcare. Genomic technologies are an increasingly large part of the evolution of modern medicine and our understanding of genomic implications is growing. The speed and repertoire of diagnostics more generally is increasing. And informatics advances are making discoveries and connections at an enormous pace.

This is the dawn of a new era in medicine that will need to move and evolve at the scale and pace of scientific and technological advances if real improvements for patients and the public are going to be made. Figure 4 sets out the changes we might see in the coming decade.

Clinical advice and leadership is vital. We have been working with the Academy of Medical Sciences to develop exemplar clinical pathways in key priority areas, such as diabetes and cardiovascular disease, where there is a real opportunity to improve outcomes for patients and our population. We will continue to work with the Academy as well as with the Academy of Medical Royal Colleges, its constituent colleges and other professional groups, to build the evidence base and clinical understanding.

Figure 4



4.2 The building blocks are already in place

In the NHS, we already have the foundations in place to bring the science and data together, through our integrated informatics and genetic laboratory infrastructure.

And we are continuing to develop them by:

- further strengthening our informatics capability and developing data standards with NHS Digital through the Paperless2020 programme;
- creating the infrastructure for personalised medicine through our 13 Genomic Medicine Centres;
- developing our specialist genetic and molecular pathology laboratories – through NHS England’s forthcoming re-procurement and designation to create a national genomics laboratory structure for England;
- investing in the data and informatics infrastructure for the NHS Genomic Medicine Centres; and
- working with Health Education England to develop the workforce capability and expertise to deliver genomic and personalised medicine.

Over the coming years, we will work with our partners to pave the way for personalised medicine approaches to be adopted across the NHS.

We will work with Genomics England, NHS Digital, Department of Health, Health Education England, Public Health England and other partners to:

Engage and involve the public, patients and patient groups, clinicians, academics, industry and others to inform and shape the NHS’s approach to personalised medicine

Build the commissioning, data and informatics infrastructure

Develop the enabling framework to ensure that personalised medicine approaches are proactively adopted based on strong evidence, value and ethics, learning from the 100,000 Genomes Project, and other health initiatives

Roll out a personalised medicine approach in a small number of exemplars, linked to NHS England’s clinical priority areas

4.3 How to get involved

This document has sought to explain why a move away from the current 'one size fits all' approach in healthcare has many benefits, for individuals, for the NHS and for our economy. It is not a simple task; there are a number of challenges including ethical, equitable and economic implications that we will need to address. It is clear that for the NHS to benefit from a personalised medicine approach, we will need to continue to build relationships with patients and their families, academics and industry. We have seen through the delivery of the 100,000 Genomes Project that the NHS is well placed to rise to this challenge.

Over the coming months we will be working with our partners, patients and the public, and leading experts to develop our approach.

If you want to get involved, or just find out the latest information, there are a number of ways you can stay in touch:

- Get in touch with your local NHS Genomic Medicine Centre about their contributions to the 100,000 Genomes Project
- Find out more about the 100,000 Genomes Project from [Genomics England](#).
- Watch out for updates from [NHS England](#) or email england.personalisedmedicine@nhs.net
- Find out more about genomic NHS staff training opportunities from [Health Education England](#).
- If you are from industry and want to find out more about working with the NHS you can contact your local [Academic Health Science Network](#).

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