BIVDA

British In Vitro Diagnostics Association

Leveraging partnerships to realise the UK's potential in genomics

Final Report

CRA Charles River Associates

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Acronyms

ADR	adverse drug reaction
BIVDA	British In Vitro Diagnostics Association
ChT	adjuvant chemotherapy
CRA	Charles River Associates
CRG	clinical reference group
ctDNA	circulating tumour DNA
GDx	genomic diagnostics
GLH	genomic laboratory hub
HCP	healthcare professional
HTA	health technology assessment
ICS	integrated care system
IVD	*in vitro* diagnostic
IVDD	In Vitro Diagnostic Directive
IVDR	In Vitro Diagnostic Medical Device Regulation
MHRA	Medicines and Healthcare products Regulatory Agency
NGS	next-generation sequencing
NGTD	National Genomic Test Directory
NHS	National Health Service
NHSE	National Health Service England
NHS GMS	NHS Genomic Medicine Service
NICE	National Institute for Health and Care Excellence
NSCLC	non-small cell lung cancer
PCR	polymerase chain reaction
RCT	randomised control trial
UC	ulcerative colitis
UK	United Kingdom
US	United States
WES	whole exome sequencing
WGS	whole genome sequencing

Foreword

Dany Bell
Strategic Advisor Treatment, Medicines,
Genomics Macmillan Cancer Support

This report details the value of and explores barriers in genetic and genomic diagnostics delivery and access, making recommendations on how the Genomic Medicine Service infrastructures across the United Kingdom (UK) can overcome them, as well as potential implications for policy review.

Macmillan has a strong relationship with the National Health Service Genomics Medicine Service in England due to wanting to understand how as an organisation we might be able to support people with cancer to benefit from genomics, ensure equity of access, as well as have the right information to enable shared decision making. This requires the professionals that support them to be adequately prepared and able to embed innovation and technology such as genomics into clinical practice, as well as translate often complex information to their patients.

The significant progress and increase in the advances in diagnostics and personalised medicine in cancer care can have an impact on outcomes for people with cancer if utilised appropriately. Equally facilitating diagnosis of rare diseases enabling treatment if the technologies are sustainably translated into clinical practice. However, the translation of cutting-edge technologies such a genomics, despite the progress made since the launch of the genomic medicine services, into pathways and clinical practice, is often challenging, especially when it may require the workforce and the health system to review existing pathways and processes, as well as ensure adequate learning and knowledge at a time when both are under pressure.

This report commissioned by the British In-Vitro Diagnostics Association to identify real life examples of genetic and genomic diagnostics to understand and demonstrate value, as well as the barriers faced by clinicians and the system, has recommendations that should help the NHS Genomics Medicine Services infrastructure. Some of the barriers are known but the examples of partnerships and the need for collaborative working are evident in the real-life examples.

The reference to genomic medicine infrastructure within the UK outside England is not well represented in this report but the messages apply to all four nations within the UK. However, it is important to understand the infrastructure for all nations and how they are working together to achieve the Genome UK strategy, also to ensure there is not inequity across the Genomic Medicine Services for patients within the UK. To complement this work, it would be good to see patient engagement as the next step to building an understanding of the value and barriers to support progression of embedding genetic and genomic diagnostics within pathways across the UK.

This report is a good start in outlining continued barriers and the potential to leverage partnerships to realise improved access to genetic and genomic diagnostics within the National Health service in the UK and I hope it will facilitate discussion and action.

Foreword

Philip Beer
Chair, BIVDA Genomics Working Group

A key learning from the COVID-19 pandemic is that rapid progress can be made when healthcare, academia and industry work together towards a singular goal. An obvious question then arises: can this success be repeated in other areas such as the diagnosis and treatment of cancer?

BIVDA's Genomics Working Group set out in early 2021 to examine the genomics ecosystem in the UK, with an initial focus on oncology. Cancer is a disease of the genome and a lead exemplar for genomic medicine, having already yielded many examples of successful genomically-directed therapy. The NHS has shown great vision in recent years in prioritising personalised medicine and planning an infrastructure to deliver a genomic medicine service. However, despite the UK's position as a leader in genomic innovation, patient access remains suboptimal.

BIVDA commissioned Charles River Associates to undertake an independent review of the provision of genomic testing in the NHS, with a focus on two key areas:

1. to articulate and evidence the value framework for advanced in vitro diagnostics;
2. to determine the key enablers of new partnership models, and how such models might improve patient access.

This review identifies key challenges that are currently limiting patient access to genomic testing in the UK. Importantly, this work characterises potential solutions to these problems, through the improved utilisation of industry-healthcare partnerships, licensed by national policy change.

Democratised access to genomic diagnostics has the potential to significantly impact the lives of those with cancer, through the development of new drugs and the improved use of existing therapies. Benefits to the wider healthcare system include more efficient use of financial and personnel resources. Revenue generating opportunities for the UK include the growth of an advanced diagnostic technology ecosystem and the creation of an optimal infrastructure for the delivery of clinical trials of biomarker associated therapies.

This report describes a framework for a reinvigorated approach to the delivery of genomic medicine, based on deeper and more effective collaboration between healthcare and industry. Creating an environment to foster such partnerships has the potential to accelerate the process of unlocking the full utility of genomics in medicine.

Foreword

BIVDA, is the UK industry association representing IVD companies active in the UK, whether they are UK manufacturers, distributors or the UK subsidiaries of global organisations. One of our roles is to amplify the voice of the industry through activities such as the publication of this report.

The role of *in vitro* diagnostics (IVDs) in healthcare has become much more widely recognised since 2020 and IVDs will play an increasing role in the future in areas such as enabling faster diagnosis, as well as better management of resources such as reduction in admissions to secondary care and more targeted drug treatment. Significantly, IVDs will allow more accurate treatment and improved outcomes for the population.
As the knowledge of genomics increases, so does the significance of using diagnostics to allow greater precision in drug use and truly individualised medical care. To realise this potential will require the right infrastructure and a partnership with both the pharmaceutical and diagnostics industry sectors.
So, I commend this report, commissioned by the BIVDA Genomics Working Group under the leadership of its Chair, Dr Philip Beer.

Doris-Ann Williams MBE
Chief Executive

Executive summary

Genetic and genomic diagnostics (GDx) are becoming increasingly important for patients, the health system and society. Some of the many ways in which GDx deliver value in the United Kingdom (UK) are by optimising diagnosis and treatment, alleviating pressure on the healthcare system, and supporting economic growth – contributing to two of the Prime Minister's five priorities for 2023.[1] But despite the UK's position as a leader in genomic innovation, patient access to these innovative technologies as part of standard clinical practice remains limited. For example, the UK currently ranks 19th in Europe for uptake of next-generation sequencing in non-small cell lung cancer (NSCLC).[2]

Charles River Associates (CRA) was asked by the British In Vitro Diagnostics Association (BIVDA) to investigate real-life examples of GDx to understand the value they deliver, the barriers they face and the role of partnerships in overcoming these barriers and improving patient access to GDx. We were asked to draw on this experience and develop policy recommendations that would deliver opportunities to ensure UK patients and the National Health Service (NHS) don't miss out on the value of these technologies.

Four key challenges are limiting patient access, as set out in Box 1.

Box 1: Key challenges limiting patient access to GDx in the UK

- The evolving UK regulatory framework for GDx, including development of new approaches for assessing software, has created an uncertain environment which risks causing bottlenecks that could exacerbate delays to patient access.
- There is a lack of centralised guidance on the applicability of different funding pathways for different genomic technologies in the UK, often resulting in access delays and inequity, with tests being available in some NHS trusts but not others.
- Current value assessment models fail to fully capture the value of GDx, and a positive value assessment outcome is not linked to the decision to reimburse the test, resulting in a lack of incentive for evidence generation.
- Despite the strength of the NHS Genomic Medicine Service, gaps remain in the broader infrastructure required or uptake of testing, such as a lack of accessible education for physicians and patients, leading to variability in use across the UK.

Six partnerships were examined in detail and a taxonomy of types of partnership models was defined. Partnerships with two primary objectives were identified: (1) partnerships aimed at promoting the adoption of new technologies, (2) partnerships aimed at developing the GDx infrastructure. Within the category of partnerships aimed at adopting new technologies, we distinguish between those that support the establishment of clinical reference centres and those that are larger-scale implementation pilots.

Many lessons can be learned from the examples of successful partnerships between the health system and the diagnostics industry that have provided patient access to novel, cutting-edge genomic technologies. For example, the NHS has partnered with the GDx manufacturer GRAIL to pilot the adoption of a new cancer detection GDx in 140,000 patients across England to help inform the future of cancer screening in the UK.[3] Through such 'learning by doing' approaches, several ways in which partnerships can help overcome the described challenges and support patient access have already been found, as set out in Box 2.

[1] https://www.gov.uk/government/news/prime-minister-outlines-his-five-key-priorities-for-2023 [Accessed April 2023]
[2] Normanno, N. et al. (2022) Access and quality of biomarker testing for precision oncology in Europe. European Journal of Cancer. 176:70–77.
[3] https://grail.com/clinical-studies/nhs-galleri-trial-clinical/ [Accessed April 2023]

Box 2: The role of partnerships in overcoming access challenges

- Partnerships can set out key roles and responsibilities for regulatory knowledge management and data handling between stakeholders, establishing new ways of working and best practices to inform future regulatory policy.
- They can provide a means for NHS trusts to access new technologies in the absence of or preceding a national reimbursement decision and can catalyse national commissioning decisions, supporting faster patient access.
- The evidence generated through adopting novel GDx on a pilot basis can facilitate UK evidence generation to support a downstream value assessment and evidence-based guidelines for the adoption of new tests.
- Partnerships can provide a cornerstone for establishing new GDx infrastructure within the NHS, with companies able to provide capacity and capabilities that would be too resource-intensive for individual NHS trusts and laboratories to establish.

Despite the clear value of these industry–healthcare system partnerships in providing solutions to the challenges surrounding patient access, barriers to their implementation and impact remain. There is no systematic approach to matching up service needs to service offerings. Further, engaging only where a clearly defined business case meets a clearly defined clinical need restricts opportunities for the NHS to benefit from new disruptive technologies that do not yet have a clearly defined position in the clinical pathway.

There is an opportunity now for proactively fostering such partnerships through targeted policy action, including establishing more efficient pathways for new technologies to be identified and piloted in the NHS, developing guidelines for the collection and publication of evidence that is generated over the course of partnership, and creating a forum for documenting and sharing lessons from the implementation of new technologies.

However, this alone is unlikely to resolve all challenges associated with integrating novel GDx routinely and sustainability into clinical practice across the UK. Beyond supporting the growth and expansion of partnerships, targeted policy intervention is also required to address the root causes of the impeded adoption of GDx technologies in the UK health system and support routine patient access, as set out in Box 3.

Box 3: The role of policy change in addressing the root causes of UK access barriers

Policy change could address the root causes of UK access barriers in several ways:

- Effectively implementing a new regulatory framework covering GDx in the UK, learning from international experiences and providing appropriate guidance and support for companies to avoid access bottlenecks
- Providing greater clarity and guidance on pathways into regulatory approval and commissioning novel GDx across the UK, minimising the need for individual duplication of efforts and decisions at a subnational level and thus preventing inequity and delays in access
- Optimising the role of value assessment in informing funding decisions and uptake of novel GDx by increasing the efficiency of evidence generation and incentivising evidence generation through linking this more strongly with funding and access
- Supporting adoption of GDx through a more proactive approach towards horizon scanning and preparedness for new, increasingly digital technologies, introducing key performance indicators to monitor implementation, and providing accessible and appropriate education for clinicians, patients and decision makers

1. Introduction

Charles River Associates ('CRA') was commissioned by the British In Vitro Diagnostics Association ('BIVDA') to undertake a review of the UK genomics landscape focusing on patient access to genomic testing, particularly in England.
he aim was threefold:

- To demonstrate the value of genomic diagnostics (GDx) and include evidence for the real benefits they bring to patients and the health system in the UK
- To identify and describe any outstanding barriers to access to GDx that may prevent the full value of these technologies from being realised in the UK
- To understand the role of partnerships between the diagnostics industry and the UK health system in facilitating improved patient access to genomics and implications for policy change

1.1. Background

The use of genetic and genomic testing to diagnose and optimise treatment has increased substantially in recent years, driven by rapid advances in scientific understanding and technological development. This has enabled significant progress to be made in the field of personalised medicine, allowing prevention, diagnosis and treatment approaches to be tailored to individuals and groups of individuals. Between 2016 and 2020, the number of marketed personalised medicines almost doubled, from 132 to 236.[5] More recently, during the COVID-19 pandemic, the power of advanced diagnostics was put to the test from a public health perspective. Between March 2020 and February 2022, the UK sequenced over two million SARS-CoV-2 genomes,[5] using the data to inform local, national and international policy decisions and contributing to the curbing of viral spread. More broadly, genomic testing has also become a standard practice in many disease areas, particularly in the identification of rare diseases, the optimisation of cancer treatment, and in prenatal and neonatal screening programmes.[6]

The UK has been at the forefront of genomics since the sequencing of the first human genome in the Human Genome Project between 1990 and 2003, with British scientists contributing to the international collaborative effort.[7] Since then, the UK government and health services across the devolved nations have invested substantial resources in harnessing the potential of genomics for the benefit of UK patients. In England, this has been driven by the multi-year 100,000 Genomes Project and the subsequent establishment of the National Health Service Genomic Medicine Service (NHS GMS) in 2018, which aims to build on the achievements of the 100,000 Genomes Project and integrate genome sequencing into routine NHS clinical practice.[8],[9] The NHS Long Term Plan published in 2019 set out a commitment that the NHS GMS would sequence 500,000 whole genomes by 2023/24.[10] In October 2022, four years on from the creation of the NHS GMS, NHS England outlined an ambitious strategy for embedding genomic medicine in the NHS and creating a "world leading, innovative service model".[11] Shortly after, in March 2022, the UK government, working with health ministers from the devolved nations of Scotland, Wales and Northern Ireland, also published a set of over 30 shared commitments for UK-wide implementation of genomic healthcare,[12] indicating an ongoing political willingness.

[4] Personalized Medicine Consortium (2020) "The Personalized Medicine Report: Opportunity, Challenges, and the Future". Available at: https://www.personalizedmedicinecoalition.org/Userfiles/PMCCorporate/file/PMC_The_Personalized_Medicine_Report_Opportunity_Challenges_and_the_Future.pdf [Accessed April 2023]
[5] https://www.gov.uk/government/news/uk-completes-over-2-million-sars-cov-2-whole-genome-sequences [Accessed April 2023]
[6] Krier, J. B., Kalia, S. S. and Green, R. C. (2022) Genomic sequencing in clinical practice: applications, challenges, and opportunities. Dialogues in Clinical Neuroscience. 18(3): 299–312.
[7] https://www.genome.gov/11006939/ihg-sequencing-centers [Accessed April 2023]
[8] Turnbull, C. et al. (2018) The 100 000 Genomes Project: bringing whole genome sequencing to the NHS. BMJ. 361:k1687.
[9] https://www.england.nhs.uk/genomics/nhs-genomic-med-service/ [Accessed April 2023]
[10] https://www.england.nhs.uk/genomics/nhs-genomic-med-service [Accessed April 2023]
[11] NHS England (2022) Accelerating genomic medicine in the NHS. Available at: https://www.england.nhs.uk/longread/ accelerating-genomic-medicine-in-the-nhs/ [Accessed April 2023]
[12] UK Government (2022) Genome UK: 2022 to 2025 implementation plan for England. Available at: https://www.gov.uk/government/publications/genome-uk-2022-to-2025-implementation-plan-forengland/genome-uk-2022-to-2025-implementation-plan-for-england [Accessed April 2023]

However, successfully integrating novel, cutting-edge technologies such as genomic diagnostics into clinical practice presents great challenges to healthcare systems. Despite the availability of an increasing quantity and quality of GDx, data shows these tests are underutilised across many indications. This is not unique to the UK. One study based in the United States (US) found that <10% of paediatric patients with phenotypes suggestive of genetic disease received genetic testing.[13] Another showed that, despite all stage IV non-small cell lung cancer (NSCLC) patients being eligible for tumour sequencing, only 22% of patients had been tested, and only 3% were treated with a targeted therapy.[14] A recent European patient survey, which included patients in England, found that 80% of breast cancer patients eligible for genomic testing are not told it is available to them.[15] Despite the political support and advances made in the UK from a research perspective, evidence indicates that access to genetic and genomic testing in a clinical setting also remains a challenge in the UK.[16] For example, although a high percentage of precision oncology medicines are reimbursed in the UK, there is typically at least a one-year lag between reimbursement of a targeted oncology medicine and reimbursement of the associated genetic test.[17] Total uptake of genomic testing is also low, with the UK ranking 19th in Europe for uptake of next-generation sequencing (NGS) in NSCLC.[18] Several reasons for this have been discussed in the literature, such as the limitations in funding and in NHS capacity,[19] even though many genomic tests have the potential to save the health system both time and money once implemented.

In this report, we develop new evidence of the value of genomic testing in the UK health system, the barriers that currently impede timely and widespread patient access, and the role of partnerships in overcoming these barriers.

Definitions

This report uses the term 'genomic diagnostics' (GDx) to refer to any in vitro diagnostic (IVD) that serves to detect clinically relevant variations in the genome, transcriptome or proteome of an individual, or their microbiome. These include, but are not limited to, whole genome sequencing (WGS), whole exome sequencing (WES), circulating tumour DNA (ctDNA) testing and RNA sequencing. We focus primarily on diagnostics that involve the analysis of multiple genes or entire genomes, rather than single or limited gene sequencing, as these technologies represent the latest paradigm shift in clinical pathways and therefore are expected to experience novel access challenges and complexities. We exclude direct-to-consumer genomic testing, despite the rise of its popularity, as this report focuses on testing within the NHS to inform policy changes that can impact patient access to genomic testing in a clinical setting across the UK.

[13] Schroeder, B. E. et al. (2021) The diagnostic trajectory of infants and children with clinical features of genetic disease. NPJ Genomic Medicine. 6(1): 98.
[14] Behera, M. et al. (2022) Molecular testing and patterns of treatment in patients with NSCLC: An IASLC analysis of ASCO CancerLinQ Discovery Data. Journal of Clinical Oncology. 40:16 suppl. 9128.
[15] https://cancerpatientseurope.org/myc-first-european-wide-patient-survey-in-genomic-testing-in-breast-cancer/ [Accessed April 2023]
[16] Turner, R. M. et al. (2020) Pharmacogenomics in the UK National Health Service: opportunities and challenges. Pharmacogenomics. 21(17): 1237–1246.
[17] Normanno, N. et al. (2022) Access and quality of biomarker testing for precision oncology in Europe. European Journal of Cancer. 176:70–77.
[18] Normanno, N. et al. (2022) Access and quality of biomarker testing for precision oncology in Europe. European Journal of Cancer. 176:70–77.
[19] Turner, R. M. et al. (2020) Pharmacogenomics in the UK National Health Service: opportunities and challenges. Pharmacogenomics. 21(17): 1237–1246.

1.2. Methodology

Our research involved three key steps:

- A literature review of recent trends in the field of genomics, including case studies demonstrating the value of genomic testing, and a review of the access environment for such technologies in the UK, focusing on England
- An analysis of partnerships between the diagnostics industry and the UK health system
- An interview programme with senior executives from the advanced diagnostics industry, including companies with innovative testing technologies as well as service providers, to gather their perspective on the value of genomic testing and partnerships

1.2.1. Literature review

CRA undertook a literature review of governmental, non-governmental, industry and academic literature to collect recent evidence of the impact of genomic testing on patients, healthcare systems, societies and economies. Information on the access pathway for GDx in the UK was also gathered from these sources, with an additional targeted search of governmental and NHS websites. A variety of search terms were used in combination, including: 'genomic testing', 'in vitro diagnostics', 'access', 'funding', 'reimbursement' and 'value assessment'. The literature review conducted between October 2022 and December 2022 included global studies as well as a detailed analysis of UK-specific literature, with a focus on England given the larger population size. Over 40 academic articles and over 150 grey literature sources were reviewed in total.

To gain a more in-depth understanding of the level of access to GDx in the UK and the value this has brought, we also searched for recently published case studies of specific technologies that have been implemented in the UK at a national and sub-national level. In total, 20 case studies were identified through news sources, academic literature, and press releases published by diagnostic companies, NHS England, and Genomics England; a subset of these case studies that most clearly evidence the value of genomic diagnostics are described in the report.

1.2.2. Partnership analysis

In parallel with the literature review, we identified and assessed publicly available examples of partnerships between the NHS or Genomics England and the GDx industry. Our definition of partnerships covered any agreement between the health service (NHS England, individual NHS trusts, or Genomics England) and the GDx industry that directly contributed to increasing patient access to GDx.

These examples were primarily identified from press releases and results from such collaborations that have been published in academic journals. The goal of the analysis was to catalogue the types of partnership models that have been employed and evidence of the benefits these deliver, and to understand their role in supporting patient access to GDx in the UK. Six partnership examples were identified and assessed based on secondary research (Table 1).

Table 1: Identified genomic testing partnership models in the UK

Health system partner	Diagnostics industry partner	Description of partnership
Manchester University NHS Foundation Trust	Genedrive plc	Implementation trial of rapid point-of-care genotyping in acute neonatal setting to avoid antibiotic-induced hearing loss[20]
The Royal Marsden NHS Foundation Trust	Guardant Health	Establishment of in-house liquid biopsy testing facility for cancer diagnostics in an NHS trust[21]
Genomics England	Illumina	Delivery of whole genome equivalents for 100,000 Genomes Project and NHS Genomic Medicine Service[22]
Genomics England	Congenica	Provision of Diagnostic Decision Support Services in delivering the NHS Genomic Medicine Service[23]
NHS England	GRAIL	Trial to evaluate potential for NHS adoption of a blood test for multiple cancer detection alongside existing cancer screening[24]
NHS England	Genomics plc	Pilot of integration of polygenic risk scores into current GP clinical practice for prevention of cardiovascular disease[25]

1.2.3. Interview programme

To complement the secondary research, we conducted a set of 10 interviews with senior executives from companies that develop genomic diagnostic technologies or provide services to support the genomics industry in the UK. These were conducted in November and December 2022. The interviews provided insight on the access pathway for genomic technologies in the UK and challenges that companies face in bringing their technologies to the UK, the value they deliver and partnerships.

The findings from these interviews are described in aggregate throughout the report and do not reflect any individual company's perspective. References to specific proprietary technologies and partnerships throughout the report are based only on publicly available data and information.and Genomics England; a subset of these case studies that most clearly evidence the value of genomic diagnostics are described in the report.

1.3. Structure of this report

The structure of this report is as follows:

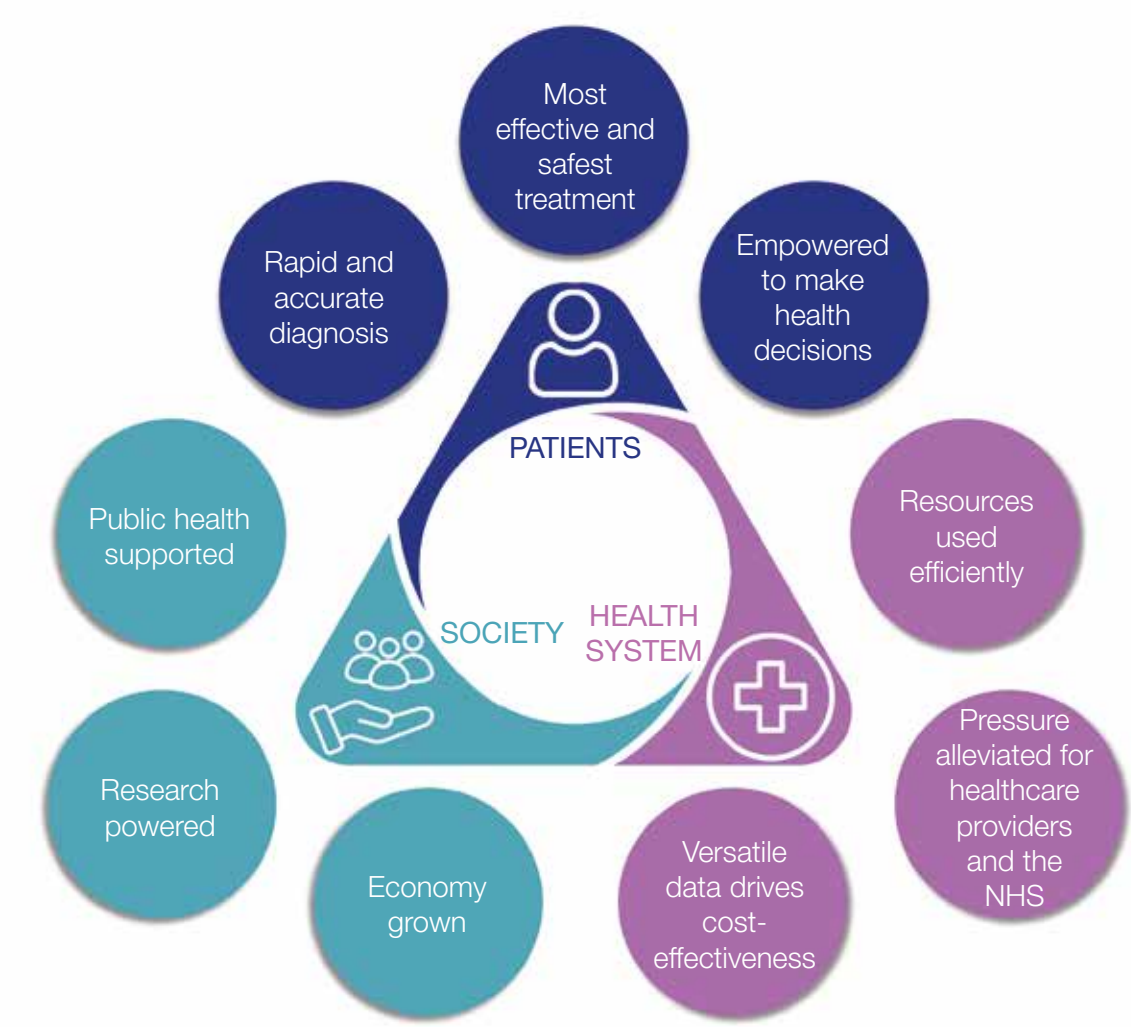
- Chapter 2 provides evidence of the value of genomic testing to UK patients, to the system of healthcare providers, and to the UK's society and economy.
- Chapter 3 reviews the current access pathway for novel GDx in the UK and identifies challenges that can impede timely and widespread patient access.
- Chapter 4 assesses the role of partnerships between the diagnostics industry and the UK health system.
- Chapter 5 identifies policy changes needed to support the development of effective partnerships and address the underlying issues in the access environment.

[20] McDermott, J. H. et al. (2022) Rapid Point-of-Care Genotyping to Avoid Aminoglycoside-Induced Ototoxicity in Neonatal Intensive Care. JAMA Pediatr. 176(5): 486–492.
[21] https://investors.guardanthealth.com/press-releases/press-releases/2021/Guardant-Health-and-The-Royal-Marsden-NHS-Foundation-Trust-Announce-Partnership-to-Establish-First-Guardant-Health-Liquid-Biopsy-Testing-Service-Based-in-the-United-Kingdom/default.aspx [Accessed April 2023]
[22] https://www.genomicsengland.co.uk/news/genomics-england-and-illumina-sequence-whole-genomes-for-nhsgmsNHSGMS [Accessed April 2023]
[23] https://blog.congenica.com/2018/10/17/congenica-earns-major-role-supporting-worlds-first-routine-nationalgenomic-medicine-service [Accessed April 2023]
[24] https://www.nhs-galleri.org/about-the-trial [Accessed April 2023]
[25] https://www.genomicsplc.com/news/successful-world-first-pilot-using-improved-genomic-risk-assessment-incardiovascular-disease-prevention-in-the-nhs/ [Accessed April 2023]

2. The value of genomic diagnostics

Developments in science and technology have led to an acceleration in the abundance and availability of genomic diagnostics.[26] There is an existing literature that documents how GDx provide significant value to patients, healthcare systems and society. Drawing on primary and secondary research, we sought to capture the full breadth of value that GDx can offer to patients and clinicians in the UK, to the UK health system and to society more broadly (summarised in Figure 1).

Figure 1: The value of genomic testing to patients, health systems and society



Source: CRA analysis

[26] NHS England (2022) Accelerating genomic medicine in the NHS. Available at: https://www.england.nhs.uk/longread/accelerating-genomic-medicine-in-the-nhs [Accessed April 2023]

2.1. Value for patients

Enabling rapid and accurate diagnosis

The primary benefit of GDx is providing a patient with an improved diagnosis.[27] GDx have proven to be powerful tools in unlocking diagnoses in the most complex and rare of cases, and in enabling more rapid diagnoses across disease areas:

- Patients with rare diseases can suffer from lengthy diagnostic odysseys, which have a significant impact on their health and well-being.[28] Patients may have to undergo many invasive tests, and misdiagnoses might lead to use of treatments with little benefit and/or potential harm to the patient.[29] GDx with a broad scope, such as WGS, can be of immense value in such cases, ending – or increasingly preventing – diagnostic odysseys.[29] For example, Olmsted syndrome (OS) is a very rare disease, occurring in fewer than 1 in 1,000,000 people, causing atypical skin growth and joint abnormalities, resulting in chronic severe pain.[30] In one case, a patient in the UK reported a diagnostic odyssey of greater than 40 years, with severe impacts to their mental health. After WGS, the patient was diagnosed with OS and could be treated; within 24 hours, the patient's symptoms began to ease.[31]
- GDx also provide significant diagnostic value to patients with the most common diseases. For example, ~375,000 people in the UK are diagnosed with cancer every year.[32] Emerging technologies such as ctDNA screening can detect cancer earlier, from a simple blood test, enabling patients to be stratified for confirmatory testing.[33] In addition, routine implementation of such technologies will make progress towards the NHS Long Term Plan's 'Ambitions for Cancer' to ensure that 75% of cancer patients are diagnosed at an early stage.[34]

Delivering the most effective and safe treatment

GDx can also enable an individual's treatment to be personally optimised to maximise effectiveness and minimise adverse events:

- Novel clinical decision support diagnostics can be used to predict the effectiveness and/or safety of a given pharmaceutical intervention based on the genome of an individual, in socalled pharmacogenomics.35 A recent Europe-wide multicentre randomised controlled trial in nearly 7,000 patients demonstrated the potential of such diagnostics; genotypeguided treatment using a 12-gene pharmacogenetic panel significantly reduced the incidence of clinically relevant adverse drug reactions.[36]
- The utility of such technologies extends beyond analysis of an individual's genome; socalled pharmacomicrobiomics involves metagenomic profiling of a stool sample to determine the biodiversity, abundance and functions of bacteria in the gut microbiome. In Crohn's disease and ulcerative colitis (UC), many patients go through a trial-and-error process of 3-6 months on each biologic to find the optimal therapy. Pharmacomicrobiomics can predict each patient's individual response to biologics, informing clinicians' decisions regarding the most efficacious therapy and thus mitigating the long and arduous treatment journey for the patient.[37],[38]

[27] CRA analysis
[28] Hay, E. et al. (2022) The Diagnostic Odyssey in rare diseases; a Task and Finish Group report for the Department of Health and Social Care [version 1; not peer reviewed]. NIHR Open Res 2022, 2:3
[29] https://www.genomicseducation.hee.nhs.uk/glossary/diagnostic-odyssey [Accessed April 2023]
[30] Duchatelet, S. and Hovnanian, A. (2015) Olmsted syndrome: clinical, molecular and therapeutic aspects. Orphanet J Rare Dis 10, 33
[31] https://www.genomicsengland.co.uk/patients-participants/stories/alan [Accessed April 2023]
[32] https://www.cancerresearchuk.org/health-professional/cancer-statistics-for-the-uk [Accessed April 2023]
[33] Campos-Carrillo, A. et al. (2020). Circulating tumor DNA as an early cancer detection tool. Pharmacology & therapeutics. 207, 107458.
[34] https://www.england.nhs.uk/cancer/strategy [Accessed April 2023]
[35] Royal College of Physicians and British Pharmacological Society (2022) Personalised prescribing: using pharmacogenomics to improve patient outcomes. Available at: https://www.rcp.ac.uk/projects/outputs/personalised-prescribing-using-pharmacogenomics-improve-patientoutcomes [Accessed April 2023]
[36] Swen, Jesse J. et al. (2023) A 12-gene pharmacogenetic panel to prevent adverse drug reactions: an open-label, multicentre, controlled, cluster-randomised crossover implementation study. The Lancet 401.10374 347–356.
[37] https://www.microbiometimes.com/microbiome-based-diagnostics-and-biomarkers-changing-the-paradigm-inmicrobiology- and-medicine/ [Accessed April 2023]
[38] http://newcastle.mic.nihr.ac.uk/impact_posts/evaluating-a-test-for-improving-treatment-of-inflammatory-boweldisease [Accessed April 2023]

- The side effects of many medications can vary dramatically, depending on an individual's genome, and severe adverse drug reactions (ADRs) can be avoided with appropriate pharmacogenomic screening.[39] ADRs account for 6.5% of UK hospital admissions, imposing significant pressure on the NHS, but many such events are avoidable.[40] For example, broad spectrum aminoglycoside antibiotics used in the treatment of sepsis can cause hearing loss in patients with a certain variant of the mitochondrial (MT) RNR1 gene, affecting as many as 1 in 500 people. Testing for this variant is available in the UK, but turnaround takes several weeks.[41] However, a novel GDx, which entered the National Institute for Health and Care Excellence (NICE)'s Early Value Assessment Programme (EVAP) evaluation in September 2022, can deliver a result in just 26 minutes, avoiding the high-risk use of aminoglycosides in predisposed patients and thereby preventing avoidable hearing loss.[42],[43]

Empowering patients to make health decisions

GDx can deliver knowledge that empowers individuals to make informed decisions about their own health and well-being:[44]

- GDx can provide new knowledge that enables individuals to make informed changes to their behaviour to minimise health risks. For example, the HEART study undertaken in North East England uses novel software to predict an individual's risk of heart disease from WGS of a blood sample taken in a routine GP appointment, equipping patients with the knowledge to make lifestyle changes that can reduce their risk of heart disease.[45],[46]
- GDx can also empower expectant parents to make informed decisions about their pregnancy. For example, a blood sample from an expectant mother can be screened for cell-free DNA shed from the placenta, enabling non-invasive prenatal testing (NIPT) to screen for inherited diseases or syndromes including Down's, Patau's and Edwards'.[47],[48] This empowers parents with knowledge about the health of their child, and the UK National Screening Committee has recommended the introduction of NIPT as part of the NHS foetal anomaly screening programme (FASP)49, with several NHS trusts including St George's and Nottingham having also begun offering this service privately.[50],[51]

  Furthermore, NIPT based screening for familial retinoblastoma was made available (via the NHS GMS) in 2022 to families with a history of the rare cancer.[52],[53]

[39] Royal College of Physicians and British Pharmacological Society (2022) Personalised prescribing: using pharmacogenomics to improve patient outcomes. Available at: https://www.rcp.ac.uk/projects/outputs/personalised-prescribing-using-pharmacogenomics-improve-patientoutcomes [Accessed April 2023]
[40] UK Government (2020) Genome UK: The future of healthcare. Available at https://www.gov.uk/government/publications/genome-uk-the-future-of-healthcare [Accessed April 2023]
[41] Royal College of Physicians and British Pharmacological Society (2022) Personalised prescribing: using pharmacogenomics to improve patient outcomes. Available at: https://www.rcp.ac.uk/projects/outputs/personalised-prescribing-using-pharmacogenomics-improve-patientoutcomes [Accessed April 2023]
[42] McDermott, J. H. et al. (2022) Rapid Point-of-Care Genotyping to Avoid Aminoglycoside-Induced Ototoxicity in Neonatal Intensive Care. JAMA Pediatr. 176(5): 486–492.
[43] http://www.genedriveplc.com/press-releases/gdr_-_nice_(26.09.22).pdf [Accessed April 2023]
[44] McAllister, M. (2016) Genomics and patient empowerment. In Genomics and society (pp. 39–68). Academic Press.
[45] https://www.genomicseducation.hee.nhs.uk/blog/nhs-launches-new-polygenic-scores-trial-for-heart-disease [Accessed April 2023]
[46] https://www.genomicsplc.com/news/successful-world-first-pilot-using-improved-genomic-risk-assessment-incardiovascular- disease-prevention-in-the-nhs [Accessed April 2023]
[47] https://www.genomicseducation.hee.nhs.uk/blog/nhs-launches-sight-saving-nipt-test [Accessed April 2023]
[48] Carbone, L. et al. (2020) Non-invasive prenatal testing: current perspectives and future challenges. Genes. 12(1):15.
[49] https://www.gov.uk/government/publications/screening-for-downs-syndrome-edwards-syndrome-and-pataussyndrome- non-invasive-prenatal-testing-nipt [Accessed April 2023]
[50] https://www.nuh.nhs.uk/about-the-nipt-test [Accessed April 2023]
[51] https://www.stgeorges.nhs.uk/service/maternity-services/your-pregnancy/fetal-medicine-unit/the-safe-test [Accessed April 2023]
[52] https://www.genomicseducation.hee.nhs.uk/blog/nhs-launches-sight-saving-nipt-test [Accessed April 2023]
[53] https://www.england.nhs.uk/2022/05/babies-to-get-new-test-for-eye-cancer-in-the-womb-to-save-their-sight [Accessed April 2023]

- Furthermore, GDx can help equip parents to make informed decisions regarding the care of their child. For example, many novel gene therapies (GTx) are only prescribed on the basis of genetic diagnoses.[54],[55],[56] At least 334 potentially durable non-oncology gene therapies were in development as of mid-2022,57 but parents may face uncertainty surrounding the treatment of their newborn with novel gene therapies; genetic diagnoses empower parents to make an informed decision in such a sensitive situation.[58] Additionally, studies suggest that at least 3,000 babies per year could benefit from lifesaving or life-changing treatment thanks to WGS; thus, the Newborn Genomes programme, launched in December 2022,59 will pilot WGS in 100,000 newborns to provide parents with crucial knowledge about the genomic health of their child, informing treatment decisions for thousands more families.[60]

2.2. Value for healthcare providers and the healthcare system

Alleviating pressure on healthcare professionals and the NHS

Healthcare professionals (HCPs) – from healthcare assistants, nurses and general practitioners to specialist consultants – are highly valuable assets of the NHS. The NHS system as a whole is currently experiencing some of the most severe pressures in its 70-year history.[61],[62] GDx can deliver significant value in alleviating this pressure. Diagnosing diseases earlier and more efficiently, and empowering individuals with knowledge about their own health, contribute to this by reducing unnecessary contact with the NHS, thus freeing up capacity.

- As well as their impact on the patient, diagnostic odysseys are significantly burdensome for the healthcare system. By enabling rapid and accurate diagnoses, GDx can deliver relief of this burden. In an example from just one individual, a 10-year-old girl who was part of the 100,000 Genomes Project, her diagnostic odyssey spanning seven years had involved multiple intensive care admissions and over 307 hospital visits at a cost of £356,571. Genomic diagnosis enabled her to receive a curative bone marrow transplant (at a cost of £70,000), and predictive testing of her siblings showed no further family members were at risk.[63]
- A specific example is the Oncotype DX Breast Recurrence Score® Test, an established technology that can predict the effectiveness of adjuvant chemotherapy (ChT) in early breast cancer patients, thus minimising its use in patients for whom ChT is likely to be ineffective.[64] As well as its value in identifying patients for whom the benefit of ChT is unlikely to outweigh the risk, and in reducing the significant costs of ChT to the UK economy,[65] this also prevents unnecessary hospital trips, saving valuable time for oncologists and nurses and alleviating a degree of NHS pressure.[66]

[54] https://www.nice.org.uk/guidance/hst15 [Accessed April 2023]
[55] https://www.nice.org.uk/guidance/hst11 [Accessed April 2023]
[56] https://www.nice.org.uk/guidance/hst7 [Accessed April 2023]
[57] Vockley, J. et al. (2023) The evolving role of medical geneticists in the era of gene therapy: an urgency to prepare. Genetics in Medicine. 100022.
[58] Marshall, D. A. et al. (2019) The value of diagnostic testing for parents of children with rare genetic diseases. Genet Med. 21(11): 2662.
[59] https://www.qmul.ac.uk/media/news/2022/smd/uk-government-launches-newborn-genomes-programme.html [Accessed April 2023]
[60] https://files.genomicsengland.co.uk/documents/Newborns-Vision-Final_SEP_2021-11-02-122418_jjne.pdf [Accessed April 2023]
[61] https://www.bma.org.uk/advice-and-support/nhs-delivery-and-workforce/pressures/an-nhs-under-pressure [Accessed April 2023]
[62] https://www.bbc.co.uk/news/health-64142614 [Accessed April 2023]
[63] 100,000 Genomes Project Pilot Investigators (2021) 100,000 genomes pilot on rare-disease diagnosis in health care – preliminary report. New England Journal of Medicine. 385(20): 1868–1880.
[64] McVeigh, T. P. et al. (2017) Clinical use of the Oncotype DX genomic test to guide treatment decisions for patients with invasive breast cancer. Breast cancer (Dove Medical Press): 9, 393–400.
[65] Parsekar, K. et al. (2021) Societal costs of chemotherapy in the UK: an incidence-based cost-of-illness model for early breast cancer. BMJ Open 11:e039412.
[66] CRA Analysis

- Pharmacogenomic treatment optimisation can also significantly alleviate pressure on the NHS, both on staff time and economically. Ensuring patients receive effective treatment could deliver sizeable cost savings. The UK spends at least £16.8 billion on prescription drugs per year; improving the effectiveness of these prescriptions would deliver significant efficiency improvements.[67] Furthermore, ensuring maximal safety is not only beneficial for patients but has great economic value – 8,000 UK hospital beds are occupied by patients suffering from ADRs at any one time, at a cost of £1.6 billion per year.[68]

Driving value for the healthcare system through providing versatile data

As well as providing value for HCPs and the NHS, GDx provide value to the wider healthcare system, including to payers. The fundamental nature of genomic data confers versatility in its application, meaning that the data delivered by GDx can inform clinical decisions over a patient's lifetime, maximising cost-effectiveness for payers.[69]

- Where the variant of a particular gene has implications for multiple facets of healthcare, data about this gene can be highly valuable.[70] For example, the enzyme encoded by the CYP2C19 gene metabolises at least 10% of drugs and prodrugs currently in clinical use, including blood thinners, anxiolytic drugs and anti-seizure drugs.[71] Different variants of the gene encode enzymes of increased or decreased activity, meaning the dose of the drug might have to be altered to have the same physiological effect in different patients.[72],[73] Novel diagnostics can deliver CYP2C19 variant results from a cheek swab in as little as one hour,[74] generating data that can influence many prescription decisions throughout the lifetime of the patient.[75]
- Broader data obtained from use of GDx, such as a whole genome sequence, is versatile and can be stored for the patient's lifetime, with only the relevant elements of the data analysed at the relevant time.[76] As part of the Newborn Genomes Programme, the whole genome sequence obtained can be analysed in the newborn setting to screen for curable diseases, and potentially the same data analysed with the patient's consent later in life in any context (e.g., to enable a rare disease diagnosis or inform risk reduction and prevention).[77] Alternatively, as the cost of sequencing continues to drop, a 'sequenceand-delete' model could become standard practice; such a model might help to address privacy and storage concerns regarding the retainment of genomic data.

[67] Turner, R. M. et al. (2020) Pharmacogenomics in the UK National Health Service: opportunities and challenges. Pharmacogenomics. 21(17): 1237–1246.
[68] Turner, R. M. et al. (2020) Pharmacogenomics in the UK National Health Service: opportunities and challenges. Pharmacogenomics. 21(17): 1237–1246.
[69] CRA Analysis
[70] Beitelshees, A. L. et al. (2020) Evaluating the extent of reusability of CYP2C19 genotype data among patients genotyped for antiplatelet therapy selection. Genet Med. 22(11): 1898–1902.
[71] https://medlineplus.gov/genetics/gene/cyp2c19 [Accessed April 2023]
[72] Koopmans, A. B. et al. (2021) Meta-analysis of probability estimates of worldwide variation of CYP2D6 and CYP2C19. Translational Psychiatry. 11(1): 141.
[73] Lee, C. R. et al. (2022) Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2C19 Genotype and Clopidogrel Therapy. Clinical Pharmacology & Therapeutics. 112(5): 959–967.
[74] https://www.nice.org.uk/guidance/gid-dg10054/documents/final-scope [Accessed April 2023]
[75] Beitelshees, A. L. et al. (2020) Evaluating the extent of reusability of CYP2C19 genotype data among patients genotyped for antiplatelet therapy selection. Genet Med. 22(11): 1898–1902.
[76] Chrystoja, C. C. and Diamandis, E. P. (2014) Whole genome sequencing as a diagnostic test: challenges and opportunities. Clinical chemistry. 60(5):724–733.
[77] https://www.genomicsengland.co.uk/initiatives/newborns [Accessed April 2023]

2.3. Value for society

Underpinning public health protection

GDx serve as a vital means to collect samples whose analysis can underpin crucial public health decisions.

- Nowhere has this been more evident than throughout the COVID-19 pandemic.[78] Samples collected for PCR tests to diagnose SARS-CoV-2 infection were subjected to WGS to monitor the emergence and transmission of novel viral variants, and between March 2020 and February 2022 the UK sequenced over 2 million SARS-CoV-2 genomes.[79] This genomic data was leveraged to generate epidemiological models estimating risk to the healthcare system, and to inform decisions on local and national restrictions, contributing to the curbing of viral spread.
- Wastewater surveillance sampling is an important diagnostic technique to detect the presence of pathogens excreted by members of the public at a population level.[80] Between February and June 2022, multiple poliovirus isolates were detected through metagenomic profiling of wastewater samples in London, underpinning the Joint Committee on Vaccination and Immunisation (JCVI) recommendation that all children aged between one and nine years old in London should be offered a booster dose of the inactivated polio vaccine (IPV).[81]

Supporting research

With the execution of every genomic test, additional data can be added to an ever-growing genomic dataset. Increasing the size of a genomic dataset, and the representation of different patients within the data, increases the validity of the data and thus its utility to all in society. Genomic datasets of greater validity allow for more accurate diagnoses and predictions of effectiveness, safety and risk, strengthening the future delivery of GDx, and thus enhancing the value previously described.

- More broadly, datasets of greater validity support stronger research in genomics and pharmaceuticals, and initiatives such as the National Institute for Health and Care Research (NIHR) BioResource and the UK Biobank collect genomic data specifically for this purpose.[82],[83]
- In an example of how such data can support research, the arcOGEN Consortium performed genome-wide meta-analysis on data from the UK Biobank to discover novel therapeutic targets for osteoarthritis (OA), and thus identify existing drugs that may be useful as new treatments for OA.

Growing the economy

While little evidence of the value of GDx to the UK economy has been systematically captured, it is clear that investment in this sector will deliver widespread and meaningful returns. The development and delivery of GDx introduces high-paying, high-skilled jobs into the economy, contributing to the ~270,000 jobs in the UK life sciences industry.[85] The generation of these jobs and the purchase of goods and services also positively impacts the performance of other sectors in the UK economy.[86]

[78] CRA Analysis
[79] https://www.gov.uk/government/news/uk-completes-over-2-million-sars-cov-2-whole-genome-sequences [Accessed April 2023]
[80] https://www.nature.com/articles/s41564-022-01201-0 [Accessed April 2023]
[81] https://commonslibrary.parliament.uk/research-briefings/cbp-9618 [Accessed April 2023]
[82] https://bioresource.nihr.ac.uk [Accessed April 2023]
[83] https://www.ukbiobank.ac.uk [Accessed April 2023]
[84] Tachmazidou, I. et al. (2019) Identification of new therapeutic targets for osteoarthritis through genome-wide analyses of UK Biobank data. Nat Genet. 51(2): 230–236.
[85] https://www.gov.uk/government/statistics/bioscience-and-health-technology-sector-statistics-2020/bioscience-and-health-technology-sector-statistics-2020 [Accessed April 2023]
[86] Boyce, T. and Brown, C. (2019) Economic and social impacts and benefits of health systems: report. World Health Organization. Regional Office for Europe.

Furthermore, this drives investment into building state-of-the-art research and development, manufacturing and distribution facilities, creating new hubs of economic activity and boosting economic growth. The delivery of the NHS GMS through regional Genomic Laboratory Hubs (GLHs) contributes to spreading investment in the NHS GMS across the country, and creating more equitable access to GDx will likely ensure opportunity and economic growth is spread across the length and breadth of the UK.[87],[88]

- Development of GDx in the UK contributes to growth of the country's genomics sector, which employs over 5,000 highly skilled people in a market worth over £5 billion.
- The value delivered to patients and the healthcare system can also translate into economic growth as patients receiving targeted therapy have a higher quality of life and can remain at work for longer or return sooner.[90] Diabetic patients diagnosed with monogenic diabetes through the use of GDx can receive oral sulfonylureas, eliminating the need for burdensome insulin injections.[91] NSCLC patients diagnosed with KRAS G12C can receive oral sotorasib, eliminating the use of side-effect-heavy ChT.[92] In early breast cancer alone, the costs of ChT due to societal productivity losses from short- and long-term work absences amount to over £130 million, so GDx that can reduce ineffective ChT can deliver significant value to the economy.[93]
- An additional indirect benefit of GDx to the growth of the economy includes a reduction in caregiver burden, although this benefit is more difficult to quantify.[94]

2.4. Summary

Box 4: Summary of key findings related to the value of GDx in the UK

GDx deliver broad and meaningful value for patients, healthcare providers, the healthcare system and society:

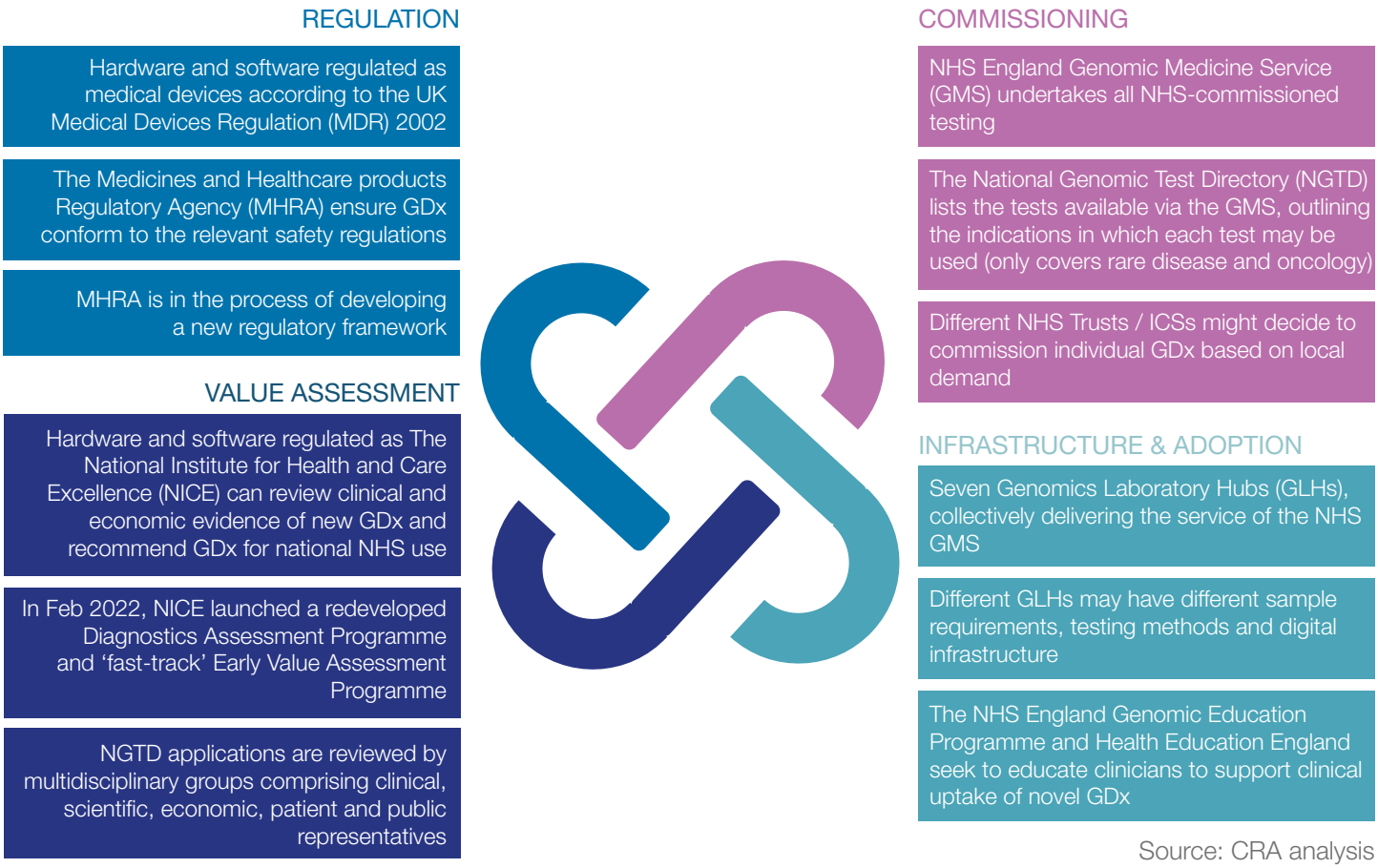
- For patients, GDx can enable rapid and accurate diagnoses across rare disease and cancer, ensuring appropriate and targeted treatment to maximise outcomes. The implementation of pharmacogenomics in routine clinical practice can ensure patients receive the safest and most effective treatment, minimising adverse drug reactions that account for 6.5% of UK hospital admissions.[95] Improvements in genetic risk profiling, prenatal and newborn screening empower individuals to make informed decisions about their health and that of their children.
- GDx can alleviate pressure on healthcare professionals and the NHS in multifarious ways: eliminating costly diagnostic odysseys, preventing unnecessary use of ineffective therapies, and ensuring patients receive the most effective and safe treatment. The versatility of data provided by GDx also drives value for the healthcare system; information about a single gene can have many implications, and expansive patient data such as a whole genome sequence has abundant potential to inform future treatment decisions.
- GDx technologies such as WGS have underpinned crucial public health decisions in recent years, with its use during the COVID-19 pandemic and in detecting poliovirus isolates in wastewater samples in London demonstrating two crucial examples of the value that such technologies deliver for our societal well-being. The execution of GDx also supports research in expanding genomic datasets, ensuring diversity and representation across society to increase the validity of the data. Finally, widespread adoption of GDx into society has the potential to deliver profound economic growth across the entire UK, creating new jobs and increasing the number of economically active individuals.

[87] CRA Analysis
[88] UK Government (2020) Genome UK: The future of healthcare. Available at https://www.gov.uk/government/publications/genome-uk-the-future-of-healthcare [Accessed April 2023]
[89] https://www.bioindustry.org/news-listing/new-report-reveals-strength-of-the-uks-thriving-genomics-sector.html [Accessed April 2023]
[90] Mathur, S. and Sutton, J. (2017) Personalized medicine could transform healthcare (Review). Biomedical Reports, 7(1): 3–5.
[91] Zhang, H. et al. (2021) Monogenic diabetes: a gateway to precision medicine in diabetes. J Clin Invest. 2021;131(3):e142244.
[92] https://www.england.nhs.uk/2022/03/hundreds-of-patients-to-benefit-from-revolutionary-lung-cancer-drug-on-the-nhs [Accessed April 2023]
[93] Parsekar, K. et al. (2021) Societal costs of chemotherapy in the UK: an incidence-based cost-of-illness model for early breast cancer. BMJ Open 11:e039412.
[94] Information from interview programme with representatives from the diagnostics industry, November–December 2022

3. Challenges in ensuring patient access to genomic testing

Despite the significant value that GDx can deliver for patients, for the healthcare system and for wider society, there is evidence of a number of barriers to access that can prevent these benefits from being realised to their full extent in the UK. Broadly, these challenges occur in one of four distinct yet interrelated components of the access landscape for GDx in the UK (Figure 2). In this section, these components are discussed in turn and eight access challenges are described.

Figure 2: The access landscape for genomic diagnostics in the UK



Source: CRA analysis

3.1. The evolving regulatory landscape

Challenge 1: There is uncertainty surrounding the implications of new genomic diagnostic regulatory requirements in the UK

The requirements to achieve regulatory conformity for a novel IVD depend on the risk class of that device.[96] Currently most GDx fall into the lowest risk class (termed general IVDs), and can be self-declared as conforming to the regulations by the manufacturer, allowing for prompt regulatory conformity decisions and ensuring patients have swift access to innovative technologies.[97] Higher risk devices require a conformity assessment review to be undertaken by a UK Approved Body: an Approved Body Assessment (ABA).[98] Changes to this system are expected to come into force in July 2024 and are likely to result in as many as 90% of GDx requiring an ABA, and increased requirements for manufacturers to submit ongoing proactive evidence following demonstration of regulatory conformity.[99] This greater scrutiny on GDx, it is argued, will ensure patients continue to have access to the safest, most effective and most relevant technologies as the pace of innovation in GDx increases.

[95] UK Government (2020) Genome UK: The future of healthcare. Available at https://www.gov.uk/government/publications/genome-uk-the-future-of-healthcare [Accessed April 2023]
[96] https://www.ukri.org/councils/mrc/facilities-and-resources/find-an-mrc-facility-or-resource/mrc-regulatory-support-centre/developing-healthcare-products/medical-devices-and-in-vitro-diagnostics [Accessed April 2023]
[97] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[98] https://www.ukri.org/councils/mrc/facilities-and-resources/find-an-mrc-facility-or-resource/mrc-regulatory-support-centre/developing-healthcare-products/medical-devices-and-in-vitro-diagnostics [Accessed April 2023]
[99] Information from interview programme with representatives from the diagnostics industry, November–December 2022

However, manufacturers of GDx have little experience of the ABA process, given that most GDx on the market today have not required this review to date.[100] Implementation of new IVD regulations will therefore likely increase uncertainty (at least for a period of time) and require increased investment in terms of human capital and resources from regulators, manufacturers and Approved Bodies.[101] Whilst some efficiencies exist (for example, healthcare laboratories are exempt from many regulatory requirements when manufacturing new diagnostics services in-house to be used on their own patients), there is a risk that new requirements for external manufacturers and service providers could create a bottleneck for new tests entering the UK market, exacerbating current delays in time to patient access and potentially creating an unlevel playing field for technology and service providers. This may pose a particular challenge for smaller companies with limited resources, which comprise a significant proportion of the GDx industry. Of the GDx companies interviewed as part of this research, the number of employees ranges from only three up to 9,100, and thus there are varying levels of resources available to be allocated to navigating the new regulatory process.

Challenge 2: There is uncertainty surrounding the implementation of new regulation for software used in genomic testing

Software plays a critical and increasingly prominent role in the delivery of GDx.[102] The application of software in GDx is wide ranging, from interpretation, reporting and clinical decision support tools, to the use of artificial intelligence (AI) in specific tasks such as genome annotation, variant classification and phenotype-to-genotype correlation.[103],[104],[105]

However, software can be regulated as a stand-alone medical device (commonly referred to as Software as a Medical Device – SaMD), with additional regulatory requirements imposed by Data Coordination Board (DCB) clinical risk management standards and international information security management systems (ISMS) standards.[106] New regulations surrounding the use of software in medical devices are beginning to be developed globally, with the US Food and Drug Administration (FDA) recently setting out guidance on the regulation of Clinical Decision Support software.[107] The UK is also following suit, with the Medicines and Healthcare products Regulatory Agency (MHRA) expected to include new requirements for software within their future regulatory system.[108]

In the interim, the MHRA has published guidance to assist manufacturers in navigating this changing regulatory situation;[109] however, there is a concern that the disparate mix of regulatory requirements will not be optimal given the unique nature of software.[110] For example, software optimisation is a quick and iterative process, with updates that can be released on a much more frequent basis than for a physical diagnostic. GDx software developers lack clarity on how new regulations might account for such differences – for example, whether a GDx would need to undergo a regulatory re-evaluation following each software update.[111] There is therefore a risk that an increase in the evidence threshold applied to GDx software, although intended to maximise patient safety, could potentially impede access and innovation.[112]

[100] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[101] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[102] https://www.globenewswire.com/en/news-release/2022/11/22/2561069/0/en/Precision-Medicine-Software-Market-is-expected-to-generate-a-revenue-of-USD-3-20-Billion-by-2028-Globally-at-8-57-CAGR-Verified-Market-Research.html [Accessed April 2023]
[103] Austin-Tse, C. A. et al. (2022) Best practices for the interpretation and reporting of clinical whole genome sequencing. npj Genome Medicine. 7, 27.
[104] De La Vega, F. M. et al. (2021) Artificial intelligence enables comprehensive genome interpretation and nomination of candidate diagnoses for rare genetic diseases. Genome Medicine 13, 153.
[105] Dias, R. and Torkamani, A. (2019) Artificial intelligence in clinical and genomic diagnostics. Genome Medicine. 11, 70.
[106] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[107] https://www.cov.com/en/news-and-insights/insights/2022/10/5-key-takeaways-from-fdas-final-guidance-on-regulation-of-clinical-decision-support-software-fda-outlines-significant-changes-for-cds [Accessed April 2023]
[108] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[109] https://www.gov.uk/government/publications/medical-devices-software-applications-apps [Accessed April 2023]
[110] CRA Analysis
[111] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[112] Information from interview programme with representatives from the diagnostics industry, November–December 2022

Challenge 3: The application of data protection regulation to genomic diagnostics remains unclear

Delivery of GDx requires the processing of vast amounts of genetic information, but both primary and secondary research have evidenced that legal uncertainty remains over the application of the UK Data Protection Act (2018) and the UK General Data Protection Regulation (UK GDPR), collectively (together, 'UK data protection law'), to this information.[113],[114],[115],[116]

The distinction between personal data, pseudonymised data and anonymised data is important because it determines the scope of application of the UK data protection law: personal data and pseudonymised data are subject to UK data protection law, whereas anonymised data is not.

During processing and interpretation, genetic data is deconstructed for analysis, but there is uncertainty about the circumstances in which genetic data are no longer personal data and the UK data protection law ceases to apply (i.e. when genetic data loses its 'individuality' and therefore can be considered 'anonymous'). Indeed, a recent government consultation suggested that "more could be done to help organisations understand what needs to be done to anonymise data" and that "[g]reater use of effective anonymisation could help to better protect individuals' personal information, reduce risks for organisations and provide the opportunity for broader economic and societal benefits through an increase in the availability of data".[117]

The collection of excess sequencing data and identification of incidental findings also remain crucial areas of legal uncertainty for diagnostics providers, as are concerns over how and where genetic data should be securely stored.[118]

Uncertainty in these areas limits innovation and creates hurdles in establishing UK access to such technologies. Differences in interpretation among collaborators lead to significant resources being expended on time-consuming negotiations. And, even where an agreement is reached, there is typically a lack of clarity regarding how to apply the principles of UK data protection law to the information at stake.[119],[120] While the NHS has confirmed that there are different mechanisms to host personal confidential data outside the UK,[122] our interviews with companies in the GDx space indicated some instances whereby negotiations between companies and NHS trusts stalled due to requirements that all data generated by use of the technology in that trust be stored in the UK. This may create barriers to international companies bringing new genomic technologies to the UK, where they may not have the capacity or resources to establish local data storage capabilities locally. Further, uncertainties or ambiguities within the NHS around the implications of GDPR can delay or prevent adoption of new innovative GDx entirely, preventing the value of these technologies from being realised.[123]

[113] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[114] https://www.phgfoundation.org/blog/how-does-the-gdpr-apply-to-genomic-data [Accessed April 2023]
[115] https://www.phgfoundation.org/report/the-gdpr-and-genomic-data [Accessed April 2023]
[116] https://www.genome.gov/sites/default/files/media/files/2020-11/GDSPolicy_Mitchell_Nov2020.pdf [Accessed April 2023]
[117] UK Government (2021) Data: A new direction. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1022315/Data_Reform_Consultation_Document__Accessible_.pdf [Accessed April 2023]
[118] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[119] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[120] https://www.genome.gov/sites/default/files/media/files/2020-11/GDSPolicy_Mitchell_Nov2020.pdf [Accessed April 2023]
[121] https://digital.nhs.uk/data-and-information/looking-after-information/data-security-and-information-governance/nhs-and-social-care-data-off-shoring-and-the-use-of-public-cloud-services [Accessed April 2023]
[122] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[123] Information from interview programme with representatives from the diagnostics industry, November–December 2022

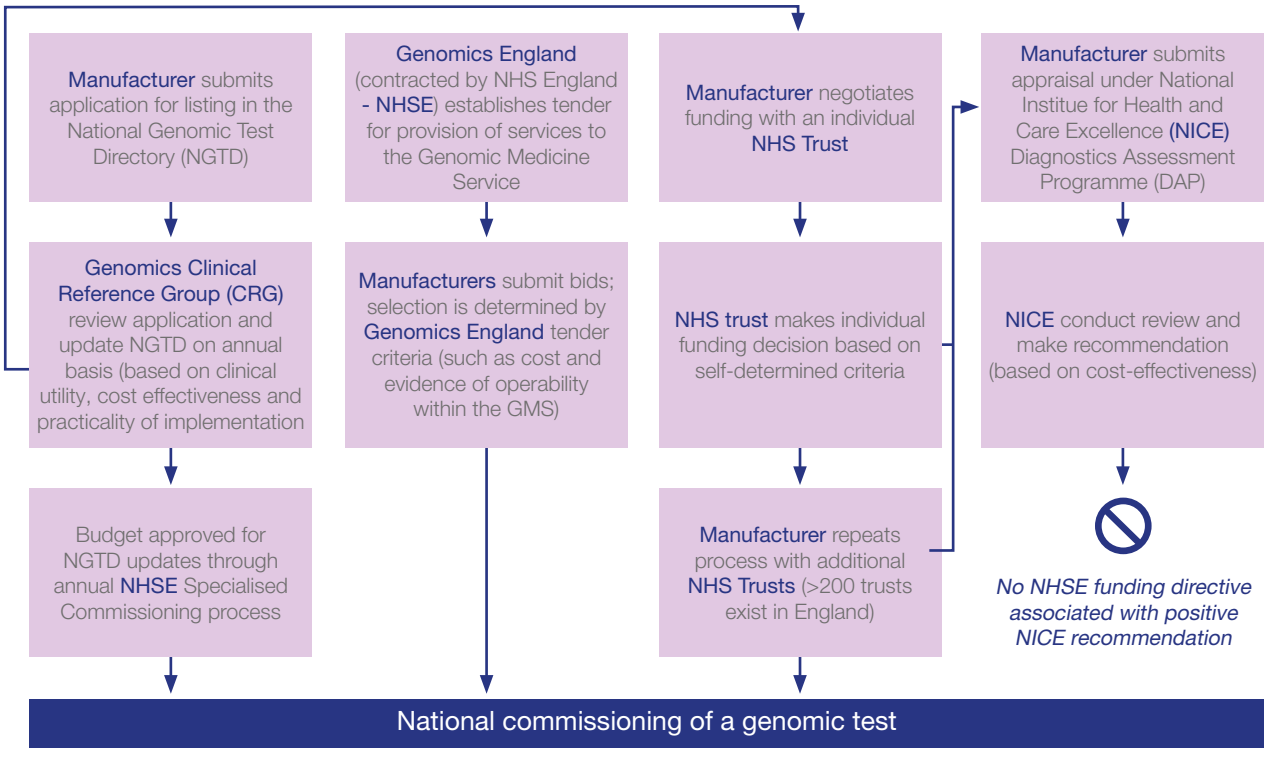
3.2. The limitations of current commissioning models

Note: The below description of the commissioning processes for GDx focuses on NHS England; those of the devolved nations were not investigated in detail.

Challenge 4: There is a lack of clarity over the process for national commissioning

Currently, the National Genomic Test Directory (NGTD) specifies which genomic tests in rare disease and oncology are commissioned at a national level by NHS England, including the indications for which the test is covered and which patients are eligible.[124] However, there are also a number of other processes for evaluation and funding of new GDx within England (described in Figure 3). There is a lack of centralised guidance for manufacturers of innovative GDx on the applicability of different pathways for different technologies, and thus the companies we interviewed reported very different experiences.[125] The most frequently cited access route was via negotiations with individual NHS trusts or integrated care systems (ICSs). However, this was seen to result in inefficiencies for both the NHS and the manufacturer, and in delayed and inequitable access across England.

Figure 3: The multiple routes to genomic test commissioning in England



Source: CRA analysis

National commissioning decisions can also be made independently of a company-initiated process; some companies cited experiences of only being informed of their involvement in the NHS national commissioning process by practising physicians, rather than through formal consultation with the NHS.[126]

[124] NHS England (2020) National Genomic Test Directory: Frequently Asked Questions. Available at: https://www.england.nhs.uk/wp-content/uploads/2020/12/National-Genomic-Test-Directory-FAQs-v4-Dec-2020.pdf [Accessed April 2023]
[125] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[126] Information from interview programme with representatives from the diagnostics industry, November–December 2022

The lack of a clear and coherent national funding pathway was seen as a significant problem. There is no clear source of national funding following recommendation by the National Institute for Health and Care Excellence (NICE) (if a health technology assessment (HTA) evaluation is conducted at all). Funding is not mandated in this scenario for diagnostics as it is for pharmaceuticals, requiring GDx test manufacturers to go to individual NHS trusts to negotiate funding from a variety of local sources or from pharmaceutical companies (for example, Myriad Genetics delivering HRD testing funded by AstraZeneca on behalf of a partner NHS Genomic Laboratory Hub), which is highly resource intensive and results in regional inequity of access. There is also concern that the devolution of GDx commissioning decisions to local ICSs will further contribute to regional inequality of access.

Siloing of budgets and the lack of an integrated approach to NHS funding appears to have resulted in a narrow approach to recognising the value of GDx. For example, although implementation of a new GDx might result in net cost savings to the health system – by alleviating pressure on the NHS or delivering versatile data that can inform clinical decisions over a patient's lifetime – funding decisions for the GDx typically consider the increased cost of adopting a new technology in the short term, rather than the potential wider cost savings across the NHS in the long term.

Challenge 5: The National Genomic Test Directory is not working for all types of genomic diagnostics technologies

In our interviews, some companies expressed a clear understanding of the NGTD and its role in national commissioning and impact for patients, but to many this remained unclear.

Anyone can apply to update the NGTD, but applications are only reviewed on an annual basis by the Genomics Clinical Reference Group (CRG) and test evaluation working groups (comprising clinical and scientific experts, and patient and public voice representatives).[131] The NGTD covers a large number of indications (357 rare disease indications and 203 cancer indications),[132] meaning that for established technology types such as next-generation sequencing, the NGTD can provide a valuable route to access for patients affected by rare disease or cancer. However, many patients who could benefit from the use of GDx in other disease areas or in different ways (such as through pharmacogenomic treatment optimisation) are currently not covered by the NGTD.[133]

Even for those tests included in the NGTD, inclusion does not guarantee patient access or a test becoming used in standard practice. Recent analyses have shown that, despite having some of the best availability of next-generation sequencing technologies in Europe, the UK is one of the worst-performing nations in uptake of the testing capability for use in standard clinical practice. For example, in NSCLC, only 9% of tissue biopsies are analysed with NGS technology in the UK, compared to as many as 75% in Denmark.[134]

Specific proprietary technologies can only be listed in the NGTD if they have been assessed and recommended by NICE; thus, bottlenecks arising in the NICE process (as detailed in Section 3.3) limit the ability of GDx manufacturers to deliver patient access.[135] Furthermore, for emerging technologies delivered from a single centre of excellence, the NGTD is viewed as exclusionary; only tests that are delivered by the NHS Genomic Medicine Service (NHS GMS) can be listed, thus impeding patient access to innovative technologies.[136]

[131] https://www.england.nhs.uk/genomics/the-national-genomic-test-directory [Accessed April 2023]
[132] NHS England (2022) Accelerating genomic medicine in the NHS. Available at: https://www.england.nhs.uk/long-read/accelerating-genomic-medicine-in-the-nhs [Accessed April 2023]
[133] https://www.england.nhs.uk/publication/national-genomic-test-directories [Accessed January 2023]
[134] Normanno N. et al. (2022) Access and quality of biomarker testing for precision oncology in Europe. European Journal of Cancer, 176, 70–77
[135] https://www.england.nhs.uk/genomics/the-national-genomic-test-directory [Accessed April 2023]
[136] Information from interview programme with representatives from the diagnostics industry, November–December 2022

3.3. The role of value assessment

Challenge 6: Current value assessment approaches are not aligned to the evidence generation process for genomic diagnostics

Given the costs involved and the small target patient populations, randomised control trials (RCTs) are not economically feasible for most new GDx technologies.[137] Further, RCTs are increasingly complex to design and conduct as tests are now rarely developed for use in a single indication. Once a genomic sequence has been obtained, it can be used for many clinical purposes across a patient's lifetime, which is not possible to evaluate with a single clinical trial. Instead, evidence generation typically occurs more pragmatically through the generation of real-world evidence (RWE).

This creates challenges for assessing the value of new technologies to inform funding decisions. The current approach towards value assessment of GDx in England is not fit-for-purpose for several reasons:

- There are two distinct processes, with different approaches and evidence requirements: NICE's Diagnostics Assessment Programme (DAP) for evaluating the cost-effectiveness of new diagnostics,[138] and NHS England and NHS Improvement's process for updating the NGTD, which considers the clinical utility, cost-effectiveness and workforce required to deliver the testing (although in practice, demonstration of cost-effectiveness is not routinely requested).[139],[140] This results in inefficiencies and duplication of effort across NICE and NGTD evaluations, as well as confusion for manufacturers regarding the role and remit of each process. Ultimately, NICE does not currently play a strong role in informing evidence-based decisions on the adoption of new GDx in England, with NICE guidance only having been published for a limited number of GDx to date.[141]
- It is challenging for companies with novel GDx technologies to meet NICE's cost-effectiveness thresholds, as the DAP is not tailored to the unique attributes of GDx relative to more traditional diagnostics. The lack of suitability of current value assessment approaches for GDx has been well documented in the literature, with GDx sharing some of the evaluation challenges common to all diagnostics (such as complexity of the analysis given multiple clinical applications) and presenting new challenges (such as the inability to capture the full value of testing and the difficulty of modelling incidental findings).[142] The impact of these challenges in the UK is evident through recommendations published by NICE, which cite significant uncertainties in the estimated cost-effectiveness of GDx technologies.[143]
- Companies interacting with NICE describe varying experiences in terms of speed and guidance, but for most the process is slow.[144] For example, the NICE guidance on 'Tumour profiling tests to guide adjuvant chemotherapy decisions in early breast cancer' [DG34] was last updated in 2018, and as of January 2023, the NICE website still lists this guidance as due for its next review in 2021.[145] This slow progress means that tests might remain unavailable to patients or clinicians, despite these tests having established evidence in that indication. There is also evidence that the UK is significantly lagging behind other markets: for example, Oncotype DX has been reimbursed in the US since 2006.[146] NICE's recommendation was only published seven years later in 2013, with the reimbursement decision taking another two years.[147]

[137] Lu, C. Y. et al. (2018) A proposed approach to accelerate evidence generation for genomic-based technologies in the context of a learning health system. Genetics in Medicine. 20: 390–396.
[138] https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-diagnostics-guidance [Accessed April 2023]
[139] https://www.england.nhs.uk/wp-content/uploads/2020/12/Updating-the-National-Genomic-Test-Directory-v1-Dec-2020.pdf [Accessed April 2023]
[140] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[141] https://www.nice.org.uk/guidance/published?ndt=Guidance&ngt=Diagnostics%20guidance&ps=2500 [Accessed April 2023]
[142] Bouttell, J. et al. (2022) Economic evaluation of genomic/genetic tests: a review and future directions. International Journal of Technology Assessment in Health Care. 38(1): e67, 1–8.
[143] https://www.nice.org.uk/guidance/dg34 [Accessed April 2023]
[144] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[145] https://www.nice.org.uk/guidance/dg34 [Accessed April 2023]
[146] Trosman, J. R., Van Bebber, S. L. and Philips, K. A. (2010) Coverage Policy Development for Personalized Medicine: Private Payer Perspectives on Developing Policy for the 21-Gene Assay. J Oncol Pract. 6(5): 238–242.
[147] https://www.prnewswire.com/news-releases/following-nices-exclusive-recommendation-nhs-england-agrees-to-access-program-for-oncotype-dx-breast-cancer-test-300031258.html [Accessed April 2023]

- In addition, because a NICE recommendation is not associated with a funding directive for diagnostics, and because GDx are not protected by patents, there is no economic incentive to generate the evidence required for value assessment.[148] There is also a need to account for the impact this has on competition and innovation. The current model imposes a 'penalty on innovation', as the first manufacturer to introduce a new GDx must take on the burden and cost of evidence generation, while those coming later benefit from the already established infrastructure and evidence.[149],[150]

3.4. The wider infrastructure for adoption of genomic testing

Challenge 7: The genomics diagnostics infrastructure – comprising the NHS GMS, Genomics England and services provided by private industry – could be better integrated

Upon its launch in 2018, the NHS Genomic Medicine Service (NHS GMS) represented a step change in the use of genomics in the NHS. The NHS GMS is a service commissioned nationally by NHS England's Genomics Unit, comprising seven consolidated laboratory networks – the Genomic Laboratory Hubs (GLHs) – each providing services across a defined geography through engagement, with between 18 and 45 NHS trusts in each, resulting in a complex interconnected network of stakeholders.[151] Since its establishment, over 35,000 whole genomes have been sequenced, and diagnoses have been provided or confirmed for around 40% of children tested.[152] Despite the immense successes, there are challenges in integration across the NHS GMS to ensure GDx are widely and consistently accessible.[153]

- There has not been a comprehensive review of the role of technologies and services developed in-house by individual NHS trusts and GLHs, versus those that have been developed and can be provided by external companies and service providers.[154] Executing a specialised assay in a global centre of excellence, or interpreting sequencing data using proprietary software, are both processes involved in delivering diagnostics outside of the NHS GMS that are growing in abundance and importance, but there is no clear way that such services might be integrated into routine clinical practice in the NHS.[155] This issue is compounded by the lack of consistency across the NHS GMS – for example, in sample requirements, test requesting methods and digital infrastructure;[156] as such, there is no one model to integrate into.

- Within the NHS GMS, the GLHs are not well integrated; external service providers reported having to negotiate different contracts with each stakeholder – NHS England, different NHS trusts and ICSs and individual GLHs – adding unnecessary complexity and inconsistency, and thus delaying patient access.

[148] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[149] https://medtech.pharmaintelligence.informa.com/MT147394/Why-EU-Must-Reform-Regulation-And-Funding-For-Life-Saving-Cancer-Biomarker-Tests [Accessed April 2023]
[150] Johnston, K. et al. (2019) Genomic screening costs in modelling – a penalty for innovation? ISPOR Europe 2019, Copenhagen, Denmark
[151] NHS England (2022) Accelerating genomic medicine in the NHS. Available at: https://www.england.nhs.uk/long-read/accelerating-genomic-medicine-in-the-nhs/ [Accessed April 2023]
[152] NHS England (2022) Accelerating genomic medicine in the NHS. Available at: https://www.england.nhs.uk/long-read/accelerating-genomic-medicine-in-the-nhs/ [Accessed April 2023]
[153] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[154] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[155] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[156] ABPI (2022) Harnessing the UK's genomics expertise to improve patient outcomes. Available at: https://www.abpi.org.uk/publications/harnessing-the-uk-s-genomics-expertise-to-improve-patient-outcomes [Accessed April 2023]

Challenge 8: There is a lack of suitable educational infrastructure

Patients lack a full awareness of the value of GDx, and harbour concerns and questions surrounding their involvement with GDx and their data privacy, as highlighted by a survey of patients involved in the 100,000 Genomes Project.[158] These questions and concerns might result in suboptimal patient input into, and thus equity of, genomic data.[159]

Despite the establishment of a Genomics Education Programme[160] by Health Education England to support the NHS GMS in educating the NHS workforce, challenges in this area remain. Clinicians, despite commonly having an interest in genomics, typically lack education and confidence with the topic, which may translate into an uncertainty on how and when to request GDx for patients, leading to poorer outcomes for patients.[161],[162] The evidence shows that this educational gap arises even in the early years of clinical training (throughout the undergraduate and junior doctor years),[163] and a recent review commissioned by Genomics England described a lack of genomic education as one of the most significant barriers to the implementation of GDx in standard clinical practice.[164] However, clinicians are currently facing immense workload pressures, and given the pace of change in genomics, may not be able to engage with GDx unless solutions are delivered in a manner that integrates with current workstreams.[165]

3.5. Summary

There are a number of barriers to access that can prevent the benefits of GDx from being realised to their full extent in the UK. These barriers span regulatory, commissioning, value assessment and uptake components of the access landscape, as summarised in Box 5.

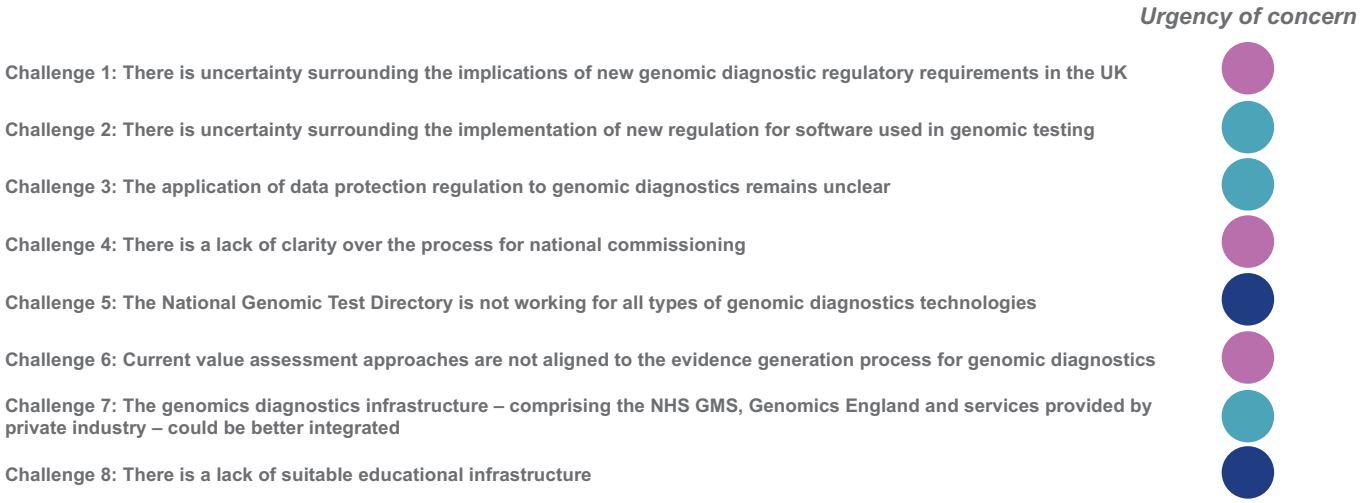
Box 5: Summary of key challenges impacting access to GDx in the UK

- Uncertainty surrounding the implications of new GDx regulatory requirements in the UK may require increased investment from regulators, manufacturers and Approved Bodies, exacerbating delays in time to patient access and potentially creating an unlevel playing field for technology and service providers. There is also uncertainty surrounding the implementation of new regulations for software used in genomic testing, and the application of data protection regulation to genomic diagnostics remains unclear.
- Research identified a lack of centralised guidance for GDx manufacturers on the different pathways for evaluation and funding of new GDx, resulting in inefficiencies and regional inequality of access. In addition, the NGTD is not working for all types of GDx. Inclusion in the NGTD does not guarantee patient access or that a test will be used in standard clinical practice, and the exclusion of tests delivered from a single centre of excellence limits patient access to innovative technologies.
- Current value assessment approaches are not aligned to the evidence generation process for genomic diagnostics; RCTs are not economically feasible for most new GDx technologies, and current models don't consider prospective evidence generation. The slow pace of interaction with NICE and the lack of an associated funding directive create barriers for manufacturers seeking to enable patient access.
- The genomics diagnostics infrastructure in the UK requires better integration to ensure consistent access to GDx. This involves addressing issues such as the lack of consistency across the NHS GMS and difficulties in integrating external services. There is also a lack of suitable educational infrastructure for patients and healthcare professionals, which can result in suboptimal patient input into genomic data and poorer outcomes for patients.

[157] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[158] Dheensa, S. et al. (2019) Fostering trust in healthcare: Participants' experiences, views, and concerns about the 100,000 genomes project. Eur J Med Genet. 62(5): 335–341.
[159] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[160] https://www.genomicseducation.hee.nhs.uk [Accessed April 2023]
[161] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[162] Slade, I. et al. (2016) Genomics education for medical professionals - the current UK landscape. Clinical medicine. 16(4): 347–352.
[163] Just, K. S. et al. (2017) Medical education in pharmacogenomics—results from a survey on pharmacogenetic knowledge in healthcare professionals within the European pharmacogenomics clinical implementation project Ubiquitous Pharmacogenomics (U-PGx). European Journal of Clinical Pharmacology 73, 1247–1252
[164] Alarcón Garavito, G. A. et al. (2022) The implementation of large-scale genomic screening or diagnostic programmes: A rapid evidence review. European Journal of Human Genetics. 1–14.
[165] Information from interview programme with representatives from the diagnostics industry, November–December 2022

Figure 4 summarises the eight key challenges in ensuring patient access to genomic testing that are set out in this section, and ranks them based on urgency.

Figure 4: A ranked summary of the challenges in ensuring patient access to genomic testing



Source: CRA analysis

4. The role of partnerships

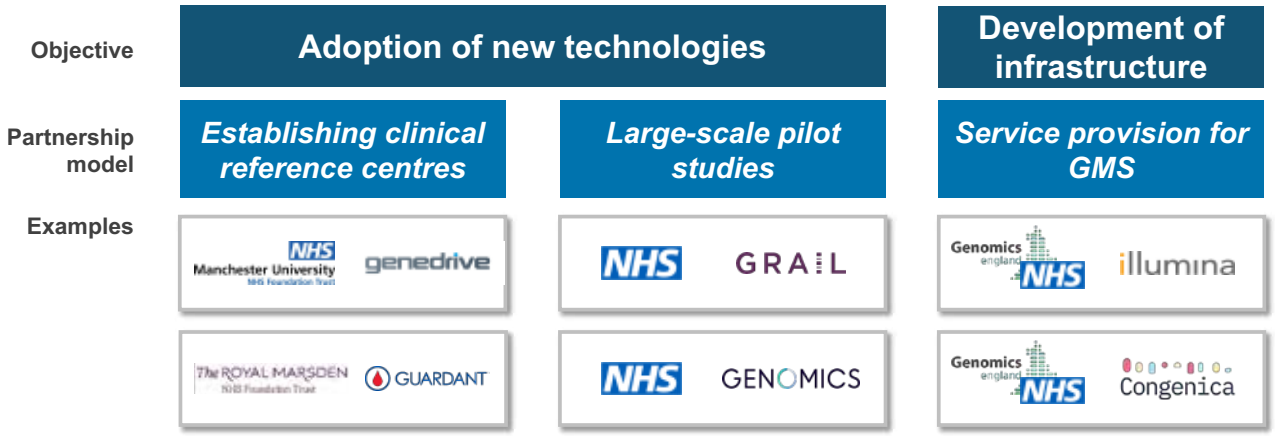
A key objective of this study was to understand the role of partnerships between the UK health service and the wider genomics ecosystem in realising the value of GDx and overcoming challenges to patient access.

4.1. A novel taxonomy of partnership models

Drawing from the six partnerships included in our assessment, we established a taxonomy of types of partnership. We use this taxonomy to investigate factors fundamental in the establishment of different types of partnerships and the value these partnerships can deliver for patients.

In the taxonomy, partnerships with two different primary objectives were identified: (1) partnerships aimed at promoting the adoption of new technologies, and (2) partnerships aimed at developing the GDx infrastructure. Within the category of partnerships aimed at adopting new technologies, we distinguish between those establishing clinical reference centres and those that are larger-scale pilots, as set out below and summarised in Figure 5. All of the partnerships discussed in our interviews fall into one of these categories.

Figure 5: A taxonomy of partnership models



Source: CRA analysis

Establishing clinical reference centres

The first type of partnership model identified involved the establishment of a clinical reference centre to drive the adoption of new GDx technology. In these partnerships, recognition of the clinical need and subsequent support from local clinicians and decision makers, as well as from the individual hospital or NHS trust, has contributed to successfully enabling patient access to the GDx. As well as enabling access for the patients of the individual hospital, these partnerships can generate evidence used to support wider adoption. For example:

- In 2022, Manchester University NHS Foundation Trust partnered with Genedrive to deploy six of their point-of-care MT-RNR1 screening systems (previously discussed) to optimise neonatal care.[166] This partnership provided access to the innovative test for neonates treated at hospitals in the Trust, but also provided important lessons to inform a potential pilot of this diagnostic in acute neonatal care across the NHS.[167]

[166] https://www.genomicseducation.hee.nhs.uk/blog/rapid-genomic-test-helps-prevent-newborn-hearing-loss [Accessed April 2023]
[167] CRA Analysis

- In 2021, The Royal Marsden NHS Foundation Trust partnered with Guardant Health to establish an in-house liquid biopsy testing facility. The Guardant 360 CDx assay provides complete genomic profiles of solid tumours from a simple blood test, quickly identifying actionable biomarkers to inform oncology treatment decisions.[168] This partnership will enhance oncology treatment for patients at the Royal Marsden NHS Foundation Trust, and learnings from this partnership could lead to an evidence generation programme that may underpin a national funding decision for this assay in the UK.[169] Furthermore, the partnership has served to inspire the development of a larger pilot study (TRACC Part C) across ~40 sites in the UK, investigating the potential of Guardant Reveal to guide adjuvant chemotherapy decisions in early colorectal cancer.[170]

Large-scale pilot studies

An alternative way to enable patient access to new GDx technologies is through a larger-scale pilot study partnered with the NHS at a national level. These types of partnership are funded from a national NHS budget, but the NHS might decide to run the pilot study in one part of the country initially, or in a time-limited manner. These partnerships are able to generate large volumes of evidence that might support national rollout of the partner technology into routine clinical practice if it is deemed a success. For example:

- In 2021, the NHS and GRAIL initiated a pilot study of their Galleri multi-cancer early detection test.[171] This test can detect the presence of more than 50 types of cancer from a simple blood sample using high intensity sequencing of circulating tumour DNA (ctDNA). The pilot study recruited its target of 140,000 participants in just ten months, and another 25,000 patients with possible cancer symptoms are to be offered testing to speed up their diagnosis. Building on the success of the partnership, the NHS has committed to the purchase of one million tests before 2024/25.[172]
- Since 2021, the NHS has partnered with Genomics plc to deliver the previously discussed HEART Pilot Study in the North East of England.[173] Genomics plc has developed a population health management tool that uses genomic data to determine polygenic risk scores (PRS). These can be integrated with non-genetic data to determine an overall risk of heart disease, to inform lifestyle changes and prescription decisions.[174]

Service provision for NHS GMS

Partnerships aimed at developing the UK's GDx infrastructure typically have a longer history. In these partnerships, the value of the partner's technology is already recognised by the NHS and the partner provides a service that forms an integral and long-term part of the NHS GMS. For example:

- Since as early as 2012, NHS England and Genomics England have partnered with Illumina to deliver the sequencing equipment and develop interpretation and reporting tools to deliver reports for the sequencing of all genomes in the proof-of-concept 100,000 Genomes Project. Following successful delivery of this project, the NHS GMS was established, and in 2020, Genomics England and Illumina announced a new agreement to extend this delivery to 500,000 whole genome equivalents before 2025.[175]
- Since the establishment of the NHS GMS in 2018, NHS England and Genomics England have partnered with Congenica to provide Diagnostic Decision Support Services in delivering the NHS GMS. Congenica develops tools for clinical analysis and genomic interrogation of sequencing data, which have reduced manual data processing by 95%, improved analysis times 20-fold and increased diagnostic yield by 50%.[176]

[168] https://investors.guardanthealth.com/press-releases/press-releases/2021/Guardant-Health-and-The-Royal-Marsden-NHS-Foundation-Trust-Announce-Partnership-to-Establish-First-Guardant-Health-Liquid-Biopsy-Testing-Service-Based-in-the-United-Kingdom/default.aspx [Accessed April 2023]
[169] CRA Analysis
[170] https://investors.guardanthealth.com/press-releases/press-releases/2023/Guardant-Health-and-The-Royal-Marsden-NHS-Foundation-Trust-partner-on-highly-anticipated-TRACC-Part-C-trial-to-use-Guardant-Reveal-blood-testto-help-guide-treatment-decisions-in-colorectal-cancer [Accessed April 2023]
[171] https://grail.com/clinical-studies/nhs-galleri-trial-clinical [Accessed April 2023]
[172] https://www.england.nhs.uk/blog/a-moment-to-celebrate-in-our-potentially-revolutionary-cancer-blood-tests-trial [Accessed April 2023]
[173] https://www.genomicseducation.hee.nhs.uk/blog/nhs-launches-new-polygenic-scores-trial-for-heart-disease [Accessed April 2023]
[174] https://www.genomicsplc.com/news/successful-world-first-pilot-using-improved-genomic-risk-assessment-in-cardiovascular-disease-prevention-in-the-nhs [Accessed April 2023]
[175] https://www.genomicsengland.co.uk/news/bioinformatics-partnership-with-illumina [Accessed April 2023]
[176] https://blog.congenica.com/2018/10/17/congenica-earns-major-role-supporting-worlds-first-routine-national-genomic-medicine-service [Accessed April 2023]

4.2. The role of partnerships in overcoming access challenges

Drawing from the experience of these case studies, we find that partnerships can serve as a tool to facilitate patient access to GDx despite the access challenges described in Chapter 3.

Regarding regulatory challenges, partnerships may set out key roles and responsibilities for regulatory knowledge management and data handling between stakeholders, establishing new ways of working and best practices to inform future regulatory policy.

- Establishing clinical reference centres is unlikely to significantly impact regulatory practices. Instead, regulatory barriers may inhibit the ability of such centres to be established, for example if there is uncertainty regarding appropriate data storage protocol.
- Large-scale pilot studies and service provision models can both occur on a large enough scale to generate enough experience of working with new GDx technologies that it can help inform regulatory best practices as described above.

Partnerships can provide a means for NHS trusts to access new technologies in the absence of or preceding a national reimbursement decision and can catalyse national commissioning decisions.

- Establishing clinical reference centres at an NHS trust or GLH level can enable a cohort of patients to access new technologies at a faster rate than if they had to wait for a national commissioning decision. In addition, the centres can foster technology transfer agreements to NHS partners, thus supporting ongoing innovation.
- Large-scale pilot studies can provide a route for companies with novel technologies to bring these to the awareness of NHS England and the NHS GMS, enabling faster and more efficient access to these technologies by generating evidence that can be used by other parts of the NHS or NHS GMS to support informed decision-making.
- Service provision models are established within existing funding pathways (national tendering), rather than to provide an alternative to traditional routes. Experiences can be used to inform more optimal tender design and implementation for future services.

In value assessment, partnerships can facilitate UK evidence generation to support a downstream evaluation, and successful partnerships can provide an alternative evidence-based guideline for the adoption of tests in the absence of a formal HTA recommendation.

- Establishing clinical reference centres can trigger and inform value assessment. For example, as a result of the evidence and learnings generated from Manchester University NHS Foundation Trust's successful partnership with Genedrive, the MT-RNR1 screening system was entered into NICE's 14-month Diagnostics Assessment Programme. In September 2022, this evaluation was transferred to the accelerated EVAP, which is expected to publish a conclusion within six months.[177]
- Large-scale pilot studies provide valuable evidence, generated in a UK setting, that can support NICE's evaluation. This data, if published in a timely manner, can also provide an alternative evidence-based guideline for the adoption of new tests to inform decision-making in the absence of or preceding a NICE appraisal.
- Service provision models bypass the need for value assessment, as a funding decision is made based on defined tender criteria. This can enable timely access to technologies whose cost-effectiveness is harder to determine, such as the decision support services that Congenica provides to NHS England and Genomics England.

[177] http://www.genedriveplc.com/press-releases/gdr_-_nice_(26.09.22).pdf [Accessed April 2023]

Partnerships can provide a cornerstone for establishing new GDx infrastructure.

- Establishing clinical reference centres can, for the NHS/NHS GMS partner, support with the development of infrastructure and capabilities on site that otherwise would not be possible (for example, that may be too resource heavy). The partner site can also become a centre for education of clinicians UK-wide and for proof-of-concept for implementation in other NHS trusts. Healthcare professionals can receive education on how to use the GDx and remain up to date with developments in the space, facilitating dissemination of practical knowledge across the UK.[178]
- Large-scale pilots may offer the opportunity to offload some of the pressure on the capacity of the NHS and healthcare professionals. For example, the partnership with GRAIL has been conducted from mobile clinics in convenient community locations, preventing unnecessary hospital or primary care visits.[179]
- Service provision models can support the long-term establishment of critical infrastructure for the delivery of genomic testing and genomic medicine in the NHS. For example, Illumina, as a key partner involved in establishing the 100,000 Genomes Project, today forms a core part of the NHS Genomic Medicine Service, with the partnership also having led to further proof-of-concept trials in other areas.[180]

4.3. The process for establishing partnerships

Our interviews with industry partners identified several key factors enabling development of these partnerships.

First, the majority of partnerships are demand-driven more than supply-driven. Identifying and articulating the clinical need within the NHS GMS or NHS is typically the first step in establishing a partnership. Key enablers include:

- Garnering clinician interest and advocacy
- Establishing a joint research partnership that has incentives to develop evidence useful to both parties

Second, formal terms need to be developed, which tend to align with one of two key models:

- Partnerships such as those involving Illumina or Congenica follow a tender-like model, with the industry provider delivering a service directly for Genomics England, which is contracted by NHS England to provide services to the NHS GMS. Such models enable rapid identification of suitable partners through the public announcement of a tender and the invitation of a large number of organisations to provide bids, with the winner being determined based on clearly defined criteria.
- Alternatively, direct negotiations with individual NHS trusts (e.g., those involving Genedrive and Guardant) or with NHS England (e.g., those involving GRAIL and Genomics plc) might define specific terms surrounding the establishment of a clinical reference centre, technology transfer, or formal implementation trial. Such terms may be agreed in a matter of months, or take years to develop as the right partner is identified and capabilities and responsibilities are understood and established.

Understanding such factors is important not only for establishing new partnerships going forward but also in considering how to optimise their development.

[178] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[179] https://www.england.nhs.uk/midlands/2021/09/13/thousands-of-people-in-east-midlands-invited-to-help-nhs-trial-new-cancer-test [Accessed April 2023]
[180] https://www.england.nhs.uk/contact-us/privacy-notice/nhs-genomic-medicine-service [Accessed April 2023]
[181] Information from interview programme with representatives from the diagnostics industry, November–December 2022

4.4. Barriers limiting the implementation and impact of partnerships

Despite the clear value of industry–healthcare system partnerships in providing solutions to the challenges surrounding patient access, our research highlighted some barriers to the implementation of partnerships:

- In certain cases, partnerships are borne out of external factors, such as geographic proximity of both parties, rather than a more systematic approach to matching up service needs to service offerings. This can result in inequality in patient access, as partnerships may cover limited geographic areas or only provide access on a temporary basis, with limited or no funding available for long-term adoption. Although the NHS is seeking to establish its Innovation Service as a single route to create opportunities for new technologies to be piloted in the NHS,[182] our research indicates that the Service has not yet provided clear and consistent opportunities for adoption of innovative GDx.[183]
- Intertwined with this issue, partnerships may have been driven by demand of the health system to arguably too great an extent thus far. For example, basing the adoption of new GDx only in situations of well-defined clinical need may restrict opportunities for the NHS to benefit from new disruptive technologies that do not yet have a clearly defined position in the clinical pathway.

4.5. Summary

Box 6: Summary of key lessons from analysis of GDx partnerships

Partnerships can serve as a tool to facilitate patient access to GDx despite the access challenges described in Chapter 3.

- Regarding regulatory challenges, partnerships may set out key roles and responsibilities for regulatory knowledge management and data handling.
- In commissioning, partnerships can provide a means for NHS trusts to access new technologies in the absence of a national reimbursement decision and can catalyse national commissioning decisions.
- In value assessment, partnerships can facilitate UK evidence generation to support a downstream evaluation, and can provide an alternative evidence-based guideline for the adoption of tests in the absence of a formal HTA recommendation.
- More broadly, partnerships provide a cornerstone for establishing new GDx infrastructure and creating opportunities for education of clinicians and patients to support adoption of novel tests.

Our research identified several significant factors in establishing partnerships that will be important in optimising their development going forwards. We also found there has been a lack of a systematic approach to establishing new partnerships thus far, and this must be addressed to prevent barriers limiting the implementation and impact of partnerships.

[182] https://innovation.nhs.uk [Accessed April 2023]
[183] Information from interview programme with representatives from the diagnostics industry, November–December 2022

5. The role of policy change

As shown in Chapter 4, successful partnerships between the UK health system and the diagnostics industry can provide an avenue for supporting both short- and long-term access to innovative genomic technologies. There are a range of policies that can make them easier to establish, more effective or deliver greater benefits. These are set out below.

However, they will not fundamentally change or address flaws in the overall access ecosystem in the UK. To support the government's vision of ensuring that patients across the UK can benefit from world-first advances in genomic healthcare, policy improvements are needed across four dimensions:

1. Supporting effective implementation of fit-for-purpose regulations
2. Providing clear and efficient funding pathways to support equitable access
3. Recognising the value of genomic tests and incentivising evidence generation
4. Removing barriers to the widespread adoption of genomic testing within the NHS

Policy improvements in these areas are discussed in section 5.2.

5.1. Policies to support the development of effective partnerships

The expansion of partnerships to enable access to innovative technologies is part of the role of the NHS GMS Alliances, and should be a key aim for the NHS moving forwards, contributing towards the key priority set out in 'Accelerating genomic medicine in the NHS' – to "enrich existing, and develop new NHS GMS relationships to support innovation and the generation of evidence to improve health and care".[184] To overcome the barriers outlined, several approaches should be considered in seeking to optimise the establishment and development of partnerships moving forward:

- The genomics market is rapidly evolving. Supply drive, horizon scanning and even patient demand functions should play a much greater role in the establishment of partnerships going forwards, to enable access by the NHS, and thus patients, to disruptive innovation in GDx. NHS England or Genomics England could adopt a proactive role in connecting companies that can provide valuable services or technologies with the parts of the health service that can benefit from these. This could promote a more systematic and efficient process for the establishment of new partnerships and eliminate the role of chance or circumstance in the way that partnerships form.
- Guidelines for the development and publication of evidence that is generated over the course of a partnership (for example, within a clinical reference centre or via a larger-scale pilot study) should also be developed to ensure that evidence of the value of implementation of new technologies in the NHS is consistently captured and used to inform decision-making.
- As new partnerships are established, it is important to consider that the taxonomy (in Figure 5) will evolve as new objectives are defined and new models demonstrated. Creating a forum for sharing lessons and experiences across the NHS would be beneficial and would help to ensure progress continues to be made.

[184] NHS England (2022) Accelerating genomic medicine in the NHS. Available at: https://www.england.nhs.uk/long-read/accelerating-genomic-medicine-in-the-nhs/ [Accessed April 2023]

5.2. Policies to address the root causes of UK access barriers

5.2.1. Supporting effective implementation of fit-for-purpose regulations

The MHRA have confirmed it is their intention to extend the implementation of the future Medical Device Regulations by 12 months, bringing the new date of application to 1 July 2024.[185] To mitigate issues with the transition to a new UK regulatory structure, the recognition of CE (Conformity to European regulations)[186] marking on the UK market for IVDs has also been granted a transition period. Neither of these intentions have been implemented in UK law at the time of this report.

For guidance:

- CE certificates or declarations of conformity to the In Vitro Diagnostic Directive (IVDD) can continue to be used to place in vitro diagnostics on the Great Britain market for up to five years, or until the certificate/declaration of conformity expires. This must be dated prior to 1 July 2024, the expected date of application of the new UK Medical Device Regulations.[187]
- CE certificates or declarations of conformity to the In Vitro Diagnostic Medical Device Regulation (IVDR) can continue to be used to place in vitro diagnostics on the Great Britain market for up to five years, or until the certificate/declaration of conformity expires. This can be dated after 1 July 2024, the expected date of application of the new UK Medical Device Regulations.[188]

  Regarding the regulation of software used in GDx, the MHRA appears to have recognised this challenge, recently announcing a new Software and AI as a Medical Device Change Programme to ensure regulatory requirements are clear and optimised for software, and to eliminate friction between the MHRA, NICE and NHS England.[189] This is expected to inform the development of new regulation to apply to software in GDx.

Our research identified several key focus areas for implementation of the new regulations:

- There is a need for an advisory or educational service (perhaps delivered by the MHRA) to guide companies, especially small to medium-sized enterprises (SMEs), through the conformity assessment process and the associated evidence requirements. Such a service would be important for GDx manufacturers, given the upcoming scale of change in the GDx regulatory landscape, and the rapid pace of innovation that creates new technological niches to which regulations might not directly translate.
- Clarifications should be made over the applicability of data protection regulations – such as UK GDPR – to genomic information in various formats. This will provide reassurance to patients about the safety of their data, and clarification to GDx manufacturers about how data should be handled and processed.
- Beyond these immediate steps, it is vital that policymakers seek to strengthen the relationship between conformity to the UK Conformity Assessed (UKCA) mark[190] and patient access, to establish a global gold standard that maximises patient access and minimises risk.

[185] https://www.gov.uk/government/publications/implementation-of-the-future-regulation-of-medical-devices-and-extension-of-standstill-period [Accessed April 2023]
[186] CE marking (from the French "Conformite Europeenne") certifies that a product has met EU health, safety, and environmental requirements, which ensure consumer safety (https://www.trade.gov/ce-marking) [Accessed April 2023]
[187] https://www.gov.uk/government/publications/implementation-of-the-future-regulation-of-medical-devices-and-extension-of-standstill-period [Accessed April 2023]
[188] https://www.gov.uk/government/publications/implementation-of-the-future-regulation-of-medical-devices-and-extension-of-standstill-period [Accessed April 2023]
[189] https://www.gov.uk/government/publications/software-and-ai-as-a-medical-device-change-programme/software-and-ai-as-a-medical-device-change-programme-roadmap [Accessed April 2023] https://www.gov.uk/government/publications/software-and-ai-as-a-medical-device-change-programme/software-and-ai-as-a-medical-device-change programme-roadmap [Accessed April 2023]
[190] UK Conformity Assessed (UKCA) marking is the product marking used for products being placed on the market in Great Britain (https://www.gov.uk/guidance/using-the-ukca-marking) [Accessed April 2023]

- Lessons should be learnt in the UK from the regulatory issues that have arisen from the implementation of new EU IVDR regulations. An insufficiency of Notified Bodies to undertake conformity assessment reviews, delays in the establishment of expert panels and reference labs to evaluate the highest-risk devices, and a lack of contingency plans have all been key sticking areas in the implementation of the IVDR, and failing to learn lessons from these issues threatens to impede patient access to novel GDx in the UK, and discourages new investments in the UK.[191],[192]

5.2.2. Providing clear and efficient funding pathways to support equitable access

The 'Accelerating genomic medicine in the NHS' strategy sets out an intention that, from the financial year 2023/24, the NHS GMS will work with the ICSs to develop a sustainable commissioning model.[193] The NHS Revenue Finance and Contracting Guidance for 2023/24 also outlines that genomic testing services will move to an activity-based payment model, which will lead to a standard set of prices across trusts; this is likely to lead to increased harmonisation across trusts, which may support greater efficiency and make the commissioning process more streamlined for all parties.[194] Going further, our research and interviews identified a range of important considerations for optimising the current funding systems for GDx to ensure clarity for technology and service providers and efficiency for the health system:

- In developing a more sustainable commissioning model, there is a need for greater clarity on the route(s) to national commissioning, as well as a need for a mandatory funding mechanism for those GDx that have demonstrated value (for example, from a NICE recommendation, or a fit-for-purpose evaluative framework, potentially including pilot studies). This will ensure that manufacturers are able to follow a clear process with a known end outcome, minimising wasted resources on navigating through a multi-step commissioning process, and expediting patient access.
- The role of ring-fenced funding for GDx should also be explored. This could help to ensure that patient access to novel GDx remains protected and equitable across the country. Evidence from the Netherlands suggests that implementing such a funding strategy in pharmacogenomic testing has not resulted in an immediate overwhelming demand for tests, but rather has led gradual growth year-on-year.[195]
- Regarding the NGTD, it is evident that the role of this NGTD must be more clearly established.[196] The NGTD should be reviewed on a more frequent basis and should consider the breadth of ways that GDx are delivered. Doing so could maximise patients' access to the most innovative of GDx technologies, regardless of the mode or location of delivery.

[191] https://www.biomedeurope.org/images/news/2021/BioMed_Alliance_IVDR_statement_final.pdf [Accessed April 2023]
[192] https://www.phgfoundation.org/briefing/what-is-the-ivdr [Accessed April 2023]
[193] NHS England (2022) Accelerating genomic medicine in the NHS. Available at: https://www.england.nhs.uk/long-read/accelerating-genomic-medicine-in-the-nhs/ [Accessed April 2023]
[194] https://www.england.nhs.uk/wp-content/uploads/2023/01/PR00021ii-guidance-on-23-24-revenue-finance-and-contracts.pdf [Accessed April 2023]
[195] Turner, R. M. et al. (2020) Pharmacogenomics in the UK National Health Service: opportunities and challenges. Pharmacogenomics. 21(17): 1237–1246.
[196] Information from interview programme with representatives from the diagnostics industry, November–December 2022

5.2.3. Recognising the value of genomic tests and incentivising evidence generation

The 'Genome UK: shared commitments for UK-wide implementation 2022 to 2025' recognises the Scottish government's commitment to rethinking the approach to value assessment for WGS in rare disease to bring a more holistic and patient-centric approach, but such commitments are generally missing from current debates about genomics in the UK as a whole.[197] The role of NICE was notably missing from NHS England's 2022 strategy for accelerating genomic medicine in the NHS.[198] However, there are several improvements that could be made to optimise the role of value assessment in funding decisions for novel GDx in the UK:

- NICE could consider adapting the current 'see-to-pay' model of value assessment process for GDx, exploring a 'pay-to-see' retrospective evidence generation model that would enable patient access to innovative GDx prior to completion of the long value assessment process.[199] Such 'pay-to-see' systems already exist in the UK for innovative medicines, such as the Cancer Drugs Fund.[200] Further adaptations could include participation in international/European partnerships on data sharing, thus avoiding arduous duplication of evidence. The need for a more holistic restructure of the value assessment approach for genomic diagnostics has been proposed in the literature;[201] as world leaders in developing robust HTA methodologies, NICE could consider reviewing their current approach.
- Going forwards, NICE's role in value assessment and its relationship to the funding of a diagnostic must be more clearly established – a positive recommendation should lead to a positive funding decision. In addition, transparency on the role of and access to the NICE DAP and EVAP pathways is essential to optimise the value assessment process.
- Finally, a mechanism to incentivise innovation should be found. Given that the intellectual property (IP) protections afforded to GDx and the incentives to invest in developing new technologies and generate the volume of evidence required are all seen as too low, there is a need to consider the market returns to innovators. A working group comprised of key stakeholders across the health system and genomics field should be established to evaluate potential mechanisms.

[197] UK Government (2022) Genome UK: shared commitments for UK-wide implementation 2022 to 2025. Available at: https://www.gov.uk/government/publications/genome-uk-shared-commitments-for-uk-wide-implementation-2022-to-2025 [Accessed April 2023]
[198] NHS England (2022) Accelerating genomic medicine in the NHS. Available at: https://www.england.nhs.uk/long-read/accelerating-genomic-medicine-in-the-nhs/ [Accessed April 2023]
[199] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[200] https://www.england.nhs.uk/cancer/cdf [Accessed January 2023][Accessed April 2023]
[201] Bouttell, J. et al. (2022) Economic evaluation of genomic/genetic tests: a review and future directions. International Journal of Technology Assessment in Health Care, 38(1): e67, 1–8.

5.2.4. Removing barriers to the widespread adoption of genomic testing within the NHS

The 'Accelerating genomic medicine in the NHS' strategy commits NHS GMS services to further integration with (or delegation to) the newly established ICSs, and the NHS GMS Alliances play a role in supporting the embedding of genomics in standard clinical practice, which may go some way to improving integration and efficiency of the uptake of genomic testing across the service [202] To improve clinician awareness of test availability, Health Education England has committed to support the NHS GMS in educating the NHS workforce by establishing a Genomics Education Programme.[203] However, there are limited commitments to the education of patients and decision makers.

Meanwhile, the NHS Innovation Service has been established to provide guidance to manufacturers on the processes involved in getting a new product approved and reimbursed in the NHS, but the application of this service to GDx remains underdeveloped, resulting in ongoing uncertainty for GDx manufacturers.[204]

- It is important to consider the continued and rapid evolution of the GDx space, and any solution should consider establishing a means for innovative technologies, such as computerised decision support services, to readily integrate into NHS systems and workflows.[205],[206] Part of this solution may involve optimisation and extension of the NHS's horizon scanning functions, currently undertaken by the Accelerated Access Collaborative (AAC),[207] to increase preparedness for integration, but should also make available to GDx manufacturers clearer information on current NHS working practices so that services may be designed with these in mind.
- As suggested by the Association of the British Pharmaceutical Industry (ABPI),[208] the introduction of key performance indicator reporting at the GLH level would help to elucidate the areas for infrastructure optimisation.
- Furthermore, in areas where no products currently exist on the market, healthy competition should be promoted between services developed within the NHS and those provided externally by the GDx industry, to maximise innovation and patient access. Initiatives to foster innovation in these areas of clinical need should be considered – for example, the model used in the Rapid Acceleration of Diagnostics (RADx) programme launched by the National Institutes of Health (NIH) in the US.[209] By outlining a set of capability requirements and by opening applications to a wide range of stakeholders, healthy competition can be promoted, delivering more opportunities for innovation and entrepreneurship and enabling the NHS – and thus patients – to take advantage of the best technology available.
- The processes involved in seeking conformity assessment and reimbursement for a new product should be clarified and optimised. Part of this solution might involve continued and focused investment in and improvement of the advisory capacity of the NHS Innovation Service.

[202] NHS England (2022) Accelerating genomic medicine in the NHS. Available at: https://www.england.nhs.uk/long-read/accelerating-genomic-medicine-in-the-nhs/ [Accessed April 2023]
[203] https://www.genomicseducation.hee.nhs.uk [Accessed April 2023]
[204] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[205] Turner, R. M. et al. (2020) Pharmacogenomics in the UK National Health Service: opportunities and challenges. Pharmacogenomics. 21(17): 1237–1246.
[206] Information from interview programme with representatives from the diagnostics industry, November–December 2022
[207] https://www.england.nhs.uk/aac [Accessed April 2023]
[208] ABPI (2022) Harnessing the UK's genomics expertise to improve patient outcomes. Available at: https://www.abpi.org.uk/publications/harnessing-the-uk-s-genomics-expertise-to-improve-patient-outcomes [Accessed April 2023]
[209] https://www.nih.gov/research-training/medical-research-initiatives/radx [Accessed April 2023]

- An interconnected educational infrastructure is needed (as called for in Genomics England's recent review),[210] managed by all stakeholders, and to educate all stakeholders, with frequent updates to reflect the rapidly changing landscape for GDx technologies. However, education alone is not enough, and it is important to consider how the topics surrounding and the findings generated by GDx can be communicated in a way that integrates with the current work of healthcare providers. In Europe, the INSTAND programme has been established to optimise the workflow for NGS of samples from cancer patients, with a focus on communicating findings in a way that can be easily understood by patients and can inform bedside clinical decisions.[211] Other solutions could consider leveraging the NHS app – now used by over 30 million people – to support patient education and access, helping patients feel more in control of their own health and genomic data.[212]
- Finally, it is necessary to enable the demand drive and clinical need signalling of the NHS to be more appropriately captured and actioned upon to maximise integration of this function into the GDx infrastructure. For example, clinicians who have started to develop or successfully developed new technologies or approaches should be encouraged to expand these into more widespread NHS offerings, with support available for navigating the broader regulatory imposition associated with such expansion.

[210] Alarcón Garavito, G. A. et al. (2022) The implementation of large-scale genomic screening or diagnostic programmes: A rapid evidence review. European Journal of Human Genetics. 1–14.
[211] https://www.instandngs4p.eu [Accessed April 2023]
[212] https://www.nationalhealthexecutive.com/articles/nhs-app-achieves-30-million-downloads [Accessed April 2023]

5.3. Summary

Box 7: Summary of main policy recommendations

The value of partnerships can be observed through their widespread implementation, but an optimised process for establishing partnerships requires political and legislative support. Such support should include:

- Establishing more efficient pathways for new technologies to be identified and piloted in the NHS
- Developing guidelines for the collection and publication of evidence that is generated over the course of partnership
- Creating a forum for documenting and sharing lessons from the implementation of new technologies

However, further targeted policy intervention is also required, to address the root causes of the impeded adoption of GDx technologies in the UK health system and to support routine patient access:

- Effective implementation of the new regulatory framework covering GDx in the UK, learning from international experiences and providing appropriate guidance and support for companies to avoid access bottlenecks.
- Greater clarity and guidance on pathways into commissioning of novel GDx across the UK, minimising the need for individual duplication of efforts and decisions at a subnational level and thus preventing inequity and delays in access.
- Optimising the role of value assessment in informing funding decisions and uptake of novel GDx by increasing the efficiency of evidence generation and incentivising evidence generation through linking this more strongly with funding and access.
- Supporting adoption of GDx through a more proactive approach towards horizon scanning and preparedness for new, increasingly digital technologies, introducing key performance indicators to monitor implementation, and providing accessible education for clinicians, patients and decision makers.

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