

Together we will beat cancer



CANCER
RESEARCH
UK

EARLY DETECTION AND DIAGNOSIS OF CANCER

A ROADMAP TO THE FUTURE



1 | FOREWORD

The early detection and diagnosis of serious disease, including cancer, changes outcomes substantially. If cancer can be intercepted at the earliest clinically relevant timepoint this gives a much better chance of survival and an improved quality of life. Generally, it also leads to safer, more limited and more widely available treatment. For many cancers earlier diagnosis would lead to transformed outcomes with existing treatments.

Early detection and diagnosis (ED&D) is therefore rightly emerging as a priority for organisations across the UK and globally as an important tool for extending and saving lives. Many organisations are setting ambitious targets for detecting cancers at earlier, more treatable stages. But this challenge is considerable and requires coordinated action across a range of sectors and organisations in order to make progress. Cancer Research UK has done great work to develop a document setting out the possible future of ED&D and a series of actions that serve as a roadmap to getting there.

The process identified major challenges and proposes addressing them through funding new research and technology innovation, investing in platforms and data access to support such research, developing new models of healthcare and engaging the public and patients meaningfully in designing the solutions.

The mix of skills, resources and infrastructure in the UK give us the potential to lead ED&D research and development, accelerating health impact and creating a significant opportunity for the UK economy. Academia and industry can accelerate patient benefit by working together to ensure rapid transition from research and development into policy and practice. Engaging the ED&D ecosystem (including researchers, industry, the NHS, regulators and importantly the public and patients) was important in developing this roadmap and will continue to be important for putting it into practice.

Due to COVID-19 we are now in a particularly difficult time for health services and research. Many in the ED&D ecosystem have undoubtedly been affected significantly. Reacting to the pandemic is important but so too are many other health priorities; these have not gone away. One of these is cancer ED&D and its potential for the UK and globally. We should not allow COVID-19 to stop the progress that was being made and the ambition to go further. Earlier diagnosis of cancer can be transformative of peoples lives, and we need to continue to undertake the planning and research to achieve it.



Professor Chris Whitty

Chief Medical Officer for England and
Chief Scientific Adviser for the Department of
Health and Social Care

This report was developed by Cancer Research UK in consultation with the Early Detection and Diagnosis Roadmap Steering Committee, workshop participants and external representatives.

Project team: Nicole Lyons, David Crosby, Rose Dixon, Emma Greenwood, Samantha Harrison, Sara Hiom, Jodie Moffat, Talisia Quallo, Emlyn Samuel, Ian Walker

IN CONSULTATION WITH:



CONTENTS

1 FOREWORD	2
2 EXECUTIVE SUMMARY	5
3 EARLY DETECTION AND DIAGNOSIS OF CANCER ROADMAP	10
4 INTRODUCTION	11
Current Early Detection and Diagnosis landscape	11
Accelerating action and research – uniting behind a shared Roadmap	14
Scope of this Roadmap	15
Impact of COVID-19 on this Roadmap	15
Key terminology used in this Roadmap	16
Putting it into perspective	16
5 VISION FOR THE FUTURE OF ED&D	17
6 ED&D ROADMAP THEMES & ACTIONS	20
Theme 1: Understanding risk and prognosis: biology to technology	20
Action 1: Longitudinal deep characterisation of early cancer and pre-cancerous lesions	22
Action 2: Using routine patient touch-points with the NHS as a platform for risk stratification, early detection research and clinical practice	24
Action 3: Flexible risk-adapted screening for national screening programmes	26

Theme 2: Biomedical data science and systems	27
Action 4: Using electronic health records and AI/machine learning methods to deliver assessment of cancer risk in early symptomatic patients	29
Putting it into perspective	31
Action 5: Novel AI risk stratification technologies for ED&D in the asymptomatic public	32
Action 6: Wearables and other technology for real-time monitoring and risk management	35
Putting it into perspective	37
Action 7: Digital health twin	38
Theme 3: Incentivising and supporting development and commercialisation	40
Action 8: A health economic model for ED&D	42
Action 9: A health innovation incubator for ED&D	44
Action 10: A platform for validation and evaluation of new diagnostics in cancer referral pathways in hospitals	46
Putting it into perspective	47
Theme 4: Healthcare system innovation and accelerating adoption	49
Action 11: Mapping the ED&D pipeline and developing Target Product Profiles	50
Action 12: Generating cancer site-specific ED&D roadmaps	52
Action 13: A phased approach to automate diagnostic clinical pathways	54
Action 14: Dynamic patient and public health consultation	56
Putting it into perspective	57
7 POLICY RECOMMENDATIONS	58
8 CONCLUSION: REALISING THE VISION FOR ED&D	62
9 CASE STUDY: THE JOURNEY OF CYTOSPONGE®-TFF3	63
10 APPENDIX 1 - ED&D ROADMAP DEVELOPMENT PROCESS AND CONTRIBUTORS	66
References	69

2 | EXECUTIVE SUMMARY

Progress over the last 50 years has transformed the prospects for people diagnosed with cancer in the UK. In the 1970s, only one in four cancer patients survived their disease for 10 years or more. By 2010, this had risen to two in four, and survival continues to improve [1]. This is due to groundbreaking research, screening programmes, data-led improvements to healthcare pathways, innovative new treatments, and the tireless efforts of staff across the National Health Service (NHS).

However, there is still much to be done. Cancer remains the leading cause of death in the UK [2]. A growing and ageing population with increasingly complex needs means that cancer incidence continues to rise at an alarming rate, with a stark projection of rising incidence to over half a million cases per year by 2035 [3]. We also see lower survival in the UK than in comparable countries around the world, and significant variation in outcomes across the UK too [4]. Critical to addressing these challenges, at home in the UK and globally, is to see a paradigm shift in our ability to detect and diagnose cancer at an early stage. Patients diagnosed early, at stages 1 and 2, have the best chance of curative treatment and long-term survival. For example, 92% of patients with bowel cancer diagnosed at stage 1 survive their disease for at least five years, compared to 10% of patients diagnosed at stage 4 [5]. But in England, for example, we are currently only diagnosing just over half of patients at an early stage [6], demonstrating significant opportunity for improvement.

The importance of this challenge is recognised by the UK and devolved nations' governments [7]. The NHS England Long Term Plan makes the commitment to detect 75% of cancers at an early stage by 2028 [8], and similar ambitions are set out in cancer strategies in the devolved nations. These ambitions cannot be met through better implementation of known cancer diagnostics alone – research and development to bring in new, impactful early detection and diagnosis (ED&D) approaches will be vital. Not only will ED&D save lives, but it will likely be cost-saving for health systems in the long-term as the high cost of late stage disease treatment is reduced.

The future of healthcare lies not solely in firefighting symptomatic disease, but in health maintenance – a holistic, proactive approach to understanding disease risk, early detection of deviations away from health and intervening appropriately. Such an approach will ultimately deliver disease prevention (through interception of consequential pre-disease). While this **Roadmap for the Early Detection and Diagnosis of Cancer** primarily focuses on cancer, it lays out plans to work towards a health maintenance research, development, regulation and implementation system that applies across health generally; cancer may be used as an exemplar to establish technologies and approaches that will deliver benefit in many disease areas.

In addition to the clear potential for health benefit through ED&D, there is also significant potential to create a world-leading environment for research, development and commercialisation of ED&D technologies, contributing to the growth of the UK economy. Historically, industry and private finance investment into ED&D development has been limited, but the tide is turning globally [9], [10], [11], [12]. Increasing biological insight and technological progress are enabling a new wave of commercial activity in this space; the UK has many of the ingredients to be a world-leader in this developing ED&D industry, capitalising on its science base and the NHS to attract investment from corporations and private finance on a global scale. This clearly aligns with UK government's ambitions to become a global science superpower, with plans to increase investment on research and development to 2.4% of the UK's GDP by 2027 [13].

Given the strong survival benefit for patients and the global growth of industrial and private finance interest in this space, it is clear that ED&D research, innovation and healthcare provision should form a central pillar of the UK's approach to realising our ambitions in both cancer and research. However, the field is beset by a historic lack of research funding and infrastructure, a market failure leading to lack of industry investment due to high research and development costs, significant regulatory hurdles and unclear adoption pathways, and an undervaluing of ED&D technologies by the healthcare system. Beyond cancer, many of

the recommendations outlined in this Roadmap including streamlined regulatory processes, access to health data for research, and opportunities for industry investment, engagement and collaboration, represent a gateway for progress in multiple diseases.

Through extensive consultation with multiple sectors and organisations, this **Roadmap for the Early Detection and Diagnosis of Cancer** aims to bring the entire ED&D ecosystem together to build an integrated, shared vision for the future, and to identify clear recommended 'Actions' to overcome major hurdles and accelerate progress in ED&D. Although this process was convened by Cancer Research UK (CRUK), this Roadmap represents the views of, and recommendations for, the ED&D ecosystem as a whole. Progress in ED&D of cancer will only be possible through collegiate action from many sectors and stakeholders as part of an interlinked ecosystem.

In addition, while the Roadmap was developed with a primary focus on the UK, it considers global activities in ED&D. The UK must recognise and build upon learnings from international efforts to deliver ED&D approaches that are nationally focussed but of global relevance. The models described could benefit health systems worldwide, with the UK acting as the exemplar.

This Roadmap aims to:

- Define a shared vision across all stakeholder sectors (e.g. academia, industry, regulators, investors, research funders, patients, the public, health professionals in primary and secondary care and healthcare system commissioners/ payers) for the future of ED&D.
- Build on the momentum, interest and initial work from CRUK and others [14] to identify the key challenges in ED&D and the opportunities to overcome these challenges.
- Define Actions to progress from the current state to the shared vision – outlining how the ED&D ecosystem can work together to achieve progress and impact on health – and 'Policy Recommendations' for the UK government and governments of the devolved nations to enable the Actions and address cross-cutting barriers.
- Ensure ED&D is delivered ethically, equitably and transparently throughout the UK with extensive involvement with patients and the public, thereby reducing health inequalities. For some cancers, the most socioeconomically deprived parts of society are subject to the highest rates of late cancer diagnosis [15] – the health system is duty-bound to address this inequality.

VISION

A future where the early detection and diagnosis of cancer (ED&D) is prioritised, incentivised and routinely embedded in UK research, development and health systems, as part of a paradigm shift towards proactive health management of individuals. ED&D will have a thriving multi-disciplinary and cross-sector research ecosystem that yields comprehensive insight into minimally invasive, cost-effective and publicly acceptable solutions, with a state-of-the-art system for evaluation, regulation and uptake, to ensure ED&D is a routine reality. Patients and the public will be actively engaged in ED&D, championing its transformative potential to improve health outcomes.

The following four 'Themes' emerged for the future of ED&D research, development and healthcare, highlighting major challenges and recommended Actions for the ecosystem. Underlying these Themes is a fundamental need for more research, both in academia and industry, to better understand early cancer signals and how to detect them reliably. This foundational knowledge generated by discovery research and technology innovation is essential as a critical first step for the Actions recommended in this Roadmap, alongside the translation of research to commercialisation and healthcare practice.

THEME 1



Understanding risk and prognosis; biology to technology: This Theme addresses the current uncertainty around identifying who is most at-risk (and so should be tested), and whether the early cancers (or pre-cancers) that are detected will progress to consequential/lethal disease or not. Resolving this uncertainty will be needed to optimise detection and minimise risk of overtreatment.

This Theme recommends the following Actions:

1. **Longitudinal study of a cohort of individuals with particular type(s) of very early or pre-cancerous lesions** to find factors that predict progression to consequential/lethal disease and development of technologies capable of detecting and prognosing.
2. **Using existing NHS patient touch-points as a platform for risk stratification and early detection research** (including sample and data capture) and clinical practice.
3. **Bringing flexible risk-adapted screening to the UK's national cancer screening programmes;** through research, identify mechanisms to risk stratify the population (through genomic or other means) and then integrate clinically- and cost-effective risk stratification into existing national screening programmes to maximise appropriate ED&D.

THEME 2



Biomedical data science and systems: This Theme addresses the current barriers to data access for ED&D research and the lack of data science and platforms for integration of biomolecular data with personal/health system/population data to inform ED&D healthcare. It recommends the following Actions to be delivered in an ethically sound way, with data privacy and protection for individual health data at the forefront:

4. **Using e-health records and artificial intelligence (AI)/machine learning methods to deliver assessment of cancer risk in early symptomatic patients presenting to primary care;** research to identify signals from missed diagnostic opportunities and then translation to methods for use of live data to support general practitioner decision-making.
5. **Generation of novel AI risk stratification technologies for ED&D in the asymptomatic public;** a phased approach to identify (through data science) and test (through emerging technology) the asymptomatic general public at risk. Building in data streams including e-health records, genomic sequence, family history, age, behavioural factors, web search history, emerging test technologies, etc. to identify individuals at high risk or with early deviations from health who should be screened for cancer.
6. **Development and evaluation of wearable and other technology for real-time monitoring and risk management;** identify and develop opportunities for wearable, implantable and/or mobile technologies and digital literacy to enable real-time health monitoring of the public for ED&D.
7. Building on the research insights and outcomes of Actions 4, 5 and 6, **creation of a 'Digital Health Twin' system:** a lifelong, personalised digital model mirroring an individual's health history updated with each risk, symptom, diagnostic, test, intervention, examination, etc. that would flag-up risks and provide guidance to proactively manage an individual's health.

THEME 3



Incentivising and supporting development and commercialisation: This Theme explores the current lack of incentives and the blockers to developing, investing in and commercialising new ED&D approaches. It recommends the following Actions:

8. **Creation of a health economic model for ED&D** to establish the economic viability of ED&D as a paradigm, and to be able to suggest the performance characteristics that a new test would have to achieve in order to be cost-effective in a given set of circumstances of use. This would seek to encourage more investment from the public and private sectors in ED&D development because of this economic viability.
9. **Establish a 'Health Innovation Incubator' for ED&D** to assist start-up companies by providing them with initial seed investment, physical space, mentorship and resources (on trial design, regulation, health economics and health systems insight, securing funding, etc.) to design and build an efficient, sustainable business model.
10. **Create a platform for validation and evaluation of new diagnostics in cancer referral pathways in hospitals;** a network of NHS-based platforms to design and deliver rapid evaluation and validation of ED&D signatures and tests in a real-world clinical environment (i.e. Clinical Trials Units for ED&D).

THEME 4



Healthcare system innovation and accelerating adoption: This Theme addresses challenges of ED&D regulation and commissioning not being fit-for-purpose, and the further evolution that is required. It recommends the following Actions:

11. **Creation of a national body to map, define and conduct an evidence assessment of the ED&D product pipeline in the UK and globally, and to set Target Product Profiles (TPPs)** (e.g. desired performance characteristics for new tests to work towards), with a UK government and NHS commitment to rapidly adopt tests which meet these TPPs.
12. **Generate cancer site-specific ED&D delivery roadmaps;** addressing the duplication, fragmentation and limited impact caused by poor linkage of the ED&D ecosystem by galvanising cancer site-specific roadmaps for ED&D research and clinical practice, for priority cancers with poor stage of diagnosis at present.
13. **A phased approach to optimising NHS ED&D diagnostic pathways** via systematic mapping of current pathways to identify opportunities for standardisation, optimisation and future automation through the development and application of technological approaches (e.g. AI) to reduce demand on workforce and optimise detection.
14. **Dynamic patient and public ED&D consultation;** develop and support a multi-disciplinary initiative to investigate patient and public attitudes, baseline knowledge and preferences regarding ED&D approaches. This would be a managed resource to support all academic and industrial research and development (R&D), and government policy in this space.

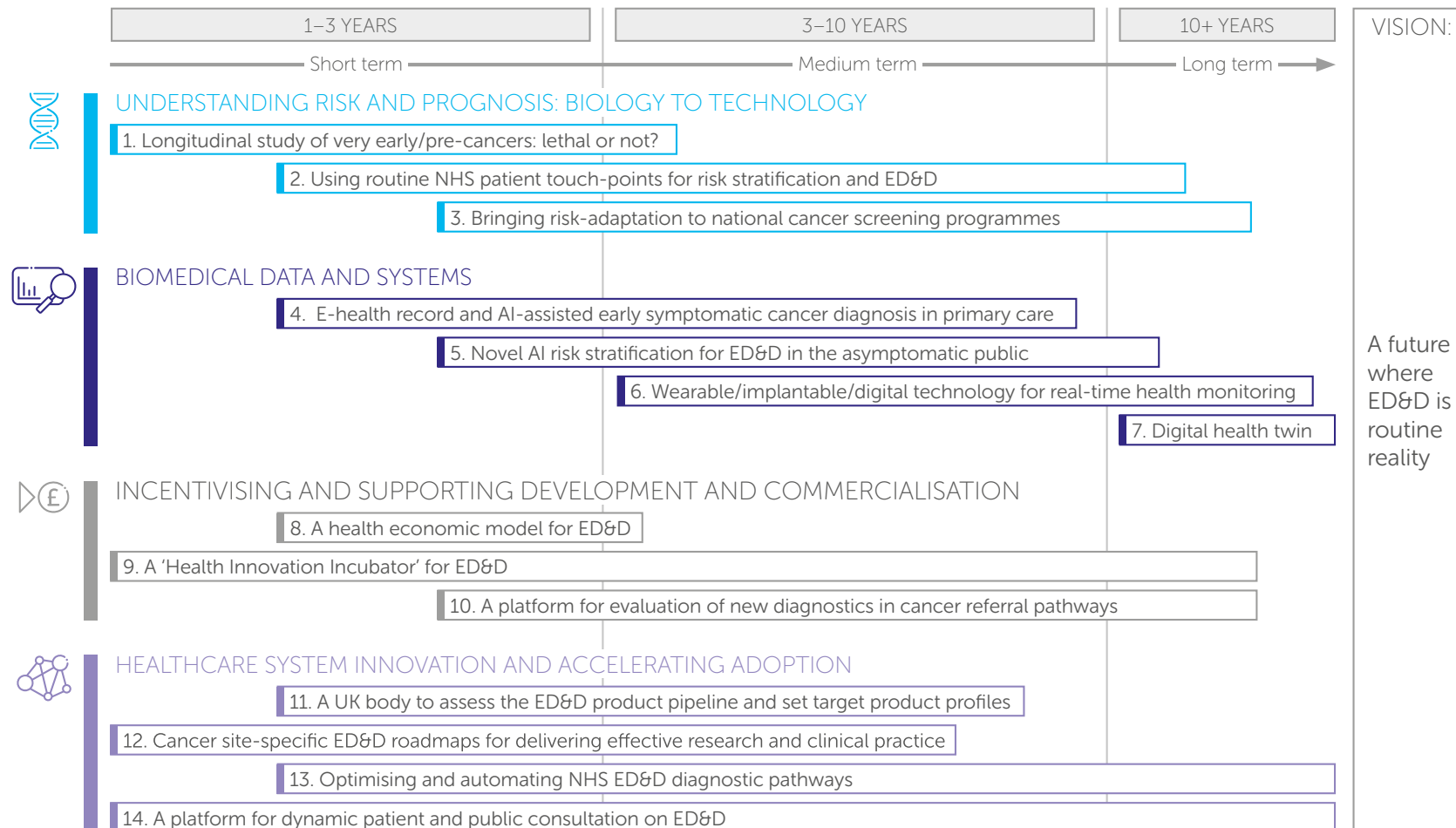
In addition, several cross-cutting barriers emerged during the consultation that, if not overcome, will impede progress towards achieving the shared vision of this Roadmap. Given the underpinning nature of these barriers, the UK and devolved nations' governments and other national bodies have a clear role to play in addressing these and facilitating a world-leading environment for ED&D. While there has been some positive progress to date, including greater emphasis on ED&D in the Life Sciences Industrial Strategy [16] and £79m committed to the Accelerating Detection of Disease programme [17], much more can and must be done. This is not only in the interests of improving health, but also wealth, given the potential economic benefit that could be developed as a result of the UK realising its role as a world-leader in this field.

Policy Recommendations to address the cross-cutting barriers to ED&D:

- 1. The UK government should make ED&D a central tenet of the UK R&D roadmap**, investing appropriately and addressing barriers to ensure a flourishing ecosystem for ED&D R&D.
- 2. The UK government and devolved nations' equivalents must address the market failure experienced in the commercialisation and adoption of ED&D technologies.** A taskforce should be established to develop an action plan to remove barriers, incentivise industry and investors into the ED&D space and accelerate adoption of technology. A vital part of this must be considering how diagnostic tests are valued in the health service and their pathway to adoption, building on the development of the NHS England and National Institute for Health and Care Excellence (NICE) MedTech Funding Mandate [18], and committing to quickly commission technologies that meet a well-defined TPP. This review should also explore a model of earlier roll-out of tests showing impact on reducing late stage diagnosis, followed by real-world evaluation of longer-term impact (e.g. on mortality).
- 3. The UK government and devolved nations' equivalents must invest to increase health service capacity – workforce, equipment and infrastructure – now and in the future, to support the ED&D agenda.** The UK government and governments of the devolved nations must be bold and provide adequate funding to train and maintain the primary and secondary care workforce that the healthcare system needs, both to meet future patient demand and to support research and innovation. Healthcare services should also explore how investment can be shifted to support and incentivise ED&D approaches more effectively, and ensure resource is available to support ED&D research.
- 4. The UK government should significantly boost investment to accelerate robust collection, interoperability and access to patient data for ED&D research, while maintaining public trust.** This should include: 1) accelerating delivery of central points of access and mechanisms for ED&D researchers to access patients' health data in a streamlined, real-time, low-burden and ethically-sound way (partnering with, building and delivering on the work of the National Disease Registration Service (NDRS), NHS Digital, Health Data Research UK (HDR UK), CRUK and others), and 2) reviewing how biological samples taken in routine practice can be utilised for research.
- 5. The UK government and devolved nations' equivalents should strategically scope and explore creating a new model of community-based health-check centres** to check (ostensibly) healthy, asymptomatic people and find early disease and/or markers of future disease and risk. Scoping of this potential future model should involve identification of, and support for, the emerging paradigm-changing research and technology development findings in the ED&D space, building on the research and systems proposed in this Roadmap. To promote equity of access, alternative routes for touch-points with the public should be explored through, for example, community pharmacies, health-check stations in supermarkets, etc.
- 6. The UK government and devolved nations' equivalents should create a clear and visible system of leadership and accountability for ED&D and diagnostics**, spanning imaging, pathology, endoscopy, genetic testing and *in vitro* diagnostics. This should involve the creation of a national leadership role for pan-disease ED&D in the NHS, and a national cadre of NHS 'Cancer ED&D Champions'.

The time to prioritise and action ED&D is now. With a growing ecosystem and emerging technological capabilities, there is an unprecedented opportunity to transform health outcomes for patients and the public by harnessing efforts to enable effective ED&D.

3 | EARLY DETECTION AND DIAGNOSIS OF CANCER ROADMAP



POLICY RECOMMENDATIONS The UK government and devolved nations' equivalents should:

1. Make ED&D a central tenet of the UK R&D roadmap
2. Address the market failure in ED&D; appropriate valuation and adoption
3. Invest in health service capacity for ED&D delivery and research
4. Accelerate quality, ethical collection and access to patient data for ED&D
5. Explore a new model of health-check centres for asymptomatic public
6. Create a system of leadership and accountability for ED&D and diagnostics

4 | INTRODUCTION



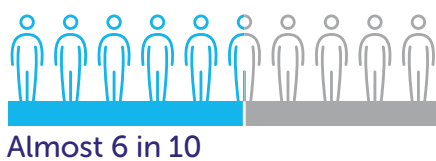
Current Early Detection and Diagnosis landscape

Detecting cancers at an early stage has the potential to revolutionise patient outcomes. At an early stage (stages 1 and 2), there are more treatment options (and more options for treatment with curative intent), causing a positive shift in patient survival and quality of life (Figure 1). Whereas at the later stages of cancer (stages 3 and 4), fewer, if any, curative options are available, response to treatments can be poor, and survival decreases greatly (Figure 2). A major reason why cancer outcomes in the UK lag behind comparable countries, particularly for some cancer types, is that cancers tend to be diagnosed at a later stage [19], [20]. For decades, whilst treatments for cancer have made revolutionary steps forward, ED&D has presented a persistent scientific and clinical challenge. Indeed, in England, 45% of all cancers with a known stage are still detected at stages 3 and 4 [6].

Early detection and diagnosis (ED&D) is defined as the identification and characterisation of a consequential cancer or pre-cancerous change (i.e. those which will cause mortality or significant morbidity within the individual's expected lifespan) at the earliest possible point at which an intervention might be made.

Figure 1: Five-year survival by stage at diagnosis

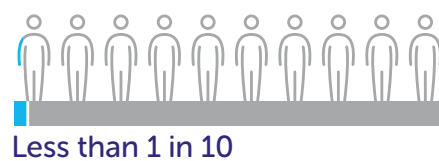
Diagnosed at earliest stage



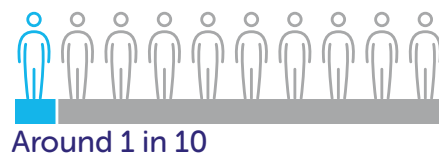
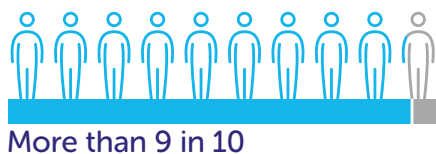
Lung



Diagnosed at latest stage



Bowel

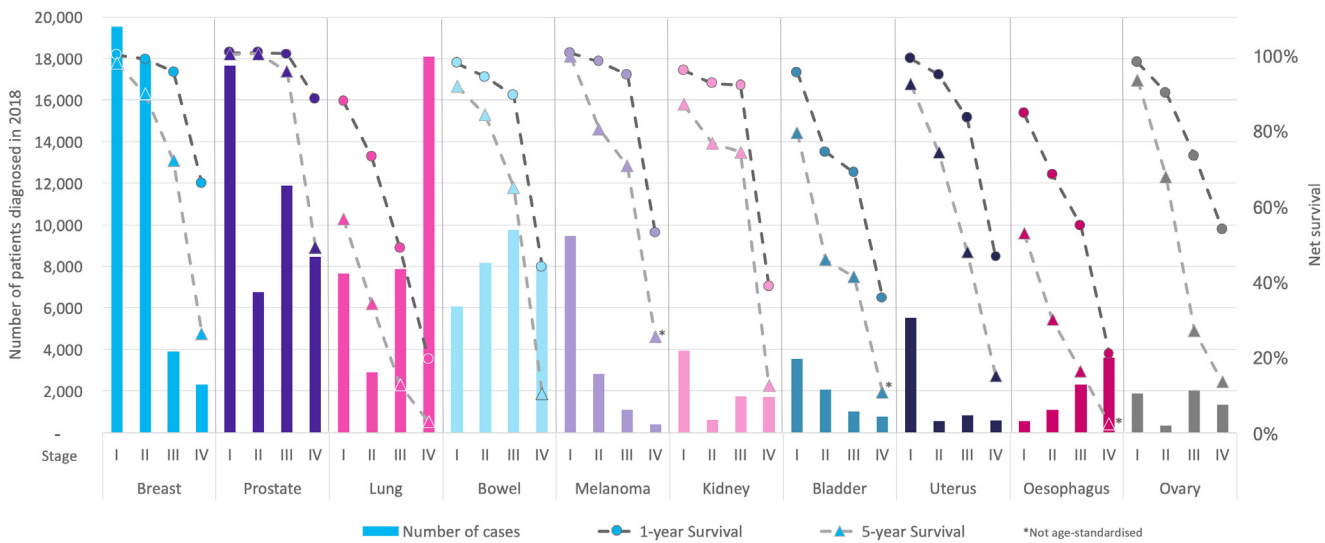


Earliest stage = stage 1; latest stage = stage 4.

Data is age-standardised net survival for adults (aged 15 to 99 years) in England in 2012-2016 followed up to 2017.

Source: Cancer survival in England. ONS/PHE, 2019.

Figure 2: Incidence by stage (2018) with one-year and five-year age-standardised net survival by stage in England



Produced by the CRUK Cancer Intelligence team using data from ONS & PHE Cancer survival in England.

Positive steps have been taken, as improved ED&D is now recognised by governments across the UK as a key strategy to improve prospects for cancer patients [7], [21]. For example, the NHS Long Term Plan sets bold ambitions to improve cancer survival in England by aiming to diagnose 75% of cancer patients at an early stage by 2028 (up from 54% of patients in 2017). This is a hugely positive ambition, but it is also a monumental challenge to achieve. It will require significant efforts across the pipeline from the basic understanding of how cancer develops to embedding new ways to detect and diagnose cancer in front-line healthcare. Furthermore, the UK government has announced plans to support the Accelerating Detection of Disease challenge, which represents a paradigm-changing research platform aiming to recruit a cohort of 5 million healthy volunteers. This platform will enable development and evaluation of new ways to detect and prevent the development of diseases, serving as an unparalleled and critical resource [17].

Stage 1 usually means that a cancer is relatively small and contained within the organ it started in.

Stage 2 usually means that the tumour is larger than in stage 1, but the cancer has not started to spread into the surrounding tissues. Sometimes stage 2 means that cancer cells have spread into lymph nodes close to the tumour. This depends on the particular type of cancer.

Stage 3 usually means the cancer is larger. It may have started to spread into surrounding tissues and there are cancer cells in the lymph nodes in the area.

Stage 4 means the cancer has spread from where it started to another body organ. This is also called secondary or metastatic cancer.

The ED&D ecosystem is defined as the web of stakeholders critical to progress in early detection and diagnosis of cancer (e.g. academia, industry, regulators, investors, research funders, patients, the public, healthcare professionals, commissioners/payers).

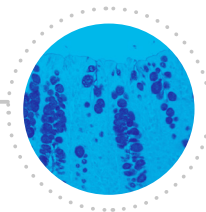
In the UK, lives have been saved by the existing national cervical, colorectal and breast screening programmes [22], [23], [24]. Nevertheless, their contribution to ED&D is relatively small, with only 6% of all cancer patients diagnosed through the UK's national screening programmes and uptake in those eligible being far from complete [25]. Early detection methods in other cancers are largely unsatisfactory or absent.

Inconsequential disease: pre-cancerous or cancerous lesions that will never cause clinically relevant morbidity or death during a patient's ordinarily expected lifetime.

Primary care plays a crucial role in the timely diagnosis of cancer but deciding the best course of action for patients presenting with a myriad of non-specific symptoms, and/or comorbidities is a complex task, and disparities remain in symptomatic presentation to primary care across different populations [26]. Despite an increase in ED&D research, there are significant challenges that impede the research itself and the translation and implementation of novel technologies and approaches into routine healthcare, as described in the sections below [14]. Further, ED&D is a comparatively nascent and siloed research field and lacks an integrated research community. Research in this field often struggles to achieve proper validation due to numerous factors including:

- complex and unclear biology,
- lack of quality sample availability (particularly repeated samples taken over time, including pre-diagnosis),
- insufficient funding for validation and translation,
- relatively limited interest from large industry players due to the lack of a clear economic model for ED&D technologies,
- a lack of specialist investors,
- a complex regulator/payer environment,
- historically poor returns from investment in this space,
- hurdles to market access,
- unclear protectability of biomarkers and algorithms,
- lack of visibility of, and collaboration within, the field.

The current requirement for evidence of impact on survival in order for ED&D approaches to be implemented leads to the requirement for complex, lengthy, large-scale and expensive trials. The challenges faced by the ED&D ecosystem are further explored in this Roadmap (Section 6), As a result of these and other challenges, a large proportion of cancers are still diagnosed at stage 3 or 4, when the prognosis is poorer, and there are fewer treatment options [25].



Accelerating action and research – uniting behind a shared Roadmap

CRUK has set an ambitious goal to drive change and progress in the field of ED&D in the UK and globally, acknowledging that this cannot be achieved by individual and fragmented efforts. The entire ED&D ecosystem, from research to healthcare delivery, needs to come together to set a shared vision for the future, to identify and resolve the major hurdles to progress and to build consensus and buy-in from a diverse range of key stakeholders. To support this effort, CRUK recruited a Steering Committee (Appendix 1) of visionary leaders, chaired by Professor Chris Whitty (Chief Medical Officer for England and Chief Scientific Adviser for the Department of Health and Social Care) to set the framework for this **Early Detection and Diagnosis of Cancer Roadmap** (ED&D Roadmap).

The development of this Roadmap was also informed by a two-day workshop held in late 2019; over 80 representatives (Appendix 1) from across academia, industry, government and research funders were brought together with healthcare professionals, patient representatives, and investment and regulation experts to critically discuss and prioritise a set of recommendations for action and a shared vision of the way forward for the ED&D ecosystem. CRUK's Cancer Insights Panel (a panel of people affected by cancer) was also consulted to gather patients' perspectives on key elements of this Roadmap; these views are integrated throughout this report.

This ED&D Roadmap collates the input of all major stakeholder sectors, organisations and groups to ensure that the vision for the future is integrated, and that the recommendations for action are inclusive and effective. The outputs of this Roadmap are intended to shape not only CRUK's ED&D strategy, but the ED&D ecosystem at large.

A roadmap is a high-level strategic plan that defines a goal or desired outcome and includes the major steps or milestones needed to reach it.

This Roadmap aims to:

- Define a shared vision, across all stakeholder organisations and sectors of the ED&D ecosystem, for a future where the ED&D of cancer is a routine reality.
- Build on previous work from CRUK and others (e.g. CRUK-Academy of Medical Sciences 'Accelerating the translation of early detection and diagnosis research in cancer' report [14]), to further define the current state of the field, the challenges faced in working towards the vision for the future and the contextual needs, trends and driving factors which will affect its delivery.
- Define Actions to progress from the current state to the shared vision in the near (one to three years), mid (three to 10 years) and longer-term (10+ years), outlining how the ED&D ecosystem can work together to achieve progress and impact on patient survival and quality of life.

Scope of this Roadmap

This Roadmap was developed with a primary focus on the UK but considers global activities and models in ED&D to inform the recommended Actions detailed in this report; proposed Actions and Policy Recommendations are focussed on where the largest health impact in the UK healthcare systems could be. This Roadmap acknowledges that the recommended Actions need to be nationally focussed but globally relevant, with new ED&D innovations and approaches gaining crucial clinical evidence, clinical pathway relevance and health economic support within the UK, but with a vision of global application. These innovations and approaches should extend and apply the

foundational groundwork and findings from the UK to progress ED&D commercial and healthcare opportunities in other nations.

For relevant Actions, it is noted whether the Action is applicable in symptomatic versus asymptomatic populations, as the resources, gaps and objectives are often different in these two groups; there is a clear need to address both populations. This is a Roadmap for the future of the ED&D ecosystem and it relies on the coalescence of the efforts of key stakeholders to deliver the recommended Actions; no single organisation can affect progress alone.

Impact of COVID-19 on this Roadmap

The bulk of this consultation occurred in late 2019 and early 2020 before the emergence of increasing pressures on many different facets of life, including healthcare services and research, due to COVID-19.

Without question, COVID-19 has had a devastating impact on cancer services and patients, with access to screening, diagnostics, referrals, treatments and care significantly affected [27]. The impact on medical research will create aftershocks for the ED&D research community, and for the discovery and translation of innovation for patient benefit, for years to come. We are far from understanding the full impact of SARS-CoV-2 infection (and the immune and inflammatory responses it provokes) on the human immune system, or what interaction that might have with early cancers or pre-cancerous changes and risk factors.

But throughout it all, the NHS has shown an energising flexibility to adapt at an unprecedented rate; there has been rapid infrastructure creation (NHS Nightingale Hospitals), some successful efforts to create additional workforce capacity [28], and acceleration of timelines for guidance [29], collectively helping to expedite and spread good practice. The shift to digitalisation that was already underway has been accelerated, most obviously through the increase in 'online' and telephone consultations in primary care [30], and reflected across the healthcare service. The pandemic has created an opportunity for research, which has been seized with vibrant collaborations, agile research proposals, and opportunities to test innovations in different areas across the healthcare system [31].

These challenging times offer us a learning opportunity and an unparalleled showcase of what can be achieved through collaboration and unification of efforts and expertise. All the elements that have been shown to be crucial and thus made possible in this pandemic are equally important for, and can be carried into, efforts to make ED&D of cancer a routine reality. High-quality and rapid data collection, linkage and access; timely application of high-quality scientific evidence; and agile approaches across multi-disciplinary and organisational boundaries to bring research into practice have been proven as essential foundations to progress. These factors, combined with the critical importance of clear and consistent communication with the public and having the workforce and infrastructure in place to make plans a reality, underscore success. These themes are prominent in this Roadmap and the lessons learned in this pandemic can undoubtedly help shape future actions and solutions for ED&D. This is not the time to be complacent but the time to press forward thoughtfully, intelligently and strategically, unlocking the transformative potential of ED&D for the UK and globally, for the benefit of cancer patients now and in the future.

Key terminology used in this Roadmap

Actions: Recommendations for action in research and technology development/infrastructure that will help the ED&D ecosystem progress from the current state to the desired future vision. These Actions may be:

- Pragmatic: Actions that deal with the current status quo of ED&D (and the current biological and technological state of the art) and may represent relatively 'easy-wins' likely to be applicable to the nearer-term.
- Disruptive: Actions that are highly innovative, may require a considerable shift in focus, resource and investment; these may be higher-risk and may require more time to deliver.

Contextual needs, trends and driving factors in the ED&D ecosystem: The current realities, challenges and opportunities that exist in the ED&D ecosystem (and those which are anticipated to emerge in the foreseeable future) and may relate to, for example, social, demographic, ethical, research, technology, economic and/or political/legislative factors. This may include any observed inadequacies in current policy/legislation that potentially slow the progress of ED&D approaches.

ED&D: The identification and characterisation of a consequential cancer or pre-cancerous change (i.e. those which will cause mortality or significant morbidity within the individual's expected lifespan) at the earliest possible point at which an intervention might be made.

The ED&D ecosystem: The web of stakeholders critical to progress in early detection and diagnosis of cancer (e.g. academia, industry, regulators, investors, research funders, patients, the public, healthcare professionals, commissioners/payers).

Enabling platforms, infrastructure, technologies, capabilities and resources: Resources that will facilitate the delivery of the recommended Actions.

Inconsequential disease: Pre-cancerous or cancerous lesions that will never cause clinically relevant morbidity or death during a patient's ordinarily expected lifetime.

Pan-disease: Applicable to diseases beyond cancer.

Policy Recommendations: Specific recommendations that the UK government and devolved nations' governments should address to overcome the challenges identified in this Roadmap and to support the proposed Actions.

Roadmap: A high-level strategic plan that defines a goal or desired outcome and includes the major steps or milestones needed to reach it.

Putting it into perspective

"When diagnosed with lung cancer, survival wasn't thought to be an option. All I had going for me was the fact that I'd presented early which means the importance of early detection and diagnosis is firmly embedded in my psyche. I remember the surgeon's words after waking from surgery to remove half of my left lung, 'Well Terry, I'm satisfied we've caught it early.' It was decided that the planned chemotherapy and radiotherapy wouldn't be needed! Looking at the statistics surrounding lung cancer at the time, I have to admit, yes, I was caught early. I see ED&D as the way forward in catching cancer before it spreads and saving more lives. I find myself echoing the surgeon's comment 'we've caught it early!' which is really why I'm still here. Detect and diagnose is the key to surviving cancer.

The impact ED&D would have for patients would be phenomenal. Consider hospital visits, hospital stays, not to mention the anxiety, effect on the family and getting back to work, so much of this can be avoided; ED&D can give patients their lives back.

The Roadmap workshop was a real eye opener for me. Never did I consider that so many disciplines could be involved in mapping out the direction research should take to nip cancer in the bud. As a patient, being part of the bigger plan was both moving and gratifying."

Terry Kavanagh, CRUK Cancer Insights Panel Representative



5 | VISION FOR THE FUTURE OF ED&D

To realise the full potential of ED&D for improving patient survival and quality of life, the ED&D ecosystem needs to set ambitious goals to work towards in the near and long-term, with consensus, endorsement and engagement from key stakeholder groups.

VISION

A future where the early detection and diagnosis of cancer (ED&D) is prioritised, incentivised and routinely embedded in UK research, development and health systems, as part of a paradigm shift towards proactive health management of individuals. ED&D will have a thriving multi-disciplinary and cross-sector research ecosystem that yields comprehensive insight into minimally invasive, cost-effective and publicly acceptable solutions, with a state-of-the-art system for evaluation, regulation and uptake, to ensure ED&D is a routine reality. Patients and the public will be actively engaged in ED&D, championing its transformative potential to improve health outcomes.

To realise this vision, the following key outcomes are needed for a world where ED&D is part of routine reality; these outcomes describe the enabling platforms, infrastructure, technologies, capabilities, resources and activities that will need to occur in order to overcome the current challenges in ED&D to progress to the shared vision. These key outcomes are grouped using the four research Themes that are further explored in Section 6 of this Roadmap.

THEME 1



Understanding risk and prognosis; biology to technology: Understanding who is at higher risk of developing cancer and the appropriate ED&D approaches to apply to those most at-risk to detect disease and make a prognosis.

- Research will have delivered new minimally invasive, cost-effective and publicly accepted ED&D technologies with the requisite sensitivity and specificity to detect and appropriately triage the earliest cancers and pre-cancerous changes.
- There will be a clear conceptual pathway for dealing with risk and indeterminate pre- and early cancer. This will be revealed by biological research, which integrates ED&D and a deep understanding of biology/prognosis/disease trajectory with clear direction on monitoring and intervention strategies. There will be clear management options for cancers too small to visualise and/or be surgically resected, but for which molecular and structural profile information from ED&D tests will be available.
- The UK health system will avoid unnecessary tests and medicalisation of those not at increased risk. To enable this, future ED&D strategies may, at least in part, be targeted to high-risk groups based on genomics, biomarker changes, lifestyle and other such stratifying factors.
- The epidemiology of cancers will change as demographics, risk factors and behaviours change; ED&D technologies and approaches will incorporate these changes to achieve maximum patient benefit, in an equitable and ethical way.
- Risk-benefit research for ED&D through coordinated, large-scale research programmes will enable a deeper understanding of potential risks and benefits of ED&D and interventions in order to minimise false negatives, false positives, psychological harm and unnecessary further testing and/or treatment.

THEME 2



Biomedical data science and systems: Ensuring access to health data for research and unlocking the potential of health data to enable effective ED&D.

- Patient/NHS data will be readily available and accessible for ED&D research. Researchers in the ED&D field will be able to access this data in a timely way to enable real-world validation of their ED&D technology and/or approach to accelerate translation and health impact. This will require continued and concerted efforts to ensure patient data is protected and used responsibly.
- An open dialogue with patients and the public regarding what is and is not wanted in ED&D, and potential barriers to uptake, will deliver insights to inform new ED&D approaches. There will be a comprehensive understanding of where and on what basis the public wants ED&D tests to take place (e.g. home, mobile community outlets, primary care), to inform a shift to proactive health management delivered by the NHS (as opposed to primarily treating symptomatic disease).
- Research will yield AI and smart systems to aid ED&D and supporting research to help inform its quality assurance and regulation. This will include deeper insights and resources to support interactions between practitioners and patients.
- Accessible and curated longitudinal data will be collected through a variety of minimally invasive tests (e.g. collected via smart phones, wearables, blood, breath, urine, acoustics, imaging, etc.) assessed continuously for the individual and understood in the context of their individual risk stratification (e.g. via genomics, environment, history, etc.). These tests may have stand-alone capabilities but will also usefully be part of a cascade of triaging and subsequent confirmatory testing in the diagnostic pathway (e.g. blood or urine-based triage tests routinely available and validated which then trigger further testing, e.g. molecular imaging).
- All necessary data systems will be interoperable to maximise the usability and information potential of both routine health system- and research-generated data in ED&D.
- There will be a commonplace approach of digitised imaging and pathology in the NHS.

THEME 3



Incentivising and supporting development and commercialisation: Placing ED&D development and commercialisation as a high priority for the UK government and devolved nations' governments and health systems to enable an attractive, growing ED&D ecosystem.

- ED&D research will be a cornerstone of cancer research, with a significant proportion of investment in cancer R&D allocated to it, across public, private and third sector funding.
- The UK government and devolved nations' governments and health systems will appropriately reward and reimburse ED&D, and investors and industry will see a strong business model to support and pursue ED&D research, development and commercialisation. The health economic benefits of ED&D will be acknowledged and drive uptake, with the flow of budgets and funding within the NHS supporting this agenda.
- The public will understand and engage in ED&D, providing further incentive to commercialise promising ED&D technologies and approaches.
- There will be a clear pathway for health economic evaluation and adoption of ED&D that works in conjunction with evolving UK regulations and guidance (e.g. NICE guidance, Scottish Intercollegiate Guidelines Network guidance, etc.).
- There will be incentivisation for industry collaboration with the NHS in ED&D. There may be a revenue share model between industry and the NHS (e.g. money flowing

back into the NHS from R&D). Industry will have used early detection of cancer recurrence as a stepping stone to initially engage and see the value and feasibility of ED&D of primary disease.

- ED&D will be prioritised by the UK government, industry and academic sectors to raise the profile of the ED&D field with strategic plans to attract and retain talent. There will be a vibrant, multi-disciplinary innovation ecosystem in ED&D with individual science and corporate successes recognised.
- Research will deliver novel, minimally-invasive ED&D technologies and approaches alongside highly sensitive and specific biomarker signatures.
- There will be a clear process for understanding, establishing and assessing the economic feasibility of ED&D approaches, which is embedded at the outset of new ED&D technology development.

THEME 4



Health system innovation and accelerating adoption: Building on the strengths of the current healthcare system, ensuring sufficient resource to support ED&D and evolving existing infrastructure to support validation and implementation of new ED&D approaches.

- Healthcare systems will shift a greater proportion of resources upstream into ED&D. The NHS will have the necessary resource, including appropriate workforce planning, to deliver appropriate interventions as well as timely treatments as a result of ED&D.
- There will be thorough and transparent ongoing evaluation of current national cancer screening programmes and other centrally funded ED&D interventions to build on learnings from these programmes and to further develop and iterate future ED&D interventions. These programmes will also be optimised as platforms for further research.
- The system of the NHS will enable low-cost/marginal-cost testing of new ED&D technologies, including covering of related diagnostics and treatment costs.
- Cancer will become one of a number of chronic diseases which are prevented/detected/managed together, and NHS infrastructure will enable delivery of this. A pan-disease approach to managing detection and multi-morbidity, and an appropriately trained health system workforce to utilise pan-disease platform technologies will be needed. For cancers where the role of ED&D is of significant and of critical importance for patient survival, cancer-specific approaches will be necessary.
- A diversified healthcare system and new business models will extend availability of screening and prevention beyond the current NHS model which is largely based on an 'illness' model of care, responding to patients with signs and symptoms. There will be a system to detect early deviations away from health in the asymptomatic public, thus unburdening primary care, ensuring maintenance of health without medicalising healthy individuals.
- There will be increased public education and awareness to promote public health and willingness to participate in cancer prevention and screening unveiled by quality social and behavioural research, with conversations around ownership of individual health data and uptake of screening, and supportive policies and investment which remove barriers and address inequalities.
- There will be a large-scale, prospective cohort(s) within integrated primary and secondary healthcare systems to better inform and support ED&D research and development.
- The health system workforce will be trained on appropriately assessing and communicating risk of cancer.
- There will be visible, visionary clinical leaders for integrated ED&D care systems.

6 | ED&D ROADMAP THEMES & ACTIONS

This Roadmap makes several recommendations for research and development, enabling platforms and health system evolution (Actions) which have the potential to drive the ED&D ecosystem towards the vision outlined above. These have been organised into the four Themes referenced in Section 5 for the future of ED&D research, translation and implementation:

THEME 1: Understanding risk and prognosis: biology to technology

THEME 2: Biomedical data science and systems

THEME 3: Incentivising and supporting development and commercialisation

THEME 4: Health system innovation and accelerating adoption

Throughout each Theme, major challenges of relevance to the Theme are highlighted, and a series of recommended Actions are presented that were developed and prioritised through consultation with cross-ecosystem stakeholders (see Appendix 1). This Roadmap recommends these Actions should be taken to overcome the current challenges to work towards the shared vision for ED&D. Many of these Actions are interrelated and interdependent, and some should be sequential; this is illustrated in the Roadmap diagram in Section 3 and described in the Action tables below. Underpinning all the recommended Actions is the need for more discovery research to better understand early cancer biology and technology innovation to develop new ways to detect and diagnose cancers earlier.

Additionally, developing the shared vision also brought to light several cross-cutting barriers impeding progress in ED&D across and beyond the four Themes. These cross-cutting barriers are explored in Section 7 and are addressed by a series of Policy Recommendations to the UK government, the devolved nations' governments and the NHS. These Policy Recommendations (Section 7) are needed in order to support and deliver the described Actions, address the cross-cutting barriers and enable progress towards the shared vision.

These Actions cannot be successfully delivered by fragmented efforts. To realise a future where ED&D is part of routine reality, these recommended Actions will need to be strategically delivered through meaningful collaborative efforts.

THEME 1

Understanding risk and prognosis: biology to technology



This Theme addresses the current uncertainty and future opportunity around 1) identifying the most at-risk populations in which to apply ED&D approaches and 2) determining what the likely progression will be of very early/pre-cancerous lesions, once detected. This Theme recommends large-scale research programmes to address these uncertainties, through biological insight and technology development/test innovation, and provides recommendations for initiatives to translate research into tests and risk stratifying clinical decision support systems in the NHS. It outlines a broader approach to understanding risk than is currently used, bridging biomolecular data with population data, using this insight to

proactively screen those at risk, and bringing in novel technologies.

Underlying this Theme is a fundamental need for more research, both in academic and industry settings, to better understand early cancer biology and spark novel approaches in test technology. This foundational knowledge is a critical first step for the Actions recommended in this Roadmap; this includes discovery biology informing what to look for in a biomarker, preclinical models of early disease, basic research into how the tumour microenvironment does or does not respond to the development of a tumour and technology innovation to foster new ways to detect and diagnose cancers earlier.

THE CHALLENGE:

At present, we lack a clear understanding of:

- 1) Who is at most risk of cancer and therefore in whom should ED&D tests be applied, and how should those tests be interpreted? A better understanding of this will enable optimal detection and minimal overdiagnosis (i.e. the detection and over-treatment of inconsequential disease).
- 2) What the likely progression will be of pre-cancerous/very early cancerous lesions, once detected? This will inform assessment of consequentiality and therefore clinical decisions around whether to treat or monitor these lesions.

There is a need to stratify the population (using genomic, clinical, family history and other risk factors) based on their risk of disease before the main age of onset and identifying those lying above the threshold of clinical utility for targeted screening, early detection and/or prevention.

Barriers to overcome in risk and prognosis:

- There is significant lack of biological insight into early lesions in many cancers, meaning that if detected, prognosis is uncertain (e.g. is it a potentially lethal lesion, or one which may remain indolent and inconsequential?) and therefore, tailored clinical decision making (monitoring/treatment) is challenging. Knowing which lesions should be investigated further, monitored, biopsied, treated or left alone is a critical challenge, including the terminology of early lesions being labelled as 'pre-cancer' or 'carcinoma *in situ*' when the trajectory of the lesions is uncertain.
- Early stage disease samples are lacking, and longitudinal, repeat samples from the same individuals pre- and post-diagnosis are almost completely lacking. Where samples exist, they are often divorced from health records and outcomes data.
- There is an immense signal-to-noise challenge in finding the earliest cancers, particularly given the many thousands of biomolecules or data points across which one might look for signals (e.g. in circulating tumour DNA, plasma proteins, exosomes, micro RNAs, imaging/radiomics, etc.). This creates a high risk of false positives and a need for mitigation strategies to deal with these.
- Beyond a handful of defined genetic risk conditions, our understanding of genetic risk/susceptibility is limited; this means that we do not necessarily know the highest-risk populations in which to develop, test and implement ED&D approaches. Additionally, there is poor education and understanding of risk by the public and therefore, less uptake of ED&D approaches.
- Most tests require biological specimens which can be invasive, thus limiting patient acceptability of repeat sampling over time, which holds back research and clinical utility.

Interrelated with this Theme is the need for access to the rich resource of health data for ED&D research to inform risk stratification and prognosis. This will be explored in Theme 2.

Through consultation, the following recommended Actions were prioritised to develop a framework to achieve progress in risk stratification and prognosis for detected early lesions. A high-level summary of each Action is included in the respective tables. These Actions are not intended to serve as comprehensive project plans and instead serve as a starting point for various stakeholders to come together, develop and champion.

Action 1: Longitudinal deep characterisation of early cancer and pre-cancerous lesions

Action: Longitudinal study of a cohort of individuals with particular type(s) of very early or pre-cancerous lesions to find factors that predict progression to consequential/lethal disease and development of technologies capable of detecting and prognosing.

Major challenge: As early detection advances, the number of pre-/early cancerous lesions of indeterminate significance that are identified grows. At present, there are several cancers that are known to have pre-/early cancerous lesions of indeterminate significance (e.g. lung, prostate, breast); information on which lesions need to be treated versus investigated further, versus monitored, versus left alone entirely, has immense implications for preventing overtreatment of patients. There are several efforts to find prognostic markers, but these are often underpowered or focused on single analyte platforms; opportunities are missed to find marker signatures across different analytes/modalities of testing. Current efforts in this space need to be built upon and accelerated.

Action description: For particular pre-/early cancer lesions, this Roadmap recommends the development and launch of a concerted research programme to recruit such early cases through the NHS (likely at a small group of major referral centres); these cases would be deeply pheno- and geno-typed at the point of diagnosis, and then followed up for a defined time period which is appropriate and sufficient for the given pre-/early cancerous lesion to know which will progress and which will not (without deviating from normal standard-of-care treatment decisions). At the point of progression, or at the end of the time period for non-progressors, samples/individuals would be reanalysed for genotypic and phenotypic traits. This would include investigation into tumour, germline and immune factors and comprehensive analysis for markers of progressors versus non-progressors through imaging, blood-borne markers, breath markers and any other modalities of measurement as appropriate. Investigations would be on a cancer type-specific basis (likely targeting a small number of cancer types initially) but would enable the opportunity for comparison and contrast between organ types.

Importance of pursuing: This Action will establish a coordinated and comprehensive approach through research to provide enhanced biological insight into early lesions and their environment in a range of cancers to inform prognostication of which lesions are consequential versus inconsequential. It will generate biological insight and identification of markers of future progression and will serve as a platform to evaluate emerging test technologies.

What needs to happen? Appropriate platforms for recruitment of patients with early, indeterminate lesions would need to be identified, such as through primary care and urgent cancer referrals, Rapid Diagnostic Centres, Targeted Lung Health Check projects, national screening programmes, etc. Healthcare professionals and patients would need to be engaged and their input sought, in order to optimise the protocol and its positioning. Care would need to be taken to ensure recruitment across all socioeconomic and demographic routes (particularly those populations which are often under-represented in sample acquisition for research) in order to ensure that results are applicable across populations. A broad and deep panel of analyses/tests to be applied to participants would need to be agreed upon through consultation across disciplines (e.g. blood proteomics [32], circulating cell-free DNA [33], [34], autoantibodies [35], breath [36], [37], metabolomics [38], tumour DNA sequencing/transcriptomics [39], imaging [40], extracellular vesicles [41], etc.).

Industry partners alongside specialist investors should be sought to invest into the platform and to bring their technologies to bear. A significant bioinformatics platform would need to be developed in order to accommodate the high-dimensional and multi-modal data generated, and to look for biomarker signatures across the different tests and data types.

It is suggested that lung cancer could be an exemplar for this approach, harnessing the Targeted Lung Health Checks which are currently being run in select areas in England, including low-dose CT scan screening for lung cancer in high-risk individuals. These CT screening tests will uncover many indeterminate lung nodules which may not be removed initially due to invasiveness of the excision procedure and risk/benefit balance, so affording a window of opportunity to study progression longitudinally.

Links to:

This Action should consider existing initiatives like the **CRUK Grand Challenge investigating ductal carcinoma in situ in breast cancer^a** [42], **research on lung dysplasias** [43], the **Accelerating Detection of Disease platform^b** [17] (a non-cancer-specific cohort of 5-million volunteers to support research), **Genomics England^c** [44] and the global efforts of the Pre-Cancer Atlas [45], so learnings in shared areas of interest can be built upon.

Key stakeholders:

The NHS, research funders including CRUK, the International Alliance for Cancer Early Detection (ACED), the National Cancer Research Institute (NCRI), industry, academics from biomarker discovery/validation science, pathology, imaging epidemiology, data science, public health, genomics, bio-repositories and patients.



a <https://www.cancerresearchuk.org/funding-for-researchers/cancer-grand-challenges/Preventing-unnecessary-breast-cancer-treatment>
b <https://www.ukri.org/innovation/industrial-strategy-challenge-fund/accelerating-detection-of-disease/#pagecontentid-0>
c <https://www.genomicsengland.co.uk/>

Action 2: Using routine patient touch-points with the NHS as a platform for risk stratification, early detection research and clinical practice

Action: Improve ED&D using the existing infrastructure of routine patient touch-points with the NHS (e.g. NHS Health Checks and equivalents) to target ED&D at the most appropriate groups in a cost-effective way through a multi-phase process:

Phase 1 – Capture current data and samples collected via routine touch-points in a way that can be accessed for research.

Phase 2 – Broaden sample collection and data capture beyond current practice to better enable ED&D research, in order to identify and validate detection markers, and identify classifiers to build into risk stratification models.

Phase 3 – Use the existing infrastructure of routine touch-points as a platform for trialling emerging ED&D tests for evaluation in a real-world scenario.

Phase 4 – Use the existing infrastructure of routine touch-points as a mechanism to appropriately direct patients into screening in routine clinical practice, based on outcomes of risk stratification and detection/triage test approaches built in Phases 1 to 3.

Major challenge: Existing infrastructure in the NHS needs to better enable ED&D research and healthcare approaches. Current initiatives with touch-points with ostensibly disease-free adults in the NHS like the NHS Health Checks and equivalents or national screening programmes could be harnessed and expanded to help address sample and data scarcity in ED&D research and enable real-world test validation platforms. Use of existing delivery mechanisms may help to provide a more favourable economic case.

Action description: This Roadmap recommends a multi-phase approach to use the existing infrastructure of routine health touch-points within the NHS to help better identify and validate ED&D markers and risk factors, and ultimately to risk stratify patients into appropriate ED&D clinical pathways. For example, the NHS Health Check is a health check-up for ostensibly disease-free adults in England aged 40 to 74. These checks are offered every five years and are designed to spot early signs of stroke, kidney disease, heart disease, type 2 diabetes and/or dementia; they do not currently collect any indices intended to detect cancer. This Action seeks, in the near term, to fully utilise existing touch-points with ostensibly disease-free adults in the NHS (e.g. NHS Health Checks and beyond) to gather samples and other health data to inform ED&D biomarker discovery, validation and risk stratification approaches (Phases 1 and 2) to, over time, build a rich, accessible research resource. Additionally, it seeks to expand the use of routine touch-points to include capability for real-world trials of emerging ED&D approaches (Phase 3). Phase 3 could be expanded to analyse the data collected in Phases 1 and 2 on a large scale using networks of Trusted Research Environments (e.g. building on current approaches for cardiovascular research in relation to COVID-19 [46]). In the longer-term, the insights gained from this research (and other research aiming to risk stratify the population) will then be used to implement cancer risk assessment and early detection as part of routine health check-in practice (Phase 4), subject to clinical and cost-effectiveness.

The Roadmap acknowledges that a review of the NHS Health Checks is currently underway [47], and that the opportunity of harnessing the NHS Health Checks will be dependent on the outcome of that review. Learnings from this review should inform a strategic approach to shape future touch-points with ostensibly disease-free adults in the NHS to include indices to enable ED&D.

Importance of pursuing: As new ED&D approaches can be expensive and time consuming to develop, it's important to capitalise on the existing infrastructure in the healthcare system. This Action has the potential to dramatically impact ED&D for the population accessed via existing touch-points in public health.

What needs to happen? This Roadmap recommends a progressive build on existing infrastructure and initiatives to deliver a potentially clinically- and research-rich resource for driving change in ED&D. Subsequent to ensuring buy-in from a large range of stakeholders, mostly within the healthcare system, a pilot study would need to be developed for an 'enhanced' version of routine touch-points within the NHS (Phase 2) to include expanded sample collection with appropriate broad consents. The pilot will also assess the feasibility of using bio-samples for genetic tests at primary care level. It is likely that the study would start by risk stratifying people into existing screening programmes; however, there are areas where foundational knowledge is needed through research to enable risk stratification approaches. In the process of developing the pilot study, better risk models and tools for cancer risk prediction would need to be developed, as well as gaining a better understanding of the optimal age group and optimal interventions for each group. Each screening programme would be incrementally broadened to include additional data points, better connected data, better access to data and better access for the public. Over time, this could evolve to be used as a platform to trial emerging ED&D tests. Building on the risk stratification insight from the 'enhanced' routine health touch-points and detection via validated ED&D tests, patients could be directed to appropriate clinical pathways. A health economics plan would need to be worked up alongside a plan for implementation which would include behavioural research and strategies to effectively communicate risk.

This Action would need to involve a public awareness campaign and may involve the screening programmes expanding in their number of access points to maximise uptake, such as in pharmacies. Any expansion will then need to incorporate training for healthcare professionals, as well as insuring appropriate methods are in place to record consent to use health data and the security of that data. Appropriate harmonised infrastructure would need to be in place to collect, store and integrate the various data discussed, which does not universally exist across NHS practices and trusts. Therefore, fundamental infrastructure relating to health data and patient access would need to be in place before the delivery of this Action would be feasible.

Links to: Action 1, 3, 5

This Action should consider activities of, and look to synergise with, the NHS England **Targeted Lung Health Check**^a [48] and **Accelerating Detection of Disease platform**^b [17]. Phase 3 of this Action should link to the work of the **NIHR Innovation Observatory**^c [49] and the **Accelerated Access Collaborative**^d [50]. It will also relate to the **NHS Med Tech Funding Mandate**^e [18] that is currently under consideration .

Key stakeholders: Primary care networks, the NHS, NICE, NHSX, Public Health England, NHS Digital, Department for Health and Social Care, the National Data Guardian, diagnostic service providers, CRUK, HDR UK and the Academic Health Science Networks.

a <https://www.england.nhs.uk/contact-us/privacy-notice/how-we-use-your-information/our-services/evaluation-of-the-targeted-lung-health-check-programme/>

b <https://www.ukri.org/innovation/industrial-strategy-challenge-fund/accelerating-detection-of-disease/>

c <http://www.io.nihr.ac.uk/>

d <https://www.nice.org.uk/aac>

e https://www.engage.england.nhs.uk/consultation/medtech-funding-mandate/user_uploads/medtech-funding-mandate-guidance-consultation-document-v2.00--2-.pdf

Action 3: Flexible risk-adapted screening for national screening programmes

Action: Through a concerted research programme, identify mechanisms to risk stratify the population (through genomic, lifestyle and other means) to identify groups at higher risk of cancer; once utility is demonstrated by this emerging research, integrate clinically- and cost-effective risk stratification into existing national screening programmes to optimise ED&D.

Major challenge: National cancer screening programmes are currently based on age-related risk and neglects other information regarding risk. As the population increases and there is greater pressure on screening programmes, it will become increasingly important to reduce costs and time associated with unnecessary tests, to minimise the possibility of overdiagnosis/treatment and to maximise early detection by risk stratifying the population more effectively. This includes applying ED&D tests appropriately to those at highest risk, who may not currently be eligible for screening.

Action description: In the foundational phase of this Action, embarking on a coordinated research programme to identify and validate improved mechanisms to risk stratify the population is recommended, building on current research in this area. New ways to sample and infer risk scores would need to be developed (and adapted as new risk stratifying factors are discovered across e.g. germline genomics, demographics, family history, behavioural and environmental factors). Once these improved risk stratification mechanisms have been developed and their utility proven through research, it will then be important to apply these principles to the national screening programmes in order to screen a greater proportion of individuals who are at higher risk (who may not be captured in the existing screening eligibility criteria) and to minimise the risk of over-diagnosis through tailoring of screening in those at lower risk.

Importance of pursuing: Better incorporation of risk measures to target screening to those who are most in need (and at an appropriate frequency based on risk) using a selection of factors, has transformative potential to increase the efficacy and cost efficiency of the UK's national screening programmes. Furthermore, it will help to minimise participant anxiety and improve the patient experience of national screening programmes.

What needs to happen? As a first port of call for this Action, the existing screening programmes would be dynamically reviewed, building on Professor Sir Mike Richard's Independent Review of Adult Screening Programmes in England [51]. A clear and comprehensive way to risk stratify the specific populations for screening would need to be developed, starting with bowel cancer as an exemplar. This would also include looking at less invasive tests and new ways to gather insight to risk stratify patients through research and incorporating novel technology where appropriate. This Roadmap recommends focussing on the existing national cancer screening programmes, (namely breast, cervix, bowel) the Targeted Lung Health Checks and the prostate cancer risk management programmes. It will require systematic collection of risk information, such as samples, family history, lifestyle factors, genomic data, etc. Underpinning this, there would need to be research into less invasive tests in order to collect these data (e.g. blood, saliva, breath, urine, etc.). This will then need to be fed into better models of risk to identify individual risk scores, integrating and building on Actions 1, 2, 4 and 5. This would require the development of these scores and thresholds, alongside training and education for primary care practitioners (PCPs), better public education and the embedding of research nurses within the national screening programmes.

Links to: Actions 1, 2, 4 and 5

Independent Review of Adult Screening Programmes in England^a [51]

Breast cancer screening is an example of where risk-adapted screening is beginning to be integrated [52] and is a paradigm that can be used for other cancers in the future to showcase the potential of incorporating risk stratification approaches in national screening programmes. This also links with successes in cervical screening and HPV vaccination [53] and NHS efforts to modernise the national bowel screening programme.

Key stakeholders: UK National Screening Committee, Public Health England, the NHS, the National Cancer Research Institute's Screening, Prevention and Early Diagnosis Advisory Group, Genomics England, UK Biobank, healthcare professionals, patients and the public.



THEME 2

Biomedical data science and systems



Strongly linked to Theme 1, this Theme addresses the current barriers to data access for research and the lack of data science and platforms for integration of biomolecular data with health system/ population data to inform healthcare. It outlines recommendations involving unlocking NHS data for research (including for industry-led research and development in a controlled and ethical way), development of data-driven models of symptomatic

presentation for decision support in primary care, and risk in the general population, and ultimately the ambition to work towards an individual data, AI-driven model for every citizen which would inform proactive ED&D. These Actions should be delivered in an ethically sound way, with the maintenance of privacy and protection for personal health data of critical importance.

THE CHALLENGE:

At present, access to patient health data for ED&D research is difficult and access routes are variable and complex to navigate, serving as a barrier to real-world discovery and validation. Difficulty in accessing routine clinical care data is often compounded by a lack of clarity around data ownership/custodianship.

Furthermore, the research potential of NHS-derived data is held back by lack of commonality and interoperability between data systems across practices, hospitals and trusts.

^a <https://www.england.nhs.uk/wp-content/uploads/2019/02/report-of-the-independent-review-of-adult-screening-programme-in-england.pdf>

Barriers to overcome in biomedical data science and systems:

- The quality of NHS health data available for ED&D research is variable (e.g. in terms of missing data and biases in collection) and is not routinely digitised, findable, accessible, interoperable, re-useable (FAIR) or secure and steps are needed to address this [54], [55]. There needs to be the appropriate infrastructure to store and maintain high-quality health data for ED&D research.
- Collecting the correct depth of health information (e.g. granularity of coding or nuance of information from free-text GP notes) with sufficient longitudinal follow-up for ED&D research is often overlooked. NHS-derived data needs linkage across the care pathway in order to relate clinical features with cancer outcomes either for risk or diagnosis.
- It will be imperative to build an environment of strong leadership and technical skills in biomedical data science to create data that has sufficiently high utility for AI approaches, digital twinning, etc. Data engineering capability is essential to ensure data is FAIR and prioritising the adoption of open standards and tools (data elements, coding, ontology mapping, etc.) will be essential to realise the shared vision for ED&D.
- There needs to be a commitment to upskill the NHS workforce to collect high-quality data and to building strong relationships with healthcare professionals and the ED&D ecosystem to champion ED&D-relevant data collection.
- At present, there are unclear access requirements and routes for researchers, which can be fragmented (e.g. across multiple Clinical Commissioning Groups or hospital trusts), inconsistent, costly and resource intensive.
- Primary care is a crucial interface for ED&D, but GPs face significant challenges in diagnosing cancers early based on non-specific symptoms; decision-support systems which take advantage of all available data sources are lacking.

Through consultation, the following recommended Actions were prioritised to develop a framework for action to maximise the potential of biomedical data science in ED&D approaches. A high-level summary of each Action is included in the respective tables. Many of the recommended Actions work towards a pan-disease vision of data science-supported, proactive health management. These Actions are not intended to serve as comprehensive project plans and instead serve as a starting point for various stakeholders to come together, develop and champion.

In May 2018, a national data opt-out policy was introduced for the health and social care system in England, in line with the recommendations made in the National Data Guardian's Review of Data Security, Consent and Opt-Outs (July 2016) [56]. Implementation of this opt-out policy will allow patients greater control over the use of their confidential patient data (data which identifies the person it relates to and conveys some information about their health, care or treatment) for purposes outside of their own care and treatment, e.g. for research and planning [57]. Although this national programme will go some way towards building public trust in data sharing, further and more considerable action is required to improve the visibility and accessibility of anonymised/de-personalised patient data for research and to build greater trust between patients and the public and health data sharing.

Many of the challenges and Actions described below are interrelated with **CRUK's Vision for NHS Health Data in England^a** [58], which outlines a vision for unlocking the potential of health data to transform cancer outcomes.



a https://www.cancerresearchuk.org/sites/default/files/cruk_vision_for_data_jan_20_1.pdf

Action 4: Using electronic health records and AI/machine learning methods to deliver assessment of cancer risk in early symptomatic patients

Action: Research to retrospectively analyse electronic health records to identify signals from missed diagnostic opportunities and translate these into methods for use of live data to support risk assessment and GP decision-making in symptomatic patients presenting to primary care.

Major challenge: Our understanding of missed diagnostic opportunities and avoidable delays has grown over the last decade through the development and analysis of datasets like the **National Cancer Diagnosis Audit^a** (NCDA) [59], **Cancer Patient Experience Survey^b** [60] and the **Clinical Practice Research Database^c** [61]. After presenting to primary care with early, non-specific symptoms, too many patients experience multiple referrals and significant delays before a diagnosis is made [62], [63]. Primary care plays a crucial role in the timely diagnosis of suspected cancer but deciding the best course of action for patients presenting with numerous non-specific symptoms, comorbidities, etc. is a complex task [64]. Several clinical decision algorithms and tools exist to support GP decision-making including **QCancer^d** [65] and other such tools [66]. There is a significant opportunity to build on the capability of these tools and to create new tools which are applicable to more cancers, easier to use and better performing to deliver more effective ED&D.

Action description: This Roadmap recommends a coordinated research effort to build on previous initiatives to develop novel approaches capitalising on health informatic advances (e.g. AI/machine learning) to retrospectively analyse existing electronic health records to identify missed diagnostic opportunities from early symptomatic presentation in individuals who progress to a cancer diagnosis. These patterns of presentation would then be translated into automated systems which would use electronic health records to dynamically deliver cancer risk assessment to GPs for patients presenting with symptoms and recommend diagnostic courses of action. This includes linking health records between primary and secondary care and applying machine learning approaches to identify/flag cancer risk and appropriate future triaging/testing. Results of this process and the data collected over time would then feed back into the decision support model to further refine its algorithms and recommendations, creating a 'learning health system' [67]. This intervention does not encompass the development of systems to collect electronic health records.

Importance of pursuing: This approach will maximise the use of existing patient health data that currently exists in silos and will facilitate the development and refinement of decision support tools in clinical practice. It will improve patient outcomes through more timely diagnosis and commencement of treatment. It may have the potential to reduce the cost of care by delivering more timely and targeted interventions and the avoidance of repeat clinical appointments.

What needs to happen? An evidence base showing that early signs of cancer risk can be identified using health record data and demonstrating the effectiveness of clinical decision support tools for improving patient outcomes needs to be further established through research (building on existing early examples [68], [69], [70]). This needs to be developed alongside workable business models and reimbursement for clinical decision support tools that improve outcomes. To establish an evidence base, a defined set of clinical cases of patients that presented with symptoms over multiple primary and/or secondary

a <https://www.cancerresearchuk.org/health-professional/diagnosis/national-cancer-diagnosis-audit>

b <https://www.ncpes.co.uk/>

c <https://www.cprd.com/>

d <https://www.qcancer.org/>

healthcare visits (e.g. GP surgery, hospital visits) that eventually led to a cancer diagnosis needs to be collated. In the first instance, the focus could be on cancer types which have been demonstrated to manifest symptoms early in the disease course (i.e. at a tractable stage) or to have ambiguous early symptoms which are linked to missed diagnostic opportunities. Using this defined set of clinical cases as a test case, health informatic approaches such as machine learning could be used to identify potential patterns of missed and/or late diagnosis in the test case.

Following the identification of any patterns, opportunities to flag these risks to GPs and suggest changes to clinical triage pathways would be generated; these signals will need to be translated to produce informed clinical decision support tools (e.g. can the GP ask additional questions, perform a minimally invasive test, etc. to better inform the triage pathway for the patient?). These decision support systems can then be used to deliver cancer risk assessment in future patients.

Investigation into what steps of this pathway can be automated and what information and/or training for GPs is needed to trust and use these decision support tools needs to be addressed; there needs to be behavioural research to determine the most appropriate and effective points for accurate diagnosis through the integration of human decision making and decision support tools. Instrumental to this Action is the importance of safety-netting all triaging and testing (e.g. verifying patients went for recommended tests and healthcare professionals acting on the results of the tests, etc.).

To deliver this Action, there is a need for specific use-cases to demonstrate impact and further catalyse movement towards interoperable data to incentivise open-source standards. This Action recommends that interoperable data is stored in relevant, local secure environments, and federated so that researchers can analyse data across multiple datasets, without the need to always pool patient data. Part of this research programme should also be a thorough investigation of patient/public acceptability of their data for these research and development purposes, and of attitudes to GP decision support technology (this could be delivered through the system outlined in Action 14).

Delivery of this Action would be contingent on a system for streamlined access to NHS data for the research component (with appropriate data protection measures). The need for such a system and an associated policy recommendation are discussed in Section 7.

Links to:

Existing risk assessment tools and trials (e.g. **QCancer**^a [65], **Electronic Risk Assessment for Cancer (ERICA) trial**^b) [71], examples of key pieces of previous literature (non-exhaustive list):

Understanding missed opportunities for more timely diagnosis of cancer in symptomatic patients after presentation [72]

The frequency, nature and impact of GP-assessed avoidable delays in a population-based cohort of cancer patients [73]

Evaluation of risk assessment tools for suspected cancer in general practice: a cohort study [74]

Availability and use of cancer decision-support tools: a cross-sectional survey of UK primary care [66]

a <https://www.qcancer.org/>

b <https://www.cantest.org/research-projects/what-is-the-clinical-effectiveness-and-cost-effectiveness-of-embedded-risk-of-cancer-assessment-of-patients-in-primary-care-the-erica-trial/>

Symptom checking and triage applications are an increasing part of the primary care healthcare landscape (eConsult^a [75], askmygp^b [76], ISABEL^c [77]), and may have an important role to play.

In a separate initiative, this was identified by the **James Lind Alliance Early Detection Top 10 priorities^d** [78] as #8 – Can we use data from patients who have already been diagnosed with cancer to look for early warning signs that might have been missed or not investigated appropriately at first appointment?

Actions 5, 6, 7 and 14

Key stakeholders:

NHS digital initiatives across all nations, NHSX, primary care digital system suppliers (e.g. EMIS Health, SystemOne, Vision), HDR UK, DATA-CAN, UK Research and Innovation (UKRI) digital initiatives and the UK government in collaboration with data scientists, ACED, clinicians including pathologists, infrastructure suppliers, cancer risk assessment experts, health informatics experts, healthcare professionals and patients and the public.

Putting it into perspective

Through consultation with CRUK's Cancer Insights Panel, patient representatives agreed that this Action could potentially yield significant benefits, including developing a more comprehensive picture of where lessons learned from previous missed diagnostic opportunities could be used for improvement of future patient outcomes. Representatives highlighted several practical concerns that should be addressed when considering the intervention, including having the data anonymised and securely stored, with an emphasis that third parties should not have access to this data for profit. Any patient data-sharing initiative should be transparent regarding the use of data for non-profit/research intentions, thereby empowering patients to make an informed decision.



a <https://econsult.net/>

b <https://askmygp.uk/>

c <http://v4.isabelhealthcare.com/home/default>

d <https://www.jla.nihr.ac.uk/priority-setting-partnerships/detecting-cancer-early/top-10.htm>

Action 5: Novel AI risk stratification technologies for ED&D in the asymptomatic public

Action: A phased approach to develop risk stratification and GP decision support for the asymptomatic public.

Phase 1 – Research to identify signals, through AI/machine learning methods, which predict risk of cancer or early deviations away from health in the asymptomatic public. This would entail augmenting data from electronic health records with additional data streams such as genomic sequence, family history, behavioural factors, web search history, etc.

Phase 2 – Development of AI decision support tools that build on the symptomatic patient triage tools developed in Action 4 to dynamically assess the data and detect the signals developed in Phase 1 and proactively alert GPs to cases of elevated cancer risk/deviation away from health and/or need for triage/screening tests in asymptomatic members of the public registered with their practice.

Phase 3 – Integrate novel (and optimise existing) non-invasive, point-of-care triage tests in primary care, as they come online, to build upon and strengthen risk stratification models from Phase 1 and 2.

Major challenge: A new NHS model, aimed not only at treating symptomatic disease but aiming to maintain health, is needed, with the objective to identify individual deviations from health and working towards a reality where ED&D is the norm. This would enable true early detection of asymptomatic and curable cancer/pre-cancer. An increasing breadth and depth of data is available concerning each member of the public, but there is insufficient concerted effort to integrate the various disparate data types in order to specifically detect early cancer. Currently, the lack of health economic understanding of ED&D, segregation of AI skills in the UK (acknowledging strong individual private and academic capabilities), uncertainty around the approach for regulating and approving algorithms for use in clinical practice and the need to introduce a behavioural change for GPs towards ED&D serve as challenges to delivering this Action.

Action description: This Roadmap recommends a phased approach, identified through research to developing GP clinical decision support tools to better determine and act on cancer risk of members of the public; as an exemplar, it proposes to build on the application of AI/machine learning methodologies to analyse electronic health data to spot patterns linked to specific cancer risk/early deviations away from health and towards cancer, by integrating new datasets not currently linked into GP records/cancer risk-assessment in a systematic way (e.g. genomic sequence, family history, behavioural factors, web search history, shopping patterns [79], personal activity monitors, smart phone data, etc.). This work will aim to ask whether AI methodologies can link apparently unrelated health data to inform GPs of cancer risk in asymptomatic members of the public registered with their practice and provide guidance for relevant triage/screening tests.

The first phase of this Action is research to integrate data, generate algorithms and identify signals. Outputs from this first phase can then inform approaches to create implementable real-time, dynamic risk stratification and GP decision support tools (Phase 2) which will analyse health records of asymptomatic patients for patterns linked to cancer risk and proactively inform GPs to initiate the appropriate triage pathway for that patient. This approach would integrate electronic healthcare records with real-time outputs linked to clinical guidance.

In the third phase, this Roadmap recommends the integration of novel, non-invasive technologies and point-of-care testing in primary healthcare to serve as a further mechanism for additional risk stratification and triage information. Data from such tests should be integrated into the risk model arising from Phases 1 and 2. For point-of-care

testing, this includes minimally-invasive sampling approaches (e.g. urine, saliva, breath analysis, blood, etc.) and does not include invasive sampling approaches. This Action should also consider digital therapeutic technologies and platforms being used to collect longitudinal data to help improve an individual's sleep, weight management, diabetes, etc. and how to make best use of these additional, non-cancer data sources.

Importance of pursuing:

This Action offers the opportunity to take a proactive approach to health by using health data, AI and minimally-invasive point-of-care approaches to identify cancer risk in asymptomatic members of the public; it could potentially significantly shift the stage and proportion of cancers that are detected in primary care. It offers the opportunity to develop improved data utilisation through collecting data that are not routinely obtained (via questionnaires, bio-samples and emerging diagnostic modalities, etc.) that is prompted and integrated by AI modelling.

What needs to happen?

To deliver this Action, further building on risk stratification approaches from missed diagnostic opportunities (detailed in Action 4) to include additional sources of health data to analyse for patterns identifying cancers will be required. Phase 1 of this Action will also require the continuing identification of risk stratifying factors from the other datasets mentioned above (e.g. germline genomics and behavioural factors), and the integration of these factors with the risk model. AI approaches should enable this analysis and integration.

After establishment of a firm evidence-base for patterns linking signals to specific cancer types, it proposes analysis of asymptomatic patient electronic healthcare records, using the same sets of classifiers discovered and integrated in Phase 1 of this Action, to proactively risk stratify asymptomatic individuals and alert GPs of potential individuals at risk, prompting the GP to proactively suggest triage testing (Phase 2).

To enable a further mechanism for additional risk stratification, use of results from emerging minimally-invasive point-of-care tests can be fed into the risk stratification models (Phase 3); this will depend on the outputs of the previous phases but also on the emergence of validated minimally-invasive triage tests (e.g. liquid biopsies, breath tests, etc.).

Electronic healthcare records should include collecting primary healthcare data and 'Hospital Episode Statistics' data to develop AI models and link to clinical outcomes using resources like the cancer registries and the Diagnostic Imaging Dataset [80]. The developed model can then be validated, and new datasets can be added as available (e.g. information from liquid biopsies, genomic tests, etc.). The model would then be tested to see if there is an improved choice of next steps in the clinical pathway of the patient (e.g. further triage tests, imaging tests, etc.). To achieve AI-driven risk stratification, there is a need for high performance computing infrastructure to collate and integrate multiple types of health data to generate the release of one predicative model of risk.

Links to:

Action 4

Approaches should build upon existing initiatives that provide proof-of-concept in other diseases (e.g. **QRisk**^a [81] for calculating risk of cardiovascular disease).

In a separate initiative, this was identified by the **James Lind Alliance Early Detection Top 10 priorities**^b [78] as #1 and #3 respectively – 'What simple, non-invasive, painless, cost-effective, and convenient tests can be used to detect cancer early?' and 'Would increasing access to tests to diagnose cancer within General Practices improve the number of cancers detected early, and is it cost-effective?'

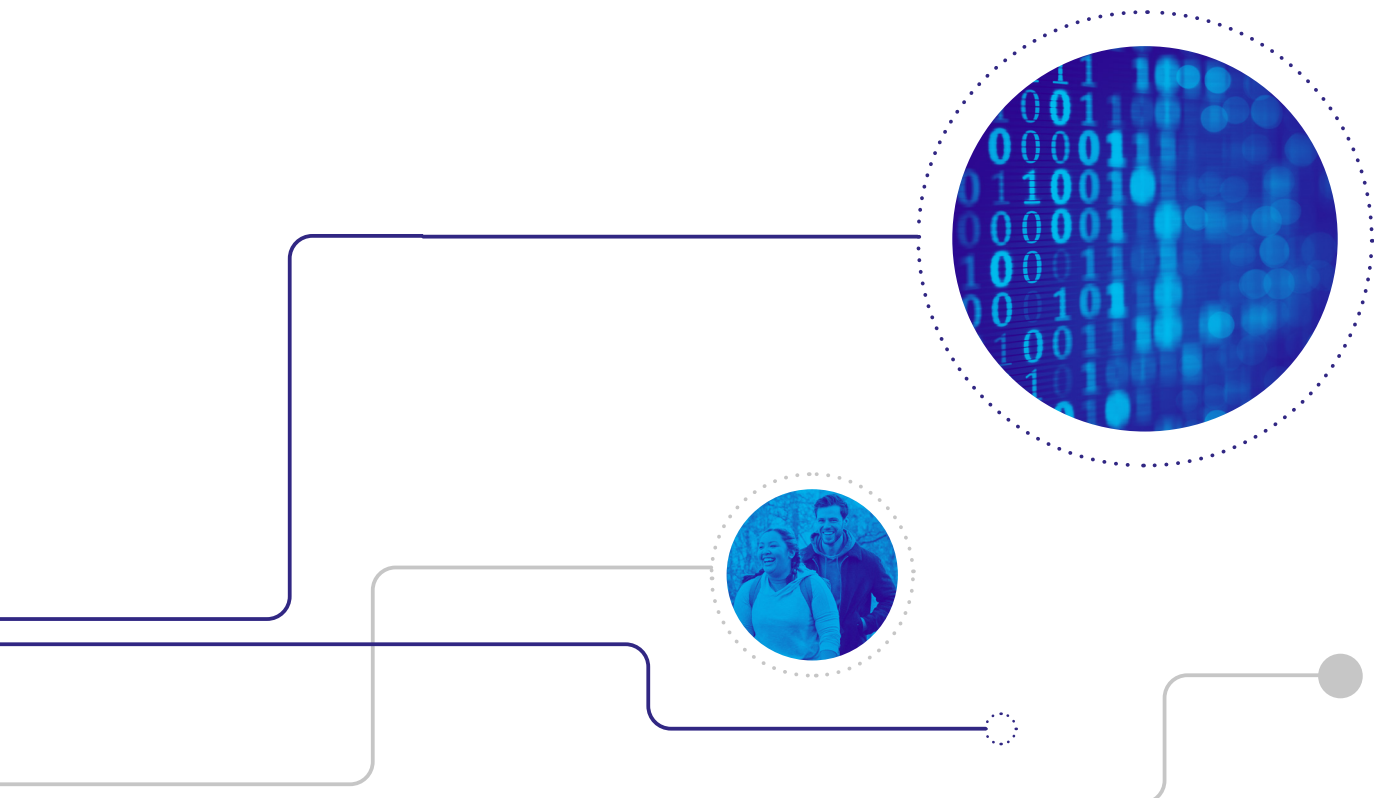
a <https://www.qrisk.org/>

b <https://www.jla.nihr.ac.uk/priority-setting-partnerships/detecting-cancer-early/top-10.htm>

Phase 3 of this Action should link to the work of CanTest^a [82], [83], the NIHR Innovation Observatory^b [49] and the Accelerated Access Collaborative^c [50]. It will also relate to the NHS Med Tech Funding Mandate^d [18] that is currently under consideration.

Key stakeholders:

Primary care health professionals, academia, the NHS, NHS Digital/X, commercial AI providers, digital health investors, key players in the *in vitro* diagnostics industry, imaging companies, charitable organisations, NCRI, HDR UK, organisations issuing UK guidelines, Royal Colleges and patients and the public.



a <https://www.cantest.org/>

b <http://www.io.nihr.ac.uk/>

c <https://www.nice.org.uk/aac>

d https://www.engage.england.nhs.uk/consultation/medtech-funding-mandate/user_uploads/medtech-funding-mandate-guidance-consultation-document-v2.00--2-.pdf

Action 6: Wearables and other technology for real-time monitoring and risk management

Action: Through research, identify and capitalise on opportunities for wearable/implantable/mobile technologies and digital literacy to enable real-time risk stratification and monitoring of the public for ED&D, acknowledging some risk factors are dynamic and can change over time.

Major challenge: There are untapped opportunities to reduce individual risk levels and detect warning signs earlier by mobilising citizens to take a proactive approach to monitoring their health via wearable, implantable and/or smartphone technologies. The cost of devices, lack of clarity in regulation standards, lack of a clear understanding of a comprehensive list of risk-factors for specific cancers, and a lack of digital engagement of citizens and healthcare professionals currently serve as major challenges. It will be essential to establish a robust evidence-base and a strong education base in digital literacy and health management to avoid unnecessary anxiety in healthy individuals and have the ability to crucially integrate data with patient records.

Action description: This Roadmap proposes a cross-ecosystem research effort to determine the feasibility of continually monitoring health status (and deviations from health towards early cancer) through wearable, implantable or smartphone devices. As an initial step, this Roadmap recommends mapping the wearable, implantable and smart device application landscape with emphasis on identifying successful exemplars from other diseases. This recommended Action proposes assessing the potential through research of a system of dynamic risk assessment via wearable/implantable/mobile device-derived data that would enable alerts to the individual to seek appropriate clinician risk assessment/diagnostic testing. This would require a coordinated academic and industry research programme involving marker validation (e.g. can signals robustly linked to ED&D be detected by wearable or implantable devices in a convenient, minimally-invasive way? Can signals that are readily measured via physiological and digital longitudinal biomarkers; such as temperature, sleep, lung function, and movement be applied to ED&D?), technology development, data analytics and integration, evaluation and user acceptability. Capitalising on digital literacy, this would help identify and monitor risk factors as identified by individualised data collected through wearable technologies. This Action aims to move towards a culture of individual health management informed by real-time data collection via one's smart devices.

This Roadmap recommends starting with technologies/devices that are being used/are already validated for ED&D in other disease applications to determine whether these approaches can potentially apply to cancer (e.g. **Apple watch for ED&D of atrial fibrillation^a**) [84]. Digital health and symptom-checking apps are likely to be a significant part of this landscape (e.g. **Evergreen Life^b**) [85]. In the initial investigational phase, this may encompass exploring potential applications to one cancer type and a limited number of motivated individuals as a pilot cohort. Data streams generated from this initial test cohort can help to further refine and modify the risk stratification approach, and depending on the outcome, could be incorporated into the NHS via a health system's smart device application to increase users and generate more evidence; there needs to be a strong evidence base to show tangible impact. After an algorithmic hypothesis is generated, it should be validated, and the impact of the intervention should be evaluated in the medium to long-term (e.g. 5+ years).

a <https://support.apple.com/en-us/HT208931>

b <https://www.nhs.uk/apps-library/evergreen-life/>

Importance of pursuing:

This Action could ultimately lead to a pan-disease approach where citizens are at the centre of health self-management, detecting pre-morbid factors to intervene early. This approach may also help to establish the link between cancer research and other research communities through the collection of individual health data for a pan-disease approach. It provides an opportunity to build public buy-in and interest due to an increased sense of ownership of one's health. The opportunity to capitalise on motivated individuals to proactively take a leading role in health self-management may provide the step-change needed for ED&D, not just for cancer but for a myriad of diseases, with appropriate steps taken to reduce inequalities.

What needs to happen?

An initial comprehensive mapping of the wearable and implantable device landscape and potential links to cancer early detection serves as the basis for this recommendation. Based on the outcomes of this mapping exercise, it should be identified whether approaches in other diseases (e.g. diabetes, cardiovascular diseases etc.) can potentially be applied to cancer. A multi-disciplinary research programme should determine which risk factors can be robustly identified using the data collected by wearable, implantable or mobile technologies. Working with technology experts, the correct sensor/data acquisition technology would need to be identified and piloted to gather evidence in the short-term as to whether this method of risk stratification works for the ED&D of cancer. An initial cohort of activated/motivated individuals, a clear understanding of which collected data can be used to inform risk and how these data can be reliably integrated into existing health system infrastructure needs to be established by this research programme. In parallel, there needs to be behavioural research on the potential barriers to adoption by the healthcare system (e.g. what type of information generated via wearable or implantable devices would healthcare professionals trust?). It will be crucial to involve behavioural, sociological and economic components to the research programme, such that any technologies developed are applicable, acceptable and available to all populations, and look to address rather than exacerbate health inequalities.

This Action should also consider current digital therapeutic technologies and platforms being used to collect longitudinal data to help improve other conditions in sleep, weight management, diabetes, etc. Opportunities may exist to harness those existing datasets to inform cancer ED&D R&D. There needs to be appropriate data sharing models with those gathering large datasets including large companies and parties developing wearable technologies for ED&D. This must be conducted in accordance with ethical data privacy and protection policies and regard protection of personal individual health data of critical importance.

It needs to be established how this will link to existing suspected cancer referral pathways and the capacity required to support further triaging/confirmatory tests in the healthcare system. There is the opportunity to link with screening results and other cohorts (e.g. digital diaries from digital therapeutic technologies and biobanks) and the opportunity to combine physiological, behavioural, genetics, microbiome information, etc. to generate more comprehensive risk profiles. There needs to be consensus on the provider of the wearable technologies, the appropriate place to discuss this intervention (e.g. in the community at remote health checks, GP surgery, etc.), and the level of support needed to those using the technology.

Links to:

Actions 4, 5 and 7

This Action should build on the technological strengths that currently exist (e.g. NHS applications, approaches in other diseases like cardiovascular disease) and the potential for increased investment in this area. This Action should consider activities of the **Accelerating Detection of Disease platform^a** [17].

a <https://www.ukri.org/innovation/industrial-strategy-challenge-fund/accelerating-detection-of-disease/>

Key stakeholders:

Technology developers (academic and industrial), the NHS, NHS Digital, HDR UK, healthcare professionals, health informatics experts, behavioural researchers, patients and the public.

Putting it into perspective

When consulting CRUK's Cancer Insights Panel, generally, most supported this concept, noting that it was a progressive way forward, providing examples of how this is used in other diseases with success (e.g. implantable technologies for monitoring heart conditions that link to smart phone applications). Patient representatives stressed the importance of this Action applying to cancer types where there is a clear agreement on how best to monitor and treat that cancer type. It was emphasised that it was critical that the user did not directly receive the raw data generated, as this may cause the user unnecessary anxiety. Representatives highlighted it was imperative that the data was reliable, and appropriately integrated with other data sources to better inform clinical decisions.



Action 7: Digital health twin

Action: Building on the research insights and outcomes of Actions 4, 5 and 6, creation of a 'Digital Health Twin' system: a lifelong, personalised digital model mirroring an individual's health history updated with each risk, symptom, diagnostic, test, intervention, examination, etc. that would flag-up risks and provide guidance to proactively manage an individual's health.

Major challenge: A long-term, visionary pan-disease approach to proactive health management that shifts away from treating symptomatic disease to maintenance of health is needed. This pan-disease approach would optimally aim to identify individual deviations from health to work towards a reality where ED&D is standard practice. Major hurdles include the currently limited understanding of big data for ED&D, lack of a transparent and robust 'digital twin' model including adaptability of the model, the ability to test and manipulate the model, and the data accessibility/security/ethics considerations of the 'digital twin' model. Appropriate data sharing and business models need to be formulated and adopted for this approach.

Action description: Building on Actions 4, 5 and 6, this Roadmap proposes an Action to research and scope the potential of mirroring an individual's lifetime story of their health via digital storage of their health history including their risks, symptoms, diagnostic tests and examinations, medications, intervention history, family history, demographic data, genome, etc. This digital model would encompass medical datasets (e.g. reported symptoms at GP surgery, health insurance claims, diagnostic test results, medical procedures) and non-medical datasets (online search history, shopping history, data from wearables and other devices, etc.). Using the comprehensive individual profile, health informatic approaches (e.g. machine learning) would recognise patterns and use the medical and non-medical data to project the individual's normal/healthy trajectory and flag up risks or deviations away from normal. For example, analysis of the data would provide an 'alert' to identify the need for screening/testing and intervention and providing guidance for clinical decision support. Data collected would need to extend beyond primary care and include other input sources, with a strong opportunity to build on cutting-edge technology. This recommended Action is broader than cancer and aims to ultimately encompass a pan-disease approach.

Importance of pursuing: This Action offers the opportunity to combine ED&D with precision therapy (with the 'digital twin' predicting response to intervention) and radically shift the diagnosis model to become, in the long-term, less resource intensive, more comprehensive and more accurate. It offers the opportunity for the healthcare system to avoid unnecessary diagnostics and treatment interventions, enables a platform to better understand diseases, provides cohorts for trials that are informed by deeper data analysis and may give rise to new treatment opportunities in early disease stages.

What needs to happen? This Roadmap proposes a long-term research Action that encompasses a pan-disease approach to health management and requires robust foundations set by Actions 4, 5 and 6. This Action will require a dramatic shift in public engagement in research, and hence an extensive and comprehensive consultation with the public needs to be undertaken. It will be critical to integrate behavioural, sociological and economic components to this approach, such that this model and any supporting technologies developed are applicable, acceptable and available to all populations, and look to minimise rather than exacerbate health inequalities.

Using evidence-based patterns linking electronic health data to clinical outcomes and integration of well curated non-medical datasets, a 'digital twin' model needs to be

established. An initial trial will need to test modelling approaches and to validate predictions via surrogate outcome measures. Informational governance will need to support this, with societal and ethical changes including behavioural research into how to motivate individuals with clear articulation of health benefits backed by evidence. The health data will need to be incorporated into algorithms, ensuring the right data is collected, sufficient quality of the data (e.g. curated effectively) and how the data is linked. To ensure the applied algorithms have sufficient predictive power, it needs to be established that the data can be read and there are sufficient volumes of training data.

In the short-term, data integration and longitudinal modelling methods will be needed, as well as deep consideration of anonymisation, security, and storage of health data. There needs to be research into dynamic monitoring markets for the 'digital twin' and conversations and transparency over ownership of data. Additionally, in the short-term, the generation of 'synthetic datasets' from Actions 4, 5 and 6 could be made available for research and interrogation by the ED&D ecosystem. In the mid-term, it is proposed there is validation and exemplars of the 'digital twin', followed by a 'digital twin' adaptive trial in the long-term.

Links to:

The ED&D ecosystem can build on the strengths of existing strong infrastructural resources (e.g. HDR UK, NIHR Biomedical Research Centres), longitudinal data stored by the NHS, proactive health initiatives and foundational knowledge of digital twin models in other sectors (e.g. civil and mechanical engineering).

Key stakeholders:

This Action will require extensive collaboration with funders, relevant pharmaceutical companies, medical technology companies, large technology companies, digital experts, NHS organisations across the UK, key organisations involved in health data and research (e.g. HDR UK, Scotland's **Mydex**^a) and patients and the public [86].

a <https://mydex.org/about-mydex>

THEME 3

Incentivising and supporting development and commercialisation



This Theme explores the current lack of incentives and the blockers to developing, investing in and commercialising new ED&D approaches. It calls for placing ED&D as a high priority for the UK government and devolved nations' governments and health systems to enable an attractive, growing and investable ED&D ecosystem to support innovation and translation. This Theme

highlights recommendations around infrastructure to support entrepreneurialism in ED&D and to nurture and grow novel ideas, start-ups and scale-ups in this space, infrastructure to support real-world evaluation of the most promising ED&D approaches in the most efficient ways, and a deeper understanding of the health economics of ED&D.

THE CHALLENGE:

There has been a historic under-investment into ED&D from the private sector, due to factors including a complex regulatory landscape, inappropriate reimbursement, lack of support for promising technologies/start-ups to establish proof-of-principle and attract investment, and an unclear health economic and business model.

There needs to be recognition of and investment in the potential of ED&D as a health and wealth driver for the UK. In order to stimulate investment into ED&D from the private sector (and thereby accelerate progress towards impact on health), the UK government and devolved nations' governments need to acknowledge the benefits of, incentivise and reward ED&D and build a strong business model for investment in ED&D technology development, ensuring there is sufficient resource and structure in place to embrace ED&D.

As the ED&D research and technology ecosystem grows, there needs to be the necessary support and infrastructure to commercialise leading approaches. At present many ED&D technologies and approaches suffer the fate of failing to reach clinical practice or of terminally slow adoption. If we want ED&D to be a routine reality, this needs to change.



Barriers to overcome in incentivising and supporting development and commercialisation of ED&D approaches:

- The UK government and devolved nations' governments and health systems (and those of the majority of nations globally) do not reward and reimburse ED&D at a level which incentivises private-sector investment in earlier-stage development of new ED&D technologies and approaches. Private investors and industry do not generally see a strong business model to support and pursue ED&D research, development and commercialisation due to the high cost and long timelines of development and the low price-point of tests. This challenge is exacerbated for low-incidence cancers.
- There has been insufficient engagement between academia and industry to ensure that early stage discovery work (e.g. biomarker discovery) is captured and translated to commercialisable tests. A good example of an approach to encourage this is the **UKRI-Cancer Research UK Integrated Diagnostics call^a** [87].
- The system currently usually requires evidence of impact on mortality from a new ED&D test, which necessitates very long and expensive trials. This requirement coupled with the under-valuation of ED&D means that most companies and private investors do not see a viable business model for investing in ED&D R&D. More could be done to link ED&D to early stage intervention; Big Pharma could see a model for investing in ED&D research if successful ED&D developed a new market for early therapeutic interventions.
- The health economic benefits of implemented ED&D are sometimes assumed (e.g. reduction in the significant costs of late stage treatment) but have not been conclusively demonstrated. The system is unsure whether up-front investment in ED&D will be cost-effective in the longer-term; a clear economic model is lacking. Health economic models that have relevance not just to UK healthcare pathways but also internationally are key to attracting investors.

- While ED&D tests are under development, they do not routinely include health economic components. This is often due to uncertainty around the targets for which they should be aiming and because characteristics such as cost-effectiveness will depend on factors beyond the test itself (such as where and how it is implemented into practice and use of the test). There is a lack of clarity around what clinical performance characteristics and what health economic consequences a test would need to have in order for it to be adopted. Too few exemplar 'wins' exist or are recognised which demonstrate that there is a business model for ED&D to be successful.
- There are significantly too few leaders responsible for championing, and charged with, the development and implementation of ED&D approaches within the NHS.

Through consultation, the following recommended Actions were prioritised to develop a framework for action to achieve progress in supporting the development and commercialisation of ED&D approaches. A high-level summary of each Action is included in the respective tables. These Actions are not intended to serve as comprehensive project plans and instead serve as a starting point for various stakeholders to come together, develop and champion.



a <https://apply-for-innovation-funding.service.gov.uk/competition/424/overview>

Action 8: A health economic model for ED&D

Action: Deeper understanding and use of health economic modelling to support ED&D implementation; creation of a health economic model to establish the cost-effectiveness of ED&D in the NHS, and to be able to suggest the performance that a new test would have to achieve in order to be cost-effective in a given set of circumstances of use.

Major challenge: The system is unsure whether investment in delivery of ED&D will be cost-effective (or even cost-saving) for the health system as a whole – does up-front investment in ED&D testing just add cost to the system, or does it deliver cost-neutrality/saving through reduction in late stage diagnosis and associated higher treatment costs? Is any cost to the system commensurate with reduction of the societal burden of late stage diagnosis and the morbidity/mortality this results in? Unlike for new therapeutic interventions such as drugs, there is no robust mechanism to decide what the healthcare system is willing to pay for a novel ED&D test; a clear economic model is lacking. Gaps in the data infrastructure required (e.g. open access to annual screening data reports, data on costs of disease therapy/management including long-term morbidity management and palliative care across cancer stages, data on health-related quality of life measures), as well as accurate estimations of the costs of ED&D tests (including their infrastructure for provision and the costs of follow-on testing, management and therapy) provide challenges in this area. Furthermore, a lack of multi-disciplinary teams specialising in health economics of ED&D presents a challenge.

Action description: This Roadmap recommends that a concerted effort is needed to develop a comprehensive and sufficiently complex health economic model for ED&D. Such a model should seek to establish the health economic viability of ED&D as a paradigm, and to be able to suggest the performance characteristics and price-point that a new test would have to achieve in order to be economically feasible. It should seek to demonstrate whether and how ED&D affects downstream costs to the system (e.g. cost of diagnostic follow-up, cost of early versus late stage treatment), and to help set parameters for how the NHS should value ED&D tests. Health economic models will be different in symptomatic versus asymptomatic instances due to their differences in resources, settings and approaches; hence, different models will need to be developed for specific scenarios, as this will not be a case of one size fits all. It should also seek to encourage more investment from the public and private sectors in ED&D development because of this economic viability and would allow new business models to be developed and tested. Bringing together key stakeholders, this Action aims to develop a fully justified health economic model that considers the current state of affairs, demonstrates the economic case for ED&D, helps to identify 'plug and play' opportunities to introduce new ED&D strategies/approaches, development of business models and starts to define an economic runway for future tests.

Importance of pursuing: With an established health economic model for ED&D, the implementation of new tests will be far simpler. This model would help define clear performance characteristics (in terms of e.g. accuracy, positive/negative predictive value and cost per test) that new ED&D tests would have to achieve (in particular circumstances) to be economically feasible/adoptable by the NHS and provide leverage to drive policy commitments to rapidly adopt tests that meet defined TPPs (feeding into Action 11). This is essential for new diagnostics, where relative merits may be compared in a fully justified manner. This model would also allow for better cost/benefit comparison of multiple competing tests within the same ED&D scenario. Furthermore, investment in this area will help to drive more global investment into diagnostic development, as there would be a better-defined pathway.

What needs to happen?

Clear articulation of current healthcare pathways and the routes to implementation of diagnostic tests is required as foundation for this Action. By bringing together a multi-disciplinary team, a worked-up plan can be created, resulting in a full health economic model to analyse new ED&D interventions against and clarify routes to implementation, including regulatory requirements. In deriving this model, the type of test will need to be considered (e.g. screening, symptomatic, triage, etc.), as well as where it sits on the clinical pathway. This model should consider and build upon the work of the NICE Diagnostics Assessment Programme [88]. This will then lead to better understanding of how new tests would alter current pathways and costs, as well as the impact of a new test on distribution of diagnoses by cancer stage and the impact this would have on downstream cost of care (diagnostic services, staffing, treatment costs, morbidity associated with late stage surgery and therapy, end of life care, etc.), leading to health economic modelling. Within the next five years, it is then expected that this team would have developed a framework for the approach and health economic evaluation of existing ED&D, followed by a mapping of the pathway for different cancer types and tests to generate a base model for each cancer type, as well as for pan-cancer approaches.

Links to:

Action 11

Key stakeholders:

Health economists, clinicians, health education institutions, the NHS, the UK National Screening Committee and representatives from the devolved nations, UKRI, HDR UK, the Department of Health, NICE, Medicines and Healthcare Products Regulatory Agency, industry representatives, investors, and patient representatives.



Action 9: A health innovation incubator for ED&D

Action: A health innovation incubator for ED&D to support growing entrepreneurship in the ED&D ecosystem, assisting start-up companies by providing them with initial seed investment, physical space, mentorship and resources (on trial design, regulation, health economics and systems insight, securing funding, etc.) to design and build an efficient, sustainable business model.

Major challenge: At present, there are a lack of mechanisms to support innovation and entrepreneurship in ED&D. Start-up companies and early stage investors in this space often struggle to understand the pathway towards commercialisation of an asset, to secure significant funding or to have their ED&D technologies/approaches be integrated into healthcare pathways. Few resources exist to provide the appropriate unbiased mentorship to change this.

Action description: This Roadmap proposes an incubator model specifically dedicated to ED&D. Incubators are a mechanism to assist start-up companies with business development by providing them with initial seed investment, physical space, mentorship and resources to design and build an efficient and sustainable business model. This model exposes start-ups to customers, key opinion leaders, investors and corporates in an efficient manner which accelerates the start-ups' progress whilst reducing common mistakes. Additionally, incubators can help to concentrate, connect and educate the corporate and investor community, which will be valuable for bridging sectors in the ED&D ecosystem. A 2019 report from the UK government (Department for Business, Energy & Industrial Strategy) highlights the positive impact of incubator models on start-ups in other sectors [89]. This ED&D incubator would be independent; the main aim is to support the validation, translation and commercialisation of ED&D technologies and approaches. This model would provide a focal point for ED&D innovations and a world-class cluster of ED&D start-ups, providing space for fleshing out new, disruptive ideas in ED&D and providing the necessary supporting structures to allow for new companies, businesses, and collaborations to be built. It would support new ED&D companies through seed funding, expert advice on study design, intellectual property development, regulatory affairs, market access, etc. and would bring these promising companies into close proximity with investors.

Importance of pursuing: At present, there is a growing ED&D ecosystem both in the academic and industry realms with the potential to generate scalable ED&D outputs to be accelerated in the NHS and internationally, where applicable. This incubator would serve as a resource for expert support, funding and collaborative opportunities for early stage start-ups and scale-ups. This could increase investment in ED&D, build the ED&D community and attract and retain talent from a broad range of disciplines. This initiative would help accelerate ED&D innovations into healthcare practice and provide a menu of disruptive ideas and focal point of talent to deliver viable and sustainable ED&D approaches.

What needs to happen? In order to establish a pipeline of relevant start-ups, academic innovation will need to be supported to encourage translation from discovery towards a commercialisable ED&D product. This might involve translational funding, commercially-minded development partnerships, entrepreneurship training, accelerator programs, etc.

This incubator model would require investment from a collection of ED&D champions; for example, this could include combined investment from the UK government, academic institutions, industry partners, charities and venture capital. The physical space for the incubator should be in close proximity to academic and clinical resources, with relevant programme support and funding for ED&D start-ups (e.g. seed funds).

The incubator offering needs to provide start-ups with access to data, clinical pathways, health economic models, key opinion leaders, corporates, investors and expertise that otherwise they would struggle to access. Collaborative teams supported by the incubator would need to be evidence-generating and reach set milestones to continue receiving financial and intellectual support and mentorship. After a defined time, companies would be expected to prove their ability to become financially stable. Measures of success for this incubator could include companies securing further funding/licensing deals/acquisitions, projects that are accelerated into healthcare system pathways, increased academic and industry collaboration, sustainable and profitable companies and national and international recognition as a hub for ED&D innovation.

Links to: This Action should build upon successful incubator and accelerator models in other sectors (e.g. **Capital Enterprise**^a [90], **Panacea Innovation**^b [91], **KQ Labs**^c [92], **Start Codon**^d [93], **Novartis Biome**^e [94], **Illumina Accelerator**^f [95], **MedTech SuperConnector**^g [96]). This Action should consider activities of the **Accelerating Detection of Disease platform**^h [17].

Actions 8, 11

Key stakeholders: A unification of efforts by the UK government, corporations with support from academic partners and charities to launch and run a non-profit ED&D incubator. It is suggested to work with the NHS Accelerated Access Collaborative to facilitate co-production with the NHS.

a <https://capitalenterprise.org/>

b <http://panacea-innovation.com/>

c <https://www.crick.ac.uk/partnerships/kq-labs>

d <https://startcodon.co/>

e <https://www.novartis.com/our-science/novartis-biome>

f <https://emea.illumina.com/science/accelerator.html>

g <https://medtechsuperconnector.com/>

h <https://www.ukri.org/innovation/industrial-strategy-challenge-fund/accelerating-detection-of-disease/>

Action 10: A platform for validation and evaluation of new diagnostics in cancer referral pathways in hospitals

Action: Create a new infrastructural network of NHS-based streamlined platforms to design and deliver rapid evaluation and validation of ED&D signatures and tests in a real-world clinical environment based in high-patient-volume hospitals (i.e. creating a resource of Clinical Trials Units for ED&D).

Major challenge: While there is a well-worn pathway for design and conduct of clinical trials of therapeutics (and considerable uptake in drug trial design innovation) and a critical mass of therapeutic trial statistical/methodological expertise in many hubs across the UK, the same cannot be said for expertise in the design of ED&D trials. Furthermore, at present in the UK health and regulatory system, critical barriers of time and cost impede the evaluation of new diagnostics. Trials aiming to show an impact on mortality from a new ED&D test are complex, large (due to low incidence of cancer), long (due to years of follow-up needed between diagnosis and death) and costly. Unless these barriers are resolved via a more streamlined and real-world process, potentially transformative diagnostic technologies will not be utilised for patient benefit and will continue to experience a high rate of attrition.

Action description: This Roadmap proposes to create a UK-wide network of NHS-based streamlined platforms for rapid and robust assessment, validation and clinical trial evaluation of ED&D signatures and tests within pathways/point-of-care in a clinical environment, maximising the potential of high-patient-volume hospitals and real-world validation environment. Consideration could be given to approach recruitment of patients via primary care as an option. This key infrastructural resource would cluster dedicated ED&D expertise in statistics, trial design and trial conduct (in a model analogous to a network of ED&D-dedicated Clinical Trial Units) and would help resolve market failure of ED&D technologies and approaches. This platform could allow for evaluation of multiple ED&D tests in parallel against current standard of care, in a basket-trial design (so increasing cost-efficiency of ED&D trials) and could even support evaluation of the potential for multiple tests to be used together to derive a more holistic diagnostic picture. Linked to Policy Recommendation 6, there is opportunity for engagement and support via creation of a national leadership role for ED&D in the NHS, with a mandate to organise ED&D across these technologies and across diseases, driving and supporting research and service delivery.

Importance of pursuing: This Action draws on the opportunity of existing clinical networks that see a high volume of patients to help validate ED&D approaches in development, in parallel to routine gold-standard diagnostic testing; at present, there is a prohibitively long, complex and expensive route to validation of diagnostic tests and pathways. This unique infrastructure also offers the opportunity to attract research from around the world to offer a platform for validation and evaluation that reduces barriers to patient access and streamlines access to health data and samples, at scale, across populations. The potential of this initiative for the provision of early health economic data would also be important. Such a platform would enable a new model of real-world evaluation of ED&D tests with NHS data linkage providing long-term follow up, potentially reducing the cost of trials in this space.

What needs to happen? This Roadmap proposes the creation of a new UK-wide network including infrastructure and staff to utilise patients and samples going through the cancer referral pathways to validate and evaluate/trial novel diagnostics in partnership with regulators and existing NHS infrastructural resources. It is suggested that strategic industry partners are given the opportunity to trial a limited number of tests for validation initially. Consideration as to whether the test to be validated is appropriate for this

environment must be determined. This resource would enable harmonised data, protocols, storage and access processes to maximise the value of the data (including health economic data) collected via this infrastructural resource. This would also build additional capacity and capability in statistics, trial methodology and provide robust governance with a patient-focussed view. This model would include transparent consent processes for patients going through the suspected cancer referral pathways. As this would provide an opportunity to test new diagnostic tests in a symptomatic environment alongside existing diagnostic tests, there needs to be clear standards of what success looks like of the trialled test versus the routinely used test. There would also need to be consideration of clinical protocols for when there is a discrepancy in trialled versus routinely used tests to ensure the best clinical care is delivered to the patient.

Links to: This Action should build on the strengths of the UK diagnostic industry, the unique research validation opportunities offered by the structure of the current UK healthcare system, and the ability to co-ordinate patients that are routinely entering the healthcare system that are enriched for cancer ED&D.

Key stakeholders: The NHS, Clinical Trials Managers, Clinical Trials Units, Experimental Cancer Medicine Centres, Rapid Diagnostic Centres, the NIHR Medtech and In vitro diagnostics Co-operatives, Cancer Alliances, the Academic Health Science Networks, UK regulatory associations, UK charities, NCRAS, UK cancer registries, patients and the public, academic researchers and industry.

Putting it into perspective

“I learnt how important early cancer detection was when my wife, Kate, was diagnosed with stage 4 colon cancer at age 34. Her chances of survival were only 5% and sadly she was not one of the lucky ones despite the amazing efforts of her doctors. I was shocked and angered when I was told that her survival chances would have been 90% if picked up at an early stage. The solution to save lives is in plain sight – detect cancer earlier – but making this a reality is hugely difficult. It needs groundbreaking science, technologies that do not yet exist, enormous amounts of investment, but above all an army of brilliant people who will not give up until the early detection challenge has been solved.

The company I had founded at Cambridge was developing a sensor technology to detect toxic chemicals and explosives. At around the time of my wife’s diagnosis, we had started working with academic researchers to see if the same technology could be used to detect the chemical markers of lung cancer on a patient’s breath. From the encouraging initial data, we decided to spin out Owlstone Medical to further develop this Breath Biopsy technology. We have been fortunate to secure over \$90M of investment from investors who see that despite the risks, challenges and uncertainty, early detection is a problem that must be solved. We have since grown to a team of 170 with a singular mission, to save 100,000 lives. Every day there are more and more scientists, start-ups and investors who are saying enough is enough and are focusing their brilliant minds and efforts on early detection. As a community we will succeed. We will no longer have to say goodbye to those we love taken by cancer before their time.”

Billy Boyle, CEO Owlstone Medical Ltd



Putting it into perspective

“The early detection and diagnosis of cancer is a field which holds immense promise. The innovations that the pharmaceutical industry have brought to bear on cancer have saved lives on a huge scale; advances in targeted drug treatment and immunotherapy have transformed the way we treat cancer. However, finding patients to receive these therapies remains too reliant on the current status quo of patient presentation and diagnosis. It is clear that detecting cancers at an earlier stage gives the best chance of successful treatment. Consequently, a new model is needed for ED&D, which not only has potential to save many lives, but may also create a significant new business model and sector of investment, development and commercialisation. I can see potential for a model that works economically for both industry and the UK government and people, with a new generation of diagnostics incentivising significant investment in ED&D. The tide is beginning to rise – more and more start-ups working on ED&D are beginning to emerge, and larger players are beginning to invest more significantly in this space. Given its strong bioscience base, the UK is poised to ride that rising tide and be at the forefront of this new model.”

Susan Galbraith, SVP Early Oncology at AstraZeneca



THEME 4

Healthcare system innovation and accelerating adoption



This Theme explores building on the strengths of the current healthcare system, ensuring sufficient resource to support ED&D, evolving existing infrastructure to support validation and implementation of new ED&D approaches and engaging in a dynamic consultation with patients and the public on ED&D approaches.

THE CHALLENGE:

The healthcare system needs a clear forward view of novel technologies that are approaching readiness for implementation, and an understanding of how and when to implement them into healthcare practice. There needs to be agreement on the requirements to acceptably demonstrate validation and utility for emerging detection/diagnostic biomarkers and technologies. A clear pathway is needed for the health economics and adoption of ED&D evolving in conjunction with emerging technologies and UK regulations and guidance. The healthcare system must evolve to best make use of disruptive technologies.

Barriers to overcome in healthcare system innovation and adoption of ED&D approaches:

- The NHS is under-staffed and under-trained to deliver effective ED&D even with existing approaches (e.g. there are currently bottlenecks due to lack of primary care practitioners, radiologists, endoscopists, pathologists and other diagnostic staff) and this problem will be exacerbated as new screening and ED&D tools come online, through detecting more patients requiring confirmatory diagnosis.
- Insufficient NHS budget is dedicated to implementation of ED&D, and clarity is lacking around division of responsibility between the NHS and UK government and devolved nations' governments in this space. The NHS is built to treat patients who are symptomatic, not to maintain health in the asymptomatic population.
- The division of secondary clinical care into organ-centric systems can slow detection of cancer in early cases with non-specific symptoms.
- In many cancers, in current clinical practice, detection of very early lesions would lead to clinical uncertainty, with few clear pathways and treatment options for early, indeterminate and pre-cancerous lesions.

- The regulatory and adoption pathway for detection/diagnostic technologies is highly unclear, with no current mandate for adoption of tests approved by NICE and no clear threshold of performance to be achieved by tests in development.

Through consultation, the following recommended Actions were prioritised to develop a framework for action to achieve progress in health system innovation and adoption of ED&D approaches. A high-level summary of each Action is included in the respective tables. These Actions are not intended to serve as comprehensive project plans and instead serve as a starting point for various stakeholders to come together, develop and champion.

Action 11: Mapping the ED&D pipeline and developing Target Product Profiles

Action: Creation of a national body to map, define and conduct an evidence assessment of the ED&D product pipeline in the UK and globally, and to set Target Product Profiles (TPPs) for new tests to work towards.

Major challenge: Numerous companies and academic centres are now clinically trialling technologies and approaches to detect and diagnose cancer early, and many more approaches are in the developmental pipeline; the UK health system lacks a clear evidence base to understand what the overall pipeline is, which approaches are closest to being ready for implementation (and should therefore be piloted, or considerations made for the system changes needed to adopt them), and what the evidence gaps are which would impede uptake. Furthermore, it is unclear to the test developers where the 'goalposts' are for the test which they are developing; what are the test performance characteristics and evidence levels required to convince the healthcare system decision makers that an ED&D test should be implemented?

Action description: This Roadmap proposes that a dedicated, funded and sustained effort is made to specifically map the pipeline of emerging ED&D technologies and approaches globally, to inform future NHS system planning/readiness, to identify evidence gaps and to set the objectives that emerging tests should seek to reach, by defining a series of TPPs for particular cancers and particular ED&D scenarios. It will be important not just to map the individual tests emerging but also look at how they can be combined either in parallel or sequentially. A body could be established to do this mapping and evidence evaluation on an on-going basis and prioritise new ED&D approaches for piloting in the NHS as they reach a defined evidence threshold. This body should also develop relevant TPPs to define clear standards of what is needed for emerging ED&D approaches to be successful (a TPP defines the ideal hypothetical test in terms of e.g. its sensitivity, specificity, positive and negative predictive value, cost and circumstances of use). When tests are developed which meet these TPPs, that would be the trigger for piloting implementation within the NHS. Where products appear to be close to NHS adoption ready, they should be proactively put forward as candidates for evaluation by NICE.

Importance of pursuing: With a more well-understood, integrated pipeline and a better idea of what is happening in the field, we can gather the evidence for what is needed regionally and nationally and therefore achieve meaningful patient impact earlier. It will be particularly important for the NHS to have a clear forward view of emerging disruptive ED&D technologies which might require significant system change (e.g. diagnostic pathways, staffing, follow-up) in order to make best use of them. Building on this knowledge and on an understanding of current clinical unmet need and shortcomings in existing tests/ED&D approaches, defining a series of TPPs for particular cancers would establish clear 'goalposts' for which emerging tests should aim. This will support and incentivise companies seeking to commercialise ED&D approaches and accelerate progress towards impact on health.

What needs to happen? This Roadmap proposes a funded initiative to complete a systematic and comprehensive mapping and review process, requiring strong engagement across academia, research funders, industry and innovation partners in the UK and abroad, and robust knowledge management utilising technology developments. It is recommended that a funded body of experts establish a dynamic approach to mapping the ED&D pipeline (e.g. on-going and not a one-off initiative) with robust links to the NHS to inform the NHS of what is in the ED&D pipeline. This should be a body endorsed by

the UK government that meets regularly; in addition to mapping, this body should contribute to developing TPPs to provide clarity around standards required for emerging ED&D approaches. The proposed body would, over time, define a TPP for missing/required tests for each cancer type and each particular circumstance of use (e.g. a national/risk stratified screening programme versus a point-of-care triage test versus a confirmatory referral test, etc.). In order to define these TPPs, the proposed body would also need to fully understand current clinical practice and diagnostic pathways, incidence statistics, current ED&D test performance and the health economics of the particular scenario. The TPP would also define the acceptable cost of the test for its given performance characteristics (and therefore projected impact on morbidity and mortality, analogous to the manner in which NICE defines and evaluates cost per quality-adjusted life-year gained for new therapeutic interventions).

Links to:

The horizon scanning activity of the proposed body would capitalise on work currently on-going within the National Cancer Research Institute's Screening, Prevention and Early Diagnosis Advisory Group (white paper in progress detailing the ED&D portfolio within the context of a National Cancer Imaging Translational Accelerator) [97], [98]. It would also build upon the work undertaken in developing this Roadmap, bringing many of the relevant stakeholders together to launch a coordinated ED&D pipeline mapping exercise. It should also link to, learn from and build on (but go beyond) the work of the **NIHR Innovation Observatory^a** and the **Accelerated Access Collaborative^b** [49], [50]. It will also relate to the **NHS Med Tech Funding Mandate^c** that is currently under consideration [18].

Key stakeholders:

NHS representatives, UKRI and other UK-based funding bodies, international funding bodies, industry partners, specialist investors, specialist city analysts, NICE, the National Cancer Research Institute's Screening, Prevention and Early Diagnosis Advisory Group, charities, technology companies, service providers, and academics.

a <http://www.io.nihr.ac.uk/>

b <https://www.nice.org.uk/aac>

c https://www.engage.england.nhs.uk/consultation/medtech-funding-mandate/user_uploads/medtech-funding-mandate-guidance-consultation-document-v2.00--2-.pdf

Action 12: Generating cancer site-specific ED&D roadmaps

Action: Addressing the duplication, fragmentation and limited impact caused by poor linkage of the ED&D ecosystem by galvanising disease-specific roadmaps for ED&D research and healthcare system practice, for cancers with poor stage diagnosis at present (with lung cancer as an exemplar).

Major challenge: There is currently a lack of coherent strategies for disease-specific ED&D. While a new generation of multi- or pan-cancer ED&D tests are in development, many others are specific to cancers with a particular tissue of origin, each with its own challenges and characteristics (e.g. incidence, risk factors, biomarkers, ease of access for sampling etc.). In order to make near to mid-term progress in ED&D of a given cancer type, a holistic view is needed of the clinical state-of-the-art, the challenges and unmet needs, the aspirations of what an ideal ED&D health system would deliver, a view of the current research and development landscape and emerging ED&D approaches, and recommendations for progress.

Action description: To enable a flexible and specific approach to each cancer site, there needs to be a greater understanding of the individual barriers and requirements for each cancer type. Therefore, this intervention proposes the development of cancer site-specific roadmaps (i.e. for lung cancer, pancreatic cancer, ovarian cancer, liver cancer, etc.) that detail concrete ED&D recommendations specific to a cancer type, based on the unique needs and current state-of-the-art, taking into consideration the over-arching Themes of this Roadmap. This Roadmap proposes the development of a multi-disciplinary group to provide oversight and guidance on the development of disease-specific roadmaps; the specific roadmaps would then be convened by experts in that cancer type. This would require the involvement of the full breadth of stakeholders across the ecosystem and should include financial backing from the UK government, as the roadmaps will serve as a valuable resource for prioritising government funding to deliver on recommendations and incentivising private investment for specific cancers to drive meaningful change. These site-specific roadmaps would cover research and development, and clinical service provision. Analysis of the current clinical landscape and test pipeline would highlight key gaps and unmet needs, so highlighting opportunities for targeted discovery research and technology innovation, and directing funders, investors and companies to target resource in these areas.

Importance of pursuing: In the context of this wider ED&D Roadmap, greater clarification of what is required within each specific cancer site is essential to allow a better understanding of the individual requirements in each cancer type (for example in lung, a lung ED&D roadmap would need to be built around an understanding of the ongoing NHS pilot of low-dose CT scan for screening high-risk individuals, the challenges of indeterminate lesions found through this process, the development of liquid biopsy tests, as well as triage and diagnosis in primary care, etc.). A better understanding of individual requirements and hurdles will allow coordination of research efforts and national resources in these disease-specific areas, as well as affording economic benefits to the NHS. Without a clear ED&D strategy for different cancer types, and therefore an undefined clinical case, there is minimal incentive for the private market to engage, which is required to enable progression in the ED&D field. These activities will also offer an opportunity to see where strategies can apply across cancers, and to other diseases where relevant.

What needs to happen? This Roadmap proposes the convening of an independent multi-disciplinary group to provide oversight and guidance on the development and scope of disease-specific ED&D roadmaps; key leaders in the disease-related field would be brought together to decide on a plan of action for each cancer site. Starting with a workshop to bring

together key leaders in that field, the group would work together to identify a tailored approach and targeted disease-specific interventions. It is proposed to build on the disease area landscaping work of the NCRI and to use expertise in the cancer site-related area to lead on the roadmaps.

An initial exemplar cancer should be prioritised, using factors such as incidence, high proportion of late stage diagnoses, defined risk groups and known impact of ED&D. Such an exemplar should be used as a proof-of-concept to be rolled out as a model for other cancer sites, acknowledging that some lessons learned will be different for different cancer types. It is suggested that lung cancer would meet these requirements as an exemplar (including the opportunity provided by the lung health check pilots), but other cancers could also be strong candidates. To define these requirements, a hub of multi-disciplinary ED&D expertise is required to generate guidelines for prioritisation and to ensure the disease site-specific requirements are catered for in the cancer-specific roadmaps. This multi-disciplinary group would help define the scope of the cancer-specific roadmaps and suggest the relevant experts to be involved in delivering the roadmap. This group could then provide insight into linkages between different cancer types (and potentially pan-cancer insights) and facilitate knowledge exchange and collaboration between cancer types where applicable.

Each model would also need to consider how to evolve with a rapidly changing climate seen within some cancer types. This Action recommends disease-specific areas being tackled simultaneously and in line with the changing policy landscape.

Links to:

Actions 8, 11

The broader work of this Roadmap, **National Cancer Research Institute organ specific groups^a** [99], **CRUK's cancers of unmet need^b** [100].

Key stakeholders:

In the development of a lung-specific ED&D roadmap for example, the key stakeholders required to deliver the recommendations of the roadmap may include bioengineers, clinicians (primary and secondary care), health economists, data and computer scientists, policy makers, bioinformaticians, radiologists, statisticians, patient advocates, quality of life specialists, healthcarers and the private sector, alongside the NHS, NHS advisory groups (e.g. the Lung Advisory Group, the National Cancer Programme's Clinical Advisory Group, etc.), the National Cancer Research Institute's Screening, Prevention and Early Diagnosis Advisory Group, site-specific experts and the CRUK Lung Cancer Centre of Excellence. In parallel, an evaluation of the policy landscape would need to take place to enable any recommendations outlined in the disease-specific roadmaps.

a <https://csg.ncri.org.uk/view-our-ncri-groups/>

b <https://www.cancerresearchuk.org/funding-for-researchers/our-research-strategy/tackle-cancers-with-substantial-unmet-need>

Action 13: A phased approach to automate diagnostic clinical pathways

Action: A phased approach to standardising, optimising and automating NHS diagnostic pathways via:

Phase 1 – Systematic mapping of ED&D diagnostic pathways to identify opportunities for standardisation, optimisation and future automation.

Phase 2 – Using the areas mapped in Phase 1, the application of technological approaches e.g. AI to automate relevant aspects of ED&D diagnostic pathways to facilitate optimisation of these pathways.

Major challenge: Efficient ED&D is impeded in clinical practice by a lack of standardised diagnostic pathways, within and between hospitals and trusts. Opportunities are missed to identify, share and implement best practice in these pathways and to reduce inefficiency. Diagnostic staff shortages currently create bottlenecks, slowing diagnosis; there are a number of opportunities that have not yet been capitalised on to integrate technology into ED&D clinical care pathways and there is a lack of system preparedness to capitalise on the opportunities that AI and other technologies will provide to automate and optimise ED&D.

Action description: This Roadmap proposes a two-step approach to spot opportunities in current ED&D pathways for optimisation: this first includes comprehensive mapping of ED&D diagnostic pathways to determine which parts of the pathways can be standardised and optimised (reducing inefficiency, redundancy and discrepancy between different hospitals and trusts; defining and implementing best practice). In doing this mapping, Phase 1 would also identify opportunities for future automation of processes. Phase 2 would consist of the identification and application of emerging technology (e.g. AI) to these identified parts of the ED&D diagnostic pathways in order to achieve automation and reduce utilisation of human resource as ED&D demands on workforce increase. This will enable enhanced standardisation, efficiency and accuracy in ED&D diagnostic pathways.

Importance of pursuing: To make best use of limited NHS resources (by reducing repetition, unnecessary testing and streamlining workflow) and ensure the rapid and cost-effective integration of new interventions, there is a clear need for optimised diagnostic pathways in the existing healthcare system, including in primary care. This intervention represents an opportunity for reducing bottlenecks within the existing system and to play to the strengths of technology within the UK. This will address a crucial need to make the care pathway more efficient and more cost-effective, and may lead to enhanced patient satisfaction, reduction of clinical harm and improved patient outcomes. Automation, standardisation and optimisation via technology assistance lends itself towards more timely and accurate diagnosis whilst minimising overdiagnosis. Where implemented effectively, this affords the opportunity to improve quality of care and capacity.

What needs to happen? This Action requires identifying opportunities to integrate existing technology into the healthcare system via systematic mapping of ED&D pathways. This should be driven by the NHS to provide insight on the most efficient ED&D pathways, and to provide clarity on which parts of the pathway can be realistically automated within the existing healthcare infrastructure. Furthermore, it needs to be determined through research and pilot studies where the opportunities for automation may have maximum patient health benefit. This will require building an evidence-base for what technology has reached the appropriate level of evidence, and should be added into the existing infrastructure, as well as comparison of technology against current standards of care.

The primary changes would be to validate elements of the pathway and have an impact on workflow, harms, patient satisfaction and opportunity costs, followed by mortality in the medium term and eventually arise at evidence-based optimal clinical pathways. As the pathway is developed, a culture shift is required to embrace and adapt to new technologies amongst healthcare professions and patients. To do so, it is imperative training is provided to allow staff to operate within the new frameworks (e.g. automated reporting/radiographer triage), which will again require NHS buy-in. Cancer ED&D Champions may help to make this a reality – as clinical pathways shift to enable better personalisation and ED&D, Cancer ED&D Champions can offer support by creating knowledge-sharing networks.

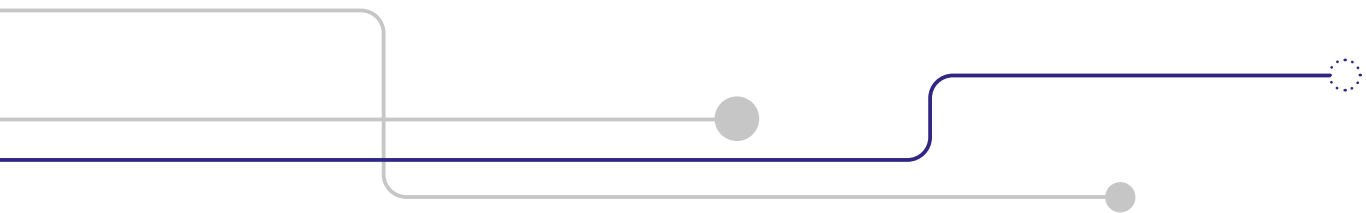
Links to:

Action 12

This Action needs to build on the strong foundations of the Industrial Strategy Challenge Fund Digital Pathology and Imaging Centres [7], [101]. Emerging technologies which could further optimise ED&D pathways e.g. highly positive results emerging from the application of machine learning techniques to automate reading of mammograms to assess risk and identify early breast cancers; results from Imperial College/DeepMind and from MIT [102], [103].

Key stakeholders:

UK government, the NHS, technology developers and providers, UK regulatory bodies, UK charities, UKRI Digital Pathology and Imaging Centres, HDR UK.



Action 14: Dynamic patient and public health consultation

Action: Develop and support a multi-disciplinary and phased initiative to investigate patient and public perspectives, baseline knowledge and preferences regarding ED&D approaches.

Major challenge: A deeper understanding of the needs and perspectives of patients and the public is required to ensure that all ED&D technologies and approaches bear these in mind to enable true line-of-sight to clinical and population health impact. Without acceptance and uptake from the public, new screening approaches will not have impact, as current uptake of screening programmes is not universal across demographic or socioeconomic groups. The reasons for this are not fully understood and interventions to enhance uptake have not resolved the problem; there is a need to understand and act on modifiable factors which prevent these populations from participating in screening and/or reporting of symptoms. One challenge is that many tests in development do not seek to (or do not have the capacity to) fully engage the public to understand their perspective. Patients and the public also need to be more thoughtfully engaged in the use of health data for research in a coordinated and comprehensive way, both through further support of existing campaigns (e.g. 'Data Saves Lives' campaign [104]) and new initiatives. There is a need to better understand the patient and public perspective at each stage of the pipeline, informing research, development, service delivery and government policy. Furthermore, a lack of such understanding of the patient and public perspective has resulted in healthcare inequalities in ED&D, with poor uptake of screening and lower rates of symptom reporting in hard-to-reach-populations.

Action description: This Roadmap proposes the development and funding of a phased and dynamic initiative to holistically and comprehensively explore patient and public attitudes, baseline knowledge and preferences regarding ED&D. This may take the form of a series of virtual citizen debates on key ED&D approaches and challenges (e.g. ED&D Virtual Town Halls) or may include the building of an online community/platform to consult patients and the public on ED&D topics as and when hot topics arise. This could be a platform to support government and NHS decision-making, academic research and industry test development.

Importance of pursuing: It is unclear how supportive the public and patients are of accepting and engaging in ED&D approaches, how far they would go in order to achieve ED&D as routine reality, what level of monitoring and data openness they would consider acceptable, and preferences for organisation and delivery of care. In the COVID-19 era, diagnostic tests have a prominence in the public consciousness like never before, but it is unclear whether and how this extends to cancer ED&D. Few actions to support ED&D can be done without the engagement of public and patients and thus, there is a significant need to better engage with and understand the public's appetite for early detection and diagnosis, monitoring and screening. This includes their understanding of risk and their views on participation in research, use of patient data and acceptability of tests. Such understanding should help to address inequalities, particularly in areas like uptake of screening.

What needs to happen? This Action should include consideration of what key building blocks might be needed to support, from a societal perspective, a progressive and sustained shift away from an 'illness' model of health service, to a 'maintenance of health' model, the ethical and moral considerations of increasingly sophisticated and risk stratified approaches to ED&D, increasing research access to NHS data and appropriate consideration of

variation, such as by socio-demographic factors. With shifts occurring in the understanding and diagnosis of diseases other than cancer, it will be important to consider interactions, considerations and opportunities through a wider disease lens. This consultation needs to be far-reaching beyond those that are currently engaged in this dialogue, and to be dynamic, to capture perspectives in this evolving space. This, for example, may include a series of virtual citizen debates or an online community platform where the perspectives of patients and the public are consulted on specific ED&D topics and/or approaches.

Links to: Actions 1, 2, 3, 4, 5, 6, 7, 12 and 13

Key stakeholders: Funders, UK charities, NCRI, the public, patients, NHS, research organisations including universities, public health clinicians and behavioural scientists.

Putting it into perspective

“My wife, Pam, was misdiagnosed three times over 18 months before finally being admitted to hospital via Accident & Emergency, where, following tests and surgery she was diagnosed with incurable bowel cancer. She died 12 months later, aged just 52. Such events devastate families and I was determined to do whatever I could to ensure as few families as possible went through the experience we went through and so I began volunteering and fundraising for CRUK. I’m particularly passionate about early detection and diagnosis as you’re more likely to survive your cancer if it is caught early, but currently only around half of people actually are diagnosed in the early stages. Right now, there are too many people each year who are diagnosed too late to give them the best chance of survival. I’m particularly excited about the development of an Early Detection and Diagnosis of Cancer Roadmap and proud that as a member of the Cancer Insights Panel I’ve had an early opportunity to give some feedback to CRUK’s Prevention & Early Detection team on the development of this Roadmap. This, I’m sure will make a real difference, helping to transform lives and ensure more people are diagnosed early, resulting in successful treatments and increased survival rates.”

Patrick McGuire, CRUK Cancer Insights Panel Representative



7 | POLICY RECOMMENDATIONS TO ADDRESS THE CROSS-CUTTING BARRIERS TO THE EARLY DETECTION AND DIAGNOSIS OF CANCER

Throughout the challenges and Actions described above for Themes 1 to 4, several cross-cutting barriers emerged that, if not overcome, will impede progress towards achieving the shared vision outlined in this Roadmap (Section 5). These barriers span the entire research and implementation pipeline, encompassing challenges in research, translation, development, adoption, healthcare system delivery and engagement with patients and the public.

Addressing these cross-cutting barriers should be explored by, and kept at the forefront of the minds of, all stakeholders working in the ED&D ecosystem. However, given the underpinning nature of these barriers, the UK and devolved nations' governments and other national bodies have a clear role to play in addressing these and facilitating a world-leading environment for ED&D. While there has been some positive progress to date, including greater emphasis on ED&D in the Life Science Industrial Strategy and £79m committed to the **Accelerating Detection of Disease programme^a**, much more can and must be done. This is not only in the interests of improving health, but also wealth, given the potential economic benefit that could be developed from the UK realising its role as a world-leader in the ED&D ecosystem.

While this Roadmap has identified specific recommendations to address these barriers, in many respects they are interconnected and ideally should be considered holistically. The major cross-cutting barriers to progress in ED&D, and the Policy Recommendations to address them, are:

A. ED&D research has been chronically under-prioritised and consequently, under-funded by both public and private sectors. There are several contributing factors to this including, but not limited to: a historical focus on research to support treatment of late stage disease due to the predominance of late stage patients in clinical care, the perceived difficulty of working on early cancer due to biological complexity and lack of early stage models and samples, and the technological limits for sufficient sensitivity and specificity of tests. In addition, there are challenges in accessing NHS data and samples, unclear pathways to adoption and the low value placed on diagnostics by the health service. These issues have created a market failure associated with commercialising early detection technologies in the UK, limiting industry and private financial investment. Making ED&D research a true national priority would promote health and wealth in a progressive way; it would accelerate progress towards the goals to improve early diagnosis in the NHS England Long Term Plan and ambitions set out by the devolved nations, and would support the growth of a burgeoning industry in this country. The UK has the potential to be a world-leader in this space.

Policy Recommendation 1: The UK government should make ED&D a central tenet of the UK R&D roadmap, investing appropriately and addressing barriers to ensure a flourishing ecosystem for ED&D research and development.

a <https://www.gov.uk/government/news/uk-to-innovate-new-life-saving-treatment-and-diagnosis-technology>

B. The UK lacks a clear, agile and streamlined system to evaluate the clinical and cost-effectiveness of ED&D approaches, to value them appropriately and to ensure their uptake and implementation into the healthcare service. Unlike for therapeutic interventions, the regulatory and adoption pathway for detection/diagnostic technologies is highly unclear. The healthcare service does not have a system that appropriately values and reimburses ED&D tests or ensures that approved tests are universally implemented. Required evidence levels can be prohibitively high for most test developers; the requirement for a new ED&D screening test to show impact on mortality means that trials must involve vast numbers of participants studied over many years, requiring at least tens of millions of pounds of investment. Timelines for development and approval are inordinately long and the price-point of diagnostics is low. All of this presents a massive financial barrier to industry and private financial investment in developing and marketing ED&D tests in the UK, resulting in a market failure.

A longer-term view is needed of 'cost-effectiveness'. More appropriate models for ED&D diagnostic cost-effectiveness evaluation must be investigated to address, for example, the current lack of uptake of new diagnostic approaches due to the requirement to be cost-neutral or pay back within a year. Savings from ED&D may be realised some years later (through reduction in the proportion of late stage diagnoses and associated high treatment costs). Further, even when cost-effectiveness has been demonstrated, there is currently no clear system to ensure nationwide adoption of a new test. The development of a MedTech mandate by NHS England and NICE is a positive initiative in this space.

Policy Recommendation 2: The UK government and devolved nations' equivalents must address the market failure experienced in the commercialisation and adoption of ED&D technologies. A taskforce should be established to develop an action plan to remove barriers, incentivise industry and investors into the ED&D space and accelerate adoption of technology. A vital part of this must be considering how diagnostic tests are valued in the health service and their pathway to adoption, building on the development of the NHS England and NICE MedTech Funding Mandate, and committing to quickly commission technologies that meet a well-defined Target Product Profile. This review should also explore a model of earlier roll-out of tests showing impact on reducing late stage diagnosis, followed by real-world evaluation of longer-term impact e.g. on mortality.

C. UK health systems do not have enough resource to deliver even the effective ED&D approaches we do have access to, nor to support research or readiness for novel approaches. This includes critical shortages in staff capacity, equipment and technology which limits the health system's ability to diagnose patients in a timely way and to innovate in order to develop and adopt further new detection technologies. Staff shortages have persisted for many years and have been the result of poor planning, unclear accountability and lack of investment in training of staff. In addition, while early diagnosis is a key strategy in the NHS England Long Term Plan, for example, insufficient prioritisation is given to ED&D in NHS budgeting [105] – the same can be said for other UK nations. Without due attention to budget challenges and considerations, and solutions that create incentives rather than disincentives, it will be impossible to fully realise the potential of research and innovation to make ED&D a routine reality. There is also often a lack of provision of staff time for sufficient clinical engagement in the research and development of new ED&D approaches, as well as difficulties implementing them into practice.

Policy Recommendation 3: The UK government and devolved nations' equivalents must invest to increase health service capacity – workforce, equipment and infrastructure – now and in the future, to support the ED&D agenda. The UK government and devolved nations' governments must be bold and provide adequate funding to train and maintain the primary and secondary care workforce that the healthcare system needs, both to meet future patient demand and to support research and innovation. Healthcare services should also explore how investment can be shifted to support and incentivise ED&D approaches more effectively, and ensure resource is available to support ED&D research.

D. Patient-level NHS data provides an enormous opportunity for ED&D research but currently data is difficult to access or inaccessible in reasonable timeframes. It is imperative that NHS data is readily available, in an ethical and timely way, to researchers; this would allow real-world discovery and validation of new technologies. However, streamlined, centralised points of data access are lacking for real-time clinical data. Furthermore, robust, consistent and complete data collection is lacking in some areas of care and there remains fragmentation and lack of interoperability of data systems between NHS practices, hospitals and trusts. These challenges

all limit data utility for ED&D research. A recent report from the Association of the British Pharmaceutical Industry articulates these challenges and suggests ways forward [106].

Governments across the UK recognise the potential of health data for research. For example, the creation of HDR UK and its work to develop an **Innovation Gateway**^a to create a 'single front door' to allow responsible access to patient datasets for research purposes is a clear signal of intent [107]. Initiatives such as Northern Ireland's 'encompass' programme, are seeking to introduce digital integrated care records but should go further to allow integration with primary care systems and to enable access for researchers in addition to healthcare professionals [108]. **The National Cancer Diagnosis Audit**^b (NCDA) has succeeded in collecting and linking the detailed primary care records of over 56,000 people in England alone (similar collections are underway in Scotland and Wales) leading up to their diagnosis of cancer in 2018 [109]. The NCDA was only made possible by CRUK taking the lead and pump-prime funding a partnership between the charities, Public Health England, the Royal College of General Practitioners and NHS England, and will cease to exist as a critical data collection platform unless a way can be found to automate or the UK government/NHS England takes over future funding.

There is clearly still much more work to do, at pace, to better join up care records, genome sequencing, imaging and other data types, and make this more readily available to ED&D researchers. To enable this, it is paramount that work continues to engage with and inform patients about the use of their data and research to ensure trust is maintained. There is also a need to improve access to excess biological samples (e.g. tissue, blood, etc.) taken in routine clinical practice, at an anonymised individual patient level.

Policy Recommendation 4: The UK government should significantly boost investment to accelerate robust collection, interoperability and access to patient data for ED&D research, while maintaining public trust. This should include: 1) accelerating delivery of central points of access and mechanisms for ED&D researchers to access patients' health data in a streamlined, real-time, low-burden and ethically-sound way (partnering with, building and delivering on the work of NDRS, NHS Digital, HDR UK, CRUK and others), and 2) reviewing how biological samples taken in routine practice can be utilised for research.

E. The healthcare system approach to ED&D service delivery remains too siloed. The long-term future of ED&D of cancer, and any shift towards proactive maintenance of health (rather than treatment of later stage disease), cannot exist in isolation. ED&D is an increasingly important prospect for an array of diseases including neurodegeneration, diabetes, arthritis, cardiovascular disease and many more. By its own definition, early detection and diagnosis operates at a point in the pathway prior to establishment of disease type and so should operate from a platform broadly agnostic to this. Such an approach could enable a shift towards proactive health management in the asymptomatic public, provide an opportunity to engage 'hard-to-reach' demographics and remove some burden from the primary care workforce. However, a new model of care should be developed to achieve this aim.

Building on platforms such as the Rapid Diagnostic Centres, Diagnostic Hubs, NHS Health Checks (and equivalents in devolved nations), and the Accelerating Detection of Disease initiative, a long-term view of cross-disease detection and diagnosis is needed. Further research and development will be needed before a model is feasible. Understanding the public's needs and tolerances around health maintenance and early disease detection will be crucial (as per Action 5 and 14). This potential new model would be a platform for sample collection and research as well as clinical detection and investigation/treatment referral.

Policy Recommendation 5: The UK government and devolved nations' equivalents should strategically scope and explore creating a new model of community-based health-check centres to check (ostensibly) healthy, asymptomatic people and find early disease and/or markers of future disease and risk. Scoping of this potential future model should involve identification of, and support for, the emerging paradigm-changing research and technology development findings in the ED&D space, building on the research and systems proposed in this Roadmap. To promote equity of access, alternative routes for touch-points with the public should be explored through, for example, community pharmacies, health-check stations in supermarkets, etc.

a <https://www.healthdatagateway.org/pages/about>

b <https://www.cancerresearchuk.org/health-professional/diagnosis/national-cancer-diagnosis-audit>

F. There is a lack of leadership and accountability for ED&D within the healthcare service, with no clear responsibility for its advancement and delivery. Responsibility for component fields such as imaging, pathology, endoscopy, genetic testing and *in vitro* diagnostics is fragmented and siloed across organ- or disease-centric specialties. Individual hospitals/trusts do not tend to have senior positions specifically responsible for research, development and implementation of cancer ED&D; as such, accountability for innovation is lacking and progress is impeded. Furthermore, there is a lack of national coordination, leadership and accountability for ED&D diagnostics across diseases and technologies (see opportunity for integration in Action 10); with no clear central responsibility, a fragmented picture is presented for how a new test might find a route to adoption, who is accountable for supporting research and innovation, or how resource should be managed across diseases and technologies. This last point was brought into sharp focus by the severe impact the COVID-19 crisis had on cancer diagnosis, which may have been ameliorated by clearer central responsibility for diagnostics.

Policy Recommendation 6: The UK government and devolved nations' equivalents should create a clear and visible system of leadership and accountability for ED&D and diagnostics, spanning imaging, pathology, endoscopy, genetic testing and *in vitro* diagnostics. This should involve the creation of a national leadership role for pan-disease ED&D in the NHS, with a mandate to organise ED&D across these technologies and across diseases, driving and supporting research and service delivery. This should also involve creation of a national cadre of NHS Cancer ED&D Champions: every relevant hospital should appoint an ED&D Cancer Champion to drive cancer ED&D as a mission within their hospital, to engage relevant decision makers and practitioners to ensure implementation of the best approaches and to engage in research opportunities. This would be a high-profile role with a national forum for the ED&D Cancer Champions to share best practice, working closely with key ED&D roles in Health Boards, Cancer Alliances and NHS regions and feeding into the recommended national leadership role for ED&D in the NHS.



8 | CONCLUSION: REALISING THE VISION FOR ED&D

This Roadmap serves as a compass for the ED&D ecosystem, providing a high-level direction of travel, shaped by the knowledge and expertise of the cross-ecosystem stakeholders that were consulted in its development. Through this consultation, it was evident that the talent and enthusiasm of a growing ED&D ecosystem can propel paradigm-changing approaches. We are already beginning to see the tide is starting to turn, as broadening interest and investment in the ED&D space takes shape. Now is the time to accelerate ambition; this ambition for ED&D is far-reaching and future-facing, but achievable through a strategic, phased and coordinated approach.

The UK has the potential to be the global leader in research, development and commercialisation in this space, capitalising on the unique resource of the NHS and the UK's fantastic pedigree in biomedical research and innovation. To realise this potential, there needs to be a renewed focus on building a deeper understanding of the biological insights achieved through research and using these insights to strategically inform ED&D approaches. Additionally, many of the Actions featured in this Roadmap have potential to feed into (or be informed by) solutions for other diseases. The future vision is one of maintenance of health, rather than firefighting symptomatic disease – this will ultimately make a pan-disease approach essential. Although this Roadmap is primarily focused on the UK, the ED&D sector needs to consider and embark on collaboration on an international scale, having the foresight, open-mindedness and flexibility to adapt to emerging research and technology to spot and deliver opportunities for the ED&D of cancer and other diseases. Should the UK realise its potential as a world-leader in ED&D, the approaches developed here may attract global investment and may set the tone for a global shift towards ED&D,

both in developed nations in the near term, and also ultimately translating to a global health impact as technologies evolve and become more affordable.

The Actions presented in this Roadmap are meant to serve as a foundation on which future success will be built. The different Themes presented in this report are highly linked, with many of the Actions building in a step-wise manner to a shift towards proactive health management. Only through an integrated, multi-disciplinary, multi-organisational approach will success of this vision be realised.

At the heart of it all lies the life-changing opportunity to impact population health in an unprecedented way. Patients and the public need to be considered on every step of this journey and in the delivery of each of the Actions presented here. The ED&D ecosystem needs a deeper understanding of the needs and perspectives of patients and the public to ensure that all ED&D technologies and approaches bear these in mind to enable true line-of-sight to clinical and population health impact.

The ED&D landscape is complex, and the ambition of this Roadmap is significant. If we are to defeat cancer, ED&D is arguably the single most important and impactful objective we can have. Progress in this mission will only be possible through concerted, collaborative action from an array of sectors and stakeholders, supported and enabled by government policy. We need to work co-operatively to unite fragmented efforts, pool expertise and resources and build on the talent and energy of the growing ED&D ecosystem. Now is the time to act; together let's make the progress needed to make ED&D a routine reality.

9 | CASE STUDY: THE JOURNEY OF CYTOSPONGE®-TFF3

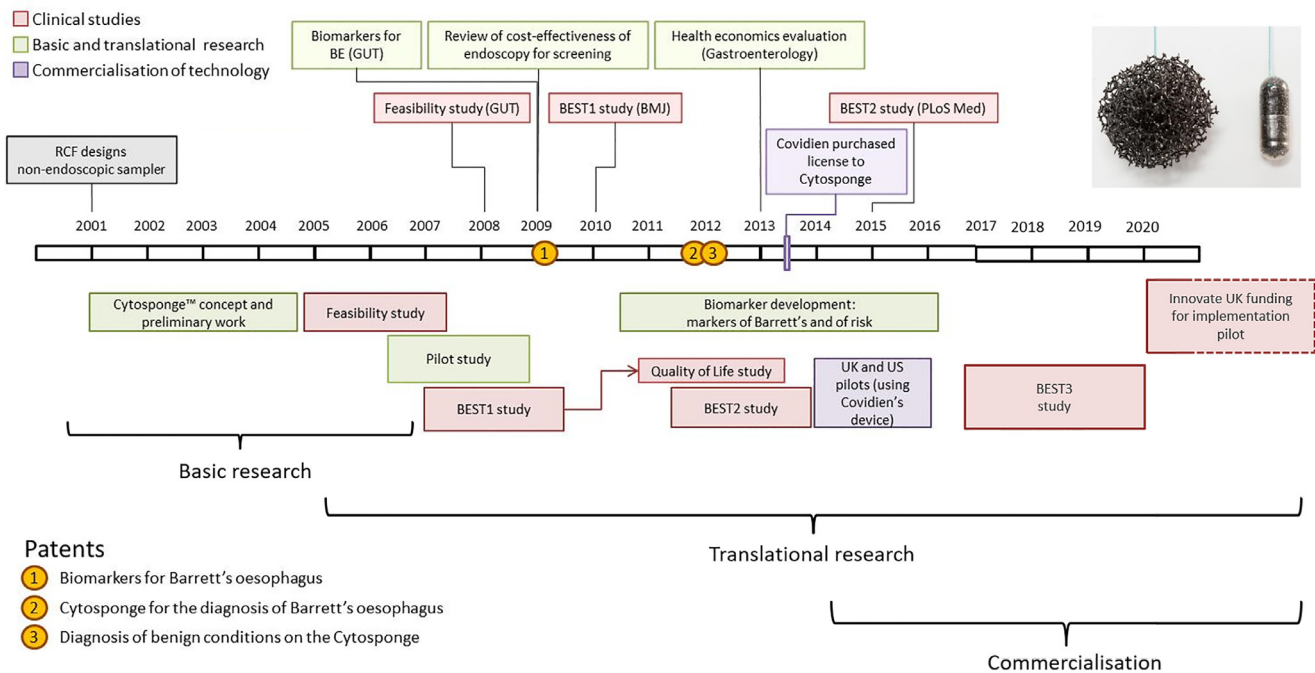
The development of innovative technologies and approaches for the ED&D can yield transformative benefits for patient survival and quality of life. However, achieving this impact is rarely straight-forward – the development and adoption of novel ED&D technologies can be a lengthy process with complexities in navigating the pathway to translation.

over 19 years from the early days of conception of the device to the present time where over 13,000 patients who are on medication for heartburn were invited to take part in the randomised BEST3 study, with results published in August 2020 [110].

One example of this is the Cytosponge®-TFF3, an innovative test for Barrett’s oesophagus – a condition that can increase a person’s risk of developing oesophageal (food pipe) cancer. It’s an inexpensive and straight-forward test that can be done in a GP surgery instead of a referral to hospital for an endoscopy.

The journey of the Cytosponge®-TFF3 test spans

Cytosponge®-TFF3 timeline



A novel idea is born (2001)

Professor Rebecca Fitzgerald developed the early conception for the idea of a less-invasive test to detect Barrett's oesophagus. In these early days, she explored different models for the design complexity of the device and investigated feasibility of the device.

Early models and exploring biomarkers (2001–2009)

The first sampler is designed; this original model is very different from the current Cytosponge®-TFF3. Rebecca decided to move away from a rigid catheter to deliver the sampling device to a capsule which would be less dependent on a highly skilled operator to deliver the test. In parallel to designing the device, Rebecca realised that a biomarker would be required to specifically identify any Barrett's or cancerous cells from this heterogeneous and copious cell sample which collects cells from the stomach as well as the oesophagus and oropharynx. A series of experiments were undertaken to find a suitable biomarker for diagnosing Barrett's and she decided on a protein-based approach, as this assay would be highly stable and detectable by antibody immunohistochemical assays that are standard in all hospital laboratories. Hindsight clearly outlined the need to keep stringent records and the consideration of intellectual property (IP) at the early stages (e.g. the potential to further protect commercial interests in an antibody or assays). This sheds light on some key learnings:

- When involving lab-based processing as an element of your ED&D approach, you need to consider the pros and cons of a centralised processing model versus multiple labs.
- Thoughtfully debate the optimal assay methodology considering whether it needs to be very high-throughput and quantitative. Consider future iterations that might supersede the original assay and how the evidence base can be transferred.
- To be most impactful in cancer, your biomarker approach may need to combine biomarkers for quality control, detection of the condition (e.g. pre-cancer) and stratification of the degree of future risk or stage of the cancer. When multiplexing is an option, consider implications for IP.
- Developing strong IP and look to bundle where applicable; having this knowledge at very early days will help inform future iterations of the device and assay selection.
- Your methodology needs to be scalable. How does your implementation and business model of assay of choice fit into the current infrastructure of the health system? Can parts of this be automated to ensure standardisation?

Testing feasibility in clinical trials (2008–2015)

Assessing the health economics of where the test would be best situated within the clinical pathway revealed complexities. The over-arching goal was to develop a test suitable for the primary care setting and the BEST1 feasibility study was conducted in primary care. There was extensive consultation with patients to understand acceptability and inform trial recruitment.

- You need a firm grasp on the health economics of your technology in the early days, including how the health systems operate in reality, the different budgets that will be required for each step in the development pathway; simulations need to reflect real-world spending of health economics to best inform placing of your technology and ED&D approach.
- It is important from the outset to understand what patients want. Champions that lend their story to strengthen the message of the potential impact of the technology and ED&D approach are invaluable.

Overcoming roadblocks in design and materials (2010)

A major challenge arose, as it surfaced that the materials of the device needed to be changed to meet stringent regulatory requirements. There were also questions about ensuring the scalability of the manufacturing process which had been heavily manual up to this point. There were hurdles in understanding how commissioning works. A trademark for the Cytosponge®-TFF3 was secured, which helped build its presence and visibility over time. The major lessons learned were:

- For devices, involve experts in material sciences in the early days of development of design and selection of materials.
- You are committed early on to the properties of the device once clinical trials are underway; changing materials of the device may change the performance characteristics and require the trials to be re-run to recollect evidence.
- Consider scalability of manufacturing processes.

Commercialisation of the Cytosponge®-TFF3 (2014–2017)

The options of commercialisation routes for the test were deliberated. Extensive interactions with companies regarding investment and licensing opportunities were time intensive. A dilemma was whether this technology was more suited to the devices industry or an *in vitro* diagnostic company since its function is two-fold. After discussions with potential investors, two options were pursued. There was the offer of investment for a start-up company or to license to an existing devices company. The Medical Research Council advised that licensing was the least risky option and a license deal was made with Covidien (makers of ablation treatment catheters used to treat dysplasia in Barrett's) in 2014. Soon afterwards Covidien was bought out by the global devices company Medtronic, which naturally added some delays in the translation of the Cytosponge®-TFF3.

- Comprehensive, unbiased advice to see how your technology fits within the wider early detection picture is invaluable and often difficult to obtain. Seeking mentorship without vested interest to receive coaching and advice at every stage of the process is key.
- When thinking of potential investors and partners, carefully consider their expertise and interest in your approach to help drive progress. Solid partnerships are pivotal in a complex translation environment. At an early stage, think beyond border limits to attract investment opportunities in markets larger than the UK and seek partners that may provide expertise and know-how to infiltrate larger markets.
- Dealing with competition is inevitable and having realistic expectations about the timeframes to adoption and success against other approaches is challenging.

Continuing to build the evidence base for the Cytosponge®-TFF3 (2013–present)

BEST2 was designed to test the accuracy of the Cytosponge®-TFF3 and BEST3 was conducted to provide the level of evidence (e.g. randomised trial) for adoption by the NHS, commissioning, NICE guidelines, etc. Undertaking a randomised trial in early detection requires large numbers of patients and is complex to navigate. BEST2 and BEST3 were supported by CRUK in partnership with NIHR clinical networks and is an example of strong partnerships between government, charity funders and the NHS enabling support for innovative approaches in ED&D. Rebecca and her team have now established a spin-out diagnostics company (Cyted) to provide the lab testing and AI-assisted diagnostics.

- The journey of the Cytosponge®-TFF3 isn't over yet and the next stage is implementation. Establishing changes in clinical practice and behaviour is a long journey and is difficult to achieve. Perseverance is key!

Key links to this Roadmap's Themes and Actions

Throughout the journey, progress was made possible in part by a strong appetite to support novel ideas in ED&D by academic funders, with opportunities to secure long-term funding to support the longevity of projects; this key role of funders was vital at critical stages of the Cytosponge®-TFF3 journey. Regulatory approval processes were complex and difficult to navigate, adding significant time and costs (Action 8, 11). The journey of the Cytosponge®-TFF3 has required the integration of different disciplines to realise success, including the collation of efforts from multi-disciplinary experts in trial design and statistics, health economics, assay expertise, device manufacturing, material sciences, and engineering. A clear grasp on the health economics and an in-depth understanding of how the device could fit within existing health pathways was key to progress (Action 8). Central to success is a comprehensive understanding and dynamic consultation of the views of patients and the public throughout the journey to gather insight on acceptability and uptake (Action 14).

10 | APPENDIX 1 – ED&D ROADMAP DEVELOPMENT PROCESS AND CONTRIBUTORS

CRUK recruited a Steering Committee of visionary leaders, chaired by Professor Chris Whitty (Chief Medical Officer for England and Chief Scientific Adviser for the Department of Health and Social Care) to inform and set the framework for this ED&D Roadmap. This Steering Committee met in June and September 2019 to define the major challenges and vision for the ED&D Roadmap through a series of one-day meetings and offline consultation. This work helped set the foundations for a two-day workshop in October 2019, in which over eighty cross-sector delegates contributed. The Steering

Committee and workshop delegates provided a series of potential interventions for discussion during the October 2019 workshop. Co-design and co-facilitation of the workshop processes was supported by Andrew Gill and Imoh Ilevbare, Industrial Associates, University of Cambridge Institute for Manufacturing. Through round-table and plenary discussions and an individual voting exercise, a series of 14 Actions were prioritised. Workshop participants were asked to consider the following criteria of assessment:

Opportunity factors

- Health benefit – lives improved and survival enhanced through ED&D
- Health economics – economic tractability of the proposed intervention (e.g. cost benefit in reduction of later stage treatment and cost of intervention)
- Wider UK PLC economic benefits – creates attractive commercial opportunities
- Reducing inequalities in access to ED&D interventions

Feasibility

- Technical feasibility – understanding of nature or detection requirement and ability to deliver required performance characteristics
- Health system adoptability – workforce capability and governance, effectiveness of referral pathways
- Patient and public acceptability
- Government policy in current political climate

Following prioritisation, mixed-sector groups worked on developing high-level plans for each of the prioritised interventions, which are reflected in the Action tables in this Roadmap. Further consultation via email was completed in 2020 to finalise the recommended Actions and Policy Recommendations.



ED&D Roadmap Steering Committee

Andy Richards | Entrepreneur & Investor
Billy Boyle | Owlstone Medical
Bob Steele | National Screening Committee & University of Dundee
Cally Palmer | The Royal Marsden NHS Foundation Trust
Caroline Dive | University of Manchester
Chris Hudson | Roche Diagnostics
Chris Whitty | Department of Health and Social Care (Chair)
David Hunter | University of Oxford
Fiona Walter | University of Cambridge
George Hanna | Imperial College London
Harpal Kumar | Grail
Jem Rashbass | Public Health England
Karin Oien | University of Glasgow
Mike Richards | NHS
Peter Sasieni | King's College London
Rebecca Fitzgerald | University of Cambridge
Sam Janes | University College London
Stan Kaye | The Royal Marsden NHS Foundation Trust
Sue Hill | NHS England
Tony Newman Sanders | NHS

ED&D Roadmap Workshop Participants

Adam Hill | Oncimmune
Alan Davies | Digital & AI Innovation National Network
Alison Ward | NHS Digital
Andrew Reynolds | AstraZeneca
Andy Howlett | NHS Improvement
Andy Richards | Entrepreneur & Investor
Antonis Antoniou | University of Cambridge
Aurora Callaghan | CRUK
Ben Gordon | HDR UK
Ben Moody | techUK
Bina Rawal | CRUK
Bissan Al-Lazikani | Institute of Cancer Research
Bob Steele | UK National Screening Committee
Cally Palmer | NHS England
Caroline Dive | University of Manchester
Charles Le Faou | Philips
Chris Hodkinson | Owlstone Medical Ltd
Chris Whitty | Department of Health and Social Care
Craig Buckley | Siemens
David Baldwin | NCRI Screening Prevention & Early Diagnosis Group
David Crosby | CRUK
David Hunter | University of Oxford
Doris-Ann Williams | British In Vitro Diagnostics Association
Emily Lam | Patient Representative
Fergus Gleeson | University of Oxford
Fiona Walter | University of Cambridge
George Hanna | Imperial College London
Helen Campbell | NIHR
Helen Compton | NIHR
Iain Foulkes | CRUK
Iain Frame | NCRI
Ian Lewis | NCRI

Ian Walker | CRUK

Ian Young | Department of Health Northern Ireland

Ilaria Mirabile | NHS England and NHS Improvement

Imran Rafi | St George's, University of London

Jack Cuzick | Wolfson Institute of Preventive Medicine, Bart's Cancer Institute

James Somauroo | HS Ventures

James Squires | Academy of Medical Sciences

Jamie Foster | Hill Dickinson

Jessica Brand | CRUK

Jo Waller | University College London

Joanne Hackett | Genomics England

Jodie Moffat | CRUK

John Spindler | Capital Enterprise

Julie Barnes | Abcodia

Karin Oien | University of Glasgow

Katriina Whitaker | University of Surrey

Lauren Harper | Roche Diagnostics

Mark Friend | CRUK

Merewyn Loder | Department for Business, Energy and Industrial Strategy

Mike Richards | NHS

Nandita deSouza | Institute of Cancer Research

Nick Crabb | NICE

Nicole Lyons | CRUK

Parker Moss | Owkin

Paul Davis | EMIS Health

Penny Wilson | Innovate UK

Peter Johnson | University of Southampton, NHS England

Peter Sasieni | King's College London

Philippa Hemmings | Engineering and Physical Sciences Research Council

Ranjit Manchanda | Bart's Cancer Institute, NHS Innovation Accelerator Fellow

Richard Lee | The Royal Marsden NHS Foundation Trust

Roger Spencer | The Christie NHS Foundation Trust

Rosalind Onions | CRUK

Rose Dixon | CRUK

Ross Hawkins | National Institute for Biological Standards and Control

Sam Janes | University College London

Sara Hiom | CRUK

Sarah Byron | NICE

Shabnam Shabbir | NHSX

Shonit Punwani | University College London

Sophie Whyte | University of Sheffield

Stan Kaye | The Royal Marsden and Institute of Cancer Research

Stephen Oakeshott | Medical Research Council

Sue Hill | NHS England

Terry Kavanagh | Patient Representative

Tim Aitman | University of Edinburgh

Tom Haswell | Patient Representative

Tony Hickson | CRUK

Tony Ng | King's College London

Triin Parik | Roche

Wendy Clark | NHS Digital

Yoryos Lyratzopoulos | University College London

Zoe Martin | CRUK

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References

- [1] "Cancer survival statistics," [Online]. Available: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/survival#heading-Zero>. [Accessed September 2020].
- [2] "Cancer mortality for all cancers combined," [Online]. Available: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/mortality/all-cancers-combined#ref-> [Accessed September 2020].
- [3] C. R. Smittenaar, K. A. Petersen, K. Stewart and N. Moitt, "Cancer incidence and mortality projections in the UK until 2035," *Br J Cancer*, vol. 115, no. 9, pp. 1147-1155, October 2016.
- [4] M. Arnold, M. J. Rutherford, A. Bardot, J. Ferlay, T. M.-L. Andersson, T. Å. Myklebust, H. Tervonen, V. Thursfield, D. Ransom, L. Shack, R. R. Woods, D. Turner, S. Leonfellner and S. Ryan, "Progress in cancer survival, mortality, and incidence in seven high-income countries 1995–2014 (ICBP SURVMARK-2): a population-based study," *Lancet Oncol*, vol. 20, no. 11, pp. 1493-1505, November 2019.
- [5] O. f. N. Statistics, "Cancer survival in England – adults diagnosed," August 2019. [Online]. Available: <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancersurvivalratescancersurvivalinenglandadultsdiagnosed>. [Accessed September 2020].
- [6] Public Health England, "Case-mix adjusted percentage cancers diagnosed at stages 1 and 2 by CCG in England," May 2020. [Online]. Available: <https://www.gov.uk/government/statistics/case-mix-adjusted-percentage-cancers-diagnosed-at-stages-1-and-2-by-ccg-in-england>. [Accessed September 2020].
- [7] A. Downey, "Government pledges £50m for AI to improve diagnosis of deadly disease," September 2020. [Online]. Available: <https://www.digitalhealth.net/2020/08/government-pledges-50m-for-ai-to-improve-diagnosis-of-deadly-disease/>.
- [8] NHS England, "NHS Long Term Plan," January 2019. [Online]. Available: <https://www.longtermplan.nhs.uk/publication/nhs-long-term-plan/> [Accessed September 2020].
- [9] "Cancer Diagnostics Market Worth \$249.6 Billion By 2026," February 2019. [Online]. Available: <https://www.grandviewresearch.com/press-release/global-cancer-diagnostics-market>. [Accessed September 2020].
- [10] "Grail's third VC round brings funding total to \$1.5B," May 2018. [Online]. Available: <https://www.fiercebiotech.com/medtech/grail-s-third-vc-round-brings-funding-total-to-1-5-billion> [Accessed September 2020].
- [11] "Early Cancer Detection Technology Receives Record Venture Investment," June 2019. [Online]. Available: <https://hub.jhu.edu/2019/06/03/cancerseek-blood-test/>. [Accessed September 2020].
- [12] "Cancer Diagnostics Market," [Online]. Available: <https://www.marketresearchfuture.com/reports/cancer-diagnostics-market-1962> [Accessed September 2020].
- [13] Department for Business, Energy & Industrial Strategy, "New publication showcases record investment in research and development programmes," August 2018. [Online]. Available: <https://www.gov.uk/government/news/new-publication-showcases-record-investment-in-research-and-development-programmes>. [Accessed September 2020].
- [14] Academy of Medical Sciences and Cancer Research UK, "Accelerating the translation of early detection and diagnosis research in cancer," The Academy of Medical Sciences, 2018.

- [15] G. Lyratzopoulos, G. A. Abel, C. H. Brown, B. A. Rous, S. A. Vernon, M. Roland and D. C. Greenberg, "Socio-demographic inequalities in stage of cancer diagnosis: evidence from patients with female breast, lung, colon, rectal, prostate, renal, bladder, melanoma, ovarian and endometrial cancer," *Ann Oncol*, vol. 24, no. 3, pp. 843-850, March 2013.
- [16] Office for Life Sciences, "Life Sciences Industrial Strategy," August 2017. [Online]. Available: <https://www.gov.uk/government/publications/life-sciences-industrial-strategy>. [Accessed September 2020].
- [17] UK Research and Innovation, "Accelerating Detection of Disease," [Online]. Available: <https://www.ukri.org/innovation/industrial-strategy-challenge-fund/accelerating-detection-of-disease/>. [Accessed September 2020].
- [18] NHS England and NHS Improvement, "Consultation on the proposals for the MedTech Funding," 2019. [Online]. Available: https://www.engage.england.nhs.uk/consultation/medtech-funding-mandate/user_uploads/medtech-funding-mandate-guidance-consultation-document-v2.00--2-.pdf. [Accessed September 2020].
- [19] M. Araghi, M. Arnold, M. J. Rutherford, M. G. Guren, C. J. Cabasag, A. Bardot, J. Ferlay, H. Tervonen, L. Shack, R. R. Woods, Saint-Jacques, D. P. N, C. McClure, G. Engholm, A. T. Gavin, E. Morgan, P. M. Walsh, C. Jackson and G. Porter, "Colon and rectal cancer survival in seven high-income countries 2010–2014: variation by age and stage at diagnosis (the ICBP SURVMARK-2 project)," *Gut*, Vols. *gutjnl-2020-320625*, June 2020.
- [20] S. Walters, C. Maringe, M. P. Coleman, M. D. Peake, J. Butler, N. Young, S. Bergström, L. Hanna, E. Jakobsen, K. Kölbek, S. Sundström, G. Engholm, A. Gavin, M. L. Gjerstorff, J. Hatcher, T. B. Johannesen, K. M. Linklater, C. E. McGahan, J. Steward, E. Tracey, D. Turner, M. A. Richards, B. Rachet and ICBP Module 1 Working, "Lung cancer survival and stage at diagnosis in Australia, Canada, Denmark, Norway, Sweden and the UK: a population-based study, 2004–2007," *Thorax*, vol. 68, no. 6, pp. 551-564, June 2013.
- [21] A. Downey, "Government pledges £250m for National AI Lab to improve diagnostics," August 2019. [Online]. Available: <https://www.digitalhealth.net/2019/08/government-250-million-artificial-intelligence-lab-diagnostics/>.
- [22] R. Landy, F. Pesola, A. Castañón and P. Sasieni, "Impact of cervical screening on cervical cancer mortality: estimation using stage-specific results from a nested case-control study," *Br J Cancer*, vol. 115, no. 9, pp. 1140-1146, 25 October 2016.
- [23] NHS, "Breast Cancer Screening; Benefits and risks," March 2018. [Online]. Available: <https://www.nhs.uk/conditions/breast-cancer-screening/why-its-offered/> [Accessed September 2020].
- [24] P. Hewitson, P. Glasziou, E. Watson, B. Towler and L. Irwig, "Cochrane systematic review of colorectal cancer screening using the fecal occult blood test (hemoccult): an update," *Am J Gastroenterol*, vol. 103, no. 6, pp. 1541-1549, June 2008.
- [25] Cancer Research UK, "Cancer in the UK 2019," 2019. [Online]. Available: https://www.cancerresearchuk.org/sites/default/files/state_of_the_nation_april_2019.pdf
- [26] P. C. Hannaford, A. J. Thornton, P. Murchie, K. L. Whitaker, R. Adam and A. M. Elliott, "Patterns of symptoms possibly indicative of cancer and associated help-seeking behaviour in a large sample of United Kingdom residents—The USEFUL study," *PLoS One*, vol. 15, no. 1, p. e0228033, 24 January 2020.
- [27] Cancer Research UK, "Over 2 million people waiting for cancer screening, tests and treatments," 1 June 2020. [Online]. Available: <https://scienceblog.cancerresearchuk.org/2020/06/01/impact-of-coronavirus-on-cancer-services-revealed-over-2-million-people-waiting-for-screening-tests-and-treatments/>. [Accessed September 2020].

- [28] "NHS steps up coronavirus fight with two more Nightingale Hospitals," 10 April 2020. [Online]. Available: <https://www.england.nhs.uk/2020/04/nhs-steps-up-coronavirus-fight-with-two-more-nightingale-hospitals/>. [Accessed September 2020].
- [29] The National Institute for Health and Care Excellence, "Coronavirus (COVID-19)," [Online]. Available: <https://www.nice.org.uk/covid-19>. [Accessed September 2020].
- [30] NHS, "Appointments in General Practice July 2020," August 2020. [Online]. Available: <https://digital.nhs.uk/data-and-information/publications/statistical/appointments-in-general-practice/july-2020> [Accessed September 2020].
- [31] M. di Pietro, I. Modolell, M. O'Donovan, C. Price, N. D. Pilonis, I. Debiram-Beecham and R. C. Fitzgerald, "Use of Cytosponge as a triaging tool to upper gastrointestinal endoscopy during the COVID-19 pandemic," *Lancet Gastroenterol Hepatol*, vol. 5, no. 9, pp. 805-806, September 2020.
- [32] C. A. K. Borrebaeck, "Precision diagnostics: moving towards protein biomarker signatures of clinical utility in cancer," *Nat Rev Cancer*, vol. 17, no. 3, pp. 199-204, March 2017.
- [33] A. M. Lennon, A. H. Buchanan, I. Kinde, A. Warren, A. Honushefsky, A. T. Cohain, D. H. Ledbetter, F. Sanfilippo, K. Sheridan, D. Rosica, C. S. Adonizio, H. J. Hwang, K. Lahouel, J. D. Cohen and C. Douville, "Feasibility of blood testing combined with PET-CT to screen for cancer and guide intervention," *SCIENCE*, vol. 369, no. 6499, July 2020.
- [34] G. R. O. Minetta C Liu, E. A. Klein, C. Swanton, M. V. Seiden and C. Consortium, "Sensitive and specific multi-cancer detection and localization using methylation signatures in cell-free DNA," *Ann Oncol*, vol. 31, no. 6, pp. 745-759, June 2020.
- [35] J. Edelsberg, D. Weycker, M. Atwood, G. Hamilton-Fairley and J. R. Jett, "Cost-effectiveness of an autoantibody test (EarlyCDT-Lung) as an aid to early diagnosis of lung cancer in patients with incidentally detected pulmonary nodules," *PLoS One*, vol. 13, no. 5, p. e0197826, May 2018.
- [36] M. S, W. T, A. S, C. ST, R. A, N. K, E. B, C. D, M. M, J. Lagergren and H. GB, "Assessment of a Noninvasive Exhaled Breath Test for the Diagnosis of Oesophagogastric Cancer," *JAMA Oncol*, vol. 4, no. 7, pp. 970-976, July 2018.
- [37] Owlstone Medical, "Clinical Trial Launches to Develop Breath Test for Multiple Cancers," January 2019. [Online]. Available: <https://www.owlstonemedical.com/about/news/2019/jan/3/clinical-trial-launches-develop-breath-test-multip/>. [Accessed September 2020].
- [38] V. Erben, M. Bhardwaj, P. Schrotz-King and H. Brenner, "Metabolomics Biomarkers for Detection of Colorectal Neoplasms: A Systematic Review," *Cancers (Basel)*, vol. 10, no. 8, p. 246, July 2018.
- [39] J. C. M. Wan, C. Massie, J. Garcia-Corbacho, F. Mouliere, J. D. Brenton, C. Caldas, S. Pacey, R. Baird and N. Rosenfeld, "Liquid biopsies come of age: towards implementation of circulating tumour DNA," *Nat Rev Cancer*, vol. 17, no. 4, pp. 223-238, April 2017.
- [40] J. V. Frangioni, "New Technologies for Human Cancer Imaging," *J Clin Oncol*, vol. 26, no. 24, p. 4012-4021, August 2008.
- [41] N. Kosaka, A. Kogure, T. Yamamoto, F. Urabe, W. Usuba, M. Prieto-Vila and T. Ochiya, "Exploiting the message from cancer: the diagnostic value of extracellular vesicles for clinical applications," *Exp Mol Med*, vol. 51, no. 3, pp. 1-9, March 2019.
- [42] Cancer Research UK, "Cancer Grand Challenges. Preventing unnecessary breast cancer treatment," [Online]. Available: <https://www.cancerresearchuk.org/funding-for-researchers/cancer-grand-challenges/Preventing-unnecessary-breast-cancer-treatment>. [Accessed September 2020].

- [43] V. H. Teixeira, C. P. Pipinikas, A. Pennycuick, H. Lee-Six and D. Chandrasekharan, "Deciphering the genomic, epigenomic, and transcriptomic landscapes of pre-invasive lung cancer lesions," *Nat Med*, vol. 25, no. 3, pp. 517-525, January 2019.
- [44] "Genomics England," [Online]. Available: <https://www.genomicsengland.co.uk/>.
- [45] S. Srivastava, G. Sharmistha, K. Jacob, M. Richard and N. C. I. H. Implementation, "The Making of a PreCancer Atlas: Promises, Challenges, and Opportunities," *Trends Cancer*, vol. 4, no. 8, pp. 523-536, August 2018.
- [46] "Trusted Research Environment service for England," [Online]. Available: <https://digital.nhs.uk/coronavirus/coronavirus-data-services-updates/trusted-research-environment-service-for-england> [Accessed September 2020].
- [47] Department of Health and Social Care, "Personalised health checks to be considered in new review," August 2019. [Online]. Available: <https://www.gov.uk/government/news/personalised-health-checks-to-be-considered-in-new-review>. [Accessed September 2020].
- [48] NHS England, "Evaluation of the Targeted Lung Health Check programme," [Online]. Available: <https://www.england.nhs.uk/contact-us/privacy-notice/how-we-use-your-information/our-services/evaluation-of-the-targeted-lung-health-check-programme/>. [Accessed September 2020].
- [49] "NIHR Innovation Observatory," [Online]. Available: <http://www.io.nihr.ac.uk/>. [Accessed September 2020].
- [50] The National Institute for Health and Care Excellence, "Accelerated Access Collaborative (AAC)," [Online]. Available: <https://www.nice.org.uk/aac>. [Accessed September 2020].
- [51] P. S. M. Richards, "Independent Review of Adult Screening Programmes in England," 2019.
- [52] D. G. Evans, S. Astley, P. Stavrinou, E. Harkness, L. S. Donnelly, S. Dawe, I. Jacob, M. Harvie, J. Cuzick, A. Brentnall, M. Wilson, F. Harrison, K. Payne and A. Howell, "Improvement in risk prediction, early detection and prevention of breast cancer in the NHS Breast Screening Programme and family history clinics: a dual cohort study," *Programme Grants for Applied Research*, August 2016.
- [53] Public Health England, "Ten years on since the start of the HPV vaccine programme – what impact is it having?," June 2018. [Online]. Available: <https://publichealthmatters.blog.gov.uk/2018/06/18/ten-years-on-since-the-start-of-the-hpv-vaccine-programme-what-impact-is-it-having/>. [Accessed September 2020].
- [54] S. van der Bij, N. Khan, P. Ten Veen, D. H. de Bakker and R. A. Verheij, "Improving the quality of EHR recording in primary care: a data quality feedback tool," *J Am Med Inform Assoc*, vol. 24, no. 1, pp. 81-87, January 2017.
- [55] R. A. Verheij, V. Curcin, B. C. Delaney and M. M. McGilchrist, "Possible Sources of Bias in Primary Care Electronic Health Record Data Use and Reuse," vol. 20, no. 5, p. e185, May 2018.
- [56] National Data Guardian, "Review of data security, consent and opt-outs," 6 July 2016. [Online]. Available: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/535024/data-security-review.PDF [Accessed September 2020].
- [57] NHS Digital, "National data opt-out operational policy guidance document," 4 March 2019. [Online]. Available: <https://digital.nhs.uk/services/national-data-opt-out/operational-policy-guidance-document>. [Accessed September 2020].

- [58] Cancer Research UK, "Vision for NHS Health Data in England," January 2020. [Online]. Available: https://www.cancerresearchuk.org/sites/default/files/cruk_vision_for_data_jan_20_1.pdf. [Accessed September 2020].
- [59] Cancer Research UK, "National Cancer Diagnosis Audit," [Online]. Available: <https://www.cancerresearchuk.org/health-professional/diagnosis/national-cancer-diagnosis-audit>. [Accessed September 2020].
- [60] "National Cancer Patient Experience Survey," [Online]. Available: <https://www.ncpes.co.uk/>. [Accessed September 2020].
- [61] "Clinical Practice Research Datalink," [Online]. Available: <https://www.cprd.com/> [Accessed September 2020].
- [62] G. Lyratzopoulos, R. D. Neal, J. M. Barbiere, G. P. Rubin and G. A. Gary, "Variation in number of general practitioner consultations before hospital referral for cancer: findings from the 2010 National Cancer Patient Experience Survey in England," *Lancet Oncol*, vol. 13, no. 4, pp. 353-365, April 2012.
- [63] G. A. Abel, S. C. Mendonca, S. McPhail, Y. Zhou, L. Ellis-Brookes and G. Lyratzopoulos, "Emergency diagnosis of cancer and previous general practice consultations: insights from linked patient survey data," *Br J Gen Pract*, vol. 67, no. 659, pp. e377-e387, June 2017.
- [64] W. Hamilton, F. M. Walter, G. Rubin and R. D. Neal, "Improving early diagnosis of symptomatic cancer," *Nat Rev Clin Oncol*, vol. 13, no. 12, pp. 740-749, December 2016.
- [65] "QCancer," [Online]. Available: <https://www.qcancer.org/>. [Accessed September 2020].
- [66] S. Price, A. Spencer, A. Medina-Lara and W. Hamilton, "Availability and use of cancer decision-support tools: a cross-sectional survey of UK primary care," *Br J Gen Pract*, vol. 69, no. 684, pp. e437-e443, July 2019.
- [67] C. P. Friedman, N. J. Allee, B. C. Delaney, A. J. Flynn, J. C. Silverstein, K. Sullivan and K. A. Young, "The science of Learning Health Systems: Foundations for a new journal," *Learn Health Syst*, vol. 1, no. 1, p. e10020, November 2016.
- [68] O. Kostopoulou, T. Porat, D. Corrigan, S. Mahmoud and B. C. Delaney, "Diagnostic accuracy of GPs when using an early-intervention decision support system: a high-fidelity simulation," *Br J Gen Pract*, vol. 67, no. 656, pp. e201-e208, March 2017.
- [69] J. Hippisley-Cox and C. Coupland, "Development and validation of risk prediction algorithms to estimate future risk of common cancers in men and women: prospective cohort study," *BMJ Open*, vol. 5, no. 3, p. e007825, March 2015.
- [70] Macmillan Cancer Support, "Clinical Decision Support Tool for Cancer (CDS) Project," 2014.
- [71] "What is the clinical-effectiveness and cost-effectiveness of embedded risk-of-cancer assessment of patients in primary care: the ERICA trial," [Online]. Available: <https://www.cantest.org/research-projects/what-is-the-clinical-effectiveness-and-cost-effectiveness-of-embedded-risk-of-cancer-assessment-of-patients-in-primary-care-the-erica-trial/>. [Accessed September 2020].
- [72] G. Lyratzopoulos, P. Vedsted and H. Singh, "Understanding missed opportunities for more timely diagnosis of cancer in symptomatic patients after presentation," *Br J Cancer*, vol. 112, no. 1, p. S84-S91, 31 March 2015.
- [73] R. Swann, G. Lyratzopoulos, G. Rubin, E. Pickworth and S. McPhail, "The frequency, nature and impact of GP-assessed avoidable delays in a population-based cohort of cancer patients," *Cancer Epidemiol*, vol. 64, p. 101617, February 2020.

- [74] W. Hamilton, T. Green, T. Martins, K. Elliott, G. Rubin and U. Macleod, "Evaluation of risk assessment tools for suspected cancer in general practice: a cohort study," *Br J Gen Pract*, vol. 63, no. 606, pp. e30-e36, January 2013.
- [75] "Econsult," [Online]. Available: <https://econsult.net/>. [Accessed September 2020].
- [76] "askmyGP," [Online]. Available: <https://askmygp.uk/>. [Accessed September 2020].
- [77] "Isabel Healthcare," [Online]. Available: <http://v4.isabelhealthcare.com/home/default>. [Accessed September 2020].
- [78] "Detecting Cancer Early Top 10," [Online]. Available: <https://www.jla.nihr.ac.uk/priority-setting-partnerships/detecting-cancer-early/top-10.htm>. [Accessed September 2020].
- [79] "Cancer Loyalty Card Study (CLOCS)," [Online]. Available: <https://www.clocsproject.org.uk/>. [Accessed September 2020].
- [80] "Diagnostic Imaging Dataset," [Online]. Available: <https://www.england.nhs.uk/statistics/statistical-work-areas/diagnostic-imaging-dataset/>. [Accessed September 2020].
- [81] "QRISK," [Online]. Available: <https://www.qrisk.org/>. [Accessed September 2020].
- [82] "CanTest," [Online]. Available: <https://www.cantest.org/>. [Accessed September 2020].
- [83] F. M. Walter, M. J. Thompson, I. Wellwood, G. A. Abel, W. Hamilton, M. Johnson, G. Lyratzopoulos, M. P. Messenger, R. D. Neal, G. Rubin, H. Singh, A. Spencer, S. Sutton, P. Vedsted and J. D. Emery, "Evaluating diagnostic strategies for early detection of cancer: the CanTest framework," *BMC Cancer*, vol. 19, no. 1, p. 586, June 2019.
- [84] "Heart health notifications on your Apple Watch," [Online]. Available: <https://support.apple.com/en-us/HT208931>. [Accessed September 2020].
- [85] "Apps Library. Evergreen Life," [Online]. Available: <https://www.nhs.uk/apps-library/evergreen-life/>.
- [86] "Mydex," [Online]. Available: <https://mydex.org/about-mydex>. [Accessed September 2020].
- [87] "Enabling integrated diagnostics for early detection," [Online]. Available: <https://apply-for-innovation-funding.service.gov.uk/competition/424/overview>. [Accessed September 2020].
- [88] "Diagnostics Assessment Programme," [Online]. Available: <https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-diagnostics-guidance>. [Accessed September 2020].
- [89] Department for Business, Energy and Industrial Strategy, "The impact of business accelerators and incubators in the UK," [Online]. Available: <https://www.gov.uk/government/publications/the-impact-of-business-accelerators-and-incubators-in-the-uk>. [Accessed September 2020].
- [90] "Capital Enterprise," [Online]. Available: <https://capitalenterprise.org/>. [Accessed September 2020].
- [91] "Panacea Innovation," [Online]. Available: <http://panacea-innovation.com/>. [Accessed September 2020].
- [92] "KQ Labs," [Online]. Available: <https://www.crick.ac.uk/partnerships/kq-labs>. [Accessed September 2020].
- [93] "Start Codon," [Online]. Available: <https://startcodon.co/>. [Accessed September 2020].

- [94] "Novartis Biome," [Online]. Available: <https://www.novartis.com/our-science/novartis-biome>. [Accessed September 2020].
- [95] "Illumina Accelerator," [Online]. Available: <https://emea.illumina.com/science/accelerator.html>. [Accessed September 2020].
- [96] "MedTech SuperConnector," [Online]. Available: <https://medtechsuperconnector.com/>. [Accessed September 2020].
- [97] "Screening, Prevention and Early Diagnosis (SPED) Advisory Group," [Online]. Available: <https://csg.ncri.org.uk/groups/advisory-groups/sped/> [Accessed September 2020].
- [98] "National Cancer Imaging Translational Accelerator (NCITA)," [Online]. Available: <https://ncita.org.uk/> [Accessed September 2020].
- [99] "National Cancer Research Institute Groups," [Online]. Available: <https://csg.ncri.org.uk/view-our-ncri-groups/>. [Accessed September 2020].
- [100] "Tackle cancers with substantial unmet need: our research strategy," [Online]. Available: <https://www.cancerresearchuk.org/funding-for-researchers/our-research-strategy/tackle-cancers-with-substantial-unmet-need>. [Accessed September 2020].
- [101] "Artificial Intelligence to help save lives at five new technology centres," November 2018. [Online]. Available: <https://www.gov.uk/government/news/artificial-intelligence-to-help-save-lives-at-five-new-technology-centres>. [Accessed September 2020].
- [102] S. M. McKinney, M. Sieniek, V. Godbole and J. Godwin, "International evaluation of an AI system for breast cancer screening," *Nature*, vol. 577, no. 7788, pp. 89-94, January 2020.
- [103] A. Yala, C. Lehman, T. Schuster, T. Portnoi and R. Barzilay, "A Deep Learning Mammography-based Model for Improved Breast Cancer Risk Prediction," *Radiology*, vol. 292, no. 1, pp. 60-66, July 2019.
- [104] "Data Saves Lives," [Online]. Available: <https://datasaveslives.eu/>. [Accessed September 2020].
- [105] Cancer Research UK, "How can we best incentivise world class cancer services in England," September 2019. [Online]. Available: https://www.cancerresearchuk.org/sites/default/files/how_can_we_best_incentivise_world_class_cancer_services_in_England.pdf [Accessed September 2020].
- [106] The Association of the British Pharmaceutical Industry, "Unlocking the promise of UK Health Data," 2020. [Publication pending]
- [107] "Health Data Research Innovation Gateway," [Online]. Available: <https://www.healthdatagateway.org/pages/about> [Accessed September 2020].
- [108] "encompass," [Online]. Available: <http://www.hscboard.hscni.net/encompass/>. [Accessed September 2020].
- [109] "National Cancer Diagnosis Audit," [Online]. Available: <https://www.cancerresearchuk.org/health-professional/diagnosis/national-cancer-diagnosis-audit>. [Accessed September 2020].
- [110] R. C. Fitzgerald, M. di Pietro, M. O'Donovan, R. Maroni, B. Muldrew, I. Debiram-Beecham, M. Gehrung, J. Offman, M. Tripathi, S. G. Smith, B. Aigret, F. M. Walter, G. Rubin, BEST3 Trial team and P. Sasieni, "Cytosponge-trefoil factor 3 versus usual care to identify Barrett's oesophagus in a primary care setting: a multicentre, pragmatic, randomised controlled trial," *Lancet*, vol. 396, no. 10247, pp. 333-344, August 2020.

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