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# Accelerating the translation of early detection and diagnosis research in cancer

**Summary of a workshop held by the Academy of Medical Sciences and Cancer Research UK, 7 February 2018**

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The Academy of Medical Sciences is the independent body in the UK representing the diversity of medical science. Our mission is to promote medical science and its translation into benefits for society. The Academy's elected Fellows are the United Kingdom's leading medical scientists from hospitals, academia, industry and the public service. We work with them to promote excellence, influence policy to improve health and wealth, nurture the next generation of medical researchers, link academia, industry and the NHS, seize international opportunities and encourage dialogue about the medical sciences.

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The Academy of Medical Sciences' FORUM was established in 2003 to recognise the role of industry in medical research, and to catalyse connections across industry, academia and the NHS. Since then, a range of FORUM activities and events have brought together researchers, research funders and research users from across academia, industry, government, and the charity, healthcare and regulatory sectors. The FORUM is a major component of the Academy's work to deliver the strategic objective of 'linking academia, industry and the NHS' and its success relies on supporter organisations who make an annual donation. We are grateful for the support provided by the members and are keen to encourage more organisations to take part. If you would like further information on the FORUM or becoming a member please contact [FORUM@acmedsci.ac.uk](mailto:FORUM@acmedsci.ac.uk) or visit our website.

Opinions expressed in this report do not necessarily represent the views of all participants at the event, the Academy of Medical Sciences or its Fellows, or Cancer Research UK

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# Executive summary

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**The increasing emergence of early detection and diagnosis technologies has the potential to substantially reduce mortality from cancer. However, historically healthcare systems have been slow to fully understand how to measure their clinical and cost benefits, and how to use this evidence to drive adoption of research outputs into clinical practice.**

Therefore on 7 February 2018, the Academy of Medical Sciences and Cancer Research UK held a joint FORUM workshop on '*Accelerating the translation of early detection and diagnosis research in cancer*'. The workshop explored the 'state of play' in early detection and diagnosis (EDD) research, highlighting emerging developments in EDD science whilst also exploring the challenges experienced in translating this science into the health system. Participants specifically discussed the key challenges from discovery to translation and ways to address these, and considered what a roadmap for EDD translation could look like. The key points of discussion are outlined below under two themes.

## Generating the right evidence

- **Understanding the applications of EDD research early in development** including what clinical need it is addressing, where it may fit in a clinical pathway and the economic impact and wider value. Developing a '**Target Product Profile**' which encompasses these factors at an early stage was proposed.
- More broadly, there was recognition of the **importance of balancing the need for robust evidence with faster access** to these technologies. Safety, clinical utility and an economic case are key factors to consider for new technologies.
- The value of building a **strong economic rationale for commissioners** was emphasised, especially given the financial climate in the NHS. Highlighting the future benefits of EDD technologies is crucial as it is likely that cost savings may accrue years downstream of introducing an EDD test. Therefore a holistic, long-term view of the benefits is needed including health outcomes, clinical pathways and impact for patients and the health system, that is aligned to the information needs of decision-makers.
- **Challenges to building the evidence base for diagnostics** include the need for multi-disciplinary teams and capacity in the health system to deliver trials of EDD technologies, and a **lack of access to, and availability of, high-quality samples** for discovery and validation. Participants proposed a centralised repository of longitudinal samples linked to clinical data to support discovery and validation of EDD markers. There is potential opportunity to better define evidence generated during clinical use ('real world' evidence) to further support the evidence base for EDD technologies.

## The research and translation infrastructure and culture

- **A national model of 'Clinical Trial Units (CTUs) for diagnostics' may be needed.** Whilst the current network of CTUs have great strengths in supporting design,

development and delivery of clinical trials, they focus on therapeutic interventions and the demands for trialling diagnostics are significantly different.

- There is a need to **address heterogeneity in access to, and implementation of, new technologies** across regions as well as by individual clinicians. This includes ensuring appropriate **capacity, capability and awareness in the NHS workforce** to deliver EDD research findings into practice, with consideration as to the type of skills needed amongst healthcare professionals.
- The importance of **collaboration across all key stakeholders** such as academia, industry and the NHS, and others involved in the developmental pathway such as health economists and commissioners, was highlighted.
- Historically, the NHS has placed emphasis on treatment and disease management rather than EDD, and would benefit from a **shift to focus more on EDD**, particularly within primary care. This would help to increase awareness of this field, improve participation in research and further ready the system for translation and implementation. It is important that the system manages the different levels of 'risk' for patients through a risk-stratified approach to screening.

Overall, **a system change is needed** to ensure better development, evaluation, translation and implementation of EDD tests. Delegates **advocated the value of developing a roadmap for translation** of EDD research that incorporates these factors and particularly addresses evidence and clinical needs at the various stages in translation. This may be challenging to establish across all types of EDD research and so any roadmap needs to consider the nuances of using different types of biomarkers, amongst other aspects. This could **build on existing frameworks for biomarker development** that are in development such as through the CanTest initiative.<sup>1</sup>

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<sup>1</sup> [www.cantest.org/](http://www.cantest.org/)

# Introduction

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**It has been shown that for almost all cancers, there is a marked improvement in survival following diagnosis at an earlier stage. However, despite the increase in early detection and diagnosis research, there are still significant challenges in translating this research into effective technologies. Healthcare systems are then slow to adopt these technologies in clinical practice. This highlights the need to find ways to tackle the barriers and accelerate access to potentially transformative technologies which can improve health outcomes for cancer patients.**

Early detection research seeks to enable the detection of cancer or pre-cancerous states at the earliest possible time at which an effective intervention might be made; early diagnosis research seeks to understand the role of patients, healthcare professionals and healthcare providers, and to develop interventions in a population or clinical context. As outlined, such research can improve survival compared with detection at later stages (acknowledging lead time challenges).

There are clear areas of unmet clinical need that may be addressed by early detection and diagnosis (EDD) technologies. For example, later diagnosis of pancreatic cancer when it becomes symptomatic is accompanied by a very limited chance of curative treatment. There is an urgent need to develop better tools to detect pancreatic cancer at the earlier stages when symptoms are either not present or vague. Opportunities to increase the pace and efficiency of discovery and translation across the EDD research pathway need to be identified and exploited to maximise patient benefit. This spans the entirety of the pathway from biomarker discovery and validation for diagnostic development through to NHS adoption, dissemination and commissioning.

# The landscape for early detection and diagnosis research

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**Participants heard views from key stakeholders on the landscape for EDD research and opportunities for this field. Case examples illustrated the challenges in translation of EDD research and how these might be addressed in the future to accelerate access.**

## Opportunities for EDD research

Some screening programmes have significantly lowered cancer mortality rates, as best exemplified by bowel scope, a one-off lifetime screening test using flexible sigmoidoscopy that has been shown to reduce invasive cancers by ~40%.<sup>2</sup> To improve benefit-harm ratios, screening can be targeted to populations who are at high-risk. However, new biomarkers are needed to improve sensitivity and specificity in existing programmes, and to provide detection methods for cancers where no screening programme currently exists. There is also a need to avoid false positives and over-diagnosis in areas such as prostate cancer, where this could prevent unnecessary and invasive procedures (for example, transrectal biopsies). In addition, the effectiveness of screening programmes depends on coverage – requiring engagement with the public and high uptake – reinforcing the need to stratify populations and target screening to those most at risk. There is an opportunity for new technologies such as artificial intelligence and support systems in managing and triaging patients for new tests.

### Supporting and integrating systems to drive translation

It was highlighted that the majority of cancers present with symptoms in primary care, rather than national screening programmes. It is therefore key to ensure the appropriate capacity and capability in primary care for EDD including an evolution of the GP consultation to accommodate EDD processes. In addition, new biomarkers are needed to improve detection; notably, there are still only two widely used blood-based cancer biomarkers in primary care, the same markers that were used 25 years ago, which illustrated the challenges in translation and adoption. The evaluation of new biomarkers must be accompanied by raising awareness of cancer signs and how to act upon them, and wider system change to ensure better development, evaluation and implementation of tests.

An example of an initiative aiming to improve care pathways by integrating cancer systems

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<sup>2</sup> Atkin W, et al. (2017). *Long-term effects of once-only flexible sigmoidoscopy screening after 17 years of follow-up: the UK Flexible Sigmoidoscopy Screening randomised controlled trial*. *Lancet*, **389**, 10076, 1299-1311.

into secondary care is the lung cancer programme for early diagnosis, run by the UCLH Cancer Collaborative.<sup>3</sup> This targeted hard-to-reach populations and trialled the feasibility of low-dose CT scans, which was highly successful for increasing reach to the at-risk, low socioeconomic population. The study emphasised the importance of a collaborative approach to EDD research across industry, academia and the NHS, to deliver an effective, integrated system for EDD.

## Preparing the system

It was emphasised that EDD technologies typically take 15 years from initial investment to market, and so a realistic and holistic vision of the route to market is needed that documents the necessary scientific and financial steps, and the risks and costs at each stage of development. There was agreement on the need to map out translation and adoption pathways early in development to determine feasibility and likelihood of success, including an early consideration of the value of EDD technologies, the target market and the reimbursement process. This should include: an understanding of the clinical pathways such as where a technology fits; the stakeholders involved and who needs to be engaged in the process; potential barriers to adoption such as availability of funding; and processes for building and iterating the evidence base on value and utility. More specifically, it should ensure that there is a robust clinical adoption plan that will enable the generation of high integrity data that fulfils regulatory requirements.

There is a need to fully understand the clinical pathways and context for delivery. For example, in order to decide whether a product is designed for point-of-care or as a laboratory test, with advantages and disadvantages of each. These considerations include time to reach result, accuracy, cost and regulation. For example, point-of-care testing may deliver results quickly but a more controlled, laboratory-based environment may deliver greater 'value' (in terms of accuracy). Ultimately, these product development choices aim to strike a balance between accuracy and cost.

### The value of EDD technologies

Understanding the economic impact of technologies and using this to form a strong health economics argument is essential for a finance-limited NHS, particularly at a local commissioning level. There was consensus that this 'value' should be more holistic as the benefits of technologies extend beyond simple cost-savings, and views on value will differ across stakeholders. One speaker described two perspectives on the value of diagnostic tests as an 'essentialist' view which defines value by the trustworthiness of results (accuracy and validity), and a 'consequentialist' view based on impact on broader health outcomes and utility.

It was highlighted that a compelling value proposition is particularly important for investors when slow translation into clinical practice from initial investment can deter investment, and especially when other sectors have shorter timeframes and faster returns. Industry speakers noted that a strong intellectual property (IP) portfolio is needed as part of this value to encourage investors, but this can risk impeding innovation.

### The evidence base

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<sup>3</sup> [www.uclh.nhs.uk/OurServices/ServiceAZ/Cancer/NCV/Documents/UCLH%20Annual%20review%20201718.pdf](http://www.uclh.nhs.uk/OurServices/ServiceAZ/Cancer/NCV/Documents/UCLH%20Annual%20review%20201718.pdf)



Industry delegates noted that large-scale validation is needed following product development to demonstrate clinical relevance and validate a product in a heterogeneous population to ensure clinical utility. However, this scale of validation can be particularly challenging to carry out in an academic setting. In some circumstances, there is the potential to use novel methods for gathering evidence. For example, Owlstone Medical's Breath Biopsy has been made open-source to encourage other researchers to use it and add to the evidence base on its efficacy. It was suggested that regulatory pathways could support a faster route to market for products following demonstration of safety, by facilitating use of real world evidence for aspects such as mortality-benefit studies.

### Adoption in the NHS

The slow adoption of new technologies demands a realistic approach to timelines for implementation. It was proposed that medical guidelines should be made more adaptable and quicker to adopt new technologies and methods to accelerate this. Regulatory approval does not guarantee market access so it is key to engage early with stakeholders such as clinicians, commissioners and patients, as well as multiple NHS Trusts with differing priorities. Speakers emphasised the value of engaging the right people at the right time, and ensuring a full understanding of stakeholder needs. For example, change to clinical pathways requires confidence to be built amongst clinicians, so it is important to understand the capability and capacity needed to introduce a new technology.

# How can we overcome the challenges to translating EDD research?

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**With the emergence of new biomarkers and EDD technologies, there is a need to support the translational pathways for this research from discovery through to delivery in order to benefit patients. Participants discussed the barriers to translation and possible solutions and in parallel, considered how the healthcare system can be prepared to fully realise the potential of this research. Priorities for a roadmap for translation were discussed and four key areas emerged: capacity and capability; evidence generation for EDD technologies; understanding the value of EDD research and its place in the healthcare system; and adoption in the NHS.**

## Capacity and capability

### Multidisciplinary of EDD research

Participants highlighted the multidisciplinary of EDD research, which not only requires skilled teams for a given research question but also the engagement of other stakeholders involved in the translation process. One proposal was to develop Clinical Trials Units (CTUs) specifically for diagnostics. The CTUs, which currently focus on therapeutics, are valuable for supporting design, development and delivery of clinical trials, however, the technical and logistical demands of diagnostics trials are significantly different. Another point raised was that areas such as health economics, statistics and IP need to be considered alongside basic science skills. Each trial currently recruits this expertise, which is 'lost' when it ends. This does not incentivise skilled individuals to specialise in diagnostics and so a national model of diagnostic CTUs could centralise fragmented expertise and build critical mass, as well as raising standards and providing a career structure for specialists.

Participants discussed incentives for those working in the EDD field. For example, it can be difficult for early career researchers (ECRs), as publications can be more challenging in this field of research, but are regarded as criteria for success. These challenges are attributable to various factors including the relatively low success rates of biomarker research, and lengthy

studies such as those required to demonstrate mortality benefit in a 'healthy' cohort. Participants discussed the value of taking a 'team science' approach and considering the team composition and support for available ECRs. It was suggested that demonstrating impact on healthcare could be used as a metric for success, however, this is complicated by the potentially lengthy timescales for such visible impact in the system, as well as difficulty in foreseeing and understanding where such impact may occur. It was noted that specific fellowships for EDD ECRs would help draw and retain ECRs in the field, and support them through the challenges that the EDD field faces.

## Building the clinical workforce for EDD

The skillset in the NHS reflects its focus on treatment and disease management so the current workforce is not best equipped to engage with the EDD agenda. To prepare the system, it is key to understand the number and type of healthcare professionals needed to deliver an EDD technology and the training required. Clinical capacity is already a challenge – for example in radiology and endoscopy – and the system needs to be better prepared for the rise in workload that may accompany the new technologies. It was noted that Health Education England's Cancer Workforce plan should help to build this workforce but is not sufficient to support the breadth and quantity of skills required to effectively deliver EDD research.<sup>4</sup>

The shift towards implementation of EDD technologies in primary care can be supported, in part, by an evolution of the GP consultation process and guidance for decision-making by approving more biomarkers for primary care. Support is particularly needed for cancers of greater unmet need that are either difficult to detect or have non-specific symptoms. Geographical variation in clinical diagnostic capabilities is challenging and differences in success rates and practice were noted; for example, variation in triaging due to different GP referral thresholds. This variation will widen if more EDD is introduced into primary care, and so effective training is needed in primary care for sampling, referral and decision-making processes.

## Awareness and engagement

Participants discussed the importance of wider engagement throughout development and ensuring buy-in from stakeholders and key groups such as pathologists. In addition, it is important to raise patient awareness and understanding of symptoms and how to act upon these. Moreover, the role of the more knowledgeable, empowered individual needs to be considered, with the public increasingly coming forward for follow-up screening and lifestyle guidance. It was suggested that overall, behaviour change including awareness and motivation may be as important as the technologies.

## The importance of collaboration

Participants recognised that collaboration across sectors such as academia, industry and the NHS, is critical to accelerating translation by capitalising on capabilities across sectors and addressing different stakeholder needs. There are often differences in the expectations and priorities between industry and academia. Careful consideration must be given to IP exchange and ownership across organisations. It was noted that there are opportunities to work alongside the NHS, and the example was cited of the joint roll-out of a lung screening trial by UCLH and a US biotech company which built upon a pilot by the NHS Cancer Vanguard.<sup>5</sup>

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<sup>4</sup> Health Education England (2017). *Cancer Workforce Plan*. [www.hee.nhs.uk/sites/default/files/documents/Cancer%20Workforce%20Plan%20phase%201%20-%20Delivering%20the%20cancer%20strategy%20to%202021.pdf](http://www.hee.nhs.uk/sites/default/files/documents/Cancer%20Workforce%20Plan%20phase%201%20-%20Delivering%20the%20cancer%20strategy%20to%202021.pdf)

<sup>5</sup> <https://cancervanguard.nhs.uk/>

# Evidence generation for EDD products

## Sample collection and datasets

Participants emphasised the paucity of samples; one reason put forward for the 'failure' of technologies is that the majority of discovery research uses small sample sets that lack statistical validity. More samples and larger datasets are needed to build a more robust evidence base for discovery and validation, enabling 'go' or 'no-go' decisions to be reached more quickly. There is a dearth of samples in some types of cancers, notably those that are rarer and harder to diagnose. Participants proposed multiple ways to address this such as:

- Better standardisation of sampling.
- Establishment of consortia to aid data and sample collection.
- A more comprehensive, larger biobank of samples from a diverse population, including longitudinal data and linkage to other datasets such as clinical records. It was noted that useful sample banks such as the NIHR Bioresource and UK Biobank already exist and there is a need to capitalise on samples that have already been collected, however, existing resources may be insufficient for the demand of the field.
- It was proposed that samples could be collected from all patients at two-week wait clinics but this would require the associated infrastructure to be established.

More high-quality follow-up data is also needed and there are sometimes limitations in utility for specific research protocols owing to the way that samples have been collected. It was also cautioned that the maintenance of large biobanks is expensive and it is challenging to futureproof samples for all possible requirements.

Standardisation of sample collection and storage, and the associated datasets, can help to support their use for studies. Although use of retrospectively collected datasets is helpful, it was argued that in some cases, there is more value in prospective data collection from the correct cohort tailored to a well-defined research question. It was suggested that the Cancer Alliances in England could facilitate such prospective data collection as well as building on initiatives such as the Scotland SHARE database of blood samples.<sup>6</sup> Participants warned that prospective data collection can be difficult and costly if data are not collected in the right way.

## A proportionate approach to evidence generation

A specific challenge identified was the requirement to demonstrate mortality benefit from diagnostics when (particularly given the low price point of these products) generating this evidence can be so lengthy as to be unaffordable. There was a strong emphasis on proportionality in EDD technology development to balance safety and a sufficiently robust evidence base with rapidly widened access. One suggestion was that once a product is CE-marked, real-world mortality studies could be conducted post-approval during clinical use, as the diagnostics carry a low safety risk. Earlier adoption followed by real-world pragmatic conditions (i.e. routine care) to collect evidence could be an effective way to accelerate access to EDD research, with a view to withdrawing products from use if they do not demonstrate value. This could be piloted through the NHS Cancer Alliances in England and rolled out more widely.

It was noted that there should be different evidence requirements and a more proportionate approach for introducing iterative technologies that improve on a product already in use, when compared to novel technologies. For example, most technologies will require an RCT but

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<sup>6</sup> [www.goshare.org.uk/](http://www.goshare.org.uk/)

this may not be relevant for incremental improvements. The current system does not allow for this stepwise iteration. Finally, progress is needed on the ability to use linked evidence for EDD research. For example, when studies have already shown that a novel EDD approach enables earlier detection of cancer, prior studies showing that early detection leads to improved outcomes in the same cancer could be better utilised to support evidence on outcomes.

The MHRA's Innovation Office can offer clarity on the regulatory and technical framework for evidence generation to individual companies on a case-by-case basis. In addition, the NIHR Medtech and In-vitro diagnostic Co-operatives (MICs) can assist with early evidence generation and performance testing.<sup>7</sup>

## Funding for EDD research

Participants highlighted that historically, competition for research funding of biomarker discovery and validation has not been particularly successful. It was suggested that some research applications may lack sufficient methodological rigour, often due to the lack of funding available for sufficient evidence generation, and appropriate consideration needs to be given to these funding needs. The funding gap between early discovery and late-stage development was noted, with the observation that evidence generation needs to be flexible and strategic, incorporating the options above to overcome resource barriers. In addition, it was suggested that challenges exist around the notion of 'novelty' where innovations may be iterative and improvements rather than truly disruptive. Further, validation studies may not be a priority or of interest for researchers, and better recognition of efforts to bridge this translational gap through validation could incentivise research activity in this area.

# Understanding value and place in the health system

## Understanding the applications and early value of research

There was detailed discussion around the need for researchers to understand the potential value and applications of an EDD technology, and its positioning in the healthcare system, *early* in the development process; otherwise this can impede later translation. It was felt that health economics models should be integrated as early as possible in development of novel markers/technologies and iterated throughout so the right data on outcomes is collected with an understanding of impact on patients, clinical pathways and the wider system. This would facilitate earlier engagement with NHS Trusts and commissioners to discuss their evidence needs (and outcomes of interest) so that research meets these requirements. This idea of value was encompassed by the suggestion of developing '*Target Product Profiles*' for new technologies – that is, what a new EDD technology would need to do in order to change practice. These may include clinical need, the competitive landscape, the context for delivery, and explicitly defining desirable figures for sensitivity, specificity and cost.

The importance of balance was recognised and whilst foresight is important, it was argued that early R&D should not be too deterministic and that the best context for implementation may not be clear at the outset. It was noted that if health economics is incorporated *too* early

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<sup>7</sup> [www.nihr.ac.uk/about-us/how-we-are-managed/our-structure/infrastructure/Documents/medtech-and-in-vitro-diagnostic-co-operatives.htm](http://www.nihr.ac.uk/about-us/how-we-are-managed/our-structure/infrastructure/Documents/medtech-and-in-vitro-diagnostic-co-operatives.htm)

then it could constrain innovation and it should not be over-prescriptive.

## Health economics for EDD technologies

Health economics has a wider role beyond understanding the value of a technology. It is also key for exploring the impact of early diagnosis on health service planning and delivery. There is often a lack of understanding around this, with focus on the direct cost of a product rather than a more holistic view of where it fits within the system or what the health system can afford. Health economics can try to balance outcomes of interest, which may differ across stakeholders, for example patient measures such as quality of life. It was recognised that the term 'health economics' can be ambiguous and it may be more useful to focus on the 'value proposition' of a technology, which may not be cost-saving in the short-term but still has a wider value for the system in other ways.

Delegates noted the importance of carefully considering the harms and benefits of testing. For example, the appropriate level of testing for symptomatic patients is different to putting a healthy population through tests and procedures which could cause 'harm'. It was also emphasised that there is a need to better understand where harms truly exist. One such example is consideration of the harms resulting from potential over-screening. It was highlighted that the assumption that earlier detection saves more costly and complicated future management is not always right, and other considerations are needed including whether there is an effective treatment available, and if there are complications or potential adverse effects of treatment.

# Uptake and adoption in the NHS

## Preparing the system for access and uptake

Uptake and adoption of EDD technologies in the NHS was felt to be slow. Participants described issues around length of time to implementation, particularly in the UK, with multiple examples of slow (or even absence of) adoption even when technologies have been shown as beneficial with 'overwhelming' evidence. For example, it was argued that the UK has been very slow to adopt HPV screening for cervical cancer which was introduced in the US in 2003. There has been a similar experience with the faecal immunochemical test (FIT) for colorectal cancer, which has been shown to improve outcomes.<sup>8</sup> Access to diagnostics can vary across the country and within different demographics, and equity of access is paramount. It was highlighted that stronger advocacy could support adoption in the UK and that there is potential to capitalise on the opportunity afforded by integrated healthcare systems. Academic Health Science Networks (AHSNs), NHS Cancer Alliances and other UK structures might also help to drive translation into practice.

The Accelerated Access Review sets out steps to improve access to innovative technologies in the NHS.<sup>9</sup> However, some participants explained that this will only apply to a few products in the first instance, and whilst originally intended to cover EDD technologies, much of the downstream work has focused on therapeutics. In general, participants emphasised the need

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<sup>8</sup> Moss S, et al. (2017). *Increased uptake and improved outcomes of bowel cancer screening with a faecal immunochemical test: results from a pilot study within the national screening programme in England* Gut. 66, 1631-1644.

<sup>9</sup> Accelerated Access Review (2016). [www.gov.uk/government/publications/accelerated-access-review-final-report](http://www.gov.uk/government/publications/accelerated-access-review-final-report)

for the NHS and Government to focus on EDD research and other technologies as well as medicines.

## NHS commissioning and value

There was consensus that one of the biggest challenges to adoption lies in commissioning. It is essential for developers to understand the commissioning structure to ensure adoption, but it was noted that this is complex for diagnostics which sit between specialised and local commissioning. Ultimately, few cancer tests are endorsed by the NHS and there needs to be greater understanding of why this is and what 'success' looks like for the NHS. One proposal was to establish a Standard Operating Procedure for commissioning of EDD technologies to allow better insight into NHS decision-making. This would help to ensure that research incorporates expected outcomes from commissioners, clinicians and others, as perspectives on value of these technologies will differ from therapeutics. For example, EDD tests may help reach a diagnosis but because the treatment and management is not directly attributable to the technology, there is only indirect evidence of how these tests may impact outcomes.

It is essential to consider where and how testing will be delivered so that the system and commissioners can be prepared. Products should be fit-for-purpose and optimised for use in the clinic and target populations. Firstly, commissioners need to be convinced of the value of EDD through health economics modelling and the product will need to be delivered at reasonable cost. Costs of associated laboratory/pathology tests must also be considered. There is often a tension between short-term financial views in the NHS demanding rapid cost-savings, and the long-term value of EDD – or cost-effectiveness – with potential savings downstream that may not deliver benefit for some time (particularly for diagnostics). It was suggested that there is recognition that screening does not necessarily need to be cost-saving in the short-term but must ultimately be cost-effective and deliver value. Demonstrating value in practice is often needed, which requires more long-term investment in mid-phase evidence generation from developers. There is also an *opportunity cost* of commissioning a new pathway which will impact the system elsewhere. Therefore a strong argument is needed for EDD technologies on potential impact and return on investment in order to justify the re-direction of funds. One participant proposed that an alternative value proposition can be made through '*theranostics*' – that is, targeted therapies linked to companion diagnostics where it is easier to demonstrate value and generate funding for the diagnostics.

Commissioning decisions are further complicated by siloed budgets and negotiations across multiple stakeholders such as different NHS Trusts. This can make collaboration difficult and means that those who fund the development of a product may not derive direct benefit from it. Multiple Trusts and stakeholders may have different outcomes of interest, for example across geographical regions, and this also needs to be taken into consideration.

## NHS culture

A culture change is required to focus on EDD as well as treatment in the NHS, particularly in primary care if more EDD is to be undertaken by GPs. This can be instigated through training and decision-support, incentives for testing and referral and the infrastructure to support at-scale testing in primary care. Participants noted the opportunity to build on the previous success with moving cervical screening services into primary care.

Instigating change in the NHS can be challenging, particularly due to the heterogeneity across multiple Trusts and other organisations, as well as many individuals with different beliefs. Participants proposed that some form of centralised process may be necessary for effective uptake of EDD research, as well as incentivising change through a potential share of IP for the NHS. It was noted that political tenure can affect the long-term landscape in the UK as short-

term parliamentary positions and processes do not align with the long process of implementing a product in practice.

### Risk stratification of patients

Participants discussed the opportunity to stratify patients before and after screening, and implement different strategies for at-risk groups and those with the highest need.

There was a suggestion that this should be accompanied by an evolution of the National Screening Committee's model of definitive diagnosis in comparatively broad populations, towards identification of higher-risk groups. One participant suggested that risk models should be developed to identify those at risk of a diagnosis in five or ten years' time, allowing individuals to be screened according to risk. It is important to distinguish between screening for individuals at risk in the future and those at immediate risk as the clinical pathways for each will be different, involving surveillance and prevention strategies for the former and early treatment for the latter.



# A roadmap for translation

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**To prepare the research, development and healthcare systems, it was agreed that a comprehensive, clear roadmap is needed that details the various steps along the EDD research pathway. This should help inform development from idea and conception, through testing and evaluation, to clinical delivery.**

An EDD roadmap should encompass 'what good looks like' for the translational pathway. Participants noted that it should not suggest an overhaul of current systems and should instead build upon the processes currently in place. There was strong support for a framework for biomarker development, and this could be expanded more broadly to incorporate other technologies and devices. It was proposed that the NCRI Screening, Prevention and Early Diagnosis Group could advise on this framework, with collaboration across all essential stakeholders whether the NHS, industry, funders, health economists, IP lawyers or others.

Participants identified the following priorities for a future roadmap:

- Clear guidance on the level of evidence that needs to be generated, and parameters that are required at each decision point, to enable progression to the next stage, including the overall body of evidence needed for commercialisation. This includes an understanding of the supportive studies required to progress as well as what factors might affect progress or decision-making, particularly with the emergence of a more holistic focus on specifications beyond specificity and accuracy, such as accessibility and cost. These evidence requirements will require consensus across key stakeholders and should note, in particular:
  - o Guidance is helpful for the proof-of-concept stages around sensitivity, specificity and validation, and then how a product can be scaled up beyond this to a larger test or across multiple sites.
  - o Proportionality and guidance on using different types of evidence to support a technology (e.g. real world evidence).
  - o To address aspects beyond evidence generation on clinical utility including economic viability and cost-benefit information, along with how developers and other key stakeholders might understand whether an innovation is realistic for an EDD context and where it would sit within the healthcare system.
- Advice on when to consult different stakeholders along the pathway to help direct research. This includes the needs at all stages of the roadmap so that necessary engagement can occur with key decision-makers early in the process.
- Clarity around regulatory validation and defining the different regulatory pathways and checkpoints along the pathway. The framework must allow for regulatory agility and recognise some of the accelerated pathways available in the UK.
- Proportionality and flexibility to account for the different needs of completely novel technologies compared with refinements or incremental improvements in existing technology/pathways.
- Agreement around terminology used and appropriate accountability and cohesion across sectors for different parts of the pathway. This includes building patient and public involvement into the pathway and also an exploration of the wider consequences of EDD research such as over-diagnosis.

- The roadmap should take into consideration and build upon similar initiatives that already exist rather than duplicate work. The CanTest initiative funded by Cancer Research UK was referenced as an example. This is an international collaboration seeking to improve diagnosis by exploring ways to develop and implement cancer diagnostics in primary care by building a framework for the development, evaluation and implementation of diagnostic tests.

It was agreed that the roadmap should offer a helpful tool for developers to think ahead and successfully manage challenging parts of the translational pathway, rather than a 'tick box' resource that potentially hampers innovation and instead creates more regulatory and governance barriers.

The meeting chair, Professor Peter Johnson CBE FMedSci, Professor of Medical Oncology at the University of Southampton, concluded the meeting by noting the need for appropriate investment in this field and infrastructure to make it easier to develop and implement EDD testing. This requires support along the translational pathway from understanding the evidence generation, clinical need and positioning of a technology in the healthcare system at the outset of EDD research, through to preparing the healthcare system for its delivery and supporting widespread uptake and diffusion.

## Annex 1: Attendees List

### Chair

**Professor Peter Johnson CBE FMedSci**, Professor of Medical Oncology, University of Southampton

### Speakers and panellists

**Dr Elisabeth Adams**, Managing Director, Aquarius Population Health

**Professor Patrick Bossuyt**, AMC Principal Investigator, Academisch Medisch Centrum

**Mr David Browning**, Chief Executive Officer, Oxford Cancer Biomarkers

**Professor Jack Cuzick CBE FRS FMedSci**, Director, Wolfson Institute of Preventative Medicine, Queen Mary University of London

**Dr Craig Eagle**, Vice President and Head of Oncology, Pfizer

**Dr Emma Greenwood**, Director of Policy and Public Affairs, Cancer Research UK

**Mr Geoffrey Hamilton-Fairley**, Chief Executive Officer, Oncimmune

**Professor George Hanna**, Professor of Surgical Sciences and Head of Division, Imperial College Healthcare NHS Trust

**Dr Rory Harvey**, Consultant Gastroenterologist and Divisional Medical Director, Bedford Hospital NHS Trust

**Professor Richard Neal**, Professor of Primary Care Oncology, University of Leeds

**Dr Daniel O'Connor**, Expert Medical Assessor, Medicines and Healthcare products Regulatory Agency

**Dr Karin Oien**, Reader in Pathology, University of Glasgow

**Professor Kathy Pritchard-Jones FMedSci**, Chief Medical Officer, UCLH Cancer Collaborative and Cancer Programme Director, UCL Partners AHSN

**Professor Robert Steele**, Senior Research Professor, University of Dundee

**Dr Marc van der Schee**, Head of Clinical, Owlstone Medical  
Participants

### Participants

**Professor Eric Aboagye FMedSci**, Director, Comprehensive Cancer Imaging Centre, Imperial College London

**Professor Tim Aitman FMedSci**, Chair of Molecular Pathology and Genetics, University of Edinburgh

**Dr Wendy Alderton**, Early Detection Programme Manager, CRUK Cambridge Centre

**Professor David Baldwin**, Honorary Professor of Medicine, University of Nottingham

**Dr Julie Barnes**, Founding CEO and Chief Scientific Officer, Abcodia

**Ms Meena Bhagat**, Consumer Representative, NCRI Screening, Prevention and Early Diagnosis Advisory Group

**Professor Andrew Biankin FMedSci**, Regius Chair of Surgery, University of Glasgow

**Professor Kevin Brindle FMedSci**, Professor of Biomedical Magnetic Resonance, University of Cambridge

**Professor Robert Brown**, Head of Division of Cancer, Imperial College London

**Dr Helen Campbell**, Portfolio Manager, Department of Health Research Networks, Clinical Research Facilities, and Cancer Research

**Professor Brendan Delaney**, Chair in Medical Informatics and Decision Making, Imperial College London

**Professor Caroline Dive CBE FMedSci**, Deputy Director, Cancer Research UK Manchester Institute

**Mr Will Dracup**, Chief Executive Officer, Biosignatures

**Professor Stephen Duffy**, Professor of Cancer Screening, Queen Mary University of London

**Professor Douglas Easton FMedSci**, Director of the Centre for Cancer Genetic Epidemiology, University of Cambridge

**Professor Gareth Evans**, Professor of Medical Genetics, University of Manchester  
**Dr Ciaran Fulton**, Head of Diagnostics, LifeArc  
**Professor Richard Gilbertson FMedSci**, Head of Department of Oncology, University of Cambridge  
**Dr Vincent Gnanapragasam**, University Lecturer in Uro-oncology, University of Cambridge  
**Dr Liz Harrington**, Head of Translational Sciences UK Oncology, AstraZeneca  
**Dr Shirley Henderson**, Cancer Scientific Adviser, Genomics Implementation Unit, NHS England  
**Professor Sam Janes**, Professor of Respiratory Medicine, University College London  
**Dr Philip Jordan**, Business Analyst, Wellcome Trust  
**Dr Maria Kapi**, Senior Medical Advisor, Roche Diagnostics  
**Professor Stanley Kaye FRSE FMedSci**, Professor of Medical Oncology and Research Director, RM Partners  
**Dr Teresa Klinowska**, Senior Project Director, AstraZeneca  
**Professor Martin Leach FMedSci**, CRUK Cancer Imaging Centre, Institute of Cancer Research  
**Ms Claire Levermore**, Senior Programme Manager (Earlier Diagnosis), UCLH Cancer Collaborative and Cancer Programme  
**Dr Leila Luheshi**, Associate Director, Clinical and Translational Research, Oxford Nanopore  
**Professor Yoryos Lyratzopoulos**, Professor of Cancer Epidemiology, University College London  
**Dr Athena Matakidou**, Head of Clinical Genomics, AstraZeneca  
**Dr Iain Miller**, Founder and CEO, Healthcare Strategies Group  
**Ms Teri Morgan**, Consumer Representative, NCRI Screening, Prevention and Early Diagnosis Advisory Group  
**Dr Clive Morris**, Chief Medical Officer, Inivata  
**Dr Declan Mulkeen**, Chief of Strategy, Medical Research Council  
**Dr Claire Palles**, Birmingham Fellow, Institute of Cancer and Genomic Science  
**Dr Ivana Poparic**, Research Collaboration Manager, NIHR Office for Clinical Research Infrastructure  
**Dr John Pritchard**, Entrepreneur in Residence (Diagnostics and Devices), Cambridge Academy of Therapeutic Sciences  
**Professor Helen Reeves**, Professor of Translational Hepatology, Newcastle University  
**Dr Nitzan Rosenfeld**, Group Leader, CRUK Cambridge Institute  
**Dr Chris Rowe**, Lead Technologist - Stratified Medicine Innovation Platform, Innovate UK  
**Professor Peter Sasieni**, Professor of Biostatistics and Cancer Epidemiology, King's College London  
**Ms Sophia Turner**, Patient Representative  
**Dr Hayley Whitaker**, Reader in Cancer Biology, University College London

#### **Secretariat**

**Ms Ola Bykowska**, Policy Intern, Academy of Medical Sciences  
**Dr David Crosby**, Head of Early Detection Research, Cancer Research UK  
**Dr Katy Davidson**, Early Diagnosis Officer (Cancer Outcomes), Cancer Research UK  
**Ms Liberty Dixon**, FORUM Policy Manager, Academy of Medical Sciences  
**Ms Samantha Harrison**, Senior Manager (Early Diagnosis and International Cancer Benchmarking Partnership), Cancer Research UK  
**Ms Sara Hiom**, Director of Early Diagnosis & Cancer Intelligence, Cancer Research UK  
**Dr Lauren Kerr**, Early Detection Programme Manager, Cancer Research UK  
**Dr Jodie Moffat**, Head of Early Diagnosis, Cancer Research UK  
**Ms Florence Mowlem**, Policy Intern, Academy of Medical Sciences  
**Mr David Osuna De La Pena**, Intern, Cancer Research UK  
**Mr James Squires**, Policy Officer, Academy of Medical Sciences

## Annex 2: Agenda

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| 10.00-10.10   | <p><b>Introduction and welcome</b><br/>Professor Peter Johnson CBE FMedSci, Professor of Medical Oncology, University of Southampton</p>   |
| <b>The landscape for translating early detection and diagnosis research</b> |  |
| 10.10-10.30   | <p><b>Overview of EDD research and the translational pathway</b><br/>Professor Richard Neal, Professor of Primary Care Oncology, University of Leeds</p>   |
| 10.30-10.45   | <p><b>The potential of EDD research and exemplars</b><br/>Professor Jack Cuzick CBE FRS FMedSci, Director, Wolfson Institute of Preventative Medicine, Queen Mary University of London</p>   |
| 10.45-11.00   | <p><b>Implications of advances in EDD biomarkers and technology</b><br/>David Browning, Chief Executive Officer, Oxford Cancer Biomarkers</p>  |
| 11.00-11.15   | <p><b>Navigating the translation of EDD research – learning from the UCLH Cancer Collaborative</b><br/>Professor Kathy Pritchard-Jones, Chief Medical Officer, UCLH Cancer Collaborative</p>   |
| 11.15-11.30   | <p><b>Creating a system for translation of innovation: case study 1</b><br/>Geoffrey Hamilton-Fairley, Chief Executive Officer, Oncimmune</p>  |
| 11.30-11.45   | <p><b>Creating a system for translation of innovation: case study 2</b><br/>Dr Marc van der Schee, Head of Clinical, Owlstone Medical</p>  |
| 11.45-12.00   | <p><b>Creating a system for translation of innovation: case study 3</b><br/>Dr Craig Eagle, Senior Vice President and Head of Oncology, Pfizer</p>   |
| 12.00-12.45   | <b>Lunch</b>   |
| <b>Defining and meeting the challenges of the future</b>                    |  |
| 12.45-13.00   | <p><b>The value of EDD technologies</b><br/>Dr Elisabeth Adams, Managing Director, Aquarius Population Health</p>  |
| 13.00-14.00   | <p><b>Panel discussion: What are the challenges for EDD research and technologies and how do they fit into the broader healthcare landscape?</b></p> <ul style="list-style-type: none"> <li>• David Browning, Chief Executive Officer, Oxford Cancer Biomarkers</li> <li>• Professor Robert Steele, Chair, UK National Screening Committee</li> <li>• Geoffrey Hamilton-Fairley, Chief Executive Officer, Oncimmune</li> <li>• Professor Kathy Pritchard-Jones, Chief Medical Officer, UCLH Cancer Collaborative</li> <li>• Dr Karin Oien, Reader in Experimental Therapeutics, University of Glasgow</li> </ul>   |
| 14.00-14.20   | <b>Coffee and refreshment break</b>  |
| <b>Preparing the system for EDD research and technologies</b>               |  |
| 14.20-14.25   | <p><b>Introduction to afternoon</b><br/>Professor Peter Johnson CBE FMedSci, Professor of Medical Oncology, University of Southampton</p>  |
| 14.25-14.55   | <p><b>What do we need to know to prepare the system?</b><br/>Professor Patrick Bossuyt, AMC Principal Investigator, Academisch Medisch Centrum</p>   |
| 14.55-16.05   | <p><b>Break-out sessions: filling the gap for translation of EDD technologies</b></p> <ul style="list-style-type: none"> <li>• Group 1 – chaired by Professor George Hanna, Professor of Surgical Sciences and Head of Division, Imperial College Healthcare NHS Trust</li> <li>• Group 2 – chaired by Professor Patrick Bossuyt, AMC Principal Investigator, Academisch Medisch Centrum</li> <li>• Group 3 – chaired by Professor Caroline Dive CBE FMedSci, Deputy Director, Cancer Research UK Manchester Institute</li> <li>• Group 4 – chaired by Professor Martin Leach FMedSci, CRUK Cancer Imaging Centre, Institute of Cancer Research</li> </ul> |

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|-------------|--|
| 16.05-16.50 | <b>Panel discussion – Preparing the system for EDD technologies</b> <ul style="list-style-type: none"><li>• Dr Daniel O'Connor, Expert Medical Assessor, MHRA</li><li>• Dr Rory Harvey, Consultant Gastroenterologist, Bedford Hospital NHS Trust</li><li>• Emma Greenwood, Director of Policy and Public Affairs, Cancer Research UK</li><li>• Professor George Hanna, Professor of Surgical Sciences and Head of Division, Imperial College Healthcare NHS Trust</li></ul> |
| 16.50-17.00 | <b>Summary and close</b> <p>Professor Peter Johnson CBE FMedSci, Professor of Medical Oncology, University of Southampton</p>  |



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