



Early detection and diagnosis of cancer

Towards a roadmap for Wales

Moondance Cancer Initiative is a new, not-for-profit company established to find solutions so that more people in Wales survive cancer. We want to help achieve significant and sustained improvements in cancer survival outcomes over the next ten years. What we do:

- We identify and trial new pathways, practices, and technologies, so that more people in Wales survive cancer
- We work in partnership with the Welsh health community and beyond – connecting great people across different disciplines, sectors, and regions
- Our work is evidence-informed, rigorous, and adventurous: we see value in moving quickly, trying and learning
- We bring funding, research intelligence, and an ethos of collaboration to the table

We're a not-for-profit company (company number 12305964), privileged to be funded by the Moondance Foundation.

Published by:

Moondance Cancer Initiative
12 Cathedral Road
Cardiff, CF11 9LJ
Wales, UK

Tel: +44 (0) 2921 113990

Email: info@moondance-cancer.wales

www.moondance-cancer.wales



VISION

Proactive Care

Creating capacity to engage in case-finding of early cases, not gatekeeping

Enabled Workforce

A bolstered, innovative workforce, enabled by digital infrastructure

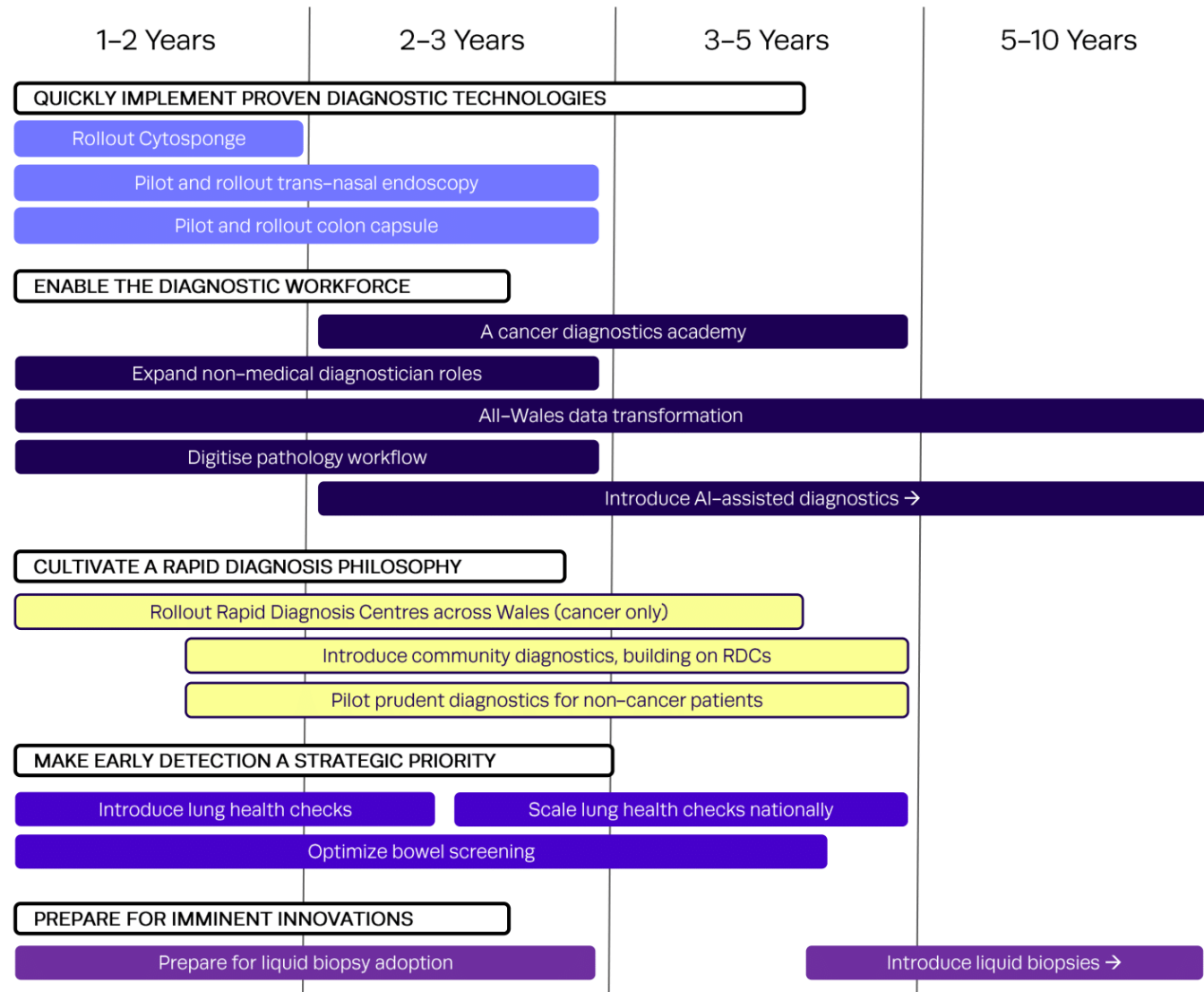
Rapid Diagnosis

A rapid diagnostic philosophy, with elective pathways and accessible community hubs

Early Detection

Optimized and effective bowel screening and lung health checks

ROADMAP



Contents

Purpose and context of this paper.....	5
<i>In this paper</i>	5
<i>A note on awareness and early presentation</i>	6
<i>The impact of Covid-19</i>	6
Articulating a vision for future cancer ED&D services.....	7
<i>Proactive care: from gate-keeping to case-finding</i>	7
<i>A service with a relentless, shared focus on early detection</i>	8
<i>Diagnostic services in communities</i>	8
<i>A tech-enabled, combined diagnostic workforce</i>	9
How can we get there? An emerging roadmap for cancer ED&D in Wales.....	10
1. Quickly implement proven diagnostic technologies.....	12
<i>Cytosponge</i>	12
<i>Transnasal endoscopy</i>	12
<i>Colon capsule</i>	13
<i>How innovative triage can help</i>	13
2. Enable the diagnostic workforce.....	14
<i>A Diagnostics Academy?</i>	14
<i>Key opportunity: clinical scientist of the future</i>	14
<i>Digital transformation</i>	15
<i>Reducing duplication, increasing coordination</i>	17
3. Cultivate a rapid diagnosis philosophy.....	18
<i>How rapid diagnosis might be evolved</i>	20
4. Make early detection a strategic priority.....	22
<i>Bowel cancer screening</i>	22
<i>Lung Health Checks</i>	23
5. Get ready for imminent innovations.....	25
<i>Key opportunity: plan for liquid biopsies</i>	25
Concluding remarks	26
Annex 1: the ED&D roadmap and Welsh Government cancer quality goals.....	27
Annex 2: Contributing organisations.....	28
References.....	29

Purpose and context of this paper

The early detection and diagnosis (ED&D) of cancer is one of the most important factors in reducing cancer-related illness, death, and the strain on our healthcare system. It is acknowledged as a key priority in the Wales Cancer Quality Statement¹ and in the 'A Healthier Wales'² plan for health and social care.

Wales has historically struggled to diagnose cancer early (50% of patients presented at stages III–IV in 2018)³. The COVID backlog,⁴ workforce pressures in radiology⁵ and pathology,^{6,7} and steadily increasing diagnostic waiting times,^{8,9} indicate this picture is worsening.

In recent years, a wave of services, technologies and workforce innovations for effective cancer ED&D have emerged or are emerging across the world. Wales has implemented some of these innovations in limited settings, such as in the rollout of rapid diagnostic centres (RDCs).¹⁰

We believe that these innovations, in combination with policy motivation, create a significant opportunity to transform ED&D in Wales over the next decade, speeding up time-to-diagnosis across all cancers – with a direct meaningful impact on cancer outcomes.

Wales needs a roadmap to achieve this goal.

In this paper

The emerging roadmap presented in this paper is the product of scoping, systematic review, and consultation with a multi-disciplinary sample of expert NHS Wales clinicians.

- In our ED&D scoping paper, published in Summer 2021, we systematically reviewed innovations in ED&D which could improve Welsh service provision. To see the underpinning methods and evidence supporting this roadmap, you can download the paper from our website¹¹
- Taking our scoping paper as an input, we hosted a short series of discussions with a sample of relevant clinicians across NHS Wales, from medical directors to diagnostic and screening specialists. In these sessions we validated and expanded our innovations list and discussed realistic priorities for improving Welsh ED&D.

We hope this paper will serve as a constructive contribution to the start of a programme towards earlier cancer detection and diagnosis in Wales. It builds on the work, energy and ideas already in the system as well as drawing from exciting developments elsewhere. This roadmap is not comprehensive, and there are undoubtedly further exciting innovations that Wales can harness in coming years.

It is a beginning, and we hope it will inform thinking and debate across the Welsh health system.

A note on awareness and early presentation

Any improvement to the delivery of cancer detection and diagnosis services, and access routes into them, will benefit those people who engage early with health services.

According to recent evidence, approximately 20% of newly diagnosed cancer patients present as emergencies.¹² These acute symptoms often correlate with the cancer being at a late stage. There are many intertwined reasons as to why people don't come forward earlier with possible cancer symptoms, but we do know that a disproportionate number live in Wales' most deprived areas. Emerging evidence also shows that even more people avoided healthcare services despite experiencing potential cancer symptoms during the COVID-19 pandemic.¹³

Continued investment in innovations targeted towards awareness and engagement are therefore **essential** alongside transformation of ED&D provision if we want the benefit to reach everyone.

To make the scope of this roadmap manageable, we have not addressed awareness and early presentation here. However, it is of equal importance and Moondance Cancer Initiative has commissioned an evidence review to inform thinking about our own future investment in awareness and early presentation.

The impact of Covid-19

We know that the public health measures taken to protect NHS capacity during the Covid-19 pandemic have discouraged people from presenting with cancer symptoms, and compromised the ability of the NHS to serve them when they do (alongside other conditions). The Welsh Government has signalled it is likely to take a full Senedd term to fully tackle the backlog.¹⁴

The pandemic is not yet over. In our discussion series, clinicians confirmed media reports that they and their colleagues are deeply fatigued and that their capacity to think and to innovate is squeezed by simply responding to daily demands.

We acknowledge that the starting point for this roadmap, in Winter 2021-22, takes place within the context of a continuing pandemic and an over-stretched NHS. Despite this, numerous clinicians have told us that the hope of improving and transforming services through innovation gives them energy whilst they continue to respond to backlog demand.

Articulating a vision for future cancer ED&D services

The principal objective of cancer ED&D services, as described in the Welsh Cancer Quality Statement,¹ is that *'More cases of cancer are detected at earlier, more treatable stages through more timely access to diagnostic investigations'*.

We hope that the vision articulated here will also deliver on other objectives, such as closing inequities in access to cancer diagnosis, and delivering services in a resource-efficient way that benefits workforce and patients in and outside of cancer care. For a summary of how our vision could achieve multiple aims set out in the Cancer Quality Statement, see Annex 1.

So what might ED&D services that achieve these principles and outcomes by 2031 or thereabouts *actually look like*? The following key elements consistently emerged in this study:

Proactive care: from gate-keeping to case-finding

One long-term goal, articulated to us by colleagues in the WICKED team at Bangor University, is to make good on the policy aspiration for prevention made in *A Healthier Wales*² by shifting from a health system dominated by reactively gate-keeping to one proactively engaged in case-finding. This would mean equipping community services and national screening programmes to increase work that pro-actively identifies cancer risk in the community and offers diagnostic and preventative interventions.*

“We aspire to shift from gate-keeping to case-finding”

This aspiration captures a desire for culture change as well as system transformation – which came through strongly in our roundtables. As a statement, it affords long-term direction and ambition to this developing roadmap; however for many, the time and resources for case-finding also feel a long way off.

*There are different views as to whether a shift to case-finding means increasing funding and by how much; the case of Denmark is cited as an example in which gate-keeping was removed and the system ‘wasn’t flooded’ – but also acknowledgement that this shift took place in a very different fiscal and health context).

A service with a relentless, shared focus on early detection

Cancer screening holds significant potential impact on cancer survival. It offers the chance of identifying cancer at an asymptomatic earlier stage, when for many cancer types curative treatment is much more likely.

Early detection via screening is therefore a leading priority, and was identified as such in our discussions by clinicians working across multiple disciplines. This emerging roadmap for cancer detection thus includes full optimisation and rapid adoption of proven screening approaches *at scale*. For example, the underpinning evidence for lung health checks is strong and rapid national adoption as soon as possible was widely supported in our discussions. While a more distant prospect, there is clear appetite to prepare for cancer detection or screening using liquid biopsies when the technology matures.

While responsibility for delivery of screening services sits with Public Health Wales, numerous clinicians recognised the need and potential for wider, shared ownership of screening participation.

Diagnostic services in communities

The emerging collective vision for diagnostic services is for people with potential cancer symptoms to access protected elective diagnostic services separately from emergency and acute care and preferably within or close to their own communities:

- Where diagnostic tests can be undertaken in local primary care, they are, so that treatment can start as soon as possible
- Where needed, patients can also be referred to a community-based diagnostic service within a short period of time (drawing on both the rapid diagnosis centre modelled in Wales and the ideas in Professor Sir Mike Richards' report¹⁵). Depending on the character and needs of each community, community diagnostics may include pop-up or mobile clinics to improve access too
- Community diagnostic services, protected from acute care demands, can then provide (most) patients with a diagnosis within days, if not on the same day; staff in these services have time to explain results, next steps, and support options to patients.
- Diagnostic pathways with broad provision, graduated workups, and sensible use of nonmedical interventions prevent 'referral tennis' between primary care and specialist secondary sites.

The shared belief is that these diagnostics services will also become much more efficient when decoupled from acute care and additionally result in improved services in acute settings.

A tech-enabled, combined diagnostic workforce

This collective vision is only deliverable by a well-equipped, well-trained, and well-staffed workforce.

A shift to community diagnostics presents an exciting opportunity to bridge the primary and secondary care 'gap' by combining skills in new community diagnostics teams, with some rapid diagnosis centres seen as early exemplars. Moreover, many envisage future diagnostic teams to include many more non-medical roles, with staff enabled to work and participate in MDTs both on and off-site as technology permits.

Future integrated information systems planned for NHS Wales are also expected to help streamline case management, and to provide much richer, real-time management information so that care can be coordinated between GPs and community diagnostics services, ensuring every patient reaches a clear diagnosis as soon as possible.

How can we get there? An emerging roadmap for cancer ED&D in Wales

The outline vision in the chapter above summarises a collective view of 'where we want to go' on early detection and diagnosis in Wales that emerged from our research. The key question we now address is more complex: 'how can Wales get there?'

The emerging roadmap presented comprises five key priority areas for the next 10 years:

1. **The fast implementation of proven diagnostic technologies** – to triage patients at risk of cancer, and reduce pressure on diagnostic services
2. **Enable the diagnostic workforce** – supporting with digitized and integrated infrastructure, connecting diagnostic training & development, and actively supporting the expansion of non-medical diagnostics careers
3. **Cultivate an elective rapid diagnosis philosophy** – based on principles of patient-centred accessibility, separation from acute care, generic diagnostic workup, and sensible use of nonmedical and social prescribing. More resource-intensive elements of this approach could be supported by expanded nonmedical workforce, and digital infrastructure
4. **Make early detection a strategic priority** – facilitated by digital infrastructure, and relief on diagnostic services by innovative triage, providing a world-leading screening system; to include bowel screening optimized to maximise case finding, and an ambitious national lung health check (LHC) service
5. **Get ready for imminent innovations** – most pressingly for the coming revolution of liquid biopsies

In Figure 1, below, we present these priority areas visually, focussed on the next 3–10 years. In Annex 1, we also map how the actions presented in this roadmap would contribute toward achieving the goals set out in the Wales Quality Statement for Cancer.¹

Then in the five following chapters, we discuss each priority area in more detail, proposing concrete steps that together can help to move Wales forward, toward innovative, effective cancer ED&D provision.

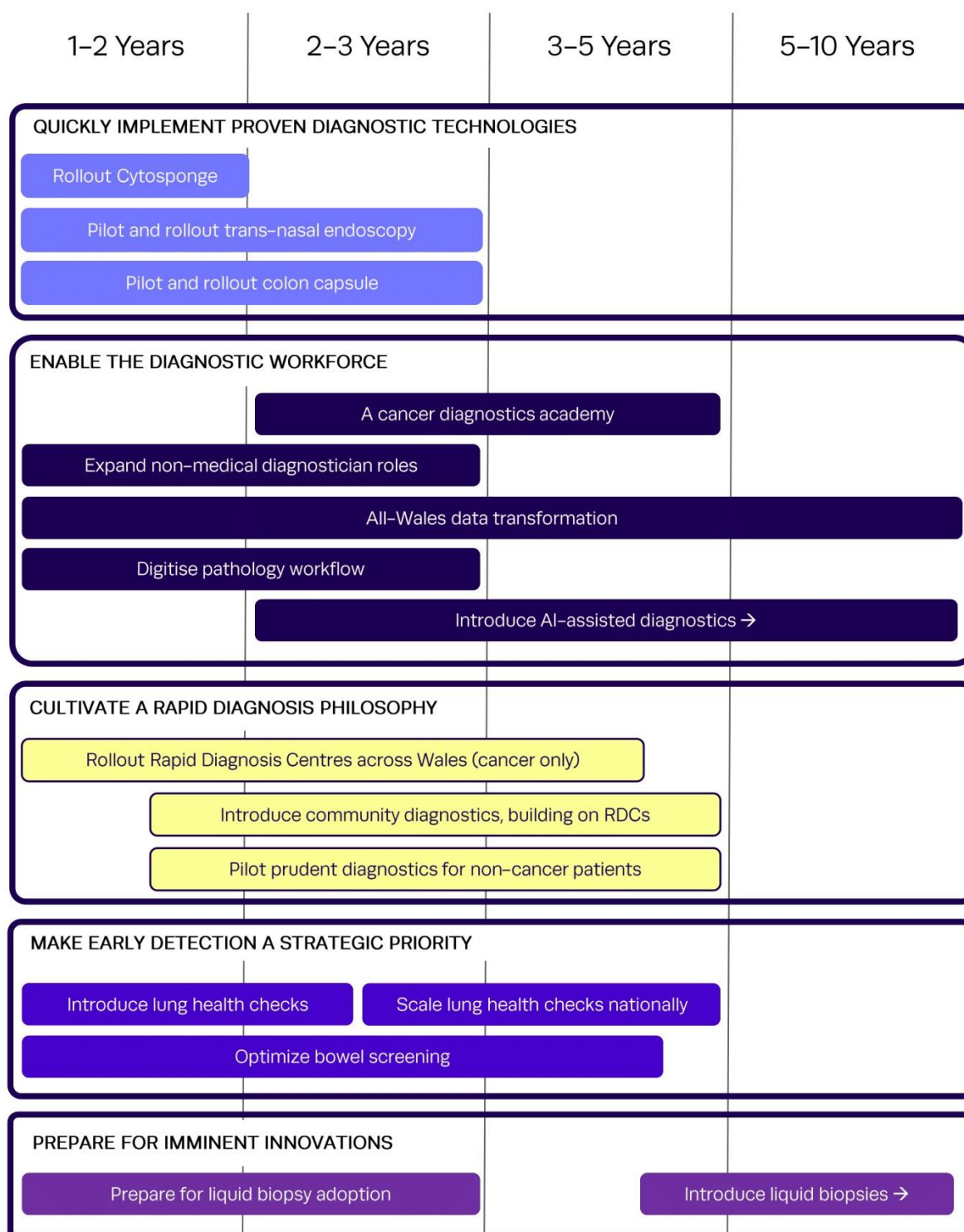


Figure 1. A roadmap towards earlier cancer detection and diagnosis in Wales

1. Quickly implement proven diagnostic technologies

A key immediate priority for innovation in cancer ED&D is to address the pressures and waiting times for diagnosis in secondary care, described by Senedd researchers as 'a mountain to climb'.¹⁶ In particular, endoscopy services are beset by waiting times that were already increasing before the pandemic.⁸ Solutions are needed, both to help deal with the pandemic backlog, and to improve sustainability in the longer-term.

A series of novel diagnostic technologies are emerging which could help safely triage patients, and reduce pressure on diagnostic services. Our exploration of novel diagnostics focussed on GI cancers, given the recognised backlog in endoscopy, and suggested the following offer real potential:

Cytosponge

Cytosponge is a swallowed 'device on a string' used to test for Barrett's Oesophagus (BE), a pre-cancer condition. It has proven effective (and cost-effective) in clinical trials in patients with reflux symptoms and those on surveillance for BE. It may have a role in triaging waiting lists, safely identifying patients who do not require endoscopies and prioritising those who do, accelerating their cancer diagnosis.^{17–19} Unpublished data from national rollout of Cytosponge in Scotland showed that it reduced gastroscopy waiting lists by ~80%. Administration requires one nurse, is short (~7 minutes) and has straightforward training requirements. Finally, it can be positioned within primary or secondary care.

With a high-quality evidence base, straightforward training requirements, and ongoing rollout in Scotland and England, it appears that cytosponge could play an important role in the short term to reduce pressure on diagnostic services. Moondance Cancer Initiative is in discussion to fund the introduction of Cytosponge for endoscopy triage in Betsi Cadwaladr UHB and Powys THB, which could form the basis of adoption by all health boards across Wales.

Transnasal endoscopy

Trans-nasal endoscopy (TNE) involves the application of an ultrathin endoscope via the nose in locally anaesthetised patients. Maintaining a comparable degree of diagnostic accuracy to traditional endoscopy,^{20–22} TNE is more tolerable, with the vast majority of patients finding discomfort absent or minimal. It takes less time, and is associated with fewer complications than traditional endoscopy.^{22–24}

Requiring only one nurse, and less hospital time for patients to recover from sedation, TNE is also more resource efficient.

TNE is standard practice in many countries (such as Japan, which has specialized in dealing with historically high volumes of upper GI cancer), including many hospitals in England and Scotland.²⁵

TNE appears to represent a valid method to make endoscopy services more efficient and patient-acceptable in the long-term. Moondance Cancer Initiative is funding an implementation pilot of TNE in Cardiff and Vale UHB and Cwm Taf Morgannwg UHB in Winter 2021-22.

Colon capsule

Colon capsule, or PillCam, is a swallowed device, which captures and analyses images of the colon. It can be used for triaging of colonoscopy waiting lists, having been shown to reduce colonoscopy need by between 43–70%.^{26–29} It also has favourable diagnostic accuracy compared to other non-invasive measures, such as CT scan. National rollout of colon capsule is ongoing in Scotland.^{30,31}

Colon capsule could be administered in primary or community care, even self-administered at home, and could be rolled out in Wales in the short-to-mid term future. We are aware that the National Endoscopy Programme are looking at adoption of this technology in Wales, though the scale and timelines are unclear.

How innovative triage can help

The three technologies profiled above are available now. Whilst endoscopy-focused, these innovations could also afford indirect benefit across the diagnostic workforce: for example, fewer unnecessary endoscopies means fewer biopsies to report for pathology, and fewer failed endoscopies means fewer CT scans for radiology reporting.

“Triaging using innovative technology will be our way forward.”

Relieving caseload pressure using innovations available now could not only help tackle the pandemic backlog, and speed up time to cancer diagnoses, but also help to free up capacity for other necessary innovations in ED&D – some of which are discussed below.

2. Enable the diagnostic workforce

Our initial scoping paper¹¹ focussed on technology and pathway innovations with the potential to transform early detection and diagnosis of cancers in Wales. The roundtable discussions with clinicians placed strong emphasis on the need to put people at the heart of this roadmap. The successful introduction of any ED&D innovation will depend on the having the right combination of professional staff from across primary and secondary disciplines, working well in teams, appropriately equipped and trained.

While there were understandable calls for more staff of nearly all types, in our discussions there was widespread agreement on the need to reconfigure and equip the diagnostic workforce too. The following practical areas for action were emphasized:

A Diagnostics Academy?

The challenges facing the clinical diagnostic workforce in Wales have been well documented in recent years.⁷ This workforce is struggling to meet increasing diagnostic demand alongside a decline in numbers, and a demographic indicating large numbers of retirements soon.

If cancer ED&D is to innovate and improve, it is clear that our diagnostic workforce needs to be adequately supported. Whilst some of this support can come from nonmedical diagnostician roles, digital transformation, and quality improvement processes, the continued importance of clinical diagnosticians – as bridges between diagnosis, through MDTs, to treatment decisions – was also emphasized. A central workstream of this roadmap is therefore the extension of active investment in training and development for these roles.

Clinicians praised the work of the National Imaging Academy, with nearly 80 trainee radiologists in the system. We believe that similar schemes could be established for endoscopy and pathology services within a 5–year timescale. One clinician suggested these efforts could valuably be connected or combined, becoming a diagnostics ‘academy’ for Wales.

**“It’s about training
the cancer workforce
of the future”**

Key opportunity: clinical scientist of the future

Pressure on the diagnostic pathway could be alleviated by nurturing the emerging nonmedical diagnostician workforce in Wales, trained in the performance and reporting of radiology, pathology, and endoscopy diagnostic procedures. Such

nonmedical diagnosticians provide support by gathering and reporting diagnostic data, allowing clinicians to perform tasks best utilizing their skills and experience – such as focussing on more complex cases, and leading in settings such as MDT meetings. Such roles might be particularly well suited to elective-only diagnostic centres, such as RDCs and CDHs (see Theme 3: Cultivate a rapid diagnosis philosophy).

Some individual schemes have been initiated in Wales, including training for nonmedical (and nurse) endoscopists,³² and pathologists which have been funded by Moondance Cancer Initiative.³³ These developments are promising but so far piecemeal, creating pockets of opportunity. As yet, matters of career paths, ideal training requirements and skillsets, where best to deploy these roles, and their medicolegal responsibilities, have not been fully addressed.

Consequently, the full potential of the emerging nonmedical diagnostician workforce has not yet been exploited. Further development, crucially with HEIW input, seems a ripe opportunity.

Digital transformation

Faster diagnosis of cancers in Wales will be facilitated by a transition to a digital infrastructure that affords access to comprehensive patient records; connects all stages of the pathway; enables distance working; supports use of AI to augment clinicians work and workflow; and allows for the production of rich management and research insights, drawing on both clinical and administrative information to drive continuous improvement.

In simplest terms, we understand there are two phases of digital health transformation that will help Wales to realise the full potential of ED&D: making the move to a fully digitised infrastructure, which then provides the platform for deployment of AI-assisted diagnostics.

Digital Architecture

Clinicians reinforced with us, as has been reported in the NHS Wales Digital Architecture Review,³⁴ that digital infrastructure is inconsistent across Wales. Different healthcare applications are often siloed from one another with health records that do not cross application/health board boundaries, and health boards independently developing and employing digital solutions which cannot communicate with the rest of Wales.

To demonstrate how this affects cancer care, one clinician described the process to refer and report a radiology appointment – involving three separate and time consuming transfers from digital records to a paper referral, which has to be physically delivered. They emphasised that the time and resource savings of an entirely digital system would be enormous, both for patients and clinicians.

“The one big advance we could do is collaborative, linked clinical systems, saving rafts of bureaucracy.”

A modern digital infrastructure, where electronic health records are laid across a comprehensive all-Wales data pool, with interoperable settings (e.g. primary and secondary care) and applications (e.g. referrals, patient histories, imaging), should form the backbone of an effective Welsh ED&D provision. Planned publication of standards (and creation of APIs) to link in new digital applications can then facilitate ongoing digital ED&D innovation, such as AI tools for cancer recognition at GP surgeries.³⁵ Inspiration can be taken here from countries with world-leading digital health infrastructures, such as Denmark.³⁶

We understand that DHCW is currently detailing a once-for-Wales package of digital transformations to move Welsh health and care services towards these aims. Mapping how and when this transformation will impact real-life cancer care will be essential to realising the full benefits for cancer patients.

Digitizing Pathology

Alongside radiology and endoscopy, pathology is the major workhorse in the diagnosis and staging of cancer. Whilst traditional pathology mostly involves the indexing and analysis of physical slides, a digitized pathology workflow involves the scanning of a digital whole slide imaging (WSI) for digital storage and analysis.³⁷ This approach is widely regarded as the next step in pathology, is associated with increased workforce efficiency, removal of geographical barriers and delays, and faster reporting, without loss of accuracy, is essential for AI-assisted diagnosis, and is endorsed by the Royal College of Pathologists.^{38–42}

We understand that some progress has been made toward a digitized pathology platform, for instance being trialled in Betsi Cadwaladr UHB.⁴¹ To maximise the benefits, digitized pathology should of course be underpinned by an efficient all-Wales digital architecture. With this in place, it was indicated that health boards could make the short-term investment into equipment to digitize their pathology programmes, within an overall 3 year timescale.

AI assistance for diagnostic imaging

Artificial intelligence platforms have shown very high accuracy for the diagnosis of cancer from both pathology and radiology images,^{43–47} and hold promise to be a powerful tool to improve Welsh ED&D provision, by acting as a decision aid and triaging tool for diagnosticians. For instance, AI has been integrated into the first of two reads in breast cancer screening, cutting down workload of the second read radiologist by 88% without compromising accuracy,^{46,48} and could perform other tasks, such as prioritization of reporting for cases likely to represent more advanced cancers.

“AI doesn’t replace radiologists: it makes them more efficient.”

Efficient use of AI does require an efficiently digitized imaging infrastructure. However, once this is in place in Wales, with a number of regulator-approved suppliers available, for instance with mammography AI in use already in 15 English hospitals,⁴⁹ we believe Wales could tune and implement some AI within a 3 year timescale, both by individual health boards, and bodies such as DHCW and PHW, where national programmes are appropriate.

Data quality improvement

Clinicians consistently indicated to us that availability of patient-level and patient-reported outcomes and other performance measures in cancer care is invaluable for research and continual improvement of cancer services. For example, the OpenSafely collaborative demonstrates how availability of national patient-level data can enable impactful research.⁵⁰ We understand the national data resource (NDR), being developed by DHCW, will represent an interrogatable All-Wales data pool. When access and training for clinicians and researchers is delivered, it could facilitate powerful research and quality improvement.

Reducing duplication, increasing coordination

Clinicians also told us they feel there is currently a lack of connection and collaboration across health boards on cancer services. This pattern was highlighted first in terms of simple information exchange – swapping insights, learning together, knowing who’s trialling which new approaches, and so on. Some forums are available – such as the Wales Cancer Network site groups, and MacMillan’s events, amongst others. Addressing this appetite for more connection therefore needs to start with further exploration before identifying ways to meet it; ‘more’ meetings are unlikely to be effective, especially given the demands of patient workloads.

“In a country like Wales, we can be collaborative, collegiate, and really get some great things going.”

A desire for greater coordination was also evident when we discussed making the most of the diagnostic workforce (& equipment). Some see regional working as both inevitable, and desirable if managed well and especially if digitised – which would reduce the need to travel and enable workloads to be shared. Some saw diagnostic hubs as a potential regional collaboration too – though balanced with the opportunity to locate these closer to the communities served.

3. Cultivate a rapid diagnosis philosophy

With pilot projects in and outside Wales demonstrating reduction in time to diagnosis,⁵¹ positive patient and clinician experiences,⁵² in more deprived populations,^{53,54} and doing so cost-effectively,⁵¹ Rapid Diagnosis Centres (RDCs) for vague cancer symptoms are being expanded across Wales. At the same time, evidence is beginning to emerge that some community diagnostic hub (CDH) models in England can shift stage of diagnosis earlier,⁵⁵ and in the wake of the Independent Review of Diagnostic Services for NHS England by Prof Sir Mike Richards,¹⁵ CDHs are being rapidly rolled out across England.⁵⁶

Whilst no RDC or CDH is completely identical, they share a set of design principles, which have the potential to serve patients with faster, more accessible diagnosis. These principles offer promise as a core philosophy for Wales' cancer diagnosis pathways of the future.

Separating elective and acute

Accelerated by necessities of the pandemic, the concept of 'cold' diagnostic services, separated from acute care, is generally recognised as an important factor for efficient diagnostic services.^{15,57} Clinicians explained to us that, if forced to choose, they will understandably prioritise acute over elective needs. However, doing so reduces the efficiency of elective diagnostics, and increases the chances of the same patients later presenting to acute care.

“Faced with acute care, you can't be in two places at once... everything else gets pushed aside”

Whilst some argue a 'bricks and mortar' approach is best, with diagnostic hubs built on repurposed NHS estate, located on the high street, or using mobile provision, this philosophy can also be implemented in traditional healthcare settings. For example, the Neath–Port Talbot RDC is delivered inside Neath Port Talbot hospital – an existing non-acute services location. In each case, the core and most important principle is the *protection* of elective diagnostic provision from acute care demands.

This protection can even be additionally achieved by workforce practices. One clinician described to us a 'cancer physician of the week' scheme, where one clinician a week was reserved solely for elective cancer diagnostics – just one example of how this philosophy can begin to be implemented at a workforce level.

Generic diagnostic workup

A principle aim of vague symptom RDCs is to prevent 'communication tennis', where patients are sent back and forth between primary and specialised secondary care for a particular cancer site. This delays diagnosis (thereby worsening prognosis), adds unnecessary pressure to stretched secondary diagnostic care, and worsens patient care through the stress of multiple waits for cancer diagnosis.

Evidence suggests that RDCs with generic diagnostic provision work well, to ensure accurate referrals for patients with vague cancer symptoms, for a cancer yes/no decision on patients with low-but-not-no risk symptoms, and for non-cancer diagnoses (such as COPD in patients with lung symptoms), all without repeated referrals back and forth between primary and secondary care.

**“You have to
avoid this
communication
tennis”**

Patient-centred care and accessibility

Planning for easy accessibility is also key to rapid diagnosis, especially for more deprived populations. More accessible locations, such as shopping centres and mobile units have shown their ability to drive attendance of people from more deprived groups.

Alternative referral methods may also play a role, such as pharmacy referrals⁵⁸ or via GP-endorsed letters, which in a Manchester CT study enabled patients to go straight to their diagnostic hub.⁵⁹ Despite fears of overuse by the 'worried well', clinicians indicated that targeted use of direct self-referral to CDHs could work well in specific deprived populations.

A diagnosis-in-a-day philosophy

Underpinning all of this, a rapid (ideally one-day) philosophy is essential. Evidence shows that experiences such as long waiting lists, or a hospital appointment leading to no progress (e.g. after a failed colonoscopy or inappropriate referral), are hugely detrimental to patient engagement and help-seeking behaviour.

**“If somebody turns up with a problem, they have to
leave with a problem solved.”**

A rapid centre, with short waiting times, and where for instance a failed colonoscopy could be followed up immediately with a colon CT scan, would be beneficial for patients, and more efficient for diagnostic services.

Prudent healthcare and diagnostic capacity

Some clinicians suggested that this philosophy, in combination with prudent healthcare principles,⁶⁰ could also better serve non-cancer patients, whilst increasing diagnostic capacity for patients with suspected cancer.

In one example, a senior Welsh diagnostician asked if a patient with suspected sciatica was best served by being put on an MRI waiting list for diagnosis by their GP, where they could delay diagnosis of suspected cancer patients? Or whether graduated workup could take them to a physiotherapist to address symptoms, who was empowered to refer onwards to MRI if the case was sufficiently severe?

A more prudent, less medicalized approach to non-cancer patients, utilizing a generic workup, and social and nonmedical prescribing, could better serve both patients with and without cancer, and improve diagnostic capacity. We estimate that pilots investigating these prudent nonmedical pathways could be established by health boards within the short to medium term.

How rapid diagnosis might be evolved

Health boards across Wales have committed to the introduction of RDC pathways for vague symptoms that could be cancer. In parallel, the idea of community diagnostic hubs for all/most elective diagnostic pathways is gaining traction too. Both offer significant potential value to better cancer ED&D in Wales. Accelerating this transition towards rapid diagnostics could make a real difference to cancer survival outcomes, wider health outcomes and patient experience.

Speeding up this transition will be easier when diagnostic services are relieved of some pressure through efficient triage, and as improved digital-enabled systems are ready. Redesigning services and engaging the diagnostic workforce in training and delivering the desired changes will however remain significant tasks.

At this point in time, if this ambition for rapid diagnosis is accepted, it seems there are two routes forward. First, the ongoing rollout of RDC pathways might be expanded, to support the extension of the one-day philosophy from vague symptoms to more suspected cancers, responding appropriately to the specific needs and infrastructure of each locality. (Moondance Cancer Initiative is supporting the Swansea Bay RDC to begin this expansion in 2022 and 2023).

Second, building from existing elective diagnostic infrastructure where it is already independent of acute demands, several models of CDH could be piloted with a focus on patient-centred accessibility. (We understand pilots are being discussed in some health boards). These CDHs could be primary care-led, and

supported by an innovative nonmedical diagnostician workforce, who would be well suited for the elective-only, non-prescribing diagnostic workload.

Eventually it seems likely that cancer-focussed RDC pathways may appropriately be absorbed into future CDHs, if that can be done without risking the shared philosophy and practices that we anticipate RDC teams across the country will embrace.

4. Make early detection a strategic priority

There is real appetite to focus and invest more in early detection as the most effective known way to reduce deaths from cancers in Wales.

At this point in time, evidence points strongly to two specific innovations – bowel screening optimisation, and lung health checks – as evidenced ways to reduce premature deaths from cancer that are ready for implementation as soon as the health system has the capacity to deliver them.

Bowel cancer screening

Bowel cancer is the second most common cancer in Wales.³ It has an identifiable, modifiable pre-cancer phase, and curative surgical and endoscopic treatments have a very high success rate if the cancer is detected early.

The Bowel Screening Wales (BSW) programme has been in existence since 2000. It has maintained the highest level of quality assurance in its delivery but has still not been able to fully optimise its service in terms of reach, currently detecting approximately 10% of the cancers diagnosed in Wales each year. The minimum eligibility age has seen its first reduction in 2021 to 58 and the cut-off for onward referral remains at 150µg/g blood in faeces as it has done since the programme commenced. In this respect, it is behind top comparator countries in efforts to detect as many bowel cancers as early as possible (Figure 2). The aspiration is to reduce eligibility age to 50 and sensitivity level to 80µg for onward referral, though timelines are currently unclear, and heavily dependent on endoscopy capacity.

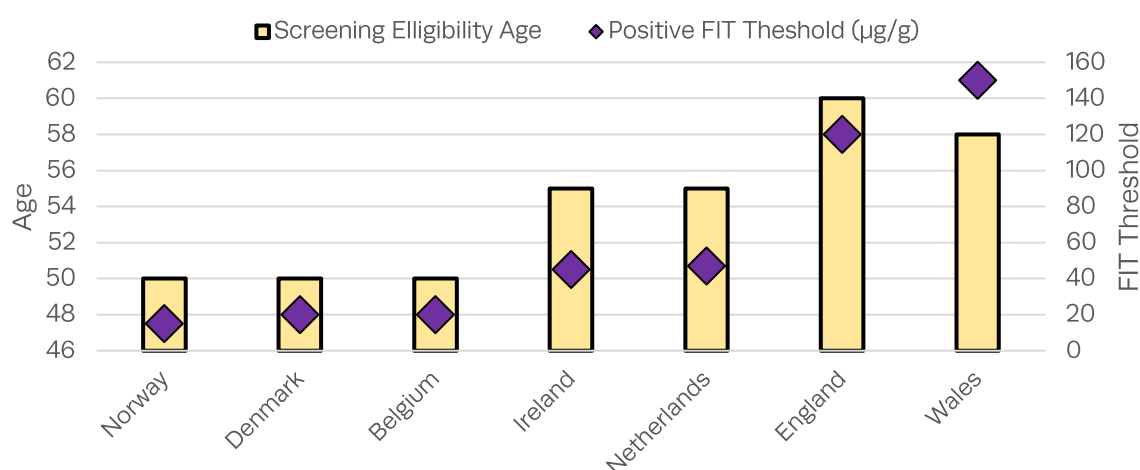


Figure 2. Bowel screening eligibility and threshold for onward referral in countries comparable to Wales.

Reducing the age of eligibility and FIT sensitivity threshold will identify more people with early stage and pre-cancer.^{61,62} Commitments to lowering age of eligibility, and eventually lowering the positive threshold are a significant step in the right direction.⁶³ Endoscopy capacity is a limiting step to the pace of full optimisation. Innovative endoscopy triage and upscaled non-medical endoscopist workforce recruitment, as outlined above, could help accelerate timescales.

It is important for Wales' long-term success to start optimizing as fast as possible: clinicians told us that the fewer cancers picked up by screening leads to a greater demand from emergency and acute presentation and poorer outcomes as evidenced during the pandemic.

The process of bowel screening needs as much innovation as any other part of the pathway. A pragmatic approach will need to be taken to optimise the programme without an unacceptable compromise of quality. For example, in light of the known correlation between quantitative FIT measure and risk of bowel cancer,^{64,65} a pilot could be conducted, where patients could be prioritised for colonoscopy according to their FIT score, ensuring patients most in need of diagnosis are given a colonoscopy as soon as possible. This may be particularly relevant with the long waits in some Health Boards during recovery from the endoscopy pandemic backlog.

Lung Health Checks

“I’ve seen the difference lung health checks make to people’s lives... it’s astonishing”

Lung cancer is the most common cancer, and by far the largest cause of cancer deaths in Wales.⁶⁶ High quality international data shows that lung health checks (LHCs) that combine low-dose diagnostic CT scan and smoking cessation interventions lead to earlier diagnoses, more curative-intent surgery, and fewer deaths from lung cancer, cost-effectively. With over 20 LHC already sites running in England based on this evidence, it is clear that this innovation could represent a huge step forward for cancer ED&D in Wales.^{67–72}

Meeting implementation challenges

There are some challenges to implementing LHCs in Wales, but adaptive solutions are available – and we are aware these are being considered in current early stage plans for an NHS Wales LHC ‘implementation pilot’.

- First, numerous approaches are available to ensure LHCs are targeted at the appropriate at-risk population, which incorporate information as simple as age and smoking history. These are being compared in trial settings now.^{59,70,73}

- Second, an efficient LHC programme will need to be underpinned by a digitized platform, for which solutions exist and could be integrated with digitized radiology platforms in Wales. Experts advise that AI is being deployed in English LHC programmes to safely filter ‘normal’ lung scans and send others on to radiologists, saving diagnostic capacity. There is further potential for nonmedical diagnosticians to carry out this service, reducing overall cost.
- Finally, we recognise that a national LHC programme would incur significant short-term costs. However, studies have consistently shown LHCs to be a cost-effective use of limited resources,^{55,71,74,75} which can bring about long-term reductions in the number of patients receiving expensive therapies for advanced disease.

Accessibility and Deprivation

Both smoking and lung cancer are strongly associated with deprivation in Wales.³ Through both targeting and programme design (e.g., conducting LHCs in a community location and using non-medical language), LHC programmes have successfully engaged people from deprived areas, who were otherwise less engaged with healthcare.^{59,73,76} Well designed and deployed LHCs thus offer an immediate evidence opportunity to improve survival outcomes and help to reduce Wales’ significant inequalities in cancer outcomes.

Introducing LHCs

As mentioned above, we understand that planning is underway for an implementation pilot of LHCs in Wales.⁷⁷ Given the potential benefit, and evidence of effective implementation in similar contexts elsewhere in the UK, there is a strong argument for this introduction to be as large scale as possible. After an implementation framework is established, clinicians informed us that – if prioritised by government and the NHS together – a sustainable all-Wales LHC service could be achieved well within the timescale of this roadmap.

5. Get ready for imminent innovations

At a time when dozens of innovative, disruptive cancer diagnostic technologies are under development globally, from liquid biopsies being clinically trialled, 'breath biopsies' for screening,⁷⁸ or even purchasing history as a detection method,⁷⁹ clinicians made it clear to us that Wales needs to have an eye towards the future of cancer diagnosis and detection.

“There’s a tendency in Wales for innovation to be fragmented.”

Key opportunity: plan for liquid biopsies

Both single-cancer detection tests, such as Epi ProColon and CanSense for bowel cancer,^{80–82} and multi-cancer detection tests (MCDT), such as PinPoint and GRAIL,^{83–86} are growing their clinical evidence base. It is becoming clear that a revolution of high throughput, low-resource intensity liquid biopsies is on the horizon for cancer ED&D. Most notably, the NHS Galleri trial, depending on the data generated, has the potential to motivate a paradigm shift in the way we screen for cancer.⁸⁷

For Wales to adopt this potentially powerful technology effectively, clinicians indicated to us that a number of questions need to be answered, for example:

- How do we decide how to use different liquid biopsies – for example, asymptomatic screening, a screening alternative for those refusing more invasive methods, triage for symptomatic patients?
- What are the operational and demand implications of introducing these tests? What setting should tests be deployed in, and how should staff be trained?
- How do you ethically communicate the potentially complex output of an MCDT to patients?
- Who will be financially responsible for liquid biopsy provision, who will procure them, and how will we make sure we understand the market and manage commercial relationships effectively?

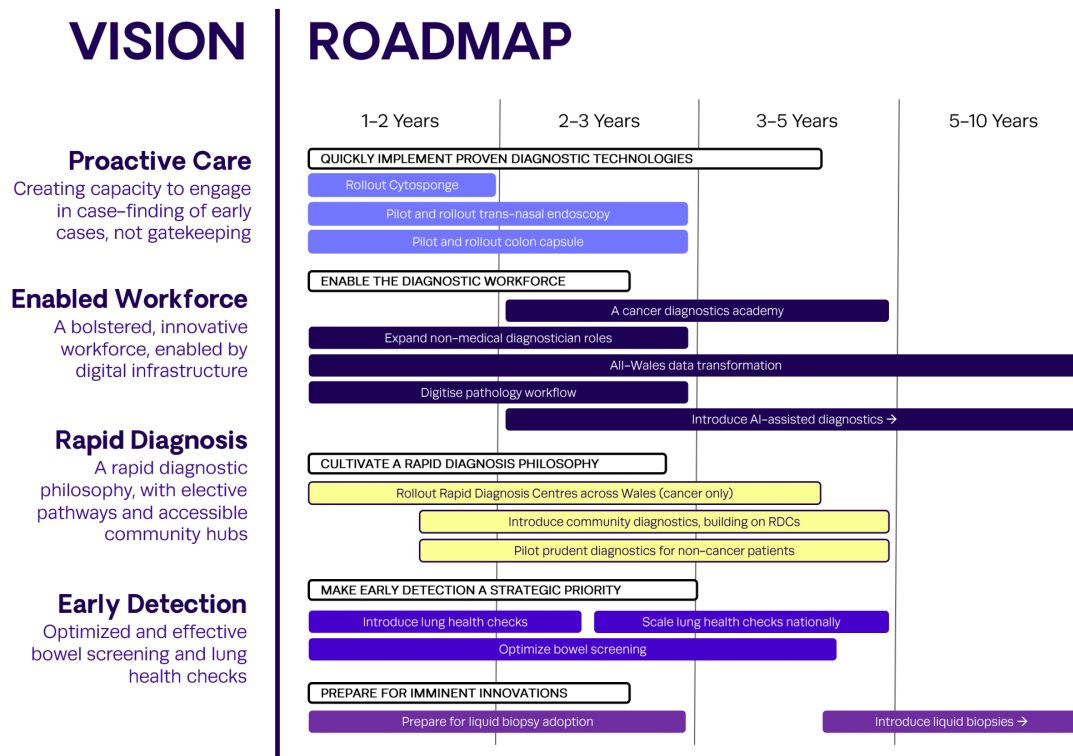
**“Liquid biopsies
are coming.
What are we
going to do when
they arrive?”**

Clinicians have expressed enthusiasm for the creation of a team or unit tasked to consider and advance-plan for the introduction of liquid biopsies into Wales. The team could discuss these questions (and more), liaise with health boards and liquid biopsy providers, and potentially have the authority to publish guidance on the topic. The right team would draw talent from liquid biopsy trials, the cancer clinical community, Public Health Wales, Life Sciences Hub, Health Technology Wales, Welsh Government, industry and others.

Concluding remarks

Earlier detection and diagnosis of cancer is a challenge that Wales must meet. Effective ED&D provision is vital for the future of Welsh cancer care, and therefore to the sustainability of NHS services overall.

In this paper, we have presented an emerging vision and roadmap for how cancer ED&D could transform over the next 10 years – one which we believe holds potential to radically improve the experiences of cancer patients and healthcare professionals across Wales, and to help more people live beyond their cancers.



Built on literature review and consultation with stakeholders, this emerging vision and roadmap is intended as a constructive contribution to both action and ongoing debate. Here at Moondance Cancer Initiative, this paper is directly informing our partnerships and funding strategy going forward. We hope that it will be of value to colleagues across cancer services, strategy and policy too, and we encourage it to be shared across Wales.

If the ideas discussed here provoke any questions or ideas, please don't hesitate to get in touch.

Annex 1: the ED&D roadmap and Welsh Government cancer quality goals

The following table maps the actions contained in this emerging roadmap to the Welsh Government's Cancer Quality Statement.

Cancer quality statement	This roadmap
An immediate system-level focus on recovering the pre-pandemic waiting list volume	Diagnostic technologies proven safe and effective are used to triage secondary care diagnostics.
Clinicians working in cancer pathways work at the top of their licence or are supported to improve their skill mix and are also enabled to take part in the quality assurance cycle and research activity	<p>The diagnostic workforce is recruited to and upskilled by diagnostic academies.</p> <p>Clinicians are supported by an innovative nonmedical diagnostician workforce.</p> <p>Efficient digitized and AI-assisted diagnostics enable clinicians to work at the top of their licence.</p>
The cancer patient record is delivered on a modern and resilient IT platform that enables greater integration of care and provides the relevant data to guide service development	A once-for-Wales interoperable digital infrastructure seamlessly underpins diagnostic service provision.
Cancer services collaborate through the clinical network to ensure transparency and support equity of access and consistency in standards of care	<p>A culture of information sharing and collaboration is encouraged between health boards and trusts.</p> <p>Regional diagnostic hub and lung health check services are designed to benefit those most disadvantaged by cancer in Wales.</p>
Person-centred cancer care is culturally embedded and supported by a common approach to assessing and managing people's needs	<p>A patient-centred rapid diagnostic philosophy is implemented, supported by rapid and community diagnostic centres.</p> <p>Compassionate social and nonmedical prescribing is sensibly deployed across Wales.</p>
Recommended population and targeted screening programmes are available, uptake meets service standards and participation is equitable	<p>Enabled by a more efficient diagnostic service, bowel cancer screening is optimized into a world-leading service.</p> <p>Lung health checks are implemented across Wales.</p>
Horizon scanning of transformative innovations supports more rapid and widespread local adoption	Incoming innovations, such as liquid biopsies, are planned for by Wales-representative landing committees.
More cases of cancer are detected at earlier, more treatable stages through more timely access to diagnostic investigations	By these combined innovations, more cancers are detected at earlier stages, enabling better treatment, better quality of life, and more people surviving their cancers.

Annex 2: Contributing organisations

We give our thanks to members of the following organisations who participated in discussions that informed this roadmap:

- Aneurin Bevan University Health Board
- Betsi Cadwaladr University Health Board
- Cardiff and Vale University Health Board
- Cwm Taf Morgannwg University Health Board
- Swansea Bay University Health Board
- Velindre NHS Trust
- Public Health Wales
- Digital Health and Care Wales
- National Imaging Academy Wales
- Bangor University
- Cardiff University
- Telemedicine Clinic
- Cancer Research UK

References

1. Welsh Government. The quality statement for cancer. <https://gov.wales/quality-statement-cancer-html> (2021).
2. Welsh Government. *A Healthier Wales: our Plan for Health and Social Care*. (2018).
3. WCISU. *Cancer Incidence in Wales, 2002–2018*. <https://phw.nhs.wales/services-and-teams/welsh-cancer-intelligence-and-surveillance-unit-wcisu/cancer-incidence-in-wales-2002-2018/> (2021).
4. BBC News. Cancer consultant fears for patients in Wales. 1–8 <https://www.bbc.co.uk/news/uk-wales-58677549> (2021).
5. BBC News. Covid : Radiologist shortage adds to Wales ' NHS pressures. 1–12 <https://www.bbc.co.uk/news/uk-wales-56906674> (2021).
6. The Royal College of Pathologists. *Briefing: The pathology workforce in Wales*. (2019).
7. CRUK. *Cancer Research UK position paper: The diagnostic workforce in Wales*. https://www.cancerresearchuk.org/sites/default/files/cancer_research_uk_workshop_on_ai_and_the_diagnostic_workforce_meeting_note_0.pdf (2018).
8. StatsWales. Diagnostic and Therapy Services Waiting Times by week.
9. StatsWales. Suspected cancer pathway (closed pathways): The number of patients starting their first definitive treatment and those informed they do not have cancer by local health board, tumour site, age group, sex, measure and month. <https://stats.wales.gov.wales/Catalogue/Health-and-Social-Care/NHS-Hospital-Waiting-Times/Cancer-Waiting-Times/Monthly/suspectedcancerpathwayclosedpathways-by-localhealthboard-tumoursite-agegroup-gender-measure-month>.
10. BBC News. New cancer clinic 'cuts waiting times by 92%'. (2020).
11. Moondance Cancer Initiative. Early detection & diagnosis. <https://moondance-cancer.wales/research-insights/insight-early-detection-diagnosis>.
12. CRUK. *Early Detection and Diagnosis of Cancer: A Roadmap to the Future*. <https://www.cancerresearchuk.org/funding-for-researchers/research-opportunities-in-early-detection-and-diagnosis/early-detection-and-diagnosis-roadmap> (2020).
13. Quinn-Scoggins, H. D. *et al.* Cancer symptom experience and help-seeking behaviour during the COVID-19 pandemic in the UK: A cross-sectional population survey. *BMJ Open* **11**, 1–15 (2021).
14. BBC News. Covid: Welsh NHS warns waiting list backlog could take years to clear. 1–7 <https://www.bbc.co.uk/news/uk-wales-58698189> (2021).
15. Richards, M. Diagnostics: Recovery and Renewal. Report of the Independent Review of Diagnostic Services for NHS England. 98 (2020).
16. Worthington, P. Hospital waiting times: a mountain to climb. *Senedd Research* 1–8 <https://research.senedd.wales/research-articles/hospital-waiting-times-a-mountain-to-climb/> (2021).
17. Fitzgerald, R. C. *et al.* 634 Results From the Barrett's Oesophagus Trial 3 (Best3): a Randomised Controlled Trial Comparing the Cytosponge™–Tff3 Test With Usual Care To Identify Oesophageal Precancer in Primary Care Patients With Chronic Gastroesophageal Reflux. *Gastroenterology* **158**, S–136 (2020).
18. Fitzgerald, R. C. *et al.* Cytosponge–trefoil factor 3 versus usual care to identify Barrett's oesophagus in a primary care setting: a multicentre, pragmatic, randomised controlled trial. *Lancet* **396**, 333–344 (2020).
19. Offman, J. *et al.* Barrett's oEsophagus trial 3 (BEST3): Study protocol for a randomised controlled trial comparing the Cytosponge–TFF3 test with usual care to facilitate the diagnosis of oesophageal pre-cancer in primary care patients with chronic acid reflux. *BMC Cancer* **18**, (2018).
20. Shariff, M. K. *et al.* Randomized crossover study comparing efficacy of transnasal endoscopy with that of standard endoscopy to detect Barrett's esophagus. *Gastrointest. Endosc.* **75**, 954–961 (2012).
21. Arantes, V. *et al.* Effectiveness of unsedated transnasal endoscopy with white–light, flexible spectral imaging color enhancement, and lugol staining for esophageal cancer screening in high-risk patients. *J. Clin. Gastroenterol.* **47**, 314–321 (2013).
22. Parker, C., Alexandridis, E., Plevris, J., O'Hara, J. & Panter, S. Transnasal endoscopy. No gagging no panic! *Frontline Gastroenterol.* **7**, 246–256 (2016).
23. Lin, L. F., Ma, K. Z. & Tu, H. L. A prospective randomized study comparing transnasal and peroral 5–mm ultrathin endoscopy. *J. Formos. Med. Assoc.* **113**, 371–376 (2014).
24. Wang, C. H. *et al.* Use of transnasal endoscopy for screening of esophageal squamous cell carcinoma in high-risk patients: Yield rate, completion rate, and safety. *Dig. Endosc.* **26**, 24–31 (2014).
25. Tanuma, T., Morita, Y. & Doyama, H. Current status of transnasal endoscopy worldwide using ultrathin videoscope for upper gastrointestinal tract. *Dig. Endosc.* **28**, 25–31 (2016).
26. Hassan, C., Zullo, A., Winn, S. & Morini, S. Cost-effectiveness of capsule endoscopy in screening for colorectal cancer. *Endoscopy* **40**, 414–21 (2008).
27. Spada, C. *et al.* Meta-analysis Shows Colon Capsule Endoscopy Is Effective in Detecting Colorectal Polyps. *Clin. Gastroenterol. Hepatol.* **8**, 516–522.e8 (2010).
28. Möllers, T. *et al.* Second-generation colon capsule endoscopy for detection of colorectal polyps: Systematic review and meta-analysis of clinical trials. *Endosc. Int. Open* **09**, E562–E571 (2021).

29. Kroijer, R., Kobaek-Larsen, M., Qvist, N., Knudsen, T. & Baatrup, G. Colon capsule endoscopy for colonic surveillance. *Color. Dis.* **21**, 532–537 (2019).
30. BBC. Pill camera procedure launched in fight against bowel cancer. <https://www.bbc.co.uk/news/uk-scotland-tayside-central-55130655> 1–7 (2020).
31. NHS England. NHS rolls out capsule cameras to test for cancer. 1–3 <https://www.england.nhs.uk/2021/03/nhs-rolls-out-capsule-cameras-to-test-for-cancer/> (2020).
32. HEIW. NHS Wales Clinical Endoscopist Training Programme. 10–11 <https://heiw.nhs.wales/news/nhs-wales-clinical-endoscopist-training-programme/> (2021).
33. Moondance Cancer Initiative. Innovating the pathology workforce. 2–5 <https://moondance-cancer.wales/projects/bowel-cancer-programme/pathology-training> (2021).
34. NHS Wales & Welsh Government. Digital Architecture Review – Final Report. https://digitalhealth.wales/sites/default/files/2020-04/WG_Digital_Architecture_Review_2019.pdf (2019).
35. Signs, C. C–the Signs – The Tool. <https://cthesigns.co.uk/tool> doi:10.1049/pbpc010e_ch16.
36. Schmidt, M. *et al.* The Danish health care system and epidemiological research: From health care contacts to database records. *Clin. Epidemiol.* **11**, 563–591 (2019).
37. Retamero, J. A., Aneiros-Fernandez, J. & del Moral, R. G. Complete digital pathology for routine histopathology diagnosis in a multicenter hospital network. *Arch. Pathol. Lab. Med.* **144**, 221–228 (2020).
38. Evison, M. *et al.* Implementation and outcomes of the RAPID programme: Addressing the front end of the lung cancer pathway in Manchester. *Clin. Med. J. R. Coll. Physicians London* **20**, 401–405 (2020).
39. Barbieri, A. L., Fadare, O., Fan, L., Singh, H. & Parkash, V. Challenges in communication from referring clinicians to pathologists in the electronic health record era. *J. Pathol. Inform.* **9**, 1–14 (2018).
40. Hanna, M. G. *et al.* Validation of a digital pathology system including remote review during the COVID-19 pandemic. *Mod. Pathol.* **33**, 2115–2127 (2020).
41. Babawale, M. *et al.* Verification and validation of digital pathology (whole slide imaging) for primary histopathological diagnosis: All Wales experience. *J. Pathol. Inform.* **12**, 4 (2021).
42. Corvò, A. *et al.* Visual analytics in digital pathology: Challenges and opportunities. *Eurographics Work. Vis. Comput. Biol. Med. VCBM* **2019** 129–143 (2019) doi:10.2312/vcbm.20191240.
43. Ström, P. *et al.* Artificial intelligence for diagnosis and grading of prostate cancer in biopsies: a population-based, diagnostic study. *Lancet Oncol.* **21**, 222–232 (2020).
44. Ström, P. *et al.* Pathologist-level grading of prostate biopsies with artificial intelligence. *arXiv* (2019).
45. Baldwin, D. R. *et al.* External validation of a convolutional neural network artificial intelligence tool to predict malignancy in pulmonary nodules. *Thorax* **75**, 306–312 (2020).
46. McKinney, S. M. *et al.* International evaluation of an AI system for breast cancer screening. *Nature* **577**, 89–94 (2020).
47. Kim, H. E. *et al.* Changes in cancer detection and false-positive recall in mammography using artificial intelligence: a retrospective, multireader study. *Lancet Digit. Heal.* **2**, e138–e148 (2020).
48. Killock, D. AI outperforms radiologists in mammographic screening. *Nat. Rev. Clin. Oncol.* **17**, 134–134 (2020).
49. NHSx. Mia mammography intelligent assessment. 1–4 <https://www.nhsx.nhs.uk/ai-lab/explore-all-resources/understand-ai/mia-mammography-intelligent-assessment/> (2021).
50. Wong, A. Y. S. *et al.* Association between oral anticoagulants and COVID-19 related outcomes: two cohort studies. *medRxiv* 2021.04.30.21256119 (2021).
51. Sewell, B. *et al.* Rapid cancer diagnosis for patients with vague symptoms: A cost-effectiveness study. *Br. J. Gen. Pract.* **70**, E186–E192 (2020).
52. Vasilakis, C. & Forte, P. Setting up a rapid diagnostic clinic for patients with vague symptoms of cancer: a mixed method process evaluation study. *BMC Health Serv. Res.* **21**, 1–11 (2021).
53. Sindhar, J. *et al.* The success of the Rapid Diagnostic Clinic (RDC) in detecting cancer in patients with non-localizing symptoms. *J. Clin. Oncol.* **38**, 303–303 (2020).
54. Dolly, S. O. *et al.* The effectiveness of the Guy's Rapid Diagnostic Clinic (RDC) in detecting cancer and serious conditions in vague symptom patients. *Br. J. Cancer* **124**, 1079–1087 (2021).
55. Hinde, S. *et al.* The cost-effectiveness of the Manchester 'lung health checks', a community-based lung cancer low-dose CT screening pilot. *Lung Cancer* **126**, 119–124 (2018).
56. UK Government. Press release: 40 community diagnostic centres launching across England. <https://www.gov.uk/government/news/40-community-diagnostic-centres-launching-across-england> (2021).
57. NHS Wales Collaborative. A Framework for the Reinstatement of Cancer Services in Wales during COVID-19. 1–7 (2020).
58. Holland-Hart, D. *et al.* Feasibility and acceptability of a community pharmacy referral service for suspected lung cancer symptoms. *BMJ Open Respir. Res.* **8**, 1–10 (2021).
59. Crosbie, P. A. *et al.* Implementing lung cancer screening: Baseline results from a community-based 'Lung Health Check' pilot in deprived areas of Manchester. *Thorax* **74**, 405–409 (2019).
60. Welsh Government. Prudent healthcare. *Welsh Gov.* 1–2 (2016).
61. Brenner, H. & Werner, S. Selecting a Cut-off for Colorectal Cancer Screening With a Fecal Immunochemical Test. *Clin. Transl. Gastroenterol.* **8**, e111 (2017).
62. Terhaar Sive Droste, J. S. *et al.* Higher fecal immunochemical test cutoff levels: Lower positivity rates but still acceptable detection rates for early-stage colorectal cancers. *Cancer Epidemiol.*

- Biomarkers Prev.* **20**, 272–280 (2011).
63. Eluned Morgan. Written Statement : Optimising Wales ' Bowel Screening Programme. *Welsh Government* 1–2 <https://gov.wales/written-statement-optimising-wales-bowel-screening-programme> (2021).
 64. Bailey, J. A. *et al.* Quantitative FIT stratification is superior to NICE referral criteria NG12 in a high-risk colorectal cancer population. *Tech. Coloproctol.* **25**, 1151–1154 (2021).
 65. D'souza, N., Georgiou Delisle, T., Chen, M., Benton, S. & Abulafi, M. Faecal immunochemical test is superior to symptoms in predicting pathology in patients with suspected colorectal cancer symptoms referred on a 2WW pathway: A diagnostic accuracy study. *Gut* **70**, 1130–1138 (2021).
 66. WCISU. Cancer mortality in Wales, 2001–2017. https://publichealthwales.shinyapps.io/wcisu_cancer_mortality_in_wales_2017/.
 67. CRUK. Lung Health Checks. 1–6 <https://www.cancerresearchuk.org/about-cancer/lung-cancer/getting-diagnosed/lung-health-checks> (2021).
 68. Zhao, Y. R. *et al.* NELSON lung cancer screening study. *Cancer Imaging* **11**, 79–84 (2011).
 69. Yousaf-Khan, U. *et al.* Risk stratification based on screening history: The NELSON lung cancer screening study. *Thorax* **72**, 819–824 (2017).
 70. de Koning, H. J. *et al.* Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial. *N. Engl. J. Med.* **382**, 503–513 (2020).
 71. Field, J. K. *et al.* UK Lung Cancer RCT Pilot Screening Trial: Baseline findings from the screening arm provide evidence for the potential implementation of lung cancer screening. *Thorax* **71**, 161–170 (2016).
 72. Ebell, M. H., Bentivegna, M. & Hulme, C. Cancer-specific mortality, all-cause mortality, and overdiagnosis in lung cancer screening trials: A meta-analysis. *Ann. Fam. Med.* **18**, 545–552 (2020).
 73. Crosbie, P. A. *et al.* Yorkshire Lung Screening Trial (YLST): protocol for a randomised controlled trial to evaluate invitation to community-based low-dose CT screening for lung cancer versus usual care in a targeted population at risk. *BMJ Open* **10**, e037075 (2020).
 74. Du, Y. *et al.* Cost-effectiveness of lung cancer screening with low-dose computed tomography in heavy smokers: a microsimulation modelling study. *Eur. J. Cancer* **135**, 121–129 (2020).
 75. Tomonaga, Y. *et al.* Cost-effectiveness of low-dose CT screening for lung cancer in a European country with high prevalence of smoking—A modelling study. *Lung Cancer* **121**, 61–69 (2018).
 76. Crosbie, P. A. *et al.* Second round results from the Manchester a € Lung Health Check' community-based targeted lung cancer screening pilot. *Thorax* **74**, 700–704 (2019).
 77. Eccles, S. LUNG HEALTH CHECK WALES: Summary of Scoping Project. (2021).
 78. Altomare, D. F. *et al.* Chemical signature of colorectal cancer: case-control study for profiling the breath print. *BJS Open* **4**, 1189–1199 (2020).
 79. Brewer, H. R., Hirst, Y., Sundar, S., Chadeau-Hyam, M. & Flanagan, J. M. Cancer Loyalty Card Study (CLOCS): protocol for an observational case-control study focusing on the patient interval in ovarian cancer diagnosis. *BMJ Open* **10**, e037459 (2020).
 80. Lamb, Y. N. & Dhillon, S. Epi proColon® 2.0 CE: A Blood-Based Screening Test for Colorectal Cancer. *Mol. Diagnosis Ther.* **21**, 225–232 (2017).
 81. Shirley, M. Epi proColon® for Colorectal Cancer Screening: A Profile of Its Use in the USA. *Mol. Diagnosis Ther.* **24**, 497–503 (2020).
 82. Jenkins, C. A. *et al.* A high-throughput serum Raman spectroscopy platform and methodology for colorectal cancer diagnostics. *Analyst* **143**, 6014–6024 (2018).
 83. Leeds in Vitro Diagnostics Co-operative. PinPoint Cancer joins forces with Leeds big data experts. 25–26 (2021).
 84. West Yorkshire and Harrogate Cancer Alliance. What Is The PinPoint Test? 1–4 (2021).
 85. Liu, M. C. *et al.* Sensitive and specific multi-cancer detection and localization using methylation signatures in cell-free DNA. *Ann. Oncol.* **31**, 745–759 (2020).
 86. Klein, E. A. Clinical validation of a targeted methylation-based multi-cancer early detection test. Oral presentation at: American Association for Cancer Research; April, 2021; LB013. in.
 87. NHS. NHS Galleri Trial: detecting cancer early. 9–11 <https://www.nhs-galleri.org/> (2021).



MOONDANCE
CANCER INITIATIVE

Moondance Cancer Initiative helps find solutions so that more people in Wales survive cancer. We actively support people and projects with potential to transform survival outcomes across the country, and we undertake research and insight to inform our work.

www.moondance-cancer.wales

© Moondance Cancer Initiative 2021. Not to be reproduced without permission.