10 years on: accelerating early diagnosis evidence into practice

Highlights from
Cancer Research UK's
fifth biennial Early Diagnosis
Research Conference
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Together we will beat cancer

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The early diagnosis ‘movement’ – 10 years on

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Ten years ago, it was clear that we needed to build an evidence base from which we could translate early diagnosis research into action. The Cancer Reform Strategy[1] for England in 2007 was the first national cancer plan to have a major focus on early diagnosis. This manifested as the National Awareness and Early Diagnosis Initiative (NAEDI),[2] which coordinated action and research across the diagnosis pathway; acknowledging that reducing late stage diagnosis was a multifaceted issue that needed to be tackled on a range of fronts.[3] When the governance arrangements of NAEDI came to an end, the action and research to achieve earlier diagnosis continued. Today we have a thriving, collaborative, multidisciplinary early diagnosis community that works together to forge progress and impact, evidenced by the breadth and quality of research showcased at this year’s conference, and the constructive challenge and enthusiasm with which it was met.

In the past 10 years, investment in targeted activities has encouraged the public to seek help for symptoms sooner and led to more patients being urgently referred. These campaigns have shown that they can shift both public and health professional behaviour and, in some cases such as lung cancer, we have been able to measure stage shift and improved diagnosis.[4]

A decade ago we had three national cancer screening programmes in place. The newest of these, for bowel cancer screening, is now well embedded; and the introduction of more effective screening technologies has improved population screening, including faecal immunochemical testing (FIT) in the bowel screening programme, and the introduction of human papillomavirus (HPV) as the primary test in cervical screening.

The International Cancer Benchmarking Partnership has highlighted the contribution of stage at diagnosis to international survival differences, and has explored several other potential contributory factors. This included the finding that GPs in the UK have a lower propensity to refer patients for tests at the earliest opportunity than counterparts in comparable countries.

Looking back, the role of primary care in early diagnosis was poorly understood 10 years ago, but there is now an active and productive research effort in this area. Our understanding has been boosted by studies investigating symptomology of patients prior to a diagnosis. This has helped to inform cancer referral guidelines and has supported policy to increase GP direct access to tests. Primary care research has underpinned the development of guidance to support GPs, ensuring that patients can receive the attention they need in a timely and effective manner.

We've also seen a transformation in our understanding of what's needed in diagnostic pathways. For too long, GPs depended on red flag two-week referral pathways. Now, we have the emergence of multidisciplinary centres (MDCs) or rapid diagnosis centres (RDCs) – a pathway that GPs can refer patients with serious non-specific symptoms on to. These pathways have increased the rapidity of diagnosis and prevent the shuttling of patients between primary and secondary care.

This research and action has been made possible by major improvements in data and intelligence over the last decade. The publication of national staging data shines a light on areas of need and provides a baseline from which to measure improvement. We have started to embed audit in primary care in a way that we couldn't before, with the National Cancer Diagnosis Audit (NCDA), and we are now able to understand the whole pathway by linking cancer registration records to primary care data. The Routes to Diagnosis methodology allows us to identify the way in which cancer patients are diagnosed and the impact this has on survival, showing us how critical it is to avoid emergency presentations.

A decade on, however, late stage diagnosis of cancer is still a problem. Cancer Research UK has, for several years, had an ambition for 3 out of 4 cancers to be detected at stage I and II by 2034, accompanied by a reduction in late stage disease. Recently in England, the NHS has set an even more ambitious target, seeking 3 in 4 at stage I and II by 2028. Such ambitions seek to increase impetus and accelerate progress and impact. This year's conference celebrates the collective advances we have made, the evidence we now have and the opportunity this presents in terms of tackling the key drivers of late diagnosis. Now we need to galvanise our efforts to get us closer to this ambitious goal within the next decade.

This is a bold target, and one we definitely won't meet unless we come together as a community and challenge ourselves to accelerate progress.

Keynote:
Professor Sir Mike Richards,
former National Cancer Director and Trustee of Cancer Research UK

We have made progress, but there is 'unfinished business' in closing the cancer survival gap, Professor Sir Mike Richards said in his keynote presentation.

He began by reflecting on how far we have come since the 1970s when he qualified as a doctor, a time he referred to as 'the dark ages', when there was a strong feeling of fatalism associated with cancer, and a lack of strategies or clinical guidelines. The early diagnosis 'alarm' was then raised in 1995 with the Calman-Hine report,[5] but it was only in 2007 with the Cancer Reform Strategy[1] that an evidence-based focus on early diagnosis truly began.

Although there is now a strong consensus that late stage diagnosis plays an important role in the UK's lagging cancer survival figures, this was not the view 20 years ago, Sir Richards said, when concerns were instead expressed about validity of cancer registration and there was little in the way of primary care research.

Even so, we haven't made as much progress as hoped, Sir Richards said, because the burden of cancer is ever increasing, in part because of an ageing population. The UK's tight gate-keeping model in primary care and issues such as poor diagnostic access and difficulties getting a GP appointment contribute to some of the challenges in securing a timely cancer diagnosis. The solution, Sir Richards argued, is a major programme of engagement with patients and GPs. We need to engage the public because we know they are worried about wasting GP time. But we also need to engage GPs, who in the UK are less likely to investigate symptoms or refer than in other countries.

Workforce is also an issue, Sir Richards warned. Despite a number of commitments in the NHS Long Term Plan to achieve an ambition of diagnosing 3 in 4 patients at an early stage by 2028,[6] this will only happen with proper investment and a focus on workforce, he said. It's an ambition worth going for, he concluded, but now we've got to go for it wholeheartedly.

Keynote: CT lung cancer screening – after NELSON

Professor Harry De Koning, Professor of Public Health and Screening, Erasmus University

The NELSON trial is the second largest randomised lung cancer screening trial to date and provides unique evidence because of its long-term follow-up. Results so far show that CT scanning decreased deaths from lung cancer by 26% in high-risk men and up to 61% in high-risk women over a 10-year period – revealing an important gender difference.[7] In his keynote, Professor De Koning discussed whether lung cancer screening studies present an opportunity to learn more about the natural history of lung cancer; as the amount of cancers you detect provides an idea of duration of disease. In NELSON, for example, nearly 7 in 10 cancers detected through screening were early stage IA or IB, but many of the interval cancers were late stage.

Professor De Koning also raised the issue of over-diagnosis, and the costs and benefits of lung cancer screening, and drew comparisons with existing cancer screening programmes. New data on cost-effectiveness and age were presented, which suggested that the starting age does not matter (starting ages of between 50 and 70 have similar cost-effectiveness), but if you stop screening too early, the cost-effectiveness reduces because most risk occurs in later age, especially in smokers. In terms of intervals, annual screens look to be the most cost-effective, but Professor De Koning commented on the continued need to look to the future and for opportunities for more intelligent, tailored screening, with the first screen providing data with which to individualise the interval for subsequent screens.

> “I loved listening to the progress being made as well as plans for future developments”
>
> Conference attendee

A decade’s difference in lung cancer

In his reflections on Day One, **Professor Sir Mike Richards** commented that 10 years ago we could not have filled a two-hour conference session on the topic of lung cancer early diagnosis research – a clear demonstration of the progress that has been made in this area. Introducing the Spotlight on Lung Cancer session earlier in the day, **Dr Mat Callister, Leeds Teaching Hospitals NHS Trust**, shared evidence from the Leeds Early Lung Cancer campaign that symptom awareness and more public and health professional action could be translating into better outcomes, with a 9% reduction in lung cancer mortality coinciding with the post-campaign period.[8] The challenges of the evaluation design mean it is not possible to be certain that the findings were caused by the campaign, but they are highly encouraging.

One of the take-home messages from this session was the need for multi-faceted, integrated, community-based interventions for those at most risk of lung cancer. **Dr Grace McCutchan, Cardiff University**, shared data from interviews with people at high risk of lung cancer in the UK’s most deprived communities, exploring symptom attribution and help seeking. Among the common themes was a perception of feeling unworthy of seeking medical help, and the importance of not being judged. It was suggested that the primary messaging used in current awareness interventions may not be specific enough for this group: a persistent cough would not be relevant for chronic obstructive pulmonary disease (COPD) sufferers, for example. There may be a benefit to focusing on a change in what is normal for them – a message which is often found in supporting campaign material, but not always featured prominently across the range of media.

Interestingly, **Dr Aradhna Kaushal, University College London (UCL)**, showed that the attribution of cough and breathlessness to cancer is no different in people with comorbidities such as asthma and COPD, but found that women were more likely to contact a GP about these symptoms.

Building on Professor De Koning’s evidence for lung cancer screening, we heard from **Dr Sammy Quaife, UCL**, about the importance of understanding its psychological impact. She presented a comparison of anxiety levels in lung cancer screening participants and those who have never been offered screening. Anxiety levels were higher in the screening group, but there was no evidence of clinically significant adverse impact. She suggested that future screening services should monitor psychological responses and use evidence-based communication strategies to minimise potential distress.

Dr Hilary Robbins, US National Cancer Institute and the International Agency for Research on Cancer (IARC), provided a fascinating insight into the management of ground glass opacities (GGOs) – partial filling of air spaces in the lungs – identified through CT screening. Current US guidance (Lung-RADS) has a high diameter threshold for GGOs: those larger than 20mm are managed with six-month scans and those smaller than 20mm by annual screening. But retrospective analysis suggests this management misses cancers. Analysis of diameter-specific malignancy probability for both solid nodules and GGOs suggests that GGOs smaller than 20mm should receive closer follow-up than is currently the case in the US.

Although still lagging behind other cancers, the net survival from lung cancer has slightly increased.[9] But with this comes a new challenge – an increased likelihood of a second cancer. **Professor Robert Rintoul, Cambridge University**, presented data showing that lung cancer survivors, particularly women, have an increased incidence of smoking-related primary cancers for at least a decade after their first lung cancer. Those aged 50–79 are particularly at risk. The incidence rates of a second different primary cancer, and of a second primary lung cancer, continue to rise after routine five-year follow-up. This raises the question of whether follow-up should be extended from five to 10 years, especially for people aged 50–79.

Diagnosing rare and less common cancers earlier

Keynote: Closing the ovarian cancer survival gap
Mr John Butler,
Consultant Gynaecological Oncology Surgeon, The Royal Marsden NHS Foundation Trust

Survival from ovarian cancer is lower in the UK than in many other countries. In his keynote speech, Mr Butler described evidence from the International Cancer Benchmarking Partnership (ICBP) which is helping to explain this survival gap – and it seems there are multiple factors at play.

First, a vignette study revealed that when posed with the same potential ovarian cancer case studies, fewer than 40% of GPs in England, Northern Ireland or Wales would refer or investigate, compared to over 60% in Australia and Canada, where cancer survival is much better.[10]

Second, in Denmark, PET CT scanning alongside lymphadenectomy has been introduced, which has resulted in a stage shift towards more advanced disease, but better survival. So, it appears that patients diagnosed without PET CT are likely have their disease stage underestimated and potentially receive treatment that is too conservative.

Data from ICBP module 1 suggest that treatment differences could underlie the poorer outcomes in this country, because the UK has lower survival of people with stage III and IV ovarian cancer compared to other nations. The main determinant of survival of advanced ovarian cancer is whether residual disease remains after surgery. This might be helped by the further centralisation of ovarian cancer surgery,[11] meaning more operations are performed by accredited gynaecological oncologists. However, an unpublished survey of UK gynaecological oncologists suggests that there is not enough radical surgery taking place: 78% of respondents gave an average operating time of less than three hours. This is further complicated by the fact that most women requiring surgery in the UK are over 70 and have multiple comorbidities. Undertreatment may therefore be an important factor in the UK's poorer outcomes.

> ...night sweats were among the five most frequently reported symptoms in four of nine cancer groups that were identified, and could represent a key symptom to raise awareness of ...

Rare and less common cancers provide even greater challenges to GPs and patients alike when it comes to recognising and acting on signs and symptoms. **Jane Lyons, CEO of Cancer52**, an alliance of nearly 100 charities working in rare and less common cancers, chaired this session on some of the efforts being made to track back from a rare cancer diagnosis to find clues that could help with earlier diagnosis.

Dr Fiona Walter, Cambridge University, kicked off this session with insights gained from conducting interviews with people diagnosed with brain tumours soon after their diagnosis. The goal was to understand the patient perspective on symptom appraisal, seeking help and their routes to diagnosis. Conversations with 39 patients and their families suggest that people experience 'changes' rather than symptoms, often first noticed by others. These included headaches, seizures, changes in sleep and changes in cognition, but were often blamed on stress, tiredness, age, mental health, recent events or existing illness, rather than a new medical condition. Approaches to remedy some of these issues could include exploring the development and impact of a triage tool that includes cognitive assessment.

The incidence of bladder and kidney cancer in women is increasing, while survival is getting worse. **Dr Yin Zhou, Cambridge University**, presented results from a systematic review assessing factors that affect the quality of diagnosis for these cancers. She found that up to two-thirds of people with blood in their urine received no further evaluation up to six months later. Women were also much less likely to be referred in accordance with guidelines and had longer diagnostic intervals than men. The results suggest that a urinary tract infection (UTI) diagnosis can be a decoy and can mask other, more serious diagnoses, and that digital technology developments which help to flag the right patients may help to better stratify risk.

We also heard from **Dr Monica Koo, UCL**, about the lack of epidemiological evidence for symptoms of cancer in teenagers and young adults (TYA). Patient survey data show that the majority of TYAs present with multiple symptoms; in fact, in the BRIGHTLIGHT cohort there were 357 unique symptoms combinations and the 10 most frequent combinations only accounted for 37% of patients. Time to presentation also varied by symptom. The large spectrum of symptoms makes it hard to identify targets for early diagnosis. However, night sweats were among the five most frequently reported symptoms in four of nine cancer groups that were identified, and could represent a key symptom to raise awareness of in this patient group.

Optimising patient pathways

Keynote:
Professor Willie Hamilton CBE, Professor of Primary Care Diagnostics, Exeter University

Professor Willie Hamilton CBE kicked off Day Two of the conference with a keynote speech that took us all back to the 1960s, when cancer was not really something that was prioritised in primary care. Indeed, most GPs never found out what happened to the people they had referred on, so there was no feedback on whether symptoms turned out to be important or not. Then came the growing awareness that UK cancer outcomes were poor, and through ICBP we began to see that our tendency to refer was low compared with other nations.[12] Cancer recognition and referral was revolutionised by the two-week-wait pathway[13] and the subsequent increase in referrals has supported improved patient outcomes, albeit at the cost of tensions between primary and secondary care. Coming two years after the CanTest Collaboration[14] was launched, Professor Hamilton is still sure that the future impact lies in the right tests, at the right time, for the right patient and at the right cost.

How well are patient and GP motivations aligned during a consultation? According to research presented by **Dr Georgia Black, UCL**, a consultation is a dynamic process – a constantly evolving negotiation over symptom attribution and next steps. Analysis of 200 video recordings of GP-patient consultations showed that problems can arise when GPs don't adequately address patients' emotional concerns and instead focus on clinically interpreting the symptoms. As a result, patients may not attend follow-up appointments, may change GPs and lose trust in the healthcare system.

One avoidable delay in diagnosis is the 'ping-pong' effect when patients are shuttled between primary and secondary care before being given (or not) a definitive cancer diagnosis. **Mr Alexander Thomson, Epsom and St Helier University Hospitals NHS Trust**, discussed a pilot pathway using Physician Associate Telephone Assessment Clinics in patients who have concerning symptoms but do not meet the two-week-wait referral criteria. Of 130 patients triaged, 3% were found to have colon, lung or stomach cancer. These patients were likely to have otherwise been referred back and forth, delaying their diagnosis.

Repeat referrals was also covered by **Dr Henry Jensen, Aarhus University**, who explained how non-specific digestive tract symptoms and the loose referral criteria for bowel cancer in Denmark cause challenges for GPs. A study of 110,000 initially negative cancer diagnostic investigations showed that after six months, 6.1% started a second cancer-site specific pathway, and 0.6% of those had cancer. Some were missed cancers, but others were within the same anatomical area, suggesting that a whole digestive system referral pathway might be needed.

In some countries, multiparametric magnetic resonance imaging (mpMRI) is routinely used in prostate cancer diagnosis and staging, but this is not the case in the UK. **Dr Sam Merriel, Exeter University**, presented the outcomes of a mapping study looking at mpMRI availability across England. Although 13 of 19 cancer alliances had some access to mpMRI, its use varied. NHS England has developed a handbook[15] for service providers to deliver a timed prostate pathway, which includes use of mpMRI. Yet there is still work to be done to optimise how and when this technology is used, and the capacity of equipment and workforce presents a challenge.

We also heard from **Dr Sarah Price, Exeter University**, that the same workforce strain may be hindering the impact of the 2015 National Institute for Health and Care Excellence (NICE) cancer recognition and referral guidelines on time to diagnosis (NG12). Preliminary analysis of diagnostic intervals since the NG12 guidance was published showed that results varied by cancer site. For ovarian cancer, where changes to recognition and referral guidelines were made in 2011, there was evidence of a reduced time to diagnosis. The pooled diagnostic interval (across all cancer types) showed an increase in the time to diagnosis, but this may reflect the challenges the health service faces in dealing with the demand generated by the lower referral threshold.

Advances in breast cancer and cervical screening

Targeted screening in breast cancer

Risk-stratified breast cancer screening would mean that women at higher risk have more frequent mammograms and women at lower risk get less frequent mammograms. The Predicting the Risk of Cancer at Screening (PROCAS) studies are looking at integrating breast cancer risk scores into screening. Risk is based on self-reported information about health, hormones, diet and lifestyle, and the Tyrer-Cuzick model, which incorporates family history and breast density.

Professor David French, Manchester University, presented data from the first PROCAS study on the psychological impact of receiving breast cancer risk estimates. Women were slightly more anxious if waiting for results, or if found to be at higher risk, but overall had fairly low anxiety levels.

Dr Louise Donnelly, Manchester University Hospital NHS Foundation Trust, shared the results from focus groups with healthcare professionals looking at the feasibility of automating risk estimation as a routine part of screening (PROCAS2). These results highlighted the importance of explaining the concept of 'high risk', and ensuring a clear pathway of next steps and concerns around whether all participants would be in a position to make an informed choice, with potential implications for widening inequalities. Workforce concerns and system restraints were also flagged as a key consideration.

In the final session, **Professor Gareth Evans, Manchester University**, spoke of the future and whether polygenic risk scores are ready to be used in breast cancer screening. He argued that single nucleotide polymorphisms (SNPs) are far more useful than extended gene panels, and could meaningfully change the risk in half of the breast cancer screening population.

As a follow-up to PROCAS2, he said they would do some work with low-risk women to work out what screening intervals would be acceptable.

Spotlight on cervical screening

In the context of declining coverage, and the roll-out of HPV testing as the primary test in the national cervical screening programme, this spotlight session focused on women's perceptions around HPV and cervical cancer risk.

Professor Jo Waller, UCL, presented data on awareness and understanding of HPV, and the psychological impact of different HPV results. She found much higher awareness in people with recurrent HPV, suggesting awareness is not being raised at the most appropriate time. In those aware of HPV, the least understood aspect was that HPV does not usually require treatment. Women in the HPV-positive group were the least likely to be 'moderately' or 'very' confident that they understood their result. This suggests that different approaches may be needed to communicate changes to the screening programme.

Women who 'intend' to go for screening make up the largest group of non-attendees. **Mairead Ryan, UCL**, discussed the practical barriers that prevent this group making it to their appointment. Among the most common reasons were difficulty getting through to a receptionist or challenges with calling the practice during opening hours, forgetting to book after reading the invitation letter, lack of choice for appointment times, and queries about being able to change the appointment after booking. Endorsement of these barriers by 'maintainers' – those who regularly attended their appointments – suggests that both groups would benefit from more support with appointment booking.

Women aged 50 to 64 are increasingly less likely to be screened for cervical cancer, yet with the introduction of the HPV vaccination protecting younger women, it will be the 50 to 64 age group that will have the highest cervical cancer incidence rates in the immediate future. **Laura Marlow, UCL**, presented results from a study which tested whether presenting information about the timeline of HPV would increase the perceived risk of cervical cancer in older women, as well as improve their intention-to-attend screening. She conducted an online experimental study involving women aged 50 to 64 who do not intend to go for screening when next invited. It was found that when providing information about the timeline of HPV, intention strength and risk perception increased, and there was a statistically significant improvement in agreement (from 53% to 88%) of the statement 'I understand how HPV can cause cervical cancer'. However, the study also shows that shifting perceptions is difficult and we don't yet know whether this shift in understanding would translate into behaviour change.

...women who 'intend' to go for screening make up the largest group of non-attendees in cervical screening...

And finally, **Robert Music, Jo's Cervical Cancer Trust**, asked whether the myths and stigma associated with HPV risk would put people off attending their screening appointment. Survey work conducted by the charity has demonstrated shame or fear associated with HPV; with 39% of people being worried about what people would think if they told them they had HPV, 42% worrying that their partner had been unfaithful, and 48% being put off having sex with their partner. With an increase in the number of HPV-related helpline calls and online searches already, there is a need to reduce the anxiety surrounding the virus to ensure women understand what their result means and that they are not ashamed or scared of it.

"It was fantastic to have the opportunity to hear and meet so many key people in the fast developing field of ED research and to share learnings from across the country"

Conference attendee

What is FIT fit for?

25% of people who had a positive FIT have not had a follow-up appointment yet

Keynote:
Professor Robert Steele CBE,
Senior Research Professor,
University of Dundee

Professor Robert Steele CBE, Chair of the UK National Screening Committee, used his keynote to outline what makes a good screening programme, before reflecting on the introduction of the faecal immunochemical test (FIT) into the bowel cancer screening programme in Scotland. He reminded the audience of the necessary criteria for population screening, and the bias that can occur in interpreting outcomes of screen-detected versus symptom-detected disease.

In November 2017, FIT went live in the Scottish bowel cancer screening programme, using a threshold of 80µg Hb/g faeces for determining a positive result referral. FIT has advantages over the Guaiac faecal occult blood test (FOBT) as it is quantitative and easier to do, requiring only a single poo sample. As a result, he said, Scotland has seen increased uptake of bowel cancer screening – with the greatest increase in men and people living in the most deprived areas. This higher uptake and sensitivity of FIT has increased colonoscopies by 100%.

So given FIT's credentials, could we be even smarter with it? Professor Steele asked whether in the future we could vary the cut-off threshold by screening interval, or vary interval by the faecal haemoglobin level. And could using FIT in the symptomatic population support better use of endoscopy services?

> "I found the talks to be so relevant and insightful, and the atmosphere to be collaborative and genuine"
>
> Conference attendee

FIT for people with symptoms of colorectal cancer

In 2017, NICE published diagnostic guidance[16] that recommended the adoption of FIT in primary care, using a threshold of 10µg Hb/g faeces, to guide referral for suspected colorectal cancer (CRC) in people without rectal bleeding who have unexplained symptoms but do not meet the criteria for a suspected cancer pathway referral.

Dr Lance Saker, Transforming Cancer Services Team for London, shared the steps needed to support FIT being rolled out in a resource-poor setting in London. He talked through the process of setting up a steering group, and agreeing a pathway and a network pathology model. There were some issues still to be worked through, for example how best to safety net patients who have a negative FIT result. Key insights from implementation were that regular meetings and communication are crucial, as the landscape changes quickly as evidence evolves, and how to achieve early diagnosis while managing the increase in service demand.

Dr Brian Nicholson, Oxford University, presented his experience of adopting FIT for symptomatic patients in Oxford. The profile of patients referred for colonoscopy showed that there were some red flag symptoms, but it is possible for GPs to assess a patient with a red flag symptom as low risk overall. They found that FIT had a 21.4% positive predictive value (PPV) for colorectal cancer (FIT threshold 10µg/g), and that 10µg Hb/g faeces seemed best for balancing false positive and negative results overall.

Determining the optimum threshold for FIT was also discussed by **Dr Sarah Bailey, Exeter University**, who presented data from an ongoing evaluation of the South West Cancer Alliance FIT programme. Initial results showed that 25% of people who had a positive FIT have not had a follow-up appointment yet (although this could be due to missing data), and they had not seen the hoped for reduction in colonoscopy referrals so far. It was too early to report on stage of detected cancers, and missing data meant they did not have a picture of the number of negative FIT results.

Finally, **Mr Nigel D'Souza, Croydon University Hospital**, described the NICE FIT study, which is investigating whether FIT can be used to exclude bowel cancer in people with suspect symptoms referred via the two-week-wait (2WW) pathway, contributing to the evidence on using FIT in high-risk patients.

One of the takeaway messages from this session was the difficulty of having two different drivers for using the test – preventing everyone on a 2WW pathway going straight to colonoscopy (high-risk use), and also ruling some people in who don't meet the symptoms for the urgent 2WW pathway (low-risk use).

How are we doing with data?

We might not yet be leading the world in cancer survival, but we have access to data that will help us to close that gap. Chairing one of two sessions focused on cancer data, **Dr Jem Rashbass, Public Health England**, reminded us how much the data landscape has changed in the past decade, with a focus on developments in England.

The situation has moved from having only basic incidence, mortality and survival data, to detailed data on patient demographics, use of chemotherapy and radiotherapy (through the systemic anti-cancer therapy [SACT] database and radiotherapy dataset [RTDS], respectively), routes to diagnosis, and more detailed staging data. The future, Dr Rashbass said, is to take a pathway approach to data, such as the Prostate Cancer Pathway tool, which allows visualisation of 200–300 'events' per patient, capturing the entire pathway from detection of inherited prostate cancer risk to death, and shining a light on opportunities for improvement.

In subsequent sessions, **Dr Thomas Round, Kings College London**, described using data to study associations between referral practice and cancer mortality. Data from a cohort of more than 1.4 million patients, from 2011/12 to 2015/16, showed that higher use of urgent referral lowered patient mortality by 4–5% over five years for all cancers, and decreased late stage disease for all but colorectal cancer.

Dr Sean McPhail, Public Health England, presented analyses which further explore emergency referrals and presentations; trying to unpick the route of these cases and their interaction with primary care. Delving into Routes to Diagnosis and NCDA datasets, Dr McPhail set out to answer two questions: 1) what proportion of emergency presentation patients have prior contact with GPs; and 2) how do emergency referrals and emergency presentations inter-relate? He reported a complex picture: of the 3,319 emergency presentation cases captured in the audit (patients diagnosed in 2014), around a third had no prior contact with their GP, a further third had contacted their GP and not been referred, and the remainder had a progression of their cancer during the referral or investigation process. Dr McPhail's original hypothesis was that GPs were unaware of the presentation status of some emergency presentations. Although not untrue, the data tell us that this is not the full story and that the 'standard' narrative of clearly separated emergency and elective routes is a significant over-simplification. The presentation illustrated how, by using linked data, it becomes possible to meaningfully categorise emergency presentations according to their place on the primary care cancer pathway. The linked data are available from Public Health England via the Office for Data Release.

Also using NCDA data, **Dr Ruth Swann, Cancer Research UK and Public Health England**, studied delays to diagnosis that GPs considered to be 'avoidable', and looked at the impact on overall time from presentation to diagnosis. Of 17,042 patients in the analysis, almost a quarter (24%) had an avoidable delay.[17] Among the results, she found that people with a greater number of comorbidities were most likely to have an avoidable delay, as were those with pancreatic, bowel, stomach, rectal or oral/oropharyngeal cancer. The proportion of avoidable delay varied by route – those from a routine referral had the highest odds of an avoidable delay, followed by urgent referrals and emergency presentation. The phase in the pathway where the avoidable delay occurred also varied by cancer site. For example, in breast cancer, help-seeking was the area where most avoidable delay was reported, whereas in stomach cancer the avoidable delay was in waiting for tests or test results.

Finally, **Dr Josephine French, Public Health England**, presented her analyses of pre-diagnostic prescription data. The project exemplifies the interest in big data and whether it is possible to identify an early signal of cancer diagnosis. She looked at prescription data in the nine months prior to a diagnosis with bowel or lung cancer and compared this with a matched cohort, and found a cancer site-specific increase in certain prescriptions for both. The next step is to apply machine learning to the data to investigate the predictive value of different prescription combinations.

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Spotlight on national cancer pathways

Gregor McNie, Head of External Relations (Devolved Nations) at **Cancer Research UK**, chaired a session focusing on opportunities to improve pathways to diagnosis with increased efficiency, investment and recruitment – challenges faced by all nations of the UK. There was much discussion about the need for greater collaboration between healthcare professionals and those working on the early diagnosis research pipeline, to enable optimal pathway design and implementation.

Professor Tom Crosby OBE, Cardiff Velindre Cancer Centre, shared the experience of implementing a Single Cancer Pathway in Wales. The pathway was announced in November 2018 by Vaughan Gething from the Welsh Government, and has been implemented from June 2019. For the first time, health boards will record how long patients wait from the point a cancer is first suspected until it is diagnosed, regardless of the way they enter the healthcare system. The aim is to reduce the intervals to diagnosis for cancer patients, regardless of the route to diagnosis, and will require optimal capacity and effective measurement processes and systems.

Margaret Kelly, Scottish Government, discussed the work of the National Cancer Framework Consultancy, which is building a picture of how well individual health boards achieve their cancer waiting time targets. This involves reviewing responsibilities, organisational structures, referral processes, pathway tracking/reporting, capacity and the use of MDTs, while engaging with and facilitating conversations with stakeholders across the pathway. The process will lead to local recommendations on how to improve cancer diagnosis and will facilitate the development of service improvement plans.

David Fitzgerald, Director of the NHS Cancer Programme in England, presented on how the NHS Long Term Plan for England aims to accelerate the early diagnosis of cancer. An implementation framework was published in June 2019, and improved governance through engagement of clinical staff and key opinion leaders is proposed. Mr Fitzgerald echoed many of the points that Cally Palmer, National Cancer Programme Director, made in her keynote session but described how the plans are going to be operationalised, highlighting the importance of collaboration with partners and this research community at the conference to ensure progress is made. He also emphasised that the scale of the early diagnosis challenge is different across distinct cancer types.

> I thoroughly enjoyed the 3 days and greatly appreciated having the opportunity to hear about the pioneering research being conducted.
>
> Conference attendee

Highlights from Cancer Research UK's fifth biennial Early Diagnosis Research Conference

Are Multidisciplinary Diagnostic Centres working?

Multidisciplinary Diagnostic Centre (MDCs) based pathways were piloted as part of the Accelerate, Coordinate, Evaluate (ACE) programme supported by NHS England, Cancer Research UK and Macmillan Cancer Support. There have also been projects in other parts of the UK. The MDC pathway is intended for patients with vague or non-specific but concerning symptoms that could be indicative of several cancers, where a clear referral route does not currently exist. In this session, we heard emerging evidence from four MDCs.

Clare Pearson, Cancer Research UK, an analyst for the ACE programme, provided context for the MDC pilots with an overview of the differences in diagnostic routes for people with 'vague' versus 'obvious' symptoms. Data from the NCDA (2014) showed that patients with vague symptoms were more likely to present via an emergency route, be of a later stage at diagnosis and have longer intervals during the diagnostic pathway.

Dave Chapman, also from the ACE programme and based at **Cancer Research UK**, spoke about what we can learn from combining evidence from the MDC pilots. He highlighted that the patient profiles of people who meet the criteria for MDC referral were complex: of 239 cancers diagnosed across 10 MDCs in ACE (an 8% conversion rate), more than half were less common or rare cancers, and covered more than 30 different tumour types. There were also non-cancer conditions diagnosed through MDCs, especially digestive diseases, which they plan to analyse in more detail.

Dr Brian Nicholson, Oxford University, shared his perspective of implementing the Oxford Suspected CANcer (SCAN) pathway. The pathway has three steps: 1) triage (blood test, FIT, CT); 2) referral to a site-specific pathway; or 3) referral to an MDC. The pilot raised several questions. Some patients referred via an MDC had red flag symptoms, prompting questions as to why they were not referred via a cancer-specific pathway. Another finding was that using CT in the stage 1 triage led to diagnosis of many lung nodules and cysts. The conversion rate is 10.2% so far, with the majority diagnosed at stage III or IV. Dr Nicholson concluded that the MDC pathway was better for patient experience, and that GPs were positive because it provided a referral route for complex cases, but it is too early to look at whether and how it affects cancer outcomes. Workforce (e.g. having the right roles – data analyst, GP, patient navigator and a true generalist MDC clinician) was critical to the operation of the MDC pathway.

Finally, **Dr Gareth Davies, Wales Detecting Cancer Earlier Programme**, **Dr Heather Wilkes, Neath Port Talbot Hospital**, and **Dr Bernadette Sewell, Swansea University**, described a pilot Rapid Diagnostic Centre (RDC) implemented by the Wales Cancer Network. GPs can refer patients aged 18 or older to the RDC if they have a clinical suspicion of cancer but there's no suitable referral pathway. Patients need to be well enough to go through a morning of tests to exclude any site-specific symptoms. The patient stays in a day room with refreshments while the results are discussed by the multidisciplinary team (a physician, radiologist and clinical nurse specialist), before having the next steps (management plan) explained to them. They are either referred to a site-specific pathway, a non-cancer pathway, back to their GP or for further investigation. The referring GP receives a letter with all the details within 24 hours. They reported a conversion rate of around 11%, with respiratory onward referrals being the most common.

Closing reflections – a call to arms for the next 10 years

Over the past 10 years, a thriving community has coalesced around the challenge of reducing late stage diagnosis of cancer. This anniversary conference truly highlighted the culture of working together, learning from each other, and challenging ourselves and others, which has helped to accelerate our field's progress. In the past decade we have transformed our understanding of the root causes of late diagnosis and we are starting to make real inroads in tackling them.

When tackling the root causes and striving to meet our ambitious targets, it is meaningful reduction in late stage diagnosis that we seek. We are here to make a significant dent in the tens of thousands of people who are currently diagnosed with late stage cancer each year and die as a result.

It is clear that there is unwarranted and unacceptable variation in cancer diagnosis and outcomes across the UK, unequivocally linked to inequalities. We need to address this. If we can tackle this variation locally, regionally and nationally, then our cancer outcomes will be up there with the best in the world.

While we must include all cancers in our efforts to improve cancer outcomes, including those which are rare or less common, we must also acknowledge that each cancer type is at a different point and, for some, optimising the research pipeline to ensure effective interventions in the future is key.

We need to keep tackling all parts of the pathway, for all cancers, and become more sophisticated in the way we do it. From identifying and reaching those at risk, to understanding who needs which tests, when and where. There is much still to work through in terms of optimising and organising care – such as how RDCs can learn and evolve from MDCs, and how we streamline the interface between primary and secondary care.

Central to our ability to transform diagnostic pathways will be considering the NHS capacity to deliver these new models of care. As well as investment in workforce, we need to seek opportunities to release capacity within existing funding.

If we get this right, the benefits will stretch beyond achieving early diagnosis – from opportunities to link screening up with prevention, to the impact of detecting and treating other conditions, to ensuring patients have the care and support they need from the earliest point that they need it.

Whether the ambition to shift late stage diagnosis and achieve 3 in 4 cancers diagnosed early is by 10 or 15 years from now, both trajectories are ambitious, and will require a coordination and acceleration of effort.

What does this look like? Well, this largely depends on all of us. Every two years, this conference gets bigger and better than ever, with attendees enthusiastically and openly sharing their data, expertise and experience, and joining in the lively discussion and debate. But we need to maintain the energy and the action in between these milestones and continue to direct our efforts in the best way. If you have ideas for how we at Cancer Research UK can support this, then we want to hear from you.

The easiest way to get in touch is by emailing earlydiagnosis@cancer.org.uk

Endnotes

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