Evidence Review: Early diagnosis of cancer

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1. Executive Summary

The national target for increasing the proportion of cancers diagnosed at an early stage is set to 75% by 2028. The most recent publicly available data (2017) suggests BCWB is at 50%.

The Black Country & West Birmingham (BCWB) Academy is starting a population health project focusing on increasing the number of cancers diagnosed at an early stage. To help inform this project the academy commissioned an evidence scan to explore the following research questions:

- What evidence is available to inform cancer site specific targets for early identification?
- What are the reasons for late diagnosis?
- What is the effectiveness of interventions to improve early identification?

A summary for each of the research questions is presented below.

1.1 Evidence to inform cancer site specific targets for early identification

In general, for **most cancer types earlier diagnosis leads to increased survival chances**.

Data presented in this evidence scan shows that the three cancer types demonstrating the highest five-year survival estimates (testis, melanoma, and thyroid) mirror the cancer sites with the highest percentage of cancers diagnosed at stages 1 and 2. Similarly, the cancer types with the lowest percentage of cancers diagnosed at stages 1 and 2 (oesophagus, pancreas, stomach and lung) are also among the cancer types demonstrating the lowest five-year survival estimates.

For some cancer sites however the stage of diagnosis is reported to be less important. For example, hodgkin lymphoma survival is generally high regardless of stage. Data for prostate cancer shows high survival rates for stages 1 to 3, however significant declines for stage 4.

The latest figures for cancers diagnosed at stages 1 and 2 in England report a **wide variation between cancer sites,** ranging from 13.5% (oropharynx, base of tongue, tonsil, soft palate, and uvula) to 92.0% (testis). Nationally, **seven cancer sites are already achieving an early diagnosis of 75% or above**: bladder (75.8%), cervix (80.3%), uterus (80.8%), breast (85.8%), thyroid (88.9%). Melanoma (89.2%) and testis (92%).

The total number of people diagnosed with cancer across sites also varies widely. Cancer sites with the highest number of stageable cancers diagnosed include prostate (44,759), breast (43,658) and lung (36,552). Cancer sites with the lowest number of stageable cancers diagnosed include Larynx (1,565), Hodgkin lymphoma (1,605) and Testis (1,869).

Some of the cancer sites with the highest percentage of cancers diagnosed at an early stage have low total number of stageable cancers diagnosed. Cancer of the testis is reported to have

the highest percentage of cancers diagnosed at an early stage (92%), however the total number of stageable cancers diagnosed (1,869) is the third lowest of the 21 cancer sites reported. Thyroid cancer has the third highest percentage of cancers diagnosed at an early stage (88.9%), however also records a relatively low total number of stageable cancers diagnosed (2,669). **In contrast, due to the lower early diagnosis percentage for lung cancer (28.9%) as well as the high number of total people diagnosed with lung cancer (36, 552) this has been suggested a key cancer site to target.** It is also thought to be the cancer type affected most by the COVID-19 pandemic due the symptoms of COVID-19 being similar to the alarm symptoms for lung cancer.

Overdiagnosis relates to the diagnosis of a condition that would otherwise not go on to cause symptoms or death. Diagnosis of these conditions means the patient receives further investigation, and treatment, but without the benefits. **Improving early diagnosis programmes must consider the risk of overdiagnosis.** UK research suggest four cancer sites; uterine, prostate, oral and thyroid, where incidence and mortality trends are suggestive of overdiagnosis. Trends in melanoma and kidney cancer also suggest potential overdiagnosis.

1.2   Reasons for late diagnosis

Analysis of data from the English National Cancer Diagnosis Audit (NCDA) on patients diagnosed with cancer in 2014 found **24% were deemed to have had an avoidable delay to their diagnosis.** A breakdown of the avoidable delays shows **13% were deemed to have occurred pre-consultation, 49% within primary care, and 38% within secondary care.**

Delays in cancer diagnosis relate to three main time periods in the cancer pathway: patient delay; doctor / primary care delay; and system delay.

The patient interval concerns the time from when a patient becomes aware of the first symptom that may indicate an underlying cancer, to the point where they consult a GP for the first time. **Patient symptoms and symptom knowledge influence patient delays. This includes the type of alarm symptoms experienced, the process and ability to appraises those symptoms, and psychosocial factors that influence symptom appraisal and help-seeking behaviour. Patient demographics such as socioeconomic status, ethnicity, age, sex, and rurality may also influence patient presentation, however the evidence presents a mixed picture.**

The doctor / primary care interval concerns the length of time from first presentation to specialist referral. **Primary care delays are typically related to failure to appreciate the significance of symptoms leading to lack of examination and/or no referral or incorrect referral (e.g. non-urgent, wrong specialty). Factors, such as nature of presenting symptoms, patients' demographics, presence of comorbidities and communication are potential contributing factors.**

System delay refers to the interval between referral and definite diagnosis or treatment. **System delays can relate to delays in referral and delays in hospital care. Factors such as primary care access, the GP gatekeeper role, and waiting times for tests are reported to delay diagnosis.**

1.3   Interventions to improve early identification

Secondary, synthesised evidence evaluating interventions targeting earlier diagnosis identified a range of interventions which we categorised into the following types of interventions: Faecal immunochemical tests, Cancer Decision Support Tools, Rapid Diagnostic Centres, Primary Care (spanning targeting behaviour, improving screening uptake, and safety netting), Cancer awareness (spanning campaigns, patient education and provider education), and Lung Health Checks. A brief summary for each is provided below.

1.3.1   Faecal immunochemical tests (FIT)

FIT can be used to screen asymptomatic people through the bowel screening programme, as well as triage symptomatic patients. **Evidence from trials has shown that screening take up rates improved by 7% including among groups with low participation rates such as men, people from ethnic minority backgrounds and people in more deprived areas. Two systematic reviews report FIT is useful for triaging symptomatic patients, one focused on low risk patients and the other more generally.**

1.3.2   Cancer Decision Support (CDS) Tools

CDS tools can be used to predict the current risk for undiagnosed patients with symptoms, or predict future incident disease for asymptomatic individuals. **Evidence from systematic reviews indicates that CDS improves physician performance and the ordering of diagnostic tests, however evidence on clinical outcomes such as stage at diagnosis and survival remains lacking.** In their guidelines on suspected cancer NICE recognise that the use of CDS is an emerging area of interest, but conclude **more research is needed to assess the effectiveness of those interventions in referral for suspected cancer.**

1.3.3   Rapid Diagnostic Centres (RDCs)

RDCs build on ten Multidisciplinary Diagnostic Centre (MDC) service models piloted with Cancer Research UK, which focused on diagnosing cancers where patients often present with non-specific symptoms and may go to their GP many times before being sent for tests, such as blood and stomach cancers. The MDC evaluation found that across the programme 79% of cancers diagnosed had staging data and of those 26% were diagnosed at an early stage (one or two). The report highlights that **many of the cancer types diagnosed within the MDC will present when disease is already advanced, so early diagnosis for some of these cancers may not be possible.** A review exploring one-stop clinics for symptoms that could be indicative of cancer also reports that

while **one-stop clinics are associated with reduced time from GP referral to testing and diagnosis, it is still unknown whether one-stop clinics are associated with earlier cancer stage at diagnosis or increased survival.** Analysis of the ongoing NHS Rapid Diagnostic Centre programme will add to the evidence base. The Strategy unit are part of a consortium led by Ipsos Mori who are currently undertaking a national evaluation of the programme.

1.3.4   Primary Care (spanning targeting behaviour, improving screening uptake, and safety netting)

Target behaviour - Think cancer

The Wales Interventions and Cancer Knowledge about Early Diagnosis (WICKED) programme is currently trialling a target behaviour intervention, involving GPs thinking of and acting on clinical presentations that could be cancer.

Improving screening uptake

Interventions to improve participation in cancer screening services include **pre-screening reminders, general practice endorsement, personalised reminders for non-participants and offering a more culturally acceptable screening test.**

Safety netting

Safety netting can be defined as a consultation technique to communicate uncertainty, provide patient information on red-flag symptoms, and plan for future appointments to ensure timely re-assessment of a patient's condition. Safety netting is recommended in NICE clinical guidelines on suspected cancer. Patients can play a role in achieving an earlier diagnosis of cancer by monitoring and re-appraising symptoms after initially presenting to primary care however **a systematic review of interventions that involve patients identified no studies of such interventions.**

1.3.5   Cancer awareness (spanning campaigns, patient education and provider education)

Campaigns

Interventions that promote cancer awareness and early presentation **have shown promise, although few report long-term outcomes.** The Public Health England 'Be Clear on Cancer' campaigns reported a small, but significant, increase in the proportion of lung cancers diagnosed at a stage amenable to surgical resection (stage I tumours).

Patient Education

Patient education is reported to increase awareness of symptoms **but it is unclear from the evidence identified whether this impacts stages of cancer.**

Provider education

Evidence from two campaigns that included an additional education element for health professionals reported positive results in terms of increased referrals and reductions in the diagnostic interval, **but it is unclear whether this impacts stages of cancer.**

1.3.6   Lung Health Checks

The high-quality US National Lung Screening Trial published in 2011 found that for ever-smokers aged 55–74 years low-dose computed tomographic screening **resulted in a significant mortality reduction of 20%**. Within Europe, the results of the European Dutch-Belgian randomised lung cancer screening study (Nederlands–Leuvens Longkanker Screenings Onderzoek [NELSON]) have been eagerly awaited. The results of the NELSON trial were published in February 2020, and reported **significantly lower lung-cancer mortality among those who underwent volume CT screening compared to those who underwent no screening.**

The UK Lung Cancer Screening (UKLS) Trial (Field et al., 2016) piloted a trial of low-dose CT screening for lung cancer in at UK. A total of 1994 participants underwent CT scanning: 42 participants (2.1%) were diagnosed with lung cancer; 36 out of 42 (85.7%) of the screen-detected cancers were identified as stage 1 or 2, and 35 (83.3%) underwent surgical resection as their primary treatment. In the UKLS trial, transport difficulties as well as emotional barriers were reported as barriers to participation (Crosbie et al., 2020). Alterations to increase participation have included, basing the service in convenient community locations, and inviting participants to a 'lung health check' rather than 'lung cancer screening'.

Within the UK several areas have been piloting lung health checks. The UK Accelerate, Coordinate, Evaluate (ACE) Programme trialled four projects: The Liverpool Healthy Lung Programme (LHLP), The Nottingham Lung Health MOT Pilot, The Manchester Lung Cancer Early Diagnosis Service, and the University College London (UCL) Lung Screen Uptake Trial (LSUT). **The ACE programme sites have reported a reduction in the stage at diagnosis compared to the general population.**

It is not currently known what the impact on diagnosis rate would be at a population level, however. The Yorkshire Lung Screening Trial (YLST) (Crosbie et al., 2020) which is currently underway should provide useful evidence in this respect.

A recent review **considering the readiness to implement CT screening for lung cancer highlights some useful considerations, including**: selecting the right population; ensuring engagement with the hard-to-reach; deciding what the optimum screening model is between commissioner, primary care and provider; adopting a broader lung health intervention rather than concentrating solely of cancer screening; ensuring harm reduction through evidence-based algorithms; and considering key infrastructure such as engagement strategies, the service model, CT resource, reporting capacity and quality assurance, and the impacts on diagnostic and treatment providers.

2. Introduction

The national target for increasing the proportion of cancers diagnosed at an early stage is set to 75% by 2028. The most recent publicly available data (2017) suggests BCWB is at 50%.

The Black Country & West Birmingham (BCWB) Academy is starting a population health project focusing on increasing the number of cancers diagnosed at an early stage. To help inform this project the academy commissioned an evidence scan to explore the following research questions:

- What evidence is available to inform cancer site specific targets for early identification?

- What are the reasons for late diagnosis?

- What is the effectiveness of interventions to improve early identification?

2.1 Methodology

Medline and HMIC searches were conducted in October 2020 (see Table 1 for example search strategy).

Table 1. Medline search strategy

1	exp NEOPLASMS/
2	"EARLY DETECTION OF CANCER"/
3	Exp "EARLY DIAGNOSIS"/
4	((early OR rapid OR timely OR fast*) ADJ3 (diagnos* OR detect*)).ti,ab
5	("diagnos* centre*" OR "diagnos* service*" OR "diagnos* pathway*" OR "diagnos* clinic*").ti,ab
6	exp *"DIAGNOSTIC SERVICES"/
7	exp *"PATIENT CARE MANAGEMENT"/
8	exp *"HEALTH CARE QUALITY, ACCESS, AND EVALUATION"/
9	4 AND (5 OR 6)
10	4 AND (7 OR 8)
11	1 AND (2 OR 3 OR 9 OR 10) *[DT 2010-2020] [Document type Review]*

Additional keywords and follow up searches were completed using seminal papers.

Grey literature searches were conducted across search aggregators and search engines which included Google Scholar, NHS Evidence, TRIP and OpenGrey. Additional searches were conducted on specific web sites including NHS England and NHS Improvement, Public Health England, NICE, National Cancer Registration and Analysis Service (NCRAS), and Cancer Research UK.

To manage the volume of literature, the review prioritises secondary evidence (i.e. reviews). Other secondary research from the grey literature and UK-based literature including primary research is

included where there is insufficient secondary evidence, or to provide relevant contextual UK evidence.

Screened results were managed in Excel. Papers were categorised so that evidence maps could be created to aid the structure of the evidence scan.

3. Policy Background

The NHS Long Term Plan (NHS England, 2019a) sets out an ambition that, by 2028, the proportion of cancers diagnosed at stages 1 and 2 will rise from around half now to three-quarters of cancer patients. The plan also highlights several ways in which this will be achieved, including:

- raise greater awareness of symptoms of cancer;

- lower the threshold for referral by GPs;

- accelerate access to diagnosis and treatment; and

- maximise the number of cancers that are identified through screening.

Initiatives to realise these ambitions include the use of personalised and risk stratified screening and testing family members of cancer patients where they are at increased risk of cancer.

Primary care is expected to play a key role in delivering the NHS LTP ambitions to diagnose cancers earlier (BMA and NHS England, 2019). The updated GP contract agreement for 2020/21-2023/24 (BMA and NHS England, 2020), sets out the new service specification for supporting early cancer diagnosis. The specification states from 1 April 2020 PCNs will 'take reasonable steps to improve rates of early cancer diagnosis for their registered population' (NHS England and Improvement, 2020a). It is expected PCNs will:

1. review referral practice for suspected cancers, including making use of Clinical Decision Support Tools and Rapid Diagnostic Centre pathways;

2. contribute to improving uptake of national cancer screening programmes; and

3. support the delivery of these aims through a community of practices enabling peer-to-peer learning.

In line with COVID-19 guidance issued in March 2020, the contractual start date for this work is now 1 October 2020.

The updated GP contract agreement for 2020/21-2023/24 (BMA and NHS England, 2020), also sets out revised quality improvement (QI) requirements on the early diagnosis of cancer (NHS England and Improvement, 2020b). The aims of the Early Diagnosis module are to (BMA and NHS England, 2020):

- improve participation in the national breast, cervical and bowel cancer detection and screening programmes; and

- improve referral and safety netting practices for patients suspected of having cancer, and intended to support the roll out of the PCN early cancer service specification.

Due to COVID-19 QOF requirements have been simplified. Quality improvement actions for early cancer diagnosis are now focused upon restoration of delivery of screening services with a focus on cervical screening and ensuring patients who require urgent referral are identified, supported and managed in line with NICE guidance (NHS England and Improvement, 2020c). The updated guidance for GMS contract 2020/21 in England (NHS England and Improvement, 2020c) sets out the following actions for practices:

- restoring cervical screening uptake to pre-COVID-19 levels;
- building public confidence that general practice and other healthcare settings can be accessed safely;
- returning referrals to pre-COVID-19 levels, improving the quality of referrals; and awareness of referral and testing pathways; and
- having robust and consistent systems in place for safety netting.

In addition, to the GP contracts focusing on cancer diagnosis a new standard for faster diagnosis standard was intended to be introduced in April 2020 (NHS England, n.d.), but is currently on hold due to COVID-19. The Faster diagnosis standard requires that patients who are referred for the investigation of suspected cancer are told whether or not they have cancer after an urgent referral from their GP or a cancer screening programme, within 28 days.

A recent review of diagnostic services commissioned by NHS England and Improvement (2020d) before the pandemic sets out ambitions for future delivery of diagnostic services and takes into account COVID-19. The review highlights that in order to achieve many of the NHS Long Term Plan commitments, including increasing the proportion of cancers diagnosed at stages 1 and 2, major expansion of diagnostic capacity was already clearly identified as being needed before the pandemic. The COVID-19 pandemic has further amplified the need for 'radical change'.

> *"Services will require major investment in facilities, equipment and workforce, alongside replacement of obsolete equipment. Training of additional highly skilled staff will take time but should start as soon as possible. International recruitment should be prioritised when possible but national workforce solutions will also be critical. Alongside this, skill-mix initiatives involving more apprenticeships and assistant practitioners, and using qualified staff at the top of their licence will be essential, as will learning lessons from staff flexibility and roles undertaken during the Covid-19 pandemic."* (NHS England and Improvement, 2020d)

4. What is early diagnosis

4.1 Definition of early diagnosis

"Early detection and diagnosis (ED&D) is defined as the identification and characterisation of a consequential cancer or pre-cancerous change (i.e. those which will cause mortality or significant morbidity within the individual's expected lifespan) at the earliest possible point at which an intervention might be made." (Cancer Research UK, 2020)

Staging data record how advanced a person's cancer is at diagnosis. Staging data is determined by the TNM staging system which stands for Tumour, Node, Metastasis. TNM looks at:

- the size of the tumour (T);

- whether there are any cancer cells in the lymph nodes (N); and

- whether the cancer has spread to a different part of the body (M).

TNM staging is then used to provide number staging. Number staging typically has four stages. Stage 1 usually means that a cancer is small and contained within the organ it started in. Stage 4 means the cancer has spread from where it started to another body organ. Early diagnosis is classified as diagnosis of cancer at stage 1 or 2.

4.2 Why earlier diagnosis is important

Cancer survival data demonstrate the importance of early diagnosis. The Office for National Statistics (2019) have explored 1 year and 5-year survival estimates for adults diagnosed with cancer between 2012 and 2016 for individuals diagnosed with cancer at different stages (1 to 4). Stage data were calculated for 27 cancer sites, excluding pancreatic and non-Hodgkin lymphoma. The analysis found that generally, those who are diagnosed at an earlier stage have a better chance of survival. However, for some cancer the stage of detection is less important. Hawkes (2019) highlight cancers where data from the ONS analysis suggested early stage of diagnosis was important, and cancers where the stage of detection seems less important:

Data shows early diagnosis important:

- **Colorectal cancer:** one-year survival if detected at stage 1 is 97.7%, falling to 43.9% if detected at stage 4.

- **Lung cancer:** one-year survival if detected at stage 1 is 87.3%, falling to 18.7% if detected at stage 4.

Data shows stage of detection less important:

- **Hodgkin lymphoma:** survival is generally high regardless of stage. Even when detection is at stage 4, one-year survival is 86.7%.

- **Prostate cancer:** extremely high one-year survival rates (around 100%) whether it is detected in stages 1, 2, or 3, falling to 87.6% if detected in stage 4. Five-year survival follows a similar but steeper decline—100% or near for stages 1, 2, and 3, but down to 47.7% for stage 4.

The Nuffield Trust (2020a) present the ONS five-year net survival estimates for adults (aged 15-99 years) in England diagnosed with one of the 29 most common cancers between 2013 and 2017, and followed up to 2018 (see Figure 1). The cancers with the lowest five-year survival estimates are mesothelioma (6.5%), pancreatic cancer (7.3%) and brain cancer (12.2%). The highest five-year survival estimates can be seen in patients with testicular cancer (95.3%), melanoma of skin (91.3%) and thyroid cancer (87.4%).
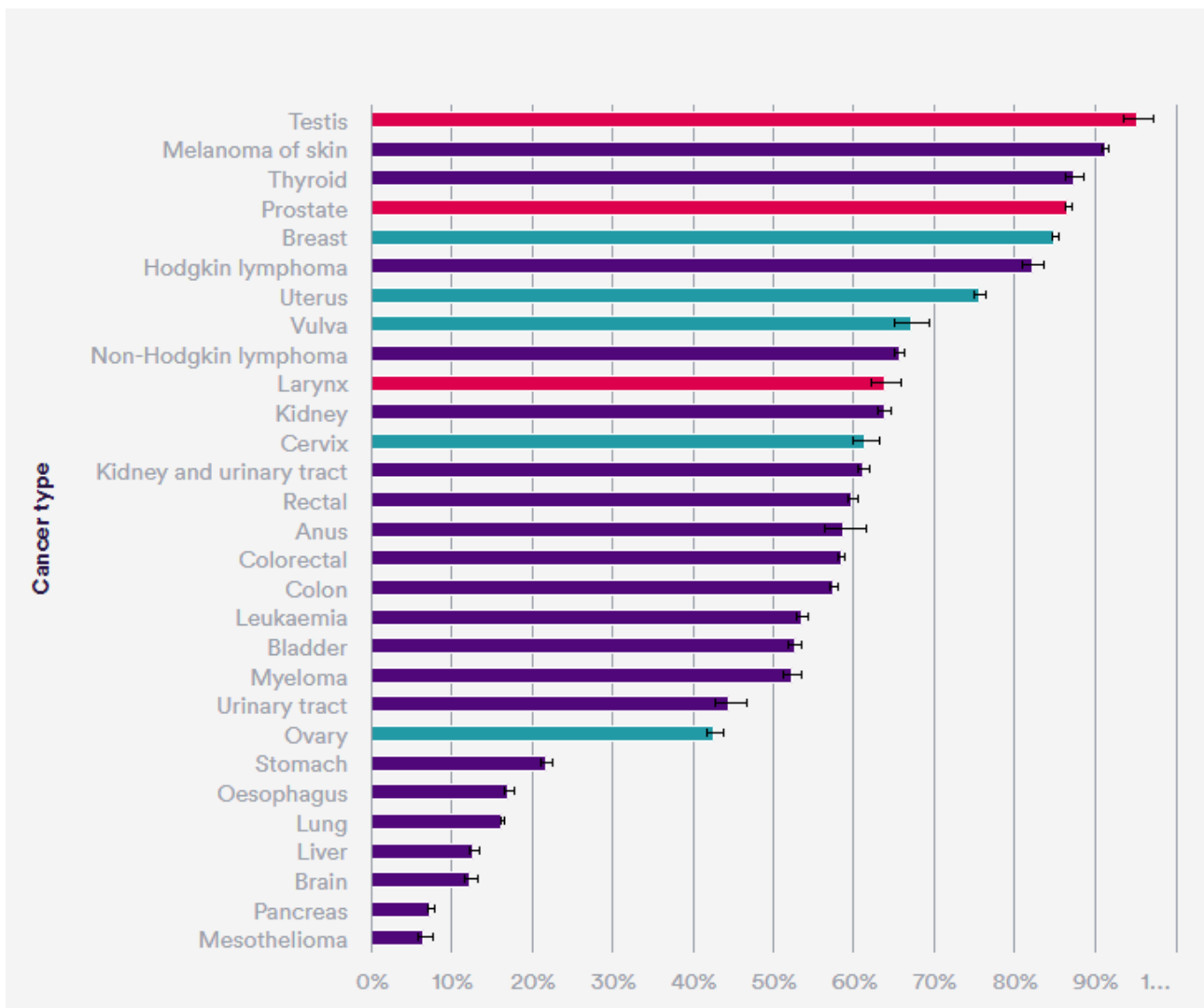

Figure 1. Fiver-year survival estimates for adults (aged 15-99 years) in England diagnosed between 2013 and 2017, and followed up to 2018 (taken from Nuffield Trust, 2020a).

The three cancer types demonstrating the highest five-year survival estimates (testis, melanoma, and thyroid) mirror the cancer sites with the highest percentage of cancers diagnosed at stages 1 and 2 in 2018 as shown in Table 2 in the following section. Whilst the cancer sites reported differ slightly across the survival estimates in Figure 1 and the percentage of cancers diagnosed at stages 1 and 2 in Table 2, the cancer types with the lowest percentage of cancers diagnosed at stages 1 and 2 (oesophagus, pancreas, stomach and lung) are also among the cancer types demonstrating the lowest five-year survival estimates.

4.3 Current achievement of early diagnosis

The International Cancer Benchmarking Partnership (ICBP) explores international variation in cancer survival, incidence and mortality, across eight countries including Canada, Denmark, Australia, Norway, New Zealand, Sweden, Ireland, and the United Kingdom.

Analysis from the ICBP looked at data on 3.9 million people with cancer from 1995 to 2014 in seven countries (Australia, Canada, Denmark, Ireland, New Zealand, Norway, and the UK) to analyse changes in survival, alongside incidence and mortality, in people with cancers of the oesophagus, stomach, colon, rectum, pancreas, lung, and ovary (Arnold et al., 2019). The study found that cancer survival continues to increase across high-income countries; however, international disparities persist, with the UK generally performing worse or near to worse.

Late diagnosis is thought to be a factor contributing to poorer cancer survival rates in the UK compared to some other countries. Data from the ICBP on stage distribution for colon, rectal and ovarian cancers is presented by the International Agency for Research on Cancer (2020). The stage distribution for ovarian cancer is similar across countries (see Figure 4), however the distribution for colon cancer (see Figure 2) and rectal cancer (see Figure 3) shows the UK lags behind others. Differences between staging data means the countries included in analysis varies.
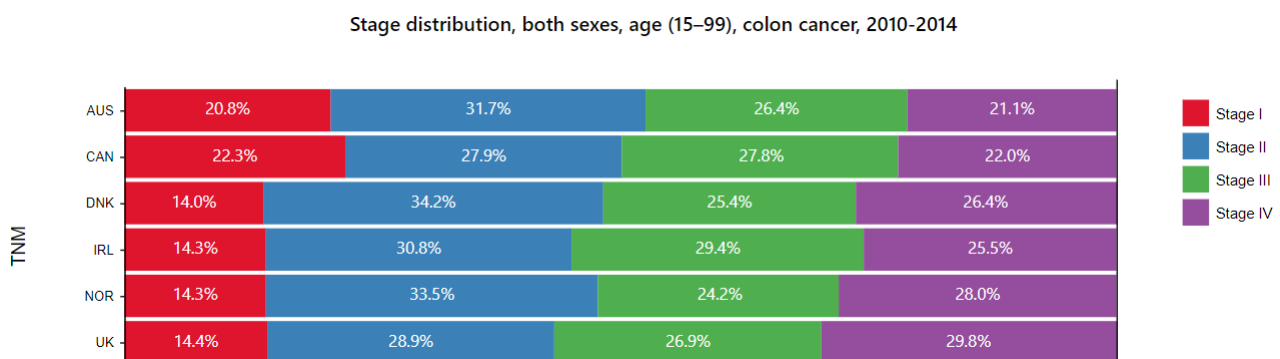
Stage distribution, both sexes, age (15–99), colon cancer, 2010-2014

Figure 2. ICBP data on stage distribution for colon cancer

Stage distribution, both sexes, age (15–99), rectal cancer, 2010-2014

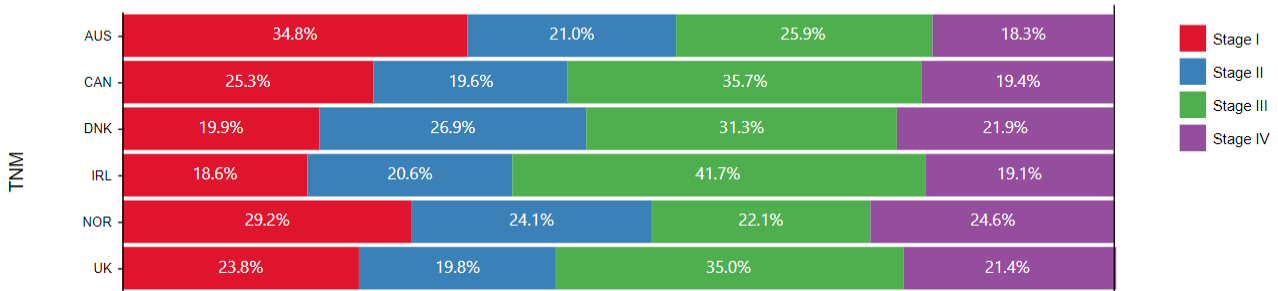| TNM	Stage I	Stage II	Stage III	Stage IV
AUS	34.8%	21.0%	25.9%	18.3%
CAN	25.3%	19.6%	35.7%	19.4%
DNK	19.9%	26.9%	31.3%	21.9%
IRL	18.6%	20.6%	41.7%	19.1%
NOR	29.2%	24.1%	22.1%	24.6%
UK	23.8%	19.8%	35.0%	21.4%

Figure 3. ICBP data on stage distribution for rectal cancer

Stage distribution, age (15–99), ovarian cancer, 2010-2014

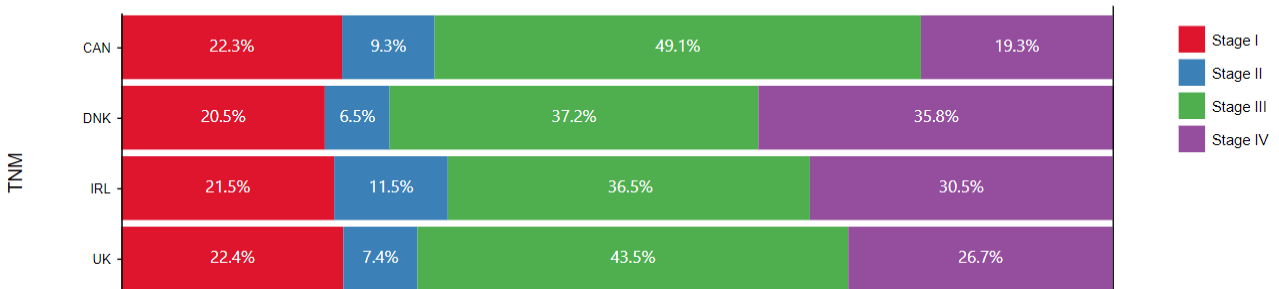| TNM	Stage I	Stage II	Stage III	Stage IV
CAN	22.3%	9.3%	49.1%	19.3%
DNK	20.5%	6.5%	37.2%	35.8%
IRL	21.5%	11.5%	36.5%	30.5%
UK	22.4%	7.4%	43.5%	26.7%

Figure 4. ICBP data on stage distribution for ovarian cancer.

The ICBP data for colon and rectal cancer has also been published in the journal Gut (Araghi et al., 2020). The authors conclude that differences in cancer registration practice and different staging systems across countries may have impacted the comparisons (Araghi et al., 2020). The proportion of colon cancer patients with missing stage at diagnosis was highest in the UK (TNM: 39.5%; SEER: 37.2%) and lowest in Canada (TNM: 7.5%; SEER: 6.4%). For rectal cancer, a similar pattern was seen i.e. proportion with missing TNM stage was 39.4% (SEER: 37.0%) in the UK and 10.8% (SEER: 6.8%) in Canada.

The latest data on cancers diagnosed at stages 1 and 2 in England (Public Health England, 2020b) finds that:

- In England, there were 242,346 cancers diagnosed with a recorded stage (1 to 4) in 2018. Of these, 55% were diagnosed at stages 1 and 2. The unadjusted range by CCG was 48% to 64%, which is comparable to the previous year (2017) when the unadjusted percentage was 54%, ranging from 47% to 60%;

- The most recent 3-year case-mix adjusted percentage figures (2016 to 2018) show that 55% of cancers were diagnosed at stages 1 and 2 – the case-mix adjusted range by CCG was 50% to 58%.

The percentage of cancers diagnosed at stages 1 and 2 varied by cancer site – in 2018, this ranged from 13.5% (oropharynx, base of tongue, tonsil, soft palate, and uvula) to 92.0% (testis). The analysis included 21 cancer groups that are defined as those with at least 1,500 cancers diagnosed annually in England and 70% staging completeness (see Table 2. Percentage of cancers diagnosed at stages 1 and 2 by cancer site in 2018 (Public Health England, 2020b)

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Table 2. Percentage of cancers diagnosed at stages 1 and 2 by cancer site in 2018 (Public Health England, 2020b)

Cancer site	Total number of stageable cancers diagnosed	Number of cancers diagnosed at stages 1 and 2	Percentage (%)
Testis	1,869	1,720	92.0
Melanoma of skin	13,786	12,297	89.2
Thyroid	2,669	2,374	88.9
Breast	43,658	37,456	85.8
Uterus	7,507	6,066	80.8
Cervix	2,075	1,667	80.3
Bladder	7,384	5,594	75.8
Kidney, except renal pelvis	8,004	4,556	56.9
Prostate	44,759	24,428	54.6
Larynx including anterior surface of epiglottis	1,565	796	50.9
Oral cavity, hard palate, and lip (inner aspect)	2,529	1,175	46.5
Hodgkin lymphoma	1,605	725	45.2
Colon	21,401	9,638	45.0
Rectum and rectosigmoid junction	10,678	4,592	43.0
Ovary, fallopian tube and primary peritoneal carcinomas	5,574	2,229	40.0
Non-Hodgkin lymphoma	9,980	2,992	30.0
Lung	36,552	10,562	28.9
Stomach excluding cardia and gastroesophageal junction	2,707	742	27.4
Pancreas	7,199	1,625	22.6
Oesophagus including cardia and gastroesophageal junction	7,571	1,627	21.5
Oropharynx, base of tongue, tonsil, soft palate, and uvula	3,274	443	13.5

Cancer of the testis is reported to have the highest percentage of cancers diagnosed at an early stage (92%), however the total number of stageable cancers diagnosed (1,869) is the third lowest of the 21 cancer sites. Thyroid cancer has the third highest percentage of cancers diagnosed at an early stage (88.9%), however also records a relatively low total number of stageable cancers diagnosed (2,669).

The United Kingdom Lung Cancer Coalition (2020) present data from 2017 and argue lung cancer offers an important contribution to achieving the ambitions of the Long Term Plan (see Figure 5). Lung cancer has a percentage that is much lower than many other cancer types, as well as high numbers of people impacted.
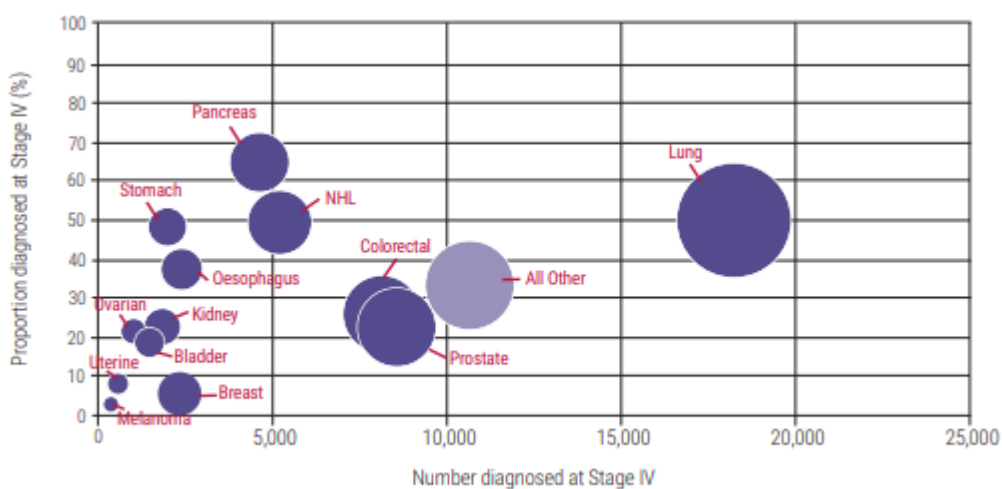

Figure 5. Number and Proportion of Cancer Cases Diagnosed at Stage IV, England, Cancer Research UK (2017) (taken from United Kingdom Lung Cancer Coalition, 2020)

A report prepared for Cancer Research UK in 2014 (Incisive Health, 2014) looked at variations in the proportion of patients who are diagnosed with cancer at an early stage for colorectal, lung and ovarian cancer across CCGs. Analysis showed that:

- colorectal cancer had nearly a threefold variation between the highest and lowest performing CCGs;

- lung cancer had nearly a fourfold variation between the highest and lowest performing CCGs; and

- ovarian cancer had nearly a fivefold variation between the highest and lowest performing CCGs.

The report acknowledges the recording of stage of cancer is variable across England, for example for ovarian cancer, one CCG had nearly two thirds of patients unstaged, whereas others managed to stage all patients. Furthermore, some CCGs with a high proportion of patients recorded as

having early stage cancer also have a very high proportion of unstaged cancer, suggesting that some of those patients where stage is not recorded may have been diagnosed late.

The reporting of cancer staging data is improving. The National Audit Office (2015) reports that the percentage of cancers diagnosed with staging data recorded increased from 40% in 2010 to 62% in 2012. The latest available data for 2017 reports that the staging data were complete for nearly 82% of all cases of cancer (Public Health England, 2020a).

In line with the improvement in staging data variations is the proportion of patients who are diagnosed with cancer at an early stage across CCGs. The 2nd Atlas of variation in risk factors and healthcare for respiratory disease (Public Health England and NHS Rightcare, 2019) looks at the variation in percentage of lung cancer patients diagnosed at an early stage (stage 1 and 2) by CCG between 2015 and 2017. Data showed that CCG values ranged from 16.6% to 37.5%, which is a 2.3-fold difference between CCGs. The England value for 2015 to 2017 was 25.8%.

4.4   Impact of COVID-19 on early diagnosis

Screening, case identification, and referral in symptomatic cancer diagnosis have all been affected by the COVID-19 pandemic (Jones et al., 2020).

Breast Cancer Now (2020) has estimated that around 986 000 women in the UK missed mammograms since March, when services were stopped in an effort to reduce the spread of covid-19 and release emergency NHS resources.

Cancer Research UK have published several analysis highlighting concerns relating to cancer diagnosis and outcomes. Less urgent suspected cancer referrals have been reported, with an estimated 350,000 fewer people referred for urgent suspected cancer between April and August 2020 (Cancer Research UK, 2020a). Considerable reductions have also been seen in diagnostic tests. In England, there was a 39% drop in the number of these 7 key diagnostic tests between March and July this year, which is equivalent to around 3.2 million fewer tests compared to the same period last year (Cancer Research UK, 2020a). As a result, waiting lists for diagnostics will continue to grow. As of May 30th, there were more than 180,000 people in England waiting for an endoscopy - a rise of 44% from the same time in 2019 (Cancer Research UK, 2020b). And of these people, 66% are waiting six weeks or longer for these vital tests. Compared to last year:

- 51% more people are waiting for colonoscopies and 46% more for flexi-sigmoidoscopies, which are used to detect bowel cancer

- 44% more patients are waiting for gastroscopies, which help diagnose oesophageal and stomach cancer

- 23% more people are waiting for a cystoscopy, used for bladder cancer diagnosis

- around 2.3 million fewer tests that help diagnose cancer have taken place since lockdown compared to the same time last year.

Cancer Research UK (2020c) also warn about lung cancer becoming the 'forgotten disease' of the coronavirus pandemic. At least 14,000 fewer people have been urgently referred for lung cancer tests since March, with Cancer Research UK highlighting this is the hardest hit cancer of all cancer types. It is thought that initial advice for people to stay at home and isolate if they had a new, continuous cough could have led to some people delaying seeking help. At the end of August, the number of people sent for urgent review and tests in England was still at only around 60% of pre lockdown figures.

Researchers at Cardiff University have launched a UK-wide project to investigate the impact of the Covid-19 pandemic on diagnosis of cancer (Cardiff University, 2020).

4.5 Risk of overdiagnosis

Overdiagnosis relates to the diagnosis of a condition that would otherwise not go on to cause symptoms or death (Elmore and Fletcher, 2012). Diagnosis of these conditions means the patient receives further investigation, and treatment, but without the benefits. Nicholson (2017) highlights the importance of prospective evaluation of early diagnosis initiatives to assess where overdiagnosis may occur.

A study examining trends in UK cancer incidence and mortality by cancer site and assessment of the potential for overdiagnosis (Oke et al., 2018) found that for four cancer sites; uterine, prostate, oral and thyroid, incidence and mortality trends are suggestive of overdiagnosis. Trends in melanoma and kidney cancer also suggest potential overdiagnosis and an underlying increase in true risk, whereas for cervical and breast cancer, trends may also reflect improvements in treatments or earlier diagnosis.

5. Causes of late diagnosis

Delays in cancer diagnosis can happen anywhere along the cancer diagnosis pathway. Analysis of data from the English National Cancer Diagnosis Audit (NCDA) on 17,042 patients diagnosed with cancer in 2014 explores GP-assessed avoidable delays in cancer patients (Swann et al, 2019). Among all analysed patients (n = 14,259), 24% (3372) were deemed to have had an avoidable delay to their diagnosis. The median diagnostic interval for patients with a reported avoidable delay was 92 days compared to 30 days for those without a delay. A breakdown of the avoidable delays shows 13% were deemed to have occurred pre-consultation, 49% within primary care, and 38% within secondary care.

When undertaking research into delays in diagnosis in Demark, Olesen et al (2009) defined the three main time periods of the pathways as patient delay, GP delay and system delay. The pathway has been adapted by others to explore delays in the cancer diagnosis pathway. Figure 6 shows an adaptation of the pathway presented by Merriel and Hamilton (2020).
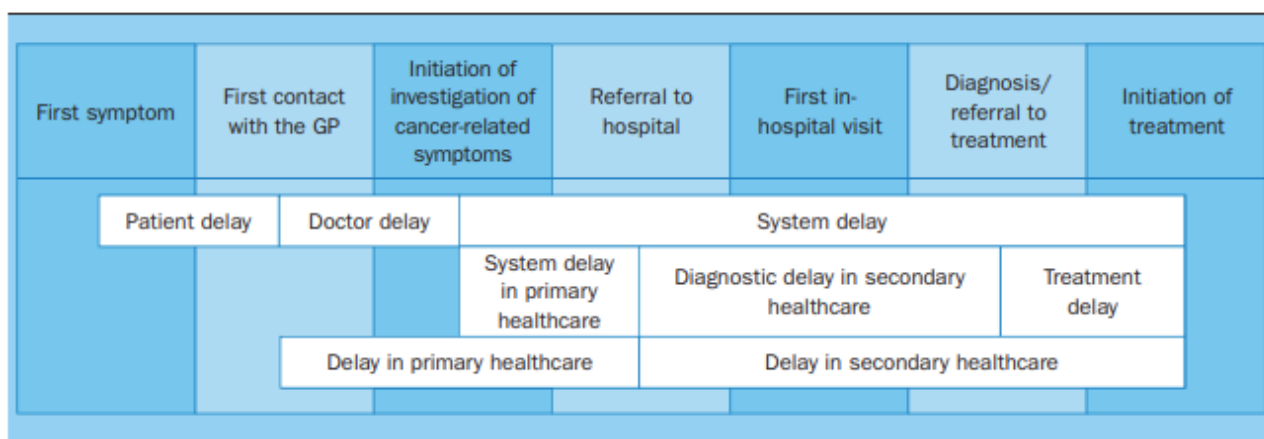

Figure 6. Model of diagnostic delay (taken from Merriel and Hamilton, 2020)

In the following sections we discuss factors that influence delays according to patient, doctor / primary care, and system.

5.1 Patient delays

The patient interval concerns the time from when a patient becomes aware of the first symptom that may indicate an underlying cancer, to the point where they consult a GP for the first time. Patient symptoms and symptom knowledge influence patient delays. This includes the type of alarm symptoms experienced, the process and ability to appraises those symptoms, and psychosocial factors that influence symptom appraisal and help-seeking behaviour. Patient demographics such as socioeconomic status, ethnicity, age, sex, and rurality may also influence patient presentation, however the evidence presents a mixed picture.

5.1.1 Symptoms and symptom knowledge

5.1.1.1 Alarm symptoms

Hamilton et al (2016) consider pre-presentation factors affecting early diagnosis. They highlight differences in symptoms with some symptoms recognised as 'alarm' symptoms and recognised as possible cancer e.g. breast lump, whereas recognition of other symptoms, such as fatigue, is less simple. A systematic review exploring risk factors for emergency presentation with colorectal cancers (Mitchell et al, 2015) demonstrates differences in recognising symptoms for colorectal cancers. Rectal bleeding was not found to be associated with emergency presentation for colorectal cancer, possibly because of patients seeking help earlier with what they might consider to be a more alarming symptom. Instead, emergency presentations of people with colorectal cancers have been found to be linked to symptoms, such as pain, obstruction, and weight loss.

UK analysis

Analysis of data from the English National Cancer Diagnosis Audit (NCDA) on 10,297 English patients subsequently diagnosed with one of 18 cancers (bladder, brain, breast, colorectal, endometrial, leukaemia, lung, lymphoma, melanoma, multiple myeloma, oesophageal, oro-pharyngeal, ovarian, pancreatic, prostate, renal, stomach, and unknown primary) showed that the overall median recorded patient interval was 10 days, with a range of 0–38 days (Keeble et al., 2014). Prompt presentation was defined by the authors as 14 days of onset of symptoms. 56% of patients were recorded as a prompt presentation, however this varied significantly between cancer types. Prompt presentation was most frequent for bladder and renal cancer (74% and 70%, respectively); and least frequent for oro-pharyngeal and oesophageal cancer (34% and 39%, respectively). The authors suggest that variation in prompt presentation is likely to reflect how recognisable symptoms are as being indicative of cancer. For example, unexplained bleeding is often associated with shorter patient intervals which is likely to explain why bladder and renal cancer have prompt presentation as patients often present with haematuria.

More recent analysis of data from the English National Cancer Diagnosis Audit 2014 analyses 20 common presenting symptoms of cancer and stage at diagnosis (Koo et al., 2020). The proportion of patients diagnosed with stage IV cancer varied substantially by presenting symptom, from 1% for abnormal mole to 80% for neck lump. Three of the examined symptoms (neck lump, chest pain, and back pain) were consistently associated with increased odds of stage IV cancer, whether reported alone or with other symptoms, whereas the opposite was true for abnormal mole, breast lump, postmenopausal bleeding, and rectal bleeding.

5.1.1.2 Symptom appraisal

Hamilton et al (2016) highlight three main factors influencing symptom appraisal:

- the 'normalization' of common symptoms (where they are perceived as an expected part of life, e.g. menopause);

- the failure to interpret the symptom(s) as requiring medical attention; and

- the difficulties in recognizing new symptoms in the presence of other comorbidities.

Review on delays in diagnosis focusing on specific cancers also highlight these factors. For example the diagnosis of gynaecological cancers has been shown to be delayed by patients due to many women putting 'bodily sensations' down to menopause or a non-gynaecological cause, as well as patients lacking knowledge of the symptoms of ovarian, cervical, and endometrial cancer (Williams et al., 2019). A narrative review exploring men's cultural beliefs about changes to their bodies relevant to prostate cancer and how these affect interpretation of bodily changes and help-seeking actions found the belief that urinary symptoms such as dribbling, cystitis and urinary hesitancy were transient and related to ageing, normality and infection significantly delayed symptom appraisal and help-seeking (King-Okoye et al., 2017).

Evidence concerning the emergency presentation on cancer reports mixed evidence concerning the impact of coexisting morbidity on presenting behaviour.   Zhou et al (2017) report co-morbid illness has been consistently reported to be a risk factor for emergency presentation, highlighting numerous studies where patients with increasing comorbidities (especially 3 or more) are more likely to be diagnosed with cancer in an emergency setting. When looking at specific conditions however they report that patients with dementia and those with cerebrovascular disease are more likely to present as emergencies than those without these comorbid conditions, whereas for chronic respiratory disease, diabetes and cardiovascular disease no associations between comorbidity and emergency presentation risk were reported.

Another review exploring comorbidities and emergency presentations of cancer concludes there is conflicting evidence about the impact of coexisting morbidity on presenting behaviour (Mitchell et al., 2015). In their review on risk factors for emergency presentation with lung and colorectal cancers they found half of the studies evaluating the impact of comorbidities found that it increased the likelihood of emergency presentations, while the other half found that it did not. This finding was consistent across both types of cancer. Mitchell et al (2015) highlight that methods of identifying (national cancer audit, cancer registry, hospital records) and classifying comorbidity (individual conditions, Charlson score, Deyo score) varied across studies, which may have impacted on the consistency of findings.

5.1.1.3 *Psychosocial factors*

Hamilton et al (2016) highlight a study concerning colorectal cancer by Hall et al., 2015 that suggests symptom appraisal and help-seeking are also influenced by psychosocial and cultural contexts, including a fear of stigma, cancer diagnosis and treatment, and fatalism, as well as

practical barriers to help-seeking, such as a lack of access to healthcare and lack of sufficient time and/or transport to attend a consultation.

Williams et al (2019) highlight research by the International Cancer Benchmarking Partnership that examined the effect of cancer awareness and beliefs on cancer survival in different countries. It found that the UK had the 'highest mean barriers to symptomatic presentation', for example, embarrassment and worry about what the doctor might find, when compared with other high-income countries.

A narrative review exploring help seeking behaviour of men with prostate cancer King-Okoye et al (2017) found that men held the belief that sexual changes, such as impotence and ejaculation dysfunction were private, embarrassing and a taboo, which impeded timely help-seeking. Cultural beliefs, spirituality and the role of wives/partners were significant for men to help appraise symptoms as requiring medical attention thus sanctioning the need for help-seeking.

Evidence reviews exploring reasons for emergency presentations of colorectal cancer have found evidence that being unmarried (and in some cases divorced or widowed) increased the likelihood of EP (Zhou et al., 2017; Mitchell et al (2015).

5.1.2   Patient demographics

Numerous patient demographics groups have been thought to influence the patient interval. Demographics considered include socioeconomic status, ethnicity, age, sex, and rurality.

5.1.2.1   Socioeconomic status

Williams et al (2019) explored the association of socioeconomic status (SES) on the diagnostic journey of gynaecological cancers. They found four articles covering a range of cancers including gynaecological cancers that demonstrated a lack of influence of socioeconomic status (SES) on the diagnostic journey, although one study demonstrated diagnostic delay in patients of lower SES diagnosed with endometrial cancer.

A systematic review and meta-analysis exploring socio-economic inequalities in stage at diagnosis for lung cancer patients including 39 papers (20 from the UK) in the review and seven in a final meta-analysis found no evidence of socio-economic inequalities in late stage at diagnosis in the most, compared to the least, deprived group. However, reviews focusing on lung cancer patients presenting via emergency presentations report an association between measures of lower socioeconomic status and greater risk of diagnosis of cancer as an emergency (Newsom-Davis, 2017; Mitchell et al., 2015). The association between measures of lower socioeconomic status and greater risk of diagnosis of cancer as an emergency has also been reported in an evidence review across cancer types (Zhou et al., 2017), although Mitchell et al. (2015) suggest the evidence of a relationship with presentation for colorectal cancer was less conclusive.

Cancer Research UK (2020e) cite research by Niksic et al., (2015) that found in England people from more deprived populations are less likely to recognise signs and symptoms of cancer than those in the least deprived. People from the most deprived populations were half as likely to recognise signs and symptoms such as 'unexplained lump or swelling' or 'change in appearance of a mole', as a potential symptom for cancer. Cancer Research UK is currently surveying members of the public to understand their awareness of the signs/symptoms of cancer, and will be looking at variations by deprivation and how this changes over time.

5.1.2.2 Ethnicity

Martins et al (2013) review ethnic inequalities in time to diagnosis of cancer. Five studies focused on breast cancer were identified that investigated ethnic differences in patient delay. Three out of the five studies found longer patient and pre-hospital delays in ethnic minority women compared to their white counterparts, while the remaining two reported no difference. The authors highlight methodological issues with the two studies that reported no difference.

Evidence from patients who have an emergency presentation of cancer reports some evidence of a higher prevalence in Asian ethnicity (Newsom-Davis, 2017; Zhou et al., 2017) and non-white patients (Zhou et al., 2017) in the UK. Evidence is limited to one study for Asian ethnicity and one study for non-white ethnicity across the two reviews. The two reviews also include limited evidence of differences in people of Pacific origin in New Zealand and in the African-American population in the USA.

5.1.2.3 Age

Research focusing on gynaecological cancers identifies age as a factor in the late diagnosis of cancer (Williams et al., 2019). Williams et al (2019) found three studies found that females aged 75 years and over, and those who were housebound were more likely to present earlier, along with those patients who were retired. Females of working age were more likely to delay presentation.

Cancer patients at the either extremes of age (the youngest and the very old patients) are more likely to be diagnosed as emergencies (Zhou et al., 2017; Lyratzopoulos et al., 2015). We identified two reviews demonstrating increasing age and emergency presentation of cancer for lung cancer (Newsom-Davis, 2017; Mitchell et al., 2015) and colorectal cancer (Mitchell et al., 2015).

5.1.2.4 Sex

A review focusing on emergency presentation of lung cancer (Newsom-Davis., 2017) reports an unclear association with gender. Some studies listed female gender as being associated with EP, but others report no association with either sex.

Research focusing on gynaecological cancers identifies rurality as a factor in the late diagnosis of cancer (Williams et al., 2019). Three studies demonstrated that rurality and distance from health care increased delay.

5.2 Doctor / primary care delays

The doctor / primary care interval concerns the length of time from first presentation to specialist referral. Primary care delays are typically related to failure to appreciate the significance of symptoms leading to lack of examination and/or no referral or incorrect referral (e.g. non-urgent, wrong specialty). Factors, such as nature of presenting symptoms, patients' demographics, presence of comorbidities and communication are potential contributing factors which we discuss below.

5.2.1 Symptoms and difficult to diagnose cancers

As well as influencing the patient interval, the nature of presenting symptoms can also critically influence the length of time from first presentation to specialist referral (the primary care interval) (Koo et al., 2018).

The first stage of a diagnosis differs greatly between cancer types; some are relatively simple, such as checking for the presence of a breast lump or a pigmented skin lesion, whereas others are notoriously difficult to diagnose conclusively, particularly when the symptoms are common features of benign conditions (Hamilton et al., 2016). A review focusing on the diagnosis of gynaecological cancers reports non-specific, atypical, and gastrointestinal symptoms are more likely to be associated with delay (Williams et al (2019). Hamilton et al. (2016) defining 'difficult to diagnose' cancers as having three or more primary care attendances before diagnosis and highlight analysis of the 2010 National Cancer Patient Experience Survey in England showing a wide variation in the proportion of patients who had visited their general practitioner three or more times before hospital referral: 7·4% for breast cancer; 10·1% for melanoma; 41·3% for pancreatic cancer; and 50·6% for multiple myeloma.

In their review concerning the effect of different presenting symptoms on diagnostic intervals Koo et al. (2018) propose a taxonomy of cancer sites considering their symptom signature and the predictive value of common presenting symptoms. Symptom signature is used to denote the nature and relative frequency of symptoms. Symptom signatures are described as 'narrow' when most patients present with a particular symptom (as is the case for breast lump in the context of breast cancer) or 'broad' when patients present with a larger range of symptoms (as is the case for colorectal cancer). Predictive value is used to represent diagnostic difficulty of common presenting symptoms. The taxonomy proposed considers cancers in three groups:

- Cancers with a narrow symptom signature of sufficiently high predictive value (e.g., breast, bladder cancers);

- Cancers with a broad symptom signature of varying predictive value (e.g., colorectal, gastric, lung, oesophageal, oropharyngeal, ovarian, renal cancers);

- Cancers with a broad symptom signature of low predictive value (e.g., brain / CNS, haematological cancers).

5.2.2 Patient demographics

As well as influencing the patient interval, some patient demographics groups have been shown to influence GP referrals. Demographics considered include socioeconomic status, ethnicity, and age.

5.2.2.1 Socioeconomic status

A review focusing on the diagnosis of gynaecological cancers (Williams et al., 2019) highlight a cohort study from Denmark that reports GPs were less likely to delay referring women with higher socioeconomic status, as well as evidence from a systematic review that found lower educational status was associated with referral delay.

5.2.2.2 Ethnicity

Martins et al (2013) review ethnic inequalities in time to diagnosis of cancer. They found one study relating to colorectal cancer and one study relating oesophagogastric cancer, both demonstrating longer referral delay among Asian and Black people. A review focusing on the diagnosis of gynaecological cancers reports that the effect of ethnicity was mixed (Williams et al., 2019). They found one study that demonstrated black or ethnic minority women in the UK were more likely to require three or more visits to their GPs before referral, and two studies that demonstrated no link with ethnicity and delay.

A review paper by Lyratzopoulos et al. (2015) highlights potential language barriers as the cause for delay; *"lack of interpretative support may impede effective patient–doctor communication, with some epidemiological evidence suggesting that suspecting the diagnosis of cancer is less prompt (i.e., requiring a greater number of pre-referral consultations) in older ethnic minority patients with symptoms (Lyratzopoulos et al, 2012)."*

5.2.2.3 Age

Lyratzopoulos et al. (2015) warn of 'epidemiological optimism' bias that can make prompt suspicion of the diagnosis of cancer even harder in low-risk patient groups even when they complain of symptoms that may be due to cancer. Such groups include young persons. A review focusing on the diagnosis of gynaecological cancers (Williams et al., 2019) highlights a UK study that found patients under 55 years old diagnosed with ovarian cancer were found to be more likely to have had more than three consultations before referral.

5.2.3 Comorbidity

The presence of other known non-cancer comorbid conditions can make the consideration of a cancer diagnosis is particularly challenging (Lyratzopoulos et al., 2015).

5.2.4 Communication

Ineffective doctor-patient communication may account for instances of missed opportunities (Lyratzopoulos et al., 2015; Williams et al., 2019). Williams et al (2019) found evidence to suggest poor communication can lead to patients not re-presenting with persistent symptoms or follow-up. A lack of follow-up can lead to delays in diagnosis.

5.3 System delays

System delay refers to the interval between referral and definite diagnosis or treatment. System delays can relate to delays in referral and delays in hospital care. Factors such as primary care access, the GP Gatekeeper role, and waiting times for tests are reported to delay diagnosis.

5.3.1 General practice characteristics

A narrative review exploring how healthcare systems influence speed of cancer diagnosis (Brown et al., 2014) cites evidence from an earlier systematic review that suggests primary care access is an important factor in earlier cancer diagnosis, with healthcare providers playing an important role in facilitating or impeding treatment delay.

A review exploring emergency presentation of cancer (Zhou et al.,2017) found two English studies that exploring the association between practice characteristics and emergency presentations. The first paper found poorer in-hours primary care access (as measured by patients' ability to get an appointment within two days was found to independently predict the risk of emergency presentation (all cancer site). The same paper also reported a higher than average proportion of non-UK qualified practice doctors, and smaller practice list size were associated with higher odds of emergency presentation in the practice population. The second paper looked at continuity of cancer and found no association between continuity and emergency presentation.

5.3.2 GP Gatekeeper role

It has been suggested that the gatekeeper role performed by GPs delays diagnosis (Williams et al., 2019; Hamilton et al.,2016). A recent systematic review focusing on the impact of GP gatekeeping on health care use and health outcomes (Sripa et al., 2019) found one study that reported unfavourable outcomes of patients with cancer under gatekeeping. The authors also highlight research showing for England approximately three-quarters of patients with cancer who visited their GPs in in 2002 and 2014 were referred to a specialist after only one or two consultations, and about 60% of all referred patients saw a specialist within 2 weeks. The authors conclude therefore

that delayed diagnosis of cancer in England is not caused solely by gatekeeping, however acknowledge the possible association with delayed diagnosis for cancer is of significant concern.

5.3.3   Waiting times for tests

Strain on diagnostic capacity in the UK has been reported to influence the propensity of primary care in England to refer when investigating potential cancer compared to jurisdictions with similar health systems (Cancer Research UK, 2018a).

A report from Cancer Research UK in 2016 warned pathology workforce issues meant that waiting times are likely to increase as it will take longer to process and report all requests, which may delay patients' diagnosis and treatment. Further research from Cancer Research UK in 2018 shows that waiting times for tests are increasing. Following an urgent GP referral for suspected cancer, at least 93% of patients should be seen by a specialist within two weeks. The Nuffield Trust (2020b) report that between 2009 and 2014, the percentage of people with suspected cancer having their first consultant appointment within two weeks of an urgent GP referral fluctuated at around 95%. After this, performance dropped slightly to about 94%, until 2018 where it declined further. The two-week standard has been missed for the last two years. In Q4 2019/20 (January to March 2020), only 92% of patients had their first consultant appointment within two weeks.

6. Improving early diagnosis

Secondary, synthesised evidence evaluating interventions targeting earlier diagnosis identified a range of interventions which we categorised into the following types of interventions:

- Faecal immunochemical tests

- Cancer Decision Support Tools

- Rapid Diagnostic Centres

- Primary Care (spanning targeting behaviour, improving screening uptake, and safety netting)

- Cancer awareness (spanning campaigns, patient education and provider education)

- Lung Health Checks

A brief review of the key findings from the reviews follows in the rest of chapter 6, with a more detailed review for Lung Health Checks presented in section 7. This intervention had the most evidence to review. Furthermore, COVID-19 is also thought to be impacting on lung cancer diagnosis due to potential delays in presenting due to the symptoms being similar (see section 4.4).

Further interventions of interest can be explored further on request. As well as supplementary searches for interventions of interest, looking a primary research and case studies to provide further insights.

6.1 Faecal immunochemical tests

Faecal immunochemical tests (FITs) detect blood and can quantify the amount of human blood in a single stool sample. FIT can be used to screen asymptomatic people through the bowel screening programme, as well as triage symptomatic patients. There are important key differences in the use of FIT for screening asymptomatic people through the bowel screening programme compared to being used to triage symptomatic patients. Cancer Research UK (2018b) highlight the key differences.

6.1.1 FIT for bowel screening

The NHS Long Term Plan (NHS England, 2019a) commits to modernising the Bowel Cancer Screening Programme to detect more cancers at an earlier stage. Faecal Immunochemical Tests (FIT) are suggested as key to this ambition as they make the service easier to use for patients. The Long-Term Plan cites evidence from trials that has shown that take up rates improved by 7% including among groups with low participation rates such as men, people from ethnic minority backgrounds and people in more deprived areas.

The implementation of FIT began in 2019 and Cancer Research UK (2020d) reports there has been an increase in bowel screening as a result. The latest available data for the Bowel Screening programme reports a 64.5% (Public Health England, 2020c).

6.1.2   FIT for triaging symptomatic patients

NICE guidance DG30 (2017) recommends the use of FIT for symptomatic patients at 'low risk' where they do not meet the criteria for a suspected cancer pathway referral.

We identified two reviews that explored FIT for testing symptomatic patients. The first review by Westwood et al (2017) was considered in the NICE guidelines, and lead to the recommendation of FIT for symptomatic patients at 'low risk'. A more recent systematic review and meta-analysis by Pin Vieito et al (2019) explores the accuracy of FIT across the broad spectrum of possible symptoms. The meta-analysis confirms that FIT is useful for triaging referrals in people with lower abdominal symptoms, however FIT ability to rule out colorectal cancer is higher in studies solely including symptomatic patients.

6.2   Cancer Decision Support Tools

Cancer Decision Support tools (CDS), also referred to as cancer prediction tools, help predict the current or future risk of cancer. Predicting the current risk is used for undiagnosed patients with symptoms, and predicting future incident disease is used for asymptomatic individuals. Tool predicting risk may be integrated into wider intervention such as Lung Health Checks initiatives. For example the Liverpool Lung Project (LLP) risk model (www.MyLungRisk.org) has been used in the Liverpool Healthy Lung project, and the PLCO 2012 risk prediction model used in the Manchester lung cancer pilot study (Weller et al., 2019).

CDS tools use a range of rigorously researched and developed algorithms to assess a variety of information about an individual; from age and postcode through to tumour site specific cancer symptoms to generate a risk score to assist decision making (NHS England, Cancer Research UK and Macmillan Cancer Support, 2017a). The tools are mostly designed as assessment tools for GPs (Hamilton et al., 2016; Usher-Smith et al., 2015). Current tools are now usually computer based integrated into a GP's usual patient management system and may include prompt/alert boxes based on presenting symptoms, symptom checkers, or risk stratification (NHS England, Cancer Research UK and Macmillan Cancer Support, 2017a). Common tools include Cancer Risk Assessment Tool (RAT), QCancer, and Macmillan Cancer Decision Support (CDS) tools.

Evidence from systematic reviews indicates that clinical decision support improves physician performance and the ordering of diagnostic tests, however evidence on clinical outcomes such as stage at diagnosis and survival remains lacking (Hamilton et al., 2016). A recent review exploring decision support tools to improve cancer diagnostic decision making in primary care (Chima et al.,

2019) identified only one study that evaluated time to diagnosis. The authors concluded electronic clinical decision support tools (eCDSTs) improve practitioner performance and patient care, but their role in cancer diagnosis has not been adequately addressed.

The latest update to NICE (2020) guidance for suspected cancer does not recommend clinical decision support tools for the diagnosis of cancer. The guidelines do however recognise that the use of electronic health records and decision support tools is an emerging area of interest, but more research is needed to assess the effectiveness of those interventions in referral for suspected cancer.

The ACE programme, a joint initiative between NHS England, Cancer Research UK and Macmillan Cancer Support, is an early diagnosis of cancer initiative focused on testing innovations that either identify individuals at high risk of cancer earlier or streamline diagnostic pathways. One of the innovations they sought to understand was the use of Cancer Decision Support (CDS) Tools in General Practice. A learning report on the ACE Cancer Decision Support Tools (NHS England, Cancer Research UK, and Macmillan Cancer Support, 2017a) reports that the association between QCancer risk score and resulting cancer diagnosis is unclear. It was hoped that data from the projects would be able to explore association between the calculated risk score and resulting cancer diagnoses, however this proved to be particularly challenging. This was due to limited data linking QCancer risk scores with cancer diagnoses, and no data linking QCancer risk scores with cancer stage.

6.3   Rapid Diagnostic Centres

The NHS Long Term Plan (NHS England, 2019a) commits to the roll-out of new Rapid Diagnostic Centres (RDCs) across the country to upgrade and bring together the latest diagnostic equipment and expertise. The commitment to roll out RDCs forms an important part of a broader strategy to deliver faster and earlier diagnosis (NHS England and Improvement, 2019).

RDCs can be broadly categorised into two distinct pathways, based on two separate patient cohorts:

- **Non-Specific Symptoms (NSS):** Patients who have symptoms that are indicative of cancer, but symptoms do not indicate a specific cancer or an isolated body system, for which currently no cancer pathway exists.
- **Site-Specific Symptoms (SSS):** Patients who have symptoms that are indicative of a particular site of cancer (e.g. lung) for which existing urgent two week wait cancer pathways exist.

RDCs are intended to support the new Faster Diagnosis Standard (FDS), which was due to be introduced from April 2020 (NHS England and Improvement, 2019), but has been delayed due to

COVID-19. To support this NHS England (2019c) devised a set of guidelines (timed diagnostic pathways) that set out how diagnosis within 14 days and diagnosis within 28 days can be achieved for the colorectal, lung, oesophageal and prostate cancer pathways.

RDCs build on ten **Multidisciplinary Diagnostic Centre (MDC) service models** piloted with Cancer Research UK, which focused on diagnosing cancers where patients often present with non-specific symptoms and may go to their GP many times before being sent for tests, such as blood and stomach cancers (NHS England, 2019a; Cancer Research UK, 2019). The MDC evaluation Cancer Research UK, 2019) found that across the programme 79% of cancers diagnosed had staging data and of those 26% were diagnosed at an early stage (one or two). The report highlights that many of the cancer types diagnosed within the MDC will present when disease is already advanced, so early diagnosis for some of these cancers may not be possible. The MDC evaluation did however also find that of the cancers diagnosed by this service model, a high proportion were rare or difficult to detect cancers, which is the category of cancers often diagnosed at a late stage e.g. pancreatic or stomach cancer. After excluding diagnoses associated with the four most common cancers (breast, colorectal, lung and prostate), 56% of cancers diagnosed were considered as rare and less common. Rare cancers are a category of cancers often diagnosed at a late stage e.g. pancreatic or stomach cancer, and thus there may be an improvement for some tumour sites associated with very poor early stage diagnosis.

A review exploring one-stop clinics for symptoms that could be indicative of cancer also reports that while one-stop clinics are associated with reduced time from GP referral to testing and diagnosis, it is still unknown whether one-stop clinics are associated with earlier cancer stage at diagnosis or increased survival (Friedemann Smith et al., 2019).

Analysis of the ongoing NHS Rapid Diagnostic Centre programme will add to the evidence base. The Strategy unit are part of a consortium led by Ipsos Mori who are currently undertaking a national evaluation of the programme.

6.4   Primary care practitioner

6.4.1   Target behaviour - Think cancer

Symptomatic patients typically present to primary care for initial consultation therefore the clinician must first think of cancer as a possibility and must then decide whether testing is required or not (Hamilton et al.., 2016).

The Wales Interventions and Cancer Knowledge about Early Diagnosis (WICKED) programme is aiming to develop a behaviour change intervention to expedite diagnosis through primary care and contribute to improved cancer outcomes. In a protocol from the programme (Stanciu et al., 2018) a four work packages to the programme are set out:

1. Identify relevant evidence-based interventions (systematic review of reviews) and will determine why interventions do or do not work, for whom, and in what circumstances (realist review).

2. Assess cancer knowledge, attitudes, and behaviour of GPs, as well as primary care teams' perspectives on cancer referral and investigation (GP survey, discrete choice experiment [DCE], interviews, and focus groups).

3. Synthesise findings from earlier work packages using the behaviour change wheel as an overarching theoretical framework to guide intervention development.

4. Test the feasibility and acceptability of the intervention, and determine methods for measuring costs and effects of subsequent behaviour change in a randomised feasibility trial.

Findings from work package 2 have been published (Nafees et al., 2018), however searches did not find the published review or a summary of work package 3. Follow-up searches found that work package 4 is focused on a target behaviour, involving *GPs thinking of and acting on clinical presentations that could be cancer*, based on the findings from the first two Work Packages. The ThinkCancer! Intervention feasibility study started in the autumn of 2019 (Bangor University, n.d.).

6.4.2 Improving screening uptake

A rapid review of the evaluation of interventions to improve participation in cancer screening services found those that most consistently improved screening participation were - pre-screening reminders, general practice endorsement, personalised reminders for non-participants and offering a more culturally acceptable screening test. A review focused on cervical cancer screening (Musa et al., 2017) found that invitation letters alone (or with a follow up phone contact), making an appointment, and sending reminders to patients who are due or overdue for screening had a significant effect on improving participation and screening rates in populations at risk.

The ACE programme, a joint initiative between NHS England, Cancer Research UK and Macmillan Cancer Support, is an early diagnosis of cancer initiative focused on testing innovations that either identify individuals at high risk of cancer earlier or streamline diagnostic pathways. The programme team explored interventions to increase bowel screening uptake. Interventions trialled in primary care included: GP endorsement & primary care engagement; Interventions targeted specifically at non-responders; and Opportunistic Prompts (NHS England, Cancer Research UK, and Macmillan Cancer Support, 2017b)

6.4.3 Safety netting

Safety netting can be defined as a consultation technique to communicate uncertainty, provide patient information on red-flag symptoms, and plan for future appointments to ensure timely re-assessment of

a patient's condition (Jones et al., 2019). NICE (2020) describe safety netting as the active monitoring in primary care of people who have presented with symptoms, and outline two key functions:

1. timely review and action after investigations; and

2. active monitoring of symptoms in people at low risk (but not no risk) of having cancer to see if their risk of cancer changes.

Patients can play a role in achieving an earlier diagnosis of cancer by monitoring and re-appraising symptoms after initially presenting to primary care however a systematic review of interventions that involve patients identified no interventions (Heyhoe et al., 2018).

6.5 Cancer awareness

6.5.1 Campaigns

Public campaigns aim to raise awareness of the symptoms of cancer, and to promote help-seeking, with the intention of educating people and empowering them to hasten earlier presentation (Hamilton et al., 2016). A review focusing on improving early diagnosis of symptomatic cancer looked at the evidence concerning symptom awareness campaigns for achieving expedited diagnosis (Hamilton et al., 2016). The review highlights evidence from a systematic review specifically exploring interventions that promote cancer awareness and early presentation that concluded some of these campaigns have shown promise, although few report long-term outcomes. The review also highlights evidence from other evaluations such as the Public Health England 'Be Clear on Cancer' campaigns. Key findings include:

- increased public awareness of the headline symptoms of lung and bowel cancer;

- increases in attendances for symptoms by those aged 50 and over;

- more cancers diagnosed; and

- a small, but significant, increase in the proportion of lung cancers diagnosed at a stage amenable to surgical resection (stage I tumours).

6.5.2 Patient Education

Providing educational information to women and healthcare providers regarding symptoms relating to endometrial cancer may raise awareness of the disease and reduce delayed treatment. A Cochrane review (Cheewakriangkrai et al., 2020) aimed to explore health education interventions to promote early presentation and referral for women with symptoms of endometrial cancer identified no relevant trials or ongoing trials. Another Cochrane review (O'Mahony et al., 2017) exploring interventions for raising breast cancer awareness in women identified two RCTs involving 997

women. The review found a brief intervention has the potential to increase women's breast cancer awareness, however neither of the included studies reported outcomes relating to motivation to check their breasts, confidence to seek help, time from breast symptom discovery to presentation to a healthcare professional, intentions to seek help, quality of life, adverse effects of the interventions, stages of breast cancer, survival estimates or breast cancer mortality rates.

Hamilton et al. (2016) highlight a Scottish trial including a cohort of people at a higher risk of lung cancer (smokers and former smokers) that provides preliminary evidence of altered consulting patterns in this population, in response to an intervention comprising a single consultation session with a nurse and provision of a self-help manual on lung cancer symptoms.

6.5.3   Provider education

In their review focusing on improving early diagnosis of symptomatic cancer Hamilton et al. (2016) identified two campaigns that included an additional education element for health professionals, 'I'll tackle it soon' and 'HeadSmart: Be Brain Tumour Aware'. Both studies have shown positive results in terms of increased referrals and reductions in the diagnostic interval but it is unclear whether this impacts stages of cancer.:

- Data from the 'I'll tackle it soon' UK study showed that a combined public awareness campaign and GP education programme for lung cancer led to increased chest X-ray referrals by 20%, and lung cancer diagnoses by 27%, although most of these additional cancers were of an advanced stage.

- The 'HeadSmart: Be Brain Tumour Aware' charity campaign, launched in 2011 across the UK as a quality improvement strategy for expediting the diagnosis of brain tumours in children, employed guidelines for professionals alongside public awareness campaigns. This campaign reported considerable reductions in total diagnostic interval and in the median interval from first medical contact to CNS imaging.

7. Focus on: Lung Health Checks and Targeted Lung Screening

Lung Health Checks aim to identify lung cancer earlier. An initial breath test (spirometry) is performed and a discussion to assess their individual lung cancer risk, as well as smoking cessation advice where appropriate. Patients assessed as being at high risk of lung cancer are offered a low-dose CT scan. NHS England (2019b) has published guidance that sets out a high-level participant pathway (see Figure 7).
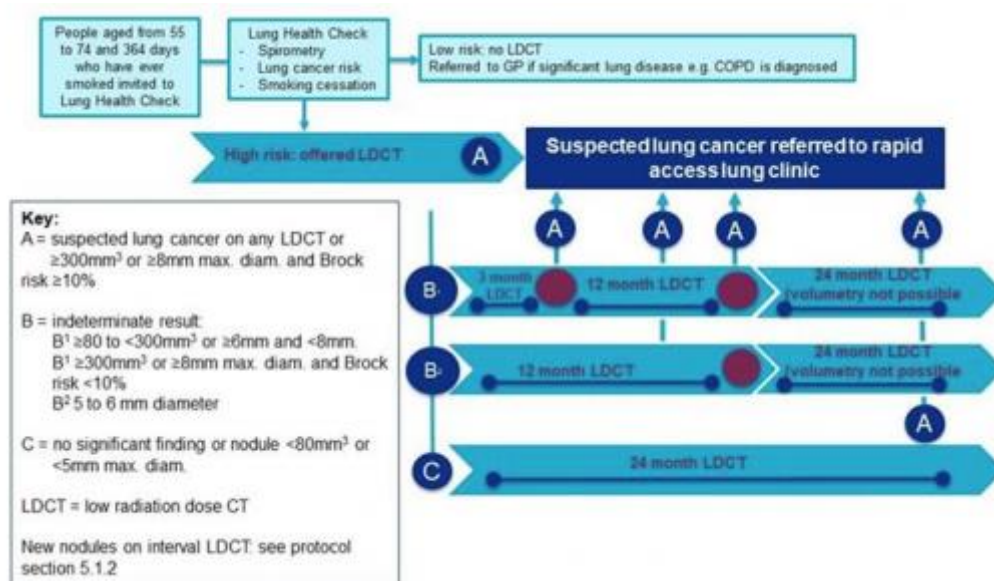

Figure 7. Targeted lung health checks - High level participant pathway (taken from NHS England, 2019b)

Lung Health Checks differ from national population screening programmes as they target people at high risk of lung cancer (NHS England., 2019b).

The NHS Long Term Plan committed to the extension of lung health checks, building on encouraging results in Liverpool and Manchester.

7.1 Impact

A narrative review of CT screening for lung cancer (Balata et al., 2019) highlights the high quality US National Lung Screening Trial published in 2011 that found for ever-smokers aged 55–74 years low-dose computed tomographic screening resulted in a significant mortality reduction of 20%. This lead to many American bodies, including the US Preventive Services Task Force (USPSTF) recommending screening with low does CT for ex-smokers aged 55-80, however the authors highlight that due to the absence of a second confirmatory randomised controlled trial (RCT) widespread implementation in the US has been limited post-2011.

Within Europe, the results of the European Dutch-Belgian randomised lung cancer screening study (Nederlands–Leuvens Longkanker Screenings Onderzoek [NELSON]) have been eagerly awaited (United Kingdom Lung Cancer Coalition, 2020; Balata et al., 2019). The trial was initiated in 2000, and aimed to show a reduction in lung-cancer mortality of 25% or more with volume-based, low-dose CT lung-cancer screening in high-risk male participants at 10 years of follow-up. A report published by the United Kingdom Lung Cancer Coalition in January 2020 highlights the establishment of a national screening programme for lung cancer in the UK rests on the publication of the findings from the NELSON trial into low-dose CT screening.

The results of the NELSON trial were published in February 2020 (de Koning et al., 2020) and concluded that there was significantly lower lung-cancer mortality among those who underwent volume CT screening compared to those who underwent no screening. The cumulative rate ratio for death from lung cancer at 10 years was 0.76 (95% confidence interval [CI], 0.61 to 0.94; P=0.01) in the screening group as compared with the control group, similar to the values at years 8 and 9. Analyses of data from the small subsample of women (with a known date of lung-cancer diagnosis) showed the rate ratio was 0.67 (95% CI, 0.38 to 1.14) at 10 years of follow-up, with values of 0.41 to 0.52 in years 7 through 9. The discussion of the published trial also highlighted analysis of the trial data that showed volume CT screening in the NELSON trial led to a substantial shift to lower-stage cancers at the time of diagnosis as well as to more frequent eligibility for curative treatment (mainly surgical).

The UK Lung Cancer Screening (UKLS) Trial (Field et al., 2016) piloted a trial of low-dose CT screening for lung cancer in at UK thoracic centres with expertise in lung cancer imaging, respiratory medicine, pathology and surgery (Liverpool Heart & Chest Hospital, Merseyside, and Papworth Hospital, Cambridgeshire). A total of 1994 participants underwent CT scanning, of which 42 (2.1%) were diagnosed with lung cancer. 36 out of the 42 (85.7%) of the screen-detected cancers were identified as stage 1 or 2, and 35 (83.3%) underwent surgical resection as their primary treatment.

In the UKLS trial, transport difficulties as well as emotional barriers were reported as barriers to participation (Crosbie et al., 2020). Alterations to increase participation have included, basing the service in convenient community locations, and inviting participants to a 'lung health check' rather than 'lung cancer screening'.

Within the UK several areas have been piloting lung health checks. The UK Accelerate, Coordinate, Evaluate (ACE) Programme, an early diagnosis of cancer initiative, trialled four projects focusing on low dose CT scans to subjects at particularly high risk of lung cancer: The Liverpool Healthy Lung Programme (LHLP), The Nottingham Lung Health MOT Pilot, The Manchester Lung Cancer Early Diagnosis Service, and the University College London (UCL) Lung Screen Uptake Trial (LSUT). NHS

England, Cancer Research UK, and Macmillan Cancer Support (2018) report on the projects, key findings include:

- Reduction in the stage at diagnosis compared to the general population - 80% of lung cancer diagnoses were at early stages (I and II) in the Liverpool, Nottingham, and Manchester.

- Sign of potential economic benefit from respiratory health clinic and CT screening - Taking into account the limitations of the health economic evaluation, the data suggested that evidence exists on the potential of respiratory health and CT screening projects to be cost effective. Based on the diagnoses of lung cancer alone, cost per quality adjusted life-year (QALY) gained are £13,087 for the Liverpool project and £19,453 for the Nottingham project.

- Patients express a good level of satisfaction in being invited to attend a respiratory health clinic - Patient satisfaction was high in all three projects and ease of access was reported in Nottingham and Manchester. A need for further or simpler information about the process was reported in Liverpool, reflecting the importance of ensuring all communication is appropriately designed for participants.

The Yorkshire Lung Screening Trial (YLST) which is currently underway (Crosbie et al., 2020) will also evaluate a community lung health check programme. The randomised controlled trial aims to assess the impact of lung cancer screening at a population level.

Below we set out further evaluations of the UK lung health check programmes reported to date.

7.1.1 London

The London Lung Screen Uptake Trial (LSUT), evaluating the impact of 'targeted, stepped and low burden' invitation materials on attendance of a 'lung health check' appointment, reported in October 2020 (Ruparel et al., 2020).

The trial selected patients aged 60 to 75 years, who had been recorded as 'current smokers' within the seven preceding years from primary care practices falling within three London Clinical Commissioning Groups (CCGs): Islington, Camden, and City and Hackney. Patients were sent an invitation letter from their usual general practice doctor inviting them to a lung health check. The lung health check included an eligibility screen (i.e. smoking and medical history), spirometry test, CO reading, smoking cessation advice (for current smokers), and for those eligible, a low dose CT scan.

The study reports that out of the 2012 invited, 1058 (52.6%) attended a 'lung health check'. 768 out of 996 (77.1%) underwent a low-dose CT scan. 92 (11.9%) and 33 (4.3%) participants had indeterminate pulmonary nodules requiring 3-month and 12-month surveillance, respectively; 36 lung cancers (4.7%) were diagnosed (median follow-up: 1044 days). 72.2% of lung cancers were stage 1 or 2, and 79.4% of non-small cell lung cancer had curative-intent treatment.

7.1.2 Manchester

NHS England (2019b) report that the Manchester trial resulted in 65% of lung cancers being diagnosed at stage 1 and 13% at stage 4, compared to 18% at stage 1 and 48% at stage 4 before the trial.

Baseline results from the community-based 'Lung Health Check' screening pilot in deprived areas of Manchester were published by Crosbie et al. in 2019.

The pilot invited ever smokers, age 55-74, from 14 Manchester GP practices, to attend lung health checks, next to local shopping centres. The lung health check included an assessment of respiratory symptoms, spirometry and 6-year lung cancer risk, alongside smoking cessation advice. Those at high-risk were offered an immediate access to a low dose CT scan.

The study reports that out of 1,384 individuals screened 3% (95% CI 2.3-4.1%) had lung cancer (80% early stage) of whom 65% had surgical resection. A cost-effectiveness study (Hinde et al., 2018) of the pilot concluded the pilot was a cost-effective use of limited NHS resources. The programme cost £663, 076. It diagnosed 42 patients with lung cancer resulting in a gain in population health of 88.13 discounted life years, equivalent to 65.85 QALYs. This implied an incremental cost-effectiveness ratio of £10,069/QALY.

7.1.3 Liverpool

The evaluation of the Liverpool Healthy Lung Programme was published in 2019 (Ghimire, et al., 2019).

The programme invited patients aged 58-75 years with a history of smoking or a diagnosis of chronic obstructive pulmonary disease (COPD) according to their general practice records for a lung health check with a respiratory nurse in a community health hub setting. The first invitation letter was followed by a second one in case of non-attendance, and if there was no response to the second letter either, the patient was contacted by telephone. The lung health check included a detailed risk assessment using information from the subject's medical history and other risk factor information, and spirometry to assess lung function in those without a pre-existing diagnosis of COPD. Patients with abnormal lung function were referred for further investigation. Patients with a 5% or greater five-year risk of lung cancer as estimated using the 'MyLungRisk' calculator, were

referred for a low dose CT scan. All smoking patients were also offered smoking related advice and referred to the National Health Service (NHS) smoking cessation clinics if they consented to this.

The study reports 4566 patients attended the appointment for risk assessment and 3 591 (79%) consented to data sharing. Of those attending, 63% underwent spirometry and 43% were recommended for a CT scan. A total of 25 cancers were diagnosed, of which 16 (64%) were stage one. Comparison with the national stage distribution implied that the programme was reducing lung cancer mortality by 22%.

7.2   Implementation lessons

A recent review considering the readiness to implement CT screening for lung cancer (Balata et al., 2019) highlights some useful considerations which we have summarised in Table 3.

Table 3. Considerations when implementing Lung Health Check initiative

Consideration	Why important and potential solutions
Selecting the right population	Increasing the precision of screening reduces harms and improves efficacy. Different methods have been used to identify target populations, with age and smoking history being common selection criteria. Several risk prediction models have been established to improve selection, which mostly show better results than age and smoking status.
Ensuring engagement with the hard-to-reach	It is vital that screening services are accessible to those at highest risk, and therefore most likely to benefit. Demographic factors linked with lung cancer risk, such as current smoking and low socioeconomic status, are also associated with lower screening uptake. Participation bias, where participants have been from more educated and affluent backgrounds, has been shown to occur in previous trials. Barriers can be practical such as travel issue getting to hospital-based services, or emotional such as fear and anxiety. Community-based lung cancer screening services such as mobile CT scanners located in more deprived areas, have been shown to engage at risk deprived populations. Organisational barriers, which include engagement, communication, screening site, and reliance on primary care physicians to opportunistically identify and refer potential participants may all contribute to poor uptake.
Optimum screening model	The optimal model of screening and most effective relationship between commissioner, primary care and provider is not yet established. Three models have been described: 1. Centralised – driven by the provider creating capacity and encouraging primary referral 2. Decentralised – based on primary care assessment and referral, with or without engagement programmes, to diagnostic providers 3. Hybrid - typically work in collaboration, providing a clear strategy for community and primary care education and engagement, and full responsibility for delivery of recruitment, assessment, diagnostics, and treatment lying with the provider. Pros and cons exist for the different models. The optimal model of care for screening is yet to be determined, but centralised or hybrid models appear most abundant in the published literature.
Broader intervention	The terminology 'lung cancer screening' can create psychological barriers. Promoting a 'Lung Health Check' (LHC) of which lung cancer screening is a part of can help downplay 'cancer screening' and may help overcome this barrier. Including screening within a broader intervention also provides an opportunity to address tobacco addiction and competing causes of premature death such as cardiovascular disease (CVD) and chronic

	obstructive pulmonary disease (COPD). This approach thus has additional benefits to increase the mortality reduction from screening.
Ensuring harm reduction through evidence-based algorithms	There is a risk, as with any screening programme, of harm to participants despite careful evaluation. In CT screening for lung cancer, the well-established concerns relate to 1) overdiagnosis, 2) radiation-induced lung cancers, 3) false positive screens and subsequently 4) investigation of benign disease including benign surgical resection rates.
Key infrastructure	Ensuring that the right participant has convenient access to a high-quality programme will require consideration of engagement strategies, the service model, CT resource, reporting capacity and quality assurance, and the impacts on diagnostic and treatment providers.

8.   Next Steps

This review aimed to help BCWB Academy understand how the national 75% early diagnosis target should be broken down between individual cancer sites. No evidence to answer this question directly was identified, so instead evidence on current trends and variations in early diagnosis, reasons for variations, and interventions to help improve early diagnosis was explored.

In seeking to help answer this question we provide a summary of what we do know and then consider further actions to help address this question.

Relevant key findings from the latest data available for cancer diagnosis in England include:

- **The percentage of people diagnosed at stages 1 and 2 varies by CCG.** In 2018, the national achievement was 55%. The unadjusted range by CCG was 48% to 64%, and the case-mix adjusted range by CCG was 50% to 58%.

- **The percentage of cancers diagnosed at stages 1 and 2 varies by cancer site**. In 2018, this ranged from 13.5% (oropharynx, base of tongue, tonsil, soft palate, and uvula) to 92.0% (testis).

- **The total number of people diagnosed with cancer across sites varies widely.** Cancer sites with the highest number of stageable cancers diagnosed include prostate (44,759), breast (43,658) and lung (36,552). Cancer sites with the lowest number of stageable cancers diagnosed include Larynx (1,565), Hodgkin lymphoma (1,605) and Testis (1,869).

- **Some of the cancer sites with the highest percentage of cancers diagnosed at an early stage have low total number of stageable cancers diagnosed.** Cancer of the testis is reported to have the highest percentage of cancers diagnosed at an early stage (92%), however the total number of stageable cancers diagnosed (1,869) is the third lowest of the 21 cancer sites reported. Thyroid cancer has the third highest percentage of cancers diagnosed at an early stage (88.9%), however also records a relatively low total number of stageable cancers diagnosed (2,669).

International evidence suggests that the UK could potentially improve diagnosis rates for colon and rectal cancers. International data exploring stage distribution of colon and rectal cancer between 2010 and 2014 shows that Australia achieved the highest diagnosis rates for colon and rectal cancers. For colon cancer, Australia achieved an early diagnosis rate of 52.5%, compared to the UK which achieved 43.3%. For rectal cancer, Australia achieved an early diagnosis rate of 55.8%, compared to the UK which achieved 43.6%. *Differences in cancer registration practice and different staging systems across countries may have impacted the comparisons, with the UK reporting the highest proportion of missing stage at diagnosis for both colon and rectal cancer.*

Table 4. Improving early diagnosis interventions

Intervention	Cancer sites targeted
Faecal immunochemical tests	Bowel cancer (colon and rectal)
Cancer Decision Support tools (CDS)	All cancer types
Rapid Diagnostic Centres (RDCs)	All cancer types (in the MDC pilots lung, colon, pancreas, non-hodgkin's lymphoma, and kidney cancer were the most common types of malignant neoplasms diagnosed)
Primary care practitioner	All cancer types (national cancer screening programmes include bowel, breast, and cervical cancer)
Cancer awareness	All cancer types (National Be Clear on Cancer campaigns cover lung, bowel, and kidney and bladder cancer)
Lung Health Checks	Lung cancers

We explored six types of interventions used to improve early diagnosis. Some of the interventions apply to all cancer sites and some are specific to individual cancer sites e.g. lung health checks (see Table 4).

Promising results from interventions suggest potential improvements in early diagnosis due to changes in clinician behaviour or patient behaviour, however evidence on the impact on early diagnosis rate is lacking. For example, evidence from systematic reviews indicates that cancer decision support tools can improve physician performance and the ordering of diagnostic tests, however evidence on clinical outcomes such as stage at diagnosis and survival remains lacking. Similarly, **some interventions may measure the impact on screening programmes but not the direct impact on early diagnosis.** For example, evidence from trials on faecal immunochemical tests for bowel screening has shown that take up rates improved by 7% including among groups with low participation rates such as men, people from ethnic minority backgrounds and people in more deprived areas. How this impacted stage of diagnosis was not reported.

The lung health check intervention trials have recorded early diagnosis rate among those that participated in the programme, however what the impact on diagnosis rate would be at a population level is not yet known. A reduction in the stage at diagnosis compared to the general population has been reported for participants in lung health check pilots. 80% of lung cancer diagnoses via lung health checks were at early stages (I and II) in the Liverpool, Nottingham, and Manchester. The Yorkshire Lung Screening Trial (YLST) (Crosbie et al., 2020) which is currently underway should provide useful evidence on what the impact on diagnosis rate is at a population level.

Further exploration of local data, intelligence and experience is required to understand how the interventions identified in this review could impact early cancer diagnosis rates in BCWB. We therefore recommend stakeholder engagement and exploration of local data to help identify the best route to achieve this. Stakeholder involvement is also likely to generate other ideas of interventions for consideration in the data and evidence.

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