Pathways to a Cancer Diagnosis:

Monitoring variation in the patient journey across Northern Ireland

2012 to 2016

The Northern Ireland Cancer Centre at Belfast City Hospital

The North West Cancer Centre at Altnagelvin Hospital

This report has been produced by analysts working in the Centre for Public Health, Queen's University Belfast, in conjunction with independent statisticians from the Northern Ireland Statistics and Research Agency (Based in the HSCNI Business Services Organisation).

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This report and further background information can be found at:

http://www.hscbusiness.hscni.net/services/3094.htm

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Executive Summary

Introduction

The circumstances under which a person is diagnosed with cancer is strongly associated with their subsequent survival. This report provides the first ever overview of the 'Routes-to-Diagnosis' of Northern Ireland (NI) cancer patients diagnosed from 2012 to 2016. An algorithm, developed by Public Health England, classified individual NI cancer patients, based on their healthcare episodes or events, into one of the following eight routes that characterises how they received their diagnosis:

1. **Screen detected**: detected via the national screening programmes
2. **Red flag referral**: urgent GP referral with a suspicion of cancer
3. **GP referral**: routine and urgent GP referrals that are not red flag referrals
4. **Other Outpatient**: an elective route starting with an outpatient appointment
5. **Inpatient elective**: an elective route where there is no earlier admission
6. **Emergency presentation**: an emergency route via A&E, GP, transfer, consultant, outpatient, or self-presentation
7. **Death Certificate Only**: only information on a cancer patient is referenced on their death certificate, even following investigation by the cancer registry
8. **Unknown**: no data available on patient

The cancer patient population diagnosed 2012-2016 were identified through the Northern Ireland Cancer Registry (NICR). In addition to data from the *Northern Ireland Cancer Screening Service* and *General Registrar Office* which were integrated into the NICR, data from inpatient or outpatient episodes from the *Patient Administration System* and waiting-time information captured on the *Cancer Patient Pathway System* (CaPPS) were all added to the database and the algorithm was applied to these sources.

This report presents Routes-to-Diagnosis for individual cancer sites (female breast, colorectal, breast, lung, prostate, cervical, melanoma) and for groupings of cancer sites under the following titles: head, upper-gastro-intestinal (GI), digestive, urinary, female-genital, blood and lymph, young person, and all cancers excluding non-melanoma

skin cancer (NMSC). Where possible, proportions of patients diagnosed through each route are broken down by sex, age, year of diagnosis, deprivation, Trust, stage of disease, and/or compared to England. Net survival (the survival that would be observed if the only possible underlying cause of death was the disease under study) after three years is reported for each Route-to-Diagnosis, with comparisons with England and breakdowns by age and stage. More detailed breakdowns are available on an interactive tool designed for an internet platform at http://www.hscbusiness.hscni.net/services/3102.htm

Summary of Results

- Of the 46,068 cancer (excluding non-melanoma skin cancer) patients diagnosed in NI from 2012-2016, one fifth were diagnosed through an emergency route-to-diagnosis, and had a poor net survival at 3 years, 23%. The proportion of emergency presentations was higher in deprived areas and among older patients.

- Red flag and routine GP routes accounted for 28% and 21% of NI diagnoses, with each route having a 3-year net survival of 72% and 71%, respectively. The proportion of patients diagnosed through the red flag route increased from around 26% in 2012 to just below 31% in 2015.

- The proportions of patients diagnosed via screening (6%) and emergency presentation route-to-diagnosis (20%) in NI were very similar to England. However, compared to England, NI has greater proportions of patients diagnosed via outpatient and inpatient elective routes, and smaller proportions of red flag and routine GP routes. The higher proportions of patients diagnosed through outpatient and inpatient Routes-to-diagnosis in NI compared to England may be partly an artefact arising from how the PHE algorithm interacts with the NI health service and data sources, which requires further investigation (See Section 1.5.3).

- Within NI, the distribution of routes-to-diagnosis differed markedly between the four main cancer sites: female breast, colorectal, lung and prostate. The most common route-to-diagnosis for colorectal (27%) and breast cancer (50%) patients was red flag

referral. Most common route-to-diagnosis for prostate cancer patients (37%) was GP referral, while for lung cancer patients (35%), it was emergency presentation.

- The cancer sites with a greater proportion of patients diagnosed via emergency route had worse survival outcomes.

- The proportion of patients diagnosed via screen-detected routes-to-diagnosis varied between the cancer sites with NI screening programmes, breast (29%), colorectal (8%), and cervix (24%), but were not different from England. Like England, survival was higher for screen-detected patients (>90%). Fewer cancer patients were diagnosed through screening with increasing levels of deprivation.

- Six in every ten patients diagnosed via screen detected route-to-diagnosis had Stage I cancer. In contrast, around seven in ten patients diagnosed via emergency presentation route-to-diagnosis had either Stage IV or unknown stage.

- With breast, colorectal and lung cancer patients, the net survival variation between different routes-to-diagnosis reflected the proportion of advanced stage of disease in each route-to-diagnosis.

- In colorectal and lung cancer, there was evidence of more advanced stage of disease at diagnosis in the red flag route compared to routine GP; this may suggest that eligible red-flag symptoms for red-flag referral are associated with more serious disease. The lung survival estimates of patients diagnosed by a red flag were lower than routine GP.

- Cancer sites with poorer survival (e.g. colorectal, lung) had high proportions of patients diagnosed with advanced disease across the range of route to diagnosis. In addition, in these sites a large proportion of patients were diagnosed through an emergency admission.

- Emergency presentation route-to-diagnosis made up around a quarter or more of the patients for blood and lymph cancer (28%), digestive cancer (42%), upper GI tract cancer (27%) and head, neck, brain and eye cancer (24%).

Recommendations

This information highlights insights for further investigation and discussion with regard to promoting earlier diagnosis in Northern Ireland and should be used by public health experts and health service planners. A number of recommendations have been made to address specific data quality issues encountered during the current project, further enhance the methodology, and to aid interpretation of results in any future iterations of this work. Some wider recommendations have also been offered with a view to firmly establishing Routes-to-Diagnosis reporting, analysis and research as business as usual within the NI health and social care family.

Conclusions

Information on the Routes-to-Diagnosis in England has helped transform the cancer patient pathway by focusing attention on promoting symptom awareness, early presentation to GP, followed by rapid diagnosis and treatment of aggressive disease. Both national cancer strategies and early diagnosis interventions can be better planned and evaluated with Routes-to-Diagnosis information. The introduction of a digital integrated care record within NI (the Encompass programme) provides a great opportunity to efficiently capture accurate information on Routes-to-Diagnosis, and capture relevant clinical information to explore variation in Routes-to-Diagnosis patterns across regions and population sub-groups.

1. Introduction

1.1 Routes-to-Diagnosis Northern Ireland

The results presented in this document are an overview of the Routes-to-Diagnosis for cancer patients in Northern Ireland. “Routes-to-Diagnosis” analysis is a novel methodology which was developed by Public Health England; the analysis uses routine healthcare activity data to work backwards from a cancer diagnosis examining the various patient pathways in order to estimate the sequence of events which led to the diagnosis of cancer.

This research aims to establish whether the Public Health England (PHE) Routes-to-Diagnosis Methodology can be applied to Northern Ireland datasets and to establish the first set of Routes-to-Diagnosis estimates for Northern Ireland. Analysis in this document is presented for all cancers (excluding non-melanoma skin cancer) in Northern Ireland with detailed analysis of Lung, Breast, Prostate and Colorectal Cancer as well as summary information for additional cancer sites.

The analysis presented shows the estimated proportion of cancers diagnosed through each of the main routes and contains comparisons with England as well as key demographic breakdowns and indications of outcomes through survival analysis. The project commenced in February 2018 and reports findings for cancers diagnosed between 2012 and 2016 in Northern Ireland.

The analysis has been carried out by researchers from the Centre for Public Health in Queen’s University Belfast and has been facilitated by the Honest Broker Service within the HSC Business Services Organisation who linked the various datasets and applied the PHE algorithms. Support was provided from the Northern Ireland Cancer Registry, particularly with respect to the base cancer patient data.

The Honest Broker Service facilitates the provision of anonymised patient level data for health research purposes through a safe research environment hosted within the HSC Business Services Organisation.

The research was funded by the Health Foundation, an independent charity committed to bringing about better health and health care for people in the UK, through its Applying Advanced Analytics (AAA) Programme.

We would like to thank all the contributors to this work including the Health Foundation, the Northern Ireland Cancer Registry, Public Health England and our Steering Group for their valuable advice and input throughout the project.

1.2 Background

Analysis of the routes by which patients are diagnosed with cancer were first published in England in 2010 and the award winning study has now presented 10 years of data with over 3 million cancers analysed.

The National Cancer Intelligence Network website provides an array of tools through which the English data can be explored.

http://www.ncin.org.uk/publications/routes_to_diagnosis

Routes-to-Diagnosis uses routinely collected data sources to work backwards through patient pathways to examine the sequence of events that led to a cancer diagnosis. The methodology identifies over 70 individual pathways and then categorises patients into one of eight broad Routes.

The eight broad routes identified in England (English specific terminology)

Route	Description
Screen Detected	Detected via the national breast, cervical or bowel screening programmes
Two Week Wait*	Urgent GP referral with a suspicion of cancer
GP Referral	Routine and urgent GP referrals where the patient was not referred under the Two Week Wait referral Route
Other Outpatient	An elective route starting with an outpatient appointment: either self-referral, consultant to consultant, other or unknown referral
Inpatient Elective	Where no earlier admission can be found prior to elective admission from a waiting list, booked or planned

Emergency Presentation	An emergency route via A&E, emergency GP referral, emergency transfer, emergency consultant outpatient referral, emergency admission or attendance
Death Certificate Only	No data available from Inpatient or Outpatient HES, CWT or screening and with a death certificate only diagnosis flagged by the cancer registry
Unknown	No data available from Inpatient or Outpatient HES, CWT or screening

**It should be noted that in England all urgent GP referrals with suspicion of a cancer have a two week wait target hence the labelling for this route. In Northern Ireland these are referred to as Red Flag Referrals however the target waiting times differ. This route has therefore been re-labelled as Red Flag referral in the Northern Ireland analysis and when comparing with England. The GP Referral route in Northern Ireland therefore consists of non-red flag GP Referrals.*

The English Routes-to-Diagnosis analysis has highlighted differences in how patients were diagnosed, including variation in short-term survival and inequalities across different patient groups and cancers. Updates have been used to chart the impact of the National Awareness and Early Diagnosis Initiative, early diagnosis campaigns, improved treatments and the evolution of screening programmes. Results are regularly used across England to monitor the changes in the distribution of cancers, and to understand better where efforts to improve outcomes can be focused.

1.3 Methods

The Public Health England methodology on which Routes-to-Diagnosis analysis is based was described in detail in the British Journal of Cancer article "Routes-to-Diagnosis for cancer - Determining the patient journey using multiple routine datasets", which was published in October 2012.

The English analysis uses cancer registry records, Inpatient and Outpatient Hospital Episode Statistics data, National Cancer Waiting Times data as well as data from screening services. This data is joined together using NHS number and an algorithm which was developed by Public Health England is applied in order to assign the most likely Route-to-Diagnosis for each cancer.

The algorithm works by assigning an end point which is the interaction assumed to be the clinical care event that led most immediately to diagnosis. Having defined the end point, the algorithm works backwards from the end point across the different data sources in order to

assign a start point which is most likely to be the initial referral which leads to the investigation and diagnosis of cancer.

Much more detail is provided by PHE through the link above and the flow charts they present demonstrate effectively how the different routes are assigned.

The Northern Ireland analysis has been facilitated through the Honest Broker Service.

The Honest Broker Service enables the safe and secure provision of anonymised data to researchers for approved health and social care related research, which is in the overall interest of public health and the development of health and social care related policy.

The authors would like to acknowledge the help provided by the staff of the Honest Broker Service (HBS) within the Business Services Organisation Northern Ireland (BSO). The HBS is funded by the BSO and the Department of Health for Northern Ireland (DoH). The authors alone are responsible for the interpretation of the data and any views or opinions presented are solely those of the author and do not necessarily represent those of the BSO.

For a detailed breakdown of the methods applied in the Northern Ireland analysis, please see the technical documents (attached as Annexes to this main report). This includes full detail of the data preparation steps and decisions made in relation to applying the routes algorithm to Northern Ireland data sources.

A summary of the Northern Ireland data sources which informed the analysis is provided below.

1.4 Data sources

1.4.1 Northern Ireland Cancer Registry (NICR)

The NICR is a population based cancer registry collecting data on all malignant and certain non-malignant tumours diagnosed in Northern Ireland.

For this project, all cancer registrations across Northern Ireland between 2009 and 2016 inclusive were initially extracted from the NICR.

There were certain exclusions from the dataset which are outlined in more detail in the technical document.

1.4.2 Patient Administration System

Patient Administration Systems are principally used to manage and record inpatient, day case and outpatient activity within Health and Social Care hospital sites in Northern Ireland.

Hospital Inpatient System (HIS)

The Hospital Inpatient System (HIS) is formed in the HSC Data Warehouse from PAS data and provides information on admitted patient care delivered by health and social care hospitals in Northern Ireland. It is a patient level administrative data source and each record relates to an individual consultant episode.

For the pathways-to-diagnosis project, an extract containing 2008/09 to 2015/16 records was used to identify patients from the NICR with a hospital admission for any cause during the six months prior to their cancer diagnosis.

Outpatient Universe

The Outpatient Universe is formed in the HSC Data Warehouse from PAS data and provides information on outpatient appointments at Health and Social Care (HSC) hospitals in Northern Ireland. It is a patient level administrative data source.

For the pathways-to-diagnosis project, an extract containing 2008/09 to 2015/16 records was used to identify patients from the NICR with an outpatient attendance for any reason during the six months prior to their cancer diagnosis.

1.4.3 Cancer Patient Pathway System (CaPPS)

The Cancer Patient Pathway System (CaPPS) is a bespoke data system used to administer cancer treatment services within Health and Social Care (HSC) Trusts in Northern Ireland. This dataset contains patient level information and is used to monitor and report on the number of patients treated for cancer following a decision to treat being taken.

For the pathways to diagnosis project an extract containing 2008/09 to 2015/16 records was used to identify patients from the NICR who received an urgent GP referral (or 'Red Flag referral') for suspect cancer.

1.4.4 Screening Data

Flags to indicate whether a cancer patient had attended screening were indicated on the Cancer Registry data. A significant amount of work was carried out between the cancer registry and HSC screening services prior to the project in order to improve coverage and accuracy of the screening data held within the cancer registry.

1.5 Data quality

1.5.1 Private healthcare

Routes-to-diagnosis includes details of private patients treated in NHS hospitals and any such case will have a meaningful route assigned dependent on their activity. Patients treated solely in private hospitals, however, although included in the figures, will receive an 'unknown' Route-to-Diagnosis classification.

1.5.2 Data quality 2009-2011

Initially the project intended to look at Routes-to-Diagnosis for cancers diagnosed between 2009 and 2016, however, a key data source, the CaPPS, was only introduced in Northern Ireland in 2008.

It was clear that the recent introduction of this system was impacting on results 2009 to 2011 and, as a result, a large proportion of cases could not be assigned to a route for these years.

From 2012 to 2016 a consistent and stable pattern was observed in the data so only these results are presented in the analysis.

1.5.3 Inpatient and Outpatient Routes-to-Diagnosis

One of the most consistent findings from the Northern Ireland Routes-to-Diagnosis analysis, when compared to England's findings, is a higher proportion of patients were assigned to the Outpatient Route and also to the Inpatient Route.

The Public Health England definitions of an Outpatient and Inpatient route are as follows:

> ***Outpatient diagnosis (OP)*** *– patients with no inpatient episodes preceding the cancer diagnosis date (as defined above) but with an outpatient attendance preceding the*

cancer diagnosis date or with an inpatient elective admission, or were emergencies via an outpatient clinic, or were unresolved inpatient transfers.

Inpatient diagnosis (IP) *– patients with a cancer diagnosis date related to a preceding inpatient episode (excluding patients already defined as special cases). An inpatient diagnosis is defined where the cancer diagnosis date is within the start and end of an episode. In addition, due to the potential for diagnosis to be confirmed following a relevant inpatient episode, a cancer diagnosis date that is within 6 months after the end of an episode and with no outpatient activity between would also be regarded as an inpatient diagnosis.*

It would be unusual for a patient to arrive at an outpatient clinic or an inpatient setting without an earlier referral from primary care. The higher outpatient and inpatient figures in NI compared to England may be partly an artefact arising from how the PHE algorithm interacts with the NI health service and data sources.

As part of this study significant efforts were made to arrange the Northern Ireland data in as close a format as possible to the English data in order to apply the algorithm, however it was not within the scope of the study to materially adjust the settings within the algorithm itself to better match the Northern Ireland healthcare setting – this set of results therefore reflects a baseline where the Public Health England parameters have been applied to Northern Ireland data.

There are several possible issues which could be investigated in future work:

- There is an element of the algorithm called the “Consultant Overwrite”, this works backwards on an iterative basis in 6 month chunks from an outpatient appointment to see what the source of the outpatient attendance was. For selected referral sources it then overwrites the route-to-diagnosis with an earlier referral source (such as GP) where it deems this appropriate. In Northern Ireland there are a higher proportion of cases which are not subject to the consultant overwrite due to the specific referral source codings. Further investigation is required to see if the rationale for not overwriting these cases with earlier data equally applies in Northern Ireland. Any amendment to the Northern Ireland coding could potentially re-assign some cases to

other routes-to-diagnosis such as GP Referral (please see technical document for more information on this).

- In the earliest iterations of Routes-to-Diagnosis analysis, Public Health England initially reported similar rates of Inpatient Elective Routes-to-Diagnosis as reported here for Northern Ireland. Through improving their linkage to Hospital Episode Statistics over time they subsequently saw a decrease in the proportion of Inpatient Electives and an increase in the proportion of GP Referrals. Further iterative improvements to the quality of the Northern Ireland data and recalibration of the algorithm will potentially lead to similar improvements to the Northern Ireland Routes-to-Diagnosis classifications.
- For example, some of the inpatient cases in the Northern Ireland data appeared to have worse outcomes than those flagged in the English data (e.g. later stage cancer and lower survival rates); these should be looked at to ensure they aren't emergency presentations that have been miscoded and not picked up correctly by the algorithm.
- Cut off dates applied within the algorithm were developed to fit the English healthcare system; these cut off dates may not always be appropriate for Northern Ireland where the cancer related performance targets are different – this could impact the number of Red Flag referrals in particular.
- Differences in access to diagnostic tests – there are potentially differences in the range of diagnostic tests available between primary care and secondary care between Northern Ireland and England. More tests being carried out in an outpatient setting could lead to increased outpatient activity (and hence more chance of the algorithm assigning an outpatient route), however, these would usually be based on referral from primary care.
- Coverage in the CAPPS system – not every case on the cancer registry appears on the CAPPS system. There are certain low grade cancers that are not recorded on CAPPS and any cases that are not managed through a Multidisciplinary Team will not be on this system. However, as this is the source for Red Flag Referrals in the analysis, if there are coverage issues this could potentially lead to cases being incorrectly identified as inpatient/outpatient routes

- Coding Between Hospitals - As outlined in detail in the technical document (page 12) some manual work was carried out to group local codes up into a regional code to mirror the Public Health England Referral Source variable which is a key variable in establishing the outpatient route to diagnosis. Differences in how coding is carried out across Northern Ireland, as well as the process of aggregating the data into the regional code could lead to differences between the Northern Ireland and English data.

Differences in waiting times, with significantly longer waiting times on average in Northern Ireland, could exacerbate all of these issues as they increase the time frame between the initial referrals and the diagnosis and increase the chance of the algorithm missing key information.

The extent to which these issues would potentially reduce the difference in outpatient and inpatient routes-to-diagnosis between Northern Ireland and England is unknown. It is recommended, however, that these issues are investigated further in future iterations of this research and consideration given to customising the algorithm to better fit the cancer targets in and average waiting times experienced by patients in Northern Ireland.

1.5.4 Age impacts and co-morbidities

Lucy Ellis-Brookes et al in their discussion around the routes to diagnosis algorithm state

“A central assumption underlying the assumption is that it is reasonable to suppose that inpatient and outpatient hospital activity up to 6 months, and in particular the 28 days before the diagnosis is linked to the diagnosis of the cancer. This activity may not necessarily be directly caused by the cancer itself as diagnosis can result from other clinical investigations, for example, radiological examination of an unrelated condition.”

The algorithm does not attempt to match diagnosed cancers to cancer-specific inpatient or outpatient records.

This means that there could be some systemic impacts on older patients and patients with pre-existing comorbid conditions – due to the algorithm picking up a higher rate of “background” admission rates, in particular this could bias towards “non-Emergency” presentations.

See the discussion section of the 2012 British Journal of Cancer article on Routes-to-Diagnosis for more information.

1.6 Analytical techniques

1.6.1 Confidence intervals

The confidence intervals in the multiple bar charts were calculated using the standard error SE(P)=√(P*(1-P)/n), where P is the sample proportion of a Route-to-Diagnosis, and n is the number of patients in all Route-to-Diagnosis for a sample proportion, P, and assuming it has a normal distribution (95% confidence interval = $P \pm Z_{0.05} \times SE(P)$). Confidence intervals are indicative of where the true proportion lies, therefore two non-overlapping confidence intervals are indicative of a significant difference between two proportions.

However, a proper hypothesis test of the difference in two proportions would require a specific test statistic about this difference, accounting for numbers in each proportion. In addition, a correction (e.g. Bonferroni) to the p-value of the test statistic would be needed to protect against a false Type 1 error rate arising from making multiple comparisons.

1.6.2 Three year net survival

Three year net survival (Perme et al., 2012) using the complete approach (Brenner & Gefeller, 1997) was used for estimating the survival of cancer patients diagnosed from 2012-2016 followed up to the end of 2017. This guaranteed at least 3 years (2012-2014) of patient data followed up for a minimum of 3 years. In future updates to Route-to-Diagnosis analysis, it will be possible to extend follow-up and produce five-year estimates as standard. Net survival required the use of Northern Ireland lifetables to estimate the non-cancer mortality rates of cancer patients. To prevent spurious results, survival estimates were only presented when at least 50 patients contributed data; this approach reflects international cancer studies such as CONCORD (Allemani et al., 2015).

1.6.3 Control limits

A random-effects model was employed to inform the control limits of the funnel plots using a methodology described by Spiegelhalter (2005). This approach recognises two sources of variation, one that recognises variation between estimates or random effects variation, and another, sampling variation, which is a function of an estimate's sample size. In a process

control environment, when an estimate breaches the 95% control limits it is a 'warning', whereas breaching the 99.8% control limit signifies a real departure. Adopting the conservative 99.8% control limit protects against making Type 1 statistical errors.

1.6.4 Standardisation

The proportion of patients diagnosed via Route-to-Diagnosis by HSC Trusts were age-, sex- and deprivation-adjusted. This was achieved by fitting a logistic model of a dummy variable for the Route-to-Diagnosis as outcome with Trust by age interaction terms, plus main terms for sex and deprivation.

1.7 Report Structure

Each chapter is structured in a similar fashion with descriptive statistics and charts supplemented with commentary. Within each results chapter, both tables and figures are sequenced from 1 upwards.

Routes-to-diagnosis breakdowns are presented with comparisons against England where possible. The data has been broken down by key demographics such as age, gender, deprivation and geography.

Survival analysis and breakdowns by stage and Route-to-Diagnosis have been provided as key indicators of outcomes associated with the different Route-to-Diagnosis.

The commentary highlights statistically significant findings – while it is not within the remit to investigate reasons for variation, there is a discussion section at the end of each chapter where potential points of interest are suggested.

1.7.1 Conceptual Framework

The routes to diagnosis is a rich source of information. The experience in Public Health England is that it generates a lot of research questions and suggests potential avenues for further investigation. For instance, the information can be used to identify target populations, or disease or service factors for interventions to promote earlier diagnosis. Theoretical frameworks for understanding the process of how patients become aware of symptoms and present to the GP are useful for situating the Route-to-Diagnosis information. The General Model of Total Patient Delay (also known as the Andersen Model

of Diagnostic Delay) describes potential causes for delayed diagnosis in cancer patients (Figure 1) (Andersen et al., 1995).

The model described five delay intervals between a patient experiencing a symptom and seeking treatment:

1. Appraisal delay (time taken for a patient to evaluate their symptoms as illness)
2. Illness delay (time between illness inferred and decision to seek medical attention)
3. Behavioural delay (time between decision to seek medical attention and scheduling appointment)
4. Scheduling delay (time between scheduling appointment and receiving medical attention)
5. Treatment delay (time between receiving medical attention and beginning treatment for illness)

The model found appraisal delay contributed to the majority (>60%) of delay in diagnosis (Andersen et al, 1995). More recently, a review examined the application of the Andersen Model in studies which assessed cancer diagnosis, and assessed the utility of the Andersen Model in conceptualising and measuring the different stages leading to cancer diagnosis (Walter et al., 2012). Figure 2 provides a summary schema or model of the cancer patient's pathway to diagnosis, which is, not only a deliberation on the findings of the review, but also an attempt to simplify the process, and clarify definitions with a view to being able to measuring components of delay. The schema in Figure 2 is useful for considering how Routes-to-Diagnosis may be able provide evidence on different components of delay.

An emergency admission can indicate that there were delays in both the *appraisal* and *help-seeking* intervals for many patients. For various reasons, a patient does not present early in the disease's development. For some cancers, particularly in internal organs, the cancer may be advanced before there are any symptoms. In other cases, symptoms may be present but confounded with symptoms of other comorbidities, for example coughing in lung cancer patients may be caused by other respiratory conditions that smokers frequently have. In addition, patients, not being aware of the importance of specific symptoms, or being advanced in age and, possibly, with dementia, may also not act on symptoms until they become grave. These grave symptoms precipitate an emergency presentation which can be

initiated by the patient, their GP, or a hospital consultant. They are diagnosed, most likely, with advanced disease for which the curative treatment options are very limited, and their prognosis is not good.

Figure 1: The General Model of Total Patient Delay as proposed by Andersen et al. (1995). Reproduced with permission from the British Journal of Social Psychology

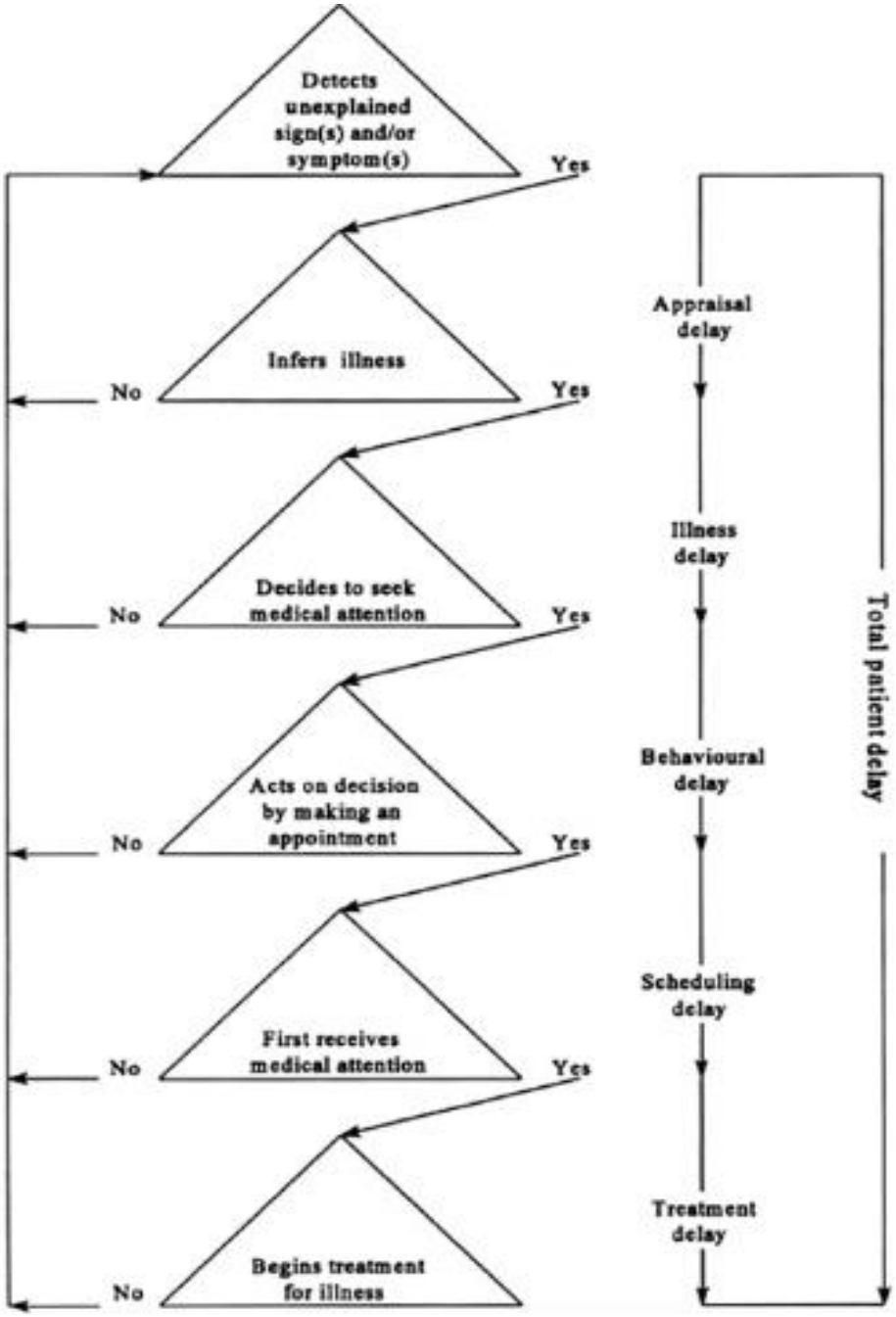

Figure 2: Model of pathways to treatment, a summary schema of review on the Anderson model by Walter et al.

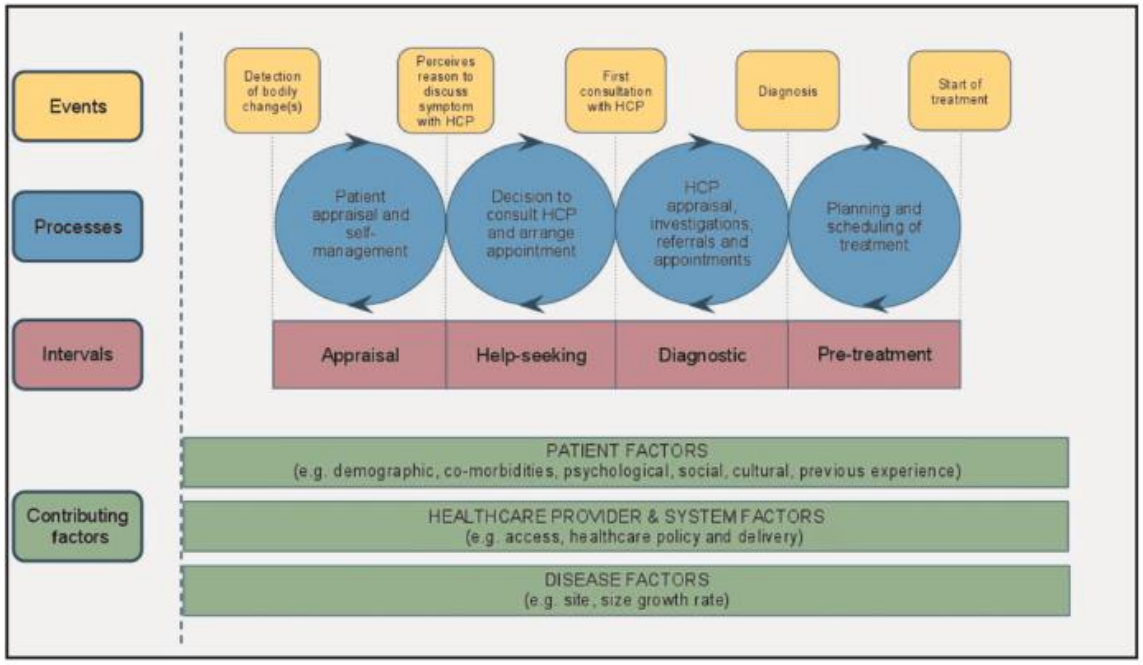

Figure 3 Model of pathways to treatment
HCP = health care provider

Almost the inverse of the emergency route, the screening route generally leads to a diagnosis without any appreciable *appraisal* or *help-seeking* interval. The disease is detected at a pre-symptomatic and early-stage, and for which the success of curative treatment is high, leading to good survival providing that the *diagnostic* and *pre-treatment* intervals are short (Figure 2). Waiting lists are long in NI, allowing the possibility of gains, through screening, being lost in delays post-diagnosis.

Between screening and emergency, Routes-to-Diagnosis that involve GPs will have *appraisal* or *help-seeking* intervals whose lengths will be influenced by a variety of patient, disease and primary care factors. In order to enter the system with a red-flag referral, the patient needs to display a specific symptom that raises suspicion of cancer and places them on a fast-track pathway. Depending on the type of cancer, and the co-existing comorbidities of the patient, there may be a specific cancer symptom that will quicken the *appraisal* and *help-seeking* intervals, e.g. rectal bleeding. If the symptom reflects early-stage disease, the red-flag system has the potential to improve outcomes by shortening the *diagnostic* interval. However, some of these symptoms are associated with already advanced disease that leads to fewer, or less effective, treatment options and poorer outcomes, despite the potential to shorten some intervals to getting treatment. Alternatively, a patient may

present with non-specific symptoms which require further investigation but do not meet the threshold for a red flag referral, and they may receive a routine GP referral. These patients being on a slower-track may experience longer delays in the *diagnostic* interval, as well as having probable delays in the *appraisal* and *help-seeking* intervals, leading to poorer outcomes.

Patients diagnosed via outpatient or inpatient routes are possibly undergoing elective treatment or treatment unrelated to cancer. Due to the more intense medical observation, cancer is opportunistically detected. Symptoms and disease may therefore be detected earlier for that patient with reduced or non-existent *appraisal* and *help-seeking* intervals, and shorter *diagnostic* interval. However, on the other hand, if the patient is unwell with non-cancer comorbidity, cancer symptoms may be masked leading to a much later diagnosis (than had they been able to appraise and seek-help) with more advanced disease, and poor survival. Comorbidity alone may also influence survival. These counteracting factors make conjecture about survival in patients diagnosed in elective Routes-to-Diagnosis less clear.

1.8 Data visualisation

In support of the main report with Routes-to-Diagnosis and discussion by site, an interactive tool has also been developed.

This tool is based on aggregate pre-prepared data which has been cleared for statistical disclosure risk and has been developed in open source software using “R Studio”.

The interactive tool is a series of HTML documents which can be downloaded from the website and opened in an internet browser.

http://www.hscbusiness.hscni.net/services/3102.htm

The tool allows users to delve deeper into the information and compare across multiple cancer sites and breakdowns which are not included in the main report.

The tool should be viewed very much as a prototype with additional scope in future for enhanced functionality including the creation of bespoke analyses by users, subject to funding and within an appropriate data governance framework.

1.9 Future Updates

This is a time limited funded study, however the intention has been to leave a methodology and set of procedures so that the analysis can be replicated.

A separate implementation plan, for consideration by internal stakeholders, has been produced outlining options for continuing this work in the future subject to longer term funding being secured.

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2. Results

2.1 All Cancers

2.1.1 Key findings

- Route-to-diagnosis is reported on 46,068 cancer patients diagnosed with cancer[1] (excluding non-melanoma skin cancer) in NI from 2012-2016 in this chapter.
- For all cancers in Northern Ireland (excluding non-melanoma skin cancer) the red flag Routes-to-Diagnosis was the most common way to receive a cancer diagnosis (28.3%) followed by the GP Route-to-Diagnosis (21.4%). The proportion of Red Flag Route-to-Diagnosis increased over the years 2012-2016 in NI reaching 30.5% in 2015.
- There was a higher proportion of patients diagnosed in Red Flag Route-to-Diagnosis in England (35.2%), whereas NI had higher outpatient and inpatient cancer diagnoses. The higher proportions of patients diagnosed through outpatient and inpatient Routes-to-diagnosis in NI compared to England may be partly an artefact arising from how the PHE algorithm interacts with the NI health service and data sources, which requires further investigation (See Section 1.5.3).
- Proportions of patients diagnosed in screening (5.7%) and Emergency Presentation Route-to-Diagnosis (20.0%) were almost equal between NI and England.
- There was an increasing gradient in proportion of Emergency Presentation Route-to-Diagnosis with deprivation quintile. The Emergency Presentation Route-to-Diagnosis was more common in older patients (aged 75 years and older).
- Three-year net survival was highest for screen detected cancers (97%), and lowest for Emergency Presentation (21.0%).

[1] 'All cancer' in this chapter is defined by ICD-10 (WHO, 2011) topological sites C01-C43, C45-C97

2.1.2 All Cancer (excluding non-melanoma skin cancer)

Cancer occurs when abnormal cells (generated by faulty cell growth signalling pathways) divide in an uncontrolled way. This uncontrolled proliferation may invade tissues; the cancer is defined according to the anatomical site in which the cells divide (Cancer Research UK, 2017a). In Northern Ireland (NI) between 2013-2017 there were 4,691 male and 4,710 female patients diagnosed with cancer (excluding Non-Melanoma Skin Cancer (NMSC)) annually; lifetime risk of developing a cancer was 1 in 3.5 for men and 1 in 3.7 for women (Northern Ireland Cancer Registry, 2020). From 2008 to 2017 the number of patients diagnosed with cancer increased due to the growing number of older people in the NI population. In NI there are 4,338 deaths from cancer (2,275 in men, 2,064 in women) annually.

2.1.2.1 Incidence and survival

The European age-standardised incidence rate for cancer is 590 per 100,000 for NI (Cancer Research UK, 2017b). Older people are more likely to develop cancer; 63% of cancers occur in people aged 65 years or older, and incidence rates were greatest amongst those aged 85-89 years (2,687 cases per 100,000) (Northern Ireland Cancer Registry, 2020). Some cancers are specific to men or women (e.g. ovarian cancer) only. In the UK between 2014-2016 incidence rates were higher for females among younger age groups, but higher amongst older males (Cancer Research UK, 2017c). Between 2013 and 2017, the most common cancers amongst males were prostate cancer, lung cancer, bowel, head & neck cancer and lymphomas, whilst breast cancer, lung cancer, bowel, uterine cancer, and ovarian cancer were most common amongst females. One- and five- year net survival in NI is 71.5% and 56.0%, respectively (diagnosis period 2007- 2011); an improvement from 1993-1996 net survival which was 60.3% and 41.3%, respectively.

2.1.3 Routes-to- diagnosis in Northern Ireland and England

2.1.3.1 Incidence of Routes-to-Diagnosis in NI and England

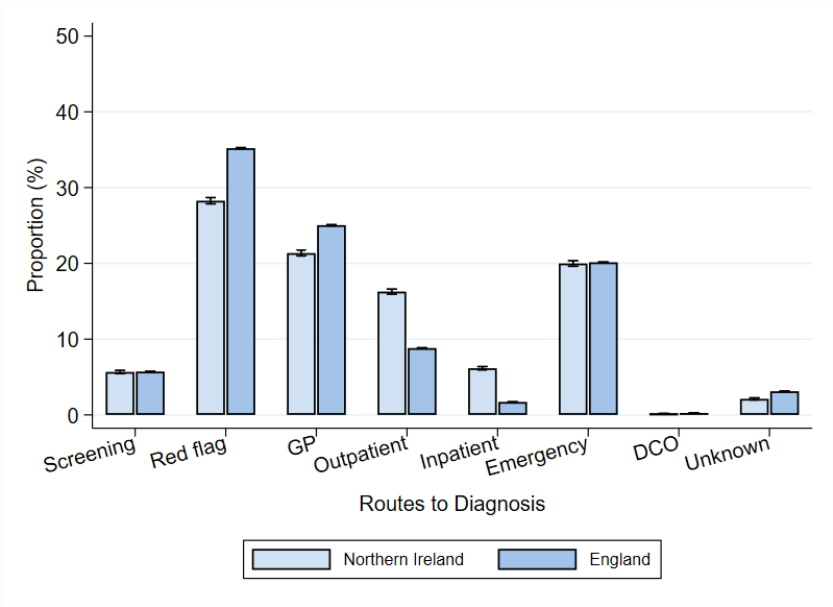
In NI, large proportions of cancer patients are diagnosed via Red Flag Route-to-Diagnosis (28.3%), GP Routes-to-Diagnosis (21.4%) and Emergency Presentation Route-to-Diagnosis (20.0%) (Table 1). The proportions of patients diagnosed via a Screening Route-to-Diagnosis

(5.7%) and Emergency Presentation Routes-to-Diagnosis (20.0%) are almost identical between NI and England (Table 1). There was a higher proportion of Red Flag Routes-to-Diagnosis in England (35.2%) compared to NI (28.3%), and GP Route-to-Diagnosis in England (25.0%) than NI (21.4%). The proportions diagnosed via Inpatient Route-to-Diagnosis and Outpatient Route-to-Diagnosis were higher in NI compared to England (16.3% vs 8.8%) (Figure 1).

Table 1: The frequency (n) and distribution (%) of Routes-to-Diagnosis of all cancer patients diagnosed in 2012-2016, by country

Route-to-diagnosis	Northern Ireland		England	
	n	%	n	%
Screening	2,612	5.7	85,588	5.7
Red Flag	13,022	28.3	527,054	35.2
GP Referral	9,840	21.4	374,999	25.0
Outpatient	7,496	16.3	132,050	8.8
Inpatient	2,837	6.2	25,554	1.7
Emergency Presentation	9,208	20.0	301,444	20.1
Death Certificate Only	77	0.2	3,881	0.3
Unknown	976	2.1	46,647	3.1
Total	**46,068**		**1,497,217**	

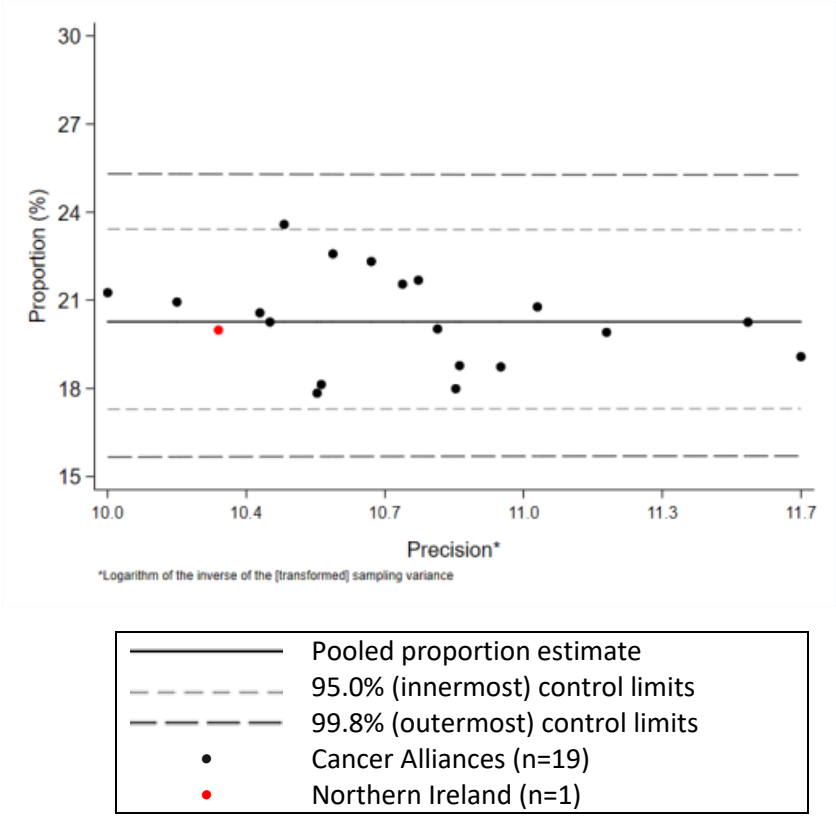
Figure 1: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with all cancer from 2012-2016, by country (Northern Ireland and England)



2.1.3.2 Northern Ireland compared to English Cancer Alliances

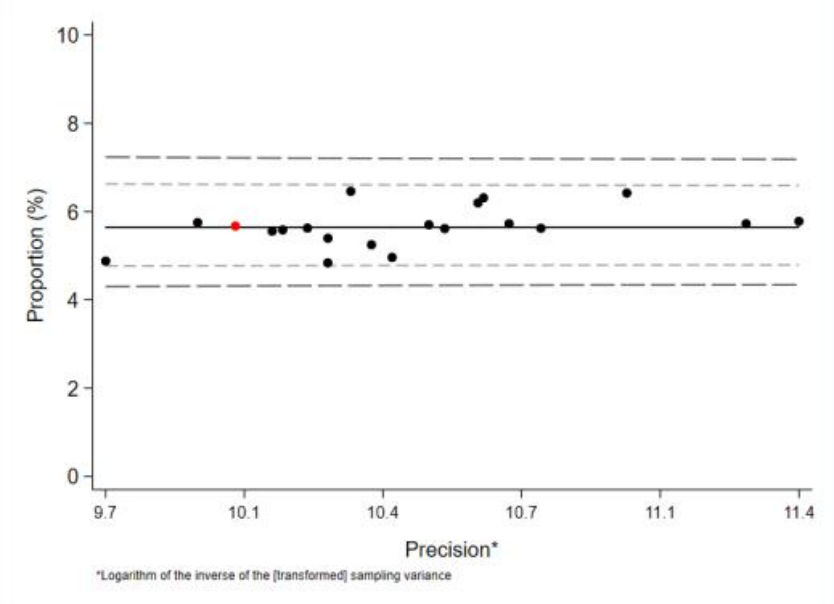
The proportion of patients diagnosed through different routes from 2012-2016 was compared between NI and the English Cancer Alliances (n=19) on a funnel plot (Figures 2-5). The pooled proportion of English Cancer Alliances estimate shown in the funnel plot will be different from the English estimate for each route observed in Table 1.

Figure 2: Proportion (%) of patients diagnosed for all cancers in 2012-2016 through an emergency presentation Route-to-Diagnosis in English Cancer Alliances (n=19) and Northern Ireland presented in a funnel plot



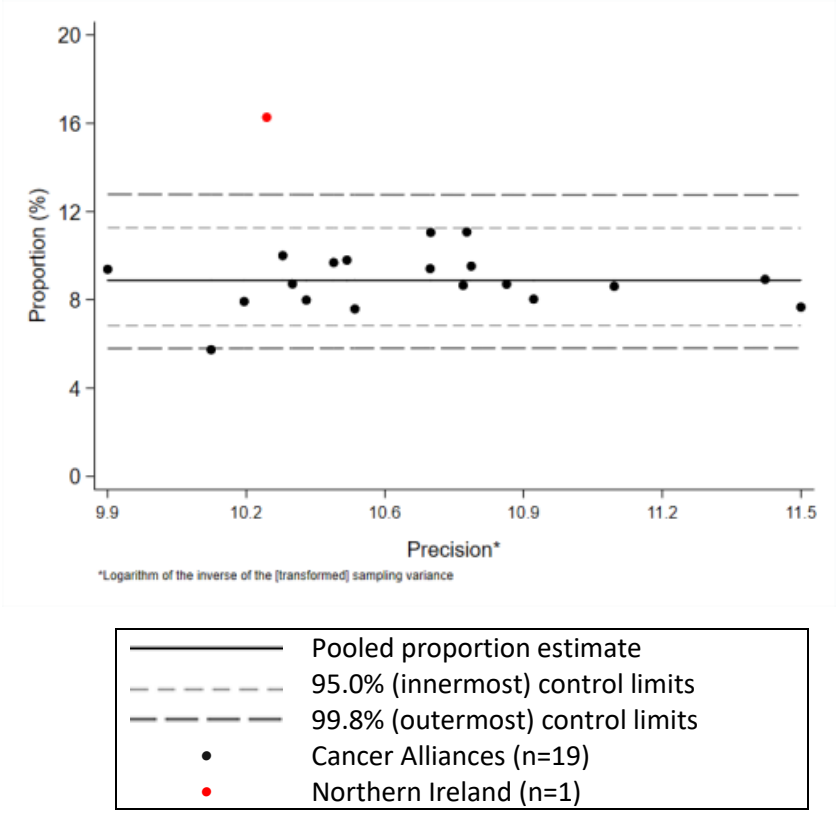
The NI proportion of Emergency Presentation Routes-to-Diagnosis (20.0%), lying within the 95% control limits, was not significantly different from the pooled proportion estimate of the English Cancer Alliances (20.3%) (Figure 2).

Figure 3: Proportion (%) of patients diagnosed for all cancers in 2012-2016 through a screening Route-to-Diagnosis in English Cancer Alliances (n=19) and Northern Ireland presented in a funnel plot



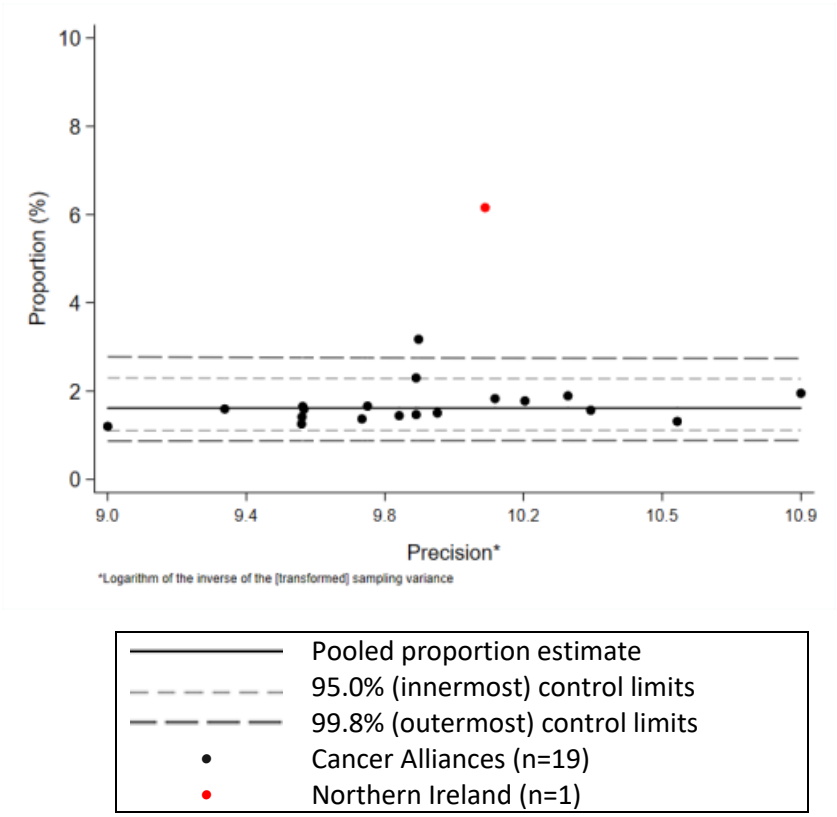
The NI proportion of Screening Routes-to-Diagnosis (5.7%), lying within the 95% control limits, was not significantly different from the pooled proportion estimate of the English Cancer Alliances (5.6%) (Figure 3). The variation between the Cancer Alliances' proportions of Screening Routes-to-Diagnosis was much lower (see width of the control limits) than the variation of Emergency Presentation Routes-to-Diagnosis (Figure 2).

Figure 4: Proportion (%) of patients diagnosed for all cancers in 2012-2016 through an outpatient Route-to-Diagnosis in English Cancer Alliances (n=19) and Northern Ireland presented in a funnel plot



The NI proportion of Outpatient Routes-to-Diagnosis (16.3%), lying outside the 99.8% control limits, was significantly different from the pooled proportion estimate of the English Cancer Alliances (8.9%) (Figure 4).

Figure 5: Proportion (%) of patients diagnosed for all cancers in 2012-2016 through an inpatient Route-to-Diagnosis in English Cancer Alliances (n=19) and Northern Ireland presented in a funnel plot



The NI proportion of Inpatient Routes-to-Diagnosis (6.2%), lying outside the 99.8% control limits, was significantly different from the pooled proportion estimate of the English Cancer Alliances (1.6%) (Figure 5).

For Red Flag Routes-to-Diagnosis and GP Routes-to-Diagnosis, NI had lower proportions of patients, breaching the 95.0% control limit but not the 99.8%, than England's pooled proportion estimates of 35.2% and 24.9%, respectively (funnel plots not shown).

2.1.4 Northern Ireland Routes-to-Diagnosis: demographic and stage breakdown

2.1.4.1 Patient Sex

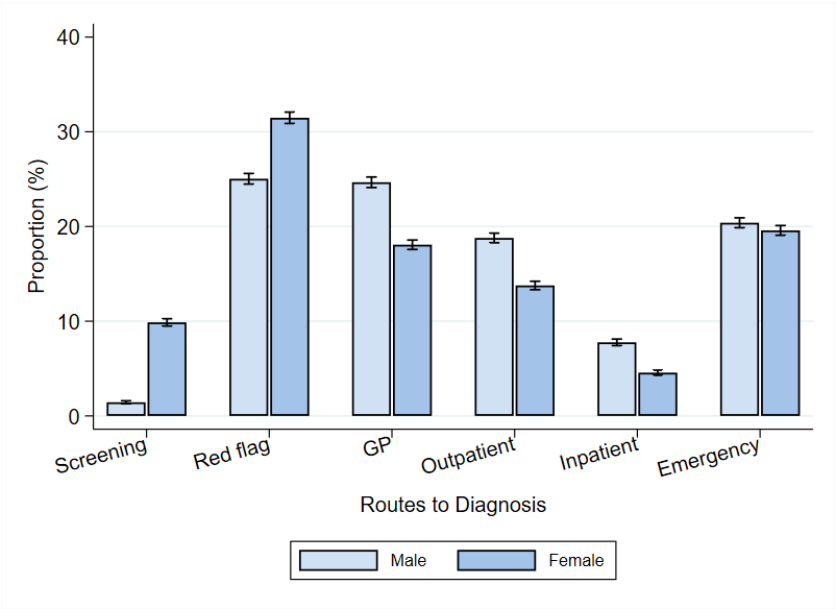
Women were more likely than men to be diagnosed via Screening Routes-to-Diagnosis (9.9% vs 1.4%) and Red Flag Route-to-Diagnosis (31.5% vs 25.0%), while men were more likely than women to be diagnosed via GP Route-to-Diagnosis (24.7% vs 18.1%), Outpatient Routes-to-Diagnosis (18.8% vs 13.8%) and Inpatient Route-to-Diagnosis (7.8% vs 4.6%). These differences are likely to be influenced by the naturally higher levels of screening in women for breast and cervical cancer. Emergency Presentation Routes-to-Diagnosis proportions were similar in both sexes at around 20% (Table 2, Figure 6).

Table 2: The frequency (n) and distribution (%) of Routes-to-Diagnosis of all cancer patients diagnosed in 2012-2016, by sex

Route-to-diagnosis	Male		Female	
	n	%	n	%
Screening	330	1.4	2,282	9.9
Red Flag	5,749	25.0	7,273	31.5
GP Referral	5,664	24.7	4,176	18.1
Outpatient	4,314	18.8	3,182	13.8
Inpatient	1,783	7.8	1,054	4.6
Emergency Presentation	4,682	20.4	4,526	19.6
Total	**22,961**		**23,107**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown-Route to diagnosis

Figure 6: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with all cancer within Northern Ireland from 2012-2016, by patient sex

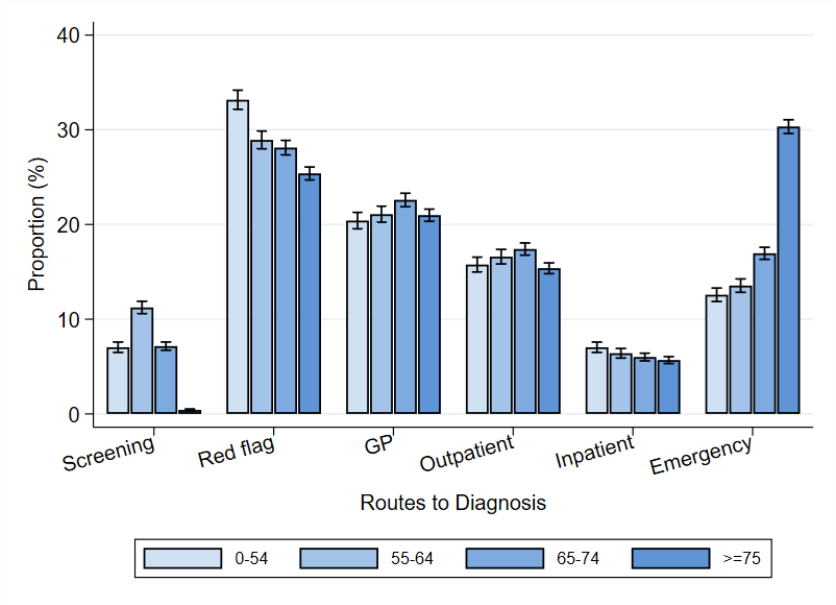


2.1.4.2 Age

The proportion of patients diagnosed via Screening Routes-to-Diagnosis peaked in the 55-64 age group at over 10%, as expected given the age range of the screening programmes in NI (breast, 50-70 years; colorectal, 50-70; cervical, 25-64). Patients in the 75+ age group had the lowest proportion of Screening Routes-to-Diagnosis (0.4%) and the largest proportion of Emergency Presentation Routes-to-Diagnosis (30.3%) (Table 3). The proportion of patients with Red Flag Routes-to-Diagnosis and Inpatient Routes-to-Diagnosis decreased for older patients, while GP Routes-to-Diagnosis and outpatient Routes-to-Diagnosis proportions increased to age groups 65-74 but declined in age group 75+ (Figure 7).

Table 3: The frequency (n) and distribution (%) of Routes-to-Diagnosis of all cancer patients diagnosed in 2012-2016, by age group								
Route-to-diagnosis	**Age groups (years)**							
	0-54		**55-64**		**65-74**		**75+**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Screening	585	7.0	1,011	11.2	951	7.2	65	0.4
Red Flag	2,758	33.2	2,603	28.9	3,737	28.1	3,924	25.4
GP Referral	1,697	20.4	1,897	21.1	3,003	22.6	3,243	21.0
Outpatient	1,311	15.8	1,494	16.6	2,314	17.4	2,377	15.4
Inpatient	585	7.0	576	6.4	798	6.0	878	5.7
Emergency Presentation	1,046	12.6	1,219	13.5	2,254	17.0	4,689	30.3
Total	**8,316**		**8,999**		**13,294**		**15,459**	
Note: frequency (n) will sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis								

Figure 7: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with all cancer within Northern Ireland 2012-2016, by age group



2.1.4.3 Year of diagnosis

Despite the short timeframe of available data, there was a significant and sizeable trend in the proportions of patients diagnosed via Red Flag Routes-to-Diagnosis in 2012-2016, peaking in 2015 (30.5%) (Table 4). A small positive trend was observed in Outpatient

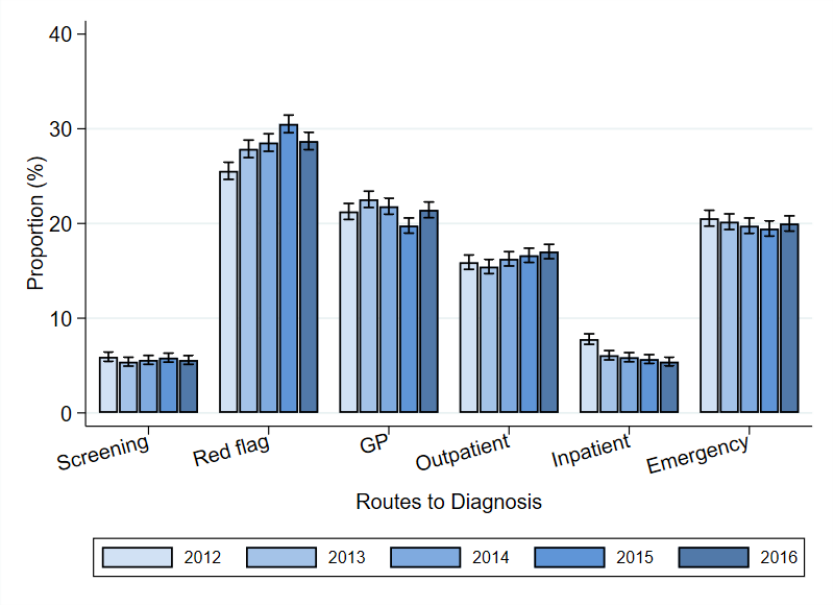
Routes-to-Diagnosis, while a slight negative trend was observed in Inpatient Routes-to-Diagnosis. There were no trends observed in GP Routes-to-Diagnosis, Screening Routes-to-Diagnosis, or Emergency Presentation Routes-to-Diagnosis proportions over the time period (Figure 8).

Table 4: The frequency (n) and distribution (%) of Routes-to-Diagnosis of all cancer patients, by year of diagnosis

Route-to-diagnosis	Year of diagnosis									
	2012		2013		2014		2015		2016	
	n	%	n	%*	n	%	n	%	n	%
Screening	532	5.9	490	5.4	513	5.6	550	5.8	527	5.6
Red Flag	2,295	25.6	2,527	27.9	2,616	28.5	2,877	30.5	2,707	28.7
GP Referral	1,910	21.3	2,044	22.6	1,999	21.8	1,865	19.8	2,022	21.4
Outpatient	1,429	15.9	1,400	15.4	1,491	16.3	1,569	16.6	1,607	17.0
Inpatient	700	7.8	552	6.1	539	5.9	536	5.7	510	5.4
Emergency Presentation	1,846	20.6	1,830	20.2	1,811	19.8	1,835	19.5	1,886	20.0
Total	**8,980**		**9,064**		**9,164**		**9,429**		**9,431**	

Note: frequency (n) will sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 8: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with all cancer in Northern Ireland 2012-2016, by year of diagnosis



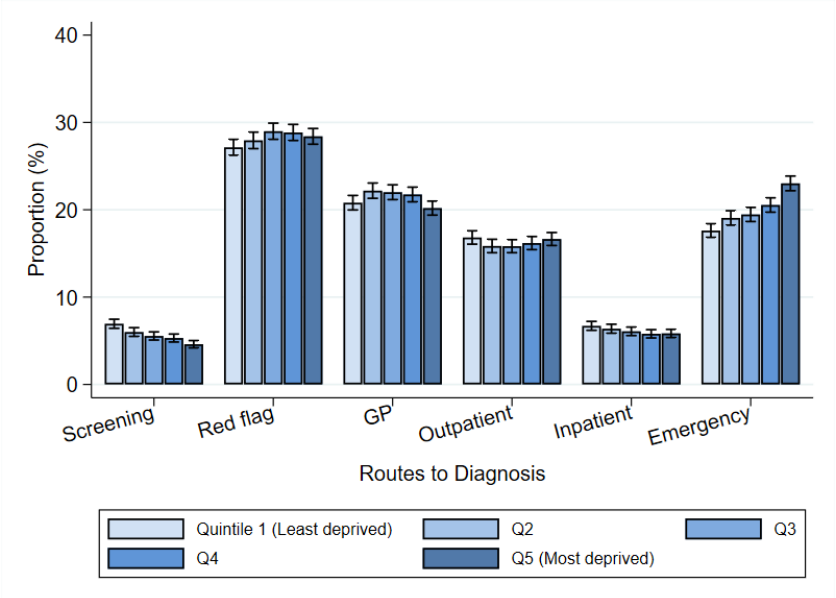
2.1.4.4 Deprivation

Deprivation in this report was measured using the Northern Ireland Multiple Deprivation Measure (NIMDM) for 2010 (Northern Ireland Statistics and Research Agency, 2010). Northern Ireland's Super Output Areas (SOA, n=890) were ranked by NIMDM and divided into quintiles. Cancer patients were assigned to deprivation quintiles according to the quintile of their SOA of residence at diagnosis.

There was a strong positive association in the proportion of patients diagnosed via an Emergency Presentation Routes-to-Diagnosis and deprivation quintile, from least deprived (17.6%, Quintile 1) to most deprived (23.0%, Quintile 5). The proportion of Screening Routes-to-Diagnosis was inversely associated with deprivation, with 6.9% in the least deprived quintile (Quintile 1) to 4.6% in the most deprived quintile (Quintile 5). The proportion of Red Flag Routes-to-Diagnosis was lower in the most affluent quintile compared to the more deprived quintiles 3 to 5 which were similar (Figure 9). There was no strong gradient of the proportion of GP Routes-to-Diagnosis, Outpatient Routes-to-Diagnosis, or Inpatient Routes-to-Diagnosis by deprivation quintile (Table 5).

Table 5: The frequency (n) and distribution (%) of Routes-to-Diagnosis of all cancer patients diagnosed in 2012-2016, by deprivation quintile										
Route-to-diagnosis	**Deprivation Quintile**									
	Quintile 1 (least deprived)		**Quintile 2**		**Quintile 3**		**Quintile 4**		**Quintile 5 (most deprived)**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Screening	640	6.9	521	6.0	512	5.6	494	5.3	444	4.6
Red Flag	2,501	27.1	2,426	27.9	2,674	29.0	2,681	28.8	2,738	28.4
GP Referral	1,917	20.8	1,926	22.2	2,030	22.0	2,021	21.7	1,946	20.2
Outpatient	1,550	16.8	1,376	15.8	1,460	15.8	1,504	16.2	1,605	16.6
Inpatient	618	6.7	554	6.4	561	6.1	539	5.8	563	5.8
Emergency Presentation	1,623	17.6	1,655	19.1	1,795	19.5	1,909	20.5	2,219	23.0
Total	**9,213**		**8,682**		**9,224**		**9,293**		**9,640**	
Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis										

Figure 9: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with all cancer within Northern Ireland 2012-2016, by deprivation quintile



2.1.4.5 Stage

As well as the frequency and percentage (%) distribution of Routes-to-diagnosis by stage (Table 6, Figure 10), the frequency and percentage distribution of stage by Routes-to-

diagnosis (Table 7 & 8, Figure 11) is presented to investigate the case-mix of patients in each Route-to-diagnosis.

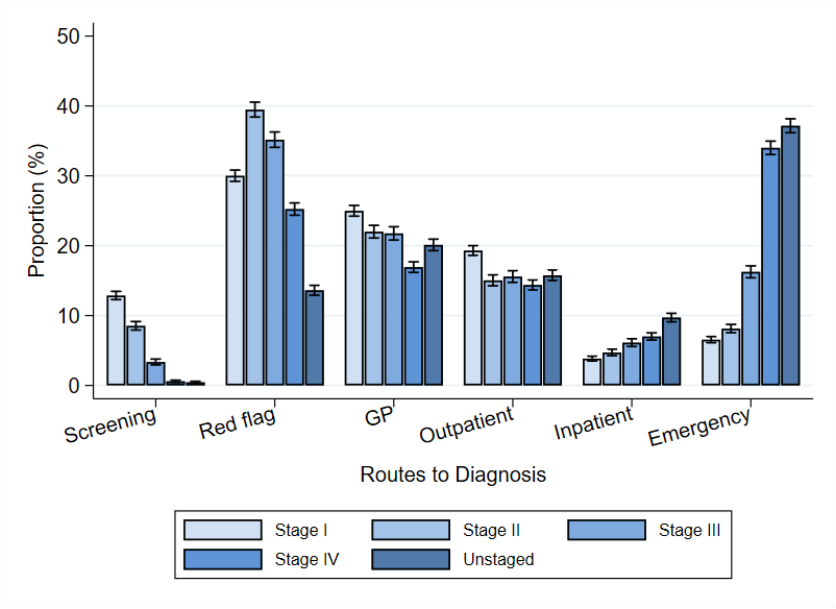
A majority (>55%) of patients with Stage I-III disease were diagnosed in either Red Flag Route-to-Diagnosis, or GP Route-to-Diagnosis, while Stage IV and unstaged patients were more likely (>33%) to be diagnosed in an Emergency Presentation Route-to-Diagnosis (Table 6). Around 13% of Stage I patients were diagnosed via a Screening Route-to-Diagnosis. Stage II and III disease patients were most likely (>35%) to be diagnosed via a Red Flag Route-to-Diagnosis than any other Route-to-diagnosis (Figure 10).

Table 6: The frequency (n) and distribution (%) of Routes-to-Diagnosis of all cancer patients diagnosed in 2012-2016, by cancer stage

Routes-to-diagnosis	Stage groups									
	I		II		III		IV		Unstaged*	
	n	%	n	%	n	%	n	%	n	%
Screening	1,585	12.9	687	8.5	243	3.4	56	0.6	41	0.5
Red Flag	3,695	30.0	3,177	39.5	2,544	35.2	2,367	25.2	1,239	13.6
GP Referral	3,077	25.0	1,771	22.0	1,574	21.8	1,588	16.9	1,830	20.1
Outpatient	2,377	19.3	1,210	15.0	1,127	15.6	1,348	14.4	1,434	15.8
Inpatient	473	3.8	380	4.7	443	6.1	657	7.0	884	9.7
Emergency Presentation	807	6.6	655	8.1	1,176	16.3	3,189	34.0	3,381	37.2
Total	**12,311**		**8,048**		**7,233**		**9,378**		**9,098**	

*cancer stage unknown
Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 10: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with all cancer within Northern Ireland from 2012-2016, by cancer stage



Patients diagnosed through a Screening Route-to-Diagnosis had a high proportion of Stage I diagnoses (60%) (Table 7), while patients diagnosed via Emergency Presentation Route-to-Diagnosis and Inpatient Route-to-Diagnosis had high proportions of Stage IV and unstaged disease (Table 8). Red Flag Route-to-Diagnosis, GP Route-to-Diagnosis, Outpatient Route-to-Diagnosis proportions were distributed more evenly among the disease stage groups although all still had their highest proportions at Stage I (Figure 11). With the exception of Screening Route-to-Diagnosis, all Routes-to-diagnosis had sizeable proportions of Stage IV disease.

Table 7: The frequency (n) and distribution (%) of cancer stage of all cancer patients diagnosed in 2012-2016, by Route-to-Diagnosis

Stage groups	Routes-to-diagnosis					
	Screening		Red Flag		GP	
	n	%	n	%	n	%
I	1,585	60.7	3,695	28.4	3,077	31.3
II	687	26.3	3,177	24.4	1,771	18.0
III	243	9.3	2,544	19.5	1,574	16.0
IV	56	2.1	2,367	18.2	1,588	16.1
Unstaged*	41	1.6	1,239	9.5	1,830	18.6
Total	**2,612**		**13,022**		**9,840**	

*cancer stage unknown

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

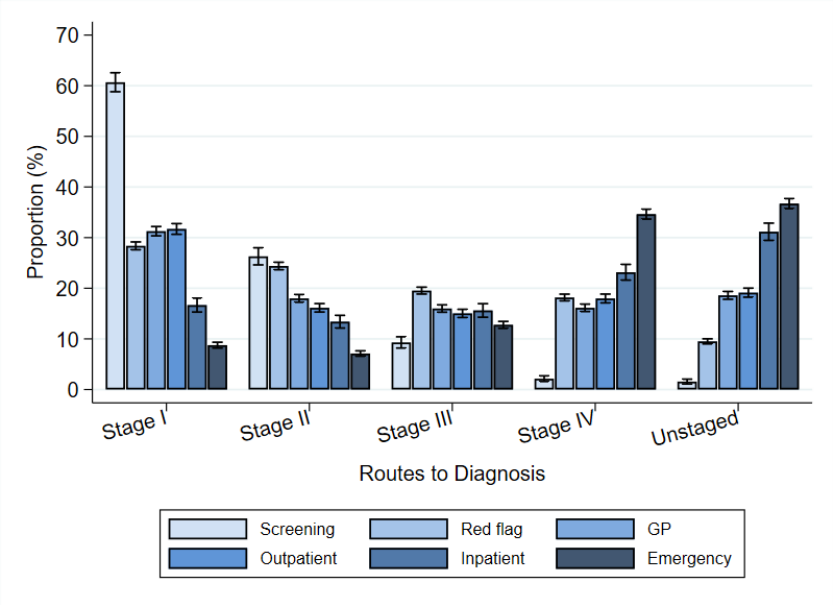
Table 8: The frequency (n) and distribution (%) of cancer stage of all cancer patients diagnosed in 2012-2016, by Route-to-Diagnosis

Stage groups	Routes-to-diagnosis					
	Outpatient		Inpatient		Emergency Presentation	
	n	%	n	%	n	%
I	2,377	31.7	473	16.7	807	8.8
II	1,210	16.1	380	13.4	655	7.1
III	1,127	15.0	443	15.6	1,176	12.8
IV	1,348	18.0	657	23.2	3,189	34.6
Unstaged*	1,434	19.1	884	31.2	3,381	36.7
Total	**7,496**		**2,837**		**9,208**	

*cancer stage unknown

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 11: Distribution (%) of stage for patients diagnosed with all cancer within Northern Ireland from 2012-2016, by Routes-to-Diagnosis

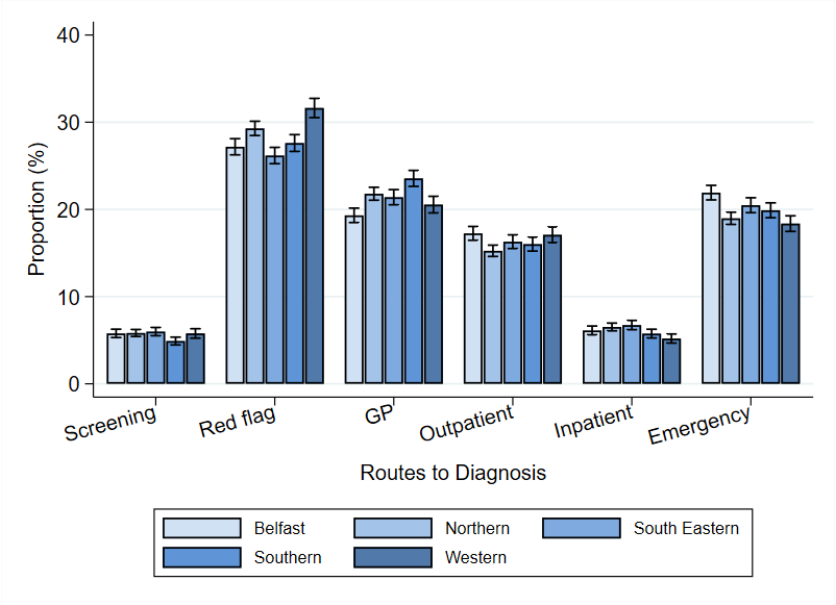


2.1.5 Geographic variation within NI Healthcare Trusts

There was a higher proportion of patients diagnosed via Red Flag Route-to-Diagnosis in the Western Trust (31.7%, Table 9), which was significant after adjustment for age group, patient sex and deprivation (Figure 12). Likewise, the Southern Trust had a greater proportion (23.7%) of GP Route-to-Diagnosis. Belfast Trust had a greater proportion of Emergency Presentation Route-to-Diagnosis (23.0%) than the other Trusts.

Table 9: The frequency (n) and distribution (%) of Routes-to-Diagnosis of all cancer patients diagnosed 2012-2016, by Trust										
Routes-to-diagnosis	**Healthcare Trust**									
	Belfast		**Northern**		**South Eastern**		**Southern**		**Western**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Screening	512	5.5	710	5.9	570	6.3	425	5.0	394	5.5
Red Flag	2,535	27.0	3,513	29.3	2,343	26.0	2,366	27.8	2,263	31.7
GP Referral	1,781	19.0	2,628	21.9	1,935	21.5	2,017	23.7	1,479	20.7
Outpatient	1,606	17.1	1,831	15.3	1,486	16.5	1,354	15.9	1,218	17.0
Inpatient	566	6.0	785	6.5	618	6.9	492	5.8	374	5.2
Emergency Presentation	2,158	23.0	2,252	18.8	1,760	19.5	1,683	19.8	1,348	18.9
Total	**9,376**		**12,001**		**9,015**		**8,514**		**7,146**	
Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis										

*Figure 12: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with all cancer within Northern Ireland 2012-2016, by Trust**



***** The presented proportions in Figure 12 were standardised to the NI population by the following factors: age, sex, and deprivation. Please see 1.6 Analytical techniques for further details.

2.1.6 Survival

The report presents net survival estimates, a theoretical statistic used for comparing groups of patients whose non-cancer or background mortality will differ (e.g. different regions or calendar periods). Net survival is defined as the probability of surviving cancer when the mortality from other causes of death is removed (see also Perme, Stare, & Estève, 2012).

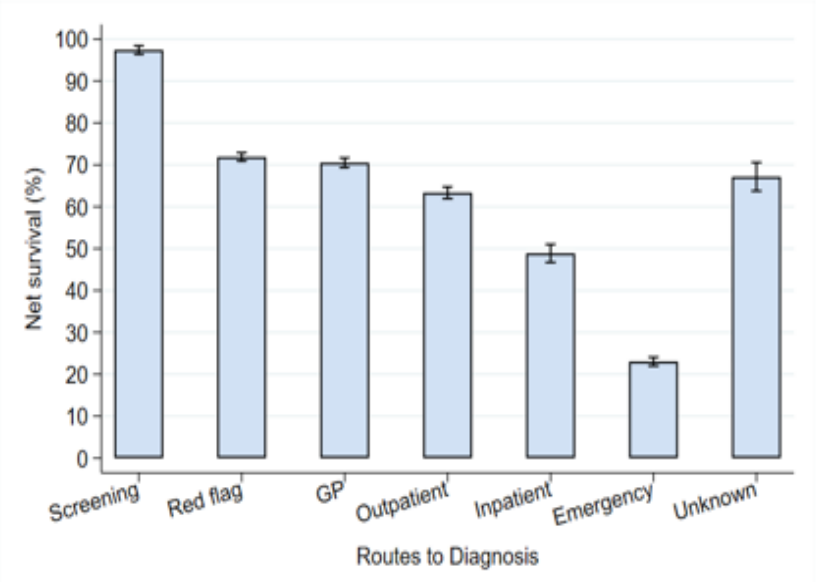
The highest three year net-survival occurred for patients diagnosed via a Screening Route-to-Diagnosis (97.4%), and the lowest survival (23.0%) was in the Emergency Presentation Route-to-Diagnosis patients (Table 10). Patients in the Red Flag Route-to-Diagnosis and the GP Route-to-Diagnosis had similar survival (71.9% and 70.5%, respectively), with lower survival in Outpatient Route-to-Diagnosis (63.3%) and Inpatient Route-to-Diagnosis (48.9%). Unknown Route-to-Diagnosis had intermediate net survival between Outpatient Route-to-Diagnosis and Red Flag Route-to-Diagnosis (Figure 13).

Table 10: Three-year net survival (ns, %) of all cancer patients diagnosed in Northern Ireland (2012-2016)

Route-to-diagnosis	Northern Ireland	
	n*	ns, %
Screening	2,549	97.4
Red Flag	12,574	71.9
GP Referral	9,451	70.5
Outpatient	6,808	63.3
Inpatient	2,754	48.9
Emergency Presentation	8,775	23.0

*some patients are not included in the survival analysis, see 1.6 *Analytical techniques*

Figure 13: Three-year net survival (%) of all cancer patients diagnosed from 2012-2016 in Northern Ireland, by Route-to-Diagnosis

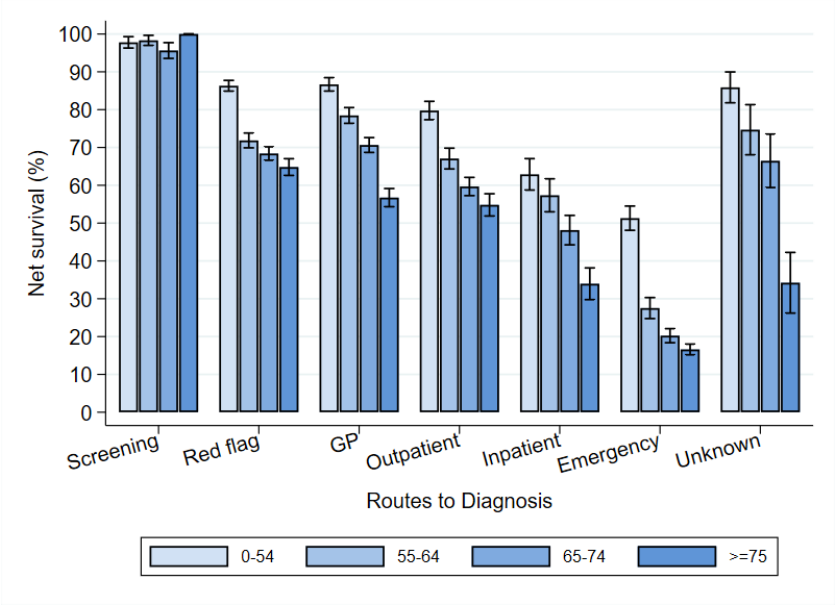


2.1.6.2 Age-group specific survival

Across all Routes-to-diagnosis, net survival was lower in older patients (Table 11) apart from in Screening Route-to-Diagnosis, which may be due to the low number of older patients in this group. Age-group gradients were steeper in patients diagnosed via GP Route-to-Diagnosis (86.7% for 0-54 age group versus 56.7% for 75+ age group), Outpatient Route-to-Diagnosis (79.8% for 0-54 year olds versus 54.8% for 75+ year olds), Inpatient Route-to-Diagnosis, and Emergency Presentation Route-to-Diagnosis (Figure 14). These gradients indicate that older patients are more likely to die from their cancer than younger patients because net survival removes their higher background mortality rates.

Table 11: Three-year net survival (ns, %) for patients diagnosed with all cancer in Northern Ireland from 2012-2016, by age group and Route-to-Diagnosis								
Routes-to-diagnosis	**Age groups (years)**							
	0-54		**55-64**		**65-74**		**75+**	
	n*	**ns, %**	**n**	**ns, %**	**n**	**ns, %**	**n**	**ns, %**
Screening	575	97.8	983	98.3	930	95.6	61	100.0
Red Flag	2,693	86.3	2,534	71.9	3,591	68.4	3,756	64.8
GP Referral	1,662	86.7	1,850	78.5	2,871	70.6	3,068	56.7
Outpatient	1,239	79.8	1,371	67.1	2,083	59.7	2,113	54.8
Inpatient	577	62.9	568	57.3	778	48.2	831	34.0
Emergency Presentation	1,022	51.3	1,170	27.5	2,147	20.2	4,436	16.6
*some patients are not included in the survival analysis, see 1.6 *Analytical techniques* **numbers too low (<50) to estimate survival								

Figure 14: Three-year age specific net survival for Route-to-Diagnosis for patients diagnosed with all cancer within Northern Ireland 2012-2016



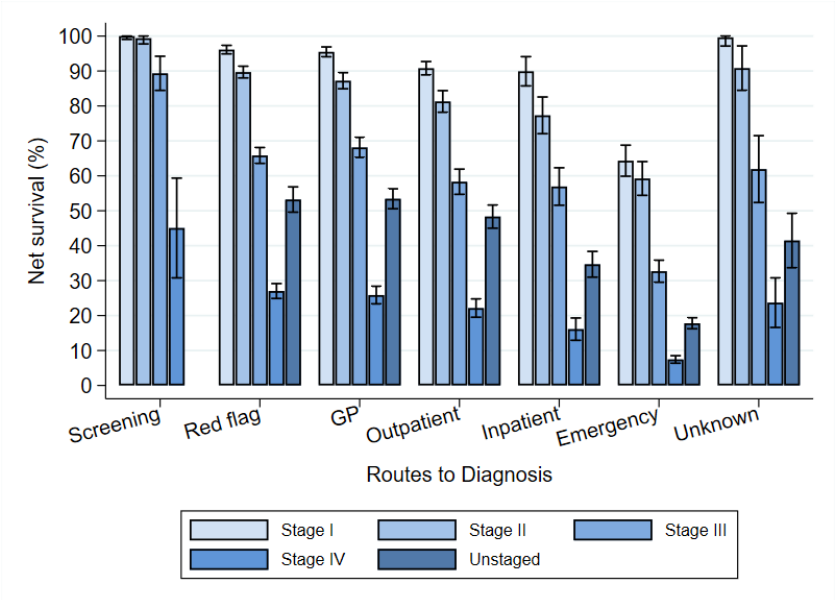
2.1.6.3 Stage specific survival

There was a steep declining gradient in net survival with advancing stage of disease in each Route-to-diagnosis (Table 12). Generally, patients with unstaged disease had intermediate survival between Stage III and IV disease. Patients diagnosed via Emergency

Presentation - Route-to-diagnosis had lower stage-specific survival (Figure 15), even though stage is the strongest prognostic factor because it captures the spread of the disease, and determines treatment options. Possibly, Stage IV in Emergency Presentation - Route-to-diagnosis patients is more aggressive (precipitating an emergency) than Stage IV in other Routes-to-diagnosis. However, it may be the case that this pattern reflects generally poorer health among patients presenting as emergency and the NI life tables overestimating non-cancer related mortality in this patient group.

Table 12: Three-year net survival (ns, %) for patients diagnosed with all cancer in Northern Ireland from 2012-2016, by cancer stage and Route-to-Diagnosis										
Routes-to-diagnosis	**Stage groups**									
	I		**II**		**II**		**IV**		**Unstaged***	
	n*	**ns, %**	**n**	**ns, %**	**n**	**ns, %**	**n**	**ns, %**	**n**	**ns, %**
Screening	1,550	100.0	668	99.4	237	89.3	55	45.1	-**	-
Red Flag	3,527	96.1	3,078	89.7	2,481	65.8	2,311	27.0	1,177	53.2
GP Referral	2,954	95.5	1,719	87.2	1,513	68.1	1,539	25.9	1,726	53.4
Outpatient	2,122	90.8	1,097	81.3	1,043	58.3	1,277	22.1	1,268	48.3
Inpatient	464	89.9	373	77.3	439	56.9	639	16.1	839	34.7
Emergency Presentation	759	64.3	628	59.2	1,138	32.7	3,082	7.4	3,168	17.8
*some patients are not included in the survival analysis, see 1.8 *Analytical techniques* **numbers too low (<50) to estimate survival										

Figure 15: Three-year stage specific net survival for Route-to-Diagnosis for patients diagnosed with all cancer within Northern Ireland 2012-2016, by cancer stage



2.1.7 Discussion

Considering all cancers together has the advantage of increasing the numbers of patients available to detect real patterns ('signal') in the data over and above random variation ('noise') in the data. Real patterns of routes to diagnosis for 'all cancer' patients are factors that affect every cancer patient, such as the health service in general or socio-cultural factors, i.e. factors that operate irrespective of cancer type, such as access to cancer services, or attitudes to visiting your GP. However, caution should be exercised in interpreting patterns as it is possible that single large cancer sites, e.g. female breast, may be driving them. Combining all cancers into one set of estimates and comparing to another country like England, with a broadly similar health-service organisation and population in general, should provide some basic quality-control, particularly as this is the first Routes-to-Diagnosis to be published for NI.

The proportions of patients diagnosed through Screening Route-to-Diagnosis and Emergency Presentation - Route-to-diagnosis were remarkably similar between Northern Ireland and England. In the case of Screening Route-to-Diagnosis, the screening programmes in both countries are very similar and the social-cultural milieu is broadly similar, both combining to give similarity in the Screening Route-to-Diagnosis results. In addition, the variation in the proportion of Screening Route-to-Diagnosis in English Cancer Alliances was relatively small. Emergency Presentation Route-to-Diagnosis is probably a function of factors, beyond the direct control of the health-service, arising from the social-cultural domain that is broadly common to NI and England.

The Routes-to-diagnosis that differ between countries– Red Flag, GP referral, Inpatient and Outpatient Routes-to-diagnosis–relate to actual cancer patient pathways that are directly shaped by separate national Departments of Health. The possibility that some of these differences are artefactual requires further investigation, as it is conceivable that the algorithm developed in England but driven by data from Northern Ireland might interact in an unintended way. The investigation will be facilitated by feedback on Routes-to-diagnosis from clinicians and health service managers, who, with their knowledge and experience, can isolate the genuine patterns from among the findings.

The greatest proportion of NI patients were diagnosed with cancer via a Red Flag Route-to-Diagnosis. England had a higher proportion of Red Flag Route-to-Diagnosis (35.2% vs 28.3%) and GP Route-to-Diagnosis (25.0% vs 21.4%) compared to NI, whereas in NI there were higher proportions of inpatient and Outpatient Route-to-Diagnosis. In NI there was an increasing trend in the Red Flag Route-to-Diagnosis proportion from 2012-2015 which decreased slightly in 2016. This reflects that stable operating of the Red Flag Route-to-Diagnosis has perhaps been reached.

Increasing proportions of Red Flag Route-to-Diagnosis in NI is an encouraging result, as this is a specialised route intended to promote early cancer diagnosis. Referrals using this route are based on a pre-defined clinical criteria established by the Northern Ireland Cancer Network (NICAN, 2012). Patients who have been 'red-flagged' will be prioritised in cancer referral waiting lists (Belfast Health and Social Care Trust, 2019). However, further research is required at the individual cancer site level (see breast chapter) to confirm if Red Flag Route-to-Diagnosis patients had a more advanced stage distribution than GP Route-to-Diagnosis. This would indirectly confirm that triaging on cancer specific symptoms is identifying the more serious cases. In 'all cancers', Red Flag Route-to-Diagnosis patients had higher Stage II-IV proportions that GP Route-to-Diagnosis, but a much lower unstaged proportion (9.5% vs 18.6%) which had a low net survival that was intermediate between Stage III & IV.

Mindful of lengthy waiting lists for appointments for a routine GP referral, GPs will aim to 'red-flag' patients if their symptoms meet the red flag criteria for a suspected cancer. Each cancer site has a list of symptoms which have been deemed 'red-flags' based on their presence being indicative of the cancer. Some red flag symptoms may be naturally harder to recognise, or the red flag symptom occurs with advanced disease stage only. For these reasons, red flag symptoms are debated amongst GPs for some cancers e.g. for gynaecological cancers there are different views as to whether ultrasound evidence is required to red-flag this cancer.

The NICE red-flag guidelines have been updated in 2015 (NICE, 2015) although NI still follow 2012 guidance until new guidelines have been commissioned by the Department of Health.

The new guidance lowers the thresholds of many diagnostic tests to red-flag cancer, which is anticipated to detect cancer earlier.

A higher proportion of women, and those aged 55-64 year were diagnosed in a screening Route-to-Diagnosis, and can be explained by the breast cancer screening programme. There was a decreasing gradient of Screening Route-to-Diagnosis proportion with deprivation (see comments on female breast cancer chapter). Older patients (75+ age group) were rarely diagnosed through a Screening Route-to-Diagnosis.

Increasing proportions of patients diagnosed via Emergency Presentation Route-to-Diagnosis were positively associated with age, but not patient sex, which may reflect competing comorbidities that hinder early detection in older patients by either making cancer symptoms less specific (Lyratzopoulos, Neal, Barbiere, Rubin, & Abel, 2012), or the patient less aware of their symptoms, e.g. dementia. A similar finding was reported in England (Elliss-Brookes et al., 2012). The positive gradient in the proportion of Emergency Presentation Route-to-Diagnosis with deprivation suggest 'barriers' that people living in deprived areas experience in approaching or accessing primary care services. Increasing proportions of Emergency Presentation Routes-to-Diagnosis in more deprived areas of England has also been reported (Herbert et al., 2018).

Net survival was lowest for those diagnosed via the Emergency Presentation Route-to-Diagnosis in NI, which was also found for Routes-to-Diagnosis in England (National Cancer Registration and Analysis Service, 2013). Stage-specific survival in Emergency Presentation Route-to-Diagnosis was the lowest of all routes suggesting more severe disease within these categories (but also could partly be explained by higher non-cancer mortality rates than found in the NI lifetable used in net survival). Abel et al., reported that 29% of those diagnosed via Emergency Presentation Route-to-Diagnosis within England reported no prior GP consultations for their cancer and were more likely to be older patients with harder to detect symptoms (Abel et al., 2017). The lower net survival for older people in NI was also as expected, as treatment options following diagnosis may be less optimal or timely due to frailty or poor health (Marosi & Köller, 2016).

Differences in the demographically-adjusted distribution of Routes-to-diagnosis for all cancers between NI Trusts were, in general, not large even though they were statistically significant. Understanding any differences, such as the higher proportion of emergency Route-to-Diagnosis in the Belfast Trust, requires further research. There are potentially a number of service-level factors which might combine to drive variation, such as delays getting appointments in GP practices, access to diagnostic imaging within Trusts, and shortage of key personnel such as radiologists.

Despite the caveats mentioned at the beginning of the discussion, the 'all cancers' results showed more pattern similarities with England than individual sites, probably due to greater numbers of patients available. In this way, it partly validates the data compilation and analysis, notwithstanding the large differences in the routes to diagnosis other than emergency and screening routes.

2.1.8 Bibliography

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2.2 Colorectal Cancer

2.2.1 Key findings

- There were 5,985 patients diagnosed with colorectal cancer[2] in Northern Ireland from 2012-2016. The most common route for colorectal cancer patient diagnosis was via a red flag (26.7%), followed by emergency (21.5%).
- NI had a higher proportion of patients diagnosed in an inpatient and outpatient route to diagnosis compared to England (20.8% vs 10.0%), the higher proportions of patients diagnosed through outpatient and inpatient Routes-to-diagnosis in NI compared to England may be partly an artefact arising from how the PHE algorithm interacts with the NI health service and data sources, which requires further investigation (See Section 1.5.3).
- For patients with Stage IV disease, the highest proportion were diagnosed as an Emergency Presentation Route-to-diagnosis (35.2%). For patients with Stage 1 disease, a sizeable proportion came via screening route (19.7%). Many unstaged patients were diagnosed in an emergency route (40.3%).
- Three-year net survival in NI was highest for patients diagnosed via screening (94.1%), and lowest for those diagnosed via an emergency route (37.9%).
- Net survival patterns were similar between NI and England.

[2] 'Colorectal cancer' in this chapter is defined by ICD-10 (WHO, 2011) topological sites C18-C20

2.2.2 Colorectal Cancer

Colorectal cancer arises in the small bowel, anus, rectum and colon. In Northern Ireland (NI), approximately 1,200 patients are diagnosed annually (Northern Ireland Cancer Registry, 2020) and it is the second highest cause of cancer-related deaths, with around 420 deaths per year.

2.2.2.1 Incidence

The age-standardised[3] incidence rate for colorectal cancer is 76.6 cases per 100,000 of the population. Risk of colorectal cancer increases with age; 71% of colorectal cancer patients are diagnosed over age 65 years. Men are more likely to develop colorectal cancer; 1 in 23 men and 1 in 33 women (Northern Ireland Cancer Registry, 2020) can expect a diagnosis in their lifetime. Breakdown by stage is as follows; Stage I (20.0%), Stage II (28.6%), Stage III (29.2%) and Stage IV (22.2%).

2.2.2.2 Survival

For NI patients diagnosed from 2007-2011, the age-standardised five-year net survival was 59.8%, an increase from 45.9% in 1993-1996 (Northern Ireland Cancer Registry, 2020). Five-year net survival decreases with more advanced stage of diagnosis (2007-2011): Stage I (98.1%), Stage II (90.2%), Stage III (66.9%) to Stage IV (8.8%).

2.2.2.3 Northern Ireland Bowel Screening Programme

The NI Bowel Cancer Screening Programme began in 2011. Every two years all men and women in NI aged between 60-74 years are invited to a screening test, the Faecal Occult Blood Test (FOBT) that detects small amounts of blood or polyps in bowel motions indicating cancer. Participation in the NI screening programme is around 60%, which is considered a success by the UK National Screening Committee. In early 2020, the screening programme will adopt the Faecal Immunochemical Test (FIT) kit to screen for colorectal cancer, as it is considered a more effective and easier to self-administer (Bowel Cancer UK, 2019).

[3] 2013 European Standard Population

2.2.3 Routes-to-diagnosis in Northern and England

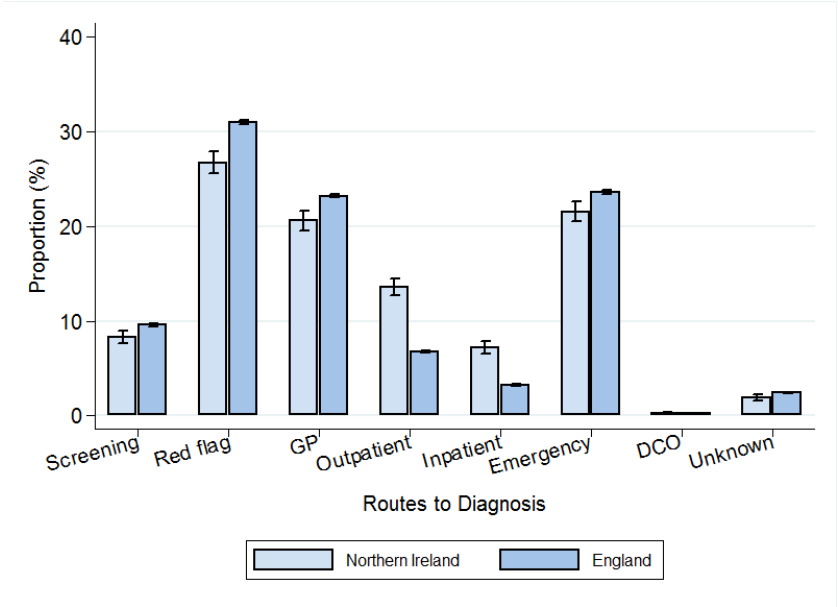
2.2.3.1 Incidence of Routes-to-Diagnosis in NI and England

The largest proportion of patients in NI were diagnosed via a Red Flag Route-to-Diagnosis (26.7%), but this proportion was lower than England (31.0%, Table 1). Compared to England, NI has higher proportions of Outpatient Route-to-Diagnosis (13.6%) and Inpatient Route-to-Diagnosis (7.2%). England had a higher proportion of GP Route-to-Diagnosis (23.2% vs 20.6%) and Emergency Presentation Route-to-Diagnosis (23.6% vs 21.5%) than NI (Figure 1).

Table 1: The frequency (n) and distribution (%) of Routes-to-Diagnosis of colorectal cancer patients diagnosed in 2012-2016, by country

Route-to-diagnosis	Northern Ireland		England	
	n	%	n	%
Screen	496	8.3	16,647	9.6
Red Flag	1,600	26.7	53,851	31.0
GP Referral	1,232	20.6	40,367	23.2
Outpatient	811	13.6	11,799	6.8
Inpatient	431	7.2	5,580	3.2
Emergency Presentation	1,289	21.5	41,051	23.6
Death Certificate Only	13	0.2	426	0.2
Unknown	113	1.9	4,187	2.4
Total	**5,985**		**173,908**	

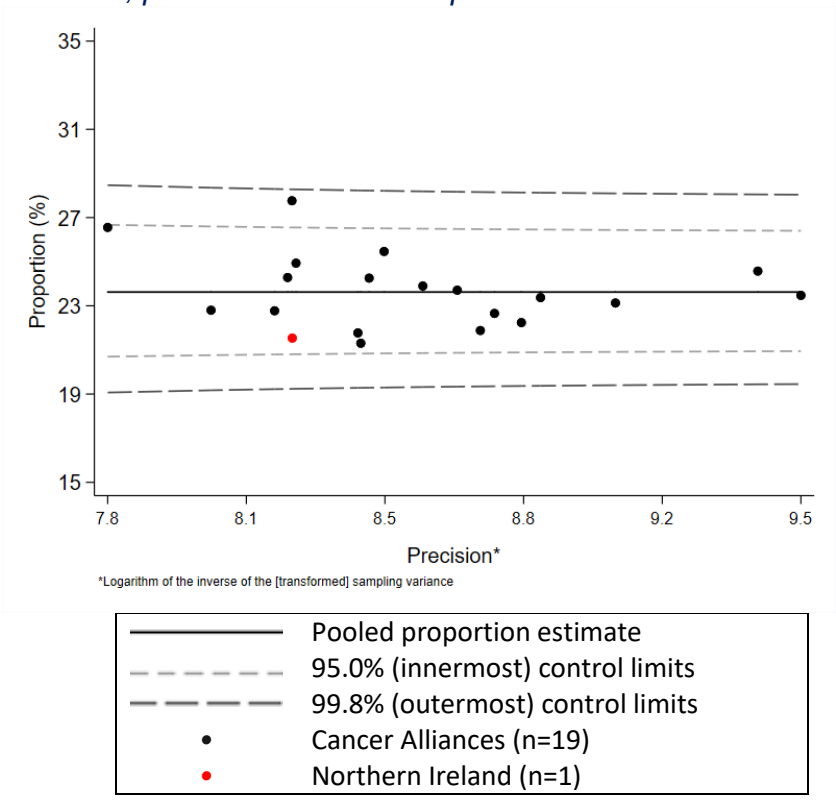
Figure 1: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with colorectal cancer from 2012-2016, by country (Northern Ireland and England)



2.2.3.2 Northern Ireland compared to English Cancer Alliances

Routes-to-diagnosis proportions were compared between NI and the English Cancer Alliances (n=19) on a funnel plot. The pooled proportion of English Cancer Alliances estimate shown in the funnel plot will be different from the English estimate for each route observed in Table 1. The proportion of NI patients diagnosed via an Emergency Presentation Route-to-Diagnosis (21.5%) lay within the 95% control limits, and therefore was not different from the pooled proportion estimate of the English Cancer Alliances (23.6%, Figure 2).

Figure 2: Proportion (%) of colorectal cancer patients diagnosed through an emergency presentation Route-to-Diagnosis in English Cancer Alliances (n=19), and Northern Ireland, presented in a funnel plot



The proportion of NI patients diagnosed via the Outpatient Route-to-Diagnosis (13.6%) lay outside the 99.8% control limits, and therefore differed significantly from the pooled proportion estimate of the English Cancer Alliances (6.8%, Figure 3).

Figure 3: Proportion (%) of colorectal cancer patients diagnosed through an outpatient Route-to-Diagnosis in English Cancer Alliances (n=19) and Northern Ireland presented in a funnel plot

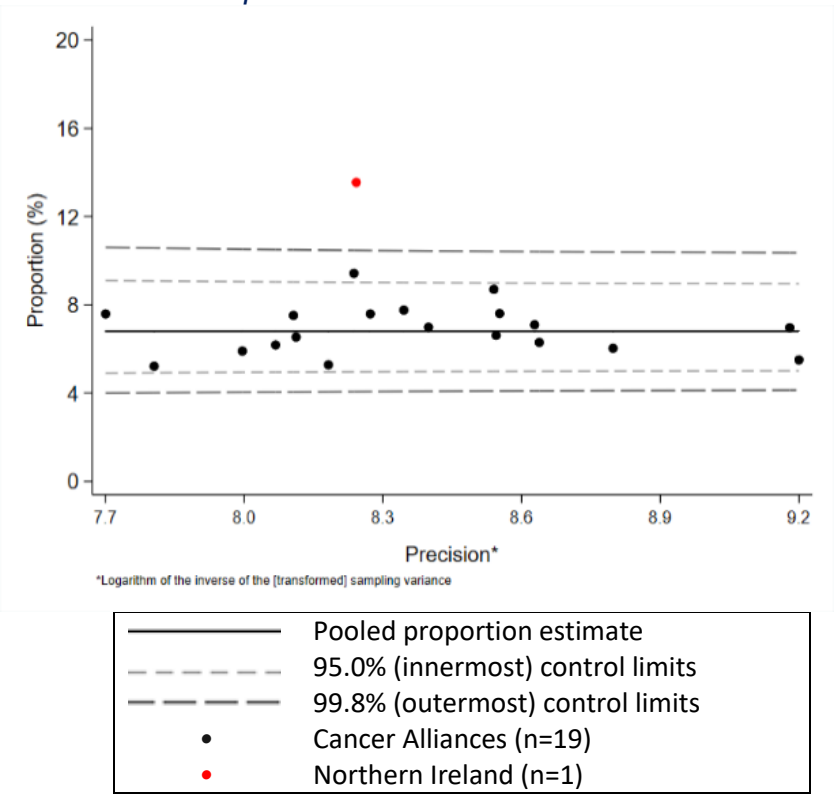
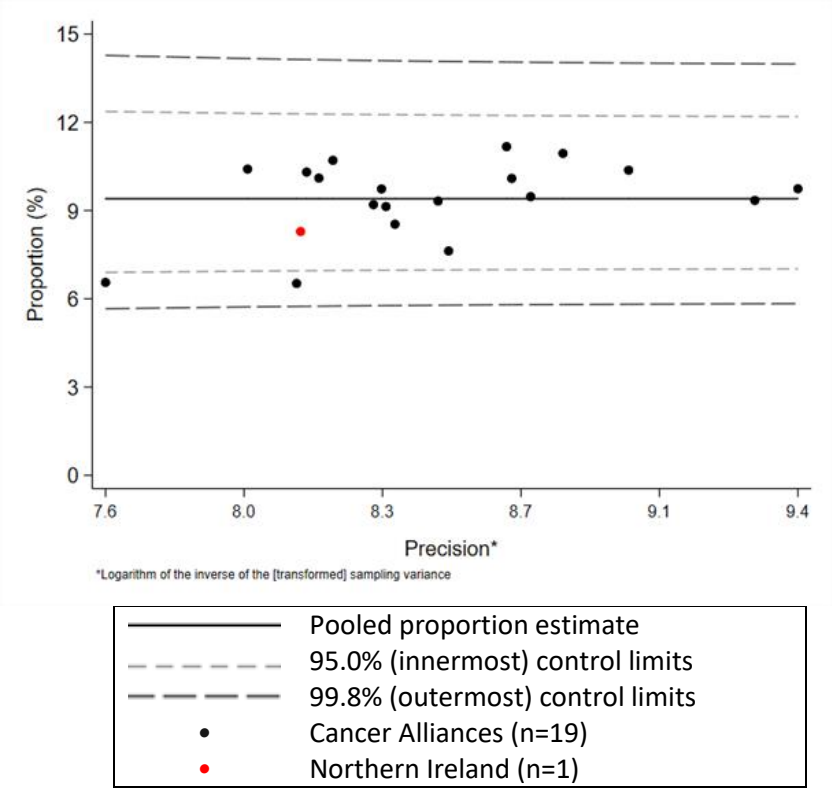


Figure 4: Proportion (%) of colorectal cancer patients diagnosed through a screening Route-to-Diagnosis in English Cancer Alliances (n=19) and Northern Ireland presented in a funnel plot



The proportion of NI patients diagnosed via Screening Route-to-Diagnosis (8.3%) lay within the 95% control limits, and therefore did not differ significantly from the pooled-mean proportion of English Cancer Alliances (9.4%, Figure 4).

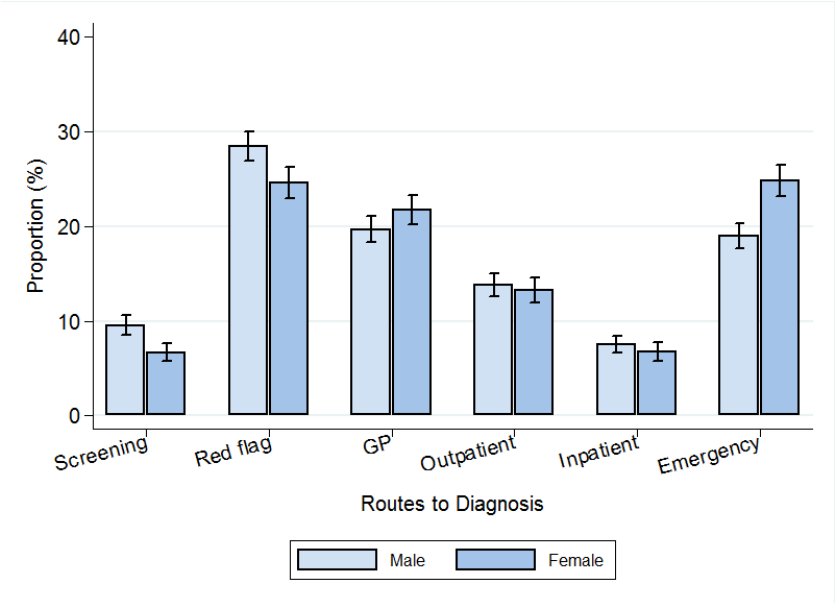
2.2.4 Northern Ireland Routes-to-Diagnosis: demographic and stage breakdown

2.2.4.1 Patient Sex

A larger proportion of women were diagnosed through an Emergency Presentation Route-to-Diagnosis (24.8% vs 19.0%, Table 2) than men. A larger proportion of men were diagnosed via Red Flag Route-to-Diagnosis than women (28.4% vs 24.6%). A higher proportion of men were diagnosed through Screening Route-to-Diagnosis than women (9.6% vs 6.7%, Figure 5).

Table 2: The frequency (n) and distribution (%) of Routes-to-Diagnosis of colorectal cancer patients diagnosed in 2012-2016, by sex				
Route-to-diagnosis	**Male**		**Female**	
	n	**%**	**n**	**%**
Screen	320	9.6	176	6.7
Red Flag	951	28.4	649	24.6
GP Referral	659	19.7	573	21.7
Outpatient	462	13.8	349	13.2
Inpatient	253	7.6	178	6.7
Emergency Presentation	635	19.0	654	24.8
Total	**3,347**		**2,638**	
Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis				

Figure 5: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with colorectal cancer within Northern Ireland from 2012-2016, by patient sex

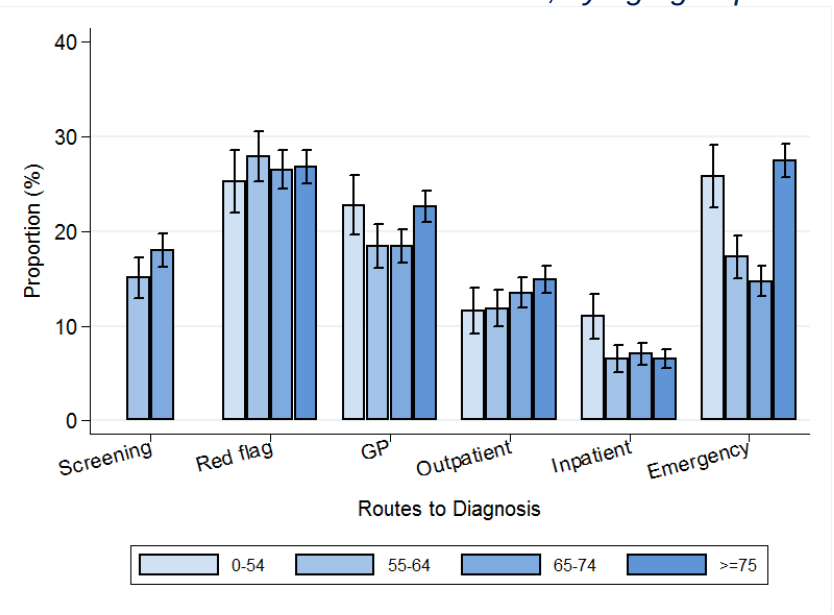


2.2.4.2 Age

There were notably higher proportions of patients diagnosed via Emergency Presentation Route-to-Diagnosis in age groups 0-54 (25.8%) and 75+ (27.4%), compared to intervening age groups 55-64 (17.3%) and 65-74 (14.7%, Table 3). There was a greater proportion of Inpatient Route-to-Diagnosis diagnoses in age group 0-54 (11.0%) compared to the older age groups (range 6.5%-7.1%, Figure 6).

Table 3: The frequency (n) and distribution (%) of Routes-to-Diagnosis of colorectal cancer patients diagnosed in 2012-2016, by age group								
Route-to-diagnosis	**Age groups (years)**							
	0-54		**55-64**		**65-74**		**75+**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Screen	-	-	164	15.1	328	18.0	-	-
Red Flag	172	25.3	303	27.9	484	26.5	641	26.8
GP Referral	155	22.8	200	18.4	337	18.5	540	22.6
Outpatient	79	11.6	129	11.9	247	13.5	356	14.9
Inpatient	75	11.0	71	6.5	129	7.1	156	6.5
Emergency Presentation	176	25.8	188	17.3	269	14.7	656	27.4
Total	**681**		**1,087**		**1,826**		**2,391**	
Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis								

Figure 6: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with colorectal cancer within Northern Ireland 2012-2016, by age group



2.2.4.3 Year of diagnosis

There was an increasing trend (Figure 7) in the proportion of patients diagnosed through the Red Flag Route-to-Diagnosis from 2012 (21.8%) to 2016 (29.8%), which corresponded to a decreasing trend in GP Route-to-Diagnosis from 2013 (23.8%) to 2016 (18.3%), suggesting a transfer of patients from GP Route-to-Diagnosis to Red Flag Route-to-Diagnosis. The

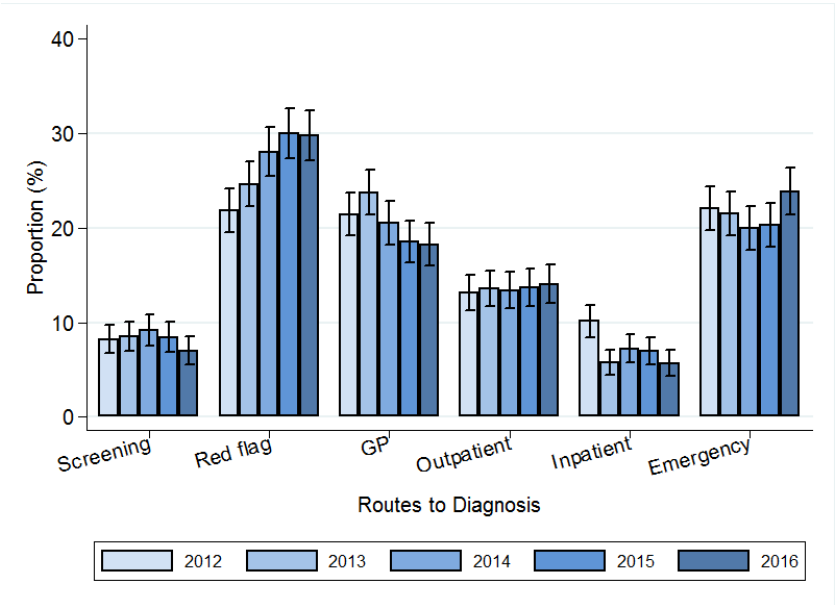
proportion of Inpatient Route-to-Diagnosis decreased from 2012 (10.1%) to 2016 (5.7%, Table 4).

Table 4: The frequency (n) and distribution (%) of Routes-to-Diagnosis of colorectal cancer patients, by year of diagnosis

Route-to-diagnosis	Year of diagnosis									
	2012		2013		2014		2015		2016	
	n	%	n	%	n	%	n	%	n	%
Screen	104	8.2	106	8.5	109	9.2	97	8.4	80	7.0
Red Flag	276	21.8	307	24.6	333	28.1	345	30.0	339	29.8
GP Referral	271	21.4	296	23.8	244	20.6	213	18.5	208	18.3
Outpatient	166	13.1	169	13.6	159	13.4	157	13.7	160	14.0
Inpatient	128	10.1	72	5.8	86	7.2	80	7.0	65	5.7
Emergency Presentation	279	22.1	268	21.5	237	20.0	233	20.3	272	23.9
Total	**1,264**		**1,246**		**1,187**		**1,149**		**1,139**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 7: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with colorectal cancer in Northern Ireland 2012-2016, by year of diagnosis



2.2.4.4 Deprivation

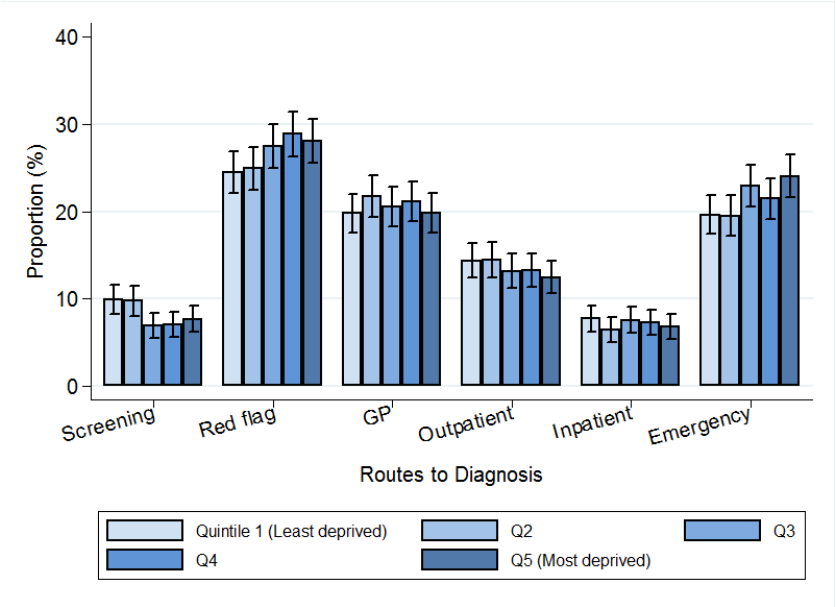
There was no strong evidence of a deprivation gradient in the proportions of patients diagnosed via each Route-to-diagnosis (Figure 8). However, whilst not significant, proportions diagnosed through Screening Route-to-Diagnosis proportions appear to decrease from the most-affluent quintile of the population (10.0%) to most deprived quintile (7.7%, Table 5). It is possible that lack of statistically significant deprivation gradients are due to small numbers of colorectal cancer patients in NI, as when routes to diagnosis by deprivation quintiles were compared for all cancer patients, strong gradients for emergency presentation and screening were observed (see Deprivation section 2.1.4.4).

Table 5: The frequency (n) and distribution (%) of Routes-to-Diagnosis of colorectal cancer patients diagnosed in 2012-2016, by deprivation quintile

Route-to-diagnosis	Deprivation Quintile									
	Quintile 1 (most affluent)		Quintile 2		Quintile 3		Quintile 4		Quintile 5 (most deprived)	
	n	%	n	%	n	%	n	%	n	%
Screen	124	10.0	112	9.8	83	7.0	84	7.0	93	7.7
Red Flag	304	24.4	286	24.9	327	27.5	344	28.9	339	28.0
GP Referral	246	19.8	250	21.8	244	20.5	252	21.1	240	19.9
Outpatient	179	14.4	166	14.5	157	13.2	158	13.3	151	12.5
Inpatient	96	7.7	74	6.4	90	7.6	87	7.3	83	6.9
Emergency Presentation	244	19.6	224	19.5	273	23.0	256	21.5	291	24.1
Total	**1,244**		**1,148**		**1,189**		**1,192**		**1,209**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 8: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with colorectal cancer within Northern Ireland 2012-2016, by deprivation quintile



2.2.4.5 Stage

As well as reporting frequency and percentage (%) distribution of Routes-to-diagnosis by stage (Table 6, Figure 9), the frequency and percentage distribution of stage by Route-to-diagnosis (Table 7, Figure 10) is presented to observe the case-mix of patients in each Route-to-diagnosis.

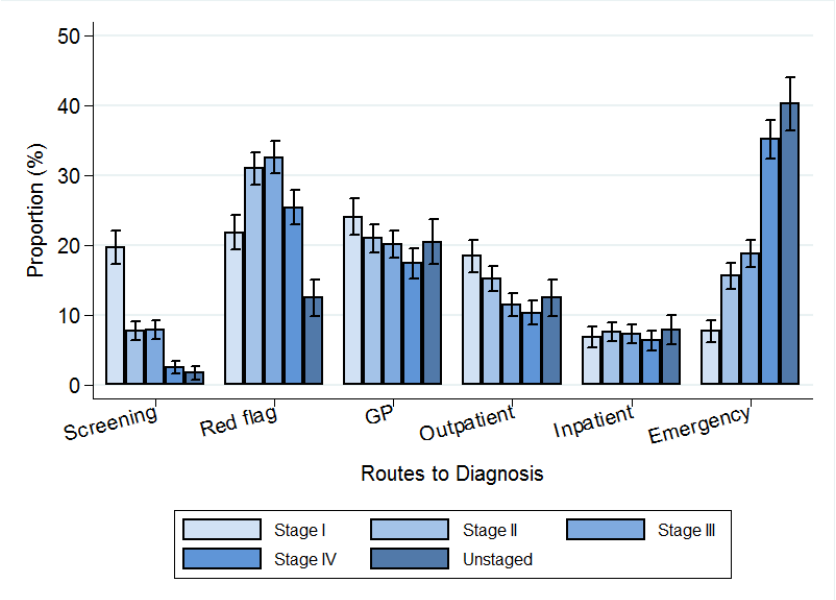
Patients with Stage IV or unknown stage disease were more likely to be diagnosed through Emergency Presentation Route-to-Diagnosis (35.2% and 40.3%, respectively) than patients with Stage I disease (7.7%, Table 8). Conversely, patients with Stage I disease were more likely to be diagnosed through Screening Route-to-Diagnosis (19.7%) or Outpatient Route-to-Diagnosis (18.5%) than Stage IV or unstaged. Patients with Stage II and Stage III were more likely (31.0% and 32.6%, respectively) to be diagnosed through a Red Flag Route-to-Diagnosis, than Stage I (21.8%) or Stage IV (25.4%). Over one-third (35.2%) of patients with Stage IV disease were diagnosed via Emergency Presentation Route-to-Diagnosis, with sizeable proportions in Red Flag Route-to-Diagnosis (25.4%) and GP Route-to-Diagnosis (17.5%, Figure 9).

Table 6: The frequency (n) and distribution (%) of Routes-to-Diagnosis of colorectal cancer patients diagnosed in 2012-2016, by cancer stage

Routes-to-diagnosis	Stage groups									
	I		II		III		IV		Unstaged*	
	n	%	n	%	n	%	n	%	n	%
Screen	209	19.7	121	7.8	124	8.0	31	2.6	11	1.7
Red Flag	232	21.8	478	31.0	508	32.6	303	25.4	79	12.5
GP Referral	256	24.1	324	21.0	314	20.2	208	17.5	130	20.5
Outpatient	196	18.5	234	15.2	179	11.5	123	10.3	79	12.5
Inpatient	73	6.9	118	7.7	114	7.3	76	6.4	50	7.9
Emergency Presentation	82	7.7	241	15.6	292	18.8	419	35.2	255	40.3
Total	**1,062**		**1,542**		**1,557**		**1,191**		**633**	

*cancer stage unknown
Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 9: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with colorectal cancer within Northern Ireland from 2012-2016, by stage



For the Emergency Presentation Route-to-Diagnosis, 32.5% of patients were diagnosed with Stage IV disease followed by Stage III (22.7%), unstaged (19.8%) and Stage II (18.7%) which were all similar. However, with the exception of Screening Route-to-Diagnosis, all Routes-to-

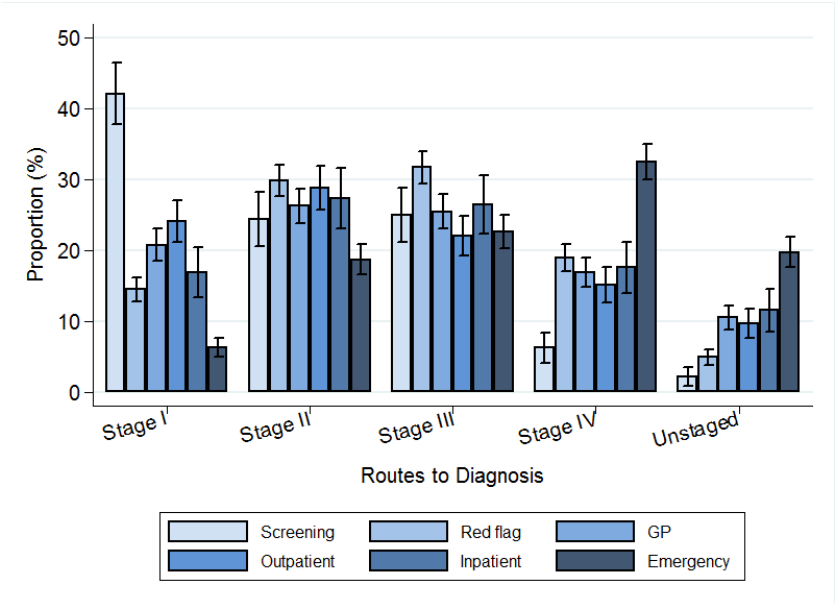
diagnosis had large proportions of patients diagnosed with Stage III (>22%) and Stage IV (>15%) disease showing late detection of disease in all Routes-to-diagnosis (Table 7). In Screening Route-to-Diagnosis, Stage I comprised 42.1% of the cases, in contrast to Stage IV (6.3%) and unstaged (2.2%). Apart from Emergency Presentation Route-to-Diagnosis, the remaining Routes-to-diagnosis had proportions of Stage II in the range 24-30% (Figure 10).

Table 7: The frequency (n) and distribution (%) of cancer stage of colorectal cancer patients diagnosed in 2012-2016, by Routes-to-Diagnosis

Stage	Routes-to-diagnosis											
	Screen		Red Flag		GP		Outpatient		Inpatient		Emergency Presentation	
	n	%	n	%	n	%	n	%	n	%	n	%
I	209	42.1	232	14.5	256	20.8	196	24.2	73	16.9	82	6.4
II	121	24.4	478	29.9	324	26.3	234	28.9	118	27.4	241	18.7
III	124	25.0	508	31.7	314	25.5	179	22.1	114	26.5	292	22.7
IV	31	6.3	303	18.9	208	16.9	123	15.2	76	17.6	419	32.5
UN*	11	2.2	79	4.9	130	10.6	79	9.7	50	11.6	255	19.8
Total	**496**		**1,600**		**1,232**		**811**		**431**		**1,289**	

*UN cancer stage unknown
Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 10: Distribution (%) of stage for patients diagnosed with colorectal cancer within Northern Ireland from 2012-2016, by Routes-to-Diagnosis



2.2.5 Geographic variation within NI Healthcare Trusts

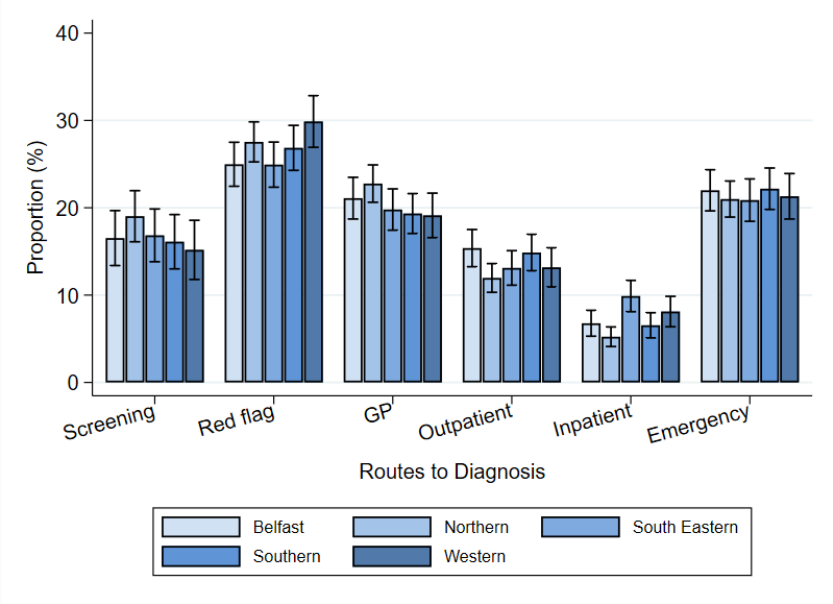
The frequency and distribution (%) of Routes-to-diagnosis by Trust are present in Table 8. On adjusting for demographic factors (age group, sex and deprivation), there was no evidence of any differences in the distribution of Routes-to-diagnosis between the Trusts (Figure 11).

Table 8: The frequency (n) and distribution (%) of Routes-to-Diagnosis of colorectal cancer patients diagnosed 2012-2016, by Trust

Routes-to-diagnosis	Healthcare Trust									
	Belfast		Northern		South Eastern		Southern		Western	
	n	%	n	%	n	%	n	%	n	%
Screen	93	7.9	135	9.0	110	9.4	89	7.6	69	7.2
Red Flag	297	25.1	408	27.3	285	24.4	314	26.8	296	30.8
GP Referral	247	20.9	343	22.9	229	19.6	230	19.6	183	19.0
Outpatient	178	15.0	182	12.2	158	13.5	173	14.8	120	12.5
Inpatient	78	6.6	80	5.3	115	9.8	76	6.5	81	8.4
Emergency Presentation	268	22.7	313	20.9	233	19.9	264	22.5	210	21.8
Total	**1,183**		**1,496**		**1,170**		**1,171**		**962**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

*Figure 11: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with colorectal cancer within Northern Ireland 2012-2016, by Trust**



***** The presented proportions in Figure 11 were standardised to the NI population by the following factors: age, sex, and deprivation. The screening proportions by Trust have screening age groups as their denominator and therefore the proportions presented are different from the observed proportions in the table which include all ages. Please see 1.6 *Analytical techniques* for further details.

Northern Ireland Healthcare Trusts compared to English Clinical Commissioning Groups (CCGs)

England's CCGs have similar numbers of patients diagnosed from 2006-2016 (11 years) to NI's Trusts for 2012-2016 (5 years), the latter's estimates were superimposed on a funnel plot of the CCG estimates. The proportion of colorectal cancer patients diagnosed via Emergency Presentation Route-to-Diagnosis for any of the NI Trusts was found to lie below the pooled proportion estimate of English CCGs (24.3%), but within the 95.0% control limits (Figure 12). The proportions of colorectal cancer patients diagnosed via Screening Route-to-Diagnosis for each of the Trusts were found to lie within the 95.0% control limits around the pooled proportion estimate of English CCGs (7.4%, Figure 13).

Figure 12: Proportion of colorectal cancer patients diagnosed through an emergency Route-to-Diagnosis for English Clinical Commissioning Groups (n=195, 2006-2016), and Northern Ireland Trusts (n=5, 2012-2016) in a funnel plot

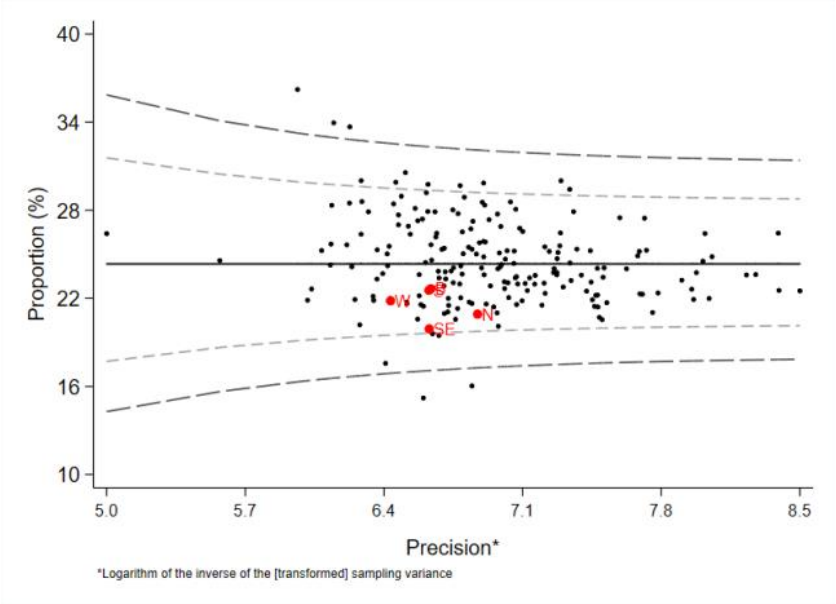
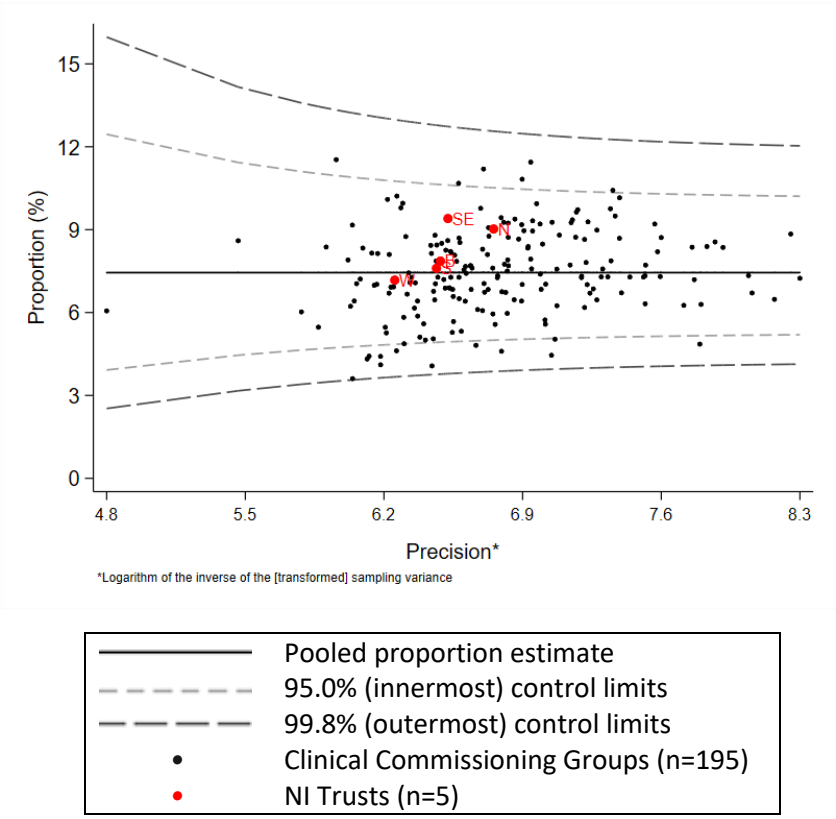


Figure 13: Proportion of colorectal cancer patients diagnosed through a screening Route-to-Diagnosis for English Clinical Commissioning Groups (n=195, 2006-2016), and Northern Ireland Trusts (n=5, 2012-2016), in a funnel plot



2.2.6 Survival

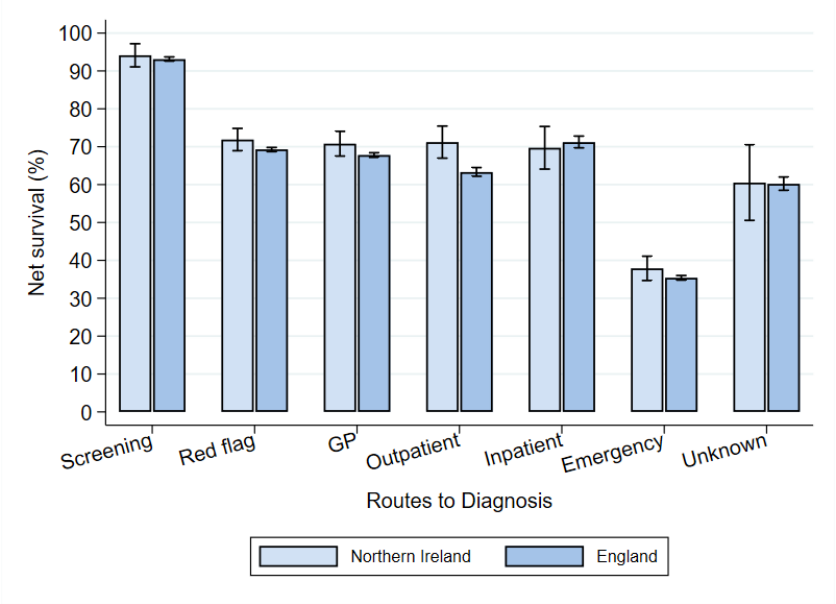
The report presents net survival estimates, a theoretical statistic used for comparing groups of patients (e.g. different regions or calendar periods) whose non-cancer or background mortality will differ. Net survival is defined as the probability of surviving cancer when the mortality from other causes of death is removed (see also Perme, Stare, & Estève, 2012).

2.2.6.1 Survival by country

Net survival in NI was highest in patients diagnosed via Screening Route-to-Diagnosis (94.1%), and lowest in the Emergency Presentation Route-to-Diagnosis (37.9%, Table 9). NI and England had comparable survival for patients diagnosed through most routes, except Outpatient Route-to-Diagnosis where survival in Northern Ireland (71.2%) was greater than England (63.3%, Figure 14). (Note the slightly different diagnosis periods of the countries' estimates).

Table 9: Three-year net survival (ns, %) of colorectal cancer patients diagnosed in Northern Ireland (2012-2016) and England (2011-2015), by route-to-diagnosis				
Route-to-diagnosis	**Northern Ireland**		**England**	
	n*	**ns, %**	**n**	**ns, %**
Screen	490	94.1	16,331	93.1
Red Flag	1,560	71.9	50,663	69.3
GP Referral	1,207	70.8	38,797	67.8
Outpatient	766	71.2	10,573	63.3
Inpatient	419	69.7	5,398	71.2
Emergency Presentation	1,249	37.9	38,936	35.4
*some patients/cases are not included in the survival analysis, see 1.6 *Analytical techniques*				

Figure 14: Three-year net survival (%) of colorectal cancer patients diagnosed from 2012-2016, by Route-to-Diagnosis and country



2.2.6.2 Age-group specific survival

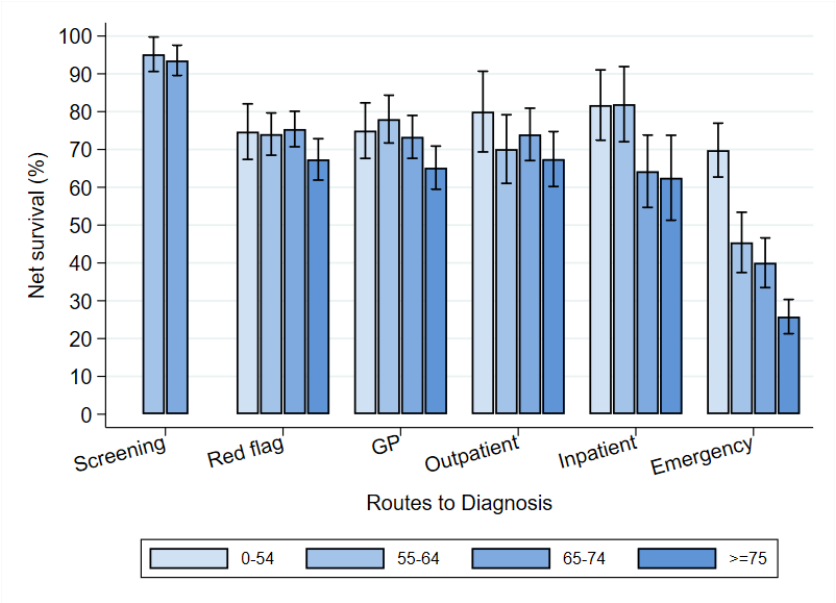
Across all Routes-to-diagnosis, apart from the Screening Route-to-Diagnosis, three-year net survival was lower in the 75+ age group (Table 10), but reached statistical significance only in the Emergency Presentation Route-to-Diagnosis, which also showed the steepest gradient in survival with age group (Figure 15).

Table 10: Three-year net survival (ns, %) for patients diagnosed with colorectal cancer in Northern Ireland from 2012-2016, by age group and Route-to-Diagnosis

Routes-to-diagnosis	Age groups (years)							
	0-54		55-64		65-74		75+	
	n*	ns, %	n	ns, %	n	ns, %	n	ns, %
Screen	-**	-	162	95.2	325	93.5	-	-
Red Flag	169	74.7	300	74.1	470	75.4	621	67.4
GP Referral	153	75.0	198	78.0	329	73.3	527	65.2
Outpatient	70	80.0	125	70.1	230	74.0	340	67.5
Inpatient	74	81.7	69	82.0	126	64.2	150	62.5
Emergency Presentation	175	69.8	184	45.4	260	40.0	630	25.8

*some patients/cases are not included in the survival analysis, see 1.6 *Analytical techniques*
**numbers too low (<50) to estimate survival

Figure 15: Three-year age specific net survival for Route-to-Diagnosis for patients diagnosed with colorectal cancer within Northern Ireland 2012-2016



2.2.6.3 Stage specific survival

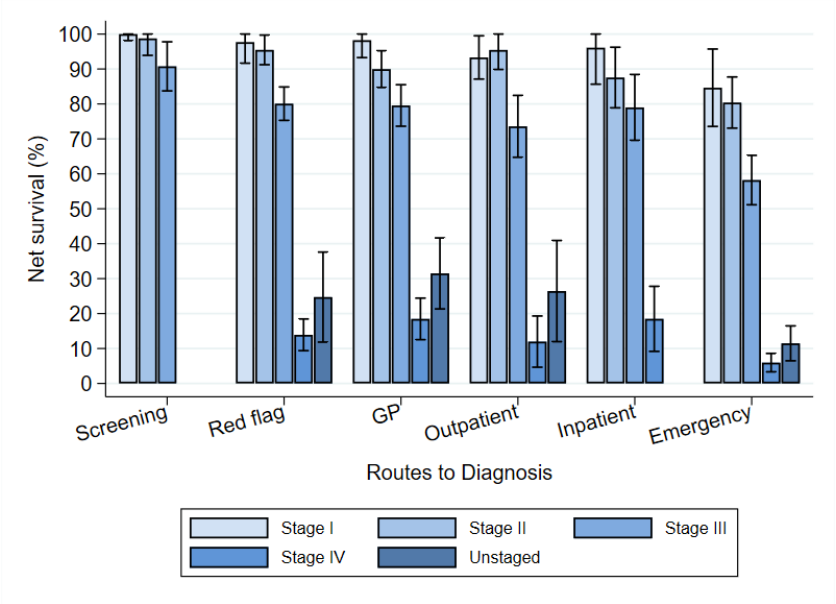
In each of the Routes-to-diagnosis, there was a consistent decline in net survival with advancing stage of disease (Figure 16). In the Red Flag Route-to-Diagnosis, Outpatient Route-to-Diagnosis, and Emergency Presentation Route-to-Diagnosis, 3-year survival for Stage III patients was lower than Stage I and Stage II, while Stage IV patients' survival was less than 20% in all Routes-to-diagnosis (Table 11). Patients with unstaged disease had intermediate survival between Stage III and IV disease in all Routes-to-diagnosis (Figure 16). There were no strong patterns in stage-specific survival across the Routes-to-diagnosis, suggesting that the NI lifetable mortality rates, used in estimating net survival, were not under-estimating the non-cancer deaths in any of the patients groups defined by the Routes-to-diagnosis (see lung cancer).

Table 11: Three-year net survival (ns, %) for patients diagnosed with colorectal cancer in Northern Ireland from 2012-2016, by cancer stage and Route-to-Diagnosis

Routes-to-diagnosis	Stage groups									
	I		II		III		IV		Unstaged*	
	n*	ns, %	n	ns, %	n	ns, %	n	ns, %	n	ns, %
Screen	206	100.0	120	98.8	121	91.6	-**	-	-	-
Red Flag	221	98.3	471	95.6	495	80.0	297	14.1	76	24.1
GP Referral	253	98.3	318	89.3	309	79.8	206	18.5	121	31.8
Outpatient	181	93.7	223	95.2	176	73.5	117	12.0	70	26.4
Inpatient	71	96.1	117	87.6	113	79.0	74	18.5	-	-
Emergency Presentation	75	86.5	237	80.2	288	58.4	411	5.7	238	11.4

*some patients are not included in the survival analysis, see 1.8 *Analytical techniques*
**numbers too low (<50) to estimate survival

Figure 16: Three-year stage specific net survival for Route-to-Diagnosis for patients diagnosed with colorectal cancer within Northern Ireland 2012-2016, by cancer stage



2.2.7 Discussion

Routes-to-diagnosis for colorectal cancer in NI follow patterns similar to England in both the distribution of the cancer patients among the routes, and the patient survival within Route-to-diagnosis groups. Lack of differences between Trusts within NI reflects homogeneity of healthcare services across NI.

Most patients in NI were diagnosed by a Red Flag Route-to-Diagnosis followed by Emergency Presentation Route-to-Diagnosis which, broadly, was observed in England. Survival by Route-to-Diagnosis between NI and England is comparable which broadly indicates a similar case-mix of patient at diagnosis reflecting similar cancer detection capability between Northern Ireland and England.

Increased levels of Emergency Presentation Route-to-Diagnosis amongst female colorectal cancer patients in NI was observed in England as well (Abel et al., 2015); where it was conjectured that the number of specific colorectal cancer symptoms was lower among women than men. Additionally, women have been reported to experience more embarrassment and discomfort whilst undergoing a colonoscopy used to diagnose colorectal cancer which may deter them from visiting their GP with symptoms. Increased Screening Route-to-Diagnosis amongst men may be linked to an increased awareness among the screening age groups that colorectal cancer is more common in males.

Higher proportions of Emergency Presentation Route-to-Diagnosis for patients aged 0-54 years indicate more barriers in suspecting and detecting colorectal cancer in this age group as is expected. Higher Emergency Presentation Route-to-Diagnosis for those aged 75+ years may be due to competing comorbidities that reduce the range of colorectal cancer-specific symptoms. Older people had worse survival than younger people even if both groups had high proportions of Emergency Presentation Route-to-Diagnosis. There was evidence of an increase in Red Flag Route-to-Diagnosis proportion over the study period (2012-2016) and a broadly corresponding reduction in GP Route-to-Diagnosis. Further investigation is required to establish whether this represents a real improvement/adoption of the red flag system.

Routes-to-diagnosis in England found differences between deprivation quintiles whilst NI found decreased screening proportions in more deprived areas, although these differences were not statistically significant. However both countries use a different measure of deprivation, and the deprivation gradient is steeper in England in absolute terms. Higher Emergency Presentation Route-to-Diagnosis in more deprived areas were reported by England (McPhail et al., 2013) along with lower Screening Route-to-Diagnosis uptake in more deprived areas (Smith, Stansbie, & Juby, 2011) which has been attributed to reduced health literacy, health inequalities and access to Screening Route-to-Diagnosis services in more deprived areas.

The survival differences between the routes were broadly explainable by their disease stage case-mix. Screening Route-to-Diagnosis patients that were predominantly diagnosed with early-stage disease had the best survival, while the converse was observed for the patients diagnosed in the Emergency Presentation Route-to-Diagnosis with predominantly advanced disease (unknown stage have intermediate survival between Stage III and IV). Apart from the Screening Route-to-Diagnosis and Emergency Presentation Route-to-Diagnosis, the other Routes-to-diagnosis had intermediate overall survival which is reflective of the less extreme patient stage case-mix, though there were relatively high proportions of advanced disease in Red Flag Route-to-Diagnosis and GP Route-to-Diagnosis.

Stage-specific survival did not vary much between the Routes-to-diagnosis, and the common survival gradient with advanced stage highlights the importance of early detection leading to a greater likelihood of successful treatment and outcome. Screen-detected colorectal cancers associated with higher survival reflects a greater proportion of cancers diagnosed at

an early asymptomatic stage through attendance at a screening appointment. Conversely, the more advanced presenting symptoms associated with Stage IV may have precipitated the Emergency Presentation Route-to-Diagnosis diagnosis. The intermediate survival of Red Flag Route-to-Diagnosis and GP Route-to-Diagnosis may be due to symptoms in the earlier stages of the cancer being confused for other health conditions, thus leading to a delay in diagnosis.

Symptoms of colorectal cancer, which include diarrhoea, constipation, rectal bleeding, weight loss, anaemia and abdominal pain, are not unique and can be mistakenly attributed to other less serious conditions such as irritable bowel syndrome (IBS). Red flag symptoms for colorectal cancer also differ by age group. Unexplained weight loss and abdominal pain are red flag symptoms to those aged 40 and older, whilst iron-deficiency anaemia or changes in bowel habits are red flag symptoms for those aged 60 and older. These differences reflect the prevalence of other health conditions in older people.

The screening programme is a public health intervention designed to improve patient outcomes/survival, and early indications from this Route-to-diagnosis study are positive. However, most solid evidence will be a reduction in the number of colorectal cancer deaths, as survival statistics can be biased upwards by length bias whereby less-aggressive slower growing tumours are more likely to be detected by screening than aggressive tumours that are detected through symptoms. However, the screening programme may be raising awareness of the risk of colorectal cancer, and indirectly encouraging the public to heed symptoms and present earlier to their GPs. As well as observing trends and geographical variation in Routes-to-diagnosis for monitoring service-delivery, information on Routes-to-diagnosis will also be useful for evaluating the effectiveness of bowel cancer symptom awareness campaigns.

2.2.8 Bibliography

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2.3 Breast Cancer

2.3.1 Key findings

- There were 6,810 women diagnosed with breast cancer[4] in NI between 2012 and 2016. Most breast cancer patients were diagnosed via red flag (49.5%) and screen Route-to-Diagnosis (29.1%).
- The distribution of Routes-to-Diagnosis in NI and England was similar. The proportion diagnosed via Outpatient Route-to-Diagnosis in NI was higher compared to England (6.5% compared to 2.6%). The higher proportions of patients diagnosed through outpatient and inpatient Routes-to-diagnosis in NI compared to England may be partly an artefact arising from how the PHE algorithm interacts with the NI health service and data sources, which requires further investigation (See Section 1.5.3).
- There was a negative gradient in the proportion of Screening Route-to-Diagnosis with deprivation.
- Older patients were less likely to be diagnosed via Screening or Red Flag Route-to-Diagnosis.
- The variation in survival between the Routes-to-Diagnosis reflected the level of Stage IV disease. Patients diagnosed via Emergency Presentation Route-to-Diagnosis had the lowest survival, but the other Routes-to-Diagnosis had high survival.

[4] 'Breast cancer' in this chapter is defined by ICD-10 (WHO, 2011) topological site C50

2.3.2 Female Breast Cancer

Breast cancer is cancer of the cells that line the milk ducts of the breast (Cancer Research UK, 2020). In NI, there were 1,398 women and 11 men diagnosed (male breast cancer not included in this chapter) with the disease each year between 2013 and 2017 (Northern Ireland Cancer Registry, 2020). A women has a 1 in 10 chance of getting breast cancer over the course of her lifetime. Every year about 300 women die of breast cancer in Northern Ireland.

2.3.2.1 Incidence and survival

The age-standardised[5] incidence rate for breast cancer is 162 per 100,000 for NI. The age-specific incidence rate is high from the age of 40 (126 per 100,000) onwards, peaking in women aged 80-84 (440 per 100,000) (Northern Ireland Cancer Registry, 2020). Nineteen percent of breast cancer cases occurred in females aged under 50 years. The distribution of disease stage at diagnosis is: Stage I (37%), Stage II (34%), Stage III (14%), Stage IV (5%), and unstaged (10%).

Breast cancer has high five-year survival at 82.1% for patients diagnosed in 2007 to 2011. Survival has improved from 73.5% in patients diagnosed in 1993-1996. Survival by stage is currently as follows: Stage I (98.9%), Stage II (92.1%), Stage III (72.2%), Stage IV (17.8%), and unstaged (56. 8%) (Northern Ireland Cancer Registry, 2020).

2.3.2.2 Northern Ireland Breast Screening Programme

The NI Breast Screening Programme invites women aged between 50 and 70 years old to attend a screening appointment once every 3 years. Uptake of breast screening is 75% (Public Health Agency, 2018). The screening procedure involves an X-ray of each breast (mammogram) to detect small changes in the breast tissue. Women who are described as being at higher risk of breast cancer (e.g. those with genetic mutations) are invited to attend screening appointments at an earlier age compared to women from the general population (defined as surveillance screening). Attendance at breast screening appointments allow earlier detection of breast cancer, as 1 in every 100 women invited for screening will receive a breast cancer diagnosis (Public Health Agency, 2014).

[5] 2013 European Standard Population

2.3.3 Routes-to-diagnosis in Northern and England

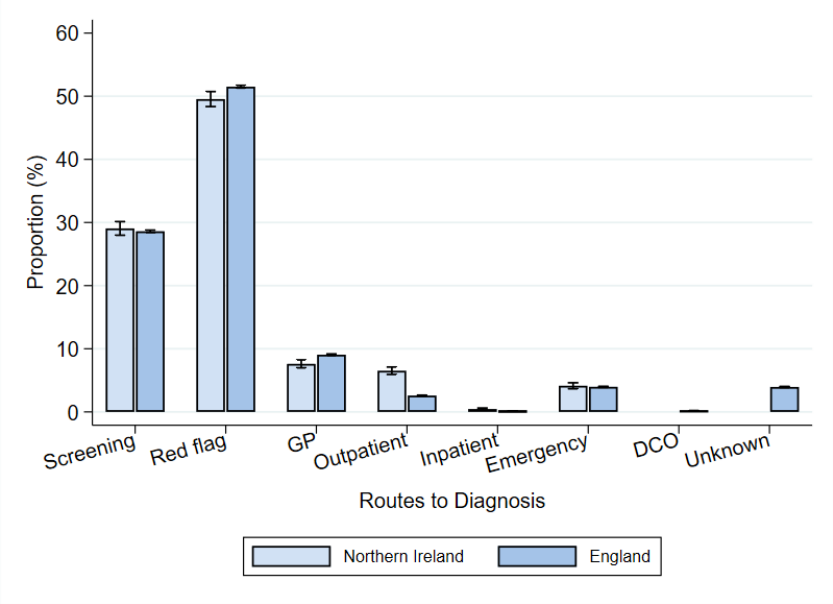
2.3.3.1 Incidence of Routes-to-Diagnosis in NI and England

In NI, a majority of women were diagnosed via a Red Flag Route-to-Diagnosis (49.5%) or Screening Route-to-Diagnosis (29.1%, Table 1). In general, the distribution of Routes-to-diagnosis in NI was similar in England, with only a slight difference in Outpatient Route-to-Diagnosis (6.5% vs 2.6%, respectively). As the frequency of Inpatient Route-to-Diagnosis was very low (n=31 in NI), this Route-to-Diagnosis will not be reported on further.

Table 1: The frequency (n) and distribution (%) of Routes-to-Diagnosis of breast cancer patients diagnosed in 2012-2016, by country

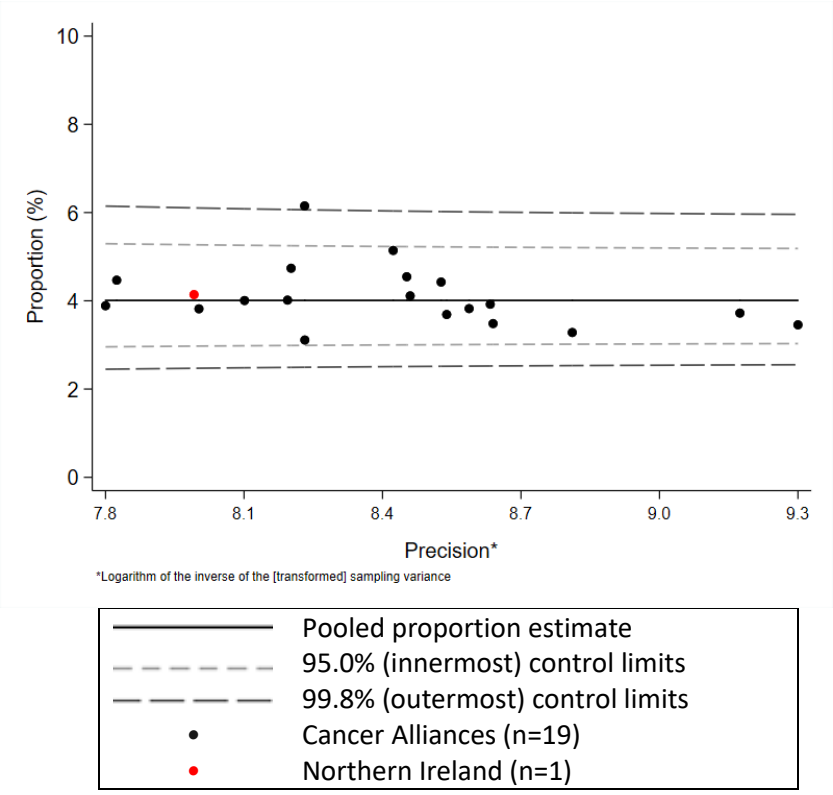
Route-to-diagnosis	Northern Ireland		England	
	n	%	n	%
Screening	1,979	29.1	64,510	28.6
Red flag	3,374	49.5	116,169	51.5
GP	518	7.6	20,435	9.1
Outpatient	444	6.5	5,832	2.6
Inpatient	31	0.5	297	0.1
Emergency Presentation	282	4.1	8,954	4.0
Death Certificate Only	<10	-	428	0.2
Unknown	≈170	<3.0	8,909	4.0
Total	**6,810**		**225,534**	

Figure 1: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with breast cancer from 2012-2016, by country (Northern Ireland and England)



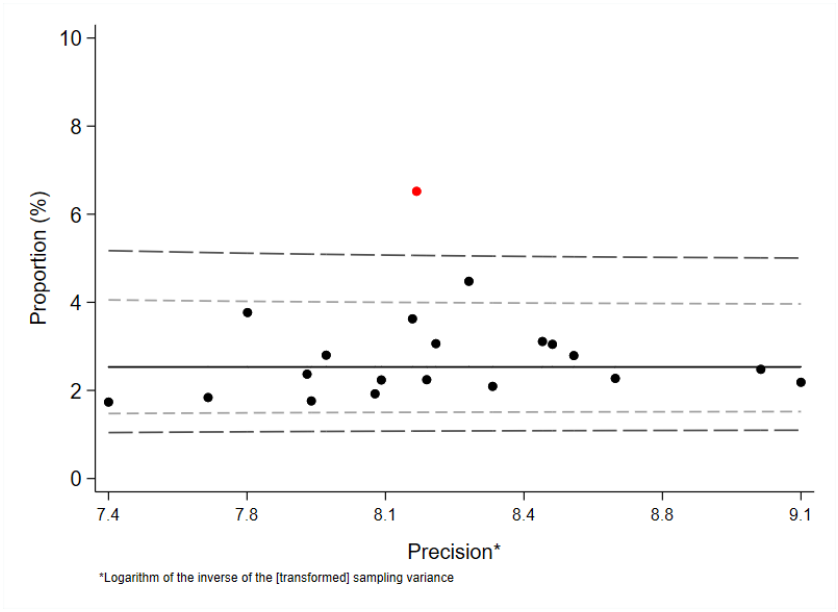
2.3.3.2 Northern Ireland compared to English Cancer Alliances

Figure 2: Proportion (%) of patients diagnosed with breast cancer from 2012-2016 through an emergency referral Route-to-Diagnosis in English Cancer Alliances (n=19) and Northern Ireland presented in a funnel plot



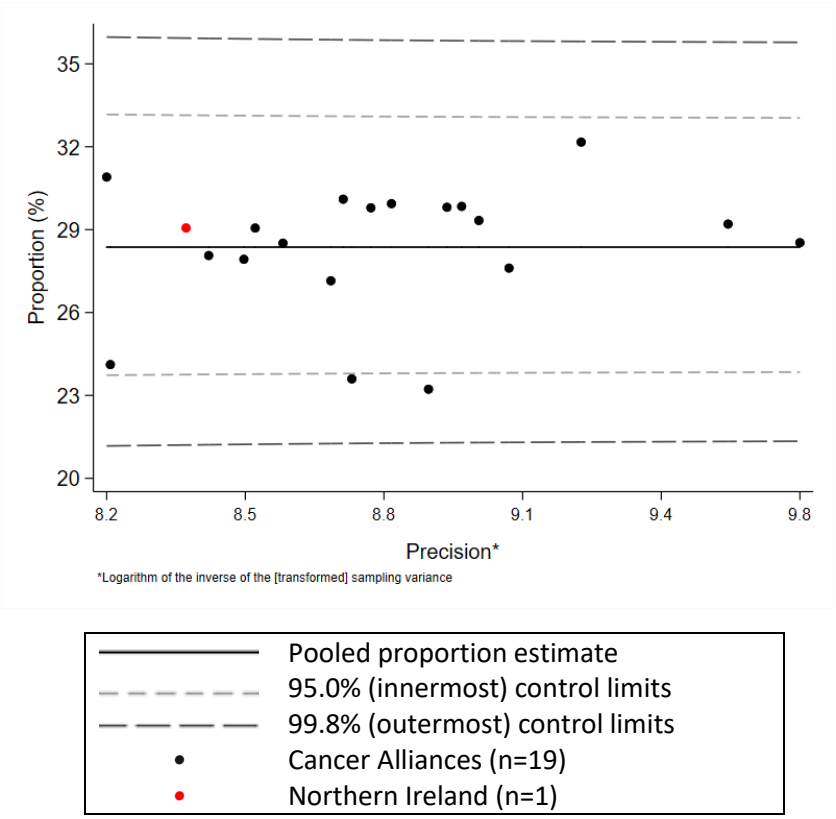
The proportion of patients diagnosed through an Emergency Presentation Route-to-Diagnosis was compared between NI and the English Cancer Alliances (n=19) on a funnel plot (Figure 2). The NI proportion (4.1%), lying within the 95% control limits, was not significantly different from the pooled proportion estimate (4.0%) of English Cancer Alliances.

Figure 3: Proportion (%) of patients diagnosed with breast cancer from 2012-2016 through an outpatient referral Route-to-Diagnosis in English Cancer Alliances (n=19) and Northern Ireland presented in a funnel plot



The NI Outpatient Route-to-Diagnosis proportion (6.5%), lying outside the 99.8% control limits, was significantly different from the pooled proportion estimate (2.5%) of English Cancer Alliances (Figure 3).

Figure 4: Proportion (%) of patients diagnosed with breast cancer from 2012-2016 through a screening Route-to-Diagnosis in English Cancer Alliances (n=19) and Northern Ireland presented in a funnel plot



The NI Screening Route-to-Diagnosis proportion (29.1%), lying within the 95% control limits, was not significantly different from the pooled proportion estimate (28.4%) of English Cancer Alliances (Figure 4).

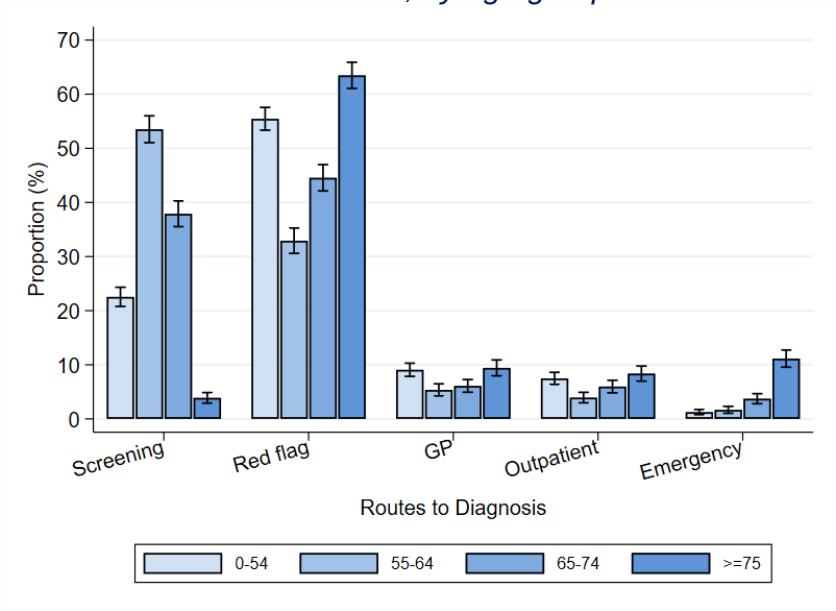
2.3.4 Northern Ireland Routes-to-Diagnosis: demographic and stage breakdown

2.3.4.2 Age

Women in the 55-64 age group had the largest proportion of Screening Route-to-Diagnosis (53.5%) followed by age group 65-74 (37.9%) reflecting the range of ages (50-70) that women are invited by the Breast Screening Programme (Table 2). Age groups that are not included in the Screening Programme had the largest proportions of Red Flag Route-to-Diagnosis (0-54, 55.5%; 75+, 63.5%). The proportion of patients diagnosed via the Emergency Presentation Route-to-Diagnosis increased with age group to 11.1% in the age group 75+ (Figure 5).

Table 2: The frequency (n) and distribution (%) of Routes-to-Diagnosis of breast cancer patients diagnosed in 2012-2016, by age group								
Route-to-diagnosis	**Age groups (years)**							
	0-54		**55-64**		**65-74**		**75+**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Screening	482	22.6	829	53.5	609	37.9	59	3.9
Red Flag	1,185	55.5	510	32.9	716	44.6	963	63.5
GP Referral	194	9.1	83	5.4	98	6.1	143	9.4
Outpatient	160	7.5	61	3.9	96	6.0	127	8.4
Emergency Presentation	27	1.3	26	1.7	60	3.7	169	11.1
Total	**2,137**		**1,549**		**1,607**		**1,517**	
Note: frequency (n) will not sum to total due to exclusion of Inpatient, Death Certificate Only, and Unknown Routes-to-diagnosis								

Figure 5: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with breast cancer within Northern Ireland 2012-2016, by age group

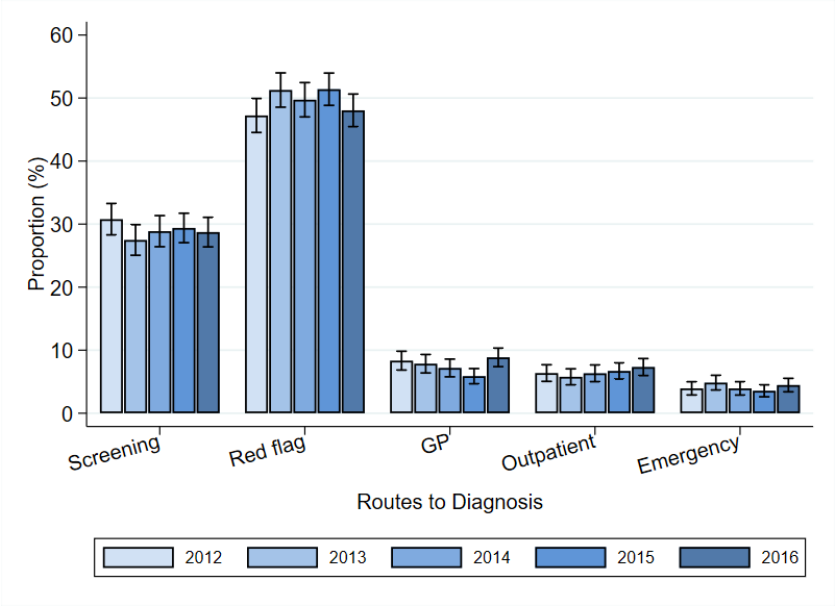


2.3.4.3 Year of diagnosis

There was no evidence of trends in the proportions of patients in the Routes-to-diagnosis from 2012-2016; this may reflect too short a period to measure change in a service that is well-established and stable (Table 3, Figure 6).

Table 3: The frequency (n) and distribution (%) of Routes-to-Diagnosis of breast cancer patients, by year of diagnosis										
Route-to-diagnosis	**Year of diagnosis**									
	2012		**2013**		**2014**		**2015**		**2016**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Screening	406	30.8	357	27.5	374	28.9	430	29.4	412	28.7
Red Flag	623	47.2	666	51.3	644	49.7	752	51.4	689	48.0
GP Referral	110	8.3	102	7.9	93	7.2	86	5.9	127	8.9
Outpatient	84	6.4	75	5.8	82	6.3	98	6.7	105	7.3
Emergency Presentation	52	3.9	63	4.8	51	3.9	52	3.6	64	4.5
Total	**1,319**		**1,299**		**1,295**		**1,463**		**1,434**	
Note: frequency (n) will not sum to total due to exclusion of Inpatient, Death Certificate Only, and Unknown Routes-to-diagnosis										

Figure 6: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with breast cancer in Northern Ireland 2012-2016, by year of diagnosis



2.3.4.4 Deprivation

There was evidence of a positive gradient of the proportion of patients diagnosed via Red Flag Route-to-Diagnosis with deprivation (Q1, 44.7%; Q5, 55.7%) and a negative gradient of the proportion of Screening Route-to-Diagnosis with deprivation (Q1, 31.9%; Q5, 25.8%; Table 4). There were no differences in proportions in GP Route-to-Diagnosis, Outpatient

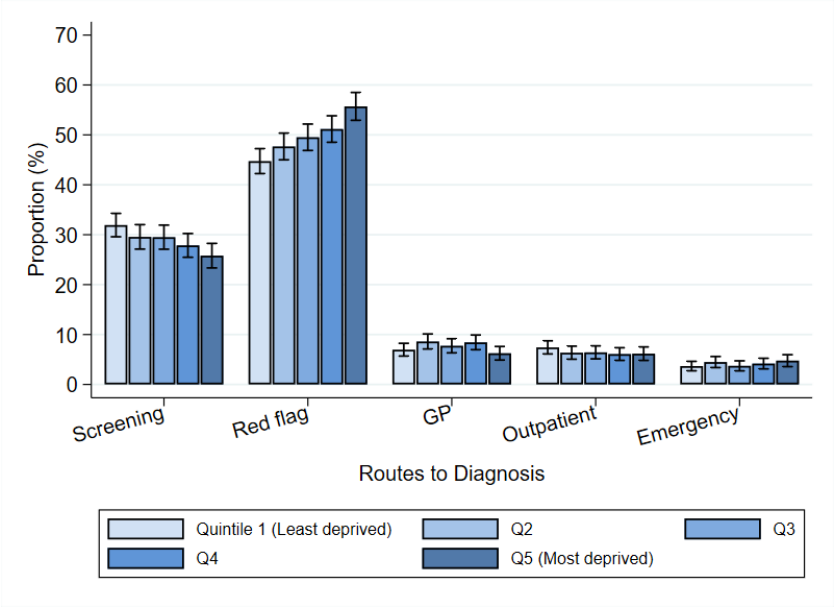
Route-to-Diagnosis, and Emergency Presentation Route-to-Diagnosis between the deprivation quintiles (Figure 7).

Table 4: The frequency (n) and distribution (%) of Routes-to-Diagnosis of breast cancer patients diagnosed in 2012-2016, by deprivation quintile

Route-to-diagnosis	Deprivation Quintile									
	Quintile 1 (least deprived)		Quintile 2		Quintile 3		Quintile 4		Quintile 5 (most deprived)	
	n	%	n	%	n	%	n	%	n	%
Screening	486	31.9	395	29.6	404	29.5	380	27.9	314	25.8
Red Flag	681	44.7	637	47.7	678	49.5	698	51.2	678	55.7
GP Referral	106	7.0	115	8.6	106	7.7	115	8.4	76	6.2
Outpatient	113	7.4	85	6.4	88	6.4	83	6.1	75	6.2
Emergency Presentation	56	3.7	60	4.5	51	3.7	57	4.2	58	4.8
Total	**1,522**		**1,336**		**1,369**		**1,364**		**1,217**	

Note: frequency (n) will not sum to total due to exclusion of Inpatient, Death Certificate Only, and Unknown Routes-to-diagnosis

Figure 7: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with breast cancer within Northern Ireland 2012-2016, by deprivation quintile



2.3.4.5 Stage

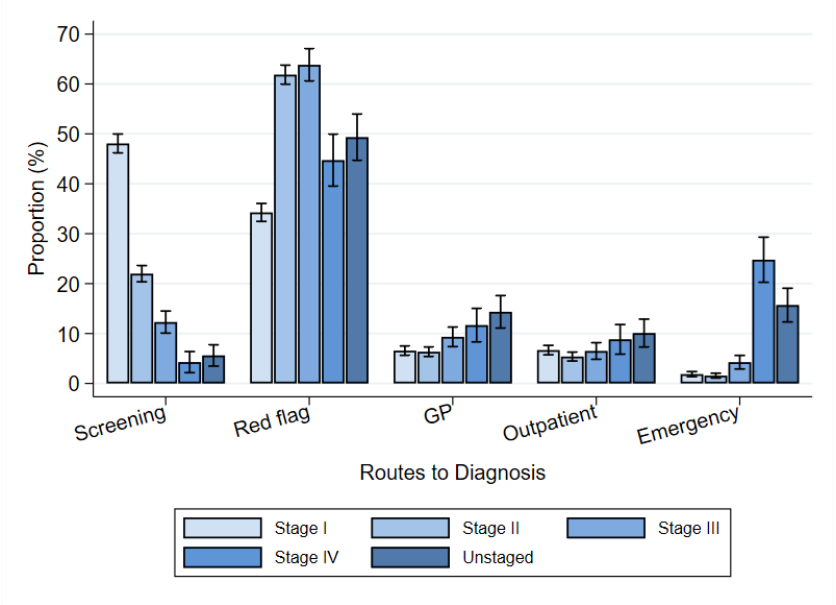
As well as the frequency and percentage (%) distribution of Routes-to-diagnosis by stage (Table 5, Figure 8), the frequency and percentage distribution of stage by Route-to-diagnosis

(Table 6, Figure 9) is presented to investigate the case-mix of patients in each Route-to-diagnosis.

The proportion of patients diagnosed via Screening Route-to-Diagnosis decreased with more advanced stage at diagnosis (48.1% at Stage I compared to 4.3% at Stage IV, Table 5). A reverse pattern of increasing proportions with more advanced disease Stage was broadly observed in GP Route-to-Diagnosis, Outpatient Route-to-Diagnosis, and Emergency Presentation Route-to-Diagnosis (Figure 8). Over 60% of Stage II & III patients were diagnosed by Red Flag Route-to-Diagnosis, while less than 50% of Stage I (34.3%), Stage IV (44.7%), and for unstaged patients (49.3%) of patients were diagnosed by Red Flag Route-to-Diagnosis.

Table 5: The frequency (n) and distribution (%) of Routes-to-Diagnosis of breast cancer patients diagnosed in 2012-2016, by cancer stage										
Routes-to-diagnosis	**Stage groups**									
	I		**II**		**III**		**IV**		**Unstaged***	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Screening	1,288	48.1	547	22.0	104	12.3	15	4.3	25	5.6
Red Flag	918	34.3	1,539	61.9	540	63.8	157	44.7	220	49.3
GP Referral	176	6.6	158	6.4	79	9.3	41	11.7	64	14.3
Outpatient	179	6.7	134	5.4	55	6.5	31	8.8	45	10.1
Emergency Presentation	50	1.9	39	1.6	36	4.3	87	24.8	70	15.7
Total	**2,679**		**2,488**		**846**		**351**		**446**	
*cancer stage unknown Note: frequency (n) will not sum to total due to exclusion of Inpatient, Death Certificate Only, and Unknown Routes-to-diagnosis										

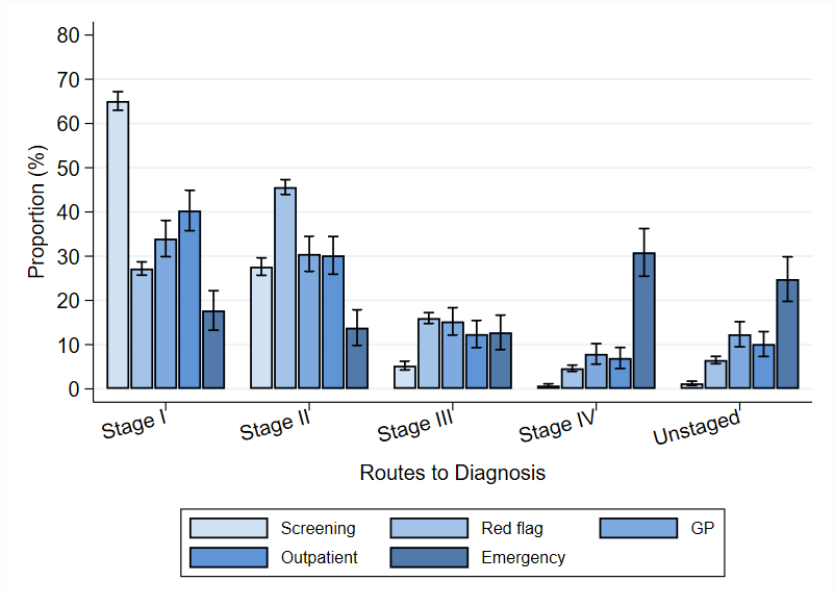
Figure 8: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with breast cancer within Northern Ireland from 2012-2016, by cancer stage



The majority of patients diagnosed through a Screening Route-to-Diagnosis were Stage I (65.1%) or Stage II (27.6%; Table 6). Stage II patients make up the largest proportion of Red Flag Route-to-Diagnosis (45.8%) followed by Stage I (27.1%). Although having sizeable proportions (>12%) in each stage group, most Emergency Presentation Routes-to-Diagnosis were Stage IV (31.1%) or unstaged (24.6%). GP Route-to-Diagnosis and Outpatient Route-to-Diagnosis had similar stage distribution with a majority of early-stage (I & II, Figure 9).

Table 6: The frequency (n) and distribution (%) of cancer stage of breast cancer patients diagnosed in 2012-2016, by routes-to-diagnosis										
Stage groups	**Routes-to-diagnosis**									
	Screening		**Redflag**		**GP**		**Outpatient**		**Emergency**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
I	1,288	65.1	918	27.2	176	34.0	179	40.3	50	17.7
II	547	27.6	1,539	45.6	158	30.5	134	30.2	39	13.8
III	104	5.3	540	16.0	79	15.3	55	12.4	36	12.8
IV	15	0.8	157	4.7	41	7.9	31	7.0	87	30.9
Unstaged*	25	1.3	220	6.5	64	12.4	45	10.1	70	24.8
Total	**1,979**		**3,374**		**518**		**444**		**282**	
*cancer stage unknown										

Figure 9: Distribution (%) of stage for patients diagnosed with breast cancer within Northern Ireland from 2012-2016, by Routes-to-Diagnosis



2.3.5 Geographic variation within NI Healthcare Trusts

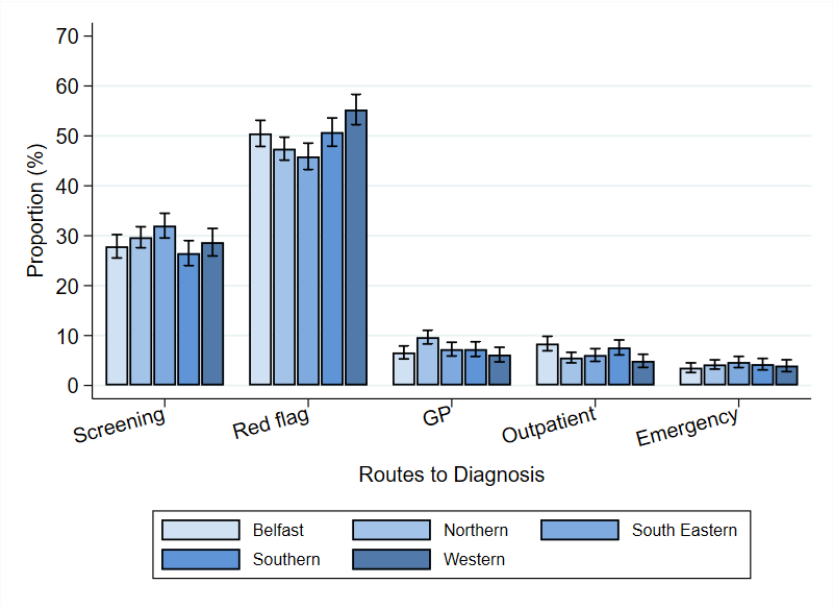
There was a lower proportion of patients diagnosed via Red Flag Route-to-Diagnosis in the South Eastern Trust (45.9%) than the Western Trust (55.3%, Table 7). However, apart from this difference, the distribution of Routes-to-diagnosis between the Trusts, when adjusted for age-group, sex and deprivation, was similar (Figure 10).

Table 7: The frequency (n) and distribution (%) of Routes-to-Diagnosis of breast cancer patients diagnosed 2012-2016, by Trust

Routes-to-diagnosis	Healthcare Trust									
	Belfast		Northern		South Eastern		Southern		Western	
	n	%	n	%	n	%	n	%	n	%
Screening	392	27.9	537	29.7	436	32.0	317	26.5	297	28.7
Red Flag	710	50.5	858	47.4	625	45.9	607	50.8	572	55.3
GP Referral	93	6.6	175	9.7	99	7.3	87	7.3	64	6.2
Outpatient	118	8.4	101	5.6	83	6.1	91	7.6	51	4.9
Emergency Presentation	50	3.6	76	4.2	64	4.7	51	4.3	41	4.0
Total	**1,406**		**1,809**		**1,362**		**1,196**		**1,035**	

Note: frequency (n) will not sum to total due to exclusion of Inpatient, Death Certificate Only, and Unknown Routes-to-diagnosis

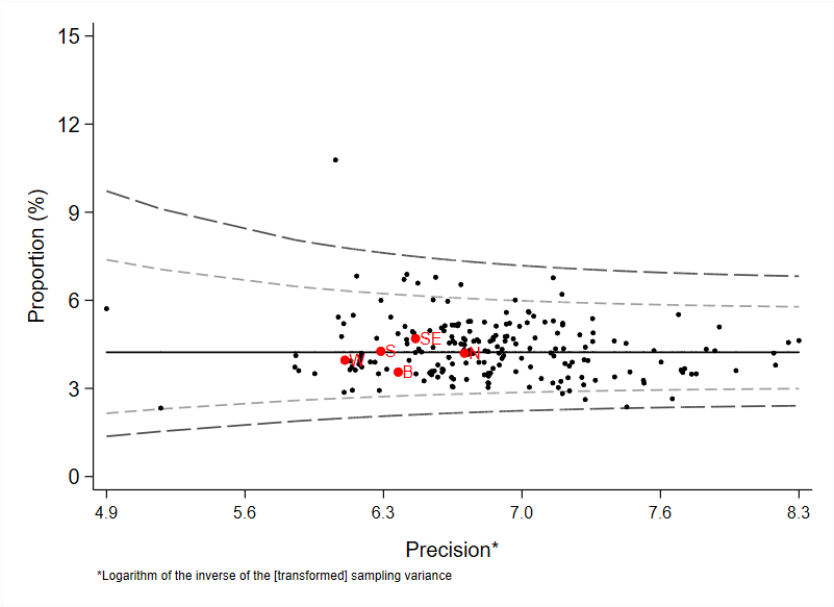
*Figure 10: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with breast cancer within Northern Ireland 2012-2016, by Trust**



***** The presented proportions in Figure 10 were standardised to the NI population by the following factors: age, sex, and deprivation. Please see 1.6 *Analytical techniques* for further details.

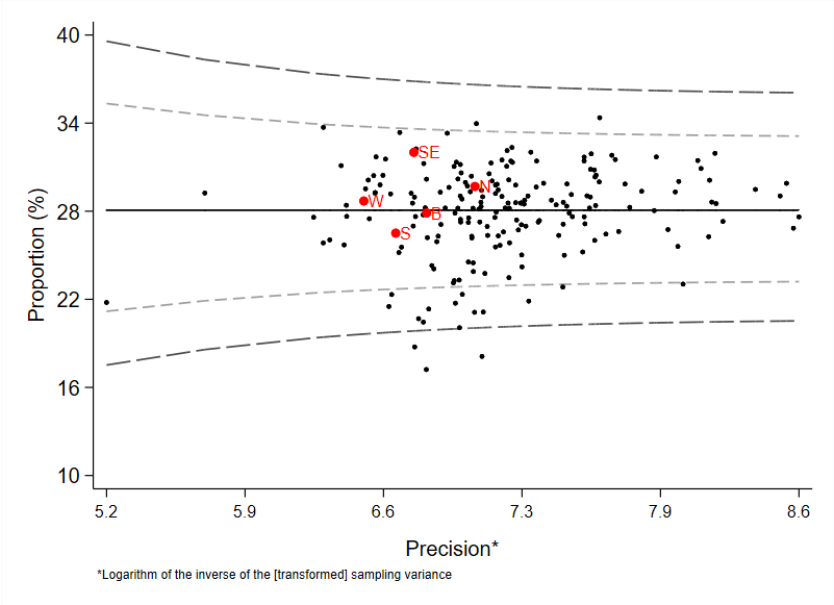
2.3.5.1 Northern Ireland Healthcare Trusts compared to English Clinical Commissioning Groups (CCGs)

Figure 11: Proportion of patients diagnosed with breast cancer through an emergency Route-to-Diagnosis for English Clinical Commissioning Groups (n=195, 2006-2016), and Northern Ireland Trusts (n=5, 2012-2016) in a funnel plot



England's CCGs have similar numbers of patients diagnosed from 2006-2016 (11 years) to NI's Trusts for 2012-2016 (5 years), the latter's estimates were superimposed on a funnel plot of the CCG estimates. The proportion of patients diagnosed via Emergency Presentation Route-to-Diagnosis for any of the Trusts lay between 95% control limits, and thus did not differ from the pooled proportion estimate for English CCGs (4.2%) (Figure 11).

Figure 12: Proportion of patients diagnosed with breast cancer through a screening Route-to-Diagnosis for English Clinical Commissioning Groups (n=195, 2006-2016), and Northern Ireland Trusts (n=5, 2012-2016) in a funnel plot



The proportion of patients diagnosed via Screening Route-to-Diagnosis for any of the Trusts lay between 95% control limits, and thus did not differ from the pooled proportion estimate for English CCGs (28.1%) (Figure 12).

2.3.6 Survival

The report presents net survival estimates, a theoretical statistic used for comparing groups of patients whose non-cancer or background mortality will differ (e.g. different regions or calendar periods). Net survival is defined as the probability of surviving cancer when the mortality from other causes of death is removed (see also Perme, Stare, & Estève, 2012).

2.3.6.1 Survival by country

The three-year net survival for patients diagnosed via the Screening Route-to-Diagnosis in NI was 99.0% (Table 8), indicating few breast cancer deaths during follow-up. Survival in the Red Flag Route-to-Diagnosis, GP Route-to-Diagnosis, Outpatient Route-to-Diagnosis, or Unknown Route-to-Diagnosis were not significantly different, but had survival intermediate

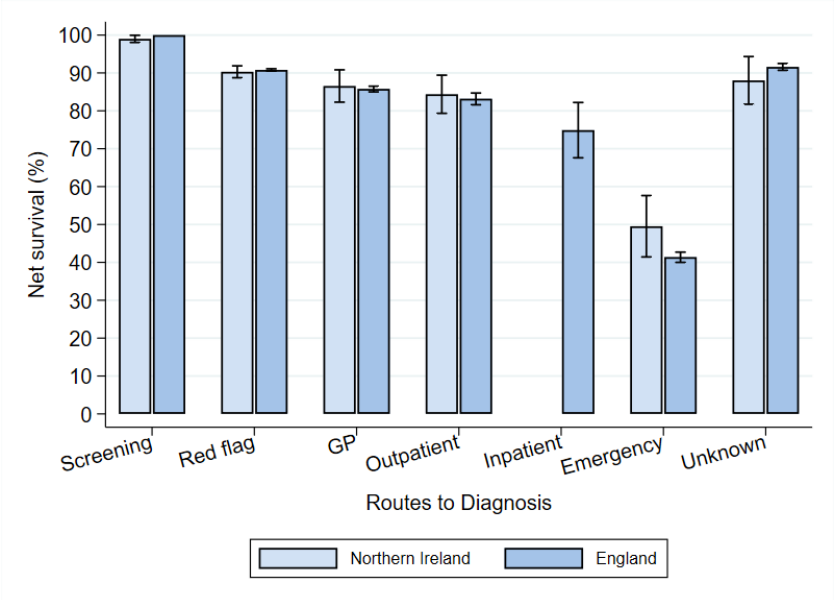
between Screening Route-to-Diagnosis (99.0%) and Emergency Presentation Route-to-Diagnosis (49.5%), which had the lowest survival. There were no significant differences between NI and England survival estimates for any of the Routes-to-diagnosis (Figure 13).

Table 8: Three-year net survival (ns, %) of breast cancer patients diagnosed in Northern Ireland (2012-2016) and England (2011-2015) by route- to-diagnosis

Route-to-diagnosis	Northern Ireland		England	
	n*	ns, %	n	ns, %
Screening	1,947	99.0	61,660	100.0
Red Flag	3,273	90.3	107,093	90.8
GP Referral	496	86.6	16,717	85.8
Outpatient	415	84.4	3,698	83.2
Emergency Presentation	268	49.5	7,949	41.4

*some patients are not included in the survival analysis, see 1.6 *Analytical techniques*

Figure 13: Three-year net survival (%) of breast cancer patients diagnosed from 2012-2016, by Route-to-Diagnosis and country



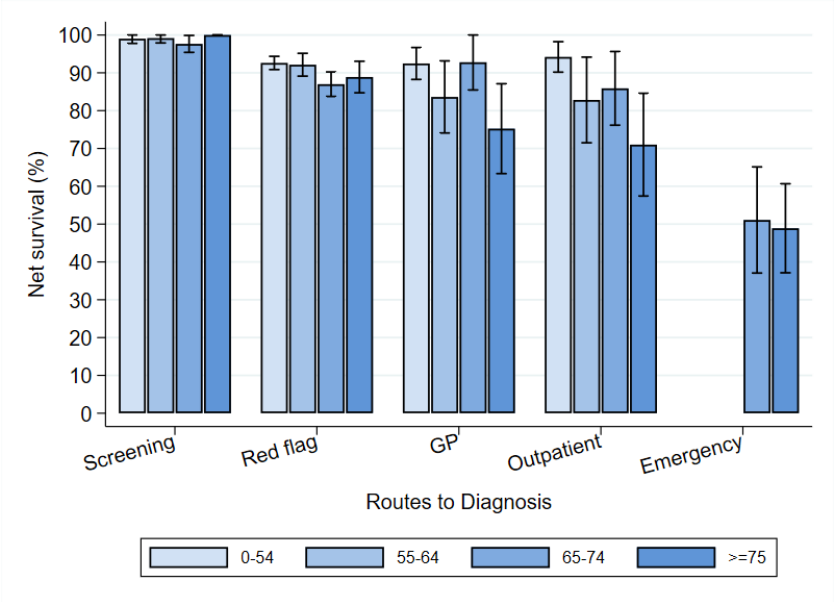
2.3.6.2 Age-group specific survival

There was no strong evidence of a survival gradient with age group in NI for any of the Routes-to-diagnosis (Table 9, Figure 14), particularly in screening-RD and red flag-RD where

estimates were more precisely estimated due to sufficient numbers, than the other Routes-to-diagnosis.

Table 9: Three-year net survival (ns, %) for patients diagnosed with breast cancer in Northern Ireland from 2012-2016, by age group and Route-to-Diagnosis								
Routes-to-diagnosis	**Age groups (years)**							
	0-54		**55-64**		**65-74**		**75+**	
	n*	**ns, %**	**n**	**ns, %**	**n**	**ns, %**	**n**	**ns, %**
Screening	472	99.0	815	99.2	601	97.6	58	100.0
Red Flag	1,161	92.6	498	92.1	686	87.0	928	88.9
GP Referral	190	92.5	81	83.6	93	92.8	132	75.2
Outpatient	152	94.2	55	82.8	88	85.9	121	71.0
Emergency Presentation	-**	-	-	-	57	51.1	160	48.9
*some patients are not included in the survival analysis, see 1.6 *Analytical techniques* **numbers too low (<50) to estimate survival								

Figure 14: Three-year age specific net survival for Route-to-Diagnosis for patients diagnosed with breast cancer within Northern Ireland 2012-2016



2.3.6.3 Stage-specific survival

Due to relatively small numbers (<50 patients), it was only possible to estimate Stage IV survival in Red Flag Route-to-Diagnosis (33.6%) and Emergency Presentation Route-to-Diagnosis (23.5%). It was not possible to estimate survival in patients diagnosed via an Emergency Presentation Route-to-Diagnosis in stage groups I-III. Survival of patients in Stage I & II was >90% irrespective of Route-to-diagnosis, while in Stage III, apart from Screening

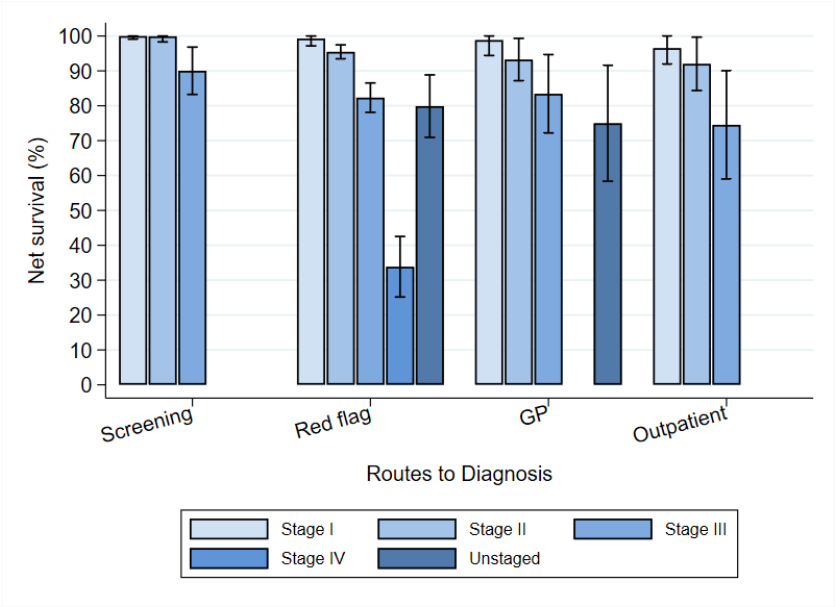
Route-to-Diagnosis (90%), survival in other Routes-to-diagnosis was lower than 85%. These findings demonstrate the poorer survival outcomes associated with late stage breast cancer and Routes-to-diagnosis (Table 10, Figure 15).

Table 10: Three-year net survival (ns, %) for patients diagnosed with breast cancer in Northern Ireland from 2012-2016, by cancer stage and Route-to-Diagnosis

Routes-to-diagnosis	Stage groups									
	I		II		III		IV		Unstaged*	
	n*	ns, %	n	ns, %	n	ns, %	n	ns, %	n	ns, %
Screening	1,267	100.0	540	99.9	103	90.0	-**	-	-	-
Red Flag	873	99.4	1,509	95.5	528	82.5	153	33.6	210	79.2
GP Referral	165	98.8	155	93.3	77	83.4	-	-	59	75.0
Outpatient	164	96.5	130	91.8	51	74.5				
Emergency Presentation	-	-	-	-	-	-	85	23.5	65	53.1

*some patients are not included in the survival analysis, see 1.6 *Analytical techniques*
**numbers too low (<50) to estimate survival

Figure 15: Three-year stage specific net survival for Route-to-Diagnosis for patients diagnosed with breast cancer within Northern Ireland 2012-2016, by cancer stage



2.3.7 Discussion

The majority of breast cancer patients in NI were diagnosed via Red Flag Route-to-Diagnosis (49.5%) or Screening Route-to-Diagnosis (29.1%), with a small proportion of Emergency Presentation Route-to-Diagnosis (4.1%); this closely matched the English Routes-to-Diagnosis pattern. NI had a higher proportion of Outpatient Route-to-Diagnosis which could reflect differences in diagnostic pathways or availability of tests between the two countries (Timmins, 2007).

Net survival was highest in the Screening Route-to-Diagnosis (99.0%), lowest in the Emergency Presentation Route-to-Diagnosis (49.5), and intermediate for Red Flag Routes-to-Diagnosis (90.3%), GP Routes-to-Diagnosis (86.6%) and outpatient Routes-to-Diagnosis (84.4%). These differences in survival reflect the proportions of patients with Stage IV or unstaged breast cancer. Net survival between NI and England was similar for all the Routes-to-diagnosis though some of the NI net survival estimates were imprecise due to small numbers.

Screening Route-to-Diagnosis proportions were higher among the patient age groups that overlapped the Screening Programme invitation age range, 50-70 years. The other age groups had higher proportions in the Red Flag Route-to-Diagnosis which perhaps reflects patients visiting their GPs with symptoms instead of being diagnosed by chance via screening. Higher proportions of older patients were more likely to present via GP Route-to-Diagnosis, Outpatient Route-to-Diagnosis, or Emergency Presentation Route-to-Diagnosis, though these proportions were typically less than 12%.

High net survival was found for all patients except those diagnosed via Emergency Presentation Route-to-Diagnosis. Emergency Presentation Route-to-Diagnosis has which has a relatively low occurrence which is perhaps due to the existence of breast cancer-specific symptoms such changes to the breast like a lump, swelling or redness, that facilitates early awareness and detection in both patients and healthcare professionals. In addition, the existence of a national Breast Screening Programme, and breast cancer symptoms campaigns increase the awareness of symptoms in the public.

The Screening Route-to-Diagnosis patients had an early-stage profile of disease, with almost no breast cancer specific mortality up to 3 years of follow-up. The high survival is partly a

success reflecting the effectiveness of screening in detecting cancer earlier, but it could partly be due to length-bias (whereby slow-growing, less-aggressive tumours are more easily detected by screening), and lead-time bias (whereby survival time is inflated by advancing the diagnosis date of a very aggressive cancer without any real improvement in the patients outcome). In women outside the screening age group, GPs may need to be vigilant regarding red flag breast cancer symptoms in young women who are unsuspecting of cancer. This is likewise in elderly women who have other health conditions (Shachar, Hurria, & Muss, 2016), including dementia, that make detection more difficult, and increases the risk of a precipitated Emergency Presentation Route-to-Diagnosis. In the UK older women present with breast cancer at a later stage and with lower net survival (McPhail et al., 2013).

Differences in breast cancer incidence rate by age have led to the development of different red flag criteria symptoms by age group. A persistent breast lump for those aged 30 years or older warrants investigation, while a breast lump which enlarges, is fixed, hard or for whom there is a family history of breast cancer is a red flag for younger women aged <30 years old (NICAN, 2012).

In the more deprived areas of NI, proportionately more patients were diagnosed via Red Flag Routes-to-Diagnosis and less through Screening Routes-to-Diagnosis. This could be due to a lack of screening uptake linked to a lower awareness of a disease whose incidence is lower in more deprived areas. Moreover, a higher proportion of screen detection in affluent areas may be due to the increased trend of 'self-referral' (National Cancer Registration and Analysis Service, 2010). The English Routes-to-Diagnosis project found Emergency Presentation Route-to-Diagnosis was more common in deprived areas (Abel, Mendonca, McPhail, Zhou, & Elliss-brookes, 2017) perhaps due to reduced health literacy or limited access to screening services. Deprivation gradients for Emergency Presentation Route-to-Diagnosis within NI were not found, but NI as a whole is more deprived compared to England and hence there is less potential for a similar gradient to express. In addition, the small numbers of Emergency Presentation Routes-to-Diagnosis in NI may have made it more difficult to detect a gradient.

NI national cancer awareness programmes such as 'Be Breast Aware' (Public Health Agency, 2019) may raise the knowledge and awareness of breast cancer symptoms in the general

public, which was reported after English breast cancer awareness publicity campaign launches (National Cancer Registration and Analysis Service, 2016). Breast cancer is a 'high profile' cancer, with a Breast Cancer Awareness Month every October (Breast Cancer Now, 2019).

A higher proportion of Stage IV disease among those with an Emergency Presentation Route-to-Diagnosis for breast cancer suggests a group of women who have not attended screening services or GPs for their symptoms. Previous research into women in NI who have not attended or infrequently attended breast screening appointments found that these women were more likely to be disadvantaged, single and in better health (Coyle et al., 2014).

Breast cancer receives a lot of investment in NI due to the large numbers who develop the disease; there are dedicated screening facilities established for breast cancer across NI. Awareness campaigns should continue to be implemented in order to ensure greater uptake in screening, and that those with potential breast cancer symptoms attend their GP. The British Medical Association (BMA) recently conducted a review of current NI breast cancer screening services, and found that existing resources are stretched (British Medical Association Northern Ireland, 2019). This comes against recent UK reports of 'a plateau in progress' as the incidence of breast cancer increases (Breast Cancer Now, 2017).

2.3.8 Bibliography

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2.4 Lung Cancer

2.4.1 Key findings

- There were 6,313 patients diagnosed with lung cancer[6] in Northern Ireland (NI) between 2012 and 2016. The most common Route-to-Diagnosis was emergency presentation (34.8%), which is similar to England.
- England had a slightly higher proportion of patients diagnosed through a Red Flag referral Route-to-diagnosis (27.5% vs 22.1%) and GP referral Route-to-diagnosis (22.5% vs 17.5%) than Northern Ireland (NI). NI had a higher proportion of Outpatient Route-to-diagnosis than England (18.2% vs 11.7%). The higher proportions of patients diagnosed through outpatient and inpatient Routes-to-diagnosis in NI compared to England may be partly an artefact arising from how the PHE algorithm interacts with the NI health service and data sources, which requires further investigation (See Section 1.5.3).
- Fifty-six percent (56.1%) of patients diagnosed through an emergency Route-to-diagnosis had Stage IV disease, while 41% of patients diagnosed through outpatient Route-to-diagnosis had early stage (Stage I or II).
- Three-year net survival in Northern Ireland was lowest for emergency presentation Route-to-diagnosis (5.8%) and highest amongst patients presenting via outpatient referral Route-to-diagnosis (30.6%).
- Net survival patterns were similar to England, except for inpatient referral Route-to-diagnosis, where 3-year survival in England was twice that of NI (15.4% vs 8.2%).

[6] 'Lung cancer' in this chapter is defined by ICD-10 (WHO, 2011) topological sites C33-C34

2.4.2 Lung Cancer

Lung cancer is abnormal cell division and tumour formation in any part of the trachea, bronchus or lungs (Cancer Research UK, 2020a). In Northern Ireland (NI) an average of 680 men and 610 women are diagnosed annually with the disease in 2013-2017; 1 in 22 men and 1 in 26 women can expect a lung cancer diagnosis in their lifetime (Northern Ireland Cancer Registry, 2020).

2.4.2.1 Incidence

The European age-standardised incidence rate for lung cancer is 86.4 per 100,000 for NI (Cancer Research UK, 2020b). Lung cancer incidence rates increase with age; 76% of lung cancer cases occur in patients aged older than 65 years, with highest incidence amongst men aged 85-89 years old and women aged 75-79 years old (Northern Ireland Cancer Registry, 2020). Incidence rates are higher in men compared to women.

2.4.2.2 Survival

Lung cancer patients have poor survival outcome. For patients diagnosed in 2007-2011, one- and five-year net survival was 32.9%, and 11.0%, respectively. Five-year net survival decreases with more advanced stage at diagnosis: Stage I (44.0%), Stage II (31.4%), Stage III (8.5%), Stage IV (1.5%). While still low, five-year survival has improved from 7.5% in patients diagnosed in 1993-1996 (Northern Ireland Cancer Registry, 2020).

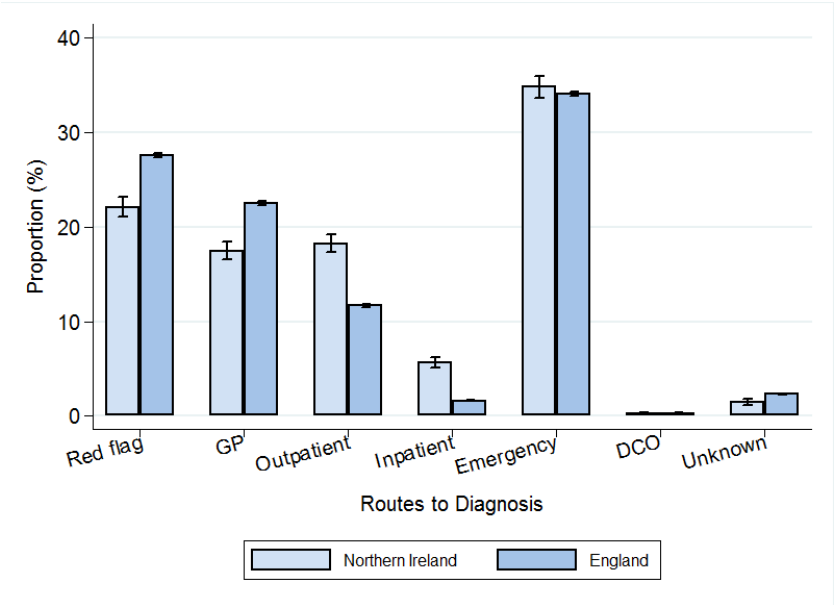
2.4.3 Routes-to-diagnosis in Northern and England

2.4.3.1 Incidence of Routes-to-Diagnosis in NI and England

The largest proportion of patients in NI was diagnosed via an Emergency Presentation Route-to-Diagnosis (34.8%) followed by a Red Flag Route-to-Diagnosis (22.1%, Table 1). The largest proportion of patients was also diagnosed in England as Emergency Presentation Route-to-Diagnosis (34.1%). NI had a higher proportion of Inpatient Route-to-Diagnosis (5.6%) and Outpatient Route-to-Diagnosis (18.2%) compared to England, whereas England had higher proportions of patients diagnosed via Red Flag Route-to-Diagnosis (27.5%) and GP Route-to-Diagnosis (22.5%; Figure 1).

Table 1: The frequency (n) and distribution (%) of Routes-to-Diagnosis of lung cancer patients diagnosed in 2012-2016, by country				
Route-to-diagnosis	**Northern Ireland**		**England**	
	n	**%**	**n**	**%**
Red Flag	1,395	22.1	52,139	27.5
GP Referral	1,103	17.5	42,634	22.5
Outpatient	1,152	18.2	22,113	11.7
Inpatient	356	5.6	3,006	1.6
Emergency Presentation	2,197	34.8	64,470	34.1
Death Certificate Only	18	0.3	560	0.3
Unknown	92	1.5	4,384	2.3
Total	**6,313**	**100.0**	**189,306**	**100.0**

Figure 1: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with lung cancer from 2012-2016 by country (Northern Ireland and England)

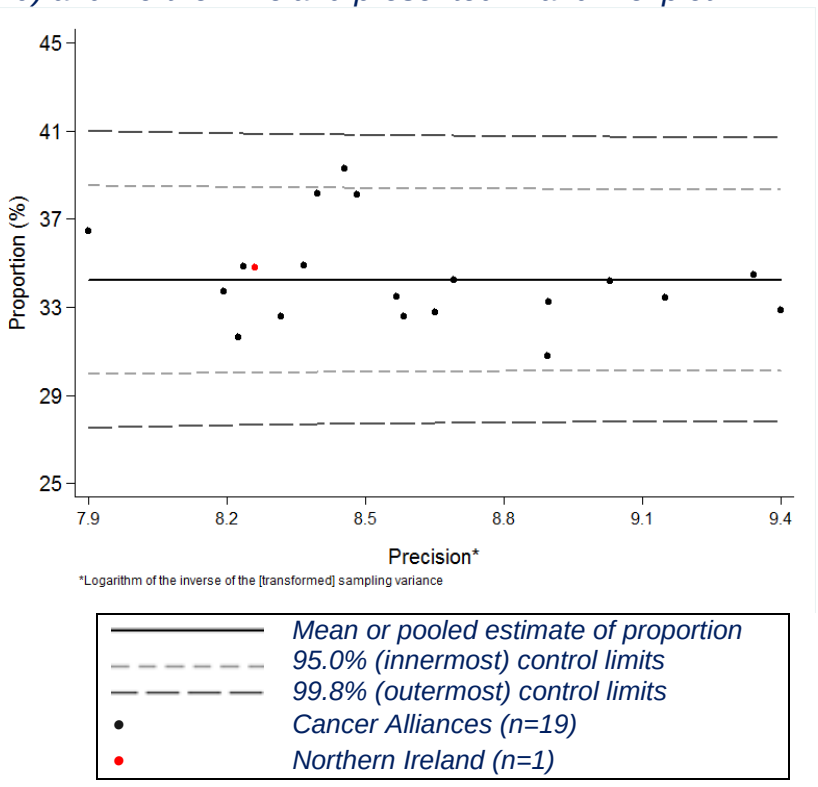


2.4.3.2 Northern Ireland compared to English Cancer Alliances

The proportion of patients diagnosed through an emergency Route-to-Diagnosis was compared between NI and the English Cancer Alliances (n=19) on a funnel plot (Figure 2). The pooled proportion of English Cancer Alliances estimate shown in the funnel plot will be different from the English estimate for each route observed in Table 1.

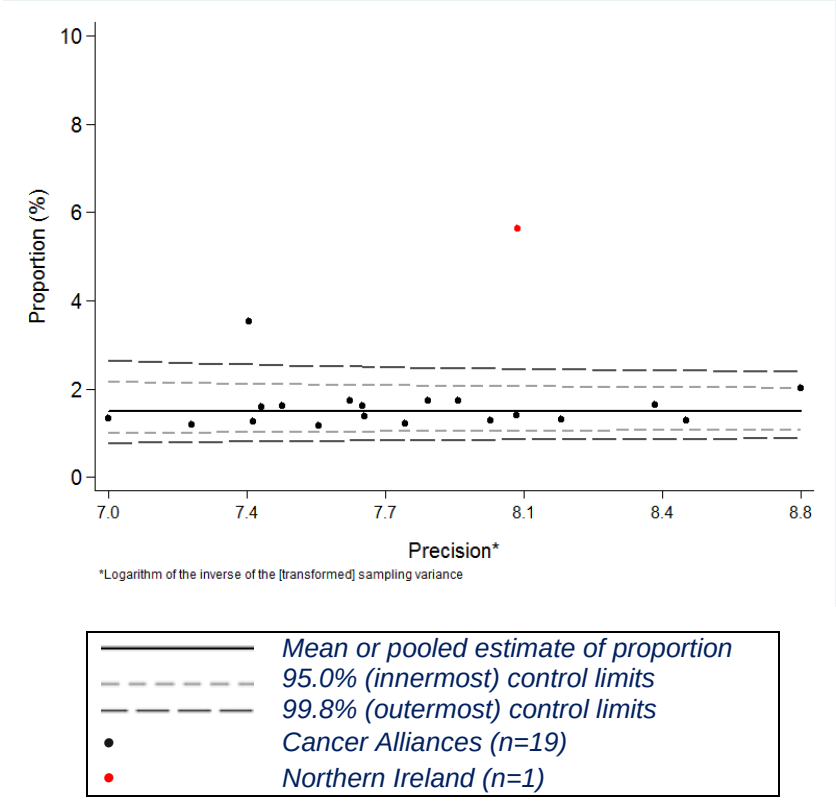
The NI proportion, lying within the 95% control limits, was not significantly different from the pooled proportion of English Cancer Alliances.

Figure 2: Proportion (%) of patients diagnosed with lung cancer from 2012-2016 through an emergency presentation Route-to-Diagnosis in English Cancer Alliances (n=19) and Northern Ireland presented in a funnel plot



While inpatient proportions were low (<10%), Northern Ireland has a greater proportion of patients diagnosed via Inpatient Route-to-Diagnosis than the pooled proportion estimate of English CALS, lying outside the 99.8% control limits (Figure 3). Possible reasons for this higher proportion are discussed later (see Discussion 2.4.7).

Figure 3: Proportion (%) of patients diagnosed with lung cancer from 2012-2016 through an inpatient referral Route-to-Diagnosis in English Cancer Alliances (n=19) and Northern Ireland presented in a funnel plot



2.4.4 Northern Ireland Routes-to-Diagnosis: demographic and stage breakdown

2.4.4.1 Patient Sex

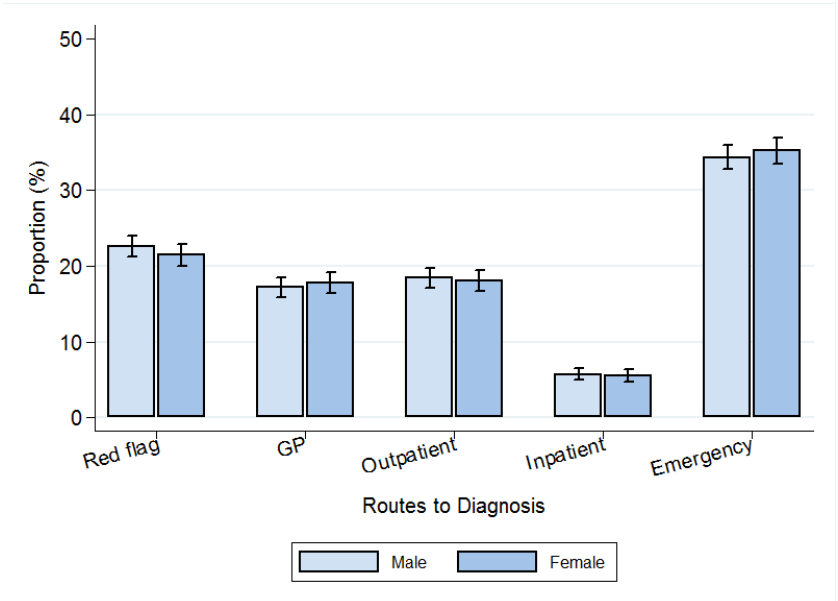
The distribution (%) of Routes-to-diagnosis in NI by sex was similar (Table 2, Figure 4), unlike for other cancer sites such as colorectal cancer.

Table 2: The frequency (n) and distribution (%) of Routes-to-Diagnosis of lung cancer patients diagnosed in 2012-2016, by sex

Route-to-diagnosis	Male		Female	
	n	%	n	%
Red Flag	757	22.6	638	21.5
GP Referral	576	17.2	527	17.8
Outpatient	617	18.5	535	18.0
Inpatient	192	5.7	164	5.5
Emergency Presentation	1,150	34.4	1,047	35.3
Total	**3,344**		**2,969**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 4: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with lung cancer within Northern Ireland from 2012-2016, by patient sex



2.4.4.2 Age

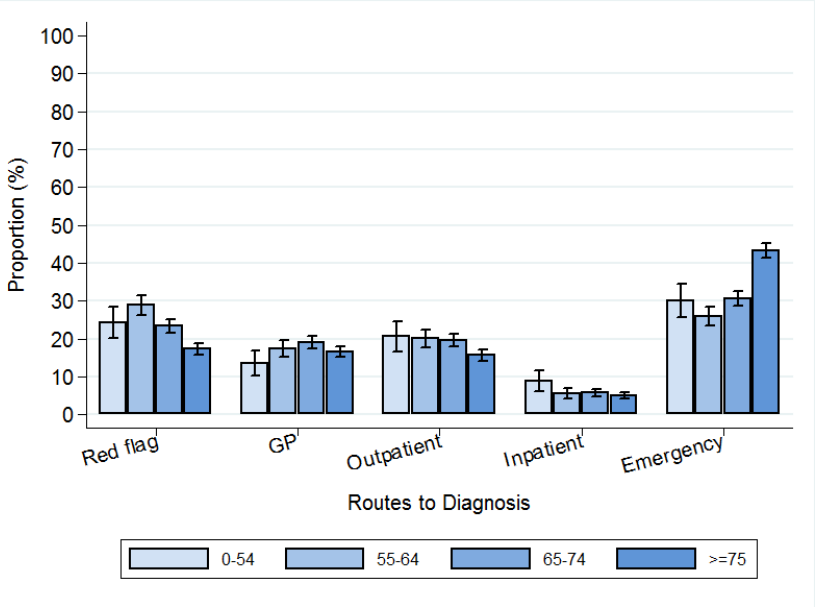
As with other cancer sites, differences in routes to diagnosis were strongly associated with age with a higher proportion of Emergency Presentation Route-to-Diagnosis lung cancers in the 75-99 age group (43.4%), while Red Flag Route-to-Diagnosis and Inpatient Route-to-Diagnosis were more common among the younger patients (Table 3, Figure 5). The proportion of patients in the 75-99 age group diagnosed through the Outpatient Route-to-Diagnosis (15.7%) was lower than the younger age groups (range, 19-20%).

Table 3: The frequency (n) and distribution (%) of Routes-to-Diagnosis of lung cancer patients diagnosed in 2012-2016, by age group

Route-to-diagnosis	Age groups (years)							
	0-54		55-64		65-74		75-99	
	n	%	n	%	n	%	n	%
Red Flag	99	24.4	339	28.9	521	23.4	436	17.4
GP Referral	55	13.5	204	17.4	427	19.2	417	16.6
Outpatient	84	20.7	236	20.1	439	19.7	393	15.7
Inpatient	36	8.9	65	5.5	129	5.8	126	5.1
Emergency Presentation	122	30.1	305	26.1	682	30.6	1088	43.4
Total	**396**		**1,149**		**2,198**		**2,460**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 5: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with lung cancer within Northern Ireland 2012-2016, by age group



2.4.4.3 Year of diagnosis

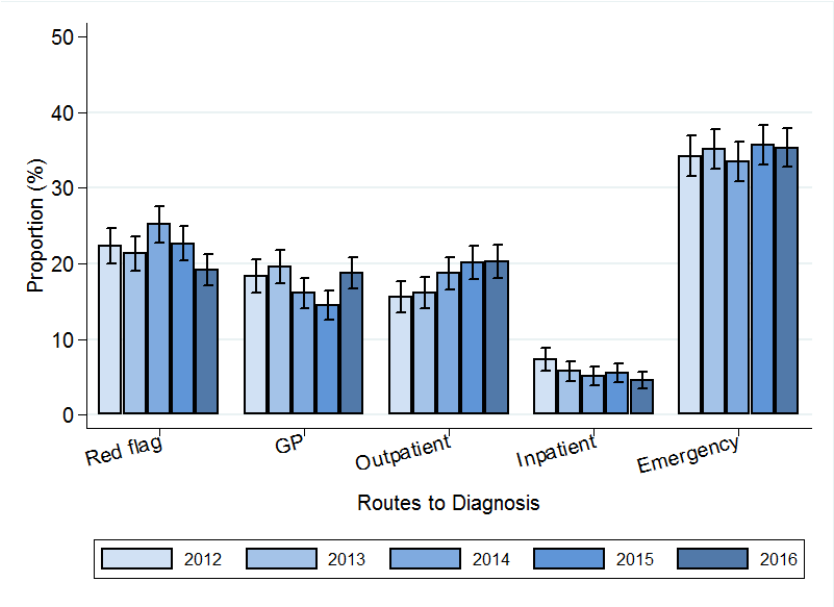
There was no strong evidence of trends in the proportions of patients within individual Routes-to-diagnosis, due to the short calendar period and the natural variation of the estimates. Proportions of Outpatient Route-to-Diagnosis appeared to increase, while Inpatient Route-to-Diagnosis showed a decline (Figure 6). The proportions in Red Flag Route-to-Diagnosis (25.2% in 2014 compared to 19.2% in 2016) and GP Route-to-Diagnosis (14.5% in 2015 compared to 18.8% in 2016) differed between the years.

Table 4: The frequency (n) and distribution (%) of Routes-to-Diagnosis of lung cancer patients, by year of diagnosis

Route-to-diagnosis	Year of diagnosis									
	2012		2013		2014		2015		2016	
	n	%	n	%*	n	%	n	%	n	%
Red Flag	267	22.3	265	21.4	316	25.2	288	22.7	259	19.2
GP Referral	220	18.4	243	19.6	202	16.1	184	14.5	254	18.8
Outpatient	187	15.6	200	16.1	235	18.7	256	20.2	274	20.3
Inpatient	88	7.4	72	5.8	64	5.1	70	5.5	62	4.6
Emergency Presentation	410	34.3	436	35.2	421	33.5	453	35.7	477	35.3
Total	**1,197**		**1,240**		**1,255**		**1,270**		**1,351**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 6: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with lung cancer in Northern Ireland 2012-2016, by year of diagnosis



2.4.4.4 Deprivation

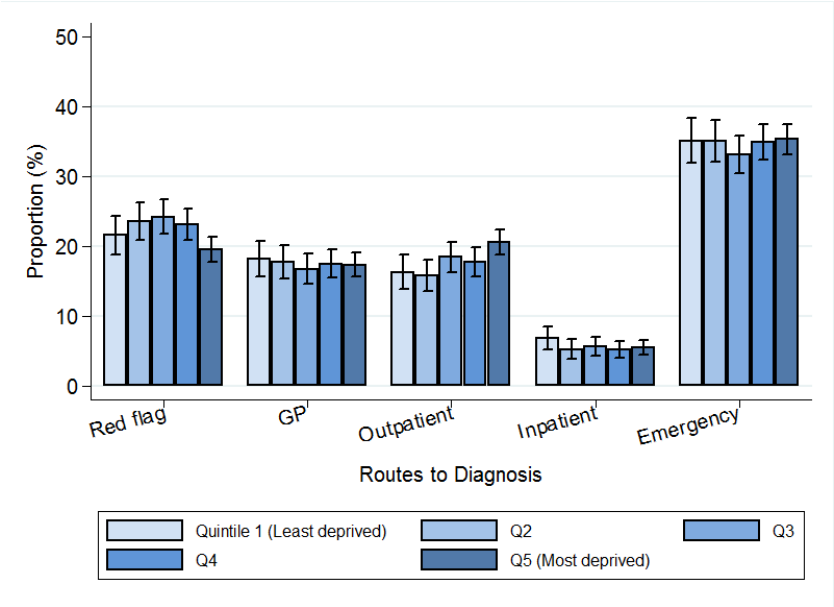
There is no statistical evidence of a deprivation gradient in the proportions of patients diagnosed within any route (Figure 7). This is at odds with Routes-to-Diagnosis for England, which found higher proportions of Emergency Presentation Route-to-Diagnosis lung cancer patients in more deprived areas (Maringe et al., 2018). However, previous research has found that NI as a whole is more deprived than England (Abel et al., 2016), and therefore NI deprivation gradients may be less steep compared to England.

Table 5: The frequency (n) and distribution (%) of Routes-to-Diagnosis of lung cancer patients diagnosed in 2012-2016, by deprivation quintile

Route-to-diagnosis	Deprivation Quintile									
	Quintile 1 (most affluent)		Quintile 2		Quintile 3		Quintile 4		Quintile 5 (most deprived)	
	n	%	n	%	n	%	n	%	n	%
Red Flag	185	21.6	231	23.6	289	24.2	313	23.1	377	19.6
GP Referral	156	18.2	174	17.8	200	16.8	238	17.6	335	17.4
Outpatient	140	16.3	155	15.8	220	18.5	241	17.8	396	20.6
Inpatient	59	6.9	52	5.3	68	5.7	71	5.2	106	5.5
Emergency Presentation	301	35.1	344	35.1	395	33.1	474	35.0	681	35.4
Total	**857**		**980**		**1,192**		**1,356**		**1,926**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 7: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with lung cancer within Northern Ireland 2012-2016, by deprivation quintile



2.4.4.5 Stage

As well as the frequency and percentage (%) distribution of Routes-to-diagnosis by stage (Table 6, Figure 8), the frequency and percentage distribution of stage by Route-to-diagnosis (Table 7, Figure 9) is presented to investigate the case-mix of patients in each Route-to-diagnosis.

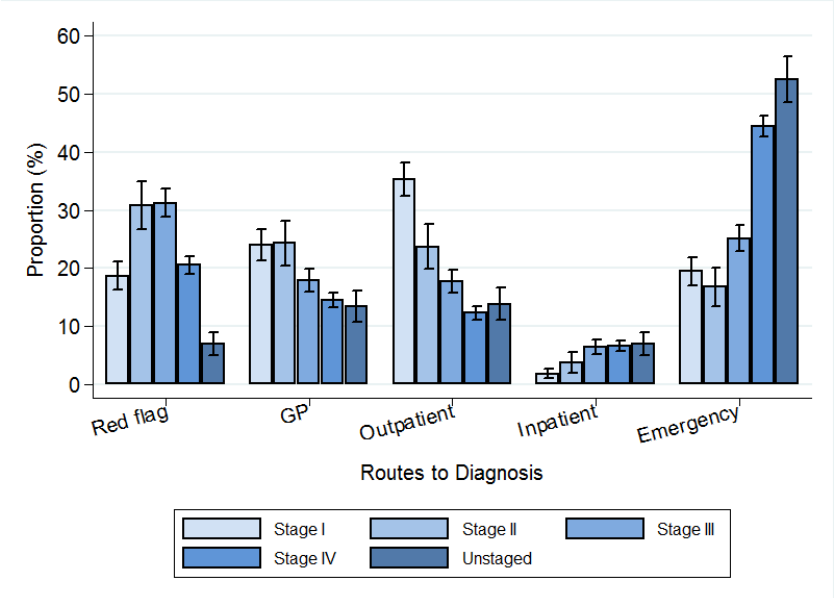
In Table 6, patients with Stage IV or unknown stage were over twice as likely to be diagnosed through Emergency Presentation Route-to-Diagnosis (44.5% and 52.6%, respectively) than patients with Stage I disease (19.5%). Conversely, patients with Stage I disease were more likely (35.3%) to be diagnosed through Outpatient Route-to-Diagnosis than Stage IV (12.3%) or unstaged (13.9%), and a similar pattern occurred in GP Route-to-Diagnosis. Patients with Stage II and Stage III were more likely (30.9% and 31.2%, respectively) to be diagnosed through a Red Flag Route-to-Diagnosis, than Stage I (18.7%) or Stage IV (20.6%). Less than half (44.5%) of patients with Stage IV disease were diagnosed via Emergency Presentation Route-to-Diagnosis, with large proportions in GP (14.5%), Red Flag (20.6%), and Outpatient Route-to-Diagnosis (12.3%) making up the remainder.

Table 6: The frequency (n) and distribution (%) of Routes-to-Diagnosis of lung cancer patients diagnosed in 2012-2016, by cancer stage

Routes-to-diagnosis	Stage groups									
	I		II		III		IV		Unstaged*	
	n	%	n	%	n	%	n	%	n	%
Red Flag	191	18.7	147	30.9	443	31.2	570	20.6	44	7.0
GP Referral	245	24.0	116	24.4	255	18.0	403	14.5	84	13.4
Outpatient	360	35.3	113	23.7	251	17.7	341	12.3	87	13.9
Inpatient	19	1.9	18	3.8	92	6.5	183	6.6	44	7.0
Emergency Presentation	199	19.5	80	16.8	357	25.1	1,232	44.5	329	52.6
Total	**1,020**		**476**		**1,420**		**2,771**		**626**	

*cancer stage unknown
Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 8: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with lung cancer within Northern Ireland from 2012-2016, by stage



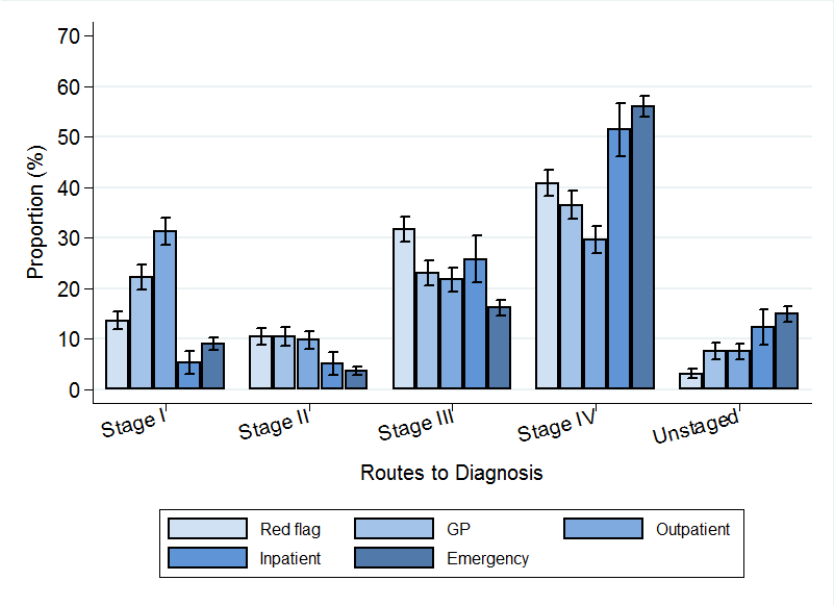
In Table 7, in both Inpatient Route-to-Diagnosis and Emergency Presentation Route-to-Diagnosis, Stage IV disease (51.4% and 56.1%, respectively) made up the largest proportion of patients. However all Routes-to-diagnosis had large proportions of Stage III and Stage IV patients, showing the difficulty of detecting this disease early, irrespective of Route-to-diagnosis. Both Inpatient Route-to-Diagnosis (5.3% for Stage I and 5.1% for Stage II) and Emergency Presentation Route-to-Diagnosis (9.1% for Stage I and 3.6% for Stage II) had low proportions of early-stage disease. The differences in stage distribution reflect differing case-mix of patients diagnosed via each Route-to-diagnosis.

Table 7: The frequency (n) and distribution (%) of cancer stage of lung cancer patients diagnosed in 2012-2016, by Routes-to-Diagnosis

Stage groups	Routes-to-diagnosis									
	Red Flag		GP		Outpatient		Inpatient		Emergency Presentation	
	n	%	n	%	n	%	n	%	n	%
I	191	13.7	245	22.2	360	31.3	19	5.3	199	9.1
II	147	10.5	116	10.5	113	9.8	18	5.1	80	3.6
III	443	31.8	255	23.1	251	21.8	92	25.8	357	16.2
IV	570	40.9	403	36.5	341	29.6	183	51.4	1,232	56.1
Unstaged*	44	3.2	84	7.6	87	7.6	44	12.4	329	15.0
Total	**1,395**		**1,103**		**1,152**		**356**		**2,197**	

*cancer stage unknown
Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown route to diagnosis

Figure 9: Distribution (%) of stage for patients diagnosed with lung cancer within Northern Ireland from 2012-2016, by Routes-to-Diagnosis

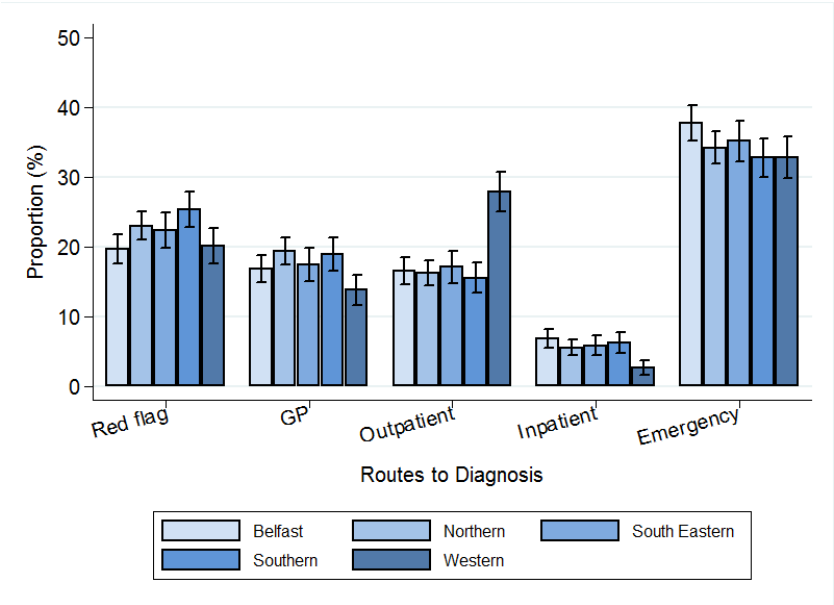


2.4.5 Geographic variation within NI Healthcare Trusts

In Table 8, there was a markedly higher proportion of patients in the Western Trust (28.5%) diagnosed through Outpatient Route-to-Diagnosis compared to the other Trusts (range, 15.5% to 16.8%). A higher proportion of patients of the Southern Trust were diagnosed through Red Flag Route-to-Diagnosis (26.1%) compared to the Belfast Trust (18.9%, Figure 10).

Table 8: The frequency (n) and distribution (%) of Routes-to-Diagnosis of lung cancer patients diagnosed 2012-2016, by Trust										
Routes-to-diagnosis	**Healthcare Trust**									
	Belfast		**Northern**		**South Eastern**		**Southern**		**Western**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Red Flag	286	18.9	375	23.3	242	22.6	290	26.1	202	20.0
GP Referral	258	17.0	309	19.2	187	17.5	209	18.8	140	13.9
Outpatient	254	16.8	259	16.1	180	16.8	172	15.5	287	28.5
Inpatient	105	6.9	91	5.7	64	6.0	69	6.2	27	2.7
Emergency Presentation	582	38.4	551	34.2	375	35.1	358	32.3	329	32.6
Total	**1,516**		**1,609**		**1,069**		**1,109**		**1008**	
Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis										

*Figure 10: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with lung cancer within Northern Ireland 2012-2016, by Trust**

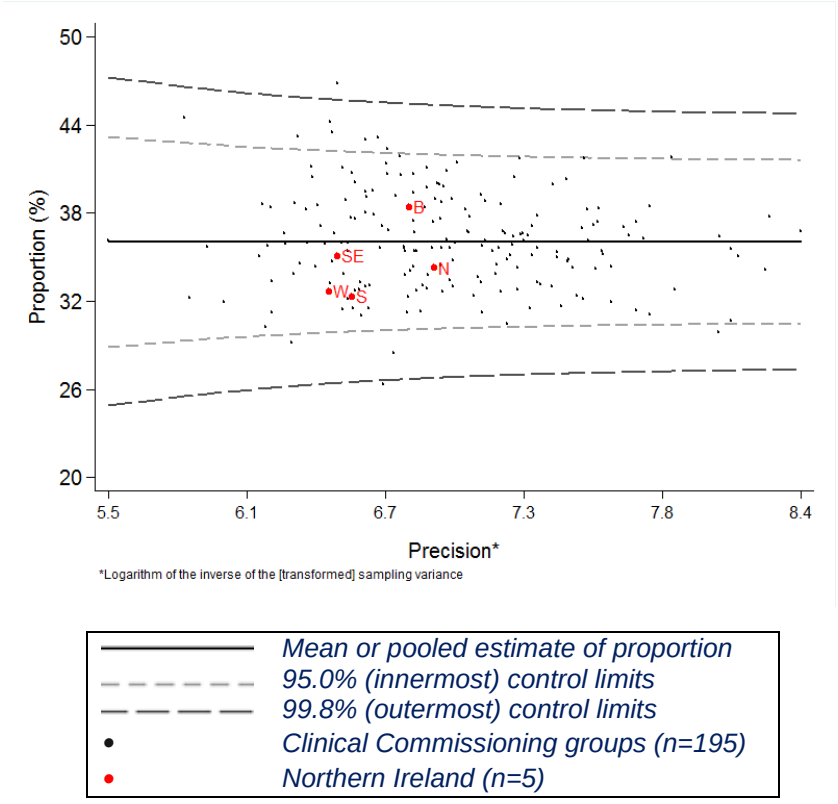


***** The presented proportions in Figure 10 were standardised to the NI population by the following factors: age, sex, and deprivation. Please see *1.6 Analytical techniques* for further details.

Northern Ireland Healthcare Trusts compared to English Clinical Commissioning Groups (CCGs)

For English CCGs, proportions of patients diagnosed in each Route-to-Diagnosis are available for the Emergency Presentation Route-to-Diagnosis. England's CCGs have similar numbers of patients diagnosed from 2006-2016 (11 years) to NI's Trusts for 2012-2016 (5 years), the latter's estimates were superimposed on a funnel plot of the CCG estimates. The proportions of patients diagnosed via Emergency Presentation Routes-to-Diagnosis for each of the Trusts were found to lie between control limits.

Figure 11: Proportion of patients diagnosed with lung cancer through an emergency Route-to-Diagnosis for English Clinical Commissioning Groups (n=195, 2006-2016), and Northern Ireland Trusts (n=5, 2012-2016) in a funnel plot



2.4.6 Survival

The report presents net survival estimates, a theoretical statistic used for comparing groups of patients whose non-cancer or background mortality will differ (e.g. different regions or calendar periods). Net survival is defined as the probability of surviving cancer when the mortality from other causes of death is removed (see also Perme, Stare, & Estève, 2012).

2.4.6.1 Survival by country

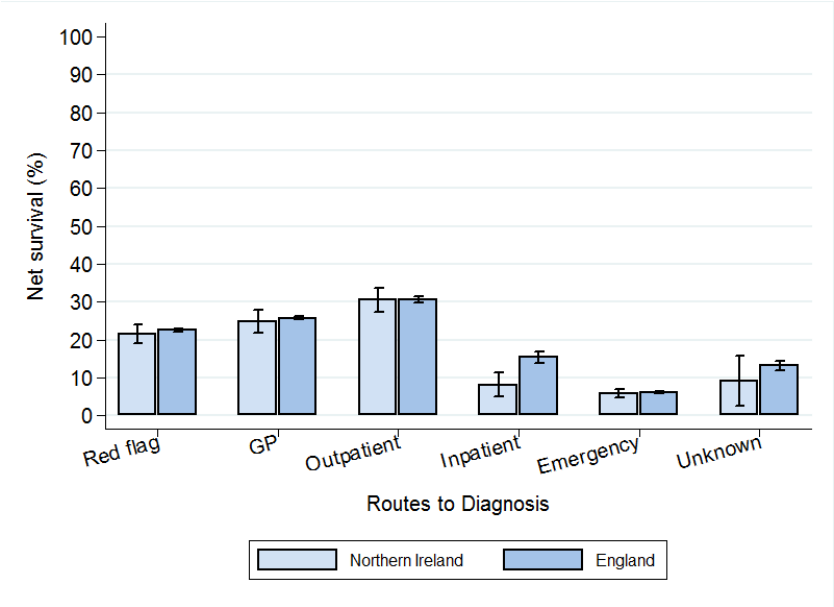
Net survival was highest in patients diagnosed via Outpatient Route-to-Diagnosis (30.6%), and lowest in the Inpatient Route-to-Diagnosis (8.2%) and Emergency Presentation Route-to-Diagnosis (5.8%). NI and England had comparable survival for patients diagnosed though most routes except Inpatient Route-to-Diagnosis, with survival in England (15.4%) twice that of Northern Ireland (Table 9).

Table 9: Three-year net survival (ns, %) of lung cancer patients (n) diagnosed in Northern Ireland (2012-2016) and England (2011-2015) by route- to-diagnosis

Route-to-diagnosis	Northern Ireland		England	
	n*	ns, %	n	ns, %
Red Flag	1,390	21.5	50,496	22.6
GP Referral	1,096	24.8	39,331	25.8
Outpatient	1,136	30.6	19,905	30.6
Inpatient	351	8.2	2,941	15.4
Emergency Presentation	2,182	5.8	62,452	6.1

*some patients are not included in the survival analysis, see 1.6 *Analytical techniques*

Figure 12: Three-year net survival (%) of lung cancer patients diagnosed from 2012-2016, by Route-to-Diagnosis and country



2.4.6.2 Age-group specific survival

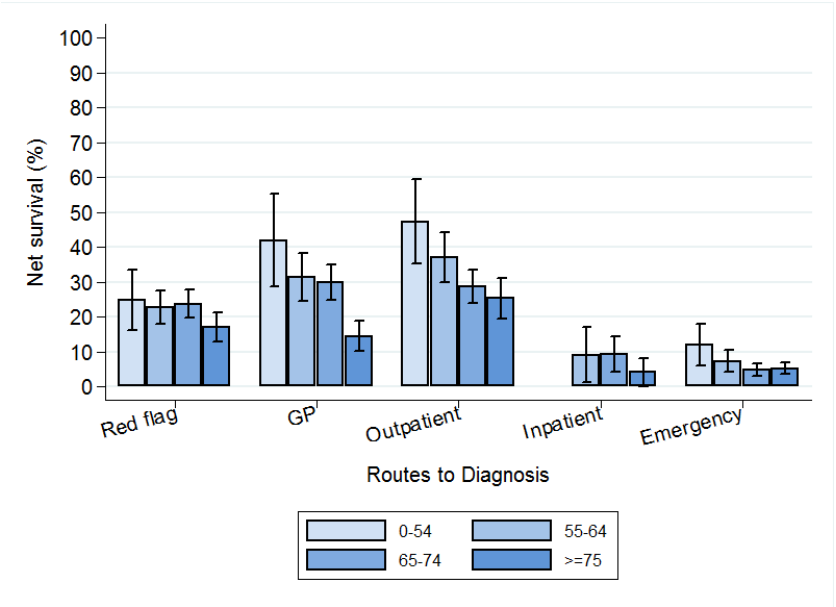
Across all Routes-to-diagnosis, net survival was lower in older patients (Table 10). Age-group gradients were steeper in patients diagnosed via GP Route-to-Diagnosis (42.0% for 0-54 year olds to 14.5% for 75-99 year olds) and Outpatient Route-to-Diagnosis (47.3% for 0-54 year olds to 25.3% for 75-99 year olds, Figure 13).

Table 10: Three-year net survival (ns, %) for patients diagnosed with lung cancer (n) in Northern Ireland from 2012-2016, by age group and Route-to-Diagnosis

Routes-to-diagnosis	Age groups (years)							
	0-54		55-64		65-74		75-99	
	n*	ns, %	n	ns, %	n	ns, %	n	ns, %
Red Flag	99	24.8	337	22.8	518	23.7	436	17.1
GP Referral	55	42.0	202	31.4	424	29.9	415	14.5
Outpatient	84	47.3	231	37.0	436	28.8	385	25.3
Inpatient	-**	-	65	9.1	129	9.2	122	4.1
Emergency Presentation	122	12.0	303	7.4	678	4.9	1079	5.2

*some patients are not included in the survival analysis, see 1.6 *Analytical techniques*
**numbers too low (<50) to estimate survival

Figure 13: Three-year age-group specific net survival for Route-to-Diagnosis for patients diagnosed with lung cancer in Northern Ireland 2012-2016

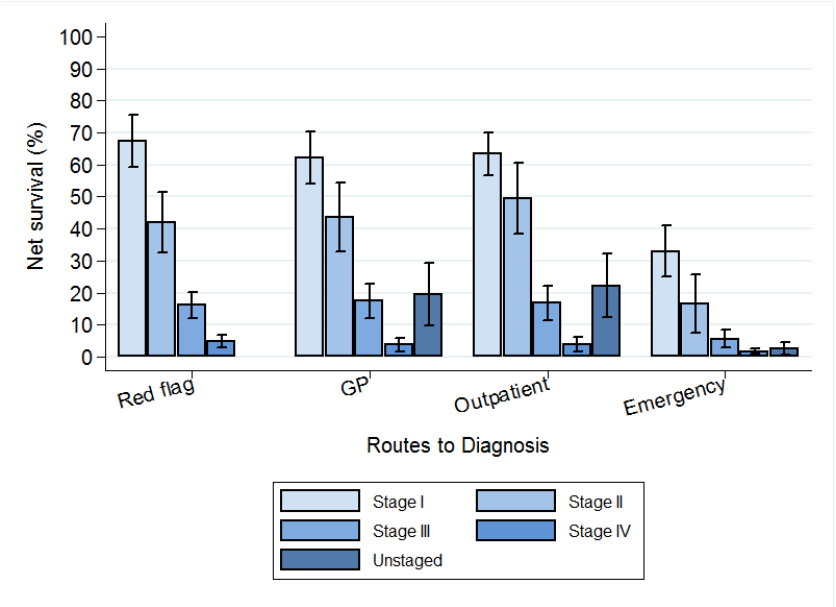


2.4.6.3 Stage specific survival

As expected for each of the Route-to-diagnosis, there was a steep declining gradient in net survival with advancing stage of disease (Table 11). For GP Route-to-Diagnosis and Outpatient Route-to-Diagnosis, patients with unstaged disease had intermediate survival between Stage II and III disease, but in Emergency Presentation Route-to-Diagnosis survival was intermediate between Stage III and IV. Patients diagnosed via Inpatient Route-to-Diagnosis and Emergency Presentation Route-to-Diagnosis had lower stage-specific survival, even though stage is the largest prognostic factor. The national NI lifetable mortality rates, used to adjust for non-cancer deaths in net survival, probably underestimate the mortality rates of patients diagnosed via Inpatient and Emergency Presentation Routes-to-Diagnosis patients who might have higher smoking-related respiratory and cardiac disease; this biases excess cancer mortality upwards, and net survival downwards.

Table 11: Three-year net survival (ns, %) for patients diagnosed with lung cancer (n) in Northern Ireland from 2012-2016, by cancer stage and Route-to-Diagnosis										
Routes-to-diagnosis	Stage groups									
	I		II		III		IV		Unstaged*	
	n*	ns, %	n	ns, %	n	ns, %	n	ns, %	n	ns, %
Red Flag	187	67.3	147	41.9	442	16.2	570	4.9	-**	-
GP Referral	241	62.3	116	43.6	254	17.5	403	3.7	82	19.5
Outpatient	351	63.4	113	49.6	249	16.8	340	3.9	83	22.3
Inpatient	-**	-	-	-	92	7.7	183	2.9	-	-
Emergency Presentation	198	33.0	80	16.6	357	5.5	1,231	1.7	316	2.6
*some patients are not included in the survival analysis, see 1.6 *Analytical techniques* **numbers too low (<50) to estimate survival										

Figure 14: Three-year stage specific net survival for Route-to-Diagnosis for patients diagnosed with lung cancer in Northern Ireland 2012-2016, by cancer stage



2.4.7 Discussion

The proportion and survival of lung cancer patients diagnosed through different Routes-to-Diagnosis are broadly similar in Northern Ireland and England, with the largest proportion of lung cancer patients diagnosed via Emergency Presentation Route-to-Diagnosis (34.9% NI and 34.1% England). However, Northern Ireland has a higher proportion (15.4%) of patients diagnosed through Inpatient Route-to-Diagnosis than England (8.2%). Survival of patients in English Inpatient Route-to-Diagnosis is twice that of NI, indicating case-mix differences in patients between the two countries. Patients diagnosed through the inpatient route in NI have late stage disease and poorer outcomes. Different inpatient and outpatient proportions in NI could be due to the diagnostic pathway in the system, and requires further study.

Differences in Route-to-diagnosis proportions were found between the Healthcare Trusts. There was a higher proportion of Outpatient Route-to-Diagnosis in the Western Trust. The lack of significant differences by deprivation quintile does not agree with England where increased proportions of Emergency Presentation Route-to-Diagnosis were found in the most deprived areas (National Cancer Intelligence Network, 2015). NI is more deprived than England, with possibly a less steep deprivation gradient. However, similar to England, the lung cancer incidence in Northern Ireland is 41% higher in the most-deprived communities (Northern Ireland Cancer Registry, 2020).

Just over a third of lung cancer patients are diagnosed via an Emergency Presentation Route-to-Diagnosis, among whom the majority have Stage IV disease and poor survival outcomes. Understanding the case-mix differences by Route-to-diagnosis will assist in understanding the overall poor survival of lung cancer patients in NI. Stage-specific net survival estimates are lower in patients with Emergency Presentation Route-to-Diagnosis. The NI lifetable mortality rates that are used to adjust for non-cancer deaths in net survival probably underestimate the true non-cancer mortality rates of Emergency Presentation Route-to-Diagnosis patients who may have higher smoking-related respiratory and cardiac disease; this will bias their net survival downwards.

Poor lung cancer survival was also found by Public Health England (McPhail, Johnson, Greenberg et al., 2015), and lung cancer is the leading cause of cancer-related death in the world (Blandin Knight et al., 2017). UK lung cancer survival lags behind other countries with

similar health-care service (Walters et al., 2013). Walters et al., reported that poor lung cancer stage distribution in the UK indicated later diagnosis, and lower stage-specific survival for lung cancer in the UK points to less timely and optimal treatment (i.e. surgery, chemotherapy or radiotherapy) (Walters et al., 2013). The high proportion of late stage lung cancer diagnoses may be due lack of awareness of symptoms amongst the public, or in delays in the healthcare system diagnostic pathways (Hubbard & Baldwin, 2010).

Patient awareness of lung cancer symptoms may influence their eventual routes to diagnosis. A UK cohort study found that the majority of those diagnosed through an emergency route did not report any symptoms previously to their GP (Barrett & Hamilton, 2008) despite experiencing at least one symptom. The main risk factor for lung cancer, smoking, can cause a number of other conditions of the lung. Therefore the symptoms of lung cancer can be incorrectly attributed to other smoking-related conditions which delay cancer diagnosis and lead to later stage disease. In a similar manner, older people are more likely to have more complex comorbidities and cognitive impairment which may make diagnosing lung cancer difficult, leading to a higher proportion of advanced-stage diagnoses. Research in England found lung cancer Emergency Presentation Route-to-Diagnosis to be associated with older age and comorbidity (Newsom-Davis, 2017).

Delays in diagnosis means that the disease will be more aggressive and advanced on diagnosis; this highlights the importance of awareness campaigns to provide information about lung cancer symptoms to the public, particularly smokers. Campaigns in England to raise awareness of lung cancer symptoms increased public knowledge of symptoms of the disease (Ironmonger et al., 2014). England has introduced ‘lung cancer scanning trucks’ to encourage early diagnosis (NHS England, 2019). Northern Ireland has developed and implemented a cancer awareness programme of lung cancer symptoms (Public Health Agency, 2015). Route-to-diagnosis information can be used in the evaluation of the effectiveness of such interventions.

Higher proportions of Stage IV disease were also diagnosed in Red Flag Route-to-Diagnosis, GP Route-to-Diagnosis, and Outpatient Route-to-Diagnosis, a finding reported in England (Elliss-Brookes, 2016) also. This highlights the poor sensitivity and specificity of many of the red flag referral symptoms (lethargy, hoarseness, chest pain, haemoptysis, finger clubbing) in detecting early-stage aggressive disease, and which can be worse in older age groups. Lung cancer can be asymptomatic at earlier stages, with the more noticeable red flag symptoms for lung cancer like haemoptysis (coughing up blood) only occurring at an advanced stage of lung cancer.

In Northern Ireland, GP direct access to chest x-ray services has facilitated the diagnostic process, notwithstanding a level of false negative results. Other diagnostic tests like computerized tomography (CT) scanning are not available to GPs across all of Northern Ireland; some GPs have to refer patients to Trusts which have access to CT which generates referral pressure (Nursing Standard, 2015). Further work could be undertaken to evaluate the efficacy of such arrangements alongside consideration of further initiatives to support GPs.

The NICE Guideline Development Group recommends referring patients in a timely manner, taking into account patients' smoking history, to ensure earlier stage diagnoses and minimising the number of patients inappropriately diagnosed (National Institute for Health and Care Excellence, 2015).

NICE red flag referral guidelines were updated in 2015 (NICE, 2015) however the NI healthcare system still follows 2012 NICE red flag referral guidelines (NICAN,2012). A new recommendation in the NG12 guidelines was the addition of unexplained haemoptysis for patients aged 40 or older as a red flag criteria for lung cancer patients (NICE, 2015). NICE guidelines acknowledge that this would increase the number of chest x-rays requested by GPs, but that there was evidence to support the effectiveness of 'red-flagging' this symptom.

The higher proportion of Outpatient Route-to-Diagnosis in Stage I disease patients could be explained by incidental diagnoses. Patients may visit respiratory clinics for other conditions like COPD (Chronic Obstructive Pulmonary Disorder) or emphysema. The chest x-rays done there can assist the detection of early-stage lung cancer. In conclusion, lung cancer has a

higher proportion of Emergency Presentation Route-to-Diagnosis, and poorer survival for all Route-to-diagnosis compared to other cancer sites. These results are comparable to England, and suggest the need for interventions to improve early diagnosis through greater public awareness supported by more accurate and timely diagnosis.

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2.5 Prostate Cancer

2.5.1 Key findings

- There were 5,586 patients diagnosed with prostate cancer[7] in NI between 2012 and 2016. GP referral was the most frequently utilised route (36.7%) which was similar to England. However, England had a higher proportion of Red flag Routes-to-Diagnosis compared to NI (44.4% vs 28.2%). NI had higher proportions of prostate cancer patients diagnosed by inpatient and outpatient routes than England. The higher proportions of patients diagnosed through outpatient and inpatient Routes-to-diagnosis in NI compared to England may be partly an artefact arising from how the PHE algorithm interacts with the NI health service and data sources, which requires further investigation (See Section 1.5.3).
- A high proportion of men aged ≥85 (32.9%) were diagnosed in an emergency route to diagnosis.
- In Northern Ireland, low 3-year net survival (43.8%) was observed only in patients in the emergency Route-to-Diagnosis due to sizeable proportions of Stage IV (38%) and unstaged (42.5%). All other routes to diagnosis had high survival levels indicating limited excess mortality from prostate cancer among the patients during follow-up, even when sizeable proportions of advanced disease are present.
- NI and England had similar survival outcomes for all Routes-to-diagnosis, and probably reflects the two-fold reality of diagnosis via emergency presentation or not.
- Understanding the symptom development of patients diagnosed through an emergency route to diagnosis may assist in identifying and raising awareness of the specific symptoms for life-limiting aggressive prostate cancer.

[7] 'Prostate cancer' in this chapter is defined by ICD-10 (WHO, 2011) topological site C61

2.5.2 Prostate Cancer

Prostate cancer arises when cells begin to divide and grow in an uncontrolled way in a man's prostate gland (Cancer Research UK, 2020). In Northern Ireland (NI), approximately 1,100 patients are diagnosed annually (Northern Ireland Cancer Registry, 2020) with around 270 deaths per year. It is the most common type of cancer amongst men in NI making up 24% of cancer incidence and 12% of cancer deaths. With increased clinical use of prostate-specific antigen (PSA) biomarker in detecting prostate cancer, it is generally accepted that there is over-diagnosis of non-aggressive disease. Therefore survival statistics can be influenced by the level of PSA testing rather than the earlier detection of aggressive disease. The age-standardised death rate has remained constant at 48 deaths per 100,000 men since 2010.

2.5.2.1 Incidence & Survival statistics

The age-standardised[8] incidence rate for prostate cancer is 163.0 cases per 100,000 of the population. Risk of colorectal cancer increases with age; 72% of prostate cancer patients are diagnosed at 65 years of age and older. Men have a 1 in 12 odds (Northern Ireland Cancer Registry, 2020) of being diagnosed in their lifetime. The distribution of stage of diagnosis is: Stage I (32%), Stage II (22%), Stage III (19%), Stage IV (19%) and unstaged (9%). The five-year net survival for men with prostate cancer is high at 88.3%, but varies by stage: Stage I & II (100%), Stage III (97%), Stage IV (32%), and unstaged (81%).

2.5.3 Routes-to-diagnosis in Northern and England

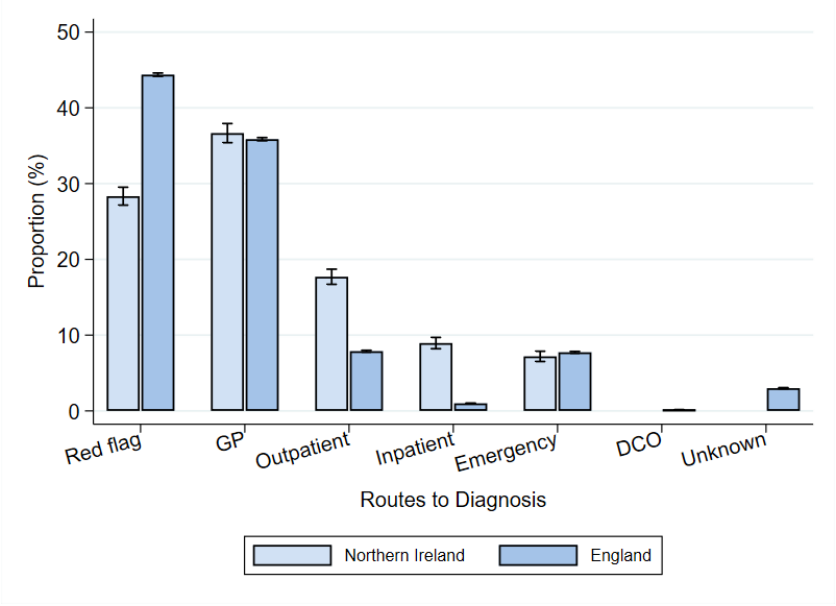
2.5.3.1 Incidence of Routes-to-Diagnosis in NI and England

There were 5,586 men diagnosed with prostate cancer in NI in the years 2012-2016. The largest proportions of patients in NI were diagnosed via a GP Route-to-Diagnosis (36.7%), Red Flag Route-to-Diagnosis (28.3 %), and Outpatient Route-to-Diagnosis (17.7%, Table 1). In England, more patients were diagnosed via Red Flag Route-to-Diagnosis (44.4%), and much less through Outpatient Route-to-Diagnosis (7.9%, Figure 1). Northern Ireland had a sizeable proportion of patients diagnosed in an Inpatient Route-to-Diagnosis (9.0%). The proportion of men diagnosed via an Emergency Presentation Route-to-Diagnosis was comparable between NI and England (7.2% vs 7.7%).

[8] 2013 European Standard Population

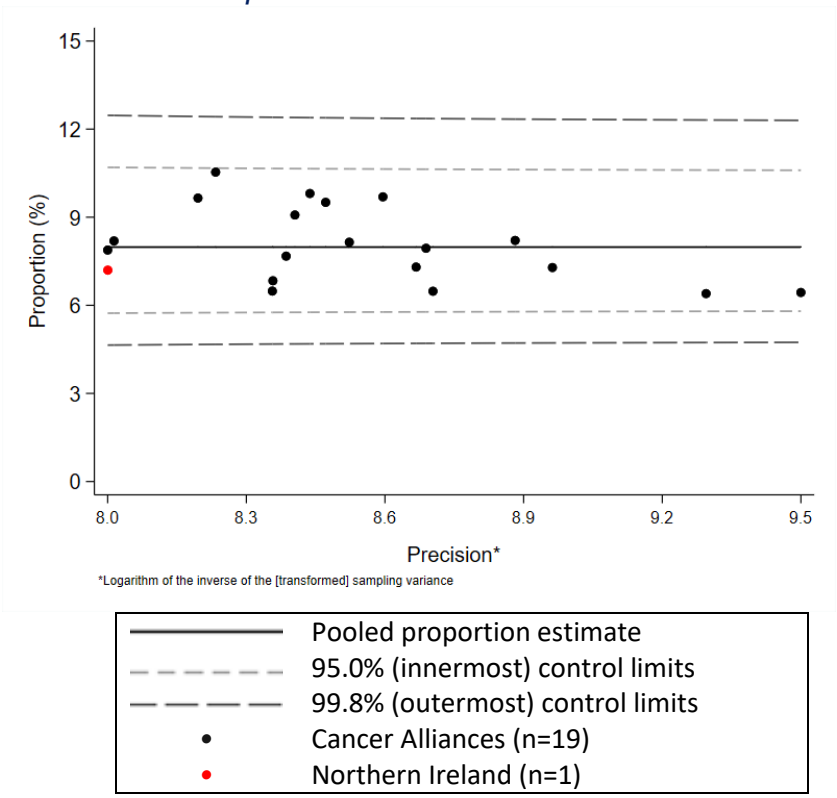
Table 1: The frequency (n) and distribution (%) of Routes-to-Diagnosis of prostate cancer patients diagnosed in 2012-2016, by country				
Route-to-diagnosis	**Northern Ireland**		**England**	
	n	**%**	**n**	**%**
Red Flag	1,583	28.3	89,543	44.4
GP Referral	2,048	36.7	72,362	35.9
Outpatient	989	17.7	15,901	7.9
Inpatient	500	9.0	2,001	1.0
Emergency Presentation	402	7.2	15,599	7.7
Death Certificate Only	<10	-	310	0.2
Unknown	≈55	-	6,051	3.0
Total	**5,586**		**201,767**	

Figure 1: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with prostate cancer from 2012-2016 by country (Northern Ireland and England)



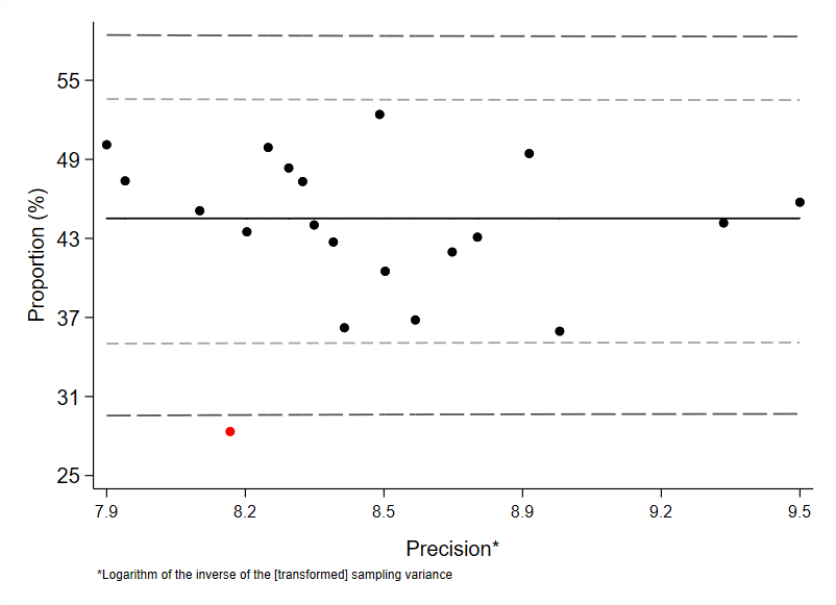
2.5.3.2 Northern Ireland compared to English Cancer Alliances

Figure 2: Proportion (%) of patients diagnosed through an emergency presentation Route-to-Diagnosis 2012-2016 in English Cancer Alliances (n=19) and Northern Ireland presented in a funnel plot



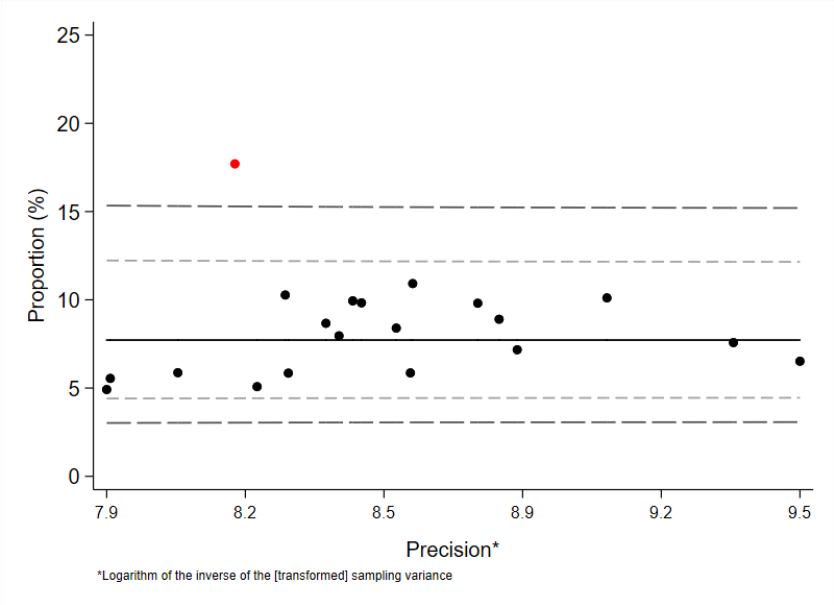
The proportion of patients diagnosed through an Emergency Presentation Route-to-Diagnosis was compared between NI and the English Cancer Alliances (n=19) on a funnel plot (Figure 2). The NI proportion (7.2%), lying within the 95% control limits, was not significantly different from the pooled proportion estimate (8.0%) of English Cancer Alliances.

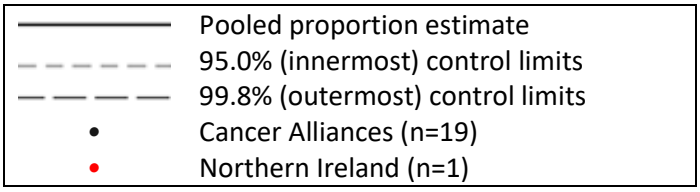
Figure 3: Proportion (%) of patients diagnosed through red flag Route-to-Diagnosis 2012-2016 in English Cancer Alliances (n=19) and Northern Ireland presented in a funnel plot



Northern Ireland had a lower proportion (28.3%) of patients diagnosed via Red Flag Route-to-Diagnosis than the pooled proportion estimate of English CALS (44.5%), lying outside the 99.8% control limits (Figure 3).

Figure 4: Proportion (%) of patients diagnosed through outpatient Route-to-Diagnosis 2012-2016 in English Cancer Alliances (n=19) and Northern Ireland presented in a funnel plot





NI had a higher proportion (17.7%) of patients diagnosed via Outpatient Route-to-Diagnosis than the pooled proportion estimate of English CALS (7.7%), lying outside the 99.8% control limits (Figure 4).

2.5.4 Northern Ireland Routes-to-Diagnosis: demographic and stage breakdown

2.5.4.2 Age

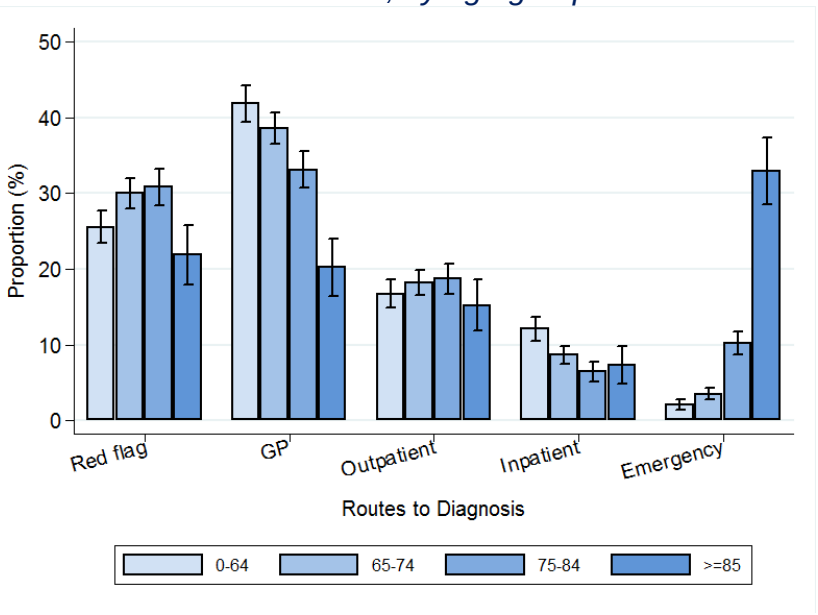
There was a strong declining gradient in the proportion of men diagnosed via a GP Route-to-Diagnosis with advancing age group from 41.8% in age group 0-64 to 20.3% in the age group ≥85 (Table 2). Conversely, there is a strong increasing gradient in the proportion of men diagnosed via Emergency Presentation Routes-to-Diagnosis with patients in the ≥85 age group (32.9%) higher than the younger age groups (<11%). For age groups <85, the largest proportion of patients were diagnosed through GP Route-to-Diagnosis, followed by Red Flag Route-to-Diagnosis and then Outpatient Route-to-Diagnosis (Figure 5).

Table 2: The frequency (n) and distribution (%) of Routes-to-Diagnosis of prostate cancer patients diagnosed in 2012-2016, by age group								
Route-to-diagnosis	**Age groups† (years)**							
	0-64		**65-74**		**75-84**		**≥85**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Red Flag	406	25.6	628	30.0	454	30.8	95	21.9
GP Referral	664	41.8	808	38.6	488	33.1	88	20.3
Outpatient	266	16.8	381	18.2	276	18.7	66	15.2
Inpatient	192	12.1	181	8.7	95	6.4	32	7.4
Emergency Presentation	34	2.1	74	3.5	151	10.3	143	32.9
Total	**1,587**		**2,092**		**1,473**		**434**	

†age groups use ICSS definition for international survival studies

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 5: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with prostate cancer within Northern Ireland 2012-2016, by age group



2.5.4.3 Year of diagnosis

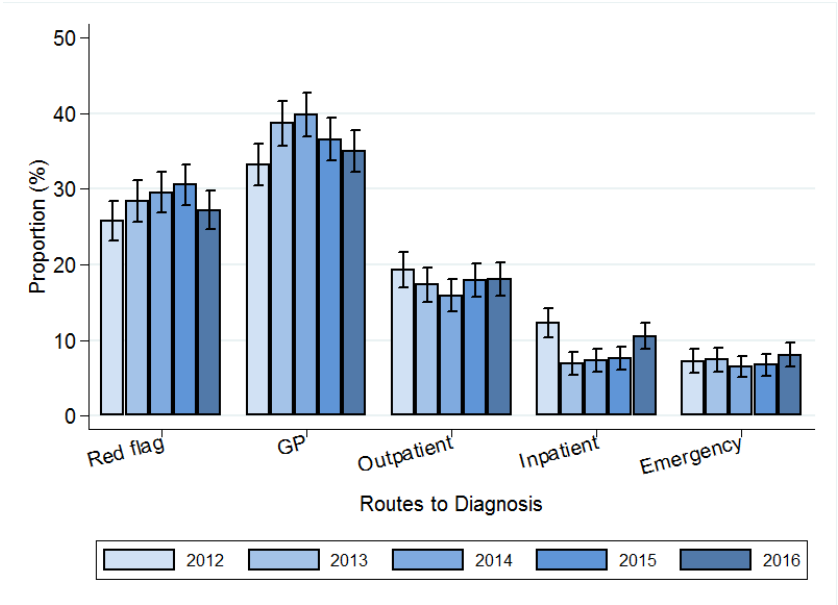
There was no strong evidence of trends in the proportions of patients diagnosed via individual Routes-to-diagnosis, due to the short calendar period and the natural variation of the estimates. Proportions of Inpatient Route-to-Diagnosis in 2012 were higher than the years 2013-2015 (Table 3, Figure 6).

Table 3: The frequency (n) and distribution (%) of Routes-to-Diagnosis of prostate cancer patients, by year of diagnosis

Route-to-diagnosis	Year of diagnosis									
	2012		2013		2014		2015		2016	
	n	%	n	%*	n	%	n	%	n	%
Red Flag	281	25.8	295	28.4	340	29.6	350	30.6	317	27.2
GP Referral	362	33.2	401	38.7	458	39.8	419	36.6	408	35.0
Outpatient	211	19.4	180	17.4	183	15.9	205	17.9	210	18.0
Inpatient	134	12.3	72	6.9	84	7.3	87	7.6	123	10.6
Emergency Presentation	79	7.3	77	7.4	75	6.5	77	6.7	94	8.1
Total	**1,089**		**1,037**		**1,150**		**1,145**		**1,165**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 6: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with prostate cancer in Northern Ireland 2012-2016, by year of diagnosis



2.5.4.4 Deprivation

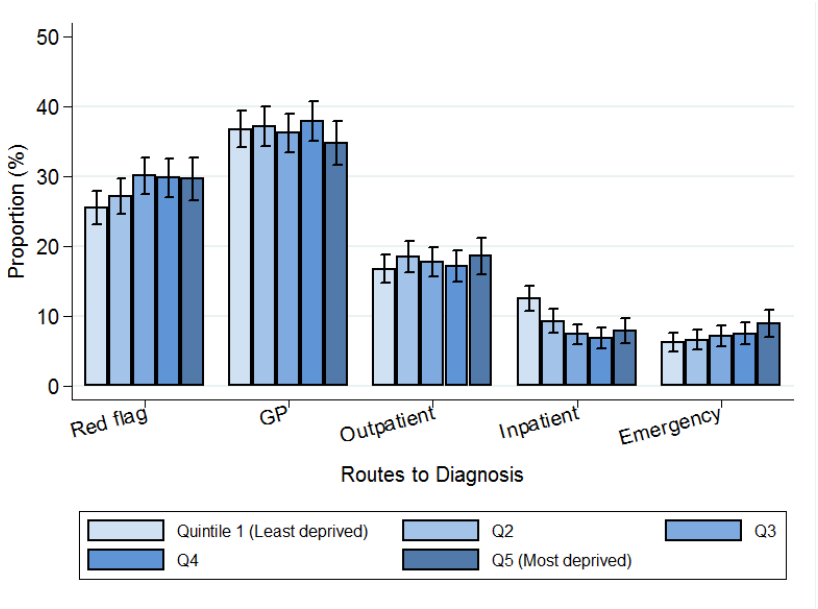
There was no statistical evidence of a deprivation gradient in the proportions of patients diagnosed in the Routes-to-diagnosis, apart from Inpatient Route-to-Diagnosis where there was a decline from 12.5% in the most affluent quintile to 7.9% in the most deprived quintile (Table 4, Figure 7). It is possible that lack of statistically significant deprivation gradients are due to small numbers of prostate cancer patients in NI, as when routes to diagnosis by deprivation quintiles were compared for all cancer patients, strong gradients for emergency presentation and screening were observed (see Deprivation section 2.1.4.4).

Table 4: The frequency (n) and distribution (%) of Routes-to-Diagnosis of prostate cancer patients diagnosed in 2012-2016, by deprivation quintile

Route-to-diagnosis	Deprivation Quintile									
	Quintile 1 (most affluent)		Quintile 2		Quintile 3		Quintile 4		Quintile 5 (most deprived)	
	n	%	n	%	n	%	n	%	n	%
Red Flag	324	25.5	311	27.2	369	30.1	324	29.8	255	29.7
GP Referral	467	36.8	426	37.2	444	36.2	412	37.9	299	34.8
Outpatient	213	16.8	212	18.5	218	17.8	186	17.1	160	18.6
Inpatient	159	12.5	107	9.3	91	7.4	75	6.9	68	7.9
Emergency Presentation	79	6.2	76	6.6	88	7.2	82	7.5	77	9.0
Total	**1,269**		**1,145**		**1,226**		**1,087**		**859**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 7: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with prostate cancer within Northern Ireland 2012-2016, by deprivation quintile



2.5.4.5 Stage

As well as the frequency and percentage (%) distribution of Routes-to-diagnosis by stage (Table 5, Figure 8), the frequency and percentage distribution of stage by Route-to-diagnosis (Table 6, Figure 9) is presented to investigate the case-mix of patients in each Route-to-diagnosis.

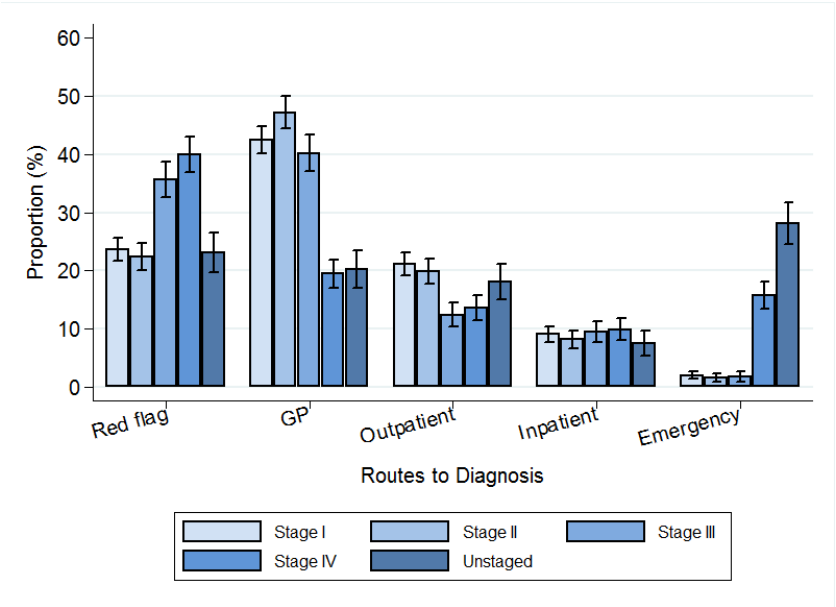
Patients with Stage IV disease were most likely to present via Red Flag Route-to-Diagnosis (40.0%) with sizeable proportions in GP Route-to-Diagnosis (19.5%), Outpatient Route-to-Diagnosis (13.7%), and Emergency Presentation Route-to-Diagnosis (15.8%, Table 5). Over 65% of Stage I-III patients were likely to proceed through a Red Flag Route-to-Diagnosis or GP Route-to-Diagnosis. Of the unstaged patients the greatest proportion were diagnosed via an Emergency Presentation Route-to-Diagnosis (28.2%); very few patients Staged I-III (≤2%) were diagnosed through an Emergency Presentation Route-to-Diagnosis (Figure 8).

Table 5: The frequency (n) and distribution (%) of Routes-to-Diagnosis of prostate cancer patients diagnosed in 2012-2016, by cancer stage

Routes-to-diagnosis	Stage groups									
	I		II		III		IV		Unstaged*	
	n	%	n	%	n	%	n	%	n	%
Red Flag	419	23.7	279	22.4	350	35.6	395	40.0	140	23.1
GP Referral	751	42.5	587	47.1	395	40.2	192	19.5	123	20.3
Outpatient	374	21.2	248	19.9	122	12.4	135	13.7	110	18.2
Inpatient	161	9.1	102	8.2	93	9.5	98	9.9	46	7.6
Emergency Presentation	36	2.0	21	1.7	18	1.8	156	15.8	171	28.2
Total	**1,766**		**1,245**		**982**		**987**		**606**	

*cancer stage unknown
Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

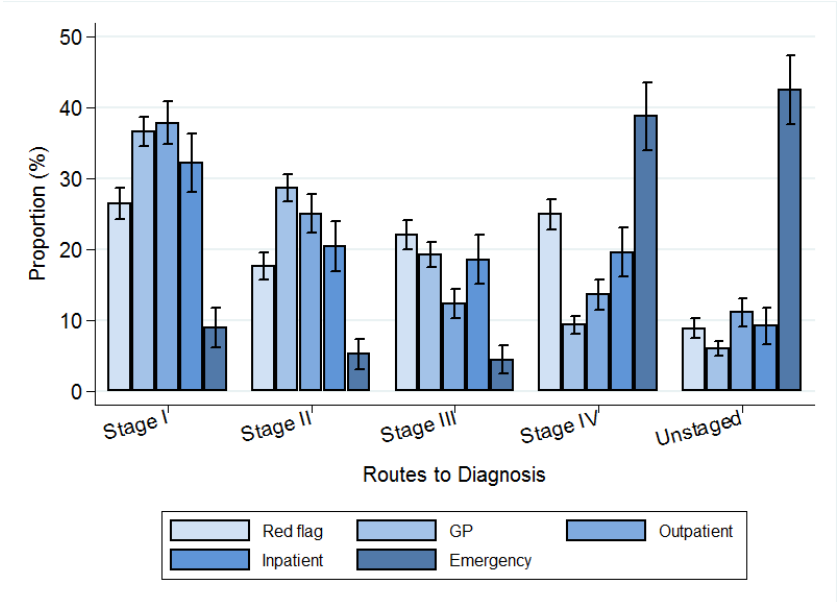
Figure 8: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with prostate cancer within Northern Ireland from 2012-2016, by cancer stage



The stage distribution in GP Routes-to-Diagnosis, Outpatient Routes-to-Diagnosis, and Inpatient Routes-to-Diagnosis were weighted towards early-stage disease (Table 6), while in Emergency Presentation Routes-to-Diagnosis the bulk on the distribution was in Stage IV (38.8%) and unstaged (42.5%, Figure 9). The Red Flag Route-to-Diagnosis has sizeable proportions (>17%) in stage groups I-IV.

Table 6: The frequency (n) and distribution (%) of cancer stage of prostate cancer patients diagnosed in 2012-2016, by Routes-to-Diagnosis										
Stage groups	**Routes-to-diagnosis**									
	Red Flag		**GP**		**Outpatient**		**Inpatient**		**Emergency Presentation**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
I	419	26.5	751	36.7	374	37.8	161	32.2	36	9.0
II	279	17.6	587	28.7	248	25.1	102	20.4	21	5.2
III	350	22.1	395	19.3	122	12.3	93	18.6	18	4.5
IV	395	25.0	192	9.4	135	13.7	98	19.6	156	38.8
Unstaged*	140	8.8	123	6.0	110	11.1	46	9.2	171	42.5
Total	**1,583**		**2,048**		**989**		**500**		**402**	
*cancer stage unknown Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown route to diagnosis										

Figure 9: Distribution (%) of stage for patients diagnosed with prostate cancer within Northern Ireland from 2012-2016, by Routes-to-Diagnosis



2.5.5 Geographic variation within NI Healthcare Trusts

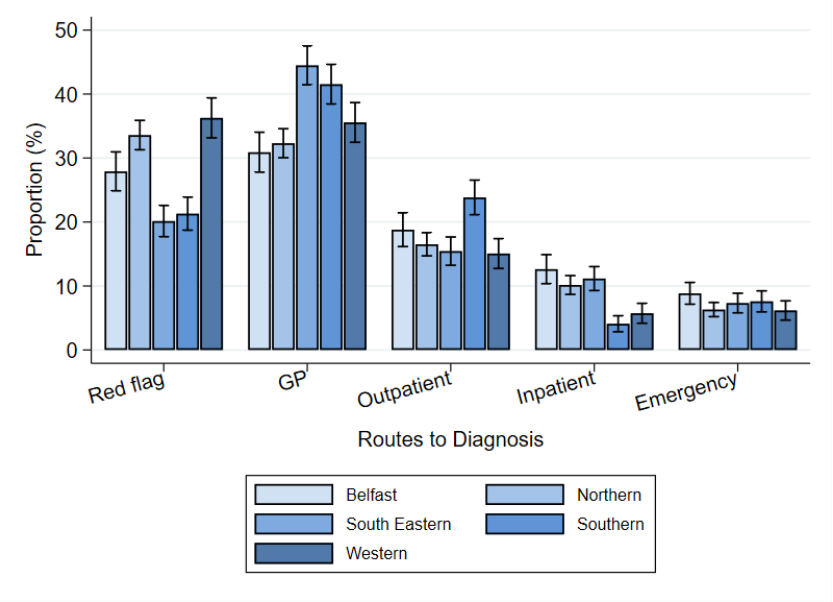
The Southern and South Eastern Trusts had lower proportions of patients in the Red Flag Route-to-Diagnosis (21.3% and 20.0%, respectively) but higher proportions of GP Route-to-Diagnosis (41.9% and 44.3%, respectively, Table 7), in comparison to other Trusts. The Southern Trust had a high proportion of patients diagnosed via Outpatient Route-to-Diagnosis (23.8%), but had a low proportion of Inpatient Route-to-Diagnosis (4.1%) similar to the Western Trust (5.3%, Figure 10).

Table 7: The frequency (n) and distribution (%) of Routes-to-Diagnosis of prostate cancer patients diagnosed 2012-2016, by Trust

Routes-to-diagnosis	Healthcare Trust									
	Belfast		Northern		South Eastern		Southern		Western	
	n	%	n	%	n	%	n	%	n	%
Red Flag	246	27.6	554	33.7	221	20.0	210	21.3	352	36.7
GP Referral	268	30.1	531	32.3	489	44.3	414	41.9	346	36.1
Outpatient	169	19.0	271	16.5	170	15.4	235	23.8	144	15.0
Inpatient	110	12.4	167	10.1	132	11.9	40	4.1	51	5.3
Emergency Presentation	89	10.0	105	6.4	75	6.8	74	7.5	59	6.2
Total	**890**		**1,646**		**1,105**		**987**		**958**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

*Figure 10: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with prostate cancer within Northern Ireland 2012-2016, by Trust**

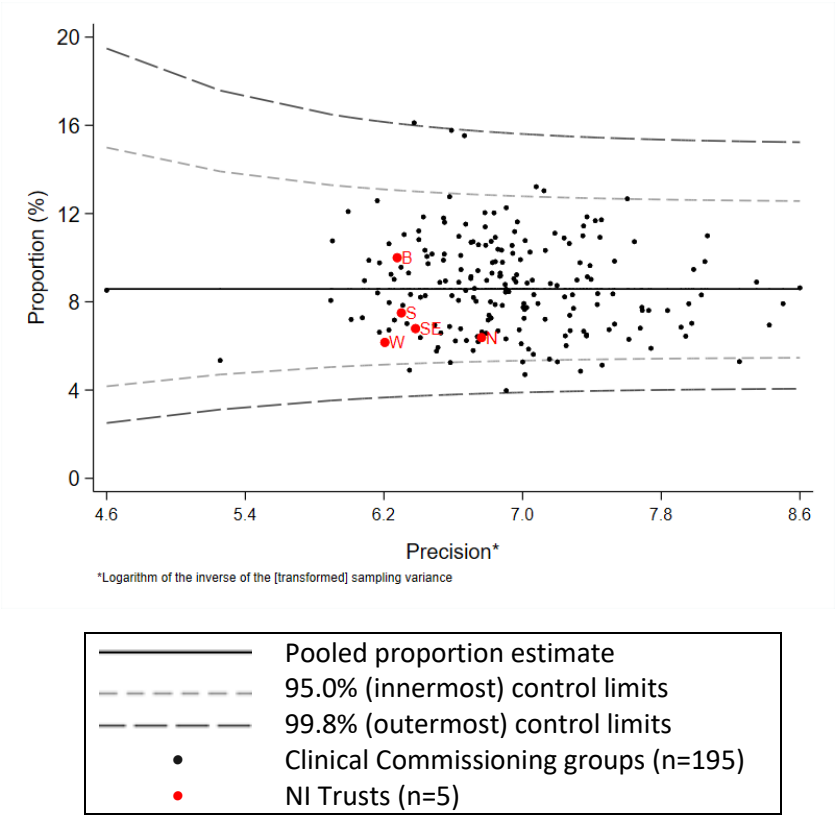


***** The presented proportions in Figure 10 were standardised to the NI population by the following factors: age, sex, and deprivation. Please see 1.6 *Analytical techniques* for further details.

Northern Ireland Healthcare Trusts compared to English Clinical Commissioning Groups (CCGs)

England's CCGs have similar numbers of patients diagnosed from 2006-2016 (11 years) to NI's Trusts for 2012-2016 (5 years), the latter's estimates were superimposed on a funnel plot of the CCG estimates. The proportion of patients diagnosed via Emergency Presentation Route-to-Diagnosis for each Trust lay between the 95% control limits, and therefore was not significantly different from the pooled proportion estimate of English CCGs (8.6%) (Figure 11).

Figure 11: Proportion of patients diagnosed through an emergency Route-to-Diagnosis for English Clinical Commissioning Groups (n=195, 2006-2016), and Northern Ireland Trusts (n=5, 2012-2016) in a funnel plot



2.5.6 Survival

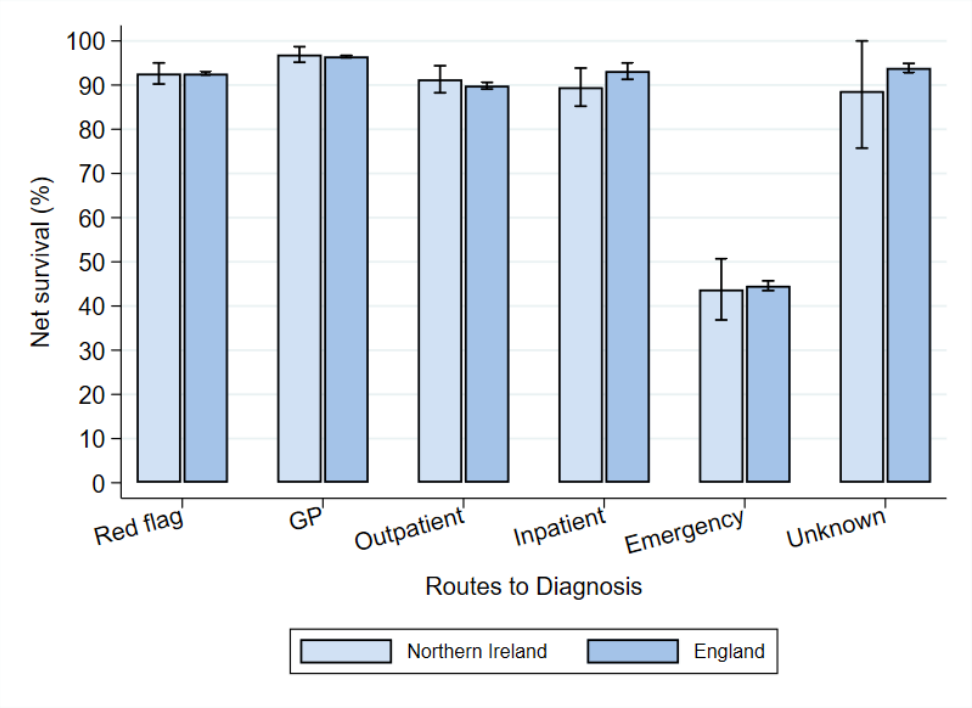
The report presents net survival estimates, a theoretical statistic used for comparing groups of patients whose non-cancer or background mortality will differ (e.g. different regions or calendar periods). Net survival is defined as the probability of surviving cancer when the mortality from other causes of death is removed (see also Perme, Stare, & Estève, 2012).

2.5.6.1 Survival by country

Net survival in Northern Ireland was high (≈90%) in all Routes-to-diagnosis except Emergency Presentation Route-to-Diagnosis (43.8%, Table 8). The NI survival was not significantly different to England in any of the Routes-to-diagnosis; survival was highest in patients diagnosed via GP Route-to-Diagnosis in both countries (Figure 12).

Table 8: Three-year net survival (ns, %) of prostate cancer patients diagnosed in Northern Ireland (2012-2016) and England (2011-2015) by route- to-diagnosis				
Route-to-diagnosis	**Northern Ireland**		**England**	
	n*	**ns, %**	**n**	**ns, %**
Red Flag	1,583	92.6	81,636	92.6
GP Referral	2,048	96.9	73,699	96.5
Outpatient	986	91.3	15,946	89.9
Inpatient	498	89.5	2,138	93.2
Emergency Presentation	397	43.8	14,297	44.6
*some patients are not included in the survival analysis, see 1.6 *Analytical techniques*				

Figure 12: Three-year net survival (%) of prostate cancer patients diagnosed from 2012-2016, by Route-to-Diagnosis and country

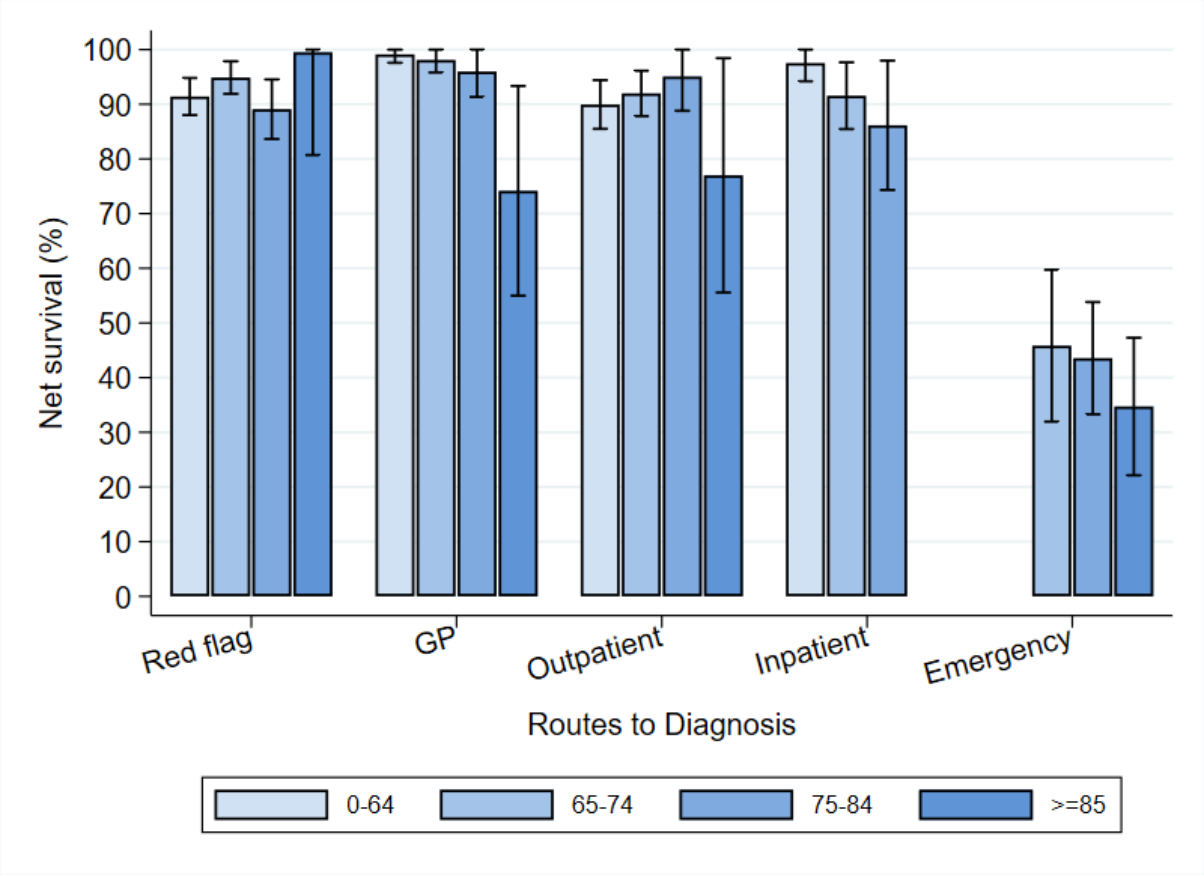


2.5.6.2 Age-group specific survival

There were no significantly different patterns in the distribution of Routes-to-diagnosis between age groups (Table 9, Figure 13); the survival estimate in the ≥85 age group was imprecise (large confidence intervals) due to small numbers (the age groups chosen for prostate cancer were the ICSS definition used in international survival studies).

Table 9: Three-year net survival (ns, %) for patients diagnosed with prostate cancer in Northern Ireland from 2012-2016, by age group and Route-to-Diagnosis								
Routes-to-diagnosis	**Age groups (years)**							
	0-64†		**65-74**		**75-84**		**≥85**	
	n*	**ns, %**	**n**	**ns, %**	**n**	**ns, %**	**n**	**ns, %**
Red Flag	406	91.4	628	94.9	454	89.1	95	99.5
GP Referral	664	99.1	808	98.1	488	96.0	88	74.2
Outpatient	266	90.0	381	92.0	276	95.1	63	77.0
Inpatient	192	97.5	181	91.6	93	86.2	-	-
Emergency Presentation	-**	-	74	45.8	150	43.6	139	34.7
*some patients are not included in the survival analysis, see 1.6 *Analytical techniques* **numbers too low (<50) to estimate survival †age groups use ICSS definition for international survival studies								

Figure 13: Three-year age specific net survival for Route-to-Diagnosis for patients diagnosed with prostate cancer within Northern Ireland 2012-2016



2.5.6.3 Stage specific survival

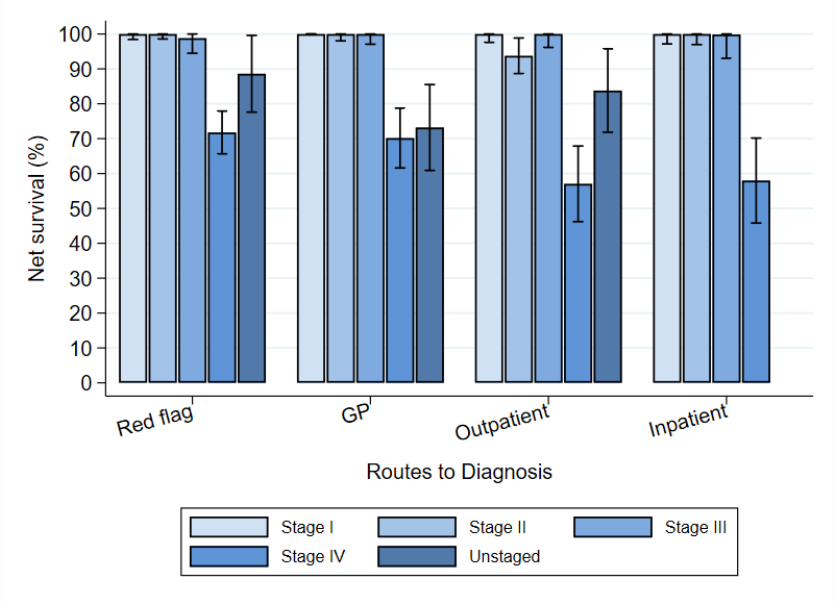
Three-year net survival was high (≈100.0%) for patients with Stage I-III disease in all Routes-to-diagnosis except Emergency Presentation Route-to-Diagnosis for which there were no estimates due to small numbers of Stage I-III (Table 10). Patients with Stage IV disease had lower survival across all Routes-to-diagnosis with Emergency Presentation Route-to-Diagnosis having the lowest survival (21.2%) (Figure 14).

Table 12: Three-year net survival (ns, %) for patients diagnosed with prostate cancer in Northern Ireland from 2012-2016, by cancer stage and Route-to-Diagnosis

Routes-to-diagnosis	Stage groups									
	I		II		III		IV		Unstaged*	
	n*	ns, %	n	ns, %	n	ns, %	n	ns, %	n	ns, %
Red Flag	419	100.0	279	100.0	350	98.8	395	71.8	140	88.6
GP Referral	751	100.0	587	100.0	395	100.0	192	70.2	123	73.2
Outpatient	374	100.0	248	93.8	122	100.0	135	57.0	107	83.8
Inpatient	161	100.0	102	100.0	93	99.9	98	58.0	-	-
Emergency Presentation	-**	-	-	-	-	-	156	21.2	166	45.1

*some patients are not included in the survival analysis, see 1.6 *Analytical techniques*
**numbers too low (<50) to estimate survival

Figure 14: Three-year stage specific net survival for Route-to-Diagnosis for patients diagnosed with prostate cancer within Northern Ireland 2012-2016, by cancer stage


Net survival (%)
100
90
80
70
60
50
40
30
20
10
0
Red flag
GP
Outpatient
Inpatient
Routes to Diagnosis
Stage I
Stage II
Stage III
Stage IV
Unstaged

2.5.7 Discussion

The largest proportion of prostate cancer patients were diagnosed via GP Route-to-Diagnosis in NI (36.7%). The pattern of Routes-to-Diagnosis for prostate cancer in NI differs from England where a greater proportion of 'red flag' prostate cancer cases were reported (44.4% vs 28.3% in NI). Conversely, patients in NI are more frequently diagnosed in inpatient and outpatient routes. Three-year net survival by Routes-to-Diagnosis were similar between countries. However, this probably reflects a two-fold survival pattern existing in both countries, patients with an Emergency Presentation Route-to-Diagnosis have low survival, whereas patients in other Routes-to-diagnosis have similarly high survival with the GP Route-to-Diagnosis performing particularly well in this regard (96.0%).

The high 3-year net survival (>90%) of patients in Stages I-III is probably due to over-diagnosis of non-aggressive early-stage prostate cancer, and to an effective hormone treatment that can extend life by up to five years for men with more advanced disease at diagnosis. The excess deaths due to prostate cancer that occurs in patients diagnosed with advanced-stage disease explains the poor survival in Emergency Presentation Route-to-Diagnosis of whom 81% were Stage IV or unstaged. However, there was high survival (>89.5%) in Routes-to-diagnosis where the proportion of Stage IV and unstaged disease was sizeable such as Red Flag Route-to-Diagnosis (33.8%) and inpatient (29.8%). Stage IV patients diagnosed via Red Flag Route-to-Diagnosis and GP Route-to-Diagnosis had moderately good survival (>70%) compared to Stage IV patients diagnosed in an Emergency Presentation Route-to-Diagnosis (21.2%). It is possible, therefore, that patients whose symptoms precipitated an Emergency Presentation Route-to-Diagnosis had very advanced disease whose particular symptom development could be further investigated with a view to early-detection interventions.

To improve the outcomes of men with prostate cancer it is necessary to identify those who have aggressive disease early, and hence there is ongoing research to find biomarkers, besides PSA, that can specifically detect aggressive disease. However, there is also the potential for improving the early-detection of symptoms associated with aggressive disease as there are differences in the proportion of Emergency Presentation Route-to-Diagnosis in different demographic sub-groups of the population. For instance, older people more likely to be diagnosed via Emergency Presentation Route-to-Diagnosis in NI as perhaps their

cancer symptoms are less likely to be acted on because other related-comorbidity or cognitive impairment (Silberstein, Pal, Lewis, & Sartor, 2013). Difficulty urinating, a symptom for prostate cancer, is also associated with older age in the non-cancer population. Across deprivation quintiles there was a non-significant increasing Emergency Presentation Route-to-Diagnosis proportion gradient from most-affluent to most–deprived in NI which has also been found for English Routes-to-Diagnosis (National Cancer Intelligence Network, 2015), suggesting earlier-detection rates in more affluent areas.

In order to improve specificity of prostate cancer symptoms, in 2015 NICE updated the red flag referral symptoms for prostate cancer to include visible haematuria and age-specific PSA reference ranges for different age groups of the population (National Institute for Health and Care Excellence, 2015). Better definitions of symptoms/or tests for aggressive disease combined with greater symptom-awareness in the community and GP practice could improve earlier detection of aggressive disease before it precipitates an emergency presentation. There is lack of consensus among clinicians about the PSA test, which has high levels of false positive tests for life-limiting aggressive prostate cancer disease. Therefore some patients have had unnecessary invasive and painful investigations and treatments, when others are managed by active surveillance. This inconsistency of approach may affect the public perspective regarding the usefulness of symptoms in detecting the aggressive disease, leading men to ignore particular symptoms that could point to aggressive disease.

While there were interesting differences between the patterns of Routes-to-diagnosis among the Trusts, the proportion of patients diagnosed via Emergency Presentation Route-to-Diagnosis were similar and these are the patients for whom survival outcomes are worse. The higher proportion of patients in GP Route-to-Diagnosis over Red Flag Routes-to-Diagnosis in the Southern and South-Eastern Trusts may reflect well-established referral and treatment pathways involving the Belfast Trust predating the red flag referral option. The higher Outpatient Route-to-Diagnosis in NI compared to England may be due to specific diagnostic pathways through outpatient clinics in Belfast. For instance, magnetic resonance imaging is only offered in the Belfast Trust, and as of March 2019, around 18,000 patients were waiting for a magnetic resonance imaging test (Department of Health, 2019).

The patients with the worst survival outcomes generally present with advanced disease in an Emergency Presentation Route-to-Diagnosis, and proportions of such patients were

consistent between NI and England. These patients are likely to have symptoms of aggressive life-limiting prostate cancer which precipitated the emergency presentation. Investigations into the natural development of these symptoms may identify specific symptoms that can detect early development of aggressive disease, and awareness of these symptoms should be raised in the public and clinical community.

2.5.8 Bibliography

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2.6 Cancer sites grouped

2.6.1 Key findings

- The highest proportion of cervical cancers were diagnosed via Screening Route-to-Diagnosis (24.4%) although GP Route-to-Diagnosis had the highest net survival.
- Some cancer site domains had highest proportions diagnosed via Red Flag Route-to-Diagnosis (e.g. melanoma skin cancer and female genital cancer) which were associated with high net survival.
- Outpatient Route-to-Diagnosis and GP Route-to-Diagnosis were most common amongst younger patients and for those diagnosed with urinary cancer.
- Blood and lymph cancer, digestive cancer, upper GI tract cancer and head, neck, brain and eye cancer all had significant proportions of patients diagnosed via Emergency Presentation Route-to-Diagnosis.

2.6.2 Cancer groupings reported

Table 1: Cancer site groupings reported in chapter	
Cancer Site Domain*	ICD-10 code (WHO, 2011)
Cervix uteri	C53
Malignant melanoma	C43
Head & neck, eye and brain	C00-C14, C30-C32, C69, C70,C71,D32,D33,D35.2-D35.4, D42, D43, D44.3-D44.5
Upper GI: oesophagus, stomach, small intestine	C15,C16,C17
Digestive: liver, gallbladder, pancreas	C22,C23,C24
Urinary: kidney, bladder, other	C64, C67, C65-66
Female genital: vulva, vagina, cervix, corpus uteri, ovary, other	C51,C52,C53,C54-C55,C56, C57
Blood and Lymph: lymphoma, multiple myeloma, leukaemia, other	C81-86,C90,C91-95,C88,C96
Young person (aged 0-24)	C01-C97,D32,D33,D35.2-D35.4,D42,D43,D44.3-D44.5
*the following cancer site domains were not reported on because a single large caseload site (that has a dedicated chapter) would dominate: Respiratory: *lung (C33-34)*, mesothelioma (C45) Lower GI: *colon (C18), rectum (C19-C20)*, anus (C21) Male genital: *prostate (C61)*, testis (C62), penis (C60) *in some cancer site domains a comparison with England was not possible	

2.6.3 Cervical Cancer

Cervical cancers occur in the cervix almost exclusively caused by the Human papillomavirus (HPV) as this virus causes changes in the cells lining the cervix (Public Health Agency, 2020a). Cervical cancer occurs only in women. Between 2013 and 2017, 83 patients were diagnosed annually with the disease. Over three quarters (77%) of patients were diagnosed between 25-59 years with highest incidence rates amongst those aged 30-34 years. Cervical cancer has a screening programme designed to detect early pre-cancerous changes to cervix cells; invitations are issued to women aged 25-49 years every 3 years and to those aged 50-64 years every 5 years. A sample of cells (smear test) is taken, with 1 in 10 results on average showing abnormal cell changes (Public Health Agency, 2020b). Five-year net survival was 66.6% for patients diagnosed between 2007 and 2011 (Northern Ireland Cancer Registry, 2020a).

Routes-to-diagnosis in Northern Ireland

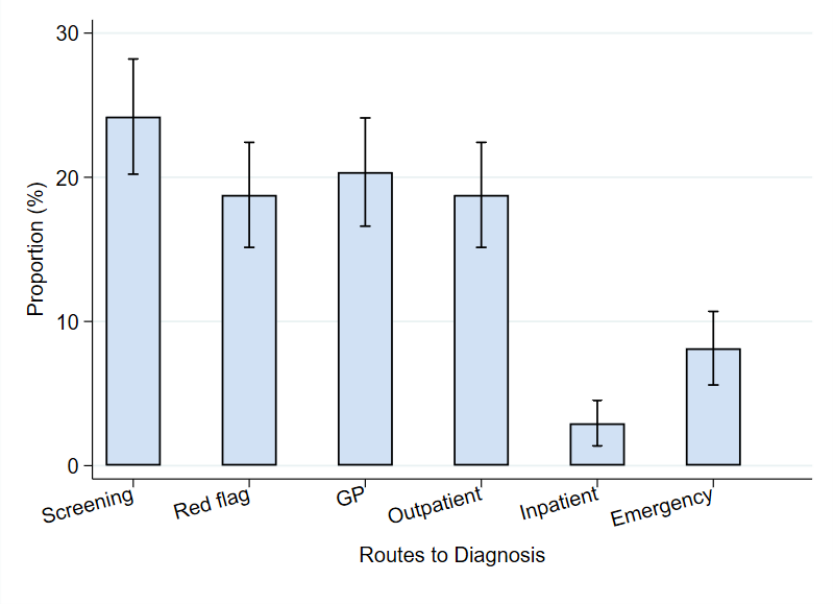
The largest proportion of women were diagnosed via Screening Route-to-Diagnosis (24.2%), but with sizeable and similar proportions in Red Flag Route-to-Diagnosis, GP Route-to-Diagnosis, and Outpatient Route-to-Diagnosis.

Table 2: The frequency (n) and distribution (%) of Routes-to-Diagnosis of cervical cancer patients diagnosed in 2012-2016 in Northern Ireland

Route-to-diagnosis	Northern Ireland	
	n	%
Screening	107	24.2
Red Flag	83	18.8
GP Referral	90	20.4
Outpatient	83	18.8
Inpatient	13	2.9
Emergency Presentation	36	8.1
Total	**442**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 1: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with cervical cancer from 2012-2016 in Northern Ireland



Net Survival

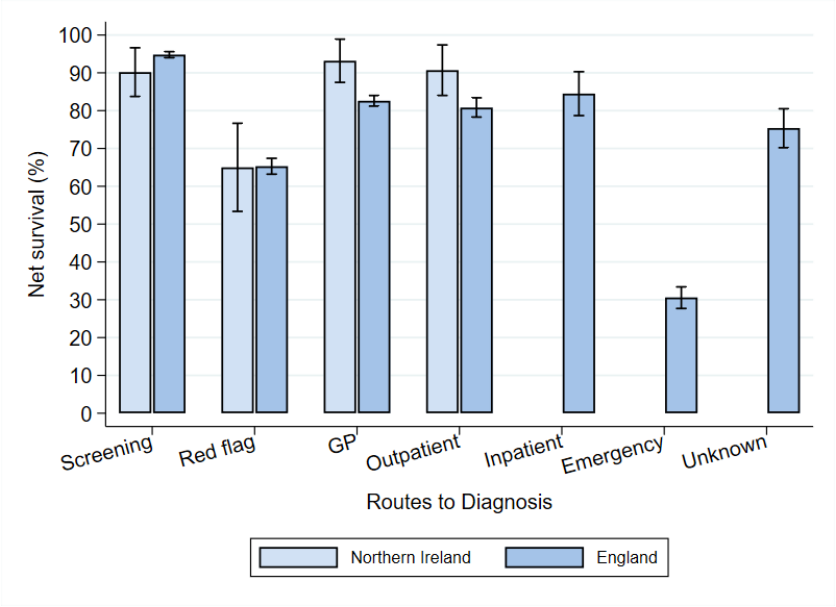
Survival was highest for patients diagnosed via GP Route-to-Diagnosis (93.2%) and lowest for Red Flag Route-to-Diagnosis (65.0%). We have not been able to estimate emergency survival rates for Northern Ireland due to low numbers, however England's Screening Route-to-Diagnosis patients had highest net survival (94.8%), similar survival for Red Flag Route-to-Diagnosis, and lowest survival for Emergency Presentation Route-to-Diagnosis (30.6%) (Table 3, Figure 2).

Table 3: Three-year net survival (ns, %) of cervical cancer patients diagnosed in Northern Ireland (2012-2016) and England (2011-2015) by route- to-diagnosis

Route-to-diagnosis	Northern Ireland		England	
	n*	%	n	%
Screen	107	90.2	3,531	94.8
Red Flag	83	65.0	2,652	65.3
GP Referral	88	93.2	3,754	82.6
Outpatient	83	90.7	1,085	80.8
Inpatient	-**	-	175	84.5
Emergency Presentation	-	-	1,204	30.6
Unknown	-	-	315	75.4
Total	**361**		**12,716**	

*some patients are not included in the survival analysis, see 1.6 *Analytical techniques*
**numbers too low (<50) to estimate survival

Figure 2: Three-year net survival (%) of cervical cancer patients diagnosed from 2012-2016, by Route-to-Diagnosis and country



2.6.4 Melanoma Skin Cancer

Malignant melanoma is a type of skin cancer, starting as proliferation of the melanocyte cells found in the skin between the dermis and epidermis. Ultraviolet radiation can cause sunburn, damaging the DNA in the melanocytes (Cancer Research UK, 2020a). Between 2013 and 2017 in NI, there were 174 men and 203 women diagnosed with malignant melanoma skin cancer annually (Northern Ireland Cancer Registry, 2020b). Incidence increases with age, with approximately 70% of patients diagnosed aged over 50 years old. Overall incidence by sex was similar but women appear to have a more gradual increase in incidence upon growing older compared to men whose incidence increases rapidly with older age. From 2007 to 2011, five-year net survival was higher for women (92.3%) compared to men (89.2%) (Northern Ireland Cancer Registry, 2020b).

Routes-to-diagnosis in Northern Ireland

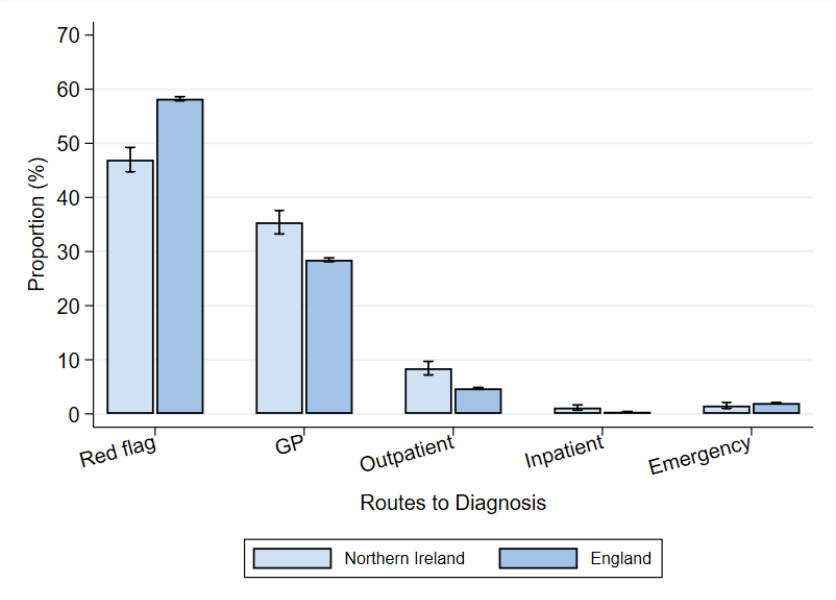
The largest proportion of NI patients were diagnosed via a red flag Route-to-diagnosis (47.0%) followed by GP referral (35.4%). In England, a larger proportion (58%) of patients were diagnosed via red-flag, and smaller proportions via GP Route-to-Diagnosis, and Outpatient Route-to-Diagnosis.

Table 4: The frequency (n) and distribution (%) of Routes-to-Diagnosis of melanoma skin cancer patients diagnosed in 2012-2016, by country

Route-to-diagnosis	Northern Ireland		England	
	n	%	n	%
Red Flag	885	47.0	37,365	58.2
GP Referral	667	35.4	18,272	28.5
Outpatient	159	8.4	3,030	4.7
Inpatient	22	1.2	252	0.4
Emergency Presentation	29	1.5	1,286	2.0
Total	**1,884**		**64,172**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

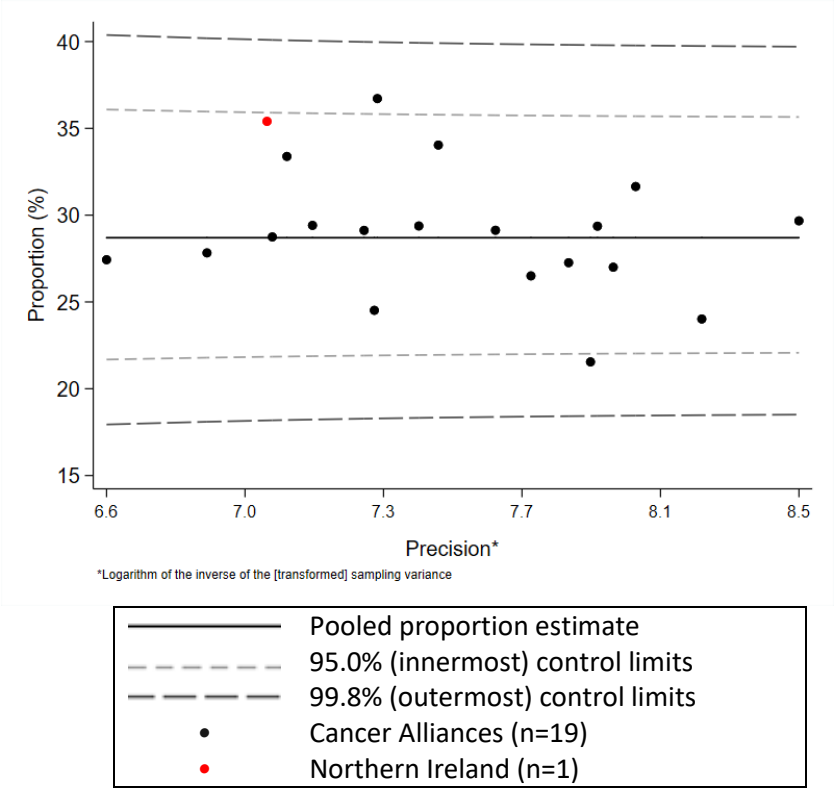
Figure 3: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with melanoma cancer from 2012-2016 in Northern Ireland



Northern Ireland compared to English Cancer Alliances

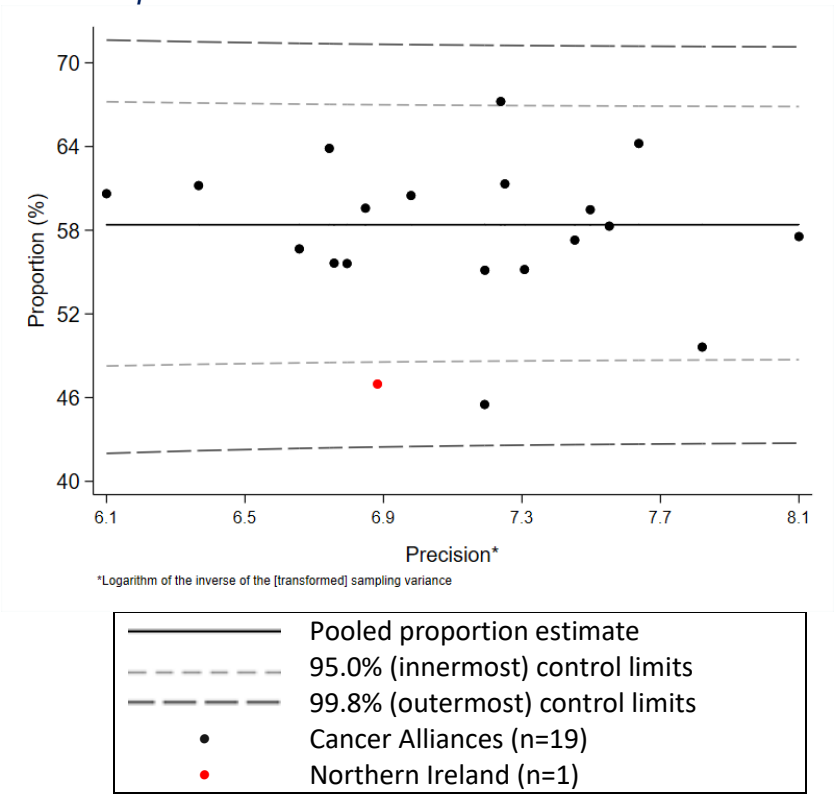
The NI GP Route-to-Diagnosis proportion (35.4%) lay within the control limits, and therefore was not different from the pooled proportion estimate of the English Cancer Alliance estimates (Figure 4).

Figure 4: Proportion (%) of melanoma patients diagnosed through an routine GP presentation Route-to-Diagnosis in English Cancer Alliances (n=19) and Northern Ireland presented in a funnel plot



The NI Red Flag Route-to-Diagnosis estimate (47%) lay outside the 95.0%, but within the 99.8% control limits showing a 'warning' regarding a difference from the English Cancer Alliances pooled proportion estimate (Figure 5).

Figure 5: Proportion (%) of melanoma patients diagnosed through an red flag Route-to-Diagnosis in English Cancer Alliances (n=19) and Northern Ireland presented in a funnel plot



Net Survival

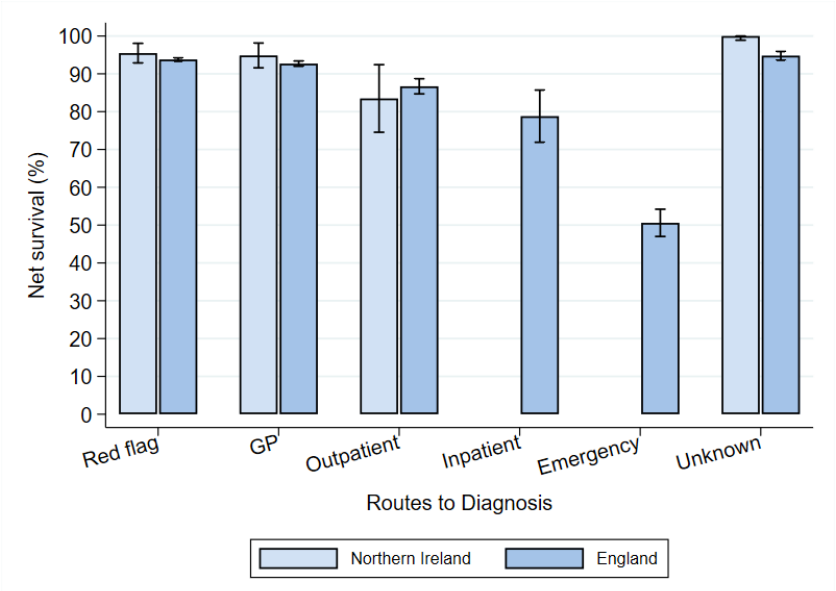
Net survival was highest for patients with Red Flag Route-to-Diagnosis (95.5%) and GP Route-to-Diagnosis (94.9%, Table 5). Similar patterns were also found for England (Figure 6).

Table 5: Three-year net survival (ns, %) of melanoma skin cancer patients diagnosed in Northern Ireland (2012-2016) and England (2011-2015) by route-to-diagnosis

Route-to-diagnosis	Northern Ireland n*	Northern Ireland %	England n	England %
Red Flag	882	95.5	33,480	93.8
GP Referral	662	94.9	16,779	92.7
Outpatient	151	83.5	2,598	86.7
Inpatient	-**	-	225	78.8
Emergency Presentation	-	-	1,136	50.6
Unknown	119	100.0	3,911	94.8
Total	**1,814**		**58,129**	

*some patients are not included in the survival analysis, see 1.6 *Analytical techniques*
**numbers too low (<50) to estimate survival

Figure 6: Three-year net survival (%) of melanoma skin cancer patients diagnosed from 2012-2016, by Route-to-Diagnosis and country



2.6.5 Head & neck, eye and brain cancer

This grouping represents particular types of tumours that occur in a range of anatomical organs in the head. The bulk of these cancers in NI are (with yearly number, and 5-year survival) head and neck (328, 55%), invasive brain (150, 24.5%) and non-invasive brain (243, 91.3%) (Northern Ireland Cancer Registry, 2020c).

Routes-to-diagnosis in Northern Ireland

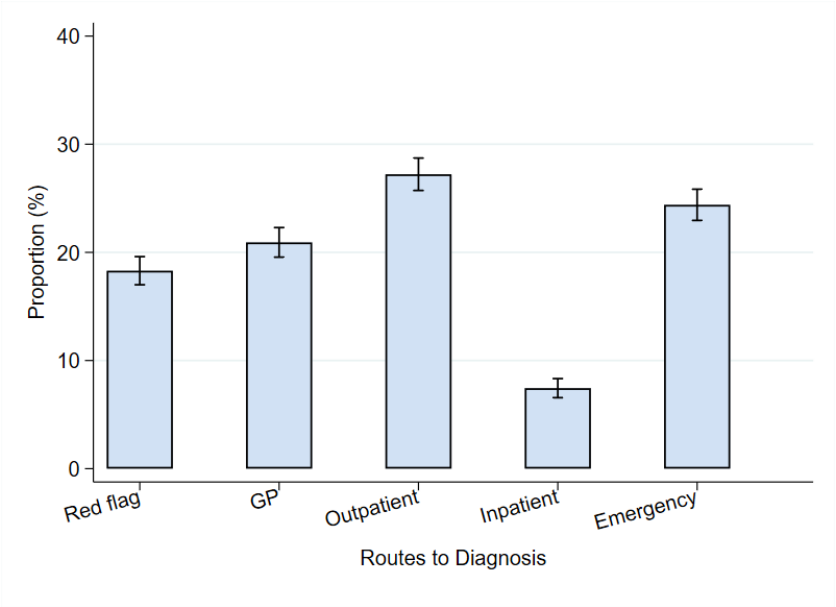
The largest proportion of patients diagnosed with head, neck, brain and eye cancer were diagnosed by Outpatient Route-to-Diagnosis (27.2%) followed by Emergency Presentation Route-to-Diagnosis (24.4%) (Table 6, Figure 7).

Table 6: The frequency (n) and distribution (%) of Routes-to-Diagnosis of head & neck, eye and brain cancer patients diagnosed in 2012-2016 in Northern Ireland

Route-to-diagnosis	Northern Ireland	
	n	%
Red Flag	622	18.3
GP Referral	711	20.9
Outpatient	925	27.2
Inpatient	253	7.4
Emergency Presentation	829	24.4
Total	**3,398**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 7: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with head & neck, eye and brain cancer from 2012-2016 in Northern Ireland



Net Survival

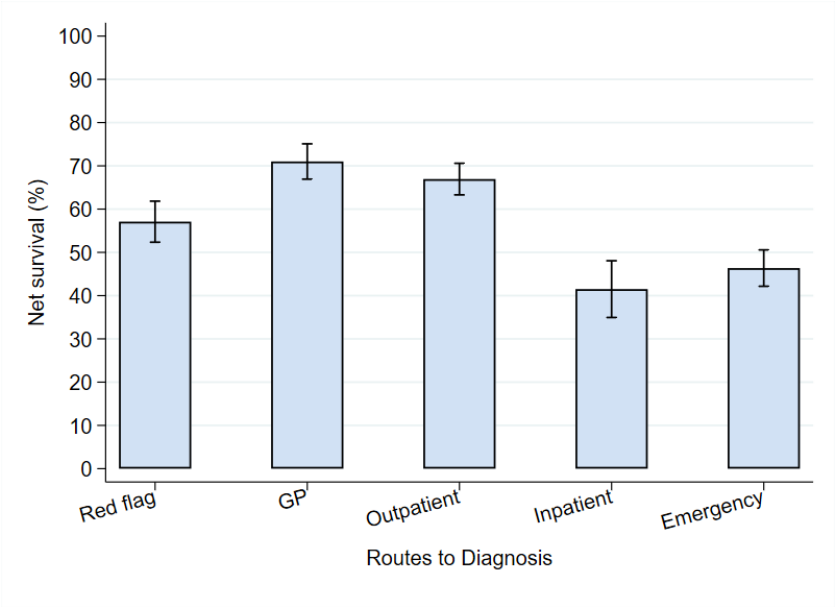
Three year survival was less than 72% for patients diagnosed in all routes. It was highest for GP Route-to-Diagnosis (71.0%) and lowest for Inpatient Route-to-Diagnosis (41.5%) and Emergency Presentation Route-to-Diagnosis (46.4%) (Table 7, Figure 8).

Table 7: Three-year net survival (ns, %) of head & neck, eye and brain cancer patients diagnosed in Northern Ireland (2012-2016)

Route-to-diagnosis	Northern Ireland	
	n*	ns, %
Red Flag	614	57.1
GP Referral	703	71.0
Outpatient	887	66.9
Inpatient	248	41.5
Emergency Presentation	812	46.4
Total	**3,264**	

*some patients are not included in the survival analysis, see 1.6 *Analytical techniques*
Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 8: Three-year net survival (%) of head & neck, eye and brain cancer patients diagnosed from 2012-2016, by Route-to-Diagnosis



2.6.6 Upper GI Tract cancer

Upper GI Tract cancers occur in the stomach, small intestine and oesophagus. In NI, 217 cases of stomach (Northern Ireland Cancer Registry, 2020d), and 218 cases of oesophageal (Northern Ireland Cancer Registry, 2020e) are diagnosed annually. These cancers have higher incidence rates amongst older people; 79% of those diagnosed with oesophageal cancer and 82% with stomach cancer are aged older than 60 years. Oesophageal lifetime risk of developing this disease was 1 in 84 for men and 1 in 268 for women. The lifetime risk of developing stomach cancer was 1 in 116 for men and 1 in 246 for women. In NI between 2007 and 2011, five-year net survival for oesophageal cancer was 18.6% and for stomach cancer was 21.1% (Northern Ireland Cancer Registry, 2020d & 2019e).

Routes-to-diagnosis in Northern Ireland

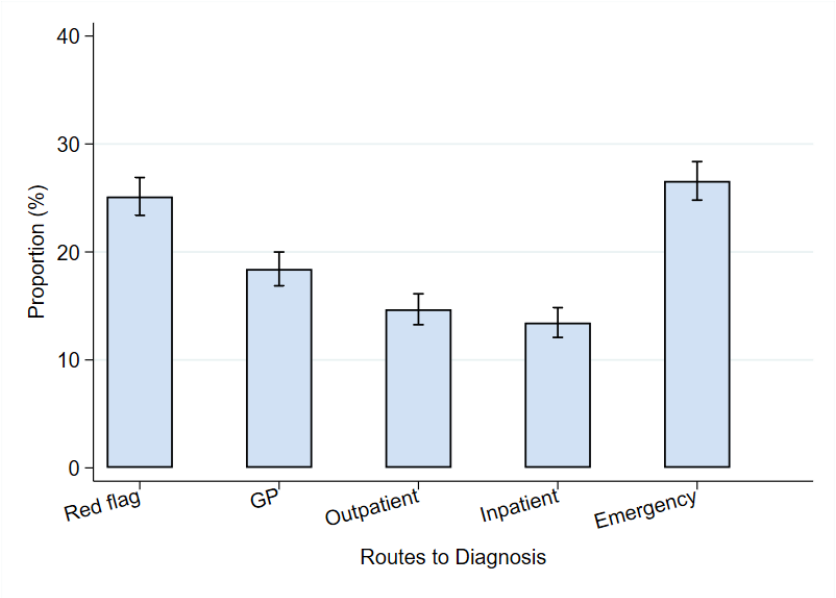
The largest proportion of patients diagnosed via an Emergency Presentation Route-to-Diagnosis (26.6%) and Red Flag Route-to-Diagnosis (25.1%) (Table 8, Figure 9).

Table 8: The frequency (n) and distribution (%) of Routes-to-Diagnosis of upper GI cancer patients diagnosed in 2012-2016 in Northern Ireland

Route-to-diagnosis	Northern Ireland	
	n	%
Red Flag	592	25.1
GP Referral	434	18.4
Outpatient	346	14.7
Inpatient	317	13.5
Emergency Presentation	626	26.6
Total	**2,355**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 9: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with upper GI cancer from 2012-2016 in Northern Ireland



Net Survival

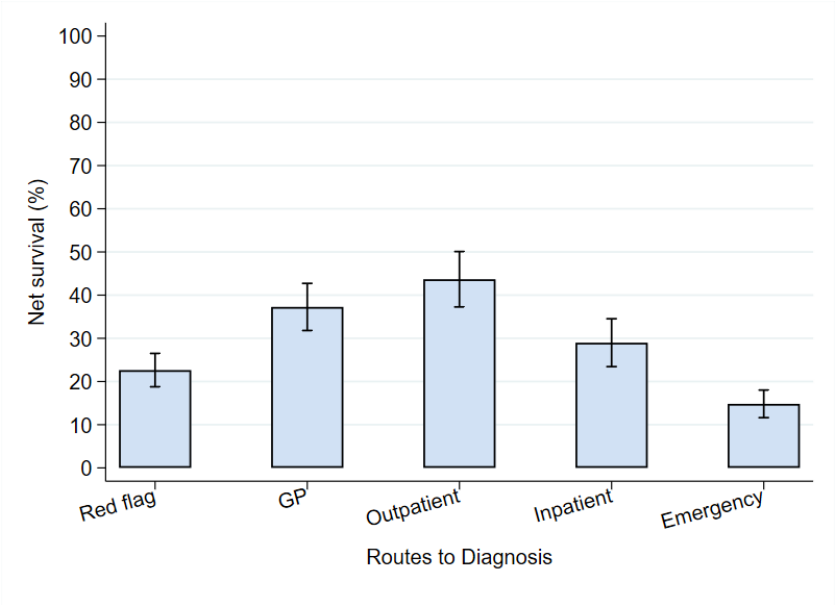
Three-year net survival was highest for those diagnosed via an Outpatient Route-to-Diagnosis (43.7%) and by GP Route-to-Diagnosis (37.3%). There was lowest survival for Emergency Presentation Route-to-Diagnosis (14.8%) and Red Flag Route-to-Diagnosis (22.6%) (Table 9, Figure 10).

Table 9: Three-year net survival (ns, %) of upper GI cancer patients diagnosed in Northern Ireland (2012-2016) by route- to-diagnosis

Route-to-diagnosis	Northern Ireland	
	n*	ns, %
Red Flag	590	22.6
GP Referral	426	37.3
Outpatient	335	43.7
Inpatient	315	29.0
Emergency Presentation	617	14.8
Total	**2,283**	

*some patients are not included in the survival analysis, see 1.6 *Analytical techniques*

Figure 10: Three-year net survival (%) of upper GI cancer patients diagnosed from 2012-2016, by Route-to-Diagnosis



2.6.7 Digestive Cancer

Digestive cancers occur in the liver, gallbladder and pancreas. These cancers have very poor prognosis because they can remain asymptomatic until an advanced disease stage. Symptoms of pancreatic cancer include weight loss, jaundice and indigestion (Pancreatic Cancer UK, 2020a) and liver cancer symptoms are a swollen abdomen and abdominal pain (Cancer Research UK, 2020b) which can be confused with symptoms of other health conditions. In Northern Ireland, 255 people are diagnosed annually with pancreatic cancer (Northern Ireland Cancer Registry, 2020f), and 133 with liver cancer (Northern Ireland Cancer Registry, 2020g). Five-year net survival for pancreatic and liver cancer is 4.9% and 8.6%, respectively (Northern Ireland Cancer Registry, 2020f & 2020g).

Routes-to-diagnosis in Northern Ireland

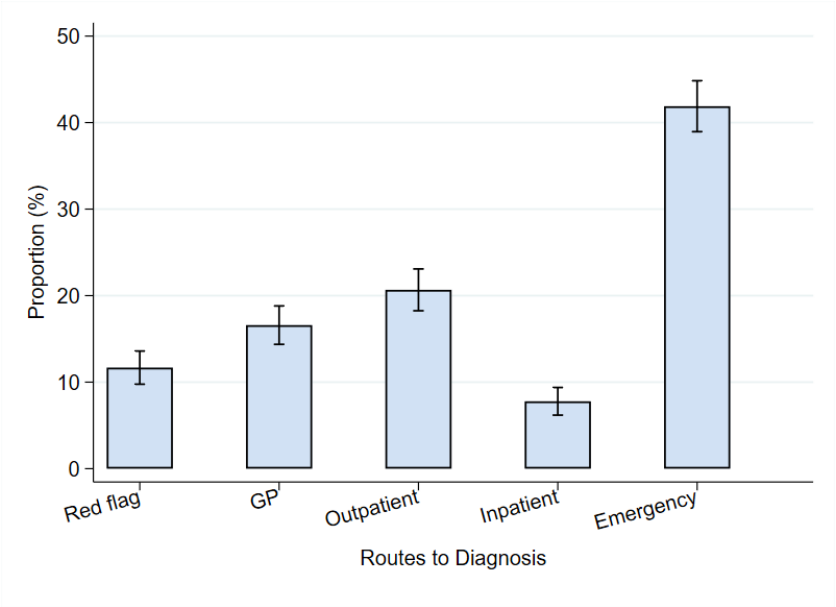
The largest proportion of digestive cancer patients were diagnosed via Emergency Presentation Route-to-Diagnosis (41.9%) followed by Outpatient- Route-to-diagnosis (20.7%) (Table 10, Figure 11).

Table 10: The frequency (n) and distribution (%) of Routes-to-Diagnosis of digestive cancer patients diagnosed in 2012-2016 in Northern Ireland

Route-to-diagnosis	Northern Ireland	
	n	%
Red Flag	126	11.7
GP Referral	179	16.6
Outpatient	223	20.7
Inpatient	84	7.8
Emergency Presentation	452	41.9
Total	**1,079**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown route to diagnosis

Figure 11: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with digestive cancer from 2012-2016 in Northern Ireland



Net Survival

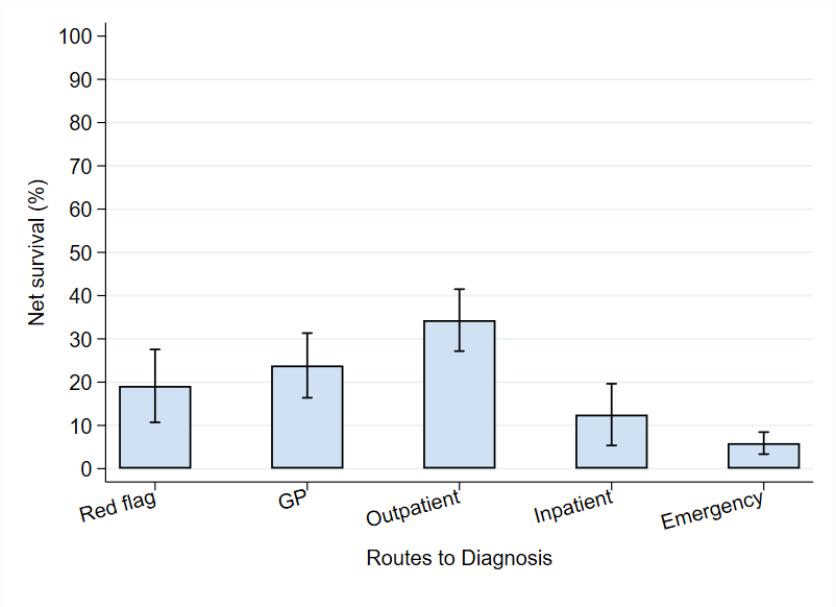
Outpatient Route-to-Diagnosis patients had the highest three-year net survival (34.3%) in contrast the lowest net survival route for Emergency Presentation Route-to-Diagnosis (5.9%) (Table 11, Figure 12).

Table 11: Three-year net survival (ns, %) of digestive cancer patients diagnosed in Northern Ireland (2012-2016) by route- to-diagnosis

Route-to-diagnosis	Northern Ireland	
	n*	ns, %
Red Flag	125	19.1
GP Referral	179	23.9
Outpatient	222	34.3
Inpatient	84	12.5
Emergency Presentation	443	5.9

*some patients are not included in the survival analysis, see 1.6 *Analytical techniques*

Figure 12: Three-year net survival (%) of digestive cancer patients diagnosed from 2012-2016, by Route-to-Diagnosis



2.6.8 Urinary Cancer

Urinary cancers occur largely in the kidney and bladder. Every year in NI, 315 cases of kidney cancer are diagnosed (Northern Ireland Cancer Registry, 2020h), and 219 of bladder cancer (Northern Ireland Cancer Registry, 2020i). Incidence of bladder cancer was higher for men, as 1 in 120 men and 1 in 374 women will be diagnosed during their lifetime. Kidney cancer is more common; lifetime risk was 1 in 67 for men and 1 in 129 for women. Five-year net survival for kidney cancer was 58.7% and for bladder cancer was 55.9% between 2007 and 2011 (Northern Ireland Cancer Registry, 2020h & 2020i).

Routes-to-diagnosis in Northern Ireland

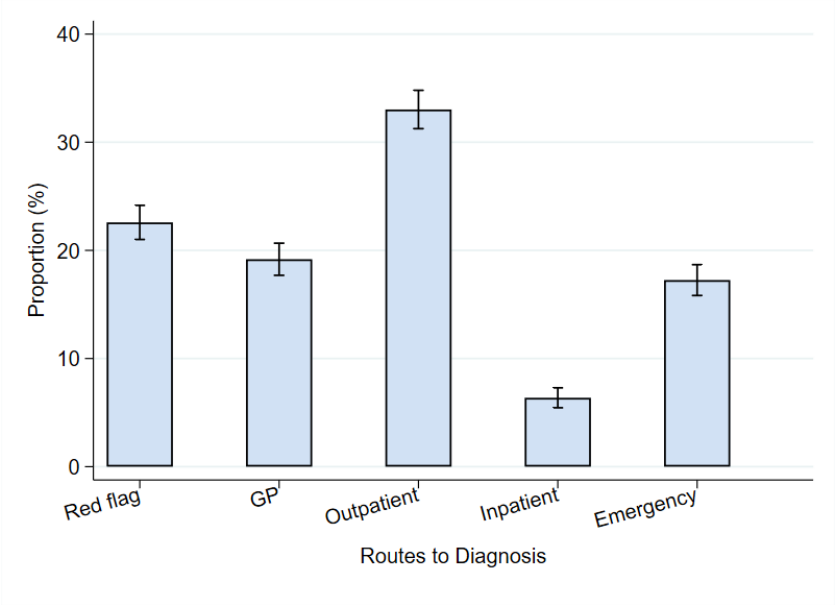
The largest proportion of urinary cancer patients were diagnosed by Outpatient Route-to-Diagnosis (33.0%) followed by Red Flag Route-to-Diagnosis (22.6%). Sizeable proportions were diagnosed through GP Route-to-Diagnosis and Emergency Presentation Route-to-Diagnosis (Table 12, Figure 13).

Table 12: The frequency (n) and distribution (%) of Routes-to-Diagnosis of urinary cancer patients diagnosed in 2012-2016 in Northern Ireland

Route-to-diagnosis	Northern Ireland n	%
Red Flag	610	22.6
GP Referral	518	19.2
Outpatient	892	33.0
Inpatient	172	6.4
Emergency Presentation	466	17.3
Total	**2,701**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 13: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with urinary cancer from 2012-2016 in Northern Ireland



Net Survival

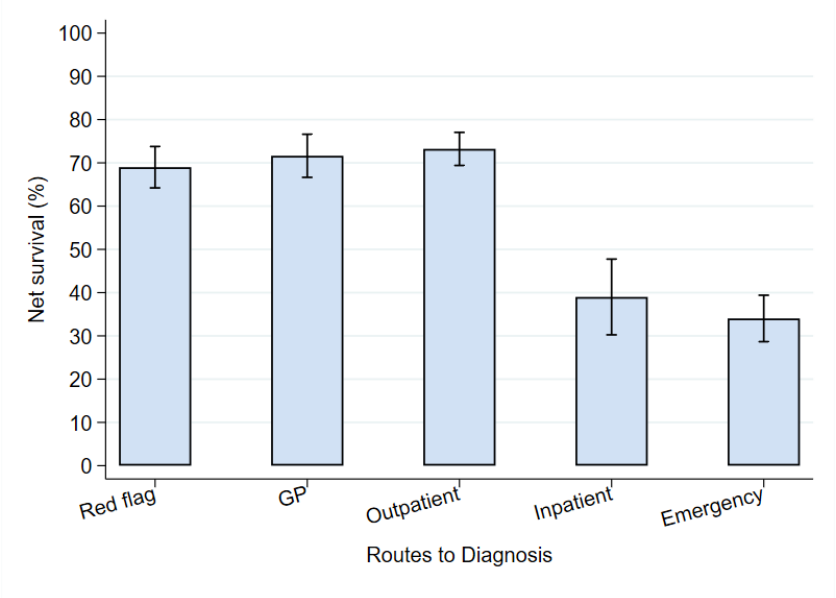
Survival was highest for patients diagnosed via Outpatient Route-to-Diagnosis (73.2%), roughly twice that of Emergency Presentation Route-to-Diagnosis (34.0%) (Table 13, Figure 14).

Table 13: Three-year net survival (ns, %) of urinary cancer patients diagnosed in Northern Ireland (2012-2016) by route- to-diagnosis

Route-to-diagnosis	Northern Ireland	
	n*	ns, %
Red Flag	608	69.0
GP Referral	512	71.6
Outpatient	867	73.2
Inpatient	167	39.0
Emergency Presentation	451	34.0
Total	**2,605**	

*some patients are not included in the survival analysis, see 1.6 *Analytical techniques*

Figure 14: Three-year net survival (%) of urinary cancer patients diagnosed from 2012-2016, by Route-to-Diagnosis



2.6.9 Female genital cancer

Female genital cancer occurs in the cervix, vulva, uterus and ovary (sometimes referred to as gynaecological cancers). The bulk of these patients are diagnosed with cervical cancer (83, annual incidence in NI), ovary (217), and uterus (249). Five-year net survival for cervical cancer is 66.6% , ovarian cancer is 41.5% and cancer of the uterus is 78.7% (Northern Ireland Cancer Registry, 2019c).

Routes-to-diagnosis in Northern Ireland

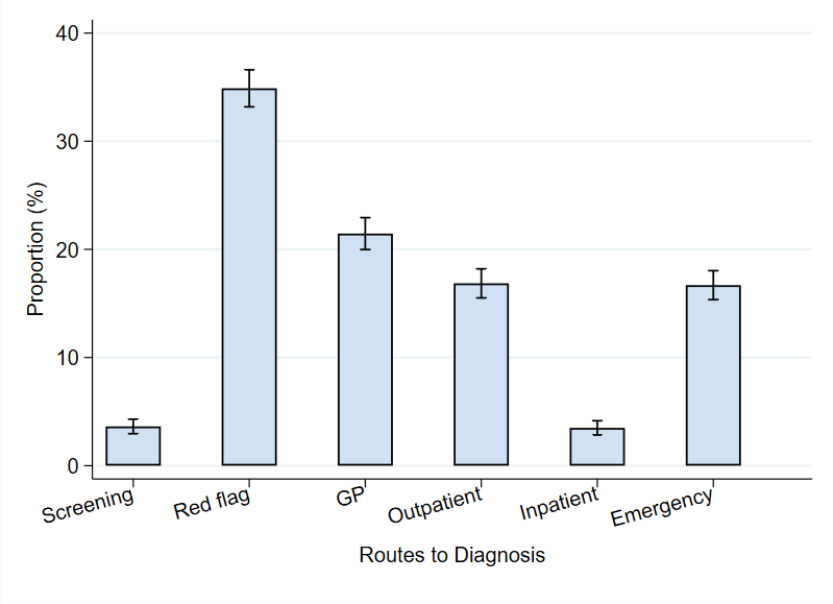
The largest proportion of female genital cancers were diagnosed via a Red Flag Route-to-Diagnosis (34.9%) and with sizeable proportions in GP Route-to-Diagnosis, Outpatient Route-to-Diagnosis and Emergency Presentation Route-to-Diagnosis (Table 14, Figure 15).

Table 14: The frequency (n) and distribution (%) of Routes-to-Diagnosis of female genital cancer patients diagnosed in 2012-2016 in Northern Ireland

Route-to-diagnosis	Northern Ireland	
	n	%
Red Flag	1,039	34.9
GP Referral	639	21.5
Outpatient	502	16.9
Inpatient	104	3.5
Emergency Presentation	497	16.7
Total	**2,781**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 15: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with female genital cancer from 2012-2016 in Northern Ireland



Net Survival

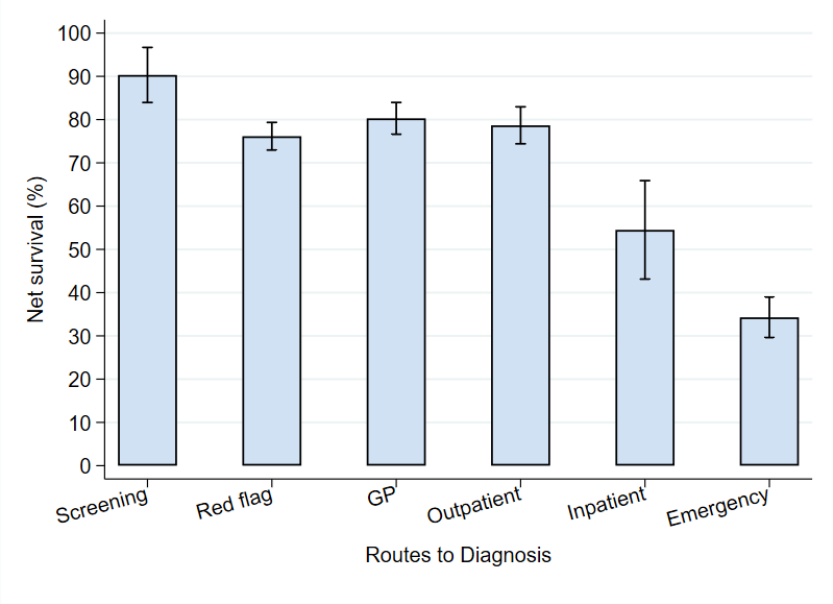
The three-year net survival of patient diagnosed via GP Route-to-Diagnosis, Red Flag Route-to-Diagnosis and Outpatient Route-to-Diagnosis were similar, greater than 76%. Net survival was lowest for Emergency Presentation Route-to-Diagnosis (34.3%) (Table 15, Figure 16).

Table 15: Three-year net survival (ns, %) of female genital cancer patients diagnosed in Northern Ireland (2012-2016)

Route-to-diagnosis	Northern Ireland	
	n*	ns, %
Red Flag	1,015	76.2
GP Referral	631	80.3
Outpatient	478	78.7
Inpatient	103	54.5
Emergency Presentation	487	34.3
Total	**2,714**	

*some patients are not included in the survival analysis, see 1.6 *Analytical techniques*

Figure 16: Three-year net survival (%) of female genital cancer patients diagnosed from 2012-2016, by Route-to-Diagnosis



2.6.10 Blood and Lymph Cancer

Blood and lymph cancer comprise of lymphoma, leukaemia and myeloma. These are cancers of blood cell formation (haematopoietic neoplasms). Lymphoma affects lymphocytes, leukaemia affects the white blood cells (lymphocytes and myelocytes) and myeloma affects the cells of the bone marrow (Klauser, 2001). In Northern Ireland (NI) there were 782 patients diagnosed with blood and lymph cancer annually between 2013 and 2017 (Northern Ireland Cancer Registry, 2020c). Incidence of blood and lymph cancer increases with age, however there is a peak in leukaemia incidence for patients aged between 0 to 4 years. By sex, incidence rates of blood and lymph cancer are higher amongst men compared to women. Five year net survival for blood cancer types is as follows: lymphoma (65.7%), leukaemia (55.6%), and myeloma (52.6%) (Northern Ireland Cancer Registry, 2020c).

Routes-to-diagnosis in Northern Ireland

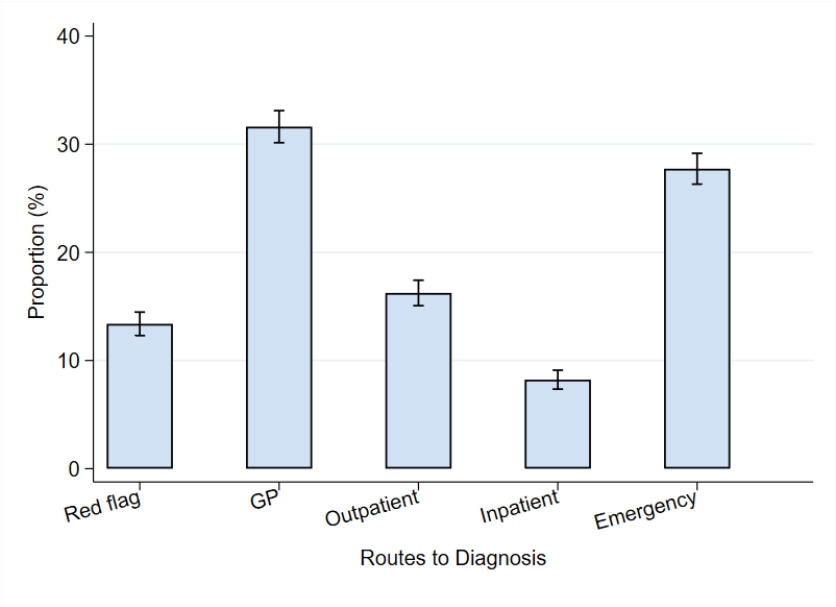
The highest proportion of blood and lymph cancer patients were diagnosed via GP Route-to-Diagnosis (31.6%) followed by Emergency Presentation Route-to-Diagnosis (27.7%) (Table 16, Figure 17).

Table 16: The frequency (n) and distribution (%) of Routes-to-Diagnosis of blood and lymph cancer patients diagnosed in 2012-2016 in Northern Ireland

Route-to-diagnosis	Northern Ireland n	%
Red Flag	506	13.4
GP Referral	1,195	31.6
Outpatient	614	16.2
Inpatient	311	8.2
Emergency Presentation	1,048	27.7
Total	**3,779**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 17: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with blood and lymph cancer from 2012-2016 in Northern Ireland



Net Survival

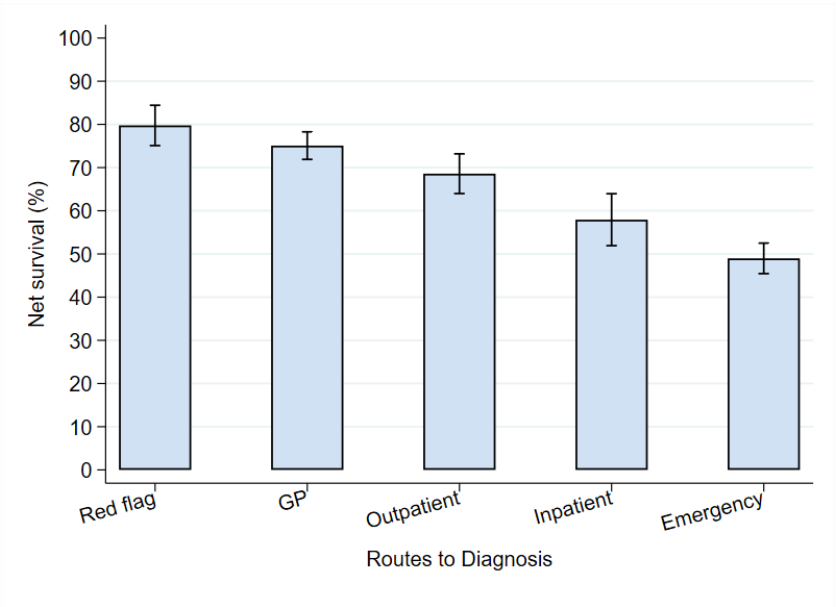
Three year net survival was highest for patient diagnosis via Red Flag Route-to-Diagnosis (79.8%) and lowest for Emergency Presentation Route-to-Diagnosis (49.0%). Inpatient Route-to-Diagnosis patients had intermediate survival between emergency Route-to-Diagnosis and Outpatient Route-to-Diagnosis, GP Route-to-Diagnosis, and Red Flag Route-to-Diagnosis (Table 17, Figure 18).

Table 17: Three-year net survival (ns, %) of blood and lymph cancer patients diagnosed in Northern Ireland (2012-2016) by route- to-diagnosis

Route-to-diagnosis	Northern Ireland	
	n*	ns, %
Red Flag	506	79.8
GP Referral	1,186	75.1
Outpatient	610	68.6
Inpatient	310	57.9
Emergency Presentation	1,034	49.0
Total	**3,646**	

*some patients are not included in the survival analysis, see 1.6 *Analytical techniques*

Figure 18: Three-year net survival (%) of blood and lymph cancer patients diagnosed from 2012-2016, by Route-to-Diagnosis



2.6.11 Young person's cancer

Young person's cancer describes cancer which occurs in a patient aged 24 years or younger. These cancers make up less than 1% of all cancers diagnosed in the UK between 2014 and 2016 (Cancer Research UK, 2020c). By sex, incidence rates were broadly similar, 58% of young person's cancer in the UK are diagnosed amongst women, whilst 42% were diagnosed for men. The three most common cancer types in UK young people are lymphomas, carcinomas and germ cell tumours (Cancer Research UK, 2020c; Birch et al., 2002).

Routes-to-diagnosis in Northern Ireland

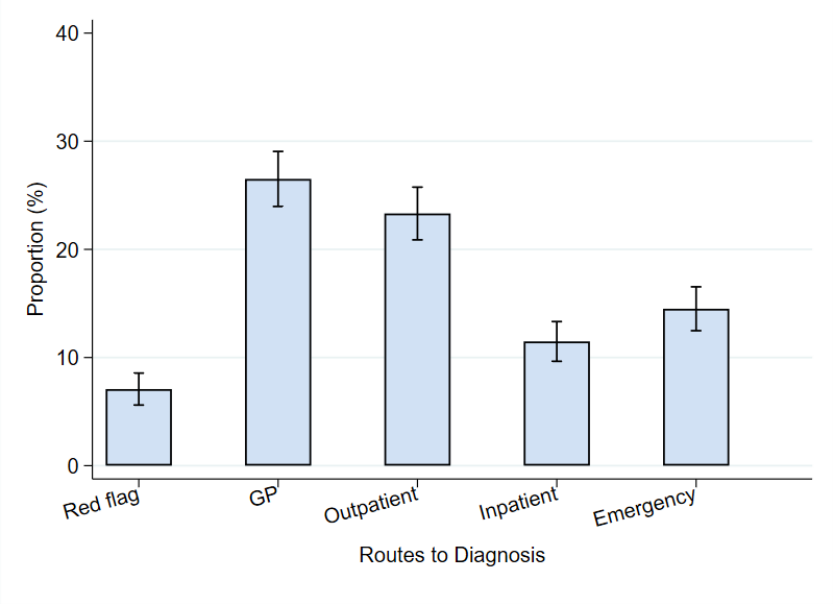
The highest proportion of young person's cancer were diagnosed by GP Route-to-Diagnosis (26.5%) followed by Outpatient Route-to-Diagnosis (23.3%). Around 14.5% of young people presented as emergencies. A large proportion of young people's route to diagnosis was unknown (not shown in Table 18, Figure 19)

Table 18: The frequency (n) and distribution (%) of Routes-to-Diagnosis of young person cancer patients diagnosed in 2012-2016 in Northern Ireland

Route-to-diagnosis	Northern Ireland	
	n	%
Red Flag	82	7.1
GP Referral	307	26.5
Outpatient	270	23.3
Inpatient	133	11.5
Emergency Presentation	168	14.5
Total	**1,158**	

Note: frequency (n) will not sum to total due to exclusion of Death Certificate Only and Unknown routes to diagnosis

Figure 19: Distribution (%) of Routes-to-Diagnosis for patients diagnosed with young person cancer from 2012-2016 in Northern Ireland



Net Survival

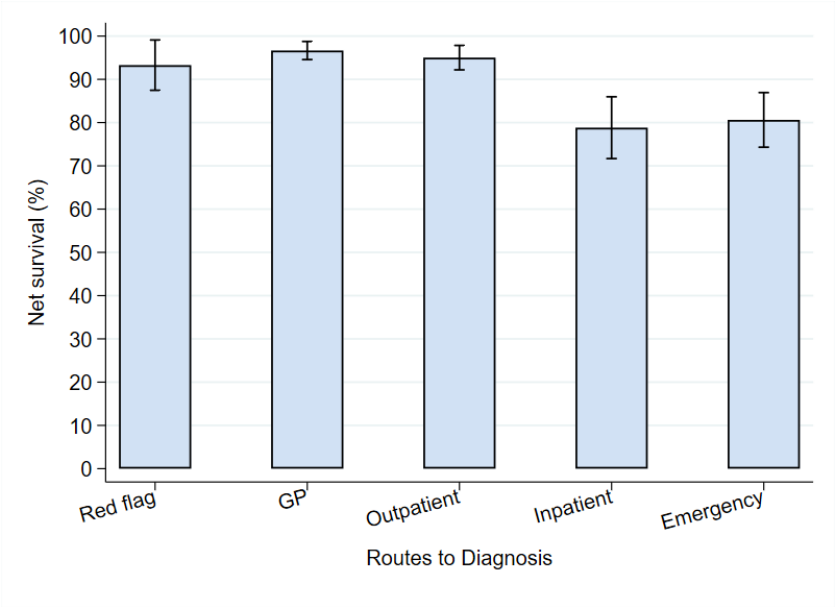
Survival was highest for patients diagnosed via GP Route-to-Diagnosis (96.7%), Red Flag Route-to-Diagnosis (93.3%) and Outpatient Route-to-Diagnosis (95.0%). Net survival was lower for Inpatient Route-to-Diagnosis (78.8%) and Emergency Presentation Route-to-Diagnosis (80.6%) (Table 19, Figure 20).

Table 19: Three-year net survival (ns, %) of young person cancer patients diagnosed in Northern Ireland (2012-2016) by route- to-diagnosis

Route-to-diagnosis	Northern Ireland	
	n*	ns, %
Red Flag	81	93.3
GP Referral	305	96.7
Outpatient	266	95.0
Inpatient	131	78.8
Emergency Presentation	166	80.6
Total	**949**	

*some patients are not included in the survival analysis, see 1.6 *Analytical techniques*

Figure 20: Three-year net survival (%) of young person cancer patients diagnosed from 2012-2016, by Route-to-Diagnosis



2.6.12 Discussion

Patterns of Route-to-diagnosis distribution for patients varied a lot among the different cancer groupings. In addition, survival of the Route-to-diagnosis varied between the cancer sites, although Emergency Presentation Route-to-Diagnosis patients had consistently the worst outcomes. Although, there is adequately complete staging information for some of the cancer site groupings, it was, for the purposes of this report, raising patient disclosure issues when cross tabulating Routes-to-diagnosis by stage, and other demographic factors. The Route-to-diagnosis dataset will need to accumulate data in the coming years before meaningful cross-tabulation and analysis of Routes-to-diagnosis by patient clinical and demographic factors is possible. The tables presented above, however, do highlight some issues to motivate hypotheses for service improvement, and in conjunction with insights from the cross-tabulations of the four large caseload cancer sites (breast, bowel, lung and prostate), these hypotheses may be enriched if assuming basic commonalties (e.g. age or sex associations with Routes-to-diagnosis) is sensible.

Cervical cancer patients were diagnosed through all routes in similar proportions (ranging from 18-24%). The Red Flag Route-to-Diagnosis had much lower survival (65%) compared to the GP Route-to-Diagnosis, Screening Route-to-Diagnosis and Outpatient Route-to-Diagnosis (>90%). This finding was broadly similar to England, where sufficient data was available to

estimate poorer outcome in Emergency Presentation Route-to-Diagnosis (30.6%). These observed variations in survival indicate the great potential there is to improve outcomes, through focusing research and interventions of patients that have been diagnosed via Red Flag Route-to-Diagnosis and Emergency Presentation Route-to-Diagnosis. These explorations may discover sub-groups of the patient population who were not aware of symptoms or the value of screening leading to their advanced stage of disease at diagnosis.

The survival outcome for melanoma skin cancer patients in NI has been higher than the UK in general in recent decades, and so the lower proportion of Red Flag Route-to-Diagnosis patients is not indicative of poorer practice but of pre-established pathways that continue to serve well. The funnel plot of Red Flag Route-to-Diagnosis proportions in England showed a wide variation which implies that there may be a legitimate variation in cancer pathways in dealing with this disease.

A common finding across many of the cancer site groupings is the poorer outcome of patients diagnosed via Inpatient Routes-to-Diagnosis, and although these proportions are not sizeable many approach 10%. These patients may represent incidental findings in patients admitted in hospitals with other serious conditions, and whose cancer is advanced. Further research could amalgamate these patients across cancer site groups and investigate their demographic and clinical profile for strong associations that may prove causal and be generate potential interventions.

More frequent use of Red Flag Route-to-Diagnosis for some cancer site domains such as melanoma skin cancer and female genital cancer is an encouraging result as this is the referral pathway generated to promote early cancer diagnosis. High net survival for melanoma skin cancer reflects this, but the lower net survival for inpatient and Emergency Presentation Route-to-Diagnosis diagnosed female genital cancers may reflect confusion of symptoms with other health conditions which makes timely diagnosis difficult e.g. ovarian cancer symptoms are often confused with pregnancy, Irritable Bowel Syndrome (IBS) or menopause (Macmillan Cancer Support, 2017).

Outpatient Route-to-Diagnosis was also frequently used to diagnose cancer for site domains head, neck, brain and eye cancer and urinary cancer. These cancers may be more likely to be incidentally diagnosed through CT and MRI scans used to diagnose other cancers. Symptoms

of head and neck cancer include a swollen neck and sore throat, which could be confused with other health conditions particularly as the cancer is uncommon (Radiology Information, 2020). In 2018 the Kidney Cancer UK Patient Survey found that around half of all kidney cancer patients are initially misdiagnosed with other conditions such as respiratory problems and urine infections (PharmaTimes, 2018).

The highest proportion of patients were diagnosed via Emergency Presentation Route-to-Diagnosis for upper GI cancer, digestive cancer and blood and lymph cancer. This is likely due to the symptoms associated with these cancers, which are commonly misdiagnosed for other health conditions e.g. pancreatic cancer symptoms include abdominal pain, indigestion and jaundice which are associated with a number of health conditions (Pancreatic Cancer UK, 2020a). In light of calls for more structured referral pathways for pancreatic cancer patients due to their poor survival, the updated 2015 NICE red flag guidelines (National Institute for Health and Care Excellence, 2015) have included a section on pancreatic cancer for the first time (Pancreatic Cancer UK, 2020b). High Emergency Presentation Route-to-Diagnosis for blood and lymph cancer have been described as due to heterogeneity in these cancers (i.e. some present aggressively like Burkitt Lymphoma whilst others are incurable but indolent like follicular lymphoma) and symptoms which can be confused for other health conditions (Kane et al., 2017). Routes to diagnosis in England reported emergency presenters amongst oesophagogastric cancer patients were more likely to be older and with comorbidities (Palser et al., 2013).

Younger patients were most frequently diagnosed via GP Route-to-Diagnosis, which differs from Routes to diagnosis in England which found the highest proportion of cancers were diagnosed via Emergency Presentation Route-to-Diagnosis (although it is important to note that age groups differed; England defined patients as being aged 15-24 years) (Cancer Research UK, 2020c). Higher GP diagnoses could reflect perceptions that cancer is rare in younger people or younger patients may not present with the usual red flag symptoms, particularly at early stage disease (Dommett et al., 2019).

2.6.13 Bibliography

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3. Conclusions and recommendations

3.1 Concluding Remarks

This has been a challenging piece of research in terms of assembling a fit-for-purpose linked dataset, adapting the PHE Routes-to-Diagnosis algorithms to run on NI data and exploring observed differences between NI and England. Whilst it is encouraging to see so much similarity between the two countries, indicating a high level of consistency in respect of service delivery, the higher proportions of NI patients being diagnosed in an outpatient, and to a lesser extent, inpatient setting begs further investigation. Identifying such differences in the pattern of care exemplifies the value of this resource in identifying potential target populations and services for optimisation of care pathways, service improvement and potentially to promote earlier diagnosis. While possible reasons for such differences were highlighted in the Introductory Section (see para 1.5.3), it is beyond the scope of the routes-to-diagnosis to fully explain such variation. Given the variation in patient survival by diagnostic pathway noted across the cancer sites studied, it would be important to establish to what extent this variation can be explained by real service differences rather than simply being an artefact of the data.

The development of a supporting interactive monitoring tool using 'R Studio' freeware should provide practitioners with the ability to explore the results in much more detail and all data tables will be made available in CSV format to facilitate reuse. The interactive tool, however, should be very much regarded as a prototype with significant scope for enhancement. All outputs currently within the tool have had to be pre-defined and cleared for publication to ensure compliance with Honest Broker Service data governance arrangements. Moreover, the raw data have had to be destroyed upon completion of the project. In future, however, it may be possible to secure agreement to retain anonymised project datasets, within an appropriate data governance framework, to facilitate secondary research. This will be important to help explore the many questions to which work of this nature inevitably gives rise.

It will also be important to keep abreast of developments in NI HSC data systems. The introduction of a digital integrated care record within NI, via the Encompass programme, will provide fresh challenges in carrying out work of this nature. However, if the Routes-to-

Diagnosis algorithms can be successfully adapted and built into the new system then, over the longer term, there will be opportunities to automate the derivation of the diagnostic routes within a research dataset and provide ad-hoc analysis functionality to a wide range of HSC users.

This current report plugs a significant gap in cancer information within NI and has identified a range of issues for further research. A set of Standard Operating Procedures (SOPs) have also been developed in order to facilitate the future repetition of the study. As it stands, however, the research findings only provide a benchmark against which to judge the new NI Cancer Strategy (in development), the effectiveness of early diagnosis interventions and of public awareness campaigns. If the desired goal of improved patient outcomes is to be fully realised, then it is vitally important that the derivation of Routes-to-Diagnosis is properly resourced and becomes embedded as business as usual within the NI HSC family. How this work should be taken forward is ultimately for the Department of Health and other stakeholders to consider but there are also clear opportunities for collaboration with the voluntary sector. The availability of this type of information is reputed to have transformed the delivery of cancer services in England and there is no reason why, if properly resourced, NI patients could not similarly benefit.

3.2 Recommendations

During the course of the research project, the team identified a range of things that could be improved in further updates. These are listed below.

Methodological/Data Quality

- The PHE Routes-to-Diagnosis algorithms be thoroughly reviewed and sensitivity tested with input from service professionals. This would help establish whether any recalibration of key algorithm parameters is warranted to better fit the NI context, for example, given our longer waiting times compared to England.

- Exploration as to whether Clinical Communication Gateway (CCG) data could be incorporated into future Routes-to-Diagnosis analysis. This system is used in the majority of GP practices and provides rapid, secure and auditable transfer of

referrals, electronically, from primary to secondary care. The system is integrated with the GP practice clinical information system from which it extracts relevant data for inclusion in the referral.

- Improvement to the consistency of coding of outpatient records. Whilst regional codes are available, the historical and continued use of local codes across NI HSC Trusts has necessitated a lot of manual intervention to reclassify records to the same coding scheme as used by the Routes-to-Diagnosis algorithms. This issue should be raised with Trusts via the Information Standards Board.

- Significant work was carried out between the NI Cancer Registry and NI Screening Services in order to make sure the screening records held by the Cancer Registry were as accurate as possible. This is a key element of the Routes-to-Diagnosis algorithm so it is important that the quality of this information is maintained for future iterations.

- Further exploration of routes at smaller geographical levels as further years of fit-for-purpose data become available increasing the size of the analysable dataset.

Service Improvements

- A dedicated Route-to-Diagnosis team be established, including both analytical and service professional input, with a remit to exploring significant variation in diagnostic routes. The marked difference between NI and England in respect of inpatient and, in particular, outpatient routes should be prioritised for further investigation

- Discussion of existing data governance arrangements, in collaboration with NI HSC Trusts and, if applicable, the NI Honest Broker Governance Board, with a view to developing an appropriate governance framework which facilitates reuse of Routes-to-Diagnosis datasets and promotes secondary research.

- Development of a server based solution on which to host the online monitoring tool and enhancements to its functionality including the ability for users to create their

own outputs. This could further expand into a dedicated Routes-to-Diagnosis website as a one-stop shop for new reports, innovative analysis and other related resources.

- Continued liaison with Encompass team to allow for Routes-to-Diagnosis field derivation, standard reporting and ad-hoc analysis functionality to be taken account of in the development of the new system specification.

Wider Developments

- There are significant opportunities for collaborative projects in this area with colleagues in PHE and when the new Welsh study begins to produce their own Routes-to-Diagnosis results. The possibility of further developing the range of available analysis and linking to patient experiences should also be explored. The resource available to undertake such work could potentially be enhanced through collaboration with cancer charities such as CRUK and Macmillan.

- The research findings from this work, and its potential to positively impact service delivery in the cancer field, should continue to be disseminated and promoted at relevant conferences and via journal articles.

4. Authorship and acknowledgements

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We were very grateful for the support and advice of our Steering Group throughout the project, comprising (in alphabetical order):

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This project is part of the Health Foundation's Applying Advanced Analytics programme.

The Health Foundation is an independent charity committed to bringing about better health and health care for people in the UK. Their aim is a healthier population, supported by high quality health care that can be equitably accessed. From giving grants to those working at the front line to carrying out research and policy analysis, they shine a light on how to make successful change happen. They use what they know works on the ground to inform effective policymaking and vice versa. They believe good health and health care are key to a flourishing society. Through sharing learning, collaborating with others and building people's

skills and knowledge, they aim to make a difference and contribute to a healthier population.

The authors would like to acknowledge the help provided by the staff of the Honest Broker Service (HBS) within the Business Services Organisation Northern Ireland (BSO). The HBS is funded by the BSO and the Department of Health for Northern Ireland (DoH). The authors alone are responsible for the interpretation of the data and any views or opinions presented are solely those of the author and do not necessarily represent those of the BSO.

5. Glossary

Cancer

A disease resulting from the breakdown in the normal growth of body cells as a result of faults or damage to the genes that control for cell growth.

Cancer Site

The location in the body that a cancer originates in, e.g. lung, breast or prostate.

Carcinoma In-situ

A group of abnormal cells that remain in the place where they first formed. They have not spread. These abnormal cells may become cancer and spread into normal tissue. Also called 'Stage 0' diease.

Comorbidity

The presence of one or more disorders (or diseases) in addition to a primary disease or disorder.

Confidence Interval

The range of values calculated to have a specified (usually 95%) probability of containing the true value of an observation. Thus the 95% confidence interval for a survival rate is the range of values within which there is a 95% probability of finding the true value for the survival rate.

Diagnosis

The process whereby the nature of a patient's illness is identified through medical examination.

European Standard Population

A standard population using the age distribution per 100,000 persons in Europe. The same age distribution is used for males and females.

Expected Survival

The survival expected from of a group of patients based upon the life table of the general population from which they are diagnosed.

ICD10

The tenth edition of the International Statistical Classification of Diseases and Related Health Problems, which is published by the World Health Organisation (WHO). It provides a detailed description of known diseases and injuries and is used in the production of morbidity and mortality statistics.

Incidence

The number of new cases of a cancer diagnosed in a particular period for a particular population.

Lead-time bias

The systematic error of apparent increased survival from detecting disease in an early stage.

Length bias

The systematic error from detecting disease with a long latency or pre-clinical period.

Life Table

A table that shows the life expectancy of a person at each age and sex. Also included in Northern Ireland life tables are:

- The probability that a person of a given age will die before their next birthday;
- The number of people out of 100,000 live births who survive to a given age;
- The number of people who die at a given age.

Malignant Tumour

A cancerous tumour that can invade and destroy nearby tissue and spread to other parts of the body.

Mortality

For the purposes of this report mortality refers to the number of patients whose primary cause of death for a particular period was cancer. In a wider context this refers to all causes of death.

Net survival

Net survival is an estimate of survival where the effect on survival of background population mortality rates has been removed.

Pathway Group

A classification that is created for each tumour according to the presence or absence of inpatient and outpatient hospital activity data in the 6 months prior to diagnosis.

P-value

The probability of an event occurring given a null hypothesis is true. In any statistical tests in this report the null hypothesis is taken to be that there is no difference between two mean values or rates. A small p-value (typically less than 0.05) suggests that the two means or rates tested are significantly different.

Quintile

One of five groups of equal size into which the population is divided, with the division depending upon the value of a particular variable (e.g. deprivation levels).

Route-to-Diagnosis

A 'Route-to-Diagnosis' is defined as the sequence of interactions between the patient and the healthcare system which lead to a diagnosis of cancer, based on the end point, the pathway and the referral route into secondary care. Depending on context it might either be a 'detailed' route, e.g. IP-C-O4, or a broad summary route, e.g. "Emergency Presentation".

Route start-point

The start point is the first recorded clinical care event that the Route-to-Diagnosis Algorithm picks up.

Route end-point

The end-point was assumed to be the clinical care event that led most immediately to diagnosis.

Staging

A measure of how far a malignancy has spread in the body. The higher the stage the greater the disease has spread and the less favourable the prognosis for the patient.

Standardisation by age, sex and deprivation

A method whereby a statistic, e.g. a proportion, is adjusted to a standard population of the same age, sex and deprivation structure in order to provide for a more like-for-like comparison.

Statistically significant

A difference between two values that has a low probability (typically less than 5%) of being a result of a random occurrence.

Screening

A method of checking for the presence of disease when there are no signs or symptoms.

Tumour

An abnormal mass of tissue resulting from uncontrolled cell growth and causing a swelling of the body. Tumours may be benign or malignant.

Unstaged Cancer

A cancer for which there is not enough information to indicate a stage and may result from patients not receiving a full diagnostic evaluation.