Geographic variations in access to cancer services and outcomes along the cancer care pathway

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Abstract

The poorer cancer survival in England in comparison to countries of comparable wealth may be explained by variations in diagnostic and treatment practices, and in disease stage. This highlights the importance of General Practitioners (GPs) in facilitating earlier diagnosis and access to secondary care. Poor access to secondary care has been associated with poorer cancer outcomes. As GPs are the first point of contact with health services for most patients, it is possible that some problems associated with access in secondary care originate from poor GP access. Despite this, there is little evidence describing the relationship between access to GPs and cancer outcomes. This research examines the association between geographical accessibility and cancer outcomes along the cancer care pathway, with a focus on access to the GP.

The research begins by reviewing policies on improving access to cancer services, and finds some trade-offs that result when meeting contrasting policy goals. For example, centralisation may improve efficiencies, but may increase inequities in access. One study found that cancer services in England may not be located according to need, but are more likely to be concentrated in urban areas where incidence rates are lower. The other studies examine how geographical access associates with outcomes related to primary care, secondary care and the interface between these two. These studies found that longer travel to primary care has an opposite association on outcomes in rural compared to urban areas, and, has important implications on the mode of cancer diagnosis in secondary care. Additionally, longer travel to both primary and secondary care, and living in an urban area is associated with worse survival, furthermore, times delays and disease stage may be important mediators for these associations.

This research generates original evidence showing that geographical access to primary care for diagnosis may have important consequences for cancer outcomes. The findings suggests that rural areas may not necessarily experience poorer outcomes, warranting future research on access issues amongst patients living in urban areas.

Author Declarations

The author took the lead role in designing all studies, in obtaining approval for data access (**Annex E, Annex F, Annex G** and **Annex H**) in the analysis of data, and in writing all manuscripts and the final thesis. Contribution by other individuals is reported in the list below and in the acknowledgements section of the thesis.

The following is a list of output (publications, poster abstracts and conference presentations) that has been generated from this research:

Chapter Two – A review of the development of cancer policies in England; evaluating the progress of policy objectives

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Chapter Three - Geographical disparities in access to cancer management and treatment services in England

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Chapter Four – Impact of travel time and rurality on presentation and outcomes of symptomatic colorectal cancer: a cross-sectional cohort study in primary care

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Oral presentation at the Cancer and Primary Care Research International Network (CaPRi) conference, Aarhus, Denmark, May 21st - 20th, 2015

Chapter Five – Geographical access to general practitioners and modes of cancer diagnosis in England: a cross-sectional study of linked cancer registry and hospital data

Manuscript in preparation and will be submitted for publication

Oral presentation at the Public Health England National Cancer Registration and Analysis Services (PHE NCRAS) Cancer Data and Outcomes Conference, Manchester UK, June 13th – 14th, 2016

Chapter Six – Do time delays and advanced disease explain the association between access to health services and colorectal cancer survival?

Manuscript in preparation and will be submitted for publication.

Collaborative poster presentation by Peter Murchie (University of Aberdeen), Line Jensen (Aarhus University), Peninah Murage (University of East Anglia), Andy Jones (University of East Anglia), Peter Vedsted (Aarhus University), Melanie Turner (University of Aberdeen) and Shona Fielding (University of Aberdeen). *Comparing the literal cancer journey for colorectal cancer patients between Denmark, England and Scotland.* Presented at the Cancer and Primary Care Research International Network (CaPRi) conference, Edinburgh, Scotland, April 18th - 20th, 2017.

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Chapter 1

General Introduction

1.1 Introduction

Cancer is the leading cause of death in the UK (Independent Cancer Taskforce 2015; National Records for Scotland 2013), resulting in over 160,000 deaths per year (Cancer Research UK 2016a). It is estimated that half of those born post 1960 will be diagnosed with cancer at some point in their lifetime (Ahmad et al. 2015). The UK also has poorer cancer survival rates in comparison to other countries of equal wealth (Coleman et al. 2010; De Angelis et al. 2013).

These differences in survival may be explained by differences in factors operating at the patient, health practitioner, or health system level. For instance, disease stage may be an explanatory factor and it has been suggested that patients in the UK present with more advanced disease stage at diagnosis than their European counterparts (Coleman et al. 2010; Walters et al. 2013). Another suggestion is that the survival differences may be as a result of differences in how cancer is diagnosed and treated (Coleman et al. 2010). The latter is particularly important because survival rates in the UK are similar to Denmark, another European country that shares a similar primary care system to the UK, whereby GPs (General Practitioners) control access to secondary care services for diagnosis and treatment. There are suggestions that the system of GP gatekeeping may determine cancer outcomes; one study has reported lower survival rates in healthcare systems with a primary care gate keeper (Vedsted & Olesen 2011). Identifying the mechanisms that may explain how primary care influences the cancer outcomes that are reported farther up the cancer care continuum is an area that warrants further investigation. Access issues are felt most acutely by patients with a long standing illness because of their need to access services more frequently (Haynes & Bentham 1982). Most cancer patients would have sought both primary and secondary care a number of times in the course of the disease, which emphasises the need to investigate issues related to accessing cancer services.

1.2 Access to cancer services and cancer outcomes

Examining variations in access to diagnosis and treatment may contribute to understanding the variations in cancer survival. Access has been a central tenet in the NHS since its inception with the goal of providing free access on the basis of clinical need and not ability to pay (NHS 2015). The NHS is considered as one of the most equitable service in the western world due to its provision of universal access (The Commonwealth Fund 2010). Despite this, the NHS has had some shortcomings in terms of its overall performance, and some of these shortcomings are related to accessibility issues that will be explored in more detail in this research.

Although the goal of universal access has alleviated some barriers in access such as those associated with affordability, patients are still required to pay for some social and economic costs of use. Some social costs may be associated with accessing GPs, whereby opening hours may not be convenient for those unable to obtain appointments during working hours (Carr-Hill et al. 1997), and this may particularly affect those in employment. Some economic costs include costs associated with travel, and the opportunity costs of time that is spent on travelling or waiting for an appointment (Carr-Hill et al. 1997). These costs are important in the context of understanding barriers in access to services because greater access costs act to lower the utilisation of the health services. Geographical inaccessibility my further amplify the effect of these social and economic costs, and this may have implications for cancer outcomes.

Previous studies have reported associations between poor access to secondary care services and cancer outcomes. One study based in England showed that longer travel to the hospital of treatment was associated with lower odds of obtaining optimal treatment in patients with lung and rectal cancers (Jones et al. 2008). Other studies based in northern Scotland showed that greater distances to a specialist cancer centre were associated with more advanced disease stage and with poorer survival from lung, prostate and colorectal cancers (Campbell et al. 2001; Campbell et al. 2000) . Poorer access to hospital services has also been associated with worse outcomes in other parts of the world (Dejardin et al. 2008; Dejardin et al. 2014; Wan et al. 2012; Silva et al. 2011).

There is less evidence on the association between access to early diagnosis services and cancer outcomes. One study that looked at access from the perspective of the ease of obtaining a GP appointment found practices that provided more timely access to primary care had fewer self-referred visits to the emergency departments (Cowling et al. 2013). Another study based in the USA found that poor geographical access to primary care significantly increased the risk of late breast cancer diagnosis (Wang et al. 2008). There is limited evidence on the association between access to the GP and cancer survival in the UK.

Investigating the influence of access to primary services on cancer outcomes is important; firstly, with the exception of emergency services, access to secondary care services for diagnosis and treatment can only be obtained by referral from primary care services. Thus, restricted access to primary care may in turn reduce access to secondary care (Carr-Hill et al.

1997). Furthermore, the likelihood of GPs to make referrals may be influenced by accessibility to services, and by consideration of the journeys that their patients may make (Carr-Hill et al. 1997; Sladden & Thomson 1998; Haynes & Bentham 1982). Thereby, when the opportunity cost of access is high (such as longer journey time), GPs may refer fewer patients into secondary care (Carr-Hill et al. 1997), making it plausible that some of the poor outcomes associated with access to secondary care may have originated from decisions made in primary care. Additionally, inaccessibility to primary care services may influence patient decisions to consult their GPs with symptoms. For example, one previous study found GP consultation rates to decline with increasing distance (Haynes & Bentham 1982). Poor access may have a greater deterrent effect when the perceived risk or benefit of treatment is lower (Carr-Hill et al. 1997), and may be more apparent when symptoms are deemed low risk. The combination of GPs' and patients' perceptions of accessibility may therefore determine treatment options, and ultimately clinical outcomes.

1.3 Defining and measuring access

Healthcare utilisation is the most commonly applied proxy of access to services and assumes that use of health services is evidence of access to those services (Allin et al. 2007). Use of utilisation to estimate access raises conceptual and methodological concerns. This is because service utilisation does not account for variations in the use of health care, such as those related to differences in preferences, cultural or financial barriers, or other factors such as differences in levels of risk aversion (Oliver & Mossialos 2004; Allin et al. 2007). Utilisation rates may therefore not fully reflect need which is a useful measure in investigating health inequalities (Allin et al. 2007).

A more comprehensive definition of access has been suggested as 'opportunity to access' and has been be articulated as *'the ability to secure a specified range of services, at a specified level of quality, subject to a specified maximum level of personal inconvenience and cost, while in possession of a specified amount of information'* (Allin et al. 2007) (pg.4). This definition recognises the distinction between the possibility of using a service if required (potential access) and actually using a service (utilisation) (Allin et al. 2007).

Access to healthcare can thereby be classified into two dichotomous groups at the broadest level; potential vs. revealed (actual) access. These broad groups can be further categorised into

geographical/spatial and non-geographical/aspatial access (Wang 2006; Khan 1992), whereby the former is moderated by space or distance to services, and the latter is normally conditioned by social barriers. **Table 1.1** shows these high-levels dimensions of access.

Table 1.1 Dimensions of access to healthcare

	Geographical	Non-geographical
Potential	Potential Geographical access	Potential non-geographical access
Realized	Revealed Geographical access	Revealed non-geographical access

Source: Khan, 1992

Although this research will focus on revealed geographical access, it will also examine how geographical access relates to other dimensions of access. This is because there are considerable overlaps in the dimensions; as an example, it is likely that individual and system level factors such as socio-cultural (acceptability), cost (affordability) and waiting times (availability) may interact with geographical location or distance to influence health seeking decisions (Thiede & Akweongo 2007).

1.3.1 Measuring geographical accessibility

There are three commonly applied measures of geographical accessibility. The simplest one is the use of supply-demand ratios to calculate the ratio of population vs. providers within a common geographical or administrative boundary (McGrail & Humphreys 2009a). This method is popular with policy makers because is it intuitive. However, it is overly simplistic as it does account for movement across administrative boundaries (McGrail & Humphreys 2009a). A more appropriate measure of accessibility is one that does not assumes that individuals are static and tied to a geographic unit, and recognises that people and places are dynamic and interacting entities (Vallée & Chauvin 2012).

Another commonly used and widely acceptable in measuring accessibility to health services is travel impedance, which computes accessibility as either travel time or distance from the point

of interest to a health service (McGrail & Humphreys 2009b). The limitation of this method is that it doesn't account for capacity of the service provider, or the size of the population i.e. availability (Wang 2006; McGrail & Humphreys 2009a). Use of travel impedance is therefore advocated for when demand of services is less of a concern (Wang 2006) such as in rural and remote areas where demand for services is reduced.

The most robust but also most challenging measure of spatial access uses variations of gravity models that employ a 'distance decay' function, which assumes that service use diminishes with longer distance. These models can be further enhanced by also factoring in both the supply and demand of services (Luo 2004; Luo & Qi 2009; Wang 2006). However, gravity models have been criticised for their difficulty in determining the distance decay function, which is estimated from actual physician-patient interaction, and varies by service type and population under study (Guagliardo 2004; McGrail & Humphreys 2009a).

1.3.2 Rurality

The terms rurality and geographical accessibility have been used interchangeably when examining the association between access to health services and health outcomes. This is in recognition of the lower service accessibility and higher geographical isolation that exists in rural areas. For example, the average estimated journey time to the nearest hospital in rural areas is nearly twice as much as that in urban areas; this rural urban difference is greatest when using public transport (22 vs. 40 minutes) and when cycling (14 vs. 40 minutes), but less marked when driving (7 vs. 12 minutes) (Department for Transport 2014a).

There is a widely held view that people who reside in rural areas have better health outcomes such as mortality (Jones & Lake 2013; Haynes 1987), but other views suggest that poor health amongst the rural poor is hidden by the by favourable averages of health and deprivation measures (Haynes & Gale 2000). Poor health is less associated with deprivation in rural than in urban areas, but this may be a statistical artefact produced by inconsistent scale of analysis and the distribution of rich and poor in rural and urban areas (Haynes & Gale 2000). For instance, large areas of inner city neighbourhoods tend to concentrate people with similar socio-economic status, while small rural areas have less homogenous populations (Haynes & Gale 2000). Rural disadvantage may also manifest as having higher levels of chronic conditions (Douthit et al. 2015) as a result of a more elderly population; who may be further disadvantaged

by residing in more remote areas that experience the greatest loss of health services (Haynes 1987; Haynes & Bentham 1982; Bentham & Haynes 1985).

Studies looking at rural and urban differences in cancer outcomes have also had contrasting findings. Research conducted in France and Australia has shown lower odds of presenting symptoms to the GP amongst patients living in rural areas (Launoy et al. 1992; Emery et al. 2013). Another Australian study showed increased time delays from presentation to obtaining a diagnosis amongst the most remote female patients with ovarian cancer (Jordan et al. 2010). In contrast, research from the USA reveals a rural reversal, whereby risk of later stage colorectal cancer was found in urbanised areas, negating previous assumptions of rural-disadvantage on the basis of poor access (McLafferty & Wang 2009). Similarly, a study looking at primary care access and visits to the emergency departments in England found that rural practices had significantly lower visits than those located in urban areas (Cowling et al. 2013).

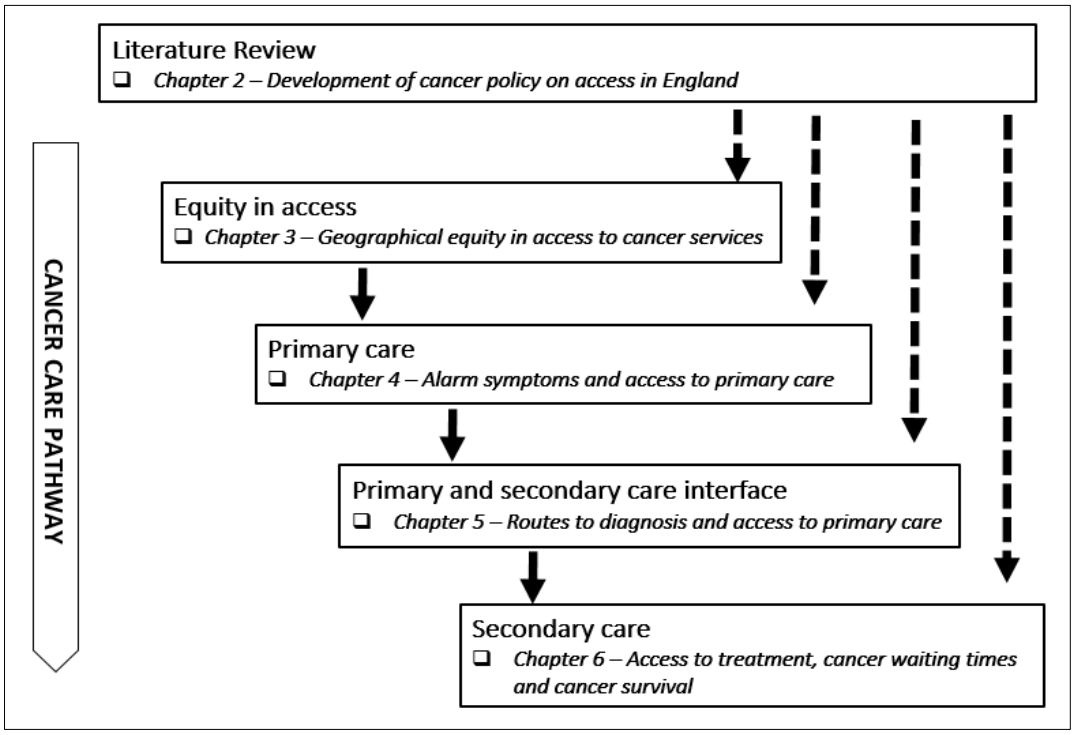
So far, there is inconclusive evidence on the rural and urban differences in cancer outcomes. This research will consider rurality as a dimension of geographical access, in a similar manner to other measures of access such as distance or travel times. It will use the Department for Environment Food and Rural Affairs (DEFRA) definition of rurality which classifies settlements with populations of less than 10,000 as rural (DEFRA 2013b).

1.4 Structure of thesis

The objective of this research is to investigate the potential influence of geographical access on cancer outcomes along the cancer care continuum. The implicit assumption is that of a vertical progression of disease from symptom/s presentation to diagnosis, treatment and survival or death. This progression correlates with patients' care along the care pathway that begins from early detection, to primary care, proceeding to secondary care, and ending with palliative care; although the latter is beyond the scope of this study. Although a linear processes is assumed, the research also recognises that the complex nature of how health services are organised means that receipt of cancer care is anything but linear. There is also a recognition that geographical access may be intertwined with the other dimensions such as cost or financial factors and socio-cultural acceptability of utilising health services.

The research is presented in seven chapters which includes this introduction (Chapter One) and a conclusion chapter (Chapter Seven). The relationship between these chapters is represented in **Figure 1.1**. The dashed line shows that the findings from the literature review feed into the analytical chapters by helping formulate relevant research questions. The bold lines show the connection between the chapters, whereby the analysis begins by taking an area level perspective in Chapter Three, and thereafter, drilling down onto specific aspects of the cancer pathway in the subsequent chapters.

Figure 1.1- Flowchart showing the connection between the thesis chapters



Chapter Two is a narrative review that traces the development of national cancer policy in England with a specific focus on policies on improving access. This Chapter is an in-depth review of five policy documents: A Policy Framework of Commissioning Cancer Services, hereafter referred to as the 'Calman and Hine report' (Calman & Hine 1995), the NHS Cancer Plan (Department of Health 2000), the Cancer Reform Strategy (Department of Health 2007), Improving Outcomes Cancer Strategy (Department of Health 2011a) and Achieving World Class Cancer Outcomes (Independent Cancer Taskforce 2015).

Three of the five policy documents, NHS Cancer Plan, Cancer Reform Strategy and Improving Outcomes were led by the respective Governments of the time, whereas the other two strategies, Calman and Hine report and Achieving World Class Outcomes, were developed by senior physicians and an Independent Taskforce, respectively. This difference in authorship makes an interesting comparison when examining the recommendations and implementation of the proposed policies. The strategies will be examined in order to assess their position on how to achieve the four broad objectives of healthcare policies that are commonly applied when judging health system performance; improving access, narrowing inequalities, improving quality and reducing inefficiencies (Le Grand 1993; Palfrey 2000; The Commonwealth Fund 2010). Any progress in meeting the policy objectives will be assessed, as well as any interaction and/or trade-offs between the objectives. Other sources of evidence will also be reviewed to support the findings.

Chapter Three will build on the findings of the narrative review. The chapter will assess any intrinsic overlaps between the four policy objectives and examine whether any trade-offs that may exist in meeting policy objectives have any measurable impact on outcomes. To do this, the chapter will use publicly available area level data, to examine geographical equity in cancer services, by investigating the extent to which cancer management and treatment services in England are located according to need. Equity in access to healthcare is an important policy objective in England. Indeed, the NHS was founded on the principle that services would meet everyone's needs, and would be based on clinical need and not ability to pay (NHS 2015). It is important to investigate the progress of this principle nearly seven decades since the inception of the NHS. This analysis conducted at an area level will generate hypotheses that can be explored in depth using more granular datasets in subsequent chapters.

The rest of the chapters (Four, Five and Six) use individual level datasets to investigate the relationship between access to GPs and cancer outcomes. Primary care is the first point of contact with the health services for most patients in the UK. Furthermore, GPs in the UK facilitate access to secondary care services which makes it plausible that some of the poor outcomes observed in secondary care may actually originate from poor access in primary care (Carr-Hill et al. 1997; Haynes & Bentham 1982); an example would be the use of emergency

services which may be a marker of inaccessibility of GP services. Access will be studied from the perspective of travelling time to services and as rural or urban residency.

Chapter Four uses a Scottish cancer registry dataset linked with primary care records to assess whether geographical access to GPs affects how patients present to their GP with symptoms that may be related to cancer. Symptoms related to cancer can be broadly categorised based on their ease of diagnosis; thus symptoms such as rectal bleeding may be considered alarming, whereas others such as constipation are considered vague due to their atypical nature. The prospect of longer journeys may make patients less inclined to attribute these symptoms to cancer. Therefore, it is likely that inaccessibility may reduce the odds of obtaining a diagnosis following presentation with atypical symptoms. The considerable rurality in northern Scotland makes this area a good case study for investigating any geographical and socio-cultural variations in symptoms presentation.

Chapters Five and Six employ a record level dataset from the English cancer registries that has been linked with hospital records, with information on screening and with cancer waiting times. This linkage has enabled the ascertainment of the route that patients took to obtain a cancer diagnosis. Routes such as emergency presentations have previously been associated with poorer outcomes. However, it is not clear the extent to which this is because of poor access. Chapter Five investigates whether access to the GP determines the routes to diagnosis and will compare the associations between access and desirable routes (screening and urgent referrals), with the association between access and less desirable routes (emergency presentations and death certificate only diagnoses).

Chapter Six examines how access to the GP, and to the hospital of treatment is associated with cancer waiting times, disease stage and cancer survival. This Chapter also investigates potential mechanisms that may explain these associations using cancer waiting times and disease stage as two potential mediators.

This research benefits from the high-quality data information collected by the UK Cancer Registries; the data has an estimated case ascertainment completeness of up to 99% (Moller 2011) and contains socio-economic, demographic and clinical variables that are important for research purposes. The quality of the registry data has been improved by linkage with

complementary datasets such as Hospital Episode Statistics (HES), which has improved the accuracy of common variables such as disease stage, and has enabled the use of information on comorbidities. Further linkage with other routine datasets such as screening and Cancer Waiting Times (CWTs) datasets makes it possible to perform analysis that integrates different processes and outcomes on the care continuum. Additionally, the registry dataset spans a period of several decades, offering a wide window of opportunity for studying the development and impact of health policies that normally take lengthy periods to implement, and for their impact to manifest.

Chapter 2

A review of the development of cancer policies in England; evaluating the progress of policy objectives

2.1 Background

The five strategies on cancer published between 1995 and 2015 describe comprehensive policies of improving cancer care and outcomes (Calman & Hine 1995; Department of Health 2000; Department of Health 2007; Department of Health 2011a; Independent Cancer Taskforce 2015). Their content and approach has been influenced by a myriad of social, economic and political changes that have spanned the last two decades. These include but are not limited to five governments, significant NHS (National Health Service) re-organisation, advances in information technology, and economic fluctuations. The various polices may therefore have had varying levels of achievements in meeting their intended objectives.

Service re-organisation in the delivery of cancer services have at times been coordinated with wider reforms related to changes in government. At other times though, changes have occurred in isolation of government involvement. The earliest and perhaps most significant restructuring of cancer services that was instigated by the Calman and Hine report (Calman & Hine 1995) was not related to any wider reforms, and was entirely independent of government. The report had policy recommendations that had far reaching consequences in the configuration of cancer services in England and Wales. Some of the policies such as the creation of specialised cancer centres to cater for rare cancers and specialised treatment, and cancer units to manage the more common cancers continue to be enacted two decades since they were proposed.

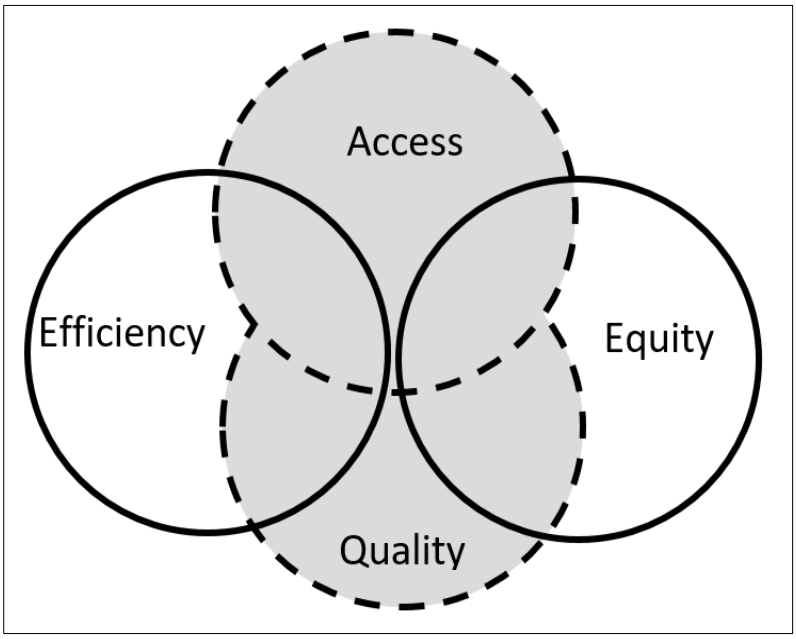
Although the majority of Calman and Hine recommendations had the full support of health professionals, they were only fully realised after the first national Government strategy on cancer, the NHS Cancer Plan (Department of Health 2000), provided the necessary resources and leadership needed to fully implement the policies (Haward 2006). Since the NHS Cancer Plan, there have been two further Government strategies on cancer; the Cancer Reform Strategy (Department of Health 2007) and Improving Outcomes Strategy on Cancer (Department of Health 2011a). The most recent cancer strategy, Achieving World Class Cancer Outcomes, was however independent of government, and was developed by an Independent Taskforce on behalf of NHS England and five other national arm's length bodies (Independent Cancer Taskforce 2015).

Decisions to reform health services are often met with resistance because they are not only associated with significant expenses and service disruption, but are also perceived as a threat

to the existing workforce or to the institutional culture. However, the pressure to reform may at times be necessary, in cancer care; the increase in cancer incidence and cost of treatment necessitates adoption of cost-effective approaches that do not compromise quality of care, or exacerbate inequalities. Reforms may thereby be considered necessary in order to introduce changes in the system.

All the five cancer strategies endeavour to make improvements in the delivery of services in order to improve cancer outcomes. In so doing, they all propose numerous changes in the commissioning and provision of cancer care. At the heart of these changes are overarching policy objectives that can be broadly categorised into four goals; reducing inefficiencies, improving quality and access and narrowing inequalities. These goals are consistent with the benchmark applied in judging the performance of health systems (Le Grand 1993; Palfrey 2000; The Commonwealth Fund 2010). These four policy objectives however do not operate in isolation as demonstrated in **Figure 2.1**. Equity and efficiency are normally considered to lie at the opposing end of each other. For example, a trade-off ultimately ensues in the attempt of equitably distributing a scarce resource like healthcare. Both equity and efficiency are additionally interlinked with goals to improve quality and access. The inter-relatedness between the different policy objectives will be explored in more detail in subsequent sections of this chapter.

Figure 2.1 – Conceptual framework of the interplay between the four health policy objectives



Another important consideration in the process of reviewing policy statements is that the NHS is a highly politicised organisation that different political parties have use as leverage for swinging the electorate in their favour (Baggott 2007). For example, the Labour administration won the 1997 elections on the back of a commitment to address the under-funding crisis in the NHS (Crinson 2009). Despite the political and societal importance of health policies, their effectiveness and impact on health outcomes is seldom evaluated (World Health Organization 2010; Buse et al. 2012; Walt et al. 2008; Embrett & Randall 2014).

This lack of evaluation of policy impact can be attributed to a number of challenges such as the failure to set up systems of monitoring and evaluation alongside policy initiation (Le Grand 1993). There are also methodological challenges in unpicking the multifaceted causal chains required in identifying and quantifying cause and effect relationships (Buse et al. 2012; World Health Organization 2010). Other challenges include the long time-lags between policy implementation and observation of outcomes, which create difficulties in demonstrating policy effect on outcomes, and may be a disincentive for evaluation (World Health Organization 2010). The mismatch in time frames is yet another challenge; the relatively slow pace of research vs. the rapidity of political decision-making is a barrier to collaboration between policy makers and researchers (World Health Organization 2010). Time conflicts may also exist between the long term nature of policy development and implementation, and the short term nature of some research (Walt et al. 2008). Further, there are conceptual challenges in objectively quantifying abstract factors such as power, values and ideologies that are central to the policy process (Walt et al. 2008; Douglas 1984). Lastly, findings from policy analysis are not always transferable; the analytical process takes into account political, social and economic contexts which might be area specific but my not be generalizable to other areas (World Health Organization 2010).

Despite the difficulties, understanding the impact of government policies in health and assessing whether they achieve their intended goals should be prioritized. This knowledge would aid in informing policy making by linking political ideology with the desired social and health outcomes, it would also inform the debate on the most efficient and effective use of scarce resources (World Health Organization 2010). Some suggested methodologies for evaluating the effect of health policy involve retrospective analyses, which involves piecing fragments of facts together methodically (World Health Organization 2010). Other

recommended methodologies that are frequently employed in humanities and social sciences involve summarising complex processes by use of conceptual frameworks and logic models (World Health Organization 2010; Kelly et al. 2010).

2.1.1 Chapter Objective

This chapter is a retrospective narrative review whereby existing evidence is assessed in order to map the development of policy objectives proposed on improving cancer care in England. Specific focus is given on the policy objective to improve access to cancer services. Alongside access, policy objectives on quality, efficiency and quality are also considered, in recognition of the considerable overlap between access and these other policy objectives. Findings from this review have been used to shape the research questions, and to provide the policy context in the analytical Chapters Three to Six.

The chapter is divided into three sections; the first section describes the methodology used in reviewing the evidence. The second section summarises the progress on the aforementioned objectives during the period of study, this section also provides some narrative of how progress may have been influenced by the policy making process, and offers some reflection on the interrelationship between access and the other three objectives. The last section gives a summary of the key findings, and offers some thoughts on the direction on future policies on access to drive better cancer outcomes.

2.2 Methodology

Key policy documents on cancer have been reviewed in order to identify the overarching objectives of cancer policy, and the approach to policy implementation. Other sources of evidence have also been reviewed to assess the progress to date of the identified objectives. These sources of evidence include peer reviewed publications, books, policy opinions, expert analyses and reports from leading health policy charities and Think Tanks such as the King's Fund, Cancer Research UK and Macmillan Cancer Support. In addition, the findings are supplemented by quantitative analysis of existing datasets where the data is available (Buse et al. 2012).

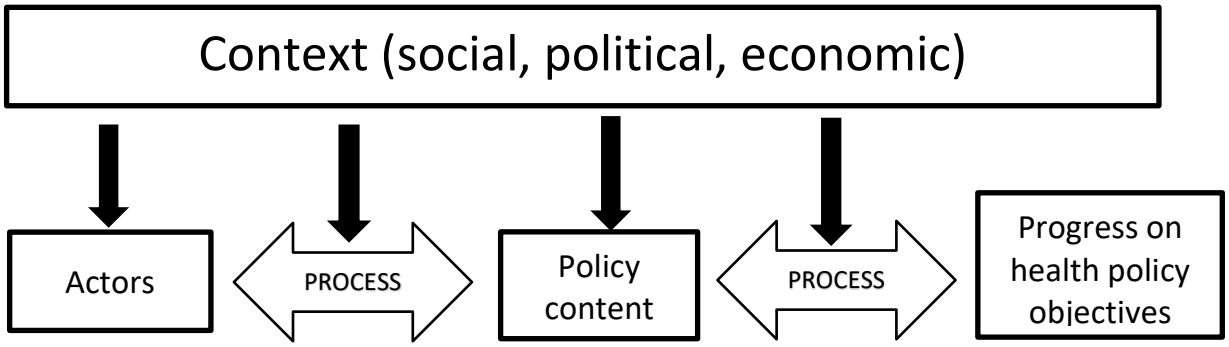
The review of literature begins by identifying the outcome of interest and works backwards to trace potential influencers along the way. This approach has been suggested as a useful means

of yielding insights into the outcomes associated with policies implemented at population level (World Health Organization 2010). The approach is also recommended in analysis of policy where true experiments cannot be carried out, and where there are no control groups (World Health Organization 2010). One major limitation to this methodology is that it is susceptible to observation bias which may lead to contradictory findings, and may make the findings unattractive to decision makers (World Health Organization 2010). An example of observation bias is when personal values influence the analysis, the research question and/or the findings. Use of multiple sources may help improve the validity of the findings and minimise such bias (Buse et al. 2012). In this narrative review, qualitative findings from secondary sources have been supplemented with the quantitative analysis of trend data, where possible.

The study period covered in the review coincides with the period covered by the national policies on cancer in England; beginning with the Calman and Hine report written in 1995, to the most recent strategy on cancer developed by the Independent Taskforce that was published in 2015. **Table 2.1** provides a brief summary of the policy documents reviewed in relation their approach on improving access, narrowing inequalities, reducing inefficiencies and improving quality. This summary (**Table 2.1**) gives a glimpse of how these objectives have been translated into policy and some direction on implementation. The content in **Table 2.1** has been explored in more depth in the rest of this Chapter where policy statements are reviewed alongside secondary sources to help identify any levels of success of failure.

Some understanding of the policy making process is important in order to help with understanding why some national policies meet their objectives and others do not. Policies are akin to a 'web of decisions' (Crinson 2009) in recognition of the challenges encountered in the process of making these decisions. This process of decision making takes place in a complex environment (context) of competing goals (content) and involves multiple influencers (actors) (Buse et al. 2012). The interaction between these different factors determines the success or failure of policy implementation and of achieving the intended objectives. These relationships are conceptualised in **Figure 2.2**.

Figure 2.2 - Conceptualising the influence of the policy process on health policy objectives



Source: Adapted from Buse et al, 2012.

In this conceptual framework, context indicates the prevailing systematic factors such as social, political and economic local factors that may have an impact on the making or implementation of health policy. Contextual factors may be in the form of 'situational' factors, such as an increasingly elderly population. They may also be structural factors such as the prevailing political or judicial system, or may come in the form of cultural factors such as attitudes that may influence the acceptance, access or delivery of health interventions (Buse et al. 2012).

Actors, as shown in **Figure 2.2,** are individuals or groups, who participate in the policy process, and have a varying influence based on their power and interest (Alford 1975). Actors in healthcare have in the past been broadly categorised into three groups; 'professional monopolisers' who control medical knowledge, 'corporate rationalisers', who plan and finance health care and 'equal-health advocates' who represent an alternative viewpoint and/or demand improvements in health services (Alford 1975). Decisions in the making of health policy are based on ongoing negotiations amongst actors (Alford 1975). Over the years, there have been changes in terms of the number of actors and the roles they represent that has introduced important paradigm shifts in terms of the assertiveness and the competition amongst actors. One notable change is in the loss of the medical profession's economic and political autonomy, and the corresponding rise in a patient-driven service where patients play an increasingly active role in their healthcare (Crinson 2009; Klein 2006; Borras et al. 2014). In cancer care, this paradigm change can be broadly summed up as a shift from a disease-focused management to a patient-centred approach, where more attention is given to psychosocial aspects, quality of life, patients' rights and empowerment (Borras et al. 2014).

Process **(Figure 2.2)** refers to the way in which policies are initiated, developed, negotiated, communicated, implemented and evaluated (Buse et al. 2012). The policy making process is an iterative one that involves several stages, with the key ones being; problem identification, policy formulation, option analysis, policy implementation and evaluation (Buse et al. 2012). These processes react to contextual changes and influences from the actors. The example below demonstrates how this framework might have worked in the context of the recommendations proposed by the Calman and Hine report

Context**:** - Changes in delivery of cancer services in the UK were driven by the social, political and economic climate of the 1990s. There was increasing public and political interest in improving the worse cancer outcomes in England in comparison to other wealthy countries. Poor outcomes were thought to be driven by funding cuts in the NHS and by the 'postcode lottery' in access to services (Haward 2006).

Actors**:** - The recommendations were drafted by the 'Expert Advisory Group on Cancer' that was chaired by the most senior advisors on health (Chief Medical Officers (CMO) in England and Wales) and supported by a selected group of 12 health professionals. The group also sought input from a national consultation exercise which contributed to over 300 responses (Calman & Hine 1995; Haward 2006).

Content: - The report set out principles for cancer care in England and Wales. The key recommendation was a new structure of cancer services to ensure that the benefits of specialised care were available to all patients. The authors purposely kept the report broad in scope and refrained from specifying costs; references to cost might have posed serious risks to the publication of the report in view of the political climate of the day (Haward 2006).

Process: - There was general professional consensus of the recommendations proposed by the Calman and Hine report. But despite this, full implementation of the policies was difficult to achieve. The key setbacks to implementation were a shortage of manpower and resources, the loosely defined objectives, and a lack of national monitoring and accountability (Haward 2006; Rachet et al. 2009). Full implementation was only achieved after a change in the political climate. The new government incorporated the

Calman and Hine recommendations in its cancer strategy and allocated resources to deal with the shortfalls in manpower and facilities. To oversee the full implementation of the policies, a national cancer director was appointed and progress was to be monitored against clearly laid out objectives and process targets (Haward 2006) .

Table 2.1- Summary of key objectives of cancer policies in England

Strategy's Timeline	Policy document	Approach to efficiency, quality, equity and access
1995 -2000 **John Major's Conservative Administration**	A Policy Framework for Commissioning Cancer Services (1995) Also known as the Calman - Hine Report	This policy framework was initiated in response to the increase in cancer incidence, the variations in outcomes and treatment, and the huge economic consequences resulting from cancer. The Chief Medical Officers for England and Wales put forward the following main recommendations that are relevant to this review; - To minimise inequalities in access to diagnosis and treatment - To ensure the highest quality of care that would be achieved by increased specialisation - A change in the commissioning of cancer services whereby cancer units and cancer centres would provide an integrated network of care. Cancer units would manage common cancers while the management of rare cancers and provision of specialist treatment such as radiotherapy would be provided by Cancer Centres
2000 – 2006 **Tony Blair's Labour Administration**	NHS Cancer Plan; A plan for action, a plan for investment (2000)	This strategy incorporated the Calman and Hine recommendations on developing a national plan that would deliver improvements in all aspects of cancer care. The strategy's main commitments that are relevant to this review were as follows; - A funding commitment of an extra £570 million a year to modernise cancer services and offset years of underfunding. This would pay for additional services in order to end postcode lottery in service provision - A move from the 'internal market' model to a new model where power was devolved to Primary Care Trusts. Central Government will still have a role of setting standards, monitoring performance and system inspection. - The introduction of performance monitoring in order to improve quality. Targets would also help monitor progress; for example, the national inequalities targets would monitor areas such stop smoking services that were set up to reduce social-economic inequalities by targeting manual workers. - Improved access would be achieved by introducing targets on waiting times for diagnosis and treatment; these include a maximum one month of waiting time from urgent referral for suspected cancer to treatment
2007 – 2010 **Gordon Brown's Labour Administration**	Cancer Reform Strategy (2007)	The Cancer Reform Strategy built on the momentum of the Cancer Plan to enhance the proposals developed by the Cancer Plan. In this respect, these two strategies are not radically different. The main proposal set out by the Cancer Reform Strategy are;

		- In order to improve outcomes and reduce inequalities as set out in the previous strategy, the Cancer Reform Strategy needed access to good quality information and intelligence. This marked the establishment of the National Cancer Intelligence Network (NCIN) - Cancer Networks were established so as to help deliver more value for money by strengthening commissioning, the networks would do so by coordinating services and fostering collaborations across organisational boundaries - The National Cancer Equality Initiative (NCEI) was established to help reduce inequalities in treatment and outcomes by helping to develop research proposals on cancer inequalities, to test interventions and to advise on policy development - The National Awareness and Early Diagnosis Initiative (NAEDI) was launched in recognition that late diagnosis is a major contributing factor to poor cancer survival rates in the UK. NAEDI would help coordinate activities to help increase symptoms awareness and encourage earlier presentation.
2011 – 2015 **David Cameron's and Nick Clegg's** **Conservative and Liberal Democrats Coalition**	Improving Outcomes, a Strategy for Cancer (2011)	The strategy was preceded by an economic recession and was enacted alongside a major reform of the English health services. Some of the policy content and approach to implementation were ideologically different from the Cancer Plan and Cancer Reform Strategy in the following ways; - The strategy had a significant emphasis on efficiency savings; the 2011/12 NHS Operating Framework aimed to achieve up to £20bn efficiency savings within a period of four years - The government challenged the NHS to meet efficiency goals without compromising on quality, this was to be delivered under the Quality Innovation, Productivity and Prevention (QIPP) programme. The resources saved would be invested back into services to improve quality. - It was expected that information transparency would help scrutinise quality of care and reduce inequalities. Focusing activity on the most vulnerable was also deemed to have the greatest scope for improving outcomes. - Initiation of a bottom-up-approach' where individuals, groups and communities were encouraged to play a greater role in participation, raising awareness and in creating partnerships, a concept referred to as 'big-society' - There was a big push to focus on outcomes and abolish performance measures and targets such as waiting times. However waiting times were retained following a review that showed an overwhelming public and professional support

2015 – 2020 **David Cameron** **Conservative Administration (up to 2016)** **And** **Theresa May's Conservative Administration (present)**	Achieving World Class Cancer Outcomes. A Strategy for England 2015 - 2020	This strategy is unique as it was developed by an Independent Taskforce on behalf of arm length bodies. This independence from government strikes similarities with the Calman and Hine report. The following are its key proposals; - Similar to the Calman and Hine report, the strategy re-emphasises the importance of striking a balance between improving quality through specialisation and ensuring equitable access to services - The importance of general practitioners in improving survival was re-emphasised. This would be achieved by reducing late diagnosis and improving optimal access to services. The roll-out of Multidisciplinary Diagnostic Centres (MDCs) that offer same day testing on relevant symptoms is proposed. - Emphasis on improving patient experience with the objective of establishing patient experience to be on par with clinical effectiveness and safety. - A recognition of the shortfall in the investment that is required to offset current workforce and equipment deficits. - An overhaul of the current commissioning to develop services that are better co-ordinated along the care pathway. This would improve earlier diagnosis, reduce costly emergency admissions, and deliver efficiency savings. - A recognition that changes in commissioning and improving patient experience in the most marginalised would reduce inequalities in access and variations by sub-groups (socio-economics, ethnicity, age).

2.3 Access to services

All the four strategies recognise that optimal access to cancer services is crucial to improving cancer outcomes and reducing inequalities. Access is intrinsically linked with the other three healthcare objectives assessed in this review. As an example, timely access is advocated as a means of improving quality, and which was a key driver to the introduction of cancer waiting time standards (waiting times will be covered in more detail subsequent sections). Access is also a key ingredient in measuring health equity; a common definition of equity in health is 'equal access for equal need' (Allin et al. 2007; Oliver & Mossialos 2004). Similarly, healthcare utilisation is a commonly applied metric in estimating productivity in health (Office of National Statistics 2015b). The extent of the overlap between access and these other policy objectives is explored in more detail in sections 2.4, 2.5 and 2.6 of this chapter.

The multi-dimensional nature of access makes it challenging to define, to measure and to monitor. Access can take three interconnected dimensions; affordability (ability to pay), acceptability (social-cultural) and availability (physical/locational or appointments) (Thiede & Akweongo 2007). In the UK, the introduction of the NHS ensured universal access to healthcare for all, hence removing barriers in access related to affordability. This universal access to healthcare has been accorded support by the public, professionals and even politicians; despite differences in political ideologies in the latter. This support has had the advantage of safeguarding free accessibility. However, one dis-benefit of the popularity of the NHS is that is has become a 'political party football' and is often a major issue for political debate often with the goal of achieving election victory (Baggott 2007). Nevertheless, the NHS has generally been spared from the extensive privatisations that took place in other nationalised industries during the 1980s (Baggott 2007), and this can be credited to the support accorded to a national health service that offers free and universal access (Baggott 2007).

The acceptability dimension of access refers to how services are perceived by individuals and communities, and how services accommodate patients' beliefs and attitudes (Thiede & Akweongo 2007). These attitudes may be influenced by differences in demographic characteristics such as age, sex, ethnicity, language, cultural beliefs and socio-economic status or by geographical location. The availability dimension of access encompasses both spatial 'geographical' or aspatial 'non-geographical' perspectives summarised in **Table 1.1.** The monitoring of access to health care in the English NHS is dominated by the 'non-geographical'

dimension of accessibility with a specific emphasis on waiting lists and waiting times (Godden & Pollock 2009). Cancer waiting times were introduced by the Cancer Plan (Department of Health 2000) as a means of promoting more rapid access which was thought to improve cancer survival. **Table 2.2** summarises the cancer waiting time that were initially proposed in 2000 by the Cancer Plan and which later on evolved following the proposals developed by the Cancer Reform Strategy. Interestingly, the subsequent cancer policy published in 2011, Improving Outcomes (Department of Health 2011a), advocated for a disbandment of all process measures, including cancer waiting time targets, and in their place proposed a greater focus on outcomes measures (Department of Health 2011b).

Table 2.2 - Summary of cancer waiting times targets

- Maximum two-week wait for first outpatient appointment for patients referred urgently with suspected cancer by a GP
- Maximum one month wait from urgent GP referral to treatment for acute leukaemia and children's and testicular cancers
- Maximum one month wait from date of decision to treat to first treatment for breast cancer
- Maximum two month wait from urgent GP referral to first treatment breast cancer
- Maximum one month wait from date of decision to treat to first treatment for all cancers;
- Maximum two month wait from urgent GP referral to first treatment for cancer
- Maximum 31-day wait for subsequent treatment where the treatment is surgery
- Maximum 31-day wait for subsequent treatment where the treatment is an anticancer drug regimen
- Maximum 62-day wait from a consultant's decision to upgrade a patient's priority to first treatment for all cancers
- Maximum 62-day wait from a referral from an NHS screening service to first treatment for all cancers
- Maximum two-week wait for first outpatient appointment for patients referred with breast symptoms, where cancer was not initially suspected

Source: Department of Health Review of Cancer Waiting Time Standards, 2011

2.3.1 Access to early diagnosis services

All the five strategies reviewed recognise the importance of access to services for the earlier detection and earlier diagnosis of cancer. The Cancer Plan extended the age range of access to breast cancer screening to include women aged 65 to 70, with availability for request for those over 70 years of age. Access to early diagnosis was also prioritised in the Cancer Reform Strategy and culminated to the establishment of the National Awareness and Early Diagnosis Initiative (NAEDI). NAEDI's advocacy work has pushed for an increased recognition in the role of GPs in improving cancer outcomes. The two most recent cancer strategies, Improving

Outcomes Strategy and Achieving World Class Outcomes, indicate a significant shift from the focus on cancer treatment to giving more attention to early diagnosis. This shift has been driven by the recognition that later diagnosis in England is a major determinant for poor survival rates, and that between 10,000 and 11,000 deaths could be avoided every year by earlier diagnosis (Department of Health, 2011a; Independent Cancer Taskforce, 2015). The current early diagnosis initiatives are piloting the efficacy of alternative diagnostic pathways to be prioritised in areas where GP access is poor; these will include self-referrals and referral pathways from other primary health professionals besides GPs (Independent Cancer Taskforce 2015). Another proposed development in the referral pathways is the introduction of multi-disciplinary diagnostic centres (MDC) which are single testing locations offering multiple tests on symptoms on the same day. In addition to offering diagnostics for more typical symptoms, MDCs would also offer diagnostics for atypical symptoms; thereby resolving some of the challenges associated in determining appropriate referral pathways for non-specific symptoms that maybe related to cancer (Independent Cancer Taskforce 2015).

2.3.2 Policies on geographical access

The geographical accessibility of cancer services was a central theme in the Calman and Hine report. The authors recommended that, *'all patients should have access to a uniformly high quality of care wherever they may live, and that this care should be provided as close to the patient's home as is compatible with high quality, safe and effective treatment'* (Calman & Hine 1995) (pg. 6). The authors also recommended service reconfiguration whereby cancer units would focus on the management of common cancers, and specialised cancer centres would provide management for both common and rare cancers as well as offer specialised diagnostics and treatment (Calman & Hine 1995). A positive outcome of increased specialisation of cancer services in England has been the improvement in cancer survival (Oliphant et al. 2013). However, this may have inadvertently exacerbated inequalities in access and subsequently in outcomes. In particular, specialist hospitals tend to be concentrated in large cities which means some patients have had to travel further to access cancer care (Gatrell & Elliott 2015).

Despite the trade-off that results in attempting to meet somewhat competing policy objectives such as the simultaneous improvements in quality and access, three of the five cancer strategies do not address the obvious but inadvertent consequences of increased specialisation on geographical accessibility to services. These three strategies also coincidentally happen to be

the Government led strategies that were proposed between 2000 and 2011; the Cancer Plan, Cancer Reform Strategy, and Improving Outcomes Strategy on cancer (Department of Health 2000; Department of Health 2007; Department of Health 2011a). This shortcoming has been rectified in the most recent strategy, Achieving World-Class Cancer Outcomes (Independent Cancer Taskforce 2015). This recent strategy shares similarity with the Calman and Hine report in recognising the importance of geographical accessibility in achieving optimal utilisation of diagnosis and treatment services. The strategy also reiterates the importance of balancing service specialisation, against creating variations in access that may disadvantage patients who travel the farthest (Independent Cancer Taskforce 2015). **Table 2.3** lists the four recommendations set out in this most recent strategy in relation to reviewing, updating and implementing the evidence on geographical access to cancer services. Thus far, the recent strategy has been the most comprehensive in describing issues pertaining to poor geographical accessibility of cancer services and in suggesting a course of action.

Table 2.3 - Cancer strategy recommendations related to geographical access to services

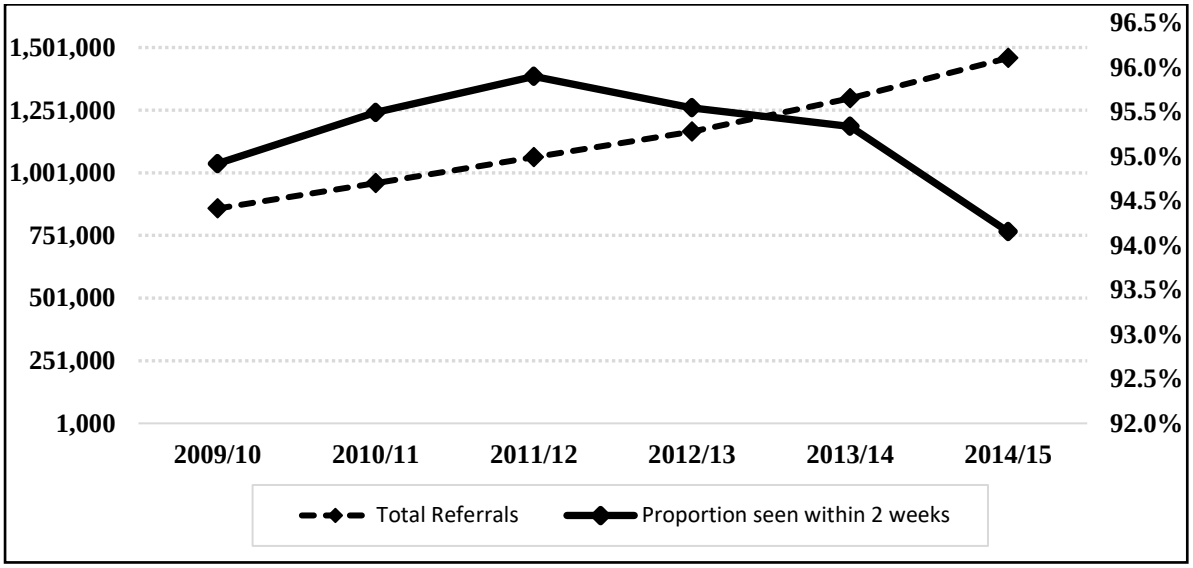
Recommendation 26: CRGs should regularly evaluate emerging evidence to determine whether service configuration for surgery merits further centralisation and to advise NHS England accordingly.
Recommendation 27: NCIN should undertake an up-to-date evaluation of the impact on cancer outcomes of patients living different distances from a cancer Centre. Historical data suggested that longer distance from a Centre results in lower probability of curative treatment.
Recommendation 29: From autumn 2015, NHS England should commence a rolling programme of replacements for LINACs as they reach 10-year life, as well as technology upgrades to all LINACs in their 5th year. All LINACs that are already ten years old should be replaced by the end of 2016 at the latest. This should be driven through a national capital fund, overseen in the first 2-3 years by a small implementation team, who will also need to ensure that equipment is geographically distributed to serve local populations optimally.
Recommendation 43: NHS England, working through the CTYA Clinical Reference Group should: • Consider whether paediatric treatment centres should be reconfigured to provide a better integrated network of care for patients and families. • Establish clear criteria for designation and de-designation of treatment centres for TYA patients. • Ensure that any transition gap between children's' and adult services is addressed. • Assess impact of proposals on travel times for families.

Source: Achieving world-class cancer outcomes, 2015

2.3.3 Progress on the objective to improve access

Monitoring timely access to cancer services in England has been by measured by how rapidly patients referred with suspected cancer receive a consultant appointment (see **Table 2.2**). The national operational standard for this target is for 93% of the referred cancer patients to have their first outpatient attendance within two weeks of referral (NHS England 2015). These standards take into account that some local variations at provider level will exist based on provider's case mix or patients' choice (NHS England 2015). **Figure 2.3** shows that at a national level this target has been consistently met. The proportion of patients seen within two weeks of a GP referral rose between 2009 and 2012, but has been in decline since (**Figure 2.3**). This decline may be explained by the increase in referrals through the two-week wait route (**Figure 2.3**, dashed line). Two things may be happening concurrently, firstly, it is possible that waiting time targets have increased utilisation of treatment as GPs increase the number of referrals into secondary care. Secondly, this increase in referrals may make it more difficult to meet the waiting time target as staff and other resources such as workforce and equipment may have remained static.

Figure 2.3- Two week wait from GP urgent referral to first consultant appointment

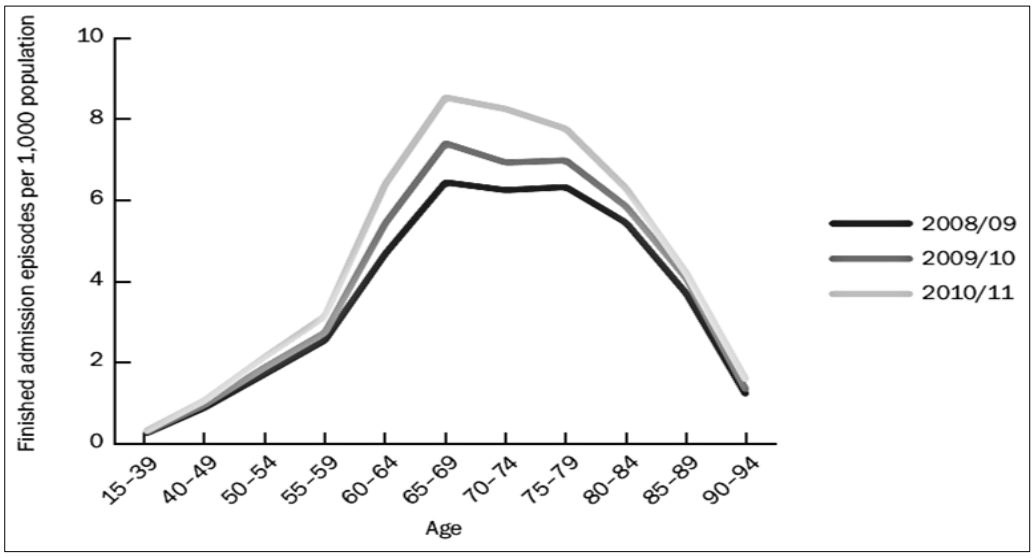


Source: NHS Cancer Waiting Time Statistics. Data collected before December 2008 is not comparable due to changes in how the data is collected

The evidence on the effectiveness of waiting times reductions on cancer mortality is so far inconclusive (Neal 2009). One study has shown that decreasing waiting times from diagnosis to surgery has little impact on breast cancer survival (Redaniel et al. 2013), whereas other studies have reported a 'waiting time paradox' whereby patients with short diagnostic intervals have higher mortality than patients with long diagnostic intervals (Ramos et al. 2007; Rupassara et al. 2006). This paradox may be explained by the fact that patients with poor prognosis are given medical priority (Tørring et al. 2011) or it could also be due to differences in tumour progression; symptoms in a fast growing tumour are likely to progress rapidly leading to faster diagnosis but poorer outcomes (Neal 2009). Despite the lack of consensus on their clinical effectiveness on cancer survival, waiting times policies were retained in the 2010 health reforms because of the perceived psychological benefits they have on patients. There was a unanimous view from patient groups, cancer charities, and health professionals that the cancer waiting time standards have helped to drive service improvement and have reduced patients' anxiety related to delays with diagnosis and treatment (Department of Health 2011b).

When access to healthcare is viewed from the perspective of 'utilisation', notable variations that may be related to different attitudes towards health and illness, or to differences in clinical practice have been reported. As an example, there is increasing evidence to suggest that older patients are less likely to receive the most clinically effective treatment for their cancer, this may be linked to the poorer outcomes reported in older people (Royal College of Surgeons of England 2012; Macmillan Cancer Support 2012). **Figure 2.4** shows a consistent decline in the rate of colorectal excision procedures after the age of 69 years. This decline in treatment rates does not correlate with the increased incidence of colorectal cancers and diverticular disease in older patients (Royal College of Surgeons of England 2012). Rather, the differences may be explained by a combination of factors such as presence of comorbidities, patient choice or clinical attitudes towards treating older patients; which include misunderstanding of the toxicities and side effects of treatments, or even challenges in providing appropriate community support for older cancer patients (Department of Health 2010).

Figure 2.4 - Rate of elective colorectal excision procedures by age



Source: The Royal College of Surgeons and Age UK, 2012 ©. Reproduced with permission

With regards to achieving geographical accessibility, there is ample evidence demonstrating the association between geographical accessibility to secondary services and poorer outcomes (Campbell et al. 2001; Campbell et al. 2000; Jones et al. 2008; Crawford et al. 2009; Sauerzapf et al. 2008). There is also some evidence on the influence of rurality on health seeking behaviour such as consultation with the GP, or reporting symptoms (Haynes & Bentham 1982; Emery et al. 2013). Despite this, there is presently no national indicator to measure or monitor progress on geographical access to health services and so it is not known to whether there has been any improvements in achieving equality in access to all regardless of location, or whether the implications of not achieving equitable access remain a concerning issue.

2.4 Efficiency of cancer services in England

An efficient healthcare system is one that maximizes the quality of care and outcomes with the given resources, and at the same time ensures that investments yield net value over time (The Commonwealth Fund 2010). The simplest measure of healthcare efficiency is productivity, which uses multiple information such as inputs (labour, goods and services), outputs (hospital, GP services), and computes productivity at the desired scale i.e. national, hospital or disease level (Langabeer II & Ozcan 2009; Office of National Statistics 2015b). Measuring efficiency of cancer services at a national level presents several challenges as it is dependent of the availability of reliable data at the disease level, the information required to do this for cancer care in England is not yet readily available.

2.4.1 Commissioning of cancer services

The commissioning process can be described as a process of developing, planning, purchasing and coordinating the delivery of health services in order to improve population health (Crinson 2009). Commissioning therefore determines whether efficiencies or productivity will be accrued; as health commissioners aim to make the most optimal use of health resources to achieve the intended outcomes (National Audit Office 2010b).

The period covered in this review has seen major changes in healthcare commissioning. To begin with, the authors of the Calman and Hine report recognised the importance of informed commissioning, thus aptly referring to this report as 'A Framework for Commissioning Cancer Services' (Calman & Hine 1995). Despite this explicit reference to commissioning, this report steered clear of any explicit references to money, due to the risk in publication posed by the political climate of the day (Haward 2006). During the 1990s, and at around the time of publishing the Calman and Hine report, the Conservative Government had introduced a significant change in how NHS funds were utilised. The new system was referred to as 'internal market' and it divided the NHS into 'purchasers' such as GP fundholders and health authorities and 'providers' such as hospitals. Purchasers were given a budget which they could use to secure services for their population, and 'providers' were to compete for these services (Baggott 2007). This system was expected to generate efficiencies as providers competed for business, there are some accounts of increased productivity measured by changes in activity relative to resources, which increased by around 7 per cent between 1991 and 1996. On the other hand, there is also evidence of inequities that stemmed from variation in access to hospital services between patients of fund-holders and non-fundholding GPs (Baggott 2007).

GP fundholders were replaced by Primary Care Trusts (PCTs) when the Labour Party came into power in 1997. The Government sought to increase efficiencies by developing a system of incentive payment to the more efficient providers, this system was referred to as a 'supplier market' (Crinson 2009). PCTs were responsible for commissioning cancer services, via a lead clinician on cancer, whose role was to contribute to developing cancer networks that would enable better coordinated care along the care pathway (Department of Health 2000). PCTs were also to provide logistical support to GPs to enable them to effectively plan the needs of their population (Crinson 2009). Cancer Networks in turn were to support PCTs in their commissioning role by helping maintain dialogue with clinical teams and users (Department

of Health 2007). The incoming Labour Government supported the Calman and Hine proposals fully, however, the full implementation of major recommendations such as increasing specialist cancer care required a balance between the critical mass required to achieve optimal care (Department of Health 2007), equity in access (Munro 2001), and efficient collaboration across care pathways (Department of Health 2007). This was to be achieved by commissioning services across a network based on care pathways as opposed to organisational boundaries; Cancer Networks were best placed to do this because they provided the required critical mass of approximately one to two million people (Department of Health 2007).

The commissioning landscape changed once more in 2010 when the coalition Government transferred the function of PCTs to the GP commissioners under the newly formed Clinical Commissioning Groups (CCGs). At a national level, NHS England was also established to oversee the commissioning of specialised services such as diagnostics and treatment of rare cancers. Public Health England was also established to oversee services that require national level coordination such as cancer screening. Efficiency savings were to be realised under the Quality Innovation Productivity and Prevention (QIPP) challenge (Department of Health 2011a). Although QIPP had been established by the Labour administration under the umbrella of NHS Institute for Innovation and Improvement, its role was strengthened by the Coalition administration, and the programme was rebranded as the NHS Improving Quality. Under QIPP, NHS organisations were encouraged to demonstrate efficiency savings that had been re-invested back into services in order to improve quality (Department of Health 2011a).

The Improving Outcomes Cancer Strategy also recognised the role of Cancer Networks as specialist advisers to commissioners, however, it also hinted at changes to the networks, ranging from their complete eradication, to a reduction of their remit to early diagnosis only (Department of Health 2011a). The intention to bring changes to the networks was apparent when GP commissioners were given freedom to obtain commissioning advice from elsewhere (Department of Health 2011a). This move was opposed by many who recognised the contribution of Cancer Networks in improving outcomes, in maintaining an integrated service across the entire pathway, and in ensuring service users are meaningfully involved in the whole commissioning cycle (All Party Parliamentary Group on Cancer 2011; MacMillann Cancer Support 2011). The landscape of the Cancer Networks has been in constant evolution, their role was largely retained in 2013 but under the umbrella of newly formed Strategic Clinical

Networks (SCN) (NHS 2012). SCN would build on the strength of the Cancer Networks but would cover a wider remit of disease areas, thus ensuring commissioners would have a broad range clinical expertise (NHS 2012). The most recent cancer strategy published in 2015 has proposed the establishment of Cancer Alliances that are in many ways reminiscent of the abolished Cancer Networks. These Alliances will bring together key partners at a sub-regional level in order to drive improvements and support integrated care pathways (Independent Cancer Taskforce 2015), as well as provide strategic support and leadership (MacMillan Cancer Support 2015).

2.4.2 Funding in cancer services

Labour and Conservative Governments have had different approaches towards investing in health services. The Cancer Plan, produced under the Labour administration, had an unparalleled commitment to investment in comparison to the subsequent government strategies on cancer. The Labour administration was responding to concerns of poorer survival in England in comparison to other European countries. There were also concerns about large inequalities in cancer mortality, and on less funding for cancer care in comparison to other European countries (Department of Health 2000). The Labour Government responded by scaling up England's spending by an estimated £570 million a year, it was expected that this extra funding would correct decades of neglect and under-investment by the previous administration (Department of Health 2000). The funding was aimed at tackling the deficit in the cancer workforce, investing in cutting edge diagnostic equipment, and strengthening research (Department of Health 2000).

Subsequent cancer strategies have been much more conservative on their approach towards spending. For instance, the Cancer Reform Strategy, whilst re-affirming continuity in vital investments, also emphasised the monitoring of variations in spending in order to improve efficiencies, and reiterated the importance of cancer networks as advisors to cancer commissioners (Department of Health 2007). Efficiency savings was once again emphasised in the Improving Outcomes Strategy on Cancer. The concern over inefficiencies coincided with a period of low economic growth that followed a major financial recession, but it was also informed by ideological differences; as an example, the incoming Coalition Government was driven by a belief that the Labour Government had been prolifically wasteful (Conservative

Party, 2010)*. These differences in ideology are exemplified by the Improving Outcomes Strategy's challenge to the NHS to deliver efficiency savings of £20billion within four years (Department of Health 2011a). These savings were deemed necessary in the face of rising cancer incidence and increasing demand for expensive treatments. However, implementing such enormous cost savings measures without compromising quality presents a considerable challenge to a health service that is already overstretched.

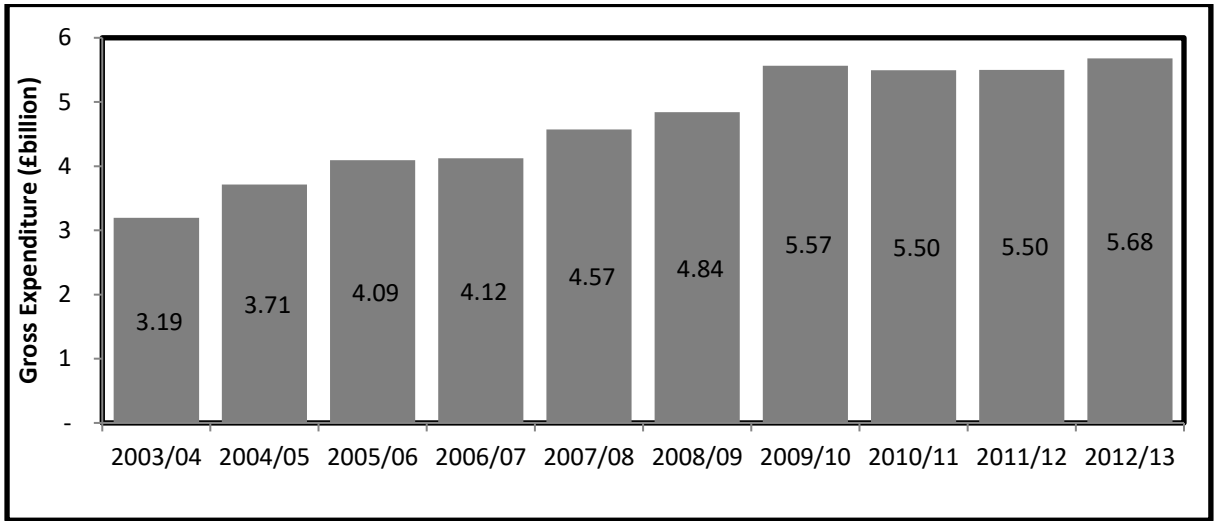
The gross NHS expenditure on cancer over the past decade is shown on **Figure 2.5**, which reveals a steady increase in spending between 2003/04 and 2009/10. Spending however plateaued between 2010 and 2012 before continuing to increase slightly in 2012/13. **Figure 2.5** suggests that the Cancer Reform Strategy's (Department of Health 2007) pledge to cut unnecessary spending from 2007 onwards may not have had any impact on the total spend, however, the spending cuts announced in the 2010 NHS reforms may have had some impact on cancer expenditure. Analysis of the NHS expenditure statistics shows that real expenditure on cancer rose by 2.9% in the 2008/09 financial years, and by 11.2% in 2009/10 (Cancer Research UK 2012). However, there was a 2.6% real terms decrease in cancer spend in 2010/11 (averaging an estimated 3.4 per cent per population head) (Cancer Research UK 2012). This decline was as a result of low nominal growth in the total NHS expenditure, a reduction in the proportion of the NHS budget allocated to cancer, and high inflation (Cancer Research UK 2012). These patterns observed in cancer spend are observed across the entire NHS expenditure; healthcare expenditure grew strongly between 1997 and 2009 with an annual average growth rate of 8.1% but growth slowed after 2009 with an annual average growth rate of 1.4% between 2009 and 2011 (Office of National Statistics 2013a).

Healthcare spending on cancer is associated with better health outcomes, even after controlling for need (to factor in that areas with higher need have more expenditure) (Centre for Health Economics 2007). Perhaps in recognition of this association, the most recent strategy on cancer observes that offsetting the current spending deficit will be required in order to deliver a modern high quality service (Independent Cancer Taskforce 2015). The strategy proposes necessary investments such as; an increase in workforce, updating radiotherapy equipment, improving access to new cancer treatment and allocating more funds for cancer research

* There are 19 mentions of 'waste' in the 2010 Conservative Manifesto

(Independent Cancer Taskforce 2015). The total cost of meeting the recommendations set out in the this strategy is estimated as £400m per annum (Independent Cancer Taskforce 2015).

Figure 2.5 - Programme budgeting aggregate PCT expenditure for England for cancers and tumours – 2003/04 to 2012/13



Source - DH Programme budgeting, 2014

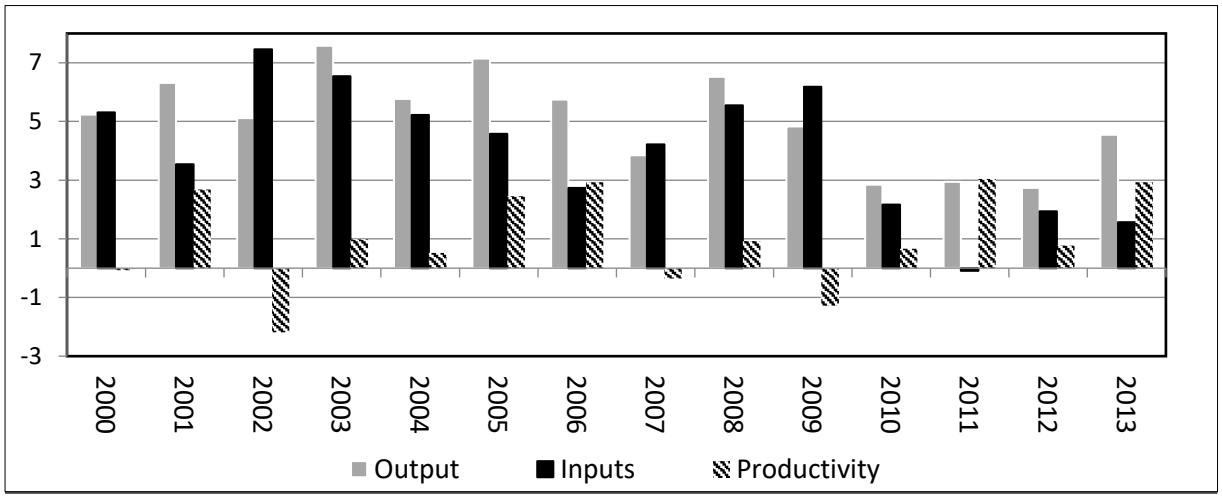
2.4.3 Delivering value for money

There are methodological issues in ascertaining value for money from investments made on cancer services. The Office of National Statistics methodology uses productivity estimates (Office of National Statistics 2007) which estimate the amount of output which is produced for each unit of input. These estimates can be criticised as they do not measure value for money, nor wider performance. As an example, productivity estimates cannot determine whether inputs were purchased at the lowest possible cost or whether the desired outcomes were achieved (Office of National Statistics 2015b). Nevertheless, productivity estimates measure efficiency up to a certain point, because increasing productivity is a sign of greater efficiency in producing outputs from given inputs (Office of National Statistics 2007). ONS productivity statistics are not disease specific so it is difficult to relate them specifically to cancer services. Also healthcare productivity is measured at UK not England level and so cannot be related to health policies implemented in England. Nevertheless, these ONS productivity statistics are the closest to determining the value of money in the NHS investments over time.

The estimated trend of healthcare productivity since 2000 is shown in **Figure 2.6**. The reduced volume of inputs from 2010 onwards coincides with the QIPP efficiency challenge, which

required the NHS in England to make £20 billion of savings by the end of the spending review period (Office of National Statistics 2015b). Productivity increased in most years, with an annual average growth rate in quality adjusted productivity of 0.8% (Office of National Statistics, 2015).

Figure 2.6 - Growth rates for healthcare output, inputs and productivity, UK 2000-2013



Source: ONS, 2015

There is no definitive evidence to ascertain whether cancer services offer value for money. This is despite the fact that efficiency is a key policy objective in cancer care. An evaluation of the impact of the Cancer Reform Strategy on efficiency found that there may be some measurable improvements in efficiency such as in treating more people as day cases, and in reductions in the length of stay (National Audit Office 2010a). Studies looking at individual aspects of care have shown an association between proactive case management by Clinical Nurse Specialists and increased efficiency savings (Baxter 2011). There is also evidence associating the increase in doctors' specialisation with value for money (Max Bachmann et al. 2003); increases in surgical volume is associated with lower costs, but only up to a specific threshold beyond which higher volume begins to incur higher costs. So far there is no conclusive evidence on the cost-effectiveness of the increasing service centralisation of cancer services (Ke et al. 2012). A counter argument to centralisation is that any benefits such as cost savings on the NHS may be transferred to patients who have to incur the cost of travelling farther for care, additionally, longer journey may reduce the likelihood of compliance with and uptake of treatment (Ke et al. 2012).

2.5 Improvements in Quality

High quality care is care that is effective, safe, coordinated and patient-centred (The Commonwealth Fund 2010). Effectiveness in healthcare is determined by the appropriateness in preventing or in treating a condition, or in controlling chronic illnesses (The Commonwealth Fund 2010). Cancer survival rates are used as a marker of quality of services because better survival is a reflection of improvements in early diagnosis and in effective treatment (Richards 2009). Clinical effectiveness and safety has historically received greater prominence than patient experience, however, the last two cancer strategies have reinforced the importance of using cancer patient experience is as a marker of service quality (Department of Health 2011a; Independent Cancer Taskforce 2015). The most recent strategy goes as far as proposing for patient experience to be given equal parity with clinical effectiveness (Independent Cancer Taskforce 2015).

Information on cancer patient experience in England is collected by the NHS Cancer Patient Experience Survey (CPES) that was established by the Cancer Reform Strategy; earlier cancer patient surveys were conducted before the introduction of CPES, in 2000 and in 2004 and were the basis of the CPES Programme. Cancer patient surveys are now conducted annually and the feedback obtained is expected to help drive quality improvements and thereby improve cancer outcomes. However, evidence suggests that the surveys have had minimal impact in terms of quality improvements (Department of Health 2012a), which has led to endorsements to incorporate the surveys into quality improvements; such as using feedback from patients to inform the design and delivery of services (Department of Health 2011a; Independent Cancer Taskforce 2015). The increasing importance in monitoring patient experience indicates a paradigm shift from a disease focused to a patient-centred approach (Borras et al. 2014; Crinson 2009), and it may be a demonstration of the increasing power of patients as an interest group.

All the five strategies on cancer acknowledged that cancer survival in England lagged behind that of other comparable European countries, thereby identifying improvements in survival as a key policy objective. The Cancer Plan had a bold ambition to deliver the fastest improvement in cancer services in Europe in five years and to match the survival rates of the best European countries by 2010 (Department of Health 2000). The EUROCARE statistics on one year relative survival rates for cancers diagnosed between 1995-1999 and 2000-2007 show that seven years after the Cancer Plan, England was yet to catch up with Sweden (Europe's best)

(**Table 2.4**). However, there has been some progress as England has one of the fastest increase in relative survival in Europe, and this has been increasing at nearly the same speed as that of Sweden (**Table 2.4**).

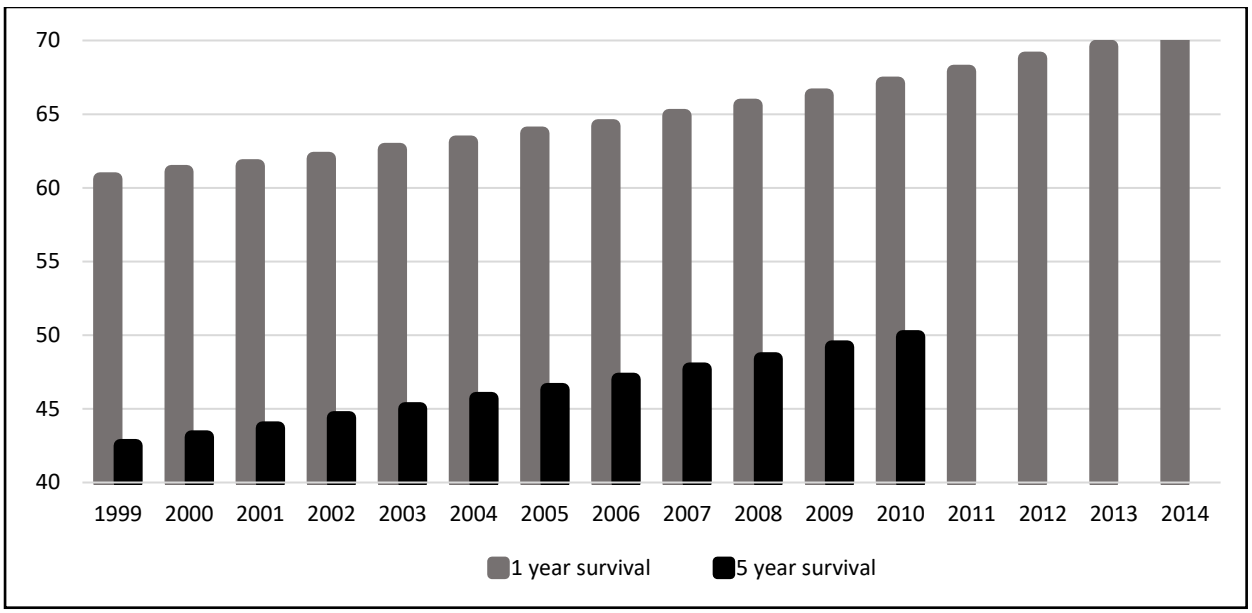
Table 2.4 - One year age standardised relative survival (%) for all malignant neoplasms in adults patients, diagnosed in the 1995-1997 and 2000-2007

1995 – 1999		2000 - 2007		Increase in relative survival
Sweden	76.03	Sweden	81.13	5.10
UK England	63.14	UK England	68.14	5.00
European Average	69.55	European average	72.53	2.98

Source - EUROCARE 4 and 5 Database

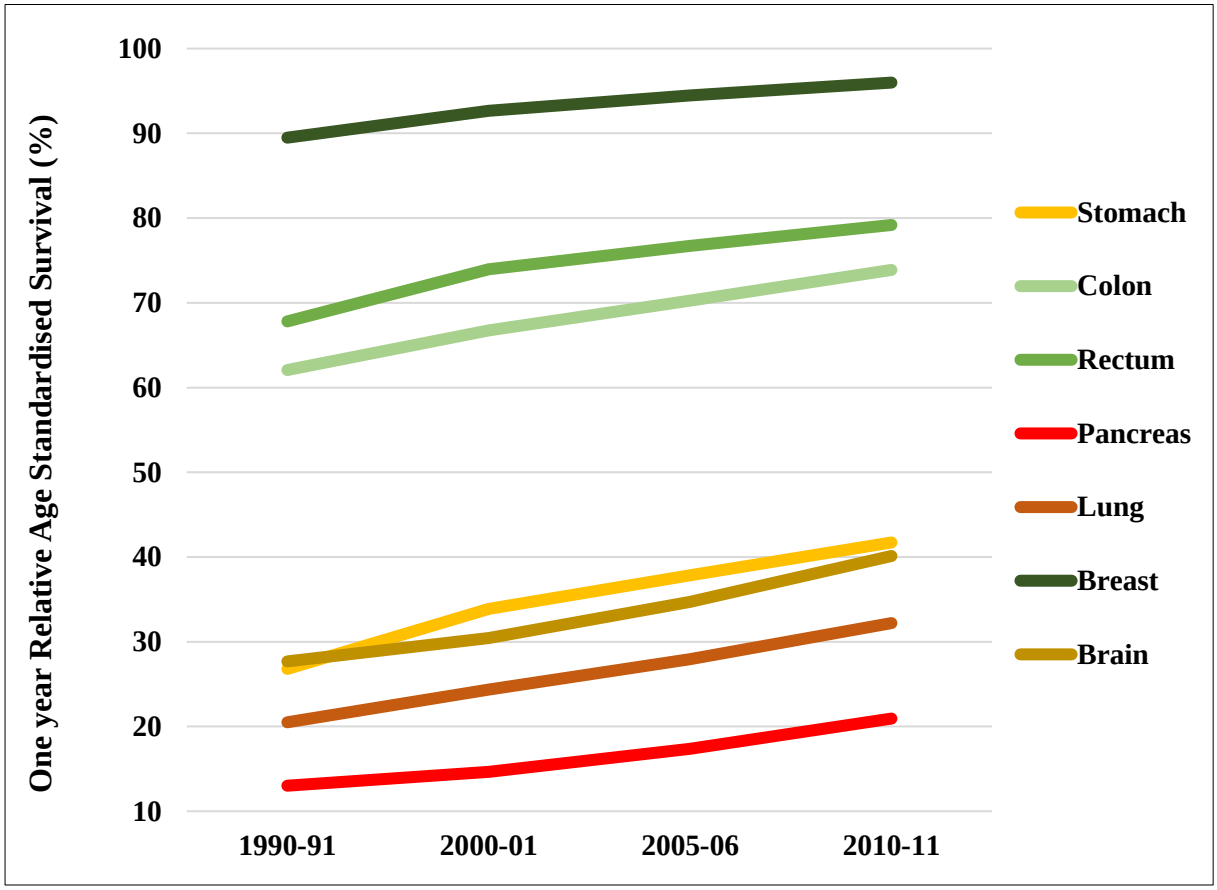
Cancer survival rates in England have been consistently improving for all combined cancer types (**Figure 2.7**). There have also been steady improvements in individual cancer types, although there is a clear survival difference between cancers of good prognosis such as breast, prostate and colon and rectum cancers and cancers of poor prognosis such as stomach, lung, brain and pancreatic sites **(Figure 2.8).**

Figure 2.7 - One and five year survival index for all cancers combined, by calendar year of diagnosis (15-99 years), 2000 – 2014



Source – Office of National Statistics, 2016

Figure 2.8 - Trend in age adjusted one year index of survival (%) for selected cancer sites in adults (15-99 years) in England



Source – Quaresma et al, 2015

2.5.1 Policy impact on cancer survival

There is some evidence showing that the observed increase in cancer survival may be directly attributed to some of the governments' policies on cancer. A comprehensive assessment of the impact of the NHS Cancer Plan on cancer survival rates in England attributed the accelerated rate of increase in one year relative survival to this strategy (Rachet et al. 2009). Survival rates were generally improving before the Cancer Plan and so there were methodological difficulties in ascertaining the contribution of the policy to any improvements in survival. The assessment therefore focused on the acceleration in the survival trend between three distinct periods; 1996 - 2000 (before the cancer plan), 2001 - 2003 (policy initialisation), and 2004 - 2006 (policy implementation), and compared the progress in England with that of Wales. The Welsh national policy on cancer was published six years after the English Cancer Plan and therefore any impact of the Cancer Plan would be determined if survival rates in England accelerated more rapidly

in England than in Wales following several years of latency (Rachet et al. 2009). The study concluded that although cancer survival was very similar in England and Wales, the gains in 1-year survival were more marked in Wales during 1996–2000 and 2001–2003, whereas gains in England were more marked from 2004 onwards. The improvements in Wales were associated with the implementation of recommendations by a report from the Welsh Office (Cancer Services Expert Group 1996) post 1997. Whereas England's survival improvements maybe related to the implementation of the cancer plan (Rachet et al. 2009; Richards 2009).

It is difficult to ascertain which individual policy changes should be attributed to the improvements in cancer survival rates. In England, it is most likely that it is the contribution of the sum of all; service redesign, increased funding, multidisciplinary working, clinical audits, better information being key factors amongst others. There is some evidence to associate increased specialisation (as advocated by the Calman-Hine report and endorsed in subsequent strategies) with improvement in survival; for instance, surgical specialisation has been shown to improve colorectal cancer survival, with survival differences reported in patients treated by specialist vs. non-specialist surgeons (Oliphant et al. 2013).

The association between increases specialisation and survival improvements may be as a result of greater experience amongst specialist surgeons, making them more likely to perform thorough investigations (M Bachmann et al. 2003). Specialist hospitals are also able to offer better clinical care on aspects such as nursing, nutrition and palliation (M Bachmann et al. 2003). Increased specialisation also extends to the use of Clinical Nurse Specialists (CNS) whose utilisation has also led to improvements in quality (Gurzick & Kesten 2010; Moore et al. 2002). Other studies have shown that the emotional support that CNS offer patients is also highly regarded (Liebert & Furber 2004), in addition, the national Cancer Patient Experience Survey found that patients with an allocated CNS gave more positive scores on almost all questions compared to those without (Department of Health 2012a). However, the reported variability in access to specialist treatment and to CNS has important equity implications for patients who are unable to access these services (Campbell et al. 2000; Sauerzapf et al. 2008; Ream et al. 2009; Department of Health 2012a; Independent Cancer Taskforce 2015).

Use of Multidisciplinary Teams (MDTs) has also been championed as a means of improving clinical decision making, although there is lack of consensus on their benefits. Evaluations of

the clinical impact and effectiveness of MDTs conclude that the cost of the meetings are very high but produce minimal clinical impact (Fleissig et al. 2006; Chinai et al. 2013). This has resulted to some recommendations for MDTs to focus on the very complex cases rather than on all cancer patients (Fleissig et al. 2006; Chinai et al. 2013).

Another practice recommended by cancer policy that may have led to overall quality improvements is the undertaking of clinical audits and ensuring clinical governance. One of the earliest audits in cancer care was commissioned to review the progress of Calman and Hine recommendations, to provide an assessment of the current state of services and provide a baseline for measuring future progress (Department of Health 2000). At present, there are four established cancer specific clinic audits; the National Lung Cancer Audit (LUCADA), National Bowel Cancer Audit (NBOCAP), National Head and Neck Cancer Audit (DAHNO) and Oesophago-gastric Cancer Audit (Department of Health 2011a). These audits have been credited to improving service quality (Department of Health 2011a), and there are proposals for them to be extended to more cancer sites such a prostate cancer, as well as the establishment of a primary care cancer diagnosis audit (Department of Health 2011a).

More improvements in cancer survival are anticipated because of current initiatives in improving early detection and diagnosis. The National Awareness and Early Diagnosis Initiative (NAEDI) established by the Cancer Reform Strategy has been at the forefront of coordinating activities and research in early diagnosis. The importance of early diagnosis in improving England's cancer survival on par with other European countries is iterated in all cancer strategies reviewed. The most recent strategy, Achieving World-Class Cancer Outcomes, projects that 11,000 deaths annually can be prevented by improvements in early diagnosis (Independent Cancer Taskforce 2015).

Alongside recognising the impact of earlier diagnosis on improving cancer survival, there is also an acknowledgement of the difficult task that GPs have in suspecting cancer, in making appropriate referral when the symptoms are non-specific (Department of Health 2011a). The referral guidelines for suspected cancer that were first published in 2000 to support GPs in making referral decisions have been updated twice since to incorporate current evidence. The most recently revised referral guidelines are noteworthy in their efforts to improve early diagnosis by referring patients with non-alarming or vague symptoms. Previous guidelines

were inconsistent with regards to the risk threshold for referral, and investigation for referral was rarely initiated where positive predictive values (PPV)† were below 5% (NICE 2015). The revised guidelines have now included symptoms with a PPV of as low as 3% , and it is anticipated that this will is improve earlier diagnosis (NICE 2015) which will consequently improve survival.

2.6 The Equity Challenge

Inequalities in cancer can manifest as differences in the cancer care experience or outcomes in relation to an individual's socio-economic status, cancer type, race, age, gender, disability, belief, sexual orientation and geographical location (All Party Parliamentary Group on Cancer 2009).

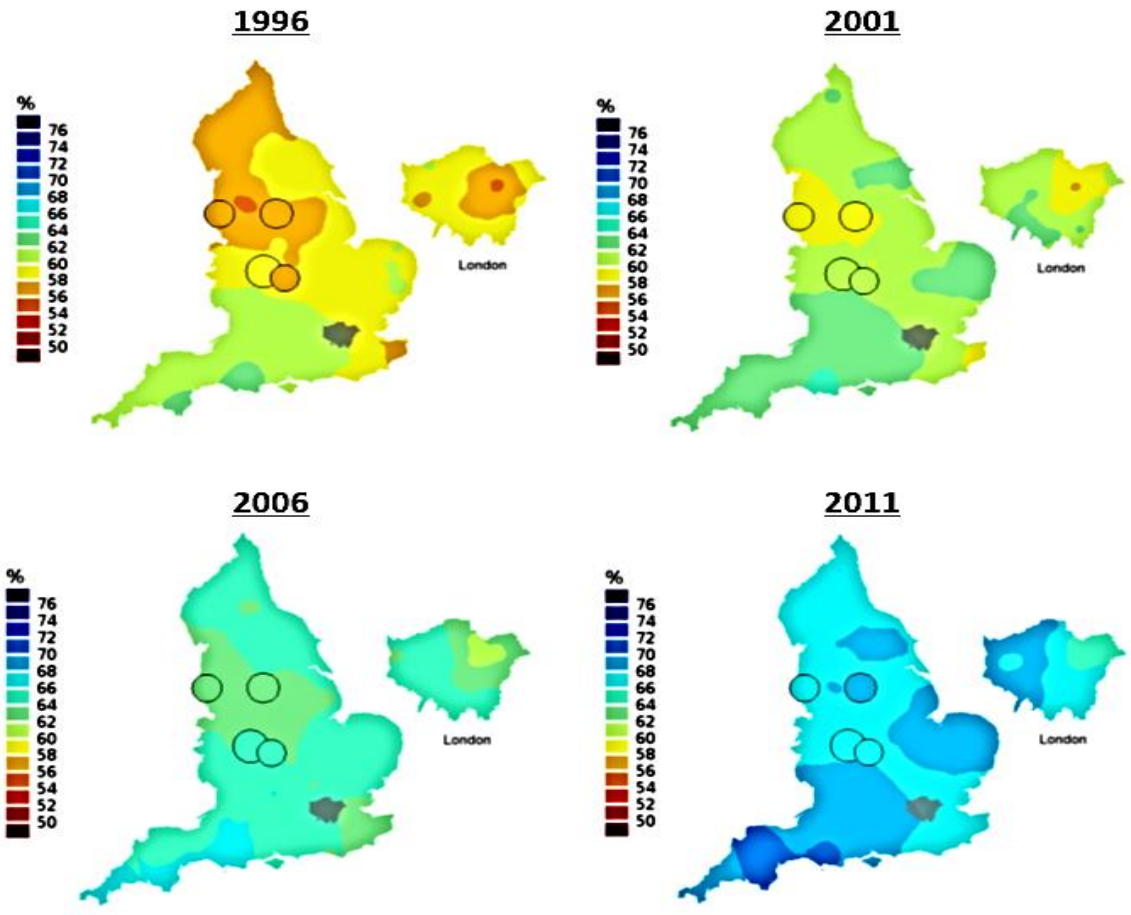
Tackling inequalities has been at the forefront of all the cancer strategies reviewed. The Cancer Plan recognised the presence of acute inequalities in cancer care and outcomes stating that; *'People from deprived backgrounds are more likely to get some types of cancer, and overall are more likely to die from it once they have been diagnosed'* (Department of Health 2000) (pg. 19). This strategy sought to reduce inequalities by targeted efforts in the most deprived such as efforts to reduce smoking rates in manual groups (Department of Health 2000). The Cancer Reform Strategy also highlighted inequalities as a priority, declaring that a lack of evidence on their nature was a hindrance to addressing the issue. In response, the Government set up the National Cancer Equality Initiative (NCEI) which was mandated to optimise data collection in order to enable a better understanding of inequalities, to promote research and evidence on cancer inequalities, and to spread good practice (Department of Health 2007). More recently, the Improving Outcomes Strategy on cancer has attributed England's poorer outcomes to the worse outcomes observed in vulnerable groups and deprived areas; *'Higher morbidity and mortality in disadvantaged groups and areas are a key driver for our poor average outcomes'* (Department of Health 2011a) (pg. 3). The most recent strategy, Achieving World-Class Outcomes Cancer Strategy, also reiterates the impact of socio-economic variations and attributes 15,300 cases and 19,200 deaths per year to the gap between the most and least deprived (Independent Cancer Taskforce 2015).

† Positive Predictive Value (PPV) is the risk of having the disease of interest given a specific symptom

Cancer inequalities in England manifest as; higher cancer incidence and mortality in deprived groups, in older people, in some ethnic minorities and in men. The exception here is breast cancer where women who are more affluent have higher incidence, although they also have lower mortality than the less affluent women. Cancer incidence is generally lower amongst ethnic minority groups, with the exception of prostate cancer where incidence is greater amongst Black African and African-Caribbean men. Liver cancer incidence is higher among South Asians, and mouth cancer is highest among Bangladeshis (Department of Health 2010). Inequalities have also been reported in levels of patient experience, with black and minority ethnic groups reporting poorer experience of care (Department of Health 2012a). Some older people also experience clinically inappropriate under treatment, which may be attributed to the slower rate of improvements in mortality in older people in comparison to younger age groups (Department of Health 2010).

There are also known geographical inequalities in cancer diagnosis, treatment and outcomes in England that are intrinsically related to how services are organised and how patients access them. These geographical inequalities have been reported as the regional differences in survival whereby survival rates are generally lower in Northern England than in the South of the country (Walters et al. 2010). Trend data shows that the north-south divide has become less pronounced over time (Office of National Statistics 2013b); **Figure 2.9** demonstrates the narrowing of cancer survival rates between Clinical Commissioning Groups located in the north and south of England. This reduction in geographical inequality is particularly significant in breast cancer survival, which has been attributed to the successful implementation of the NHS Cancer Plan recommendations (Walters et al. 2010).

Figure 2.9 - Smoothed maps of the one-year survival index (%) for all cancers combined in 211 Clinical Commissioning Groups: England, 1996, 2001, 2006 and 2011, patients' ages 15-99 years



Source - ONS, 2013 ©. Re-used with permission. Licence for re-use is available at http://www.nationalarchives.gov.uk/doc/open-government-licence/version/3/

Analysis of individual level data reveals geographical inequalities that are associated with access to cancer services. For instance, poor geographical access has been associated with decreased likelihood of histological diagnosis (Crawford et al. 2009) and poorer uptake of optimal treatment (Sauerzapf et al. 2008; Jones et al. 2008). Proximity to specialist services has been associated with uptake of care, in lung cancer; large variations in resection rates has been linked to local provision of specialist thoracic surgeons, whereby, presence of a surgeon at a lung MDT, has been associated with higher resection rates (Lau et al. 2013). Another study found that specialist thoracic surgical services have higher resection rates for patients referred directly to them compared to those patients referred from the wider and much larger catchment areas that they serve (Khakwani et al. 2013).

2.6.1 Closing the gap

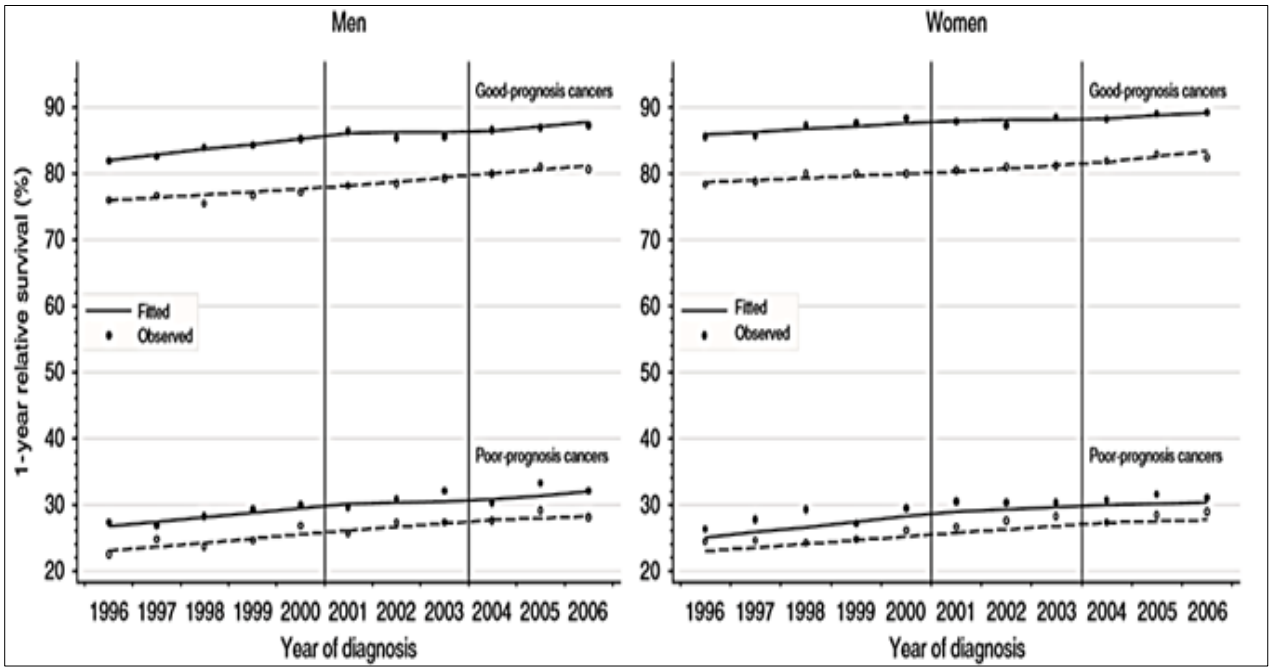
Despite the consistent policy attention on tackling unjustified inequalities, there has been little progress in closing the inequality gap. For example, inequalities by socio-economic groups have persisted despite the universal access to health in the UK. The exact origins of these inequalities remain unclear, but it is likely that they arise from complex interactions of factors that operate at different levels; biological, behavioural or psychosocial and health system levels (Munro 2005). Thus, inequalities may be as a result to differences in tumour aggression (Woods et al. 2006), disease stage (Møller et al. 2009), or comorbidity (Møller et al. 2012). At a behavioural level, inequalities may be as a result to different attitudes towards seeking health care (Niksic et al. 2015; Moffat et al. 2017). They may also arise due to factors operating at the health system level such as differences in clinical practice (King's Fund 2011), or as a result of environmental factors such as variations geographical and locational access to services (Munro 2005).

It is estimated that closing the gap in survival between the most and least affluent would prevent anywhere between 7,000 (Ellis et al. 2012) to 19,200 deaths (Independent Cancer Taskforce 2015) in England only. Whilst understanding healthcare inequalities requires the rigour of scientific investigation, addressing them fully requires political will power that involves addressing inequalities of the wider determinants of health that operate outside the health system (Navarro 2009; Whitehead & Popay 2010; Marmot et al. 2017). It is therefore welcoming that most of the cancer strategies reviewed had a political commitment to addressing inequalities, by targeted action on determinants of poor survival such as diet, smoking, alcohol consumption and physical activity, and focussing initiatives on the most disadvantaged groups and areas (Department of Health 2011a; Independent Cancer Taskforce 2015; Department of Health 2000).

The extent to which cancer strategies have successfully achieved the objective to reduce inequalities is not fully known. An assessment on the impact of the Cancer Plan on the equity goal found that the strategy was successful in improving cancer survival rates, but was unsuccessful in reducing the socio-economic gap in survival (Rachet et al. 2010). **Figure 2.10** shows the consistency of the survival gap in 1 year relative survival rates between the most and least deprived groups. Secondly, the assessment found that the socio-economic gap in relative survival differed between cancers of good vs. poor prognosis; socio-economic inequalities

were wider for cancers of good prognosis‡ (**Figure 2.10**). Lastly, the assessment reported *'persistent and wide socioeconomic inequalities in the excess hazard of death in the period immediately after a cancer diagnosis'* (Rachet et al. 2010) (pg. 452), suggesting that more attention should be given to earlier diagnosis and prompt access to optimal treatment across all socioeconomic groups (Rachet et al. 2010).

Figure 2.10 - Trends in 1-year relative survival for the most deprived (solid line) and most affluent (dashed line) groups, by cancer prognosis, England 1996–2006. Lines are the regression plots fitted in a single model, which comprises every survival estimate by deprivation and calendar year.



Source – Rachet et al, 2010, Re-used with permission. Licence for re-use is available at https://creativecommons.org/licenses/by-nc-sa/3.0/

Most of the socioeconomic deficits in survival occur shortly after diagnosis, and they tend to attenuate or disappear with time since diagnosis (Rachet et al. 2008; Møller et al. 2012). In colorectal cancer for instance, excess mortality (survival deficit) in the most deprived groups is a short term phenomenon, that is largely confined to the first year (colon cancer) and two years (rectal cancer) after diagnosis (Møller et al. 2012). As described earlier in this section, these variations in survival may explained by differences in patient and disease characteristics

‡ Cancers of good prognosis are bladder, breast, cervix, colon, Hodgkin's disease, kidney, larynx, leukaemia, melanoma, myeloma, Non-Hodgkin lymphoma, ovary, prostate, rectum, testis and uterus. Cancer of poor prognosis are brain, lung, oesophagus, pancreas and stomach, (Rachet et al, 2010).

and a number of studies have demonstrated this. Another suggested explanations is in relation to the organisation and quality of cancer care services (Møller et al. 2009), inequalities from this may arise as a result to variations in optimal access to early diagnosis and treatment services (Richards 2009; Rachet et al. 2010). As described elsewhere in this section, there is evidence showing how the structure of treatment services may exacerbate inequalities in cancer outcomes (Khakwani et al. 2013; Lau et al. 2013). The extent by which access to early diagnosis services may generate or perpetuate any inequalities in cancer outcomes is largely unknown, this research will contribute to towards generating evidence for this.

2.7 Highlighting the key findings from a policy perspective

Achieving health policy goals in cancer care presents significant challenges to policymakers and healthcare providers. Increase in life expectancy and improvements in early detection has led to an increase in cancer incidence, whilst improved treatment has increased survivorship. On the other hand, the health resources required to manage and treat the disease are increasingly scarce, and this ultimately results in a trade-off when attempting to meet competing policy goals such as equity and efficiency. The other challenge lies in measuring and monitoring some policy objectives such as access that have no universal definition and have a wide scope that encompasses spatial and non-spatial aspects. There are also numerous methodological difficulties in evaluating the impact of policy, the shortage of meaningful evaluation means policy makers often have limited evidence on the progress of their recommendations.

A review of literature suggests that the NHS productivity has been increasing by an annual average of 0.8% (Office of National Statistics 2015b), which may be indicative of greater efficiencies in the health system (Office of National Statistics 2007). Productivity estimates are not available at disease level and so the efficiencies specific to cancer services remain unclear. The goal to improve quality on the other hand has had unquestionable success, as demonstrated by improvements in survival rates and in patient experience. The increase in survival rates has been attributed to efforts implemented following the publication of the Cancer Plan (Rachet et al. 2009). In contrast, the equity goals also outlined in the Cancer Plan have not been met and for some cancers the inequality gap in survival has widened (Rachet et al. 2009). Policy objectives to improve access to cancer services have focused on monitoring cancer waiting times, although their impact on clinical outcomes has been inconclusive (Department of Health 2011b). Other dimensions of access such as geographical access continue to have significant

implications on outcomes, nearly two decades since the Calman and Hine report identified this as an issue of concern. Despite this, geographical access has failed to receive policy consideration in the three Government strategies, although it has now received attention in the most recent strategy (Independent Cancer Taskforce 2015).

2.7.1 Politicking and the development of health policy

Political ideologies can be traced in the Government policies on health, and this has had an impact on policy content, on the approach to policy implementation, and on the achievement of policy objectives. Differences in political ideologies have meant that change is inexplicably linked with the delivery of healthcare, the following quote articulates the constancy of change within the NHS; *'Change is a permanent feature of the NHS, organisations are revamped, funding flows are redirected, and lines of accountability redrawn as the political tide sweeps remorselessly backwards and forwards. Acronyms appear and disappear as the fraught politics of the NHS demand that a new working group be established or a redundant committee be dispatched…if the never-ending public clamour for improved state health services is to be assuaged, policies must be produced, lobbies satisfied and still further promises made'* (Salter 1998) (pg.4).

The narrative review has highlighted some of the key changes as they pertain to cancer services, some of which may be deemed necessary, for example, establishing specialist cancer centres for the management and treatment of rare cancers. However, the relevance of other changes can be questioned due to the disruption they cause to the health system. Political analysts use the term 'path dependency' to describe the process where incoming governments initiate some changes but retain elements of their predecessors' policies (Baggott 2007). The abolition of Cancer Networks to create Strategic Clinical Networks (SCNs) is an example of path-dependency, whereby the incoming Conservative Government of 2010 had intended to get rid of Cancer Networks but instead rebranded them as SCNs. These newly formed SCNs were to advise commissioners on a wide range of diseases and not just cancer. Although this sharing of knowledge may prove to be useful, it might come at the expense of cancer care if the SCNs resources are spread too thinly. Perhaps in the recognition of the shortcomings of the SCN, the most recent cancer strategy has proposed the establishment of Cancer Alliances which bear striking resemblance to the disbanded Cancer Networks, particularly with regards to driving

improvements by promoting service integration along the cancer care pathway (Independent Cancer Taskforce 2015; MacMillan Cancer Support 2015).

Despite ideological differences and the political rhetoric, there are numerous similarities between the different strategies examined. Such congruence tends to be on areas where there is indisputable clinical evidence. For instance, the Labour administration's Cancer Plan fully endorsed the National Screening Programmes that were rolled out by the previous Conservative Government. The Cancer Plan went further to provide resources to extend the age range covered by breast cancer screening and to enable screening programmes for other cancer types. There is also full agreement in terms of the focus on early diagnosis across all the strategies. The National Awareness and Early Diagnosis Initiative (NAEDI) that was established by the Labour Government gained momentum under the Coalition and Conservative administrations. Another area where there has been full consensus is in the role of information and intelligence to inform practitioners and commissioners. This culminated to the establishment of National Cancer Intelligence Network (NCIN) which has been recently rebranded as the Public Health England National Cancer Registration and Analysis Service (PHE NCRAS), although it has retained its function of driving improvements in cancer care and outcomes through information and intelligence.

One notable paradigm shift that may undoubtedly have an impact on the policy making process is the increasing importance of the patient group. Patients have historically possessed the least 'power' in the policy making process as they have been viewed as receivers not co-owners of the medical model (Borras et al. 2014). The initiation a Cancer Patient Experience Survey (CPES) marked a collective attempt towards a more patient centred care. The initial shortfalls in the full utilisation of the cancer patient survey have been overcome, and this may be credited to recent policy recognition of the patients' voice importance in informing commissioning and making service improvements (Department of Health 2011a; Independent Cancer Taskforce 2015)

One persistent challenge that policy makers have is in demonstrating the effectiveness of government policies on health (World Health Organization 2010). Overcoming this may require the combined effort between research, policy makers and health practitioners (Embrett & Randall 2014). The many parallels between evaluating the impact of health policy and

evaluating public health interventions may present opportunities for collaborations (Kelly et al. 2010). The first parallel is in methodological difficulties, both types of evaluation experience long and complex causal chains between intervention or implementation to health outcome, which presents challenges in demonstrating cause and effect, and makes it impossible to conduct true experimental studies (World Health Organization 2010; Kelly et al. 2010).

The second methodological difficulty arises in the normative aspect of public health and health policy concepts such as equity or power that may imply judgement or blame on certain individuals, groups or organisations. This may be regarded unattractive by researchers or even as threatening to professional and political interests (Embrett & Randall 2014). The challenge for public health researchers when investigating clinical factors that influence health and well-being, is to consider the political environment where decisions are made, where policies are implemented, and any socio-political factors that may act as a barrier to policy adoption. This is because *'the way in which an intervention is delivered, the systems infrastructure and the nature of the recipient population are at least as important in determining outcome as the intervention itself and are an integral part of the causal chain'* (Kelly et al. 2010) *(pg. 1060)*. Unfortunately, guidelines for doing this nature of research are currently unavailable which makes most public health researchers ill-equipped to attempting such research (Marmot et al. 2010).

Whilst not proposing to attempt policy analysis at any length, the studies presented in the rest of this thesis will make explicit reference to present and past cancer policies that pertain to health care accessibility. In so doing, the research will use policy as a lens to identify gaps in the evidence and to help with framing the research questions. Having a comprehensive understanding of the wider policy perspective will assist in interpreting the findings, by highlighting potential implications that are of relevance to police makers and health practitioners.

2.7.2 Future policies of geographical access to cancer services

One finding from the review is that more work is needed to characterise how other dimensions of access beyond cancer waiting times determine cancer outcomes. This will involve investigating other areas that may have been overlooked, such as issues pertaining to

geographical access to primary care, socio-cultural factors that may influence service utilisation, and the interactions between these dimensions.

The existing evidence to date demonstrates that issues of geographical accessibility are particularly acute with access to specialised services such as radiotherapy and surgery. Some of the gaps in the current evidence are highlighted in the most recent cancer strategy (**Table 2.3**). Unlike the previous cancer strategies, the recent strategy has tasked various key players to lead on implementing its 96 recommendations. PHE NCRAS and Clinical Reference Groups (CRGs) have been assigned to lead on the recommendations on the impact of geographical accessibility to services by reviewing the evidence on the merits of service configuration and further centralisation (**Table 2.3**). The successful implementation of this task will require combined efforts of which academic research will undoubtedly play a role, such as in evidence generation.

In this recent cancer strategy, service configuration to create specialist centres has been attributed to improving of cancer outcomes, as a result of bigger centres having better experience of rescuing the patient if something goes wrong; even though the strategy recognises that the rate of complication is the same in both specialist and non-specialist centres (Independent Cancer Taskforce 2015). Given the known benefits of creating centres of excellence, there is a need to balance the benefits of greater specialisation with the dis-benefits of more patients traveling further, and as such, the strategy recommends an assessment of the impact on cancer outcomes on patients living farther from a cancer centre (Independent Cancer Taskforce 2015). This is particularly crucial amongst patients residing in the most remote areas, whereby travelling for treatment has been estimated to account for nearly 13% life post diagnosis, in addition to incurring the financial burden on longer travel, as well as social and emotional separation from family and friends who may struggle to make visits (Baird et al. 2000).

The recent cancer strategy also recommends an assessment of the impact of travel times for children, young people and families (Independent Cancer Taskforce 2015). These proposals are timely and point to the need of going further than what the existing evidence has highlighted. This is because the impact of poor access on outcomes disproportionally affects the most vulnerable groups; those with chronic conditions, the elderly, young families, the

disabled and deprived groups (Bentham & Haynes 1985; Mungall 2005). These groups of patients may require more frequent access, may have pre-existing mobility issues (Bentham & Haynes 1985; Mungall 2005), or may experience relatively greater cost dis-benefits of paying for travel. More research is required to characterise the access issues in these vulnerable groups.

Lastly, a common theme across all the cancer strategies was the recognition of earlier diagnosis as a key driver to improving to improving outcomes, however, all strategies failed to acknowledge that geographical access to primary care diagnosis is a prerequisite to optimal access of earlier diagnosis. For instance, access to the GP may have important implications for obtaining planned referrals to secondary care, and for reducing uptake of emergency admissions, there is however very little empirical evidence to show this.

Given the important of access in the evolution of cancer policy in the UK, the next chapters explore how access continues to be associated with cancer outcomes. These chapters will answer pertinent questions related to the geographical accessibility of cancer services that were apparent following this review. To do this, the analysis will combine statistical and geographical analytical techniques, focussing on the access objective, but also taking into consideration how this objective overlaps with the objectives of equity, quality and efficiency. To begin with, the next chapter investigates the issue of geographical equity in access that was highlighted in the Calman and Hine recommendations over two decades ago. That chapter will assess the current state of equity in access to cancer management and treatment services in England by investigating whether these services are located according to population need.

Chapter 3

Geographical disparities in access to cancer management and treatment services in England

3.1 Background

As discussed in Chapter Two, equity in access to healthcare is an important policy objective in England. The NHS was founded on the principle that services would be available to everyone and would be free at the point of delivery (NHS 2015). Equity is also embedded in the operating model for the commissioning of specialised services, where NHS England seeks to provide consistent services to all regardless of location (NHS England 2012). The provision of equitable cancer services is dependent on how they are organised. In England, service configuration since the 1990s has been informed by the Calman and Hine report, which recommended high quality and also accessible cancer care (Calman & Hine 1995). The report stated that, *'All patients should have access to a uniformly high quality of care as close to the patient's home as possible' and that 'services should be planned to minimise travelling times whilst maintaining the highest standards of specialist care'* (Calman and Hine, 1995, p.6). These recommendations have been endorsed by consecutive Governments with particular attention paid to improving quality by establishing specialised cancer centres (Department of Health 2000; Haward 2006). Indeed, some improvements in cancer survival in England have been attributed to this increase in specialisation (Haward 2006; Oliphant et al. 2013).

The Calman-Hine recommendations also introduced a dilemma with regards to centralisation of services that ensures all patients have access to specialist care without having to travel too far for it (Munro 2001). Healthcare providers and policymakers are thus faced with the substantial challenge of delivering geographically equitable cancer services within the constraints of finite healthcare resources and in the face of rising cancer incidence rates. Some geographical inequalities in access are inevitable (Gatrell & Wood 2012) because certain populations, such as rural residents, will always need to travel farther to access specialist services. Inequalities in access are however unacceptable when they lead to avoidable disadvantages in health, and when they disproportionally affect those most in need (Gatrell & Wood 2012).

Access issues are felt more acutely by those with the greatest need for healthcare, such as patients with chronic conditions who require regular hospital visits, those with lowest mobility such as elderly or disabled patients and also the most deprived (Bentham & Haynes 1985; Mungall 2005). Poor access is also known to amplify the effect of deprivation, whereby patients with the longest travel times and also in the most deprived areas are least likely to have

a histological cancer diagnosis and optimal treatment (Crawford et al. 2009). In the UK, studies using individual level data have shown a negative association between travel to hospital and uptake for cancer treatment (Jones et al. 2008; Sauerzapf et al. 2008; Lau et al. 2013) and increased odds of diagnosis at death (A. P. Jones et al. 2010). Longer distance to specialist cancer centres has also been associated with higher cancer stage at diagnosis (Campbell et al. 2001) and with poorer survival (Campbell et al. 2000). These findings have been replicated outside the UK; in France, road distance to the nearest cancer centre was associated with worse survival (Dejardin et al. 2008). Studies that have employed alternative measures of healthcare accessibility have reached similar conclusions. For instance, one North American study used a derivative of the gravity model to capture the availability (supply) as well as the attractiveness (demand) of services (Wang 2006), the study demonstrated an association between poor geographical access and advanced cancer stage (Wang et al. 2008).

3.1.1 Multidisciplinary Teams (MDTs)

MDTs in cancer care were suggested as model for managing cancer care by the Calman and Hine report (Calman & Hine 1995), and were later endorsed in subsequent cancer strategies. MDTs are made up of relevant specialists such as surgeons, oncologists, radiologists, pathologists, cancer nurse specialists and other specialist physicians who meet to discuss their patients and make treatment plans (Raine et al. 2014). There is an estimated 1500 cancer MDTs in England (National Cancer Action Team 2010). Their clinical effectiveness is disputed because of lack of evidence linking multidisciplinarity with more effective decision-making, rather, factors such as good team climate and clear goals and processes have been suggested as better indicators of effective decision making (Raine et al. 2014). MDTs have also been criticised for failing to implement decisions made at the meetings, particularly for patients living in more deprived areas (Raine et al. 2014). Despite their shortcomings, MDTs are beneficial because discussing each patient's care at these meeting ensures their treatment is considered by professionals with specialist knowledge of their cancer type. These discussions also provide a safeguard against errors (Raine et al. 2014) and they ensure continuity of care by promoting good communication along the care pathway.

3.1.2 Chemotherapy, Radiotherapy and Surgery

Chemotherapy, radiotherapy and surgery are the three main types of curative cancer treatments available on the NHS that will be considered in this chapter. Chemotherapy is administered as

a single or a combination of drugs that aim at killing cancer cells. Radiotherapy treatment can be administered externally using x-ray or particle beams. It can also be administered internally (brachytherapy) where radioactive implants are put inside or close to a tumour, or radioactive liquids are given as a drink or injection (Cancer Research UK 2016c). Surgery is one of the main treatments for cancer and it may provide a cure where cancer has not spread. The treatment involves removing the tumour and/or some normal tissue and lymph nodes nearest the cancer cells in case they contain cancer cells (Cancer Research UK 2016c). These three treatments are used separately or in combination. As an example, chemotherapy and radiotherapy may be used to shrink a cancer before surgery, or to prevent it from spreading after surgery. These three treatments may also be used as palliative treatment where the aim is to relieve symptoms by reducing pain, or to help patient live longer and more comfortably where curing the cancer is not possible (Cancer Research UK 2016c).

3.1.3 Estimating geographical access, equity and need

This chapter will investigate geographical inequities in access at a population level. Previous evidence that shows the association between poor access and poorer outcomes may be an indication of geographical inequities in the location of cancer services, however, such inequities have not been demonstrated in research.

Geographical access will be defined as travel times in minutes from area of residence to the nearest hospital for cancer management or treatment. Equity in healthcare normally encompasses three principles; ‘equal access to health care for those in equal need’, ‘equal utilisation of health care for those in equal need’ and ‘equitable health outcomes’ for example as measured by quality adjusted life expectancy (Oliver & Mossialos 2004). This analysis will use the first principle ‘equal access for equal need’ as this is the definition of equity that is most generally accepted by policy makers (Oliver & Mossialos 2004; Allin et al. 2007).

Need is a problematic concept to define because it does not have a universally accepted definition (Haynes 1987; Oliver & Mossialos 2004; Allin et al. 2007). The earliest definition of need takes a humanitarian perspective and focuses on the identification of human suffering without taking into account the limitation of resources (Acheson 1978). This chapter will adopt a more agreeable definition that suggests that need for medical care exists only when an individual has an illness or disability for which there is effective and acceptable intervention

to prevent or treat it (Matthew G 1971; Wright et al. 1998). Healthcare need at a population level can be measured by the 'level of ill health' (Allin et al. 2007) and epidemiological measures such as prevalence or incidence can be used to describe 'how much of it there is' and 'where it is located' (Acheson 1978; Wright et al. 1998).

In this study, geographical inequities in access will be determined where areas with higher need also have poorer access to cancer services. Additionally, geographical access will be associated with relative survival rates to determine whether areas with poor access also have the worst outcomes. Lung, breast and colorectal cancers are among the commonest cancers totalling to about 40% of all cancer incidence the England, and amounting to approximately 120,000 cases annually (Cancer Research UK 2016b). Treatment for these requires access to MDT, chemotherapy and radiotherapy, and so they are appropriate cancer sites for this work.

3.2 Methodology

The study will be a cross sectional ecological design, with measurements and inferences at the level of NHS Primary Care Trust (PCT), as this is the scale at which data was available. It was not possible to obtain data on lower geographies for this study.

The information on the location of cancer hospital sites was obtained from multiple sources. In England, this information is collected by the National Peer Review Team (National Peer Review Programme 2013) which holds details on the location of hospital sites that provide cancer treatment (chemotherapy and radiotherapy), and sites providing cancer management via multidisciplinary teams (MDTs). The Peer Review Programme collects this information as a part of a quality assurance process to ensure clinical teams comply with national measures on quality improvement, safety and patient experience (National Peer Review Programme 2013).

In order to account for the 'edge-effect' whereby patients in some parts of England may receive treatment in Wales and Scotland, similar data was obtained from the Welsh Health Directory (NHS Wales Informatics Services 2014). At the time of the analysis, the Welsh Health Directory had complete information on the North Wales Cancer Network, but information was incomplete on the South Wales Cancer Network. Missing information was supplemented by Freedom of Information (FOI) requests from the Welsh Health Boards that are part of the South Wales Cancer Network. Data was also obtained from the Information Services Division

Scotland (Information Services Division 2015) on hospital sites located in the southern Scotland Health Boards that may serve some English patients; Dumfries and Galloway, Borders, Ayrshire and Arran, Lanarkshire, Lothian and Greater Glasgow and Clyde. The Scottish data did not have information on MDT presence, and therefore hospitals offering chemotherapy were used as a proxy for presence of a MDT. Finally, information on hospital sites offering cardiothoracic surgical for lung cancer treatment in England, Wales and Scotland was obtained from the Society for Cardiothoracic Surgery in Great Britain and Ireland (SCTS) (Society for Cardiothoracic surgery 2015).

3.2.1 Geographical units and measurements

Geographical access was estimated as travel times in minutes from all LSOA population weighted centroids in England to the nearest hospital site offering treatment or management for the specified cancer. LSOAs are small geographic areas in England and Wales that are designed to improve the reporting of small area statistics. There are 32,844 LSOAs in England each with a population range of 1,000 to 3,000 residents (Office of National Statistics 2015c). Population weighted centroids are summary reference points at the centre of the population in a geographical unit, they represent the spatial distribution of the population in a given geography such as an LSOA in this instance (Office of National Statistics 2013d). The most recent 2011 LSOA centroids were obtained from the Office of National Statistics digital geographical boundaries (Office of National Statistics 2013d).

A geographical Information System (GIS) (ArcGIS 10.3, Esri Inc.) was used to estimate the travel times. This part of the research was done by creating a road network using Ordnance Survey Meridian 2 data, which included all motorways, A, B and minor roads (Ordnance Survey 2013). The road network was then intersected with Developed Land Use Area (DLUA) boundaries (also obtained from the Meridian 2 data) to delineate urban areas, and to determine which road sections were in urban and in rural settings. Thereafter, each section of the road was assigned an average speed based on its road classification and whether it was in a rural or urban area, this was done using the average speeds developed in a previous study (Bateman et al. 1996). The road network was used within the Network Analyst module of the ArcGIS software, and travel times were estimated from all 2011 LSOA population centroids in England, to all postcodes from the identified hospital sites.

Postcodes are geographical reference points in the U.K that are used to identify postal delivery areas (Office of National Statistics 2015a).There are about 1.8 million postcodes in the U.K; around 1.75 million of these are 'small user postcodes' and 0.7 million are 'large user postcodes' (Office of National Statistics 2015a). A single small user postcode may contain anywhere from 15 to 100 single addresses. Larger addresses that receive numerous mail items per day such as hospitals are normally be assigned to a single large user postcode (Office of National Statistics 2015a).

The generated travel times were then aggregated to the PCT level. PCTs are English health administrations responsible for commissioning cancer services. They occupy a large geographical area with a median resident population of 203,000 (Office of National Statistics 2013e). There were 152 PCTs in England at the time of this analysis.

The National Radiotherapy Advisory Group (NRAG) recommend travel of no longer than 45 minutes for radiotherapy treatment (National Radiotherapy Advisory Group 2007) and therefore this was used as an important threshold for radiotherapy and surgical treatment. For travel to MDT and Chemotherapy, 20 minutes marked an important threshold as this was the approximate average travel time to hospitals in England during the study period (Department for Transport 2014b). The proportion of the population in England whose travel may exceed these thresholds was further quantified using ONS 2009 mid-year population estimates (Office of National Statistics 2013e; Office of National Statistics 2013c).

3.2.2 Statistical analysis

The measure of population need adopted for this analysis was the number of cases of (breast (ICD-10 C50), colorectal (ICD-10 C17-21 and C26) and lung (ICD-10 C33-34) cancer in a PCT. This was obtained as a three year average for 2008 - 2010 from the publicly available National Cancer Intelligence Network (NCIN) dataset of newly diagnosed cancer cases per year (National Cancer Intelligence Network 2010).

Primary outcomes were identified as one and five year PCT relative survival rates for each cancer, also obtained from the NCIN public dataset (National Cancer Intelligence Network 2014a). These relative survival rates were estimated nationally by NCIN using the actuarial

method that divides observed with expected survival rates to give a population level relative survival rate (Parkin & Hakulinen 1991; National Cancer Intelligence Network 2014b). The 'observed one year survival rates' were estimated as the number of persons diagnosed with the specified cancer between 2010 and 2012 with mortality follow up to the end of 2013. The 'observed five year survival rates' were also estimated in the same way but for patients who had a diagnosis between 2002 and 2004 and followed up to 2009. The 'expected survival rates' were based on the population life tables matched by age, sex and period of observation (Parkin & Hakulinen 1991; National Cancer Intelligence Network 2014b).

Every effort was made to match the timescale covered by the estimated travel times with that of the incidence and survival data. This was achieved for travel to radiotherapy as there were fewer sites involved. Thus, travel time to radiotherapy was restricted to sites in operation before 2010 to match the incidence data. The three new radiotherapy hospital sites that opened after 2010 were excluded from the analysis; Bracknell Clinic, Fazackerley site of Clatterbridge Cancer Centre and The Christie at Royal Salford. For the regression analysis, hospital sites identified as above were also used in the analysis, because the cancer cases used to estimate relative survival rates would have been diagnosed in the same decade as the incidence data; 2010 - 2012 for 1 year survival and 2002 - 2004 for 5 year survival. It was however not possible to discern MDT and chemotherapy sites by year of operation, and therefore the most recent data at the time of the analysis (November 2014) was used. The discrepancies between the time of data collection and study period might have a slight effect on the results, but this effect may not be substantial because English hospital sites would not have changed substantially during this decade.

Deprivation and ease of obtaining a general practitioner (GP) appointment were identified as potential confounders as they are independently associated with cancer survival. PCT level deprivation data was obtained from the English indices of multiple deprivation (Department for Communities and Local Government 2010). Good access to primary care is important in the early diagnosis and later prognosis of cancer and has previously been associated with lower rates of emergency admissions to secondary care (Cowling et al. 2013). Ease of obtaining a GP appointment was measured as the percentage of patients in a GP practice who were able to get an appointment to see or speak to a health professional during their most recent appointment, without the need to call back closer to or on the preferred appointment date. This information

is collected on an annual basis by the national GP Patient Survey of 2.75 million adults registered with a GP in England (NHS England 2013)

Statistical analysis was conducted on using Stata (Version 13.1; StataCorp, College Station, TX, USA). Spearman's rank correlation was used to correlate the unadjusted PCT cancer cases (need) with the estimated mean PCT travel times (access). Linear regression was used to examine the association between cancer relative survival rates and PCT level mean travel times, adjusting for age, sex, year, area deprivation and ease of GP access. Models were tested to ensure they met the following assumptions of the linear regression models; linearity, normality and homoscedasticity of the residuals. Sensitivity analysis was performed by modelling travel times both as a continuous measure and a grouped measure and examining any changes in the results. Standard errors of the relative survival rates were estimated to help determine the extent to which they were influenced by sampling variation (Ederer et al. 1961). A p-value (<= 0.05) was used to identify statistical significance in all analyses.

3.3 Results

The distribution of the estimated mean PCT travel times is shown on **Table 3.1**. Radiotherapy and surgery were provided at the fewest number of hospital sites and therefore incurred the longest journey times 23.70 minutes and 31.93 minutes respectively. Aggregating travel time to PCT level conceals the variation experienced at lower geographies. As an example, the highest LSOA level travel times are; 76.33 (Breast MDT), 85.14 (Colorectal MDT), 76.33 (Lung MDT), 83.91 (Chemotherapy), 102.69 (Radiotherapy) and 172.84 (Lung Surgery). The PCT equivalents are markedly lower (**Table 3.1**). Thus, it is likely that PCT level analysis underestimates the full extent of geographical access issues. This is illustrated in **Figure 3.1** that shows how PCT level averages mask areas with the longest estimated travel times in the peripheral parts of the country.

Table 3.1 - Number of cancer services and estimated PCT mean travel times in England, Wales and Scotland*

Type of service	Number of hospital sites	Travel times in minutes PCT (LSOA)					
		Lowest	Mean	Highest	25th Quartile	Median	75th Quartile
Breast MDT	214	3.97 (0)	13.5 (15.2)	35.2 (76.3)	9.5 (8.2)	12.4 (12.7)	17.1 (19.6)
Colorectal MDT	226	3.84 (0)	13.3 (15.0)	35.2 (85.1)	9.1 (8.0)	12.2 (12.5)	16.3 (19.6)
Lung MDT	219	3.84 (0)	13.5 (15.2)	35.2 (76.3)	8.9 (8.0)	12.4 (12.7)	16.4 (19.9)
Chemotherapy	231	3.55 (0)	13.1 (14.9)	35.2 (83.9)	8.7 (7.8)	11.9 (12.3)	15.7 (19.4)
Radiotherapy	61	3.97 (0)	23.7 (25.6)	61.0 (102.7)	13.8 (14.0)	22.4 (23.6)	32.0 (34.5)
Lung Surgery	41	4.4 (0.4)	31.9 (36.1)	151.8 (172.8)	15.8 (17.2)	26.3 (29.0)	41.1 (46.8)

*Scottish data was obtained from the southern Health Boards only; Dumfries and Galloway, Borders, Ayrshire and Arran, Lanarkshire, Lothian and Greater Glasgow and Clyde. MDT, multidisciplinary team. LSOA, Lower Super Output Area

The population estimates were grouped by travel time thresholds **Table 3.2** to determine the percentage of the population in England living in the longest travel categories. The PCT level analysis for MDT and Chemotherapy suggests that on average between 1% and 2% of the population in England live more than 30 minutes from a facility (this estimates is markedly higher (around 9%) when examined at the LSOA level (**Table 3.2**).

Likewise, PCT level analysis shows that an estimated 6% and 24% of the population lived longer than 45 minutes from a radiotherapy and surgical facility for lung cancer (respectively). Again, this is markedly higher when using LSOA estimates (10% and 27% respectively) (**Table 3.2**). The distribution of travel times to cancer services in England are mapped in **Figure 3.1(A&B)**, the areas with the poorest access are highlighted in red.

In **Table 3.3**, access to radiotherapy services is used as an example to demonstrate the distribution in deprivation score by travel time categories in the three cancer sites examined. Using the mid-2009 PCT population, an estimated 3 million (5.72%) people and of whom over 6,000 were breast, colorectal and lung cancer patients, lived more than 45 minutes from a radiotherapy facility during the study period

Figure 3.1 (A) Map of mean travel times to MDT and chemotherapy services estimated at PCT and LSOA level

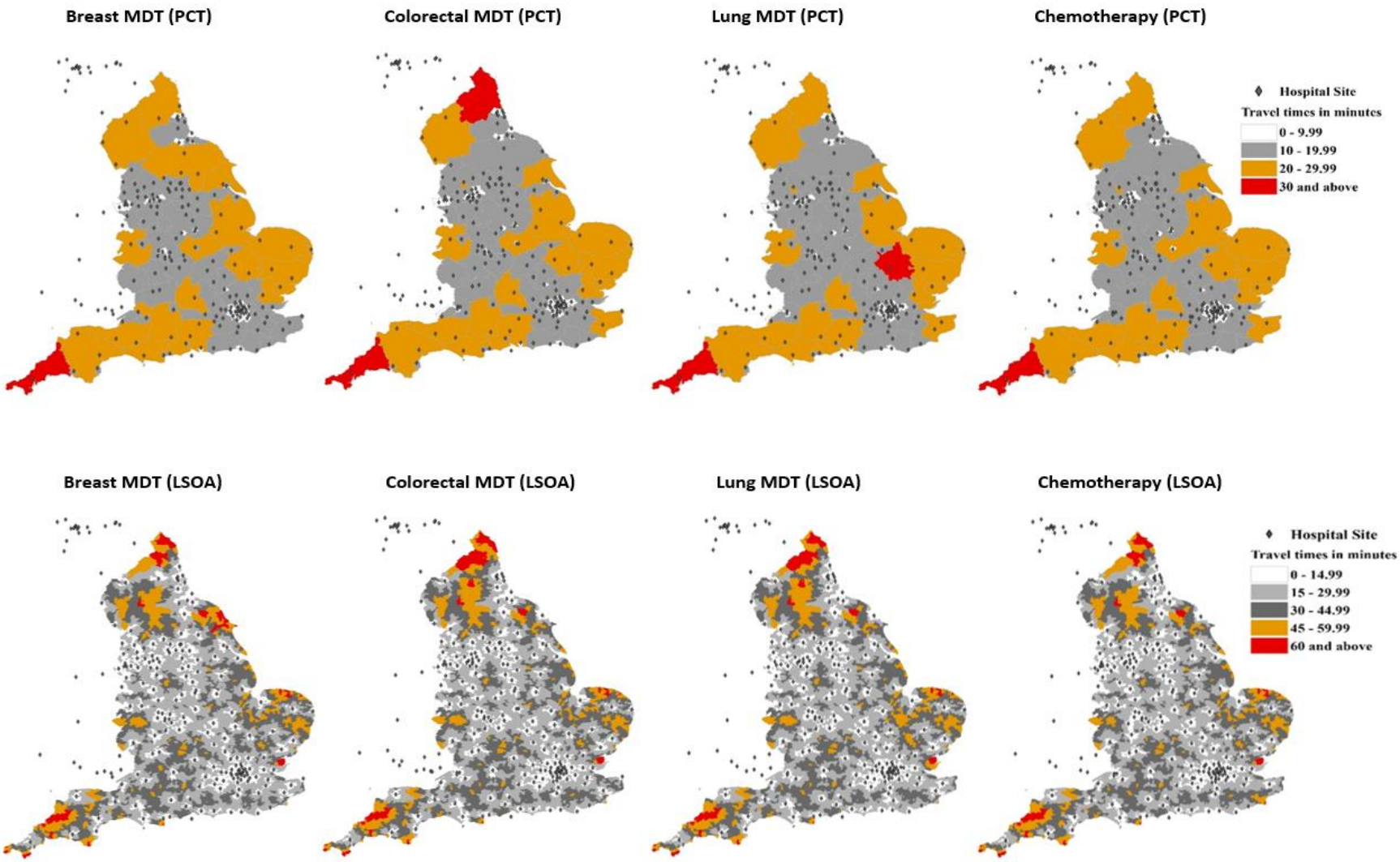


Figure 3.2 (B) Map of mean travel times to radiotherapy and surgical services estimated at PCT and LSOA level

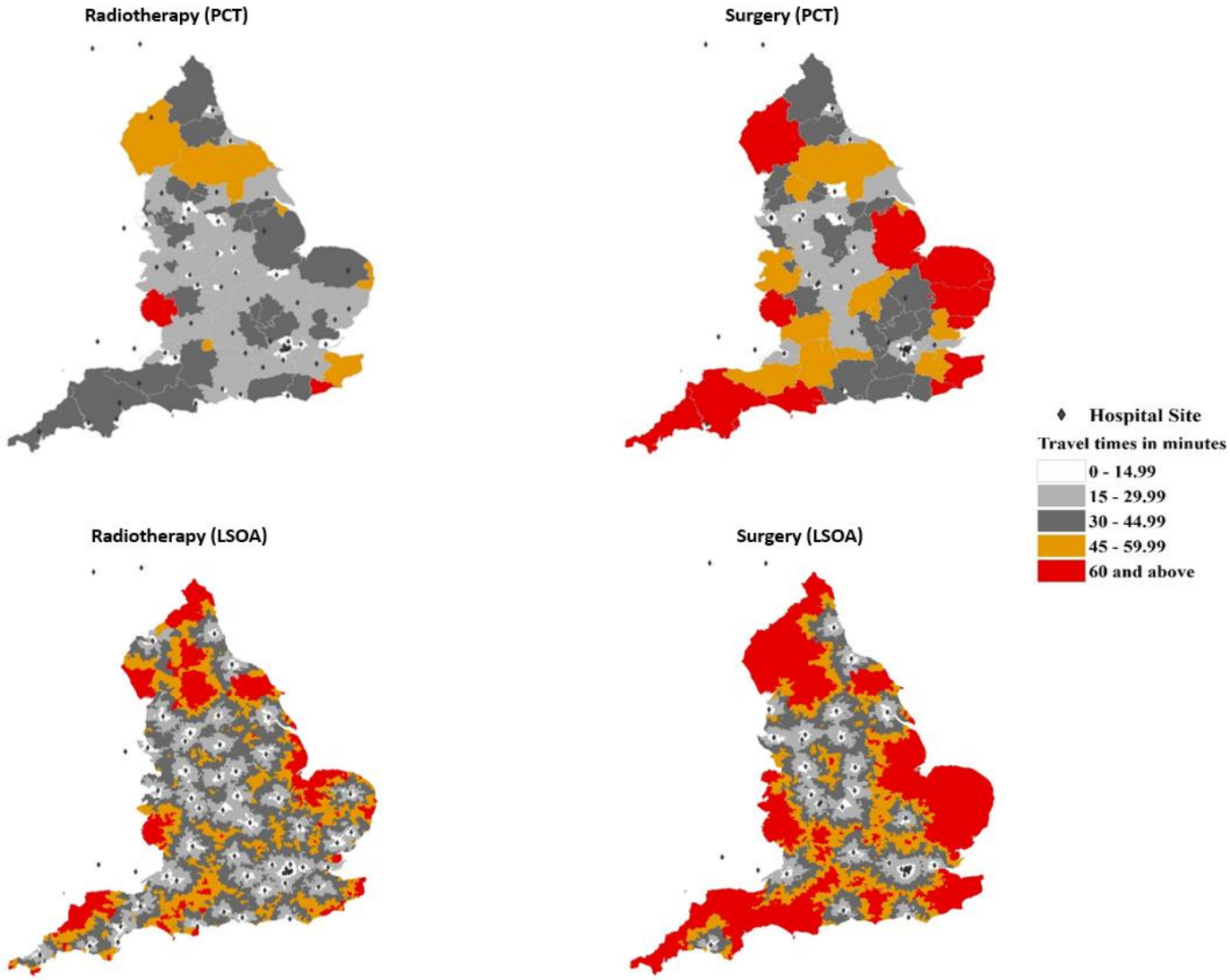


Table 3.2- LSOA and PCT populations in England grouped by estimated travel times to a) Breast MDT, b) Colorectal MDT, c) Lung MDT and d) Chemotherapy e) Radiotherapy and f) Surgical services

				Population mid 2009 estimates (% of total)
				LSOA Level
Travel times (minutes)	**a) Breast MDT**	**b) Colorectal MDT**	**c) Lung MDT**	**d) Chemotherapy**
0 – 9.99	18,453,676 (35.53%)	19,301,918 (37.17%)	18,920,250 (36.43%)	19,748,856 (38.03%)
10 – 19.99	20,900,582 (40.24%)	20,019,626 (38.55%)	20,027,080 (38.56%)	19,828,896 (38.18%)
20 – 29.99	8,157,819 (15.71%)	8,005,732 (15.42%)	8,205,517 (15.80%)	7,794,951 (15.01%)
30 plus	4,421,540 (8.51%)	4,606,342 (8.87%)	4,780,772 (9.21%)	4,560,916 (8.78%)
				PCT Level
0 – 9.99	10,765,508 (20.68%)	12,186,756 (23.41%)	11,976,508 (23.01%)	12,074,690 (23.19%)
10 – 19.99	29,963,086 (57.56%)	28,700,932 (55.13%)	29,249,622 (56.19%)	28,812,996 (55.35%)
20 – 29.99	10,800,810 (20.75%)	10,327,228 (19.84%)	9,697,036 (18.63%)	10,641,717 (20.44%)
30 plus	528,616 (1.02%)	843,105 (1.62%)	1,134,854 (2.18%)	528,616 (1.02%)

	Population mid 2009 estimates (% of total)	
	LSOA Level	
Travel times (minutes)	**a) Radiotherapy**	**b) Surgery**
0 – 14.99	14,648,231 (28.21%)	10,760,925 (20.72%)
15 – 29.99	19,538,424 (37.62%)	16,258,171 (31.31%)
30 – 44.99	12,606,802 (24.27%)	10,870,102 (20.93%)
45 – 59.99	3,611,327 (6.95%)	6,665,957 (12.84%)
60 plus	1,528,835 (2.94%)	7,375,266 (14.20%)
	PCT Level	
0 – 14.99	11,451,308 (22.00%)	9,653,462 (18.54%)
15 – 29.99	24,010,852 (46.12%)	17,170,464 (32.98%
30 – 44.99	13,616,842 (26.16%)	12,597,047 (24.20%)
45 – 59.99	2,614,793 (5.02%)	6,315,879 (12.13%)
60 plus	364,225 (0.70%)	6,321,168 (12.14%)

PCT, Primary Care Trust. LSOA, Lower Super Output Area

Table 3.3 - Population estimates and cancer cases grouped by travel times to radiotherapy services. Cancer cases are estimated using PCT mid-2009 population estimates and three year annual cancer cases (2008 – 2010)

Travel times to radiotherapy services (minutes)	**PCTs by Travel time categories**	**PCT Overall IMD average by Travel time categories**	**PCT Population mid 2009 estimates (% of total)**	**Estimated breast, colorectal and lung cancer cases**
0 – 14.99	43	28.11	11,451,308 (22.00%)	23,647
15 – 29.99	65	22.26	24,010,852 (46.12%)	49,574
30 – 44.99	34	21.24	13,616,842 (26.16%)	28,119
45 plus	8	21.36	2,979,018 (5.72%)	6,148

3.3.1 Correlations

The number of cancer cases in a PCT across the three cancer types were positively and significantly correlated with longer PCT mean travel times to all hospital sites ($p<0.01$) **(**Table 3.4**).** The correlations were higher in chemotherapy and MDT, than radiotherapy or surgery.

Table 3.4 - Correlation coefficient of mean PCT mean travel time to cancer services and PCT cancer incidence (number of new cases, annual average for 2008-2010)

Number of new cases per year	Breast MDT	Colorectal MDT	Lung MDT	Chemotherapy	Radiotherapy	Surgery
Breast	0.68**			0.68**	0.45**	
Colorectal		0.72**		0.72**	0.46**	
Lung			0.58**	0.58**	0.41**	0.35**
Surgery						0.30**

** p<0.01, * p<0.05. MDT, multidisciplinary team

3.3.2 Testing assumptions of linear regression

The test for linearity using the Stata 'nlcheck' tool (Jann 2008) showed that continuous 'travel time' and 'ease of GP access' variables failed to meet this assumption, which supported the decision to model these variables as categories. The 'Shapiro-Wilk' test for the normality of residuals also showed that some models failed to meet this assumption. However, this does not invalidate the analysis because the inferences in linear regression are robust to violations of normality so long as the sample size is reasonably large (Agresti 2015; Yan & Su 2009). Although it is recognised that non-normality does not affect the validity of the models, heteroscedasticity may affect it (Lumley et al. 2002). Four out of eighteen of the fully adjusted models did not meet this homoscedasticity assumption, these four models are for lung cancer access to MDT and Chemotherapy services (Tables 3.5 and 3.6), and hence these findings should be treated with caution. Modelling travel times as a continuous rather than categorical measure, did not alter the conclusions. Estimated standard errors of the relative survival rates across the three cancer sites, and for both one and five years were generally small compared to their associated estimates, and ranged from 0.004 to 0.049.

3.3.3 Regression results before adjustment

When estimated PCT mean travel times were regressed on cancer relative survival rates, the unadjusted models for breast and colorectal cancers showed that longer travel was positively associated with longer survival. This was mostly evident for travel to MDTs (**Table 3.5**) and to chemotherapy services (**Table 3.6**), and was statistically significant for five year relative survival rates. For example, for travel to breast and colorectal MDTs, PCTs with the longest mean travel had a significantly higher five year survival rates (breast coefficient = 1.79; SE = 0.79; t (148) = 2.26; $p<0.05$), and (colorectal coefficient = 4.10; SE = 1.16; t (148) = 3.54; $p<0.01$) (**Table 3.5**). Longer travel to radiotherapy was also positively associated with breast cancer survival although this was only statistically significant for the five year survival rates (1.27; SE = 0.59; t (148) = 2.15; $p<0.05$) **(Table 3.7**). In contrast, the lung cancer analysis showed that PCTs with the longest mean travel had significantly lower one and five year relative survival rates, this was the case across all treatment types examined (**Table 3.5**, **Table 3.6**, **Table 3.7** and **Table 3.8**).

3.3.4 Results after adjustment

Adjusting for deprivation and ease of GP access revealed a clear survival gradient whereby PCTs with longer mean travel times consistently had poorer relative survival rates. This survival gradient was observed in travel to all services across the three cancers. As an example, **Table 3.7** shows the regression output for the models of survival and access to radiotherapy treatment. The coefficients are percentage point differences in relative survival associated with each explanatory variable. The lung cancer output for example, shows that an increase in travel times from the reference category 'less than fifteen minutes', to the highest category '45 plus minutes', is associated with a predicted reduction in one year survival by -3.43 percent, $p<0.05$ (before adjusting), -4.02 percent, $p<0.01$ (after adjusting for deprivation only) and -4.60 percent, $p<0.01$ (after adjusting for deprivation and ease of obtaining a GP appointment).

In the lung cancer analysis, the travel – survival association was generally greater for one year than five year relative survival rates. For example, the lung cancer output in **Table 3.7** shows the corresponding predicted reduction in the five year relative survival is -2.40 percent, $p<0.05$ (before adjusting), -2.72 percent, $p<0.05$ (after adjusting for deprivation only) and -2.98 percent, $p<0.01$ after adjusting for deprivation and ease of obtaining a GP appointment. Lastly,

the association between travel time to radiotherapy and relative survival was greater in colorectal and lung cancer compared to breast cancer (**Table 3.7**).

The results on **Table 3.8** shows the same pattern whereby PCTs with longer estimated travel to lung cancer surgical sites have significantly poorer relative survival rates. After adjusting for deprivation and ease of obtaining a GP appointment, PCTs in the longest travel time category ’45 minutes plus’ have a -5.42 percent and -3.43 percent predicted reduction in 1 and 5 year lung cancer survival respectively, in comparison to PCTs with the shortest estimated travel.

Table 3.5 - PCT mean travel times to the nearest MDT site, associated with 1 and 5 year breast, colorectal and lung cancer relative survival rate. The table shows linear regression model outputs using 150 PCTs in England, adjusted for deprivation and ease of obtaining a GP appointment

	Not adjusted for deprivation or ease of GP appointment			Adjusted for deprivation			Adjusted deprivation & ease of GP appointment		
	Breast	**CRC**	**Lung‡**	**Breast**	**CRC**	**Lung‡**	**Breast**	**CRC**	**Lung‡**
Explanatory variables									
Outcome: 1 Year Relative Survival									
Travel times to MDT									
<10 minutes (reference)									
10 – 19.99 minutes	0.15	0.42	-2.18**	-0.36	-0.76	-3.02**	-0.30	-0.81	-3.10**
20 minutes plus	0.32	1.41	-2.20*	-0.79*	-0.46	-3.52**	-0.59	-0.98	-4.21**
Deprivation (IMD)				-0.09**	-0.16**	-0.12**	-0.09**	-0.14**	-0.10*
Ease of obtaining a GP appointment									
Quartile 1 - Difficult									
Quartile 2							-0.26	-0.17	0.07
Quartile 3							-0.46	0.15	0.28
Quartile 4 - Easy							-0.54	1.21	1.67
Intercept (Y)	96.34**	75.94**	34.31**	98.81**	80.57**	37.69**	99.23**	80.01**	36.84**
R-squared	0.01	0.02	0.07	0.27	0.18	0.12	0.30	0.21	0.14
Outcome: 5 Year Relative Survival									
Travel times to MDT									
<10 minutes (reference)									
10 – 19.99 minutes	0.75	0.43	-1.16**	-0.47	-1.51	-1.65**	-0.65	-1.67*	-1.62**
20 minutes plus	1.79*	4.10**	-1.25*	-0.87	1.04	-2.01**	-1.63*	-0.10	-2.37**
Deprivation (IMD)				-0.21**	-0.26**	-0.07**	-0.19**	-0.23**	-0.06*
Ease of obtaining a GP appointment									
Quartile 1 - Difficult									
Quartile 2							0.12	0.04	-0.17
Quartile 3							1.03	0.57	-0.39
Quartile 4 - Easy							1.61*	2.71*	0.74
Intercept (Y)	84.64**	53.02**	9.50**	90.59**	60.62**	11.44**	89.61**	59.25**	11.29**
R-squared	0.03	0.09	0.05	0.29	0.26	0.10	0.32	0.30	0.13

Numbers show the regression coefficients (standardized β). All relative survival rates are adjusted for age, sex and year. ** p<0.01, *p<0.05

‡ Lung cancer output should be interpreted with caution because these models violated the homoscedasticity linear regression assumption

Table 3.6 - PCT mean travel times to the nearest chemotherapy site, associated with 1 and 5 year breast, colorectal and lung cancer relative survival rate. The table shows linear regression model outputs using 150 PCTs in England adjusted for deprivation and ease of obtaining a GP appointment

	Not adjusted for deprivation or ease of GP appointment			Adjusted for deprivation			Adjusted deprivation & ease of GP appointment		
	Breast	**CRC**	**Lung‡**	**Breast**	**CRC**	**Lung‡**	**Breast**	**CRC**	**Lung‡**
Explanatory variables									
Outcome: 1 Year Relative Survival									
Travel times to chemotherapy <10 minutes (reference)									
10 – 19.99 minutes	0.33	0.48	-2.00**	-0.26	-0.61	-2.77**	-0.18	-0.68	-2.90**
20 minutes plus	0.34	1.45	-1.97*	-0.61*	-0.34	-3.24**	-0.40	-0.87	-3.96**
Deprivation (IMD)				-0.08**	-0.15**	-0.11**	-0.09**	-0.14**	-0.09*
Ease of obtaining a GP appointment Quartile 1 - Difficult									
Quartile 2							-0.24	-0.21	0.04
Quartile 3							-0.47	0.15	0.41
Quartile 4 - Easy							-0.57*	1.19	1.71
Intercept (Y)	96.24**	75.90**	34.17**	98.63**	80.37**	37.34**	99.06**	79.84**	36.48**
R-squared	0.02	0.03	0.06	0.26	0.18	0.10	0.29	0.21	0.13
Outcome: 5 Year Relative Survival									
Travel times to chemotherapy <10 minutes (reference)									
10 – 19.99 minutes	1.29*	0.48	-1.20**	-0.14	-1.33	-1.66**	-0.33	-1.52	-1.64**
20 minutes plus	1.62*	4.13**	-1.13	-0.71	1.18	-1.89**	-1.34	0.03	-2.25**
Deprivation (IMD)				-0.20**	-0.25**	-0.07*	-0.18**	-0.22**	-0.06*
Ease of obtaining a GP appointment Quartile 1 - Difficult									
Quartile 2							0.20	-0.01	-0.18
Quartile 3							1.00	0.60	-0.30
Quartile 4 - Easy							1.57*	2.70*	0.75
Intercept (Y)	84.41**	52.99**	9.49**	90.24**	60.38**	11.40**	89.20**	59.04**	11.21**
R-squared	0.05	0.09	0.06	0.29	0.25	0.10	0.32	0.30	0.12

Numbers show the regression coefficients (standardized β). All relative survival rates are adjusted for age, sex and year. ** p<0.01, *p<0.05.

‡ Lung cancer output should be interpreted with caution because these models violated the homoscedasticity linear regression assumption

Table 3.7 - PCT mean travel times to the nearest radiotherapy site, associated with 1 and 5 year breast, colorectal and lung cancer relative survival rate. The table shows linear regression model outputs using 150 PCTs in England, adjusted for deprivation and ease of obtaining a GP appointment

	Not adjusted for deprivation or ease of GP appointment			Adjusted for deprivation			Adjusted deprivation & ease of GP appointment		
	Breast	**CRC**	**Lung**	**Breast**	**CRC**	**Lung**	**Breast**	**CRC**	**Lung**
Explanatory variables									
Outcome: 1 Year Relative Survival									
Travel times to Radiotherapy									
<15 minutes (reference)									
15 – 29.9 minutes	-0.12	-0.15	-1.58*	-0.59**	-1.12*	-2.09**	-0.62**	-0.98	-1.94*
30 – 44.9 minutes	0.24	-0.16	-3.08**	-0.30	-1.29*	-3.68**	-0.30	-1.31*	-3.71**
45 minutes plus	0.33	-0.97	-3.43*	-0.20	-2.09*	-4.02**	0.07	-2.67*	-4.60**
Deprivation (IMD)				-0.08**	-0.17**	-0.09*	-0.09**	-0.14**	-0.07
Ease of obtaining a GP appointment									
Quartile 1 - Difficult									
Quartile 2							-0.27	-0.23	-0.30
Quartile 3							-0.50*	0.05	-0.31
Quartile 4 - Easy							-0.81**	1.27	1.14
Intercept (Y)	96.44**	76.51**	34.39**	98.67**	81.15**	36.85**	99.42**	80.31**	36.24**
R-squared	0.02	0.01	0.10	0.28	0.21	0.13	0.33	0.24	0.15
Outcome: 5 Year Relative Survival									
Travel times to Radiotherapy									
<15 minutes (reference)									
15 – 29.9 minutes	1.27*	0.50	-1.15*	0.13	-1.14	-1.44**	0.20	-0.84	-1.34**
30 – 44.9 minutes	0.77	-0.05	-1.32*	-0.56	-1.97*	-1.68**	-0.55	-2.03*	-1.69**
45 minutes plus	1.07	-0.16	-2.40**	-0.24	-2.05	-2.72**	-0.72	-3.49*	-2.98**
Deprivation (IMD)				-0.19**	-0.28**	-0.05*	-0.17**	-0.22**	-0.05
Ease of obtaining a GP appointment									
Quartile 1 - Difficult									
Quartile 2							0.10	-0.04	-0.34
Quartile 3							0.84	0.36	-0.64
Quartile 4 - Easy							1.34*	3.28**	0.40
Intercept (Y)	84.54**	53.62**	9.614**	89.99**	61.50**	11.03**	88.75**	59.20**	11.05**
R-squared	0.03	0.00	0.07	0.29	0.24	0.10	0.32	0.31	0.13

Numbers show the regression coefficients (standardized β). All relative survival rates are adjusted for age, sex and year. ** p<0.01, *p<0.05.

Table 3.8 - PCT mean travel times to the nearest cardio-thoracic hospital site for surgery, associated with 1 and 5 year lung cancer relative survival rate. The table shows linear regression model outputs using 150 PCTs in England, adjusted for deprivation and ease of obtaining a GP appointment.

	Not adjusted for deprivation or ease of GP appointment	Adjusted for deprivation	Adjusted deprivation & ease of GP appointment
Explanatory variables			
Outcome: 1 Year Relative Survival			
Travel times to Radiotherapy			
<15 minutes (reference)			
15 – 29.9 minutes	-2.23**	-3.35**	-3.34**
30 – 44.9 minutes	-3.37**	-4.96**	-5.10**
45 minutes plus	-2.98**	-4.78**	-5.42**
Deprivation (IMD)		-0.15**	-0.14**
Ease of obtaining a GP appointment			
Quartile 1 - Difficult			
Quartile 2			-0.80
Quartile 3			-0.70
Quartile 4 - Easy			1.05
Intercept (Y)	34.92**	39.50**	39.55**
R-squared	0.10	0.18	0.21
Outcome: 5 Year Relative Survival			
<15 minutes (reference)			
15 – 29.9 minutes	-1.36**	-2.05**	-2.09**
30 – 44.9 minutes	-2.05**	-3.05**	-3.14**
45 minutes plus	-1.89**	-3.01**	-3.43**
Deprivation (IMD)		-0.09**	-0.09**
Ease of obtaining a GP appointment			
Quartile 1 - Difficult			
Quartile 2			-0.67
Quartile 3			-0.95
Quartile 4 - Easy			0.38
Intercept (Y)	9.98**	12.82**	13.32**
R-squared	0.10	0.18	0.22

Numbers show the regression coefficients (standardized β). All relative survival rates are adjusted for age, sex and year. ** p<0.01, *p<0.05

3.4 Conclusions

This study shows that PCTs with more cases of breast, colorectal and lung cancer also have longer estimated mean travel times to the cancer management and treatment services identified. PCTs with longer mean travel times also have poorer relative survival rates after adjustment for area deprivation. These findings highlight the importance of examining inequalities in access to services and should inform NHS England's mandate of ensuring equitable commissioning of specialised services (NHS England 2012).

The analysis used an area level dataset. It is therefore likely that inference at this level will suffer to some extent from ecological fallacy by suggesting that relationships between areas may be related to individuals within them. Nevertheless, area based studies have several advantages, such as contributing to theory and hypothesis generation for future testing (Pearce 2000). Use of publicly available datasets have highlighted issues in access that warrant further investigation using more robust individual level datasets. The study also offers a national perspective on geographical access and augments the evidence previously conducted using smaller regions. Although incidence data is available at lower geographies, confidentiality restrictions meant is was not possible to obtain this for the study. Relative survival rates on the other hand have not been computed at lower geographies in England, because the small number of cases and deaths at lower geographies introduces difficulties in standardising by age and sex. Whilst acknowledging that using relatively large PCT geographies conceals variation present at lower geographies, these findings are still informative because commissioning of cancer services in England took place at this level (Okello et al. 2011).

By use of area level data, the study demonstrates that areas with the poorest access also have the highest cancer cases **Table 3.4**. This may be an indication that services in England may not be located according to population need. One explanation is that cancer services are more likely to be located in cities. This is contrary to the fact that the demand for these services is greater in less urban areas that carry a larger cancer burden due to larger percentage of older people. A programme commissioned by the National Cancer Action Team to model radiotherapy demand in England showed local area variation. Inner London PCTs with younger populations such as Tower Hamlets had a lower projected demand by the year 2020; 6,007 fractions per million in comparison to 20,827 fractions per million for more rural PCTs such as Devon

(Round et al. 2013). This variation is due to geographical variation in age distribution because older age carries an increased cancer burden (Round et al. 2013).

Associating PCT level mean travel times with cancer survival rates showed that areas with longer travel times to MDT and treatment have worse cancer survival rates. The unadjusted models for breast and colorectal cancers showed that areas with longer travel were more likely to have better relative survival rates. However, when the confounding effect of deprivation was removed the opposite was apparent; areas with longer travel were more likely to have poorer relative survival rates. This may be because deprived populations are more likely to live in urban areas where most hospitals are located.

The findings indicate that travel time – survival association was strongest in lung and colorectal cancers than in breast cancer, this is particularly so for radiotherapy treatment (**Table 3.7).** The travel time – survival associations for access to lung cancer surgical treatment had some of the strongest associations (**Table 3.8)**. Increasing distance from a cancer centre has been previously associated with poorer survival in lung cancer (Campbell et al. 2000). Poor survival for those with poorer access may be explained by the increased likelihood of more advanced disease stage at diagnosis (Campbell et al. 2001), but why this might vary by tumour site is less clear. Other research suggests treatment uptake also appears to vary by tumour type; breast, rectal and lung cancers patients are all less likely to receive radiotherapy if they live farther from a radiotherapy site (Jones et al. 2008). Additionally, poor access to chemotherapy for rectal and lung cancer treatment (Jones et al. 2008) and poor access to surgical treatment for lung cancer has been associated with reduced likelihood for these treatments (Jones et al. 2008; Lau et al. 2013; Khakwani et al. 2013). There is also some evidence that geographical inequalities in cancer survival has declined for breast cancer but has persisted for other cancers (Walters et al. 2011), our findings may to some extent support this conclusion.

Geographical access to radiotherapy and surgery had a stronger association with relative survival rates than geographical access to MDT and chemotherapy services. This is most likely because there are fewer sites for radiotherapy and surgical treatment than for MDT and chemotherapy. For radiotherapy treatment, NRAG recommends a threshold of 45 minutes travel for radiotherapy treatment (National Radiotherapy Advisory Group 2007). Using ONS mid 2009 PCT population estimates and mean PCT travel times, an estimated 6% (3 Million)

of the population in England lives farther than the recommended 45 minutes. It is likely that this population estimate is greater, this is because analysis at large areas such as PCTs conceals the extent of variation observed at smaller areas. For example, similar analysis at LSOA level showed that an estimated 10% (5 million) of the population in England lives over 45 minutes from a radiotherapy hospital site.

Surgical operation is the main treatment for colorectal cancer and non-small cell lung cancer (Cancer Research UK 2016c). This study shows acute geographical inequalities in access to surgical treatment for lung cancer patients, whereby over a quarter of the population in England may need to travel longer than 45 minutes to obtain this treatment. Fortunately, surgical treatment tends to involve fewer hospital visits than chemotherapy or radiotherapy that is delivered in multiple visits over a longer period of time, thus, it may be less burdensome for patients to travel to highly specialised surgical treatment centres (Independent Cancer Taskforce 2015).

In recent decades, the role of radiotherapy in cancer treatment was understated and this resulted to an under-investment of radiotherapy services in the UK (Cancer Research UK 2009). However, its curative effectiveness is now increasingly being recognised, with nearly 40% of cured cancer cases being attributed to radiotherapy treatment (National Radiotherapy Advisory Group 2007). Where used curatively in lung cancer, it is generally reserved in the treatment of inoperable tumours often in elderly patients or those with other multiple morbidities (Louie et al. 2015). It is also used often to treat rectal but not colon cancers, whilst in breast cancer, radiotherapy is used after breast reconstruction and mastectomy (Cancer Research UK 2016c). A substantial under-provision of radiotherapy services in England has been reported with an estimated 63% gap between current activity levels and optimal treatment levels, however, improvements to increase provision are underway (National Radiotherapy Advisory Group 2007). The findings in this study suggest that good access to radiotherapy treatment may be an important prognostic factor in breast, colorectal and lung cancer.

This study has a number of limitations. It is a cross-sectional study and therefore causality cannot be determined; it is plausible for example, that longer travel times might have caused poorer survival because of later diagnosis or inadequate treatment, although no data was available to let enable this analysis. Another limitation is in using number of cancer cases to

indicate population need. It could be argued that the number of cases are only an indicator of the quantity of services needed, and not of the needs of individuals who have cancer. The analysis used aggregated PCT level data as individual level data or data from smaller geographies was not available at the time of the study. Aggregated data exposes the study to the ecological fallacy meaning the findings at a population level may not be inferred at individual level. Additionally, some of the data sources did not cover the same time period. For example, there was no information to identify the location of MDT and chemotherapy hospital sites operating in the period over which the outcomes were measured, although it is unlikely that the geographical provision of services will have changed substantially over the period of this study. Data were not available on mobile chemotherapy units or GP surgeries offering chemotherapy services and so it was not possible to include them in the access measures. Another limitation is that PCTs are now obsolete geographies and have been replaced by CCGs (Clinical Commissioning Groups). At the time of this analysis it was not possible to obtain cancer specific five year relative survival rates at CCG level.

In conclusion, this study has shown that despite equity in access being a key objective in the provision of healthcare, it remains an elusive goal in the provision of cancer services in England. The findings suggest that longer travel times to services might lead to inadequate treatment and therefore poorer survival. The study also identifies some research questions that warrant more in-depth future research. Firstly, colorectal and lung survival appear to be more sensitive to poor geographical access to radiotherapy than breast cancer **Table 3.7**. Secondly, in lung cancer, geographical access issues are more strongly associated with one year over five year survival rates. Thirdly, lung cancer survival appears to be more sensitive to geographical access to chemotherapy and MDT than both colorectal and breast cancer.

Part of the challenge in meeting the equity goal may lie in the lack of a universal definition and monitoring criteria for equity in access (Allin et al. 2007). Another challenge lies in the trade-off that results when attempting to meet contrasting goals such as equity and efficiency, with resources that are increasingly scarce. This has been recognised by the recent Cancer Strategy for England that is working to develop a five year cancer survival improvement strategy (Independent Cancer Taskforce 2015). The strategy has identified a need to revisit the issue of access to services in order to enable improvements in earlier diagnosis and quality of care. Additionally, the strategy recognises the inequitable commissioning and delivery of care, and

has urged the tackling of variation to be a priority over the next five years. To achieve this, two recommendations that are relevant to this study have been put forward; an evaluation of evidence to determine whether service configuration of surgery merits further centralisation and, an evaluation of the impact on cancer outcomes of patients living distances from a cancer centre (Independent Cancer Taskforce 2015).

It is plausible that some of the associations between access and survival shown in this chapter may be influenced by accessibility to primary care. Controlling for access to primary care using a measure of ease of obtaining a GP appointment had little impact on the travel time – survival associations (**Table 3.5** - **Table 3.8**). With a few exceptions, relative survival was generally higher in PCTs where patients had the most ease in obtaining a GP appointment. For example, in access to radiotherapy treatment, a decrease in difficulty of obtaining a GP appointment from the reference category 'quartile 1 (difficult)' to the lowest category 'quartile 4 (easy)', is associated with a predicted increase in five year survival by 1.34 percent, $p<0.05$ in breast cancer and 3.28 percent, $p<0.01$ in colorectal cancer (**Table 3.7**). The area level analysis used in this chapter may mask the variations that are observed at lower geographies or at the level of individual patients; data that are more granular are required to ascertain the relationships at these lower levels. The next chapter will use individual level data to examine the association between other measures of access to the GP (such as travel times), rurality and key process and clinical outcomes.

Chapter 4

Impact of travel time and rurality on presentation and outcomes of symptomatic colorectal cancer: a cross-sectional cohort study in primary care

4.1 Background

Chapter One described how previous studies examining the relationship between access and cancer outcomes have had a focus on secondary services, whereas primary care services has been overlooked. Studies conducted in the UK have reported that people who live rurally and further away from health services have poorer cancer outcomes (Jones et al. 2008; Campbell et al. 2000). Chapter Three supported these findings by showing that areas with the poorest access also have worse survival rates, and found that this may be linked to inequities in accessing management and treatment services.

It was not possible to ascertain how access to primary service contributed to the findings in Chapter Three, although some work conducted in Australia suggests causative mechanisms may be at the general practice level; particularly with regards to rural accessibility (Emery et al. 2013). This is because rural populations may be impacted disproportionately by overall poor accessibility and by long distances travelled to obtain primary and secondary healthcare (Douthit et al. 2015; Emery et al. 2013). For example, longer distance to health services has been associated with fewer in-patient admissions (Haynes & Bentham 1982), with poorer uptake of cancer diagnosis and treatment (Jones et al. 2008; Lau et al. 2013; Crawford et al. 2009), and with lower survival (Campbell et al. 2000). Secondly, socio-cultural factors could manifest as different attitudes or stoicism in rural dwellers, with correspondingly lower rates of primary care consultation, and as a consequence, lower likelihood of general practitioners (GPs) being enabled to detect early symptoms of cancer (Emery et al. 2013; Farmer et al. 2006). Geographical location and considerations of access could also influence GP decision making if they take into account patients' journey to hospital when making referral decisions (Haynes & Bentham 1982; Sladden & Thomson 1998).

Acting together, these mechanisms could conspire against rural patients and their GPs and lead to disproportionately longer diagnostic delays, later stage presentation and poorer survival. A study from the early 2000s in Northern Scotland supports this notion by showing that longer straight-line distances from patients' homes to a cancer centre was associated with later stage at diagnosis and poorer survival from colorectal cancer (Campbell et al. 2001; Campbell et al. 2000). Rural patients are therefore more likely to experience longer distances and worse access because health services are located more sparsely in these areas. However, poorer access in

rural areas may not always translate to worse outcomes; research from the USA has provided contradictory findings by reporting increased likelihood of late stage cancer amongst urban patients (McLafferty & Wang 2009; McLafferty et al. 2011).

Achieving a true understanding of the relationship between rural residence and cancer outcomes is hindered by a focus on outcomes, survival and stage, rather than process. There have been few meaningful attempts to compare urban and rural cancer diagnosis at the level of patient - GP interactions. Cancer is easier to detect and refer when alarm symptoms are present (Jensen et al. 2014; Hamilton 2009), and harder when symptoms are atypical (Lyratzopoulos et al. 2014).

When grouped by diagnostic difficulty, cancer sites such as breast and melanoma are considered easier to detect because they present with signs and symptoms that are fairly specific. In contrast, cancers such as lung, myeloma and stomach present with non-specific symptoms that are frequently seen in primary care and this makes diagnosis of the cancer difficult (Lyratzopoulos et al. 2014). The diagnosis of colorectal cancer lies in the middle of this spectrum of diagnostic difficulty because some patients with this cancer present with specific symptoms but others present atypically (**Table 4.1**) (Lyratzopoulos et al. 2014)

Table 4.1 - Categories of diagnostic difficulty

Category	Definition
Harder to suspect	Most patients present with non-specific symptoms (e.g. multiple myeloma, pancreas, stomach, lung)
Intermediate	Some patients present with specific symptoms, but other present atypically (e.g. colon, renal, lymphoma)
Easier to suspect	Most patients present with highly specific symptoms or signs (e.g. breast, melanoma, endometrial, testicular, bladder)

Source; Lyratzopoulos et al (2014)

Subsequent diagnosis after presentation with non-alarm symptoms may therefore require more frequent engagement with health services, which may be hindered by poor accessibility; difficulties in accessing secondary care services could mean rural GPs might delay referral until symptoms are more obvious (Vedsted & Olesen 2011). It seems plausible therefore, that for rural populations, geographical inaccessibility and socio-cultural differences would

manifest as a greater likelihood to be diagnosed with colorectal cancer following presentation with alarm symptoms to GP, or following an emergency admission.

4.1.1 Referral guidelines for suspected cancer

In the UK, GP referral for suspected cancer is informed by referral guidelines such as the National Institute for Health and Clinical Excellence (NICE) and the Scottish referral guidelines for suspected cancer (NICE 2005; Health Improvement Scotland 2013; NICE 2015). The 2005 NICE referral guidelines were criticised for concentrating on typical presentations of cancer, which may have delayed diagnosis in patients with atypical presentations (Hamilton et al. 2009). These guidelines have been recently revised (NICE 2015). One key recommendation in the revised guidelines has been to lower the symptoms threshold to include any symptoms with a 3% or higher positive predictive value (PPV); the previous guidelines had few symptoms with a PPV of lower than 5% (NICE 2015).

The revised referral guidelines also aim to standardise clinical practice by minimising unwarranted variations such as in making referrals and testing for cancer (NICE 2015). Variations in clinical practice are well documented; for instance, there are known age, gender, ethnic, and tumour site variations in the number of pre-referral consultation (Lyratzopoulos et al. 2012). Patients with tumours in the pancreas, stomach, lung, colon, ovarian as well as Hodgkin's lymphoma, and multiple myeloma are more likely to consult their GP three or more times before hospital referral (Lyratzopoulos et al. 2012). Similarly, younger patients, females, and ethnic minorities are also more likely to have multiple consultations before a referral in comparison to older patients, men, and white patients, respectively (Lyratzopoulos et al. 2012). Variations in referral to secondary care that arise due to issues in access are also plausible. These may emanate from poor access to both primary and secondary services or from poor access influencing GPs referral behaviour (Carr-Hill et al. 1997; Haynes & Bentham 1982), but these relationships have not been well researched.

4.1.2 Study Objectives

This study examines rural urban differences in the diagnosis of colorectal cancer using a historical, but highly detailed database from Northern Scotland (Robertson et al. 2004). The CRUX (Comparing Rural and Urban Cancer Care) database linked detailed information from the primary care records of people diagnosed with colorectal cancer, to cancer registry and

service use data from NHS Scotland. Using this linked dataset, this chapter explores the association between rurality, travel to services and symptoms at presentation, emergency presentation, stage and survival for 926 people diagnosed with colorectal cancer between 1997/8. Also, for the first time the analysis investigates the interaction between rurality, urbanity and travelling time on these important colorectal cancer outcomes, as well as the relationship between symptoms, emergency admissions and survival.

4.2 Methodology

The study used the CRUX (Comparing Rural and Urban Cancer Care) linked dataset that contains primary care data from Northern Scotland. CRUX holds records of cancer cases diagnosed between 1997 and 1998 (Murchie et al. 2014; Robertson et al. 2004) and followed up until 2011. The GP records hold clinical information on symptoms presented at the index consultation, referral route, other comorbidities, information on diagnosis and treatment. These have been linked with data from the Scottish Cancer Registry to provide information on demographics, Dukes' stage and GP practice of registration at the time of colorectal cancer diagnosis. A final linkage with the General Register Office for Scottish Death Registry provided the date of death. We only used colorectal cancer records as this was the focus of the study.

The index consultation was determined as the first visit to the GP with a recording of potential symptoms of colorectal cancer that preceded diagnosis (Murchie et al. 2014). Patients with symptoms recorded two years before treatment were excluded, as it was judged unlikely that these symptoms were associated with the tumour (Robertson et al. 2004; Murchie et al. 2014). The presence of alarm symptoms, non-alarm symptoms, emergency admissions, later (C or D versus A or B) Dukes' stage and survival were identified as the primary outcomes. Admission types recorded as emergency and/or A&E (Accident and Emergency) were grouped into 'emergency admissions', whilst all inpatient and outpatient admissions as well as day cases and domiciliary visits were grouped as 'other admissions'. Stage at diagnosis was recorded as Dukes' stage (A, B, C or D). Survival time was measured from date of first presentation to primary care (Murchie et al. 2014).

4.2.1 Alarm and non-alarm symptoms

Expert opinion was sought on the definition of alarm symptoms (Hamilton, 2015 Personal Communication). Alarm symptoms were defined as serious symptoms that are most likely to result in a patient seeking a consultation or a GP making an urgent referral. These are rectal bleeding, palpable mass and weight loss. This grouping was consistent with a previous other study (Van Hout et al. 2011). Patients with any of these symptoms were categorised as 'Alarm'. The opposite end of the spectrum to alarm symptoms are 'non-alarm' symptoms. These are considered 'low risk, but not no risk' (Hamilton 2010); they most probably do not indicate cancer but cancer cannot be excluded (Vedsted & Olesen 2015) and are important to investigate because referral decisions are considered particularly difficult for them (Hamilton 2010; Vedsted & Olesen 2015). Following expert advice (Hamilton 2015), we identified these non-alarm symptoms as constipation, diarrhoea, abdominal pain and anaemia. Patients with any of these non-alarm symptoms (but excluding alarm symptoms above) were grouped as 'Non-alarm'.

4.3 Statistical Analysis

Geographical access was defined as estimated travel times in minutes from the patients' home postcode to the postcode of their GP practice of registration at diagnosis. These were computed using a Geographical Information System (GIS) (ArcGIS 10.3, Esri Inc.), see section 3.2.1 for more information on the methodology.

Road travel time was selected as the most appropriate measure of accessibility; a previous study had demonstrated that over 87% of cancer patients travel to hospital by motor vehicle (Haynes et al. 2006). Travel times estimated using GIS have previously been closely related to the times of actual car journeys reported by cancer patients (Haynes et al. 2006). Lastly, patients were grouped according to rural or urban residence using the (2003-04) Scottish rural-urban classifications (Scottish Executive 2004).

All data were analysed using Stata Version 13 (StataCorp College Station, TX, USA). Estimated travel time was analysed as a continuous variable. Symptoms and admissions and stage data were binary coded as 'alarm symptoms vs not', 'emergency vs not', 'early stage (CD) vs late stage (AB)'. Logistic regression was used to examine how travel time was associated with the likelihood of these outcomes. So that parameter estimates were

conservative, the models were adjusted for variables deemed to have a relationship with the outcomes; age, sex, Carstairs deprivation score (Morris & Carstairs 1991) and Charlson comorbidity index (Charlson et al. 1987). Odds ratios (OR) and 95% CI were calculated in all four models. Cox survival analysis was used to examine the relationship between travel time to GP and survival. For each patient, follow-up began at the date of their index presentation (see definition above) and ended at the date of death or was censored after three years. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated and this model was also adjusted for the above confounders.

Based on the differences in geographical accessibility and socio-cultural acceptability of care seeking between rural and urban areas (Douthit et al. 2015; Bain & Campbell 2000; Farmer et al. 2006), it was hypothesised that travel times may have a different relationship with the outcomes of interest for those living in rural compared to urban settings. To test this, interaction terms were fitted to examine if rurality moderated associations between travel times and the outcomes. Urban and rural associations were then separately plotted, and statistical significance of the differences was tested; a p-value (<= 0.05) was used to show statistical significance.

4.4 Results

The CRUX dataset had 1489 cases with a colorectal cancer diagnosis. Of these, 531 were excluded because their initial symptoms were recorded as having been presented two years before treatment, and 31 were excluded because they did not have any GP recorded symptoms. One case was missing postcode (zip code) and was also excluded. A total of 926 patients with symptomatic colorectal cancer had complete data and were used in this analysis. Just over half of these were male (56.3%) and majority (83.1%) were above 60 years of age (**Table 4.2**). Over half of the patients (52.4%) had one or more comorbidities, 825 (89.1%) had between one and three symptoms, whilst the remaining 101 (10.9%) had over more than four symptoms recorded. There were 373 patients with one or more alarm symptom, 507 patients with one or more 'non-alarm symptom', 243 patients were admitted to hospital via an emergency route and 424 patients had Dukes' stage C and D (**Table 4.2**).

The median travel time was 5.5 minutes, whereas 75% of all patients could access their GP within 10 minutes. Nearly a third (32.2%) lived in a rural area and travel times to GPs were longest for those living in rural vs urban areas (12.0 vs 6.2 minutes) and those with four or

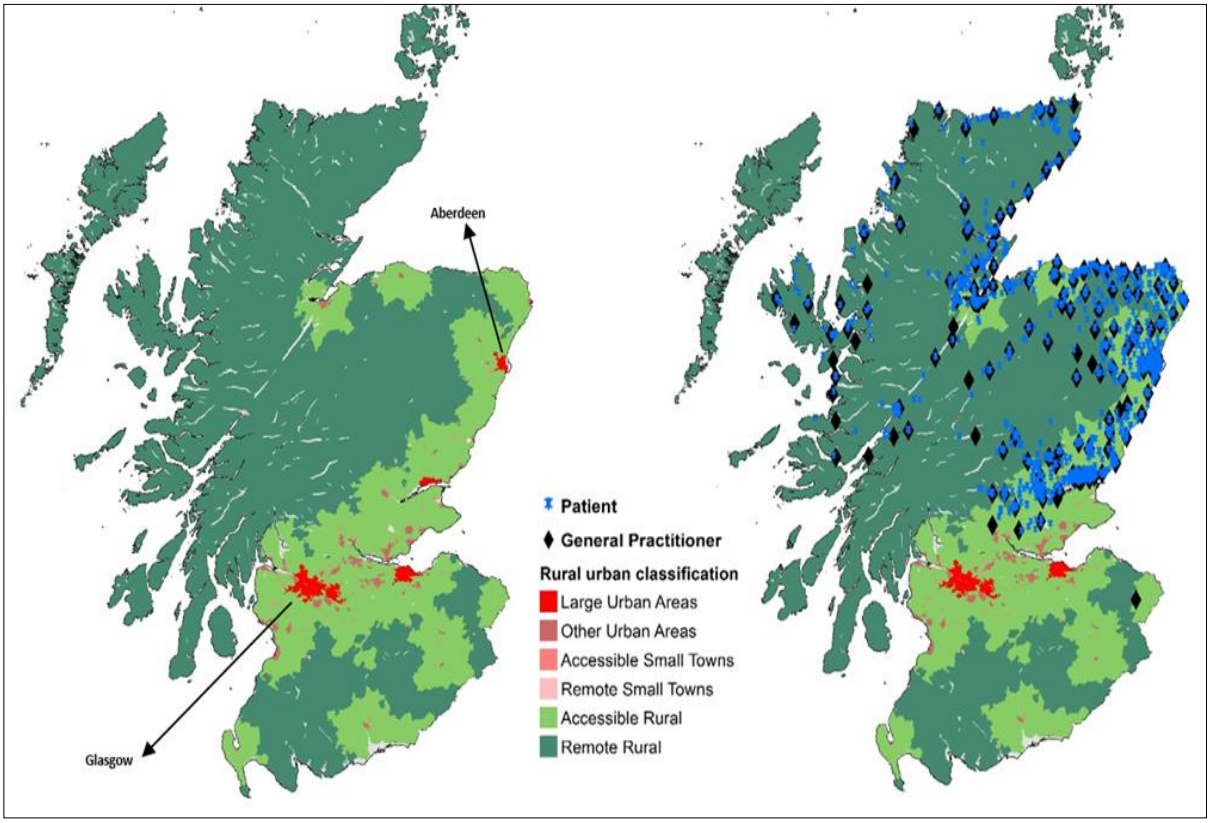
more symptoms vs one to three symptoms at the index presentation (10.7 vs. 7.7 minutes) (**Table 4.2**). There was little variation in mean travel times between the other variables. **Figure 4.1** is a map showing the geographical location of the patients, the GPs as well as the rural urban localities in the region of study. The map reveals that most of the region of study (Northern Scotland) is predominantly rural.

Table 4.2 - Sample characteristics and outcome variables

Variable	Frequency (%)	Mean travel time (minutes)	25th and 75th travel time percentile
Male	521 (56.3%)	8.8	2.8, 10.7
Female	405 (43.7%)	7.1	2.7, 10.0
Under 59 years	157 (17.0%)	8.8	3.0, 11.6
60 – 69 years	240 (25.9%)	7.6	2.2, 10.0
70 – 79 years	347 (37.5%)	8.5	2.9, 10.6
80 years plus	182 (19.7%)	7.1	2.8, 8.7
Rural	298 (32.2%)	12.0	2.6, 16.3
Urban	628 (67.8%)	6.2	2.8, 8.1
Travel time to GPs			
25th percentile	232 (25%)	2.8	
50th percentile	463 (50%)	5.5	
75th percentile	695 (75%)	10.3	
99th percentile	917 (99%)	43.8	
Least deprived Q1	191 (20.6%)	8.6	3.1, 12.7
Q2	191 (20.6%)	7.8	2.2, 10.1
Q3	171 (18.5%)	9.1	3.0, 11.2
Q4	188 (20.3%)	8.1	1.9, 9.1
Most deprived Q5	185 (20.0%)	6.5	3.9, 8.6
0 comorbidity	441 (47.6%)	7.8	2.6, 10.1
1-2 comorbidities	312 (33.7%)	8.3	3.0, 10.5
3 plus comorbidities	173 (18.7%)	8.3	2.5, 11.1
1 – 3 symptoms	825 (89.1%)	7.7	2.9, 10.3
4 plus symptoms	101 (10.9%)	10.7	2.1, 11.8
Alarm Symptoms	373 (40.3%)	7.9	2.6, 10.3
Emergency Admissions	243 (26.2%)	7.7	2.8, 10.1
Dukes' stage CD*	424 (48.9%)	7.9	2.9, 10.3

*****Information on disease stage was missing in 58 patients

Figure 4.1 - Map of the study area in Northern Scotland, showing location the geographical location of patients, GP services and rural and urban areas



4.4.1 Regression analysis

In the model without travel time – rurality interaction terms, there were no independent associations between travel time to GP, rural-urban residence, and the first three primary outcomes (alarm symptoms, emergency admissions and Dukes' stage). However, both longer travel and rural residence were significantly associated with better survival (HR 0.81 and 0.71, $p<0.01$ respectively) **(Table 4.3, model 4a&b).**

The addition of an interaction term to each model **(Table 4.3, models 1d - 4d)** showed that associations with travel time and each outcome differed between urban and rural patients. This difference was statistically significant for alarm symptoms (OR 0.62, $p<0.05$) and emergency admissions (OR 1.69, $p<0.05$). As an example, **Table 4.3**, model 1d, shows longer travel in urban areas increased the likelihood of presenting with alarm symptoms (OR 1.34, $p=0.06$),

but this likelihood was reduced in rural areas (OR 0.83, p=0.08, obtained by multiplying OR of the estimate of travel time to GP with the interaction term). Conversely, longer travel time in urban areas reduced the likelihood of having an emergency admission (OR 0.62, p<0.05) **(Table 4.3, 2d)** and of death within three years of diagnosis (HR 0.75, p<0.05) **(Table 4.3, 4d).**

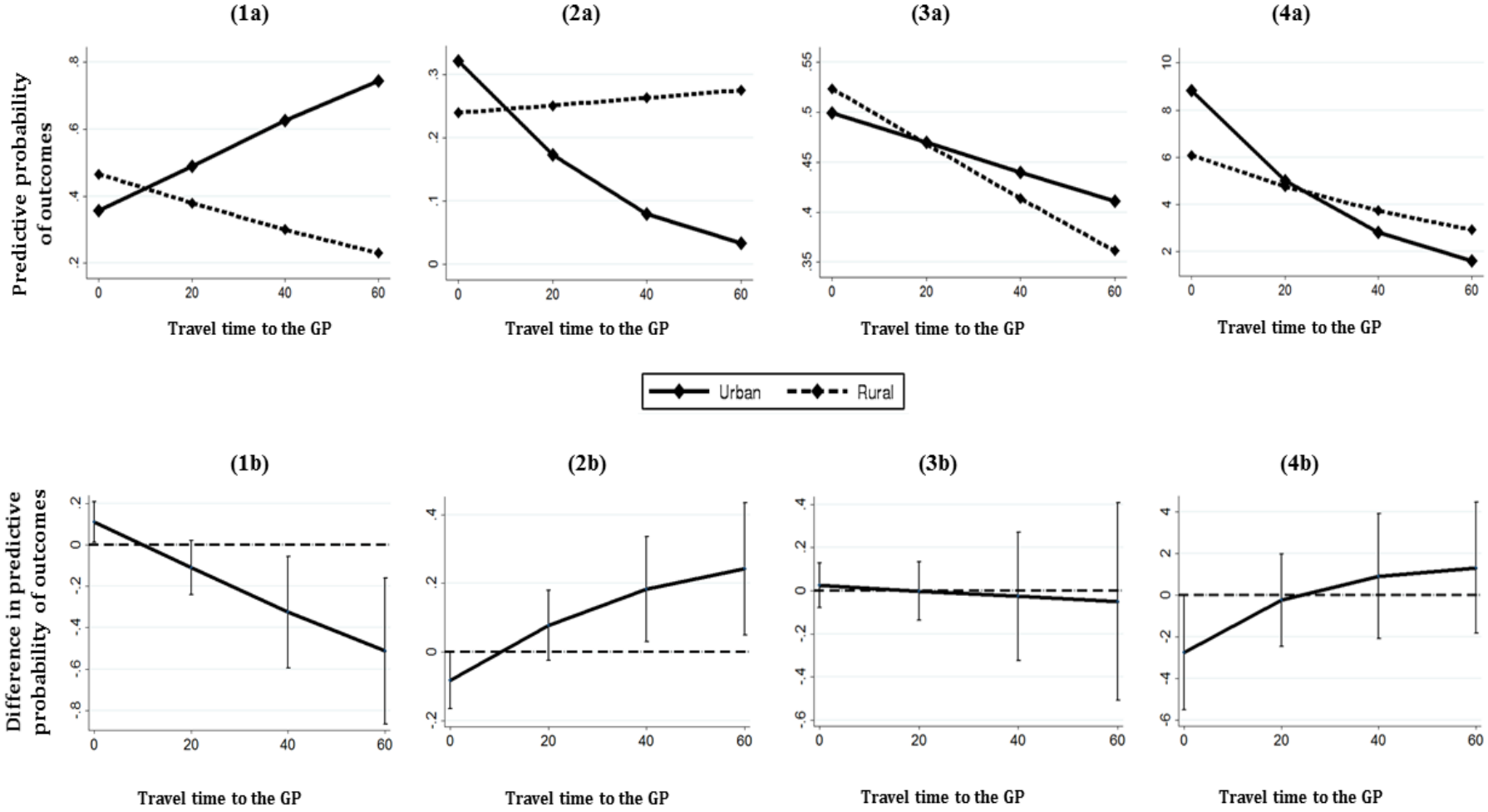
Figure 4.2 graphically illustrates the output from **Table 4.3, models 1d – 4d**. **Figure 4.2 (1a - 4a)** shows the differences in association between rural and urban areas; the lines indicate modelled association between travel time and the primary outcomes. **Figure 4.2 (1b – 4b)** shows the scale of the rural – urban difference in outcomes (solid line). This difference is statistically significance at the p<0.05 level where the 95% CI does not the cross zero marker (dashed line).

The odds of emergency admission was significantly lower in the presence of alarm symptoms (0.36, p<0.01) **(Table 4.3, model 2c).** Alarm symptoms were not significantly associated with survival, and there was no significant interaction between alarm symptoms and rural residence in the models with emergency admission and survival as outcomes.

Table 4.3 - Association between rurality, travel times to the GP, alarm symptoms and primary outcomes. Travel time is the predictor in 'a', rurality is the predictor in 'b', and alarm symptoms is the predictor in 'c'. Travel times are interacted with rurality in 'd'. All models are adjusted for age, gender, deprivation and comorbidity. For brevity, the coefficients for the covariates are only shown in the models with the interaction term (d).

	Explanatory variables	1) Alarm symptoms OR (95%CI)	2) Emergency admission OR (95%CI)	3) Dukes' Stages OR (95% CI)	4) Hazard ratio of death HR (95%CI)
	Outcome variables without interaction terms				
a)	**Travel time to GP (minutes)**	0.98 (0.84 - 1.14)	0.91 (0.75 - 1.09)	0.91 (0.78 - 1.07)	0.81** (0.72 - 0.92)
b)	**Rural**	1.08 (0.80 - 1.46)	0.83 (0.58 - 1.18)	0.99 (0.72 - 1.34)	0.71** (0.57 - 0.88)
c)	**Alarm Symptoms**	N/A	0.36* (0.25 - 0.53)	0.85 (0.64 - 1.14)	1.15 (0.94 - 1.41)
	Outcome variables with interaction terms fitted				
d)	**Travel time to GP**	1.34 (0.98 - 1.82)	0.62* (0.39 - 0.97)	0.94 (0.68 - 1.29)	0.75* (0.59 - 0.96)
	Rural	1.62* (1.05 - 2.48)	0.61 (0.36 - 1.02)	1.11 (0.72 - 1.70)	0.69* (0.51 - 0.94)
	Travel time / rurality interaction	0.62* (0.43 - 0.90)	1.69* (1.02 - 2.79)	0.95 (0.65 - 1.38)	1.18 (0.88 - 1.57)
	Alarm Symptoms	N/A	0.37** (0.26 - 0.54)	0.84 (0.63 - 1.12)	1.17 (0.95 - 1.43)
	Age (years)	1.00 (0.98 - 1.01)	1.02* (1.00 - 1.03)	0.97** (0.96 - 0.99)	1.03** (1.02 - 1.04)
	Female	0.95 (0.72 - 1.23)	0.89 (0.63 - 1.24)	0.76 (0.57 - 1.01)	0.74** (0.60 - 0.90)
	Index of deprivation (Carstairs)	0.99 (0.94 – 1.04)	0.99 (0.93 - 1.05)	1.05 (0.99 - 1.11)	1.02 (0.99 - 1.06)
	0 comorbidities (Charlson Score) (reference)	1	1	1	1
	1 – 2 comorbidities (Charlson)	0.53** (0.39 - 0.71)	4.87** (3.27 - 7.26)	0.87 (0.63 - 1.19)	1.20 (0.95 - 1.50)
	3 plus comorbidities (Charlson)	0.29** (0.20 - 0.44)	7.26** (4.63 - 11.39)	1.44 (0.97 - 2.14)	2.53** (1.98 - 3.25)

Figure 4.2 - '1a - 4a' show differences in association between rural and urban areas (Table 2, models 1d – 4d). The lines show modelled association between travel time and alarm symptoms (1a), emergency admission (2a), Dukes' stage (3a) hazard ratio of death (4a). 1b – 4b show the difference in the rural vs. urban slope along with 95% CI. These differences are statistically significant where the confidence intervals do not cross the zero line.



4.5 Conclusions

This study has examined the potential influence that rurality has on how patients present to their GP with symptomatic colorectal cancer and their subsequent outcomes. Additionally, the study has considered how rurality, urbanity and estimated travel time interact to influence the same outcomes. This work is novel because it considers for the first time whether symptomatic presentation of colorectal cancer to GPs is different in rural compared to urban areas.

One of the main finding was that rural patients had superior three year survival than their urban counterparts (OR 0.71, $p<0.01$). The association between longer travel and the primary outcomes was opposite in rural areas to that observed in urban localities. The difference was statistically significant for alarm symptoms (OR 0.62, $p<0.05$) and emergency admissions (OR 1.69, $p<0.05$). The moderation by travel times was statistically significant in urban areas but not in rural areas and may suggest that rural and urban patients may perceive geographical inaccessibility differently (Field & Briggs 2001). The presence of alarm symptoms significantly reduced the odds of emergency admissions (OR 0.36, $p<0.01$), whilst alarm symptoms were not associated with survival at three years.

Rural patients had better three year cancer survival, confirming some reports of better cancer outcomes in rural areas from the USA (McLafferty & Wang 2009). Travelling farther to GPs in urban areas increased the odds of presenting with alarm symptoms; this supports our hypothesis that poor access results in greater odds of cancer diagnosis resulting from an alarm symptom presentation. Patients presenting with alarm symptoms were less likely to be diagnosed with cancer following emergency admission, perhaps because patients with alarming symptoms are more likely to be referred using standard referral pathways (Jensen et al. 2014). Unlike previous studies that associated alarm symptoms with better survival (Dregan et al. 2013; Stapley et al. 2006), this present analysis could not confirm this finding.

The hypothesis expected that travelling farther in rural areas would also have higher odds of a diagnosis after presenting with alarm symptoms, rather, the analysis showed the opposite; longer travel time to GPs in rural areas reduced the odds of presenting with alarm symptoms. It is plausible that at the onset of such symptoms, those with the poorest geographical access in rural areas will delay seeking healthcare in comparison to their urban counterparts. Such rural - urban differences may be driven by social cultural differences in health seeking

behaviour, where the most remote rural patients may be displaying stoicism when seeking help (Emery et al. 2013; Douthit et al. 2015; Farmer et al. 2006; Elliott-Schmidt & Strong 1997). This may be supported by studies from Northern Scotland that found rural patients were more likely to present later, had lower expectations of healthcare, and may pursue their care less tenaciously (Bain et al. 2002; Bain & Campbell 2000).

Urban patients with shorter travel to their GP had the worst outcomes. This may be related to disadvantages amongst patients living in inner city deprived areas. Although area deprivation, was controlled for, the findings may suffer from residual confounding by deprivation; the Carstairs index may not fully capture individual level deprivation. Further, a measure of car ownership used in the index may not appropriately capture deprivation in rural areas where a car can be an essential possession (Information Services Division 2010).

The study has several strengths; the sample has high levels of linkage to high quality routine datasets which includes all patients diagnosed within the study period. Record linkage has enabled a detailed analysis using clinical, demographic and geographical information, and adjustment for a greater array of potential explanatory variables. Finally, the long follow-up period has made it possible to examine associations with long-term survival.

The study has a number of limitations. Except for survival analyses, it is a cross-sectional study hence the directions of cause and effect cannot be inferred. In order to allow for adequate follow up of deaths, the data is based on diagnoses made over a decade ago. Further, defining symptoms as either alarm or non-alarm is problematic in the absence of information on symptom severity. For instance, abdominal pain and anaemia have been grouped as non-alarm symptoms, but severe cases of these symptoms may be alarming enough to instigate a GP consultation or referral to hospital. Another limitation is not considering the availability of public transport, although previous work suggests this is infrequently used by cancer patients (Haynes et al. 2006).

It was hypothesised that living in rural areas and having longer travel to a GP would be associated with greater likelihood of obtaining a diagnosis from alarm symptoms, and via emergency admissions. This in turn would lead to later stage colorectal cancer diagnosis and poorer three year survival. Unexpectedly, the analysis found that rural patients and urban

patients with longer travel generally had better outcomes, were less likely to have emergency presentations, and had better survival. Further, the association between longer travel, alarm symptoms and emergency presentation was reversed between rural and urban areas.

These findings suggest that the interplay between attitudes and location is more complex than has previously been considered in research into cancer and rurality. Socio-cultural attitudes and geographical location may influence how patients present to GPs with symptomatic colorectal cancer, and this may influence differences in outcomes in ways that may be counterintuitive. Most existing research has tended to make straight comparisons between urban and rural populations or considered distance separately from constructs of rurality or urbanity. Future research should explore the mechanisms driving the interaction between location, access and outcomes. Such mechanisms may include time delays occurring at various stages of the diagnostic pathway such as patient, primary care or system delays (Neal 2009). There is also scope for more research to better understand how time delays (Weller et al. 2012) and frequency of consultation (Lyratzopoulos et al. 2013; Dregan et al. 2013) may mediate the causal pathway between geographical access and reporting of symptoms. Future research should also examine how symptoms related to cancer mediate the association between access and the other primary outcomes examined in this study.

These findings should reassure most rural cancer patients and their GPs that where they live may not be conferring the widely perceived rural diagnostic and survival disadvantages. In contrast, longer travel in urban areas may be associated with better outcomes. This has potential implications for urban GPs whose patients travel the least distance; such patients are more likely to live in the inner cities and may experience other access barriers such as longer delays due to larger GP list sizes. This has implications for defining catchment areas for urban practices that encapsulate travelling distances as well as transport options. Considering these in the context of practice list size and appointment availability could facilitate more efficient and effective healthcare access and outcomes.

The better survival amongst rural patients and patients with longer travel may be explained by the fact that these patients were also less likely to have emergency presentations. The next chapter will build on this hypothesis by undertaking an in-depth exploration of the association between access to the GP and the mode by which a cancer diagnosis was attained.

Chapter 5

Geographical access to general practitioners and modes of cancer diagnosis in England: a cross-sectional study of linked cancer registry and hospital data

5.1 Introduction

The previous chapter found that rural patients in Northern Scotland and patients with longer travel to their GP had better outcomes indicated by lower odds of obtaining a diagnosis via an emergency presentation and by better survival from colorectal cancer. This analysis was based on a small sample of data collected in the late 1990s; thus, it is necessary to examine whether those findings would be replicated using a more recent and detailed national dataset, with records from eight different cancer sites. This dataset will enable investigations on whether geographical accessibility and rurality predict the route by which a cancer diagnosis is obtained; the relationship between access and survival will be considered in the next chapter.

Identifying the pathways that lead to a cancer diagnosis is an important approach to improving access to care and consequent cancer survival. This is because the route that a patient takes to a cancer diagnosis has been shown to strongly predict survival (Elliss-Brookes et al. 2012; McPhail et al. 2013). Routes such as emergency presentations are associated with poorer survival (McPhail et al. 2013), whereas tumours detected via screening programmes have better outcomes (Brenner et al. 2014; Peto et al. 2004). There is also evidence associating increase in the GP use of two week wait (TWW) referrals with better survival (Møller et al. 2015).

In addition to potential effects on survival, there are cost-effectiveness benefits associated with specific diagnostic routes. Emergency presentations represent approximately 65% of all hospital bed-days in England, incurring heavy costs to the health services and causing significant disruption to planned inpatient admissions (King's Fund 2010a). They also account for an estimated 24% of all cancer diagnoses in England, ranging from around 5% in breast cancer to 62% in cancers of the central nervous system (Elliss-Brookes et al. 2012). Two specific diagnostic routes have been credited to the successful reduction of emergency admissions; diagnosis following screening for certain cancers and TWW GP referrals. The former increase the chances of cancer detection at the earliest stage whilst the latter ensure patients with expedited GP referrals are seen by a specialist within a two-week window. Indeed, the decline in emergency presentations in lung cancer from 39% in 2006 to 35% in 2013 may be due to increases in TWW referrals from 22% to 28% in the same time period (Public Health England 2015b). Similarly, the 3% drop in colorectal cancer emergency presentations may be explained by corresponding 4% and 10% increases in TWW referrals and screen detected diagnosis (Public Health England 2015a).

Preventing avoidable emergency admissions and other routes associated with poor prognosis requires understanding of factors that determine diagnostic routes. Some emergency admissions are unavoidable as they result from biological factors such as aggressive tumours that require sudden critical attention; these cases do not necessarily indicate failure of earlier diagnosis (Abel et al. 2015; Mitchell et al. 2015). However, many emergency admissions are potentially avoidable and are likely related to a combination of factors that operate at patient and health services levels. Patient level factors have been studied before: living in a deprived area, being elderly or female or belonging to an ethnic minority group have been associated with higher risk of emergency admissions (Abel et al. 2015; Raine et al. 2010). Health system level factors may also influence mode of diagnosis; difficulties in obtaining a GP appointment have been associated with an increase in emergency visits (Agarwal et al. 2012; Cowling et al. 2013). Geographical access to services may also determine how a cancer diagnosis is obtained. Two previous studies showed an association between poor access to hospital and screening sites and poor participation in screening programmes (Jensen et al. 2013; Maheswaran et al. 2006), likewise, access to hospital has also been reported to increase the odds of post-mortem cancer diagnosis (A. P. Jones et al. 2010).

There is limited evidence showing the relationship between access to primary care services and early cancer diagnosis. Previous work has shown that primary care inaccessibility reduces GP consultation rates (Haynes & Bentham 1982), suggesting that poor access may also determine how a cancer diagnosis is attained by lowering the likelihood of patients to engage with early diagnosis services, or by influencing GPs decision to refer patients to secondary care for diagnosis (Sladden & Thomson 1998; Haynes & Bentham 1982). Little research has looked at how associations differ between urban and rural areas. Rural areas are normally associated with poorer geographical access to services (DEFRA 2013a), but this does not necessarily translate to higher emergency department visits (Cowling et al. 2013), suggesting perhaps that rurality maybe a distinct variable that measures a different parameter to travel time.

5.1.1 Chapter objective

This is the first study to use individual patient level data to examine how travelling time to a GP, and living in a rural or urban area, is associated with the routes that patients take for a cancer diagnosis. The hypothesis is that longer travel and living in a rural area will increase the likelihood of obtaining a diagnosis from less desirable routes (emergency presentations and

death certificate only), but will decrease the likelihood of obtaining a diagnosis from routes of better prognosis (screen-detected and TWW). The findings may support early diagnosis efforts, by improving our understanding of how the prospect of longer travel determines interaction with services for a cancer diagnosis, or GPs decisions when making referrals.

5.2 Methods

The analysis uses cancer registry records of cases diagnosed between 2006 and 2010 in England. Eight cancer sites were examined; breast (ICD-10 C50), brain (C71), cervical (C53), colorectal (C18- C20), lung (C33-34), ovarian (C56-57), prostate (C61) and stomach (C16). These were selected to include both rare and commonly occurring tumours, those that are amenable to screening, and tumours with varying degrees of diagnostic difficulty (Lyratzopoulos et al. 2014). Each record contained information on the route that the patient would have taken prior to obtaining a diagnosis. This was obtained by linking data from routine datasets to provide details on interactions between the patient and the health services that preceded the diagnosis (Elliss-Brookes et al. 2012; National Cancer Intelligence Network 2013).

Record level data was retrieved from English cancer registries for all newly diagnosed malignant tumours, and linked to Hospital Episodes Statistics (HES) inpatient and outpatient records, the National Cancer Waiting Times (NCWT) monitoring dataset, and NHS Breast Screening Programme data. Screening information for cervical cancer was obtained from screening status held by cancer registries. Up to 71 distinct route combinations were identified by categorising contacts between the patient and health services according to the setting of diagnosis, the presence of inpatient and outpatient status, and the referral route (Elliss-Brookes et al. 2012). These were aggregated to give the following seven broad routes; screen-detected, Two Week Wait (TWW), GP Referral, Inpatient Elective, Other Outpatient, Emergency Presentations, Death Certificate Only (DCO) and Unknown. PHE (Public Health England) has produced a detailed description of the data linkage and methods (Elliss-Brookes et al. 2012; National Cancer Intelligence Network 2013).

Information on routes to diagnosis, age, gender, deprivation quintiles and the Charlson comorbidity index (Charlson et al. 1987) was retrieved from this linked dataset. Further linkages were made with a geographical access variable that estimated travel time in minutes

from the patients' home to their GP of registration. These travel times were computed in the ArcGIS Spatial Analyst module using the 'Cost Distance' (impedance surface) command ESRI. Firstly, roads depicted in the Meridian 2 road network (Motorway, A-road, B-road and minor roads) (Ordnance Survey 2013) were converted into a regular grid of 100 × 100 m cells, with each cell containing a value corresponding to travel-time-per-unit distance of traversing the cell. Road speeds were taken from an earlier work (A. Jones et al. 2010) and allowances were made for locations off the regular road grid (adjusted for walking speed). The resultant travel time map was used to calculate travel times from all postcodes (origins) in England to all GP practices (destinations) in England, Wales and some practices in the south of Scotland bordering England. Hospital travel times were also calculated using the same methodology, from all postcodes in England to all hospitals sites where cancer treatment was administered. ArcGIS model builder was used to iterate the computation of travel times from origins to destinations. More information on the development of the impedance surface used in this study has been described in previous literature (Sen et al. 2013; Bateman et al. 2013).

Annex A is a flowchart of the processes that were used to derive travel times for the English national cancer registry dataset obtained for this study. The entire process was computationally intensive and involved running the (GIS) software from several desktops over an estimated period of ten weeks. Road travel time was selected as the most appropriate measure of accessibility because a previous study has demonstrated that over 87% of cancer patients travel to hospital by motor vehicle (Haynes et al. 2006). Rural and urban status were assigned at postcode level using the 2011 rural-urban classification for small area geographies (DEFRA 2013b).

Primary outcomes were defined as two routes to diagnosis associated with good prognosis 'screen-detected' and 'TWW' and two less desirable routes 'emergency presentations' and 'DCO'. These were binary coded as 'screen-detected versus all other routes', 'TWW versus all other routes', 'emergency versus all other routes' and 'DCO versus all other routes'. All unknown routes and secondary tumours were excluded from the analysis.

Data were analysed using Stata Version 13 (StataCorp College Station, TX, USA). For the purpose of analysis, estimated travel time was grouped into four categories; '<10 minutes', '≥10 - 20 minutes', '>20 - 30 minutes' and '>30 minutes'. Logistic regression was used to

examine how travel time and rural – urban status was associated with the odds of each primary outcome. In a similar manner to Chapter Four (Section 4.3), interaction terms were fitted to examine whether travel times moderated the associations between rurality and the outcomes. All models were adjusted for variables deemed to have a relationship with the outcomes; age, deprivation, comorbidity, and gender (where applicable). Odds ratios (OR) and 95% CI are presented for all models.

5.3 Results

There were 749,451 unique records with a primary diagnosis of the specified cancers in England between 2006 and 2010. An estimated 88% of the population had access to their GPs within an estimated 10-minute drive (**Table 5.1**). Those with the poorest access (over 30 minutes) comprise just 0.7% of the population. Rural patients accounted for about 22% of the sample, and this was highest in prostate cancers at 24%, and lowest in cervical cancer at 16%. Routes to diagnosis varied considerably by tumour type. Breast cancer had the lowest percentage of emergency presentations with 4.5% of cancers being diagnosed via this route, whereas 62% of brain tumours were diagnosed via this route. Lung cancer had the highest percentage of DCOs with 0.7% being diagnosed post mortem (**Table 5.1**).

5.3.1 Association between travel times and primary outcomes

In the unadjusted regression models (**Table 5.2 A, B, C&D)** longer travel times were associated with increased likelihood of both emergency presentations and DCO routes. The associations were stronger for DCO than emergency presentations, and the odds ratios progressively increased from the lowest travel time category to the highest. In the unadjusted models where screen-detected and TWW were the primary outcomes, those with longer travel were less likely to have a diagnosis from these two routes; the odd ratios progressively decreased from the lowest travel time category to the highest.

After adjusting for covariates, DCOs and emergency admissions were more likely in female and older patients (**Table 5.3 A&B).** Deprivation and presence of comorbidities were also associated with higher odds of diagnosis via emergency routes but not a DCO (**Table 5.3 A&B)**. Adjusting for these covariates had a minimal effect on the associations with estimated travel time. For example, stomach cancer patients with estimated travel times of over 30 minutes were more than 10 times likely to have a post mortem diagnosis (OR 10.58, $p<0.01$).

Corresponding findings were an eight fold (OR 8.31, p<0.01), and seven fold (OR 7.29, p<0.01) elevated odds for breast and colorectal cancer patients respectively (**Table 5.3 B).** The ORs for cervical cancer when the outcome was DCO could not be estimated due to small numbers.

In the adjusted models with screen-detected and TWW as primary outcomes, female gender decreased the likelihood of diagnosis from both routes (**Table 5.4 A&B).** Deprivation was associated with lower odds of diagnosis via screening (**Table 5.4 A**). Longer travel was associated with lower odds of diagnosis via TWW, these associations were statistically significant for breast, colorectal, lung, prostate and ovarian cancers. For those travelling over 30 minutes, the odd of diagnosis via TWW for these cancer sites were; 0.87 (p<0.05), 0.68, 0.74, 0.70 and 0.53 (p<0.01) respectively compared to those with under 10 minutes of travel **(Table 5.4 B).** Longer travel was also associated with lower odds of diagnosis via screening for breast and colorectal cancer (**Table 5.4 A).**

5.3.2 Regression results for rurality and primary outcomes

Living in a rural area reduced the likelihood of a diagnosis from the emergency route but increased the likelihood for two week wait referral and screening. Adjusting for covariates had minimal effect on the associations with rurality. For example **Table 5.5 A** shows that rural patients had a lower odds of obtaining a cancer diagnosis via an emergency route, and this was statistically significant for breast, colorectal, lung, prostate (0.88, 0.93, 0.96, 0.87, p<0.01 respectively) and stomach cancer (0.93, p<0.05). Rural patients also had significantly higher odds of attaining a diagnosis following a two week wait referral for the following cancer sites: colorectal, lung, prostate, stomach and ovarian cancers (ORs 1.12, 1.15, 1.12, 1.13, 1.15, p<0.01 respectively) **(Table 5.6 B).**

Fitting a travel time – rurality interaction term suggested that the association between travel times and the outcome differed between rural and urban patients in some cancer sites. **Table A.1** of **Annex B** gives an example of the moderating effect of longer travel in rural vs. urban areas, when the outcome was diagnosis following an emergency route. Taking the example of colorectal cancer (**Model 2**), the results show that associations with travel time and this outcome differed between urban and rural patients, and the difference is statistically significant (OR 0.95, p<0.05). Longer travel in urban areas increased the odds of obtaining a diagnosis via

the emergency route (OR 1.09, $p<0.01$). Longer travel in rural areas also increased the odds of obtaining a diagnosis via this route (OR 1.04, $p<0.05$) (obtained by multiplying OR of the estimate of travel time to GP with the interaction term). In this colorectal cancer example, longer travel to the GP had a stronger moderating effect on emergency presentations in urban than in rural areas. The rest of the outcomes (TWW, DCO and screening have not been shown for brevity but they generally show similar patterns).

Table 5.1 - Characteristics of the study cohort

		Number of cases (% percentage)								
		All cancers No. (%)	Breast No. (%)	Colorectal No. (%)	Cervical No. (%)	Lung No. (%)	Prostate No. (%)	Stomach No. (%)	Ovarian No. (%)	Brain No. (%)
Age groups	**Under 59 years**	190,796 (25.5)	85,152 (44.4)	28,079 (17.6)	9,032 (73.8)	25,755 (15.3)	21,929 (13.0)	4,836 (15.1)	10,756 (36.7)	8,962 (45.4)
	60 - 69 years	202,144 (27.0)	47,616 (24.8)	41,281 (25.8)	1,156 (9.4)	45,630 (27.0)	56,963 (33.6)	6,668 (20.8)	7,330 (25.0)	4,674 (23.7)
	70 - 79 years	211,440 (28.2)	31,733 (16.5)	51,082 (32.0)	1,112 (9.1)	58,492 (34.6)	60,999 (36.0)	11,212 (35.0)	6,499 (22.2)	4,018 (20.4)
	80 years plus	145,071 (19.4)	27,487 (14.3)	39,340 (24.6)	945 (7.7)	38,985 (23.1)	29,441 (17.4)	9,339 (29.1)	4,731 (16.1)	2,070 (10.5)
Gender	**Male**	366,844 (49.0)	1,474 (0.8)	88,547 (55.4)		95,483 (56.6)		20,801 (64.9)		11,376 (57.7)
	Female	382,577 (51.1)	190,514 (99.2)	71,221 (44.6)		73,369 (43.5)		11,254 (35.1)		8,348 (42.3)
Travel time in minutes to the GP	**<= 10**	622,070 (88.1)	159,910 (87.9)	132,383 (88.2)	10,276 (88.6)	141,112 (89.4)	140,337 (87.4)	26,743 (89.5)	24,063 (87.7)	15,459 (85.7)
	10.1 – 20	70,852 (10.0)	18,782 (10.3)	15,003 (10.0)	1,105 (9.5)	14,016 (8.9)	17,385 (10.8)	2,675 (9.0)	2,786 (10.2)	2,026 (11.2)
	20.1 – 30	8,412 (1.2)	2,167 (1.2)	1,705 (1.1)	126 (1.1)	1,626 (1.0)	2,010 (1.3)	317 (1.1)	365 (1.3)	323 (1.8)
	Over 30	4,707 (0.7)	1,175 (0.7)	963 (0.6)	92 (0.8)	1,019 (0.7)	936 (0.6)	163 (0.6)	221 (0.8)	226 (1.3)
Rural- urban status	**Rural**	157,631 (21.0)	41,748 (21.8)	35,181 (22.0)	2,029 (16.6)	28,828 (17.1)	40,573 (24.0)	5,748 (17.9)	6,244 (21.3)	4,223 (21.4)
	Urban	591,820 (79.0)	150,240 (78.3)	124,601 (78.0)	10,216 (83.4)	140,034 (82.9)	128,759 (76.0)	26,307 (82.1)	23,072 (78.7)	15,501 (78.6)
Deprivation quintile	**1 least deprived**	148,868 (19.9)	42,500 (22.1)	32,718 (20.5)	1,851 (15.1)	22,977 (13.6)	39,763 (23.5)	5,178 (16.2)	5,951 (20.3)	4,319 (21.9)
	2	161,072 (21.5)	43,712 (22.8)	35,285 (22.1)	2,123 (17.3)	29,580 (17.5)	40,480 (23.9)	6,193 (19.3)	6,436 (22.0)	4,448 (22.6)
	3	157,338 (21.0)	40,839 (21.3)	34,305 (21.5)	2,369 (19.4)	34,225 (20.3)	35,567 (21.0)	6,574 (20.5)	6,340 (21.6)	4,142 (21.0)
	4	147,639 (19.7)	35,861 (18.7)	31,070 (19.5)	2,722 (22.2)	38,428 (22.8)	29,967 (17.7)	6,936 (21.6)	5,807 (19.8)	3,696 (18.7)
	5 most deprived	134,534 (18.0)	29,076 (15.1)	26,404 (16.5)	3,180 (26.0)	43,652 (25.9)	23,555 (13.9)	7,174 (22.4)	4,782 (16.3)	3,119 (15.8)
Comorbidities	**0 comorbidity**									
	1-2	644,457 (86.0)	173,959 (90.6)	133,908 (83.8)	11,290 (92.2)	131,650 (78.0)	143,572 (84.8)	25,786 (80.4)	26,096 (89.0)	17,507 (88.8)
	comorbidities	89,336 (11.9)	16,022 (8.4)	21,904 (13.7)	849 (6.9)	30,984 (18.4)	22,116 (13.1)	5,207 (16.2)	2,841 (9.7)	1,927 (9.8)
	3+ comorbidities	15,658 (2.1)	2,007 (1.1)	3,970 (2.5)	106 (0.9)	6,228 (3.7)	3,644 (2.2)	1,062 (3.3)	379 (1.3)	290 (1.5)
Routes to diagnosis	**Screen detected**	62,098 (8.3)	53,002 (27.6)	7,595 (4.8)	2,941 (24.0)					
	Two week wait	218,648 (29.2)	80,773 (42.1)	42,197 (26.4)	2,005 (16.4)	39,735 (23.5)	47,947 (28.3)	7,309 (22.8)	6,838 (23.3)	191 (1.0)
	Emergency	154,916 (20.7)	8,675 (4.5)	39,174 (24.5)	1,380 (11.3)	62,931 (37.3)	15,388 (9.1)	10,191 (31.8)	8,838 (30.2)	12,196 (61.8)
	DCO	3,442 (0.5)	608 (0.3)	737 (0.5)	16 (0.13)	1,200 (0.7)	341 (0.2)	191 (0.6)	176 (0.6)	86 (0.4)

Table 5.2 - (A,B,C,D) – Association between travel times to GP, rurality and A) emergency presentations B) DCO C) TWW and D) Screen detected, for breast, colorectal, cervical, lung, prostate, stomach, ovarian and brain cancer. Unadjusted models. Results are reported as odds ratios OR (95% CI), **p<0.01, *p<0.05

	A) Emergency Presentation						B) Death Certificate Only (DCO)					
	Urban	Rural	<= 10	10.1 – 20	20.1 – 30	Over 30	Urban	Rural	<= 10	10.1 – 20	20.1 – 30	Over 30
Breast	1	0.77** (0.73-0.82)	1	0.96 (0.89-1.04)	1.34** (1.11-1.61)	1.60** (1.26-2.04)	1	1.12 (0.93-1.35)	1	1.63** (1.24-2.16)	4.95** (3.14-7.80)	8.51** (5.20-13.92)
Colorectal	1	0.85** (0.83-0.87)	1	0.92** (0.89-0.96)	1.11 (0.99-1.23)	1.51** (1.31-1.74)	1	1.05 (0.88-1.25)	1	1.25 (0.94-1.64)	1.74 (0.90-3.37)	7.00** (4.40-11.14)
Cervical	1	0.94 (0.80-1.09)	1	0.98 (0.80-1.19)	1.49 (0.91-2.45)	0.75 (0.34-1.63)	1	0.73 (0.17-3.21)		n/a	n/a	n/a
Lung	1	0.90** (0.87-0.92)	1	1.02 (0.98-1.06)	1.04 (0.94-1.16)	1.11 (0.98-1.27)	1	0.94 (0.81-1.10)	1	1.10 (0.87-1.39)	2.46** (1.57-3.85)	2.44** (1.37-4.33)
Prostate	1	0.79** (0.76-0.83)	1	0.92** (0.87-0.98)	1.11 (0.95-1.29)	1.71** (1.42-2.08)	1	1.03 (0.80-1.32)	1	1.44* (1.02-2.03)	2.34* (1.10-4.98)	6.16** (3.03-12.51)
Stomach	1	0.83** (0.78-0.89	1	0.95 (0.87-1.04)	1.15 (0.90-1.46)	1.05 (0.75-1.49)	1	1.27 (0.90-1.80)	1	2.38** (1.50-3.80)	2.80 (0.88-8.89)	11.73** (5.05-27.22)
Ovarian	1	0.93* (0.87-0.99)	1	0.92 (0.84-1.00)	1.21 (0.97-1.52)	1.59** (1.19-2.13)	1	1.11 (0.78-1.59)	1	1.30 (0.76-2.24)	1.34 (0.33-5.44)	3.62* (1.14-11.52)
Brain	1	0.95 (0.89-1.03)	1	1.02 (0.92-1.13)	0.96 (0.76-1.21)	1.03 (0.77-1.38)	1	0.78 (0.45-1.36)	1	1.36 (0.64-2.90)	2.15 (0.52-8.92)	1.60 (0.22-11.64)

	C) Two week wait (TWW)						D) Screening					
	Urban	Rural	<= 10	10.1 – 20	20.1 – 30	Over 30	Urban	Rural	<= 10	10.1 – 20	20.1 – 30	Over 30
Breast	1	0.97** (0.94-0.98)	1	0.91** (0.88-0.94)	0.86** (0.78-0.94)	0.84** (0.74-0.96)	1	1.22** (1.19-1.25)	1	1.15** (1.11-1.19)	0.98 (0.89-1.08)	0.72** (0.62-0.84)
Colorectal	1	1.16** (1.13-1.19)	1	1.03 (0.99-1.07)	0.97 (0.86-1.08)	0.69** (0.58-0.81)	1	1.16** (1.10-1.22)	1	1.21** (1.13-1.30)	1.00 (0.80-1.26)	0.45** (0.29-0.70)
Cervical	1	1.09 (0.96-1.24)	1	0.99 (0.84-1.18)	0.70 (0.41-1.20)	0.69 (0.36-1.35)	1	0.93 (0.83-1.04)	1	1.07 (0.92-1.23)	0.83 (0.54-1.29)	1.06 (0.64-1.76)
Lung	1	1.20** (1.17-1.24)	1	1.04 (1.00-1.08)	0.96 (0.86-1.09)	0.79** (0.67- 0.92)	1					
Prostate	1	1.14** (1.11-1.17)	1	1.03 (0.99-1.06)	0.95 (0.86-1.05)	0.71** (0.60-0.84)	1					
Stomach	1	1.18** (1.10-1.26)	1	1.04 (0.95-1.14)	0.96 (0.73-1.25)	0.88 (0.60-1.31)	1					
Ovarian	1	1.21** (1.14-1.29)	1	1.11* (1.01-1.21)	0.72* (0.55-0.95)	0.54* (0.36-0.80)	1					
Brain	1	1.42* (1.03-1.95)	1	1.40 (0.93-2.12	0.98 (0.31-3.09)	1.46 (0.46-4.62)	1					

Table 5.3 - (A & B) – Association between travel to the GP and A) emergency presentations B) DCO, for breast, colorectal, cervical, lung, prostate, stomach, ovarian and brain cancer. Models are adjusted for age, gender (where applicable), deprivation and comorbidity. Results are reported as odds ratios (95% CI), **p<0.01, *p<0.05

A) Emergency Presentation

	Travel Time to the GP (minutes)				Age	Female	Deprivation quintile					Number of comorbidities		
	<= 10	10.1 – 20	20.1 – 30	Over 30			1 least	2	3	4	5 most	0	1 - 2	3+
		1.13**	1.58**	1.81**	1.07**			1.09*	1.16**	1.40**	1.72**		1.20**	2.12**
Breast	1	(1.05-1.22)	(1.30-1.92)	(1.41-2.34)	(1.07-1.07)		1	(1.01-1.17)	(1.08-1.25)	(1.30-1.51)	(1.59-1.85)	1	(1.12-1.28)	(1.86-2.41)
		1.00	1.22**	1.68**	1.02**	1.30**		1.07**	1.15**	1.29**	1.55**		1.25**	1.75**
Colorectal	1	(0.96-1.05)	(1.09-1.36)	(1.45-1.94)	(1.02-1.02)	(1.27-1.33)	1	(1.02-1.11)	(1.10-1.19)	(1.24-1.34)	(1.49-1.61)	1	(1.21-1.29)	(1.64-1.88)
		1.12	1.83*	0.84	1.05**			1.19	1.54**	1.58**	1.75**		1.07	1.76*
Cervical	1	(0.90-1.38)	(1.07-3.11)	(0.37-1.89)	(1.04-1.05)		1	(0.94-1.52)	(1.23-1.94)	(1.26-1.97)	(1.41-2.17)	1	(0.88-1.32)	(1.12-2.75)
		1.08**	1.13*	1.19*	1.03**	1.08**		1.06**	1.13**	1.22**	1.34**		1.23**	1.79**
Lung	1	(1.04-1.12)	(1.01-1.25)	(1.04-1.36)	(1.03-1.03)	(1.06-1.10)	1	(1.02-1.10)	(1.09-1.17)	(1.18-1.27)	(1.29-1.39)	1	(1.20-1.27)	(1.70-1.89)
		1.00	1.26**	1.86**	1.09**			1.08*	1.15**	1.31**	1.62**		1.42**	2.24**
Prostate	1	(0.94-1.06)	(1.07-1.47)	(1.52-2.29)	(1.09-1.10)		1	(1.0 -1.14)	(1.09-1.22)	(1.24-1.39)	(1.52-1.71)	1	(1.36-1.49)	(2.05-2.44)
		1.04	1.29*	1.15	1.03**	1.27**		1.04	1.10*	1.27**	1.51**		1.28**	1.88**
Stomach	1	(0.95-1.14)	(1.01-1.65)	(0.81-1.64)	(1.03-1.04)	(1.20-1.34)	1	(0.9 -1.14)	(1.01-1.20)	(1.16-1.38)	(1.39-1.64)	1	(1.20-1.37)	(1.65-2.14)
		0.98	1.30*	1.64**	1.03**			1.08	1.06	1.26**	1.34**		1.23**	1.98**
Ovarian	1	(0.90-1.07)	(1.03-1.64)	(1.22-2.21)	(1.03-1.03)		1	(0.99-1.18)	(0.98-1.16)	(1.15-1.37)	(1.23-1.47)	1	(1.13-1.34)	(1.59-2.46)
		1.05	1.04	1.08	1.02**	1.14**		1.04	1.07	1.19**	1.42**		0.85**	1.16
Brain	1	(0.95-1.17)	(0.82-1.32)	(0.80-1.44)	(1.01-1.02)	(1.07-1.22)	1	(0.95-1.14)	(0.97-1.18)	(1.08-1.32)	(1.28-1.58)	1	(0.76-0.95)	(0.87-1.54)

B) Death Certificate Only

	Travel Time to the GP (minutes)				Age	Female	Deprivation quintile					Number of comorbidities		
	<= 10	10.1 – 20	20.1 – 30	Over 30			1 least	2	3	4	5 most	0	1 - 2	3+
		1.84**	5.13**	8.31**	1.19**			1.07	0.89	1.23	1.08		0.66**	0.94
Breast	1	(1.39-2.45)	(3.18-8.27)	(4.91-14.08)	(1.17-1.20)		1	(0.79-1.46)	(0.65-1.24)	(0.90-1.68)	(0.76-1.53)	1	(0.49-0.89)	(0.53-1.70)
		1.36*	1.80	7.29**	1.12**	1.48**		0.81	0.91	0.88	0.94		1.01	0.61
Colorectal	1	(1.02-1.79)	(0.92-3.51)	(4.53-11.75)	(1.11-1.13)	(1.23-1.78)	1	(0.61-1.06)	(0.70-1.19)	(0.66-1.16)	(0.70-1.26)	1	(0.8-1.28)	(0.33-1.11)
Cervical		n/a	n/a	n/a	n/a			n/a	n/a	n/a	n/a		n/a	n/a
		1.15	2.66**	2.47**	1.07**	1.05		1.25	0.98	1.18	1.43**		0.71**	0.69*
Lung	1	(0.91-1.45)	(1.69-4.16)	(1.39-4.40)	(1.06-1.07)	(0.9 -1.20)	1	(0.97-1.60)	(0.76-1.27)	(0.92-1.51)	(1.13-1.80)	1	(0.59-0.86)	(0.47-1.00)
		1.46*	2.29*	4.42**	1.22**			0.94	0.63*	0.89	0.88		1.21	0.98
Prostate	1	(1.03-2.08)	(1.0 -4.92)	(2.11-9.26)	(1.20-1.24)		1	(0.67-1.32)	(0.43-0.92)	(0.61-1.29)	(0.58-1.32)	1	(0.91-1.63)	(0.53-1.80)
		2.54**	2.84	10.58**	1.08**	1.91**		0.80	0.60	0.97	0.63		0.85	0.38
Stomach	1	(1.58-4.07)	(0.89-9.13)	(4.45-25.12)	(1.06-1.10)	(1.33-2.74)	1	(0.46-1.38)	(0.33-1.07)	(0.58-1.64)	(0.35-1.13)	1	(0.53-1.37)	(0.09-1.56)
		1.45	1.21	3.17	1.13**			1.29	1.08	1.18	1.33		0.93	1.26
Ovarian	1	(0.84-2.53)	(0.29-5.02)	(0.98-10.35)	(1.11-1.16)		1	(0.73-2.29)	(0.60-1.95)	(0.65-2.14)	(0.71-2.50)	1	(0.55-1.54)	(0.46-3.48)
		1.52	2.42	1.71	1.02*	0.92		2.05	3.32*	2.94*	3.59*		1.23	0.89
Brain	1	(0.71-3.25)	(0.58-10.11)	(0.23-12.52)	(1.00-1.03)	(0.54-1.57)	1	(0.71-5.91)	(1.21-9.08)	(1.03-8.40)	(1.25-10.28)	1	(0.58-2.65)	(0.1 -6.58)

Table 5.4 - (A & B) – Association between travel to the GP and A) screen-detected B) TWW, for breast, colorectal, cervical, lung, prostate, stomach, ovarian and brain cancer. Models are adjusted for age, gender (where applicable), deprivation and comorbidity. Results are reported as odds ratios (95% CI), **p<0.01, *p<0.05

A) Screen detected														
	Travel Time to the GP (minutes)				Age	Female	Deprivation (quintile)					Number of comorbidities		
	<= 10	10.1 – 20	20.1 – 30	Over 30			1 least	2	3	4	5 most	0	1 - 2	3+
		1.09**	0.92	0.68**	0.99**			0.92**	0.89**	0.80**	0.72**		0.68**	0.37**
Breast	1	(1.05-1.12)	(0.84-1.02)	(0.59-0.79)	(0.99-0.99)		1	(0.89-0.95)	(0.86-0.92)	(0.78-0.83)	(0.69-0.74)	1	(0.66-0.71)	(0.32-0.43)
		1.11**	0.89	0.37**	0.97**	0.60**		0.96	0.92*	0.82**	0.67**		0.70**	0.37**
Colorectal	1	(1.03-1.20)	(0.71-1.12)	(0.24-0.58)	(0.97-0.97)	(0.57-0.63)	1	(0.90-1.03)	(0.86-0.99)	(0.76-0.88)	(0.62-0.73)	1	(0.65-0.76)	(0.29-0.48)
		1.02	0.67	0.97	0.95**			0.87	0.81*	0.70**	0.75**		0.82	1.10
Cervical	1	(0.88-1.19)	(0.42-1.06)	(0.57-1.65)	(0.94-0.95)		1	(0.75-1.02)	(0.69-0.94)	(0.60-0.82)	(0.65-0.87)	1	(0.65-1.03)	(0.56-2.14)

B) Two Week Wait														
	Travel Time to the GP (minutes)				Age	Female	Deprivation (quintile)					Number of comorbidities		
	<= 10	10.1 – 20	20.1 – 30	Over 30			1 least	2	3	4	5 most	0	1 - 2	3+
		0.94**	0.88**	0.87*	1.01**			1.11**	1.15**	1.19**	1.23**		1.08**	0.99
Breast	1	(0.91-0.97)	(0.81-0.97)	(0.77-0.99)	(1.01-1.01)		1	(1.08-1.14)	(1.12-1.18)	(1.15-1.22)	(1.19-1.27)	1	(1.04-1.12)	(0.90-1.09)
		1.01	0.94	0.68**	1.00	0.87**		1.03	1.04*	0.98	0.89**		0.66**	0.43**
Colorectal	1	(0.97-1.05)	(0.84-1.05)	(0.58-0.80)	(1.00-1.00)	(0.85-0.89)	1	(1.00-1.07)	(1.00-1.07)	(0.95-1.02)	(0.85-0.92)	1	(0.64-0.69)	(0.39-0.47)
		1.03	0.73	0.72	1.04**			1.12	1.03	1.20*	1.09		0.76**	0.65
Cervical	1	(0.8 -1.23)	(0.41-1.28)	(0.36-1.43)	(1.04-1.04)		1	(0.93-1.34)	(0.86-1.24)	(1.01-1.43)	(0.92-1.30)	1	(0.63-0.93)	(0.40-1.06)
		0.99	0.91	0.74**	0.98**	0.96**		1.04	1.01	0.95**	0.85**		0.55**	0.32**
Lung	1	(0.95-1.04)	(0.81-1.02)	(0.63-0.86)	(0.98-0.98)	(0.93-0.98)	1	(0.99-1.08)	(0.96-1.05)	(0.91-0.99)	(0.82-0.89)	1	(0.53-0.57)	(0.30-0.35)
		1.01	0.93	0.70**	1.01**			1.06**	1.04*	1.02	0.94**		0.72**	0.49**
Prostate	1	(0.93-1.05)	(0.84-1.03)	(0.60-0.83)	(1.01-1.01)		1	(1.03-1.10)	(1.01-1.08)	(0.98-1.05)	(0.91-0.98)	1	(0.69-0.74)	(0.45-0.54)
		1.00	0.92	0.84	0.99**	0.71**		1.04	1.07	0.95	0.92*		0.58**	0.35**
Stomach	1	(0.91-1.10)	(0.70-1.22)	(0.56-1.25)	(0.99-1.00)	(0.67-0.76)	1	(0.95-1.14)	(0.98-1.17)	(0.87-1.04)	(0.84-1.00)	1	(0.54-0.63)	(0.28-0.42)
		1.06	0.70*	0.53**	1.00*			1.06	1.03	0.90*	0.80**		0.58**	0.35**
Ovarian	1	(0.97-1.17)	(0.53-0.92)	(0.35-0.78)	(1.00-1.00)		1	(0.97-1.15)	(0.94-1.12)	(0.82-0.98)	(0.73-0.88)	1	(0.52-0.65)	(0.25-0.50)
		1.35	0.93	1.43	1.00	0.98		1.08	0.89	0.82	0.84		0.63	
Brain	1	(0.89-2.04)	(0.29-2.92)	(0.45-4.51)	(1.00-1.01)	(0.73-1.32)	1	(0.71-1.63)	(0.57-1.38)	(0.51-1.32)	(0.51-1.38)	1	(0.35-1.14)	n/a

Table 5.5 - (A & B) – Association between rural – urban status and A) emergency presentations B) DCO, for breast, colorectal, cervical, lung, prostate, stomach, ovarian and brain cancer. Models are adjusted for age, gender (where applicable), deprivation and comorbidity OR (95% CI), **p<0.01, *p<0.05

B) Emergency Presentation												
	Rural – urban status		Age	Female					Deprivation			Comorbidity
	Urban	Rural			1 least	2	3	4	5 most	0	1 - 2	3+
		0.88**	1.07**			1.09*	1.06**	1.36**	1.62**		1.20**	2.08**
Breast	1	(0.82-0.93)	(1.07-1.07)		1	(1.01-1.18)	(1.08-1.25)	(1.26-1.16)	(1.51-1.75)	1	(1.13-1.28)	(1.84-2.36)
		0.93**	1.02**	1.29**		1.07**	1.14**	1.28**	1.50**		1.25**	1.74**
Colorectal	1	(0.90-0.96)	(1.02-1.02)	(1.27-1.33)	1	(1.03-1.11)	(1.10-1.19)	(1.23-1.33)	(1.45-1.56)	1	(1.21-1.29)	(1.63-1.86)
		1.00	1.04**			1.23	1.53**	1.60**	1.78**		1.07	1.71*
Cervical	1	(0.85-1.19)	(1.04-1.05)		1	(0.98-1.56)	(1.23-1.92)	(1.29-1.99)	(1.44-2.21)	1	(0.88-1.31)	(1.10-2.66)
		0.96**	1.03**	1.08**		1.07**	1.13**	1.21**	1.32**		1.23*	1.79**
Lung	1	(0.93-0.99)	(1.03-1.03)	(1.05-1.10)	1	(1.03-1.11)	(1.09-1.17)	(1.17-1.25)	(1.28-1.37)	1	(1.2 -1.26)	(1.69-1.89)
		0.87**	1.09**			1.08**	1.14**	1.27**	1.54**		1.42**	2.21**
Prostate	1	(0.83-0.91)	(1.09-1.10		1	(1.03-1.14)	(1.08-1.21)	(1.20-1.34)	(1.46-1.64)	1	(1.36-1.48)	(2.03-2.40)
		0.93*	1.03**	1.26**		1.04	1.11*	1.24**	1.47**		1.30**	1.87**
Stomach	1	(0.87-0.99	(1.03-1.03)	(1.20 -1.33)	1	(0.95-1.13)	(1.02-1.20)	(1.14-1.34)	(1.35-1.60)	1	(1.22-1.38)	(1.65-2.13)
		0.95	1.03**			1.08	1.07	1.23**	1.31**		1.25**	1.97**
Ovarian	1	(0.89-1.02)	(1.03-1.03)		1	(0.99-1.17)	(0.99-1.16)	(1.14-1.34)	(1.20-1.43)	1	(1.15-1.36)	(1.60-2.44)
		0.99	1.02**	1.12**		1.04	1.06	1.19**	1.41**		0.84**	1.11
Brain	1	(0.91-1.06)	(1.01-1.02)	(1.05-1.19)	1	(0.95-1.14)	(0.97-1.16)	(1.08-1.31)	(1.27-1.56)	1	(0.75-0.93)	(0.85-1.46)

A) Death Certificate Only												
	Rural – urban status		Age	Female					Deprivation			Comorbidity
	Urban	Rural			1 least	2	3	4	5 most	0	1 - 2	3+
		1.20	1.15**			1.01	0.85	1.09	1.04		0.55**	0.72
Breast	1	(0.99-1.47)	(1.14-1.16)		1	(0.79-1.30)	(0.66-1.10)	(0.85-1.41)	(0.78-1.38)	1	(0.42-0.72)	(0.41-1.25)
		1.09	1.09**	1.37**		0.83	0.93	0.95	0.94		0.71**	0.45**
Colorectal	1	(0.91-1.30)	(1.08-1.10)	(1.18-1.59)	1	(0.66-1.04)	(0.75-1.16)	(0.76-1.20)	(0.74-1.21)	1	(0.57-0.88)	(0.25-0.79)
Cervical	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
		0.96	1.05**	1.00		1.07	0.91	1.06	1.23*		0.52**	0.57**
Lung	1	(0.82-1.13)	(1.05-1.06)	(0.89-1.12)	1	(0.87-1.31)	(0.74-1.12)	(0.87-1.29)	(1.02-1.50)	1	(0.43-0.62)	(0.41-0.80)
		1.00	1.21**			0.96	0.72	0.83	0.92		1.00	0.74
Prostate	1	(0.77- 1.30)	(1.19-1.22)		1	(0.71-1.31)	(0.52-1.01)	(0.59-1.17)	(0.64-1.33)	1	(0.76-1.31)	(0.41-1.37)
		1.30	1.05**	1.78**		0.77	0.72	0.91	0.82		0.54**	0.25*
Stomach	1	(0.91-1.87)	(1.03-1.06)	(1.33-2.38)	1	(0.48-1.22)	(0.45-1.15)	(0.58-1.41)	(0.52-1.30)	1	(0.34-0.85)	(0.06-1.01)
		1.08	1.10**			1.51	1.01	1.12	1.39		0.81	0.90
Ovarian	1	(0.74-1.57)	(1.09-1.12)		1	(0.95-2.42)	(0.61-1.67)	(0.67-1.86)	(0.82-2.36)	1	(0.51-1.27)	(0.33-2.47)
		1.01	1.02*	0.92		2.08	3.31*	2.87*	3.46*		1.23	0.88
Brain	1	(0.98-1.04)	(1.00-1.03)	(0.54-1.56)	1	(0.72-6.00)	(1.21-9.04)	(1.01-8.16)	(1.21-9.89)	1	(0.57-2.64)	(0.12-6.51)

Table 5.6 - (A & B) - Association between rural – urban status and A) screening B) Two Week Wait, for breast, colorectal, cervical, lung, prostate, stomach, ovarian and brain cancer. Models are adjusted for age, gender (where applicable), deprivation and comorbidity, OR (95% CI), **p<0.01, *p<0.05

A) Screening												
	Rural – urban status		Age	Female	Deprivation					Comorbidity		
	Urban	Rural			1 least	2	3	4	5 most	0	1 - 2	3+
		1.15**	0.99**			0.91**	0.89**	0.82**	0.74**		0.69**	0.37**
Breast	1	(1.12-1.18)	(0.99- 0.99)		1	(0.88-0.94)	(0.86-0.91)	(0.79-0.84)	(0.71-0.76)	1	(0.66-0.72)	(0.32-0.42)
		1.08*	0.97**	0.60**		0.95	0.90**	0.82**	0.68**		0.71**	0.37**
Colorectal	1	(1.02-1.14)	(0.97-0.97)	(0.57-0.63)	1	(0.89-1.02)	(0.84-0.97)	(0.76-0.88)	(0.63-0.74)	1	(0.65-0.77)	(0.29-0.47)
		0.93	0.95**			0.89	0.81**	0.71**	0.76**		0.83	1.03
Cervical	1	(0.82-1.06)	(0.94-0.95)		1	(0.77-1.04)	(0.69-0.94)	(0.61-0.82)	(0.66-0.88)	1	(0.66-1.03)	(0.53-2.01)

B) Two Week Wait												
	Rural – urban status		Age	Female	Deprivation					Comorbidity		
	Urban	Rural			1 least	2	3	4	5 most	0	1 - 2	3+
		0.99	1.01**			1.11**	1.15**	1.19**	1.23**		1.08**	0.99
Breast	1	(0.97-1.01)	(1.01-1.01)		1	(1.08-1.14)	(1.12-1.18)	(1.16-1.23)	(1.19-1.27)	1	(1.05-1.12)	(0.90-1.08)
		1.12**	1.00	0.87**		1.01	1.04*	0.99	0.91**		0.66**	0.43**
Colorectal	1	(1.09-1.15)	(1.00-1.00)	(0.85-0.89)	1	(0.99-1.06)	(1.00-1.08)	(0.96-1.03)	(0.88-0.95)	1	(0.64-0.69)	(0.40-0.47)
		1.05	1.04**			1.12	1.06	1.23*	1.12		0.76**	0.71
Cervical	1	(0.92-1.21)	(1.04-1.04)		1	(0.94-1.35)	(0.88-1.26)	(1.03-1.46)	(0.94-1.33)	1	(0.63-0.91)	(0.44-1.13)
		1.15**	0.98**	0.96**		1.02	1.01	0.97	0.89**		0.56**	0.33**
Lung	1	(1.11-1.18)	(0.98-0.98)	(0.94-0.98)	1	(0.99-1.07	(0.97-1.05)	(0.94-1.01)	(0.85-0.92)	1	(0.54-0.58)	(0.30-0.36)
		1.12**	1.01**			1.05**	1.04*	1.03	0.98		0.72**	0.50**
Prostate	1	(1.09-1.15)	(1.00-1.01)		1	(1.02-1.09)	(1.00-1.07)	(0.99-1.06)	(0.94-1.02)	1	(0.70-0.74)	(0.46-0.54)
		1.13**	1.00**	0.71**		1.05	1.07	0.99	0.95		0.58**	0.34**
Stomach	1	(1.06-1.22)	(1.00-1.00)	(0.67-0.75)	1	(0.96-1.15)	(0.98-1.16)	(0.90-1.08)	(0.87-1.04)	1	(0.53-0.63)	(0.28-0.42)
		1.15**	1.00**			1.04	1.03	0.93	0.83**		0.59**	0.36**
Ovarian	1	(1.07-1.23)	(1.00-1.00)		1	(0.96-1.13)	(0.95-1.12)	(0.85-1.02)	(0.76-0.91)	1	(0.53-0.65)	(0.26-0.50)
		1.35	1.00	0.99		1.11	0.94	0.82	0.97		0.67	
Brain	1	(0.97-1.88)	(0.99-1.01)	(0.74-1.32)	1	(0.74-1.67)	(0.61-1.45)	(0.51-1.31)	(0.60-1.59)	1	(0.38-1.18)	n/a

5.4 Conclusions

This study provides new evidence on how geographical access to GPs in England is associated with the routes that lead to a cancer diagnosis. Earlier diagnosis is recognised as an important approach to improving cancer survival (Cancer Research UK 2014), and the role of GPs is central because majority of cancer patients will present their symptoms to primary care (NICE 2015). Across the eight cancer sites studied, longer travel to the patients' GP significantly increased the likelihood of having a cancer diagnosis through routes that are associated with poor outcomes such as emergency or death certificate only pathways. Conversely, longer travel significantly decreased the likelihood of obtaining a diagnosis following routes that are associated with good prognosis such as screening or two week wait. When rural and urban patients were compared, the opposite was apparent; patients living in rural areas were more likely to obtain diagnosis through a route of good prognosis and less likely to have their cancer diagnosed via emergency admissions. Fitting an interaction term suggested that for some cancer sites, travel time may have a different association with the outcomes in rural compared to urban areas.

These findings may support efforts such as the National Awareness and Early Diagnosis Initiative (NAEDI) work on achieving earlier presentation (Cancer Research UK 2016d). Efforts to improve earlier diagnosis in cancer should take consideration of geographical barriers that may impede implementation. Likewise, GPs should be vigilant of accessibility issues that some of their patients may face, as these are likely to determine receipt of earlier diagnosis.

The findings presented in this study respond to requests for evidence to establish the role of access in explaining variations in the mode of diagnosis (Lyratzopoulos et al. 2015; Wallace et al. 2014). To our knowledge, this is the first study to simultaneously investigate four different routes to diagnosis and their association with geographical access to GPs. Previous studies have focused on access to hospital or screening sites or have examined single routes to diagnosis (Cowling et al. 2013; Jensen et al. 2013; Maheswaran et al. 2006). Two previous studies looking at access to screening and hospital sites showed that poor access was associated with poor participation in breast cancer screening programmes (Jensen et al. 2013; Maheswaran et al. 2006). Both studies used a smaller regional population than our study, so it is likely that their sample was more geographically homogenous. They also both estimated geographical

access using road distance rather than travel time; the latter is a better measure of access because it is closest to what patients experience (Lovett et al. 2002). Another study found longer travel times to hospital increased the odds of post mortem diagnosis (A. P. Jones et al. 2010). Similar to the findings from Chapter Four, longer travel moderated the association between rurality and emergency presentations for breast, colorectal, prostate and stomach cancer. In these cancer sites, longer travel increased the odds of an emergency presentations in both rural and urban areas, but the association was stronger in urban compared to rural areas. This supports the view that rural and urban patients may perceive geographical inaccessibility differently (Field & Briggs 2001).

These results suggest that travel to the GP may also influence patients' engagement with health services in general, and this is not limited to services offered by the GP. As an example, poor access to the GP may impede the uptake of services such as colorectal and breast cancer screening that are not offered by GPs. Similar to what other studies have reported (Abel et al. 2015; McPhail et al. 2013; Wallace et al. 2014), this study found that women were more likely to have a diagnosis following a route associated with poor prognosis. This might be because women are reportedly more fearful and experience more discomfort when undergoing investigations such as colonoscopies (Farraye et al. 2004; Kim et al. 2000).

Patients recorded to have the longest journey to their GP may indicate disconnection from primary care, such as failure to register with a GP after relocation. Although only 0.7 percent of the sample travelled longer than 30 minutes to see their GP, the poor outcomes amongst these patients is concerning. The magnitude of apparent effect for risk of diagnosis at death is particularly alarming; tenfold in stomach cancer (OR 10.58, $p<0.01$), eightfold in breast cancer (OR 8.31, $p<0.01$), sevenfold in colorectal cancer (OR 7.29, $p<0.01$) and over fourfold in prostate cancer (OR 4.42, $p<0.01$).

It is likely that the prospect of longer travel influences how patients interact with primary care for a cancer diagnosis. Geographical inaccessibility may discourage engagement with the health services, and so decrease the likelihood of health seeking behaviour such as participation in screening. Poor access may also reduce the likelihood of reporting symptoms that may be related to cancer (Emery et al. 2013), consequently increasing emergency presentations or death at diagnosis. It is also likely that poor access may influence GPs' decisions to refer for

further investigation; previous studies have shown that distance to hospital may be one of the things GPs consider when making referrals (Haynes & Bentham 1982; Sladden & Thomson 1998). Conversely, it is plausible that when GPs do make urgent referrals, patients delay attending appointments due to barriers in access.

Living in a rural area increased the likelihood of having a cancer diagnosis via screening or a TWW referral, but decreased the likelihood of emergency diagnosis. One explanation might be that rural GPs offer better continuity of care; a concept noted as one of the most essential component of general practice (Royal College of General Practitioners 2016). Continuity of care marks the extent to which patients experience an ongoing relationship with a preferred GP and how GPs assist patients with navigating complex health care systems (King's Fund 2010b; Royal College of General Practitioners 2016). This has been shown to reduce emergency admissions (Christakis et al. 2001; Menec et al. 2006) and to increase screening participation (Flocke et al. 1998). Geographical variations of continuity have been reported; patients living outside urban areas are more likely to indicate preference for a specific clinician (King's Fund 2010b).

Preference of a specific GP can however have the limitation of creating a barrier to alternative perspectives or second opinions from other clinicians (King's Fund 2010b), and this may in some cases introduce delays in the diagnostic process (Ridd et al. 2015; King's Fund 2010b). A study investigating the association between continuity of care, time to referral and time to diagnosis gave different findings for different cancer sites (Ridd et al. 2015). Patient–doctor continuity in the 24 months before diagnosis was associated with a slightly later diagnosis (time delay to diagnosis) of colorectal cancer, but not of breast or lung cancer. Conversely, patient-doctor continuity after the index consultation reduced the time to referral in breast cancer patients only (Ridd et al. 2015). The effect of continuity of care on the diagnostic process in cancer in the UK remains to be fully explored. Another more probably explanation for higher rates of emergency presentations amongst urban patients is that these patients are more likely to use emergency services because most of the close proximity to these services (Magnusson 1980). Additionally, urban patients have been shown to have a more 'detached' and 'consumerist' approach which can manifest in using a range of health services and by switching and shopping around for the most suitable services (Farmer et al. 2006).

The most recent strategy on cancer has identified earlier diagnosis and narrowing inequalities as a key mechanism to improving overall cancer survival rates in England (Independent Cancer Taskforce 2015). The strategy has set recommendations with the aim of increasing ten year survival for an additional 30,000 patients by 2020, of which 11,000 will be achieved through earlier diagnosis (Independent Cancer Taskforce 2015). Furthermore, the strategy has issued a call for evaluating the impact of cancer outcomes on patients living different distances from a cancer centre (Independent Cancer Taskforce 2015). Our findings indicate that this call should also be extended to primary care. The gatekeeping role of GPs means they control access to other services and therefore it is likely that poor outcomes related to access observed in secondary care may have their origins from poor primary care access (Bentham & Haynes 1985; Carr-Hill et al. 1997).

An estimated 0.7% patients experiencing the highest odds of delayed diagnosis are more likely to live over 30 minutes from their GP; this represents around 2,420 annual cases of all cancers diagnosed in England (Cancer Research UK 2016b). Targeted action on improving access amongst these patients may help meet the goal of reducing cancer mortality and narrowing inequalities. This is because poor geographical access is disproportionally felt by those who are either elderly, have a disability or a chronic condition that renders them unable to drive, or are too deprived to be able to afford a car (Bentham & Haynes 1985; Mungall 2005). Supporting these groups of patients to engage with the health services may include use of telephone consultations or other aspects of telehealth that have been successfully implemented in cancer care and other disease areas (Schlachta-Fairchild 2001; Shepherd et al. 2017; Win 2017; Barker et al. 2016).

This study has several strengths. The use of a large national dataset provides sufficient statistical power and adequate variation of explanatory variables, which enables control for covariates. The large dataset also enables comparisons across cancer sites that may vary in rarity, ease of detection in primary care, or by their association with deprivation. This has made it possible to undertake stratified analysis to investigate how variation in access to early diagnosis differs by cancer type. The linking of various routine datasets to obtain information on routes to diagnosis has also made it possible to examine the four different routes in parallel; comparing routes associated with good outcomes and those associated with poor prognosis. As such, the results provide a more complete picture of how physical access to primary care may

determine how a cancer diagnosis is obtained. Lastly, the inclusion of all cases registered in England over five years enhances generalisability.

There are some limitations to the study. Firstly, it is a cross-sectional study hence the directions of cause and effect cannot be inferred. Secondly, the measure of geographical access (travel time) is estimated and may not necessarily represent the actual journey time that patients might take, although previous work suggests that estimated travel times closely match the actual journeys (Haynes et al. 2006). The analysis did not consider other forms of transport such as public transport, walking or cycling although these are infrequently used for health service appointments, (Haynes et al. 2006). Also, the implications on survival were not considered, this will be examined in the next Chapter (Six). Lastly, cervical screening findings should be interpreted with caution because this data may be of poorer quality due to cancer registry variations in reporting screen detected records (National Cancer Intelligence Network 2013).

Although living in a rural areas has been related with having poorer geographical access to most services (DEFRA 2013a), this inaccessibility may not necessarily translate to poorer health outcomes as shown by the findings in this chapter. Thus, it is likely that rurality may be a distinct concept that measures a different parameter than travel time. It is therefore plausible that there are separate mechanisms mediating the association between longer travel, rurality and survival. It may also be that similar mediators exert varying levels of mediation on the access - survival causal pathway, on the basis of how access is defined (travel time or rurality). Such mechanisms are likely to operate at the patient level, the level of health services or both. The next chapter will use causal mediation techniques to examine some underlying mechanisms that may explain how longer travel and rurality impacts on cancer outcomes. The two potential mediators that will be studied are disease stage cancer waiting time; operating at the patient and health services level, respectively.

Chapter 6

Do time delays and advanced disease at diagnosis explain the association between access to health services and colorectal cancer survival?

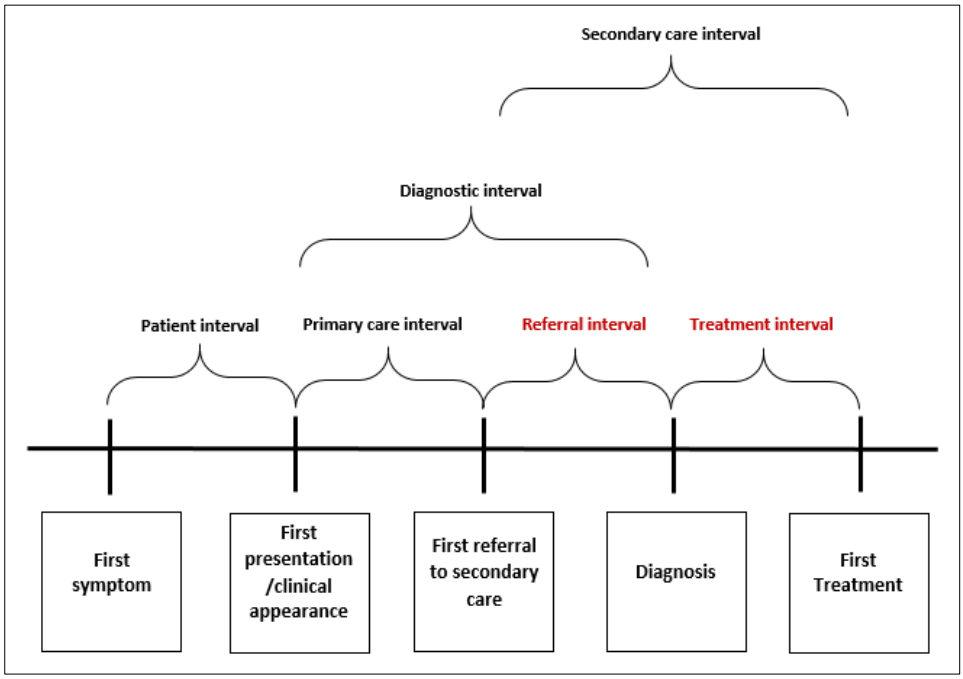
6.1 Introduction

The previous chapter demonstrated that geographical access to primary care for early diagnosis may have important consequences for how a cancer diagnosis is obtained. In that chapter, longer travel was associated with higher odds of diagnosis via an emergency presentation and post mortem diagnosis, but with lower odds of diagnosis via screening or urgent two-week referral. In contrast, living in a rural area mostly reduced the likelihood of a diagnosis from the emergency route, but increased the likelihood for two week wait referral and screening. As described in previous chapters, other studies have also reported that poor access to cancer treatment services determines lower treatment uptake and is associated with worse cancer survival (Jones et al. 2008; Campbell et al. 2000). Emerging evidence, as reported in Chapter Four, shows that access to primary care also impacts on cancer survival: rural patients, and those with greater travel to their GP in Scotland had better colorectal cancer survival rates.

The exact causal mechanisms of how access determines cancer outcomes are unknown. It is likely they are at least in part related to the decisions that patients make about when to consult their GP, or that GPs make about referral to secondary care. One result of this decision making is time delay, between symptom onset and consultation or between referral, diagnosis and treatment.

Time delays along the cancer care pathway can be defined using the Aarhus checklist that was developed to provide methodological consistency for early diagnosis research (Weller et al. 2012). **Figure 6.1** is adapted from this checklist and highlights two different time delays (referral and treatment intervals) that will be examined in more detail in the rest of this chapter. Time delays will be referred to as 'time intervals', so as to be consistent with the methodological guidance set by the Aarhus checklist (Weller et al. 2012). In England, time intervals can be derived from the Cancer Waiting Times (CWT) that were originally introduced by the NHS Cancer Plan (2000) (Department of Health 2000). It was hoped that monitoring cancer waiting times would improve outcomes by promoting rapid diagnosis and treatment. Reducing long waits was also expected to improve patient experience, and to reduce unacceptable variations in the quality and treatment type across the country (Department of Health 2000). Yet, the extent to which CWT have contributed to improving outcomes has been disputed (Neal 2009), and this has led to some suggestions for them to be abolished altogether (Department of Health 2011a).

Figure 6.1 - Time intervals in the route from first symptom until start of treatment



Source: - Adapted from Weller et al, 2012

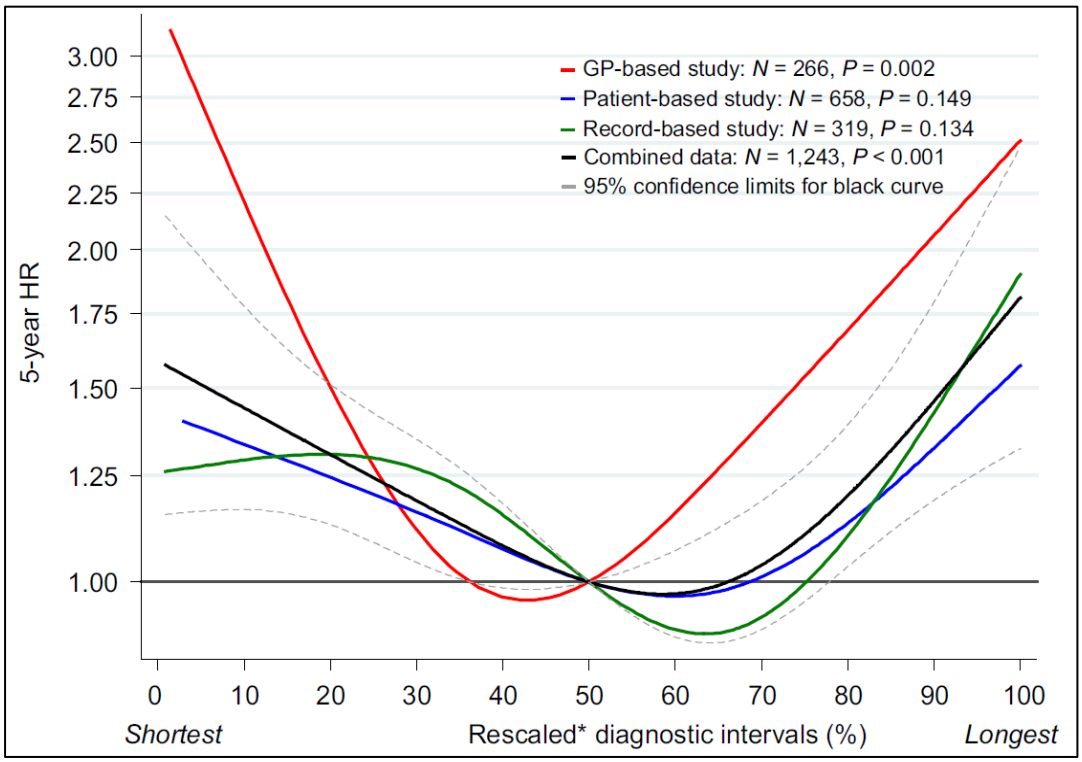
6.1.1 Waiting times and survival

Evidence on the clinical effectiveness of reducing waiting times on outcomes such as cancer survival is so far inconclusive (Neal 2009; Neal et al. 2015). However, there is evidence that shorter waits may offer psychological benefits to patients (Department of Health 2011b), and monitoring them has helped to drive service improvements (Department of Health 2011b), although this has not necessarily reduced variations in treatment (Robinson et al. 2005; House of Commons Library 2015). A systematic review of the association between time to diagnosis or treatment and clinical outcomes provided conflicting results (Neal et al. 2015). For example, in lung cancer, five of the studies reviewed found that shorter diagnostic, treatment or referral intervals were associated with more favourable outcomes, indicated by better survival and earlier stage. In contrast, 13 studies found that shorter treatment intervals was associated with poor outcomes, whereas seven studies reported no associations (Neal et al. 2015). This lack of consensus was also shown across other cancer sites.

The association between shorter delays with poorer outcomes is counterintuitive and has been referred to as the ‘waiting time paradox’. One study reported a u-shaped association between

the adjusted hazard ratio and diagnostic intervals, where patients with very short or very long waiting times from first presentation to diagnosis (known as the 'diagnostic interval') had the worst survival (**Figure 6.2**), (Tørring et al. 2012). This waiting time paradox may be explained by patients who present with more advanced disease or as emergencies being investigated more rapidly (Tørring et al. 2012; Neal et al. 2015). It is possible that any association between longer time intervals and poorer outcomes would only become apparent once the effect of expediting treatment for the most ill patients is removed. For instance, other studies have shown that the association between shorter waits and survival disappears when the analysis is controlled for emergency presentations (Neal 2009; Stapley et al. 2006), and this is because patients diagnosed via the emergency route are diagnosed more rapidly yet have worse outcomes (Tørring et al. 2012).

Figure 6.2 - Estimated 5-year hazard ratios as a function of the diagnostic interval (time from the first presentation of symptoms in primary care until diagnosis)



Source: Tørring et al, 2012. Re-used with permission.
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6.1.2 Stage as a mediator

Disease stage very likely sits on the causal pathway between access and survival, and may therefore be an important mediator in the association between measures of access and survival. Studies that have examined the association between advanced stage and geographical access have shown that patients with the worst access to a cancer centre and to primary care also have a higher odds of having an advance disease stage at diagnosis (Campbell et al. 2001; Wang et al. 2008). The evidence on rural – urban differences in stage is inconclusive: research based in France and Scotland suggests later disease stage amongst patients living in rural areas (Campbell et al. 2001; Launoy et al. 1992), whereas, studies from the USA point to a higher risk of late disease stage amongst urban patients (McLafferty & Wang 2009). It is very plausible that disease stage is a mediator between geographical access and survival, but so far the causal mechanisms that may underlie this have not been elucidated.

6.2 Chapter Objective

The primary hypothesis in this study is that geographical inaccessibility results in longer referral and treatment intervals **(Figure 6.1),** and to more advanced disease stage at diagnosis or treatment, which then results in worse cancer survival. Colorectal cancer was selected as an appropriate cancer site for this study because the association between poor access and more advanced disease stage in this cancer site has been documented in the literature (Campbell et al. 2001; McLafferty & Wang 2009), as described in Section 6.1.2. Furthermore, the association between access to the GP for colorectal cancer diagnosis is explored in detail in Chapter Four of this thesis. Also, as described in Section 6.1.1, an association between colorectal cancer and diagnostic interval (time from first presentation of symptoms in primary care to diagnosis) has also been reported (Tørring et al. 2012).

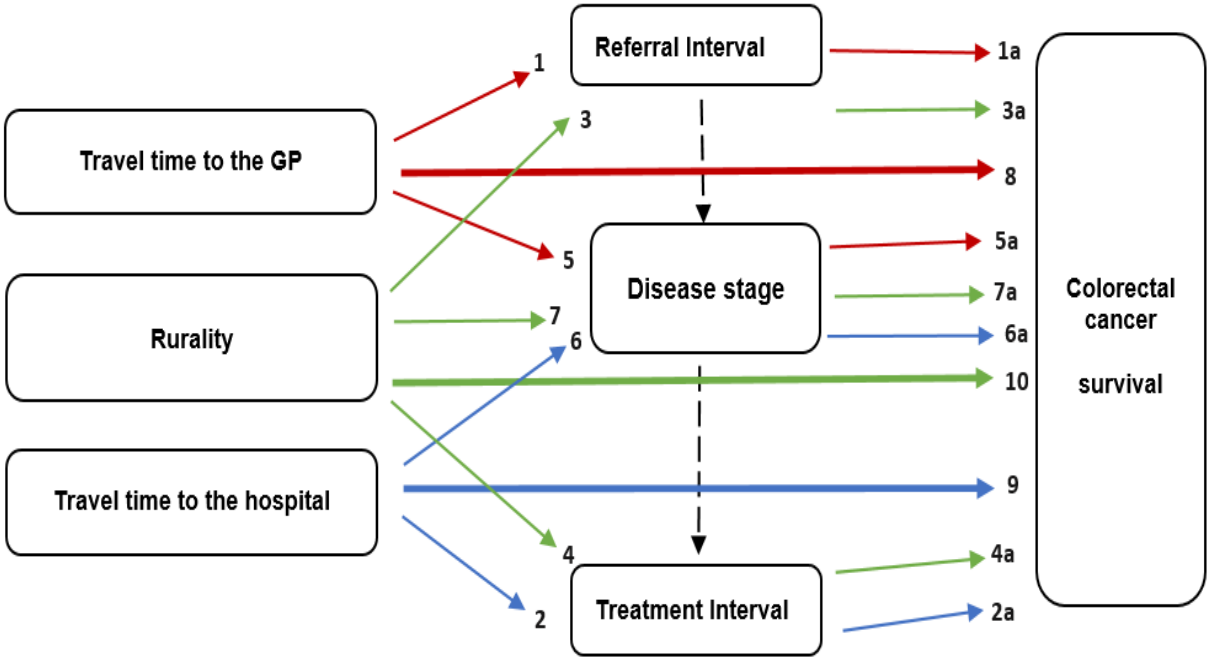
The chapter will begin by exploring the association between poor access and time intervals. The time intervals examined are time from referral to diagnosis (referral interval) and time from diagnosis to treatment (treatment interval), illustrated in **Figure 6.1**. Access will be defined as travel time from place of residence to the GP, to the hospital of initial treatment, and in terms of rural or urban status. There is only one known study that has examined the association between accessibility and time delays, which found that women living in the most remote areas of Australia were up to five times more likely to experience longer diagnostic

intervals; estimated as waiting time between the first presentation to the GP and diagnosis of ovarian cancer (Jordan et al. 2004).

The second part of the analysis will examine whether living farther from a patient's GP, and living in a rural area, is associated with survival from colorectal cancer; this too has not been investigated before in England. The chapter will also revisit the association between access to secondary services for treatment and survival.

The analysis will conclude by investigating whether two identified mediators 'time intervals' and 'Dukes' stage' can explain the association between access and cancer survival. Several predictor, mediator and outcome relationships have been identified for study and are illustrated on **Figure 6.3** . These arrows show the direction of the associations and the colour indicate the variable predicting survival; travel time to the GP (red), rurality (green) and travel time to hospital (blue). The suffix 'a' is added to show mediated relationships.

Figure 6.3 - Time intervals and disease stage as potential mediators of the association between geographical access to treatment and cancer outcomes



6.3 Methods and Materials

The study uses the national cancer registry dataset that was used in Chapter Four. Data on colorectal cancer tumours (ICD10 C18- C20) diagnosed in England between 2006 and 2010, and followed up to December 2015 for survival status were obtained for the analysis in this chapter. These records were linked with information from the hospital episode statistics (HES) inpatient and outpatient records, and with the National Cancer Waiting Times (NCWT) monitoring data. All data linkage was undertaken by the PHE NCRAS Team (Public Health England National Cancer Registration and Analysis Service).

Linkage with the HES provided information on the GP of registration, hospital of treatment, type of treatment and presence of comorbidity. Linkage to the Cancer Waiting Times (CWT) data provided information on key time points along the cancer care continuum, such as date of GP referral, date of diagnosis and treatment, and the date of death. In accordance to the Aarhus checklist **Figure 6.1,** time intervals between key time points (estimated in days) were used as a proxy for estimating time delays (Weller et al. 2012). The two time intervals examined in this chapter are: intervals between referral and diagnosis and between diagnosis and treatment, henceforth referred to as 'referral interval' and 'treatment interval'. Stage at diagnosis was recorded as Dukes' stages (A, B, C or D) and binary coded as 'early stage (CD)' and 'late stage (AB)'. Stage and the time intervals were used as the mediating variables.

Geographical access was defined as travel time from the patient to GP of registration, and to the hospital of first treatment. The treatment types used in this analysis are surgery (curative and non-curative), radiotherapy, chemotherapy and hormone therapy. All records where treatment type was recorded as 'imaging', as well as records with treatment recorded as 'unknown' were excluded in the travel to hospital analysis. Travel times were computed using a Geographical Information System (GIS) (ArcGIS 10.3, Esri Inc.), see Chapter Five for more information on the methodology used to compute travel times. The English rural – urban classifications were used to group patients according to rural or urban residence (DEFRA 2013b). These measures, as well as the information on travel times were added to the linked dataset and were used as the predictor variables.

The estimated travel times to GPs were grouped into four categories of ten minutes increment; 'less than 10 minutes', '10.1 - 20 minutes' and '20.1 - 30 minutes' and 'over 30 minutes'. The

average travel to hospital is normally longer than average travel to the GP and so travel times to hospital were grouped into four categories of 15 minutes increment; ‘less than 15 minutes’, ‘15.1 - 30 minutes’ and ‘30.1 - 45 minutes’ and ‘over 45 minutes’.

Logistic regression was used to examine the association between the access measures (travel time and rurality) and Dukes’ stage, estimated as odds ratios (OR) and 95% CI. Cox proportional hazards regression was used to examine the relationship between the access measures and time to event (time to diagnosis, treatment or death). To estimate the association between access, and time to diagnosis (referral interval), each record was followed up from the date of referral to the date of event (diagnosis), or censoring after 30 days. This was repeated to estimate the association between access, and the time to treatment (treatment interval), using date of diagnosis and date of treatment accordingly. Censoring at 30 days was selected to correspond with the national waiting times standard of no longer than one month wait from the date of decision to treat (diagnosis) and the definitive treatment (NHS England 2015).

To estimate the association between the access measures and survival, each record was followed up from the date of diagnosis to the date of death or censoring after three years. This was deemed an appropriate duration for assessing any impact of engagement with the health services for disease management or treatment. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated, and a 5% significance level was used in all the time to event models.

All models were adjusted for variables that may potentially have a relationship with the outcomes; age, sex, deprivation and comorbidity. Additionally, where time intervals were the primary outcome (**Figure 6.3, models 1, 2, 3 and 4**), the route to diagnosis was used to remove the effect of the ‘waiting time paradox’ whereby care may be expedited for the most ill patients (Stapley et al. 2006; Neal 2009) **(see Section 6.1.1)**. Two different routes were used in adjusting for this: where referral interval was the primary outcome, the waiting time paradox was corrected for by adjusting for the two week wait (TWW) route, whereas the emergency presentation route was used to correct for this paradox where treatment interval was the outcome. Linear and Cox regression analysis was conducted in Stata Version 13 (StataCorp College Station, TX, USA).

Counterfactual causal mediation analysis was conducted to estimate the direct and indirect effect of time intervals and Dukes' stage on the association between travel time, rurality and survival. Conventional methods of mediation analysis, applicable when outcome and mediating variables are all continuous, are not applicable when mediators or outcomes are categorical or are censored survival times (Imai et al. 2010). **Table 6.1** shows the mediator relationships that were examined and corresponds to **Figure 6.3.** Models 1a and 3a investigate the mediating effect of the referral interval when the predictor variables are travel time to GP and rurality respectively. Models 2a and 4a investigate the mediating effect of the treatment interval when the predictor variables are travel to hospital of treatment and rurality respectively. Lastly, models 5a, 6a and 7a investigate the mediating effect of Dukes' stage on all the access – survival associations.

Table 6.1 – List of all predictor, mediator and outcome relationships investigated

Model*	**Predictor**	**Mediator**	**Outcome**
Model 1	Travel time to the GP	n/a	Referral Interval
Model 1a	Travel time to the GP	Referral Interval	Survival
Model 2	Travel time to the hospital	n/a	Treatment Interval
Model 2a	Travel time to the hospital	Treatment Interval	Survival
Model 3	Rurality	n/a	Referral Interval
Model 3a	Rurality	Referral Interval	Survival
Model 4	Rurality	n/a	Treatment Interval
Model 4a	Rurality	Treatment Interval	Survival
Model 5	Travel time to the GP	n/a	Dukes' late stage
Model 5a	Travel time to the GP	Dukes' late stage	Survival
Model 6	Travel time to the hospital	n/a	Dukes' late stage
Model 6a	Travel time to the hospital	Dukes' late stage	Survival
Model 7	Rurality	n/a	Dukes' late stage
Model 7a	Rurality	Dukes' late stage	Survival
Model 8	Travel time to the GP	n/a	Survival
Model 9	Travel time to the hospital	n/a	Survival
Model 10	Rurality	n/a	Survival

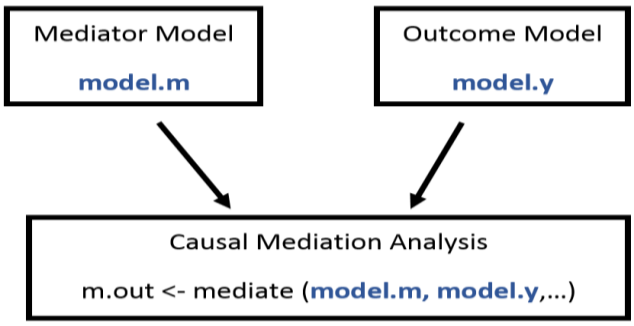
* See Figure 6.3

All mediation analysis was conducted in R, using the mediate and survreg packages. The mediate package enables the estimation of the average direct effect (ADE), the total effect and the average causal mediation effect (ACME) or indirect effect (Tingley et al. 2014; Imai et al. 2015). This package can handle different combinations of data types including linear, binary,

ordered and time to event variables (Imai et al. 2015; Tingley et al. 2014). When the outcome is time to event, the survreg package is used alongside the mediate package to fit a parametric survival regression model of accelerated failure time (AFT) (Therneau 2016; Tingley et al. 2014).

The mediation analysis conducted on Models 1a - 7a **(Table 6.1**) involved the three steps illustrated on **Figure 6.4.** The first step involved specifying a 'mediator model' to examine the association between the mediator and the predictor variable, adjusted for covariates (as described earlier). The second step involved specifying the 'outcome model' to examine the association between the predictor and outcome, also adjusted for covariates. The third step involved entering the output from steps one and two into a mediate function to compute the direct (ADE), indirect effects (ACME) and total effects.

Figure 6.4 - An illustration of the casual mediation analysis



Source: adapted from Imai, 2015

The mediation analysis used in this analysis falls within the counterfactual framework of causal inference that estimates the difference between two potential outcomes (Imai et al. 2010). The goal is to answer the following question, *'What change would occur to the outcome if one changes the mediator from the value that would be realized under the control condition $M_i(0)$, to the value that would be observed under the treatment condition $M_i(1)$, while holding the direct effect of the treatment constant?'* (Imai et al. 2010) (pg. 311). Causal mediation is zero when the predictor has no effect on the mediator, i.e. $M_i(1) = M_i(0)$ (Imai et al. 2010).

Thereby, in the analysis where the predictor was travel time **(Table 6.1 models 1a, 2a, 5a and 6a)**, the indirect effect (ACME) was estimated by capturing any changes occurring in survival,

if the mediator were to change from the value observed in the lowest travel time groups (control condition), to the value observed in the higher travel time groups (treatment condition).

Similarly, in the analysis where rurality was the predictor **(Table 6.1 models 3a, 4a and 7a)**, indirect effect (ACME) was estimated by capturing any changes occurring in survival if the mediator were to change from the value observed in the rural areas (control condition), to the value observed in urban areas (treatment condition). Further, a rurality-mediator interaction term was fitted in the 'outcome model' (Imai et al. 2015; Tingley et al. 2014) to determine whether the mediation effect varied based on rural or urban status. The statistical significance of the rurality-mediator interaction was tested using the function 'test.TMint' (Tingley et al. 2014).

6.4 Results

There were 159,768 primary colorectal tumours diagnosed during the study period (2006 – 2010). The majority of these were tumours located in the colon (102,446), followed by tumours located in the rectum (45,202), and tumours of the rectoid sigmoid junction (12,134) **(Table 6.2)**. Over 80% of patients were aged 60 years and older, and comorbidities were recorded in only a minority (17%). About half of the patients had an advanced Dukes' late stage (CD) at the time of diagnosis (**Table 6.2**).

Due to missing or incorrect GP or hospital site information, travel time to GPs was estimated for 150,054 (94%) records. Travel to hospital of initial treatment could only be estimated for 114,349 (72%) records; of these, 31,691 (20%) were excluded from the analysis because the initial treatment was marked as 'unknown', or was described as 'imaging'.

The majority of patients were in the shortest travel time categories; in the analysis considering travel to the GP, 88% of the cohort lived within a 10 minute drive-time to their GP whereas, for travel to hospital, 44% of the cohort resided within a 15 minute drive-time to the nearest hospital of treatment (**Table 6.2**). About 0.6% of patients travelled longer than 30 minutes to their GP, and 9% of patients travelled longer than 45 minutes to the hospital of first treatment (**Table 6.2**). An estimated 78% of the study population lived in an urban area.

Treatment intervals were computed in only 84% of all records because information on date of diagnosis and/or date of treatment was missing in the rest of the records. Similarly, referral interval could only be computed in 22% of the records because information on the date of referral was only available for tumours diagnosed after 2009. Of those diagnosed after 2009, only 52% had information on referral interval. Comparing the characteristics of the access variables between complete records, and those with missing information on referral and treatment intervals (**Annex C, Table A.2**) shows that missing records did not significantly differ from those that were complete.

Table 6.2 shows that diagnosis and initial treatment took place on the same day in 38,096 (48%) cases. Of these, 11,322 were emergency presentations, which makes it plausible for diagnosis and treatment to have taken place on the same day. For the rest of the cases, it is likely that a clinical histological diagnosis took place on the day of a surgical procedure. A cancer registration is based on the date a pathology sample was taken, which may also be the surgical date; even though this may have been preceded by earlier non-histological diagnosis. A smaller percentage of patients (6%) waited longer than three months for their initial treatment post obtaining a diagnosis, and nearly 5% of patients waited longer than three months from referral to obtaining a diagnosis **(Table 6.2).**

Table 6.2 - Characteristics of the study cohort

Variable	All cancers	Colon	Rectum	Rectum-Sigmoid
Travel times to GP (minutes)				
0 – 10	132,383 (88.2)	84,873 (88.3)	37,461 (88.2)	10,049 (88.1)
10 – 20	15,003 (10.0)	9,549 (9.9)	4,286 (10.1)	1,168 (10.2)
20 – 30	1,705 (1.1)	1,109 (1.2)	475 (1.1)	121 (1.1)
Over 30	963 (0.6)	629 (0.7)	265 (0.6)	69 (0.6)
Rural	35,181 (22.0)	22,703 (22.2)	9,940 (22.0)	2,538 (20.9)
Urban	124,601 (78.0)	79,743 (77.8)	35,262 (78.0)	9,596 (79.1)
Travel time to hospital (minutes)*				
0 – 15	36,486 (44.1)	24,598 (46.2)	9,240 (39.5)	2,648 (44.0)
15 – 30	26,660 (32.3)	17,277 (32.5)	7,460 (31.9)	1,923 (32.0)
30 – 45	11,802 (14.3)	7,077 (13.3)	3,862 (16.5)	863 (14.4)
Over 45	7,710 (9.3)	4,270 (8.0)	2,863 (12.2)	577 (9.6)
Referral Interval (days)				
0 (same day)	2,196 (6.3)	1,662 (7.6)	410 (3.8)	124 (4.8)
1 - 30	20,748 (59.1)	11,821 (54.2)	7,361 (68.7)	1,566 (60.1)
31 - 90	10,523 (30.0)	7,125 (32.7)	2,590 (24.2)	808 (31.0)
91 plus	1,654 (4.7)	1,185 (5.4)	360 (3.4)	109 (4.2)
Treatment Interval (days)				
0 (same day)	38,096 (47.7)	27,044 (52.8)	8,767 (38.6)	2,285 (39.1)
1 - 30	14,940 (18.7)	10,627 (20.7)	3,132 (13.8)	1,181 (20.2)
31 - 90	21,750 (27.3)	11,187 (21.8)	8,598 (37.9)	1,965 (33.6)
91 plus	5,020 (6.3)	2,396 (4.7)	2,206 (9.7)	418 (7.2)
Dukes' Stage				
Stages A&B	49,117 (49.6)	33,452 (48.8)	12,114 (52.6)	3,551 (47.1)
Stages C&D	50,011 (50.5)	35,090 (51.2)	10,930 (47.40	3,991 (52.9)
Age groups (years)				
<= 60	28,079 (17.6)	15,971 (15.6)	9,776 (21.6)	2,332 (19.2)
61 – 70	41,281 (25.8)	25,219 (24.6)	12,607 (27.9)	3,455 (28.5)
71 – 80	51,082 (32.0)	33,721 (32.9)	13,535 (29.9)	3,826 (31.5)
> 81	39,340 (24.6)	27,535 (26.9)	9,284 (20.5)	2,521 (20.8)
Male	88,547 (55.4)	53,261 (52.0)	28,239 (62.5)	7,047 (58.1)
Female	71,221 (44.6)	49,173 (48.0)	16,962 (37.5)	5,086 (41.9)
Deprivation quintiles				
1 – least deprived	32,718 (20.5)	21,125 (20.6)	9,139 (20.2)	2,454 (20.2)
2	35,285 (22.1)	22,739 (22.2)	9,845 (21.8)	2,701 (22.3)
3	34,305 (21.5)	22,069 (21.5)	9,679 (21.4)	2,557 (21.1)
4	31,070 (19.5)	19,844 (19.4)	8,909 (19.7)	2,317 (19.1)
5 – most deprived	26,404 (16.5)	16,669 (16.3)	7,630 (16.9)	2,105 (17.4)
Comorbidity				
No comorbidity	133,908 (83.8)	84,588 (82.6)	38,937 (86.1)	10,383 (85.6)
1 comorbidity	21,904 (13.7)	15,005 (14.7)	5,381 (11.9)	1,518 (12.5)
2+ comorbidities	3,970 (2.5)	2,853 (2.8)	884 (2.0)	233 (1.9)
Emergency presentation	39,174 (26.1)	30,922 (32.1)	5,731 (13.5)	2,521 (22.2)
Other routes to diagnosis	111,014 (73.9)	65,482 (67.9)	36,702 (86.5)	8,830 (77.8)

*** Excludes records where treatment is unknown or described as imaging**

6.4.1 Association between travel time, rurality, and time intervals

Those living farther from their GP of registration generally experienced shorter referral intervals (time from referral to diagnosis) **(Table 6.3A).** There was evidence of a statistically significant trend ($p<0.05$) of shorter waiting time from referral to diagnosis with increasing travel to the GP of registration. Time to diagnosis also decreased with deprivation with those in the most deprived quintile experiencing the shortest wait (HR 1.05, $p<0.05$). On the other hand, older patients, females and those with comorbidities experienced significantly longer referral intervals.

A separate analysis on the association between rurality and time intervals found that living in a rural area, compared to living in an urban area, was associated with a shorter time to diagnosis (HR 1.07, $p<0.01$) (table not shown for brevity).

In contrast, patients with longer travel to the hospital of treatment experienced longer treatment intervals **(Table 6.3B).** The likelihood of obtaining treatment within 30 days progressively declined with longer travel and was lowest for those in the longest travel time category (HR 0.78, $p<0.01$) **(Table 6.3B)**.There was statistically significant evidence of a trend ($p<0.01$) of the increase in waiting time from diagnosis to treatment with increasing travel to the hospital of initial treatment. A sensitivity analysis excluding records where diagnosis and treatment took place on the same day was also conducted. Excluding these records this did not change the patterns observed in **Table 6.3B**, although it reduced the hazard ratios, once more, those with longest travel had the lowest likelihood of obtaining treatment within 30 days (HR, 0.49**, $p<0.01$). A summary of the results are provided on **Annex C**, **Table A.2**.

Older patients, females, those with comorbidities and having and emergency presentation were all associated with significantly shorter treatment intervals **(Table 6.3B)**. Deprivation on the other hand was associated with shorter time to treatment **(Table 6.3B).**

Table 6.3 - Association between travel times, time to diagnosis and time to treatment. In A) the outcome is time to diagnosis and in B) the outcome is time to treatment. Cox proportional hazard models (hazard ratios (HR), 95%CI, ** p<0.01, * p<0.05). Larger hazard ratios indicate shorter time to event.

A) Outcome: time from referral to diagnosis (Referral Interval)		B) Outcome: time from diagnosis to treatment (Treatment Interval)	
Travel to the GP		**Travel to Hospital**	
0 – 10 minutes	Reference	0 – 15 minutes	Reference
10 – 20 minutes	1.04 (0.99 - 1.08)	15 – 30 minutes	0.94** (0.92 - 0.96)
20 – 30 minutes	1.12 (0.99 - 1.28)	30 – 45 minutes	0.80** (0.78 - 0.83)
Over 30 minutes	1.15 (0.95 - 1.39)	Over 45 minutes	0.78** (0.76 - 0.81)
Age grouped		**Age grouped**	
<= 60 years	Reference	<= 60 years	Reference
61 – 70 years	0.93** (0.89 - 0.97)	61 – 70 years	1.02 (1.00 - 1.05)
71 – 80 years	0.86** (0.83 - 0.90)	71 – 80 years	1.06** (1.03 - 1.09)
> 81 years	0.88** (0.84 - 0.92)	> 81 years	1.16** (1.13 - 1.19)
Gender		**Gender**	
Male	Reference	Male	Reference
Female	0.93** (0.90 - 0.95)	Female	1.10** (1.08 - 1.12)
Deprivation		**Deprivation**	
1 – least deprived	Reference	1 – least deprived	Reference
2	1.01 (0.97 - 1.05)	2	1.01 (0.98 - 1.03)
3	1.01 (0.97 - 1.05)	3	0.98 (0.95 - 1.01)
4	1.02 (0.98 - 1.07)	4	0.96* (0.94 - 0.99)
5 – most deprived	1.05* (1.00 - 1.10)	5 – most deprived	0.89** (0.87 - 0.92)
Comorbidity		**Comorbidity**	
No comorbidity	Reference	No comorbidity	Reference
1 comorbidity	0.93** (0.89 - 0.97)	1 comorbidity	1.05** (1.03 - 1.08)
2+ comorbidities	0.90* (0.81 - 0.99)	2+ comorbidities	1.06* (1.00 - 1.13)
Routes to diagnosis		**Routes to diagnosis**	
Other routes	Reference	Other routes	Reference
Two Week Wait	1.02 (1.00 - 1.05)	Emergency presentation	1.67** (1.64 - 1.71)

6.4.2 Association between travel times, rurality, and Dukes' stage

Longer travel to the GP and to the hospital of initial treatment increased the odds of having an advanced disease at diagnosis **(Table 6.4 A&B).** The odds of having late stage disease at diagnosis increased progressively with farther travel, for example, in comparison to those in the lowest travel time group, patients travelling between 30 – 45 minutes had a 5 % ($p<0.05$) risk of having Dukes' stage CD, the odds were highest for those travelling over 45 minutes, 1.07 ($p<0.05$) **(Table 6.4B**).

When access was measured in terms of rural-urban status, living in a rural area, compared to living in an urban area, also increased the odds of having an advanced disease at diagnosis (OR 1.04, $p<0.05$) (table not shown for brevity).

Table 6.4 - Association between travel times and Dukes' late stage. In A), stage is associated with travel to the GP and in B), stage is associated with travel to hospital. Logistic regression models, (odds ratios (OR), 95%CI, ** p<0.01, * p<0.05)

	Outcome: late Dukes' stage A) Model with travel time to the GP of registration		**Outcome: late Dukes' stage B) Model with travel time to hospital of first treatment**
Travel times		**Travel times**	
0 – 10 minutes	Reference	0 – 15 minutes	Reference
10 – 20 minutes	1.07** (1.03 - 1.12)	15 – 30 minutes	0.95* (0.92 - 0.99)
20 – 30 minutes	1.16* (1.03 - 1.31)	30 – 45 minutes	1.05* (1.00 - 1.11)
Over 30 minutes	1.15 (0.98 - 1.37)	Over 45 minutes	1.07* (1.01 - 1.14)
Age grouped		**Age grouped**	
<= 60 years	Reference	<= 60 years	Reference
61 – 70 years	0.79** (0.76 - 0.82)	61 – 70 years	0.77** (0.74 - 0.81)
71 – 80 years	0.74** (0.71 - 0.77)	71 – 80 years	0.67** (0.64 - 0.70)
> 81 years	0.75** (0.72 - 0.79)	> 81 years	0.59** (0.56 - 0.62)
Gender		**Gender**	
Male	Reference	Male	Reference
Female	1.00 (0.97 - 1.03)	Female	1.01 (0.98 - 1.05)
Deprivation		**Deprivation**	
1 – least deprived	Reference	1 – least deprived	Reference
2	1.05* (1.01 - 1.09)	2	1.00 (0.95 - 1.05)
3	1.06** (1.02 - 1.10)	3	0.99 (0.94 - 1.04)
4	1.04* (1.00 - 1.09)	4	0.95 (0.90 - 1.00)
5 – most deprived	1.12** (1.08 - 1.17)	5 – most deprived	1.01 (0.95 - 1.06)
Comorbidity		**Comorbidity**	
No comorbidity	Reference	No comorbidity	Reference
1 comorbidity	0.90** (0.87 – 0.94)	1 comorbidity	0.89** (0.85 - 0.94)
2+ comorbidities	0.92 (0.84 – 1.01)	2+ comorbidities	0.85* (0.75 - 0.95)

6.4.3 Associations between rurality, travel times, and survival

Longer travel to the GP and to hospital was associated with worse cancer survival within three years of diagnosis **(Table 6.5 A&B).** The risk of death associated with longer travel gradually increased with longer travel time. For example when travelling to access the GP, the hazard ratio increased from 1.04 ($p<0.01$) for those travelling for 10 – 20 minutes, to 1.21 ($p<0.01$) for those travelling longer than 30 minutes (**Table 6.5 A).**

In contrast, when access was measured in terms of rural-urban status, patients living in rural areas had a lower risk of death within three years of diagnosis (HR 0.96, $p<0.01$) (not shown in table for brevity).

Table 6.5 - Association between travel times and three year survival. In A) travel to the GP is associated with survival at three years. In B) travel to hospital is associated with survival at three years. Cox proportional hazard models, (HR, 95%CI, ** p<0.01, * p<0.05)

Explanatory variable		**Explanatory variable**	
A) Travel time to the GP of registration		**B) Travel time to hospital of first treatment**	
Travel times		**Travel times**	
0 – 10 minutes	Reference	0 – 15 minutes	Reference
10 – 20 minutes	1.04** (1.02 - 1.07)	15 – 30 minutes	1.02 (0.99 - 1.04)
20 – 30 minutes	1.16** (1.08 - 1.24)	30 – 45 minutes	1.10 ** (1.07 - 1.14)
Over 30 minutes	1.21** (1.11 - 1.32)	Over 45 minutes	1.13** (1.09 - 1.18)
Age grouped		**Age grouped**	
<= 60 years	Reference	<= 60 years	Reference
61 – 70 years	1.08** (1.05 - 1.11)	61 – 70 years	1.01 (0.97 - 1.05)
71 – 80 years	1.64** (1.60 - 1.68)	71 – 80 years	1.42** (1.37 - 1.47)
> 81 years	3.17** (3.10 - 3.25)	> 81 years	2.29** (2.21 - 2.37)
Gender		**Gender**	
Male	Reference	Male	Reference
Female	0.99 (0.98 - 1.01	Female	0.92** (0.90 - 0.94)
Deprivation		**Deprivation**	
1 – least deprived	Reference	1 – least deprived	Reference
2	1.07** (1.05 - 1.10)	2	1.02 (0.99 - 1.06)
3	1.13** (1.10 - 1.16)	3	1.07** (1.04 - 1.11)
4	1.23** (1.20 - 1.26)	4	1.14** (1.10 - 1.19)
5 – most deprived	1.38** (1.35 - 1.42)	5 – most deprived	1.27** (1.22 - 1.32)
Comorbidity		**Comorbidity**	
No comorbidity	Reference	No comorbidity	Reference
1 comorbidity	1.22** (1.20 - 1.25)	1 comorbidity	1.23** (1.20 - 1.27)
2+ comorbidities	1.65** (1.59 - 1.71)	2+ comorbidities	1.68** (1.57 - 1.79)

6.4.4 Indirect effects of travel times and rural residence on time to death, mediated through referral interval, treatment intervals and Dukes' stage

The results of the mediation analysis are summarised in **Table 6.6**. The columns give the estimated indirect effect (average causal mediated effect, ACME), average direct effects (ADE), total effect, and the percentage of the total effect that is explained by the indirect effect. The package 'survreg' (described in **section 6.3**) only fits accelerated failure time (AFT) models, not proportional hazards (PH) models (Therneau 2016). The coefficients are differences in mean natural logarithms of survival times, so a negative coefficient means shorter survival.

Where travel time was the predictor variable **(Table 6.6 models 1a, 2a, 5a and 6a)**, the ACME shows how the indirect effect changed as a function of travel time. Using the example of **model 1a**, the results show about 50% of the association between travelling to the GP and survival is mediated by time from referral to diagnosis (referral interval). In this model, the ACME value for those in the highest travel group (-2.20), can be interpreted as the decline in survival that would occur if those in the lowest travel group (0-10 minutes) had the same mediator (distribution of referral intervals) as those in the highest travel group (over 30 minutes). Another way of interpreting this is, if patients in the lowest travel group had the same referral intervals as those in the highest travel time group, whilst holding the travel time constant, their survival at three years would decline by 89%, ($e^{-2.20}$)[§]**.** Similarly, Dukes' late stage also significantly mediated the association between travel to the GP and survival, and explained nearly a third of this association (**Table 6.6**, **model 5a**). Once again, if patients in the lowest travel category had the same stage distribution as those in the highest travel group, their survival would decline by 86% ($e^{-1.97}$).

Treatment interval also mediated on average about 17% of the association between travel to hospital and survival (**Table 6.6 models 2a**). It was however not possible to ascertain the proportion of the indirect effect of Dukes' late stage on the travel to hospital – survival association **(Table 6.6, model 6a)**, this is because the direct and indirect effect cancel each

[§] Survival time ratio of 1 corresponds to no treatment difference (Gelfand et al. 2016). Survival time ratio of -2.20 = 0.11, therefore the difference in expected time to event (death) is 89% greater in the highest travel time group, than in the lowest travel time group.

other out when they have opposite signs (Imai et al. 2010). The positive ADE (**Table 6.6, model 6a)** suggests that longer travel to hospital may be associated with better survival at three years when the effect of Dukes' stage is controlled for.

Similarly, in the analyses where rural or urban residence was the explanatory variable **(Table 6.6, models 3a, 4a and 7a**), the percentage mediated could not be estimated, because the direct and indirect effects had opposite signs. For example, when Dukes' stage was the mediator **(Table 6.6, model 7a),** the results suggest that living in a rural area has a positive effect on survival, but higher Dukes' stage has a negative effect on survival.

Fitting a mediator – treatment interaction term in this analyses (**Table 6.6 models 3a, 4a and 7a**) revealed that the indirect effect of Dukes' stage was significantly different between rural and urban areas (ACME in Rural – ACME in Urban = -0.36, $p<0.01$) **(Table 6.6, model 7a).** The indirect effect of referral and treatment intervals did not differ between rural and urban areas.

Table 6.6 - Causal mediation estimates showing average direct effects (ADE), average causal mediation effects (ACME) or indirect effects, total effects, and percentage of total effect that is explained by the mediation effect, 95% CI, **p<0.01, *p<0.05. Coefficients are differences in mean natural logarithms of survival times, so a negative coefficient means shorter survival

Predictor and mediator variables		ACME average	ADE average	Total effect	% mediated
Mediation of effect of travel time to the GP of registration					
Model 1a) Travel time-survival, association mediated by referral interval	10 – 20 mins	-0.91*	-0.76	-1.68*	54.2%*
	20 – 30 mins	-1.64*	-1.45	-3.09*	51.8%*
	Over 30 mins	-2.20*	-2.04	-4.24**	51.0%*
Model 5a) Travel time -survival association, mediated by Dukes' stage	10 – 20 mins	-0.71**	-1.47**	-2.19**	32.9%**
	20 – 30 mins	-1.33**	-2.81**	-4.14**	31.9%**
	Over 30 mins	-1.97**	-4.04**	-6.01**	32.9%**
Mediation of effect of travel time to the hospital of first treatment					
Model 2a) Travel time - survival association, mediated by treatment interval	15 – 30 mins	-0.12	-0.74**	-0.86**	15.6%
	30 – 45 mins	-0.26	-1.42**	-1.68**	17.1%
	Over 45 mins	-0.15	-2.07**	-2.21*	18.5%
Model 6a) Travel time - survival association, mediated by Dukes' stage	15 – 30 mins	-0.11*	0.06	-0.06	N/A
	30 – 45 mins	-0.24*	0.10	-0.13	N/A
	Over 45 mins	-0.34*	0.16	-0.36	N/A
Mediation of effect of rural residence					
Model 3a) Rurality-survival association, mediated by referral interval	Rural	-1.50**	0.65	-0.82	N/A
Model 4a) Rurality-survival association, mediated by treatment interval	Rural	-0.11	1.16	1.13	N/A
Model 7a) Rurality-survival association, mediated by Dukes' stage	Rural	-1.87**	5.81**	4.29*	N/A

In 1a and 3a, the mediating variable is referral interval, in 2a and 4a, the mediating variable is treatment interval, and in models 5a, 6a and 7a, the mediating variable is Dukes' stage. Percentage mediated cannot be estimated when ACME and ADE are in the opposite directions, these entries are marked as N/A in the table.

6.5 Conclusions

This chapter begun by assessing how measures of accessibility (travel time and rurality) are associated with time intervals along the cancer care pathway. It found that travelling to health services was associated with waiting times to diagnosis and to treatment. Counterintuitively, longer travel to the GP was associated with shorter waiting time between referral and diagnosis (referral interval), whereas longer travel to hospital was associated with longer waiting time between diagnosis and treatment (treatment interval). This is believed to be the first study to examine these associations in England. The covariates used in this analyses had opposite associations when the outcome was referral or treatment intervals; older age, female gender, and having more than one comorbidity was associated with longer referral intervals, but with shorter treatment intervals. Presence of emergency presentations was also associated with shorter treatment intervals.

The analysis went on to investigate the association between access and two important health outcomes: stage and survival. The results supported findings from previous studies that showed travelling farther to hospital to obtain cancer treatment continues to have implications for colorectal cancer outcomes (Campbell et al. 2000; Dejardin et al. 2008). Furthermore, results suggested that patients who travelled farther to their GP also experienced poorer outcomes; higher odds of having advanced Dukes' stage, and worse survival at three years. Patients living in rural areas also had higher odds of having an advanced disease (OR 1.04, $p<0.05$). However, this did not translate to a higher risk of mortality as these patients had a significantly lower risk of death within three years of diagnosis (HR 0.96, $p<0.01$).

The final part of the analysis employed causal mediation inference to explore the extent by which potential mediators (disease stage and time intervals) explained the aforementioned associations. The results suggested that the indirect effects of distance to GP were most apparent. For instance, referral interval explained just over half of the association between travel to the GP and survival, and Dukes' stage mediated nearly a third of this association.

These findings have implications that may inform cancer policy and practice. Firstly, the evidence contributes to the recent call for up-to-date evaluation of the impact of living farther from a cancer centre on cancer outcomes (Independent Cancer Taskforce 2015). There is a

recognition that the current evidence may be outdated (Independent Cancer Taskforce 2015), which makes the findings in this research timely.

Secondly, the findings make a strong case for adhering to the cancer waiting times guidelines. The lack of consensus on the effectiveness of waiting times on improving cancer outcome is well documented (Neal et al. 2015; Neal 2009; Tørring et al. 2012). However, the relationship between access and waiting times has not been established, nor has the potential mediating role of waiting times on cancer outcomes. This study shows for the first time that patients who have worse access to services may also experience longer waiting times, and may therefore not be receiving some of the benefits of timely treatment, such as the previously documented psychological benefits of prompt treatment (Department of Health 2011b). The NHS operational standard for 31 days waiting time between diagnosis and treatment (treatment interval) is 96% (NHS England 2015). Healthcare providers who fall short of this standard, and other standards associated with waiting times, may be interested in understanding how alleviating barriers to access may help improve overall waiting times.

It is not clear why longer travel to the GP amounted to shorter waiting time between referral and diagnosis (referral interval). This finding will need further investigation in the future with more complete data on waiting times between referral and diagnosis, and across other cancer sites.

The results from mediation analysis suggested that a proportion of the total effect of access on survival is mediated through time intervals. The significance of this finding can be seen in the context of previous studies that have shown inconclusive results on the association between time intervals and survival (Neal et al. 2015; Neal 2009). More specifically, the finding on the mediating effect of cancer waiting times on cancer survival adds a new perspective in the understanding these previously inconclusive findings, by demonstrating the importance of examining both direct and indirect effects in future research, and emphasising the importance of adhering to Government cancer waiting times targets. The analysis also found that Dukes' stage had a stronger indirect effect when the estimates of travel time to the GP, rather than travel time to hospital predicted survival. This suggests that there are other prognostic factors besides disease stage that may have a stronger indirect effect on the association between travelling to hospital and survival; some suggested factors include access to a specialised vs.

generalised units, which were not examined in this analysis. The strong indirect effect of the time intervals and Dukes' stage on travelling to GP – survival association is not surprising, although it is striking that when travelling to GPs, referral intervals had a slightly larger indirect effect than Dukes' stage.

Living in a rural area was associated with having a higher odds of Dukes' stage at diagnosis (OR 1.04, $p<0.05$), despite this, survival in rural areas remained higher than in urban areas (HR 0.96, $p<0.01$). Additional analysis revealed that this survival advantage of living in a rural area diminished when effect of Dukes' stage was controlled for (HR 1.02, $p=0.07$).

The mediation analysis confirms this effect of Dukes' stage in rural areas, by showing that living in a rural area was associated with better survival, but higher Dukes' stage in rural areas was associated with a poorer survival. It was however difficult to estimate the proportion mediated because the direct and indirect effects of Dukes' stage and rurality on survival had opposite signs (**Table 6.6, model 7a**). Nevertheless, fitting an interaction term suggested that the indirect effect of Dukes' stage varied as a function of rurality, suggesting some differences in how rural and urban residents experience the effect of Dukes' stage. There is some indication that these differences may in part be explained by the social-cultural differences in the perception of illness, which is further compounded by poor accessibility of services in rural areas. For instance, some studies have found rural – urban differences in colorectal cancer diagnosis, characterised by delays in presentation of symptoms and in diagnosis amongst rural patients (Launoy et al. 1992; Emery et al. 2013). Some mechanisms have been postulated to explain these delays, such as the loneliness experienced by rural patients, particularly women (Launoy et al. 1992), and the stoicism shown by rural patients in the presence of illness, which is characterised by a higher threshold of enduring hardship or pain (Emery et al. 2013). The interaction between these social-cultural factors and geographical factors such as the inverse relationship between distances to services and utilisation adds further complexity health seeking decision making in rural areas, and this has noticeable impact on health outcomes.

The study benefitted from the use of a large national dataset which provided enough statistical power, adequate variation for explanatory variables, and enabled adjustment for confounding variables. The analysis was enabled by data linkage across different datasets. For example, linking cancer waiting times data with the hospital episodes statistics, and with geographical

information, made it possible to examine causal effects on several models, using variables that were specific to primary care, secondary care or to both. Lastly, the inclusion of all colorectal cancer cases diagnosed in England across five years makes the findings generalizable.

There are some limitations to the study. The mediation analysis should be interpreted with caution; it was not possible to conduct sensitivity analysis that is advised in causal mediation analyses (Imai et al. 2010; Imai et al. 2015), because the 'mediate' package does not currently support sensitivity analysis for time to event models (Tingley et al. 2015). This means that the validity of the average causal mediation effect (ACME) has not been tested. Nevertheless, adjusting for as many confounders as possible (as done in this study) is a means of attaining model validity (Imai et al. 2010; Caro 2015). Furthermore, the mediation analyses investigated only one intermediate variable at a time, whereas it is plausible that indirect effects could have operated through multiple mediators, for example, travel time => referral interval => Dukes' stage => treatment interval => time to death. Modelling of multiple mediators is methodologically challenging, however, and the results presented here at least indicate which of those intermediate variables are most important. The study was also limited by the incomplete records in some variables. For example, time from referral to diagnosis was only available for two out of the five years of the study period, and travel to hospital could not be computed for 28% of the study sample. Another limitation is that use of public transport was not considered, although previous research suggests this is mode of transport is not frequently used by cancer patients (Haynes et al. 2006).

In conclusion, this Chapter contributes to the current evidence in two main ways. Firstly, it demonstrates that times intervals along the cancer care continuum may be predicted by accessibility to health services. Secondly, it shows that good access to GPs is just as important as good access to hospital of treatment in improving cancer survival. The application of novel techniques to estimate causal mediation on time to event variables provides some insight into the mechanisms of how access might determine cancer survival. The findings suggest that a significant proportion of this association is mediated by cancer waiting times and Dukes' stage. Crucially, the availability of linked data from both primary and secondary care enables a comprehensive analysis along the cancer care continuum. Following from this, one important finding is that Dukes' stage is an important an mediator in the association between accessing the GP, living in a rural or urban area, and colorectal cancer survival, but, stage may have no

mediating effect in the association between access to secondary care for treatment and cancer survival.

The study has also generated new questions for future investigation. There is a need to quantify and characterise patients who have poor access to both primary and secondary care. Such work should estimate the need, and identify which sub-groups and areas most at risk, across all cancer sites. More research is also needed to identify other important mechanisms in the causal pathway between access and survival; this study has identified time delays and disease stage as potential mediators, others may include social-cultural factors that influence how patients seek healthcare, or how health professionals provide care. The successful implementation of efforts to improve access can only be achieved by fully understanding the underlying mechanisms by which poor access leads to poor outcomes.

Chapter 7

Final discussion and new directions for future research on access to cancer care

7.1 Contribution of thesis and significance of findings

The studies presented in this thesis are comprehensive investigations demonstrating associations between geographical access to cancer services and important outcomes along the cancer care continuum. These studies have identified several ways by which poor access to cancer services may be impinging on the overall goal of improving cancer outcomes.

The findings **confirmed the associations between longer travel to hospital and poor cancer outcomes** that are reported in previous studies. The research then goes a step farther to demonstrate **that longer travel to the GP also has implications on outcomes such as cancer stage and survival,** but also in terms of **influencing the pathways that patients take to attain a cancer diagnosis**.

By examining the relationships between access and outcomes from the angle of travel time and rurality, the results suggest that these two are distinct concepts that measure two different dimensions. For instance, rural patients had better survival and lower odds of presenting as emergency presentations in comparison to urban patients. Thus, **rurality should not be used in place for geographical inaccessibility.** Fitting a travel – rurality interaction term found **the association between travel and outcomes differed between rural and urban areas**, suggesting that perhaps rural and urban patients and GPs may perceive geographical inaccessibility differently.

In examining potential mediations to explain the above findings, the research found **that a significant proportion of the access effect on cancer outcomes was mediated through cancer waiting times and disease stage.** These had a significant mediating effect in the association between travelling to the GP and survival, but had little mediating effect when travelling to hospital. **The indirect effect of late stage on cancer survival may vary by rural or urban status.** The mediation analysis offers new insights in unravelling some of the complex causal pathways in the access – survival associations, and offers new directions for future research on access to cancer care

These findings are timely: the most recent national strategy on cancer (Independent Cancer Taskforce 2015) has shown that the role of service accessibility in determining cancer outcomes continues to be of interest to policy makers, health practitioners and service users,

but the evidence to inform decision making remain is dated or lacking. The Strategy has thereby identified key recommendations to respond to the knowledge gap **(Table 2.3).** The evidence generated by this research, will undoubtedly fill the gap in evidence, furthermore, the measures of travel times to GPs and hospitals in England generated from this work have been shared with PHE NCRAS who are currently using them in their response to the aforementioned recommendations. Additionally, the author works on an advisory capacity with PHE NCRAS to input on methodological issues associated with meeting the Strategy's recommendations on geographical access to cancer services.

7.2 Chapter overview

Chapter Two of this research was a narrative review of the five cancer strategy documents to assess how access of cancer services has been shaped by the policy making process. The development of the policy objective on improving access to cancer services was systematically mapped out, alongside other competing policy priorities. The review also identified gaps in evidence where further research may promote a better understanding of the access – cancer outcomes relationship; these findings helped formulate relevant research hypotheses which were then explored in the rest of the chapters.

Reviewing the five cancer strategies revealed the varying level of importance accorded by policies on geographical access over the last two decades. Only two of the five strategies recognised the important role that geographical access plays in determining cancer outcomes; incidentally, both strategies were authored independent of any government involvement. Exactly twenty years have elapsed between the publication of the first cancer strategy (Calman and Hine report), and the latest cancer strategy (Achieving World Class Cancer Outcomes). Despite progress in the delivery of cancer care, which has led to improvements in outcomes, the complex issue of how to deliver a geographical equitable service whilst maintaining the best possible outcomes remains to be resolved. The latest strategy has re-ignited focus on the geographical access by making four explicit recommendations that range from evaluating evidence of the impact of access on outcomes, to determining the merit of further service centralisation, and for the first time, an assessment on the impact of poor geographical access to services on children, young people and their families (**Table 2.3**).

Chapter Three, the first of the four analytical chapters, set the scene by examining the extent to which cancer services in England are equitably located. This Chapter began by identifying all hospital sites that may offer treatment and management for breast, colorectal and lung cancers. Correlating aggregated travel times to the identified hospital sites, and area level cancer incidence of the three cancer sites, revealed that cancer services tend to be located farther from areas with more cancer cases. This may be an indication that areas with the highest demand for services may also have the worst access. One explanation may be that cancer services are more likely to be concentrated in cities, whereas, demand for services is greater in less urban areas that carry a larger percentage of older people. Another finding from this chapter was that areas with longer average travel times are associated with worse survival after adjustment for age, sex, year, and area deprivation.

Chapter Four enabled the investigation of the association between access to general practitioner and cancer outcomes. Chapter Two had found a consistent acknowledgement of the poorer outcomes in England in comparison to other countries of comparable wealth recognition. There was also a recognition that efforts to improve earlier diagnosis are crucial to improving outcomes, which was particularly emphasised in the latter two cancer strategies (Department of Health 2011a; Independent Cancer Taskforce 2015). Despite recent achievements, such as the awareness generated by the National Awareness in Early Diagnosis Initiative (NAEDI), there is little evidence on how geographical access to early diagnosis determines cancer outcomes: Chapter Four addresses this gap in evidence. The Chapter used a dataset from the North of Scotland that holds GP clinical records that are linked with cancer registry data. The linked dataset offered two key benefits; firstly, the identification of symptoms that may have instigated a GP consultation and onward referral into secondary care. Secondly, the study cohort enabled consideration of remoteness as Northern Scotland has some of the remotest rural areas in the UK and living in these areas may come with distinct socio-cultural attitudes towards health.

The findings from Chapter Four suggested differences in outcomes between patients living in rural and urban areas, for instance, rural patients had significantly better survival within three years of diagnosis. The study also found the association between longer travel and the primary outcomes was opposite in rural areas to that observed in urban localities. For example, patients travelling farthest in urban areas were more likely to present with alarm symptoms, but this

was the opposite for patients with the longest travel in rural areas. These rural – urban differences in some of the outcomes examined may indicate socio-cultural differences in how patients present to their GP with symptoms that may be related to cancer. The most remote rural patients have previously been reported to display stoicism towards seeking healthcare, which makes them more likely to describe themselves as healthy and fit for work even when suffering from life threatening conditions (Elliott-Schmidt & Strong 1997), and to pursue their care less tenaciously (Bain et al. 2002).

Chapter Five continued with the focus on access to early diagnosis and went a step further by exploring the relationship between access and process measures such as mode of diagnosis that straddle the interface between primary and secondary care. This chapter built on the findings of the previous chapter (Chapter Four) that found a rural - urban difference in diagnosis following emergency admissions in Scotland. Chapter Five revisited that finding using a larger and more recent dataset from England. Furthermore, the comprehensive linkage of the English dataset enables the investigation of other routes to cancer diagnosis such as screening, GP two week wait (TWW) referrals and death certificate only (DCO) routes, and enabled this to be replicated across eight different cancer sites. The findings showed significant associations between geographical access and routes into diagnosis. Longer travel to the GP significantly increased the odds of obtaining a diagnosis via less desirable routes (DCO or emergency presentations), but reduced the odds of obtaining a diagnosis through a route of better prognosis (two week wait and screening). Conversely, those travelling the farthest had a reduced likelihood of obtaining a screen detected diagnosis or a diagnosis via the two week wait route. The opposite was apparent for patients living in rural areas; they were more likely to obtain diagnosis through a route of good prognosis (screening and TWW), and were less likely to have their cancer diagnosed following an emergency presentation.

These first three analytical chapters suggested that poor access may create a barrier to engagement with health services, resulting to reduced likelihood in presenting with symptoms that may be related to cancer (Chapter Four), or reducing the likelihood of participation in screening programmes, but, increasing the likelihood of emergency presentations and post mortem diagnosis (Chapter Five). These findings did not give any indication of the exact mediators that may explain the association between access and outcomes. The final analytical chapter (Chapter Six) addressed this by examining two potential mediators; time intervals

(delays) as derived from cancer waiting times, and disease stage. In addition to sitting on the causal pathway between access and survival, time intervals and stage may also mediate the association between access and routes to diagnosis. Although the latter was not explicitly examined, to investigate all the possible mediation relationships would require advanced statistical methodologies described in Section 7.5. Chapter Six did however find that emergency presentations were associated with shorter waiting times between diagnosis and treatment. This may explained by the 'waiting time paradox', whereby care for the most ill patients, such as those presenting as emergencies is fast tracked.

The use of cancer waiting times as the primary means of monitoring progress on access to cancer services was advocated in at least three of five cancer strategies 'Cancer Plan', 'Cancer Reform Strategy' and 'Improving Outcomes' (Department of Health 2000; Department of Health 2007; Department of Health 2011a). Although cancer waiting times measure an aspatial dimension of access, it is plausible that longer waits are partly predetermined by poor geographical accessibility, Chapter Six demonstrated this association using colorectal cancer as a case study. Rurality and longer travel to the GP were associated with shorter waits from referral to diagnosis, whereas travelling farther to the hospital of treatment was associated with longer waits in obtaining treatment within the one-month recommended in the national guidelines (NHS England 2015). Longer travel to both the GP and hospital also increased the odds of presenting with advanced disease, and of poorer survival at three years. Although living in a rural area was also associated with advanced disease, rural patients had significantly better survival at three years. Lastly, waiting times and disease stage were identified as important mediators; time from referral to diagnosis explained about 50% of the association between travel to the GP and survival, whereas, time from diagnosis to treatment interval explained around 17% of the association between travel to the first hospital of treatment and survival.

7.3 Main strengths and limitations

The studies presented in this research had a number of strengths. The research benefited from use of linked datasets which enabled the examination of access issues along the cancer continuum. Healthcare delivery in the NHS has been criticised for being fragmented such as by lack of co-ordination between different parts of the health services (primary, community and secondary care), which results to missed opportunities for earlier intervention, poor patient experience and outcomes (King's Fund 2015). The findings in this research offers decision

makers with some evidence that integrates different parts of the care continuum which can hopefully facilitate more joined up decision making. As an example, the mediation analysis in Chapter Six found that Dukes' stage may be an important mediator in the travel to the GP - survival association, but less so in the travel to hospital – survival association. This evidence may help in the making targeted decisions whereby resources are allocated to the parts of the care pathway that are most likely to benefit from any given initiatives.

Another major strength of the research was in obtaining data that enabled geographical accessibility to be examined from the perspectives of travel time and rurality. The evidence generated from this analysis has highlighted that these are measures of different parameters and should not be used interchangeably: with rurality possibly also capturing a social-cultural dimension in addition to physical accessibility. In addition to examining geographical aspects of access, data linkage also enable the exploration of how non-geographical dimensions of access such cancer waiting times may be impacted by proximity to cancer services.

Lastly, a key strength was in using advanced statistical methodologies that went beyond simple regression techniques. This was in part made possible by the availability of the linked datasets, whose clinical, demographic and geographical variables enabled examination of previously unexplored relationships. For example, fitting interaction terms in Chapter Four made it possible to isolate the effect of longer travel in rural vs urban areas. Likewise, employing mediation techniques in Chapter Six furthered the understanding of the potential mediators on the access – survival causal pathway.

The research has some limitations. Three of the five cancer strategy documents reviewed in Chapter Two were not independent of government, and so their content reflected the political ideologies of the governing political party. This presented methodological challenges of maintaining objectivity and keeping political persuasions at bay when reviewing the documents. In addition, the limited evaluation of policy initiatives added further challenges in ascertaining progress on the policy objectives.

There were also methodological limitations in the analytical Chapters Three to Six. Firstly, in Chapter Three, the use of area level data may have introduced ecological fallacies which means the findings may not be inferred at an individual level (Diez-Roux 1998). Although the

findings did generate interesting hypotheses for testing with more granular data. In Chapter Four, the absence of symptoms severity introduced challenges in the definition of alarming vs non-alarming symptoms: symptoms such as anaemia and abdominal pain were grouped as 'non-alarming' even though they may be deemed alarming when severe. Also, the use of a dated dataset where a cancer diagnosis was made between 1997 and 1998 can be criticised. However, the fact that some of the findings from that study have been replicated in Chapters Five and Six (association between access, emergency presentation and survival) gives assurance to the validity the dataset.

Chapter Six made use of recent advances in mediation techniques that use a counterfactual framework to estimate direct and indirect effects, which differ markedly from the traditional mediation analysis that use the framework of linear structural equation modelling (LSEM) (Imai et al. 2010). A major advantage of the counterfactual framework is that they can be applied on non-linear models (Imai et al. 2010). However, one limitation is the inability to test for potential violations of the assumptions[**] applied in identifying causal mechanisms when the outcome is time to event (Tingley et al. 2015). Approaches to investigate potential violations have already been developed for other model types (such as in discrete, binary outcomes) and it is anticipated this will be extended to all other model types (Imai et al. 2010).

Other methodological limitations are related to estimating the travel times used in the analyses; these were modelled estimates and not the actual times experienced by patients. This may not introduce bias in the findings as a study looking at the validity of GIS modelled estimates found minimal variation between estimates and actual car journeys. (Haynes et al. 2006). That study also found reported journey times contained rounding and recall errors, and were affected by traffic conditions, which makes GIS modelled estimates more representative of average conditions. Lastly, the measure of physical accessibility did not consider the service availability, for instance, as determined by availability of appointments. Availability may determine the outcomes for those living in urban areas in particular. Some suggestions on how future research can incorporate service availability are discussed in more detail in Section **7.6.**

[**] The assumptions are defined by the following four conditions: (1) No unmeasured confounders of the relationship between X and Y; (2) No unmeasured confounders of the relationship between M and Y; (3) No unmeasured confounders of the relationship between X and M; (4) No measured or unmeasured confounders of M and Y that have been affected by X. (Gelfand et al. 2016)

7.4 Implications on policy and practice

In addition to feeding into recommendations from the national strategy on cancer, it is anticipated that the evidence generated from this research will inform policy makers and health practitioners for example by feeding into ongoing local and national efforts such as the National Awareness in Early Diagnosis Initiative (NAEDI). Sections **7.4.1** and **7.4.2** summarises two specific ways in which the findings can shape current policy and practice, these are: improving our understanding of how to balance competing healthcare delivery and policy priorities, and, furthering the evidence on how rurality affects cancer health outcomes.

7.4.1 Balancing competing priorities

One issue that was apparent from this research was the challenge of providing equitable access to services without compromising quality of care and within the available resources. This is particularly relevant in relation to provision of access for specialist treatment such as surgery or radiotherapy. Health providers and policy makers need to reconcile three overlapping factors; the first one is the consideration of survival benefits of increased specialisation, for which there is now abundant evidence of its success. Specialisation is attained by increasing hospital and surgical volume, which is in turn achieved by concentrating services into fewer sites (Ke et al. 2012). This introduces the second factor: the benefits of increased centralisation of services as a means of improving efficiency through economies of scale (Ke et al. 2012). Whilst concentrating services in large hospitals may have the benefits of better outcomes and greater efficiencies, it also risks bringing about the dis-benefits of exacerbating inequalities in access, and consequently in outcomes. Thus, the third issue that health providers have to consider is how to organise services in a way that patients who travel farther continue to engage with services and do not experience poorer outcomes that may result from any disengagement, or from preferential treatment of those with better access. The recent strategy recognises this dilemma in the organisation of cancer services, and has recommended an evaluation of the evidence to determine whether service configuration for surgical treatment merits further centralisation (Independent Cancer Taskforce 2015).

So far, the evidence on the economic benefits of centralisation of cancer services is inconclusive. A systematic review of the economic impact of centralisation found that increasing surgeon volume is associated with cost reductions (Ke et al. 2012), but, these benefits may not be linear as one study found a u-shaped relationship where costs decreased

then increased again with increase in surgical volume (Ke et al. 2012; Max Bachmann et al. 2003). Although cost savings maybe an argument for improved efficiency, it may also bring about the additional costs associated with managing a larger organisation (Ke et al. 2012), and furthermore, any costs saved by health providers may be inadvertently transferred to patients and their carers who incur time and cost from travelling longer journeys (Ke et al. 2012).

With regards to primary care services, it was interesting that access was found to significantly determine the mode of diagnosis and cancer survival. This is because the relatively small land mass in England with approximately 7,900 GP practices (King's Fund 2016) would suggest that most patients have relatively reasonable journey times. Despite the presumed lack of issues that a lower land mass would suggest, the research found that a minority of patients have poor access that results to significantly poorer outcomes. This may be an indication of patients who are disengaged with primary care. It is feasible to re-engage with these isolated groups by encouraging the use of telephone consultations or other aspects of telehealth care (Schlachta-Fairchild 2001; Breen et al. 2015) in areas where these have not been applied. It is hoped that the relatively small population impacted by poor GP access would make the implementing such interventions attainable within the finite NHS resources.

The higher cost of financing cancer services from increasingly scarce resources means that more innovative approaches are required to support service design that enables services to deliver equitable care. Equity and efficiency need not sit on opposing ends. For example, Chapter Five demonstrates that improving access to primary care services may offer some economic benefits by reducing costly emergency presentations, also, better access may help increase the uptake of planned admissions and may encourage screening uptake, which would improve overall outcomes.

7.4.2 Rural health outcomes

One consistent finding from this research was that rural populations in both England and Scotland had significantly better cancer survival rates than their urban counterparts. Rural areas generally have poorer geographical accessibility to services (DEFRA 2013a). However, this research suggests that rural areas may not necessarily experience poorer outcomes that may be attributed to geographical inaccessibility. The rurality – travel time interacted models presented in Chapter Four also revealed that longer travel in rural areas reduced the likelihood to report

alarm symptoms related to cancer, but longer travel in rural areas was not associated with emergency admissions, stage or survival. On the contrary, urban patients appeared to be more sensitive to longer travel; this was an interesting finding that may indicate differences in how rural and urban patients perceive geographical inaccessibility (Field & Briggs 2001). One possibility is that rural patients have built resilience towards longer travel, accepting it as an inevitability of rural living.

Chapter Six found that patients living in rural areas had better three-year survival from colorectal cancer **Table 6.5**. This is despite the fact that they were more likely to have advanced disease stage than their urban counterparts **Table 6.4**. The clue to understanding this intriguing finding may be found in the previous chapters that found lower odds of attaining a diagnosis via less desirable routes such as emergency admissions amongst rural patients (Chapters Four and Five), and higher odds of a diagnosis via a more desirable route such as screening and two week wait (Chapter Five). This suggests that there may be some important lessons to learn from rural GPs, possibly in relation to better continuity of care found in the patient – GP relationship in rural areas (King's Fund 2010b). An ongoing relationship with a preferred GP which is a marker of better continuity of care has been previously associated with a reduction in emergency admissions (Christakis et al. 2001; Menec et al. 2006), and improvement in screening uptake (Flocke et al. 1998). It is therefore likely that continuity of care may play a role in improving cancer survival rates, this needs hypothesis to be fully investigated.

The better outcomes amongst rural patients in comparison to their urban counterparts that was found in this research supports findings in the US that have reported the risk of worse cancer outcomes amongst urban populations (McLafferty et al. 2011; McLafferty & Wang 2009). One study in particular found a J shaped curve of the association between advanced disease stage and rurality, whereby the most urbanised and the remotest rural groups had a higher risk of late stage cancer diagnosis (McLafferty & Wang 2009). In comparing the findings from the rural-urban analyses and the travel time analyses, one apparent conclusion is that rurality and travel time may be measuring two distinct dimensions which should always be examined separately.. Rurality may be capturing social or cultural experiences of place and environment that influence health seeking behaviours that are distinct from urban areas (McLafferty et al. 2011), and this distinction may be more apparent in the most isolated rural residents. Any distinct

traits may also be extended to GPs working in rural or urban areas, and may influence practices such as making onward referrals to secondary care.

7.5 Generalisability of findings outside UK

The association between access and outcomes may be expected to vary internationally and by context – based on differential experience of access in countries with significantly larger landmasses, or with different healthcare systems. Some of the studies referenced in this thesis were conducted in countries like the USA, Australia where the magnitude of isolation may be higher than in the UK. In addition, these countries and others like France have health systems that are different from the NHS. Healthcare systems in Australia and France share some similarities with the NHS in terms of offering universal coverage (The Commonwealth Fund 2016), however, there are some differences in the delivery of primary care, as neither system have a strict GP gate keeping role like that found in the UK (The Commonwealth Fund 2016). The USA healthcare system is substantially different from the UK, as it is characterised by a fragmented system of public and private funding. During the period covered by this study, healthcare in the USA was largely privately funded through personal health insurance, although those on low income and the elderly were covered by federal programmes such as Medicaid and Medicare (The Commonwealth Fund 2016).

Despite the country-level differences described above, there were no major differences between the findings reported in this research, and those reported by research conducted outside the UK. One particular area of similarity was the inverse association between distance, service utilisation and health outcomes. Similar to the UK, longer distance in the US was also associated with lower levels of utilisation, whereby a 10-mile increase in distance led to an estimated 2% decline in outpatient visits (LaVela et al. 2004). Longer distance to treatment in the US was also associated with worse survival (HR, 1.10, 1.01-1.39) (Wan et al. 2012). In France, longer distance to a cancer centre resulted to an estimated 25 percent increase in risk of death amongst patients living in the highest distance quartile (HR 1.25, 1.07-1.43), estimated at three years from diagnosis (Dejardin et al. 2008). Similarly in Australia, distance to cancer treatment facilities was also associated with lower utilisation whereby patients with the longest distance were less likely to take up radiotherapy treatment (OR 0.41, 0.23-0.74) compared to those with the least travel (Hsieh et al. 2015). Survival was also shown to progressively decline with geographical remoteness in Australia, such that breast cancer patients living in the most

remote regions had the lowest survival (HR 1.30, 1.02-1.64), followed by those living in moderately remote areas (HR 1.22, 1.00-1.48), compared to those living in major cities (HR = 1) (Chen et al. 2015).

The rural and urban differences in disease stage at diagnosis in the UK (Chapter Six) has also been previously reported in France and Australia, whereby rural patients diagnosed with colorectal cancer are more likely to present with later disease stage (Baade et al. 2011; Launoy et al. 1992). In contrast, colorectal cancer patients living in rural areas in the US have been found to be more likely to have lower disease stage, which has been described as 'rural-reversal' in outcomes (McLafferty & Wang 2009). Where the outcome of interest is cancer survival, living in a rural area in the USA in Australia and in France has been associated with worse cancer survival (Centers for Disease Control and Prevention 2017; Launoy et al. 1992; Yu et al. 2015). However, as shown in Chapters Four and Six of this thesis, the opposite was apparent for rural patients in the UK; they were significantly more likely to have better survival at three years since diagnosis.

The mechanisms to explain the differences in associations between these countries are complex and beyond the scope of this present research. They may be related to differences in the level of rural remoteness, for instance, better rural survival in the UK may come about because geographical access is not as big an issue due to the relatively smaller land mass. As such then, rural patients in the UK may be reaping the benefits of living in a rural area and the relative ease of accessing services, in comparison to rural patients in Australia or the USA who have to endure more severe isolation from living in a country with a larger land mass.

7.6 Suggestions for future research

The evidence generated from this research will improve the understanding of the how travelling to services and living in either a predominantly rural or urban area may determine cancer outcomes. At the same time, the findings have generated new questions for future study. One area that warrants further investigation is the better outcomes found amongst rural patients as outlined in Section 7.4.2.

The studies presented in this research were limited in their focus on estimated travel times to services. It was not possible to consider journey times using public transport using the time and

budget allowed for this research. Nor was it possible to consider other means such as cycling or walking. A study to validate the use of travel times generated by GIS (Geographical Information System) software found that up to 87% of journeys to hospital are by car (Haynes et al. 2006). The remaining 13% should not be overlooked particularly because as demonstrated in the Chapters Four and Six, urban patients had worse survival, and use of public transport has a higher prevalence in urban areas. Advances in the technology used in timetabling public transport means it may be possible to compute journey times from public transport with relative ease; this too needs to be considered in future studies.

Future studies should also consider applying GIS tools available to geographers that may help health providers with planning services that maximise access to underserved populations. Use of location-allocation modelling for instance may be helpful in selecting the optimal location for services within a given catchment population. Future work should also take advantage of more advanced measures of accessibility such as those that factor in both physical accessibility and availability of services (Luo & Qi 2009; Luo 2004), or that use gravity models which assume a distance decay; that the attractiveness of a service diminishes with increase in distance. Some derivatives of gravity models such as the 'enhanced two step floating catchment area' factors in both the demand and supply of services and the distance decay (Luo & Qi 2009). These more advanced techniques may be particularly relevant when studying access issues in urban areas where there access to services may be influenced by service demand that arise from larger practice list size, and longer waiting times for appointments. It is not clear to what extent these advanced techniques have been applied in designing cancer services in England, but it more likely they have not been routinely utilised (Allan 2014) perhaps because the complex set of skills required to use them may not be readily available to health providers. Collaborations between decision makers and researchers may be one way of addressing the skills shortage, and of ensuring that the research generated informs effective intervention programs.

Another area that would benefit from more in-depth investigation is with regards to fully mapping the causal pathways of the association between access and cancer outcomes. In this thesis, work has been presented that reveals the complex nature of some of the associations, but unravelling the full nature of the complex causal webs at play will require advanced statistical techniques. For example, Chapter Six identified Dukes' stage and time intervals as

two possible mediators, explaining some of the association between geographical access and survival. However, these mediation models were only able to accommodate one mediator at a time; the complex nature of the associations suggests a causal web of mediator, moderator and confounding relationships that occur concurrently. These relationships also operate at different levels; patient, health practitioner, health system. Furthermore, variables such as symptoms, routes to diagnosis, time delays and disease stage may all sit on the causal pathway between access and survival, but it not clear how they are associated with one another. Unpicking these relationships will require use of more advanced statistical techniques such as those found in structural equation modelling (SEM) that are built to handle complex relationships. Gaining a full understanding of this complexity will be crucial to implementing successful interventions.

From a policy perspective, achieving full implementation of any intervention will require national coordination and monitoring of progress. It may be necessary to develop a metric or indicator that measures geographical accessibility to health services and that decision makers can use for monitoring purposes. The use of indicators has been credited with successfully highlighting key national priorities, with improving implementation and strengthening accountability (Baggott 2007). In 2010, the Coalition Government introduced three sets of outcome measures for health and social care; Public Health Outcomes Framework, NHS Outcomes Framework and Adult and Social Care Outcomes Framework (Department of Health 2016a; Department of Health 2016b; Department of Health 2014). **Annex D** gives a summary of the indicators that may be used in evaluating the progress on cancer prevention, early diagnosis and treatment.

In relation to access to services, the NHS Outcomes Framework has an indicator that monitors access to GP services by measuring the overall experience of making an appointment (Department of Health 2012b). There are also several indicators that monitor progress in meeting cancer waiting times, as summarised in Chapter Two (**Table 2.2**). The goal of these indicators is to hold different services accountable for the outcomes they deliver, in cancer services across the entire care pathway (Department of Health 2011a). The most recent strategy on cancer has ensured that geographical accessibility to services remains on the national agenda for at least until 2020. Hopefully, this will also provide some impetus into developing and adopting a national metric to measuring and monitor this objective, which is the surest way to ensure progress in achieving geographical equity access

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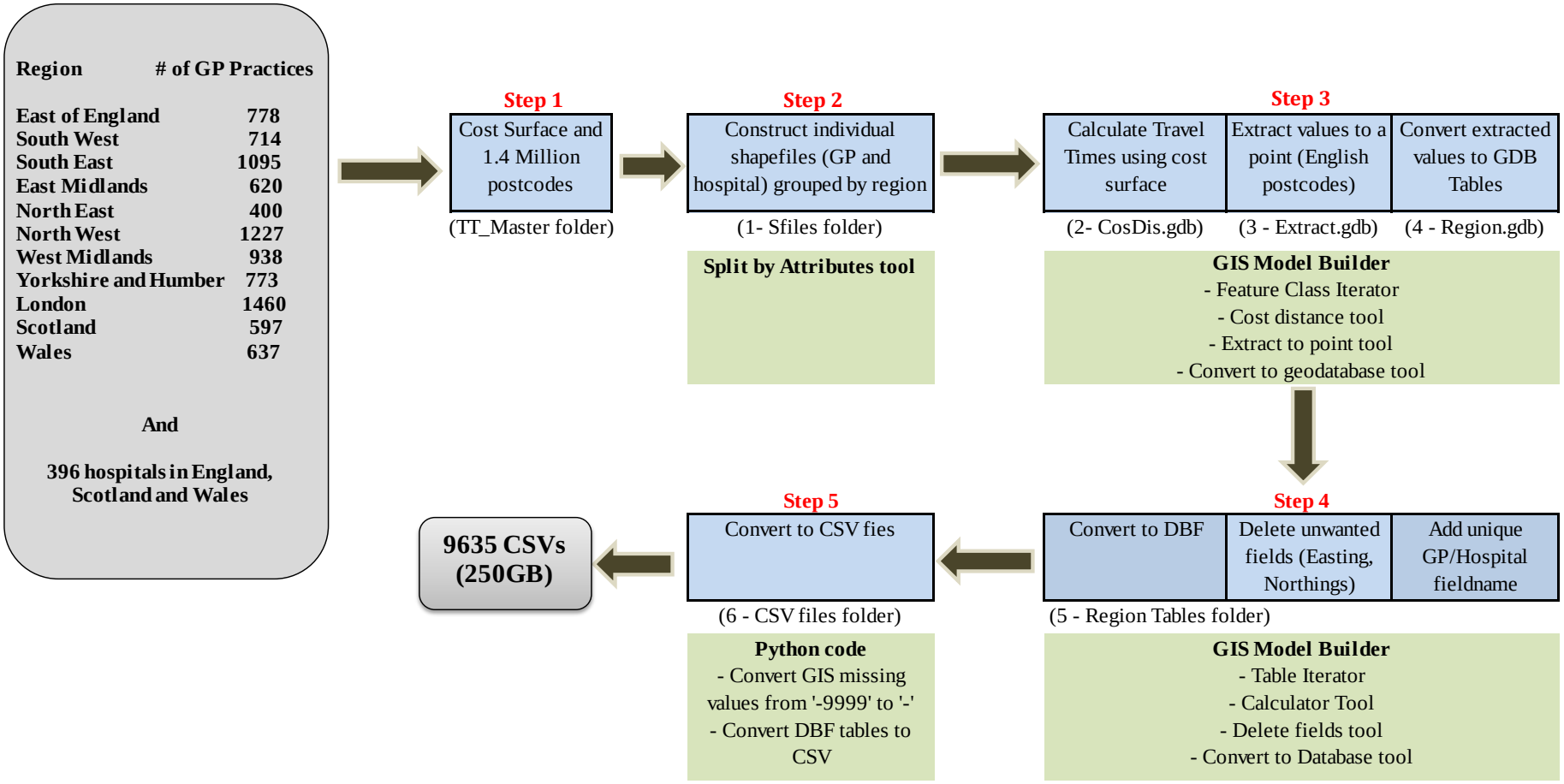
Annexes

Annex A - Flowchart showing process of computing travel times from postcodes of residence to GPs and hospitals in England, Scotland and Wales


Region # of GP Practices
East of England 778
South West 714
South East 1095
East Midlands 620
North East 400
North West 1227
West Midlands 938
Yorkshire and Humber 773
London 1460
Scotland 597
Wales 637
And
396 hospitals in England, Scotland and Wales
Step 1
Cost Surface and 1.4 Million postcodes
(TT_Master folder)
Step 2
Construct individual shapefiles (GP and hospital) grouped by region
(1- Sfiles folder)
Split by Attributes tool
Step 3
Calculate Travel Times using cost surface
Extract values to a point (English postcodes)
Convert extracted values to GDB Tables
(2- CosDis.gdb)
(3 - Extract.gdb)
(4 - Region.gdb)
GIS Model Builder
- Feature Class Iterator
- Cost distance tool
- Extract to point tool
- Convert to geodatabase tool
Step 4
Convert to DBF
Delete unwanted fields (Easting, Northings)
Add unique GP/Hospital fieldname
(5 - Region Tables folder)
GIS Model Builder
- Table Iterator
- Calculator Tool
- Delete fields tool
- Convert to Database tool
Step 5
Convert to CSV fies
(6 - CSV files folder)
Python code
- Convert GIS missing values from '-9999' to '-'
- Convert DBF tables to CSV
9635 CSVs (250GB)

Annex B – Additional Tables from Chapter Five

Table A.1 - Association between rurality, travel times to the GP and emergency presentations. Travel time is the predictor in 'a', rurality is the predictor in 'b'. Travel times are interacted with rurality in 'c'. All models are adjusted for age, gender, deprivation and comorbidity. For brevity, the coefficients for the covariates are only shown in the models with the interaction term (c).

Explanatory variables	1) Emergency presentation: Breast	2) Emergency presentation: Colorectal	3) Emergency presentation: Cervical	4) Emergency presentation: Lung	5) Emergency presentation: Prostate	6) Emergency presentation: Stomach	7) Emergency presentation: Ovarian	8) Emergency presentation: Brain
Outcome variables without interaction terms								
A) Travel time to GP (minutes)	1.10** (1.06-1.14)	1.06** (1.04-1.08)	1.06 (0.96-1.17)	1.03** (1.01-1.05)	1.08** (1.05-1.11)	1.03 (0.99-1.08)	1.06** (1.02-1.11)	1.02 (0.98-1.06)
B) Rural	0.88** (0.82-0.93)	0.93** (0.90-0.96)	1.00 (0.85-1.19)	0.96** (0.93-0.99)	0.87** (0.83-0.91)	0.93* (0.87-0.99	0.95 (0.89-1.02)	0.99 (0.91-1.06)
Outcome variables with interaction terms fitted								
C) Travel time to GP (minutes)	1.15** (1.10-1.20)	1.09** (1.06-1.12)	1.10 (0.99-1.22)	1.05** (1.03-1.07)	1.14** (1.10-1.18)	1.09** (1.03-1.16)	1.07* (1.02-1.12)	1.01 (0.96-1.07)
Rural	0.89** (0.82-0.97)	0.94** (0.90-0.98)	1.05 (0.82-1.35)	0.97 (0.93-1.01)	0.88** (0.83-0.94)	0.98 (0.89-1.08)	0.89* (0.81-0.98)	0.93 (0.84-1.04)
Travel time / rurality interaction	0.92* (0.85-0.99)	0.95* (0.91-0.99)	0.87 (0.69-1.11)	0.97 (0.93- 1.01)	0.91** (0.86-0.98)	0.88* (0.79-0.97)	1.02 (0.94-1.16)	1.04 (0.94-1.14)
Age (years)	1.07** (1.07-1.07)	1.02** (1.02-1.02)	1.05** (1.04-1.05)	1.03** (1.03-1.03)	1.09** (1.09-1.10)	1.03** (1.03-1.04)	1.03** (1.03-1.03)	1.02** (1.01-1.02)
Female		1.30** (1.27-1.33)		1.08** (1.06-1.10)		1.27** (1.20-1.34)		1.14** (1.07-1.22)
Deprivation quintiles								
1 – least deprived	1	1	1	1	1	1	1	1
2	1.10* (1.02-1.19)	1.07** (1.03-1.12)	1.20 (0.95-1.53)	1.07** (1.03-1.11)	1.09** (1.03-1.16)	1.05 (0.96-1.14)	1.09* (1.00-1.19)	1.05 (0.95-1.15)
3	1.16** (1.08-1.26)	1.15** (1.11-1.19)	1.50** (1.23-1.93)	1.13** (1.08-1.17)	1.16** (1.09-1.22)	1.10* (1.01-1.20)	1.07 (0.98-1.16)	1.07 (0.97-1.18)
4	1.37** (1.27-1.48)	1.28** (1.23-1.33)	1.55** (1.24-1.94)	1.21** (1.16-1.25)	1.29** (1.22-1.37)	1.25** (1.15-1.36)	1.25** (1.15-1.37)	1.18** (1.07-1.31)
5 – most deprived	1.66** (1.53-1.79)	1.53** (1.47-1.59)	1.72** (1.38-2.14)	1.32** (1.27-1.37)	1.57** (1.48-1.67)	1.48** (1.36-1.61)	1.33** (1.21-1.45)	1.40** (1.26-1.56)
0 comorbidities (Charlson)	1	1	1	1	1	1	1	1
1 – 2 comorbidities	1.20** (1.13-1.29)	1.25** (1.21-1.29)	1.07 (0.87-1.31)	1.23** (1.20-1.27)	1.42** (1.36-1.49)	1.28** (1.20-1.37)	1.23** (1.13-1.34)	0.85* (0.76-0.95)
3 plus comorbidities	2.12** (1.86-2.40)	1.75** (1.63-1.88)	1.75* (1.11-2.74)	1.79** (1.70-1.89)	2.23** (2.05-2.43)	1.88** (1.65-2.15)	1.98** (1.59-2.46)	1.16 (0.87-1.54)

Annex C - Additional tables from Chapter Six

Table A.2 – Comparison the frequency of travel times and rural urban status between records with and without referral and treatment intervals. A) travel to the GP, B) travel to hospital and C&D) rurality

	All records	All records with details on referral Interval	All records without referral interval
A) Travel times to GP of registration			
0 – 10 minutes	132,383 (88.2)	30,269 (88.2)	102,114 (88.2)
10 – 20 minutes	15,003 (10.0)	3,547 (10.3)	11,456 (9.9)
20 – 30 minutes	1,705 (1.1)	364 (1.1)	1,341 (1.2)
Over 30 minutes	963 (0.6)	157 (0.5)	806 (0.7)

	All records	All records with details on treatment Interval	All records without treatment interval
B) Travel time to hospital of first treatment			
0 – 15 minutes	36,486 (44.1)	34,774 (44.2)	1,712 (43.0)
15 – 30 minutes	26,660 (32.3)	25,333 (32.2)	1,327 (33.3)
30 – 45 minutes	11,802 (14.3)	11,230 (14.3)	572 (14.4)
Over 45 minutes	7,710 (9.3)	7,335 (9.32)	375 (9.4)

	All records	All records with details on referral Interval	All records without referral interval
C) Rural or urban			
Rural	35,181 (22.0)	8,406 (23.9)	26,775 (21.5)
Urban	124,601 (78.0)	26,715 (76.1)	97,886 (78.5)

	All records	All records with details on treatment Interval	All records without treatment interval
D) Rural or urban			
Rural	35,181 (22.0)	30,011 (22.4)	5,170 (20.0)
Urban	124,601 (78.0)	103,884 (77.6)	20,717 (80.0)

Table A.3 – Sensitivity analysis of Table 6.3B, Chapter 6. Results show the association between travel time to hospital, rurality and time from diagnosis to treatment (Treatment Interval)

Travel time to hospital of first treatment		Rural vs urban residence	
0 – 15 minutes	Reference		
15 – 30 minutes	0.88** (0.85 - 0.91)		
30 – 45 minutes	0.64** (0.61 - 0.68)	Urban	Reference
Over 45 minutes	0.49** (0.45 - 0.52)	Rural	1.01 (0.97 - 1.06)
Age grouped		**Age grouped**	
<= 60 years	Reference	<= 60 years	Reference
61 – 70 years	0.96 (0.91- 1.00)	61 – 70 years	0.96 (0.92 - 1.01)
71 – 80 years	0.98 (0.94 - 1.03)	71 – 80 years	1.00 (0.96 - 1.05)
> 81 years	1.10** (1.05 - 1.16)	> 81 years	1.15** (1.09 - 1.21)
Gender		**Gender**	
Male	Reference	Male	Reference
Female	1.19** (1.15 - 1.23)	Female	1.20** (1.16 - 1.24)
Deprivation		**Deprivation**	
1 – least deprived	Reference	1 – least deprived	Reference
2	0.95 (0.91 - 1.00)	2	0.94* (0.90 - 0.99)
3	0.92** (0.87 - 0.97)	3	0.91** (0.87 - 0.96)
4	0.88** (0.83 - 0.93)	4	0.92** (0.88 - 0.97)
5 – most deprived	0.80** (0.75 - 0.84)	5 – most deprived	0.89** (0.85 - 0.94)
Comorbidity		**Comorbidity**	
No comorbidity	Reference	No comorbidity	Reference
1 comorbidity	0.98 (0.93 - 1.03)	1 comorbidity	0.98 (0.94 - 1.03)
2+ comorbidities	1.01 (0.90 - 1.14)	2+ comorbidities	1.06 (0.94 - 1.19)
Routes to diagnosis		**Routes to diagnosis**	
Emergency presentation	Reference	Emergency presentation	Reference
Other routes	2.35** (2.26 - 2.45)	Other routes	2.30** (2.21 - 2.39)

Excludes records where diagnosis and treatment were on the same day.

Annex D - Indicators directly relevant to cancer care from the health and social care national Outcome Frameworks

Public Health Outcomes Framework (PHOF)

Domain 1 : Improving the wider determinants of health
1.08 Employment for those with long-term health conditions including adults with a learning disability or who are in contact with secondary mental health services
1.16 Utilisation of outdoor space for exercise / health reasons

Domain 2: Health improvement
2.09 Smoking prevalence – 15 year olds
2.10 Self-harm
2.11 Diet
2.12 Excess weight in adults
2.13 Proportion of physically active and inactive adults
2.14 Smoking prevalence – adults (over 18s)
2.19 Cancer diagnosed at stage 1 and 2
2.20 National screening programmes (breast, bowel and cervical cancers)

Domain 3: Health protection
3.01 Fraction of mortality attributable to particulate air pollution

Domain 4: Healthcare public health and preventing premature mortality
4.03 Mortality rate from causes considered preventable
4.05 Under 75 mortality rate from cancer

NHS Outcomes Framework (NHSOF)

Domain 1: Preventing people from dying prematurely
1a Potential years of life lost (PYLL) from causes considered amenable to healthcare
1.4 Under 75 mortality rate from cancer (PHOF 4.05)
- i One year survival from all cancers
- ii Five year survival from all cancers
- iii One year survival from breast, lung and colorectal cancer
- iv Five year survival from breast, lung and colorectal cancer
- v One year survival from cancers diagnosed at stage 1&2 (PHOF 2.19)
- vi Five year survival from cancers diagnosed at stage 1&2 (PHOF 2.19)

1.6 ii Five year survival from all cancers in children

Domain 2: Enhancing quality of life for people with long-term conditions
2 Health-related quality of life for people with long-term conditions (ASCOF 1A)
2.1 Proportion of people feeling supported to manage their condition
2.2 Employment of people with long-term conditions (PHOF 1.8)
2.7 Health-related quality of life for people with three or more long-term conditions (ASCOF 1A)

Domain 3: Helping people to recover from episodes of ill health or following injury
3.1 Improving outcomes from planned treatments - Total health gain as assessed by patients for elective procedures
3.6 Helping older people to recover their independence after illness or injury

Domain 4: Ensuring that people have a positive experience of care
4a Patient experience of primary care
4b Patient experience of hospital care
4.4 Improving access to primary care services
4.6 Improving the experience of care for people at the end of their lives

4.9 Improving people's experience of integrated care

Domain 5: Treating and caring for people in a safe environment and protecting them from avoidable harm
5a Deaths attributable to problems in healthcare
5b Severe harm attributable to problems in healthcare
5.6 Improving the culture of safety reporting

Adult and Social Care Outcomes Framework (ASCOF)

Domain 1 – Enhancing quality of life for people with care and support needs
1A. Social care related quality of life
1I: Proportion of people who use services, and their carers, who reported that they had as much social contact as they would like

Domain Three: Ensuring that people have a positive experience of care and support
3A. Overall satisfaction of people who use services with their care and support
3D. The proportion of people who use services and carers who find it easy to find information about support

Domain Four: Safeguarding adults whose circumstances make them vulnerable and protecting them from avoidable harm
4A. The proportion of people who use services who feel safe
4B. The proportion of people who use services who say that those services have made them feel safe and secure

Source: NHS Outcomes Framework (2016), Public Health Outcomes Framework (2016), and Adult and Social Care Outcomes Framework (2014)

Annex E - Information Governance Application

Submitted Document	Upload Date	Requirement	Criterion	Description of the required evidence
(UEA)_ODR_2014_229 _ Query on NHS IG Toolkit.msg	09/11/2014 18:46	12-223	1b	Secure transfer from PHE
(UEA)_ODR_2014_229 _ Query on NHS IG Toolkit.msg	09/11/2014 18:46	12-334	2b	Documented report or project closure document.
Certificate_Confidential Information.pdf	22/10/2014 14:36	12-120	1b	Certificate - Secure Handling of Confidential Information
Certificate_Confidential Information.pdf	22/10/2014 14:36	12-123	2a	Training certificate - Confidential Information
Certificate_Information Governance.pdf	22/10/2014 14:35	12-120	1b	Certificate - Introduction to Information Governance
Certificate_Information Governance.pdf	22/10/2014 14:35	12-123	2a	Training reports or certificates of attendance.
Certificate_Risk Management.pdf	22/10/2014 14:37	12-120	1b	Certificate - Information Risk Management
Certificate_Risk Management.pdf	22/10/2014 14:37	12-123	2a	Training certificate - Risk Management
FMH ethics application_Peninah.pdf	22/10/2014 18:04	12-220	1b	UEA - Ethics Application Form (completed)
GISP1- Risk Assessment and management.pdf	22/10/2014 19:11	12-221	1b	GISP1 - Risk Assessment and risk management
GISP12 - Secure Areas.pdf	23/10/2014 14:51	12-332	1a	UEA- Secure Areas Policy
GISP12 - Secure Areas.pdf	23/10/2014 14:51	12-332	1b	GISP12- Secure Areas
GISP17 - IT and Information Assest Management.pdf	22/10/2014 20:36	12-331	2a	GISP17 IT and Information Asset Management
GISP18 - Encryption use and key material handling.pdf	22/10/2014 19:42	12-223	1b	A document, staff handbook, or leaflet.

GISP3- Physical and Environmental Security.pdf	23/10/2014 14:51	12-332	1a	UEA - Physical and Environmental Security
GISP3- Physical and Environmental Security.pdf	23/10/2014 14:51	12-332	1b	GISP3 Physical and Environmental Security
Information Governance Certificate-Andy J.pdf	14/11/2014 13:18	12-123	2a	Training certificate (Andy)
Information Governance Certificate-Max B.pdf	09/11/2014 18:10	12-123	2a	Training certificate (Max)
PHE (potentially) identifiable data request FORM.docx	11/11/2014 18:22	12-223	1c	PHE Data Release Form
PPD Modules_ Peninah Murage.pdf	22/10/2014 14:34	12-120	1b	IG Training tool reports, certificates of attendance and attainments, or evidence of self-directed study.
PPD Modules_ Peninah Murage.pdf	22/10/2014 14:34	12-123	1c	Training records, for example, IG Training Tool reports, training certificates of attendance or attainment.
Research Protocol_Peninah.pdf	23/10/2014 16:48	12-334	1a	A documented plan.
Research Protocol_Peninah.pdf	23/10/2014 16:48	12-334	2a	Project documentation, eg project closure document or project report.
Researcher's Safety Checklist_Peninah.pdf	23/10/2014 14:49	12-332	1a	A documented risk assessment including details of any required improvements.
UEA - Conditions of Computer Use.pdf	22/10/2014 15:16	12-122	1b	UEA- Conditions of Computer Use
UEA - Conditions of Computer Use.pdf	22/10/2014 15:16	12-221	2a	Minutes/notes of meetings, briefing and awareness session materials or a list of staff signatures that they have read, understood and will comply with the procedures.
UEA - Conditions of Computer Use.pdf	22/10/2014 15:16	12-333	2a	UEA - Conditions of Computer Use
UEA - Data Protection Flyer.pdf	22/10/2014 15:53	12-123	1b	UEA - Data Protection Flyer

UEA - Data Protection Training.pdf	22/10/2014 15:52	12-123	1b	UEA - Data Protection Training
UEA - Information Security Flyer.pdf	22/10/2014 15:51	12-123	1b	UEA - Information Compliance Flyer
UEA- Correspondence with data provider (UEA)_ODR_2014_229.txt	23/10/2014 16:51	12-334	1b	The minutes of a meeting where the plan was agreed or in a note that clarifies the organisation's support.
UEA- Correspondence with data provider (UEA)_ODR_2014_229.txt	23/10/2014 16:51	12-334	1c	A note assigning responsibility, the job description of an individual or the terms of reference of a committee/group.
UEA- Dealing with Misconduct in Research.pdf	22/10/2014 15:09	12-122	1b	UEA- Procedures for dealing with allegations for misconduct in research
UEA- Information Classification Data Management.pdf	22/10/2014 19:43	12-223	1b	UEA - Information Classification and Data Management Policy
UEA- Information Classification Data Management.pdf	22/10/2014 19:43	12-331	2a	UEA - Information Classification and Data Management Policy
UEA- Research Students Handbook.pdf	22/10/2014 15:07	12-122	1b	Examples of contract clauses.
UEA- Research Students Handbook.pdf	22/10/2014 15:07	12-220	2a	Inclusion in staff handbook, or published on the Intranet, or personal copies for staff (in the latter case there may be a list of staff signatures confirming receipt of the guidance) or the evidence may be a description of the dissemination process or minutes of the meeting where this was decided.
UEA_ Good Practice in Research.pdf	22/10/2014 15:15	12-122	1b	UEA- Good Research Practice Guidelines
UEA_ Information Compliance Training.pdf	22/10/2014 15:50	12-123	1b	Written details of the training to be provided.
UEA_ Research Ethics Policy, Principles and Procedures.pdf	22/10/2014 15:13	12-122	1b	UEA- Research Ethics Policy, Principles and Procedures
UEA_ Research Ethics Policy, Principles and Procedures.pdf	22/10/2014 15:13	12-122	1c	UEA - Research Ethics Policy, Principles and Procedures

UEA_ Research Ethics Policy, Principles and Procedures.pdf	22/10/2014 15:13	12-220	1a	UEA - Research Ethics Policy, Principles and Procedures
UEA_ Research Ethics Policy, Principles and Procedures.pdf	22/10/2014 15:13	12-220	1b	A document, staff handbook, or leaflet covering consent issues around the use and disclosure of personal information.
UEA_ Research Ethics Policy, Principles and Procedures.pdf	22/10/2014 15:13	12-220	1c	Minutes of meetings, in a document or email or a personal endorsement in writing from an appropriately senior manager.
UEA_ Research Ethics Policy, Principles and Procedures.pdf	22/10/2014 15:13	12-333	1a	UEA - UEA - Research Ethics Policy, Principles and Procedures
UEA_ Research Ethics Policy, Principles and Procedures.pdf	22/10/2014 15:13	12-333	2a	UEA- Research Ethics Policy, Principles and Procedures
UEA_General Infor Security Policy.pdf	14/10/2014 16:09	12-121	1a	UEA- General Information Security Policy
UEA_General Infor Security Policy.pdf	14/10/2014 16:09	12-121	1b	UEA - General Information Security Policy
UEA_General Infor Security Policy.pdf	14/10/2014 16:09	12-122	1c	UEA - General Information Security Policy
UEA_General Infor Security Policy.pdf	14/10/2014 16:09	12-123	1a	A named individual's job description, or a signed note or e-mail assigning responsibility.
UEA_General Infor Security Policy.pdf	14/10/2014 16:09	12-221	1a	A named individual's job description, a note or e-mail assigning responsibility or the terms of reference of a group.
UEA_General Infor Security Policy.pdf	14/10/2014 16:09	12-221	1b	Documented confidentiality audit procedures which include the details of the named staff member, job role or responsible group.
UEA_General Infor Security Policy.pdf	14/10/2014 16:09	12-221	1c	Approval/sign off within the minutes of meetings, in a document or email or a personal endorsement in writing from an appropriately senior manager.
UEA_High level Infor Security Policy.pdf	14/10/2014 16:08	12-121	1a	UEA- High Level Information Security Policy

UEA_High level Infor Security Policy.pdf	14/10/2014 16:08	12-121	1b	Sign off documented on the policy document (for example - the date that it was signed-off and by whom).
UEA_High level Infor Security Policy.pdf	14/10/2014 16:08	12-123	1a	UEA - High Level Information Security
UEA_Research Data Management.pdf	22/10/2014 15:11	12-122	1b	UEA- Research Data Management Policy
UEA_Research Data Management.pdf	22/10/2014 15:11	12-122	1c	UEA - Research Data Management
UEA_Research Data Management.pdf	22/10/2014 15:11	12-220	1a	A named individual's job description, a note or e-mail assigning responsibility or the terms of reference of a group.
UEA_Research Data Management.pdf	22/10/2014 15:11	12-220	1b	UEA - Research Data Management Procedure and Guidance
UEA_Research Data Management.pdf	22/10/2014 15:11	12-220	1c	UEA - Research Data Management
UEA_Research Data Management.pdf	22/10/2014 15:11	12-333	1a	UEA - Research Data Management Procedures and Guidance
UEA_Research Data Management.pdf	22/10/2014 15:11	12-333	2a	UEA - Research Data Management Procedures and Guidance
VACS - IG Contractual Clause - signed.pdf	14/11/2014 12:23	12-122	2a	Sample contract showing that appropriate IG clauses are included in contracts.
VACS - IG Staff Declaration Form-signed.pdf	18/11/2014 11:27	12-121	2a	Inclusion in a staff handbook or by placing it on the intranet, or staff may be provided with their own copy of the policy. In the latter case there may be a list of staff signatures confirming staff have read and understood the policy.
VACS - IG Staff Declaration Form-signed.pdf	18/11/2014 11:27	12-220	2b	Notes or minutes of team meetings/awareness sessions or staff briefing materials.
VACS - IG Staff Declaration Form-signed.pdf	18/11/2014 11:27	12-223	2b	Minutes/notes of team meetings, or briefing materials from awareness sessions.

VACS - IG Staff Declaration Form-signed.pdf	18/11/2014 11:27	12-332	2b	Minutes/notes of team meetings, briefing and induction materials.
VACS - IG Staff Declaration Form-signed.pdf	18/11/2014 11:27	12-333	2b	Minutes/notes of team meetings, or briefing materials used in awareness sessions.
VACS - IG Staff Declaration Form-signed.pdf	18/11/2014 11:27	12-335	2a	A staff briefing and/or induction materials, IGP, SLSP or other equivalent policies and procedures available on desktop or local intranet, or hard copy materials handed to staff and/or placed prominently in communal areas
VACS - Improvement Plan.pdf	14/11/2014 14:22	12-120	1c	Documented IG Improvement plan.
VACS - Improvement Plan.pdf	14/11/2014 14:22	12-120	2a	Sign off should be documented on the IG improvement plan, for example the date that it was signed-off and by whom
VACS - Incident Management Plan.docx	11/11/2014 16:55	12-333	1a	UEA- Incident Reporting and Handling
VACS - Incident Management Plan.docx	11/11/2014 16:55	12-333	2a	Documented procedures and a template incident reporting form for staff.
VACS - Incident Management Plan.docx	11/11/2014 16:55	12-333	2b	Project Incident Management Plan
VACS - Incident Management Plan.docx	11/11/2014 16:55	12-333	2c	Completed incident reporting forms and reports made to senior management and where necessary to the commissioning or hosting organisation, the Information Commissioner, insurers, or the police.
VACS - Incident Management Plan.pdf	14/11/2014 16:11	12-221	2b	Project's Incident Management Plan
VACS - Incident Management Plan.pdf	14/11/2014 16:11	12-332	1b	Documented staff guidance.
VACS - Incident Management Plan.pdf	14/11/2014 16:11	12-333	1a	A named individual's job description, or a signed note or e-mail assigning responsibility.
VACS - Incident Management Plan.pdf	14/11/2014 16:11	12-333	2a	Project's Incident Management Plan

VACS - Information Asset Register.pdf	14/11/2014 17:04	12-331	2a	Documented Information Asset register.
VACS - System Level Security Policy Final.pdf	14/11/2014 12:27	12-223	1b	System Level Security Policy
VACS - System Level Security Policy Final.pdf	14/11/2014 12:27	12-223	1c	Minutes of meetings, in a document or email or a personal endorsement in writing from an appropriately senior manager.
VACS - System Level Security Policy Final.pdf	14/11/2014 12:27	12-335	1a	Documentation of the organisation's assigned responsibilities and processes for the scoping, development and approval of an IGP, SLSP or equivalent policy.

Annex F - HSCIC Level Two Information Governance Approval HSCIC Level Two Information Governance Approval

From: Nwolie Ifeoma (HEALTH AND SOCIAL CARE INFORMATION CENTRE)
<magi.nwolie@hscic.gov.uk>
Sent: 27 November 2014 09:54
To: Peninah Murage (MED)
Subject: HPOV 952160: IG Toolkit version 12 assessment - University of East
Anglia
Attachments: IGT Exemption Request Form (Vers 4 Template) - OrgName (OrgCode)
DDMMYYYY.dotx

Dear Penny,
This is to inform you that your version 12 IG Toolkit assessment has been reviewed and is satisfactory.

IG Toolkit assessments are required on an annual basis and you should ensure that version 13 is completed on or before 31 March 2016.

Just one thing to note: When you complete your version 13 assessment, you should apply for an exemption from the mobile computing requirement via the Exeter Helpdesk(exeter.helpdesk@hscic.gov.uk) rather than scoring the requirement at level 2.

Best wishes

Magi
(Ifeoma) Magi Nwolie RGN LLB(Hons)
Information Governance Delivery Manager - IG Assurance
External Information Governance Delivery
Operations and Assurance Directorate
Health and Social Care Information Centre

E: magi.nwolie@hscic.gov.uk
W: http://systems.hscic.gov.uk/infogov

Please send new IG queries to: exeter.helpdesk@hscic.gov.uk

From: DONOTREPLY@hscic.gov.uk [mailto:DONOTREPLY@hscic.gov.uk]
Sent: 18 November 2014 16:32
To: Exeter Helpdesk (HEALTH AND SOCIAL CARE INFORMATION CENTRE)
Subject: Information Governance Toolkit Assessment Publication

This e-mail has been automatically generated by the IG Toolkit because an organisation has published an IGT Assessment. The details of the IGT Assessment are as follows:
Organisation National Code: EE133853
Organisation Name: University of East Anglia
Organisation Type: Hosted Secondary Use Team/Project
Requirements Version: 12
Key Requirements Met: Yes
Purpose of Assessment: Other
(As part of requirement to obtain secondary data for a research project. No patient identifiable data has been requested, however, some fields, when used in combination pose a slight risk to identifying patients.)
Instructions to 1st Line Support: please raise a new Service Call as follows:
Call Description: <this e-mail>
Service: IGTK (3rd Line, not 2nd Line)
Call Type: IGTK Submissions

Annex G - University's Ethics Approval

Faculty of Medicine and Health Sciences Research Ethics Committee

University of East Anglia

Peninah Murage
Norwich Medical School
Faculty of Medicine and Health Sciences
University of East Anglia
Norwich,
NR4 7TJ

Research & Enterprise Services
West Office (Science Building)
University of East Anglia
Norwich Research Park
Norwich, NR4 7TJ

Telephone: +44 (0) 1603 591720
Email: fmh.ethics@uea.ac.uk

Web: www.uea.ac.uk/researchandenterprise

19th November 2014

Dear Peninah

Project title: Investigating geographic variation in cancer diagnosis and treatments; the interaction between access to services and comorbidity.
Reference: 2014/2015 07

The amendments to your above proposal have been considered by the Chair of the Faculty Research Ethics Committee and we can confirm that your proposal has been approved.

Please could you ensure that any further amendments to either the protocol or documents submitted are notified to us in advance and also that any adverse events which occur during your project are reported to the Committee. Please could you also arrange to send us a report once your project is completed.

The Committee would like to wish you good luck with your project.

Yours sincerely,

Mark Wilkinson
Chair FMH Research Ethics Committee

CC: Andy Jones

Annex H - Data Sharing Agreements, Public Health England and University of East Anglia

Public Health England

Data Re-use Agreement

Study Ref: Investigating geographic variations in cancer treatments and outcomes; the interaction between access to services and comorbidity
ODR Ref: ODR_2014_229

1.0 Organisations

This Data Re-use Agreement (the "**Agreement**") is drawn up between:

The Secretary of State for Health acting through **Public Health England ("PHE")**, of Wellington House, 133-155 Waterloo Road, London SE1 8UG, United Kingdom

And:
University of East Anglia
Norwich Medical School
Faculty of Medicine and Health Sciences
University of East Anglia
Norwich
NR4 7TJ

In this Agreement the **University of East Anglia (herein 'UEA')** and **PHE** are individually referred to as a "party" and collectively as the "parties"

2.0 Overview of Agreement

This Agreement comprises this Part 1 (Re-use Agreement), Part 2 (PHE Data Request Form) and the Schedules:

- Schedule 1: Data Specification
- Schedule 2: Permitted Users.

It sets out the terms on which the PHE agrees to share the Data with the Data Recipient.

3.0 Period of Agreement and Termination

This Agreement commences on 01/02/2015 and will terminate on 31/01/2018 unless extended by the mutual agreement of both parties in writing, in which case an Amendment (by a written modification to this Agreement) will be issued by PHE to replace this document. Either party shall be entitled to terminate this Agreement upon giving a written notice of one (1) month to the other party.

4.0 Data Retention and Disposal

The Data provided under this Agreement will be retained for the period of the Agreement, after which they will be destroyed in an auditable and verifiable manner as required by the Data Controller, as outlined in Section 12.

5.0 Data Required

Definitions from the 1998 Data Protection Act ("DPA"):

Data means information which

a) is being processed by means of equipment operating automatically in response to instructions given for that purpose,
b) is recorded with the intention that it should be processed by means of such equipment,
c) is recorded as part of a relevant filing system or with the intention that it should form part of a relevant filing system, or
d) does not fall within paragraph (a), (b) or (c) but forms part of an accessible record as defined by section 68 of the DPA;

Data controller means a person who (either alone or jointly or in common with other persons) determines the purposes for which and the manner in which any personal data are, or are to be, processed;

Data processor, in relation to personal data, means any person (other than an employee of the data controller) who processes the data on behalf of the data controller

Public Health England will supply **potentially identifiable data** as listed in Schedule 1 to UEA. These data have been extracted from the PHE Cancer Analysis System.

Data Sources/System Owner:
PHE Cancer Analysis System/ Jem Rashbass, National Director for Disease Registration.

Data Controller:
Public Health England on behalf of the Department for Health

Data Processor:
Ms. Peninah Murage on behalf of UEA.

6.0 Purpose for the Use of Data

UEA agrees not to disclose, use or reuse the data covered by this agreement except as specified in the "Investigating geographic variations in cancer treatments and outcomes; the interaction between access to services and comorbidity" protocol, summarised as:

A study to investigate if access to a GP has any impact on routes into secondary care for treatment or palliation to test the following hypotheses:

H1- Patients living farthest from GP and hospital are less likely to have their cancer detected in a national screening programme. We will test the association between distance/travel time and cancer diagnostic route.

H2- Distance to GP and to hospital of treatment is associated with the route to diagnosis and this is moderated by age, socio-economic status and rurality. We will test the association between distance to GP, and hospital of treatment with the route to diagnosis (Emergency Presentation, Inpatient Elective, Other Outpatient, GP Referral, Two Week Wait, Screen Detected and Death on Certificate).

H3- Waiting times from diagnosis to treatment are influenced by distance to GP and to hospital. We will test the association between distance and the time difference from cancer diagnosis to first treatment.

An access score for each patient will be derived using Geographical Information System (GIS).

UEA affirms that the requested data, outlined in Schedule 1, is the minimum necessary to achieve the purposes stated in this section.

UEA understands and agrees that they may not reuse the Data or any derivative data file(s) without written permission from PHE.

UEA agrees that without written authorisation from PHE, no attempt shall be made to link the Data included in Schedule 1 to any other data source.

Data access for this purpose is restricted to those named in section 8 of this agreement. Any changes in data access and data processor(s) will be notified in writing to PHE.

7.0 Specific Conditions

Nothing in this Agreement shall affect the ownership of any intellectual property rights or know-how exclusively owned by a party or existing prior to this Agreement. No right or license under any intellectual property owned by PHE is granted or implied under this Agreement.

UEA shall be permitted to use the Data for the purpose of carrying out analysis using appropriate statistical methods and the output of such analysis may be published by the UEA on its website and in peer-reviewed journals or made available directly to health professionals or members of the public. Any and all outputs must comply with the signed declaration as detailed in the PHE/UKIACR request form (annex 1) and the Health and Social Care Information Centre HES re-use protocol.

8.0 Permitted Users

Under the terms of this Agreement, UEA must ensure that access to the Data is managed, auditable and restricted to those individuals who need to process the Data for the specific purpose/s outlined in this Agreement.

UEA agrees that, access to the data covered by this Agreement shall be limited to the minimum number of individuals necessary to achieve the purpose stated in this section (i.e., individual's access to the data will be on a need-to-know basis).

No individual other than those listed in Schedule 2 ("Permitted Users") can access the Data under this Agreement.

The Data will only be accessed, processed and used within the European Economic Area only, unless permission has been granted by PHE and is stipulated in this Agreement.

9.0 User Obligations

UEA formally acknowledges the explicit commitment to maintaining the confidentiality, safety, security and integrity of any Data provided under this Agreement.

UEA continues legitimately to enter into formal agreement and/or implicit undertaking with all its clients, staff, visitors, suppliers and others, in recognition of the fact that the Data is held under the guardianship of UEA and which is pertinent to the individual client, staff member, visitor, supplier and/or other, will only be used for the explicit agreed purpose or purposes for which it has been provided, and that there will be no unlawful disclosure or loss of the same.

10.0 Audit

PHE reserves the right to undertake an audit of UEA with respect to the use and storage of the Data detailed in this Agreement, to ensure that all terms of this agreement are being abided by. UEA agrees not to withhold reasonable requests to undertake audits for the purposes set out in this clause.

11.0 Transfer of Data between PHE and UEA

The Data is categorised as Restricted and will be treated by PHE and UEA in accordance with the following protocol for the transfer and use of NHS Restricted Data.

Data Transfer Procedure:

1. Data encrypted to AES 256 standard
2. Data transferred by electronic transfer (if possible) or DVD (if necessary)
3. Decryption password communicated by telephone

12.0 Storage of Data and Data Destruction

UEA agrees to establish appropriate administrative, technical, and physical safeguards to protect the confidentiality of the data and to prevent unauthorised use or access to it.

Data will be stored securely by xx to a standard equivalent to level 2 of the Information Governance Toolkit (https://www.igt.hscic.gov.uk/) and processed within an environment that complies with the safe haven principles.

UEA agrees to ensure that computer terminals and other means to access the Data are maintained in secure premises.

The data will be destroyed by deletion from the electronic system files and shredding of any paper copies at the end of the study. UEA will issue a letter to PHE certifying destruction of all stored forms of the data within 30 days of the end of this Agreement.

13.0 Data Retention

The Data will be retained by until the end date of the Agreement. Extension of the retention period is subject to a formal review by PHE.

14.0 Publications

UEA agrees not to disclose direct findings or information derived from the Data specified in Appendix 1, with or without direct identifiers, if such findings, listings, or information can, by themselves or in combination with other data, be used to deduce an individual's identity.

UEA shall ensure that any publication derived from the Data complies with the following guidance:

(a) Anonymisation Standard for Publishing Health and Social Care Data: http://www.isb.nhs.uk/library/standard/128 ; and

(b) Anonymisation: managing data protection risk code of practice: http://ico.org.uk/for_organisations/data_protection/topic_guides/anonymisation .

15.0 Confidentiality

The parties each undertake to keep confidential and not to disclose to any third party, or to use themselves other than for the purposes of this Agreement, any confidential or secret information in any form directly or indirectly belonging or relating to the other, its affiliates, or their business or affairs, disclosed by the one and received by the other pursuant to or in the course of this Agreement, the existence and terms of this Agreement (**Confidential Information**).

Each party undertakes only to disclose the Confidential Information of the other to those of its officers, employees, agents and contractors to whom, and to the extent to which, such disclosure is necessary for the purposes contemplated under this Agreement. In the event of any incident relating to a breach of confidentiality, each party shall notify the other and initiate their reporting procedures without delay.

The obligations contained in this clause shall survive the expiry or termination of this Agreement for any reason, but shall not apply to any Confidential Information which:

- is publicly known at the time of disclosure to the receiving party; or
- becomes publicly known otherwise than through a breach of this Agreement by the receiving party, its officers, employees, agents or contractors; or
- can be proved by the receiving party to have reached it otherwise than by being communicated by the other party including being known to it prior to disclosure; or having been developed by or for it wholly independently of the other party; or having been obtained from a third party without any restriction on disclosure on such third party of which the recipient is aware, having made due enquiry; or is required by law, regulation or order of a competent authority (including any regulatory or governmental body) to be disclosed by the receiving party, provided that, where practicable, the disclosing party is given reasonable advance notice of the intended disclosure.

16.0 Breach of Conditions

Notification of breach: UEA agrees to report immediately to PHE instances of breach of any of the terms of this Agreement and to report any suspected or actual loss of Data.

Right to terminate access: The breach of any of the terms of this Agreement shall result in the immediate termination of access to the Data and the return of any Data to PHE in the manner to be advised by PHE.

17.0 Changes to Terms of Agreement

No change, modification, extension, termination, or waiver of this Agreement, or any of the provisions herein contained, shall be valid unless made in writing and signed by duly authorised representatives of the parties hereto.

18.0 Indemnity & Limitation of Liability

Nothing in this Agreement limits or excludes either party's liability for:

- death or personal injury resulting from negligence; or
- any fraud or for any sort of other liability which, by law, cannot be limited or excluded.

Subject always to the above provision, UEA shall indemnify PHE against any claims, losses, damages, costs (including all legal fees) and expenses incurred by or awarded against PHE arising out of or in connection with this Agreement, including, but not limited to, any use of Data made by UEA.

The liability of either party for any breach of this Agreement, or arising in any other way out of the subject-matter of this Agreement, will not extend to any loss of business or profit, or to any indirect or consequential losses.

19.0 No partnership or agency

Nothing in this Agreement is intended to, or shall be deemed to, establish any partnership or joint venture between any of the parties, constitute any party the agent of another party, nor authorise any party to make or enter into any commitments for or on behalf of any other party.

20.0 Governing Law and Jurisdiction

This Agreement and any dispute or claim arising out of or in connection with it or its subject matter or formation (including non-contractual disputes or claims) shall be governed by and construed in accordance with the laws of England.

The parties to this Agreement irrevocably agree that the courts of England shall have exclusive jurisdiction to settle any dispute or claim that arises out of or in connection with this Agreement or its subject matter or formation.

20.0 Agreement Signatures

For and on behalf of:
UEA

Signed:
Print Name: SUE STEEL
Post/Title: CONTRACTS MANAGER
Date: 01/02/2015

Faculty of Medicine and Health Sciences
Signed:
Print Name: ANDREW JONES
Post/Title: PROFESSOR
Date: 01/02/2015

For and on behalf of:
PHE

Signed:
Print Name: J ARMAN
Post/Title: HD OIL Sec h IS
Date: 10-2-15.

PHE Office for Data Release
Signed:
Print Name: R BRANNAN
Date: 10/02/2015

Schedule 1: Data Specification

tumour_patient_table NCDR field	Notes
tumour_pseudo_id	
patient_pseudo_id	
gppractice_psuedo_id	
travel_time_practice	based on time lookup provided by UEA
AGEATDIAGNOSISYEARS	
REGSEX	
QUINTILE2010	
DIAGDATEMONTH	
DIAGDATEYEAR	
SCREENINGSTATUS	
REGBASISCODE	
REGSITE4	4 digit ICD-10 code
REGDUKESTAGE	
REGFIGOSTAGE	
REGTNMCLIN	
REGTCLIN	
REGNCLIN	
REGMCLIN	
REGTNMPATH	
REGTPATH	
REGNPATH	
REGMPATH	
REGTNMINT	
REGTINT	
REGNINT	
REGMINT	
charlson_index	Calculated on lookback from 3 months prior to 27 months prior to diagnosis
Route_to_diagnosis	From 8 coded routes
Treatment_start_interval	Days after diagnosis to treatpent period start date as recorded in the Cancer Waiting Time system
REGSURGERYTHERAPY	Flag for surgery in 6 months post diagnosis
REGRT	Flag for RT in in 6 months post diagnosis
REGCT	Flag for Chemo in in 6 months post diagnosis
REGHORMONETHERAPY	Flag for Hormone Therapy in in 6 months post diagnosis
REGREGSITRYSUPPLYING	Cancer registrry supplying data
DCO	DCO flag

hes_table NCDR field	Notes

patient_pseudo_id	
trust_pseudo_id	
episode_pseudo_id	
interval_from_diagnosis	
diagnosis_code	
travel_time_trust	based on time lookup provided by UEA

treatment_table NCDR field	Notes
patient_pseudo_id	
trust_pseudo_id	
interval_from_diagnosis	
EVENTCODE	
EVENTDESC	
OPCS4_CODE	
RADIOCODE	
RADIODESC	
IMAGINGCODE	
IMAGINGDESC	
IMAGINGSITE	
travel_time_trust	based on time lookup provided by UEA

Schedule 2: Permitted Users

Permitted Users

Name	Institutional address (if not the same as section 1.0)	Job title	Email address
Peninah Murage		PhD Researcher	P.murage@uea.ac.uk
Andy Jones		Professor	A.P.Jones@uea.ac.uk

Annex I - Honorary contract with Public Health England

Public Health England

VISITING WORKERS / ATTACHMENT MODEL AGREEMENT BETWEEN

PUBLIC HEALTH ENGLAND

AND

University of East Anglia
Norwich Medical School
Faculty of Medicine and Health Sciences
Norwich
NR4 7TJ

And Peninah Murage, UEA Student as the Visitor

Public Health England (hereinafter called "PHE") has agreed to the attachment of the *visiting worker (hereinafter called "the Visitor")* for the purpose of acquiring experience in the National Cancer Intelligence Network (NCIN) Knowledge and Intelligence Team at PHE, subject to the following terms and conditions.

During the attachment your main point of contact is Dr Mick Peake

Status

The Visitor is not an employee of PHE and will not be entitled to PHE contractual terms and conditions for employees. No employment relationship is intended to be created by either PHE or the Visitor. The Visitor will be regarded by PHE as a volunteer worker during the attachment.

Financial Provisions

PHE shall provide the Visitor with appropriate working facilities during the attachment free of charge. However there may be circumstances under which PHE would charge bench fees (for example when using consumables) and this should be determined by the Head of Department/Unit and specified in the agreement.

PHE shall not be responsible for any payment to the *Visitor* or for any travelling and accommodation expenses incurred, except for necessary travel authorised in advance by PHE. The Visitor will be bound by the PHE Business Expense policy in respect of any such expenses.

Adherence to Regulations and Instructions

The Visitor is required to comply with the appropriate regulations and individual duties under UK Health & Safety law and the Safety Policy laid down for members of PHE staff, and PHE premises, and any reasonable instructions given by a Director or other members of PHE staff which shall be provided to the visitor on arrival.

Publication

The Visitor is required to abide by the Data re-use Agreement between UEA and PHE, attached at Annex 1 in relation to the publication, development or commercial activities, inventions or any other form of intellectual property arising from his/her work at PHE.

Confidentiality.

The Visitor shall not (except in the proper course of the services, as required by law or as authorised by PHE) during the visiting period or after its termination, use or communicate to any person, company or other organisation whatsoever (and shall use his best endeavours to prevent the use or communication of) any confidential information relating to PHE that he/she creates, develops, receives or obtains during the visiting period. This restriction does not apply to any information that is or comes in the public domain other than through the Visitor's unauthorised disclosure.

Intellectual Property Rights

The visitor shall comply with the Data Re-use Agreement in relation to any and all inventions and of all works embodying intellectual property rights made wholly or partially by him/her at any time during his/her visit.

PHE Property

On completion of the attachment *the Visitor* shall return any items of equipment or other PHE property and any books, documents or papers loaned to him/her for the purpose of his/her attachment, except any he/she is authorised in writing by the national director to retain.

Liability

PHE shall not be liable for any loss or damage to property of whatever kind caused by the negligence or default of the Visitor unless such loss or damage is caused by the negligence or fraud of PHE staff in instructing the Visitor.

Period of Agreement

This Agreement shall come into force on 01/03/2016 and shall remain in force until 30/09/2017

Termination

This Agreement may be terminated by either party giving at least one week's notice in writing.

Furthermore PHE reserves the right to terminate the Agreement forthwith if it considers any of the conditions stated herein are breached. Provisions regarding intellectual property and confidentiality shall survive the expiry or earlier termination of this Agreement.

Signed ..... Date 08/03/16
for and on behalf of PHE

Signed ..... Date 08/3/16
for and on behalf of UEA

I have read, understood and accept the conditions as set out above.

Signed ..... Date 08/03/2016
Name: Peninah Murage