Differences in Patient Access to New Blood Cancer Medicines in the United States and England: A Multi-Phase Mixed Methods Approach to Understanding the Impact of Health Technology Assessment



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There is some soul of goodness in things evil,
Would men observingly distil it out.
For our bad neighbour makes us early stirrers,
Which is both healthful and good husbandry:
Besides, they are our outward consciences,
And preachers to us all, admonishing
That we should dress us fairly for our end.

-William Shakespeare
Henry IV, Act 1V, Scene I

For Sophie Reiley Rottenberg

Who always had snacks in grad school but nearly drowned me on a white-water rafting trip. After graduation, Sophie and I shared an office at the MITRE Corporation in Baltimore. When my doctor suggested a, thankfully negative, surgical biopsy after 14 months of surveillance for breast cancer I wasn't sure who to ask to pick me up in the middle of the COVID 19 pandemic. Sophie not only volunteered but turned her home into a bed and breakfast. Groggy, high as a kite, and feeling very safe, I told her I was thinking about doing a PhD. She knew someone who went to Oxford and did what was so like her; connected friends. I applied, thinking it would be good practice before applications opened at US universities, and she was one of my first calls when I was shocked to be accepted to this program. While I adjusted to a new job and bounced between DC and Oxford, she continued to host "friendsgivings," kept me up to date with everyone, and talked for hours sitting in the car. When I was laid off, she told me it was brave, not irresponsible to move to England and finish school. She helped me pack up, organized my 27th birthday, and made time for hours of catching up when I was home. In November 2024, we travelled together to Southern Virginia to see our favorite Oxford graduate and MITRE alum get married.

Sophie was beloved by nearly every stranger she met (a BBQ joint owner and his wife in Roanoke gave her the family sauce recipe within 20 minuets). She remains beloved by friends and continues to make life more meaningful. I dedicate this work to her memory: to the laughter and care she shared so freely, and to the enduring love she left behind.

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ABSTRACT

This thesis explores how health technology assessment (HTA) influences patient access to new blood cancer medicines in the United States (US) and England. HTA is used to evaluate the clinical and economic value of new treatments and informs funding decisions. England has a formal, centralized HTA process for National Health Service (NHS) funding conducted through the National Institute for Health and Care Excellence (NICE). In contrast, the US is in the early stages of developing price negotiation policy at the national level.

Using a mixed methods approach, I examined access across three key stages: product launch, government reimbursement, and real-world utilization. I began with a quantitative analysis of regulatory approvals and launch timelines in both nations, then analyzed Medicare (US) and NICE (England) reimbursement decisions to understand their impact on coverage and funding. To add clinical context, I interviewed physicians in both countries about their experiences prescribing new treatments for blood cancer. I also carried out a scoping review to identify how researchers measure medicine access across health systems and used these findings to guide a trends analysis of new medicine utilization.

Quantitative and qualitative results indicated that the US sees earlier launches and reimbursement through government programs. US physicians generally have access to a wider range of innovative treatments, allowing more flexibility in care. In contrast, England's HTA process, while slower, tends to result in more consistent access once funding is approved. This highlights trade-offs between speed, equity, and patient centered care. While focused on blood cancers, these findings have broader relevance for how health systems manage access to innovative medicine. As the US expands price negotiation, and NHS England refines its HTA process, both systems have opportunities to learn from each other in their ongoing effort to deliver timely, fair, and meaningful care.

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LIST OF ABREVIATIONS

Abbreviation	Description of Abbreviated Term
ACA	Affordable Care Act
AMA	American Medical Association
ASCO	American Society of Clinical Oncology
AHRQ	Agency for Healthcare Research and Quality
ACTS	Accuracy and Timeliness Statistics
ATC	Anatomical Therapeutic Chemical
ABPI	Association of the British Pharmaceutical Industry
AML	Acute Myeloid Leukemia
CDF	Cancer Drugs Fund
CMS	Centers for Medicare and Medicaid Services
CAR T	Chimeric Antigen Receptor T-cell
CPAC	Clinical Priorities Advisory Committee
CI	Confidence Interval
CPI	Consumer Price Index
CLL	Chronic Lymphocytic Leukemia
VA	Department of Veterans Affairs
ESRD	End Stage Renal Disease
EMA	European Medicines Agency
EMS	Emergency Medical Service
FDA	Food and Drug Administration
GPI	Global Precision Index

HTA	Health Technology Assessment
HRU	Healthcare Resource Utilization
HI	Hospital Insurance
ICER	Institute for Clinical and Economic Review
IRA	Inflation Reduction Act
INN	International Nonproprietary Names
IQR	Interquartile Range
LCL	Lower Control Limit
MFN	Most Favored Nation
MHRA	Medicines and Healthcare products Regulatory Agency
MIDAS	Multinational Integrated Data Analysis System
MM	Multiple Myeloma
MDS	Myelodysplastic Syndromes
NCI	National Cancer Institute
NCCN	National Comprehensive Cancer Network
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NAS	New Active Substances
NHL	Non-Hodgkin's Lymphoma
OECD	Organization for Economic Co-operation and Development
ONS	Office for National Statistics
PhRMA	Pharmaceutical Researchers and Manufacturers of America
PMDA	Pharmaceuticals and Medical Devices Agency
PCC	Population Concept Context

QALY	Quality-Adjusted Life Year
RCT	Randomized Controlled Trial
SD	Standard Deviation
SEER	Surveillance, Epidemiology, and End Results Program
TA	Technology Appraisals
UCL	Upper Control Limit
UK	United Kingdom
US	United States
CUREC	University of Oxford's Central University Research Ethics Committee
WHO	World Health Organization

CHAPTER 1

A Multi-Phase Mixed Methods Approach to Understanding the Impact of Health Technology Assessment

1.1 Thesis Overview

In this thesis, I investigate how health technology assessment (HTA) contributes to differences in patient access to new blood cancer medicines in the United States (US) and England. As outlined in more detail below (see Section 2.1, *Brief History of National Insurance in the English Health System*), HTA is a process that evaluates clinical and economic implications of a health intervention, such as a new medicine. HTA is conducted with the intention of helping policymakers make informed choices about the value of a new technology. I examine the influence of HTA on patient access across three dimensions; launch, government reimbursement, and utilization (see Section 1.4, *A Note on Terminology: England vs United Kingdom* and Chapter 6, Section 6.3 for definitions of these concepts). I then contextualize these quantitative data through clinician perspectives on access to new medicines. By combining quantitative and qualitative methods across multiple phases in a mixed methods design, I aimed to provide a more comprehensive understanding of the way in which HTA influences blood cancer patient access to innovative treatments. The work undertaken for the DPhil is presented in a series of chapters, the content of which is summarized below. In writing these chapters, I aimed to make the content accessible to a broader academic audience by reintroducing key concepts and background when appropriate.

1.2 Chapter Structure and Contribution

Chapter 1 | Introduction

In this chapter, I outline key research questions, the overall structure of the thesis, and justify the use of a multi-phase mixed methods design. I clarify terminology used throughout, specifically the distinction between "United Kingdom (UK)" and "England," and explain the rationale for using the European Medicines Agency (EMA) rather than the UK's Medicines and Healthcare products Regulatory Agency (MHRA) in regulatory comparisons.

Chapter 2 | Background

I describe the health care and HTA frameworks in the US and England. I then present historic, nation-specific systemic factors that determine which patients gain access to innovative blood cancer treatment and justify the current policy relevance of this thesis. The chapter includes a rationale for focusing on blood cancer medicines.

Chapter 3 | Quantitative – Launch Data

I constructed a dataset of blood cancer medicines approved between 2011 and 2020. I assessed the availability of regulatory approval (US Food and Drug Administration (FDA) vs European Medicines Agency (EMA[1])), and market launch dates. This chapter offers a quantifiable comparison of new blood cancers launched in both the US and UK and establishes the set of medicines analyzed in subsequent chapters.

Chapter 4 | Quantitative – Reimbursement Data

Using a list of new medicines established in Chapter 3, I analyzed reimbursement decisions (Medicare vs NHS England) as measures of patient access. Chapter 4 offers a quantifiable comparison of government reimbursement for new blood cancers in both nations, estimating the proportion of technology appraisals (TAs) resulting in positive reimbursement and lag time to positive reimbursement.

Chapter 5 | Qualitative – Physician Interviews

I conducted semi-structured interviews with hematologists and oncologists in the US and England, to explore their experiences around prescribing new medicines for blood cancer. I focused on medicines with restricted or delayed funding identified in Chapter 4 and asked about broader access challenges in clinical practice. These perspectives informed the interpretation of quantitative data in Chapters 3 and 4 and guided the selection of medicines for analysis in Chapter 7.

Chapter 6 | Scoping Review

[1] For justification of EMA use see below; see Chapter 1 (Section 1.4).

I conducted a scoping review to identify appropriate data sources and methodologies for measuring access to cancer medicines. I outline how researchers measure and compare patient access across countries through utilization data. Based on findings from this review, I identified suitable sources for capturing real-world medicine use in the US and English contexts used in Chapter 7.

Chapter 7 | Quantitative – Utilization Data

I conducted a trends analysis of population-level utilization of selected blood cancer medicines using sales data from the IQVIA MIDAS[2] platform. I focused on medicines flagged by physicians in Chapter 4 as having access barriers. I evaluated whether differences in funding decisions identified in Chapter 3 reflected real-world treatment patterns.

Chapter 8 | Discussion

I synthesized findings from all chapters, drawing together findings to discuss the strengths and weaknesses of access to new blood cancer medicines in each health care system, and how HTA may shape these differences. This includes consideration of the feasibility and limitations of conducting meaningful comparative analysis across different national contexts. I conclude by evaluating the implications of introducing HTA-style mechanisms in the US, incorporating insights from the comparative analysis in Chapters 3 through 7 to inform this Chapter.

1.3 Mixed Methods Approach

This thesis used a multi-phase mixed methods design (Creswell and Plano Clark, 2011). It included two sequential phases, as shown in Figure 1.1. The design of this thesis moved from an explanatory sequential design, using quantitative research to inform the qualitative research, into an exploratory sequential design, using qualitative research to inform the final quantitative phase. A multi-phase mixed methods design involves the sequential implementation of several interconnected

[2] IQVIA MIDAS is a global pharmaceutical database that provides standardized information on drug sales and market trends across multiple countries. It is widely used in academic and industry research to analyze medicine usage, pricing, and market performance on a national and international scale. For more information on IQVIA MIDAS, see Chapters 3 (Section 3.1), 6 (Sections 6.5.2 and 6.7.1) and 7 (Section 7.2.2).

phases of research, each utilizing qualitative, quantitative, or mixed data collection and analysis strategies (Creswell and Plano Clark, 2011; Schoonenboom and Johnson, 2017). This design facilitates the progressive development, refinement, and integration of findings across phases and allows for a comprehensive examination of results and the iterative testing of research questions (Greene, Caracelli and Graham, 1989). Figure 1.1 illustrates how data were connected between phases.

Figure 1.1: Sequential Multi-Phase Mixed Methods Design

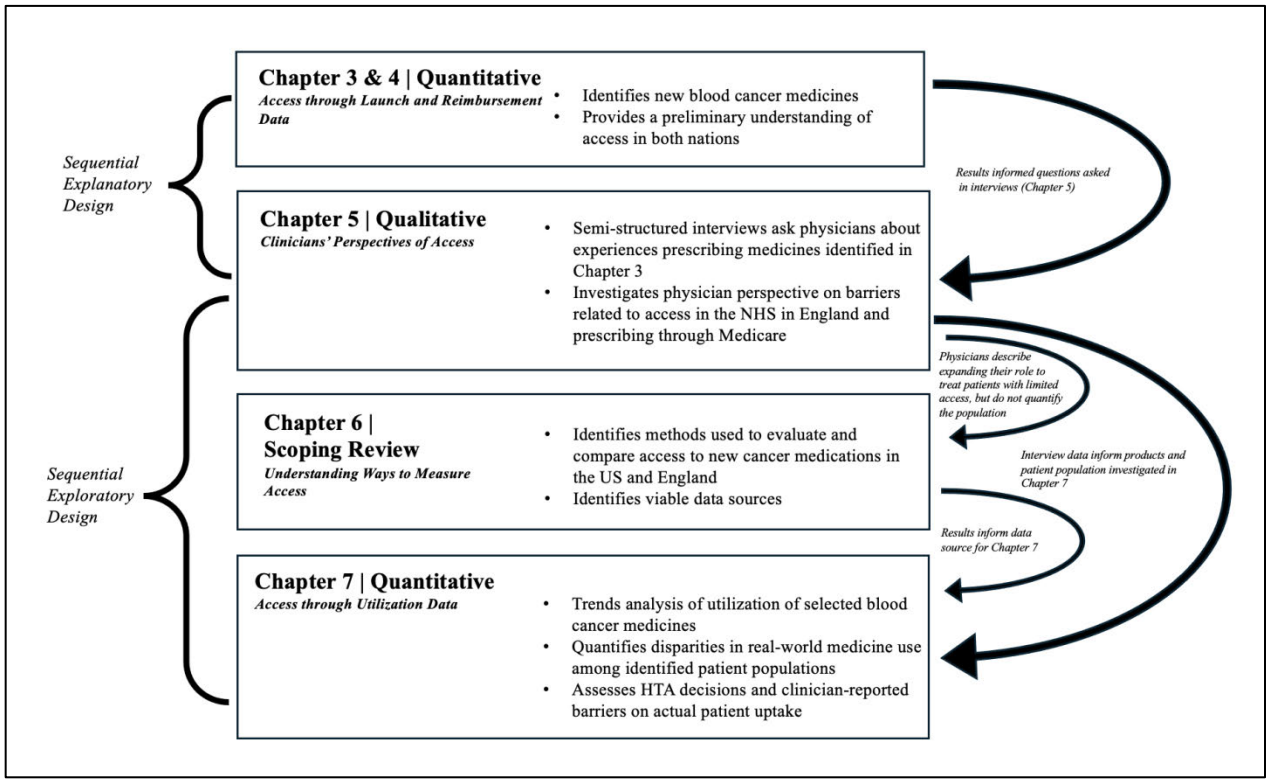


Figure 1.1 shows how quantitative analysis in Chapters 3 and 4 shaped the focus of clinician interviews in Chapter 5. Insights from interviews prompted a need to quantify the potential impact of access barriers discussed in interviews, which required identification of relevant data sources in Chapter 6. Chapter 6 supported Chapter 7 by identifying appropriate data sources to measure real-world utilization, ensuring that the final quantitative phase was methodologically grounded. Chapter 5 results further guided analysis in Chapter 7 by informing the selection of medicines and patient populations examined.

In the first phase (see Figure 1.1), quantitative analysis of access disparities between the US and England, including differences in product availability, funding status, and approval lag times, helped me develop my foundational understanding of health system variation in access. These findings were then explored in greater detail in the qualitative phase, where semi-structured interviews with physicians allowed me to contextualize these patterns. Analysis of qualitative data contributed to the development of an inductive theory about how national HTA structures shape the physician role and patient access.

In the second phase (shown in Figure 1.1), qualitative findings from interviews were used to produce a theory that HTA within the health system shapes the role of the physician in navigating access barriers, putting certain patient populations at a disadvantage in accessing new blood cancer medicines. This theory was then investigated quantitatively by looking at medicine uptake among specific blood cancer patient populations, clarifying the broader applicability and extent of qualitatively reported barriers to access.

I employed a multi-phase mixed methods design with the goals of complementarity, development, and triangulation in answering my thesis research questions (Creswell, 2009; Greene, 2007). Complementarity (Greene, Caracelli and Graham, 1989) supports the integration of quantitative and qualitative data by recognizing that each method addresses different aspects of the research topic. In this study, quantitative data captured patterns in patient access to blood cancer medicines, while qualitative data provided insight into how HTA processes influence those patterns in the US and England, together offering a more comprehensive understanding. Quantitative analyses in Chapters 3, 4, and 7 identified structural patterns in market launch, reimbursement, and utilization, while qualitative interviews in Chapter 5 provided depth and context to these findings by capturing the perspectives of physicians navigating these systems.

The sequential design of the study facilitated development (Creswell, 2011); findings from earlier phases informed the structure and focus of later phases. The medications identified in Chapter 3 as being subject to delayed or restricted reimbursement shaped the sampling and topic guide for

clinician interviews in Chapter 5, prompting the recruitment of more senior physicians with extensive experience and knowledge of NICE processes. Qualitative data collection allowed me to examine the quantitative results that surprised me in more detail (Morse, 1991). For example, after estimating overall difference in time between respective government funding in the US and England in Chapter 4, in Chapter 5 I was able to ask physician participants specifically about waiting for new products and their awareness of these products being used in other countries. Qualitative data were used to understand physician attitudes on access to new blood cancer medicines in each country (US and England). Insights from interviews then guided the selection of medications analyzed in Chapter 7, allowing for the quantitative utilization study to respond directly to qualitative insights, including patient populations of concern.

Use of a mixed methods approach also facilitated triangulation (Morse, 1991), whereby the validity of findings is enhanced in each phase by cross-verifying results across multiple sources and methods. By comparing patterns observed in launch, reimbursement, and utilization data with clinician narratives, my thesis assessed the consistency of evidence from different perspectives. This convergence of findings across methods added robustness to conclusions about how HTA mechanisms influence patient access. It also mitigates limitations inherent when relying on a single type of data.

Creswell defines mixing as meaning that data are "merged, kept separate, or combined in some way between the two extremes" (Creswell, 2009, p. 187). Mixing in this research related to the last of these approaches, combining data while maintaining elements of each source; datasets were kept separate through each phase but were connected as results were used to inform the next phase of each study. For example, Chapters 3 and 4 end with a quantitative analysis of launch and reimbursement data, establishing a foundational understanding of access disparities between the US and the UK/England. These findings informed the design of qualitative interviews in Chapter 5, where US and English physicians were asked about the specific medicines identified in Chapter 3 and their experiences prescribing them. The interviews were semi-structured (Kvale and Brinkmann, 2009), meaning participants had flexibility in guiding the discussion (Braun and Clarke, 2006; Kallio et al.,

2016). The quantitative results of Chapter 4 indicated tensions in access that helped me gain a preliminary understanding of the access picture in both nations and informed the type of participants I sought to recruit (experienced senior consultants and specialists).

Physician insights from Chapter 5 then guided development of the research question and sampling in Chapter 7 by informing the selection of medicines and patient groups for deeper investigation through utilization data. Chapter 5's analysis highlighted access dynamics, such as the clinician's role in navigating system-level constraints and perspectives on patient groups with limited access; these could not have been captured through quantitative data alone. In Chapter 5, physicians in England reported that HTA decision lag times and funding restrictions in access particularly impacted certain blood cancer patients (for example, Venetoclax for Multiple Myeloma (MM) patients). By considering these qualitative data, I was able to understand the access environment in England for specific patient groups, which informed my decision to select a small patient population for analyzing utilization data in Chapter 7 and assessing the extent to which they were affected. Data interpretation in Chapter 7 was directly shaped by physician insights from Chapter 5 as I worked to understand which patients were using restricted medicines. Figure 1.1 shows how each phase refined and extended the insights of the previous one, resulting in a more comprehensive understanding of HTA's impact on patient access.

This research is grounded in a pragmatist paradigm (Allemang, Sitter and Dimitropoulos, 2022), which shapes both its ontological and epistemological orientation. Ontologically, it adopts the view that reality is multiple and contingent, shaped by context, perspective, and practical consequences (Creswell, 2009). Epistemologically, it embraces the idea that knowledge is constructed through interaction with the world and is best judged by its capacity to generate insight and inform action (Patton, 1990). Rather than seeking universal truths (Morgan, 2007), the study is concerned with producing actionable understanding of how HTA use within a health system influences patient access to new blood cancer medicines. This stance supports a flexible methodological approach,

oriented toward real-world applicability and policy relevance (Creswell and Plano Clark, 2007; Rossman and Wilson, 1985).

1.4 A Note on Terminology: England vs United Kingdom

This thesis focuses primarily on England. NICE-led price negotiation within NHS England represents the most historic, established, and internationally influential[3] reimbursement framework among the UK's devolved health systems, especially when compared to NHS Scotland and NHS Wales. The term "UK" is used when necessary, particularly in data analysis involving broader datasets. During the development of the research plan, stakeholders highlighted that other NHS structures within the UK, such as NHS Wales and NHS Scotland, are frequently influenced by HTA decisions made by NHS England. This insight provided confidence that UK-wide data could serve as an appropriate proxy for English data when examining access trends potentially driven by HTA processes. Consequently, the term "England" and its demonym "English" are reserved for discussions related specifically to the English health system and reimbursement mechanisms, as seen in Chapters 1, 2, 4, 5, 6 and 8. In contrast, "UK" is used when referring to launch and utilization data encompassing England, Scotland, Wales, and Northern Ireland, primarily in Chapters 3 and 7, reflecting a broader national context. This deliberate distinction ensures clarity in addressing the differing scopes of data and policy relevant to each jurisdiction. Table 1.1 outlines usage of England and UK throughout this thesis.

Table 1.1: Explanation of Usage of "England" and "UK"

Term	Demonym	Relevant Sections	Usage Explanation
England	English	Chapter 1 Chapter 2 Chapter 4 Chapter 5 Chapter 6 Chapter 8	Use when referring specifically to the health system and reimbursement data related to England. This term emphasizes the geographic and administrative focus on England's NHS.
UK	British	Chapter 3 Chapter 7	Use when discussing launch and utilization data that applies to the broader United Kingdom, including England,

[3] For more on this, see Chapter 2 (Section 2.2).

			Scotland, Wales, and Northern Ireland. Though “British” refers to only England, Scotland, and Wales, it may be used colloquially in quotes or legislative titles that refer to early UK policy.

1.5 The UK vs European Regulatory Body

The initial phase of this thesis commenced in October 2020, several months following the formal exit of the UK from the European Union on January 31, 2020, commonly referred to as Brexit. The Medicines and Healthcare products Regulatory Agency (MHRA) was established in April 2003. Following input from project stakeholders and academic mentors, the European Medicines Agency (EMA) was recognized as the most influential regulatory authority for the UK (and by extension, England) during the period of the thesis study. Consequently, during the early stages of this research, particularly within Chapter 4 where regulatory decisions were examined, EMA approvals were adopted as the primary regulatory reference.

The MHRA has increased in prominence, however, the new blood cancer medicines list underpinning this thesis, constructed during data analysis phases in 2020 and 2021, encompasses new medicinal products launched globally between 2011 and 2020. Given this temporal scope, the EMA remained the most appropriate and relevant regulatory body underpinning the research.

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CHAPTER 2

Background on the Health Care Systems of England and the United States

2.1 Brief History of National Insurance in the English Health System

The establishment of the National Health Service (NHS) on 5 July 1948 marked a major transformation in the provision of health care in the UK (National Health Service Act, 1946). Early legislation, including the Public Health Acts of 1848 and 1875 (UK Parliament, 2025) and the National Insurance Act of 1911 (National Insurance Act, 1911), initiated limited state involvement in public health and employment-based health care provision. World War II exposed significant deficiencies in the existing health care system and demonstrated the feasibility of a centrally coordinated and universal health service (Webster, 1988). As discussed below, the development of the NHS was driven by political priorities, administrative innovation, and professional negotiation. This resulted in a national system based on the principles of universality, comprehensiveness, and provision free at the point of use.[4]

World War II served as a catalyst for structural reform, placing unprecedented clinical and fiscal demands on the UK's health infrastructure (Lowe, 2025). In 1939, the Ministry of Health established the Emergency Medical Service (EMS), which coordinated hospital provision across the country in response to wartime casualties (National Archives, 2025). Under the EMS, voluntary and municipal hospitals were brought under regional coordination (Health Foundation, 2025). This legislation created a de facto national hospital system that provided a temporary but practical demonstration of the administrative feasibility of centralized control in the UK. During this time, wartime medical assessments and large-scale evacuations revealed widespread levels of untreated illness, poor physical condition, and health inequalities (Webster, 1988). According to historian Rodney Lowe, these findings supported the emerging consensus that the pre-war system was inadequate and that post-war reconstruction would need to include comprehensive health reform (Lowe, 2005).

[4] See Chapter 5 (Section 5.4.1) for further discussion of intrinsic values of NHS England.

In 1942, the Beveridge Report, formally titled *Social Insurance and Allied Services*, was published under the authorship of Sir William Beveridge (Beveridge, 1942). Commissioned by the wartime coalition government, the report proposed a comprehensive welfare system to address what Beveridge described as the five "giant evils" of want, disease, ignorance, squalor, and idleness. While primarily concerned with income security, the report identified health care as an essential component of the post-war welfare state and called for a national health service to provide care based on need, funded from taxation or social insurance, and available to all citizens. The report received broad public and political support, selling over 600,000 copies and establishing expectations for health service reform after the war (Harris, 1997).

In 1944, the Ministry of Health issued a White Paper titled *A National Health Service*, outlining proposals for a state-funded, universal health service that would integrate hospitals, general practice, and community health services (Ministry of Health, 1944). It proposed that services should be free at the point of delivery and centrally administered. Though published under the coalition government (Webster, 1988), the proposals anticipated more definitive reforms that would follow the 1945 general election in which the Labour Party secured a majority and committed to implementing a national health service (Webster, 1988).

Under the leadership of Prime Minister Clement Attlee, Aneurin Bevan was appointed Minister of Health and tasked with establishing the new system (Foot, 1973). Bevan proposed the nationalization of hospitals, the integration of public health and community services, and the inclusion of general practitioners under public funding (Webster, 1988). The model Bevan advanced was based on the core principle that health care was a right of citizenship, an argument also put forward by Bevan in his 1952 book *In Place of Fear* (Bevan, 1952). However, Bevan's proposal faced substantial opposition from various quarters, specifically the British Medical Association (BMA), hospital administrators, and sections of the medical profession who were concerned about state control and the loss of clinical autonomy (Webster, 1988).

Bevan introduced several compromises to secure the cooperation of key stakeholders. General practitioners were retained as independent contractors rather than becoming salaried employees of the state (Jones et al., 2015). Hospital consultants were permitted to maintain private practice within NHS hospitals (Webster, 1988). Voluntary hospitals were absorbed into the new system but allowed to preserve elements of their administrative identity. Hospital services were managed through newly created regional hospital boards and local management committees, rather than being directly controlled by the Ministry (National Health Service Act, 1946).[5]

Following the establishment of the NHS in England, similar but distinct organizations were developed for Wales and Scotland. NHS Wales was created under the same National Health Service Act 1946 but operated with a degree of administrative autonomy to address Welsh-specific health needs and governance structures (National Health Service (Wales) Act, 1946). In Scotland, the NHS was established under separate legislation, the National Health Service (Scotland) Act 1947 (National Health Service (Scotland) Act, 1947). Both NHS Wales and NHS Scotland embraced the core principles of universality and free access to health care, while adapting their administrative structures to reflect regional needs and governance (National Health Service (Scotland) Act, 1947; National Health Service (Wales) Act, 1946).

2.2 The Creation of the National Institute for Health and Care Excellence

In recent decades, NHS England has developed a structured framework for managing the cost of new treatments, particularly pharmaceuticals. Central to this framework is the National Institute for Health and Care Excellence (NICE), a government organization established in 1999 (NICE, 2025). NICE is responsible for evaluating the clinical and cost-effectiveness of health technologies and issuing guidance on their use within the NHS (NICE, 2025). Individual regional trusts can decide to fund medicines recommended by guidance, but a positive NICE TA ensures funding by NHS providers in England within 90 days (NICE, 2025). NICE uses a standard threshold for cost-

[5] For additional reference to Regional Hospital Boards, see Chapter 5 (Section 5.4.3).

effectiveness, based on the cost per quality-adjusted life year (QALY) (NICE, 2023), to determine whether a treatment offers sufficient value for money.

Some researchers and patient activists have pointed out that the QALY is not an entirely neutral measure and may devalue the positive effect of medicine on people with disabilities (Romano et al., 2023; Sawhney, Dobes and O'Charoen, 2023). To help address this, NICE started to apply a severity modifier in 2022, which adjusts the value assigned to treatments based on the severity of the patient's condition (NICE, 2025). The severity of a condition is algorithmically classified as high, medium, or none, with high severity conditions receiving a 1.7 times weighting and medium severity conditions a 1.2 times weighting. This modifier replaces the previous end-of-life modifier and broadens support to a wider range of severe conditions, increasing the likelihood that treatments for these patients will receive positive recommendations and NHS funding (ABPI, 2024). While the severity modifier was originally designed to be opportunity cost neutral, meaning it should not increase overall NHS expenditure compared to the prior system, recent analysis suggests its current application is conservative, potentially restricting access to some high-value treatments (Holdgate, 2024). The modifier represents an important, though evolving, mechanism by which NICE balances cost-effectiveness with equity and clinical need in funding decisions for severe and life-threatening conditions.

Another adjustment made by NICE to enhance patient access to cancer treatments is the Cancer Drugs Fund (CDF). Originally introduced in 2010 in response to widespread concerns about regional disparities in access (often referred to as the "postcode lottery" (House of Commons 2010)), the CDF was restructured in 2016 to function as a managed access fund (Keogh, 2010). It provides provisional funding for promising cancer medicines while additional clinical and cost-effectiveness data are collected, allowing NICE to conduct a more comprehensive appraisal (Kang & Cairns, 2023). While the CDF has increased patient access to new cancer medicines, some critics argue that it raises ethical and economic concerns by potentially undermining the fundamental objectives of HTA

(Appleby, 2014). Given that inclusion of CDF funding may obscure the full impact of HTA, this thesis excludes data on treatments funded through it.

2.3 Brief History of National Insurance in the US Health System

The American health system has developed amid political fragmentation, powerful special interests, and a series of historical contingencies. Throughout this thesis, I discuss how these forces have produced a system that simultaneously encourages professional autonomy and market innovation, while sometimes excluding the vulnerable and underserved.

Contemporary health policy papers (Sampson & Ollendorf, 2024) argue that the US health system is moving towards the English HTA model in price negotiation. While this may seem like a dramatic shift, American health policy has long been informed by the UK model. In *Medicare and Medicaid: the Past as Prologue*, Edward Berkowitz argues that Americans interested in "sickness insurance" looked to the British National Insurance Act of 1911 as a model (Berkowitz, 2005). During the Great Depression, national health insurance was deprioritized and excluded from the 1935 Social Security Act (H.R. 7260, 1935; Gordon, 2003). As a result, the US moved toward an employer-based system almost by accident. To compete for the shortage of male workers in the US during World War II, employers raised salaries at unprecedented rates (Mills & Rockoff, 1983). The Consumer Price Index (CPI) increased by more than 35% while concern grew that excessive wage increases would destabilize the economy during wartime (Schumann, 2003). In response, Congress passed the Stabilization Act of 1942, which authorized President Franklin D. Roosevelt to fix wages and salaries at levels not higher than September 15, 1942 (Executive Order 9250, 1942). Executive Order 9250 followed, freezing wages but exempting insurance and pension benefits (Executive Order 9250, 1942). These legislative efforts excluded "insurance and pension benefits in a reasonable amount to be determined by the President" (Executive Order 9250, 1942). Employers began to offer other benefits, including insurance plans with health care coverage to compete.

World War II also reshaped US views on federalism in social policy. Berkowitz argues the war created a shift toward federal administration of large-scale programs (Berkowitz, 2005). Where

the fifty US States had previously been considered key partners in social insurance, wartime logistics and central planning highlighted their inefficiency (Itmeyer, 1966). Proposed federal health insurance bills in 1943, 1945, and 1947 sought to cover all Americans (Truman, 1961; Poen, 1979), but were repeatedly defeated under pressure from the American Medical Association (AMA), which warned of "socialized medicine" (Harry S. Truman Presidential Library and Museum , 2025; Marmor, 2000; Starr, 1992). The AMA remains an important stakeholder in US health policy and firmly opposed to universal government-run health care today (Goldstein, 2021).

In the postwar period, private insurance rapidly expanded. By 1951, over half of hospital patients had some form of health coverage, and over 40 million Americans were privately insured for physician services (Klein, 2003). As Berkowitz notes, "the private sector had scooped the public sector" (Berkowitz, 2005, p. 14), providing a solution to an unmet public need but leaving many, especially the elderly, without coverage. This gap became increasingly visible during the 1950s, as Social Security expanded but employer-based insurance failed to cover retirees.[6] Reformers began to consider the health insurance status of elderly citizens (Derthick, 1979), who could not benefit from employer-based plans and whose high morbidity made it difficult to find coverage through other private plans (Marmor, 1973). In 1952, President Harry Truman proposed a scaled-down version of his 1947 national health insurance proposal that would cover widows, orphans, and the elderly but was defeated again (Markel, 2015). However, support for federal coverage of seniors continued to grow in Congress (Corning, 1969; David, 1985) until another Democrat was elected to the US Presidency in 1961.

In his first year as President, John F. Kennedy made Medicare a legislative priority, working with private health care providers to find common ground (US Senate, 1965). On May 20, 1962, Kennedy made a direct comparison to the English system while delivering an address at a rally in Madison Square Garden, saying "The fact of the matter is that what we are now talking about doing,

[6] As Social Security became more popular in that decade and Congress passed bills raising Social Security benefit levels in 1950, 1952, 1954, 1956, and 1958 (Berkowitz, 2005).

most of the countries of Europe did years ago, the British did it thirty years ago" (Zelizer, 2015). In response, the AMA transported doctors from England to describe the "dire straits of Great Britain's insurance system" (Dickerson, 2013). Then-actor Ronald Reagan publicly argued "one of the traditional methods of imposing statism or socialism on a people has been by way of medicine" (Zelizer, 2015). The Kennedy administration backtracked to some extent; Wilbur Cohen, Kennedy's legislative aid, promised the powerful US Senator Gary Hart that unlike the UK system Medicare would "… not provide a single medical service…physicians' services would not be covered or affected and the proposal provides that the government would exercise no supervision or control over the administration or operation of participating institutions or agencies" (Cohen, 1961, p. 1).

Beyond public perception and special interests, the tax writing Ways and Means Committee of the US House of Representatives, presented a serious block to action on Medicare. Ways and Means Committee Chairman Wilber Mills was a democrat but a famous fiscal conservative and long-time opponent of health benefits tied to Social Security (Marmor, 1973). In 1960, Mills had leveraged his "one man veto" as his Committee voted against a similar bill, and the following year had held 8 days of hearings on the bill with no further action (New York Times Archives, 1964). Liberals in 1962 began to push for Senate action in the hope that Senate passage would force the House to vote on the measure (Congressional Quarterly, 1962). Kennedy succeeded in having Medicare introduced in the Senate this time, where it was promptly voted down (Congressional Quarterly, 1962). Dr Leonard W. Larson, then AMA President, went on public record saying the bill would "deprive older people of a private system of medicine which had added years to their lives and of their individual relationships with their doctors" (Congressional Quarterly, 1962, p. 192).

In 1963, President Kennedy was assassinated. The newly sworn-in, President Lyndon B. Johnson called on Congress to fulfil the agenda of his predecessor and was elected in a landslide victory in 1964. When the eighty-ninth Congress convened the following January, Chairman Mills made it clear to President Johnson's team that Medicare passage would be the first order of business

(Social Security Administration, 2025). President Johnson signed Medicare into law with President Truman standing behind him that July (Zelizer, 2015).

In 1965, the elderly (defined by the US Census as over 65 years) was the group most likely to be living in poverty; almost one third fell under the US poverty line (De Lew, 2000). This group was prioritized by Johnson in original Medicare insurance coverage which included hospital insurance (Part A) and outpatient care (Part B) (CMS, 2025). Johnson intended to expand Medicare to all citizens as part of his "Great Society" incitive, but the pressures of the Vietnam war quickly limited his domestic agenda (Heath, 2025). Medicare legislation was passed in unprecedented circumstances and remains the largest US federal insurance program today. Other federally administered government programs exist like TRICARE, the insurance program for members of the military and their dependents (Defense Health Agency, 2025). This program is significantly smaller and largely looks to Medicare for coverage decisions.

Subsequent expansions of Medicare have continued to reflect the structural limitations and political trade-offs that characterize the US health system. In 1997, under the Clinton administration, Medicare Part C was established through the Balanced Budget Act. President Bill Clinton had sought more comprehensive health reform, including the creation of a national health plan, but his efforts were blocked by a combination of partisan opposition and organized resistance from the private insurance industry (Brady and Kessler, 2010). Instead, Part C expanded the role of private insurers within Medicare, offering beneficiaries the option to receive benefits through managed care plans. A similar pattern emerged with the creation of Medicare Part D in 2003, which added outpatient prescription drug coverage but included a statutory prohibition on federal price negotiation.

President Barack Obama also pursued Medicare expansion but received pushback (Marmor, 2010). Ultimately, Obama's 2010 Affordable Care Act (ACA) extended coverage through Medicaid[7]

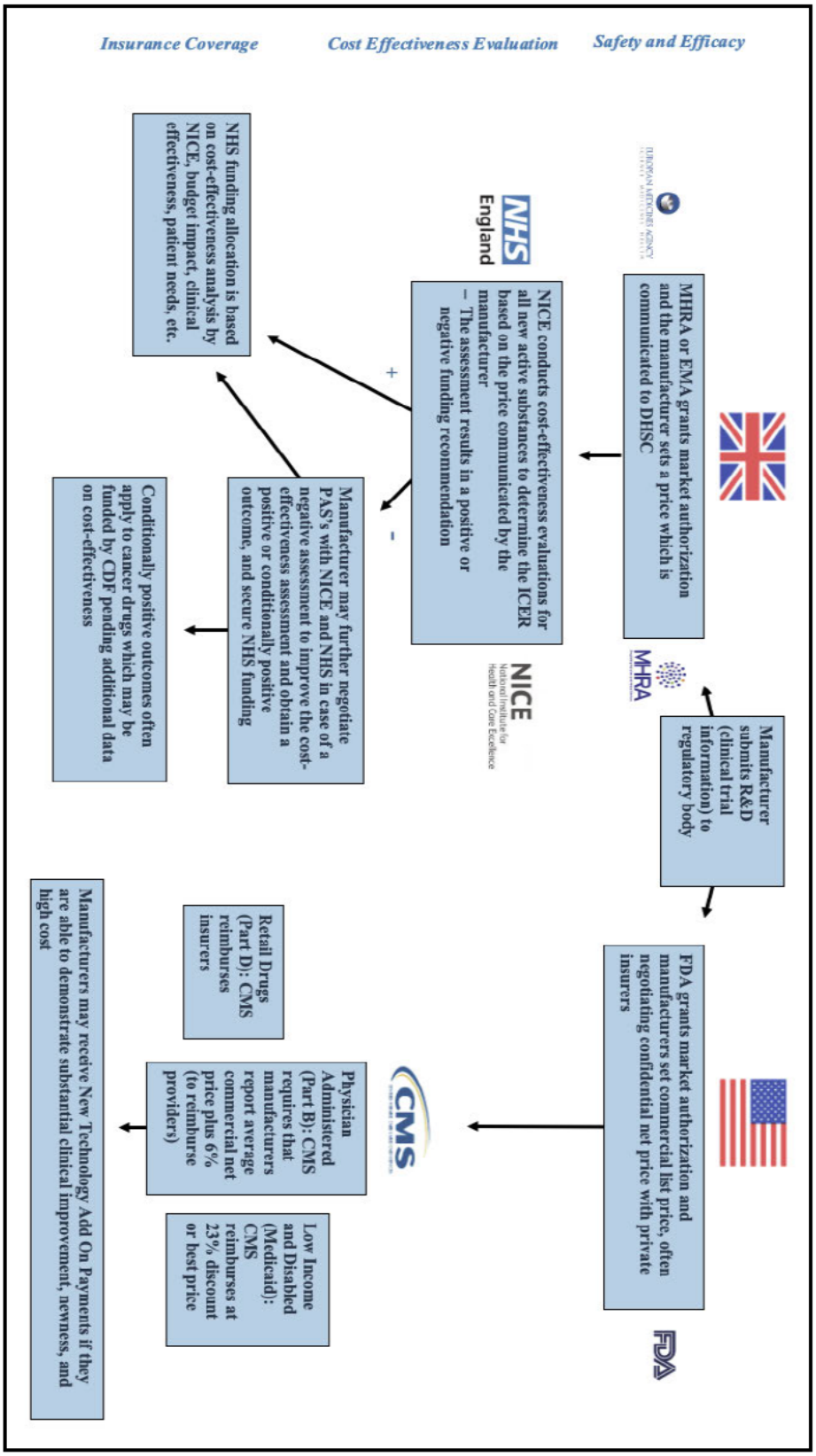
[7] Medicaid and Medicare are both US government health programs, but while Medicare primarily serves older adults and people with disabilities, Medicaid provides coverage for low-income individuals and families, with eligibility and benefits varying by state.

expansion and subsidized private insurance while preserving the central role of private insurers and excluding a single public option (H.R. 3590, 2010). Public opposition to Medicare expansion was fueled in part by rhetoric such as former Vice-Presidential Candidate Sarah Palin's widely publicized claim that price negotiation and end-of-life planning would create government "death panels," a phrase that crystallized public anxiety and further politicized cost-control efforts (Rutenberg & Calmes, 2009). Palin's statement drew on American fears of the NHS, mischaracterizing the role of NICE, which makes evidence-based decisions on treatment coverage as discussed above.

2.4 The Modern US and English Health Care Systems

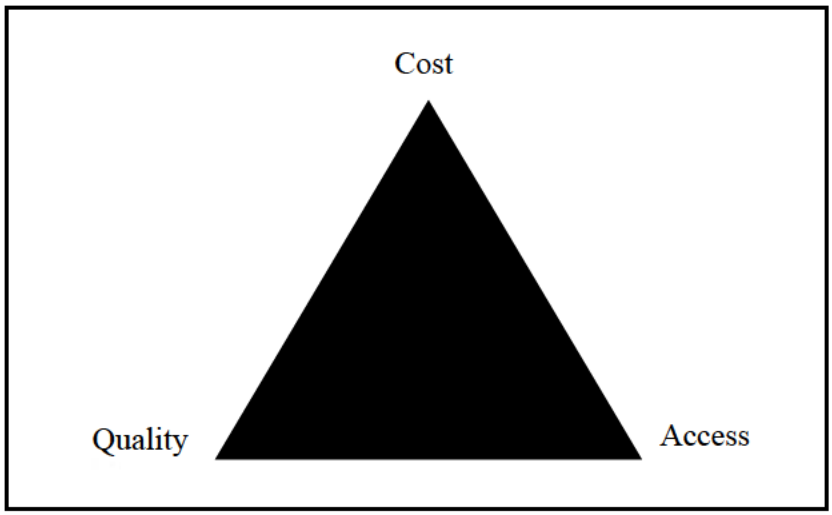
Figure 2.1 illustrates key differences between the English and US approaches to pharmaceutical price negotiation. In the former, after-market authorization by the MHRA, NICE evaluates cost-effectiveness and provides pricing recommendations. This allows the NHS, as a single-payer system, to negotiate directly with manufacturers and control costs. In contrast, the US FDA approves drugs without involvement in pricing, leaving manufacturers to set prices largely without federal negotiation. The Centers for Medicare and Medicaid Services (CMS), a US federal agency that administers Medicare, has traditionally been prohibited from negotiating drug prices, relying instead on private insurers and pharmacy benefit managers for discounts.

Figure 2.1: The English and US Health System



Governor Palin was not alone in expressing concerns about government-led price negotiation, as many critics feared that efforts to control costs could restrict access or reduce the quality of care (Cannon, 2009; Kominski, Nonzee & Sorensen, 2017; Scott, 2018). These apprehensions highlight a balancing act sometime inherent in health care policy, where improvement for one population or one aspect of care can impact others negatively. This perceived tension is reflected in William Kissick's Iron Triangle of Health Care, shown in Figure 2.2, which argues that access, cost, and quality are interlinked (Kissick, 1994).

Figure 2.2: Kissick's Iron Triangle of Health Care



In this framework, attempts to lower prices through negotiation may raise concerns that patients will face limited treatment options or diminished care standards. While many authors have opposed this idea (Bernstein, 2018; Luellen, 2017; Niles, 2015), Kissick's basic argument remains a prominent theory in US health system literature (Anderson, 1994; Beauvais et al., 2021; Carroll, 2012; Services, 2021; Terry, 2017; Van der Goes et al., 2019).

When I began my thesis program in 2020, I was convinced that the US health system policy would slowly move towards the English model. I intended to test the criticisms of the English system to understand how patient access to high quality and innovative new medicine might change in the US with the implication of price negotiation through HTA. I was also aware that concerns about price

negotiation's potential impact on patient access could be leveraged in US policymaking debates. I believed that evidence-based criteria to assess HTA's effects on patient access would be vital in these conversations.

During the evolution of this thesis, the US took initial steps toward government-led drug price negotiation, marking a shift from decades of market-based pricing. Under the Inflation Reduction Act (IRA) of 2022, CMS was granted authority to negotiate the prices of select high-cost prescription drugs covered by Medicare. This development represents a departure from previous policy and aligns the US with health system models like England's that use centralized mechanisms to control pharmaceutical spending. More recently, a revised Most Favored Nation (MFN) policy was enacted in the US via an executive order on May 12, 2025 (Executive Order 14297, 2025), introducing international reference pricing as a tool in CMS negotiations. This includes direct consideration of the UK's drug prices, tying the health systems together and underscoring the importance of this thesis topic. By investigating metrics that compare patient access in both the US and English health systems, we can gain a clearer understanding of how these systems affect patients' care. Understanding how both health systems impact patient access to new medicines is critical to identify and address delays and disparities, ultimately informing policies that promote more expansive and timely access to innovative treatments.

2.5 Rationale for Focus on Blood Cancer Medicines

This thesis focuses on patient access to new blood cancer medicines, which Siddhartha Mukherjee characterizes in *The Emperor of All Maladies* as complex and historically formidable diseases, having undergone remarkable therapeutic advances in recent years (Mukherjee, 2010). Stephen S. Hall's *A Commotion of the Blood* similarly captures the profound human and biological dimensions of blood cancers, underscoring the urgent need for innovative treatments and the success of immunotherapy (Hall, 2018). Despite these advances, new medicines such as CAR T-cell treatments, which offer potential curative outcomes for certain patients (Melenhorst et al., 2022), may

face challenges for reimbursement in England. These challenges stem from the high costs of such medicines (Wu et al., 2024) and the limited long-term evidence available at the time of HTA review, delaying or restricting patient access.

Focusing on blood cancers provides a critical lens for understanding how HTA allows health care systems to evaluate and adopt these potentially problematic medicines. This focus allows for more targeted data collection and analysis, while addressing broader questions of equity and access to oncology innovation. Investigating a single cancer allows for more straightforward comparisons between national health systems by isolating the effects of regulatory, reimbursement, and clinical decision making processes, especially those shaped by HTA.

In 2023, the US Pharmaceutical Researchers and Manufacturers of America (PhRMA), a trade association representing pharmaceutical companies, published a Global Access Report with data suggesting that the UK has lower availability of new cancer medicines than the US across all therapy areas (PhRMA, 2023). For blood cancers, 93% of new medicines launched in the US were available compared to 64% in the UK. Similar gaps exist in breast (100% US vs. 83% UK), skin (100% vs. 87%), female reproductive (100% vs. 91%), lung (96% vs. 79%), and urological cancers (90% vs. 80%) (PhRMA, 2023). These differences underscore persistent disparities in access to new oncology treatments and suggest that blood cancers warrant particular focus, given the notably larger disparity in medicine launch rates compared to other cancer types. Some evidence indicates that survival rates for patients with blood cancers are generally higher in the US than in the UK (Coleman et al., 2008). This pattern is observed specifically in 5-year survival rates for chronic lymphocytic leukemia (CLL) (Cancer Research UK, 2024; Redaelli et al., 2004) and Hodgkin lymphoma (American Cancer Society, 2024; Cancer Research UK, 2024). Furthermore, Blood Cancer UK has reported that for all major forms of blood cancer, survival outcomes in the UK lag behind those in the US (Blood Cancer UK, 2024). These differences may point to a range of contributing factors, including differences in early diagnosis, variation in the availability and uptake of new medicines, and the broader impact of health system structures such as HTA on access to treatment. Many researchers point out that while

US and UK cancer patients are comparable (Sarker et al., 2017), patient outcomes are extremely complex and difficult to compare across countries (Scowcroft, 2009). This thesis focuses on patient access and does not evaluate outcomes. However, differences in blood cancer survival rates between the two nations helped form an early point of interest in the development of the thesis topic.

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CHAPTER 3

A Preliminary Quantitative Exploration of Patient Access to New Blood Cancer Medicines in the United States and the United Kingdom: Identifying New Medicines and Validating Launch Data

3.1 INTRODUCTION

To understand patient access to new blood cancer medicine in the US and the wider United Kingdom (UK)[8], it was important that I understand the timing of the regulatory and market access process. As noted above, the US Pharmaceutical Researchers and Manufacturers of America (PhRMA) published a Global Access Report in 2023 suggesting substantial delays in patient access for new products in the UK compared to the US, especially in oncology (PhRMA, 2023). PhRMA's analysis included all new products approved by the US Food and Drug Administration (FDA), European Medicines Agency (EMA), or Pharmaceuticals and Medical Devices Agency (PMDA). While helpful for a global report on patient access, I was concerned that differences in the national regulatory processes might be the cause of reported differences in patient access. Regulatory differences can create access gaps which are not the focus of this research. For example, in my prior industry work with the Japanese Ministry of Health, we examined delays in medicine launch attributable to the Japanese regulator, the PMDA. At that time, the PMDA required that clinical trials be conducted in Japan before it would approve a new medicine because of concerns about dosage suitability for the Japanese population (FirstWord Pharma, 2023). In starting my doctoral research project, I was aware that Japanese data showing delays in global launch could have been mistakenly attributed to the national reimbursement process if regulatory approval was not considered (PhRMA, 2023). I wanted to avoid misattributing any similar regulatory differences to the HTA process in England. To get a more focused picture of the access environment in both nations, I aimed to identify new blood cancer medicines and understand what percentage of these medicines were approved by regulatory bodies in both countries. While there are other measures of patient access that will be discussed in later chapters (including reimbursement and utilization), by calculating the launch time

[8] While this thesis focuses on patient access in England, IQVIA and Pharmaprojects only offer data that applies to the wider UK. The UK is discussed in Chapter 3 to acknowledge this. In Chapter 4, more specific data on government reimbursement decisions in England is analyzed. For more on the use of UK vs English data in this thesis, see Chapter 1 (Section 1.4).

for these medicines to become available for purchase in each market I was able to build a valid preliminary picture of patient access.

As a first step, I identified which blood cancer products were introduced over a defined period from 2011 to 2020, as well as when those products were approved and launched in each country. I used two commercial datasets, the IQVIA Multinational Integrated Data Analysis System (MIDAS) and Pharmaprojects; both report regulatory approval and market launch[9] dates. Pharmaprojects is a lesser known but global database that tracks the development of pharmaceutical drugs from preclinical research to market launch (Citeline, 2025). It provides detailed information on drug pipelines, mechanisms of action, therapeutic areas, and company involvement, making it a key resource for analyzing research and development trends and competitive landscapes. IQVIA MIDAS is a global pharmaceutical sales database that tracks drug sales and market activity across more than 90 countries (IQVIA, 2025). It provides standardized data on product volume, revenue, therapeutic class, and manufacturer, enabling cross-country comparisons and market analysis. Researchers (Bassgen et al., 2023; Bucher et al., 2017; Corbacho et al., 2020; Salas-Vega et al, 2020), industry analysts (PhRMA, 2023), and policy makers (Executive Order 13948, 2020) use MIDAS to study drug utilization patterns, market access, and the impact of regulatory or pricing policies.

I found that the lists of products indicated for blood cancer reported by Pharmaprojects and IQVIA MIDAS did not align. I also found that the same product occasionally had different dates listed across the two sources. Discrepancies could bias launch time estimates, so I assesed whether these differences reflected minor discrepancies (rounding or definitional variation) or indicated more systematic inconsistencies before relying on either dataset for further analysis.

3.2 OBJECTIVE

The objective of this analysis is threefold. First, to identify new blood cancer medicines launched between 2011 and 2020. This time period was chosen at the thesis start in 2020; it spanned

[9] Launch is defined in this thesis as the date of first sale in country. For more on this, see Chapter 6 (Section 6.1).

10 years to capture any new medicines launched in the last decade. Second, to conduct a validation study comparing approval and launch dates reported by IQVIA and Pharmaprojects for all new medicines identified in the first step (identification of new medicines to treat blood cancer). Reliable datasets are essential in accurately analyzing patient access measures, so validation is important before moving on to the final step, which involves considering the impact of HTA on patient access to blood cancer medicines, and potential confounding of the reimbursement processes on access measures. To tackle the second objective, I assessed whether key dates were missing across both datasets (IQVIA and Pharmaprojects), whether the two sources reported the same values, and, where discrepancies existed, whether they reflected random variation in dates reported by the two sources or systematic differences that might bias results. I used a Bland–Altman analysis to quantify the average difference between sources and the range within which most differences fall. Bland–Altman is an effective method to test for systematic bias and was a useful way to assess whether the discrepancies pointed to random noise or something more structural. This validation step was necessary to determine whether either dataset could be used reliably in the third phase of the study, in which I calculated the percentage of products approved by regulatory authorities in both the US and UK[10] and measured the time from FDA or EMA[11] approval to market launch in each country.

3.3 METHODS

3.3.1 Phase 1 – Identification of Blood Cancer Medicines

Blood cancer medicines launched globally from 2011 to 2020 were identified from two commercial datasets, Pharmaprojects and IQVIA MIDAS, using the following approaches:

The Pharmaprojects subscription database was queried to identify drugs approved or launched in either the US or European Union[12] with indications related to blood cancers. The search applied filters for “Most Advanced Current Status” set to “approved,” and “Drug Country” set to both “UK”

[10] See Chapter 1 (Section 1.4), for distinction between UK and England relevant measures of patient access.
[11] See Chapter 1 (Section 1.5), for explanation of EMA approval use rather than MHRA.
[12] See Chapter 1 (Section 1.5), for explanation of EU indication use rather than UK.

and “US.” “Drug Country” displayed the history of a selected product in development, regulatory and launch milestones specific to a particular country. Drug indication filters were applied for “cancer” and “hematological”. Approval and launch dates were extracted from the “Event Date/type/details” columns in the results table and supplemented by reviewing the “Event History” and “Marketing” sections of each individual drug record for validation.

The IQVIA MIDAS subscription was also queried for products indicated for blood cancer. Specifically, launch dates for the UK and US markets, along with FDA and EMA approval dates, were requested by year and month. IQVIA analysts acknowledged that this data was likely to exhibit greater variability in approval dates due to factors such as EMA centralization and country-specific regulatory differences, but clarified it provides comparatively precise launch date information reflecting patient access. IQVIA defines launch date as the date of first sales to account for scenarios where marketing authorization exists but access is limited by reimbursement status. This can affect other access factors such as physician awareness and patient affordability. Date discrepancies by month may also occur due to rounding or human error.

3.3.2 Additional Verification

Product lists from IQVIA and Pharmaprojects did not fully overlap (discussed further in the Phase 1 Results Section). To validate the new blood cancer medicine list, I supplemented these sources by manually extracting all new active substances (NAS) approved for any cancer indication from the EMA, FDA, and the PMDA[13] websites. NAS identified from regulatory agency websites were compiled into a master dataset. For each NAS, I documented the agency where first approval occurred, the year of that approval, the approval date, the brand name, the active ingredient, therapy area and disease area.

[13] The Pharmaceuticals and Medical Devices Agency (PMDA) was included to provide a broader, more global perspective on innovative products entering the market, rather than relying solely on Western-centric regulatory data.

To confirm indication specificity, NAS disease and therapy areas were verified using the World Health Organization Anatomical Therapeutic Chemical (ATC) Classification codes (WHO, 2025). While regulatory listings of disease and therapy area were already captured, this step was important for verification to ensure that any future indications were captured. For example, if a product was first approved by the FDA for lung cancer but later indicated for blood cancer, checking ATC classification codes assisted in including that product in the new blood cancer medicines list. Products with cancer relevant ATC codes L01D (antineoplastic agents - antimetabolites), L01H (antineoplastic agents - protein kinase inhibitors), L01G (antineoplastic agents - alkylating agents), or L01X (other antineoplastic agents) were included. These classifications were cross-checked against therapy areas documented in the government regulatory approval listings to ensure consistency and validated again with secondary research using publicly available information on regulatory and product websites. Brand names, manufacturer details, and inconsistencies in international nonproprietary names (INN) were cross-referenced using IQVIA Analytics Link data. This step was taken to identify and resolve discrepancies when compared to the government agency regulatory approval lists.

3.3.3 Phase 2 – Validation of Data Sources

The second phase of this study was a validation analysis, a comparison to assess consistency and identify discrepancies between regulatory approval and market launch dates from IQVIA and Pharmaprojects for blood cancer medicines identified in Phase 1. The aim was to assess the consistency between these two commercial datasets to determine whether either could be used reliably for further analysis of patient access timelines. Ensuring consistency was critical because any systematic differences between data sources might distort conclusions about how quickly patients gain access to new treatments, potentially leading to misleading insights into patient access timelines.

For each product, four key dates were compared across the two sources; 1. FDA approval date, 2. EMA approval date[14], 3. US market launch date, 4. UK market launch date. Dates were recorded in year-month format to allow for calculation of continuous time differences in months. Records where dates were missing from both sources were excluded from the quantitative analysis for that date type (for example, UK market launch). Cases with one missing date were retained for Phase 3 analysis. To quantify agreement between the two datasets, the absolute difference (or the number of months between the two reported dates, regardless of which was earlier) was calculated for each product and each date type between the dates reported by IQVIA and Pharmaprojects. Differences were categorized as; Same month**,** Different by one month**,** Different by more than one month. This categorization helped me understand if the data provided by each source had occasional inaccuracies or a more systemic bias in the dates listed.

In addition to descriptive statistics, I used Bland–Altman analysis to evaluate the level of agreement. This method is particularly well suited to paired-date comparisons because it not only quantifies the average difference between two sources but also highlights the extent and pattern of disagreement, making it possible to detect systematic bias. For each date type, I calculated the mean difference between IQVIA and Pharmaprojects and the standard deviation of the differences. Limits of agreement (LoA) were defined as the mean difference ± 1.96 × standard deviation, representing the range within which most differences between the two sources are expected to fall. All data management and analysis were conducted using R Version 4.5.1 (R Core Team, 2025) in RStudio Version 2025.05.1+513 (Posit, PBC.,2025) and are recorded in Appendix 3.1.

3.3.4 Phase 3 – Assessing Approval and Launch Timing as a Measure of Patient Access

In Phase 3, I examined the timing between regulatory approval and market launch of new blood cancer medicines in the US and UK to better understand the patient access timeline in both countries. This is a descriptive analysis, intended to quantify the length of time patients may wait after

[14] See Chapter 1 (Section 1.5), for explanation of EMA approval use rather than MHRA.

a drug receives regulatory clearance before it becomes available on the market. These timelines are used as a proxy for patient access, under the assumption that longer delays may reflect slower translation of regulatory approval into real-world availability. In England, the HTA process, led by NICE, typically takes place after EMA approval and before a drug becomes routinely funded by the NHS. As such, longer launch delays in the UK may reflect, at least in part, the additional time required for HTA review and reimbursement decisions. Comparing these delays to timelines in the US, where there is no centralized HTA body and fewer formal reimbursement hurdles post-FDA approval, allows for a preliminary exploration of whether HTA contributes to slower access. This approach is not designed to establish causality. Launch delays may be influenced by a range of other factors, including manufacturer pricing strategies, supply chain readiness, national pricing negotiations, and decisions about when and where to prioritize market entry. These confounding variables mean that while regulatory-to-launch timelines offer insight into access patterns, they cannot attribute delays to specific causes such as HTA on their own. These limitations are important in interpreting the findings.

Using the validated product list from Phase 1, I extracted FDA and EMA approval dates alongside corresponding US and UK launch dates from IQVIA and Pharmaprojects datasets. Only products with complete data for both regulatory approval and launch dates in a given country were included in the timing analysis to ensure accuracy and comparability. Time-to-launch was calculated in days (rather than months to maximize precision) to define the difference between regulatory approval and commercial launch dates. Summary statistics including median, interquartile range (IQR), mean, and standard deviation (SD) were computed to describe the distribution of launch delays in each country; median and IQR were included as they are more robust to outliers, which are expected in launch timelines. This allowed for comparison of access timelines between the US and UK, with an emphasis on identifying variability and potential outliers.

All analyses were performed using R (version 4.5.1) in RStudio (version 2025.05.1+513) (See R Markdown file in Appendix 3.1 Analysis Scripts). Products missing approval or launch dates for

either country were excluded from the corresponding analyses to avoid confounding due to incomplete data.

3.4 RESULTS

The findings are presented in three phases, following the structure outlined in the Methods section. Phase 1 identifies the set of new blood cancer medicines that form the basis for all subsequent analyses. Phase 2 assesses the consistency of regulatory approval and launch dates across two commercial data sources to determine whether they can be used reliably in access timeline comparisons. Phase 3 uses this validated dataset to compare time from regulatory approval to commercial launch in the US and UK, providing insight into differences in patient access across the two countries.

3.4.1 Phase 1 – Identification of Blood Cancer Medicines

The Pharmaprojects search identified 43 products, while the IQVIA search yielded 41 products (see Appendix 3.2 for a complete list of products by source). There was a total of ten products found exclusively in one data source but not the other. Specifically, four products—pixantrone, forodesine, tagraxofusp, and quizartinib—were present in IQVIA but absent from Pharmaprojects. Conversely, six products—luspatercept, tazemetostat, crisantaspase, crizotinib, obinutuzumab, and omacetaxine mepesuccinate—were found in Pharmaprojects but not in IQVIA.

Secondary research confirmed that pixantrone, forodesine, tagraxofusp, quizartinib, crizotinib, and obinutuzumab are new active substances (NAS) indicated for blood cancer treatment, and were included in the final blood cancer product list. This verification involved cross-referencing regulatory approval documents, pharmaceutical databases, and official drug compendia to ensure the accuracy of classification and therapeutic indication. Ultimately, the New Blood Cancer Product List contained 43 Products (see Table 3.1). Four products failed to meet the inclusion criteria stated in Methods that new medicines must be indicated for blood cancer treatment and be launched globally from 2011 to 2020. These four products were excluded for the reasons stated below:

- Luspatercept: Indicated for treatment of anemia often in patients diagnosed with blood cancer but is not indicated for blood cancer treatment itself.
- Tazemetostat: Not indicated for blood cancer treatment.
- Crisantaspase: Not a classifying NAS; base component (asparaginase) was first launched in 1985.
- Omacetaxine mepesuccinate: Not a classifying NAS; first launched in 2000.

Table 3.1: New Blood Cancer Medicines

Assigned Product Number	Molecule	Brand	Company	Global Launch Year
1.	nivolumab	OPDIVO	BRISTOL-MYERS SQB.	2014
2.	acalabrutinib	CALQUENCE	ASTRAZENECA	2017
3.	belinostat	BELEODAQ	AUROBINDO	2014
4.	blinatumomab	BLINCYTO	AMGEN	2014
5.	bosutinib	BOSULIF	PFIZER	2012
6.	brentuximab vedotin	ADCETRIS	SEATTLE GENETICS	2011
7.	carfilzomib	KYPROLIS	AMGEN	2012
8.	copanlisib	ALIQOPA	BAYER	2017
9.	daratumumab	DARZALEX	JOHNSON & JOHNSON	2015
10.	elotuzumab	EMPLICITI	BRISTOL-MYERS SQB.	2015
11.	enasidenib	IDHIFA	BRISTOL-MYERS SQB.	2017
12.	ibrutinib	IMBRUVICA	ABBVIE	2013
13.	idelalisib	ZYDELIG	GILEAD SCIENCES	2014
14.	ixazomib	NINLARO	TAKEDA	2015
15.	panobinostat	FARYDAK	NOVARTIS	2015
16.	pomalidomide	POMALIDOMIDE CELGE	BRISTOL-MYERS SQB.	2012
17.	ponatinib	ICLUSIG	TAKEDA	2013
18.	venetoclax	VENCLEXTA	ABBVIE	2016
19.	pixantrone	PIXUVRI	SERVIER	2012
20.	forodesine	MUNDESINE	MUNDIPHARMA INT	2017
21.	mogamulizumab	POTELIGEO	KYOWA HAKKO KIRIN	2012
22.	axicabtagene ciloleucel	YESCARTA	GILEAD SCIENCES	2017
23.	inotuzumab ozogamicin	BESPONSA	PFIZER	2017
24.	midostaurin	RYDAPT	NOVARTIS	2016
25.	tisagenlecleucel	KYMRIAH	NOVARTIS	2017
26.	duvelisib	COPIKTRA	VERASTEM	2018
27.	ivosidenib	TIBSOVO	AGIOS	2018
28.	moxetumomab pasudotox	LUMOXITI	INTE PHARMA	2018
29.	gilteritinib	XOSPATA	ASTELLAS PHARMA	2018
30.	glasdegib	DAURISMO	PFIZER	2018
31.	polatuzumab vedotin	POLIVY	ROCHE	2019
32.	tagraxofusp	ELZONRIS	MERINI	2019
33.	quizartinib	VANFLYTA	DAIICHI SANKYO	2019
34.	selinexor	XPOVIO	KARYOPHARM THERAPE	2019
35.	belantamab mafodotin	BLENREP	GLAXOSMITHKLINE	2020
36.	brexucabtagene autoleucel	TECARTUS	GiLEAD SCIENCES	2020
37.	cedazuridine#decitabine	INQOVI	OTSUKA	2020
38.	isatuximab	SARCLISA	SANOFI	2019
39.	tafasitamab	MONJUVI	MORPHOSYS US	2020

40.	zanubrutinib	BRUKINSA	BEIGENE	2019
41.	pembrolizumab	KEYTRUDA	MERCK & CO	2014
42.	crizogtinib	XALKORI	PFIZER	2011
43.	obinutuzumab	GAZYVA	ROCHE	2013

3.4.2 Phase 2 – Validation of Data Sources

Across the 43 products in the New Blood Cancer Products List, data completeness varied by date type and data source. Table 3.2 summarizes the presence or absence of dates from IQVIA and Pharmaprojects for each date type (FDA approval, EMA approval, UK launch, US launch).

Table 3.2: Data Presence Overview Between IQVIA and Pharmaprojects Data

Date Type	Absent in Both	Only IQVIA	Only Pharmaprojects	Present in Both
EMA Approval	8	4	1	30
FDA Approval	3	1	1	38
UK Launch	13	7	2	21
US Launch	3	1	0	39

In general, FDA and US launch dates were the most consistently available across both datasets. EMA and UK launch dates showed higher rates of missingness, particularly in Pharmaprojects. Products with a date (FDA Approval, EMA Approval, US launch, or US launch) that is reported "Only in IQVIA" are more common than "Only in Pharmaprojects" for all date types except EMA Approval, suggesting IQVIA may capture some dates Pharmaprojects misses, especially for launch dates. The higher number of "Absent in both" for UK Launch dates suggests possible gaps or differences in the definition or timing of "launch" between sources or complexities in UK-specific market access. A substantial subset of products was present in both sources, Bland-Altman analysis (shown in Table 3.4) provides further insight into date differences.

Differences were evaluated and categorized for products where dates were present in both sources, (for example an EMA approval date reported by Pharmaprojects and EMA approval date reported by IQVIA). Results are summarized in Figure 3.1 and Table 3.3.

Figure 3.1: Agreement Between IQVIA and Pharmaprojects by Date Type

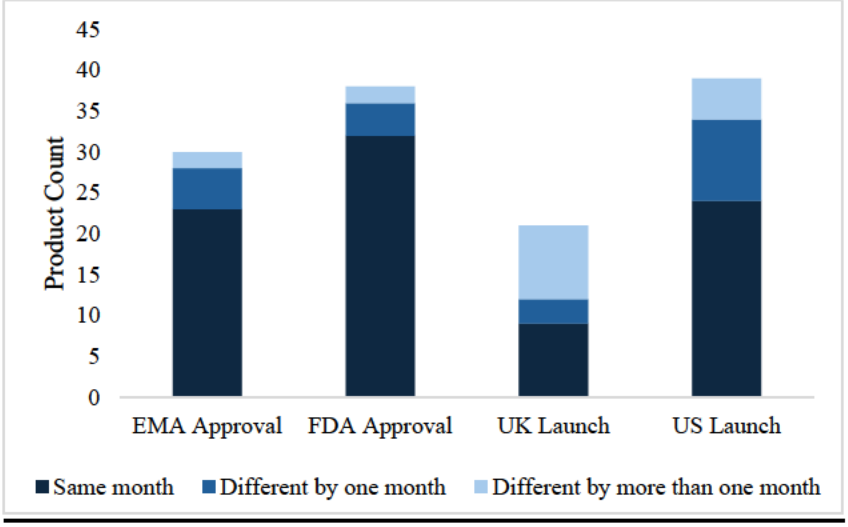


Table 3.3: Date Differences Between IQVIA and Pharmaprojects

Date Type	Difference Category	Count	Percent
EMA Approval	Different by more than one month	2.0	1.6
	Different by one month	5.0	3.9
	Same month	23.0	18.0
FDA Approval	Different by more than one month	2.0	1.6
	Different by one month	4.0	3.1
	Same month	32.0	25
UK Launch	Different by more than one month	9.0	7.0
	Different by one month	3.0	2.3
	Same month	9.0	7.0
US Launch	Different by more than one month	5.0	3.9
	Different by one month	10.0	7.8
	Same month	24.0	18.8

Table 3.3 shows a high proportion (7-25%) of close agreement (date listed as the same month) for approval dates. This indicates strong concordance for regulatory approval dates, as expected given these are key, well-documented milestones. Differences of one month occur less frequently, 2–8% depending on date type, which might be due to rounding, data entry, or slight timing differences in reporting as indicated by IQVIA Analysts. Overall, FDA and EMA approval dates showed high consistency between sources, while launch dates, particularly for the UK, were more variable. UK Launch dates show a higher rate of discrepancies, with 7% differing by more than one month and only 7% matching exactly. US Launch dates also show more spread, with nearly 12% differing by one month or more. Bland-Altman plots were used to assess the magnitude and direction of disagreement

between IQVIA and Pharmaprojects for each date type. Table 3.4 summarizes the mean difference (bias) and 95% limits of agreement (LoA) for each comparison.

Table 3.4: Bland-Altman Analysis

Date Type	Mean Diff (months)	SD Diff	Lower LOA	Upper LOA
EMA Approval	0.47	7.06	-13.4	14.3
FDA Approval	0.97	4.86	-8.55	10.5
UK Launch	-1.62	3.34	-8.16	4.93
US Launch	-0.62	1.79	-4.12	2.89

Table 3.4 presents the results of the Bland-Altman analysis, assessing the agreement between the two data sources across four key date types: EMA approval, FDA approval, UK launch, and US launch. FDA approval dates showed a mean difference of 0.97 months (SD = 4.86), with LoA ranging from 8.55 months earlier to 10.5 months later. EMA approval dates had a slightly smaller mean difference of 0.47 months (SD = 7.06) but a wider LoA, ranging from 13.4 months earlier to 14.3 months later. These results indicate that FDA and EMA approval dates differed little on average and showed narrow agreement ranges, suggesting limited bias and good consistency.

In contrast, launch dates showed greater variability. UK launch dates exhibited a mean difference of 1.62 months earlier in Pharmaprojects (SD = 3.34), with LoA from 8.16 months earlier to 4.93 months later, indicating wider variability. US launch dates were also recorded slightly earlier in Pharmaprojects, with a mean difference of 0.62 months (SD = 1.79) and relatively tight LoA ranging from 4.12 months earlier to 2.89 months later. These findings suggest that while average differences between data sources were generally modest, substantial variation, particularly in EMA approval and UK launch dates, may affect timeline accuracy.

3.4.3 Phase 3 – Assessing Approval and Launch Timing as a Measure of Patient Access

Table 3.5 presents the regulatory approval status for new blood cancer medicines in the US and UK. Of the 43 products examined, 90.7% had FDA approval, compared to 79.1% approved by the EMA. Notably, 74.4% of the medicines were approved in both regions, showing considerable overlap but also some differences in regulatory outcomes between the two countries.

Table 3.5: Regulatory Approval Status of New Blood Cancer Medicines

Category	Count	Percentage
Total Products	43	100
Approved in US (FDA)	39	90.7
Approved in UK (EMA)	34	79.1
Approved in both US and UK	32	74.4

Figure 3.2 and Table 3.6 present a comparison of launch timelines following regulatory approval for blood cancer medicines in the US and UK. The median delay from approval to commercial launch is substantially shorter in the US, with a median of 0 days (interquartile range [IQR]: 0 to 30.5 days), compared to the UK median of 61 days (IQR: 30.5 to 92 days). The distribution of launch delays in the US is notably tighter, reflected in a maximum delay of 61 days. The UK exhibits a broader range of delays, with a maximum of 608 days, indicating the presence of several outliers with extended launch times exceeding 200 days.

Figure 3.2: Time from Regulatory Approval to Market Launch

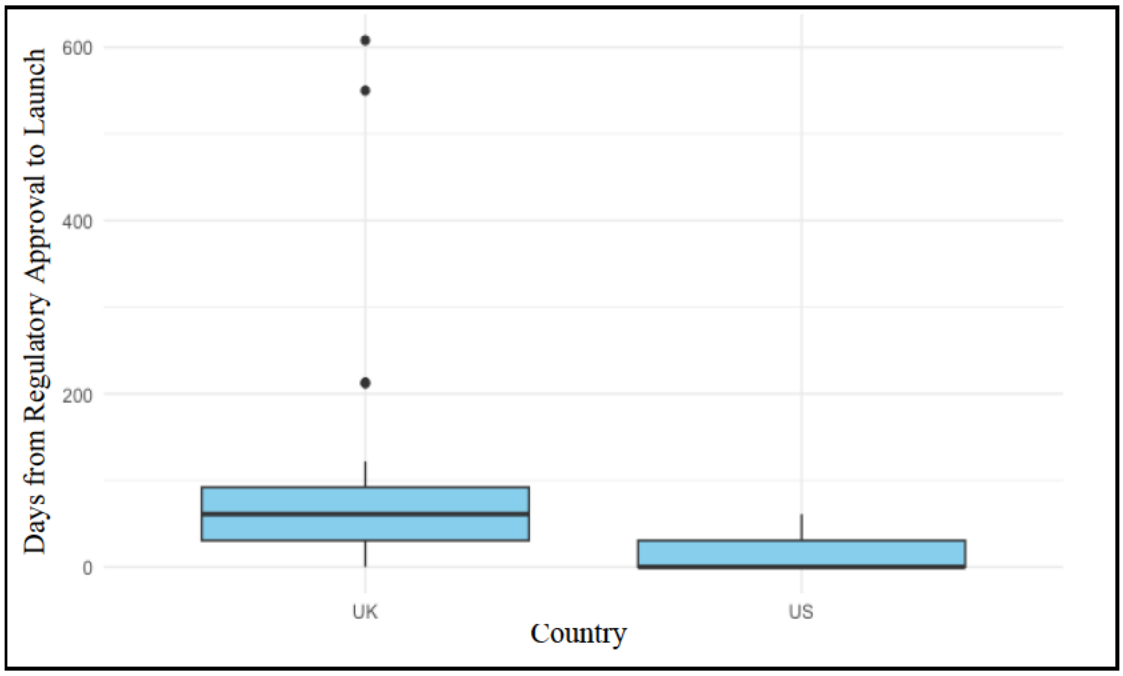


Table 3.6: Summary Statistics Time from Regulatory Approval to Market Launch

Country	N	Min	Q1	Median	Q3	Max	Mean
UK	23	0	30.5	61	92	608	109
US	31	0	0	0	30.5	61	17

3.5 DISCUSSION

3.5.1 Phase 1 – Identification of Blood Cancer Medicines

The comparison between IQVIA and Pharmaprojects identified considerable alignment in that most products indicated for blood cancer matched between datasets. However, notable discrepancies emerged. Ten products appeared in only one of the two sources, but further investigation revealed differences in classification, indication scope, and NAS status. These discrepancies illustrate how commercial databases may apply different inclusion criteria and highlight the potential for differences in whether medicines are classified as indicated for blood cancer. Desk research and regulatory cross-referencing were essential to verify which products were truly indicated for blood cancer and met the criteria for inclusion as new active substances in line with my research purposes.

Many of the products resulting from IQVIA and Pharmaprojects that were incorrectly listed as indicated for blood cancer treatment would likely be prescribed to blood cancer patients, though not for treatment of blood cancer itself. For example, Luspatercept is often prescribed to blood cancer patients to treat anemia that may result from myelodysplastic syndromes. While these treatments were not included in the analysis, they are a good reminder that treatment of a patient is often more holistic than simply curing a disease. This suggested a need for qualitative interviews with physicians to further develop understanding of how availability of other treatments and medical services could impact access to good medical care for blood cancer patients.

3.5.2 Phase 2 – Validation of Data Sources

Comparison of IQVIA and Pharmaprojects data on drug approval and launch dates revealed generally good overlap but important differences by date type. FDA approval and US launch dates showed the highest agreement, with nearly all products recorded in both sources. In contrast, UK launch dates showed notable discrepancies, with a higher proportion of products absent from one or both sources, possibly reflecting differences in market access and launch definitions. This discrepancy

between data reporting in the two nations is notable. It may indicate that IQVIA and Pharmaprojects are US-focused, perhaps because pharmaceutical companies and other potential customers are more interested in data from the larger US market (Eversana, 2021; Manufacturing Chemist, 2016; Mulcahy, 2024). IQVIA more frequently reported launch dates not found in Pharmaprojects, which may be because pharmaceutical companies report first sales data directly to IQVIA to capture patient access while Pharmaprojects tracks publicly available information. These findings suggest that while the two data sources broadly agree for many products, coverage gaps and differing data capture methodologies necessitate caution. An implication for the methodology of this thesis is that prioritizing IQVIA data, while cross-referencing with additional sources, may enhance the accuracy and reliability of drug availability timelines.

Bland-Altman analysis showed minimal systematic bias between IQVIA and Pharmaprojects dates across all date types, with mean differences ranging from -1.6 months (UK Launch) to 1.0 month (FDA Approval). Limits of agreement were wide, particularly for EMA approval dates (approximately -13 to +14 months). This may indicate that while the sources generally agree on average, individual products exhibit substantial differences in reported dates. Launch dates had narrower limits of agreement, reflecting more consistent reporting differences, with IQVIA dates tending to precede Pharmaprojects by about 1 month on average. This may be due to IQVIA's use of first sales as a proxy for launch. Results indicate that the two sources appear to differ by random error without meaningful bias, but inconsistency in recording of launch dates should be noted going forward.

3.5.3 Phase 3 – Assessing Approval and Launch Timing as a Measure of Patient Access

While most new blood cancer medicines receive regulatory approval in both the US and UK, a number are approved in only one country. These inconsistencies introduce complexity into comparative analyses, as including products lacking approval in either market risks conflating regulatory differences with subsequent access factors like HTA.

The data indicate that blood cancer medicines generally reach the market faster in the US compared to the UK. The median time from regulatory approval to commercial launch is accompanied

by a narrower range of delays and considerably shorter in the US (0 days), which means that US drugs launch on or very close to regulatory approval. Conversely, the UK exhibits a median of 61 days and wider distribution with several notable outliers experiencing delays of over 200 days, and in some cases, exceeding 600 days. The delay in the UK may suggest that factors occurring after EMA approval, such as national reimbursement decisions and HTA processes, likely play a significant role in slowing patient access to these medicines. It is also possible that the bureaucratic process conducted by NICE adds this time after regulatory approval and before product launch. The manufactures of outlier products with extreme delays may have been required to submit additional clinical data to NICE after regulatory approval to justify their cost. Understanding the economic and clinical status of the outlier drugs, and their NICE reimbursement status would be helpful in investigating the cause of this delay.

3.6 LIMITATIONS

This analysis has several limitations that should be considered when interpreting the findings. The analysis relies on two commercial datasets, IQVIA and Pharmaprojects, that report regulatory approval and market launch dates. Although a Bland–Altman analysis was used to assess agreement between these sources, discrepancies in reported dates and product indications were observed, which may affect the precision of timing estimates. Out of the 43 new blood cancer medicines identified between 2011 and 2020, approximately half had complete data for EMA regulatory approval date and UK launch. This narrowed the number of products included in the UK launch delay analysis, as calculating the time from approval to market launch required both EMA approval and UK launch dates to be present. Specifically, 23 products had complete data for both EMA approval and UK launch, whereas 31 products had sufficient data for the corresponding analysis in the US. Missing EMA approval or UK launch dates for several medicines resulted in a smaller sample size for the UK comparison, a notable gap in data completeness that could affect cross-country comparisons of patient access timelines.

While this exercise provides valuable insight into the timing of regulatory approval and market launch, it does not definitively attribute causes to the differences observed. The use of market launch date as a proxy for patient access may not capture the full complexity of real-world availability, including funding and patient uptake, which could constrain access to these medicines. Unlike the US, regulatory approval and market launch does not guarantee funding of a new cancer medicine through government insurance programs in England. In other words, launch does not mean NHS England availability.

3.7 CONCLUSION

3.7.1 Phase 1 – Identification of Blood Cancer Medicines

Relying on a single data source to identify new blood cancer medicines to examine in this thesis would have led to the omission of several relevant blood cancer treatments. Manual validation across regulatory agency records ensured that the final product list was comprehensive and consistent with the intended scope of the study. This process established a validated set of blood cancer medicines approved between 2011 and 2020. This list of NAS will form the foundation for further analysis of approval timing, launch delay, and ultimately the impact of HTA considered in this thesis.

3.7.2 Phase 2 – Validation of Data Sources

This analysis revealed greater variability and discrepancies in launch dates reported by IQVIA and Pharmaprojects compared to regulatory approval dates. This is consistent with the inherent complexities surrounding the definition and recording of launch dates in pharmaceutical markets. While launch date was considered here as date of first sale, in line with IQVIA's practice, Pharmaprojects may rely more on marketing authorization or reimbursement milestones. These methodological differences contribute to the discrepancies observed, with IQVIA typically reporting slightly earlier launch dates.

Going forward, use of launch date as a measure of patient access will be considered cautiously, understanding that the exact month can vary by a few months depending on the source. Based on the results of this study, regulatory approval dates appear to be more reliable and can serve

more effectively as anchors in considering patient access. Regulatory approval dates show tighter agreement and can be independently verified (via agency public record), so they are generally more robust for timeline analyses. Manually checking approval dates against agency records is a good validation step that will be used to strengthen this thesis dataset going forward.

3.7.3 Phase 3 – Assessing Approval and Launch Timing as a Measure of Patient Access

Most new blood cancer medicines are approved in both the US and UK, but some are approved in only one country, complicating direct comparisons. Medicines generally launch faster in the US, with shorter and less variable delays, while the UK shows wider and longer delays. Data gaps, particularly missing UK approval or launch dates, limit the analysis and highlight the need for more complete information to better compare patient access.

To avoid confounding effects of regulatory differences and to provide a clearer assessment of post-approval access barriers cause by HTA, it may be preferable to focus further analyses on the subset of medicines approved by both regulatory authorities. This approach could create a more reliable and consistent basis for comparing patient access timelines and evaluating the impact of HTA processes.

3.8 OVERARCHING CONCLUSIONS

3.8.1 Main Findings

This study identified 43 new blood cancer treatments launched between 2011 and 2020. Validation of two commercial datasets (IQVIA and Pharmaprojects) revealed close agreement on regulatory approval dates but notable inconsistencies in launch dates, particularly in the UK. Overall, medicines reached the market faster and with less variability in the US compared to the UK.

3.8.2 Methodological implications

Given the inconsistencies in reported launch dates, particularly across countries, launch data will be interpreted with caution in subsequent analyses. Regulatory approval dates, which showed stronger agreement between sources, will serve as a more reliable proxy for cross-country

comparisons. To reduce confounding from regulatory differences, the analysis will be limited to products approved by both the FDA and EMA.

3.8.3 Research Going Forward

The core product list will serve as the foundation for subsequent phases of the thesis, focused on patient access timelines. Analyses will consider regulatory approval dates to ensure consistency, while launch dates will be contextualized carefully. Further work will examine how post-approval processes, such as reimbursement decisions, affect the timing of patient access in different systems.

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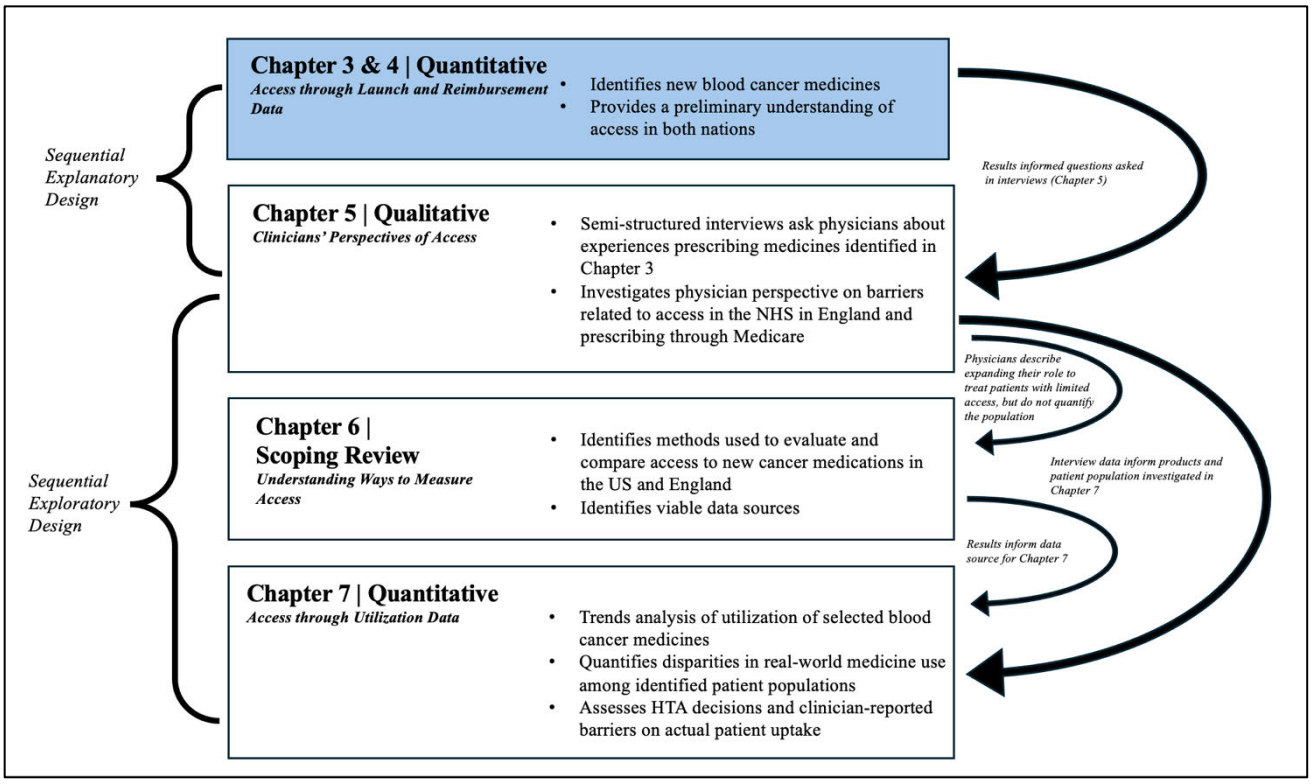
CHAPTER 4

Patient Access to New Blood Cancer Medicines in the United States and England: Reimbursement Status of New Blood Cancer Medicines Among Government Programs

CHAPTER 4 FORWARD

Chapter 4 presents a consideration of patient access through reimbursement decisions among government insurance providers in the US and England. This work has been prepared as a standalone manuscript and submitted for peer review. It builds directly on the findings from Chapter 3 and represents the next step in exploring how national policies shape patient access to innovative new medicines (see Figure 4.1).

Figure 4.1: Sequential Multi-Phase Mixed Methods Design



Chapter 3 identified inconsistencies in reported launch dates but noted that launch timing in the UK appears subject to post-regulatory approval delays. These delays may be linked to reimbursement processes, including HTA. To explore this possibility in greater depth, Chapter 4 focuses on access as defined by government reimbursement decisions and restricts the analysis to medicines that received regulatory approval in both the US and UK. This approach avoids

confounding effects introduced by differing approval timelines and allows for a more meaningful comparison of access barriers linked to HTA.

Regulatory approval dates are used as a consistent temporal anchor, enabling cross-country alignment of reimbursement timelines. This method builds on insights from Chapter 3 while incorporating a sharper focus on HTA processes and payer decisions as drivers of access. By comparing the timing and nature of these decisions across systems, this chapter contributes to a clearer understanding of where and how access diverges for the same medicines.

In adapting this article to thesis format, I have aimed to preserve the integrity of the original analysis while situating it within the thesis' broader research aims. The methodology, data sources, and limitations are presented in full within the article text but should be interpreted here as a continuation of the access narrative developed across Chapter 3 and future thesis chapters. Together, Chapters 3 and 4 investigate patient access using a quantitative approach that leverages launch and reimbursement data from both health systems, providing a preliminary quantitative understanding of patient access in the US and England.

4.2 KEY POINTS

4.2.1 Question

Do Technology Assessments (TAs) conducted by the National Institute for Health and Care Excellence (NICE) in England contribute to longer time to reimbursement qualification and limited coverage of new blood cancer medicines compared to the United States (US) insurance program Medicare?

4.2.2 Finding

This retrospective, record linkage study found that 53% of the positive TAs that were reviewed for 34 medicines funded all patients that had been approved for product use by the European Medicines Agency (EMA).[15] Patients who qualified for coverage waited a median of 3.67 years after EMA approval for funding through NICE.

4.2.3 Meaning

The findings of this study indicate that TAs conducted by NICE do have an impact on patient access to new blood cancer medications in England in both time and reach, significantly limiting and delaying reimbursement of products compared to reimbursement for US Medicare patients.

4.3 ABSTRACT

4.3.1 Importance

England determines coverage and pricing of new medicines using Technology Appraisal (TA), a systematic evaluation that has been proposed for use within the United Stated (US). However, little evidence has been published on the impact of TA on access to medicines for patients.

4.3.2 Aim

To examine medicines approved for blood cancer treatment in the US and England that have received coverage, to determine any patient population excluded from reimbursement of these medicines, and to identify delay times in coverage after regulatory approval in both countries.

[15] See Chapter 1 (Section 1.5), for explanation of EMA approval use rather than MHRA.

4.3.3 Design, setting, and participants

I conducted a retrospective, record linkage study using 34 previously identified blood cancer medicines first launched globally between 2011 and 2020.

4.3.4 Main outcomes and measures

I collected data on European Medicines Agency (EMA)[16] and US Food and Drug Administration (FDA) regulatory approval dates. I then analyzed NICE TA outcomes to determine the percentage of medicines approved for funding for each approved patient population. I calculated time to positive reimbursement from regulatory approval. The Kaplan-Meier method was used to calculate median time to funding approval to compare difference in funding outcomes between new medicines in England and the US. I then investigated difference in wait time between TAs for the same medicine.

4.3.5 Results

The search found that 34 new blood cancer medications were approved for blood cancer treatment. Of the 62 TAs that were conducted for these products, 40 (65%) TAs granted coverage to patient groups approved for treatment by the EMA, two (3%) TAs received negative recommendations, and 20 (32%) TAs were terminated. For products that received positive reimbursement, the median time from EMA approval to a positive NICE reimbursement decision was 3.67 years (95% CI: 3.06 to 5.16 years), with subsequent appraisals taking longer to reach decisions than first appraisal for the same medicine. In contrast, current US Medicare policy extends coverage immediately for all new cancer products approved by the FDA per a requirement put forth in Medicare program rules.

4.3.6 Conclusions and relevance

This retrospective, record linkage study indicates that limited coverage for new blood cancer medicines is granted by NICE. In cases where patient groups qualify for coverage, significant lag times exist after EMA approval compared to Medicare coverage after FDA approval.

[16] See Chapter 1 (Section 1.5), for explanation of EMA approval use rather than MHRA.

4.4. INTRODUCTION

Ensuring that people with blood cancer have access to the newest, most innovative medicines is challenging because treatment options are increasingly expensive personalized medicines that require development, testing, market authorization, and reimbursement before they reach patients. In England, an extra step to reimbursement which may impact patient access to new medicines, is Technology Appraisal (TA). TA is intended to limit excessive pricing and reflect the efficacy of new medicines for patients (NICE, 2022). However, it has its critics: patient groups claim that it can be leveraged as a budgetary solution for resource strained governments (Partnership to Improve Patient Care, 2020), while manufacturers argue that TA fails to account for the investment in drug development before regulatory approval (PhRMA, 2022), which is expensive and rarely successful (Kraljevic, 2004).

Medicines that achieve regulatory approval move on to apply for funding as the next step for patient access. In the US, citizens who are disabled, diagnosed with End Stage Renal Disease (ESRD), or aged over 65 qualify for the federal insurance program Medicare (Centers for Medicare & Medicaid Services, 2023). After a new medicine receives US Food and Drug Administration (FDA) approval, physicians in most cases, are immediately able to prescribe it to Medicare recipients with guaranteed reimbursement from the federal program. The European Medicines Agency (EMA) clearly specifies which indications and lines of treatment are safe and effective for patient populations, but reimbursement is not guaranteed by this approval for patients in England (Cherla et. al, 2020). English reimbursement decisions currently lie with the National Health Service (NHS) (Allen, 2019), which provides universal health care to its citizens and controls the pricing and purchase of medications. The National Institute for Health and Care Excellence (NICE) makes clinical effectiveness and cost effectiveness evaluations for new technologies including medicine, medical devices, and procedures for the NHS in England (Rawlings, 2009).

When NICE conducts a TA, it provides one of five types of recommendations: recommended, optimized, only in research, not recommended, or recommended for use in the Cancer Drugs Fund (CDF). NICE states on its public website that "85% of our recommendations have been positive (recommended, optimized, or recommended for the Cancer Drugs Fund)" (NICE, 2025). This number does not account for terminated TAs, and while an optimized TA may appear to be a positive recommendation, this may only grant reimbursement to a limited patient population.

Some research indicates that optimization has become increasingly common in NICE decision making (Bulut et al, 2020). Several peer reviewed studies compare patient access across nations through TA recommendations, but do not account for optimizations (Harricharan, 2023; Schaefer, 2021; Blázquez, 2023), or do not consider restriction with consideration of regulatory body determinations (Trouiller, 2023). To better understand the impact of TA on patient access to new blood cancer medications, I compared government insurance coverage of new products in the US and England. Though EMA decisions applied throughout the UK at the time of analysis, all funding decisions made by NICE apply only to English patients.

4.5 METHODS

I investigated the health insurance policies governing both countries' systems, then documented FDA or EMA approval decisions and dates for new blood cancer medicines. To avoid confounding from established differences in regulatory health systems between the two countries, I removed all medicines that did not receive regulatory approval from both the EMA and the FDA (Salcher-Konrad, 2020; Shah, 2013). I went on to investigate all NICE TA decisions and dates to determine reimbursement status and delay for each new medicine. In the case of TAs for combination therapies that referenced two new medicines, I used the first medicine listed. The Kaplan-Meier method was used to calculate median survival and 95% confidence intervals, censoring times for medicines that had not been assessed within the time frame of the study (2011-2020). I investigated reimbursement decisions while accounting for terminated TAs and examined difference in time to

positive reimbursement between TAs for the same medicine; I calculated proportional and average time to positive reimbursement per TA for each medicine with more than one funding decision.

4.5.1 Design

I conducted a retrospective, record linkage study using previously identified new blood cancer medicines first launched globally between 2011 and 2020. I went on to utilize the EMA and FDA public websites and document each approval status, disease indication, date of decision, approved EMA indications, product number and weblink for each of the medicines. Each of these data were extracted by myself, and all were checked by a supervisor. Medicines that were not approved by either regulatory agency were removed, and approval dates were rechecked to ensure accurate documentation within 30 days of the publication date listed by the EMA and FDA. First approval of a new medicine by the EMA and FDA was used to facilitate the most comparable analysis of English and US government reimbursement markets, though several medicines received additional regulatory approvals for new blood cancer indications after their first approval.

4.5.2 Identifying New Drug Reimbursement in England

I audited all eligible TAs conducted by NICE for blood cancer medications launched globally between 2011 and 2020; these TAs were publicly available on the NICE website and found by searching each medicine. TAs were reviewed spanning from February 26, 2014 to February 23, 2022. For each TA, I ensured the indication referenced blood cancer and removed TAs from the analysis due to non-blood cancer indications. For the remaining TAs that did indicate blood cancer, I noted the NICE recommendation decision, if the product was referred for payment through the CDF, if the TA was terminated, the TA number, the date of the publication, and the description of the official recommendation. I also noted blood cancer products included in the analysis that did not receive any TA at the time of analysis.

4.5.3 Statistical Analysis

Reimbursement delay time was calculated for all TAs that received a positive recommendation from NICE using R version 4.3.0. The R markdown file is available in the Appendix

(see A4.1). Date of EMA approval was subtracted from date of NICE recommendation, then divided by 365.25 to determine lag time in years. The confidence interval (CI), upper control limit (UCL), and lower control limit (LCL) were also calculated. In some cases, medicines had multiple positive TAs conducted by NICE, and therefore had a larger impact on the calculation of average delay time. Using the time to decision (TA decision date subtracted by regulatory approval time), I calculated the proportional and average wait time per TA for each medicine with more than one funding decision. In the case of each English patient group referenced by each TA, the "time to event" was wait time between EMA approval and a positive coverage decision. Negative or terminated TAs were considered "survivals," which would eventually lead to positive coverage decisions after a period of negotiation between the manufacturer and NICE or additional clinical data to further prove efficacy. This assumption was made to provide the most conservative assessment of negative funding decisions in England. Products with no TA and appraisals with negative TA or terminated TA were removed from this calculation as the patients in question have not yet gained coverage.

4.6 RESULTS

I found that 34 new blood cancer medicines were first launched globally between 2011 and 2020 and received both FDA and EMA approval. Table 4.1 outlines all drugs considered in the analysis including the brand name, manufacturing company, year of first launch anywhere in the world, and number of TAs conducted per product. I originally found that 43 new medicines were indicated for blood cancer treatment (see Methodology for Identifying New Blood Cancer Medicines in Chapter 3) but nine products were found to lack both EMA and FDA approval and were excluded from the analysis (see Table 4.2).

Table 4.1: Blood Cancer Medicines Included in Analysis

Molecule	Brand	Company	Global Launch Year	Number of TAs
acalabrutinib	CALQUENCE	ASTRAZENECA	2017	1
axicabtagene ciloleucel	YESCARTA	GILEAD SCIENCES	2017	1

belantamab mafodotin	BLENREP	GLAXOSMITHKLINE	2020	0
blinatumomab	BLINCYTO	AMGEN	2014	3
bosutinib	BOSULIF	PFIZER	2012	2
brentuximab vedotin	ADCETRIS	SEATTLE GENETICS	2011	5
brexucabtagene autoleucel	TECARTUS	GILEAD SCIENCES	2020	1
carfilzomib	KYPROLIS	AMGEN	2012	2
crizotinib	XALKORIS	PFIZER	2011	0
daratumumab	DARZALEX	JOHNSON & JOHNSON	2015	7
duvelisib	COPIKTRA	VERASTEM	2018	1
elotuzumab	EMPLICITI	BRISTOL-MYERS SQB.	2015	1
gilteritinib	XOSPATA	ASTELLAS PHARMA	2018	1
glasdegib	DAURISMO	PFIZER	2018	1
ibrutinib	IMBRUVICA	ABBVIE	2013	8
idelalisib	ZYDELIG	GILEAD SCIENCES	2014	4
inotuzumab ozogamicin	BESPONSA	PFIZER	2017	1
isatuximab	SARCLISA	SANOFI	2019	2
ixazomib	NINLARO	TAKEDA	2015	1
midostaurin	RYDAPT	NOVARTIS	2016	2
mogamulizumab	POTELIGEO	KYOWA HAKKO KIRIN	2012	1
moxetumomab pasudotox	LUMOXITI	INTE PHARMA	2018	0
nivolumab	OPDIVO	BRISTOL-MYERS SQB.	2014	1
obinutuzimab	GAZYVA	ROCHE	2013	3
panobinostat	FARYDAK	NOVARTIS	2015	1
pembrolizumab	KEYTRUDA	MERCK & CO	2014	2
polatuzumab vedotin	POLIVY	ROCHE	2019	1
pomalidomide	POMALIDOMIDE CELGE	BRISTOL-MYERS SQB.	2012	2
ponatinib	ICLUSIG	TAKEDA	2013	1
tafasitamab	MONJUVI	MORPHOSYS US	2020	0
tagraxofusp	ELZONRIS	MERINI	2019	0
tisagenlecleucel	KYMRIAH	NOVARTIS	2017	2
venetoclax	VENCLEXTA	ABBVIE	2016	4
zanubrutinib	BRUKINSA	BEIGENE	2019	0

Table 4.2: Blood Cancer Medicines Excluded from Analysis due to Regulatory Approval Status

Molecule	Brand	Company	Global Launch Year
belinostat	BELEODAQ	ACROTECH	2014
cedazuridine decitabine	INQOVI	ASTEX	2020
copanlisib	ALIQOPA	BAYER	2017
enasidenib	IDHIFA	BRISTOL-MYERS SQB.	2017
forodesine	MUNDESINE	BIOCRYST	2017
ivosidenib	TIBSOVO	SERVIER	2018
pixantrone	PIXUVRI	LGM PHARMA	2014
quizartinib	VANFLYTA	DAIICHI SANKYO	2019
selinexor	XPOVI	KARYOPHARM	2019

Among the 34 blood cancer medications and 62 TAs in this analysis, NICE consideration varied widely. In 6 cases (over 17% of all blood cancer medicines considered) no TAs were conducted for the new medicine (see Table 4.3).

Table 4.3: Products with No Technology Appraisal Conducted by NICE

Molecule	Brand	Company	Global Launch Year
belantamab mafodotin	BLENREP	GLAXOSMITHKLINE	2020
cedazuridine decitabine	INQOVI	OTSUKA	2020
crizotinib	XALKORI	PFIZER	2011
moxetumomab pasudotox	LUMOXITI	INTE PHARMA	2018
tafasitamab	MONJUVI	MORPHOSYS US	2020
zanubrutinib	BRUKINSA	BEIGENE	2019

Of the 62 TAs that were conducted for the remaining 28 medicines, 40 (or 65%) TAs received positive recommendations, two (or 3%) TAs received negative recommendations, and 20 (or 32%) TAs were terminated (see Table 4.4). Three additional TAs identified were replaced by a later TA for the same medicine and excluded from further analysis. These may be cases of negative

recommendations replaced with later positive ones when more evidence was submitted by the manufacturer, but details of the initial recommendation were not publicly available.

Table 4.4: The Patient Access Impact of Technology Appraisals for Blood Cancer

	Total	Negative NICE Recommendation	Termination of TA	Replacement of TA	Positive NICE Recommendation	
					Coverage for all Indications[17]	Patients Excluded from Coverage[18]
Technology Appraisals Conducted	62	2	20	3	40	
					21	19
Percent of Technology Appraisals Conducted	100%	3%	32%	-	65%	
					53% of TA with positive recommendations	47% of TA with positive recommendations

Time to positive reimbursement represents the time between EMA approval of medicine use for a specific indication and positive NICE recommendation. The 40 TAs that received positive recommendations were delayed after EMA approval by several years. For TAs that received positive reimbursement, the median difference in time from EMA approval to a positive NICE reimbursement decision was 3.67 years (95% CI; 3.06 years to 5.16 years).

For products with positive NICE recommendations, NHS coverage for all English patients approved for use under EMA guidelines is not necessarily secured. In many cases, NICE may list a medicine as recommended but specify that the recommendation only applies to a patient population that fits specific indications. To better understand how NICE TAs impact patient access, each indication was noted and compared to patient populations included in positive EMA approvals (see Table 4.4).

[17] "Coverage for all Indications" indicates a NICE TA recommendation of coverage for all indications and lines of treatment approved by the EMA.
[18] "Patients Excluded from Coverage" indicates a NICE TA recommendation that excluded patients from coverage who the EMA has approved for use of the product in question.

In 65% of the TAs that were considered in this analysis, some form of coverage under the NHS was granted to patients. However, only 34% of TAs granted coverage for all indications approved by the EMA (see Table 4.4). This means that many patients who the EMA had approved for use of a blood cancer medicine and whose medicine had a "positive reimbursement" NICE recommendation were excluded from NHS England coverage.

I calculated median and a 95% CI using the Kaplan-Meier method to compare coverage delays that patients with the same diagnosis in the US would experience. Using R Studio, I considered the "event" as achievement of positive reimbursement. In the case of each English patient group referenced by each TA, the "time to event" was delay time between EMA approval and a positive coverage decision. Negative or terminated TAs were considered "survivals," which would eventually lead to positive coverage decisions following a period of negotiation between the manufacturer and NICE or additional clinical data to further prove efficacy. This assumption was made to provide the most conservative assessment of negative funding decisions in England. I created a comparison cohort to represent the same patient groups in the US for each patient population referenced in each TA. In almost all cases, Medicare automatically covers medicines after FDA approval per a requirement put forth in the government insurance program rules (H.R.5376, 2020). This means that delay time for each US patient group was zero.

I found that in England, for medicines with multiple TAs, the proportionate time to positive reimbursement increased with the number of TAs conducted (see Table 4.5). For example, the time to decision of Ibrutinib's first indication was 827 days, while the time to decision of Ibrutinib's eighth indication was 2,409 days. In other words, patient populations considered by subsequent TAs rather than first TAs were likely to wait longer for funding decisions. Medicines with multiple TAs took longer for all funding decisions to be made, with a median of 5.64 years for later TAs compared to 1.60 years for first TAs (see Table 4.6).

Table 4.5: Average Time to Decision by Technology Appraisal

Medicine	Brand Name	Total Time (in days)	Indication 1		Indication 2		Indication 3		Indication 4		Indication 5		Indication 6		Indication 7		Indication 8	
			Time to Decision	Proportion	Time to Decision	Proportion	Time to Decision	Proportion	Time to Decision	Proportion	Time to Decision	Proportion	Time to Decision	Proportion	Time to Decision	Proportion	Time to Decision	Proportion
acalabrutinib	CALQUENCE	345	345	1														
axicabtagene ciloleucel	YESCARTA	153	153	1														
blinatumomab	BLINCYTO	1877	583	0.15	1339	0.35	1955	0.50										
bosutinib	BOSULIF	3458	1246	0.36	2212	0.64												
brentuximab vedotin	ADCETRIS	11389	1628	0.14	2057	0.18	2372	0.21	2484	0.22	2848	0.25						
tisagenlecleucel	TECARTUS	72	72	1														
carfilzomib	KYPROLIS	3813	1826	0.48	1987	0.52												
daratumumab	DARZALEX	9757	411	0.04	663	0.07	1055	0.11	1502	0.15	1951	0.20	2084	0.21	2091	0.21		
duvelisib	COPIKTRA	63	63	1														
elotuzumab	EMPLICITI	315	315	1														
gilteritinib	XOSPATA	293	293	1														
glasdegib	DAURISMO	68	68	1														
ibrutinib	IMBRUVICA	11677	827	0.07	883	0.08	988	0.08	1128	0.10	1158	0.10	1835	0.16	2409	0.21	2409	0.21
idelalisib	ZYDELIG	3405	90	0.03	405	0.12	1070	0.31	1840	0.54								
inotuzumab ozogamicin	BESPONSA	448	448	1														
isatuximab	SARCLISA	652	172	0.26	480	0.74		0		0		0						
ixazomib	NINLARO	443	443	1														
midostaurin	RYDAPT	1733	268	0.15	1465	0.85		0		0		0						
mogamulizumab	POTELIGEO	1119	1119	1														
nivolumab	OPDIVO	768	768	1														
panobinostat	FARYDAK	152	152	1														
pembrolizumab	KEYTRUDA	3557	1144	0.32	2413	0.68												
polatuzumab vedotin	POLIVY	251	251	1														
pomalidomide	DMALIDOMIDE CELG	3497	1255	0.36	2242	0.64												
ponatinib	ICLUSIG	1458	1458	1														
tisagenlecleucel	KYMRIAH	324	121	0.37	203	0.63												
venetoclax	VENCLEXTA	4506	339	0.08	815	0.18	1466	0.33	1886	0.42								

Table 4.6: Median Survival by Technology Appraisal Order Among Positive Technology Appraisals

Positive Technology Appraisals	**Total Positive Technology Appraisals** (Number of Appraisals Conducted)	**Median (in Years)**	**Lower Confidence Limit (95%)**	**Upper Confidence Limit (95%)**
First	22 (28)	1.60	0.80	3.41
Later	18 (34)	5.64	4.01	NA
Overall	40 (62)	3.67	3.06	5.16

4.7 DISCUSSION

This analysis, the first to compare NICE health coverage decisions to US Medicare coverage for blood cancer medicines, showed that only 65% of NICE funding decisions (TAs) qualified new blood cancer medicines for coverage under NHS England, while 100% of new blood cancer medication qualified for coverage through Medicare. The analysis went on to show that among the 65% of NICE approved blood cancer decisions, NICE added restrictions on coverage for 47% of TAs, limiting more expansive patient use that was previously approved by the EMA. The second analysis,

comparing delays in coverage among new blood cancer treatments in the US and England, showed that medicines in England had a median wait time of 3.67 years to qualify for funding of new blood cancer medications while US Medicare recipients experience no wait. The final analysis established statistical significance in difference in coverage wait time between the countries.

If a medicine's funding decision had been terminated, or no TA was available, patients in England did not qualify for coverage regardless of EMA determination that they may benefit from the medicine. The coverage delay among patients qualifying for NHS coverage through a positive TA should also be highlighted. In these cases, though funding is eventually granted, coverage delay is a significant impact of NICE's TA process on patient access. In the case of every medicine, NHS patients who would have been considered eligible for treatment by the EMA experienced some coverage delay. This is different in the US Medicare program, which covers a limited population but is legally structured to grant coverage immediately after regulatory approval (Bach, 2009; Cohen, 2014).

It should be noted that in 31% of the TAs analyzed (47% of TAs receiving some positive coverage), some patients who the EMA determined could benefit from a blood cancer medicine were excluded from NHS coverage by NICE recommendations. In other words, some blood cancer patients covered by NHS England had to use alternative treatments and wait nearly four years after EMA approval for NICE to approve reimbursement for new medications. According to the US Surveillance, Epidemiology, and End Results (SEER) Program, 5-year relative survival rates for Leukemia from 2012-2018 is only 55% (National Cancer Institute, 2023); hence, a three-year median wait time for qualification of treatment reimbursement of over three years is concerning. This wait time may be due to several factors, potentially including the additional leverage that the NHS holds in negotiating lower prices or the additional bureaucracy that is intrinsically involved in TA development.

It is possible that NICE is taking a more stringent approach to ensure that medicines meet the highest standard of care before qualification for reimbursement. However, I also found that wait time varied widely by the order that TAs were conducted per medicine, with later TA decisions taking a larger proportion of cumulative wait time. Medicines with multiple TAs generally took much longer

for all funding decisions to be made. For example, medicines with later TAs had a median wait time of 5.46 years after regulatory approval compared to medicines with first TA that took a median of 1.60 years. This difference is important to note and it would be helpful to understand the size and severity of disease in patient populations impacted by subsequent TAs. Whether patients face delays in NHS funding after EMA approval or encounter limitations in coverage, it is crucial to understand the access barriers confronting blood cancer patients in England and the broader impact of the NICE process on cancer patients. Significant variation in wait time occurs between TAs for the same medicine, often depending on the order in which the TA is conducted. Next steps should include investigation of the treatment alternatives that NICE considers and an estimation of the size of patient populations impacted by negative or access limiting NICE recommendations.

Furthermore, research on physician opinion of the new medicines included in the analysis, especially regarding their benefit to patient groups considered in subsequent TAs (who I found waited longer for funding decisions). As discussed, it is difficult to know if NICE is taking a more stringent approach to ensure that medicines meet the highest standards of care before approval for reimbursement or merely adding bureaucratic steps and negotiation to leverage lower reimbursement rates. Qualitative interviews with physicians on this topic would add another perspective in answering this question.

4.8 LIMITATIONS

I utilized a product list of new blood cancer medicines launched between 2011 and 2020; findings may not be generalizable to other time periods. Findings excluded non-Medicare US insurance plans, which most US citizens rely on (Gould, 2013; Su, 2019). Due to the fragmented nature of the US health insurance system, and complex reimbursement policy maintained by these plans, I limited comparisons to US patients covered by Medicare (Cebul, 2008; Kern, 2019). However, it should be acknowledged that the cost of health care for the average US citizen is significantly higher than that experienced by English citizens—which may lead to limited access for US patients non-eligible for Medicare (Fahle, 2016; Figueroa, 2021).

As discussed above, negative or terminated TAs were considered "survivals" in this analysis, creating an assumption that they would eventually lead to positive coverage decisions after a period of negotiation between the manufacturer and NICE or additional clinical data to further prove efficacy. This assumption was made to provide the most conservative assessment of negative funding decisions in England but may cause underestimation of limitations on access to new medicines in England. First approval of a new medicine by the EMA and FDA was used to facilitate the most comparable analysis of England and US government reimbursement markets, though several medicines received additional regulatory approvals for new blood cancer indications after their first approval. Orphan drug status, a status some regulatory agencies assign to a medicine intended for use against a rare condition, was not considered as full EMA approval to allow for the most conservative estimate of funding delay (Cohen, 2014). This analysis only considered formally published NICE TA decisions and excluded NICE draft guidance, which may influence local funding decisions and provide earlier access to new medicines but does not mandate funding by NHS England. Data collection for regulatory approval and NICE TA decisions took place in February 2022. These findings do not include later regulatory approval and NICE TA decisions.

Findings are limited to access for patients in England. Other research compares reimbursement across national health systems within the UK (Harricharan, 2023; Kleijnen, 2016). However, many studies comparing patient access through reimbursement decisions across nations may not take optimization into account when considering reimbursement, classifying decisions as positive or negative (Harricharan, 2023; Schaefer, 2021; Lozano-Blázquez, 2015). A strength of this study is consideration of patient populations impacted by "optimized" NICE recommendations, who are approved for use by regulatory authorities, but experience denials or delays in coverage.

4.9 CONCLUSION

This retrospective record linkage study, using 34 blood cancer products, found that only 65% of the NICE funding recommendations (TAs) reviewed qualified blood cancer patients for coverage despite the EMA previously approving them for blood cancer patient use. Patients whose medication

did receive positive TA decisions waited a median of 3.67 years after EMA approval for coverage by NICE. Findings indicate that TAs conducted by NICE may have an impact on time and reach of new blood cancer products, especially if the new medicine has multiple TAs. Patient qualification for funding of new blood cancer medications in England appears to be affected by significantly limiting and delaying reimbursement of products. With the UK government currently considering how to restructure NHS England (Kmietowicz, 2025; Wise, 2025), understanding the impact of decision making processes on patient access is crucial to inform new policies that best benefit patients. This broader policy context underscores the importance of examining clinician experiences prescribing new blood cancer medicines in the US and England directly. The following qualitative analysis explores these perspectives, highlighting how national HTA and reimbursement decisions can translate into real access challenges.

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CHAPTER 5

Physician Autonomy and Patient Equity: Tensions in Patient Access to New Blood Cancer Medicines Identified in a Qualitative Interview Study

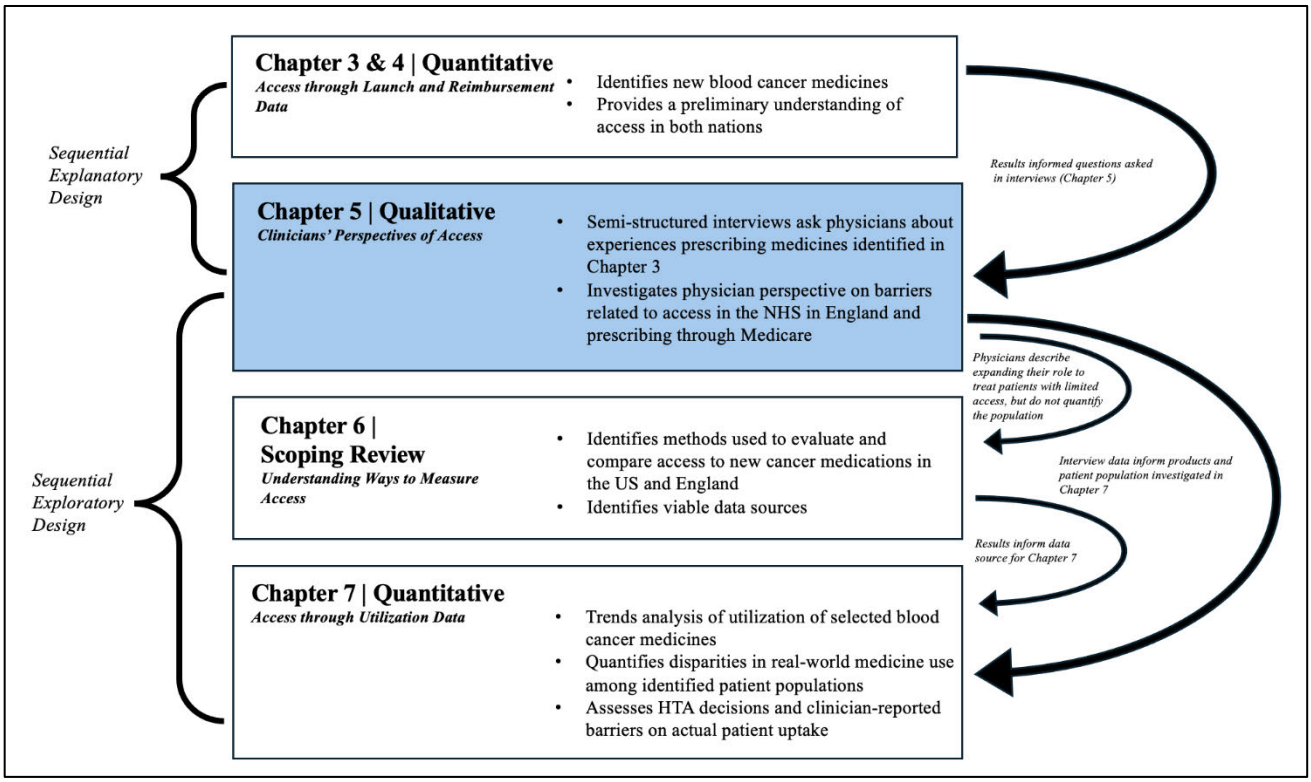
5.1 INTRODUCTION

In the previous chapter, there appeared to be significant delays and limitations in NHS England funding of new blood cancer medicines compared to Medicare in the US. Of the 34 medicines reviewed, only 53% of the TAs funded all patients that had been included in European Medicines Agency (EMA) authorizations.[19] I also found that patients who qualified for coverage waited a median of 3.67 years after EMA approval for funding through NICE. While cost negotiation processes by the NHS in England has helped keep the price of medicine to the NHS more controlled than the US (Blumenthal et al., 2024), Chapter 4 highlighted that English patients appear to get government program reimbursement of fewer new blood cancer medicines after longer periods of time.

When NICE gives a negative reimbursement decision, it typically states that the evidence available does not demonstrate sufficient cost-effectiveness or clinical benefit to justify funding for the treatment or intervention within the NHS. Physicians may testify at NICE committee hearings (NICE, 2013), but some evidence indicates that processes of NICE's HTA can undermine the evidence collected from stakeholders in committee (Hashem, Calnan and Brown, 2018). In contrast, the US government's pension program, Medicare, is required by law to immediately cover cancer products after regulatory approval (H.R.1, 2003), including off label prescriptions (CMS, 2025). Physicians working under English (NHS) or US (Medicare) national insurance programs could offer valuable perspectives on how HTA shapes the accessibility of innovative medicines within health systems. In this chapter, a qualitative comparison is presented between experiences of English and American physicians in accessing new cancer medicines. Figure 5.1 shows where this chapter sits in the multi-phase mixed methods design of the thesis.

[19] See Chapter 1 (Section 1.5), for explanation of EMA approval use rather than MHRA.

Figure 5.1: Sequential Multi-Phase Mixed Methods Design



5.2 AIM

This qualitative study aimed to investigate physician perceptions of access to new medicines indicated for treatment of blood cancer among oncologists and hematologists in the US and England. Research questions were:

1. What are the experiences of physicians in the US and England regarding the availability and funding of new cancer treatments by national health insurance programs?
2. How do physicians in the US and England perceive the value of new cancer medicines (exploring their views of clinical benefits and potential impact on patient outcomes)?
3. How do US and English physicians align and differ in their perspectives on these topics?

5.3 METHODS

I undertook a qualitative study using thematic analysis (Braun and Clarke, 2022). I obtained approval for the project from the University of Oxford's Central University Research Ethics

Committee (CUREC) (OUDCEC1A 22051). The research was conducted independently, but I benefited from supervisor guidance throughout the study. I brought a US perspective to the study and have a background in pharmaceutical industry policy. My supervisor (ST), based in England, has extensive experience in qualitative research across diverse health care settings, which helped inform aspects of the study design and analysis. I also discussed the research question with several physicians in England while developing the study protocol for feedback, who aided in my basic understanding of the health care system I wanted to learn about.

5.3.1 Sample and Data Collection

Purposeful sampling was used to identify a range of participants from across each country who could act as information-rich cases (Patton, 2002). Those sampled were knowledgeable about and experienced with the research topic (Cresswell and Plano Clark, 2011). Recruitment continued until no new major topics were heard from additional participants (data redundancy) (Bowling, 2009). I sought to ensure that the participant sample reflected variation in both geography and career stage, as this was essential for capturing a broad range of perspectives. Geographic variation was important because practices, commissioning arrangements, and local policies can differ across regions thereby shaping how access-related decisions are implemented in practice. Variation in career stage was also deliberately sought, as length of time working in the field can influence physicians' familiarity with access processes, exposure to policy changes over time, and the depth of experience informing their perspectives. Some participants were recruited through contacting professional societies, but the majority were recruited through snowballing; asking participants and professional connections to recommend colleagues with specific characteristics, knowledge, and experiences to take part. Potential participants were first approached via email, often initially from another participant they knew who made an introduction. In these cases, I followed up with an invitation outlining the study aims and what participation would involve. If a potential participant expressed interest, follow-up reminders were often sent to maximize engagement and ensure adequate representation across both countries.

Before interviews took place, participants were provided with a participant information sheet, a list of cancer medicines that might be discussed, and a topic guide for the semi-structured interview. Consent forms were signed electronically by each participant before interviews. Interviews were conducted remotely, by telephone or Microsoft Teams, depending on participant preference. I audio-recorded all interviews and transcribed them verbatim for analysis. Several adjustments were made to the topic guide as interviews progressed. For example, I became interested in learning more about the role of English pharmacists in local funding approval and the Clinical Priorities Advisory Committee (CPAC), described as a relatively little-known body that advises the NHS in England on treatment coverage decisions. ST and I agreed both were valuable topics to ask future participants about; hence, two relevant questions were added to the study topic guide for English participants (see Topic Guide in Appendix 5.1).

5.3.2 Analysis

Preliminary interpretation of data was conducted in tandem with interviewing. I recorded any ideas to arise during this early phase of analysis in a reflexive journal. As an American researcher trained in health policy and previously based in the US, I brought to this project a set of assumptions and perspectives shaped by both professional and personal experiences within a largely market-driven health system. My prior work in pharmaceutical market access and friendship with several people who have received a cancer diagnosis sensitized me to the emotional and logistical complexities of accessing new treatments. These experiences left a strong impression on how I interpreted participants' accounts, particularly those of US physicians who expressed a desire to offer new medicines to patients with limited treatment options, even when the clinical benefit was uncertain. Following the approach of Braun and Clarke (2022) to reflexive thematic analysis, I recognized that my subjectivity is not a limitation but a resource that shaped how I engaged with the data, made meaning, and developed themes. Regular supervisory discussions and peer debriefing supported an ongoing reflexive stance throughout the analysis.

During recruitment, data collection, and interpretation, I was living in England for the first time and navigating the NHS as a new resident. This experiential positioning offered me insights into the cultural and systemic contrasts between the US and English health systems but also exposed the limits of my understanding. I used moments of personal surprise in encounters with NHS England as prompts for reflection, what Braun and Clarke (2022) describe as opportunities to interrogate how one's assumptions and values shape meaning making. In conducting and analyzing interviews, I aimed to adopt a stance of humility and self-awareness, allowing participants to discuss what access and barriers meant within their own clinical and institutional contexts. While my interpretations were inevitably shaped by my cultural and experiential standpoint, I engaged reflexively with this throughout the study and analysis period, acknowledging that meaning is co-produced between researcher and data, and that the themes presented are not "found" but actively developed through my lens as a US-trained researcher newly situated within the English system (Braun and Clarke, 2022).

Thematic analysis was carried out concurrently with semi-structured interviews (Braun and Clarke, 2022). It was inductive and exploratory in nature, employed to produce themes grounded in the data. To ensure rigor and replicability, the six-phase process recommended by Braun and Clarke (2022) was observed: (1) all transcripts were read and reread to facilitate immersion in the data, and initial ideas noted; (2) each transcript was coded in its entirety using the computer program NVivo-15; (3) salient codes were clustered to generate potential themes and subthemes; (4) the candidate themes and subthemes were reviewed with reference to relevant collated data excerpts and the original transcripts; (5) the themes and subthemes were defined; and (6) the themes were elaborated in the analytic narrative (Braun and Clarke, 2022). Throughout, the analysis was reviewed and discussed with supervisor ST. Appendix 5.2 shows how the analysis moved from codes to themes and subthemes.

5.4 RESULTS

Interviews took place between December 2023-April 2024. They lasted 30-90 minutes, depending on participant availability and enthusiasm. In total, ten physicians in England and nine in

the US took part; they came from across several regions (see Figure 5.2). One physician lived in Wales but had worked in the English NHS so was included in the English cohort. Additional US physicians were contacted and expressed interest in participating, but no new topics were brought up by participants by the time the ninth interviewee from this country had taken part. I determined that data redundancy had been reached when additional interviews consistently repeated themes already identified, with no substantive new information emerging (Bowling, 2009).

Figure 5.2: Geographic Spread of Participants

United States Participants by State



Maryland: 3
Oregon: 2
Texas: 2
Virginia: 2

England and Wales Participants by Region



Anglia: 1
North West: 2
South East: 4
London: 2
Wales: 1

Both female and male physicians took part in the US (6f/3m) and England (2f/8m). Early, mid, and late career physicians participated (see Table 5.1), with later career professionals making up most participants in both countries. This was intentional, as later career physicians tended to share more opinions about their respective health system (likely because of more experience); hence, because they were information-rich sources, efforts became focused on recruiting more experienced physicians through snowball sampling. Snowballing was executed after interviewing initial

participants who met the study's core inclusion criteria (licensed physicians with experience working within the national health system under study). After each interview, participants were asked to recommend colleagues who could provide similarly substantive insights, sometimes in specific regions where participants had not yet been recruited. To guide this process, participants were requested to think of individuals who had familiarity with the new blood cancer medicines discussed and system-level knowledge.

Table 5.1: Participants by Career Stage

Number of Participants	Career Stage	Career State Definition
3	Early	*Junior Doctor (England) or Resident (US)*
6	Mid	*Middling expertise not fitting into early or late phases defined*
10	Late	*Consultant (England) or Specialist (US)*

5.4.0 Resulting Themes

The following themes were developed based on what participants said about access to new medicines for blood cancer. To illustrate and support points made, quotations from participants are presented, using EN to refer to a physician from England and US for a physician from the US.

5.4.1 Theme 1: Standardization vs Fragmentation of Protocol

Participants described how standardization or fragmentation of protocols around which new medicines are accessed by patients shaped their role as physicians. English physicians spoke about needing to follow mandated protocols for their patient to qualify for funding through NHS England, sometimes experiencing constraints on physician autonomy in the name of patient equity. While this national standardization promoted fairness in access, the bureaucracy of HTA and established treatment pathways took time and often limited their ability to tailor care to individual patients. This was particularly the case when considering new or experimental treatments but also established treatments that the English physicians saw their US counterparts using regularly.

"Essentially what is happening (in England) is you have an artificial sequence of drugs that develops which for an external medical doctor walking in from the States (US) can start to look very odd. And that looks odd because they wouldn't see that as a natural sequence that they would treat their patients

in or just doesn't make sense because why would you do this up this and so on because the type of patients who come through later would be very different. So I think from an external viewing standpoint I think it's starting to get quite challenging… but NICE can only look at it at the time things are tabled and NICE looks at it in the context of where it is cost effective. So the patients subpopulations that you kind of get to put yourself in a very very difficult position." (EN07, middle-career physician)

Several physicians (EN01, EN03, EN05) described the frustration of being barred from prescribing a medicine for their patient even when the price lowered dramatically after going off patent. Physicians explained that since no new formal HTA was prompted by the price decrease, in line with government policy[20], the drug continued to be inaccessible:

"*the price will drop in July of this year from four thousand to around £40, £50. And we explored that and asked you know beforehand the NHS commissioning group you know will this mean it's more accessible now? And no. It would still only be accessible in fourth line [treatment] for patient…*" (EN05, senior physician)

"*For example, I use something called lenalidomide which used to be over £3,000 a month. It's lost its patent so it is now £28 a month for T-cell lymphoma (which in the relapse refractory setting has very few treatment options) and almost nowhere else in the UK, very few others maybe have been able to use it even though it costs £28 a month.*" (EN03, senior physician)

Some English participants stressed that alternative drugs they would have to use (in line with NICE funding) could be more expensive yet less appropriate for their patient. This meant that certain patients received non-ideal care due to the health system limiting funding for more expensive drugs, to theoretically leave resources to fund drugs equitably across the country. Physicians noted how they would try to find alternative routes to avoid standard protocols that would require their patients to undergo chemotherapy that was likely to be ineffective, with toxic side effects, before qualifying for more promising treatments.

"It's (Venetoclax) become a sort of meaningful disease control option which now people are increasingly wanting to use in other contexts other than those for older frailer patients when their first diagnosis so it's a natural combination to want to prescribe when patients have who have had previous intensive chemotherapy have relapsed because it's much more gentle and salvage intensive chemotherapy and it's a different trip it's a very different treatment modality which we might see a response with. So in the relapse setting there's a lot of off-NICE prescribing of Venetoclax which goes

[20] Under NICE rules, only pharmaceutical manufacturers can request a technology appraisal (TA) for their product. EN03 and EN05 highlighted the disincentive for companies to seek a new TA—especially when a previous appraisal has already denied reimbursement and the product's revenue potential has dropped significantly due to patent expiry.

on and I think it's tremendously variable how different parts of the UK access that." (EN09, senior physician)

While the physician role often did not include considerations of economic value, some interviewees (like EN02 and EN05) were very aware of the price of medicine. Nearly every English participant (EN01, EN03, EN04, EN05, EN06, EN07, EN08, EN09, EN10) could list at least one medicine for blood cancer treatment that had sufficient evidence for patient use in their clinical opinion, but that they had challenges accessing for some patients because those medications had failed NICE appraisal. They described how this disadvantaged certain patients diagnosed with a cancer type whose treatment options systemically failed NICE appraisal:

"*There are a group of drugs which are approved, but are not approved in all lines of therapy. So there are things like Venetoclax for leukemia, which is not approved for (patients with) relapsed disease, only approved upfront…Venetoclax also for (patients with) myeloma… not approved. Drugs you can't access, it has been a constant feature of practicing hematology for the last 25 years. There's a steady number."* (EN04, senior physician)

More senior, specialized physicians in England, who were aware of extensive access to blood cancer medicines in other national health care systems, pushed against standardized protocols by expanding their physician role to advocate for their patients. They described contacting NHS organizations or spending extensive time applying to CPAC. In contrast, many US participants described using fragmentation within this health system as a path to access, working with extensive autonomy to prescribe off label. One US physician shared how they felt this made the US health care system more patient-centered than the English system:

"*Because the pace of oncology care is so fast and there's so many new things, new ideas, new breakthroughs, new medicines, new ways of giving medicines, new combinations…it can be hard for a big organization to come to consensus and implement that across their system….So, I think here we can be a lot more nimble. Especially if you're a patient that's got something unusual or you're not responding like we'd like you to respond…"* (US05, middle-career physician)

Other US interviewees suggested that high levels of physician autonomy resulted in equity issues, describing patients who benefited from health care innovation as individuals with access to extremely specialized physicians:

"If you're clever enough to get a highly sophisticated physician in the US, you can get better care in my view. But the large majority of Americans don't have access to that. They don't know or they're in a rural area or something. So they cannot take advantage of what is available…" (US03, senior physician)

US participants reported limits on their autonomy in private health care in ways that appeared to vary by urban/rural, academic/community, and seniority classifications. Though Medicare was described as straightforward in funding all cancer medications that were FDA approved, most patients that US physicians saw were privately insured (likely through employer-based health plans (Collins, Davis and Ho, 2005)). US residents and community care practitioners included in the study were especially likely to describe securing private funding for some medications as extremely time consuming; justifying medical treatment to insurance companies took hours, removing them from interfacing with patients, and sometimes required hiring and managing entire staff teams. One US participant, a community care practitioner in a rural area, shared that this access challenge was especially prominent for new cancer medicines:

"*If a new drug is approved by the FDA there will be a lag until insurance company updates their check boxes where it's going to be denied. And there's like no way around it that I will have to spend hours like writing letters and on the phone until I finally reach a physician at the insurance company that has the knowledge where I can say, look, this was approved by the FDA last week."* (US06, middle-career physician)

In this case, the physician described how fragmentation in the US system allowed private insurers to refuse coverage until the physician devoted resources (time, energy, staff) to fighting the initial insurance claim denial. Another US participant in a community care setting described how the additional administrative hurdles applied by private insurance companies could lead to human error that sometimes impacted their ability to provide timely care for patients:

"It's just so cumbersome…in one instance, the financial counselor used the wrong diagnostic code. By the time the insurance came back to say 'we don't approve that medication…it's not approved for this diagnosis.' I'm like, 'what diagnosis should you using?' It just happened that this patient had a diagnosis of lymphoma five or six years ago. And somehow they were using that. And I specifically put in my diagnostic code for lung cancer. So I didn't understand what was going on. Eventually the pharmacist picked up on it and said the wrong diagnostic code is being used within their system. (US09, senior physician)

In contrast, another physician who practiced at a major cancer center in the US, reported limited interaction with insurance companies by senior/specialist physicians; this was managed by their team of administrators and early career physicians (US03).

5.4.2 Theme 2: Space for Innovation

This theme explores how health system processes associated with medication access shape physicians' ability to be innovative in treatments offered to patients. Physicians described how this flexibility ultimately impacted product launch and availability within a nation. During interviews, it became clear from interviews with both US and English participants that innovative medicines were highly valued in the US health care system, where US physicians have the autonomy to prescribe new treatments as they see fit after FDA approval, going off license if they judge it will benefit their patient and spearheading clinical studies to find novel treatment options:

"*The main issue with the US (verses England) and their ability to use drugs at better lines of treatment are, going back to Hodgkin, they would absolutely use a checkpoint inhibitor second line with chemo. And they can do that because all they need is the drug license for any indication, even if that specific indication isn't licensed. As long as they got it on the NCCN[21] guidelines, most insurance companies, this is what my understanding is, will pay for it. So yeah, we do look enviously across the pond.*" (EN01, senior physician)

"…my colleagues here and at other institutions will develop these novel studies and look at drugs so it sort of pushes, you know, the field forward. We find new ways or new diseases that are responsive to it or we find correlatives of, well, this drug only works a small amount of the time in, let's say, this type of lymphoma…" (US02, senior physician)

Some US physicians described an emotional or moral imperative to find their patients better treatment options, even in cases where clinical outcomes were uncertain. Their ability to do so was shaped by the flexibility and responsiveness of the system that enabled them to prioritize individual patient needs in this way, and to show a willingness to try things, even if it was not clear how this would affect the patient's condition:

[21] The National Comprehensive Cancer Network (NCCN) is a US nonprofit group of 33 leading cancer centers. While the NCCN is a US organization, guidelines were referenced as a key source for best practice by several English physicians participating in qualitative interviews and described as standard for clinical direction in specialized cancer care. For more on the NCCN, please see Chapter 7.

"…it's easy to get lost in the passion of the patient in front of you. I've got to do something. I've got to do something. And even doing something futile offers a benefit as symbolic emotional benefit to the patient." (US03, senior physician)

Other US physicians waited for further research, in addition to FDA approval, before deciding to adopt new medicine into their regular practice. One described the flexibility within the US system for physicians to move at their own pace in beginning to prescribe new treatments:

"*I'm a middle ground adopter. There are physicians who are early adopters… at the very first hint of a positive trial are going to like try to get their patients on it…and there are those who not only want the FDA approval but they wanted like see a year's worth [of data]"* (US06, middle-career physician)

In contrast, the NHS (specifically NICE appraisals) was described as blocking physician autonomy to explore more innovative treatment options for certain patients. Some English physicians depicted the standard of care as different than other countries, classifying England as generally falling behind with later NICE approvals for cancer treatments:

"*…every now and then…I have a patient where there is a clear better standard available globally but not available locally because it's not NICE approved*." (EN10, middle-career physician)

"When we're looking at newer clinical trials it's sometimes difficult to know how that fits into our system because they compare to the standard of care across the world which might involve a drug that we don't have access to so making that comparison is more difficult for us." (EN02, early-career physician)

English participants described not having the ability to innovate early on or professionally judge evidence as more clinical studies were published, waiting years for treatments to be approved by NICE. They would communicate with US colleagues or pharmaceutical companies about potential launch in the UK. Some expressed concern that negative NICE appraisals led pharmaceutical companies to give up putting forward applications at all, or terminating appraisals out of concern that a negative NICE decision would stigmatize their product when applying for approval within other countries:

"*Drugs don't get to the UK market because innovators think that it will never be cost effective. What happens then?...the impression you're giving them is we're not open for business, we're not going to negotiate…you're not then caring for your population because you've basically said you know our doors are closed…I think that is a massive challenge*." (EN05, senior physician)

However, one participant offered a counterpoint by emphasizing that within the English health system, investment in innovative medicines necessarily entails opportunity costs elsewhere in the system. This highlighted a system-level tension specific to England between supporting innovation and maintaining balanced resource allocation across the wider health system:

"*Anything that is spent on these drugs inevitably means that there will be less that can be spent on staff or equipment or other things. There's always going to be some economic impact on it and the downside I see is that we can always compare ourselves to countries like the States and in Europe who have access to drugs."* (EN02, early-career physician)

5.4.3 Theme 3: Checks and Balances on Power

This theme relates to the constraints on decision making that physicians face when trying to secure access to new cancer medications for patients. Participants in both nations did not hold complete autonomy in securing such access; they had to work with other actors in the health system. Physicians in England described cases where their patient did not qualify for funding under the English NHS due to line of therapy; a medicine may have been approved by NICE but restricted to only be used as a third treatment option (drug C), after chemotherapy A and B regimens were tried by the patient. One physician described how unique cases, sometimes because of participation in clinical trials, could make guidelines unclear if a patient had already undergone non-NICE approved treatments:

"So if a patient has taken part in clinical trials in three prior lines you know, should they really be counted four lines of treatments or should they be counted only one line of treatment?" (EN05, senior physician)

In cases where it was unclear if the patient would qualify for funding by NICE standards, physicians explained that guidelines could be interpreted conservatively or loosely in favor of the patient by other NHS staff. This provided an additional influence in treatment decision making outside of the patient and physician. In particular, several English physicians described working with hospital pharmacists to make exceptions and have their patient approved for funding:

"*…pharmacists are meant to be the internal counter-checking…I'm blessed with having absolutely amazing colleagues there… Some who have been cancer patients themselves and who interpret the grey areas in favor of the patient. And then there are I think we're hearing of a lot of other colleagues who*

are interpreting any grey area in the most conservative way possible in terms of cost saving for the system." (EN05, senior physician)

English participants generally reported positive working relationships with pharmacists, but some talked how this role could add systemic constraints on physician autonomy:

"You have to use them (blood cancer treatments) in the right order (based on NICE approval pathways) so if there have been examples where physicians are trying to like move drugs up and use them sooner for whatever reason that the pharmacist always pick that up. And like note that you haven't given enough of this treatment to qualify for this treatment, or you know whatever… there's times like that would be when they tend to get more policeman-y." (EN06, middle-career physician)

While this approval structure furthered equity in theory, as all patients were considered under the same funding guidelines, physicians made the point that in these cases patient access ultimately was determined by the personality or leniency of the pharmacist. When access was denied, sometimes physicians took on an advocacy role to find alternative funding sources:

"I've seen cases where hospitals will pay for private medication if they feel that the risk of the medication is cheap enough and the indication is good enough…I think in the context of Venetoclax…it's not that expensive in the grand scheme of things. And it was for a young girl so who was 19 with very high risk for leukemia to have flag either with Venetoclax at induction and then another case in a different context a while back wherever Venetoclax was not licensed in the UK for the treatment of T PLL (T cell prolymphocytic leukemia) but would have been a good treatment and the hospital paid..." (EN08, early-career physician)

US physicians also described checks on their autonomy. One recalled an internal hospital influence that played a similar role to the English pharmacist; a US hospital administrator who counterbalanced treatment plans that were considered too idealistic:

"We got one guy over here…I call him the hallway monitor. His job is to keep us from doing nutty things. And he often is a roadblock to what I would like to do to help the patient...puts a check on my otherwise wild and altruistic ideas… We just did that last week and in retrospect, I think [the hallway monitor] was correct. I think it wouldn't have helped.. So there are…checks and balances in the system. And they kind of work." (US03, senior physician)

Hence, in both nations, physicians described how the role they played was shaped by tensions within their respective health care system, with checks experienced on their autonomy. To re-establish autonomy in the best interest of patients, they worked to find alternative routes to funding medicines. Participants in each country talked about connecting patients with coverage through clinical trials,

liaising with manufacturers, or helping patients apply for charity funding. However, gaining access to new medicines through alternative routes came with patient equity issues in both nations:

"... I slightly struggle with equity aspect of them (individual charity trusts). Because you can suddenly find that you've got one patient who managed to access it and another who didn't." (EN04, senior physician)

"We're fortunate, we (the hospital) give a lot of free care, we're fortunate that we're able to do that. Not everyone can do that." (US08, senior physician)

5.4.4 Theme 4: Social Deservingness and its Role in Access

This theme highlights how embedded cultural beliefs about deservingness shape patient expectations and subsequent physician experiences, particularly in the context of access to new blood cancer medicines. These beliefs were structurally reinforced by the way each health system distributes care. In the US, one participant, employed as an oncologist by the US military, made the point that someone's occupational role helped to justify the high costs that came with prescribing expensive treatments for active-duty patients. When discussing the expansive physician autonomy their government insurance program permitted, this participant noted:

"We (military health personal) also have a little bit more of a varied mission because not only do we have to take care of our beneficiaries, but you know, in a moment's notice, you have to be ready to support a war. Or when COVID was going, getting out of control, other hospitals needed help. You saw the military was sending the nurses. So it's different." (US05, middle-career physician)

In this case, the physician indicated that the high social respect for a military person in the US meant they would have access to some of the best cancer care possible. This justification for providing exceptional care was reflected in other US interviews. US participants talked about health care being tied to insurance through employment; this left patients who qualified for coverage through their work expecting the best treatment possible and advocating for exceptional treatment to their physicians. US physicians discussed treating patients who were interested in new or experimental treatments and indicated that they were more likely to challenge system-imposed constraints to encourage their physicians to innovate. In contrast, the English NHS was described by participants as fostering a more collective patient mindset, especially around end of life care:

"But in the UK system I was often really surprised and positively surprised by the patience that patients have and by the understanding that they do bring when we do explain the limitations that are truly not our making but that are the limitations of the system." (EN05, senior physician)

The NHS ensured that all patients, regardless of their economic background or other demographic factors, received the same basic standard of care. By guaranteeing a consistent standard of care regardless of economic position, the NHS implicitly affirms that all lives hold equal value within the health care system:

"And in a way the good thing about the UK is you can be anywhere in this country and have let's say aggressive lymphoma newly diagnosed and you will get recommended the same first line treatment. And that's because of the way it's set up down from NICE... So in a way it's very standardized which I think is a good thing for patients and for physicians because it means you're less likely to sit down to experience a significantly worse quality of care in a poor part of the country versus a more rich part of the country…." (EN10, middle-career physician)

This stands in contrast to US narratives, where access to care was more frequently described as stratified and associated with employment status, or insurance coverage. Views of systemic determinations of health coverage varied among US physicians, with social deservingness a notable idea within interviewees' narratives. One US participant raised the concept of patient fiscal responsibility, a consideration that does not apply in the English context where patients do not pay for treatment a point of service. The participant described variation among US patients in their willingness or ability to absorb high out-of-pocket costs, noting that some actively declined more effective treatments in order to avoid financial hardship:

"A lot of patients in the United States go both ways. There are highly fiscally responsible patients and then those that just assume the system will catch them. But for those that are, and I don't say that judgmentally, just too different approaches to life. Those that are, I'm characterizing this context as fiscally responsible, will just say, 'you know what, I'm not going to put my family in debt. This medication costs $4,000 a month. That is absolutely not tenable for us. So I would rather forgo treatment, even if it might work in lieu of transfusion, because that gets reimbursed and its not an out of pocket cost for me.'"(US04, senior physician).

In this account, the physician discussed how patients may choose an alternative treatment plan due to their insurance coverage, even if that treatment plan may be clinically suboptimal. This mirrors the non-ideal care options described by English participants in Theme 1, though this constraint it is brought about by a different health system structure.

While discussing national trends and personal experiences, some US participants used emotionally charged language and became visibly upset as they reflected on witnessing patients struggle due to funding limitations within the fragmented US health system. One US physician described a self-employed father who chose not to undertake potentially curative treatment so that he could leave his family debt free:

"*So he didn't have employer sponsored health care and was diagnosed with acute leukemia. And his out of pocket cost was also going to be about $1k per month and then hitting deductibles. So probably about $20k per year would be a reasonable out of pocket cost estimate for him. I don't remember how much he made, maybe $60k per year. Wouldn't be able to continue to work. And he made the decision to not get treatment and die so he could get the life insurance policy for his family. For his children. And for completely financial reasons… he was doing the right thing financially. Getting money for his kids instead of spending it on his care.*" (US07, middle-career physician)

Other US participants were blunter in their assessments of US culture and expectations around health insurance coverage (or other funding). For example, one interviewee (US03) stated "*kids with cancer, Boo hoo hoo"* when commenting on what they saw as a distinctly American tendency to be sympathetic to narratives involving children and galvanize public support to government policies that expand coverage to the pediatric population. Their point was not to dismiss childhood illness but to emphasis how emotional framing strongly shapes policy debates and public opinion in the US.

US participants noted that all patients are treated for acute emergency care and covered by Medicare upon turning 65 years old. They stressed that patients tended to rely on employer-based health insurance for most of their life and that variations in care coverage were common in cancer treatment. Many US participants regularly interfaced with uninsured patients:

"It happens all the time. And then they have no insurance. And then all of a sudden they have like this ginormous hospital bill and they need chemotherapy. And our social workers and our financial team are incredible at trying to get those patients access, but it is really complicated. And I had to almost treat one kid without any insurance at all. And we had to like line by line go through like what the cost of everything is going to be." (US01, early-career physician)

When discussing accessing cancer treatments in the US, some participants commented on political motivations and the history impacting coverage policies that determined which patients would qualify for health care. Rather than national consideration of health care as a human right that English participants implied, those in the US discussed social dynamics and considerations of value that led to

differing coverage policies for immigrant (US01, US07), adolescent (US01, US03), impoverished (US01, US04, US08, US09), rural (US08, US09), and elderly populations (US07, US08, US09). Participants shared that while children were often seen as innocent parties and enjoyed more generous policies (US01, US03), many other vulnerable groups could be viewed as fiscally irresponsible and received limited help (US04).

5.4.5 Overarching Theme: The Physician Role in Flux - Navigating Health System Tensions Between Physician Autonomy and Patient Equity

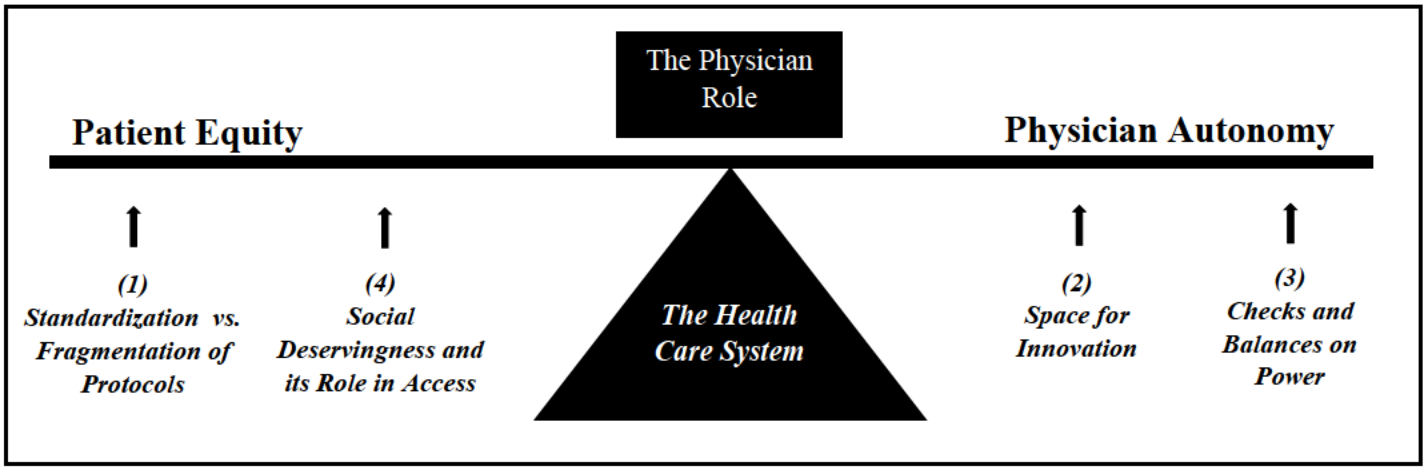
An overarching theme can be viewed as a unifying concept that captures meaning across themes: physicians consistently described their professional role as being reshaped beyond classic expectations of a doctor by tensions in the health system between promoting clinical autonomy and achieving equitable patient access to care. The former themes in this chapter operate as subthemes that illustrate specific manifestations of this broader dynamic. Together, these subthemes feed into the overarching theme by illustrating the different ways physicians navigate shortcomings in their respective health system to maximize their ability to care for patients.

Interviewees' perspectives on access to new medicines in their respective countries at first led me to feel that physician autonomy and patient equity were contrasting ideals in the US and English health systems. During analysis it became apparent that participating physicians shaped their roles to account for shortfalls within their respective health systems. This tension became an overarching theme encompassing the struggles between physician autonomy and patient equity (see Figure 5.3).

Data suggested that constraints on physician autonomy may occur in the NHS through standardized protocols for patient treatment in order to ration resources equally in the system. This encourages patient equity at face value. However, it may not be appropriate for all patients when inflexibility bars physicians from drawing on experimental new medicines that professionals believe could help. This is especially critical in fields like oncology, where new drugs may help a subset of patients but have not yet been approved for broader use. Data also suggested that in the US, emphasis on physician autonomy empowers doctors to push the boundaries of medical innovation by

experimenting with new treatments, and tailoring care to individual patients. This flexibility allows physicians to be at the forefront of therapeutic advancements, incorporating them into clinical practice at their own rate and based on their own professional judgement. The more rural/community based the practice the US physician worked within, the more they had to adopt an administrative role if innovating. Higher physician autonomy created disparities in access, with patients in well-resourced or specialized settings potentially benefiting more readily from these innovations and having more of a role in shared decision making in their treatment plan, leading to less patient equity. Many English physicians described waiting years for these same treatments to become available for use, broadening their remit to becoming advocates for wider government funding and treatment options. US physicians also described adopting an advocacy role as they argued with insurance companies, on patients' behalf, to get treatment covered, taking them away from their role as healer and caregiver.

Figure 5.3: The Physician Role in Flux - Navigating Health System Tensions Between Physician Autonomy and Patient Equity



In both systems, physicians adapted their approach in response to systemic constraints, either by advocating for patient access to new treatments or by working within existing health system frameworks to ensure fairness. These systemic differences reflected the complex balance between fostering innovation and ensuring equitable access, underscoring the critical role that physicians play in navigating these competing priorities.

5.5 DISCUSSION

This qualitative study highlights how a physician's role is shaped by the health care system they work within. This study found that in England and the US, physicians frequently broadened their remit to bring the best care possible to patients despite tensions between their own autonomy and patient equity. In the US system, physicians expanded their role to encompass advocacy, administration, welfare, health system translation, and research for their patients. In England, physicians familiarized themselves with the NICE HTA process and pushed themselves to submit economic evaluations for expanded funding through CPAC. For basic cancer treatment, the average English patient might have acceptable treatment options but not necessarily advanced or state of the art care. This led to less pressure on individual doctors to advocate for the average patient, but for specialized cases an onus fell on consultants (specialists) to draft lengthy applications to government bodies like CPAC to secure funding for treatments outside of standard guidelines.

The physician role expanding to advocacy has justice and equity implications for both health systems. Moving beyond the clinical role to manage administrative tasks, for example, is not necessarily taught in medical school and may foster inequity if certain medical groups develop and teach junior physicians better techniques. Physicians in high income settings may have more resources to devote to advocating for certain patients. Results of this study raise questions regarding the fairness of the health system applying an advocacy burden on physicians, especially specialists in England who have devoted significant time to learning clinical skills and community practitioners in the US who already work with constrained resources (both temporal and financial).

Previous research has investigated physician perspectives on uncertainty in NICE decision making (Calnan, Hashem and Brown, 2017) and health system policy (Pace et al., 2021). Pace and colleagues (2021), for example, discuss physician and consumer perspectives on accelerated access to new medicines, but focus on the regulatory pathway in an Australia context. Other researchers like Charlton and DiStefano (2024) have studied the ethical consistency and moral foundations of NICE

appraisals, finding that tensions often arise in how NICE interprets reasonableness when addressing uncertainty. However, physician perceptions on NICE's impact on access to new medicines in the clinical setting are not well documented. While existing research strives to quantify NICE impact on access to new medicine (Ball et al., 2022; Corbacho et al., 2020; Lozano-Blázquez et al., 2015; Schaefer et al., 2021), understanding the experiences of physicians working within the NHS in England is crucial as these professionals are directly impacted by HTAs and play a pivotal role in patient access to new blood cancer treatments.

Information asymmetry, an unequal distribution of knowledge between parties involved in a transaction, is a widely researched and largely accepted aspect of health care consumption (Arrow, 1963; Barile, Saviano and Polese, 2014; Bolin, Hedblom, Lindgren and Lindgren, 2010; Major, 2019; Odisho and Gore, 2017). Results of this study indicated that the existence of a national health service impacted patient expectation of care in England and established a level of trust and acceptance of limited treatment options (EN02, EN03, EN05, EN08, EN09, EN10). This institutional trust may, in turn, reinforce information asymmetry. It is possible that because patients in England feel assured of receiving basic essential care, some may have been less likely to question the availability of alternative treatments or to actively solicit more information about their treatment options. This may also mean that citizens are less likely to advocate for themselves in a clinical setting, but also for change in a health system where democratically elected officials allocate resources for funding cancer medicines (Department of Health & Social Care, 2025). While information asymmetry certainly impacts US patients (Mascarenhas, Kesavan and Bernacchi, 2013), nonexistence of a universal care system requires them to engage in health care procurement in a more involved way, which can be burdensome (Ilea and Ilea, 2024; Kyle and Frakt, 2021). Many US patients are uninsured and left behind in this system (HHS, 2024); this deeply affected US physicians who were interviewed. However, the system of US insurance based on social deservingness appeared to foster a motivated and possibly more engaged nature among US patients (as described by US07). This might lead US patients to be more aware of innovative treatment options and to exert more control over their treatment plan in

conjunction with their physician. As James C Robinson, an observer of the US system, puts it, US citizens have historically voted in favor of a health system that allows them to "*direct their own health care, with clinical advice from their physicians, financial subsidy from employers and public programs, information from the Internet and offline sources, and the support of their families and friends"* (Robinson, 2001, p. 2627). It should be noted that valuing independence nationally and undergoing care personally are distinct experiences. In the US system, increased patient choice in treatment options comes with administrative tasks for patients (Laverty, Dixon and Millett, 2015; May et al., 2014; Tran et al., 2015), who must navigate a fragmented health system and make major financial decisions while undergoing cancer treatment. Some research suggests that the burden of these tasks can result in patients in the US forgoing or delaying care (Kyle and Frakt, 2021).

5.5.1 Recommendations for Further Research

Future research could investigate the potential burden of additional treatment choice from a patient perspective. Qualitative interviews with patients would be helpful to understand patient attitudes regarding access disparities to new cancer medicine. While patients may be shielded from the inner workings of the health system and lack specialized clinical knowledge, their cultural understandings and experiences of equity issues would be valuable to learn from. Physicians interviewed for the qualitative study reported clear disparities in access to new blood cancer medicines between the US and England, which was also reflected in quantitative findings reported in Chapters 3 and 4.

5.5.2 Recommendations for Policy

Findings suggest that US health system policy practices should move towards equity, while keeping in mind limitations on physician autonomy seen in the English health care structure. Medicare, a national government administered US insurance program, provides coverage for more than 67 million people, nearly 20% of the US population (Kaiser Family Foundation, 2025). Research suggests that administrative tasks take a significant portion of US physicians' time (Sinsky et al., 2016). While Medicare was considered simple to use by interviewees and to provide expansive

coverage, US physicians regularly reported illegal denials and delaying tactics used by private insurance.

In public policy, intentional burdens placed on individuals that yield no benefits to others are referred to as ordeals (Eyal and Herlitz, 2021). Ordeals may be used intentionally as a tool to screen out those who might benefit too little to warrant the public expenditures (Heinrich, 2023). Health care is mostly paid for at the point of use among the insured US population, so insured people may be tempted to use it more than necessary. To prevent this, systems may introduce obstacles, like paperwork or other administrative steps, to discourage overuse (Zeckhauser, 2021). However, findings from this qualitative study suggest that unnecessary ordeals are regularly placed on US patients and physicians by private insurance companies, likely to reduce the cost of covering essential care. Shifting these burdens from the insurer to those seeking care raises serious concerns about justice and fairness. Increased federal oversight of private insurers could help reduce the administrative load on physicians and patients. Additionally, making it easier to report harmful practices to the US Department of Labor may contribute to their reduction or elimination.

In England, changes to policy could add flexibility to the NICE process and increase physician autonomy, patient equity, and access. For example, automatic reconsideration of products after patent expiration could be cost effective and increase access for English patients with limited treatment options. However, this would not assist with medicines never submitted for NICE appraisal, often due to manufacturer hesitation, as noted by interviewees. To address this, reframing negative or failed NICE assessments, shifting away from the stigmatizing label of "not cost-effective" and using a more neutral label such as “not funded,” could reduce reputational risk for manufacturers and potentially encourage earlier and broader market applications in England, aligning with equitable access goals listed in the 2019 NHS 10 Year Health Plan for England (NHS England, 2019).

More fundamentally, expanding access requires robust funding of the NHS. Although the NHS budget has grown by 33% in real terms over the past decade, investment in medicines has declined as a share of total health spending, falling from around 11% to 9% (ABPI, 2024). Growth in

the UK branded medicine market has been capped at between 1.1% (2014-2018) and 2% (2019-2023) per year, without consideration of inflation (Department of Health and Social Care, 2023). While the NHS in England must ration resources to provide care to all citizens, other comparable universal health systems like Italy, Germany, and France allocate nearly double the percentage of the health budget to medicines (Anandaciva, 2023). Protecting the current share of health spending on medicine could lay the financial groundwork for more innovative and flexible prescribing policies. Eventually, allocating resources to facilitate greater physician discretion to use off-label treatments could enhance patient-centered care within a universal system framework.

5.5.3 Strengths and Limitations

To ensure clear and comprehensive reporting, the study followed the COREQ guidelines for qualitative research (Tong et al., 2007). Participants included a range of physicians of different career stages, background, and regional areas who provided rich data to develop an in-depth understanding on the topic of interest. Trustworthiness was considered according to the criteria set forth by Lincoln and Guba (1985), with consideration of transferability, confirmability, credibility, and dependability. Transferability was enhanced by providing rich, detailed descriptions of the research context, participant backgrounds, and data collection procedures. This transparency allows readers to judge how the findings might apply or resonate in other similar health care settings or populations, supporting the broader relevance of the study. Since I come from an industry background my interpretation of the data could affect confirmability, but this was addressed through regular peer debriefing and feedback with my supervisor, ST, which helped strengthen the study's trustworthiness (Nowell et al., 2017). To improve credibility, I carried out a sense check of preliminary findings with some participants. This kind of member checking was used especially when there was uncertainty about interpretations to make sure their views were accurately reflected. For instance, several English interviewees referred to CPAC when discussing local decision-making processes related to new medicines. Because CPAC was not widely documented in national policy materials, I contacted the relevant participants to confirm both the existence and purpose of the committee. They clarified that

CPAC functioned as a committee within NHS England to advise on treatment coverage decisions. This feedback helped ensure that my interpretation reflected the actual organizational process rather than an inferred or assumed structure. Similarly, I sought clarification regarding repeated references to NICE policy that TA determinations were not revisited even when drug prices fell substantially. Relevant English participants confirmed that NICE did not routinely reopen previous TA decisions following significant price reductions, even when doing so could have improved patient access. Dependability was addressed by maintaining a clear audit trail of methodological decisions and data analysis processes, further enabling transparency and consistency throughout the study.

This study focused solely on the perspectives of health care professionals. While this does not undermine the credibility of the findings (given the research questions being addressed) it is important to acknowledge that decisions around access to medicines should also reflect the views and needs of others, including patients, pharmaceutical companies, health care institutions, regulators, and government bodies. Additionally, this study relied on self-reported data, which may be subject to recall bias or selective framing. Further research could benefit from incorporating observational methods like ethnographic fieldwork in clinical or policy settings. This may increase understanding of how decisions around access unfold in practice.

5.6 CONCLUSION

This study highlights the complex and often conflicting relationship between physician autonomy and patient equity in the context of new blood cancer medicines. The health care systems in both the US and England create different structures and opportunities for physicians to navigate access to new cancer medicines; each offers distinct advantages and challenges. The tension between physician autonomy and patient equity is not easily reconciled, but understanding the nuances of these tensions is critical for policymakers and health care providers alike as they work to balance innovation, cost-effectiveness, and access to care. As the US moves toward adopting elements of the English pricing model (Executive Order 14297, 2025), it is imperative to examine the structural and

experiential differences between the two systems, and to assess how price negotiation mechanisms affect patient access to care.

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CHAPTER 6

Approaches to Comparing Access to New Cancer Medicines: A Scoping Review of Evidence from England and the United States

CHAPTER 6 FORWARD

Chapter 6 presents a scoping review that examines how patient access to new cancer medicines is evaluated and compared across countries, with a particular focus on the US and England. The work underpinning this chapter has been prepared as a standalone manuscript and is currently under consideration for publication in a peer-reviewed journal. While the structure of the chapter reflects that of the submitted article, I include it here in the context of the broader thesis as it contributed to my understanding of how patient access to new medicine has been measured in the US and England and compared to other countries. It may be uncommon to include a scoping review halfway through a thesis; however, this work came at a critical point, building on previous thesis chapters and setting the direction of my final study.

This work develops from Chapters 3 and 4, which considered access to new blood cancer medicines through launch and reimbursement decisions. While launch and reimbursement are two critical stages of access, I undertook this scoping review to explore additional methodological perspectives and to identify other meaningful ways in which access has been assessed in the existing literature. Chapter 5 describes English physician reports of waiting for better availability of new blood cancer medicines and US physician reports of uninsured patients falling through the cracks. This promoted a research need to estimate the extent or generalizability of the access challenges described by interview participants. Unsure of which source to use, I undertook the scoping review in this chapter to better understand alternative methods to estimate patient access and to find a real-world data source to help me investigate how access barriers reported by physicians in my qualitative work in Chapter 5 may relate to a larger population.

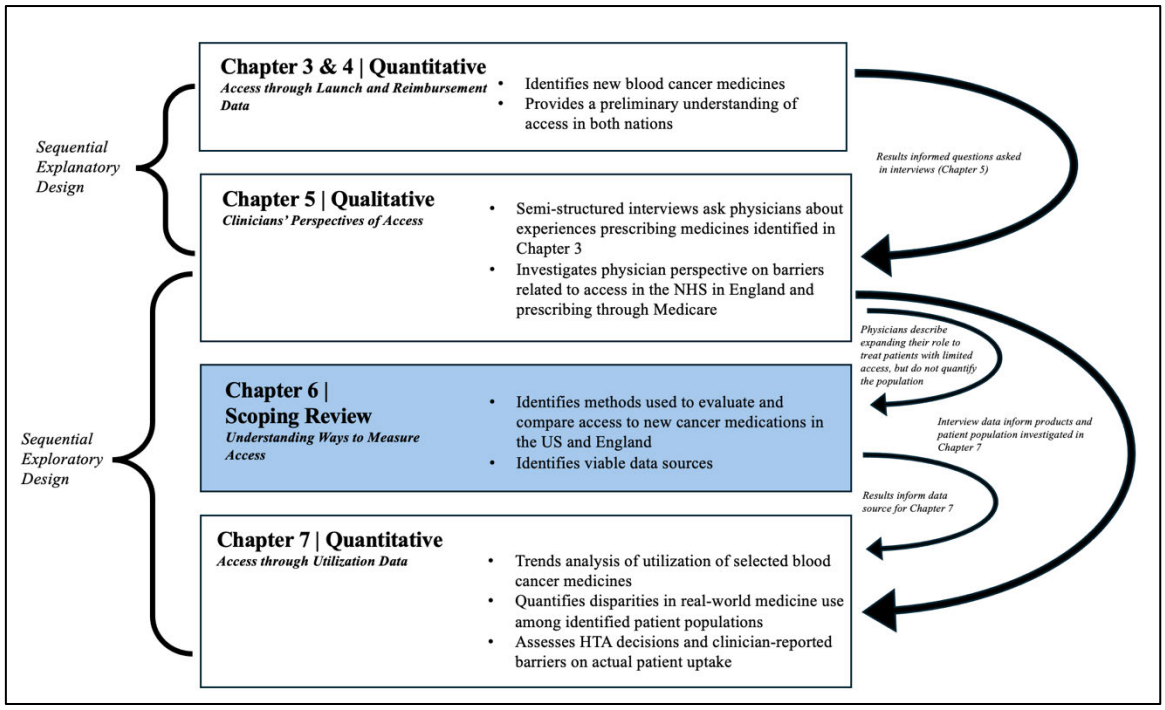
This review included 101 studies after screening over 6,000 records. Most studies evaluated access in terms of reimbursement status, typically using data from publicly available HTA records without regard to restricted approvals (discussed in Chapter 4). Only a small number assessed launch timing, an inconsistent measure of access (discussed in Chapter 3). I found that utilization, a measure

of actual uptake and use of medicines in practice, is a relatively underexplored but valuable lens through which to assess access. This observation has informed the direction of Chapter 7, particularly in my effort to identify suitable datasets for comparing real-world access to new blood cancer medicines with utilization data.

Beyond its relevance to the thesis, this review contributes new knowledge by synthesizing methods used to compare patient access to cancer medicines across countries. It highlights the importance of using data sources that reflect differences in population characteristics and health system structures. By clarifying how access disparities are measured and compared, the review supports development of more evidence-based health care policies. These insights aim to improve international understanding of barriers to new medicines and support better outcomes for patients.

In adapting this work from journal format to thesis chapter, I preserved the manuscript's analysis while also providing contextual framing that shows how this chapter informs other parts of the thesis (shown in Figure 6.1). The data sources, methodology, and limitations are described in full but should be interpreted here as part of a larger body of work that guides data source selection for Chapter 7 and, ultimately, contributes to exploring the implications of HTA negotiation on patient access to new blood cancer medicines.

Figure 6.1: Sequential Multi-Phase Mixed Methods Design



6.2 ABSTRACT

6.2.1 Aim*:* The overarching aim was to support a more systematic understanding of how access to new cancer treatments can be compared with data across countries. The review sought to identify and synthesize methods used to evaluate and compare patient access to new cancer medications in the United States (US) and England. By synthesizing methods, the review compared the different analytical approaches used in the literature and integrated them to highlight common practices and key distinctions. It also mapped methodological approaches for comparing access in these countries with other international settings.

6.2.2 Methods*:* I conducted a scoping review using the Joanna Briggs Institute methodology, guided by eligibility criteria defined in a preregistered protocol. I searched PubMed, Embase, Scopus, Business Source Ultimate, and EconLit for studies examining methods for assessing cross-country access to new cancer medications, published up until March 2024. Screening, data extraction, and analysis were conducted using predefined criteria, and results were reported in accordance with PRISMA-ScR guidelines.

6.2.3 Results*:* The search identified 6,467 unique records, of which 101 studies were included after screening and full-text review. Most studies assessed access in terms of reimbursement (94/101), with fewer studies examining launch time (2/101) or utilization (5/101). Publicly available Health Technology Assessment (HTA) records were the primary data source for access assessment in 90 studies. Although only 13 studies directly compared access between the US and England, England appeared in nearly all studies (99/101), underscoring its central role in cross-country access research.

6.2.4 Conclusion*:* This review identified methods used to assess patient access to new cancer medicines in the US, England, and other countries, with most studies evaluating access through reimbursement processes using HTA recommendations.

6.2.5 Review Registration: McKeown, S. (2024) Assessing access to new cancer medications: Approaches to international comparison. Open Science Framework (OSF). doi:10.17605/OSF.IO/2KA5X. https://osf.io/2ka5x/.

6.3 INTRODUCTION

Understanding how national reimbursement policy impacts patient access to new cancer medicines is critical, as delays or limited access can result in forgone health benefits (Bronchetti, 2023; Klein, 2025). Cross-country comparisons of patient access, whether measured through product launch, reimbursement decisions, or utilization, can provide valuable insights into how national policies shape access to care. Such comparisons are methodologically challenging due to differences in health system structure, regulatory pathways, and data availability.

In England, the National Institute for Health and Care Excellence (NICE) plays a central role in evaluating the clinical and cost-effectiveness of new medicines, making recommendations on their use within the publicly funded National Health Service (NHS) (NICE, 2012). While this centralized approach facilitates national price negotiations, it also introduces an additional step, Health Technology Assessment (HTA), which can influence both the timing and extent of access to new treatments. HTA aims to determine whether new medicines provide sufficient clinical benefit and economic value to justify their reimbursement within publicly funded health systems. However, HTA processes have been criticized by some patient advocacy groups and pharmaceutical manufacturers, who argue that they can delay or restrict access to innovative medicines (Newton, 2025; PhRMA, 2023).

In contrast, the United States (US) has a more fragmented health system. Medicare, the primary federal insurance program for adults aged 65 and older, operates within a multi-payer landscape that differs considerably from the universal, single-payer model of the NHS (H.R. 5376, 2022). Patients in the US often face additional access barriers due to co-pays, deductibles, and variation in private insurance coverage. Organizations such as the Institute for Clinical and Economic Review (ICER) and the American Society of Clinical Oncology (ASCO) conduct value assessments and issue recommendations, but they are not formally tied to coverage or reimbursement decisions in the way that NICE guidance is integrated into the NHS decision making process (ICER, 2020).

To meaningfully compare patient access across health systems, and to understand how policy changes, such as recent government-led price negotiations in the US (H.R.5376, 2022), may affect access, it is important to examine how existing studies have approached such comparisons (Centers for Medicare and Medicaid Services, 2022). This scoping review aimed to identify the methods and data sources used to assess patient access to new cancer medicines across countries, with a particular focus on studies comparing the US and England. I conceptualized patient access through three dimensions, as outlined in Table 6.1:

Table 6.1: Defining Patient Access

Launch	Availability of a new medicine (e.g. data indicating national regulatory approval and/or first sale has occurred)[22]
Reimbursement	Inclusion of a new medicine in public funding scheme (e.g. data indicating government funding/cost of medicine)
Utilization	Population adjusted use of a new medicine (e.g. data indicating the number of units sold/insurance claims records)

Scoping reviews are well suited to mapping the breadth of existing research and the methodological approaches it employs. The primary objective of this review was to identify how studies have generated evidence on patient access to new cancer medicines across countries (Grant et al, 2009; Arksey & O'Malley, 2005). A secondary aim was to explore the strengths and limitations of the existing literature and to inform future research, especially studies comparing access in the US and England. Although few of the resulting studies directly compared these nations, insights from studies that indirectly examined them in relation to other non-U.S. and non-English-speaking countries proved valuable.

6.4 METHODS

6.4.1 Study Design

I conducted a scoping review in accordance with the Joanna Briggs Institute Reviewer Manual (Peters et al, 2021) to map the methodologies used in comparative studies of patient access to cancer

[22] Regulatory approval does not guarantee that a medicine is available for patients, market launch often requires that first recorded sale is documented.

medicines. A scoping review was chosen over a systematic review to allow for the exploration of the range and characteristics of methodological approaches, rather than synthesizing clinical outcomes. The study selection process is presented using a PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Review) flow diagram (Tricco et al, 2018). The protocol was preregistered on the Open Science Framework in May 2024 (McKeown, 2024).

6.4.2 Eligibility Criteria

I developed detailed inclusion and exclusion criteria to guide reviewer decision making throughout the title/abstract screening stage as well as during full-text review. These criteria were developed with the following Population, Concept, Context (PCC) in mind, as outlined by the JBI Manual for Evidence Synthesis (Peters, 2021):

- Population: patients requiring blood cancer medicines, focusing on adults rather than children/young people
- Concept: measuring patient access.
- Context: US and England comparison with each other or with another country.

A summary of key eligibility criteria is provided in Textbox 6.1.

Textbox 6.1: Summary of Inclusion and Exclusion Criteria

Inclusion Criteria
Studies were included if they met all of the following criteria:
(i) Published in English
(ii) Addressed patient access to cancer medicines through international comparisons
(iii) Included either England or the US in the comparative analysis
(iv) Focused on oncology products
(v) Reported only quantitative results
(vi) Published in a peer-reviewed journal

Exclusion Criteria
Studies were excluded if they met any of the following criteria:
(i) Not available in English
(ii) Duplicate publications
(iii) Literature reviews or systematic reviews
(iv) Did not include oncology products
(v) Did not involve cross-country comparison, or did not including the US and/or England
(vi) Focused solely on regulatory comparisons (e.g. without including funding or patient access dimensions)
(vii) Reported only qualitative results (i.e., lack quantifiable access outcomes)
(viii) Focused exclusively on children or adolescents
(ix) Not published in a peer-reviewed journal (grey literature)

6.4.3 Search Strategy

An initial limited search of PubMed was undertaken to identify relevant articles and extract keywords and index terms from titles and abstracts. These informed a comprehensive search strategy developed in collaboration with an outreach librarian (NR) at the Bodleian Health Care Libraries.[23] The strategy was subsequently adapted for five databases: PubMed, Embase, Scopus, Business Source Ultimate, and EconLit (see Appendix 6.1). Searches were conducted and imported into Covidence as follows: PubMed (February 16, 2024), Embase and Scopus (March 5, 2024), and Business Source Ultimate and EconLit (March 7–8, 2024). Studies from all other countries were eligible if they included a comparator from the US and/or England. Only studies published in English were included.

6.4.4 Study Selection

[23] See Section 6.7.2.

Search results were uploaded to Covidence (Veritas Health Innovation, Melbourne, Australia), where duplicates were automatically removed. Two reviewers (SM and EP[24]) independently applied the eligibility criteria to a pilot sample of 100 titles and abstracts, meeting to discuss and refine the criteria where necessary. Titles and abstracts of remaining articles were then reviewed (SM and EP). Full-text articles were retrieved and reviewed by one person (SM) when abstracts met inclusion criteria or where eligibility was unclear. Reasons for full-text exclusion were recorded in Covidence and are reported in the Results section.

6.4.5 Data Extraction and Analysis

Data extraction was completed using a predefined form (Appendix 6.1) by SM. Extracted information included study design, methods, data sources, comparators, and key findings that pertained to launch, reimbursement, and utilization. The medical products considered in each study were documented to assess relevance to the review focus on access to new oncology medicines, and to distinguish these from studies addressing other therapeutic areas or health technologies.

6.5 RESULTS

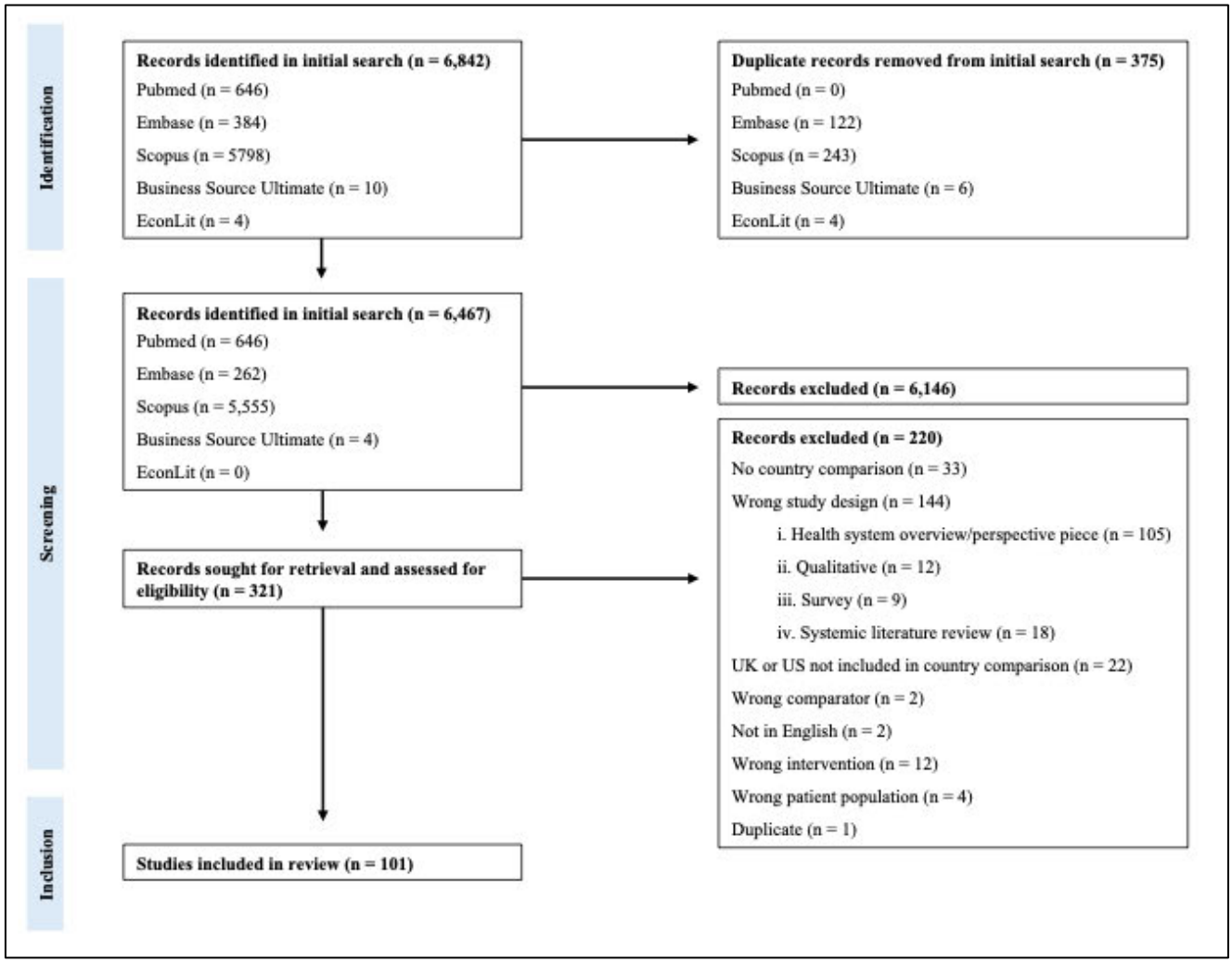
6.5.1 Study Selection

The process of study identification, screening, and inclusion is detailed in Figure 6.2. A total of 6,842 records were retrieved across five databases, with the largest number coming from Scopus, followed by PubMed, Embase, Business Source Ultimate, and EconLit. Covidence automatically removed 375 duplicates, leaving 6,467 records for title and abstract screening. Two reviewers screened all records, identifying 321 (11%) for full-text review. Of the 321 full-text articles assessed, 220 were excluded for the following primary reasons: inappropriate study design (n = 144), lack of country comparison (n = 33), no inclusion of the US or England (n = 22), irrelevant intervention or disease focus (n = 14), and ineligible patient population (n = 4). In addition, two non-English articles and one duplicate were excluded.

[24] See Section 6.7.2

A total of 101 studies met the inclusion criteria and were included in the final review. Further details on the included studies are provided in Appendix 6.2.

Figure 6.2: Identification of Studies via Databases



6.5.2 General Findings on International Access Comparisons

Among the 101 includes studies, most assessed patient access through reimbursement decisions (n = 94). Of these, 89 used datasets based on HTA recommendations. The majority of these studies (n = 86) included England in their comparisons, and most (n = 74) compared England to countries other than the US. Only a small number of the 101 studies considered access using utilization data (n = 5) (Bremner et al, 2020; Corbacho et al, 2020; Gonzalez-McQuire et al, 2018; Harries et al, 2017; Salas-Vega et al, 2020); employed methodologies are summarised in Textbox 6.2.

These studies often relied on claims data (Bremner et al., 2020), or national sales volumes (Corbacho et al., 2020, Salas-Vega et al., 2020). Launch data were used in just two studies (Bassgen, 2023, Westerling 2014), both of which focused on European countries including England. Westerling et al. (2014) assessed launch times across seven European countries, including England, noting differences of up to 22 years and highlighting the methodological difficulty of comparing launch timelines. Similarly, Bassgen et al. (2023) utilised pharmaceutical launch data from 30 European countries to assess access.

Textbox 6.2: Key Methods to Consider Patient Access Through Utilization

1. Bremner et al. (2020) used US SEER cancer registries linked to Medicare claims and the Ontario Cancer Registry linked to administrative health data to investigate End of Life cost of care estimates for patients in both countries. Using utilization data, they estimated total and resource-specific costs from public payer perspectives over the last 360 days of life by 30-day periods, by stage at diagnosis (0-II, III, IV).
2. Corbacho et al. (2020) compared TAs of anticancer medicines in Spain and England from 2008 to 2015. To assess the implementation of HTA recommendations, they assessed trends in medicine usage using regression methods. They used utilization data from 2011 to 2016, to determine if medicine utilization for 11 products does respond to the positive recommendations of HTA bodies.
3. Gonzalez-McQuire et al. (2018) used physician provided real-world health care resource utilization (HRU) to assess costs associated with different treatment regimens used in the management of patients with relapsed multiple myeloma in the UK, France, and Italy. Retrospective medical chart review of characteristics, time to progression, level of response, HRU during treatment, and adverse events (AEs) took place over six weeks in the summer of 2015, and costs were calculated based on HRU and country-specific diagnosis-related group and/or unit reference costs, amongst other standard resources.
4. Harries et al. (2017) collected retrospective data on treatment patterns among patients in France, Germany and the UK with Stage IIIB/IIIC melanoma with macroscopic lymph node involvement, using patients' medical records and a patient survey. They went on to calculate overall median distant metastases-free survival, median disease-free survival, and hospitalization frequency.
5. Salas-Vega et al. (2020) pulled utilization data from 2003–2015 to explore the relationship between cancer drug costs and drug clinical benefits. Mean total drug costs for a full course of treatment were estimated using standard dosage form for each medicine and in each country. Regression analysis was then used to test if the cost of recently licensed drugs is related to their beneficial impact for patients.

Some studies combined multiple approaches to assess patient access. For example, Bucher et al. (2017) developed HTA evaluation criteria using HTA-Accelerator data and then used IQVIA Multinational Integrated Data Analysis System (MIDAS) volume data to analyze the impact of HTA decisions on drug access across England, France, Germany, and Australia.

An overview of how the included studies assessed patient access, whether through reimbursement decisions, utilization data, or launch, is provided in Table 6.2 (please see Appendix 6.2 for further information on these studies).

Table 6.2: How Authors Consider Patient Access

	Reimbursement	Utilization	Launch
Total Papers	94	5	2
Papers Including US	14% (13/94)	33% (2/5)	0% (0/2)
Papers Including England	91% (86/94)	83% (4/5)	100% (2/2)
Papers Including Both	13% (12/94)	16% (1/5)	0% (0/2)

6.5.3 Data Sources

The included studies used a diverse range of data sources to compare patient access across countries (see Textbox 6.3). Datasets comprised of published HTA recommendations were the most popular sources used, with authors often gathering results from publicly available government websites or utilizing pre-established databases. In the sample of 101 included articles, 89 used this source.

The remaining 12 articles used a variety of other data sources. Two studies (Salas-Vega et al., 2020; Corbacho et al., 2020) used MIDAS to investigate patient access through utilization of new medicines. MIDAS is an analytics platform built on sales and medical data run by IQVIA[25], a global provider of advanced analytics and clinical research services to the life sciences industry. As discussed

[25] For more on IQVIA, please see Chapters 3 (Section 3.1) and 7 (Section 7.2.2).

above, Bassgen et al. (2023) also relied on IQVIA MIDAS data but focused on launch rather than volume as an assessment of patient access, obtaining launch data on pharmaceuticals for 30 European countries.

Other sources included medical records (Chouaid et al, 2018; Harries et al., 2017), physician-reported pricing data (Gonzalez-McQuire et al., 2018), and survey responses (Moye-Holz et al., 2022). Some authors supplemented HTA records with study questionnaires (Westerling et al., 2014), country mortality statistics (Mackenbach et al., 2013), Surveillance, Epidemiology, and End Results (SEER) Program data (Bremner et al., 2020), or platforms built and annually updated by the researchers themselves (Wang et al., 2020). In one case, authors created a value framework for the French HTA system by comparing French HTA decisions to scores calculated using the 2016 update of the ASCO Value Framework (Li, 2020).

Textbox 6.3: Datasets Utilized

Publicly Available HTA Recommendations: 89
IQVIA MIDAS: 4
Medical Records: 2
Price data: 2 (public procurement prices in LATAM/ex-factory prices in Europe; Physician reported price data)
Study Questionnaire (in addition to HTA Recommendations): 1
Country Mortality Data and Larger Epi Datasets: 1
SEER Data: 1
Platform Built by Authors: 1

6.5.4 Country Inclusion

England was more commonly included than the US in comparative analysis. England appeared in 99 out of 101 studies (98%), while the US was included in only 15 (15%). Only 13 studies (14%) directly compared the US and England, and in nearly every case where the US was included, it was compared specifically with England (please see Appendix 6.2 for further information on these studies). While only a few of the resulting studies offered direct comparisons between these nations,

those that indirectly compared them with other non-U.S. and non-English nations provided useful insights into the methodologies and data available for the review's aims.

Countries most frequently compared with the US or England included France and Germany (each in 51 studies), Canada (41), Scotland (34), and Australia (34). A complete list of countries included is shown in Textbox 6.4, and their frequency of inclusion is visualized in Figure 6.3.

Textbox 6.4: Country Inclusion: Number of Papers

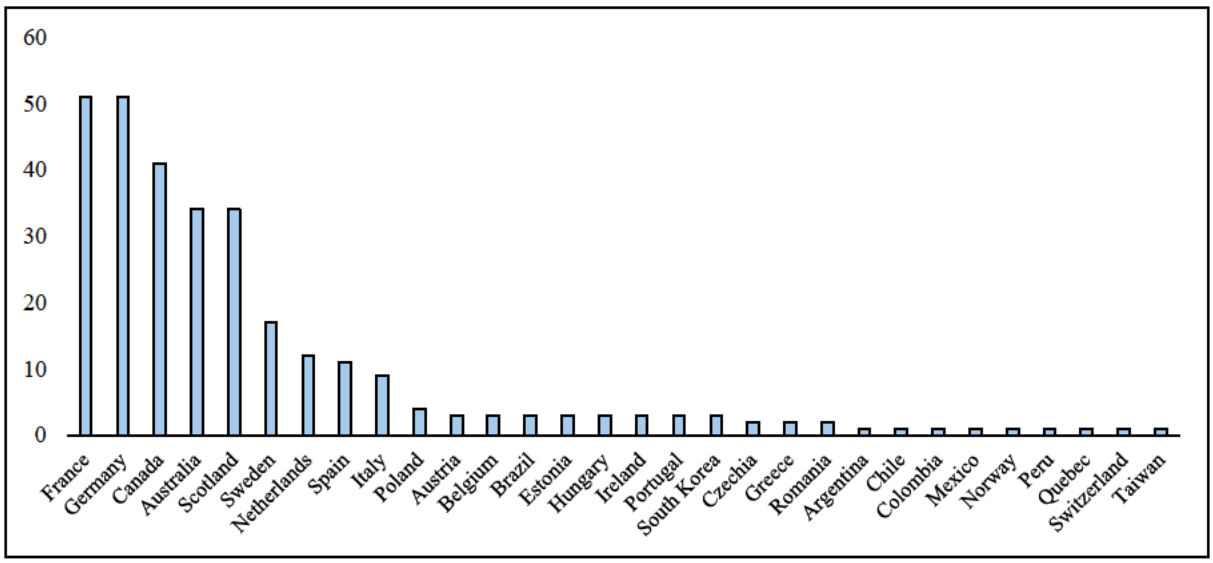
US Included: 15

England Included: 99

Direct Comparison of US and England: 13

Other Included Countries: Argentina, Australia, Austria, Belgium, Brazil, Canada, Chile, Colombia, Czechia, England, Estonia, France, Germany, Greece, Hungary, Ireland, Italy, Mexico, Netherlands, Norway, Peru, Poland, Portugal, Quebec, Romania, Scotland, South Korea, Spain, Sweden, Switzerland, Taiwan

Figure 6.3: Other Included Countries by Count



Regional groupings were occasionally used, especially for Latin America and East Asia. For example, Moye-Holz (2022) compared Chile, Brazil, Colombia, Mexico, and Peru as a group, while Ho (2017) analysed Taiwan and South Korea together. However, most studies focused on European comparisons.

6.6 DISCUSSION

This scoping review identified 101 studies that assessed patient access to cancer medicines across countries, with a primary focus on England and a smaller set of direct comparisons involving the US. Most studies (n = 94) measured access in terms of reimbursement, drawing predominantly on publicly available HTA recommendations. Grey literature studies by EFPIA and PhRMA provide comprehensive consideration of launch and utilization discussed above, but few peer-reviewed studies included in this review considered launch timing (n = 2) or utilization (n = 5) (Newton, 2025; PhRMA, 2023). England was by far the most frequently included country (99/101), while the US was considered in just 15 studies, and only 13 offered a direct comparison between the two. The review highlighted the heavy reliance on secondary datasets, particularly HTA documents, and the relatively limited use of original data sources, such as medical chart reviews or sales volume data.

A recurring theme in the included literature was the use of regional grouping, which allowed comparisons among the countries with more structurally similar health care systems. These comparisons, often involving England, France, Germany, Australia, and Scotland, provided useful insights and more homogeneous datasets. However, such groupings tended to exclude the US, particularly when access was assessed via HTA and government reimbursement. These differences underscore the challenge of comparing patient access between systems with centralized versus fragmented health governance.

Most reimbursement-focused studies centered on England and relied on HTA recommendations as a proxy for access. When US comparisons were made, researchers frequently turned to non-governmental organizations such as ICER and ASCO, or to federal agencies including the Agency for Healthcare Research and Quality (AHRQ), Centers for Medicare and Medicaid Services (CMS), and the Department of Veterans Affairs (VA). Yet, comparing these to England's single-payer NHS poses challenges. For example, Medicare, the closest analogue in the US, is limited to individuals aged 65 and over and does not guarantee cost-free access, often involving co-pays or

deductibles.[26] Comparisons based solely on national reimbursement structures can obscure deeper issues related to affordability, access inequities, and patient-level financial burden.

Recognizing these limitations, I focused on identifying methodological approaches that explored access through alternative lenses, namely launch and utilization. These frameworks, while underutilized, may offer a more nuanced view of real-world access, particularly in countries where health care systems are not centrally governed.

Other data sources were used or created by authors. Wang (2020) is one example of this, but the annual nature of this study and required partnership with pharmaceutical companies who protect proprietary sales information make it difficult to imagine replicating this method. Gonzalez-McQuire et al. (2018) also worked with physicians to conduct a retrospective medical chart review, collecting data for a month and a half between June 1 and July 15 of 2015. While this study will have provided rich data from that time, the intensive nature of data collection, ethics review, and short study period would make it complex to replicate.

For Mackenbach et al. (2013), larger trends in health system effectiveness were studied through country comparison. These authors attempted to understand patient access to health care innovations (including launch of new medicines), but their method of data collection through hand searching formularies for the first date of introduction of a drug, tracking sales data, identifying early trials, reviewing documents of professional societies and interviewing knowledgeable informants resulted in limited findings. The authors listed several challenges in their methodology, including: "*Access to data (there are significant delays in production of mortality data from some countries such as Belgium and Denmark), geographical distribution (and thus economic conditions, with countries from North, South, East and West Europe) and finally, the existence of willing partners with sufficient expertise. The research was undertaken by partners in these countries, for example, by hand searching*

[26] Peer reviewers of this manuscript also highlighted prior authorization and step therapy as access barriers unique to the US system. While physicians interviewed in Chapter 5 frequently reported encountering these barriers within the private US health care system (US01, US02, US04, US06, US07 US08, US09), several noted that such experiences were not common when treating Medicare insured patients (US01, US02, US06).

formularies for the first date of introduction of a drug, tracking sales data, identifying early trials, reviewing documents of professional societies and interviewing knowledgeable informants,"(p.1130). The authors concluded that "*the main lesson from this study is…how scarce is the evidence on, first, the ability of many common health care innovations to reduce mortality (which is, after all, one of their main objectives) and, second, on the timing, diffusion and coverage of health care interventions in Europe,*"(p.1132). Developing datasets to track health care innovations may be met with similar challenges, including access to data, expertise, willing partners, and clear information on mortality and timings. Therefore, this may be an approach to comparing access to avoid.

6.7 CONCLUSION

6.7.1 Learnings for Future Research

The overarching aim of this review was to support a more systematic understanding of how access to new cancer treatments can be compared across countries, and this review has identified several key considerations for future comparative research on patient access to cancer medicines. While most existing studies rely on HTA-based reimbursement data, particularly in England, this is an approach not easily transferrable to the US context due to structural and population-level differences in health care systems. Findings suggest that alternative approaches, particularly those using utilization data or launch timelines, may offer more feasible and informative avenues for direct comparison.

In mapping methodologies used to compare patient access internationally, I identified papers that compared utilization in the US and England. Direct comparisons of the US and England, like Salas-Vega et al. (2020), used the IQVIA MIDAS dataset to explore the relationship between cancer drug costs and drug clinical benefits. IQVIA MIDAS has been extensively used for drugs utilization studies (Choi, 2023). Its standardized and validated structure, including the Accuracy and Timeliness Statistics (ACTS) program, makes it particularly suited for consistent cross-national analysis. MIDAS provides a robust platform for tracking drug volume and market entry, allowing researchers to evaluate

access at the population level without the complexities of national reimbursement systems (IQVIA ACTS 2021).

Another promising dataset may be US SEER data used by Bremner et al. (2020), though comparable datasets in England are not obvious. This cancer registry is linked to Medicare claims data and was compared to the Ontario Cancer Registry to estimate resource specific costs from a public payer perspective over the last 360 days of life for colorectal cancer patients in the US and Canada. This resource could also be useful in understand patient access by measuring volume and patients reached.

Despite the availability of these data sources, a major limitation remains; there are few national-level datasets that provide linked information from drug launch to coverage to real-world utilization across countries. Industry-led initiatives, such as the PhRMA Global Access Report and the EFPIA Patients W.A.I.T. Indicator, represent important steps toward capturing a more comprehensive picture of patient access across countries (Newton, 2025; PhRMA, 2023). These reports integrate key measures such as time to availability and reimbursement decisions, offering valuable cross-national comparisons. While these contributions are significant there remains an opportunity to build on this work through greater engagement in the peer-reviewed academic literature which would support broader methodological development and integration into comparative research frameworks.

Alternative methods, such as building proprietary databases or conducting retrospective chart reviews, have been explored but are less practical due to limitations in replicability, time intensity, and data access. Therefore, IQVIA MIDAS may be the most viable resource for direct comparison between the US and England. SEER-Medicare is an additional dataset that also presents opportunities for deeper understanding of access dynamics within the US system. One promising methodological strategy may involve applying English reimbursement policy criteria to SEER data to estimate how many US patients would meet eligibility under a system modelled on England's. This could provide a creative and meaningful way to bridge methodological gaps between the two health systems and produce policy-relevant insights on equitable access.

This is the first scoping review to map methodological approaches to comparing patient access to cancer medicines across countries, with a specific emphasis on US and England. While HTA often provides an essential mechanism for guiding reimbursement decisions within certain national contexts, its methodological dominance in the literature narrows the lens through which access is typically evaluated, limiting the capacity for meaningful international comparison. By introducing alternative access metrics, such as utilization patterns and time to market entry, I highlight that HTA is not incorrect but insufficient for capturing the full complexity of access across diverse systems.

A key next step is to more systematically assess the strengths and limitations of different access measures, particularly comparing metrics like availability (including reimbursement approval) versus time-to-event measures, such as actual uptake or patient access timelines. The recent analysis by Li et al. (2024) offers a valuable foundation by mapping global disparities in cancer drug availability across countries from 1990 to 2022. These measures provide a clear overview of market entry though they may not fully reflect real-world access at the patient level.

In addition, future research should address the broader consequences of access disparities. Delays in access or limited availability of innovative treatments can result in significant unmet disease burden and increased health system costs. Studies such as Uyl-de Groot et al. (2020) quantify the potential life-years lost due to unequal access to cancer drugs in Europe, while Incze et al. (2022) highlight the policy and economic implications of pricing mechanisms like external reference pricing on global access and innovation. Integrating impact-focused analyses like these into access comparisons will strengthen the policy relevance of future work.

Broader metrics have to potential to inform policy decisions aimed at reducing delays and disparities in access that might otherwise be overlooked. The approaches discussed could offer meaningful ways of bridging methodological gaps between the two health systems, facilitating the generation of policy-relevant insights on equitable access to care. These insights could support the development of policies aimed at minimizing delays and reducing disparities in access to cancer care.

6.7.2 Acknowledgement

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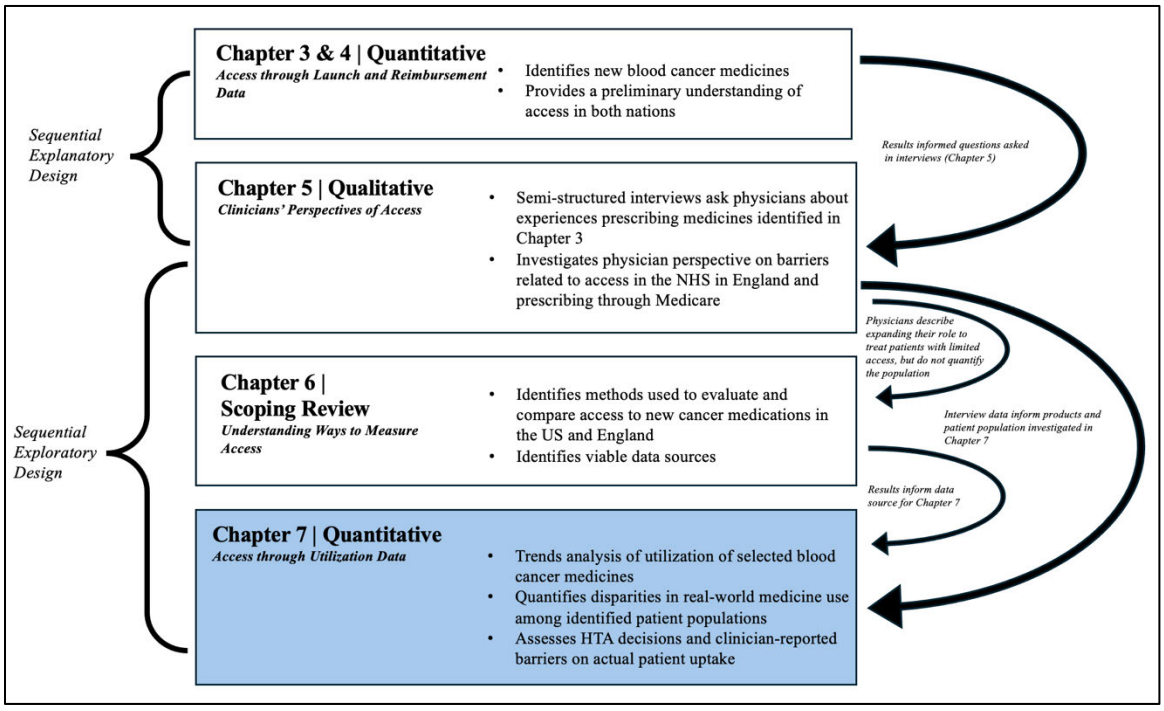
CHAPTER 7

Trends Analysis of Access by Utilization

CHAPTER 7 FORWARD

Chapter 7 explores the use of new blood cancer medicines in the US and the UK, focusing on real-world utilization patterns across three patient groups: those with acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and multiple myeloma (MM). This chapter builds on earlier findings, particularly analysis of reimbursement decisions in Chapter 4 and physician interviews in Chapter 5, by introducing quantitative data to examine whether policy restrictions and clinical access barriers may influence how medicines are used at a population level (see Figure 7.1).

Figure 7.1: Sequential Multi-Phase Mixed Methods Design



The chapter begins with a focused case study of Venetoclax, a medicine frequently cited by English physicians in Chapter 5 as clinically valuable but difficult to access due to HTA funding restrictions. Using IQVIA data, the analysis in this chapter estimates the proportion of AML patients in each country treated with Venetoclax from 2020 to 2024. This approach addresses a key question raised in earlier chapters: whether access restrictions identified in reimbursement data and qualitative reports correspond with actual differences in treatment uptake.

Part 2 of the chapter expands the scope by examining additional new AML treatments introduced during the same time period. By evaluating a broader range of medicines, this section explores whether comparably low Venetoclax use in the US may be explained by a shift toward other available medicines. The analysis suggests that US prescribing may reflect a wider treatment landscape with a more diverse set of options. Usage patterns in the UK may reflect a gradual increase following NICE decisions, with uptake potentially occurring after a delay.

Part 3 extends this analysis beyond AML, examining treatment trends for Venetoclax and other new medicines used in CLL and MM. This section aims to determine whether the patterns observed for AML are consistent across other disease groups or specific to that indication. It also considers whether NICE decisions regarding cost-effectiveness appear to shape treatment access differently in the two countries. The data suggest that while treatment uptake in the US tends to be broader and more varied, the UK shows steady increases over time, possibly in response to HTA guidance. Collectively, this analysis provides additional insight into how policy, practice, and broader system structures like HTA influence the use of new blood cancer medicine.

Part One: Utilization of Venetoclax for Treatment of Acute Myeloid Leukemia

7.2.1 INTRODUCTION

The goal of Chapter 7 is to understand utilization trends among patients using new medicine for blood cancer that were flagged by English physicians in Chapter 5 as subject to funding restrictions. In Chapter 4, I showed that 63% of TAs for 32 blood cancer medicines were positive and guaranteed reimbursement through the NHS. However, 43% of those positive appraisals excluded some patients (considered clinically appropriate for product use by the EMA) by limiting funding to a narrower indication. Data from Chapter 4 also indicated that patients who qualified for coverage waited a median of 3.7 years after EMA approval for funding through NICE TA. These findings are consistent with restricted patient access due to reimbursement policy in the UK.

During the dissemination of early thesis work, stakeholders noted that restricted reimbursement decisions may be due to uncertain clinical benefit, impact on only a small subset of patients, and that alternative routes to access may provide comprehensive care. In Chapter 5, to investigate these concerns and better understand physician experiences accessing new blood cancer medicines, I conducted 19 qualitative interviews with US and English physicians. Participants were asked about their experiences accessing new blood cancer medicines in a clinical setting, and their perceived value of these treatments. Many of these participants identified Venetoclax as a key medicine with access barriers attributable to HTA.

In Chapter 6, I conducted a scoping review to identify appropriate data sources and methodologies for measuring access, finding that utilization data is a promising means of comparison of new medicine use in the US and England. Scoping review results indicated that IQVIA was a reliable and consistently published source among peer reviewed articles for capturing real-world medicine use in the US and English contexts. Therefore, I chose to analyze the uptake of Venetoclax as a case-study of drug utilization using the IQVIA dataset.

This analysis was intended to address a limitation outlined in Chapter 4; that the lack of NICE funding for certain patient groups may affect only a small subset of the population, and that alternative access routes may still provide adequate care. I also aimed to explore whether the access barriers described by English physicians in Chapter 5, particularly those related to NICE funding restrictions, may reflect broader trends at the population level. To do this, IQVIA utilization data were analyzed for Chapter 7 to assess how many US and UK patients used Venetoclax during the years these TAs were in effect, comparing this population to the total disease prevalence in each nation. This method has drawbacks (see *Limitations*) but current literature indicates that comparing utilization counts to total disease prevalence is methodically robust (Fahr, Buchanan and Wordsworth, 2019; Sarfati, Koczwara and Jackson, 2016). For example, a similar approach to estimating the proportion of patients eligible for specific cancer medicines using population-level mortality or incidence data combined with clinical eligibility criteria was undertaken by Marquart et al. (2018). Like mortality statistics, prevalence includes patients who might not be eligible for the new medicines (due to disease stage, comorbidities, etc.), so calculated utilization percentages in Chapter 7 might underestimate true access among eligible patients and should be viewed as a limitation of this work.

7.2.1.1 Venetoclax as a case study for Acute Myeloid Leukemia

When ten English physicians were asked in interviews in Chapter 5 about new products to treat blood cancer that they considered valuable but had challenges accessing, half identified Venetoclax. This is a small sample but it is noteworthy that several of the participants mentioned this product. Other cancer medicines with access challenges were brought up by participants like teclistamab for myeloma, rituximab as monotherapy for first grade lymphoma, or lenalidomide for t-cell lymphoma, but these were each noted by only one participant and therefore had limited overlap with other flagged medicines in qualitative interviews. Participants described frustration when AML patients did not qualify for guaranteed funding through NHS England, despite seeing international colleagues prescribe the drug within wider guidelines published by regulatory

agencies e.g. the National Comprehensive Cancer Network (NCCN). The NCCN is a US nonprofit group of 33 leading cancer centers. While the NCCN is a US organization, guidelines were referenced as a key source for best practice by several English physicians participating in qualitative interviews and described as standard for clinical direction in specialized cancer care. The NCCN has published guidance on use of Venetoclax for AML, chronic lymphocytic leukemia (CLL), multiple myeloma (MM), non-hodgkin's lymphoma (NHL), and myelodysplastic syndromes (MDS) (NCCN, 2025). All of these indications are covered by the US government insurance program, Medicare (CMS, 2025).

Venetoclax was first approved by the EMA on March 2, 2016 (EMA, 2016) and by the FDA on April 11, 2016 (FDA, 2016).[27] According to the FDA, Venetoclax is used "in combination with azacitidine or decitabine or low-dose cytarabine for the treatment of newly-diagnosed AML in adults who are age 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy" (FDA, 2025). While more comprehensive coverage for CLL is currently established under several NICE TAs, AML patients receive only restricted coverage. Table 7.1 shows all TAs that have been published by NICE regarding Venetoclax reimbursement for AML patients.

Table 7.1: NICE TA Decisions for AML

TA Number	Date Published	Reimbursement Decision	Disease Area	Patient Population
TA765	02/02/2022	Positive	AML	Venetoclax with azacitidine is recommended as first line therapy (when chemo is unsuitable)
TA787	04/27/2022	Positive	AML	Venetoclax with low dose cytarabine is recommended as first line therapy (when chemo is unsuitable) only if patient has over 30% bone marrow blasts

[27] Venetoclax is prescribed by US physicians for small lymphocytic lymphoma (SLL), chronic lymphocytic leukemia (CLL), multiple myeloma (MM), T-cell prolymphocytic leukemia (T-PPL), and Acute Myeloid Leukemia (AML) (NCCN, 2025).

While both NICE TAs for Venetoclax use for AML patients are positive, they only provide reimbursement for the patient population specified in the TA. In Chapter 5, physicians repeatedly reported this as an access barrier caused by HTA, that they felt their US colleagues did not experience. Comparisons between English funding and US coverage require careful interpretation, as structural differences between the two health systems mean that the mechanisms of access barriers are not always directly comparable.

7.2.2 METHODS

This analysis combines data from two IQVIA datasets and publicly available epidemiological sources to estimate Venetoclax utilization among AML patients in the UK compared to the US. Primarily, two IQVIA data sources were employed to estimate AML patient use; MIDAS and Patient Link.*

IQVIA MIDAS has been extensively used for drug utilization studies (Choi et al., 2023). IQVIA performs an annual internal statistical program, Accuracy and Timeliness Statistics (ACTS); this is a standardized and evidence-based quality assurance program that validates purchasing data based on accuracy and timeliness through alternate sources, including manufacturers and pharmaceutical companies (IQVIA 2021). Participating manufacturers supply a total of the ex-factory quantity sold in the validated calendar year for each registered product pack, which are then compared with IQVIA's audits. In monthly updates, validation studies are conducted for each product registered in individual countries and summarized by the Global Precision Index (GPI), a quality indicator aggregating all validation results for uninterrupted 5-year national retail and hospital data. IQVIA states that this allows for comparisons of cross-national purchases (IQVIA, 2021) but a limitation of this data may be that coverage is not uniform across countries. In this study, I used IQVIA MIDAS for product-level sales data segmented by disease group.

IQVIA Patient Link provides total patient estimates based on overall units sold per product, but it does not offer disease-specific breakdowns (IQVIA, 2023). It integrates de-identified clinical data (such as prescription and medical claims) with consumer data at the

IQVIA data has been redacted for publication after review by thesis examiners.

individual level. The linkage is performed using privacy-compliant methods and is intended to support research that requires a broader view of patient characteristics, behaviors, and treatment patterns across datasets. To estimate the number of patients using a product for AML, the disease-specific proportions from MIDAS were applied to the total patient counts from Patient Link (see *Estimating Venetoclax Utilization Among AML Patients).* [28]

Additional epidemiological and population data (including incidence, prevalence, and survival) were drawn from established public sources to calculate denominator populations. The Surveillance, Epidemiology, and End Results (SEER) Program of the US National Cancer Institute (NCI) provides population-based cancer incidence and survival data, widely used for national cancer statistics and research (NCI, 2025). The American Cancer Society, a nonprofit organization, publishes annually updated cancer incidence and mortality projections based on both SEER and supplementary registry data (American Cancer Society, 2025). In the UK context, Cancer Research UK is the country's largest independent cancer research charity and maintains detailed cancer statistics, including incidence and survival trends, based on data from the National Cancer Registration and Analysis Service (Cancer Research UK, 2021). National population estimates for each year of analysis were retrieved from the US Census Bureau (US Census Bureau, 2025) and the UK Office for National Statistics (ONS, 2025) to support prevalence modeling and calculation of treatment coverage rates (see *Estimating Patient Population* in METHODS).

7.2.2.1 Estimating Venetoclax Utilization Among AML Patients

As noted above, two IQVIA data sources were used to estimate AML patient use. IQVIA Analytics Link provides data on disease grouping by units sold per product. IQVIA Patient Link provides total patient estimates based on total units sold per product. It does not provide an estimate of patients by disease grouping. To estimate the number of patients using a product by

[28] This method was verified with an IQVIA analyst in October 2022 and August 2025.

disease grouping, the total proportions from product sales was used to estimate patient count. This approach assumes that sales volumes by indication are stable and accurately reflect disease-specific utilization by IQVIA. Given that Venetoclax is approved for multiple hematologic malignancies, there is a risk of misallocating sales across indications. This assumption represents a key source of uncertainty in the analysis, and findings should be interpreted with caution unless validated by additional clinical or prescribing data. Results are shown in Table 7.2 and 7.3.

7.2.2.2 Estimating Patient Population in the United States and United Kingdom

As noted above, to calculate prevalence of AML in the US and UK, publicly available summary data on the number of individuals living with AML were combined with national population estimates. As AML prevalence is not routinely reported for every year, prevalence for missing years was approximated using incidence and average survival duration. This method provides a practical solution in the absence of consistent annual data but introduces uncertainty, as it assumes stable incidence and survival patterns over time. For the US, prevalence figures were obtained from the SEER Cancer Statistics Review, which reported 79,317 prevalent AML cases in 2022 (NCI, 2025). The American Cancer Society estimated 20,800 new AML diagnoses in 2024 and 22,010 in 2025 (American Cancer Society, 2025). From these data sets we may infer a relatively stable annual incidence of ~20,000–22,000 cases/year and a prevalence-to-incidence ratio of roughly 3.5.[29] To calculate prevalence estimates (for 2020, 2021, 2023 and 2024 as a 2022 prevalence estimate was provided by SEER) prevalence was approximated by multiplying the annual incidence of AML by the average duration of survival. This method assumes a steady-state population, which may not hold for AML given improvements in survival over time, and therefore should be interpreted as an approximation rather than a precise estimate. UK data were sourced from Cancer Research UK, which reported approximately 3,100 new AML diagnoses per year during 2016–2018 (Cancer Research UK, 2021). This model assumed gradual population

[29] The prevalence-to-incidence ratio of 3.5 is calculated by dividing reported prevalence (79,317) by incidence (22,000) and rounding down.

growth and aging would result in a modest annual increase (~1–2% per year). To estimate the number of people living with AML in any given year in the UK, the estimated number of new cases each year was multiplied by a prevalence-to-incidence ratio of three. This prevalence-to-incidence ratio reflected the lower observed survival rates in the UK (Cancer Research UK, 2021) compared to the US (NCI, 2025) (where a prevalence-to-incidence ratio of 3.5 was calculated from reported data). This method allowed for a comparable estimation of AML prevalence across both countries using accessible and up-to-date sources. Results are shown in Table 7.4.

As part of a sensitivity analysis, the impact of using alternative prevalence-to-incidence ratios (2.5 and 3.5) was explored to reflect a plausible range of survival outcomes. Under the lower-bound scenario (multiplier = 2.5), the estimated UK AML prevalence in 2024 decreased to ~7,750 patients, suggesting more limited survival duration. In contrast, applying a higher multiplier of 3.5, assuming improved survival more consistent with US trends, increasing the estimated prevalence to ~10,850 patients. Compared to the base case of ~9,300 patients (with a prevalence-to-incidence ratios of 3), this represents a range of –17% to +17% around the central estimate. This analysis highlights the sensitivity of prevalence estimates to survival assumptions and underscores the importance of accurate, region-specific survival data when modeling disease burden.

Proportion of AML patients using Venetoclax (shown in Table 7.5) was calculated using results of Table 7.5's estimate of patients using Venetoclax and Table 7.4's estimate of the AML population in the US and UK. It is important to note that this calculation uses all AML patients as the denominator, rather than the subset who are clinically eligible for Venetoclax. As a result, the uptake proportion may underestimate actual use among the eligible population and should be interpreted with this limitation in mind.

The point prevalence of AML in each year was approximated using the product of the annual incidence rate and the average duration of disease survival, scaled to the population size. Mathematically, this is expressed as:

$$\text{Prevalence}_{year} = \text{Incidence Rate (per year)} \times \text{Average Survival Duration (years)} \times (\text{Population}_{year} / 100{,}000)$$

In this calculation, the incidence rate is expressed per 100,000 population per year, and average survival duration is measured in years. This method assumes a steady-state population and disease dynamics, where incidence and survival remain relatively constant over the period of interest. The formula provides a practical approach to estimate AML prevalence in the absence of comprehensive registry data and was applied to each year by updating the corresponding population figures. See Appendix 7.1 for specific inputs per year.

7.2.3 RESULTS

IQVIA MIDAS reported other (non-AML) patient cohorts that are linked to sales of Venetoclax in the US from 2020-2024, shown in Table 7.2. To estimate the number of patients per cohort per year and ultimately compare the number of AML patients in the US and UK, the steps outlined above (see *Estimating Venetoclax Utilization Among AML Patients*) were conducted. Results are shown in Table 7.3.

Table 7.2: Volume and Proportion of Venetoclax Utilized By Disease Area

Country	Patient Cohort	Value	2020	2021	2022	2023	2024
UK	Acute Myeloid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Proportion from Total	0.22	0.18	0.23	0.19	0.24
	Chronic Lymphoid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Proportion from Total	0.78	0.82	0.77	0.81	0.76
US		Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

	Acute Myeloid Leukemia	Proportion from Total	0.15	0.14	0.13	0.13	0.09
	Chronic Lymphoid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Proportion from Total	0.68	0.68	0.66	0.66	0.66
	Multiple Myeloma	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Proportion from Total	0.07	0.09	0.12	0.11	0.13
	Non-Hodgkin's Lymphoma	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Proportion from Total	0.07	0.07	0.07	0.08	0.08
	Myelodysplastic Syndromes	Units Sold	0	[redacted]	[redacted]	[redacted]	[redacted]
		Proportion from Total	0.00	0.00	0.00	0.00	0.00
	Other Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Proportion from Total	0.03	0.02	0.02	0.02	0.03

Table 7.3 results show that volume of Venetoclax used is consistent with increased access following NHS England reimbursement among UK patients in 2022. In the US, the absolute number of AML patients using Venetoclax fell from [redacted] in 2020 to [redacted] in 2024, a reduction of nearly 100 patients. When expressed as a proportion of the total AML population, the decline is more pronounced, dropping from 2.0 to 1.3%. This highlights the importance of distinguishing between absolute patient counts and proportional trends.

Table 7.3: Estimated Patients with AML Among Patients Using Venetoclax

Country	Patient Group	2020	2021	2022	2023	2024
UK	AML Patients	397	523	953	830	1,064
	Total Patients	1,780	2,837	4,079	4,422	4,388
US	AML Patients	1,129	1,233	1,220	1,329	1,051
	Total Patients	7,590	8,851	9,515	9,975	11,133

Table 7.4 indicates that the AML patient population in the US is disproportionately larger than the UK. While the total population of the US is only 5 times the size of the UK, the US AML population is 8 times that of the UK. This disproportion reflects the higher age-adjusted incidence of AML in the US, likely driven by demographic differences such as a larger elderly population and possibly varying environmental or genetic risk factors.

Table 7.4: Estimated AML Prevalence and Patients in the US and UK Total Population

Country	Patient Group	2020	2021	2022	2023	2024
UK	AML Prevalence Estimate	14.2 per 100,000	14.3 per 100,000	14.4 per 100,000	14.5 per 100,000	14.6 per 100,000
	AML Patients	~9,525	~9,610	~9,720	~9,825	~9,925
US	AML Prevalence Estimate	21.1 per 100,000	21.4 per 100,000	23.8 per 100,000	24.0 per 100,000	24.5 per 100,000
	AML Patients	~70,000	~71,000	79,317 [30]	~80,000	~82,000

Table 7.5 indicates that the proportion of all AML patient use of Venetoclax is far smaller in the US than the UK and declined over time in the US from 2 to 1% of all AML patients. Use of Venetoclax for AML patients in the UK appears to notably exceed that of the US, especially once reimbursement was granted in 2022. In this year, the portion of AML patients using Venetoclax doubles, increasing in use from 5-10% of AML patients.

Table 7.5: Percent of US and UK AML Patients using Venetoclax

Country	2020	2021	2022	2023	2024
UK	4%	5%	10%	8%	11%
US	2%	2%	2%	2%	1%

[30] US AML Patient Prevalence supported by SEER in 2022 rather than modeled (NCI, 2025).

7.2.4 DISCUSSION

Estimated use of Venetoclax for AML patients in the UK appears to far exceed that of the US. The AML population in the US is larger as seen in Table 7.4. This may be due to higher AML incidence per capita, but also slightly longer survival rates (US 34% 5-year survival vs UK ~15%) (Cancer Research UK, 2021; NCI, 2025). The proportion of AML patient use of Venetoclax declined over time in the US; however, this estimate is based on the total AML population, not the subset of patients eligible for Venetoclax. This means the observed decline may reflect a growing overall prevalence rather than a true decrease in eligible patient uptake. In other words, because Venetoclax is not appropriate for all AML cases, it is difficult to determine if the observed decrease in use represents a change in prescribing behavior or changes in the underlying population. Nevertheless, the decline in proportion of AML patients using Venetoclax may indicate that significant access barriers like insurance coverage and cost are impacting AML patient's ability to receive care in the US. Chapter 5 results included descriptions among US physicians of regularly having to turn non-Medicare patients away from care who did not have adequate insurance coverage and fighting with insurers to cover necessary care. These barriers may be reflected in Table 7.5 results.

It is also possible that a small portion of US AML patients are being treated with Venetoclax because the standard of care in the US has already shifted to other new medicines. In Chapter 5, many participants expressed the perception that the US standard of care diverges from that in England, creating challenges for aligning global clinical development with UK HTAs. One physician interviewed for Chapter 5, who had participated in NICE TAs, explained that pharmaceutical manufacturers often face difficulties submitting trial data to NICE when the comparators used in US-based trials are not yet available in England. In the example shared, not only had the new treatment under evaluation been denied reimbursement in the UK, but the comparator used in the clinical trial had also not been launched, as it had not yet become standard of care in England.

UK utilization of Venetoclax among AML patients seemed to respond to two positive TA decisions in early 2022, increasing from 5 to 10% that year. This suggests that adoption of a new medicine happens quickly once a positive TA is published. This highlights that the UK health system appears to be robust to allow for quick patient uptake upon NICE approval, but this quick uptake may also indicate patient need and eagerness among physicians who have been waiting to use a new medicine.

7.2.5 LIMITATIONS

This data sample is limited to new medicines identified in Chapter 3 and launched from 2011 to 2020. Older medicines launched before 2011 and newer medicines launched after 2020 might be utilized by the patients considered in this analysis. In Chapter 3, I found that some IQVIA data did not include the blood cancer products Crizotinib and Obinutuzumab and some data was limited for the UK. This limitation specifically applied to missing launch dates. Results of Chapter 6 helped assure me that IQVIA is an appropriate source of utilization data for England and the US. However, incorrect reporting of sales data is a possibility.

AML patient population was estimated based on reported statistics from reputable sources (see *Estimating Patient Population*). However, this number remains a rough estimate which does not adjust for age or gender differences in national populations. Prevalence estimates were sensitive to survival assumptions, with a ±17% range observed when applying alternative prevalence-to-incidence multipliers (2.5 and 3.5) in sensitivity analysis. Uncertainty in population estimates could materially affect uptake percentage of patients using Venetoclax. Finally, this study considered the entire US population, without consideration of insurance status. Additional access barriers like health insurance coverage and cost are likely to impact the US patient population. Future research that limits results to the US Medicare population would be helpful in better comparing HTA impact on access through utilization of new blood cancer medicines.

7.2.6 CONCLUSION

I found that from 2020-2024, Venetoclax was only used by a very small percentage of AML patients in the US, decreasing from 2 to 1% in the timeframe examined. In the same timeframe, UK utilization of Venetoclax among AML patients seemed to respond to two positive TA decisions in early 2022, increasing from 5 to 10% that year. The increase after positive TA was encouraging for the importance of this thesis; it may indicate that HTA impacts patient access and UK doctors are keen to use the new medicine on a population level. Physician participants in Chapter 5 discussed their perception that the standard of care in the US shifts faster than England as new medicines are adopted. It is possible that US standards have already shifted away from Venetoclax and US physicians are using other new medicines for blood cancer treatment. To understand if this is the case, a broader look at new medicine use among AML patients was necessary.

Part 2: New Medicine Utilization Among Acute Myeloid Leukemia Patients

7.3.1 INTRODUCTION

Qualitative results in Chapter 5 indicated that standard of care in blood cancer treatment may shift faster in the US than in England. This led to a decision to examine whether the small portion of patients with AML in the US using Venetoclax (shown in Part 1 Table 7.5) could be explained by other innovative product use.

7.3.2 METHODS

This analysis employed the same core data sources and methodology outlined in Part 1 to estimate utilization of other newly approved AML medicines in the US and UK from 2020 to 2024. Primary data were drawn from IQVIA MIDAS and IQVIA Patient Link datasets. IQVIA MIDAS provided validated product-level sales, which was analyzed to identify relevant AML medicines and their usage volume by disease area. Patient Link estimates were used to approximate patient counts based on total units sold per new medicine. To estimate the number of AML patients using each new medicine, disease-specific proportions from MIDAS were applied to the total patient counts from Patient Link, consistent with the approach used to estimate Venetoclax patient utilization in Part 1. AML population estimates for the US and UK calculated in Part 1 were then used to calculate the percentage of AML patients in the US and UK using new medicines.

7.3.3 RESULTS

Between 2020 and 2024, a total of seven new medicines were identified with usage for AML in the US and UK (see Table 7.6). Among these, only three (Gliteritinib, Ivosidenib, and Midostaurin) were used in both countries. The remaining four products (Enasidenib, Cedazuridine + Decitabine, Glasdegib, and Selinexor) were utilized exclusively in the US and had no recorded sales for AML in the UK.

Table 7.6: Other New Medicines listed for AML Treatment

Product	Any USA Utilization	Any UK Utilization
Enasidenib	X	
Gliteritinib	X	X
Cedazuridine + Decitabine	X	
Ivosidenib	X	X
Midostaurin	X	X
Glasdegib	X	
Selinexor	X	

Calculations for the volume and proportion of new medicines are listed in Appendix 7.2 by disease area. Table 7.7 displays estimates of AML patients treated per new medicine. In the US, usage of newer AML medicines increased steadily from 2020 to 2024. By 2024, over [redacted] AML patients were estimated to be receiving one of these newer treatments, an increase from approximately [redacted] in 2020. Gilteritinib, Enasidenib, and Midostaurin were consistently among the most widely used new medicines, with Gilteritinib reaching over [redacted] patients annually by 2023–2024. In contrast, the UK showed more limited uptake. The total number of AML patients using new medicines rose there from [redacted] in 2020 to [redacted] in 2024, representing only about 15% of the estimated national AML population (see Table 7.8). Gilteritinib and Midostaurin accounted for the majority of UK use, while Ivosidenib only began to appear in 2024 with minimal uptake. No other new AML medicines had recorded usage in the UK during this period.

Table 7.7: Estimated Patients with AML Among Patients Using New Medicines

Country	New Medicine	Patient Group	2020	2021	2022	2023	2024
UK	Gilteritinib	AML Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Total Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

	Ivosidenib	AML Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Total Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Midostaurin	AML Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Total Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Venetoclax	AML Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Total Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
US	Enasidenib	AML Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Total Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Gilteritinib	AML Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Total Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Cedazuridine + Decitabine	AML Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Total Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Ivosidenib	AML Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Total Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Midostaurin	AML Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Total Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Glasdegib	AML Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Total Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Selinexor	AML Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Total Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	Venetoclax	AML Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Total Patients	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Table 7.8 shows the proportion of AML patients receiving newly approved medicines. Across all years, the US had higher adoption rates, with 14% to 19% of AML patients using newer treatments. The UK lagged behind, starting at just 6% in 2020 and reaching 15% by 2024. While the gap narrowed over time, US uptake remained consistently higher in both relative and absolute terms. These data suggest that the adoption of new AML treatments accelerated in both countries, but at a faster pace in the US.

Table 7.8: Percent of US and UK AML Patients using New Medicines

Country	Patient Group	2020	2021	2022	2023	2024
UK	Total AML Patients Using New Medicines	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	AML Patient Population	~9,525	~9,610	~9,720	~9,825	~9,925
	Percent of Patients Using New Medicines	6%	8%	13%	12%	15%
US	Total AML Patients Using New Medicines	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	AML Patients	~70,000	~71,000	79,317 (NCI, 2025)	~80,000	~82,000
	Percent of Patients Using New Medicines	14%	16%	16%	18%	19%

7.3.4 DISCUSSION

This study indicates that new medicine use in the treatment of AML patients is more diverse in product use in the US. New medicines like Enasdenib, Cedazuridine + Decitabine, Glasdegib, and Selinexor have no units sold in the UK, but are utilized in the US. Enasdenib is used extensively (see Table 7.7), with more AML patients treated with Enasdenib than Venetoclax. Diversity in product use could be caused by other factors like population level differences in disease onset but does reflect reports in Chapter 5 of US physicians having a better ability to tailor care for individual patients.

The percent of US AML patients using new medicines was significantly larger when additional new products to treat AML (other than Venetoclax) were added, potentially providing a more accurate picture of trends in the US for this patient group. While Table 7.5 shows only 1-2% of AML patients using Venetoclax, including other new medicines in this analysis caused that percentage to increase from 14-19% during the study period. In contrast, use of new medicines to treat UK AML patients went from 6-15% from 2020-2024. This result may support the calculated lag time of about 4 years after regulatory approval for positive NICE TAs in England in Chapter 4. Part 1 suggests that adoption happens quickly once a positive NICE TA is published. Still, even accounting for multiple therapies, only 19% of AML patients in the US were treated with new medicines in 2024.

7.3.5 LIMITATIONS

Results of Chapter 6 provide evidence of validity for IQVIA as an appropriate source of utilization data for the UK and the US. However, incorrect reporting is a possibility in this data set; in Chapter 3, I found that some IQVIA data was limited for the UK. This specifically applied to launch dates. Additionally, the data sample in Chapter 3 was limited to new medicines. As a result, well-established medicines that have been part of AML treatment for many years were not included. Hence, reported patient counts and percentages reflect only the use of newly approved medicines, rather than the full spectrum of AML care. This limitation is particularly relevant when interpreting lower adoption rates in the UK, where reliance on older, established treatments may still be prevalent. The findings should therefore be understood as a reflection of the uptake of innovative medicines, rather than a comprehensive assessment of all AML treatment.

In this analysis, patients were counted once for each product used. However, because cancer patients often receive combination therapies, or switch treatments over time, a single patient may appear multiple times in the data. Part 1 focuses specifically on Venetoclax use among AML patients, which reduced this issue by examining only one drug. However, Part 2

included multiple products, some of which may have been used by the same patient. As a result, this approach may overestimate the proportion of blood cancer patients receiving treatment with new medicines.

7.3.6 CONCLUSION

This analysis indicates greater diversity in the utilization of new AML treatments in the US compared to the UK, with several medicines used in the US absent from the UK market. When accounting for multiple new medicines, the proportion of US AML patients receiving innovative treatments appeared to increase from approximately 1-2% (Venetoclax alone) to 14–19% over the study period, while UK utilization rose from 6-15%. These findings suggest a temporal lag of approximately four years in the UK's adoption of new AML medicines relative to the US, potentially attributable to the HTA process. Despite broader availability of new treatments, only a minority of AML patients in both countries appear to receive new medicines, highlighting the presence of ongoing access barriers. However, this analysis is limited to AML patients and may not reflect utilization patterns across other hematologic malignancies. Further research was therefore needed to assess treatment trends and access barriers in the broader blood cancer population.

Part 3: Trends Analysis of New Medicine Utilization by Patient Group

7.4.1 INTRODUCTION

Results of Part 1 indicated that Venetoclax use among AML patients increased in the UK following positive HTA decisions while declining in the US, possibly due to differing access barriers and faster adoption of alternative treatments in the US. Part 2 showed that other new AML medicines have higher utilization in the US compared to the UK, suggesting a shift in treatment patterns that may explain the lower Venetoclax use in the US market.

To deepen this analysis, I examined prescribing trends for Venetoclax in other patient groups, specifically chronic lymphocytic leukemia (CLL) and multiple myeloma (MM). Exploring these additional populations helped determine whether limited utilization of new medicines was specific to AML or reflects broader differences in treatment adoption across disease areas. This comparison also shed light on fundamental differences in standards of care between the US and UK. NICE has concluded that some products, including Venetoclax, are not cost-effective for MM treatment. In Chapter 7, Part 3, I investigate whether US prescribers independently arrive at similar assessments or diverge from such guidance.

7.4.2 METHODS

I identified all new medicines utilized by CLL and MM patients according to IQVIA MIDAS data. Following Part 2 methods (see Appendix 7.2), I calculated the proportion of total products used for each blood cancer disease type. I then multiplied the proportion of products used per disease type by the total patient estimate provided by Patient Link. All patient estimates for MM and CLL patients were added to calculate the total patients treated with new medicines by disease type.

I continued to use Part 1 Methodology for calculation of point prevalence for CLL and MM during the study years. Population-based cancer incidence and survival data were sourced

from the SEER Program of the US National Cancer Institute and Cancer Research UK. The American Cancer Society provided annual projections based on SEER and supplementary registry data. In the UK, Cancer Research UK data are based on the National Cancer Registration and Analysis Service. National population estimates were obtained from the US Census Bureau and the UK Office for National Statistics to support prevalence modeling and treatment coverage calculations (see *Estimating Patient Population* in Part 1 Methods). The following formula was used for these calculations:

$$\text{Prevalence}_{\text{year}} = \text{Incidence Rate (per year)} \times \text{Average Survival Duration (years)} \times (\text{Population}_{\text{year}} / 100{,}000)$$

Total CLL and MM patients treated with new medicines were divided by the estimated point prevalence for CLL and MM patient populations to estimate the percent of blood cancer patients treated with new medicines in the US and UK by disease type.

7.4.3 RESULTS

According to IQVIA Analytics Link data, Venetoclax is utilized for five types of blood cancer. This study investigates CLL and MM, finding that like AML, additional new medicines are utilized for treatment of US patients. Table 7.10 displays these diseases, and the other new medicines utilized to treat them by country.

Table 7.10: New Medicines Utilized by Type of Blood Cancer

Cancer Type	US New Medicines Utilized	UK New Medicines Utilized
Acute Myeloid Leukemia (AML)	1. Enasidenib 2. Gliteritinib 3. Cedazuridine + Decitabine 4. Ivosidenib 5. Midostaurin 6. Glasdegib 7. Selinexor 8. Venetoclax	1. Gliteritinib 2. Ivosidenib 3. Midostaurin 4. Venetoclax
Chronic lymphocytic leukemia (CLL)	1. Ibrutinib 2. Acalabrutinib 3. Venetoclax 4. Blinatumomab 5. Bosutinib	1. Ibrutinib 2. Acalabrutinib 3. Venetoclax 4. Idelalisib 5. Zanubritinib

	6. Ponatinib 7. Enasidenib 8. Idelalisib 9. Zanubritinib 10. Midostaurin 11. Duvelisib	6. Inotuzumab Ozogamicin
Multiple Myeloma (MM)	1. Pomalidomide 2. Venetoclax 3. Carfilzomib 4. Daratumumab 5. Ixazomib 6. Elotuzumab 7. Panobinostat 8. Isatuximab 9. Cedazuridine + Decitabine 10. Midostaurin 11. Glasdegib 12. Selinexor 13. Belantamab Mafodotin	1. Pomalidomide 2. Carfilzomib 3. Daratumumab 4. Ixazomib 5. Elotuzumab 6. Panobinostat 7. Isatuximab 8. Selinexor 9. Belantamab Mafodotin

Table 7.11 displays the number of patients treated with new medicines calculated for each country by disease type. It also displays patient population estimates for the two other types of blood cancer (CLL, and MM) calculated for the US and UK for each year included in the analysis. Estimates ranged from 149,000 to 153,000 and 40,000 to 41,000 CLL patients, and 94,000 to 96,000 and 37,000 to 38,000 MM patients in the US and UK respectively. Results of Table 7.11 include estimates of the AML population previously calculated in Part 1 (see Table 7.4), and estimates of the AML population treated with new medicines previously calculated in Part 2 (see Table 7.9). These estimates are included for comparison with the other disease types.

The number of patients treated with new medicines increased over the period for all three cancer types, with particularly strong growth observed in CLL (an 85% increase in the US and a 178% increase in the UK between 2020 and 2024). In the US, the number of CLL patients treated rose from approximately [redacted] in 2020 to over [redacted] by 2024, while in the UK, the number nearly tripled from [redacted] to [redacted]. MM treatment uptake in the UK also more than doubled, increasing from [redacted] to [redacted] patients. In contrast, MM treatment numbers in the US remained relatively flat, fluctuating around [redacted] to [redacted]. For AML, treatment uptake grew more modestly, particularly in the UK, where treated patient numbers rose from [redacted] in 2020 to [redacted]

in 2024. Meanwhile, US AML patient treatment rose from [redacted] to over [redacted] during the same period.

Table 7.11: Number of Patients Treated with New Medicines and Patient Population by Disease Type

Blood Cancer Type	Country	Measure	2020	2021	2022	2023	2024
Acute Myeloid Leukemia (AML)	US	Patients Treated	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Patient Population	~70,000	~71,000	79,317 (NCI, 2025)	~80,000	~82,000
	UK	Patients Treated	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Patient Population	~9,525	~9,610	~9,720	~9,825	~9,925
Chronic lymphocytic leukemia (CLL)	US	Patients Treated	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Patient Population	~149,220	~149,445	~150,300	~151,560	~153,045
	UK	Patients Treated	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Patient Population	~40,236	~40,368	~40,506	~40,644	~40,776
Multiple Myeloma (MM)	US	Patients Treated	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Patient Population	~94,554	~94,619	~95,220	~96,288	~96,827
	UK	Patients Treated	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
		Patient Population	~37,902	~38,026	~38,128	~38,230	~38,332

Table 7.12 displays the percentage of CLL and MM patients treated with new medicines in the US and UK between 2020 and 2024. The percentage of AML patients treated with new medicines (calculated in Part 1, Table 7.4) is also included for comparison.

As noted in Part 2 (Section 7.3.3), the UK consistently lagged the US in treatment uptake for AML, though both countries showed gradual acceleration. In the US, the proportion of AML patients receiving new treatments increased from 14% in 2020 to 19% in 2024, while in the UK, it rose from 6% to 15% over the same period. CLL displayed more consistent and substantial growth in both countries. In the US, the percentage of CLL patients treated with new medicines

nearly doubled, rising from 16% to 30%. The UK also showed steady progress, increasing from 9% in 2020 to 24% in 2024, though it remained behind the US across all years. For MM, the US maintained the highest treatment percentages overall, starting at 40% in 2020 and ending at 38% in 2024, with minor fluctuations. In contrast, the UK demonstrated the most significant growth in MM treatment uptake, jumping from 13% in 2020 to 36% in 2024, indicating expanded access and adoption of new medicines.

Table 7.12: Percent of Blood Cancer Patients Treated with New Medicines in the US and UK by Disease Type

Blood Cancer Type	Country	2020	2021	2022	2023	2024
Acute Myeloid Leukemia (AML)	US	14%	16%	16%	18%	19%
	UK	6%	8%	13%	12%	15%
Chronic lymphocytic leukemia (CLL)	US	16%	20%	21%	25%	30%
	UK	9%	14%	18%	22%	24%
Multiple Myeloma (MM)	US	40%	37%	37%	35%	38%
	UK	13%	19%	26%	30%	36%

7.4.5 DISCUSSION

Data in Table 7.12 highlights meaningful differences in the uptake of new medicines across AML, CLL, and MM patients in the US and UK, revealing both cross-country and disease-specific trends in access to innovation. These results suggest growing access to and use of innovative treatments across all three blood cancers, but with lags in the UK. While the US continues to lead in uptake, particularly for CLL and MM, the UK closes the gap by the end of the five-year study period. This trend is especially apparent in MM patient utilization of new medicines, suggesting that this population may be especially impacted by delays in funding due to HTA.

CLL and MM show the highest levels of new medicine use, particularly in the US. By 2024, 30% of US CLL patients and 38% of US MM patients were treated with new medicines, reflecting a consistent upward trajectory over the five-year period. In the UK, uptake in both indications also increased but remained lower than the US, with 24% of CLL patients and 36% of MM patients treated with new medicines in 2024. The narrowing gap in MM suggests significant progress in UK utilization of new medicines, possibly driven by recent NICE approvals. The data supports earlier suggestions in Part 2 that while the UK generally lags the US by several years, uptake can accelerate once positive HTAs are in place.

Results of Chapter 7 indicate that new medicine use in the treatment of MM and CLL patients is more diverse in the US. New medicines like Blinatumomab, Bosutinib, Ponatinib, Enasidenib, Midostaurin, and Duvelisib were utilized in the US but not the UK for CLL patients. For MM patients, new medicines like Cedazuridine + Decitabine, Midostaurin, and Glasdegib were utilized in the US but not the UK. Diversity in product use could be caused by many aspects of a health care system including formulary design, reimbursement structures, clinical guidelines, and access to diagnostic tools, but continues to reflect reports in Chapter 5 of US physicians having a better ability to tailor care for individual patients.

Despite a broader range of new medicines available in the US, only 19% of AML patients in the US were treated with new medicines by 2024, compared to 15% in the UK. These figures suggest that access challenges like restrictive eligibility criteria, high treatment costs, or limited provider familiarity with new options may persist for AML patients in both systems.

7.4.6 LIMITATIONS

In Chapter 3, I identified limitations in the availability of certain IQVIA data for the UK, particularly with respect to medicine launch dates. Findings in Chapter 6 provide reassurance that IQVIA remains an appropriate and robust source of utilization data for both the UK and the US. The potential for reporting inaccuracies within the dataset should be acknowledged. While the analysis is

limited to newer medicines and may exclude older treatments launched prior to 2011 that are still in active clinical use.

Patients were counted once per product used. As noted above, cancer patients often receive multiple treatments over the course of their care, either as part of combination therapy or across successive lines of therapy. This presents a potential source of overestimation, particularly in Parts 2 and 3, which consider multiple products—some of which may be used by the same patient within a single year. By contrast, Part 1 focuses specifically on the use of Venetoclax among AML patients, reducing the impact of this limitation for that part of the analysis.

7.4.7 CONCLUSION

This analysis supports a theory that utilization of new medicines among certain patient groups (AML, MM, and CLL) is limited in the UK compared to the US. Access challenges exist in both nations, but the lag time shown in these results indicate that the role of HTA restricting government funding may contribute to delays in patient access. Although it is not possible to attribute these patterns solely to HTA within NHS England, these findings are consistent with results from earlier chapters, which indicate that HTA-driven funding restrictions may contribute to delays in access to new medicines and limit physician autonomy in England compared to the US. Utilization data analyzed in Chapter 7 suggest that US physicians do not naturally align their prescribing patterns with NICE cost effectiveness decisions but use a more diverse group of new medicines that may be better tailored to individual patient need.

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CHAPTER 8

Conclusion

8.1 Background

This thesis examined how the use of NICE HTAs to control medicine costs through England's NHS reimbursement process impacts patient access to new blood cancer medicines, drawing a comparative analysis with access patterns in the US. The US has a health care system based largely on private insurance (De Lew, Greenberg and Kinchen, 1992) and is associated with high health care costs per capita (The World Bank, 2025). Some argue this has led to minimal gains in life expectancy compared to other Organization for Economic Co-operation and Development (OECD) nations (Wager et al., 2025) and caused wage stagnation as employers limited earnings to pay for health insurance premiums (Hager et al., 2024). More importantly, the US Census Bureau reported that over 10% of US households had medical debt in years from 2017-2019 (Himmelstein et al., 2022). The US Centers for Disease Control reports that over 27 million Americans did not have health insurance in 2022 (National Center for Health Statistics, 2023).

Motivated by these economic and humane challenges, a cohort of American politicians have pushed forward major legislation intended to provide some basic level of universal care nearly every decade, often including a price negotiation policy to keep costs feasible in concert with expansive coverage.[31] In response, their opponents argue that quality and access to health care will decrease if cost is lowered (Andersen, 1994; Beauvais, 2021; Carroll, 2012), often citing a core framework developed by William Kissick, the Iron Triangle (Kissick, 1994 – see Chapter 3 and *Considering the Iron Triangle* below). President Biden's 2022 Inflation Reduction Act (IRA) initiated the practice of price negotiation in Medicare, setting the groundwork to negotiate drug prices for ten medicines currently funded by the program (H.R. 5376, 2022). More recently, a revised Most Favored Nation (MFN) policy was enacted in the US via an executive order on May 12, 2025 (Executive Order 14297, 2025), introducing international reference pricing as a tool in CMS negotiations. This includes direct

[31] For more on this, see Chapter 2 (Section 2.3 and 2.4).

consideration of England's drug prices. Understanding how patients in England are impacted by HTA is fundamental to inform developing policy on how HTA will be used in Medicare price negotiation.

8.2 Thesis Findings

My doctoral thesis sought to understand HTA impact on English patients' access to new blood cancer medicines and to compare this access with that of US Medicare patients. Using a mixed methods approach, I examined how HTA affects access across three key stages: product launch, government reimbursement, and real-world utilization. I began with a quantitative analysis of regulatory approvals and launch timelines. I used data from IQVIA and Pharmaprojects to identify 43 new blood cancer medicines launched from 2011-2020, comparing how quickly new blood cancer medicines enter the market in the US and UK. I found that while most products were approved in both countries, US patients typically gained access faster, with median launch delays of zero days following US FDA approval, compared to a 61-day median delay in the UK following EMA approval. Several UK launches experienced delays exceeding 200 days (and in some cases 600), possibly reflecting the added steps of HTA in the reimbursement decision processes. I also found notable inconsistencies between IQVIA and Pharmaprojects in how product indications and launch dates were reported, particularly in the UK, where data gaps were more common. These differences suggest that launch timing alone does not fully reflect access, and that relying solely on commercial datasets risks underestimating systemic delays. To improve accuracy, in Chapter 3 I manually validated drug approvals across regulatory sources and narrowed the analysis to medicines approved by both FDA and EMA.

I went on, in Chapter 4, to analyze reimbursement decisions from Medicare and NICE to judge how these impact coverage and funding. To remove potential confounding from different regulatory approvals, I analyzed reimbursement decisions for 34 new medicines approved by both the EMA and FDA. I found that while all new blood cancer medicines in this cohort were covered under US Medicare, only 65% received positive reimbursement decisions from NICE, thereby qualifying

them for NHS England funding. Among those approved by NICE, 47% had added restrictions that narrowed the patient population eligible for treatment compared to the EMA's broader approval. Coverage delays were also significant. NHS patients faced a median wait time of 3.67 years between EMA approval and NICE funding, whereas US Medicare patients experienced no delay due to automatic coverage following FDA approval. In some cases, delays exceeded five years, particularly for medicines with multiple TAs or those where NICE decisions came later in the process. These delays, combined with restricted coverage, suggest that NICE's reimbursement process creates meaningful access barriers for blood cancer patients in England. While Medicare covers a narrower population overall, its legal structure provides faster and more consistent coverage for newly approved medicines. Understanding the clinical implications and value of new medicines impacted by these delays, especially for patients who meet EMA criteria but are excluded from NHS coverage, was a key focus of the next stage of my research.

For the next stage, to bring in clinical context, I conducted qualitative interviews with hematologists and oncologists in England (n=10) and the US (n=9) to understand their experiences with prescribing new treatments, particularly in cases where access had been delayed or restricted. I aimed to understand and compare the experiences of physicians in these countries regarding the availability and funding of new cancer treatments by national health insurance programs. I found that physicians in both England and the US navigate significant systemic constraints that affect their ability to provide timely access to new blood cancer medicines, but in fundamentally different ways. In the US, physicians often operated with greater prescribing autonomy, allowing them to incorporate new treatments quickly based on their clinical judgment. That same autonomy came with burdensome administrative responsibilities, especially when dealing with insurance denials or delays, which many participants described as a significant distraction from their primary role as caregivers. In England, the structured nature of NHS protocols and the NICE appraisal process limited flexibility but promoted equity by standardizing treatment access across the population. Still, many English physicians reported frustration at being unable to offer promising treatments as they waited years for HTA approval,

especially for certain patient populations such as Acute Myeloid Leukemia (AML). In both systems, doctors described broadening their role by advocating for patients, navigating bureaucracy, and even contributing to economic evaluations to bridge the gap between what was clinically best for patients and what their health systems allowed. This tension between autonomy and equity was developed as an overarching theme, illustrating the ways in which physicians stretched the boundaries of their role to counterbalance the limitations of the systems they worked within.

Qualitative data provided important insight into how physicians experience and navigate access challenges in practice. To understand how these challenges affect patient access to new blood cancer medicine use on a larger scale, I carried out a scoping review to identify how researchers measure medicine access across health systems. I used these findings to guide a trends analysis of real-world drug use using IQVIA MIDAS data. This helped set a framework for the way in which policy decisions play out in actual prescribing patterns. The analysis of IQVIA MIDAS data from 2020 to 2024 showed that Venetoclax use among AML patients (who were flagged by physicians interviewed for Chapter 5 as experiencing additional access hurdles) is significantly higher in the UK than in the US, despite the US having a much larger AML population. While Venetoclax use has declined in the US, this may reflect increasing overall AML prevalence among ineligible populations and shifts to alternative standards of care. It also highlights significant access barriers such as insurance coverage and cost, as reported by US physicians interviewed for Chapter 5. In contrast, UK uptake doubled following two positive HTA decisions in early 2022, suggesting that patient access improves quickly once NICE approvals are granted.

The research in Chapter 7 found that the US also demonstrates greater diversity in AML treatment options, with several new medicines used widely in the US that were absent in the UK. This reflects qualitative reports (from interviewees - EN01, US02, US03, EN04, EN05, US05, EN07, EN08, EN09, EN10) indicating that US physicians can better tailor treatments to individual patients. Chapter 7 highlighted that when accounting for multiple new medicines, approximately 14–19% of US AML patients received innovative treatments by 2024, compared to 6–15% in the UK, supporting the

presence of a roughly four-year delay in UK adoption likely due to the HTA process. Similar patterns were observed for chronic lymphocytic leukemia (CLL) and multiple myeloma (MM), where the US leads in uptake, but the UK shows increasing access over time, narrowing the gap, particularly in MM.

Chapter 7 showed that despite broader availability of new medicines in the US, a minority of patients in both countries receive these medicines, indicating persistent access challenges influenced by regulatory delays, insurance barriers, and systemic factors. Overall, the findings suggest that HTA processes in the UK contributes to slower patient access, while US prescribing reflects a more diverse and rapidly evolving treatment landscape.

8.3 Considering the Iron Triangle

William Kissick's Iron Triangle of Health Care (see Chapter 1, Figure 1.1) argues that access, cost, and quality are in constant tension (Kissick, 1994). In this framework, attempts to lower prices through negotiation may raise concerns that patients will face limited treatment options or diminished care standards. While some authors have pushed back on this framework (Bernstein, 2018; Luellen, 2017; Niles, 2015), Kissick's basic argument remains a prominent theory in US health system literature (Andersen, 1994; Beauvais, 2021; Carroll, 2012; Services, 2021; Terry, 2017; Van der Goes et al., 2019). Medicare expansion inherently requires disciplined cost-saving measures like drug price negotiation, and critics argue that such measures would reduce the quality of and access to new medicines in the US. This thesis adds a useful piece of evidence in testing this criticism within the English system and helps understand how patient access to high quality, innovative new medicine might change in the US with the implementation of price negotiation through HTA.

Results of this thesis suggest that price negotiation mechanisms and HTA in England are correlated with reduced access to new blood cancer medicines compared to the US Medicare population. Chapters 3 and 4 show that new blood cancer medicines tend to launch and receive reimbursement more quickly in the US than in England. Chapter 7 builds on this by illustrating how those policy decisions translate into real-world utilization. In the case of Venetoclax for AML, uptake in the UK remained low until 2022, when two positive NICE appraisals led to a doubling in use, from

5% to 10% of AML patients, years after the drug was in broader use among Medicare patients in the US. Although use of Venetoclax declined in the US over time, this appears to reflect evolving clinical preferences and a shift toward other new treatments rather than reduced access. US prescribing patterns for AML were also more diverse: drugs such as Enasidenib and Glasdegib were commonly used in the US but were unavailable or rarely prescribed in the UK during the analysis period. Physician interviews in Chapter 5 contextualize these trends, with English physicians reporting frustration over access delays and limited treatment options, especially for complex or relapsed cases. US physicians described greater flexibility to tailor treatment plans to individual patient needs. These differences not only affect immediate access to new medicines but may compound over time, as regulatory and HTA applications increasingly rely on US comparators in trial data that are not yet available or funded in England. Taken together, these findings reflect the tensions outlined in Kissick's Iron Triangle, suggesting that while HTA may support cost control, it can also restrict access and limit therapeutic choice, which ultimately shapes perceptions of quality in patient care.

When the analysis is broadened to include the wider US population beyond Medicare beneficiaries, the applicability of Kissick's framework becomes more complex. Although Chapters 3 and 4 demonstrate longer delays and more restricted access to new blood cancer treatments in the UK, qualitative findings from Chapter 5 suggest that NHS physicians generally felt able to provide effective first-line treatment for most patients, particularly those with less complex cancer diagnoses. While certain diseases, such as MM, pose greater challenges in terms of access to newer medicines, English physicians consistently described being able to offer at least "some level of basic care" (EN10) or even "good care" (EN03) to nearly all patients, regardless of socioeconomic status. In contrast, US physicians frequently reported turning away uninsured patients "every day" (US08) because treatment costs were too high, regardless of clinical need. Access challenges also affected patients with private insurance, as financial and administrative obstacles often delayed treatment. Several US interviewees described spending extensive hours on the phone, navigating complicated authorization processes in attempting to secure access to appropriate medicines. These findings

complicate the narrative that broader drug availability in the US consistently leads to better care. While the NHS may limit access to high-cost medicines, it also protects patients from being excluded due to financial barriers, highlighting that affordability and equity are critical components of health care quality.

8.4 Strength and Weakness of the United States System

One of the key strengths of the US system highlighted in this thesis is its ability to deliver innovative treatments to patients more rapidly through earlier medicine launches and quicker reimbursement decisions. This enables physicians to adopt new medicines without delay, helping to push forward the standard of care in ways that can directly benefit patients. The availability of a wider range of medicines allows for more patient-centered care, where treatment decisions can be tailored to individual clinical profiles rather than being limited to a restricted set of approved options. Utilization data reported in Chapter 7 across AML, CLL, and MM indicated a greater diversity of medicines used in the US, and qualitative interviews with US physicians (Chapter 5) described a high degree of clinical autonomy in selecting treatments best suited to their patients' needs. This responsiveness, coupled with earlier access to emerging medicines, supports a system in which innovation is rapidly translated into practice, allowing patients to benefit from the latest advances in care. More broadly, the structure of the US health system plays a critical role in advancing the global standard of care by leading in pharmaceutical research and development. Many of the breakthroughs in treatment that shape cancer care worldwide are made possible by US-based investment, where pharmaceutical companies may be more willing to take financial risks knowing there is a direct pathway for reimbursement to recoup development costs after regulatory approval. Without this dynamic, many new medicines may never reach patients in the US or England.

This access comes at a considerable financial cost and may become unsustainable as the US population ages (Jones and Dolsten, 2024). As outlined in Chapter 2, Medicare, though expansive in its coverage of new treatments, operates without systematic price negotiation and remains heavily

dependent on taxpayer funding and premium contributions. Medicare Part A is financed primarily through payroll taxes, while Part B is supported by general revenues and enrollee premiums (Congressional Research Service, 2024). The 2025 Annual Report of the Medicare Trustees estimated that while the Hospital Insurance (HI) trust fund holds approximately $240 billion in reserves, it is projected to begin running deficits in 2028 and become insolvent by 2033 (Boards of Trustees of the Federal HI and Federal SMI Trust Funds, 2025). This raises serious questions about the long-term sustainability of a system that continues to absorb high drug prices without mechanisms to contain costs. Without reform, such as price negotiation or other cost-control practices, Medicare's current model may prove fiscally unsustainable as the population ages and the demand for expensive new medicine grows.

Another overriding weakness of the US system lies in the avoidable costs that are passed onto patients due to the absence of centralized coordination (NCCDPHP OHS, 2021). Unlike the NHS in England, which operates under a unified framework, the US system is fragmented across public and private payers, creating inefficiencies and administrative complexity (Sorum et al., 2023). As discussed in Chapter 5, physicians frequently described the significant administrative burden necessitated by navigating private insurance processes, with professional time and resources diverted toward securing authorizations and appealing coverage denials. This complexity contributes to higher overall system costs, much of which are ultimately borne by patients through higher premiums, co-pays, and delayed access to care (Alemayehu and Warner, 2004). At the same time, this fragmented structure supports a substantial segment of the US economy. Nearly one in every five dollars spent nationally is expended by the health care sector (Cox et al., 2024), including proliferation of intermediaries (such as benefit managers, claims processors, and administrative personnel) (Garg, 2020). While these "middlemen" may contribute to inefficiency, their role in sustaining the economic infrastructure of the health care industry cannot be overlooked. Proposals to introduce universal coverage or to consolidate administrative functions must not only address questions of justice and

access but also the broader economic implications of restructuring a system that supports millions of jobs and the current American health care structure.

8.5 Strength and Weakness of the English System

The English approach to medicine pricing, primarily led by NICE, offers a well-established model of transparency and cost containment. By applying consistent cost-effectiveness thresholds and early engagement with manufacturers and patient groups, NHS England has created a system that allows for predictable and equitable access to basic care across the population. The structure emphasizes transparency at all stages, from comparator selection to public consultation, and provides technical support to manufacturers, helping ensure methodological clarity and accountability. Overarching agreements like the voluntary scheme for branded medicines pricing and access (VPAS) ensure that NHS spending on pharmaceuticals remains within budgetary limits, preserving the financial sustainability of the public health system. These strategies allow the NHS to deliver broad access to essential medicines at lower overall costs to the system and taxpayers.

A key strength of this approach is its emphasis on equity. As highlighted in qualitative interviews in Chapter 5, English physicians reported high levels of public trust in the system and emphasized the benefits of shielding patients from the financial burden of treatment. This stands in sharp contrast to the US context, where participants described the emotional toll of denying care to uninsured patients and navigating complex reimbursement processes for those with private insurance. The absence of such barriers in the NHS framework simplifies care delivery as it promotes a more stable and equitable clinical environment.

The English system's strength in budgetary control is often counterbalanced by its limited agility. NICE prefers to consider randomized controlled trial (RCT) data, causing limited flexibility in accepting real-world data or indirect treatment comparisons. This can delay or prevent access to innovative treatments, particularly in rare diseases with an evolving standard of care as reported in Chapter 5. Lack of flexibility in interpreting evidence or accommodating long-term uncertainty can result in negative funding decisions, as seen in Chapter 4. This raises concerns about the long-term

attractiveness of the English market for investment in drug development. It may exacerbate evidence gaps as the US continues to lead innovation, the standard of care shifts, and clinical trials are developed with US comparators in mind. As a result, patients in England may experience significant delays in access to new medicines, while fewer drugs are launched and reimbursed relative to the US. While private care exists in the UK, the lack of NHS coverage likely discourages manufacturers from launching their products in England, limiting treatment options for patients across all care sectors. Because private care accounts for only a small fraction of the UK population, approximately 13% (Keith et al., 2024), manufacturers often deem the market unviable without NHS support. These structural barriers demonstrate how rigid cost-effectiveness thresholds and limited post-appraisal adaptability unintentionally hinders access to beneficial medicines, even in an otherwise well-organized universal system.

As described by participants in Chapter 5, physicians sometimes encounter situations in which lower-cost medicines offer superior clinical value for individual patients but are not reimbursed by NHS England due to prior negative NICE decisions. One significant inefficiency arises from the inflexibility of revisiting these decisions once patent exclusivity ends; if a product was denied reimbursement during its patented period, significant price reductions after patent expiry often fail to trigger re-evaluation, leaving clinically impactful and newly affordable medicines out of reach.

Another important structural limitation of the English system lies in its vulnerability to broader fiscal pressures. Unlike more decentralized systems, as in the US, the NHS is directly tied to annual government budgeting and thus may be more exposed to shifts in macroeconomic conditions. Comparative analyses of health spending trends, drawing on World Bank data (purchasing power parity-adjusted, current international dollars) and OECD recession indicators, reveal important structural differences in how the US and UK manage health care funding during periods of economic contraction (OECD, 2025; The World Bank, 2025). While both systems face financial pressures during recessions, the UK's centralized budgeting model can lead to noticeable slowdowns or even stagnation in per capita health expenditure growth. The US, despite critiques regarding inefficiency and inequity,

has demonstrated more consistent growth in health spending across economic cycles. This relative stability is partly due to the decentralized nature of the US system, which draws funding from a network of federal programs and private insurers, so is less directly influenced by annual budget negotiations. This resilience is not necessarily an indication of efficiency. It reflects a degree of structural insulation from executive control and short-term political decision making, which can preserve spending levels but may also entrench systemic waste and disparities. These patterns illustrate that health financing mechanisms are not simply economic instruments; they are also examples of national governance models and public values.

8.6 Limitations of the Research Undertaken for the Thesis

This thesis focuses specifically on access to blood cancer medicines. These medicines were chosen because of their complexity and high cost (Burns et al., 2016), which create challenges for HTA systems, but also because blood cancers themselves have seen some of the most dramatic advances in treatment in recent years (Haloupek, 2020). New medicines like CAR T-cell therapies offer potentially curative outcomes (Melenhorst, 2022) but also come with high price tags and may have limited long term clinical data at the time of HTA review. That combination makes them more formidable to fund in systems like NHS England, even when the clinical potential is clear. Focusing on blood cancers allowed for a more targeted comparison between countries, since a narrower lens helped control for variability in how different diseases are diagnosed and treated. It is important to acknowledge the limitations of focusing solely on blood cancers. The access barriers identified here may be more severe than in other cancer types or disease areas. In that sense, this thesis looked at a particularly high-stakes and high-friction part of the HTA system. Results here should not be assumed to apply across all cancer types, let alone all therapeutic areas. This narrow lens may have highlighted access challenges that are less likely to affect patients with conditions like strep throat or diabetes, which have inexpensive and highly effective treatment options. The intent of this thesis was to use blood cancers as a case study to understand how HTA can shape access to cutting-edge treatments, though it may reduce generalizability to other disease types. The findings in this thesis most relevant

to similar high-cost, high-uncertainty treatments and may not reflect the experience of patients with more common or less complex conditions.

This thesis was intended to focus entirely on Medicare patients, but Chapters 5, 6, and 7 expanded to include the entire US population. Consideration of lag in coverage and funding applied specifically to Medicare, without consideration of the uninsured and privately insured population. These are not small populations. The uninsured population in the US is an estimated 23.5 million people (Tolbert et al., 2024), while private insurance covers an estimated 180 million people (Shashikumar et al., 2024). Medicare was selected as a focus in this thesis as it provided a strong example of government insurance comparable to the NHS, though Medicare focuses on an older population while NHS England covers all age groups.

The cost of health care impacts American patients (Alemayehu and Warner 2004; Cox, Ortaliza, Wager, and Amin, 2024; Hager, Emanuel and Mozaffarian, 2024), and quantitative comparison in Chapters 3 and 4 should be read with this limitation in mind. During qualitative interviews in Chapter 5, US physicians regularly spoke about the access barriers they faced within the uninsured and privately insured populations. Utilization trends analysis in Chapter 7 included consideration of patient populations across the entire US. This was helpful for more precise investigation of the access barriers highlighted in Chapter 5 but did not include consideration of utilization specifically within the Medicare population. A need for further research in this area is discussed below.

8.7 Recommendations for Future Research

Building on the qualitative findings presented in Chapter 5, which captured physicians' experiences navigating access to new blood cancer treatments in the US and England, future research should explore the burden of treatment choice from the patient's perspective, particularly in relation to disparities in access to new cancer medicines. Qualitative interviews with patients could offer valuable insights into how individuals perceive and experience equity issues in health care, despite lacking technical knowledge of health systems. Patient-centered care during cancer therapy has been explored

in various contexts, including endocrine therapy (Yao, He and Tian, 2024; En-Nasery-de Heer et al., 2022) and radiotherapy (Bagga et al., 2024), while broader cancer care pathways and support mechanisms such as navigation have also been critically appraised (Chan et al., 2023). Current literature has begun to document patients' experiences navigating cancer care, providing important implications for understanding disparities in access to new treatments. Herb et al. (2022) identified key barriers to lung cancer care in the US, including financial toxicity, social constraints, and the importance of provider advocacy and trust. Johnson et al. (2025) focused on Black patients with endometrial cancer in Washington, D.C., revealing how delays, fragmented care, and limited treatment options contribute to inequities. In the UK context, Martins et al. (2019) highlighted how patients with primary bone cancer experienced disruptions to emotional, physical, and social well-being, with uneven access to rehabilitation services. Earlier work by Krishnasamy et al. (2007) also emphasized the evolving nature of patients' needs over time, especially highlighting diagnosis, communication, and coordination of care in lung cancer. Despite these contributions and Chapter 5's outline of systemic differences between the US and England from a physician perspective, patient voices remain underrepresented in the specific context of accessing novel cancer medicines. This is especially the case in comparative cross-national settings like the US and England. Future studies could address this gap by using observational methods like ethnographic fieldwork to enhance understanding of how access-related decisions are made in clinical and policy settings.

Supplemental research that would complement this work could measure patient impact by studying Medicare claims records in the US. Unlike the trends analysis in Chapter 7, this study would adjudicate the number of patients eligible for a new medicine under Medicare, who would not have been funded based on NHS HTA recommendations. This work would build on existing research on funding for medicine indicated for breast cancer (Sullivan et al., 2020). It would clarify the denominator of the trends analysis by identifying patients eligible for treatment according to

regulatory approval and National Comprehensive Cancer Network (NCCN) guidelines.[32] A research plan for such work, included in Confirmation of Status materials, was attempted during my DPhil. However, limitations in CMS data sharing, likely attributable to the current federal administration, prevented me accessing these data, which had previously been available under data use agreements.

Analyzing patient uptake after HTA approval provides valuable insights into the impact of HTA in England and enables comparisons with access in the US. Building on the methodology from a paper by Corbacho and colleagues (2020) titled *"Does the use of health technology assessment have an impact on the utilization of health care resources? Evidence from two European countries,"* a deeper understanding of new medicine uptake in England following HTA approval could be established. Corbacho et al. (2020) used monthly sales data from IQVIA MIDAS to compare centralized HTA in England with regional HTA in Spain, demonstrating that positive recommendations increase medicine use, though regional systems require strong coordination for consistent implementation (Corbacho et al., 2020). This study was identified in the scoping review in Chapter 6 as a key methodological reference for comparing patient access to new medicines after HTA approval. I aimed to conduct a similar analysis to investigate uptake of new medicines in England after positive HTA approval and to compare it to uptake in the US following Medicare funding. However, I was only able to secure access to annual sales data from IQVIA MIDAS, which lacked the necessary detail for this analysis.

Qualitative research in Chapter 5 highlighted that physicians in England often wait years for NHS funding of new blood cancer medicines, even after these treatments have become standard care in the US. Quantitative findings in Chapters 3 and 4 confirmed that England lags behind the US in launching and funding these medicines. Further research into actual patient uptake post-HTA approval would help confirm these findings. Comparing medicine uptake in the US and UK after funding decisions would also shed light on alternative (non-NHS England) routes to care when products are

[32] For more on NCCN guidelines, see Chapter 7 (Section 2.1).

not funded, as well as physician willingness to prescribe during HTA delays. Future studies showing high uptake of new medicines in England post-HTA approval compared to US Medicare uptake would refine understanding of patient demand and physician prescribing behavior for new blood cancer treatments nationwide.

8.8 Looking to the Future

US Medicare drug pricing policy is shifting rapidly due to the IRA (H.R. 5376, 2022), which enabled Medicare to negotiate prices for select high-cost drugs. This trend accelerated with the May 2025 executive order introducing international reference pricing (Executive Order 14297, 2025), explicitly linking US prices to countries like England. As shown in this thesis, England's long-standing use of HTA has helped contain costs while supporting equitable access to basic cancer care (Chapter 5). It has also likely contributed to delayed drug launches (Chapter 3), slower reimbursement timelines (Chapter 4), and limited blood cancer patient treatment options for more complex cases (Chapters 5 and 7). While US Medicare patients may benefit from faster access to innovation, the English system offers a model for cost control and equity. As Medicare adopts elements of HTA, recognizing both the strengths and shortcomings of England's approach is essential in shaping sustainable and patient-centered US Medicare policy (McKeown, 2024).

Ultimately, both the US and English systems exhibit distinct shortcomings and strengths. Policymakers in both nations have long pointed to the other as a model to emulate or as a cautionary tale to shape public opinion and advance specific health policy agendas. This thesis aimed to provide evidence by which to compare patient access to medicines in a space that is particularly impacted by price negotiation: blood cancer. In both systems, certain patients fare better (or worse) than their neighbors. For patients with straightforward cancer diagnoses, who may otherwise be uninsured by private plans, access to care may be timelier and more comprehensive within the equitable English NHS. For more complex or relapsed blood cancers, particularly those requiring new medicines, patients may be better served in the US system where treatment options are broader and clinical innovation is adopted more rapidly. An ideal health system can and has been defined in many ways

(Baretto, 2002; Loewy, 1998; McBride, 1985; Tomar and Cohen, 2010) but must reflect the values of its population. Depending on the lens through which a reader views the data in this thesis (equity, innovation, autonomy, patient-centered care) the US and English health systems can be judged by comparison. The central question that emerges is whether these policy structures ultimately reflect the values and priorities of the populations they must serve. My lens as an American certainly informs my interpretation of the data presented, including a personal sense of shock at learning some aspects of the English health system which I saw reflected in English colleagues as we discussed aspects of the US health system. The English universal model is not exactly right for the US and has significant access barriers like reduced physician autonomy and inflexibility. In 2020 most Americans surveyed said that they believed it was their government's responsibility to provide comprehensive health care coverage (Jones, 2020). The US is moving closer to Truman, Kennedy, and Johnson's vision[33] but has a unique opportunity to learn from England.

In completing this research, it became evident that the US delivers great value in leading the creation of new treatments for blood cancer patients and "pushing the field forward" (US02) through global scientific progress. This strength of the US health care system is often underappreciated, as it requires a level of clinical understanding that most healthy individuals hope never to need. At the same time, expert physicians working in this field who were interviewed and real-world data that were analyzed, indicated that more expansive universal health coverage options for US patients would widely increase access to new medicines. It is essential to develop US health system policy that promotes this goal while continuing to foster research, development, and access to new medicines.

[33] For more on this, see Chapter 2 (Section 2.3).

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THESIS APPENDIX

APPENDIX 3.1

A3.1: R Markdown File for Data Analysis in Chapter 3

2025-07-28

Data preparation

To begin the required packages are loaded

```
library(readxl)
library(dplyr)
```

```
##
## Attaching package: 'dplyr'

## The following objects are masked from 'package:stats':
##
##     filter, lag

## The following objects are masked from 'package:base':
##
##     intersect, setdiff, setequal, union
```

```
library(tidyr)
library(ggplot2)
```

The dataset for analysis is then loaded and checked

```
df <- read_excel("/Users/sarahmckeown/Desktop/Introduction/drug_date_comparison.xlsx")
#Load Excel data

class (df)
```

```
## [1] "tbl_df"     "tbl"        "data.frame"
```

```
#check Excel data
```

Data analysis

Validation of Data Sources

Investigate data avalability of country regulatory approval and launch dates for each source

```r
df <- df %>%
  mutate(
    IQVIA_Date = if_else(!is.na(IQVIA_Year) & !is.na(IQVIA_Month),
                         as.Date(paste0(IQVIA_Year, "-", IQVIA_Month, "-01")),
                         as.Date(NA)),
    Pharma_Date = if_else(!is.na(Pharma_Year) & !is.na(Pharma_Month),
                          as.Date(paste0(Pharma_Year, "-", Pharma_Month, "-01")),
                          as.Date(NA)),
    IQVIA_Available = !is.na(IQVIA_Date),
    Pharma_Available = !is.na(Pharma_Date),
    Availability = case_when(
      IQVIA_Available & Pharma_Available - "Present in both",
      IQVIA_Available & !Pharma_Available - "Only IQVIA",
      !IQVIA_Available & Pharma_Available - "Only Pharmaprojects",
      TRUE - "Absent in both"
    )
  )
#Create Date columns and availability flags

coverage_summary <- df %>%
  group_by(Date_Type, Availability) %>%
  summarise(Count = n(), .groups = "drop") %>%
  pivot_wider(names_from = Availability, values_from = Count, values_fill = 0)

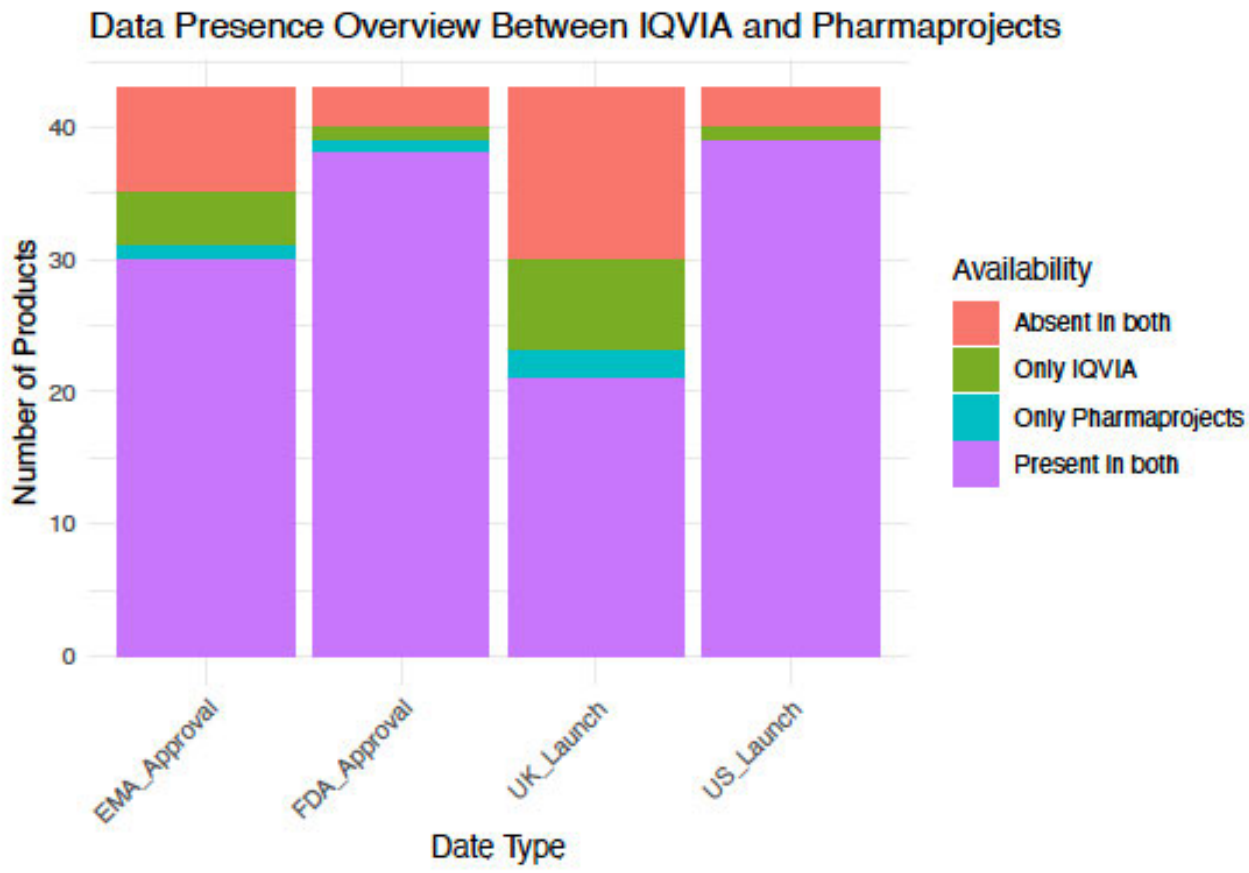
print(coverage_summary)
```

```
## # A tibble: 4 x 5
##   Date_Type    `Absent in both` `Only IQVIA` `Only Pharmaprojects`
##   <chr>                  <int>        <int>                  <int>
## 1 EMA_Approval               8            4                      1
## 2 FDA_Approval               3            1                      1
## 3 UK_Launch                 13            7                      2
## 4 US_Launch                  3            1                      0
## # i 1 more variable: `Present in both` <int>
```

```r
#Summarize counts by Date_Type and Availability
```

Check agreement Pharmaprojects and IQVIA by "Date Type"

```r
ggplot(df, aes(x = Date_Type, fill = Availability)) +
  geom_bar(position = "stack") +
  labs(
    title = "Data Presence Overview Between IQVIA and Pharmaprojects",
    x = "Date Type",
    y = "Number of Products",
    fill = "Availability"
  ) +
  theme_minimal() +
  theme(axis.text.x = element_text(angle = 45, hjust = 1))
```




```
#Create a stacked bar chart of data availability

library(lubridate)
```

```
##
## Attaching package: 'lubridate'

## The following objects are masked from 'package:base':
##
##     date, intersect, setdiff, union
```

```
#Account for interval and months functions

df_agree <- df %>%
  filter(IQVIA_Available & Pharma_Available)
#Filter to products where dates are present in both sources

df_agree <- df_agree %>%
  mutate(
    diff_months = interval(Pharma_Date, IQVIA_Date) %/% months(1),  # integer months difference
    diff_category = case_when(
      diff_months == 0 - "Same month",
      abs(diff_months) == 1 - "Different by one month",
      TRUE - "Different by more than one month"
    )
```

```
  )
#Calculate difference in months between Pharma_Date and IQVIA_Date

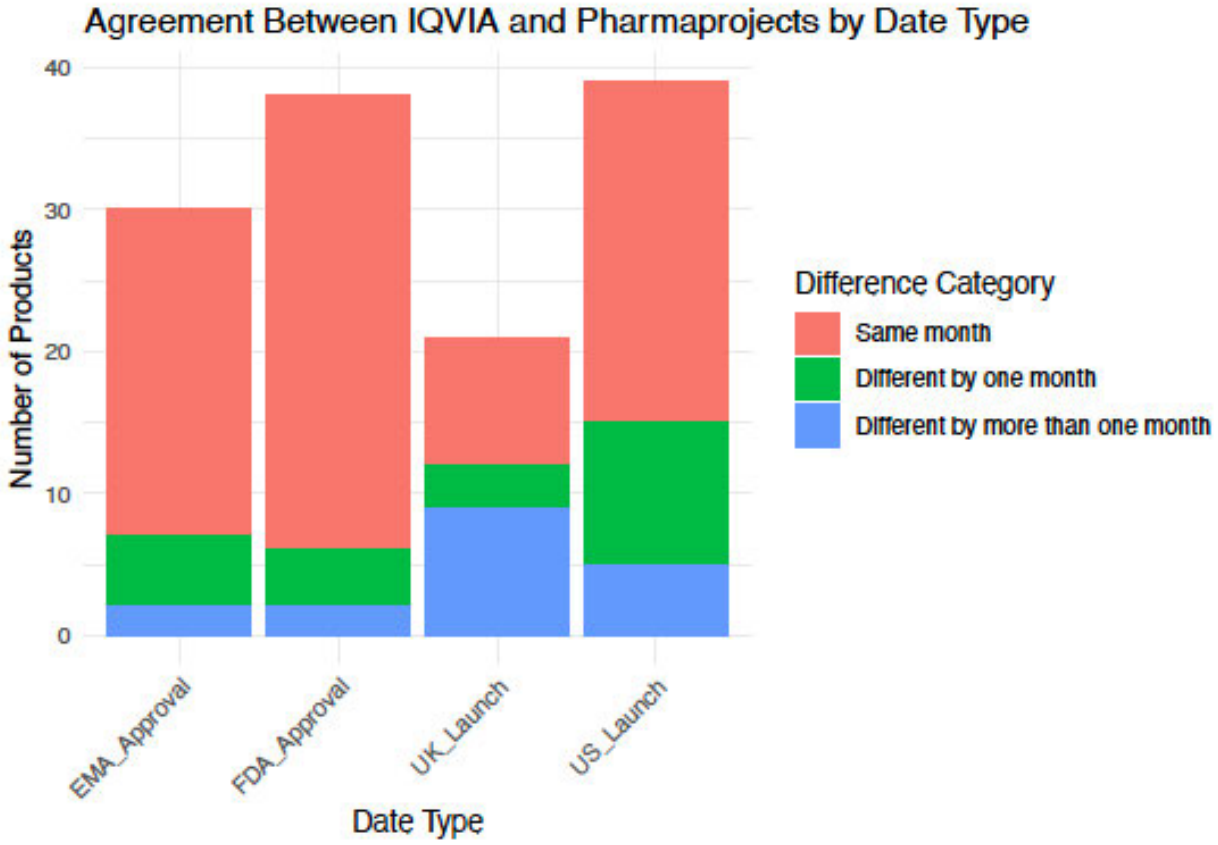
diff_summary <- df_agree %>%
  group_by(Date_Type, diff_category) %>%
  summarise(Count = n(), .groups = "drop") %>%
  group_by(Date_Type) %>%
  mutate(Percent = round(Count / sum(Count) * 100, 1))
print(diff_summary)
```

```
## # A tibble: 12 x 4
## # Groups:   Date_Type [4]
##    Date_Type    diff_category                    Count Percent
##    <chr>        <chr>                            <int>   <dbl>
##  1 EMA_Approval Different by more than one month     2     6.7
##  2 EMA_Approval Different by one month               5    16.7
##  3 EMA_Approval Same month                          23    76.7
##  4 FDA_Approval Different by more than one month     2     5.3
##  5 FDA_Approval Different by one month               4    10.5
##  6 FDA_Approval Same month                          32    84.2
##  7 UK_Launch    Different by more than one month     9    42.9
##  8 UK_Launch    Different by one month               3    14.3
##  9 UK_Launch    Same month                           9    42.9
## 10 US_Launch    Different by more than one month     5    12.8
## 11 US_Launch    Different by one month              10    25.6
## 12 US_Launch    Same month                          24    61.5
```

```
#Summarize counts and percentages by Date_Type and diff_category

df_agree$diff_category <- factor(df_agree$diff_category, levels = c("Same month", "Different by one mor

ggplot(df_agree, aes(x = Date_Type, fill = diff_category)) +
  geom_bar(position = "stack") +
  labs(
    title = "Agreement Between IQVIA and Pharmaprojects by Date Type",
    x = "Date Type",
    y = "Number of Products",
    fill = "Difference Category"
  ) +
  theme_minimal() +
  theme(axis.text.x = element_text(angle = 45, hjust = 1))
```




```
#Visualize with a stacked bar chart
```

Check date differences between Pharmaprojects and IQVIA

```
df_agree <- df %>%
  filter(IQVIA_Available & Pharma_Available)
# Filter to products where dates are present in both sources

df_agree <- df_agree %>%
  mutate(
    diff_months = interval(Pharma_Date, IQVIA_Date) %/% months(1),  # integer months difference
    diff_category = case_when(
      diff_months == 0 - "Same month",
      abs(diff_months) == 1 - "Different by one month",
      TRUE - "Different by more than one month"
    )
  )
# Calculate difference in months between Pharma_Date and IQVIA_Date

total_products <- nrow(df)
# Check total number of products in the full dataset

agree_counts <- df_agree %>%
  group_by(Date_Type) %>%
  summarise(Agree_Total = n(), .groups = "drop")
# Count total products where dates are available in both datasets by Date_Type
```

```r
summary_table <- df_agree %>%
  group_by(Date_Type, diff_category) %>%
  summarise(Count = n(), .groups = "drop") %>%
  left_join(agree_counts, by = "Date_Type") %>%
  mutate(
    Percent_Among_Total = round(Count / total_products * 100, 1),
    Percent_Among_Same_Date_Type = round(Count / Agree_Total * 100, 1)
  ) %>%
  select(Date_Type, diff_category, Count, Percent_Among_Total, Percent_Among_Same_Date_Type)
# Summarize counts and calculate percentages

print(summary_table)
```

```
## # A tibble: 12 x 5
##    Date_Type    diff_category   Count Percent_Among_Total Percent_Among_Same_D-1
##    <chr>        <chr>           <int>               <dbl>                  <dbl>
##  1 EMA_Approval Different by m-     2                 1.2                    6.7
##  2 EMA_Approval Different by o-     5                 2.9                   16.7
##  3 EMA_Approval Same month         23                13.4                   76.7
##  4 FDA_Approval Different by m-     2                 1.2                    5.3
##  5 FDA_Approval Different by o-     4                 2.3                   10.5
##  6 FDA_Approval Same month         32                18.6                   84.2
##  7 UK_Launch    Different by m-     9                 5.2                   42.9
##  8 UK_Launch    Different by o-     3                 1.7                   14.3
##  9 UK_Launch    Same month          9                 5.2                   42.9
## 10 US_Launch    Different by m-     5                 2.9                   12.8
## 11 US_Launch    Different by o-    10                 5.8                   25.6
## 12 US_Launch    Same month         24                14                     61.5
## # i abbreviated name: 1: Percent_Among_Same_Date_Type
```

```r
# Print the summarized table
```

Bland-Altman analysis of date differences

```r
bland_altman_stats <- df_agree %>%
  group_by(Date_Type) %>%
  summarise(
    Mean_Diff = round(mean(diff_months), 2),
    SD_Diff = round(sd(diff_months), 2),
    Lower_LOA = round(Mean_Diff - 1.96 * SD_Diff, 2),
    Upper_LOA = round(Mean_Diff + 1.96 * SD_Diff, 2),
    .groups = "drop"
  )
#run Bland-Altman
print(bland_altman_stats)
```

```
## # A tibble: 4 x 5
##   Date_Type    Mean_Diff SD_Diff Lower_LOA Upper_LOA
##   <chr>            <dbl>   <dbl>     <dbl>     <dbl>
## 1 EMA_Approval      0.47    7.06    -13.4      14.3
## 2 FDA_Approval      0.97    4.86     -8.56     10.5
## 3 UK_Launch        -1.62    3.34     -8.17      4.93
## 4 US_Launch        -0.62    1.79     -4.13      2.89
```

```
# Print the summarized table
```

Assessing approval and launch timing as a measure of patient access

```
library(dplyr)

# create varables for total number of products
total_products <- df %>%
  distinct(Product) %>%
  nrow()

# FDA approvals
fda_approved <- df %>%
  filter(Date_Type == "FDA_Approval" & !is.na(IQVIA_Date)) %>%
  distinct(Product) %>%
  nrow()

# EMA approvals
ema_approved <- df %>%
  filter(Date_Type == "EMA_Approval" & !is.na(IQVIA_Date)) %>%
  distinct(Product) %>%
  nrow()

# Approved in both FDA and EMA
both_approved <- df %>%
  filter(Date_Type %in% c("FDA_Approval", "EMA_Approval") & !is.na(IQVIA_Date)) %>%
  group_by(Product) %>%
  summarise(Approval_Count = n_distinct(Date_Type), .groups = "drop") %>%
  filter(Approval_Count == 2) %>%
  nrow()

# Build summary table
table5 <- tibble(
  Category = c(
    "Total Products",
    "Approved in US (FDA)",
    "Approved in UK (EMA)",
    "Approved in both US and UK"
  ),
  Count = c(
    total_products,
    fda_approved,
    ema_approved,
    both_approved
  ),
  Percentage = round(c(
    1.00,
    fda_approved / total_products,
    ema_approved / total_products,
    both_approved / total_products
  ) * 100, 1)
)
```

```
print(table5)
```

```
## # A tibble: 4 x 3
##   Category                  Count Percentage
##   <chr>                     <int>      <dbl>
## 1 Total Products               43      100
## 2 Approved in US (FDA)         39       90.7
## 3 Approved in UK (EMA)         34       79.1
## 4 Approved in both US and UK   32       74.4
```

Calculating time from regulatory approval to market launch

```
# Load libraries
library(tidyverse)
```

```
## -- Attaching core tidyverse packages ------------------------ tidyverse 2.0.0 --
## v forcats 1.0.0     v stringr 1.5.1
## v purrr   1.1.0     v tibble  3.3.0
## v readr   2.1.5
## -- Conflicts ------------------------------------------ tidyverse_conflicts() --
## x dplyr::filter() masks stats::filter()
## x dplyr::lag()    masks stats::lag()
## i Use the conflicted package (<http://conflicted.r-lib.org/>) to force all conflicts to become err
```

```
library(lubridate)
library(readxl)

# Read the Excel file
df <- read_excel("/Users/sarahmckeown/Desktop/Introduction/drug_date_comparison.xlsx")
glimpse(df)
```

```
## Rows: 172
## Columns: 6
## $ Product      <chr> "acalabrutinib", "acalabrutinib", "acalabrutinib", "acala-
## $ Date_Type    <chr> "FDA_Approval", "EMA_Approval", "UK_Launch", "US_Launch",-
## $ IQVIA_Year   <dbl> 2017, 2020, 2020, 2017, 2014, NA, NA, 2014, 2014, 2015, 2-
## $ IQVIA_Month  <dbl> 10, 11, 9, 11, 7, NA, NA, 7, 12, 11, 12, 12, 9, 3, 6, 9, -
## $ Pharma_Year  <dbl> 2017, 2020, 2021, 2017, 2014, NA, NA, 2014, 2014, 2015, 2-
## $ Pharma_Month <dbl> 10, 11, 6, 11, 8, NA, NA, 8, 12, 11, 12, 12, 9, 3, 6, 11,-
```

```
# Create a unified Date column from IQVIA_Year and IQVIA_Month
df <- df %>%
  mutate(
    Date = if_else(!is.na(IQVIA_Year) & !is.na(IQVIA_Month),
                   paste0(IQVIA_Year, "-", str_pad(IQVIA_Month, 2, pad = "0"), "-01"),
                   NA_character_),
    Date = as.Date(Date)
  )
```

```r
# Pivot data to wide format
df_wide <- df %>%
  select(Product, Date_Type, Date) %>%
  pivot_wider(names_from = Date_Type, values_from = Date)

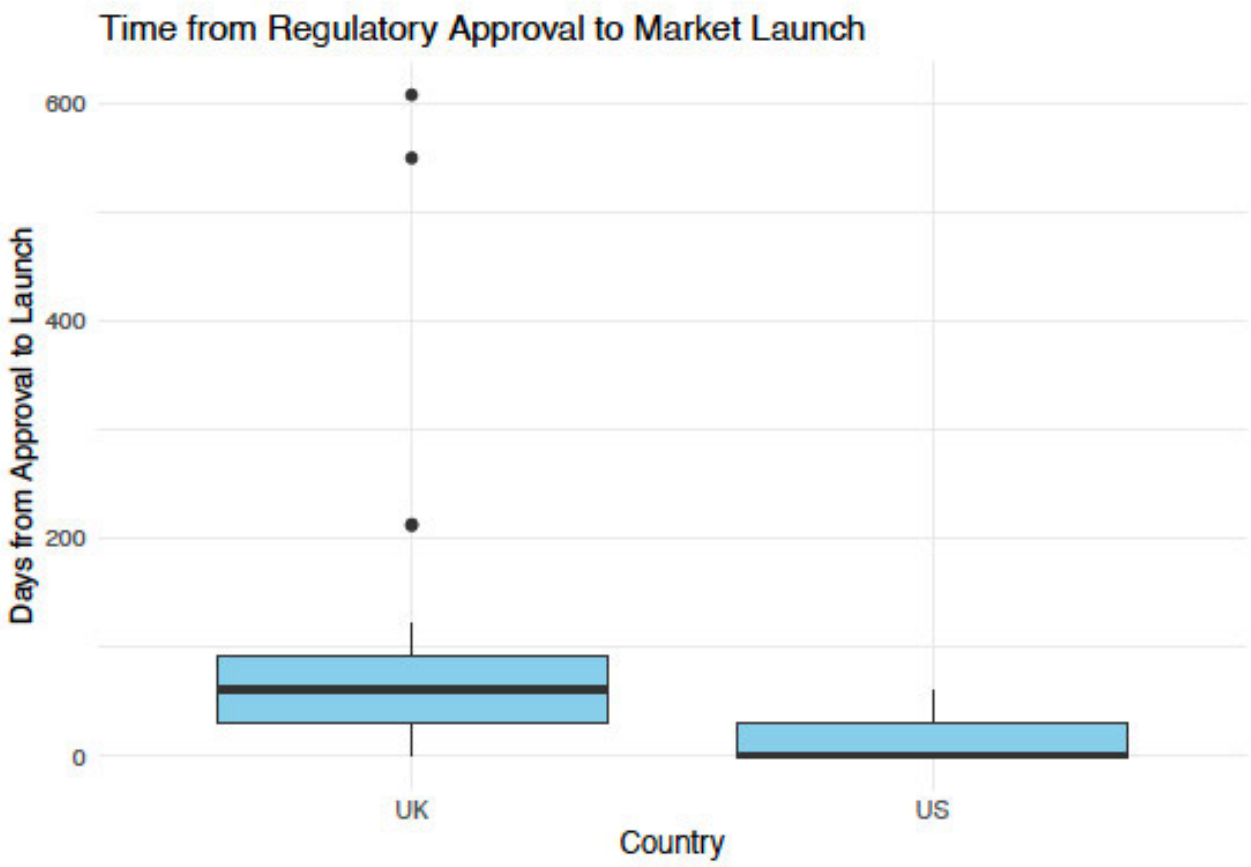
# Keep only rows with both FDA and EMA approvals
df_both <- df_wide %>%
  filter(!is.na(FDA_Approval) & !is.na(EMA_Approval))

# Calculate time from approval to launch
df_both <- df_both %>%
  mutate(
    Time_US = as.numeric(difftime(US_Launch, FDA_Approval, units = "days")),
    Time_UK = as.numeric(difftime(UK_Launch, EMA_Approval, units = "days")),
    Time_US = if_else(Time_US < 0, NA_real_, Time_US),
    Time_UK = if_else(Time_UK < 0, NA_real_, Time_UK)
  )

# Summary statistics
summary_stats <- df_both %>%
  summarise(
    Mean_US_Delay = mean(Time_US, na.rm = TRUE),
    Median_US_Delay = median(Time_US, na.rm = TRUE),
    Mean_UK_Delay = mean(Time_UK, na.rm = TRUE),
    Median_UK_Delay = median(Time_UK, na.rm = TRUE),
    Count = n()
  )

# Prepare long format data for plotting
df_long <- df_both %>%
  select(Product, Time_US, Time_UK) %>%
  pivot_longer(cols = c(Time_US, Time_UK),
               names_to = "Country",
               values_to = "LaunchDelay") %>%
  mutate(Country = recode(Country, Time_US = "US", Time_UK = "UK")) %>%
  filter(!is.na(LaunchDelay))

# Boxplot
ggplot(df_long, aes(x = Country, y = LaunchDelay)) +
  geom_boxplot(fill = "skyblue") +
  labs(
    title = "Time from Regulatory Approval to Market Launch",
    y = "Days from Approval to Launch", x = "Country"
  ) +
  theme_minimal()
```




```
# Wilcoxon signed-rank test (paired)
wilcox_test_result <- wilcox.test(df_both$Time_US, df_both$Time_UK,
                                  paired = TRUE, na.action = na.omit)
```

```
## Warning in wilcox.test.default(df_both$Time_US, df_both$Time_UK, paired = TRUE,
## : cannot compute exact p-value with ties
```

```
## Warning in wilcox.test.default(df_both$Time_US, df_both$Time_UK, paired = TRUE,
## : cannot compute exact p-value with zeroes
```

```
print(wilcox_test_result)
```

```
##
##  Wilcoxon signed rank test with continuity correction
##
## data:  df_both$Time_US and df_both$Time_UK
## V = 0, p-value = 9.03e-05
## alternative hypothesis: true location shift is not equal to 0
```

```
# Create summary table by country and metric
summary_by_country <- df_both %>%
  summarise(
    N_US = sum(!is.na(Time_US)),
    Mean_US = mean(Time_US, na.rm = TRUE),
```

```
    Median_US = median(Time_US, na.rm = TRUE),
    SD_US = sd(Time_US, na.rm = TRUE),
    Min_US = min(Time_US, na.rm = TRUE),
    Max_US = max(Time_US, na.rm = TRUE),

    N_UK = sum(!is.na(Time_UK)),
    Mean_UK = mean(Time_UK, na.rm = TRUE),
    Median_UK = median(Time_UK, na.rm = TRUE),
    SD_UK = sd(Time_UK, na.rm = TRUE),
    Min_UK = min(Time_UK, na.rm = TRUE),
    Max_UK = max(Time_UK, na.rm = TRUE)
  ) %>%
  pivot_longer(cols = everything(),
               names_to = c("Metric", "Country"),
               names_sep = "_") %>%
  pivot_wider(names_from = Country, values_from = value)

# Print and write to CSV
print(summary_by_country)
```

```
## # A tibble: 6 x 3
##   Metric    US    UK
##   <chr>  <dbl> <dbl>
## 1 N       31     23
## 2 Mean    16.6  109.
## 3 Median   0     61
## 4 SD      19.0  159.
## 5 Min      0      0
## 6 Max     61    608
```

```
write_csv(summary_by_country, "approval_to_launch_summary.csv")
```

APPENDIX 3.2

Table A3.2: Total List of Products Resulting from Pharmaprojects and IQVIA Search

Molecule	Brand	Company	Global Launch Year	IQVIA Search Results	Pharmaprojects Search Result	Reason for Exclusion
nivolumab	OPDIVO	BRISTOL-MYERS SQB.	2014	X	X	NA
acalabrutinib	CALQUENCE	ASTRAZENECA	2017	X	X	NA
belinostat	BELEODAQ	AUROBINDO	2014	X	X	NA
blinatumomab	BLINCYTO	AMGEN	2014	X	X	NA
bosutinib	BOSULIF	PFIZER	2012	X	X	NA
brentuximab vedotin	ADCETRIS	SEATTLE GENETICS	2011	X	X	NA
carfilzomib	KYPROLIS	AMGEN	2012	X	X	NA
copanlisib	ALIQOPA	BAYER	2017	X	X	NA
daratumumab	DARZALEX	JOHNSON & JOHNSON	2015	X	X	NA
elotuzumab	EMPLICITI	BRISTOL-MYERS SQB.	2015	X	X	NA
enasidenib	IDHIFA	BRISTOL-MYERS SQB.	2017	X	X	NA
ibrutinib	IMBRUVICA	ABBVIE	2013	X	X	NA
idelalisib	ZYDELIG	GILEAD SCIENCES	2014	X	X	NA
ixazomib	NINLARO	TAKEDA	2015	X	X	NA
panobinostat	FARYDAK	NOVARTIS	2015	X	X	NA
pomalidomide	POMALIDOMIDE CELGE	BRISTOL-MYERS SQB.	2012	X	X	NA
ponatinib	ICLUSIG	TAKEDA	2013	X	X	NA
venetoclax	VENCLEXTA	ABBVIE	2016	X	X	NA
pixantrone	PIXUVRI	SERVIER	2012	X		NA
forodesine	MUNDESINE	MUNDIPHARMA INT	2017	X		NA
mogamulizumab	POTELIGEO	KYOWA HAKKO KIRIN	2012	X	X	NA
axicabtagene ciloleucel	YESCARTA	GILEAD SCIENCES	2017	X	X	NA
inotuzumab ozogamicin	BESPONSA	PFIZER	2017	X	X	NA
midostaurin	RYDAPT	NOVARTIS	2016	X	X	NA
tisagenlecleucel	KYMRIAH	NOVARTIS	2017	X	X	NA
duvelisib	COPIKTRA	VERASTEM	2018	X	X	NA
ivosidenib	TIBSOVO	AGIOS	2018	X	X	NA
moxetumomab pasudotox	LUMOXITI	INTE PHARMA	2018	X	X	NA
gilteritinib	XOSPATA	ASTELLAS PHARMA	2018	X	X	NA
glasdegib	DAURISMO	PFIZER	2018	X	X	NA
polatuzumab vedotin	POLIVY	ROCHE	2019	X	X	NA
tagraxofusp	ELZONRIS	MERINI	2019	X		NA
quizartinib	VANFLYTA	DAIICHI SANKYO	2019	X		NA
selinexor	XPOVIO	KARYOPHARM THERAPE	2019	X	X	NA
belantamab mafodotin	BLENREP	GLAXOSMITHKLINE	2020	X	X	NA
brexucabtagene autoleucel	TECARTUS	GILEAD SCIENCES	2020	X	X	NA
cedazuridine#decitabine	INQOVI	OTSUKA	2020	X	X	NA
isatuximab	SARCLISA	SANOFI	2019	X	X	NA
tafasitamab	MONJUVI	MORPHOSYS US	2020	X	X	NA
zanubrutinib	BRUKINSA	BEIGENE	2019	X	X	NA
pembrolizumab	KEYTRUDA	MERCK & CO	2014	X	X	NA
crizogtinib	XALKORI	PFIZER	2011		X	NA
obinutuzumab	GAZYVA	ROCHE	2013		X	NA
luspatercept	REBLOZYL	BRISTOL-MYERS SQB.	2019		X	Not indicated for blood cancer treatment
tazemetostat	TAZVERIK	IPSEN	2020		X	Not indicated for blood cancer treatment
crisantaspase	ERWINASE	PORTON	1985		X	Launch year
omacetaxine mepesuccinate	SYNRIBO	TEVA PHARMACEUTICAL	2000		X	Launch year

APPENDIX 4.1

A4.1: R Markdown File for Data Analysis in Chapter 4

2025-07-26

Data preparation

To begin the required packages are loaded

```
library(readxl)
library(survival)
library(data.table)
```

The dataset for analysis is then loaded

```
setwd("/Users/sarahmckeown/Desktop/Chapter 2 Quant")
# Set working directory as required to navigate to file Nice Funding Manuscript

NICE_NUMBERS <- read_excel("NICE NUMBERS 07242025.xlsx")
# Final data file opened and given shorter name
```

Data analysis

Overall curve construction

The Kaplin Meiers curve for the overall data is constructed first

```
# A data table of positive indications is produced
dtx <- subset(NICE_NUMBERS, Regulatory_approval==1 & tech_appraisal_done ==1)

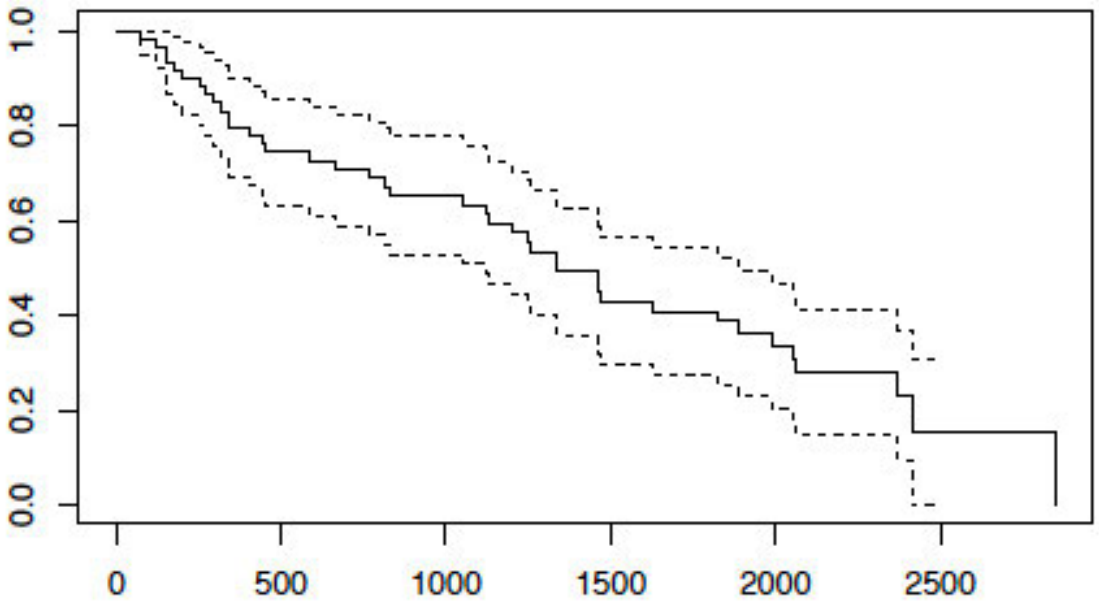
# The Kaplin Meier curve is then constructed from this table
S <- with(dtx, Surv(from_time0,recommended))
km <- survfit(S ~ 1,conf.type = 'plain')

# The summary table of the curve is called
km
```

```
## Call: survfit(formula = S ~ 1, conf.type = "plain")
##
##       n events median 0.95LCL 0.95UCL
## [1,] 62     40   1339    1119    1886
```

```
# As is the plot of the curve

plot(km)
```



Analysing indications

Having established this overall curve the effect of indication number is analyzed

```
# We first subset our data into tables of each indication number
dtx1 <- subset(NICE_NUMBERS, Regulatory_approval==1 & indication ==
1)
# This creates a data table including those treatments with regulatory approval and first indication
dtx2 <- subset(NICE_NUMBERS, Regulatory_approval==1 & indication ==
2)
# This creates a data table including those treatments with regulatory approval and second indication
dtx3 <- subset(NICE_NUMBERS, Regulatory_approval==1 & indication ==
3)
# This creates a data table including those treatments with regulatory approval and third indication
dtx4 <- subset(NICE_NUMBERS, Regulatory_approval==1 & indication ==
4)
# This creates a data table including those treatments with regulatory approval and fourth indication
dtx5 <- subset(NICE_NUMBERS, Regulatory_approval==1 & indication ==
5)
# This creates a data table including those treatments with regulatory approval and fifth indication
dtx6<- subset(NICE_NUMBERS, Regulatory_approval==1 & indication ==
6)
# This creates a data table including those treatments with regulatory approval and sixth indication
dtx7 <- subset(NICE_NUMBERS, Regulatory_approval==1 & indication ==
7)
```

```
# This creates a data table including those treatments with regulatory approval and seventh indication
dtx8 <- subset(NICE_NUMBERS, Regulatory_approval==1 & indication ==
8)
# This creates a data table including those treatments with regulatory approval and eigth indication
```

Once data tables are prepared a kaplin meier curve is constructed for first and higher indications

```
# Curves are constructed using the subsetted data tables produced above

# The method for curve construction of indications was the same as our overall curve
S1 <- with(dtx1, Surv(from_time0,recommended))
km1 <- survfit(S1 ~ 1,conf.type = 'plain')

S2 <- with(dtx2, Surv(from_time0,recommended))
km2 <- survfit(S2 ~ 1,conf.type = 'plain')

S3 <- with(dtx3, Surv(from_time0,recommended))
km3 <- survfit(S3 ~ 1,conf.type = 'plain')

S4 <- with(dtx4, Surv(from_time0,recommended))
km4 <- survfit(S4 ~ 1,conf.type = 'plain')

S5 <- with(dtx5, Surv(from_time0,recommended))
km5 <- survfit(S5 ~ 1,conf.type = 'plain')

S6 <- with(dtx6, Surv(from_time0,recommended))
km6 <- survfit(S6 ~ 1,conf.type = 'plain')

S7 <- with(dtx7, Surv(from_time0,recommended))
km7 <- survfit(S7 ~ 1,conf.type = 'plain')

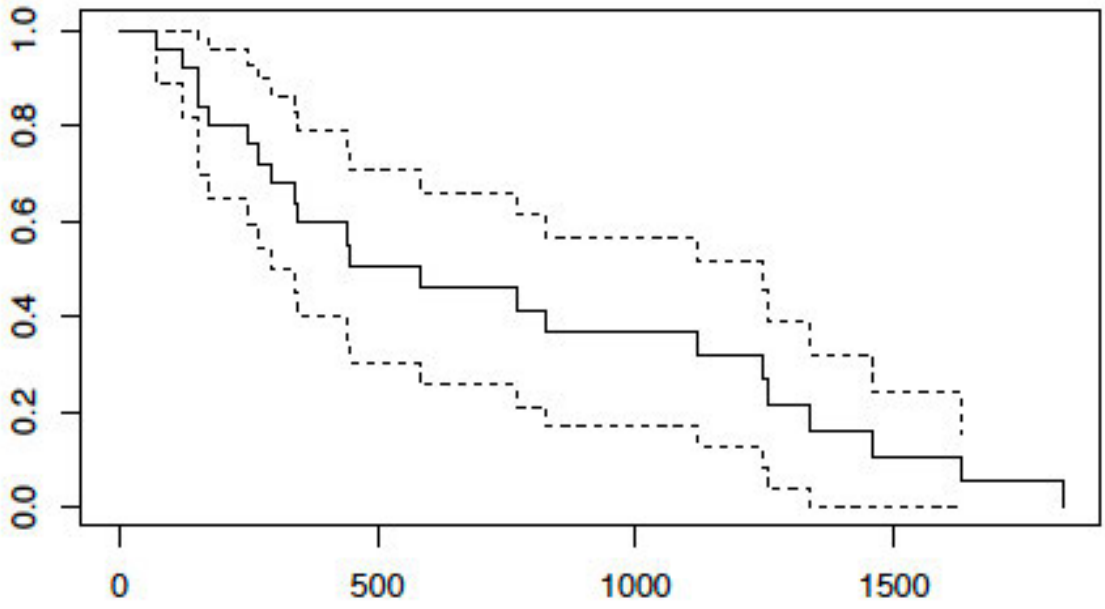
S8 <- with(dtx8, Surv(from_time0,recommended))
km8 <- survfit(S8 ~ 1,conf.type = 'plain')
```

```
# Each Kaplin Meier output table and plot is called for each indication

km1
```

```
## Call: survfit(formula = S1 ~ 1, conf.type = "plain")
##
##       n events median 0.95LCL 0.95UCL
## [1,] 28     22    583     293    1246
```

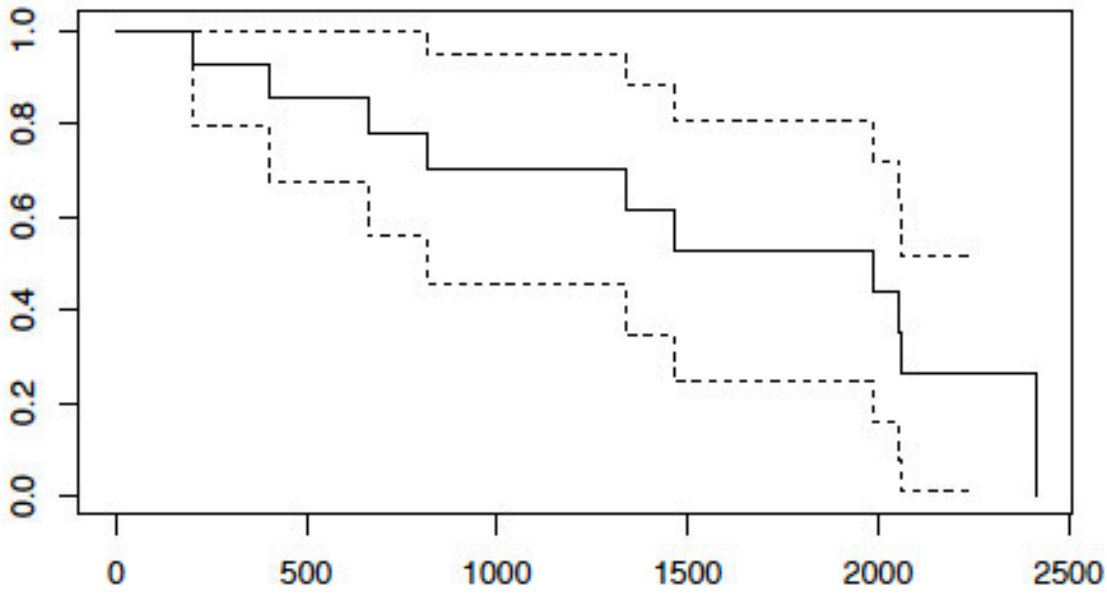
```
plot(km1)
```




```
km2
```

```
## Call: survfit(formula = S2 ~ 1, conf.type = "plain")
##
##       n events median 0.95LCL 0.95UCL
## [1,] 14     10   1987     815      NA
```

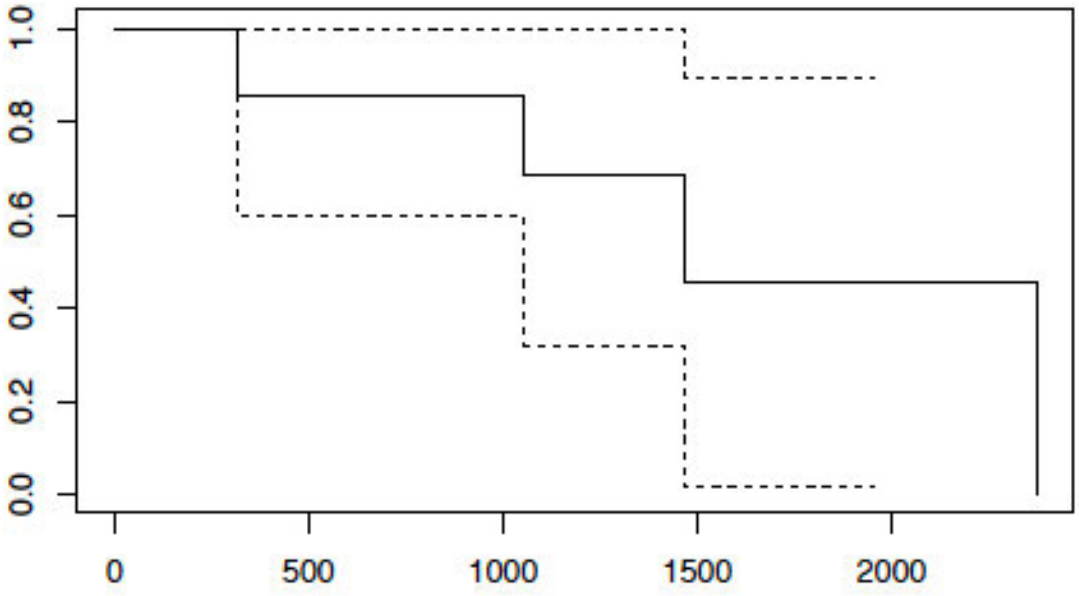
```
plot(km2)
```




```
km3
```

```
## Call: survfit(formula = S3 ~ 1, conf.type = "plain")
##
##      n events median 0.95LCL 0.95UCL
## [1,] 7      4   1466    1055      NA
```

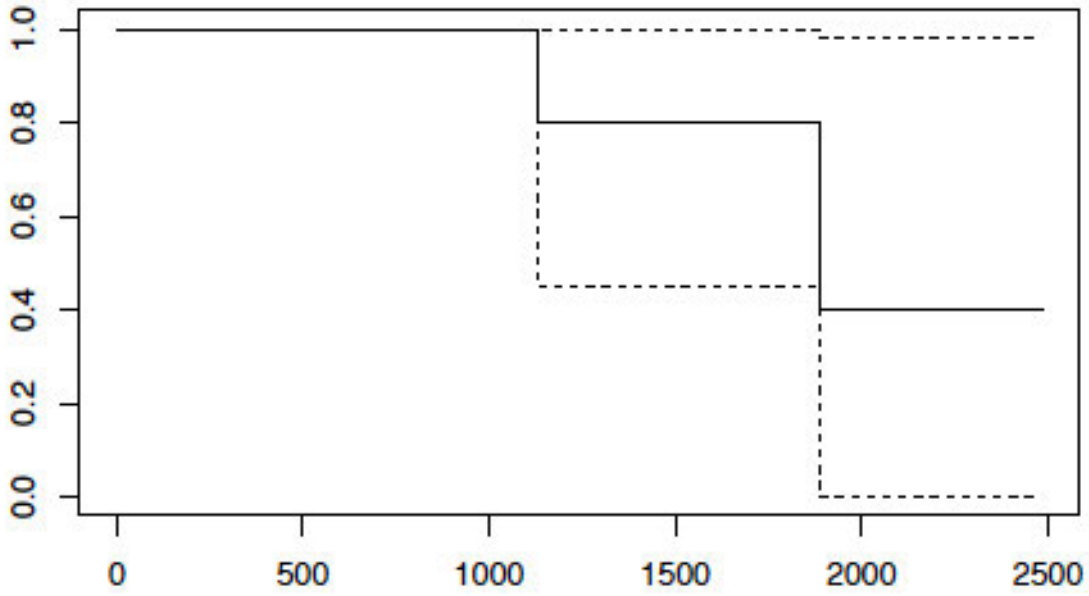
```
plot(km3)
```




```
km4
```

```
## Call: survfit(formula = S4 ~ 1, conf.type = "plain")
##
##      n events median 0.95LCL 0.95UCL
## [1,] 5      2   1886    1128      NA
```

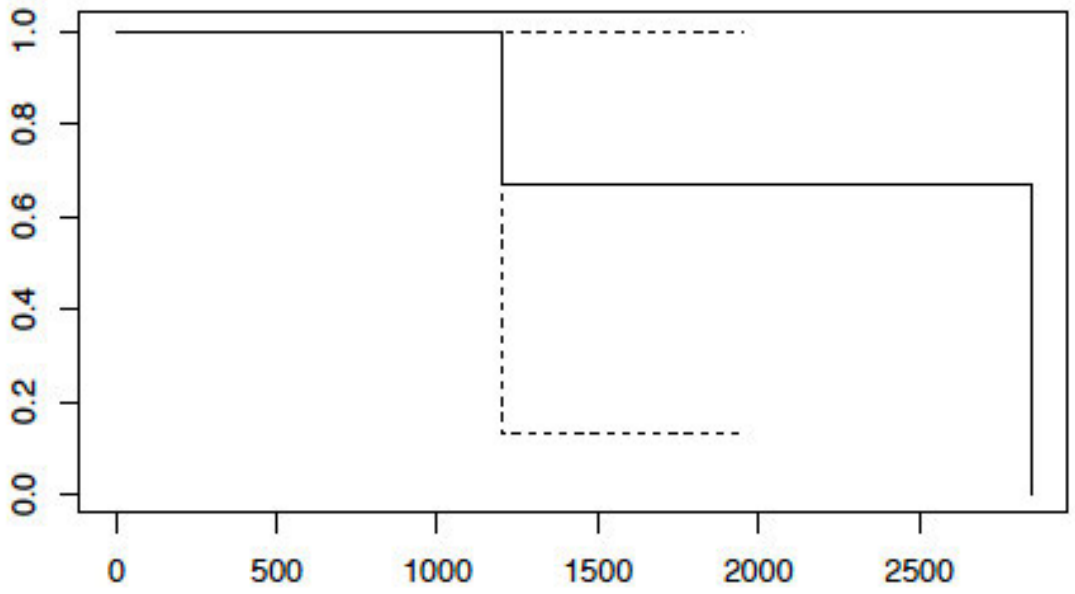
```
plot(km4)
```




```
km5
```

```
## Call: survfit(formula = S5 ~ 1, conf.type = "plain")
##
##      n events median 0.95LCL 0.95UCL
## [1,] 3      2   2848    1198      NA
```

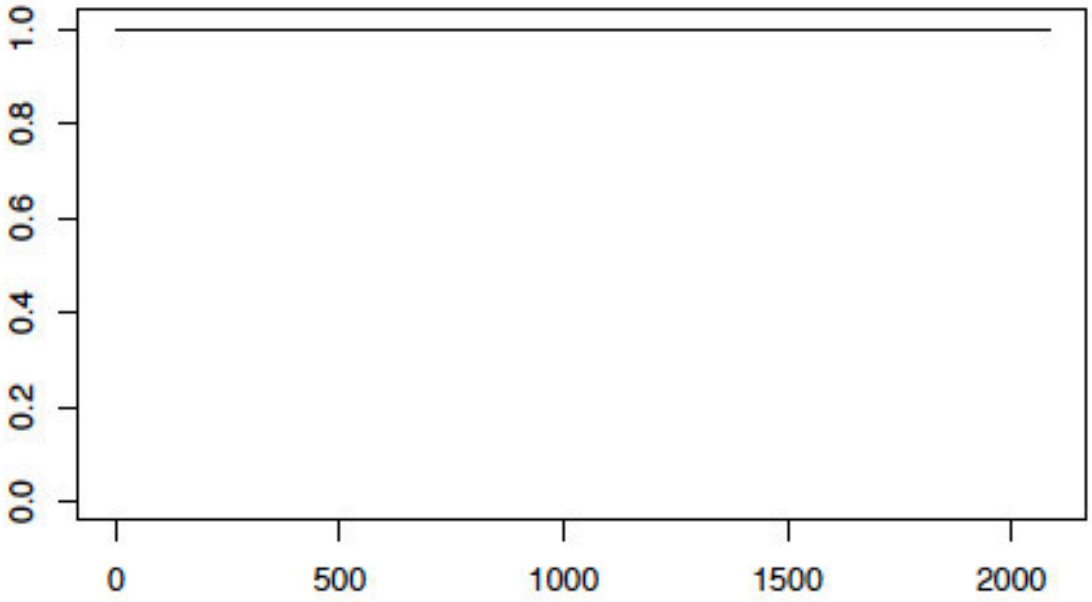
```
plot(km5)
```




```
km6
```

```
## Call: survfit(formula = S6 ~ 1, conf.type = "plain")
##
##      n events median 0.95LCL 0.95UCL
## [1,] 2      0     NA      NA      NA
```

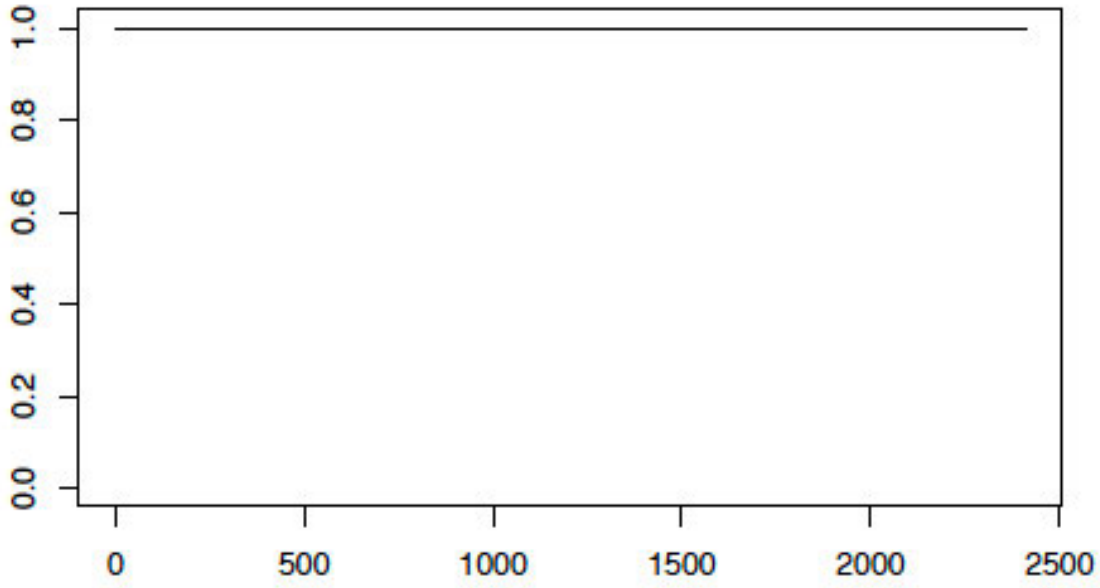
```
plot(km6)
```




```
km7
```

```
## Call: survfit(formula = S7 ~ 1, conf.type = "plain")
##
##      n events median 0.95LCL 0.95UCL
## [1,] 2      0     NA      NA      NA
```

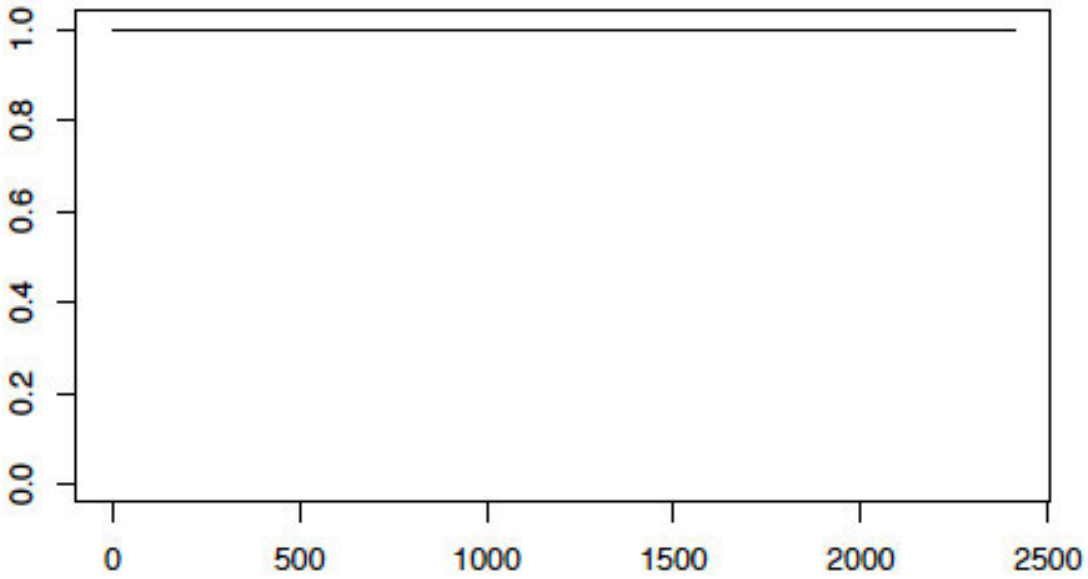
```
plot(km7)
```




```
km8
```

```
## Call: survfit(formula = S8 ~ 1, conf.type = "plain")
##
##       n events median 0.95LCL 0.95UCL
## [1,] 1      0     NA      NA      NA
```

```
plot(km8)
```



Assessment of curves and pooling of indications

For 2nd indication and beyond there does not appear to be enough data points (and occurrences within said data points) for appropriate use of a Kaplin meier curve as analysis. Pooling 2nd indications and above may therefore be a better utilization of this data set for our analysis

```
dtxlate <- subset(NICE_NUMBERS, Regulatory_approval==1 & indication >= 2)
# Indications > 1 are pooled to provide adequate data points

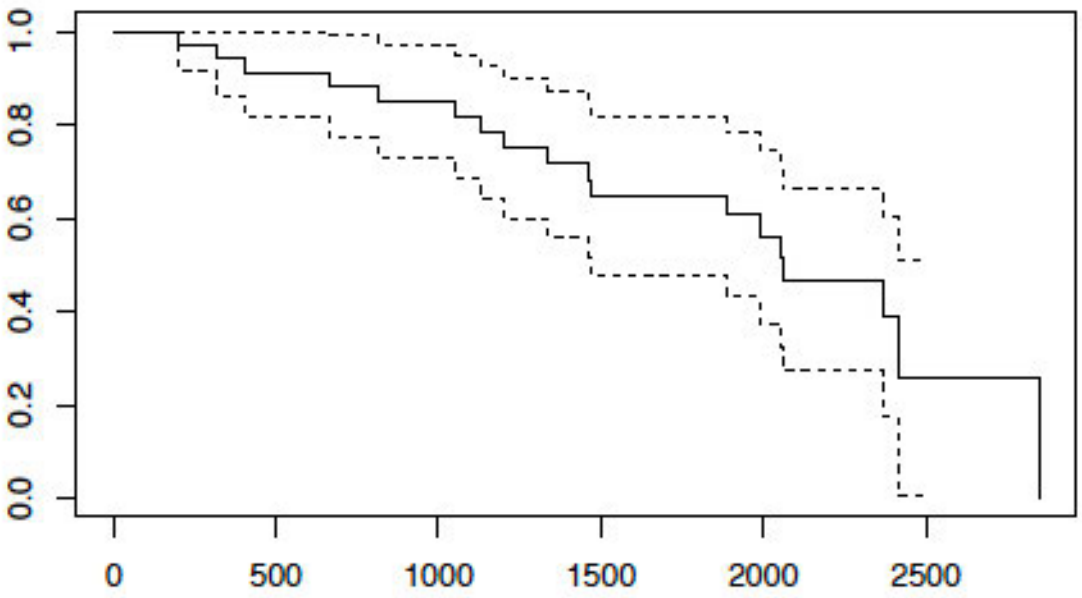
# A survival and Kaplin Meier curve is then constructed for this pooled dataset
Slate <- with(dtxlate, Surv(from_time0,recommended))
kmlate <- survfit(Slate ~ 1,conf.type = 'plain')

# The results table and plot of the curve are then called

kmlate
```

```
## Call: survfit(formula = Slate ~ 1, conf.type = "plain")
##
##       n events median 0.95LCL 0.95UCL
## [1,] 34     18   2061    1466      NA
```

```
plot(kmlate)
```



Pooling yields a Kaplin meier curve with enough data to calculate a median and lower 95% confidence interval, but not an upper confidence interval. Given that the 1st indication median is lower then the late indications median this still allows a comparison of medians. This comparison shows that later indications take additional time to reach TA approval compared to 1st indications.

Conclusions

We have shown that there are statistically significant delays between positive reimbursements. We have also shown that the magnitude of these delays increases for later indications.

APPENDIX 5.1

A5.1: Topic Guide for Interviews with Oncologists (Version 1.0: September 2022)

Health Technology Assessment Impact on Differences in Access to New Blood Cancer Medication in the US and UK: Topic Guide for Semi-Structured Interviews

The interview will take the form of a conversation. Interviewees can raise issues of importance to them. Hence, the topic guide may change as data collection progresses.

a. Thank the participant for agreeing to be interviewed
b. Brief outline of the purpose of the research
c. Reassurance about anonymity and confidentiality
d. Check it is ok to record the conversation
e. Ask about any concerns before starting
f. Make it clear it is ok to stop at any point or to refuse to answer any questions (without giving a reason)

1. My research is interested in the approval process for blood cancer treatments. What are your views on how products to treat blood cancer get approved?

2. Could you tell me about any times you've been unable to access a blood cancer medication that you think would be appropriate for a blood cancer patient?
Prompt: Barriers to prescription, feelings prompted by reported barriers, explanation to patient

3. Could you tell me about new products to treat blood cancer that you are aware of in another market (through conferences, research) that you think would be useful to your patients?

4. Could you tell me about differences you perceive in treatment norms between the US and UK?
Prompt: Cultural/societal norms, professional training/guidance, patient involvement

5a. For UK Participants only: Are you familiar with the Health Technology assessment process that National Institute for Health and Care Excellence conducts? If so, what are your perceptions of it? Are you aware of how this compares to the US system?

5b. For US Participants only: Could you tell me about any times you've interacted with a blood cancer patient that was unable to afford their treatment? Are you aware of how this compares to the UK system?

6. Could you tell me about any positive/negative approval (EMA/FDA) decisions that impacted your ability to prescribe new blood cancer medications?
Prompt: Examples

7. Could you tell me about any positive/negative reimbursement (NICE/Medicare) decisions that impacted your ability to prescribe new blood cancer medications?

Prompt: Examples

8. Could you tell me about any products that received approval or positive reimbursement decisions with an insufficient base of evidence?
Prompt: Examples

9. Could you tell me about any products on the New Medicines List that have caught your attention?

10. What do you perceive are areas for growth/improvement in the national reimbursement process?

Added Questions for English Participants

11.* Some participants have spoken about the role of English pharmacists in local funding approvals, could you tell me about that?

12.* Some participants have spoken about the Clinical Priorities Advisory Committee (CPAC) – could you tell me about that?

Is there something else we haven't covered about availability of new medicines in the blood cancer space in your country, which you think it is important for me to know?

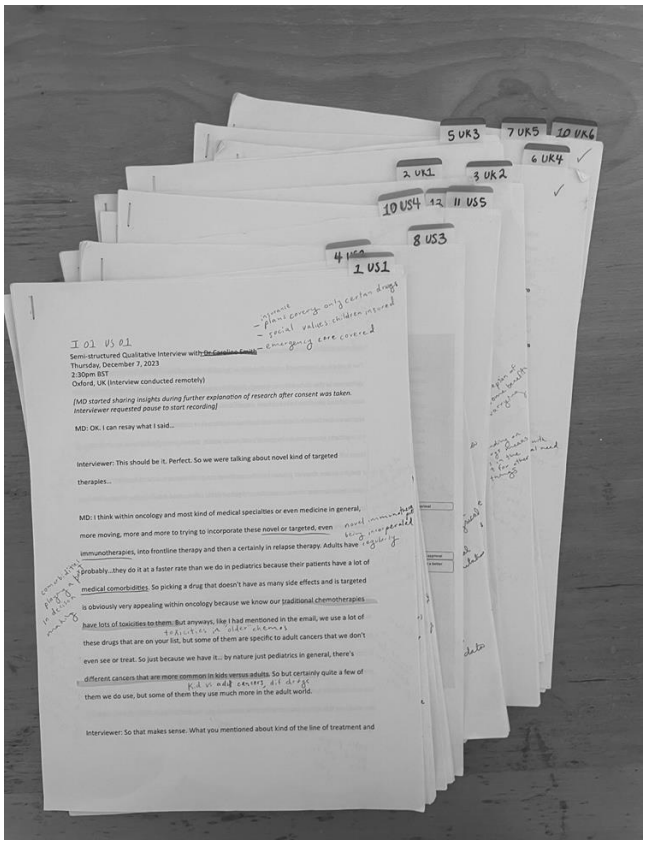
APPENDIX 5.2

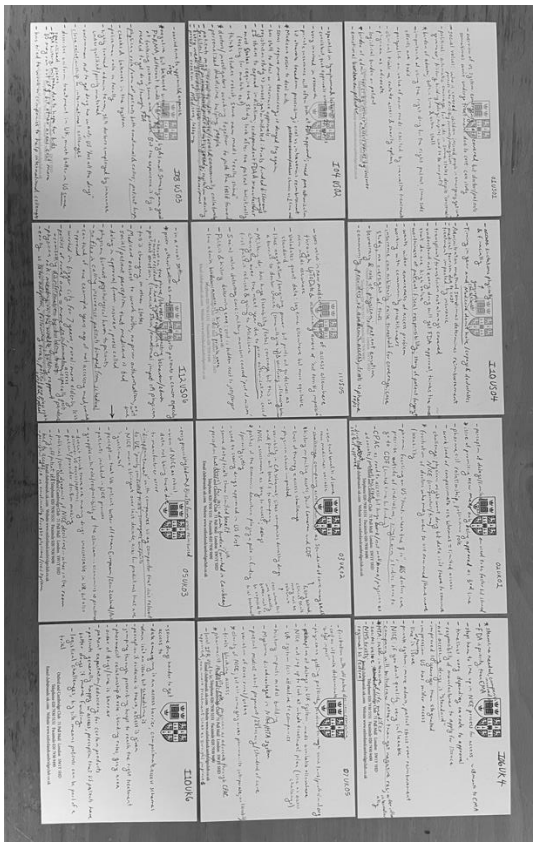
A5.2 Process of Thematic Analysis

I conducted a reflexive thematic analysis of the interview data, following the six-phase process outlined by Braun and Clarke (2022). This approach was well suited to my research aims, as it acknowledges the active role of the researcher in interpreting meaning and emphasizes the importance of reflexivity throughout the analytic process.

To begin, I transcribed all interviews verbatim. This initial step took time but allowed me to immerse myself in the data and reminded me of nuances in each interview by listening to the participant's voice and narrative. Over the following weeks, I engaged in repeated readings of the transcripts and took initial notes by hand on key ideas and impressions. I used a combination of notecards and binders during this phase to help organize early thoughts and map emerging connections across interviews (see Figures A5.1 and A5.2).

Figures A5.1 & A5.2: Materials Developed During First Phase of Thematic Analysis





Throughout the analysis, I kept a reflexive journal, which I used to record not only analytic decisions but also my thoughts, questions, and emotional responses to the material. This helped me maintain awareness of how my background, assumptions, and positionality might influence my interpretations. I was conscious of my industry experience within the field under study and my position as an American researcher. To acknowledge this, I disclosed my professional background to participants during interviews. I found that being transparent about my background helped build rapport and created space to consider how my own perspective shaped the co-construction of meaning during our conversations.

I also met regularly with my supervisor, ST, who is English, based in the UK, and comes from an academic background. These discussions were invaluable in helping me reflect on how our different professional and cultural perspectives shaped my engagement with the data. They provided a critical space to check my assumptions and situate myself within the research process more deliberately.

After the familiarization phase, I began coding all transcripts using NVivo 15 (see Figure A5.3). I coded line-by-line, aiming to stay close to the participants' words while also attending to underlying meanings. As I progressed, I revisited earlier codes and adapted them based on new insights. Once coding was complete, I collated similar codes and began organizing them into potential themes and sub-themes. I then reviewed these initial themes against the original transcripts and the coded extracts to ensure they were coherent and grounded in the data. This involved iterative reading and re-reading, and continued engagement with my reflexive journal. During this stage, I discussed my developing interpretations with ST regularly, which helped me clarify the thematic structure and ensure that the themes remained analytically meaningful.

Figure A5.3: Coding in NVivo



Once the themes and sub-themes were defined and refined, I constructed the final analytic narrative. This narrative sought to present the themes in relation to the research questions, supported by data excerpts and informed by the broader social and experiential context of the participants' accounts. Reflexivity remained central throughout this process, as I continued to interrogate how my own lens influenced the way I organized and interpreted the data. For example, I was particularly drawn to themes related to access barriers from the manufacturer's perspective, circling back to evidence gaps between FDA and HTA submission and ways that surrogate endpoints or indirect treatment comparisons might be used to make clinical trials more compelling to NICE. Meeting regularly with ST helped me reframe this issue as part of a larger theme (Space for Innovation) and put the physician as a more central actor in the access narrative. A visual overview of how the analysis progressed from initial codes to final themes and sub-themes is provided in Table A5.2.

Table A5.2: Summarizing How Analysis Moved from Codes to the Final Overarching Concept

Overarching concept	The Physician Role in Flux: Navigating Health System Tensions Between Physician Autonomy and Patient Equity			
Themes	1. Standardization vs. Fragmentation of Protocols	2. Space for Innovation	3. Check and Balances on Power	4. Social Deservingness and its Role in Access
Categories	*Going through one process* Every English doctor knows the rules, describes the blue tec form as easy to work with *Fragmentation in the US* Chaos in getting treatment approved for private patients, but can be used to the patient's advantage *Speed of process* New developments in oncology mean unique situations arise *Bureaucracy of HTA* One process means that English physicians	*Miraculous treatments* Perceptions of new medicines and interest in using them *Big Pharma* Relationship with drug manufacturers and liaison role, perception of pharmaceutical companies *Sending them a message* Health system interaction with new medicines coming to market *Perception of friendly environment* Companies watching to see if their product	*Distribution of Power in Decision making:* *Working with pharmacists* Physician experiences working with pharmacists to navigate grey areas in the English NHS coverage *Justification to insurers* Physician experiences justifying treatments to private insurers to get coverage for patients in the US *Finding care through alternative routes* Physician role in finding alternative care	*History impacting practice* Physician descriptions of cultural/historic reasoning for coverage policy *We turn down someone every day* Physician perspectives on coverage policy and phycological impact to physician *She's a good person* Descriptions of patients regarding coverage *Heroic medicine* Wanting the best care, everything to be done *Blitz mindset*

	have to work extra hard to get an exception for their patient's care	will return revenue in certain countries *Standard of care* Changing standards of care in US means clinical trials become less relevant for UK market	routes when a patient does not qualify for funding	Rationing care to leave resources for others
Codes	• Middlemen in US • Disrupters • CPAC process • Blue tec form easy to use • Patent expiration • Special exception • One process means better equity • Fragmentation improve access • Fragmentation limit access • Lines of therapy restricted • Physician as economist • Physician as advocate • Administrative burden	• Fragmentation allowing for innovation • Data gap for NICE • Certain diseases at disadvantage • Innovation in US • Easier access • England more bureaucratic • Envious of US oncology • Physician perspective of new treatments • New drugs useful • Delays typical in England • Waiting for products	• Checks and balances within the system • Insurance holds the power • Administrative time on phone • Navigating middlemen • Pharmacist relationship • Charity care • Care through hospital • Care from manufacturer • Clinical trials	• Undocumented people covered • Justifying public spending politically • Equity vs cost vs quality • Everyone gets emergency care • Fiscally reasonable patients • Pushing back care if non emergent • Private hospitals pursuing medical debt • Defining charity care • Who counts as poor • Qualifying for financial assistance • Worthy of care due to mission • American patient culture angry • Individualistic • Patient unawareness of health system problems

APPENDIX 6.1

A6.1: Sample Extraction Form

Main Data Extraction Categories	Subcategories	Description/Question
Publication Details		
Author (s)		
Journal		
Year of publication		
Source country/region		
Publication Type		
Methodology Overview		(methodology of access comparison)
Details of Comparison Methodology		
Notes:		
Study Design		
Study type		Experimental or observational study?
Design		E.g. RCT, before/after study, cohort study, etc.
Aim/Purpose/Objective		
Study population	Age Sex Diagnosis/disease Location/geography	
Sample size (if applicable)		
Methodology Limitations as Described by Author		
Comparator (if applicable)		
Outcome		
Context		
Analytics/applications		Descriptive, predictive or prescriptive?
Country/funding system		
Key Findings		
Health system implementation		Barriers and facilitators to access
Data set utilized		
Patient experience		
Study limitations		
Evidence applications		Applications for clinical practice, policymakers, industry, etc?
Other important results		

APPENDIX 6.2

Table A6.2: Studies Included in the Scoping Review

Study Number	Study Title	Author	Source	Year	US/UK Included		Primary Consideration of Access			Reference
					US	UK	Reimbursement	Launch	Utilization	
1	Appraisals by Health Technology Assessment Agencies of Economic Evaluations Submitted as Part of Reimbursement Dossiers for Oncology Treatments: Evidence from Canada, the UK, and Australia.	Ball G; Levine MAH; Thabane L; Tarride JE	Curr Oncol	2022		X	X			1
2	Comparative Assessment of Reimbursement Recommendations by NICE and HAS for Oncology New Medicines Indicated for the Treatment of Solid Tumors from 2015 to 2021.	Trouiller JB; LaramÃ©e P	Med Decis Making	2023		X	X			2
3	Real-world evidence in lung and hematologic oncology health technology appraisals: a review of six assessment agencies.	Harrichara n S; Curran E; Lin HM; Walton L; Gurjar K; Nguyen K; Forsythe A	Future Oncol	2023		X	X			3
4	Health technology assessment (HTA) in England, France and Germany: what do matched drug pairs tell us about	Schaefer R; Hernandez D; Selberg L; Schlander M	J Comp Eff Res	2021		X	X			4

	recommendations by national HTA agencies?									
5	Differences in cancer drug assessment between Spain and the United Kingdom.	Lozano-BlÃ¡zquez A; Dickson R; Fraga-Fuentes MD; MartÃnez-MartÃnez xF; Cxalleja-HernÃ¡ndez MÃ□	Eur J Cancer	2015		X	X			5
6	Oncology drug health technology assessment recommendations: Canadian versus UK experiences.	Chabot I; Rocchi A	Clinicoecon Outcomes Res	2014		X	X			6
7	Association Between the Use of Surrogate Measures in Pivotal Trials and Health Technology Assessment Decisions: A Retrospective Analysis of NICE and CADTH Reviews of Cancer Drugs.	Pinto A; Naci H; Neez E; Mossialos E	Value Health	2020		X	X			7
8	Does the use of health technology assessment have an impact on the utilisation of health care resources? Evidence from two European countries.	Corbacho B; Drummond M; Santos R; Jones E; BorrÃ s JM; Mestre-Ferrandiz J; EspÃn J; Henry N; Prat A	Eur J Health Econ	2020		X			X	(Corbacho, 2020)
9	Relative effectiveness assessments of oncology medicines for pricing and reimbursement decisions in European countries.	Kleijnen S; Lipska I; Leonardo Alves T; Meijboom K; Elsada A; VervÃ¶lgyi V; d'Andon A; Timoney A; Leufkens	Ann Oncol	2016		X	X			8

		HG; De Boer A; Goettsch WG								
10	Justifying the source of external comparators in single-arm oncology health technology submissions: a review of NICE and PBAC assessments.	Appiah K; Rizzo M; Sarri G; Hernandez L	J Comp Eff Res	2024		X	X			9
11	Is the National Institute for Health and Care Excellence (NICE) in England more 'innovation-friendly' than the Federal Joint Committee (G-BA) in Germany?	Schaefer R; Schlander M	Expert Rev Pharmacoecon Outcomes Res	2019		X	X			10
12	Patterns of Care and Costs for Older Patients With Colorectal Cancer at the End of Life: Descriptive Study of the United States and Canada.	Bremner KE; Yabroff KR; Coughlan D; Liu N; Zeruto C; Warren JL; de Oliveira C; Mariotto AB; Lam C; Barrett MJ; Chan KK; Hoch JS; Krahn MD	JCO Oncol Pract	2020	X				X	(Bremner, 2020)
13	Health Technology Assessment-Informed Decision Making by the Federal Joint Committee/Institute for Quality and Efficiency in Health Care in Germany and the National Institute for Health and Care Excellence in	Schaefer R; HernÃ¡ndez D; BÃ¤mighausen T; Kolominsky-Rabas P; Schlander M	Value Health	2023		X	X			11

	England: The Role of Budget Impact.									
14	What is driving HTA decision-making? Evidence from cancer drug reimbursement decisions from 6 European countries.	Maynou L; Cairns J	Health Policy	2019		X	X			12
15	A comparative analysis of two contrasting European approaches for rewarding the value added by drugs for cancer: England versus France.	Drummond M; de Pouvourville G; Jones E; Haig J; Saba G; Cawston H	Pharmacoeconomics	2014		X	X			13
16	Cost-effectiveness of cancer drugs: Comparative analysis of the United States and England.	Cherla A; Renwick M; Jha A; Mossialos E	EClinical Medicine	2020	X	X	X			14
17	Health Technology Assessment (HTA) Case Studies: Comparing Acceptability of Real-World Evidence (RWE) in Appraisals for Oncology Medicines	Zong J.; Pan X.; Rojubally A.; Jiao X.; Bruno A.; Gdovin Bergeson J.	Value in Health	2024		X	X			15
18	Variability in Time to Decision (TTD) Among NICE and Cadth Health Technology Assessments (HTAs)	Tzonev C.; Grieve S.; Gurjar K.; Campden R.; Igbelina C.D.; Thakur D.	Value in Health	2023		X	X			16
19	The Use of Surrogate Endpoints in Health Technology	Campden R.; Yu J.; Tzonev C.; Musat M.; Thakur D.	Value in Health	2022		X	X			17

	Assessments (HTAs) for Chronic Cancers									
20	Health Economic Modelling for HTA Assessment: A Comparison of Economic Protocols Submitted to Three HTA Bodies (HAS, NICE, CADTH)	Poignant P.; Chambry L.; Duteil E.; Leproust S.	Value in Health	2022		X	X			18
21	When and How Does RWE Impact HTA Outcomes in Oncology? A Qualitative Evaluation of Case Studies to Identify Drivers of RWE Acceptance Today and in the Future	Oswald C.; Anastasaki E.; Dunton K.; van Engen A.; Liljas B.; Mbanya Z.; Parry D.; Rosenlund M.; Szawara P.	Value in Health	2022		X	X			19
22	Health Technology Assessment and Reimbursement for Select Oncology Therapies in European Major Markets	Koka N.S.; Syed A.A.; Ahmad M.; Patel K.; Nair S.; Shah S.	Value in Health	2022		X	X			20
23	How Dual Branding of Drugs Impacts Reimbursement Decision in Multiple Myeloma?	Jagtap C.; Bhati P.; Wahal V.P.	Value in Health	2022		X	X			21
24	What Can the US Learn from Regulatory Decisions and Health Technology Assessments of New Drugs in Other Countries?	Pham C.; Le K.; Draves M.; E S.-V.	Value in Health	2022	X	X	X			22
25	Does Trial Blinding Impact Reimbursement Decisions	Jagtap C.; Mark K.; Wahal V.P.; Farinella M.	Value in Health	2022		X	X			23

	in Lung Cancer?									
26	A Comparative Analysis of Recommendations for the Post-Reimbursement Collection of Real-World DATA (RWD) in Oncology Appraisals Issued By Six HTA Agencies	Gurjar K.; Harrichara n S.; Nguyen K.; Forsythe A.	Value in Health	2021		X	X			24
27	Advancing Evidence to Action: A Comparison of Health Technology Assessment (HTA) Outcomes in England, France and Germany	Schafer R.; Hernandez D.; Schlander M.	Value in Health	2020		X	X			25
28	A Multinational Comparison of HTA Decisions for New Treatment Options in Oncology in 2019	Henry A.; Lionikaite V.; von Wilamowit z-Moellendo rff C.M.; Curry A.; Ralston S.	Value in Health	2020		X	X			26
29	Assessing the Impact of Patient-Reported Outcomes in Health Technology Assessment	Hong Y.D.; Hennig M.; Shen Q.; Alfonso R.; Kitchen H.; Marshall C.; Romero-Salerno V.; Keeley T.	Value in Health	2020	X	X	X			27
30	Global Oncology Access - The Relative Difficulty of Reimbursement Across Four Health Technology Assessment (HTA) Agencies	Nguyen K.; Forsythe A.; Azimpour K.; Vu B.K.; Tomaras D.	Value in Health	2020		X	X			28
31	Comparison of External Control Arm	Jaksa A.; Vondeling G.; Martin	Value in Health	2020	X	X	X			29

	(ECA) Critiques in Regulatory and Health Technology Assessment (HTA) Oncology Submissions	L.; Draganigo s A.; Louder A.; Rosenlund M.								
32	Health Technology Assessment for Chimeric Antigen Receptor (CAR) T-CELL Therapies for Cancer in Europe, US, and Canada	Stothard C.; Brown A.; Ralston S.; Curry A.; Cork D.; Hollier-Hann G.	Value in Health	2020	X	X	X			30
33	Health technology assessment (HTA) in England, France and Germany: What do we know about variations in cancer-related HTA outcomes?	Schaefer R.; Hernandez D.; Schlander M.	Annals of Oncology	2020		X	X			31
34	Health technology assessment acceptability of innovative survival metrics in oncology	Macaulay R.	International Journal of Technolog y Assessmen t in Health Care	2019		X	X			32
35	What Influences the Probability to Be Successful in an Oncology HTA? An Analysis of Oncology HTA Decisions in Germany, Spain and the UK	Hardtstock F.; Kocaata Z.; Wilke T.; Rebollo P.; Garcia A.; Heeg B.	Value in Health	2019		X	X			33
36	Key Drivers of Health Technology Assessment Decisions for Relapsed-Refractory Multiple Myeloma Treatments: A Country Comparison	Horsburgh S.; Nelson L.; Chadda S.	Value in Health	2019		X	X			34

37	Oncology-Related HTA Decisions in Germany, France, Spain and the UK: Assessment of Similarities and Differences	Hardtstock F.; Kocaata Z.; Wilke T.; Rebollo P.; Garcia A.; Heeg B.	Value in Health	2019		X	X			35
38	Treatment Landscape and Key Drivers for HTA Decisions in Patients with Non-Small Cell Lung Cancer without EGFR or ALK Alterations	Henry A.; Hollier-Hann G.; Ralston S.	Value in Health	2019		X	X			36
39	Parallel Scientific Advice from NICE and CADTH: Would One Submission Fit All?	Gibson S.; Atkinson M.; Beale R.; Wickstead R.; Griffiths M.	Value in Health	2019		X	X			37
40	Health Technology Assessment Decisions Over the Last Decade in the United Kingdom and the Netherlands - A Focus on Non-Small-Cell Lung Cancer	Westerink L.; Postma A.J.; Andringa H.; Martin L.; Postma M.	Value in Health	2019		X	X			38
41	Comparative Assessment of HTA Outcomes in Brazil, Canada and the United Kingdom	Boers Trilles V.; Ayoub R.; Favetta B.; Graham N.; Martin De Bustamante M.	Value in Health Regional Issues	2019		X	X			39
42	What Methods Are Applied in Assessing the Clinical and Cost Effectiveness of Health Technologies Based on the Use of Surrogate Outcomes: A Comparison	Ciani O.; Grigore B.; Taylor R.	Value in Health	2019		X	X			40

	of Evaluation Reports Across International Health Technology Assessment Agencies									
43	A Multinational Comparison of HTA Decisions for New Treatment Options in Oncology	Ralston S.; Henry A.D.; Bowe C.; von Wilamowitz-Moellendorff C.M.; Curry A.	Value in Health	2019		X	X			41
44	Did the European Financial Crisis Have an Impact on Economic Decision-Making in Health Technology Assessments?	Gizaw N.; Farinella M.; Inumerable R.V.; Rubinstein J.; Ho Y.	Value in Health	2018		X	X			42
45	Health Technology Assessment Agency Appraisal of Immuno-Oncology Cure Fraction Survival Modelling	Cameron H.L.; Brown S.; Samjoo I.; Thompson M.	Value in Health	2018		X	X			43
46	What Is the Value of Real World Evidence in Oncology in HTA Appraisals in England, France, Canada and Australia?	Ng T.; Chawla T.; Bending M.W.	Value in Health	2018		X	X			44
47	Do longer hta review times for oncology products reflect worse outcomes? A review of 482 HTAs across 5 markets	Jaksa A.; Pontynen A.; Bastian A.	Value in Health	2017		X	X			45
48	Are HTAs for oncology agents taking longer to complete? Trends in time to an HTA deicsion in 6 major markets	Jaksa A.; Pontynen A.; Bastian A.	Value in Health	2017		X	X			46

49	International comparison of health technology assessment decisions in personalized oncology therapies	Ho C.Y.; Gless P.; Lawless G.	Value in Health	2017		X	X			(Ho, 2017)
50	Access to innovative cancer drugs: Divergent outcomes of HTA bodies' appraisals in France, Germany and the United Kingdom impact on the availability of new medicines	Hartmann M.; Droeschel D.; Vollmer L.; De Paz B.; Walzer S.	European Journal of Cancer	2017		X	X			47
51	What is the response to immuno-oncology by health technology assessment agencies?	Adler B.; Blumenthal J.; Chang R.; Ho S.Y.; Jaksa A.; Lurie B.; Pontynen A.; Rubinstein E.; Sliman R.; Rubinstein J.	International Journal of Technology Assessment in Health Care	2017		X	X			48
52	Access to orphan drugs in the United Kingdom and other European countries	Garau M.; Maignen F.; aO'Neill P.; Mestre-Ferrandiz J.; Zamora B.	International Journal of Technology Assessment in Health Care	2017		X				49
53	Analysis of recent approvals of immuno-oncology drugs across England, Scotland, Germany and France	Ziomek J.; El Mouaddin N.; Ng T.; Ovcinnikova O.; Taveau C.	Value in Health	2017		X	X			50
54	Trends in oncology appraisal decisions: A comparison between the national institute for health and care excellence (NICE) and the scottish	Campbell D.J.; Clark R.S.; Meyer K.L.	Value in Health	2017		X	X			51

	medicines consortium (SMC)									
55	Does the presence of an orphan drug polcy affect HTA recommendations for oncologic orphan drugs?	Riemer J.; Hancock-Howard R.; Gauthier A.	Value in Health	2017		X	X			52
56	Health-economics evaluations in France, England, Canada and Autralia: Comparison of methodologies and impact on drugs' access to patients	Bucher D.; Abalan M.; Allou A.; Dumon L.; Vialard L.; Troubat A.; Maurel F.	Value in Health	2017		X	X			(Bucher, 2017)
57	Concordance of health technology assessment recommendations of diabetes, hepatitis, oncology and epilepsy pharmaceutical products by five agencies within europe: An interrater reliability and association analysis	Abugri I.; Braun D.; Manfred E.; Gerbsch N.	Value in Health	2016	X	X	X			53
58	Assessment of clinical value in oncology: Comparative analysis of value frameworks and HTAs	Niven C.; Hough N.M.; Zhou A.Y.; Qin L.; Alexander R.	Value in Health	2016		X	X			54
59	Untangling the Complexity of Funding Recommendations: A Comparative Analysis of Health Technology Assessment Outcomes in Four European Countries	Cerri K.H.; Knapp M.; Fernandez J.-L.	Pharmaceutical Medicine	2015		X	X			55

60	Hierarchy of clinical endpoints in HTA decision making in oncology	Kreeftmeijer J.; Ryan J.; Van Engen A.; Heemstra L.	Value in Health	2015		X	X			56
61	The validity of the Proportional Hazards assumption for the metaanalysis of time to event data to support submissions to Health Technology Assessment (HTA) authorities	Batson S.; Webb N.; Hudson P.; Greenall G.	Value in Health	2015		X	X			57
62	Consistencies in cancer therapy reimbursement recommendations made in Canada, Australia, Sweden, and United Kingdom	Samjoo I.A.; Grima D.T.	Journal of Population Therapeutics and Clinical Pharmacology	2014		X	X			58
63	Expanded data sets for HTA decision-making in oncology: Do they help to achieve positive appraisals?	Chadda S.; Mbanya Z.; Gielen V.; Chandler T.	Value in Health	2014		X	X			59
64	Comparison of oncology therapy reimbursement recommendations made by health technology assessment agencies in Australia, Canada, Sweden, and United Kingdom	Samjoo I.A.; Grima D.T.	Value in Health	2014		X	X			60
65	Similar hta, different access outcome? Comparison of orphan oncology drug assessment in	Saraf S.; Akpinar P.	Value in Health	2012		X	X			61

	South Korea, Australia and the UK									
66	Threshold values for cost-effectiveness in ahtapol and nice for cancer drug technologies	Kiljan A.; Kolasa K.; Hermanowski T.	Value in Health	2011		X	X			62
67	Comparison of anticancer drug coverage decisions in the United States and United Kingdom: Does the evidence support the rhetoric?	Mason A.; Drummond M.; Ramsey S.; Campbell J.; Raisch D.	Journal of Clinical Oncology	2010		X	X			(Mason, 2010)
68	Surrogate outcomes in HTA decision making	Sedelnikova M.; Modha R.; Lock K.; Howard P.	Journal of Population Therapeutics and Clinical Pharmacology	2010	X	X	X			63
69	Review of the decisions of health technology assessment agencies for capecitabine for the treatment of colorectal cancer	Saggia M.G.; Borges L.G.	Value in Health	2009		X	X			64
70	Agreement about Availability of Alternative Treatments for Innovative Drugs Assessed by the EMA and HTA Organizations	Madrid Paredes, J.; Versteeg, J.-W.; Vreman, R.A.; Bloem, L.T.	Clinical Pharmacology and Therapeutics	2024		X	X			65
71	Algorithms and heuristics of health technology assessments: A retrospective analysis of factors associated with HTA outcomes for new drugs across seven OECD countries	Kanavos, P.; Visintin, E.; Gentilini, A.	Social Science and Medicine	2023		X	X			66

72	Financing and Reimbursement of Approved Advanced Therapies in Several European Countries	Iglesias-Lopez, C.; AgustÃ, A.; Vallano, A.; Obach, M.	Value in Health	2023		X	X			67
73	Assessment of FDA-Approved Drugs Not Recommended for Use or Reimbursement in Other Countries, 2017-2020	Pham, C.; Le, K.; Draves, M.; Seoane-Vazquez, E.	JAMA Internal Medicine	2023	X	X	X			68
74	Does health technology assessment compromise access to pharmaceuticals?	Bassgen, M.; Stargardt, T.	European Journal of Health Economics	2023		X	X			(Bassgen, 2022)
75	A Comparative Analysis of Anticancer Drug Appraisals Including Managed Entry Agreements in South Korea and England	Lee, I.-H.; Bloor, K.; Bae, E.-Y.	Applied Health Economics and Health Policy	2023		X		X		69
76	Time to reimbursement of novel anticancer drugs in Europe: a case study of seven European countries	Post, H.C.; Schutte, T.; van Oijen, M.G.H.; van Laarhoven, H.W.M.; Hollak, C.E.M.	ESMO Open	2023		X	X			70
77	A Comparison of Seven Oncology External Control Arm Case Studies: Critiques From Regulatory and Health Technology Assessment Agencies	Jaksa, A.; Louder, A.; Maksymiuk, C.; Vondeling, G.T.; Martin, L.; Gatto, N.; Richards, E.; Yver, A.; Rosenlund, M.	Value in Health	2022	X	X	X			71
78	How do HTA agencies perceive conditional approval of medicines?	Mills, M.; Kanavos, P.	Health Policy	2022		X	X			72

	Evidence from England, Scotland, France and Canada									
79	Impact of Managed Entry Agreements on availability of and timely access to medicines: an ex-post evaluation of agreements implemented for oncology therapies in four countries	Efthymiadou, O.; Kanavos, P.	BMC Health Services Research	2022		X	X			73
80	Do Health Technology Assessment organisations consider manufacturers â€™ costs in relation to drug price? A study of reimbursement reports	Enzing, J.J.; Knies, S.; Engel, J.; IJzerman, M.J.; Sander, B.; Vreman, R.; Boer, B.; Brouwer, W.B.F.	Cost Effectiveness and Resource Allocation	2022		X	X			74
81	Value and Price of Multi-indication Cancer Drugs in the USA, Germany, France, England, Canada, Australia, and Scotland	Michaeli, D.T.; Mills, M.; Kanavos, P.	Applied Health Economics and Health Policy	2022	X	X	X			75
82	Comparison of Prices and Affordability of Cancer Medicines in 16 Countries in Europe and Latin America	Moye-Holz, D.; Vogler, S.	Applied Health Economics and Health Policy	2022		X	X			(Moye-Holz, 2022)
83	Validity of Surrogate Endpoints and Their Impact on Coverage Recommendations: A Retrospective Analysis across International Health Technology Assessment Agencies	Ciani, O.; Grigore, B.; Blommestein, H.; de Groot, S.; MÃ¶llenkamp, M.; Rabbe, S.; Daubner-Bendes, R.; Taylor, R.S.	Medical Decision Making	2021		X	X			76

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85	Determinants of Managed Entry Agreements in the context of Health Technology Assessment: a comparative analysis of oncology therapies in four countries	Efthymiadou, O.; Kanavos, P.	International Journal of Technology Assessment in Health Care	2021		X	X			78
86	Companiesâ€™ Health Technology Assessment Strategies and Practices in Australia, Canada, England, France, Germany, Italy and Spain: An Industry Metrics Study	Wang, T.; McAuslane, N.; Liberti, L.; Gardarsdottir, H.; Goettsch, W.; Leufkens, H.	Frontiers in Pharmacology	2020		X	X			(Wang, 2020)
87	Appraisal of cancer drugs: a comparison of the French health technology assessment with value frameworks of two oncology societies	Li, J.; Vivot, A.; Alter, L.; Durand-Zaleski, I.	Expert Review of Pharmacoeconomics and Outcomes Research	2020	X		X			(Li, 2020)
88	Relationship between costs and clinical benefits of new cancer medicines in Australia, France, the UK, and the US	Salas-Vega, S.; Shearer, E.; Mossialos, E.	Social Science and Medicine	2020	X	X			X	(Salas-Vega, 2020)
89	Outcomes-based reimbursement for gene therapies in practice: the experience of recently launched	Jørgensen, J.; Hanna, E.; Kefalas, P.	Journal of Market Access and Health Policy	2020		X	X			79

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91	Reimbursement of orphan drugs in Europe in relation to the type of authorization by the European medicines agency and the decision making based on health technology assessment	Malinowski, K.P.; Kawalec, P.; Trabka, W.; Sowada, C.; Pilc, A.	Frontiers in Pharmacology	2018		X	X			81
92	Adjuvant treatment patterns and outcomes in patients with stage IB-IIIA non-small cell lung cancer in France, Germany, and the United Kingdom based on the LuCaBIS burden of illness study	Chouaid, C.; Danson, S.; Andreas, S.; Siakpere, O.; Benjamin, L.; Ehness, R.; Dramard-Goasdoue, M.-H.; Barth, J.; Hoffmann, H.; Potter, V.; Barlesi, F.; Price, M.; Chirila, C.; Hollis, K.; Sweeney, C.; Wolowacz, S.; Kaye, J.A.; Kontoudis, I.	Lung Cancer	2018		X	X			82

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94	Treatment patterns and outcomes of Stage IIIB/IIIC melanoma in France, Germany and the UK: A retrospective and prospective observational study (MELABIS)	Harries, M.; Mohr, P.; Grange, F.; Ehness, R.; Benjamin, L.; Siakpere, O.; Barth, J.; Stapelkamp, C.; Pfersch, S.; McLeod, L.; Wolowacz, S.; A. Kaye, J.; Kontoudis, I.	International Journal of Clinical Practice	2017		X			X	83
95	Why do health technology assessment coverage recommendations for the same drugs differ across settings? Applying a mixed methods framework to systematically compare orphan drug decisions in four European countries	Nicod, E.	European Journal of Health Economics	2017		X	X			84
96	Health benefit assessment of pharmaceuticals: An international comparison of decisions from Germany, England, Scotland and Australia	Fischer, K.E.; Heisser, T.; Stargardt, T.	Health Policy	2016		X	X			85

97	Developing an evidence-based methodological framework to systematically compare HTA coverage decisions: A mixed methods study	Nicod, E.; Kanavos, P.	Health Policy	2016		X	X			86
98	The timing of introduction of pharmaceutical innovations in seven European countries	Westerling, R.; Westin, M.; McKee, M.; Hoffmann, R.; Plug, I.; Rey, G.; Jougla, E.; Lang, K.; PÃ¤rna, K.; Alfonso, J.L.; Mackenbach, J.P.	Journal of Evaluation in Clinical Practice	2014		X		X		(Westerling, 2014
99	Commonalities and differences in HTA outcomes: A comparative analysis of five countries and implications for coverage decisions	Nicod, E.; Kanavos, P.	Health Policy	2012		X	X			87
100	Using 'amenable mortality' as indicator of healthcare effectiveness in international comparisons: Results of a validation study	Mackenbach, J.P.; Hoffmann, R.; Khoshaba, B.; Plug, I.; Rey, G.; Westerling, R.; PÃ¤rna, K.; Jougla, E.; Alfonso, J.; Looman, C.; McKee, M.	Journal of Epidemiology and Community Health	2013		X	X			(Mackenbach, 2013)
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APPENDIX 7.1

A7.1 Calculating Point Prevalence of Blood Cancer Patient Populations

This section outlines the step-by-step methodology used to estimate the annual point prevalence of acute myeloid leukaemia (AML) in the United Kingdom (UK) and the United States (US), where complete annual prevalence data are unavailable. Estimates were generated by combining publicly reported AML incidence figures, survival estimates, and national population data. The point prevalence of AML in each year was approximated using the product of the annual incidence rate and the average duration of disease survival, scaled to the population size. Mathematically, this is expressed as:

$$\text{Prevalence}_{year} = \text{Incidence Rate (per year)} \times \text{Average Survival Duration (years)} \times (\text{Population}_{year} / 100{,}000)$$

In this calculation, the incidence rate is expressed per 100,000 population per year, and average survival duration is measured in years. This method assumed a steady-state population and disease dynamics, where incidence and survival remain relatively constant over the period of interest. The formula provides a practical approach to estimate patient prevalence by specific blood cancer in the absence of comprehensive registry data. This calculation was applied to each year by updating the corresponding population figures. Table A7.1 displays calculation inputs to estimate AML Point Prevalence in the US and UK for the years 2020-2024 (results of which are displayed in Table 7.4 in Chapter 7, Section 7.2.2.2). The Textbox A7.1 outlines definitions and sources that were used for each row in Table A7.1.

Textbox A7.1: Definitions and Data Sourcees for AML Prevalence Estimation

Incidence Rate: The number of new AML cases diagnosed within a year. Annual incidence estimates from 2024–2025 were provided by the American Cancer Society (2025) and Cancer Research UK (2021).

Average Survival Duration: The average number of years an individual lives following diagnosis with AML. Because direct survival estimates were not consistently reported for all years, this variable was operationalized through the P/I ratio. For the US, a ratio of 3.5 was applied based on SEER prevalence (NCI, 2025) and American Cancer Society (2025) incidence data. For the UK, a slightly lower ratio of 3.0 was used, reflecting differences in long-term survival and access to care as reported by Cancer Research UK (2021).

Prevalence: The total number of individuals living with AML at a given time (point prevalence). US prevalence was reported by SEER Cancer Statistics Review (NCI, 2025).

Prevalence-to-Incidence Ratio (P/I Ratio): A multiplier representing the average duration of survival with AML, used to estimate prevalence from incidence.

Population: Total national population for the given year, used to normalize prevalence per 100,000 people. US populations estimates were provided by the US Census and UK population estimates were provided by the UK Office for National Statistics.

Estimating AML Prevalence in the US started by using known prevalence data for 2022. The SEER database reported 79,317 prevalent AML cases in 2022 (see US 2022 AML Patient Estimate in Table A7.1). This served as a reference point for surrounding years. Based on American Cancer Society (2025) data, AML incidence in the US is estimated to be ~20,000–22,000 cases per year (see US 2024 Incident Rate in Table A7.1). This suggests a P/I ratio of about 3.5, as 79,317 ÷ 22,000 ≈ 3.6 (see US Average Survival Duration for 2020-2024 in Table A7.1. From 2020-2024, the estimated annual incidence was multiplied by the P/I ratio. Estimating AML Prevalence in the UK used Cancer Research UK reports of an average of 3,100 new AML cases annually from 2016–2018 (Cancer Research UK, 2021). A lower P/I ratio of 3.0 was used for the UK to reflect shorter average survival relative to the US.

Table A7.1: Calculating Point Prevalence of AML Patient Populations

		Incident Rate	Average Survival Duration	Population (Population/ 100,000)	AML Patient Estimate	Prevalence Estimate

UK	2020	3,100 (Cancer Research UK, 2021)	3	9,525	~9,525	14.2 per 100,000
	2021	3,130	3	9,610	~9,610	14.3 per 100,000
	2022	3,160	3	9,720	~9,720	14.4 per 100,000
	2023	3,190	3	9,825	~9,825	14.5 per 100,000
	2024	3,220	3	9,925	~9,925	14.6 per 100,000
US	2020	20,000	3.5	331,800	~70,000	21.1 per 100,000
	2021	20,300	3.5	333,000	~71,000	21.4 per 100,000
	2022	*Not calculated, prevalence estimate provided by SEER*	*Not calculated, prevalence estimate provided by SEER*	*Not calculated, prevalence estimate provided by SEER*	79,317 (NCI, 2025)	23.8 per 100,000
	2023	20,5000	3.5	334,000	~80,000	24.0 per 100,000
	2024	20,800 (American Cancer Society, 2025)	3.5	335,000	~82,000	24.5 per 100,000

Results of Table A.7.1 were then displayed in Chapter 7 (Section 7.2.2.2) Table 7.4.

Table 7.4: Estimated AML Prevalence and Patients in the US and UK Total Population[34]

Country	Patient Group	2020	2021	2022	2023	2024
UK	AML Prevalence Estimate	14.2 per 100,000	14.3 per 100,000	14.4 per 100,000	14.5 per 100,000	14.6 per 100,000
	AML Patients	~9,525	~9,610	~9,720	~9,825	~9,925
US	AML Prevalence Estimate	21.1 per 100,000	21.4 per 100,000	23.8 per 100,000	24.0 per 100,000	24.5 per 100,000
	AML Patients	~70,000	~71,000	79,317 [35]	~80,000	~82,000

This method assumed stable survival durations and relatively consistent incidence trends, which may not fully reflect changes in diagnostics or treatment outcomes. Prevalence estimates

[34] See Chapter 7 (Section 7.2.2.2).
[35] US AML Patient Prevalence supported by SEER in 2022 rather than modelled (NCI, 2025).

are approximations and should be interpreted within the context of population dynamics, reporting practices, and clinical advances. These estimates were intended to provide a standardized, cross-national comparison using publicly accessible data and transparent calculations.

APPENDIX 7.2

Table A7.2: Volume and Proportion of Other New Medicines Utilized By Disease Area

Country	New Medicine	Patient Cohort	Value	2020	2021	2022	2023	2024
UK	Gliteritinib	Acute Myeloid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	1.00	1.00	1.00	1.00	1.00
	Ivosidenib	Acute Myeloid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	1.00	1.00	1.00	1.00	1.00
	Midostaurin	Acute Myeloid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	1.00	1.00	1.00	0.79	0.74
		Other Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.00	0.00	0.00	0.21	0.26
US	Enasidenib	Acute Myeloid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.87	0.89	0.86	0.89	0.85
		Myelodysplastic Syndromes	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.10	0.07	0.09	0.07	0.11
		Other Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.00	0.00	0.03	0.01	0.04
		Acute Lymphoid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.02	0.03	0.02	0.00	0.00
		Chronic Lymphoid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.00	0.00	0.00	0.02	0.00
		Chronic Myeloid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.01	0.01	0.00	0.00	0.00
	Gliteritinib	Acute Myeloid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.95	0.95	0.97	0.99	0.97
		Other Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.03	0.02	0.03	0.01	0.03
			Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

		Acute Lymphoid Leukemia	Proportion from Total	0.02	0.00	0.00	0.00	0.00
		Myelodysplastic Syndromes	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.00	0.02	0.00	0.00	0.00
	Cedazuridine + Decitabine	Myelodysplastic Syndromes	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.84	0.82	0.68	0.65	0.62
		Other Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.07	0.09	0.20	0.21	0.19
		Acute Myeloid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.09	0.09	0.10	0.09	0.13
		Chronic Myeloid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.00	0.00	0.00	0.01	0.03
		Non-Hodgkin's Lymphoma	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.00	0.00	0.02	0.02	0.03
		Multiple Myeloma	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.00	0.00	0.00	0.02	0.01
		Acute Lymphoid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.00	0.00	0.00	0.00	0.00
	Ivosidenib	Acute Myeloid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.76	0.92	0.87	1.00	0.68
		Myelodysplastic Syndromes	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.02	0.08	0.10	0.00	0.32
		Non-Hodgkin's Lymphoma	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.00	0.00	0.03	0.00	0.00
		Other Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.22	0.00	0.00	0.00	0.00
	Midostaurin	Acute Myeloid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.68	0.67	0.63	0.69	0.76
		Non-Hodgkin's Lymphoma	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.22	0.20	0.21	0.23	0.19
			Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

		Multiple Myeloma	Proportion from Total	0.01	0.02	0.04	0.03	0.02
		Chronic Lymphoid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.00	0.01	0.00	0.00	0.01
		Other Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.09	0.09	0.11	0.04	0.01
		Myelodysplastic Syndromes	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.01	0.00	0.02	0.01	0.00
	Glasdegib	Acute Myeloid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.88	0.82	0.98	0.89	0.57
		Myelodysplastic Syndromes	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.03	0.17	0.00	0.11	0.18
		Other Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.04	0.00	0.00	0.00	0.14
		Chronic Myeloid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.00	0.01	0.02	0.00	0.09
		Non-Hodgkin's Lymphoma	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.00	0.00	0.00	0.00	0.02
		Multiple Myeloma	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.04	0.00	0.00	0.00	0.00
	Selinexor	Multiple Myeloma	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.92	0.99	0.94	1.00	0.93
		Non-Hodgkin's Lymphoma	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.08	0.01	0.00	0.00	0.07
		Acute Myeloid Leukemia	Units Sold	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
			Proportion from Total	0.00	0.00	0.06	0.00	0.00