Delays in lung cancer care in Mexico and the role of patient navigation programmes in early diagnosis and treatment:a mixed methods protocol

Elysse Bautista González, MD, MSc

A dissertation submitted in fulfilment
of the requirements for the degree of
Doctor of Philosophy
of
University College London.

Department of Epidemiology and Public Health
Institute of Epidemiology and Health Care
University College London

July 2, 2024

I, Elysse Bautista González, MD, MSc, confirm that the work presented in this PhD thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Abstract

Background: Prolonged cancer care intervals are highly associated with advanced-stage disease at presentation and increased public health costs. Nonetheless, lung cancer care intervals have not been quantified in Mexico. Patient navigation programs (PNP) seem promising tools to achieve early lung cancer care. However, literature on patient navigation in Mexico is scarce and previous systematic reviews have mainly relied on randomised controlled trial design or have focused solely on lung cancer screening. Thus, evidence is limited to understand the role PNP have in reducing prolonged cancer care intervals across the continuum.

Aim: This thesis aims to investigate diagnostic and treatment timeliness in lung cancer care in Mexico and the role of PNP in reducing prolonged lung cancer care.

Methods: First, a mixed-methods systematic review was conducted to retrieve evidence of the effect PNP has on diagnostic and treatment timeliness among lung cancer patients. Additionally, it critically appraised the content related to the design, population, activities, and evaluation outcomes. Secondly, stakeholders from PNP in Mexico were identified, interviewed, and case studies formulated to compare each programmes characteristics and impact on diagnostic and treatment timeliness in cancer across the continuum of care. Thirdly, a qualitative examination of patient journeys was conducted through structured interviews with lung cancer patients (N=46) admitted to the National Cancer Institute (INCAN) in 2021. Coding was conducted inductively and thematic analysis used. Journeys were classified into public, private and mixed. The profiles of typical and atypical patients were presented using joint-display of triangulated qualitative and quantitative data. Additionally, primary data was collected from electronic health records of 2645 patients admitted to the INCAN from 2004-2021 to measure intervals from symptom onset to treatment. Linear regression models evaluated the association of lung cancer care intervals with clinical characteristics and social-determinants of health. Due to skewness of data, values were fitted and log-transformed. Patients were right-censored and survival analysis undertaken. Lastly, through mixed methods, results from the interviews and the electronic health records were triangulated.

Results: Eleven articles were eligible for the systematic review. Lung

cancer PNP more frequently focused on researching the treatment interval using quasi-experimental, observational and experimental designs. Non-experimental evidence supports that PNP can increase lung cancer care timeliness, while experimental studies did not. The lack of strong evidence can be explained by heterogeneity in PNP design and evaluation, rendering the analysis with biased results. A PNP typology is built to explain why heterogeneity in evaluation and lack of design standardisation limits research conducted through systematic reviews.

Five PNP were identified in Mexico, classified under the proposed framework and found to be different types of navigational care. However, all did not measure impact in timeliness in cancer care, hindering understanding of their impact on early diagnosis and treatment.

The most frequent symptom is cough. Prolonged lung cancer care intervals are shown to be influenced by symptom appraisal, "normalisation" and disease awareness, access challenges, misdiagnosis, regional infrastructure disparities and financial constraints. Family plays a crucial role in urging patients to seek care.

The electronic health record data showed 74% of patients were diagnosed with advanced stage lung cancer. The median time from symptom onset to treatment was 192 days. Variations in the total interval were determined by characteristics such as: age (p-value 0.002), sex (p-value <0.0001), type of symptom (dyspnoea p-value <0.0001, chest-pain p-value= 0.044), cancer stage (stage IV p-value= 0.034) and cancer type (SCLC p-value= 0.010). However, the role of covariates varied in each of the intervals studied. Overall, women experienced lower hazard of dying than men (p-value= <0.0001). However, other characteristics evidence differences in survival outcomes such as: education (p-value= 0.001) and region (p-value <0.0001).

Conclusions: Results from the thesis evidence complementary, expanded, discordant, and confirmed meta-inferences of the reasons for prolonged lung cancer care intervals at the INCAN in Mexico. However, due to unstandardised PNP implementation and research (both at the international and local level), evidence does not support PNP increase timeliness across lung cancer care.

Impact Statement

The research presented in this thesis delves into the critical realm of cancer care diagnostic and treatment timeliness, particularly focusing on lung cancer in Mexico. By conducting a comprehensive investigation into the lung cancer care intervals and the potential impact of PNP implementation, this study fills significant gaps in the existing literature.

First, the findings underscore the urgent need for patient-centred interventions to address prolonged diagnostic and treatment intervals in lung cancer.

Through a mixed-methods approach, this thesis systematically evaluates the effectiveness of PNP in reducing prolonged intervals in lung cancer care. By synthesising evidence from a systematic review, case studies of PNP in Mexico, qualitative examination of patient journeys, and analysis of electronic health records, a nuanced understanding of the factors contributing to prolonged intervals emerges. Importantly, this research identifies the heterogeneity in PNP design and evaluation as a significant barrier to establishing conclusive evidence on their efficacy. The proposed typology of PNP offers a framework for understanding this diversity and highlights the need for standardisation in research methodologies.

The triangulation of results reveals multifaceted insights into the complex interplay of factors influencing lung cancer care intervals, including symptom appraisal, access challenges, misdiagnosis, and socioeconomic disparities. Notably, the study identifies gender, age, symptom type, cancer stage, and socioeconomic position as key determinants of prolonged care intervals and survival outcomes. These findings underscore the importance of tailored interventions that address the specific needs and challenges faced by diverse patient populations.

Furthermore, this research advocates for a rigorous and standardised approach to evaluating the effectiveness of patient navigation interventions across the cancer care continuum. By emphasising the importance of frameworks and methodologies that capture the impact of PNP on timeliness in cancer care, this thesis lays the groundwork for future research and policy initiatives aimed at improving access to timely care for lung cancer patients.

In light of ongoing challenges such as the COVID-19 pandemic, fragmented healthcare systems, and evolving insurance schemes, the findings of this study

hold particular relevance. Efforts to enhance access to timely care must prioritise evidence-based interventions informed by a comprehensive understanding of the patient journey and the systemic factors influencing cancer care timeliness. By addressing these challenges head-on, this research aims to contribute to improved outcomes for lung cancer patients in Mexico.

Policymakers, healthcare practitioners, and researchers possess a road map for effecting tangible improvements in lung cancer care and research and accompany an era of enhanced access, equity, and quality in cancer care in Mexico.

Acknowledgements

I would like to express my sincere thanks to the Mexican population and their family members who, despite facing the challenges of lung cancer, generously shared their experiences, contributing crucial insights to my study. Your resilience and openness have left a lasting impact on me.

To all the individuals who participated in the interviews throughout my PhD, your willingness to share your stories added depth and meaning to my research. Your contributions have been invaluable.

I extend my deepest gratitude to my family, my rock and unwavering support throughout this academic journey. To my husband David Karim, whose encouragement and love sustained me through the challenges; and to my daughter, Emma, who as a one-year-old, brought joy and perspective to each day.

I am indebted to my supervisors, Cecilia Vindrola, Anne Peasey, and Hynek Pikhart, for their guidance, wisdom, and unwavering support. Your mentorship has been instrumental in shaping the trajectory of my research and personal growth.

To my dear friends at UCL: Pamela Almeida, Carlos Valencia, Phillip Frank, Eliazar Luna, Ellie Lob, and Alejandro Maeda, thank you for providing not only camaraderie but also invaluable insights and perspectives that enriched my research. Your friendship made the academic journey more enjoyable, and one that prompted me to come back to finish the PhD.

My heartfelt appreciation goes to my parents and brother for their unwavering belief in my abilities and their enduring encouragement. Your support has been the foundation upon which I built this academic achievement. Special thanks to my Mom who cared for Emma during the last weeks in the thesis write-up.

I am also grateful for the feedback provided by Stephen Bradley and Robert Kerrison in the PhD thesis. Your constructive input has greatly contributed to the refinement of this work.

I extend my gratitude to FUNSALUD, particularly to Hector Valle, for his support during the course of my PhD. Their commitment to advancing healthcare research has been a source of inspiration.

Special thanks to Dr. Oscar Arrieta who allowed me to take on my PhD research at the INCAN. Without his involvement and support this wouldn't have happened. Also, I would like to say thank you to nurse navigator Lupita, I truly admire your work and will always remember our discussions. Thank you for sharing your workspace with me.

I will always be grateful to Dr. Alejandro Mohar and Dr. Manuel Urbina for their continuous supervision and guidance. Your expertise and commitment to my academic journey have been instrumental in shaping my professional journey.

I also want to thank Dr. Felicia Knaul, who believed in me and initiated my journey in public health. Thanks to her, I found my passion and purpose in this field.

A heartfelt thank you goes to CONACYT and the State of Hidalgo for their financial support during my PhD. Their investment in my education has been instrumental in the realisation of this academic milestone.

In conclusion, I am thankful to everyone who has played a part, no matter how big or small, in this transformative chapter of my life. Your collective influence has made this journey meaningful and has contributed to the person I am today.

Agradecimientos

Me gustaría expresar mi más sincero agradecimiento a la población mexicana y a sus familiares que, a pesar de enfrentar los desafíos del cáncer de pulmón, generosamente compartieron sus experiencias, aportando ideas cruciales a mi estudio. Su resistencia y apertura han dejado un impacto duradero en mí.

A todas las personas que participaron en las entrevistas a lo largo de mi doctorado, su disposición para compartir sus historias añadió profundidad y significado a mi investigación. Sus contribuciones han sido invaluables.

Extiendo mi más profundo agradecimiento a mi familia, mi apoyo sólido e inquebrantable a lo largo de este viaje académico. A mi esposo David Karim, cuyo estímulo y amor me sostuvieron a través de los desafíos; y a mi hija Emma, quien, siendo una niña de un año, trajo alegría y perspectiva a cada día.

Estoy en deuda con mis supervisores, Cecilia Vindrola, Anne Peasey y Hynek Pikhart, por su orientación, sabiduría y apoyo inquebrantable. Su mentoría ha sido fundamental para dar forma a la trayectoria de mi investigación y crecimiento personal.

A mis queridos amigos en UCL: Pamela Almeida, Carlos Valencia, Phillip Frank, Eliazar Luna, Ellie Lob y Alejandro Maeda, gracias por brindar no solo camaradería sino también ideas y perspectivas invaluables que enriquecieron mi investigación. Su amistad hizo que el viaje académico fuera más placentero y me impulsó a regresar para completar el doctorado.

Mi sincero agradecimiento va a mis padres y hermano por su creencia inquebrantable en mis habilidades y su constante estímulo. Su apoyo ha sido la base sobre la cual construí este logro académico. Un agradecimiento especial a mi mamá, quien cuidó de Emma durante las últimas semanas en la redacción de la tesis.

También agradezco los comentarios proporcionados por Stephen Bradley y Robert Kerrison en la tesis doctoral. Su aporte constructivo ha contribuido enormemente a la mejora de este trabajo.

Extiendo mi gratitud a FUNSALUD, en particular al Lic. Héctor Valle, por su apoyo durante el transcurso de mi doctorado. Su compromiso con el avance de la

investigación en salud ha sido una fuente de inspiración.

Agradezco especialmente al Dr. Oscar Arrieta por permitirme realizar mi investigación de doctorado en el INCAN. Sin su colaboración y apoyo, esto no hubiera sido posible. También quiero agradecer a la enfermera navegadora de pacientes Lupita, admiro sinceramente su trabajo y siempre recordaré nuestras conversaciones. Gracias por compartir el espacio de trabajo conmigo.

Siempre estaré agradecido al Dr. Alejandro Mohar y al Dr. Manuel Urbina por su supervisión y orientación contínua. Su experiencia y compromiso con mi trayectoria académica han sido fundamentales en la formación de mi camino profesional.

También quiero agradecer a la Dra. Felicia Knaul, quien creyó en mí e inició mi trayectoria en salud pública. Gracias a ella, encontré mi pasión y propósito en este campo.

Finalmente, un agradecimiento sincero a CONACYT y al Estado de Hidalgo por su apoyo financiero durante mi doctorado. Su inversión en mi educación ha sido fundamental para la realización de este hito académico.

En conclusión, agradezco a todos los que han tenido un papel, por pequeño que sea, en este capítulo transformador de mi vida. Su influencia colectiva ha hecho que este viaje sea significativo y ha contribuido a la persona que soy hoy.

Contents

List of Figures

List of Tables

Glossary

ALK Anaplastic Lymphoma Kinase

CASP Critical Appraisal Skills Programme

COFEPRIS Federal Commission for Protection against Sanitary Risks

COVID-19 COVID pandemic in 2019

CI Confidence Intervals

CT Computerised tomography

CVP Cecilia Vindrola Padros

DALYs Disability Adjusted Life Years

DGIS General Direction of Health system information

DGED General Direction of evaluation and performance

DOI Digital Object Identifier

EBG Elysse Bautista Gonzalez

EHR Electronic Health Records

EGFR Epidermal Growth Factor Receptor

FPGC National Fund for Catastrophic diseases

FUNSALUD Mexican Health Foundation

GDP Gross Domestic Product

GP General Practitioner

HIC High Income Countries

HR Hazard Ratio

IMSS Instituto Mexicano del Seguro Social- Mexican Institute of Social Security

INCAN Instituto Nacional de Cancerología- National Cancer Institute

INEGI Instituto Nacional de Estadística y Geografía - National Institute of Statistics and Geography

INSABI Instituto de Salud y Bienestar- Institute of Health and Wellness

ISSSTE Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado- Insitute of social security and social services for state workers

LC Lung Cancer

LMIC Low and Middle Income Countries

MRI Magnetic Resonance Imaging

MOH Ministry of health

MXN Mexican Pesos

NGO Non-Governmental Organisation

NSCLC Non-small Cell Lung Cancer

SCLC Small-cell Lung Cancer

OECD Organisation of Economic Development

PEMEX Petroleos Mexicanos- Mexican Petroleum Company

PNP Patient Navigation Programmes

RAT Risk Assessment Tool

RCT Randomised-controlled-trial

SEDENA Secretaria de Defensa Nacional- Ministry of National Defense

SEMAR Secretaria de Marina- Ministry of the Marines

SEP Socioeconomic position

SP Seguro Popular- Popular Insurance

SSA Secretaría de Salud- Ministry of Health

TDI Total Diagnostic Interval

TKI Tyrosine Kinase Inhibitor

TNM Tumour site, Nodule and Metastasis

UCL University College London

UHC Universal health coverage

UK United Kingdom

USA United States of America

WHO World Health Organisation

Chapter 1

Introduction to PhD Thesis

Delays in cancer care are highly associated with advanced-stage disease and mortality [1]. Prevention of delays in cancer care is crucial to achieving a reasonable time lag between disease onset, clinical progression, and an affordable treatment [1–3]. As a result, literature suggests interventions directed to avoid advanced stages of cancer should be encouraged (particularly in middle-income settings) [1]. Among the actions suggested for early diagnosis and treatment of lung cancer are: measuring delays [3], the establishment of targets (time) for each event in the cancer pathway [4, 5] and patient navigation [6–12].

This thesis aims to investigate delays in lung cancer care in Mexico and the role of PNP in increasing timeliness in lung cancer care.

Chapter 2 presents an introduction to lung cancer epidemiology and the Mexican context, elaborating on the justification for why studying delays in lung cancer care in Mexico is relevant. Additionally, it presents a literature review of policies and actions suggested to avoid late-stage diagnosis and treatment of cancer. Among them, patient navigation programmes are outlined as a useful tool. These two topics, "patient navigation" (topic I) and "delays in lung cancer" (topic II), make up the content mainly studied throughout this dissertation.

As part of the background of this project, a systematic review is presented in **Chapter 3** to explore the design of cancer patient navigation programmes found in the literature and the methods used to evaluate their impact in reducing delays in lung cancer care across the cancer continuum. As a result, this Chapter offers insights into patient navigation research gaps and the potential of patient navigation as a powerful tool in overcoming delays among lung cancer patients in a Mexican context.

Chapter 4, describes the mixed methods design, the thesis aim, specific objectives, and hypotheses.

Chapter 5 dives into patient navigation in Mexico and presents primary data as case studies of active navigation programmes. Results enhance the understanding of how these programmes tailor their activities to address the unique challenges of cancer care in Mexico. These case studies are then fitted into typologies that arise from grounded theory built during the systematic review.

This mixed-methods PhD project seeks to both understand barriers through qualitative methods and measure delays in lung cancer care. Hence, **Chapter 6** presents primary data collected through interviews (N=46) and Electronic Health Records (EHR) (N=3018). This data-rich chapter sheds light on the barriers faced by lung cancer patients in Mexico during their healthcare journey. Through triangulation of qualitative and quantitative evidence, the chapter not only describes the typical and atypical patient journeys and survival trajectories but also proposes a comprehensive classification of patient journeys to evaluate patient outcomes within the context of the Mexican health system. In addition, **Chapter 6** uncovers patient and health system delays experienced by lung cancer patients in Mexico. These delays are compared to results from the United Kingdom,

providing valuable insights into potential disparities between healthcare systems in different countries. Furthermore, the Chapter utilises quantitative methods, specifically regression modelling, to explain the causes of delays in patient care. In consequence, by identifying barriers from both proximal and distal origins, **Chapter 6** sheds light on the complex factors contributing to delays in the Mexican health system. Together, the qualitative and quantitative streams' convergence offer complementary, expanded, discordant or confirmed insights. The findings underscore the need for targeted interventions and policy development to improve lung cancer care and reduce delays. Each study within the thesis is followed by its own discussion and summary.

Chapter 7 brings together all the recommendations in research and policy for both topics: patient navigation and delays in lung cancer care. Lastly, a comprehensive general conclusion is presented at the end in **Chapter 7**, providing a synthesis of the findings across all studies. This approach ensures a thorough examination of the research results and facilitates a comprehensive understanding of the implications and contributions of the research presented in the thesis.

Chapter 2

Background

2.1 Lung cancer in Mexico

Epidemiology

Worldwide, Lung Cancer (LC) represents 14% of the new cancer cases and 20% of the cancer deaths [13]. LC incidence is generally highest in High Income Countries (HIC) [13,14]; however HIC are also experiencing declining or plateauing incidence rates. In contrast, in Low and Middle Income Countries (LMIC) like Mexico cancer incidence is still rising [1].

LC is traditionally classified into two main sub-types: Non-small Cell Lung Cancer (NSCLC) and Small-cell Lung Cancer (SCLC) [15–19]. When conducting epidemiological research, this classification is useful due to the distinct clinical features and treatment approaches associated with each one [15]. NSCLC is the most prevalent form of LC and includes sub-types such as adenocarcinoma, squamous cell carcinoma, and large cell carcinoma. Conversely, SCLC is less common but highly aggressive, with often more advanced stages of the disease on presentation [15–19]. Furthermore, risk factors and etiological factors may differ between NSCLC and SCLC. For example, while smoking is a well-established risk factor for both sub-types, SCLC is more strongly associated with smoking than

NSCLC [15–19].

Patients with either type of LC experience similar symptoms, including: chest pain or discomfort, chronic cough, breathing difficulties, wheezing, hoarseness, coughing up blood (haemoptysis), loss of appetite, and unexplained weight loss [15–19]. Other symptoms such as discomfort in the bones, cognitive confusion, seizures, and paralysis can also arise in more advanced stages of the disease [15–19].

Treatment approaches for NSCLC and SCLC can vary. Due to SCLC being diagnosed in advanced stages, treatment modalities may more often be palliative. Nonetheless, NSCLC often involves surgical resection, targeted therapies, and immunotherapies, whereas SCLC is typically treated with chemotherapy and radiation therapy [15, 20].

Overall survival depends on the stage of LC at diagnosis[1]. Prognosis and survival rates differ significantly between NSCLC and SCLC [15, 22, 23]. Metastases in LC can be solitary or oligo-metastases, especially in advanced-stage cases [15, 22, 23].

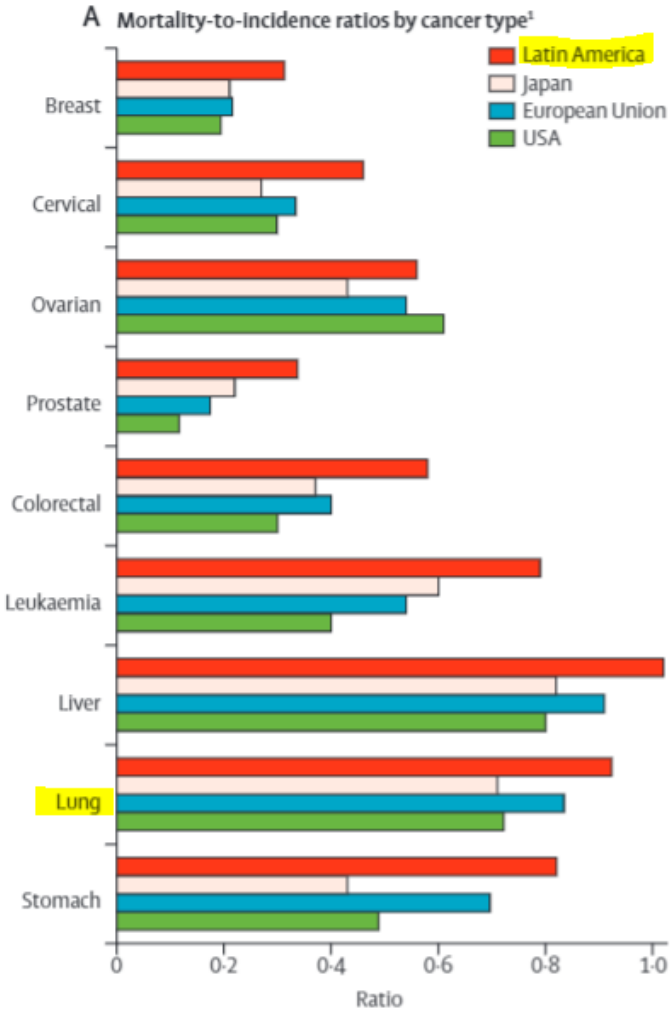
Mortality & Mortality-to-incidence inequalities

In the United Kingdom (UK), LC is the leading cause of cancer mortality, and the majority of LC cases are identified in symptomatic individuals with stages III or IV illnesses, which are less eligible for possible curative therapy [24,25]. Similarly, LC is more frequently diagnosed in stages III or IV of the disease in Mexico [20, 25].

[1]Clinical staging in cancer is part of a medical task that will define treatment and therefore prognosis [21]. The cancer stage is defined by the size of the tumour; the spread of cancer to nearby lymph nodes and spread of cancer to other parts of the body [15, 22, 23]. The higher the stage at diagnosis the worse the prognosis [21]. The Tumour site, Nodule and Metastasis (TNM) for LC is explained in ***Figures F2 and F3 in Appendix A1*** and the patient's performance status (how well a person can carry on ordinary daily activities while living with cancer) [15]

Nonetheless, although the mortality burden of cancer is large in both countries due to advanced stage diagnoses [1, 24], the mortality-to-incidence ratios are higher in Mexico [1]. For instance, in Mexico, every year there are 10,000 new LC cases [25], and approximately seven thousand people die [26].

Figure 2.1: Comparison of lung cancer mortality-to-incidence ratios across regions in the world



Source: Goss et al 2013 [1]
This image includes the UK as part of Europe. The ratio identifies whether a country has a higher or lower mortality for a condition, normalised to its incidence.

Figure 2.1 outlines different regions' mortality-to-incidence-ratios by cancer type [1]. The mortality-to-incidence ratio across different regions is worse among stomach, lung and liver cancer. Across all types of cancer, Latin America has the

Figure 2.2: Mortality-to-incidence ratio among all cancer types in the Americas

Source: Goss PE et al. 2013 [1]

The darkest colours represent higher mortality-to-incidence ratio and the stripes consider public insurance coverage >50% of the population.

worst outcomes. This image shows despite LC incidence being generally higher in HIC [13, 14], it is in the Latin-American region that mortality-to-incidence ratios are highest, reaching almost 1:1 ratio across all cancer types [1]. More importantly, when compared to other forms of cancer, LC patients have the poorest mortality-to-incidence ratio after hepatic cancer [1]. In Latin-America particularly, Mexico falls under Argentina, Suriname, Uruguay and Costa Rica's all-cancer mortality-to-incidence ratio's (see ***Figure 2.2***) [1]. This further justifies the reason

why early diagnosis and treatment should be studied and addressed in Mexico.

Unequal distribution of risk factors and unfavourable outcomes

In Mexico, most of the LC cases are associated with smoking (HR: 25) [25, 27]. Despite taxation and restrictions on tobacco marketing, labelling and packaging, and smoking restriction in public places, there are approximately 145 million smokers aged 15 years or older in Latin America [1] and tobacco use accounts for 26% of all cancer deaths and 84% of LC deaths [1]. However, in the south of Mexico, LC mortality rates are considerably lower than the northern region, and deaths are less attributable to smoking [27]. In fact, specific regions (states) in Mexico, like: Baja California, Mexico State, Guanajuato and Tabasco, have larger mortality rates due to ambient particulate matter pollution than smoking [27] (see ***Figure F4* in Appendix A1)**. Hence, besides tobacco, the Mexican population is also exposed to other environmental carcinogens that cause LC such as: radon, asbestos, exposure to wood smoke, occupational settings, and urban and rural settings [1,25,27]. People cooking and heating their homes with biomass substances such as wood, animal dung, and crop waste (that are 100 times higher than acceptable smoke levels) explain this particular pattern [1, 27][2].

Additionally, there are deep inequalities in LC outcomes in Mexico. Mortality rates due to LC are unequally distributed between population groups [1, 24, 27]. For instance, in Mexico from 1990-2016 there is a 41% decrease in LC mortality rates, but primarily driven by men [27]; and the most deprived population benefits the least from this decrease in mortality (***Figures F5 & F6*** in Appendix A1) [27]. Lastly, although Disability Adjusted Life Years (DALYs) due to LC have overall decreased in Mexico, LC has the second highest DALYs after Leukemia [27].

[2]Wood-smoke and wood by-products are carcinogenic and promote tumour growth and progression [1]

2.2 Mexico and its healthcare system

Fertility rates in Mexico have fallen from 3.4 to 2.2 births per woman and life expectancy has increased almost 5 years since 1990 [28, 29]. Current life expectancy at birth is 75.4 years, with a 5 year difference between men and women. Moreover, Mexico's population is rapidly ageing [28]. ***Table 2.1*** outlines relevant socio-demographic, economic and health-system differences between Mexico & the UK [29–33].

Table 2.1: Mexico *vs* UK health and other indicators comparison

Indicator	**Mexico**	**UK**
Total population (2021) [28]	128 Million	67 Million
GINI coeff [28]	45.4	32.6
Life expectancy at birth [33]	75 years	81 years
Global Fertility rate [29]	2.1	1.63
Obesity of pop. aged 15+ [34]	72.5 %	64.3%
Deaths from cancer per 100,000 [34]	118	216
Daily smokers % of pop. aged 15+ [34]	7.6%	15.8%
Male lung cancer incidence rate per 100k [14]	10.5	34.9
Female lung cancer incidence rate per 100k [14]	4.9	25.8
Male lung cancer mortality rate per 100k [14]	9.4	30.2
Female lung cancer mortality rate per 100k [14]	4.3	21.4
Health expenditure(%GDP) [34]	5.4	12.8
Health spending per capita [34]	1133 USD	5268 USD
Computed tomography scanners per million [34]	6	9
Radiotherapy equipment per million [34]	1.5	8.1
Medical graduates per 100,000 [35]	13.5	12.9

Indicators provided by the Organisation of Economic Development (OECD) serve as valuable tools for evaluating and contrasting the health systems of different countries, shedding light on potential public health issues. Specifically, a deliberate selection of these indicators aims to draw insightful comparisons between the epidemiological profiles of Mexico and the UK. This Table extends to identifying potential infrastructure deficits that could be critical in addressing public health concerns, with a focus on the example of LC. Furthermore, the GINI coefficient offers a crucial perspective by quantifying the extent to which income distribution

within a country diverges from perfect equality [28]. With zero representing no inequality and 100 as the most unfavourable indicator, the GINI coefficient becomes a vital measure in assessing and understanding the economic disparities within a given nation.

Mexico has experienced an epidemiological shift over the last decades. ***Figure F7 in Appendix A1*** [36] shows the causes for mortality ranked and compared from 1990 to 2017. Currently, after diabetes and cardiovascular diseases, neoplasms are ranked the third most important cause of death per 100,000 Mexican people [36]. Overall, 13.7% of total deaths in Mexico are caused by cancer [37] and from 2000 to 2013 the cancer mortality crude rate (per 100,000) in Mexico has risen from 58.7 to 65.1 [37]. Only six types of cancer account for 45% of all cancer related deaths (breast, prostate, lung, colon and endometrial cancer) [37]. Although breast and prostate cancer have raised public health concerns (due to higher incidence rates for women and men respectively) [26, 37], LC has raised public health concerns because it results in higher costs, the highest mortality rates and higher mortality-to-incidence-rations [26, 37–39].

Mexico according to the OECD

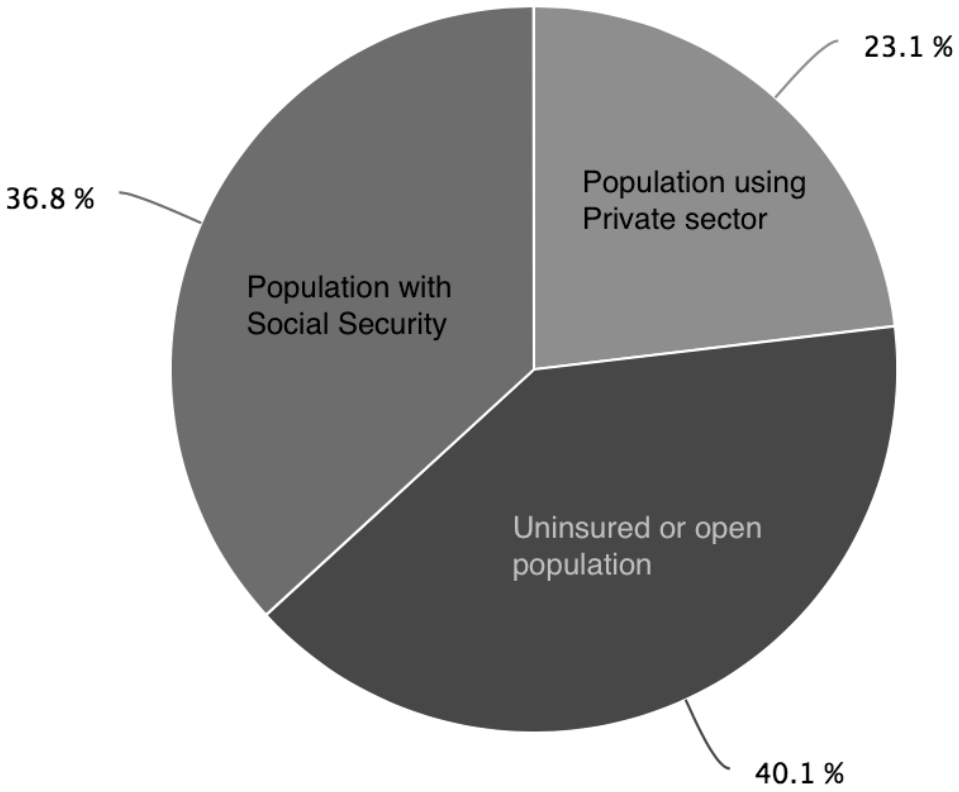
Mexico is the second most densely populated country of the OECD [35]. Despite it holding a large population (126 million inhabitants) [28], Mexico has the lowest gross national income of the OECD, making it the only middle-income country in North-America [35]. It is bordered by the United States of America (USA) in the north and Guatemala and Belize in the south.

Mexico spends 37% less of its Gross Domestic Product (GDP) on health compared to the rest of the countries in OECD; and up to 48% of Mexico's health

expenditure is made through private health spending [32]. Furthermore, in terms of the general healthcare infrastructure and human resources, large gaps exists between the supply and demand. For instance, while the OECD countries have a mean of 4.8 hospital beds per 1000 inhabitants, Mexico has a total of: 1.5 beds [40]. Magnetic Resonance Imaging (MRI) and Computerised tomography (CT) scanners also fall below the OECD's mean, with an 84% and 78% difference accordingly [41,42]. In addition, there are 2.4 doctors and 2.9 nurses per 1000 inhabitants, which is almost 6 times less than Norway which ranks the highest in this health indicator [43,44].

Mexico's fragmented healthcare system

Figure 2.3: Distribution of health system users in Mexico



Source: Instituto Nacional de Estadística y Geografía - National Institute of Statistics and Geography (INEGI), 2015 [45]

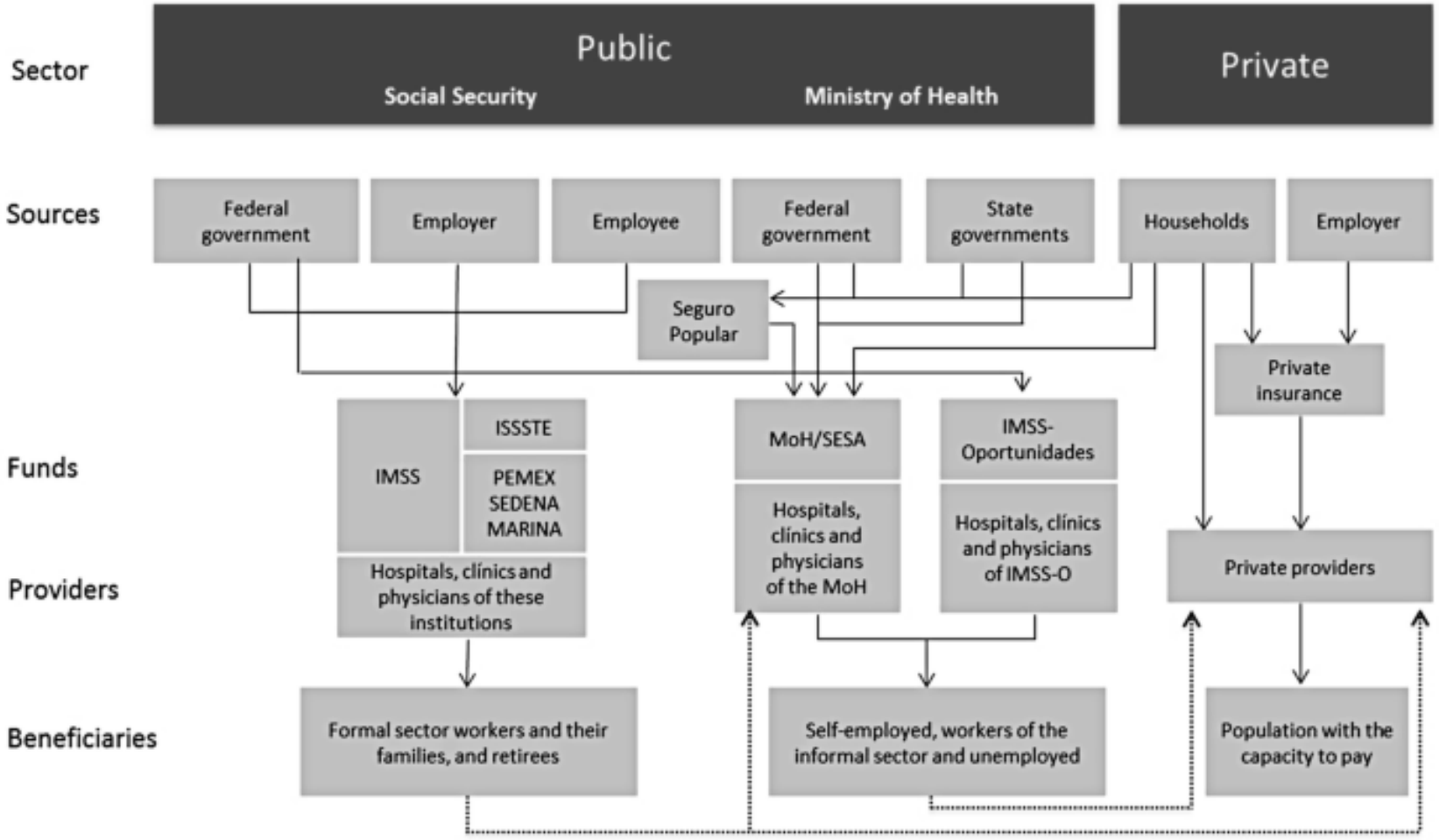
The Mexican health system is built from both private and public sectors [46].

healthcare delivery in this case is conditioned by employment status [46, 47]. As a result, there are three types of *health system users* for which different sub-systems are formulated: the population that is privately insured (23%), publicly insured (37%) or uninsured (40%) [46, 47]. Social insurance institutions provide healthcare services for the publicly insured (workers and pensioners), whereas the uninsured population is covered by the Ministry of health (MOH) [1]. ***Figure 2.3*** gives an overview of the distribution of the population using health services [45].

Previously, the uninsured population was covered by the Seguro Popular- Popular Insurance (SP). However, new reforms to the health system have been implemented in the last couple of years [48]. Currently, the SP has been dismantled and the Instituto de Salud y Bienestar- Institute of Health and Wellness (INSABI) took its place in 2020, before its formal elimination in 2022 [48]. The uninsured population has increased over the last couple of years due to the COVID pandemic in 2019 (COVID-19) and the dismantling of the SP and reductions in healthcare spending [45, 48].

There are different social insurance institutions for instance: the *Mexican Institute of Social Security* (Instituto Mexicano del Seguro Social- Mexican Institute of Social Security (IMSS)), the *Institute of Social Security and Services for State Workers* (Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado- Insitute of social security and social services for state workers (ISSSTE)), the *Mexican oil Company* (Petroleos Mexicanos- Mexican Petroleum Company (PEMEX)), the *Ministry of the Navy* (Secretaria de Marina- Ministry of the Marines (SEMAR)) or *the Ministry of National Defence* (Secretaria de Defensa Nacional- Ministry of National Defense (SEDENA)) [46, 49]. In an attempt to visually represent the health Mexican system, a previous Minister of Health developed ***Figure 2.4*** to describe the fragmented and complex system.

Figure 2.4: Visual representation of the Mexican Health System and its components



Source: Frenk J., et al 2019 [49]
The acronyms can be found in the abbreviations list.

Levels of healthcare delivery

Across the health sector (regardless of private or public), the health system is divided into three levels of healthcare delivery. The primary level is focused on general outpatient services (delivering health promotion, vaccination, disease prevention, maternal and child health and ambulatory services aligned to the community needs) [46]. The secondary level holds both out and inpatient services (preventive medicine, maternity, medical, surgical, hospital, pharmaceutical and some laboratory services) [46]. Lastly, tertiary care (third level/hospitals) serve a wider range of population through highly specialised outpatient and inpatient services [46]. Social insurance institutions: IMSS, ISSSTE, SEDENA, SEMAR and PEMEX mainly operate through tertiary and secondary level services. In contrast, the MOH holds all the levels of healthcare delivery across the 32 states of the republic. Each sovereign state has a MOH and a decentralised public body representing the national MOH. As a result 32 sub-systems exist for each state [46]. The third level of healthcare delivery is generally geographically centralised both nationally and locally [46].

The IMSS holds secondary-tertiary health services and within its social protection tasks it also covers sickness and maternity, work risk , disability, life, retirement and old-age insurance in addition to social benefits, day-care insurance and others [46]. A branch of IMSS(IMSS-bienestar) offers primary level and secondary level services to financially unprotected people in marginalised rural areas. Their services mainly focus on ambulatory, maternal and infant health. More recently, the IMSS has also allowed volunteer affiliation. Therefore, expanding the possibilities and opening it's doors to the unsecured population. The ISSSTE has social protection benefits analogous to the IMSS but they are specific for government employees, pensioners, retirees and their families. These beneficiaries

also have access to physical and mental rehabilitation services, as well as personal loans for the acquisition of property and social and cultural services. Similarly, public institutions like SEDENA, SEMAR and PEMEX hold the same social benefits as the previous, plus insurance for retirement and disability risks [46].

Health sector's Governance

Governance in the health sector is carried out by the National MOH (federal government). Strategic planning (public programmes and policies), inter-sector coordination, prioritisation and internal evaluation and health regulation are all part of the tasks of the MOH. As a result, the MOH holds agencies or departments (such as the *Federal Commission for the Protection against Sanitary Risks* (Federal Commission for Protection against Sanitary Risks (COFEPRIS)), responsible for the control and evaluation of health facilities; the prevention and control of the harmful effects of environmental factors on health; the sanitary control of products and services, and the sanitary control of the advertising of the activities, products and services [50]. Departments like the *General Directorate of Health Information* (General Direction of Health system information (DGIS)) are responsible for the managing and directing health data collection in Mexico and the *General Directorate of Epidemiology* (General Direction of evaluation and performance (DGED)) takes on other specific tasks such as: epidemiological surveillance, performance evaluations at the national and state level of priority programmes, personnel and public health services [46, 50].

Health sector's funding

As visualised in ***Figure 2.4***, each social insurance institution (the IMSS, ISSSTE, PEMEX, SEMAR, SEDENA), the MOH and the private sector are funded from different sources. Social insurance institutions raise funds through a tripartite

contribution from the employer, the employee, and the government and in turn the patients become beneficiaries of sets of social protections schemes [47]. In contrast, health services in the MOH are financed through the INSABI or previously known as the SP, which was built from contributions from the federal government, state government and individuals [46][3]. In consequence, budget allocation, costs per person or intervention, medical services, and effectiveness between institutions are heterogeneous. **Figure 2.4** visually represents the heterogeneous source of funds for each healthcare delivery institution [49].

All the above-mentioned institutions have the sovereignty to decide on what, why, how much and from whom medicines are bought; how much medical interventions cost (this includes cancer treatment and interventions) and which ones are covered for or not [47, 52], rendering an unequal patient pathway from the start. Hence, the health sub-systems are not only different in the therapeutic coverage against a specific disease, but they are also heterogeneous in the number of beds, human resources, technology and infrastructure they have. Affiliation to a specific health institution defines the dimensions of inequality at the diagnostic, control, treatment, and palliative care stage [47]. Comparisons between public insurance institutions and the MOH are summarised in ***Table 2.2*** [47,53]. This table describes the approximate amount of population covered by health institution[4] and depicts unequal characteristics of health services in Mexico. Category Secretaría de Salud- Ministry of Health (SSA) represents the uninsured population (covered by the MOH).

[3]Before 2019, health services for the uninsured population groups (the lower income population) were provided by the MOH and were financed through the *Public Insurance for social and Health protection*, better known as the SP, which was built from economic contributions from the federal government, state government, and individuals [46]. The SP served as a subsidiary insurance scheme for the uninsured population at the primary and secondary levels of healthcare delivery, while insuring against catastrophic expenses related to highly specialised medical services for beneficiaries who suffered from high-cost diseases [51]

[4]These numbers can exceed the total population, as there can be double or even triple affiliation

Table 2.2: Comparison of public insurance institutions and the Ministry of Health in Mexico

	Health institutions			
Health indicators	**PEMEX**	**SSA (MOH)**	**IMSS**	**ISSSTE**
Year of creation	1938	1943	1944	1960
Type of affiliates	Public insurance (petroleum company)	Uninsured (uninsured population)	Public insurance (private companies)	Public insurance (government workers)
Number of affiliates	12 million	55 million	62 million	13 million
Annual budget spent	$8,761 p/c	$2,852 p/c	$3,725 p/c	$4,031 p/c
# interventions covered	8000	1603	8000	8000
Doctors per 1,000	7.2	1.8	1.7	3
Nurses per 1,000	7.5	2.6	2.3	3.1
Beds per 1,000	3.7	1.2	1.1	1.6

Source: Bautista-González, E. et al. 2021 [53]

Health institutions have been over time designed to cater to distinct groups of workers and thus, contributed to the development of a fragmented health system. This system has evolved around occupation-specific institutions rather than a cohesive, unified health framework. Consequently, disparities in per capita (p/c) health spending have emerged among these institutions, giving rise to pronounced health inequalities.

2.3 Barriers for timely diagnosis and treatment in Lung cancer

Lung cancer screening and early referral

Currently, there is no national public LC screening program for high-risk populations in Mexico. However, those at high-risk have the option to pay for these through out-of-pocket expense [25]. Thus, the most well-equipped population to face a LC diagnosis are the people in higher socioeconomic groups [52]. Moreover, timely and effective referral are key to a national program for the early diagnosis of LC [25]. However, there is no referral protocol. It is assumed that many patients are lost to follow-up and that health systems are difficult to navigate.

The health system's fragmentation and the lack of Universal health coverage (UHC) contribute to low screening rates, delayed referrals, and thus delays in diagnosis and treatment and high mortality-to-incidence ratios in all types of cancer [1, 8, 37]. In LC particularly, only 5% of the new cases are detected in early stages in Mexico [25]. Thus, increasing efforts towards the prevention of cancer and avoidance of advanced stage cancer should be taken [1].

Only a few cancers may be detected asymptomatically, and even in nations with population-based screening systems, most cancer patients are identified by

symptoms [54]. Thus, in symptomatic patients, early diagnosis techniques (also known as "clinical downstaging") may improve patient outcomes [54]. Nonetheless, heterogeneous barriers to early diagnosis and treatment are experienced by LC patients in Mexico [52].

In clinical practice, testing for specific tumour characteristics helps identify cancer sub-types, predict their behaviour, and decide over treatment options [1,55]. Factors that affect cancer diagnostics include unavailability of laboratory supplies, essential equipment, skilled personnel, resources for appropriate training, and quality control [1]. However, there is insufficient physical and technological resources to diagnose and provide LC care in Mexico [1, 46]. In addition, diagnostic tests are not always performed nor covered by the insurer in Mexico. **Figure 2.5** shows genetic testing or tumour molecular analyses coverage vary by institutions [52]. These are also reported to be paid by pharmaceutical companies directly which means testing is not done exclusively at centralised laboratories as suggested by some authors [1].

The quality of tissue samples, technical handling of tissue specimens, slide preparation, and staining variability between the institutions and their providers allows for duplication of tests as results are easily ignored if not performed according to institutional standards [1]. Thus, LC delays in Mexico are also a result of non-standardised molecular testing procedures that add an additional step in the cancer pathway. Lastly, although the use of PET–CT and biomarkers are increasingly employed to guide and personalise therapeutic choices; these innovative diagnostic technologies might significantly increase diagnosis and treatment intervals [55,56].

Unequal distribution of resources for lung cancer

Highly specialised cancer services are concentrated in the centre of the country (closer to Mexico City) [46, 48]. Additionally, the first and second level of care usually lack the infrastructure to diagnose a patient with cancer (lack of CT scans or bronchoscopy). Meanwhile, third-level hospitals only provide care for patients with a confirmed diagnosis [57]. Thus, this becomes a barrier to accurate staging and subsequent treatment [1], again resulting in a breach in the cancer pathway and rendering institutions unfit to serve equally across the country.

Unequal distribution of healthcare professionals also represents a barrier to early cancer care [1]. Mexico City has most of the oncologists and equipment required to deliver cancer diagnostic and therapeutic services. Out of 269 medical oncologists registered in Mexico 44% work in Mexico City, 8% in Monterrey, and 8% in Guadalajara [1]. This means that 60% of the oncologists live in only the 3 largest cities in Mexico.

Figure 2.5: Comparison of lung cancer care coverage by healthcare institutions in Mexico

Resource	*IMSS*	*ISSSTE*	*Pemex, Sedena, Semar*	*SPS*	*Private*	*Incan*
Screening program	No	No	No	No	No	Pending resource allocation
First-line chemotherapy	Yes	Yes	Yes	No	Yes	Only for women
Second-line chemotherapy	Yes	Yes	Yes	No	Yes	Only for women
Genotyping (hospital-based)	No	No	No	No	Yes	Yes
Genotyping (surrogate by pharma)	Yes	Yes	Yes	Yes	Yes	Yes
ALK-TKI	No	No	Yes	No	No	Yes
EGFR-TKI	Yes*	Yes*	Yes	No	Yes	Yes
Bevacizumab	No	No	Yes	No	Yes	Yes
Immunoncology	Yes*	No	Yes	No	Yes	Only for patients in clinical trials
Palliative care	Yes	Yes	Yes	Yes	Yes	Yes

*Gefitinib and Pembrolizumab have recently been approved for inclusion in the Basic Medication Catalogue of IMSS.
IMSS: Instituto Mexicano del Seguro Social; ISSSTE: Instituto de Seguridad y Servicios Sociales para los Trabajadores del Estado; Pemex: Petróleos Mexicanos; Sedena: Secretaría de la Defensa Nacional; Semar: Secretaría de Marina; SPS: Seguro Popular; Incan: Instituto Nacional de Cancerología; ALK: anaplastic lymphoma kinase; TKI: tyrosine kinase inhibitor; EGFR: epidermal grouth factor receptor

Source: Gerson et al 2019 [52]

High costs and lack of lung cancer treatment coverage

Despite efforts towards UHC in the early 2000's [48], LC coverage varies depending on patients being publicly insured, privately insured or uninsured [38, 52]. LC is only partially covered in most cases, causing catastrophic patient expenditures [38, 52]. Among the uninsured population in particular, treatment is cost prohibitive [1,52]. **Figure 2.5** describes LC coverage varies by institution [52]. For instance, screening, genotyping, first- or second-line chemotherapy treatment, nor immunoncology therapy are available for the uninsured population (referred to as SPS). Instituto Nacional de Cancerología- National Cancer Institute (INCAN) represents the only hospital working for the MOH that covers treatment for the uninsured population as a third-level hospital. Nonetheless, immunotherapy is only accessible to those enrolled in clinical trials. Furthermore, up until 2019 treatment was only provided to women by the catastrophic expenditure branch of the SP: the National Fund for Catastrophic diseases (FPGC) [52]. Genotyping is only available through pharmaceutical companies.

The differences in coverage shown in **Figure 2.5** are due to the fragmented health system that has different funding and governance schemes [46, 47, 49]. Each health institution has the autonomy to choose the devices and medications depending on the institutional budget [47]. Thus, while other population groups are entitled to treatment and other forms of cancer care, the uninsured population (users of the MOH: unemployed, self-employed, and informally employed) lacks access to LC care, making it a medical and ethical concern. The lack of access against LC is even worsened by the fact that treatment is expensive, particularly when treated in more advanced stages of the disease. **Figure 2.6** shows the costs for LC per stage in Mexico [38, 39, 52]).

Although smoking is the leading cause of LC cases and that tobacco taxation generates revenue, tobacco taxes are ring-fenced for purposes other than health [52, 58]. Thus, while patients are diagnosed, they are not treated even if most patients paid taxes due to tobacco consumption [58].

Despite several breakthrough LC therapies, none of these are currently available for the uninsured population [52]. Out of the 114 currently approved and available oncology drugs in Mexico, only 14 are therapeutic options for LC. Eleven of them are available for patients who do not have actionable mutations or who aren't candidates for immune checkpoint inhibitors (4 are obsolete; 2 are standard first-line treatment options for NSCLC[5], four second line options for NSCLC[6] and one for SCLC[7]). Only 3 drugs in this catalogue are targeted therapy agents, including a Tyrosine Kinase Inhibitor (TKI) for patients with rearrangements in the Anaplastic Lymphoma Kinase (ALK), and TKI for patients with sensitizing mutations in the Epidermal Growth Factor Receptor (EGFR) gene. Unfortunately, all these targeted therapies [8] are first-generation drugs, which have clinical limitations. The latest generation of drugs [9] have managed to circumvent these limitations and offer patients better survival outcomes; however, none of these are included in the catalogue [20, 52]. Immuno-oncology agents that have shown to increase the progression-free and overall survival of LC patients, are also not included in the list of medications [20, 52].

[5] Carboplatin/pemetrexed
[6] Docetaxel, Gemcitabine, Vincristine, Vinorelbine
[7] Etoposide
[8] Crizotinib, Erlotinib and Gefitinib
[9] Afatinib, Osimertinib, Alectinib

Figure 2.6: Lung Cancer costs by disease stage and mutation status

Event	*I* *$MXN*	*II* *$MXN*	*III* *$MXN*	*IV mut-* *$MXN*	*IV mut+* *$MXN*
Diagnosis	19 353.00	30 766.92	57 156.42	83 545.93	83 545.93
Hospitalization		32 058.33	49 822.03	67 585.72	67 585.72
Surgery	9 722.00	9 722.00	9 722.00		
Intensive therapy			14 392.69	28 785.38	28 785.38
Molecular tumor profile				3 055.00	3 055.00
Chemotherapy		39 686.33	30 191.99		
Systemic treatment (mut +)					137 279.03
Systemic treatment (mut -)				46 948.28	
Radiotherapy		57 495.00	57 495.00	57 495.00	57 495.00
Monitoring	18 783.00	5 396.00	5 396.00	8 094.00	16 188.00
Total	47 858.00	175 124.57	224 176.13	295 509.31	393 934.06

Mut +: mutation positive; Mut -: mutation negative.

Source: Gerson et al 2019 [52]

Social determinants of prolonged lung cancer care

Prolonged care across the healthcare continuum are more frequently experienced by some population groups. For instance, marginalised populations have low participation in screening programmes which leads to increasing times to diagnosis and treatment and thus, progression to more advanced stages of disease [1].

According to research conducted in other countries, the factors associated with less timely care are: LC type, age, race, education, socioeconomic position, rurality, employment, insurance status, curative vs palliative radiotherapy, initial referral to a non-respiratory physician, number of diagnostic tests prior to diagnosis, number of hospitals required to obtain diagnosis, number of specialists consultations, lack of multidisciplinary team assessment, comorbidity and atypical symptoms at presentation or lack of symptoms [3, 7, 24, 54, 59–63] or even treatment delays due to surgical resection, radiation therapy have been documented [60].

Individuals face differences in cancer care and outcomes due to patients having different illness interpretations, holding diverse decision-making strategies and behaviours [60, 64, 65]. For example, indigenous people often lack thorough explanations about their illnesses, medication, and clinical instructions [1]. It is known that low levels of health literacy, fear, lack of trust in medical institutions and attitudes toward providers all contribute to personal reasons to delay cancer care [12, 62]. Additionally, health beliefs contribute to health-seeking behaviours, and these can also become reasons to delay cancer care [12, 62, 65]. Logistical issues such as: employment schedules, lack of transportation, housing or childcare might also enhance personal reasons to delay cancer care [12, 62]. As a result, it is the most deprived populations that endure greater pain and fatalism when diagnosed with cancer [6].

Disease symptoms themselves can also prolong the search for care. LC particularly, is one of the "harder-to-suspect" cancers due to its low-predictive symptom profile [54, 56]. Therefore, non-specific symptoms might not prompt high degree of clinical suspicion and cause delays in care [24, 54, 56]. Additionally, comorbidity, disability, distress, depressive symptoms, lack of appetite, sleeplessness are symptoms that might hinder access to healthcare throughout patients' journeys [12, 64].

Moreover, the health system is a barrier for timely LC care [52, 54, 60, 61]. The Mexican health system faces many challenges in preventing, diagnosing, and treating patients with LC and it is poorly equipped to deal with increasing incidence and disproportionate mortality rates [1]. The silos generated by the coexisting health subsystems (institutions) are strong barriers for the portability, accessibility and delivery of health services [46]. Similarly, distance to facilities, inadequate communication between healthcare professionals, a low cancer suspicion index, shortage of staff, lack of diagnostic and therapeutic infrastructure all leads to worse outcomes in the population. As a result, both individual and health system characteristics have an impact in access, continuity of healthcare and thus cancer outcomes [60, 61, 63, 66, 67].

On the part of health professionals, cultural misconceptions, misunderstanding of traditions and differences in communication, can also negatively impact the patients experience when seeking for oncology services [1]. Patients can also experience a sense of discomfort with the doctor-patient relationship [65].

2.4 Policies, interventions and tools to reduce prolonged intervals across the lung cancer care continuum

Primary prevention is key to reduce LC incidence. In Mexico, public policies that aim to reduce environmental carcinogens and smoking are already promoted as a primary line of preventive action in Mexico [27]. However, policymakers and researchers suggest increasing efforts towards the avoidance of advanced stage disease through early diagnosis and opportune treatment [1, 54]. These are crucial to achieve a reasonable time lag between disease onset, clinical progression and an affordable treatment [1], otherwise known as "clinical down-staging". Early diagnosis and opportune treatment can contribute to better clinical outcomes and overall improve patient experience [54]. Some of the interventions suggested to reduce delays in cancer care are:

- LC screening [24, 25]
- Risk Assessment Tool (RAT) [24, 68]
- Centralised genetic testing and tumour molecular analysis [1]
- Care coordination [3, 8, 69]
- Universal access to treatment [38, 52, 58] & unification of healthcare system [70]
- Reduction in time for approval for drugs [1]
- Electronic health records [71, 72]
- Measurement of delays to care as part of quality assurance [3]
- Patient navigation [6–12, 69]

2.4. Policies, interventions and tools to reduce prolonged intervals across the lung cancer care continu

Delays in cancer care are highly associated with advanced-stage disease and mortality [1].Thus, LC screening has been outlined as a potential intervention to achieve earlier diagnoses of LC among the people at risk. In this context, in LC screening for every 320 people, one could be saved [25]. If high-risk patients are further selected, the number of patients to study goes down to 161 [25]. However, not all studies have been able to verify the association of screening and early detection. In the Mexican context LC screening has been controversial due to risk or radiation for the patient and most importantly, due to the lack of infrastructure and human resources to achieve screening interventions [25]. A new study is taking place at the INCAN that will evaluate the effect of screening campaigns.

In addition to LC screening programmes, the use of RAT prompts physicians to investigate potential LC more effectively [68]. RAT encourages doctors to think about referral thresholds and potentially lead to earlier diagnosis. Hence, there is a possibility that using RAT may improve mortality rates [68].

Furthermore, according to the literature, genetic testing and tumour molecular analyses should be done at centralised laboratories to ensure quality and efficiency throughout the process [1]. Efforts by the Ministry of Health and the National Cancer Institute in Brazil exemplify this approach [1]. In Mexico, genetic testing and molecular analysis are not conducted at a centralised centre. Therefore, a large investment in infrastructure and political will is required to achieve this goal.

Another intervention that improves timeliness in cancer care is care coordination [3]. Studies show that multidisciplinary clinics are associated with increased rates of active treatment. Similarly, a “two-stop” diagnostic process that expedites investigation through multidisciplinary meetings via teleconference [3], is shown to reduce the median time from first specialist visit to surgery by 50% [3].

Patients are studied by CT, biopsy and/or other diagnostic tests at the initial visit and a treatment is developed during the multidisciplinary meeting within 3 days [3].

National policies towards universalising health-care, unification of medical institutions and LC coverage have been previously suggested to be among the most important lines of intervention to reduce late diagnosis, treatment and therefore LC mortality [52,58,70]. However, the different funding schemes and governance have not allowed the Mexican health system to become unified. For LC particularly, policy makers have suggested research be conducted to accelerate the diagnosis and treatment in earlier stages before creating national policies for expensive treatment coverage with very short survival span [25, 52, 54].

From a regulatory perspective, reducing delays for the approval of new cancer drugs also represent an accessibility issue in Latin America [1]. In the USA for example, new cancer drugs were responsible for >50% of the improvement in survival rates, contributing >10% to the total improvement in life expectancy of its citizens [1].

EHRs have also been suggested as technological tools that ameliorate the informational continuity of cancer care along the pathway [71–73]. By allowing portability of patient information from one institution to another, EHR help reduce duplicating diagnostic and therapeutic efforts [71–73]. Therefore, several attempts to regulate and implement the EHR have been made in Mexico. Since 2013 the EHR use was suggested throughout the health sector. However, none of them have been successful [71, 74]. There has been no political will to implement it. For example, the EHR is not yet contemplated in the General Law of Health, which reduces the legal strength for its universal instrumentation [72].

Moreover, when taking into consideration both the structural and individual barriers to health care, interventions directed to increase access or help overcome barriers are encouraged to reduce delays in cancer care [3, 75, 76]. As a result, Patient Navigation Programmes (PNP) have been outlined as potential interventions that can improve the overall timeliness of LC care [8, 9, 75, 77–79]. Patient navigation is defined as a personalised and coordinated healthcare delivery support model with *"the core function of eliminating barriers to timely delivery of health care for individual patients across the healthcare continuum"* [6]. PNP aim to facilitate the patient's passage through the health system [10, 12]. From promoting timely, regular screenings and faster diagnostic resolution (often with large differences between navigated and non-navigated populations) [8, 9] to facilitating treatment and recovery, PNP have become an innovative intervention that seeks to reduce clinical upstaging and provide cost-effective and timely access to care among undeserved patients [10, 11].

Lastly, measuring delays in cancer care might also be a way to raise awareness of the issue, serve as basal measurement and inform policy [3, 54]. For instance, the UK British Thoracic Society and the National Health Service Cancer Strategy announced LC detection and treatment time intervals in 1998. In addition, the 2000 UK National Health Service Cancer Strategy set targets for rapid cancer treatment. In parallel, the RAND Corporation developed quality indicators for prompt diagnosis and treatment, concentrating on the time from the first abnormal radiography to diagnosis and diagnosis to therapy [3, 24, 56].

Chapter 3

Systematic Literature Review: Patient Navigation in Lung Cancer

3.1 Background

Patient navigation is defined as "a healthcare delivery support system with the principal function of eliminating barriers to timely delivery of health care for individual patients across the healthcare continuum" [6]. PNP are bio-psycho-social interventions that seek to reduce health inequalities and ameliorate health outcomes [8–11, 77, 78, 80–85].

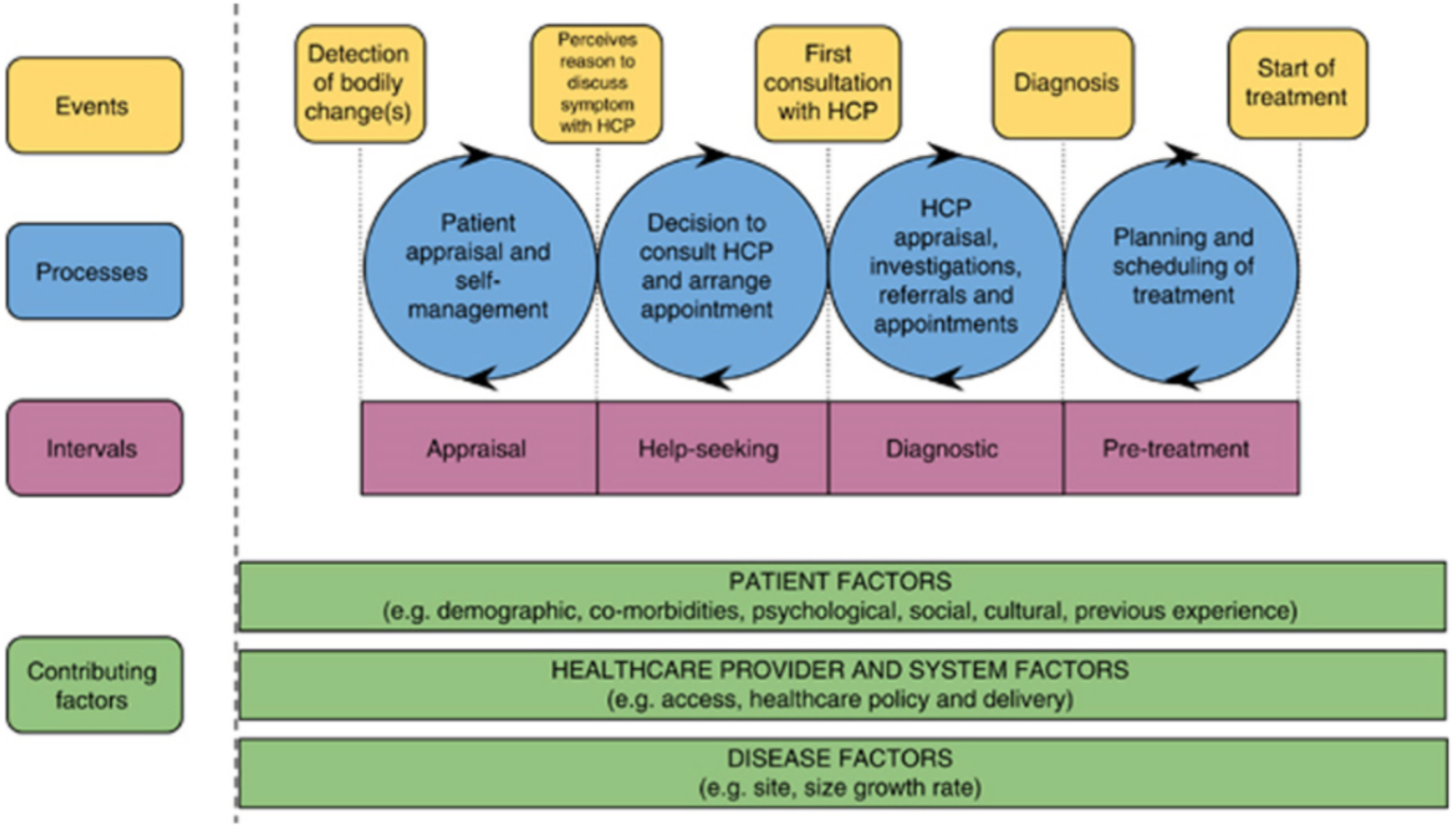
The concept of "patient navigation" was initially developed in the United States as a strategy to address the disparities in cancer outcomes between low-income, minority, and immigrant populations [86, 87]. In 1989, the *"Report to the Nation on Cancer in the Poor"* found poor people faced substantial barriers to obtaining cancer care, which lead to great hardship. Soon after, Doctor Harold Freeman pioneered the first patient navigation program among breast cancer patients in Harlem, New York, in 1990 [86]. These programmes generally target individuals and communities most at risk for delaying or skipping care, with the goal *"to facilitate timely access to quality cancer care that meets cultural needs and standards of care*

for all patients" [87].

The pathway to cancer treatment has great relevance when studying patient navigation and wanting to understand its origins. It delineates relevant clinical events, patient and healthcare processes that take place throughout time (see ***Figure 3.1***) [88]. These events and processes happen simultaneously and are determined by the social determinants of health [88]. These influence the success of patients in achieving access to healthcare. As a result, there are cancer patients who face multiple barriers to care across the cancer continuum. These barriers have been narrowed down to four major categories: patient factors, navigation process factors, navigator factors, and external factors [89]. For instance, people with a lower socioeconomic position face substantial barriers to obtaining cancer care [6,62,90,90–92]. This contributes to disparities in health outcomes [62,90–92]. Consequently, patient navigation interventions seek to address the breakdown of the pathway to cancer treatment and facilitate access to care.

Many researchers have used this patient navigation for diseases such as: surgery, chronic disease, cancer, etc. Moreover, PNP thrives in diverse care settings, spanning hospitals, community health centres, mobile clinics, and even platforms. This adaptability aims for accessibility and seamless navigation for patients [87,93].

Figure 3.1: Walter's pathway to cancer treatment



Source: Walter et al 2012.

Events mark the start and end of the different time intervals that lead to the final event: the start of treatment (yellow boxes). In parallel, there are patient and healthcare processes that take place during each time interval (blue circles). All of these events, processes and time intervals are in turn affected by the proximal or distal determinants of health, i.e., patient factors, healthcare provider and system factors, and the diseases factors themselves (green boxes). [88]

Elements of patient navigation programmes

PNP have four basic elements: case identification, detection of structural and individual barriers, the development of a personalised plan to address those barriers, and a systematic follow-up to track progress across the health continuum [87, 94]. Unlike case management, which organises patient care activities and services with different providers and seeks quality of service, optimal utilisation, and lower costs, a PNP aims to reduce health inequalities by taking into account the patient's context and perspective [12]. Although there are elements of patient navigation that frequently overlap with managed care, case management, advocacy, and social work, navigation is distinguished from these services by its focus on identifying and addressing logistical, psycho-social, and personal barriers to care [6, 10, 12, 95, 96].

Relevant stakeholders

The navigation process can begin at any point in time throughout the health continuum. There are three main actors in the navigation process: the user (patient or family member), the navigator, and the medical team embedded within the health system. Navigators are patient advocates that help patients overcome barriers in the health system through collaborative efforts with their caregivers or family members [12, 97].

Navigation programmes vary in the professionals they employ. Some programmes seek out cancer survivors as navigators [98], and sometimes navigators are nurses, health professionals, social workers, or community representatives with little or no previous experience in the medical field and no clinical training. Some studies also report a mix of patient navigator professional backgrounds. Other programmes go beyond professional background and may also seek to employ navigators with race and language in concordance to their patients' characteristics

in order to increase the effectiveness of the program [12, 99].

Patient navigators can be trained. Different resources have been developed over time through different collaborations to develop training. Content such as basic health promotion, privacy, end of life, advanced directives and visit guides are some examples of the content developed to train navigators [100].

Activities

PNP have a multifaceted landscape, with diverse services, target populations, and adaptability to care settings. Although their focus might help patients from promoting screening, diagnostic resolution [8, 9, 77, 78] to facilitating treatment and recovery [10, 11, 80, 101], PNP seek to facilitate the patients' passage through the health system [10, 12]. Hence, each PNP brings unique expertise, tailoring support to meet individual patient needs [102] in their particular context.

The navigators' activities may include scheduling diagnostic and follow-up appointments; facilitating referrals; providing language or translation services; coordinating communication between patients and with the physician; assisting with insurance paperwork; linking patients to hospital or community services; and providing health education [73, 81–84, 93, 96, 103, 104]. Moreover, as navigators are linked to resources outside the health system (i.e., other healthcare providers, social services and community programmes), they connect patients to community-based programmes to help overcome their personal barriers, including proactively connecting patients to external resources, following patients after referral, and providing information and encouragement [105]. The scope of services, in turn, plays a crucial role in enhancing the patient' satisfaction and health outcomes [85].

Depending on the barriers found, navigation models vary widely in "touch" level or intensity of the program. Meanwhile some involve only brief, remote communication between the patient and navigator, and the intervention implies mainly provision of information, advice, and encouragement. Others involve much more extensive interaction and multiple in-person meetings. Depending on the program, the role of a navigator consists of providing social support, encouraging the patient while supporting the patients autonomy, helping the patient understand the medical information that is given and coordinating personalised care across the different departments. In some cases, the navigator may accompany the patient on visits or interface directly with healthcare providers, insurers, and others the patient's behalf [73, 93, 96, 97, 104].

Navigator programmes have been implemented in both clinical and community-based settings. Evidence suggests both types of navigator programmes are similarly effective in improving patients' knowledge and behaviours [93]. Community-based navigators have shown to have more in-person interaction with patients, and to undergo training on a somewhat broader range of topics. [93]. However, navigators in both settings played similar roles, providing information, identifying, and addressing barriers, encouraging and sharing personal histories, and providing logistical and language support [93].

In a qualitative study, the navigator's relationship with the patients was described to be business-like, professional and/or friendly [89]. Differences in the approach chosen envisioned different outcomes, the most important being building trusting relationships. Authors emphasised the importance of the navigator's emotional support and the fact that the navigator was "there" as a continuous, supportive resource [12, 101]. Persistence and assertiveness were also found to influence the patient navigation program, as well as being empathetic and flexible

with the patient's needs [89].

Evidence of effect

Opportune screening

Studies have found dramatic increases in timely cancer screening [8, 77, 78, 97]. Other studies infer increases in the overall number of screenings or increase in the proportion of diagnoses that are less severe (suggesting that the program led to diagnoses of cancer at earlier, more treatable stages [77]. These results were particularly beneficial to those who previously reported to experience prolonged time to care [77].

Rapid referrals and diagnostic resolution

A pilot PNP study in Mexico registered a 97% success rate of patients being navigated (referred) to a specialised centre for [57]. Similarly, benefits such as reduction in missed or cancelled appointments and better preparation for diagnosis are mentioned in the literature [57]. There is also evidence that navigation leads to faster diagnostic resolution, often with large differences between navigated and non-navigated populations [8, 9]. For example, navigated women were much more likely to adhere to follow-up testing and receive diagnostic resolution than the control group [101, 106]. Navigated women were also more likely than non-navigated women to complete follow-up testing within the recommended period [101, 106].

Treatment access, completion, and adherence

There is mixed but generally positive evidence that navigation increases compliance with treatment recommendations and leads patients to begin treatment soon after diagnosis [97, 107]. For example, the average number of days between receiving a definitive breast cancer diagnosis and initiating therapy was significantly reduced

with patient navigation, and effect was even more pronounced among Hispanic women, eliminating the disparity between Hispanic and other women in timeliness of treatment [108].

Outcomes such as reduction of inappropriate treatment, reduction of clinic visits or emergency room visits and depression were significantly associated with the patient navigation program [8, 9]. In addition, healthcare providers reported navigation programmes to improve treatment adherence and completion rates, particularly among patients at greater risk for non-compliance [80, 101].

Follow-up

Patient navigation can also reduce the rates of loss to follow-up [109, 110]. For example, a study in 2007 found that a patient navigator after controlling for age, race, insurance status, reason for referral, and source of referral, women who had access to the navigator had 39% greater odds of having timely follow-up [109]. However, in a lay navigator program targeting under-served populations in Tampa who had an abnormal breast or colorrectal cancer screening, did not find a significant effect from navigation on the time to diagnostic resolution or the percentage of patients achieving diagnostic resolution within 180 days [102].

Self-efficacy

Through the continuum of care PNP have been attributed to increase cancer knowledge and risk perception among patients [62]. As a result, there are positive effects on patient empowerment or self-efficacy among cancer patients who have access to navigation [12, 80, 105, 109–111]. For example, women in an Randomised-controlled-trial (RCT) receiving navigation services reported feeling more confident about their ability to take care of their health in the future [112].

Quality of life

There is also some evidence of positive effects on self-reported quality of life and emotional well-being of cancer patients who have access to navigation [8,109–111]. Patients receiving navigation reported significant increases in several components of quality of life and experienced fewer hospital stay days in comparison with the control group [8, 113].

Other authors emphasised the importance of the navigator's emotional support and the fact that the navigator was "there" as a continuous, supportive resource [101, 112]. Loskutova et al. 2016 studied a program that used patient navigators to connect diabetes patients to community-based programmes to help them manage their condition, including proactively connecting patients these programmes, following patients after referral, and providing information and encouragement [105]. The authors found both improved clinical outcomes and greater self-efficacy among navigated patients after the intervention.

Survival rate

Evidence also suggests improvements in the 5-year survival rate (i.e., breast cancer increasing from 39% to 70% of their patients) have been achieved [6, 94]. Earlier studies also demonstrate fewer patients present advanced stages of cancer [97]. Although the impact on survival is much less understood [8, 85], after the introduction of patient navigation, enrolment in hospice before death and home death increased, while the use of chemotherapy and use of emergency department, intensive care unit and acute care visits decreased [8].

Patient satisfaction with healthcare services

Navigators are encouraged to manage the needs and expectations of patients so that the flow through the care continuum runs as smoothly as possible [12]. In studies reporting patient satisfaction measures, patients typically report high satisfaction

with navigator services and their healthcare services [103]. These effects on patient satisfaction are present even in programmes that fail to produce significant impacts on treatment or quality of life.

PNP also foster trust and empowerment [62, 80]. In an RCT studying a nurse navigator program for patients recently diagnosed with breast, colorrectal, or LC, patients reported significantly fewer problems with their care, especially psycho-social care, care coordination, and information [8, 114].

Funding & Costs

Patient navigation programmes have been reported to be cost effective, cost saving and even profitable from the health services perspective [77]. Researchers calculate the incremental cost-effectiveness ratio to be $95,625/life years saved [77]. Nonetheless, results suggest a navigation system adds to the expenditures and is only seen as an investment when the model's focus is on diagnosing in early stages of the disease (clinical downgrade) [115]. In addition, many do not believe it is a sustainable model when applied to all patients and should just be used in marginalised minorities for it to be targeting the people who most need it at a lower cost [116].

Reducing inequalities

Evidence suggests patient navigation reduce health inequalities by mostly benefiting the most economically deprived population (such as the urban poor, remote rural and indigenous communities) who have poorer health outcomes owing to common structural barriers that prompt in-opportune cancer-care [6, 7]. These also foster patient-centred oncology practices and have positive effects along the continuum of care [6, 7].

Systematic Reviews on Navigation in Cancer

One systematic review previously evaluated the effect of PNP in chronic diseases [82]. Although, this review included population with all-types of cancer, and diabetes, dementia, and chronic kidney disease, instead of a single-disease approach, this review was particularly interesting as it was the first approach to capturing the effect of PNP across the disease continuum. ***Figure F8 in Appendix A1*** shows the effect of PNP across the continuum of care in particular processes for each disease.

Among the systematic reviews exclusively within the realm of cancer care, two were centred solely on breast cancer [117, 118] and one addressed breast and colon cancers [119]. Another systematic review focused on summarising intervention characteristics, outcomes of interest, and validity components [120]. However, most of them relied exclusively on RCT, thereby neglecting the consideration of alternative study designs [118–120].

Another systematic review focused on cancer excluded articles not focused on under-served populations or those lacking information on adherence rates, diagnosis, or treatment effects [121]. This systematic review also disregarded secondary articles and those lacking presentation of results [121], potentially resulting in the exclusion of some content relevant to the design of the PNP. Notably, this systematic review also reported a lack of literature on LC [121].

Only one systematic review was found on PNP for LC particularly by *Shusted et al* [122]. Although it focused on screening, it described articles found across the cancer continuum. From the n=26 studies found by *Shusted et al*, most LC navigation programmes were paired with other types of cancer. Only

four were developed for LC particularly. Among them, only one study is an RCT [122], meanwhile the others were retrospective chart reviews. This suggests quasi-experimental design with no control group [123].

Positive effects were found by *Shusted et al*. For instance, increasing screening uptake, increasing molecular testing, reduction in time from suspicion to treatment initiation, reduction in time from referral to treatment, reduction in time from referral to radiation and increased earlier diagnosis from 32% to 48% (p-value= 0.0006) [122]. ***Figure F11*** in **Appendix A1** shows a summary of the findings from the systematic review on LC conducted in 2019 [122].

Gaps in the literature

Although systematic reviews have narrowed down reviews from chronic disease to cancer and then particularly to LC, only one systematic review in LC was found. However, this systematic review was originally intended to search for screening, potentially leaving out literature on early LC diagnosis. Hence, there is an imperative need to update the evidence on LC navigation. Additionally, the sample sizes, study design and overall quality of the studies found in 2019 by *Shusted et al* lacks external validity. Although PNP have been developed for other types of cancer [6, 82] and have been successful in increasing cancer care timeliness [122], there is not enough evidence to support whether PNP for LC will be effective in increasing early diagnosis and treatment of patients, particularly in Mexico. In consequence, a closer and updated look should be placed in LC navigation impact in timeliness, in addition to programme design, outcome measurement, and biases.

3.2 Methods

This chapter identified and compared international literature on PNP by using a health systems research approach. The research question for this systematic review was: *Do patient navigation programmes increase diagnostic and treatment timeliness in lung cancer?*. Hence, the main objective of the systematic review was to produce statements to guide decision making [124]. Through systematic review methodology [124], the programmes effect on timeliness, design (activities, levels of healthcare navigated, type of navigator, cancer type, etc.), study design outcome measurement, and biases were identified, extracted, and analysed. Results should inform practice, policy and research gaps [124].

Eligibility criteria

The main intervention was patient navigation for patients diagnosed with LC (from symptom onset to treatment). Studies for which the population included paediatric, imprisoned, psychiatric, cognitively impaired, or disabled patients were excluded as their navigation needs might differ. This did not include PNP focusing on vaccination (such as HPV), behavioural change that reduces the risk of cancer, surgical procedures, or transplantation around cancer nor rehabilitation. PNP focusing on screening were not eligible for inclusion as these are used for population health management purposes and fall outside the pathway to treatment model [88]. All types of study designs were eligible. Control groups were not required to be included in the review, but if found, they were reported. Results were not mandatory for inclusion. Both published and unpublished literature were eligible for inclusion. However, systematic reviews and meta-analyses were excluded from the searches. Furthermore, articles in languages other than English or Spanish were not included. Abstracts, conference papers, and trial registries were also excluded from the search.

The main outcomes collected in each identified study are:

- PNP design
  - Cancer type
  - Navigation activities
  - Focus in the pathway to cancer treatment according to Walter's framework
  - Type of navigator
- Quantitative outcomes of navigation programmes
  - Clinical (cancer stages, survival/mortality, etc)
  - Patient-reported outcomes

    Patient satisfaction,

    Health-literacy,

    Quality of life

    Other
  - Administrative outcomes

    The timeliness of care (i.e., time to diagnosis, time to treatment, etc)

    Percentage of follow-up

    Percentage of diagnosed patients

    Percentage of treated

    Other
- Qualitative outcomes of navigation programmes

Search strategy

PubMed, Cochrane , EBSCO host, CINAHL Plus, ProQuest and LILACS were selected to proceed with the search in September 2021. A range of text words and indexed terms related to *"patient navigation"* and *"cancer"* was used in the searches. Following the initial systematic review conducted, an update of the search was deemed necessary to capture the latest literature on patient navigation by december 2023. This prompted a new search in PubMed, which incorporated lessons learned from the previous experience. Notably, the search criteria excluded articles with specific words in the title, namely: screening, systematic review, scoping reviews, and surgical navigation. The search strategy used for each database is available in ***Table 3.1***.

The systematic review was registered in **PROSPERO:** `CRD42019154044` by the name ***"Patient navigation core metrics and typologies: a systematic review of models focused on cancer from symptom onset to treatment"***. [1]

[1]This systematic review sought to gather information across all cancer types. Only results in LC are presented in this Chapter. The rest of the cancer types are currently being still updated and worked with a larger team from NCI in 2024.

Table 3.1: Search strategy for systematic review in 2021 and updated version in 2023

Source	Search strategy
1 PUBMED 2021	*((((((neoplasm*[Title/Abstract]) OR cancer*[Title/Abstract]) OR lung-cancer[Title/Abstract])OR lung cancer""[Title/Abstract])) AND ((patient-navigation""[Title/Abstract]) OR patient navigation""[Title/Abstract]))"*
2 COCHRANE	*Title Abstract Keyword AND patient-navigation in Title Abstract Keyword OR "patient navigation" in Title Abstract Keyword*
3 NICE	*"patient navigation" and cancer*
4 LILACS	*(ti:("Patient navigation")) AND (ti:(cancer)) OR (ti:(neoplasm)) OR (ti:("lung cancer"))*
5 CINALH EBSCO	*TI patient navigation OR TI "patient navigation" AND TI (neoplasms or oncology or cancer)*
6 PUBMED 2023	*("NSCLC"[Title/Abstract] OR "SCLC*"[Title/Abstract] OR "lung cancer"[Title/Abstract] OR "lung-cancer"[Title/Abstract]) AND ("patient navigation"[Title/Abstract] OR "patient-navigation"[Title/Abstract]) NOT (screening[Title] OR "Surgical navigation"[Title] OR "systematic review*"[Title] OR "scoping review"[Title])*

Data collection

Elysse Bautista Gonzalez (EBG) screened the retrieved references for eligibility independently in each search engine. A total of four additional researchers[2] were supervised and trained by EBG to make decisions regarding whether the studies met the inclusion/exclusion criteria, and those that did were selected for inclusion in the review, while those that didn't were rejected. Any disagreements were resolved by discussion or by involving a third reviewer until consensus was reached. When necessary, authors sought out relevant missing data, for instance, in trial registries or other publications related to the article found through the systematic review search.

A data extraction spreadsheet was designed, piloted, and used by EBG for evidence synthesis process. The data extraction sheet poured qualitative and quantitative data into a single form and helped identify the characteristics of the navigated sample, the disease focus, the study design, a description of the navigation intervention, and their results (if available). The data extraction sheet can be found in ***Appendix A6***.

Analysis

Quantification of qualitative data was employed to capture the frequency of the emergence of PNP per year, across the globe, type of cancer, population studied and navigator type. Additionally, data comparison was conducted to capture differences in the activities conducted and technological resources used by PNP found. Similarly, all PNP found were compared with regards to the type of outcome measurements employed in each study (i.e., clinical, patient reported outcomes, administrative). This included the description of survey tools employed if any.

[2] one medical doctor with a Masters in health policy; one Masters Student; two medical oncologists

Furthermore, narrative synthesis of the results was used to discuss and compare the effect on clinical, administrative, and non-clinical outcomes using a critical view of the PNP's internal and external validity.

A separate analysis was conducted only for the RCT's using the Critical Appraisal Skills Programme (CASP). EBG assessed the risk of bias independently. A judgement of 'low risk' or 'high risk' of bias was provided for each domain.

3.3 Results

3.3.1 PRISMA flow chart

The systematic review began with the identification of 1919 articles using six different search engines in 2021. Among the literature found, 683 were duplicates. Subsequently, 1235 articles underwent screening, leading to the exclusion of 1045 based due to interventions being related to screening or interventions that were not aligned with the review's scope.

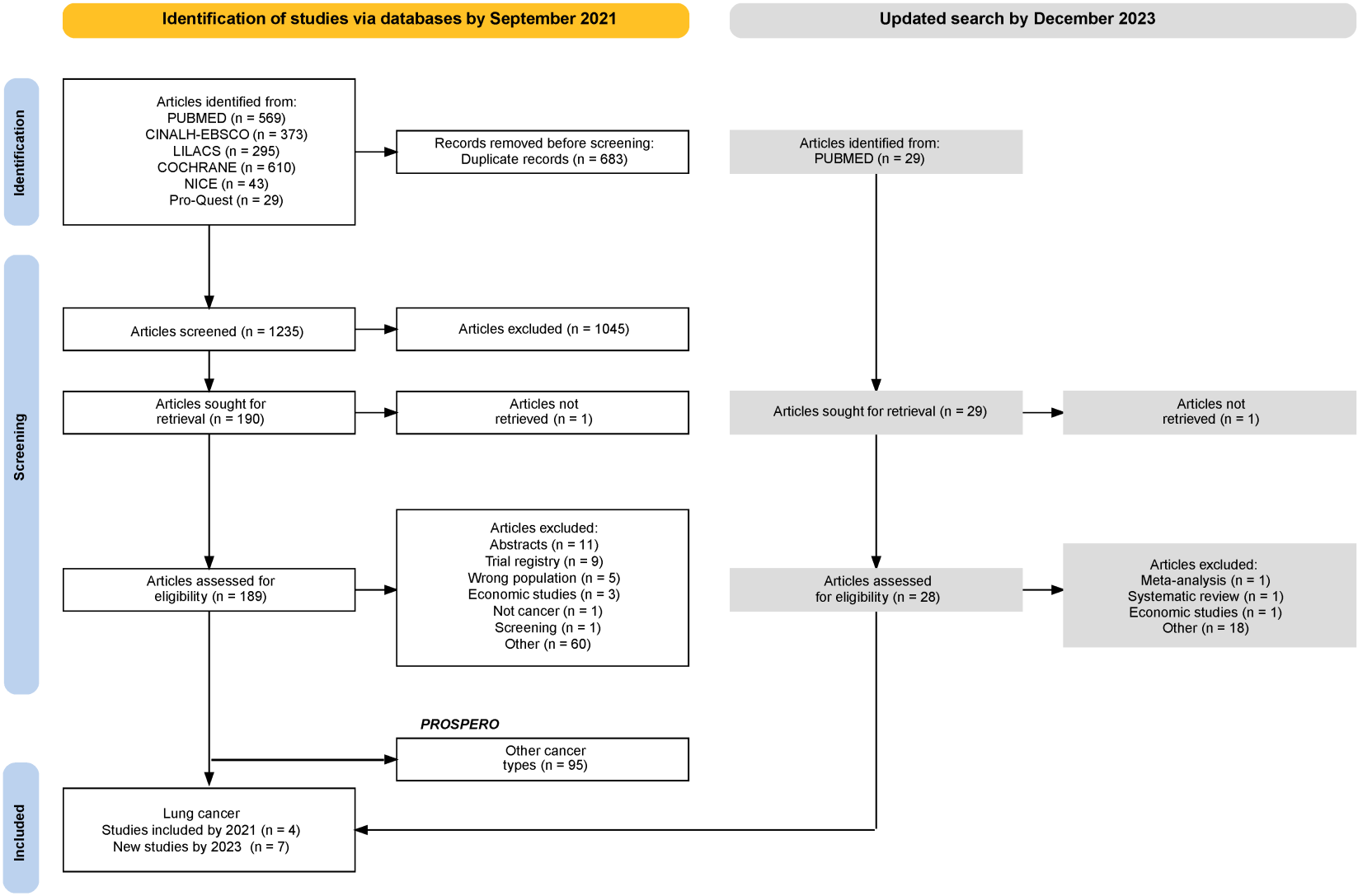
This refinement process resulted in 190 articles that were further sought for retrieval. Unfortunately, one article was not found. A thorough eligibility assessment was then conducted on the remaining 189 articles, leading to the exclusion of 90. This left a total of 99 articles related to patient navigation in cancer, with a subset of 4 specifically addressing LC.

The excluded literature, following a comprehensive assessment, was categorised into distinct groups. The "Other" category, comprising 60 articles, included those discussing patient navigation but focusing on historical background, justification of navigation, measurement of navigation intensity, navigation training, navigator relationships, navigation types, perceptions of navigation in cancer,

studies evaluating barriers that justified the need for navigation interventions, and navigation programmes focused on increasing trial participation. Although these articles were within the broader subject, they did not specifically address a particular navigation program, its design, evaluation methods, or results. Additionally, 11 abstracts and 9 trial registries were excluded as they did not contain sufficient information for inclusion in the review. Three economic studies were also identified, describing the cost of implementing patient navigation programmes or conducting cost-effectiveness analyses. Moreover, one of the articles was unrelated to cancer (focused on chronic disease patients), and five studies focused on cancer but targeted specific population groups outside the review's scope, such as incarcerated, paediatric, or adult patients who navigated for other comorbidities. One study specifically referred to navigation during screening. Consequently, all these articles were excluded from the analysis, resulting in a final sample of 99 articles addressing patient navigation in cancer.

The updated search yielded a total of 29 articles, all of which were retrieved for assessment. Subsequently, only seven articles met the inclusion criteria and were included in the analysis. The remaining 21 articles were excluded for reasons such as study type (systematic review, meta-analysis), economic studies, or being categorised as "Other". The PRISMA flow diagram in ***Figure 3.2*** depicts the flow of information through the different phases of a systematic review. Combining the results of the search conducted in 2021 with the updated search in 2023, the final selection for inclusion in the analysis comprises a total of 11 articles. This ongoing process reflects the commitment to staying current with the literature and ensuring a comprehensive and up-to-date understanding of patient navigation in the field. This Chapter will delve into the literature found in LC to capture the design and focus of PNP in the world. It will analyse the role LC PNP have increasing timeliness across the cancer continuum.

Figure 3.2: PRISMA flow chart

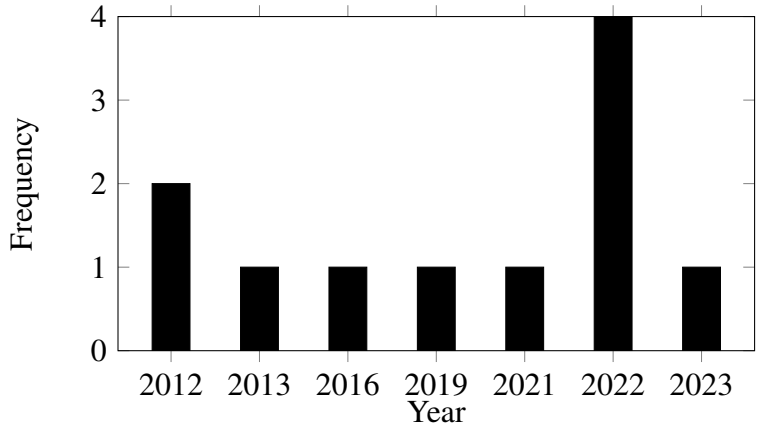


Source: Own work

3.3.2 Quantification of qualitative data

Results from this systematic review (n=11 articles) support patient navigation is more commonly published in the Unites States and is overall more common in the global north. Five articles were from USA (40%), two from Canada (20%) and Germany, Denmark, Netherlands, and Hungary had each one publication on a navigation programme for LC. ***Figure 3.3*** describes the distribution of the literature found on LC patient navigation per year up to December 2023.

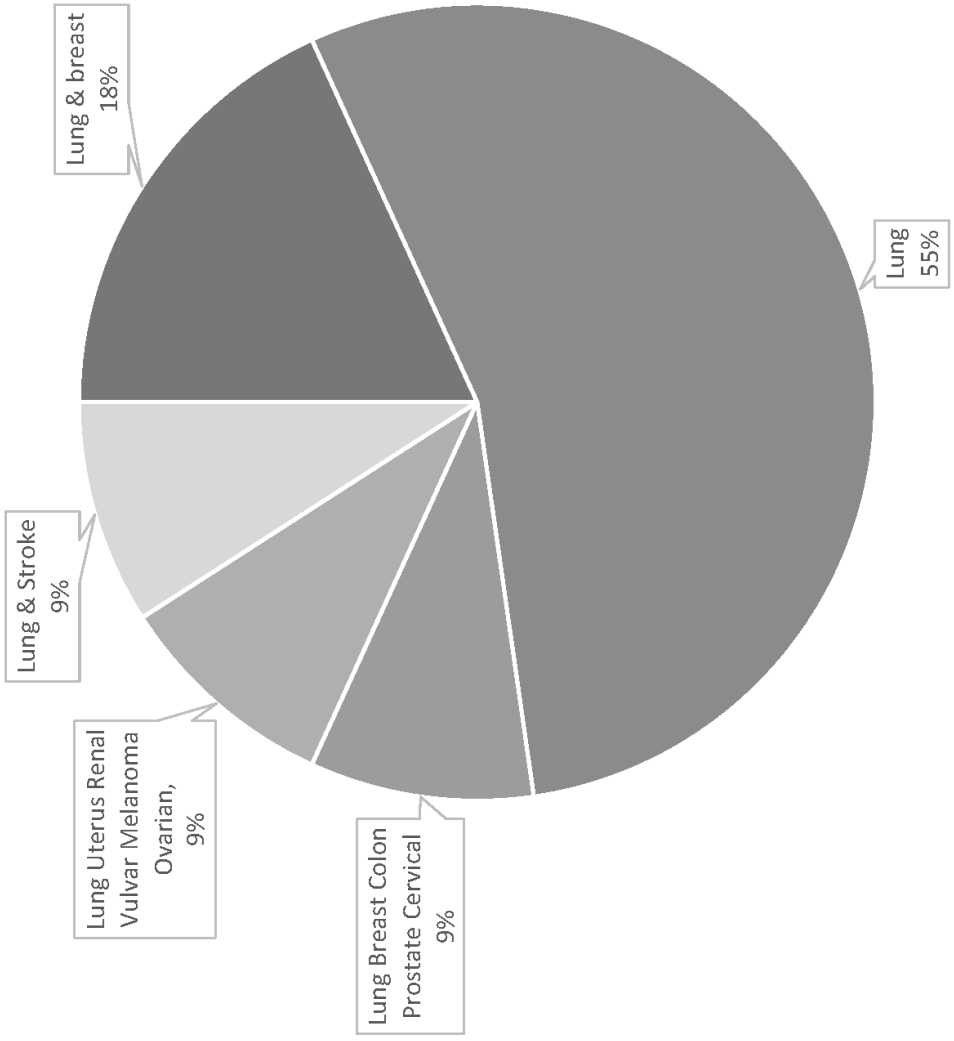
Figure 3.3: Distribution of the literature on Lung cancer patient navigation published by year found through the systematic review (N=11)



Source: Own work

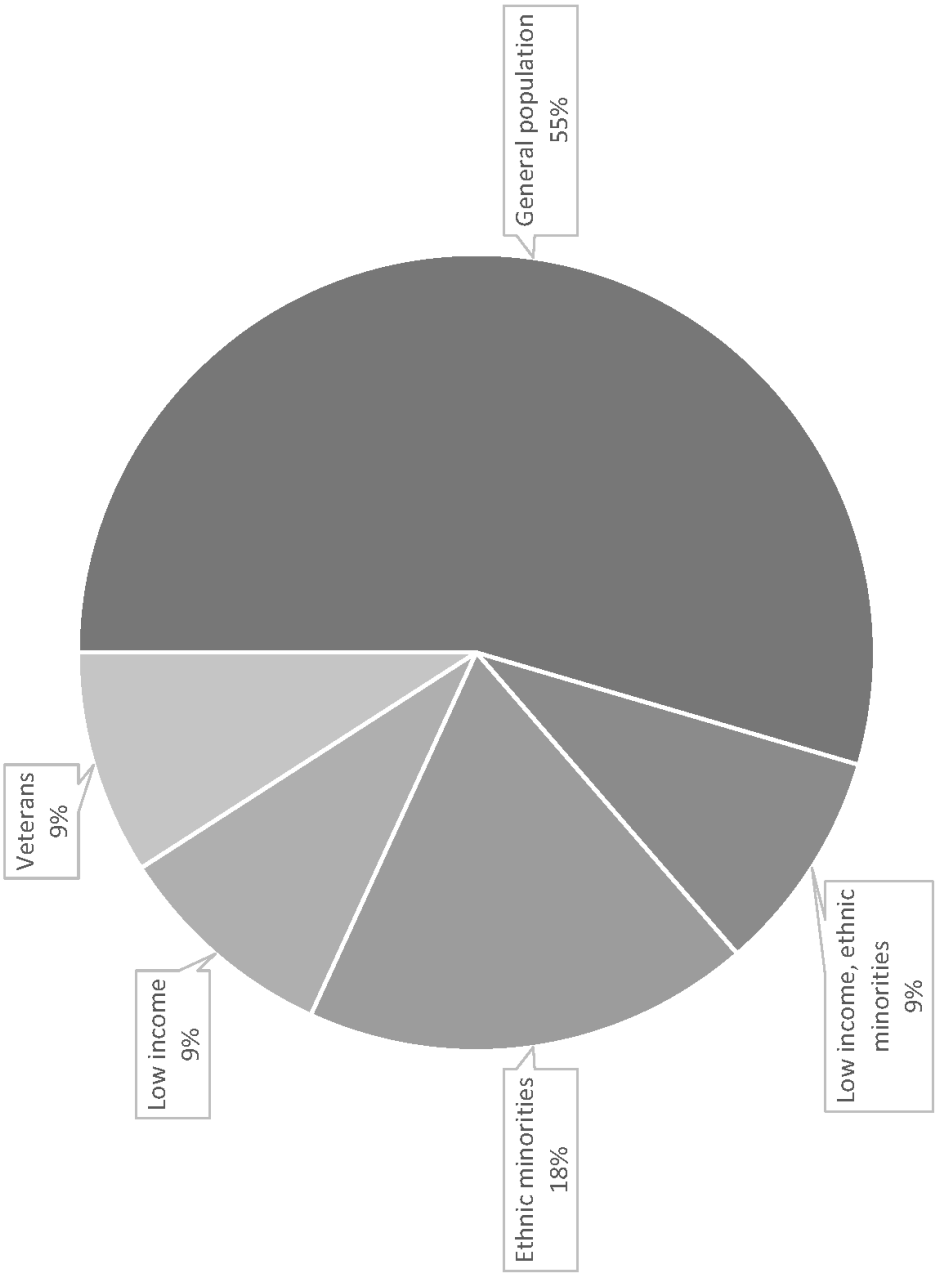
PNP found through this systematic review were almost half the times paired with another cancer type or chronic disease. The most common pairing was with breast cancer patients, followed by other cancer types and stroke ***(see Figure 3.4)***. Furthermore, the population studied also varied. For instance, some studies only recruited veterans, low income population groups or ethnic minorities. ***Figure 3.5*** shows the different population groups eligible for inclusion in the interventions across the literature.

Figure 3.4: Lung cancer patient navigation programmes and their combinations with other diseases found through the systematic literature review (N=11)



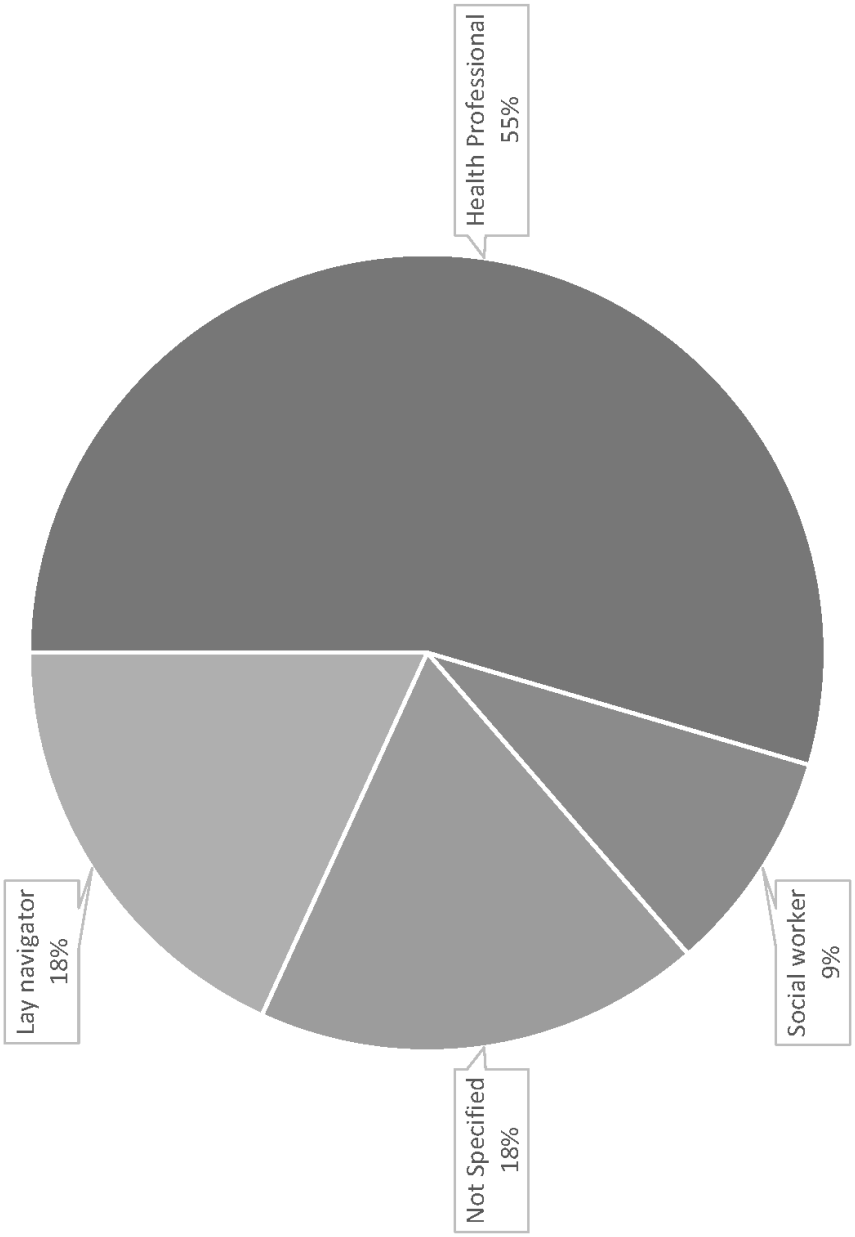
Source: Own work

Figure 3.5: Population studied by lung cancer patient navigation programmes found through the systematic literature review (N=11)



Source: Own work

Figure 3.6: Types of patient navigator found through the systematic literature review (N=11)



Source: Own work

Figure 3.6 shows programmes varied greatly in the profile, characteristics, and training of the navigators they employ. Some programmes used cancer survivors as navigators and sometimes navigators were not specified. In most cases navigators were either health professionals with experience in the medical field or some clinical training.

3.3.3 Data comparison

Study design in lung cancer patient navigation

Seven studies were not RCTs. These were rather quasi-experimental design (pre-post with non-equivalent control), observational (time series), cross-sectional or a retrospective cohort. Only four studies were RCTs. ***Table 3.2*** describes the study design for the full list of articles found through this systematic review.

Table 3.2: Study Design of Patient navigation programmes found through the systematic review (N=11)

No. (ref)	Study Type	Kind of Study	Randomisation	Sample Size	Power Calculation
1 [125]	Pre-post with non-equivalent control	Quasi-experimental	No randomisation	162 quasi-experimental group vs 165 comparison	Yes
2 [126]	Pre-post with non-equivalent control	Quasi-experimental	No randomisation	263 quasi-experimental group vs 305 concurrent comparison vs 1798 retrospective comparison	Yes
3 [127]	Pre-post with non-equivalent control	Quasi-experimental	No randomisation	44 participants	Yes
4 [128]	Retrospective cohort	Observational	No randomisation	123 intervention vs 173 control	No
5 [129]	Pre-post with non-equivalent control	Quasi-experimental	No randomisation	Not provided	No
6 [130]	RCT	Experimental	Yes	113 intervention vs 107 control	Yes
7 [131]	RCT	Experimental	Stratified randomisation	42 intervention vs 47 control	Yes
8 [132]	Cross-sectional	Observational	No randomisation	29 participants	No
9 [133]	RCT	Experimental	Yes	259 intervention vs 259 control	Yes
10 [75]	Time series	Observational	No randomisation	2007-2010 <100	No
11 [134]	RCT	Experimental	Yes	60 intervention vs 60 control	Yes

Source: Own work

Lung cancer patient navigation activities

Patient navigation programmes varied substantially in their implementation, frequency, level of intensity, profile of the navigators, and location. Meanwhile some involved only brief, remote communication between the patient and navigator, and consist mainly of information, advice, and encouragement, others involve much more extensive interaction and multiple in-person meetings. In some cases, the navigator may accompany the patient on visits or interface directly with healthcare providers, insurers, and others the patient's behalf.

In comparing the activities across PNP, a binary coding system was employed (yes=1, no=0). ***Table 3.3*** reveals a varied spectrum of services offered by PNP. The navigation activities in the PNP reveal three prominent themes, each emphasising distinct aspects of patient care. The first theme centres around providing emotional support to patients, acknowledging the profound impact of emotional well-being on the overall healthcare experience. Programmes adopting this theme, exemplified by programmes 7, 8 and 9, prioritise activities such as Emotional Support, recognising the importance of addressing the psychological challenges that patients may face during their medical journey. Navigators in these programmes play a crucial role in offering empathy, counselling, and support to enhance the holistic well-being of patients.

The second theme encompasses a broad spectrum of activities, extending beyond emotional support to include Transportation, Legal Support, and Lobbying/Advocacy. Programmes 3, 5 and 6 exemplify this comprehensive approach, acknowledging that patient needs extend beyond the clinical setting. Navigators in these programmes engage in diverse activities to tackle logistical, legal, and systemic challenges, advocating for policy changes and ensuring patients

Table 3.3: Lung cancer patient navigation activities found through the systematic literature review (N=11)

	1	2	3	4	5	6	7	8	9	10	11
Administrative & Logistics	■	■	■		■					■	■
Patient Education	■	■	■		■	■			■		■
Navigator Training	■	■	■								
Infrastructure Navigation	■	■	■		■	■					■
Emotional Support			■				■	■	■		■
Referrals			■		■		■		■	■	■
Supportive Care			■			■				■	
Transportation			■		■						
Clinical Activities						■				■	
Legal Support						■					
Lobbying/Advocacy						■					

Source: Own work
Outcomes in grey indicate YES, white indicate NO.

have access to a range of supportive services.

The third theme revolves around guiding patients through the complexities of healthcare systems. Programmes 1, 2, and 11, exemplify this theme by prioritising activities such as Referrals and Infrastructure Navigation. Navigators in these programmes serve as guides, helping patients navigate intricate healthcare processes, connect with appropriate medical services, and overcome barriers to access. This theme underscores the importance of ensuring patients receive timely and well-coordinated care within the complexities of the healthcare landscape. Collectively, these themes showcase the diversity of patient navigation approaches, each tailored to address specific facets of the patient experience and healthcare challenges.

Use of technology in lung cancer patient navigation

The tools employed by patient navigation programmes encompass a comprehensive array designed to enhance healthcare delivery. Notably, real-time warning systems emerge as a pivotal component, adept at promptly identifying unmet care

milestones. These systems, often fortified by supportive IT platforms, contribute to timely interventions by alerting healthcare providers to potential lapses in patient care. Moreover, the integration of management software packages facilitates streamlined coordination, while the utilisation of diverse communication channels such as phone calls, email, and telephone, ensures efficient and accessible patient interaction. Online questionnaires, electronic surveys, and platforms like Redcap further enrich the toolkit, offering a versatile means of gathering patient data and feedback. Collectively, these tools empower patient navigation programmes with the agility to address emerging healthcare challenges and facilitate proactive, patient-centred care.

Outcome focus in lung cancer patient navigation

In comparing the outcome measures across PNP, a binary coding system was employed (yes=1, no=0) to quantify the presence or absence of administrative, clinical or patient reported outcomes. ***Table 3.4*** shows administrative outcomes exhibited a high frequency, with programmes consistently incorporating these measures. Clinical outcomes and patient reported outcomes, on the other hand, displayed more variability, with programmes showing mixed utilisation.

Table 3.4: Outcomes studied in each patient navigation programme found through the systematic review (N=11)

Observation	1	2	3	4	5	6	7	8	9	10	11
Administrative Outcomes	■	■			■	■	■	■	■	■	■
Clinical Outcomes				■		■	■		■		■
Patient Reported Outcomes			■			■	■	■			■

Source: Own work

Outcomes in grey indicate YES, white indicate NO.

Diverse set of survey tools aimed at comprehensively assessing various aspects of patient experience and outcomes. The instruments employed included the

Cancer Needs Distress Inventory (CaNDI) [130], which gauges distress levels and requirements specific to cancer patients, alongside general patient satisfaction measures. Additionally, the review incorporated the use of a survey and the distress thermometer to evaluate broader socio-legal aspects and distress levels. Furthermore, the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) [135, 136] was utilised in conjunction with the distress thermometer, the Symptom Management Self-Efficacy Scale tailored for breast cancer patients, and the Patient Satisfaction (Cancer Care Scale) to comprehensively assess quality of life, self-efficacy, and patient satisfaction. Finally, the medical consumption questionnaire and the Vulnerability Screening Instrument were employed to capture aspects related to healthcare resource utilisation and vulnerability screening, respectively. This array of survey tools facilitated a comprehensive evaluation of PNP across multiple dimensions, providing valuable insights into their effectiveness and impact on diverse patient outcomes.

3.3.4 Narrative synthesis

From the 11 articles found through this systematic review, only three RCTs studied the impact PNP had on timeliness in cancer care. Outcomes such as patient satisfaction, quality of life, self-efficacy, self-activation, distress, trust in medical care, health costs, supportive care use, were of frequent interest to researchers [130, 131, 133, 134]. The first four articles in **Table 3.5** are RCTs and shows the outcomes studied in both RCT and non-RCT studies.

Among the eleven studies found through the systematic literature review search, none of the PNP reported negative outcomes. Fifty-five percent of the studies showed positive effects, 27% had both (positive effects and no effects)

across different outcomes and 18% had no results.

Only two studies focused on reducing health inequalities [125, 126]. In this case, the intervention was built to compare outcomes between black and white ethnic backgrounds. Nonetheless, the social determinants of health are somewhat considered in some articles by adjusting for race, age, insurance status and other social determinants of health. However, it is not the focus of their design and implementation.

Non-RCT appraisal

Two studies showed promising results and support the implementation of a navigation programme. First, Cykert et al showed increased odds of treatment completion (1.6 OR $p<0.04$) and Increased proportion of patients receiving treatment (80% retrospective control, 83% concurrent control 88% intervention). However, when reporting the results, the study did not discriminate between lung and breast cancer patients [125].

The second by Charlot et al showed positive results, evidenced a reduction in time to surgery (from 34 days in retrospective control, 33 days in concurrent control, to 23 days in intervention) [126]. Additionally, the study found the proportion of patients being treated within 56 days increased (73% retrospective control, 72% concurrent control to 86% intervention), higher likelihood of patients being treated before 56 days (1.14 OR in all intervention vs all retrospective controls and 1.16 OR in all intervention vs all concurrent controls, $p<0.01$) and higher likelihood of patients being treated before 42 days (1.23 OR all intervention vs all retrospective controls and 1.20 OR in all intervention vs all concurrent, $p<0.01$) [126]. However, this study only included patients in stages I and II of the disease and with NSCLC

Table 3.5: Outcome measurements in RCTs and non-RCTs found through the systematic review (N=11)

N=11 [a]	Clinical outcomes	Patient reported outcomes	Administrative outcomes
Battaglia et al 2022 [130] **RCT**	Distress	Patient satisfaction	Time to event (treatment)
Berezowska et al 2021 [131] **RCT**	Distress	Patient satisfaction Quality of Life Self-efficacy Self-care knowledge[b]	Supportive care use
Langballe et al 2022 [133] **RCT**	Treatment adherence Survival Psychosocial outcomes	Quality of life Self-activation	Time to event (treatment) Process evaluation Health-costs
Godde et al 2023 [134] **RCT**	Distress Treatment adherence Smoking, daily activity Loneliness Sleep Re-hospitalisation 1-year survival	Patient satisfaction Quality of life[c]	Time to event (treatment) Cost-effectiveness Utilisation of medical care Inpatient care, Emergency department use, Therapy, Rehabilitation Feasibility indicators[d]
Cykert et al 2019 [125]			Treatment completion Proportion of patients being treated
Charlot et al 2022 [126]			Time to event (treatment-surgery) Patients being treated Patients being treated <56 days Patients being treated <42 days
Fleisher et al 2012 [127]		Patient satisfaction Cognitive affective measures	
Pitter et al 2023 [128]	Survival		
Zibrik et al 2016 [129]			Time to event (treatment interval)
Lorhan et al 2013 [132]		Patient satisfaction Continuity from primary to tertiary care	
Hunnibell et al 2012 [75]			Time to event (diagnostic/treatment)

[a] Green indicates significant results in the outcome. Red indicates non-significance (p-value > 0.05). Gray indicates: no results.

[b] questions concerning daily functioning, physical activity, emotions, nutrition, fatigue, referral, recovery, smoking cessation, and employment; Symptom-Management Self-Efficacy daily functioning, physical functioning, emotions, nutrition, fatigue, employment, and sexuality; Patient Satisfaction with received answers, advice, and empathy regarding daily functioning, physical functioning, emotions, nutrition, fatigue, recovery, employment, and sexuality

[c] General and symptom-based quality of life

[d] acceptance, demand, implementation, and practicality according to ethnographic results

diagnosis, specifically [126].

In Fleisher et al's study, there was no control group, there was a small sample size (n=44) and only 6% of the sample was LC and did not focus on measuring timeliness in care as an outcome. However, their results showed increased knowledge in cancer, a reduction in worry about diagnosis, higher scores on the importance of adhering to treatment plans, and improvements in the management of distress, financial issues, and appointments [127]. No effect was found in patient satisfaction [127].

The only mixed-methods study by Lorhan et al focused in LC and in understanding the barriers themselves in addition to measuring patient satisfaction with the PNP. There were only 29 participants in the evaluation of patient satisfaction using a Likert scale [132]. However, through the qualitative arm, this research evidence increased continuity from primary to tertiary care and higher patient satisfaction.

Pitter et al focus was on LC survival [128]. Although they initially found a reduction in hazard ratio of death (HR: 0.63, p=0.039), after adjustment the effect was lost [128]. They also had a small sample size and did not measure timeliness of care as an outcome.

Zibrik et al's study was particularly interesting, as they mention a reduction in the time to systemic treatment [129]. Their focus was set in LC specifically, but the article does not have any data on the methods used nor the sample.

A time series was also found in this systematic review by Hunnibell et al [75]. This study did not carry out any statistical analysis but found changes in the time

from suspicion to treatment (117 to 52 days from 2007 to 2010). Additionally, from 2007 to 2010, the median days to CT scan decreased from 8 to 6, PET turnaround improved from 15 to 11 days, and pulmonary referral reduced from 13 to 10 days [75].

RCT appraisal

From the studies found (N=11), four were designed as RCTs. However, only two of these studies show results, and the other two (CoreNavi and Navigate) are feasibility studies or protocols [133, 134]. Three of four RCTs employed quantitative methods [130, 131, 133] and only one used mixed-methods [134]. Only one study analysed LC and particularly NSCLC patients, whereas the rest paired the intervention with breast cancer, uterus cancer and stroke patients.

The appraisal of each study was conducted taking into account only the results related to timeliness in cancer care. Results suggest that the studies generally meet several key criteria for methodological rigour. Results from the CASP for the RCTs are presented in **Table 3.6**.

The research question is clearly defined, and randomisation and participant accounting are appropriately conducted. The studies that do present results do not indicate potential issues in baseline comparability and care consistency. The reporting of intervention effects and precision of the estimate are varied, with some aspects well-documented and others lacking clarity or simply being descriptive. However, concerns arise in areas such as blinding, where the intervention and some outcome assessments lack concealment, potentially introducing bias. Notably, the intervention's value in comparison to existing alternatives raises concerns, and careful consideration of potential harm and benefits is required. Despite these

challenges, the results are generally applicable to the local population, and the study provides insights into timeliness in cancer care research among PNP, highlighting areas for improvement in future research and clinical practice.

Table 3.6: RCT-CASP Results found through the systematic review (N=4)

Study	1 [130]	2 [131]	3 [133]	4 [134]
1. Clear research question				
2. Randomised Assignment of Participants				
3. Accounting for Participants				
4. Blinding				
5. Similarity of Study Groups				
6. Equality of Care				
7. Reporting of Intervention Effects				
8. Precision of the estimate of the intervention				
9. Benefits outweigh harm				
10. Application of results to local population				
11. Intervention provides greater value than existing				

Source: Own work

Green indicates: low risk. Red indicates: high risk. Orange indicates: not enough information is available. Grey: No results

Project SUPPORT by Battaglia et al in 2022, compared standard navigation to navigation coupled with legal services. Results did not support enhanced navigation programmes with legal support led to earlier care [130]. However, they found distress decreased at 6 months due to the intervention [130]. The results were broken down by cancer type, but only 8% of the sample had LC [130]. Thus, although this study shows the use of good methodology, their sample size (113 intervention and 107 control) might have influenced the intervention and the estimates found.

The study conducted by Berezowska et al in 2021, focused on other outcomes not related to timeliness in care [131]. Descriptive measures were used to evaluate the effect size i.e., percentage of patient satisfaction with cancer care before and after. Results are not stratified by LC. Additionally, this article mentioned potential self-selection bias due to a sample that consisted of patients whose need for patient navigation was most likely low [131]. Hence, there are limitations

on the evidence collected to support PNP increase patient satisfaction and other self-reported outcomes.

The two other RCTs conducted were very clear and explicitly defined their outcome measurements and periodicity. However, these two are published as protocols and therefore do not present any results. In **Table 3.6** the cells are marked in grey when results are not yet available and thus when appraisal is not available. Although these protocols seem to be properly built, one study is paired with two additional interventions: physical activity and symptom monitoring (NAVIGATE) [133]. The primary outcome of interest is survival among NSCLC patients [133].

3.3.5 Patient navigation typology

PNP found through this systematic review were explored in-depth as case studies. Each study was analysed and classified according to a modified version of *Walter's Model of "pathways to treatment"* (***Figure 3.1***) and through constant comparison of their activities and their intervention in specific time intervals, these were fitted into the framework. As a result, grounded theory was developed [137]. This process allowed for the discovery and refinement of theoretical concepts in navigation that are grounded in the data, leading to the generation of new theories that explain the observed patterns and relationships [137].

Walter's framework describes a linear pathway to treatment [88]. However, there are processes and events beyond the treatment phase and instead of a linear approach, this can be tortuous and cyclical resulting in inaccessibility to medical-care, prolonged diagnosis and/or treatment [1, 46, 138, 139]. Hence, a modification in the pathway to cancer care is proposed in this thesis allowing for

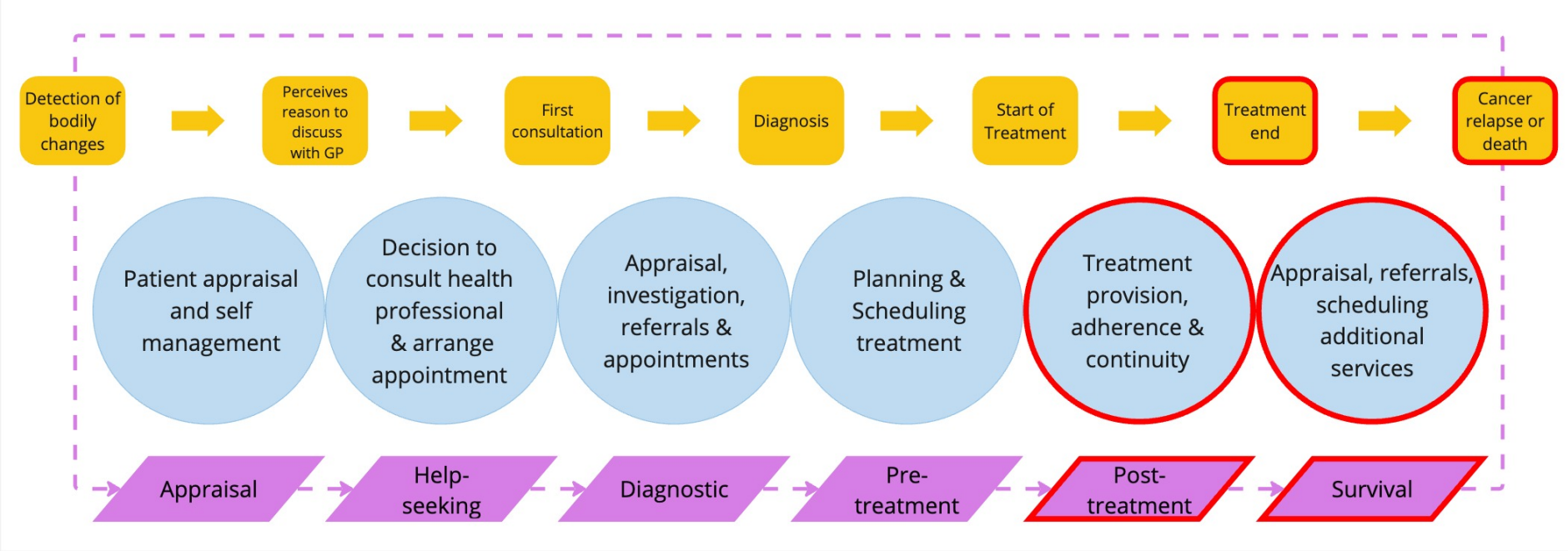
cyclical path or one that extends beyond treatment, reaching survival-free of disease or continuous treatment due to progression of the disease. The pathway to treatment model proposed by *Walter et al 2012* [88] was modified to generate the *cancer appraisal-to-survival pathway* The proposed modifications to this framework are visible in ***Figure 3.7***.

The changes to the original framework include two additional events: 1) treatment end and/or 2) cancer relapse, survival, or death. Similarly, there are two new processes and two new time intervals. From the time the treatment begins until the treatment ends (post-treatment interval). Within these intervals there are processes that ensure treatment adherence and continuity, etc. In the survival interval, new symptom appraisal, scheduling other services such as palliative care or breast surgery and new referrals are included as potential processes[3]. The last event of the post-treatment/survival interval represents disease-free survival or patient death. Processes included in this additional step should come after systemic or local treatment and could be palliative care, preservation of fertility, psychological therapy or support, to mention a few.

Results from this systematic review show PNP's act in at least one of the time intervals (***see Figure 3.8***), acting in specific processes between events in the pathway to cancer treatment and beyond the treatment phase. After fitting the different programmes into this framework, results show PNP focus on different moments in the *cancer appraisal-to-survival pathway*. Hence, "Navigating the patient" held a different meaning for each programme and entailed a different process. Even when the PNP's had similar objectives and activities. As a result, a new patient navigation typology was generated.

[3]This last interval could also be called the inter-treatment interval in patients with cancer reactivation.

Figure 3.7: The "cancer appraisal-to-survival pathway"



Source: Own work
The changes to the original framework include two additional events marked in red.

Figure 3.8: Lung cancer patient navigation programmes (N=11) classified by the "cancer appraisal-to-survival pathway"

Source: Own work.
Purple marks where in the cancer pathway the programmes intervene on.

3.4 Discussion

Patient navigation reflections, what is it for, who is interested, why is it growing?

When screening the literature, a significant portion did not focus on patient navigation in cancer but rather on various chronic or acute diseases. It proved intriguing to observe the expanding body of work dedicated to the subject of patient navigation. The emergence of patient navigation as a field suggests that medical practitioners may face a challenging responsibility, namely reducing barriers, alongside their existing clinical duties throughout the patient journey. Consequently, patient navigators play an increasingly crucial role in bridging the gap between access and care. Whether this dynamic has always existed or is a consequence of escalating medical tasks and barriers is not within the scope of this thesis discussion. However, it does serve as a potential explanation for the growing body of literature on this subject, despite conflicting evidence regarding its effectiveness. Regardless of the debate over its merits, there is a fundamental human need for patients to feel supported and patient navigators are progressively assuming the role of the closest point of contact within the healthcare system.

This thesis found three major themes on which PNP intervene on. There are programmes focused on resolving the emotional impact cancer has in the patients and caregivers; in reducing difficulties arising from navigating the healthcare system (administrative, referrals, etc,); or acting in a broader spectrum of activities such as advocating for access, legal support, and transportation services. The theme chosen by each one of these PNP found through this thesis was based on the barriers that stakeholders found relevant.

It is noteworthy that universities, foundations, and local hospitals frequently

collaborated in crafting the PNP. While the articles do not explicitly outline responsibilities and role distribution, it is important to identify the entities from which these PNP initiatives originate. Only one study provided a detailed account of the actors involved in the navigation programme [140]. The range of stakeholders, spanning from funding sources to expert steering committees, was explicitly delineated. This elucidation sheds light on the pertinent actors and highlights potential collaboration models, including private or public-private partnerships. Such insights are increasingly crucial in the implementation of patient navigation programmes. Thus, the provision of such information is encouraged. Similarly, further research is warranted to ascertain whether these programmes are rooted in genuine patient needs or if they predominantly follow a top-down approach.

PNPs appear to be more widespread in countries such as the USA. As indicated by the systematic review, literature on cancer navigation is more abundant in high-income countries, irrespective of whether their health systems are privately or publicly funded. This prompts the question: why? Further research is needed to explore the reasons behind the lesser prevalence of PNP in LMIC and whether the economic and health system structures play a role in shaping the global prevalence of such programmes. Alternatively, PNP might not be publishing their results in an academic environment, thus explaining why the literature in LMIC is scarce on PNP.

Evidence to support the implementation of navigation programmes to increase diagnostic and treatment timeliness in Lung Cancer care

Overall, research on patient navigation is large. However, very little research is available to evaluate the impact patient navigation has in LC care. Unfortunately,

the research agenda con early cancer diagnosis and patient navigation are not matched together by the objective of timeliness. Thus, this thesis vouches for the generation of a single agenda among both academic and non-academic stakeholders in order to further the impact PNP have in increasing diagnostic and treatment timeliness in cancer care.

In previous efforts, research had not considered literature not developed as RCT and the design of the PNP. This research reduces the literature gap and finds Cykert et al [125], Charlot et al [126] and Lorhan et al's [132] support the implementation of a PNP for LC early care. Despite the potential selection bias, small sample, and lack of focus on the minimisation of prolonged care intervals, these studies share promising evidence and could potentially lead to better results if outcomes were measured in a larger sample and more rigorous outcome evaluation. Although with positive results, Hunnibel's work demonstrates weak evidence to support PNP for LC. The rest of the articles found do not provide enough evidence to support the implementation of PNP for LC early care.

Difficulty in measuring results in patient navigation

The definition of patient navigation presents several challenges. Firstly, variations in the design of navigation interventions, as observed in the literature, make it increasingly difficult to compare their effects. Secondly, the mixed and sometimes conflicting outcomes reported in the literature regarding cancer patient navigation may not solely stem from differences in population groups or biases. Instead, they could be attributed to diverse interventions that, while aiming for the same outcome, are delivered in substantially different ways. This chapter points to PNP are in fact different models that are intervening in care at different moments in the disease continuum. Consequently, evaluating and comparing the effects of

patient navigation through systematic reviews or other methods may not be the most effective means of capturing the success or failure of interventions when the interventions themselves differ significantly. Thus, guidelines to support the implementation and research of patient navigation should be developed to be able to support evidence-based decisions through systematic reviews and meta-analyses.

The uptake of the definitions of PNP as models of care, might help solve the increasing and persistent issues regarding measurement of effectiveness in patient navigation. By clearly stating the interval in the pathway intervened on, processes, activities and thus outcomes are more easily delineated and thus could serve to standardise what PNP evaluate. Results from this chapter suggest a consistent emphasis on administrative outcomes, potentially reflecting the prioritisation of program efficiency and logistics. The diversity in the utilisation of clinical and patient-reported outcomes may indicate a need for standardised approaches in these domains. Moreover, the implications of such variations underscore the importance of establishing a consensus on outcome selection to ensure comprehensive and comparable assessments across patient navigation initiatives, fostering evidence-based practices and enhancing the overall impact of these programmes on patient care and health outcomes.

Another issue found was the lack of stratification of results. In this case, one article perfectly described the trial and had considered stroke patients too [134]. Nonetheless, LC patients were separated from recruitment to the analytical phase, making it easier to determine if the results are relevant or not. Thus, if a single cancer type evaluation is not possible, stratification must be done to allow for further research to be conducted in PNP.

PNPs while holding promise in healthcare delivery, exhibit design shortcomings

that warrant scrutiny. Notably, there exists a discernible pattern of excluding specific demographic cohorts. Exemplifying this trend is the conspicuous absence of men within breast cancer navigation initiatives. Furthermore, exclusions extend to individuals with a cancer history, recent cancer treatment recipients (within the last five years), those concurrently undergoing cancer treatment, individuals whose primary language is non-English, patients under the age of 18 or lacking decisional capacity, and those institutionalised, incarcerated, or afflicted with cognitive impairment (e.g., dementia or conditions induced by metabolic, medication, or drug-related factors). This phenomenon underscores a methodological concern in public health research, revealing a predilection towards investigating populations perceived as optimally poised to benefit from patient navigation initiatives. Consequently, the discernible proclivity to include only idealised subjects raises pertinent questions regarding the external validity and translational potential of research findings.

The non-reporting of comorbidity within individual studies raises substantial concerns regarding the potential repercussions on result variability across the literature. The implications of overlooking variables such as depression or diabetes when evaluating the efficacy of PNP are considerable. Patients with multiple comorbidities may exhibit distinct responses to navigation interventions. For instance, individuals with depression may manifest heightened disengagement during the navigation process, thereby introducing a nuanced layer to the assessment of program success. The bio-psycho-social ramifications of concurrent diseases can significantly influence clinical outcomes. Consequently, a comprehensive evaluation of PNPs effectiveness necessitates a meticulous consideration of the diverse comorbidity prevalent among the patient population under scrutiny. Failure to account for these multifaceted health dynamics could compromise the validity and generalisability of findings within the broader

healthcare landscape.

This systematic review shows patient navigation are sometimes paired with other interventions. For instance, some studies have paired their intervention with real-time warning systems, a certified nurse navigator, a patient registry, web-based social determinants of health platform to identify and address barriers to care and physical exercise in a person-centred delivery model [125, 126, 133, 140]. Although this might seem in practice quite pragmatic, using alternative study designs might help evaluate if the patient navigation itself is what is making the outcomes better—the sum of all of them together or just a part of it. Otherwise, the noise generated by the other interventions will shift the effect of different cancer outcomes.

Walter's Modified pathway to treatment model: a systematic review of its application in patient navigation programmes

The development of the framework emerged as a pragmatic response to the observed heterogeneity in outcome measurement practices across studies. It is offered as a tool to aid stakeholders in navigating the complex landscape of outcome selection, ensuring relevance and consistency in assessing the impact of patient navigation interventions.

In the literature PNP's focus on tackling different barriers through different activities. Therefore, this typology helps establish a framework to standardise the evaluation outcomes needed to measure timeliness in care and health inequalities. Hence, this typology clearly determines the set of activities and time intervals a PNP should measure to ultimately evaluate their role in earlier diagnosis and treatment of cancer.

Until now PNP's had not been classified according to the time-interval in the *cancer appraisal-to-survival pathway* in which the navigation takes place. This framework is particularly relevant for middle and low-income-countries where the cancer mortality-to-incidence ratio is highest, and research is needed to increase timeliness in cancer care. Thus, this framework should help stakeholders take on the task of measuring the intervals they act upon and build future evidence on the effect PNP's have on earlier diagnosis and treatment of cancer.

Recommendations for patient navigation research

A notable observation is that most studies fail to contribute their findings to platforms like Cochrane and the International Clinical Trials Registry Platform by World Health Organisation (WHO). Frequently, this section remains empty. This practice poses challenges for researchers engaged in systematic reviews or individuals seeking information on the topic, as locating dispersed publications becomes a cumbersome task. This practice poses challenges for researchers engaged in systematic reviews or individuals seeking information on the topic, as locating dispersed publications becomes a cumbersome task. In some favourable instances, researchers provide the Digital Object Identifier (DOI) of their results on the website, serving as a link to the publications. Hence, it is advisable for researchers to actively return to clinical trial registry websites to ensure the posting of their results, enhancing accessibility and facilitating comprehensive reviews of the literature.

Some studies had multiple articles [125, 126], published by different authors in different years. Hence, it is important to keep the trial registry number or the title of the patient navigation programme easily reachable for the researchers. Also,

it would also help if the previous published literature is outlined in the subsequent articles to make it easier to put the story together. Exploratory reviews like this one, allows you to you go back and forward between documents and capture the full idea of the navigation programme, its implementation, and results.

3.5 Limitations

The original purpose of the PROSPERO registration was to conduct a systematic review for all types of cancer. Although this systematic review identified PNP for other cancer types and extracted the information in all the other cancer types (N=95), these results are not shown in the dissertation. During the extraction of data, difficulties in the extraction sheet were found. The different researchers that collected the information had been trained in the topic and data collection. However, this task proved to be too specific for them and when reviewing 10% of the extracted data, all of them showed miss-classification of the PNP or study type, which overall led to wrong appraisal. As a result, for the purpose of the thesis, EBG verified the content of the LC literature only[4].

Several limitations should be considered when interpreting the findings of this systematic review. Firstly, the literature search was conducted in two phases, each utilising different code names. While this approach was adopted to expedite the retrieval of more recent and relevant results after the initial search, it may have introduced a potential bias by narrowing the scope of the review. The use of distinct code names for each phase aimed to streamline the process and enhance efficiency by bypassing content deemed not immediately relevant to the systematic review objectives. However, this strategy may have inadvertently

[4]EBG is currently working with the NIH and WHO to verify the content found for other cancer types. This task will eventually be broken down by cancer type and serve as guidelines for the WHO

excluded some pertinent studies or introduced an element of subjectivity in the selection process. Additionally, the reliance on specific code names could impact the comprehensiveness of the literature coverage, potentially omitting relevant contributions that used alternative terminology (i.e., case navigation, case management). Despite these limitations, the chosen approach was deemed necessary to balance the need for timely updates with the practical constraints of sifting through an extensive body of literature. Researchers should exercise caution in generalising the findings beyond the defined scope and consider potential omissions resulting from the search strategy employed.

This study faced a notable limitation common in patient navigation literature—difficulty in performing a meta-analysis due to disparate measurement approaches across studies. The key finding underscores the pressing need for a standardised framework for outcome measures selection in the realm of cancer research in patient navigation programmes. However, this thesis primarily aimed to gather evidence supporting the implementation of patient navigation in the context of LC in Mexico, rather than undertaking a comparative analysis of the diverse methods employed to evaluate these interventions. While one of the analytical phases inadvertently led to the development of a framework designed to guide stakeholders in the selection of outcomes for patient navigation programmes, it's essential to clarify that the thesis does not extensively delve into the intricacies of the methods associated with outcome measurement.

It is imperative to recognise that the framework proposed is a step towards enhancing the methodological rigour in future research, guiding researchers and practitioners in the selection of outcomes without delving into the intricate details of measurement methods. Future research endeavours should focus on establishing consensus guidelines that enable researchers to select and apply relevant outcome

measures consistently across studies. Only through such concerted efforts can the field progress towards a more rigorous and comparable evidence base for patient navigation interventions.

In some cases, researchers presented their methods and background rationale, but not their results. Hence, although some studies might be considered in this chapter to compare navigation types, etc., some might not be able to show results as research is still ongoing.

3.6 Summary

1. Experimental studies evidence PNP don't increase timeliness in LC care.
2. Quasi-experimental and observational studies describe PNP can reduce LC care intervals.

   Bias arise in areas such as blinding, reporting of intervention effects and precision of the estimates.

   Sample size, study design and evaluation methods limit the strength of the evidence

   55% of the studies pair LC to other diseases.
3. 60% of the literature comes from North American
4. Lung cancer PNP more frequently focuses on researching the treatment interval

1. Health inequalities are not the main scope of analysis.
2. Administrative outcomes are the ones more frequently used.
3. PNP found are actually different models of navigational-care, therefore limiting the comparison of interventions.
4. Rigorous and standardised research is needed to evaluate the effect PNP has throughout the LC continuum.
5. The *cancer appraisal-to-survival pathway* can serve as a guide to establish standardised outcome measurements in PNP.

The systematic review discussed PNP in the context of LC. In most cases, research was conducted to evaluate the effect of navigation in the diagnostic and treatment interval and earlier in the cancer continuum. The findings from quasi-experimental and observational studies indicated a favourable impact of PNP in increasing LC care timeliness. Meanwhile no effect has been found through experimental studies. Biases and limitations for each are discussed in this Chapter. However, the most important limitation of these studies and the systematic review is the heterogeneity of PNP. With diverse intervention designs PNP exhibited substantial variability even when pursuing the same objectives. Moreover, when engaged in similar activities during the same time-frame across the care continuum, the measurement methods employed differed significantly. Consequently, the evidence pertaining to LC navigation lacked comparability and can explain the differences in the results found. There appeared to be an overall improvement in patient satisfaction with the implementation of PNP. Hence, despite the literature's limitations, results offer a compelling avenue for further exploration and potential

implementation within clinical settings.

According to this systematic review, PNP can hold different objectives, designs, activities, and focus on different cancer types. The patient navigation typology developed in this thesis helps set a standardised framework to analyse programmes according to the patient's *cancer appraisal-to-survival pathway*. Stakeholders interested in designing PNP should take into account the steps in the *cancer appraisal-to-survival pathway* they are targeting, as these will be intertwined with standardised objectives, activities, and evaluation methods they will use to measure success.

Lastly, this systematic review yields specific recommendations for future research in patient navigation. These include the imperative to update clinical registry portals, enhance transparency regarding collaborative efforts and the rationale underlying programme development, define the healthcare levels involved in navigation, incorporate minorities in trials to ensure comprehensive outreach to the most marginalised demographics, elucidate the specific time intervals of interventions, and conduct further research on outcomes measurement. Additionally, it is paramount to embed a research agenda addressing health inequalities, aligning with the original purpose of patient navigation.

Chapter 4

Literature gaps, project aim and objectives

4.1 Gaps in the literature

In **Chapter 2**, I explored LC in the Mexican context and the high mortality-to-incidence ratios among these patients. I also identified interventions recommended in the literature to increase timeliness in cancer care. For instance, ongoing research at the INCAN focused on LC screening [25], while the Mexican Health Foundation (FUNSALUD) is in the planning stages for legislation concerning EHR usage [71, 72]. Noteworthy recommendations also include achieving universal access to treatment [38, 48, 52, 58], unifying the health-care system [48, 70], expediting treatment approval processes [1], and establishing a centralised infrastructure for genetic testing and tumour molecular analysis [1]. While these interventions are pertinent, it is crucial to acknowledge that their implementation may necessitate substantial investments from the Ministry of Economy, and political factors could influence their roll-out. This dissertation will not delve into an exhaustive examination of these topics, recognising the complexity and broader implications that extend beyond the scope of the current study.

In addition to the interventions suggested, some gaps were found in the literature. Despite it being essential for the development of health policies [54], no evidence was found on how long the patient and system intervals are among LC patients in Mexico [141], nor whether there are inequalities in these. Similarly, no mixed methods or qualitative studies were found on the pathways to care, or barriers being faced particularly by LC patients throughout the disease continuum in Mexico [141]. The only relevant local evidence found was on breast cancer, describing multiple delays in different hospitals [138, 139, 142, 143].

Previous research only found one systematic review on PNP for LC screening [122]. Results showed improved screening rates and patient satisfaction, but no measurement of the impact on increasing timeliness in LC care [122]. After conducting a systematic review on patient navigation, eleven studies were found for LC (see **Chapter 3**). Of these, not a single programme was implemented in Mexico. Thus, no evidence of Mexican LC navigation was found. More research is needed to understand PNPs in Mexico, their design, objectives, and role in timeliness throughout LC care in Mexico.

In summary, a series of questions arise:

1. *Do PNPs increase cancer diagnostic and treatment timeliness in Mexico and how do they evaluate their effect?*

2. *What are the barriers for LC care in Mexico, and how do these barriers influence journeys and affect the timeliness of cancer care?*

3. *How long are lung cancer care intervals among LC patients in the INCAN and what is the duration of the intervals compared to findings in the international literature?*

4.2 Aim & Objectives

This mixed-methods doctoral research [144–147] aims to investigate diagnostic and treatment timeliness in LC care in Mexico and the potential role PNP have in mitigating prolonged care intervals. This thesis will particularly focus on the uninsured population (unemployed, self-employed, or informally employed) and not people who are privately insured or through social insurance institutions. To achieve this, this thesis involves two concurrent research topics: 1) PNP and 2) the LC journey. Hence, to address these two topics, the dissertation incorporates journey case studies, quantitative analyses of intervals across the continuum of care, and patient navigation case studies.

Research topic 1 (PNP) is addressed through a series of case studies. In research topic 2 (the LC journey), a qualitative stream (2a) precedes the quantitative stream (2b). Equal weight is given to both components (2a and 2b) and primary data collection is conducted in parallel. However, the analysis of the qualitative stream (2a) precedes the quantitative stream (2b). A summary of the findings are presented at the end of each chapter and the results from both streams are triangulated and presented in a single mixed methods chapter. Finally, all sub-studies lead to a final single and unified conclusion. **Table 4.1** dives deeper into the different topics' research methods and design, data collection tools, the population sample and sub-samples, and the analytical strategy planned.

Table 4.1: Summary of PhD research methods

TOPIC	STREAM	OBJECTIVE	DESIGN	RESEARCH METHODS	DATA COLLECTION	POPULATION	DATA ANALYSIS
1	Patient navigation programmes in Mexico	To identify and compare patient navigation programmes in Mexico, their underlying design, outcome measurement, and their role in secondary prevention of cancer.	Case studies (Descriptive)	Qualitative	Semi-structured interviews	6 PNP representatives	Thematic Analysis Narrative synthesis Data comparison
2 (a)	The lung cancer patient journey	To assess structural and individual barriers encountered by patients throughout their LC journey and their role in delaying care	Case studies (Explanatory)	Mixed methods	Structured interviews	46 patients (nested sample)	Quantification of Qualitative data Narrative profile-formation Thematic analysis Triangulation
2 (b)	Delays in lung cancer care & patient trajectories	To assess the association between structural and individual barriers encountered by LC patients and their role in modifying time to cancer care	Cross-sectional	Quantitative	EHR (2005-2021)	3018 EHR	Time-to-event Linear [log] regression Survival

Hypotheses

- PNP will increase timeliness in cancer care and share similar objectives, outcome measurements, resources, and activities.
- Different barriers to LC care will be faced by patients. Barriers will lead to prolonged care intervals and condition different journey types.
- Diagnostic and treatment intervals in LC care will be longer than the international literature and similar to previously published breast cancer intervals in Mexico.

Although qualitative studies are inductive in nature [147], these hypotheses are made to be consistent with the structure of the Chapter. Thus, the horizon of the hypothesis will be broader than the one pasted here.

Chapter 5

Patient navigation: Case Studies A-E from Mexico

5.1 Background

While various PNP's have been implemented in Mexico there is limited evidence available to understand the effect they have in increasing timeliness in cancer care across the continuum. Hence, there is a need for the programmes to be identified, analysed, compared, and added to the literature. As a result, this Chapter will use case study methodologies to be able to understand how PNP have been implemented in Mexico, their design, activities, and evaluations outcomes.

Case studies involve an in-depth examination of valuable real-world applications of interventions [148–150]. The case study design is particularly justified for examining PNP due to its ability to provide a comprehensive and detailed exploration of specific program characteristics within their contextual settings [148–150]. By focusing on selected cases, this approach allows for an in-depth analysis of how patient navigation programs are structured, implemented, and experienced by stakeholders [148–150]. Through methods such as interviews with program managers, navigators, and healthcare providers, document analysis

and possibly observations, the case study design enables researchers to uncover insights into the operational dynamics, challenges, and successes of these programs [148–150]. This depth of exploration is crucial for gaining a thorough understanding of how different program characteristics contribute to program effectiveness, thereby informing improvements and strategies for scaling or adapting patient navigation initiatives in diverse public health contexts.

Case studies can showcase what PNP do in diverse healthcare settings and populations, helping to identify best practices and areas for improvement [148–150]. Ultimately, the findings from these case studies can influence policy development and practice guidelines [148–150], supporting the integration of PNP into healthcare policies or promoting its inclusion as a standard component of cancer care services. Thus, the primary goal of this Chapter is to conduct a detailed examination of program characteristics and contextual factors through stakeholder interviews.

5.2 Methods

A qualitative cross-sectional case study research design was employed to investigate multiple PNP. This sought to conduct a detailed examination of programme characteristics in Mexico through the generation of case studies [148–150] and comparison of contextual factors such as: origin, population, disease focus, aim and objectives, resources, activities, evaluation outcomes and effect in increasing cancer care timeliness across the continuum. Additionally, through thematic analysis, key themes, patterns, and commonalities across PNP were identified. Lastly, utilising a grounded theory approach [150], this Chapter also classified the PNP according to the framework developed in the systematic review ***(See Figure 3.7)***.

Five different PNP in Mexico were identified through snowballing from January to March 2019 (Case studies A-E). The first PNP was contacted by EBG due to previous knowledge of the programme. Thereafter, all programmes identified during a period of two weeks in Mexico during fieldwork were contacted. Inclusion criteria for PNP included holding elements of patient navigation such as case identification, detection of barriers, development of personalised plan and a systematic follow-up [87, 94] and providing services to suspected or confirmed cancer patients. One stakeholder from each PNP was recruited, informed of the objective of the research and if interested signed the consent form to be part of the study.

From the five PNP contacted, all agreed to participate. Data was collected through funnel-semi-structured interviews among the patient navigation providers. Stakeholders decided whether the person interviewed was the patient navigator or the director of the program. Topic guides were developed to structure the conversation between the researcher and the PNP representative. These guides were informed by the systematic review on patient navigation and revised by a second reviewer (Cecilia Vindrola Padros (CVP)). Interview questions included describing their role, the origin of the program, the actors, activities, and collaborations, the navigation process, data collection techniques, and evaluation methods. The interviews were audio-recorded. Transcripts were imported to NVivo. Coding was informed by the systematic review and topics emerging on the data. After a stage of familiarisation with the data, EBG identified key topics and labelled them inductively. Codes: origin, population navigated, insurance type, cancer type, place, and type of organisation arise. Similarly, activities and resources were coded and then compared across PNP. Then, the Braun and Clark framework was employed for thematic analysis [151].

5.3 Case studies

CASE STUDY A:

This PNP seeks to help the patient reach quality health-care at the community level; suggesting that if navigating the health sector on their own, patients would then face less access to quality health-care service. They tackle economic, logistical and communication barriers. This PNP helps the uninsured patient navigate from the primary to the second or third level of care in an indigenous region of Mexico. A social worker, in collaboration with the medical doctor and a driver, navigate the patient. The social worker and doctor identify the barriers and match them with interventions at the community level. The driver transports the patient to the closest hospital, translates for the patient if necessary and mediates with the doctor at the hospital to reach appointments sooner. Thereafter, the social worker communicates with the patient through telephone or Whats-App. The navigation activities include introducing the indigenous patient to the health system environment, aid in administrative tasks (i.e., filling documentation in Spanish), appointment management, and mediation between the doctor and uninsured ethnic minority patients. Due to the nature of the organisation, this navigation program not only linked patients with other collaborators (i.e.,other Non-Governmental Organisation (NGO), donors), but also donated resources geared to tackle economic barriers as a result of transportation and shelter access difficulties. In some cases, this PNP also donated diagnostic procedures (i.e., cancer confirmation in private clinic). Additionally, a key objective within this PNP is the provision of information with regards to diagnosis, treatment, and close relationship with the patient throughout the cancer continuum. This is mainly done by the navigator in close relationship with the patient's physician. Although this PNP did not systematically include psychological services as an activity, mental health services were always available through another hospital program. Lastly, in terms of evaluation methods, this PNP only collects information on the number of barriers found and the number of patients being navigated per year. One economic evaluation was conducted as part of a dissertation by someone connected to the program; however, results were not provided.

CASE STUDY B:
The aim of PNP B is not access to health-care but rather to improve the cancer care experience at the hospital level. This is conducted through peer-to-peer navigation in conjunction with a psychologist and a nurse. The navigator communicates with the uninsured patients through telephone, direct messaging, and a specific hospital line to help the patient reach a greater understanding of their disease. Their activities included: introducing all cancer patients to the hospital environment, maintaining a personalised and friendly environment, aid in administrative tasks (i.e., filling documentation), appointment management and mediation between the doctor and patient. They tackled economic barriers mainly through collaborations with external resources (i.e., free regional transportation, discounts in hotels, food, medicines and diagnostic procedures). They provided information and emotional support for all cancer-patients. This PNP has a direct line for patients, an educational website, and a psychological support group for each type of cancer. In addition, the patient can directly speak to the navigator for emotional support. After being treated, patients are supported through wellness and work re-integration programmes. To evaluate their impact, this PNP has measured patient satisfaction and has quantified barriers. Currently, they are looking to conduct a survival follow-up.

CASE STUDY C:

PNP C aims to navigate the patient across the health-care system. Their objective is to tackle economic barriers among patients with lung, prostate, testicular, breast, ovarian, cervical, and other haematological cancer types. They aim to increase access to cancer diagnostic and treatment services, provide emotional support, and ensure adherence to treatment despite the type or lack of insurance. The navigator is a social worker, and they communicate with the patient through social media, telephone line and Whats-App. After identifying barriers, this PNP continuously evaluates the barriers being tackled and re-evaluates barriers through-out the cancer continuum. This NGO introduces the patient both to the health-system and hospital environments. They aid in administrative tasks such as filling documentation or appointment management. To tackle economic barriers, this PNP not only donates food and diagnostic tests, but actively funds cancer treatment. Additionally, they also link the patient to external resources (i.e., state transportation, other NGO, legal services). TO evaluate impact, this PNP collects information on the number of barriers found, the number of patients being navigated per year and the cost per patient.

CASE STUDY D:

PNP D focuses on navigating the patient to get access to other cancer related services such as: fertility preservation or the ability to receive breast implants for breast reconstruction that are not entirely covered by the current insurance schemes. The navigators are psychologists and communicate with the patient through social media, telephone lines and Whats-App. Although they do help the patient with some administrative, logistical, mediation and linkage with external resources tasks, these are not their core objective. This PNP navigates the patient in the hospital environment and mainly provides emotional support, and psychological therapy to breast cancer patients under the age of 40. This privately funded organisation also donates private diagnostic services and treatment for some patients. This PNP only conducts psychological evaluations throughout the provision of care.

CASE STUDY E:
PNP E aims to reduce time to treatment initiation. They only navigate admitted LC patients at the hospital level. The navigator is a nurse, and they communicate with the patient through a telephone line or Whats-App. Their core activities are introducing the patient to the clinic, managing their appointments, and mediating when these are not suitable for the patient. This PNP donates LC treatment for the uninsured population through the acquisition of grants. In addition, they provide the patient with information on cancer and link the patient with external resources to tackle personal barriers to care. Although this PNP did not systematically include psychological services as an activity, mental health services were available at all times through another clinic. This PNP does not collect any information on the patients navigated nor evaluate its impact. They are planning to conduct a retrospective time-to-treatment analysis.

Case study comparison

Five PNP in Mexico were interviewed. Each PNP in this study varied by type and size of population, cancer focus, funding sources and settings. All the PNP interviewed were created from 2010 onwards.

PNP navigated a different range of patients (from 500 to 1100 newly diagnosed patients per year); whose health coverage varied from uninsured, privately insured and publicly insured. Meanwhile, some were part of the public health sector, others were independent NGO. PNP implemented their programme in either clinical (hospital based) or community-based settings. Patient navigators' professional backgrounds were: nurses, health professionals (doctors), social workers and cancer survivors. All PNP navigated at least some cancer patients, but while some only navigated specific types of cancer (i.e., LC others navigated patients with multiple types of cancer and in different stages of the cancer continuum. An overview of PNP can be found in ***Table 5.1***.

PNP held different aims and navigation implied a diverse set of activities. ***Table 5.2*** shows the activities found in each programme, i.e., patients were identified, and barriers were matched with interventions such as: introduction to health-care environment; help in administrative documentation; appointment management; mediation with doctor; donation or linkage to resources that facilitate access to care; provision of information; emotional support; or even psychological therapy. ***Table 5.3*** evidence the technological resources used to navigate the patient, i.e., Whats-App and direct telephone line.

Findings presented in ***Figure 5.1*** illustrate that all interviewed PNPs are actively engaged in one or more of the defined time intervals, processes, and events [1]. In consequence, the term "navigating the patient" takes on distinct meanings and involves different sets of activities and processes, even among PNPs focusing on similar healthcare levels or having similar objectives. Upon integrating the programmes into this framework, results reveal that PNPs concentrate on different stages within the "*cancer appraisal-to-survival pathway*". For instance, **PNP D** exclusively guides the patient after accessing treatment and undergoing other patient and system processes. In contrast, **PNP A** navigates individuals from an earlier stage until the patient is scheduled to receive treatment. This implies that PNPs are not merely programmes but, in fact, distinct navigation models varying in scope and action. **PNP C**, takes intervenes in a different set of processes: from the first consultation with the General Practitioner (GP) until the death, cancer relapse or disease-free survival. There are two models acting in the same activities and intervals: **PNP B** and **PNP E**.

[1] In Chapter 3, Walter's model underwent adaptation and modification to formulate an encompassing framework for the classification of PNPs. This adaptation was specifically tailored to address the unique needs and challenges confronted by cancer patients across various stages of their healthcare journey. The refined "*cancer appraisal-to-survival pathway*" extends Walter's model by incorporating additional dimensions and criteria, resulting in a more comprehensive classification system.

Table 5.1: Patient Navigation Programme Comparison: Case Studies A-E from Mexico

Case study	Origin	Navigated	Population characteristics	Cancer type	Place	Type of organisation
Case A	**2013**	**500/year**	Uninsured population Ethnic minority groups from State of Chiapas	All types	Community-based (rural)	Non-governmental organisation
Case B	**2010**	**330/year**	Uninsured population	All types (mainly breast cancer)	Hospital-based (urban)	Public health sector
Case C	**2013**	**1100/year**	Publicly insured, Privately insured, & uninsured population	Lung, prostate, testicular breast, ovarian, cervical & Haematologic cancer	Community & Hospital-based (urban)	Non-governmental organisation
Case D	**2014**	**100/year**	Uninsured women aged <40	Breast cancer only	Hospital-based (urban)	Non-governmental organisation
Case E	**2015**	**400/year**	Uninsured population	Lung cancer only	Hospital-based (urban)	Public-health sector

Results from Case studies A-E interviewed in 2019 by EBG. This table shows how many patients are navigated per year, the insurance status of the population, the cancer type the PNP provides services to, where the navigation is taken place (community vs hospital) and the type of organisation leading the PNP.

Source: Own work

Table 5.2: Activities comparison from patient navigation programmes in Mexico: Case studies A-E

CASE STUDIES		A	B	C	D	E
Basic navigation activities						
Patient identification	Activity related to the active search of eligible patients [2]	Yes	Yes	Yes	Yes	Yes
Barriers and resource identification	Identification of barriers in access to healthcare.[3]	Yes	Yes	Yes	Yes	Yes
	Activity related to the identification of resources already found in the patients context.	Yes	Yes	Yes	Yes	Yes
Continuous evaluation	Based on previous barriers, a continuous evaluation of barriers is conducted.			Yes		
	Active identification of new barriers			Yes		
Specific activities						
Infrastructure navigation	Teach patients how to navigate the hospital and/or health sector	Yes	Yes	Yes		Yes
Administrative documentation	Provision of support to fill internal documentation	Yes	Yes	Yes	Yes	
	Provision of support to fill external documentation	Yes	Yes	Yes		
Appointment management	Schedule appointment with the medical team	Yes	Yes	Yes	Yes	Yes
	Appointment reminders for all the appointments, including the first	Yes				
Mediation between doctor and patient	Communication process between the medical team and the patient [4]	Yes	Yes		Yes	Yes
Donation of resources	Donation of the cancer treatment		Yes	Yes		
	Donation of food			Yes		
	Donation of transportation to travel to hospital/clinic	Yes		Yes		
	Donation of shelters/hotel stay during the patients	Yes				
	Donation of diagnostic (lab-tests) and treatment (not cancer related)	Yes		Yes	Yes	Yes
Linkage with external resources	Connection with state transportation services and / or shelter services	Yes	Yes	Yes		Yes
	Connection to NGO 's resources		Yes	Yes	Yes	Yes
	Linkage to Hotel, medicines, transportation, and food discounts	Yes	Yes	Yes		
	Legal advice			Yes		
	Job re-integration support		Yes			
	Wellness activities		Yes			
Provision of information	Provision of information on cancer, diagnosis, treatment, survival, and other cancer related topics	Yes	Yes	Yes		Yes
	Information on which external resources are available	Yes	Yes	Yes	Yes	
	Communication with the patient throughout the navigation experience	Yes	Yes	Yes	Yes	
Psychological support	Create and administer support group		Yes	Yes	Yes	
	Generate a direct communication line with the navigator for emotional support		Yes	Yes	Yes	
	Sexual health therapy				Yes	
	Psychological therapy				Yes	

Source: Own work

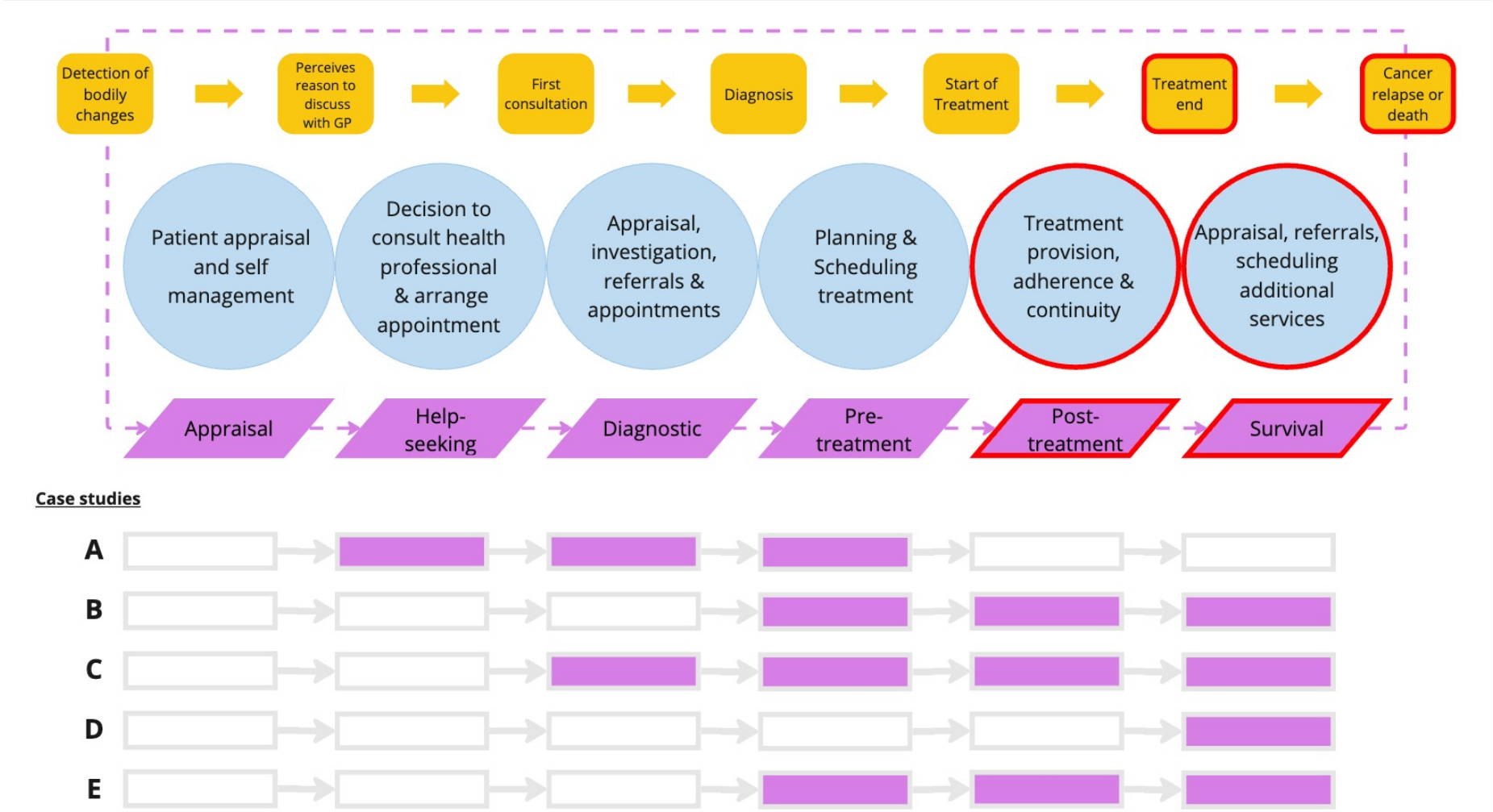
Results from semi-structured interviews conducted by EBGin 2019. Stakeholders interviewed included navigators and/or head of PNP.

Table 5.3: Resources used by patient navigation Case Studies A-E

	Type	A	B	C	D	E
Technology Resources	EHR		Yes			Yes
	Social Media			Yes	Yes	
	Telephone line	Yes	Yes	Yes	Yes	Yes
	Info-Cancer Telephone line		Yes			
	Whats-App	Yes		Yes	Yes	
	Website		Yes			

Source: Own work
Based on the semi-structured interviews conducted by EBG

Figure 5.1: Classification of patient navigation Case studies (A-E) according to the: *cancer appraisal-to-survival pathway* framework



Source: Own work

The shapes in red mark the modifications to Walter et al 2012 pathway to cancer treatment framework [88]. From diagnosis to treatment:Pre-treatment interval, from treatment to treatment end (post-treatment interval), and the time from treatment end to death or cancer relapse: survival. The pre-treatment interval corresponds to the treatment interval according to the Aarhus statement.

5.3.1 Thematic Analysis

Six themes emerged from the analysis: 1) Effect in Timely Cancer Care and Discrepancies in Program Development and Evaluation 2) Identifying barriers to care, 3) Navigation in the context of overcoming fragmented health systems, 4) Patient navigation as a changing practice, 5) Resourcing patient navigation and 6) Unveiling the Hidden Potential in Everyday Heroes

Theme 1: Effect in Timely Cancer Care and Discrepancies in Program Development and Evaluation

Many of these programmes were established as NGO's with the primary mission of "serving the vulnerable population." However, these PNP described the lack dedicated teams to systematically assess their long-term impact and often fail to consistently collect relevant data. The common refrain among these programmes is the scarcity of resources, which results in limited evaluation efforts, typically focused on quantifying the number of barriers addressed and the number of patients navigated each year. Some programmes include additional outcome measures such as: patient satisfaction, quality of life assessments across the cancer continuum, and psychological evaluations. However, a notable gap exists as none of them have gathered data on time-to-diagnosis or treatment intervals, leading to a lack of evidence demonstrating a increase in cancer care timeliness.

Moreover, a common issue among the programmes is the absence of objectives developed according to a logic model [152]. Consequently, these programmes often feature activities that do not align with their intended goals and evaluation indicators that are not comprehensive in covering all activities conducted. In some cases, PNP have basic evaluation of administrative outcomes but without a focus on measuring the impact in cancer care timeliness. Overall, the evaluation methods employed exhibit significant heterogeneity, but no clear evidence on reducing time to event.

A thorough comparison of the objectives, and the evaluation methods employed by PNP can be found in ***Table 5.4***.

Table 5.4: Aim and evaluation mechanisms of Patient Navigation Programme Case Studies A-E

Case study	Aim	Currently evaluated	Suggested intervals
Case A	**To increase access to quality health-care and tackle barriers to medical care**	Quantification of barriers Number of patients	Help-seeking interval diagnostic interval pre-treatment interval
Case B	**To better the cancer care experience and inform patients**	Patient satisfaction Quantification of barriers Survival follow-up (planned)	Pre-treatment interval treatment interval & Survival
Case C	**To navigate the patient across the health-care system, throughout the disease continuum**	Quantification of barriers Number of patients	Diagnostic interval Pre-treatment interval Treatment interval Survival
Case D	**To help patients reach access to cancer care**	Patient satisfaction Quality of life Psychological evaluation	Survival
Case E	**To reduce time to cancer care**	Number of patients per year	Pre-treatment interval Treatment interval Survival

Source: Own work

Results based on the Case Studies A-E drawn from semi-structured interviews conducted by EBG. Suggested intervals column are based on the Aarhus statement.

Theme 2: Identifying barriers to care

PNP's interviewed tackle a specific set of barriers and offer to intervene in the navigation process with a particular set of pre-defined interventions. The barriers found by PNP were most commonly: referrals to higher levels of care (second or third level), navigating the different health systems, transportation towards health-care settings, shelters close to the hospital, food for family members during the patients' stay at the hospital, logistical issues and insufficient funds for diagnosis or treatment.

Although PNP aimed to intervene throughout the cancer continuum using different activities, they all sought to help those who were most at risk for delaying or not accessing care or those who were at risk of catastrophic expenditures.

Theme 3: Navigation in the context of overcoming fragmented health systems

In the backdrop of Mexico's tiered healthcare system, characterised by three levels of care, this theme delves into the intricate challenge of navigating patients through the fragmented health landscape. The disparities among these levels, with the specialised third tier being both crucial and scarcely accessible, lay the groundwork for understanding the dynamics of patient navigation within the country's healthcare structure.

Chapter 2 established Mexico's healthcare tiers, emphasising the concentrated infrastructure and resource allocation in larger cities, particularly affecting the availability of specialised care in the third level [46]. The delineation of the first level as community clinics, typically overseen by a single medical doctor, and the second level as an intermediary further sets the stage for comprehending the challenges patients face while traversing these healthcare tiers [46].

This theme scrutinises the PNP activities based on the healthcare delivery level they address. While the distinctive characteristics and available resources guide the PNP's focus, this analysis introduces an additional layer – the healthcare level from which patients embark on their navigation journey.

Drawing a contrast to the previous examination of activities in ***Table 5.2 and Table 5.5*** strategically aligns navigation activities with the specific healthcare levels involved in each case study. Rather than emphasising the sheer number of activities, this approach underscores the importance of understanding navigation intensity in terms of the healthcare levels traversed. This nuanced perspective challenges the

conventional measurement of a PNP's effectiveness solely through activity count and suggests that the intensity of navigation should be more accurately portrayed by the diversity of healthcare levels engaged.

Table 5.5: Navigation intensity according to number of activities, health-care level navigated and number of levels navigated.

PNP	# of activities	Health-care level	Levels navigated
A	17	Primary to 2nd/3rd level	3 levels
B	18	Within 3rd level	1 level
C	22	Secondary to 3rd	2 levels
D	14	Within 3rd level	1 levels
E	10	Within 3rd level	1 levels

Source: Own work

Results based on the Case Studies A-E drawn from semi-structured interviews conducted by EBG

Theme 4: Patient navigation as a changing practice

The Patient Navigation programmes (PNP) in Mexico utilise the concept of "patient navigation," defined as a strategy to guide individuals into the healthcare system and help them navigate the pathway to care. Over time, these programmes have evolved to address changing challenges, adopting various emerging activities.

PNP in Mexico have shown adaptability to the dynamic healthcare landscape. For instance, with the improved survival rates resulting from innovative cancer therapies, navigation programmes strive to make these treatments accessible. However, economic barriers pose challenges. Consequently, PNP adjust their fundraising efforts to cover the costs of pricier treatment schemes and support patients over extended periods of time. To illustrate, breast cancer treatment is fully covered by public insurance, whereas the same is not true for lung cancer. As a result, guiding a breast cancer patient requires less financial effort. As barriers shift and healthcare coverage changes, interventions for navigated populations also evolve. Initially, PNP donations focused on unfunded cancer treatments. However,

as some therapeutic schemes became entirely covered by the health system, patient navigation shifted towards addressing psychological, logistical, or other barriers.

This adaptation highlights a noticeable prioritisation in the activities undertaken for each type of cancer, making PNP an integral part of enhancing patient experiences in the healthcare system. An insightful perspective from a stakeholder in Case C emphasises the evolving nature of patient navigation. According to the stakeholder:

> *"...it is not a finished model, it is a model that came from the need of that group of patients... You have to give medicine, but we realise that medicine today is becoming an impossibility every day and more expensive and longer schemes, right? With this chronicity of cancer, we have patients that last up to five years, don't we? Then you have to start moving this model where? Well, to another place ..."* **-Navigator from Case C-**

Theme 5: Resourcing patient navigation

Within the dynamic context of patient navigation in Mexico, this study unveils the intricate interplay of organisational dynamics and funding models crucial for providing support to patients. Navigators assume a central role in establishing connections beyond the health system. Their proactive activities include linking patients with external healthcare providers, social services, and community programmes, employing a holistic approach to surmount personal barriers and provide continuous post-referral support. This is similar to approaches conducted in the literature [105].

A notable feature of Mexican PNP lies in the diverse funding models at play. This study reveals that only two PNP in Mexico receive public funds. The majority

depend on private funding, drawing support from grants, seed funding, donations, and collaborations with private entities like shelters, restaurants, and laboratories. This funding diversity introduces different dynamics to the organisational structure of PNPs, significantly impacting their objectives, scope, and sustainability.

Despite the divergence in funding sources, a common thread unites these PNPs is the universal commitment to connecting patients with external resources. This shared goal, irrespective of funding origin, underscores the importance placed on linking patients to essential support networks. ***Table 5.6*** compares the funding sources across Case studies A-E.

Table 5.6: Funding sources used by patient navigation programme Case Studies A-E

	Type	A	B	C	D	E
Funding sources	Agreements with private providers	Yes		Yes		
	Grants and seed funding	Yes	Yes	Yes	Yes	Yes
	Public resources		Yes			
	Donations		Yes	Yes	Yes	Yes

Source: Own work

Results based on the Case Studies A-E drawn from semi-structured interviews conducted by EBG

Theme 6: Unveiling the Hidden Potential in Everyday Heroes

In Mexico, the patient navigator profile holds a mixed professional background. Like other programmes found in the literature, the Mexican cases also seek out cancer survivors as navigators [98]. In addition, programmes go beyond professional background and may also seek to employ navigators with race and language in concordance with their patients' characteristics to increase the effectiveness of the program [12, 99]. **Table 5.7** show the different actors involved as navigators in each programme. Nonetheless, this theme emphasizes the need for a more inclusive and flexible approach to patient navigation, acknowledging that effective assistance can come from unexpected sources within the community.

In the case study of a PNP C operating in an indigenous region of Mexico, the unique role of a taxi driver as a patient navigator emerges as a pivotal element. The program aims to facilitate access to quality healthcare for uninsured patients by addressing economic, logistical, and communication barriers. However, a crucial aspect of this initiative is the unconventional involvement of a taxi driver, whose lack of formal training is overshadowed by the practical relevance of their role in navigating patients through the complexities of the healthcare system.

Unlike traditional patient navigators who typically undergo specialized training, the taxi driver in this case study brings a distinct perspective. The emphasis here is on the practical skills and local knowledge possessed by the driver, proving that sometimes, real-world experience may surpass formal training. The driver's ability to transport patients, translate, and mediate with healthcare professionals highlights the importance of on-the-ground expertise. This challenges the conventional notion that only formally trained professionals can effectively navigate patients through the healthcare system.

The case study raises an intriguing question: can anyone be a navigator in the patient care process? The involvement of a taxi driver suggests that individuals with a deep understanding of the community, strong communication skills, and a willingness to assist can play a crucial role in patient navigation. This challenges the notion that navigators must have a specific background in healthcare or social work. It prompts a broader perspective on the potential contributions of community members and non-traditional actors in improving healthcare access.

Table 5.7: Human resources used by patient navigation programme Case Studies A-E

	Type	A	B	C	D	E
Human Resources	Social worker	Yes		Yes		
	Psychologist		Yes		Yes	
	Nurse		Yes			Yes
	Peer-to-peer		Yes			
	Taxi-driver	Yes				

Source: Own work

Results based on the Case Studies A-E drawn from semi-structured interviews conducted by EBG

5.4 Discussion

This study does not systematically map all the PNP available in Mexico. However, it captured programmes that have been developed in the last ten years, in different areas in Mexico. It shows the population that is navigated holds different insurance coverage schemes and the heterogeneity in cancer focus, objectives, resources employed, funding and evaluation methods. Most importantly, although it does not find any evidence of the intervention to increase cancer care diagnostic or treatment timeliness, it examines programmes being implemented in Mexico in real time.

In the literature, PNP focus on navigating patients with a single type of cancer [153, 154] or multiple types of cancer. This study presents organisations that simultaneously navigate different types of cancer patients through heterogeneous funding sources, as well as a single cancer type. More research should be conducted to evaluate the effect on cancer outcomes when navigating multiple types of cancer vs a single type of cancer.

Unfortunately, because these are “opt-in” programmes, it is potentially those who were best fitted to navigate the system in the first place that reached a navigation program or in fact, the treatment phase. Moreover, barriers and their matching interventions were determined by PNP and not by patients. This

does not imply that the actively tackled barriers are not there, but rather that some barriers might not be tackled at all if the patients are not involved in the identification process. Thus, to avoid barriers being excluded at the time the program is created, a needs assessment through the participation of community stakeholders is encouraged. The National Comprehensive Cancer Network Distress Thermometer and Problem list can be used as a standardised way to measure and report barriers [155]. Other PNP have performed a needs assessment or interviewed patients before developing a strategy to capture the barriers through the patients' lens [156]. However, if new barriers are identified by PNP, ethical and economic challenges might arise if not equipped with enough resources to tackle new additional barriers [155].

Similar to the literature, PNP actively sought out patients, detected similar structural and individual barriers and developed a personalised plan to address them. However, not all PNP in this study developed a systematic follow-up to track progress across the health continuum, despite longitudinal follow up being widely encouraged [87,94,155]. This restricts navigation to a certain period in time and does not take into account the variation in barriers across time and the cancer continuum. As a result, lack of follow-up on the barriers being tackled might hinder potential positive effect navigation has in survival and other cancer outcomes.

The thematic analysis in this thesis reveals six key themes: the effect in timely cancer care and discrepancies in program development and evaluation, identifying barriers to care, navigation in the context of overcoming fragmented health systems, patient navigation as a changing practice, resourcing patient navigation, unveiling the hidden potential in everyday heroes.

The fragmented health-care system, lack of universal health coverage, and

personal barriers to health (i.e., language, education, and beliefs) are known to be the most important causes for advanced stage diagnosis and delayed treatment of cancer in Mexico [139, 143]. In this thesis, the identification of barriers to care is a central theme, showcasing how PNPs target specific barriers with pre-defined interventions to assist individuals at risk of delayed or insufficient access to care. The navigation process is examined in the context of Mexico's tiered healthcare system, emphasising the disparities among different healthcare levels and the challenges patients face in navigating this fragmented landscape.

PNP in Mexico have failed to introduce accurate evaluation methods to measure impact across time and particularly the time to event intervals. This is similar to what has been found in the literature [8, 9, 84, 87, 157]. It seems there are no incentives for these programmes to evaluate the effect the PNP has had in timely access to care or cancer outcomes across populations and time. Hence, there is no evidence PNP reduce time-to-diagnosis or treatment in Mexico.

Despite the fact that the resources are limited, every PNP has developed their own strategy to achieve economic resources to fund their program. Although public resources are mentioned, they are not the most relevant funding source. Thus, these case studies are a great example of other non-public sources of funding. This might be relevant for PNP where financing sources have become problematic. Furthermore, reaching funding opportunities might be easier if PNP demonstrate positive impacts in cancer outcomes. PNP are encouraged to make use of theoretical frameworks and tool-kits for the evaluation of their aim, objectives and activities [83, 158]. They could also employ a logic model to operationalise their results and evaluate their intervention [152].

Similar to the results obtained through the systematic review, PNP activities

were heterogeneous. However, the systematic review found three major activities being conducted by navigators: emotional support, infrastructure navigation and advanced navigation activities (legal support); whereas this chapter found administrative and logistical aid, emotional support, and provision of resources as the overarching activities. This, variation might be due to changes in the barriers found in the population navigated. Potentially, patients in LMIC face wider accessibility barriers than in HIC. Thus, the provision of resources and donations are a result of social determinants of health acting having a deeper effect in patient outcomes.

Variations in the activities conducted might be due to the health system in itself: the levels of care navigated and whether the population is insured or not. Thus, this thesis proposes a shift in focus from measurement of activity quantity to the depth of healthcare levels navigated and the time intervals. It encourages a more refined and comprehensive portrayal of the program's impact on healthcare accessibility and patient journeys. Lastly, this chapter advocates for a re-calibration of metrics to better capture the program's effectiveness in overcoming the challenges posed by a fragmented health system.

Depending on the program, the role of a navigator consisted of providing social support, encouraging the patient while supporting the patients autonomy, helping the patient understand the medical information that is given and coordinating personalised care across the different departments. In some cases, the navigator accompanied the patient on visits or interface directly with health-care providers, and others the patient's behalf.

The theme of unveiling the hidden potential in everyday heroes challenges traditional notions of patient navigators, emphasising the diverse backgrounds of

individuals involved in patient navigation, including cancer survivors and even a taxi driver. This underscores the importance of community-based and non-traditional actors in improving healthcare access.

The integration of innovative technologies facilitates a smoother patient journey [85]. These case studies show the technology used by PNP in Mexico, and their usage variation. This could be useful in the future to develop technologies particularly directed to navigate patients. Future research should be conducted to study how prevalent or effective the usage of these communication tools is and if it varies between patients due to low levels of literacy or availability. PNP should be cautious on implementing tools in contexts where technological literacy is low. Moreover, research is encouraged to define rules to ensure boundaries between the navigator and the patient when using digital communication tools [159].

Moreover, PNP in Mexico have not taken steps towards reducing outcome inequalities within their population. Patient navigation is distinguished from other services by its focus in reducing health inequalities [62, 152]. In order to stick to the original task, PNP in Mexico should not only tackle barriers individually, but also design interventions that eliminate disparities between the population groups. They can do this by making use of the guides available to create interventions that include a health inequalities perspective [160–163]. Hendren et al are a good example of PNP were interventions seeking to reduce health inequalities have been accurately integrated [160].

Remarkably, the presence of these PNP in the academic world is virtually non-existent. Their evaluations are notably absent from systematic literature reviews and other peer-reviewed journals. It remains unclear whether this absence is due to a lack of resources inhibiting research and evidence-based interventions

or stems from the fact that these programmes are often developed by patient organisations that may not inherently possess an academic scope. This raises questions about the potential limitations imposed by organisational structures and objectives.

In charting future directions for research, it is imperative to delve into the intricacies of the multifaceted interplay of organisational dynamics and resource challenges. A nuanced investigation into public and private institutions can unveil how bureaucratic processes or profit-driven motives influence the development and evaluation of PNP. Similarly, exploring the impact of international versus national grants and donations on each programmes objectives provide insights into the global-local dynamic. The unique perspective of patient-driven organisations warrants further examination, considering how their inherent patient-centred approach shapes PNP goals and methods, while also acknowledging potential limitations in research endeavours. These future research trajectories will enhance the efficacy, sustainability, and academic integration of PNP across diverse contexts.

5.5 Limitations

It is essential to recognise that the five case studies have both strengths and limitations. While they offer valuable insights into specific contexts and unique experiences, their findings may not always be broadly applicable or generalisable to larger populations.

This study does not systematically map all active PNP in Mexico. Although this study captures some programmes in different regions of Mexico, these results are not generalised. In addition, the snow-ball sampling process might also lead to selection bias.

During the data collection process, stakeholders from different ranks (i.e., navigators, administrators, leaders, founders) were interviewed. Thus, differences in the type of involvement each stakeholder had in the program might affect the data collected.

5.6 Summary

1. PNP in Mexico vary widely in activities and scopes, but do not focus on increasing timeliness in cancer care.
2. Lack of data on time-to-diagnosis or treatment intervals hinders understanding of their impact on early diagnosis and treatment.
3. PNP in Mexico address administrative, logistical, emotional needs, and provide resources. Whereas the systematic review found three major activities being conducted by navigators: emotional support, infrastructure navigation and advanced navigation activities (legal support).
4. Patient navigators with varied backgrounds, including a taxi driver, demonstrate the importance of community expertise.
5. The adapted framework reveals navigation programmes are different navigation models, focused on different time intervals across the cancer continuum.

1. Mexico's tiered healthcare system poses challenges; navigation intensity varies based on healthcare levels traversed.
2. PNP adapt to healthcare landscape changes, focusing on access to evolving treatments and shifting healthcare coverage.
3. Diverse funding sources impact PNP dynamics; public and private sectors collaborate to connect patients with external resources.
4. Heterogeneous evaluation methods for PNP requires standardisation.

Five PNPs were identified in Mexico and interviewed for the purposes of this thesis. The examination of PNPs reveals a complex landscape where the concept of "navigating the patient" extends beyond a standardised model. Building on the identified theoretical concepts described in the systematic review, this thesis provided a structured and comprehensive way to categorise PNPs based on their intervention in specific cancer care intervals (see ***3.7***). The findings presented underscore the active engagement of all interviewed PNPs across various time intervals, processes, and events within the refined "cancer appraisal-to-survival pathway."

The diverse activities undertaken by PNPs highlight the distinct meanings and scopes associated with the term "navigating the patient." Even among PNPs with similar healthcare focuses or objectives, the navigation models vary significantly. Similar to the themes found in the systematic review, programmes focused on: emotional support, infrastructure navigation and advances navigation. In addition, this Chapter adds a fourth theme: the provision of resources and donation of

resources.

The evolving nature of patient navigation as a practice is highlighted, showcasing how PNPs adapt to changing healthcare landscapes, particularly in response to economic barriers and shifting healthcare coverage. The crucial role of organisational dynamics and funding models in resourcing patient navigation is unveiled, with private funding playing a significant role in shaping the objectives, and sustainability of PNPs.

PNPs in Mexico, as PNPs found in the systematic review, did not focus on intervening nor evaluating timeliness in cancer care. If both agendas were matched, the impact of patient navigation could be demonstrated in the Mexican context and funding opportunities might blossom.

Lastly, the discrepancies in program development and evaluation highlight the heterogeneity in objectives, and evaluation methods among PNPs. The absence of dedicated teams for systematic assessment, limited data collection, and a lack of academic presence raises questions about the potential limitations imposed by organisational structures and objectives.

Chapter 6

The lung cancer patient journey in Mexico: a mixed methods study

6.1 Background

In every pathway to care, there are important events to be studied over time [3]. In addition, there are processes and decisions that the patient and the healthcare professionals go through and decisions both patients and healthcare providers must make in between events [3]. Understanding the cancer care pathway and its intervals is crucial for establishing standard milestones to achieve timely treatment [4, 164].

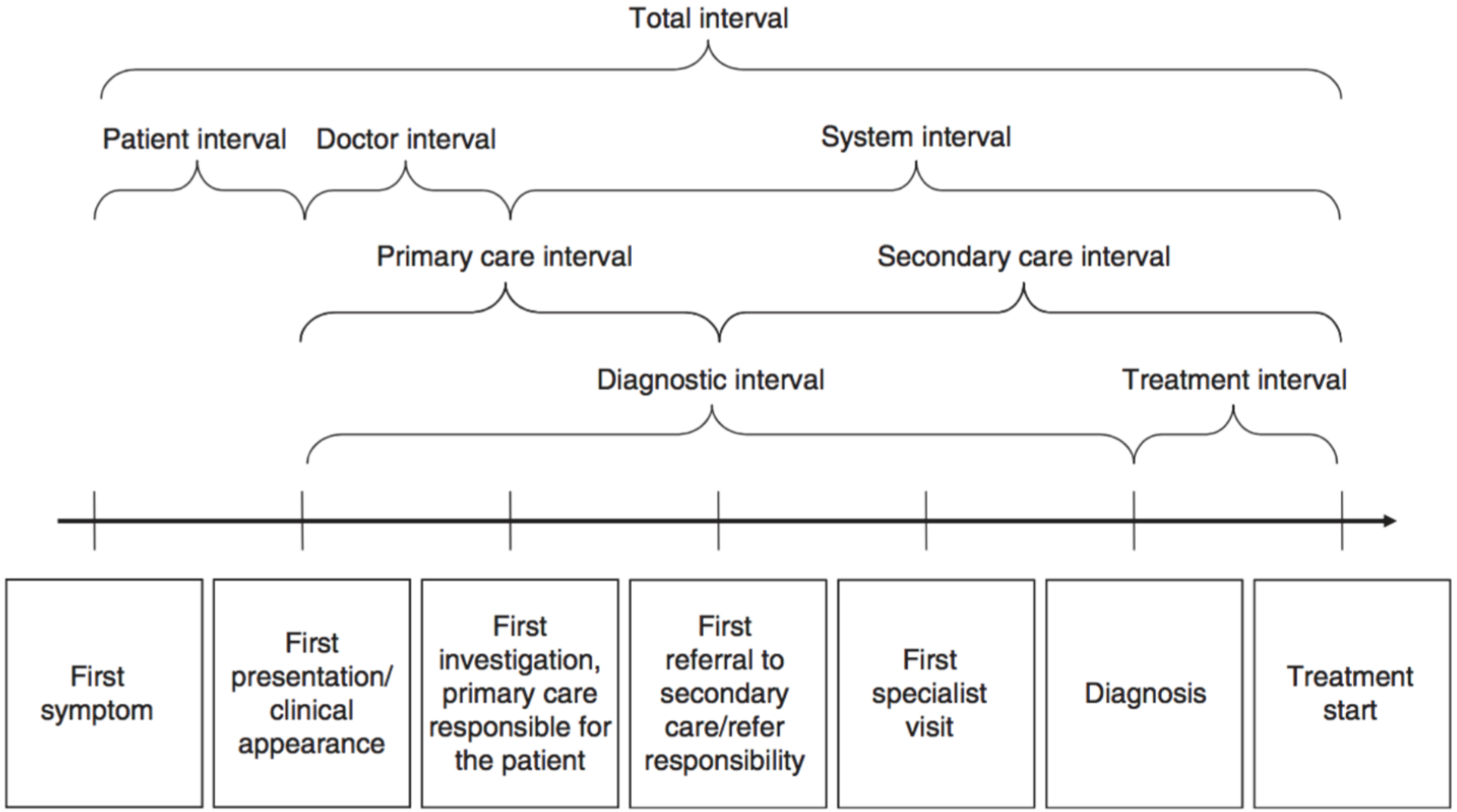
Many theoretical models have been constructed to represent the events, characterise care intervals, and define processes that lead to symptomatic cancer diagnosis and treatment. The processes, events and cancer care intervals have been studied by *Andersen et al., 2009* and *Walter et al., 2012* [64, 88]. In previous sections of this PhD thesis, Walter's work was presented in ***Figure 3.1***. This framework described the patients' pathway to cancer treatment, the patients' and systems' processes, events, and the contributing factors, all-together seen under the scope of time (intervals) [88].

Research on LC care intervals are characterised by their heterogeneity in study design, patient population, interval definitions, thereby limiting cross-study comparisons [3]. In fact, amongst the most relevant issues found in studying LC care intervals through a systematic review in 2014, authors concluded calculating time was a complicated task and standardised definitions and procedures to be implemented to improve understanding of timeliness in managing LC [79].

As a result of the heterogeneity in research in early cancer diagnosis, specific events and intervals were defined by researchers as guidelines to improve the design and reporting of studies on early cancer diagnosis [2, 5]. These guidelines are referred to as "The *Aarhus statement"* [2, 5].

Figure 6.1 shows the milestones and time intervals in the route from first symptom (first event), until the start of treatment [2, 5]. The time the patient takes to decide to reach for care is referred to as the *"Appraisal interval"*. In addition, the doctor from the primary care clinic takes some time to start investigating the patient's case, this is referred to as the *"Doctor interval"*. Similarly, the system (secondary level or above) also takes some time to respond to the patients' needs, this is referred to as the *"System interval"*. The "total interval" includes all of the intervals mentioned before, broken down into smaller bits of the cancer continuum to place further analysis in the intervals' differences across levels of care (*"primary care" vs "secondary care")* and the *"diagnostic interval"* and *"treatment interval"* [2, 5].

Figure 6.1: Olesen's cancer milestones and time intervals definitions according to the Aarhus Statement



Source: Olesen et al. 2009 and Weller et al 2012 [2, 5]

Timeliness in lung cancer care in the literature

Across the literature, many researchers have studied LC care intervals through quantitative methods and defined some gold standards of care. For example, a systematic review evaluating delays in LC care found a 13-day average between the primary care visit and referral for specialist evaluation [3]; and less than 14 days from referral to first specialist [3]. The median time to LC diagnosis ranged from 8–60 days and treatment ranged from 30–84 days [3]. A recent primary care records study of LC patients in England reported a median of 112 days in the total diagnostic interval (between first symptomatic presentation and diagnosis) [165]. Although results are different across the world, it seems countries in the Global South experience even longer care intervals [79]. This can be explained by the start of an anti-tuberculosis pathway [79] or health-system infrastructure deficiencies [1].

Meanwhile, some studies study intervals according to the initial symptoms [24], other studies also compare median times between LC types. For example, in the USA, the median time from diagnosis to treatment was 27 days for NSCLC patients and 18 days for SCLC patients [56, 166]. Additionally, research has also been conducted to understand the association between number of consultations and timeliness [167, 168]. For instance, one third of patients with LC experienced three or more pre-referral consultations and long median primary care intervals (14 days) [167, 168].

In other cases, the association between timeliness and outcomes (i.e., survival) has also been studied [3, 169]. Nonetheless, some reported of better survival in patients who received less timely care [3, 169]. This might be explained by diagnosis being shorter amongst late stages of the disease [3, 24] and palliative therapy being administered before curative ones [169]. In addition, prolonged

intervals predominantly manifest in less symptomatic patients, concomitant with a more favourable prognosis for those already with symptoms [79].

Cancer care intervals in Mexico

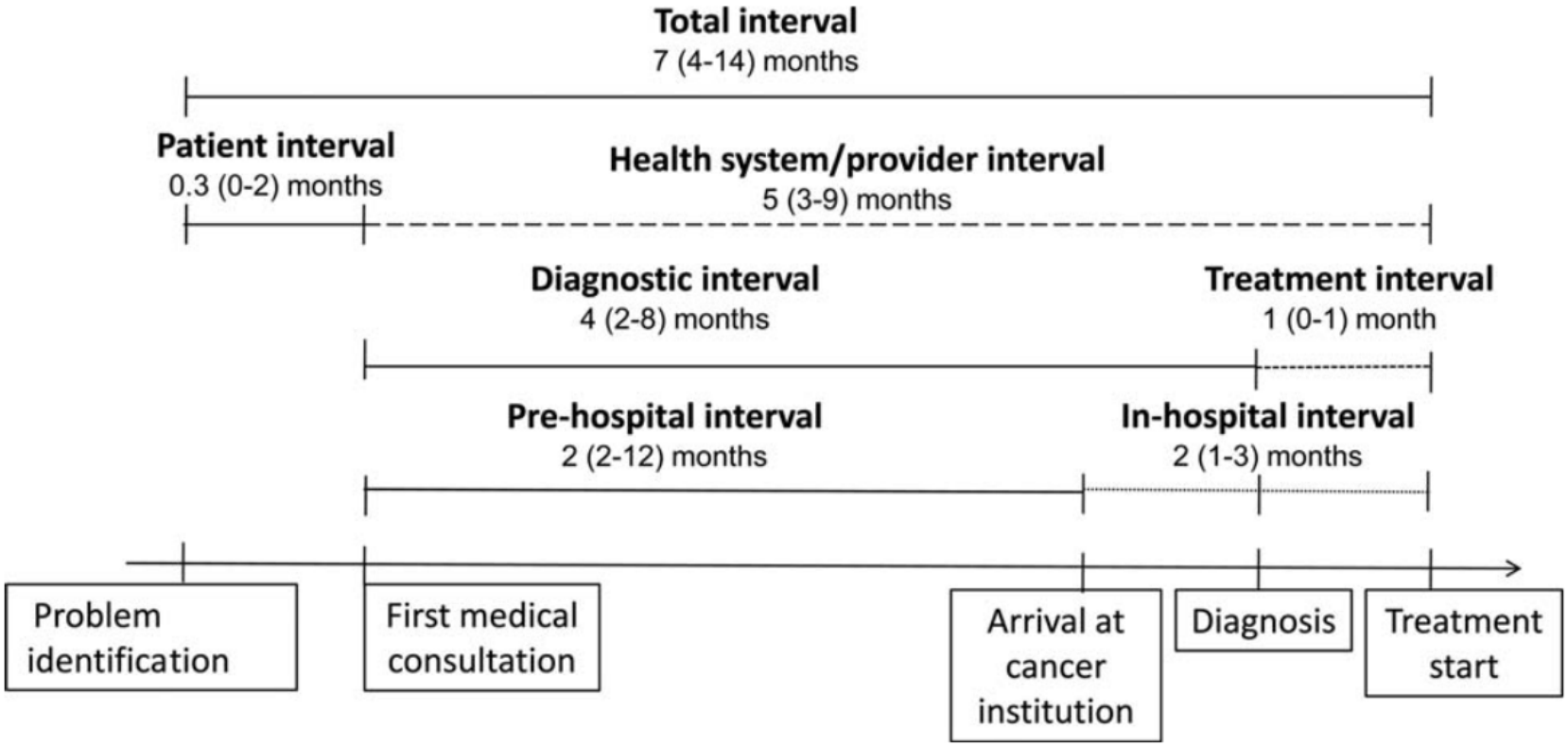
Despite the importance of qualitative research in studying the patient journey and timeliness in cancer care, there remains a notable scarcity of such studies, especially in countries with fragmented and unequal healthcare systems [170]. Studies like those are more prevalent in the global north [170] or Australia [60, 171, 172]. In Mexico, for example, there is a lack of research discussing and describing patient journeys, particularly in LC cases. Conducting further qualitative research in this area is crucial to address this knowledge gap and gain a comprehensive understanding of the unique challenges faced by LC patients in accessing timely care [170].

Similarly, European countries and the UK have more frequently examined the timeliness of LC care, the association between LC timeliness and outcomes (i.e., survival) or interventions to improve LC intervals across the continuum [3, 4]. Regrettably, in Mexico, patient, doctor, and system intervals in cancer care have not been thoroughly examined or addressed. In fact, the available research in cancer care timeliness in Mexico concentrates solely on breast cancer, particularly diagnosis by *Unger et al.* [139]. Only recently, there has been some interest among other authors to study timeliness among other types of cancer [141], but the work is still ongoing.

To contextualise previously determined frameworks to a Mexican context, *Unger et al.* developed a new set of definitions for time intervals and added a *"Pre-hospital interval" & "In-hospital interval"* [139]. In *Unger's* research, the

interval from initial medical consultation to breast cancer treatment in Mexico City was delayed by a median of five months and seven months from suspicion to treatment [139]. These results however cannot represent LC care intervals. It often takes longer to be diagnosed and treated for LC [3]. Despite modern diagnostic and treatment options, sluggish, fragmented, and poorly coordinated treatment have complicated LC care [3] and thus, should be studied independently. ***Figure 6.2*** describes the time intervals found for breast cancer in a study conducted in Mexico. Compared to the Aarhus statement and Walter's pathway to treatment frameworks, this adds a "pre-hospital" and "post-hospital" intervals.

Figure 6.2: Breast cancer intervals found in Mexico according to Unger's interval definition



Source: Unger et al. [139]
This image shows time intervals in the Mexican context for breast cancer.

UK Cancer targets and results

To track and tackle barriers in cancer care and avoidable delays, the *NHS* in England targets prolonged time to events by establishing operational standards. The current targets are: following an urgent GP referral for suspected cancer, patients must be seen by a specialist in $\leq$ 14 days (two-week-wait) [4]. Similarly, from initial referral to treatment (secondary care interval [5]), patients must be treated in $\leq$ 62 days; and no more than 31 days should pass between diagnosis/treatment plan and start of treatment [4].

In 2021, the operational standard stated that 93% of patients should be seen within 14 days of the referral, 96% of patients should be treated $\leq$ 31 days of the decision to treat date and 85% of patients should receive a first definitive anti-cancer treatment within $\leq$ 62 days of the urgent referral date [4]. Results show only 88.7% reached the two-week-wait goal, 95.0% were treated within the 31-day target and following a GP referral, only 74.3% reached the 62-day wait target [4].

Mexico, in contrast, has not established interval standards or measurements, so they go unnoticed. Literature suggests assessing the cancer care intervals themselves and implementing a continuous evaluation plan will improve outcomes [3].

Patient pathway, patient journey and patient trajectories

In theory a cancer pathway should bring the patient promptly into a medical environment where cancer will be dealt with. Pathways are biomedical tools that chronologically mark key activities and goals in the healthcare process [173, 174]. The cancer care pathway is defined as the patient-centred services that ultimately lead to the patient's diagnosis and treatment to enhance service quality, efficiency,

and clinical outcomes. The objective of a pathway is to use of the right therapy, for the right patient, at the right time, and this in turn has implications on risk–benefit ratios and treatment costs [1, 52].

The patient pathway examines the various steps, processes, and interactions involved in cancer [173, 174], from perceiving the first symptoms to accessing the healthcare system, receiving a diagnosis, initiating treatment, experiencing remission or relapse, survivorship or end-of-life care [88]. The objective of integrated pathways is improvement in the continuity of care and better outcomes [174]. However, pathways may not align with patients' expectations and values [173]. The "patient journey" or "healthscapes" encompass the collective set of potential care and treatment options that patients envision, contribute to, and navigate [173]. Unlike pathways, journeys are inherently patient-centred, ever-changing, unpredictable, and shaped by the interactions of human and non-human factors within the health-related landscape [173]. Patient journeys are mostly a result of narratives, thus studied by qualitative methods. The patients' social determinants of health embody the journey the patient will navigate, despite the milestones marked by the pathway.

Not every journey is linear and unidirectional. The journey to cancer care can be tortuous and cyclical before resulting in diagnosis and treatment, leading to worse outcomes i.e., death, elongated intervals from patient suspicion to treatment, disease progression (clinical upstaging) and higher costs [25, 38, 64, 88].

Moreover, each event in the patient journey will then (as a chain of events), increase the risk of the subsequent event and overall mark the trajectory of unequal outcomes. The term "patient trajectory" refers to the long-term view of one dimension of an individual over time [175]. Bringing the term back from

life course epidemiology [175, 176], its aim is to elucidate the characteristics of patients' journeys and how they influence the development of diseases or in this case, subsequent worse outcomes. By using the chain of risk model[1], patient trajectories provide a fresh perspective on explanations for outcome inequalities in health [175]. **Table 6.1** shows a brief comparison of the three similar terms used throughout this document.

Table 6.1: Comparison of pathway, journey and trajectory definitions

Concept	Description	Example
Patient Pathway	A series of predefined biomedical milestones that guide each patient's route from diagnosis to treatment.	For LC, the pathway may include steps such as initial symptoms appraisal, medical consultation, diagnostic tests, treatment planning, and follow-up care.
Patient Journey	The holistic experience of patients as they navigate through potential care and treatment options, facing barriers and prolonged intervals in accessing healthcare services.	A LC patient's journey may involve seeking multiple medical opinions, dealing with financial constraints, and encountering difficulties in accessing specialised treatments, all influencing their experience.
Patient Trajectories	Observing multiple patients' journeys from an outcome-focused perspective, comparing quantitative differences.	By analysing the patient trajectories, researchers can identify variations in treatment timeliness among different groups of LC patients and understand factors contributing to such differences.

[1] One model is that each exposure not only increases the risk of the subsequent exposure but also has an independent effect on disease risk irrespective of the later exposure [175]

6.2 Mixed methods design, data collection and population sampling

This chapter is considered a mixed methods study [144, 177, 178]. It integrates qualitative data and quantitative data on multiple levels (design, methods, interpretation, and reporting), as suggested by the literature [177]. It extracts dates, symptoms, diagnoses, and demographic characteristics from historical medical records and detailed explanations, descriptions, and personal narratives capturing experiences, preferences, or attitudes, in addition to important dates, symptoms, and diagnoses from structured interviews. Thus, while the qualitative stream of this study seeks to characterise the journeys taken by LC patients (particularly the participants' appraisal of specific body symptoms as well as service and pathway issues), the quantitative stream calculates the exact number of days related to the patients' journeys and their clinical and demographic profile.

For the purpose of this Chapter, ethical approval was sought both at the INCAN in Mexico and through University College London (UCL). Data-sharing agreements, data management plans, risk assessments, translation of consent forms and patient information sheets were developed. All these documents can be found in **Appendix A3, A4, and A5**.

In this quantitative cross-sectional study, the population studied were patients with suspected or confirmed LC that had an INCAN ID and an EHR. Patients with cancer on more than one organ at the same time or patients with secondary LC (metastasis) were excluded from this study. Similarly, patients under the age of 18 were not eligible for inclusion.

The list of ID's was drawn from the INCAN's epidemiological registry of

patients historically identified to have a lung cancer diagnosis. From the identified ID's, primary data was collected through EHR that were digitally available from 2004 to 2021 *N=3018*. For the quantitative analysis, a data extraction sheet was developed to download EHR data into REDcap. The approaches to data collection, analysis and reporting were based on the recommendations of the *Aarhus statement* [2]. The data extraction sheet was used by EBG and two members of the clinical staff who were previously trained by researcher (EBG) to assist in downloading the data into the extraction sheet. Most of the clinical data was found unstructured in text format. Thus, the data uploaded into the REDcap extraction sheet was previously collected from the clinical narrative and written down in the EHR by the healthcare providers at the time of the medical consultation. The EHR data extraction sheet can be found in the ***Appendix A7***. Lastly, the REDcap file was exported into STATA and underwent data cleaning.

Additionally, from the patients being admitted to the INCAN at the time the data on EHR was being collected, a sub-sample of LC patients were purposefully selected for structured interviews. In this case, patients that were considered too ill participate were not invited to participate. The sample size was determined based on data saturation, ensuring that enough data is collected to achieve comprehensive insights *(N=46)*. The structured interviews consisted of close-ended and open-ended questions allowing participants to elaborate on their responses, providing rich qualitative insights. Interviews were conducted in-person from June 2020 to December 2020. Recommendations from the literature were used to implement the questionnaire [24, 138]. For instance, it was determined that the best moment for the structured interview to take place was during the first visit to INCAN. At this moment, patient cooperation and recall of dates and events prior to the arrival were maximised and interference with institutional procedures was minimised [138]. Like previous research, the question 'What was the first thing

or symptom you noticed that made you think something might be wrong?' [24] was used to initiate the qualitative interview. The remaining sections contained items about other symptoms, and demographic and clinical details [24]. The full questionnaire can be found in the ***Appendix A8***.

Participants' responses were audio-recorded, transcribed, and securely stored in Data Safe-Haven . For analytical purposes a data extraction sheet was developed to download all interview data into REDcap.[2]. Qualitative sections of the data extraction sheet were transcribed into Nvivo. Patient interviews were merged with clinical data from the EHR.

This Chapter has a convergent parallel mixed design, it is divided into two sections: analytical methods and results from the structured interviews paired data from the EHR (2020-2021); and methods and results from the historical EHR (2004-2021). The study will integrate both quantitative and qualitative streams, each independently discussing validity and trustworthiness. Quantitative studies strive for external and interval validity; meanwhile, qualitative studies seek to achieve trustworthiness [179, 180]. Mixed methods, on the other hand, seek legitimacy for the results found [179, 180]. At the end of the study, in the interpretation and reporting levels, data integration will involve generating meta-inferences [177]. These are defined as explanations looking for additional value or conclusions in the form of a narrative, story, or theoretical statement generated [177]. In this process, both findings are compared by assessing confirmation, complementarity, expansion, and discordance [177]. All inferences from each stream are based on frameworks and literature previously published (knowledge-based-inferences). Results were not subjective or based on the

[2]All interviews were conducted in Spanish. The translation into Spanish or English was supervised by CVP using backward and forward translation practices

experience of the researcher (experience-based-inferences). The inferences in this study were data-driven.

6.3 Qualitative stream

6.3.1 Analytical Methods

Five methodological approaches were used to analyse the LC journey.

As a result of the primary data collected through structured interviews, coding was done inductively to identify common patterns across the participants' responses. After a stage of familiarisation with the data picked up by the interviews, EBG identified key topics and labelled them inductively. The process of coding was iterative, refining and organising the codes: diagnostic pathway, actors, navigation type, type of institution, level of healthcare navigated patients.

First, a narrative profile formation was conducted to present the reader with the typical LC patient journey. This was done by capturing the most common patient characteristics found among the 46 interviewees and building a case study from it (the Case of Juan). Although the Case Study can be interpreted as the typical LC case seen at the INCAN, other patients have different characteristics. Therefore, to not reduce the patient's narrative to a single story, the 46 patients' characteristics are described in a table where qualitative data was quantified.

Through triangulation of qualitative and quantitative of data, a joint display of results was drawn to analyse each one of the 46 patients interviewed. This compares the patients' socio-demographic profiles (age, sex, city, education level), diagnostic pathway (symptoms, screening or clinical finding), the combination of actors/institutions encountered throughout their journey. The different institutions were coded:

- UMF IMSS (second level of care)= A
- National Health Institute = B

- Hospital MOH (third level of care) = C
- Private hospital = D
- Private pharmacy doctor = E
- Private laboratory = F
- first level of care MOH = G
- Hospital IMSS (third level of care) = I
- Hospital ISSSTE (third level of care)= J

Furthermore, utilising a grounded theory approach [150], this Chapter also classified the patient journey according to health-system user type. The navigation type was broken down into public, private or mixed. If public or mixed were found, the institution they encountered and the healthcare navigated 1, 2 or 3 was annotated. As a result of the sum of dates available through the interviews and the EHR, the last column describes the outcomes in time intervals according to the Aarhus statement (total time, patient interval and health system interval) [2], when available.

Thereafter, out of the 46 interviewees, five were chosen due to their atypical nature. In contrast to the case of Juan, these journeys are either outliers in time intervals, or they are diagnosed through a different pathway (clinical finding or screening). Hence, through triangulation of qualitative and quantitative collected data, a joint display was drawn to explore each one of these atypical cases and their characteristics: navigation type (public, private or mixed), health institution that referred the patient, levels of healthcare navigated (1, 2 or 3) and time intervals according to the Aarhus statement (total time, patient interval and health system interval [2]), based on results drawn from interviews and dates collected through the EHR. Additionally, each one of these atypical cases is more closely described through visual representations of patient journeys. Each event in the cancer pathway

is provided with a descriptive icon and the date it took place, considering the milestones relevant in the Mexican context [88, 139]. Time intervals were drawn according to the Aarhus statement [2] and presented. Additionally, survival was also calculated when available.

Lastly, key themes, patterns, and commonalities across patient journeys were identified. Thus, the Braun and Clark framework was employed for thematic analysis [151]. The interpretation of the proximal and distal determinants of timeliness in care was guided by a thorough review of existing literature. Theoretical frameworks from *Jessica Krok-Schoen, J.L. et al.*, *Ashanya Malalasekera et al* and *Fiona Walter et al* enabled the exploration of both the proximal and distal factors contributing to the observed barriers and prolonged intervals, providing a nuanced perspective on the research findings [7, 60, 88]. These frameworks are available in **Figures F9 and F10 in Appendix A1**.

6.3.2 Results

6.3.2.1 The case of "Juan": the typical Lung cancer case

CASE

Juan, a 62-year-old husband and father was residing in Mexico City. Juan was a hardworking man, earning an average monthly income from his job. He lived with his wife, Maria, and their two children. Little did he know that his life was about to take an unexpected turn.

One day, Juan started experiencing a persistent cough that wouldn't go away. Concerned, he confided in his family members about his worrying symptom. They urged him to seek medical advice, and so, Juan went to see the first doctor available in their neighbourhood. However, to his surprise, the doctor dismissed his symptoms as a simple respiratory infection and prescribed him an antibiotic.

As the days passed, Juan's cough persisted, and he began to feel fatigued and noticed some weight loss. Worried about his health, Maria, his loving wife, encouraged him to visit another doctor. This time, the doctor suspected cancer and referred Juan for further tests, including a chest X-ray and tomography. Unfortunately, the doctor's clinic was not equipped to perform a biopsy, so Juan had to visit yet another doctor for that procedure.

The journey to find a proper diagnosis was a frustrating and time-consuming experience for Juan and his family. It took them an average of 18 days to seek appropriate medical care. Along the way, they visited a total of three doctors before finally receiving a LC diagnosis. With the diagnosis confirmed, Juan and Maria faced another challenge – the financial burden of treatment. They had no health insurance, making the cost of LC treatment at the prestigious INCAN an overwhelming burden for their family. They contemplated selling some of their belongings to afford the treatment but ultimately decided to seek help from government assistance programmes.

CASE *(continuation...)*

The journey to the INCAN was an arduous one, as the hospital was located quite far from their home. The family had to spend nearly two hours commuting to and from the hospital, mostly relying on public transportation or taxis.

Despite the challenges, they remained determined to seek the best possible care for Juan's LC. Throughout the process, Juan's health fluctuated, and he had to stop some of his regular activities due to the disease's toll on his body. Despite the hardships, he and Maria relied on their strong support system, leaning on each other and their family for emotional and financial support.

As Juan began his treatment at the INCAN, the medical team worked tirelessly to address his care needs. The hospital staff provided care and personalised treatment to ensure the best possible outcome for his condition. This gave Juan hope and reassurance that he was in good hands.

6.3.2.2 Quantification of Qualitative data

From the 46 people interviewed, 63% of them were men and 37% women, with a mean age of 57 years (64 median). 76% were from were from the metropolitan area: Mexico City (46%) and State of Mexico (30%), whilst the rest were from Hidalgo, Tlaxcala, Veracruz, Puebla, Guanajuato, Michoacan and Chihuahua. In terms of education, 13% of them were uneducated, but only 7% did not know how to read and write. Their marital status was most commonly married (54%), followed by single (22%), widowed (17%) and divorced (7%). The average monthly earning was $3729 Mexican Pesos (MXN)($5500 MXN median) amongst those who were employed (20%) or retired (7%). However, 41% of the sample of patients were unemployed and 33% had never worked (mainly women). **Table 6.2** provides an overview of the population interviewed.

Table 6.2: Socio-demographic and clinical characteristics of the population with lung cancer studied through structured interviews amongst patients (N=46)

Parameters	**Percentage/Numbers/Other**
Patients interviewed	46
Gender distribution	63% men (29), 37% women (17)
Age	57 years (mean) 64 years (median)
Median age	64 years
Metropolitan area residents	76% (Mexico City, State of Mexico) Other states: Hidalgo, Tlaxcala, Veracruz, Puebla, Guanajuato, Michoacan, Chihuahua
Marital status	Married - 54% (25), Single - 22% (10) Widowed - 17% (8), Divorced - 7% (3)
Monthly earning	Average: $3729 MXN - 171 GBP Median:$5500 MXN - 253 GBP
Pathway	Patients with initial symptoms - 89% (41) Diagnosed through clinical procedures - 9% (4) Diagnosed during routine check-up- 2% (1)
Smoking	Current smokers - 22% (10) Former smokers - 30% (14) Never smoked - 22% (10)
Patients who never had their lungs checked	76% (35)

Common symptoms	Weight loss, cough, fatigue, dyspnoea, loss of appetite, shoulder or chest pain, back pain, and others
Most common first symptom	Cough - 37% (17)
Other first symptoms	Dyspnoea - 15% (7), Back pain - 7% (3) Weight loss - 4% (2), Chest pain - 4% (2) Other symptoms - 22% (10)
Advanced disease symptoms	Dyslalia, loss of sight, seizures, depression, palpebral ptosis, headaches
Patients who had to stop activities/work due to cancer	54% (25)
Communication about symptoms	78% (36) with family members, 46% (21) relatives led them to seek care
Average time to talk to family members	18 days
Patients who never suspected cancer-related	80% (37)
Insurance Type	Patients with no insurance 50% (23) Patients insured by IMSS 17% (8) Patients insured by ISSSTE 2% (1)

Type of diagnosis	LC diagnosis after first medical appointment 11% (5) Cancer suspicion after first appointment 37% (17) Other diagnoses after first appointment 52% (24) (disease of infectious origin, allergy, asthma, musculoskeletal issues, pulmonary oedema, etc.)
Anti-inflammatory or antibiotic prescription	48% (22)
Tests and procedures after first appointment	Biopsy - 4% (2), Tomography - 30% (14) X-rays - 41% (19), Sputum citology - 2% (1) Other - 13% (6)
Patients with no laboratory/imaging follow-up	22% (10)
Patients referred to another doctor	15% (7)
Average number of doctors visited	2.5 (ranging from 1 to 13)
Average travel time to INCAN	119 minutes
Median travel time to INCAN	105 minutes
Common transportation to INCAN	Car, taxi, other public transport
Special cases transportation to INCAN	1 took a plane, 1 could walk to the hospital

Source: Own work

Results from the 46 interviews conducted

6.3.2.3 Building journey typologies

Table 6.3 presents a joint-display of information regarding the journey of the patients (N=46). The most common combinations of actors encountered during the patient journey were: DD (17.39%), DDD (13.04%), DDDD (4.34%), DDDB(4.34%), DDC(4.34%) [3]. Thus, the private journey seems to be one that is more prevalent. In contrast, the patients very rarely started to navigate the health system from public primary care.

Results from **Table 6.3** identified distinct groups of patients based on their healthcare utilisation patterns. As part of a inductive integration exercise, the prevalence of the combinations derives into three health system users: private healthcare users, public healthcare users and mixed users.

1. Private healthcare users: This typology represents LC patients who predominantly seek and receive their healthcare services from private healthcare facilities. These individuals may have private health insurance or the financial means to afford private healthcare services.

2. Public healthcare users: This typology comprises LC patients who primarily

[3]

- UMF IMSS (second level of care)= A
- National Health Institute = B
- Hospital MOH (third level of care) = C
- Private hospital = D
- Private pharmacy doctor = E
- Private laboratory = F
- first level of care MOH = G
- Hospital IMSS (third level of care) = I
- Hospital ISSSTE (third level of care)= J

rely on public healthcare facilities for their medical needs. These individuals may not have private health insurance or have limited financial resources, making public healthcare the more accessible and affordable option for them.

3. Mixed users: The mixed users typology includes LC patients who utilise a combination of private and public healthcare services. These individuals may access certain specialised treatments or diagnostic tests through private facilities while seeking general care and support from public healthcare providers.

Table 6.3: Joint display of qualitative and quantitative data of patient journey case studies (1 of 7)

ID	Patient Overview	Diagnostic pathway	The LC patient journey				Outcomes	
			Combination of actors	Navigation type	Public health institution encountered	Level of care navigated	Total Time	Time
1	**Male, 45 years Mexico City University**	Medical consultation (fatigue and neurological symptoms)	B	Public	SSA	3		P: 38 days HS: ?
2	**Female, 75 years Mexico City, Middle school Widow**	Routine Check-up	CB	Public	SSA	2/3,3	111 days	P: 42 HS: 69
3	**Male, 58 years Mexico City University Single**	Clinical finding (CT-scan for other neurological disease)	CCBG	Public	SSA	2/3,3,1		P: X HS: ?
4	**Male, 64 years Guanajuato University**	Medical consultation (cough)	D	Private				P: 139 days HS: ?
5	**Female, 50 years, Mexico City University**	Medical consultation (dyspnoea, cough)	DD	Private			60 days	P: 6 days HS: 54 days
6	**Male, 73 years Mexico City Middle school Smoker**	Medical consultation (dyspnoea)	DD	Private				P: 101 days HS: ?
7	**Male, 77 years Puebla Elementary Smoker**	Medical consultation (Back pain)	DD	Private				P: 336 days HS: ?

Table 1 of 7 (Own work)

Levels of health care navigated 1, 2 or 3. P= patient, HS= health system; Navigation type: public, private or mixed depending on stakeholders

ID	Patient Overview	Diagnostic pathway	The LC patient journey				Outcomes	
			Combination of actors	Navigation type	Public health institution encountered	Level of care navigated	Total Time	Time
8	**Male, 83 years Mexico State Elementary Smoker, Retired IMSS**	Clinical finding (Fall)	DD	Private			589 days	P: 522 HS: 67
9	**Male, 81 years Mexico City No education Previous smoker**	Clinical finding (COVID-19 Case)	DD	Private				P: X HS: ?
10	**Male, 45 years Mexico City University**	Medical consultation (cough)	DD	Private				P: 119 days HS: ?
11	**Male, 39 years Mexico City Middle school**	Medical consultation (cough)	DD	Private				P: 92 days HS: ?
12	**Female Elementary Mexico State Single**	Medical consultation (cough)	DD	Private				P: 797 days HS: ?
13	**Male, 67 years Michoacán University Widow**	Medical consultation (Fatigue cough)	DDD	Private			2378 days	P: 1923 days HS: 455 days
14	**Female, 29 years Mexico City University Previous smoker**	Medical consultation (loss of eyesight)	DDD	Private				P: 51 days HS: ?

Table 2 of 7 (Own work)

Levels of health care navigated 1, 2 or 3. P= patient, HS= health system; Navigation type: public, private or mixed depending on stakeholders

ID	Patient Overview	Diagnostic pathway	The LC patient journey				Outcomes	
			Combination of actors	Navigation type	Public health institution encountered	Level of care navigated	Total Time	Time
15	**Male Chihuahua Elementary Previous smoker + wood smoke Flies to Hospital**	Medical consultation (cough)	DDD	Private				P: 119 days HS: ?
16	**Male Mexico City No education Widow Smoker + Biomass**	Medical consultation (Weight-loss)	DDD	Private			324 days	P: 281 HS: 43
17	**Female Mexico City High-School Widow, Smoker**	Clinical Finding	DDD	Private			85 days	P: X HS: 85 days
18	**Male, 75 years Mexico State Wood smoke**	Medical consultation (?)	DDD	Private				P: ? HS: ?
19	**Female, 44 years Mexico City No education**	Medical consultation (cough)	DDD	Private			189 days	P: 15 days HS: 174 days
20	**Male, 48 years Mexico City Middle school Smoker**	Medical consultation (limb weakness)	ED	Private				P: 34 days HS: ?
21	**Female, 72 years State of Mexico Elementary**	Medical consultation (dyspnoea)	DDDD	Private			167 days	P: 97 days HS: 70 days

Table 3 of 7 (Own work)

Levels of health care navigated 1, 2 or 3. P= patient, HS= health system; Navigation type: public, private or mixed depending on stakeholders

ID	Patient Overview	Diagnostic pathway	The LC patient journey				Outcomes	
			Combination of actors	Navigation type	Public health institution encountered	Level of care navigated	Total Time	Time
22	**Male, 54 years Morelos High-School Never smoked**	Medical consultation (aphasia)	DDDD	Private			49 days	P: 8 days HS: 41 days
23	**Female, 58 years, Tlaxcala Elementary Previous smoker**	Medical consultation (Limb pain and ptosis)	DDDDD	Private				P: 6 days HS: X
24	**Male, 44 years Hidalgo Middle school Previous smoker**	Medical consultation (cough)	DDDDD DDD	Private				P: 65 days HS: ?
25	**Female, 76 years Mexico City No education Wood smoke IMSS**	Medical consultation (bakc pain)	DEDD	Private				P: 8 days HS: ?
26	**Female, 81 years State of Mexico Elementary**	Medical consultation (cough)	FD	Private			80 days	P: 37 HS: 43
27	**Male, 50 years Hidalgo High-School Previous smoker**	Medical consultation (dyspnoea)	CDD	Mixed	SSA	2/3		P: 61 days HS: ?
28	**Male, 39 years Veracruz High-school IMSS**	Medical consultation (cough)	DDDB	Mixed	SSA	3		P: 17 days HS: ?

Table 4 of 7 (Own work)

Levels of health care navigated 1, 2 or 3. P= patient, HS= health system; Navigation type: public, private or mixed depending on stakeholders

ID	Patient Overview	Diagnostic pathway	The LC patient journey				Outcomes	
			Combination of actors	Navigation type	Public health institution encountered	Level of care navigated	Total Time	Time
29	**Male, 73 years Mexico City Middle school IMSS retired**	Medical consultation (cough)	DAD	Mixed	IMSS	2		P: 8 days HS: ?
30	**Female, 40 years Mexico City Master's degree IMSS**	Medical consultation (shoulder pain)	DDAADD DDDDDD	Mixed	IMSS	2		P: 30 days HS: ?
31	**Female, 66 years Mexico State Middle school**	Medical consultation (fatigue, nausea, vomit)	DDC	Mixed	SSA	2/3		P: 16 days HS: ?
32	**Female 71 years Mexico City**	Medical consultation (back pain)	DDC	Mixed	SSA	3	114 days	P: 83 HS: 31
33	**Male, 70 years Mexico State Elementary**	Medical consultation (cough)	DDCDD	Mixed	SSA	2/3		P: 7 days HS: ?
34	**Male, 68 years, Mexico City Middle school**	Medical consultation (cough with blood)	DI	Mixed	IMSS	2/3	61 days	P: 15 days HS: 46 days
35	**Male 58 years Mexico State No education**	Medical consultation (fatigue and cough)	EA	Mixed	IMSS	2	726 days	P: 62 days HS: 664 days

Table 5 of 7 (Own work)

Levels of health care navigated 1, 2 or 3. P= patient, HS= health system; Navigation type: public, private or mixed depending on stakeholders

ID	Patient Overview	Diagnostic pathway	The LC patient journey				Outcomes	
			Combination of actors	Navigation type	Public health institution encountered	Level of care navigated	Total Time	Time
36	**Male, 61 years Tlaxcala Middle school**	Medical consultation (cough)	EADI	Mixed	IMSS	2, 2/3	204 days	P: 149 HS: 55
37	**Female, 44 years Guanajuato University**	Medical consultation (chest pain)	EDB	Mixed	SSA	3	1004 days	P. 319 days HS: 685 days
38	**Male, 43 years Mexico State Middle school**	Medical consultation (dyspnoea and fatigue)	EDC	Mixed	SSA	2/3	338 days	P: 4 HS: 334
39	**Female, 35 years Mexico City Middle school**	Medical consultation (throat and headache)	EDDDDB	Mixed	SSA	3		P: 2 days HS: ?
40	**Male, 46 years Mexico State No education IMSS**	Medical consultation (cough)	EDID	Mixed	IMSS	2/3,		P: 92 days HS: ?
41	**Female, 67 years Mexico State Middle School Never smoked Biomass**	Medical consultation (cough)	EIAIDD	Mixed	IMSS	2/3, 2, 2/3,	295 days	P: 295 HS: 83 days
42	**Male, ? Mexico City University IMSS Previous smoker**	Medical consultation (dyspnoea)	EID	Mixed	IMSS	2/3		P: 5 days HS: ?

Table 6 of 7 (Own work)

Levels of health care navigated 1, 2 or 3. P= patient, HS= health system; Navigation type: public, private or mixed depending on stakeholders

ID	Patient Overview	Diagnostic pathway	The LC patient journey				Outcomes	
			Combination of actors	Navigation type	Public health institution encountered	Level of care navigated	Total Time	Time
43	**Female, 68 years Mexico City University Previous smoker**	Medical consultation (cough)	FB	Mixed	SSA	3		P: 73 days HS: ?
44	**Male, 75 years Mexico City Master's degree ISSSTE- retired Previous smoker**	Medical consultation (shoulder pain)	FJD	Mixed	ISSSTE	2/3		P: ? HS: ?
45	**Male, ? Mexico State University Previous smoker**	Medical consultation (chest pain)	GDDDD	Mixed	SSA	1		P: 1 day HS: ?
46	**Male, 18 years Mexico City University**	Medical consultation (weight-loss)	GGDC	Mixed	SSA	1, 2/3		P: 5 days HS: ?

Table 7 of 7 (Own work)

Levels of health care navigated 1, 2 or 3. P= patient, HS= health system; Navigation type: public, private or mixed depending on stakeholders

6.3.2.4 Atypical journeys and delays in lung cancer care

The five atypical cases are drawn from the full sample (N=46) and briefly described in **Table 6.4**. Overall, results show shorter time to diagnosis when patients are screened vs longer when patients are symptomatic. However, in Case 5 the time from symptoms to seek for medical care was only 6 days through private spending and then the patient was quickly treated, all within 60 days. The first symptom to presentation however was dyspnoea and cough, which could quickly lead to emergency care. Therefore, differences in symptoms might play a role in timeliness in cancer care. In contrast, a patient whose fall led to a clinical finding suggests prolonged appraisal interval and shortened days to treatment. Hence, differences in the pathway to diagnosis potentially lead to differences in outcomes. More research needs to be done to evaluate the role of pathways in timeliness in cancer care. Lastly, heterogeneity in the time (interval) results point to further analysis through quantitative methods to be able to capture the effect each one of these characteristics has in cancer intervals across the continuum of care.

Table 6.4: Joint display of qualitative and quantitative data of atypical patient journey case studies

		The LC patient journey			Outcomes	
ID	**Diagnostic pathway**	**Navigation type**	**Public health institution**	**Level of care navigated**	**Total**	**Patient/ Health system**
2	Screening	Public	SSA	2/3,3	111 days	P: 42 HS: 69
5	Medical consultation (dyspnoea, cough)	Private			60 days	P: 6 days HS: 54 days
8	Clinical finding (Fall)	Private			589 days	P: 522 HS: 67
13	Medical consultation (Fatigue cough)	Private			2378 days	P: 1923 days HS: 455 days
35	Medical consultation (fatigue and cough)	Mixed	IMSS	2	726 days	P: 62 days HS: 664 days

Source: Own work.

Levels of health care navigated 1, 2 or 3. P= patient, HS= health system; Navigation type: public, private or mixed depending on stakeholders

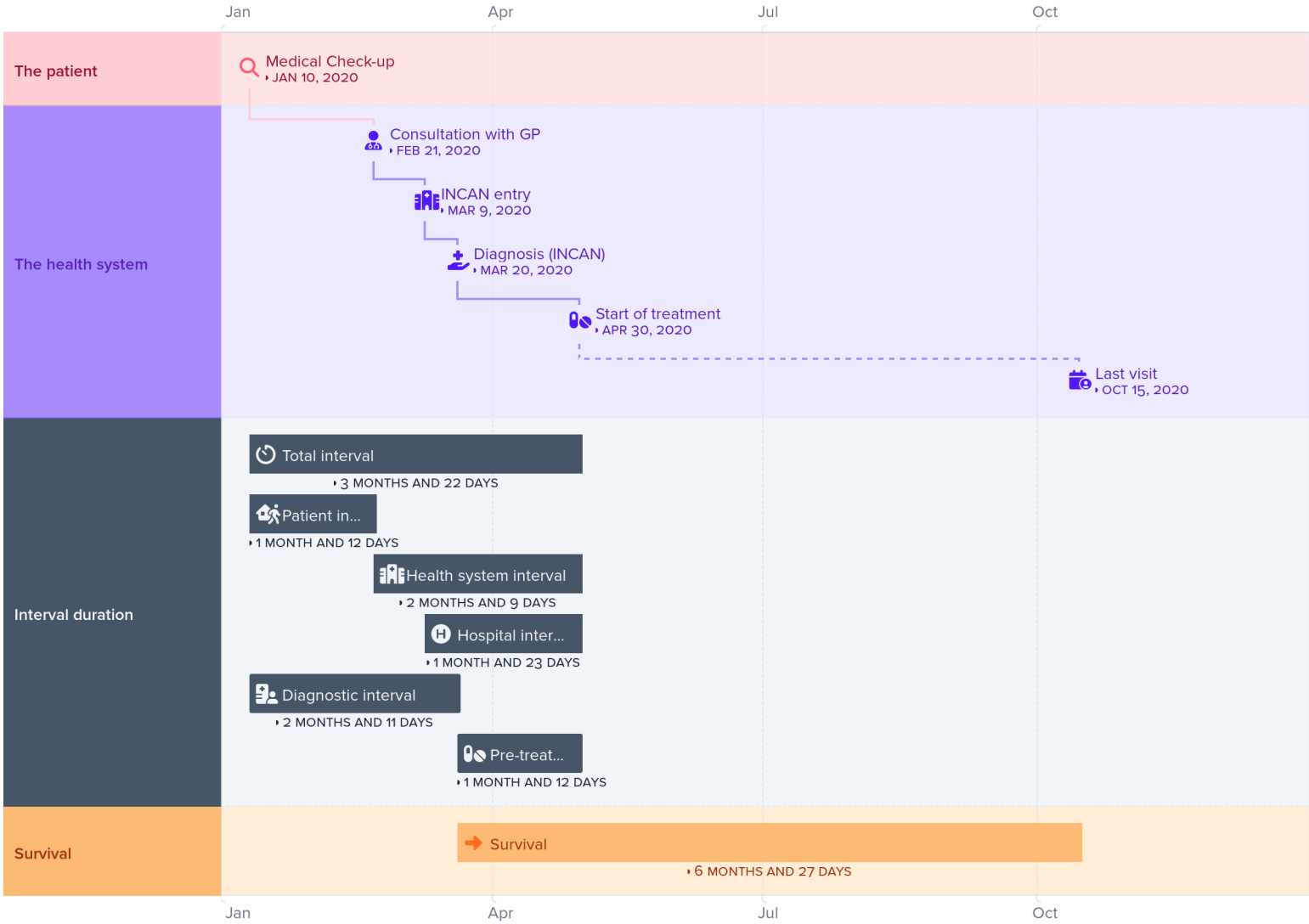
The aforementioned atypical cases are also visually represented through **Figures 6.3, 6.4, 6.5, 6.6** and **6.7**. In these Figures, the patient journey is based on results drawn from interviews (patient/appraisal interval marked in pink and health system interval in purple). Additionally, dates collected through the EHR complemented the visual representations of journeys. As a result of the sum of dates available, time intervals are drawn and presented in the blue (darker) section. If there were dates available for the last visit or date of death, survival time was included (marked in orange). Each event is provided with an descriptive icon and the date it took place, considering the milestones relevant in the LC pathway in the Mexican context [88, 139].

Results from **Figures 6.3, 6.4, 6.5, 6.6** and **6.7** show heterogeneity in the patient journey. In some cases (case 5 and 13), patients mention having spoken to their family member about their worrying symptom; in one case it quickly resolves and seeks for care and in the other seeking for care is prolonged.

In the case of the clinical finding, the patient was aware of the symptom before falling and injuring themselves. This suggests difficulty in self-appraisal of symptoms, understanding of severity and unawareness of potentially risk factors. Once in the health system and if not insured by the IMSS (Case 35), it seems patients resolve rather quickly and become treated. These results suggest, the atypical cases experience long appraisal intervals and quicker health system time intervals.

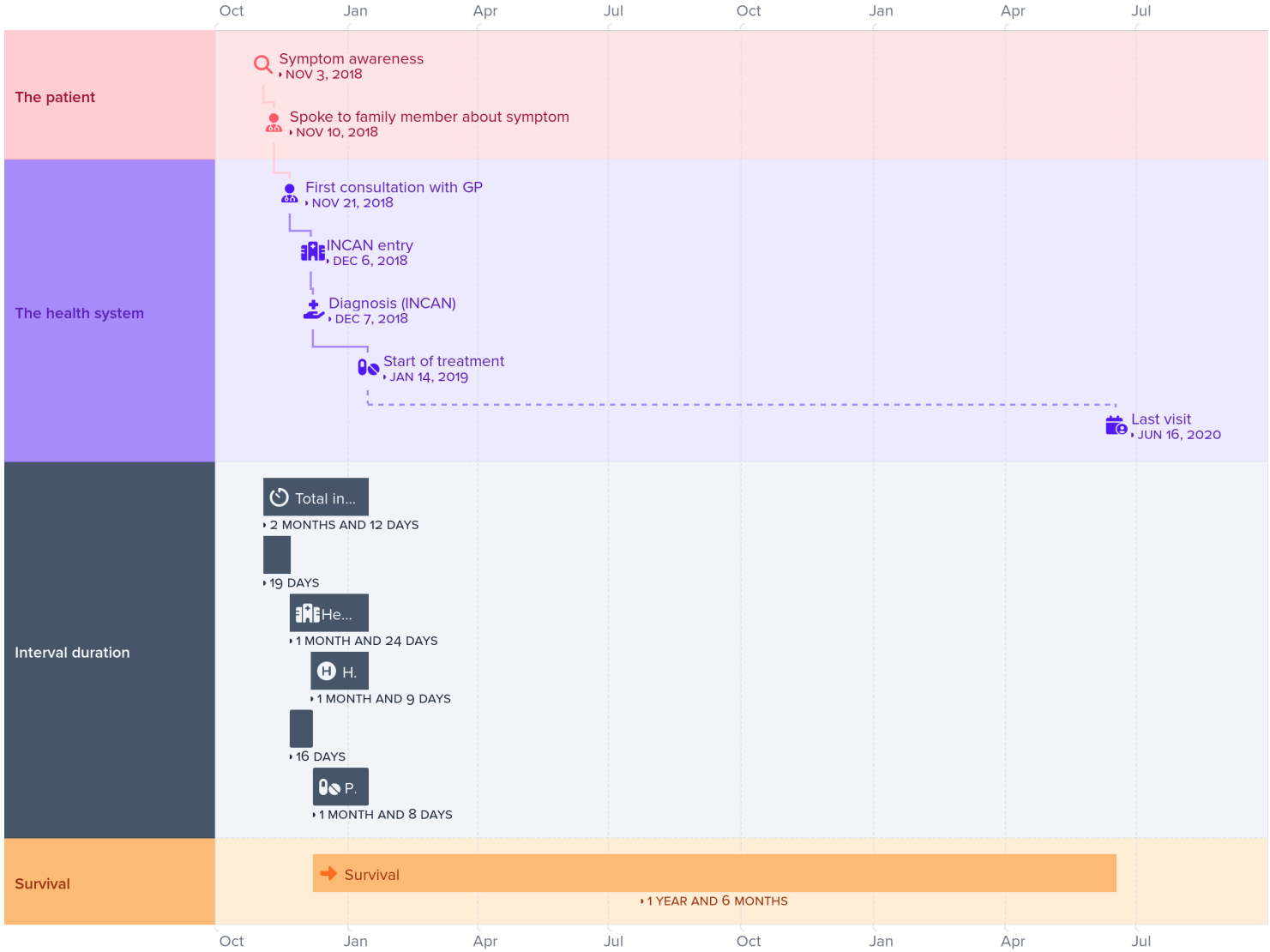
Survival seems to be unrelated to the journeys the patients take. This might have to do with clinical characteristics, stage of the disease, age, and other factors. More research should be done to find determinants of differences in survival outcomes.

Figure 6.3: Lung Cancer Journey Case Study No. 2



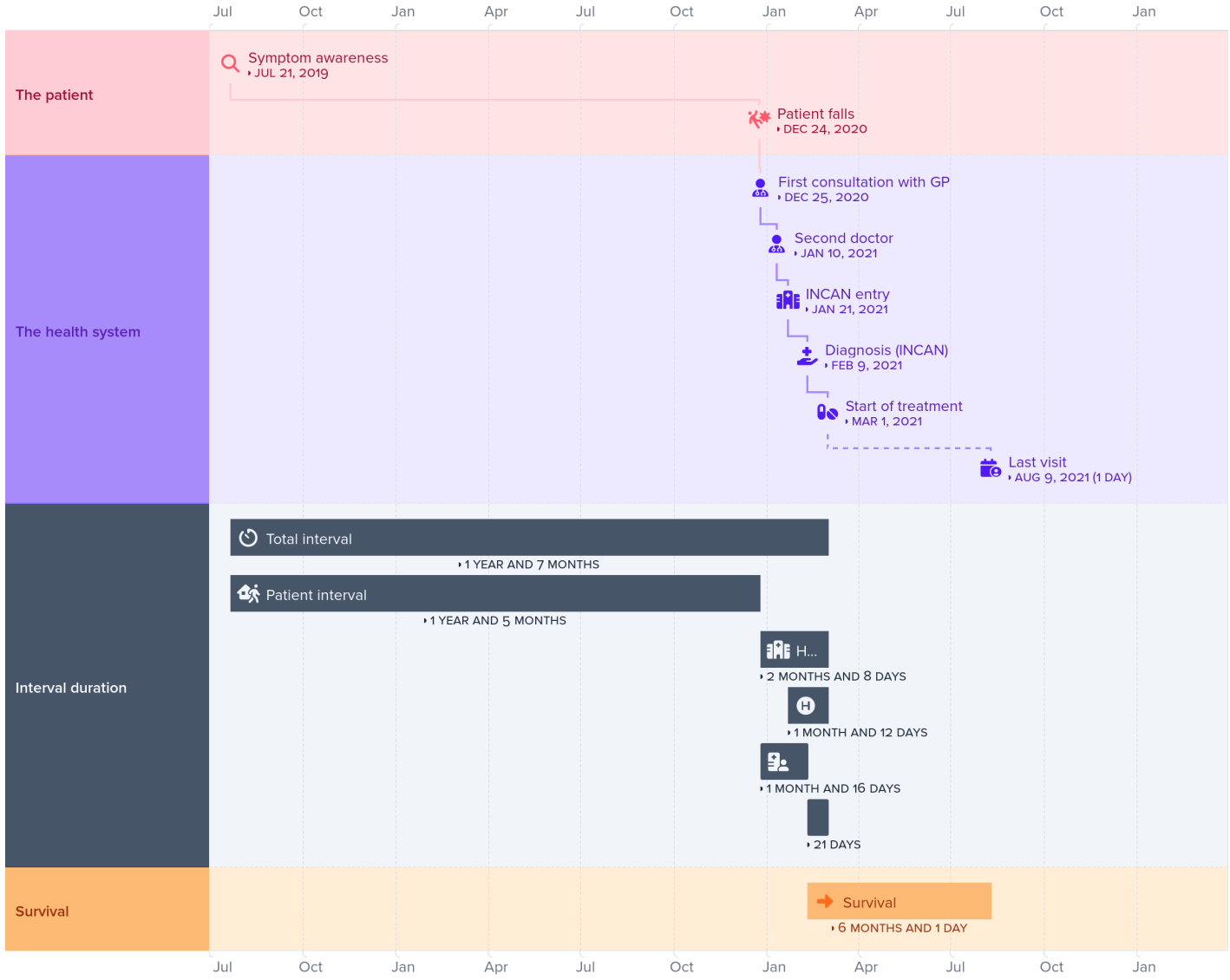
Source: Own work.
Appraisal interval: pink, Health system interval: purple, Survival: orange

Figure 6.4: Lung Cancer Journey Case Study No. 5



Source: Own work.
Appraisal interval: pink, Health system interval: purple, Survival: orange

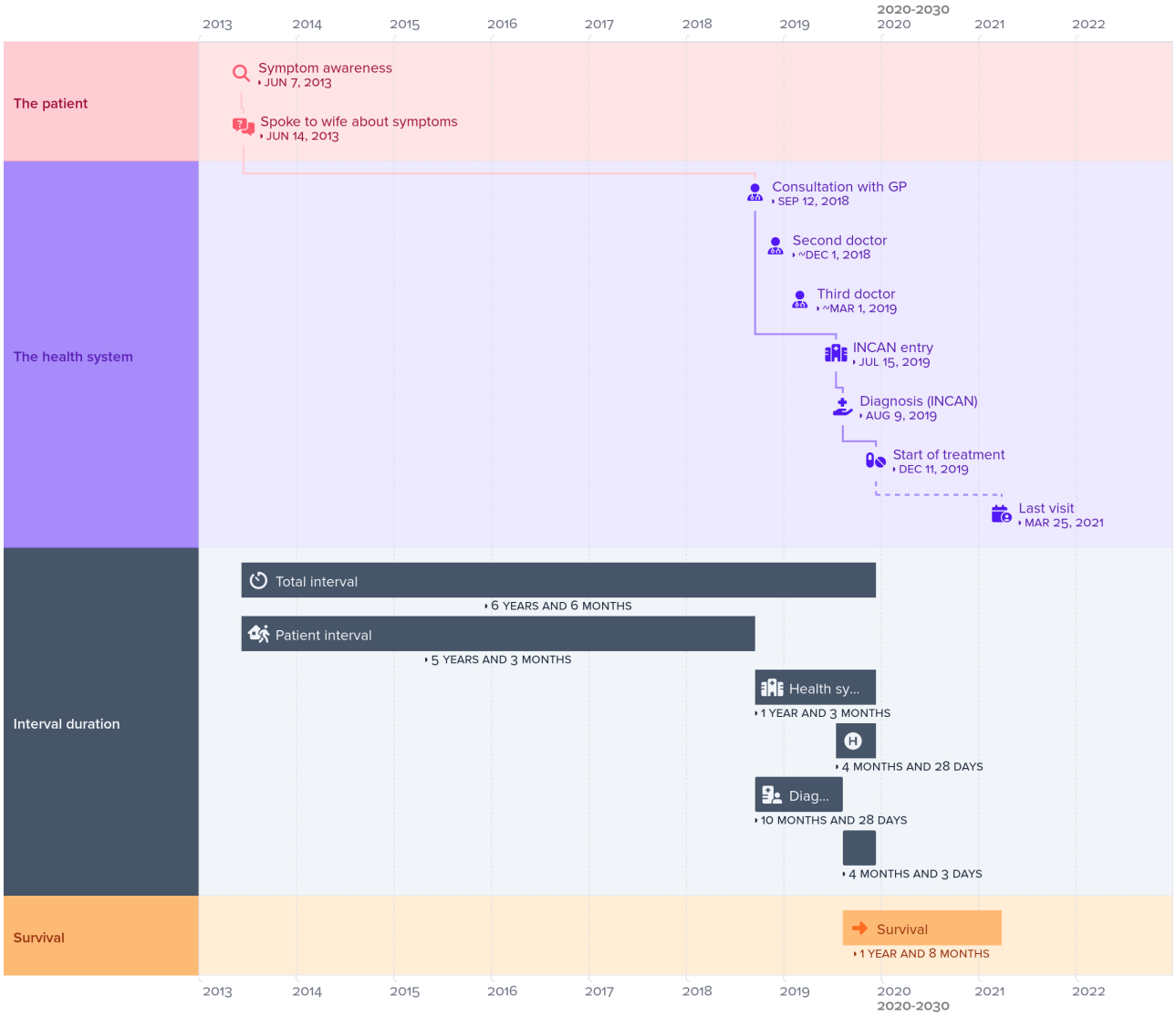
Figure 6.5: Lung Cancer Journey Case Study No. 8



Source: Own work.

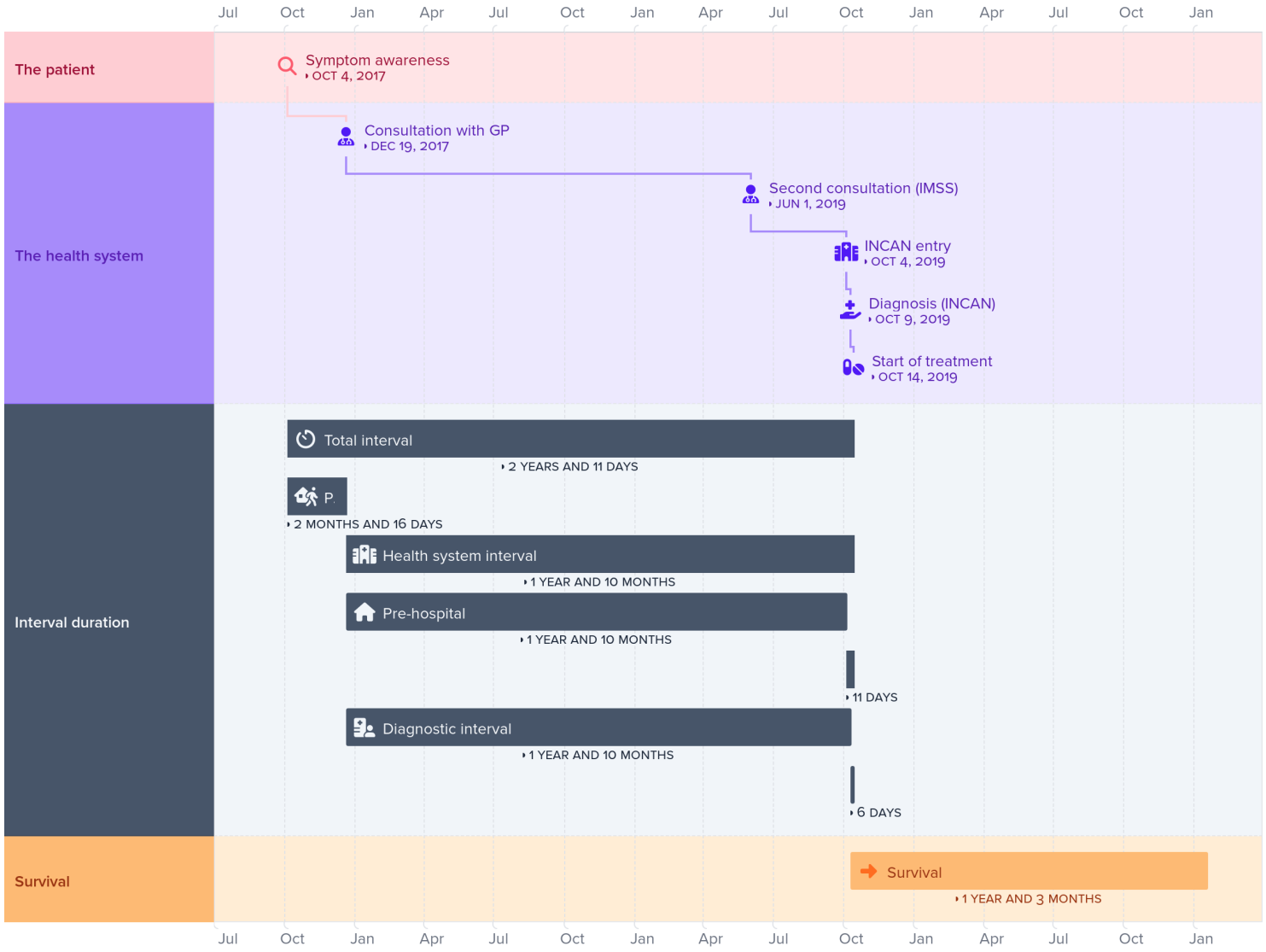
Appraisal interval: pink, Health system interval: purple, Survival: orange

Figure 6.6: Lung Cancer Journey Case Study No. 13



Source: Own work.
Appraisal interval: pink, Health system interval: purple, Survival: orange

Figure 6.7: Lung Cancer Journey Case Study No. 35



Source: Own work.
Appraisal interval: pink, Health system interval: purple, Survival: orange

6.3.2.5 Thematic Analysis

The data was consolidated by bringing together themes that represent participants' healthscapes (journeys): 1) Symptom appraisal: cultural interpretations and beliefs, 2) Access to care, fear and duties, 3) Risks and medical education, 4) Family support, diagnosis and guilt, 5) Difficult choices due to treatment inequalities in a fragmented healthcare system, 6) Informal referral pathways and their role in timely LC care, 7) Unequal distribution of resources and their role in timely LC care, 8) Catastrophic expenses and LC dropouts, and 9) LC journey during COVID-19 pandemic.

Symptom appraisal: cultural interpretations and beliefs

The pathway to treatment amongst cancer patients starts with the detection of bodily changes during the appraisal interval [88]. At this moment the patient self-manages the bodily symptoms and appraises whether they are worthy of seeking for medical care and advice or not [88]. In this study, only 89% of the patients initially had symptoms, the rest of them were diagnosed with LC due to another medical procedure (9%) and only a few cases were in for a routine medical visit and diagnosed with LC (2%).

In the literature, patients with LC frequently exhibit both lung-specific and systemic symptoms for several months before seeking medical attention, regardless of the stage of their disease at the time of diagnosis [24, 181]. In this study, the first symptom appraised and reported was cough (37%), dyspnoea (15%), back pain (7%), weight loss (4%), chest pain (4%), other symptoms (22%) (i.e., fatigue, loss of sight, soar throat, loss of sensibility in limbs, nausea, shoulder pain and aphasia). In addition to the first symptom, the most common symptoms across patients' cancer continuum were: weight loss, cough, fatigue, dyspnoea, loss of

appetite, shoulder or chest pain, back pain and less commonly haemoptysis.

Similar to other studies, cough was the amongst the common symptom found [24] and was appraised as non-serious or associated with factors such as ageing, lifestyle, smoking habits, or other existing health conditions [24]. Additionally, coughing in this study was interpreted as a sign of inflammatory or allergic reaction. Patients described it as "normal" as they referred to have always had cough throughout their life due to how they cooked (wood) or where they worked (wood or carbon oven, pesticides, coal, etc.). As a result, explanatory models of illness [182] led to prolonged intervals from suspicion to the time that the patient reaches out for aid in the healthcare system.

This study shows patients believe symptoms are "momentary" or that the main symptom would succumb with alternative non-allopathic remedies or through self-medication. Other studies have found similar results [183]. In fact 30% of patients in this study thought their symptom would disappear. However, once the patients realised their cough wouldn't go away or was suspiciously not contagious, then they became worried or perceived reason enough to discuss with a medical doctor.

> *"The cough was very persistent, there was no way to stop it, I drank tea and that was the only way it would calm down, until I went to a doctor and they asked me for the X-ray. I thought it was a an infection."*

"I thought it was because I was overweight, but I mean, I never imagined that I had any lung problem. In fact, I thought that the symptoms I had were related to the smoke from making the tamale (zacahuil), because I used a brick oven. We have been making zacahuil for 23 years. We did not know that the smoke caused that. Just like smoking causes cancer."

> *"I was more concerned about the cough and the headache, but initially I thought it was just a normal sore throat. I thought it had turned into asthma or some other respiratory disease. But I never thought about cancer. Initially I took an anti-inflammatory, steroids and antibiotics."*

Weight-loss for example was appraised as "normal" due to the patients' association of the symptom with the husband's recent death or even as a result of poverty, making it really hard for the patient to discern when the weight-loss had become over-bearing. Ultimately, family members or close friends would comment on their loss of weight and suggest seeking for care.

Dyspnoea symptoms and fatigue were normalised by patients due to their age. Patients had the cultural perception that "it was normal to be old and useless" and therefore have dyspnoea as a normal symptom of old age. In contrast, patients were more risk aware and thought the dyspnoea was related to their body-mass-index. However, when patients where younger dyspnoea was reported to be incapacitating and thus the patients would seek for health rather quickly. Hence, not only the type of symptom has an effect on the time the patients appraise the symptom and seeks for care, but age might also be an effect modifier.

> *"I was suffocating, I was tired. I lost a lot of weight. But then I fell and then the doctors realised that I had a shoulder injury and that I had a lung injury with an X-ray."*

The lack of pain was also something that interfered with the patients' appraisal and help seeking interval. Because pain was absent or very low, patients believed

that if nothing was hurting, then there was no point on seeking for health or burdening they family or caregivers with their symptom appraisal and severity suspicion. Hence, when pain was apparent, patients would seek for health more rapidly.

As previous studies have shown [183], patients refer many challenges in appraising their own symptoms and therefore take some time to interpret their severity [182]. Amongst the cases that held more advanced disease, symptoms like aphasia, loss of vision, involuntary movements, changes in sensibility, seizures were also described. When patients experienced more "severe symptoms" patients thought it was related to something in their brain and they sought for a specialist right away; ultimately relating it to LC. This suggests patients with a specific set of symptoms might be more at risk at delaying or accelerating their search for care.

> *"I had involuntary movements in my left arm and left leg, I went up the stairs and fell and hit my head. When they did a CT scan, they diagnosed me with brain metastases of unknown origin and from there they realised it's from the lungs. At first I thought it could be Parkinson's and later we saw that it wasn't."*

> *"I did a check-up because I was tired and then I got worse and they took me to the neurology hospital because we thought it was my head due to my balance symptoms, I was going leaning to the left and I couldn't speak. So I didn't know what it was. I felt very worried because I was going sideways."*

In consequence to the symptoms, more than half (54%) of the patients had to stop activities due to the disease. Regardless of the type of symptom, 63% patients in this study finally decided to reach for medical aid thinking their initial symptom could worsen.

In the minority of cases there were no symptoms yet. One patient was going to be treated for cataracts and during the medical screening before the surgical intervention a brain-tumour was found that ultimately was related to a primary LC site. Similarly, two other metastatic cases due to falls among elderly patients were diagnosed with LC. Lastly, there was only one case that was conducting a yearly medical routine check-up and then LC was diagnosed.

> *"They were going to operate on me for a cataract but they didn't want to because they wanted the result of the neurologist due to my diagnosis of schizophrenia and they found a tumour... I had complications, severe pain in my stomach and back. They gave me paracetamol. Everything stopped because emotionally it affected me a lot... But when all the pain started, then we looked for help and went to the hospital and then they said that it was cancer."*

Access to care, fear, and duties

Fear was an important factor that interfered with the patients' need to seek for medical attention. In fact, 20% of the patients referred fear being a barrier and delayer of care. Additionally, patients reported to be afraid of being revised by a medical doctor and therefore withheld from seeking care. Fear of doctors and fear to knowledge (or truth) in the literature has been previously found to have an effect

on cancer care timeliness [65].

Moreover, 24% of patients referred not being able to seek for care the first time because they couldn't get off work. In addition, 9% referred not being able to seek for care due to having to care for someone (child, elderly or other). In the interviews, patients were worried of losing their job or losing money over seeking for care.

Lastly, participants describe access to care that first time was very easy 30%, 22% somewhat easy, 9% neutral, 7% not so easy and 7% not easy a all.

Risks and medical education

Similar to other studies [184], patients believed there was not enough information available for them regarding LC risks and disease. However, once asked this study reveals 22% patients reported to currently smoke, 30% referred to smoke in the past and 22% had never smoked. The patients interviewed were most frequently living in houses built with concrete or brick, but 7% reported to live in houses made of asbestos. Lastly, 22% of the patients were exposed to biomass combustion due to use of wooden stoves to cook or heat their homes since childhood. Despite the risk factors 76% of the patients had never had their lungs checked.

> *"[Patient cries], we don't have the education to take care of ourselves and that there is nothing that teaches us in basic education about how to prevent LC. It's like administration, you do a job and you learn but they don't teach you how to manage resources..."*

Once patients got an appointment with the first medical doctor, 11% reported

to receive a LC diagnosis, 37% mentioned "cancer suspicion" and 52% gave them another diagnosis: disease from infectious origin, allergy, asthma, musculo-skeletal related, pulmonary oedema, chronic pulmonary disease, cardiopathy, gastritis, urinary infection or even COVID-19. In fact, 48% of the patients were prescribed and anti-inflammatory or antibiotic during their first consultation.

Regardless of the symptoms or the potential diagnosis, the first doctors visited by the patients decided to get X-rays in 41% of the cases, biopsy in 4% of the cases, tomography 30%, sputum citology 2% or other (13%). Nonetheless, 22% had no laboratory or imaging follow-up. Overall, 15% of patients were eventually referred to another doctor. This was a particularly interesting finding, as the first doctor patients seek does not seem to be acquainted with the positive predictive values for LC and the further investigations needed to reach a diagnosis. Although, X-ray remains the chosen method for diagnosis with sensitivity ranging 77%–80% for the diagnosis of symptomatic LC [185], some patients were directly sent to a tomography scan or biopsy, potentially due to infrastructure and economic barriers that lead to further increase in the diagnostic interval.

Furthermore, tuberculosis had to be ruled out in some cases and this has also been mentioned in the literature from middle-income countries [185]. More research needs to be done to understand what specific interventions should be done in endemic tuberculosis regions in Mexico to prioritise diagnosis and treatment and thus avoid further health inequalities amongst the least privileged groups i.e., Chiapas.

Unfortunately, the unequal distribution or specialised personnel with adequate training also represent a barrier to cancer in this study. LC care requires a complex algorithm that demands multi-disciplinary, trained personnel to determine

standard-of-care therapy [1,52]. Thus, this study suggests patients were not satisfied with the empirical knowledge shown by the doctors they approached.

> *"The doctors are not prepared, they could not establish a diagnosis.."*

> *"I was at the IMSS, they gave me an appointment with the oncologist and then he told me that he was going to admit me to do studies, but apparently you have to be almost dying for them to tend to one. The doctor told me that I was fine and that there were others that were worse and they only gave me painkillers. I arrived at a very advanced stage and I think that perhaps I could have arrived earlier, although perhaps not. The orthopaedist did not realise that I already had bone metastases. You spend what you don't have because you want to survive. It is both physical and monetary exhaustion"*

Moreover, once the diagnosis had been provided, these results suggest not enough information was provided to patients regarding their cancer prognosis. Patients were under the impression that the information provided by their oncologist was insufficient. These results are similar to other studies [186].

Family support, diagnosis, and guilt

Even if the patient had perceived enough reason to discuss their symptoms with a doctor, the patient would prefer not to be a burden to the family or to avoid the family members spending money on them. This sense of guilt overcoming the patients urge to seek for care has been previously found in the literature [65, 187]. Eventually, the patient most frequently (78%) spoke to their family members

(husband, wife, sons and daughters, brothers and sisters or parents) about their worrying symptoms and not a doctor. Overall, it took patients in this study an average of 18 days to talk to family members about their symptom appraisal (7 days, median).

> *"First I told my children to leave me, yes, not to do anything to me. That I stay like this. But they insisted that they cure me. Well then whatever."*

> *"I thought it wasn't very serious, but now I don't know...I don't even know what I have yet. It wasn't a very intense pain. I do not eat now. I thought it might be related to cancer because my sister died of cancer."*

Chronic cough, dyspnoea and the symptoms outside of the lungs were the ones that caused the patient and family members to worry the most and seek for care. Thereafter, up to 46% of patients interviewed were advised by a family member or care giver to seek for medical care, despite the fear, economic burdens, the lack of pain, etc. Other patients and carers described knowledge of family history with cancer and thus became the most important factor for reaching medical care.

Upon receiving a diagnosis of advanced LC, the initial response of the majority of patients is disbelief, often expressing sentiments like "this can't be true" or "it must be a mistake" [187]. In this study, 80% of the patients report they would have never suspected symptoms were cancer-related. Nevertheless, as time progresses, patients gradually come to terms with the reality of their diagnosis and begin to comply with the treatment plan recommended by their healthcare provider [187].

The journey through LC is marked by moments of introspection and self-awareness [187]. During this period of self-reflection, patients actively explore possible factors that might have contributed to their illness, seeking to understand any personal behaviours or habits that could have played a role in the development of their condition [187].

Difficult choices due to treatment inequalities in a fragmented healthcare system

A large amount of the population in Mexico lack health insurance [46]. Results from this study show more than half of the patients referred to have no insurance (80%), 17% reported to be insured by the IMSS, and 2% by the ISSSTE. All these institutions provide different levels of care, through disparate facilities. Each one of these institutions has different funding schemes and mechanisms and as a result the materials, devices and medications utilised are particular to each institutional budget [47,52]. Patients are restricted to services within their institutional premises. Hence, institutions prevent patients to navigate the health system freely throughout their cancer pathway, increasing time to cancer care. As a result, patients refer to not know whether they can be suitable candidates for any type of treatment at any institution or not (28% were worried their lack of insurance would render them ineligible for diagnosis and treatment). As a result, patients report feeling despair and a sense of being lost in the system. Sometimes patients would pause their search for care for a while, until a family member persisted and achieved access.

Moreover, in the background section in **Chapter 2**, the Mexican healthcare system was described. Then ***Figure 2.5*** presented the differences in treatment across health/social insurance institutions. These treatment inequalities were very much visible during the patient interviews in this study. Results show patients are restricted to health services within their institutional premises, depending on their

social insurance scheme. For example, even if the public or private healthcare sector had the available infrastructure and human resources to diagnose and treat a patient in the patients' post-code, they would not provide care if they weren't affiliated to their public insurance scheme or if they weren't able to pay for private treatment. As a result, patients had to sometimes travel via plane or several hours via public transportation to reach the health care institution that would provide for care. However, despite eventually reaching for care, sometimes diagnosis and treatment were not even granted. This caused patients frustration, anger and worry about their prolonged time to care. Thus, patients' healthscapes became stiff and faced tough choices.

In fact, patients un-enrolled themselves from the IMSS to be able to be treated at the INCAN. However, from the public health point of view this rendered the patients with the risk of being covered for LC treatment at the INCAN, however not being insured for anything else (i.e., COVID-19, surgical procedures, diabetes, etc). Patients refer having made the difficult choice to choose this path even if they put themselves and their family members at risk. One patient explained:

> *"I will be able to pay for the metformin or the appendicitis, but I would never be able to pay for LC treatment in the private sector... that's why I preferred not having IMSS."*

Even though in the literature there seems to be more opportunity for patients to be treated in the INCAN [52]. It is unclear if these patients experienced enough barriers that they gave up on the search for care, or if they died before they could come back to the hospital.

Informal referral pathways and their role in timely lung cancer care

This study demonstrates that even when patients have similar needs, their healthcare journeys can vary significantly. For example, one patient may require referral to another hospital due to inadequate diagnostic or therapeutic facilities, while another patient might face prolonged time to care due to changes in their social insurance coverage. These differences in circumstances can lead to diverse pathways to care and further reduction in timely medical attention.

For instance, a patient from the IMSS was informally referred to the INCAN. These are two different health institutions and they do not share infrastructure or costs. As mentioned before, there is no way to bring the patients information from one system to another. However, the oncologists can work in either institution or in both. Hence, they themselves can serve as a facilitator for navigation into another institution.

> *"The truth is that we waited a long time at the IMSS, Dr. XXX recommended that we come here due to our economic situation. This journey was difficult because the hospital is far away. We tried to enter here initially, but they didn't accept us. We sent an email, and they didn't accept us either. They only accepted us when we mentioned that Dr. XXX recommended us."*

Another example is a privately insured LC patient reached the end of the insurance budget for cancer care. As a result, the patients fell into catastrophic expenditure and became affiliated to the open population scheme (INSABI). However, there is not a consolidated referral pathway for patients who are referred from private services to the INCAN. Thus, the patient would have to personally navigate the health system to achieve care in a public hospital. In fact, the most common case found through these interviews were patients being referred by their private doctors to seek for healthcare in the public system. Patients particularly mention the INCAN as a potential hospital that could provide service to them. Sometimes, private practising physicians even asked the patient to ask for specific protocols or seek for specific doctors, they provided personal names and sometimes even telephone numbers of doctors (that they previously knew) who worked there. In contrast, doctors that didn't know anyone working at the INCAN did not share this type of information with their patients and thus they navigated the health system blindly, on their own. In consequence, only those medical doctors who might know someone or have knowledge of the INCAN's programmes, might informally refer the patient in the direction of access to care rather quickly, the rest would not.

Another example of informal referral pathways leading to prolonged cancer care intervals would be a patient having lost affiliation to IMSS due to unemployment (potentially due to the disease itself, COVID-19 or other) and therefore discontinuing LC treatment at that institution. Similar to the previous case, there is not a consolidated referral pathway for patients who are referred from the IMSS services to the INCAN and therefore each journey becomes different for every patient. Eventually these types of patients would seek for healthcare at the INSABI or private care and have multiple subsequent visits with one and/or the other to analyse their options. However, the clinical and administrative burden these patients would carry would reflect severe delays in cancer care. Untimely

care was mostly due to 1) not being able to transfer the medical file and having to explain what had happened so far and being examined by the doctor (again): 2) sometimes having to take diagnostic tests every time they would meet another doctor (private or public); 3) the search for multiple second-third opinions and economic viability; 4) transportation to hospitals that are farther away from home and 5) individual barriers such as fear, family context, the progression of the disease or even COVID-19.

Unequal distribution of resources and their role in timely lung cancer care

The LC pathway in Mexico is unique. In clinical practice, testing for specific tumour characteristics helps identify cancer sub-types, predict their behaviour, and decide over treatment options [1]. However, there is insufficient diagnostic infrastructure in Mexico to engage in accurate diagnosis, staging and subsequent treatment [1]. In countries like India and South Africa (that share similar infrastructure deficits with Mexico), the availability of resources has also been outlined as an issue during the patient pathway [61, 183]. In this study patients refer waiting for a long time for diagnosis or sometimes being given a wrong diagnosis or having to spend on private care to reach an earlier diagnosis.

> *"The second doctor sent me to take an X-ray and told me that it was fine. I trusted her because she said it was fine. That happens if you don't go to the specialist. But the cough wouldn't go away, and she gave me a syrup and salbutamol. She said I had an infection."*

Other factors that affect cancer diagnostics include the availability of laboratory supplies, essential equipment, resources, and quality control [1, 46].

In Mexico, the unequal distribution of infrastructure is a barrier for timely access to LC care [52]. Highly specialised cancer diagnostic and treatment services are more prevalent in the centre of the country (closer to Mexico City) [46]. For example, a LC diagnosis requires a multidisciplinary approach, including high-level imaging and potentially an invasive biopsy [1]. These results suggest patients refer having to go to other hospitals to reach diagnosis. However, this was sometimes difficult for them as they were not able to pay for them or they did not have the means of transportation to reach their appointment. As a result, some of the patients lost their appointments due to having to travel to another city or another state. In other cases, patients went to the hospital and the essential equipment did not work and they were not given information on when it would work again. No follow up was given and thus both diagnosis and treatment were delayed.

> *"I come to the state capital (Pachuca to H. Gral) and the oncologists told me that they didn't have the infrastructure to do the studies or the therapies and so they sent me here (INCAN)."*

The quality of tissue samples, technical handling of tissue specimens, slide preparation, and staining are also relevant factors for LC diagnosis and treatment. However, patients sometimes faced the need to duplicate their biopsies due to not being performed according to institutional standards. This has also been described by other authors [1].

> *"They never gave me a diagnosis. They took fluid from me many times and the diagnosis did not come out and it hurt a lot."*

Catastrophic expenses and lung cancer dropouts

Other studies have found financial constraints play a role in the cancer journey. Through the interviews conducted, almost half of patients were worried about not being able to cover for their disease expenses (48%) and 28% were worried their lack of insurance would render them ineligible for diagnosis and treatment.

LC treatment can involve a range of costly interventions, including surgery, chemotherapy, radiation therapy, targeted therapies, and immunotherapies. The expenses associated with these treatments, along with additional costs such as consultations, diagnostic tests, and supportive care, can accumulate rapidly. For individuals without adequate health insurance coverage or financial resources, the financial burden of LC treatment can become overwhelming, leading to catastrophic expenses.

Catastrophic expenses refer to the financial burden incurred by individuals or families when faced with high healthcare costs that exceed their ability to pay, often resulting in significant economic hardship. In the context of LC, these expenses can have a profound impact on patients, leading to hospital dropouts or discontinuation of treatment.

> *"The truth is that it also took us a long time to go to the oncologist because the bronchoscopy and the tomography were very expensive."*

The impact of catastrophic expenses on LC patients is multi-faceted. Firstly, the financial strain may force patients to make difficult choices, such as prioritising basic needs like food, housing, and transportation over healthcare expenses. This can result in delayed or interrupted treatment, sub-optimal adherence to prescribed medications, and compromised follow-up care. Ultimately, these factors can lead

to poorer treatment outcomes and decreased survival rates.

> *"I already died just listening to the amount we had to pay. We have no other source of income other than our store".*

Moreover, the stress and anxiety associated with financial hardship can have detrimental effects on patients' mental and emotional well-being. The constant worry about financial stability and the fear of being unable to afford necessary treatments can contribute to increased psychological distress and decreased quality of life. The psychological impact may further exacerbate the decision to drop out of hospital care due to overwhelming financial constraints.

> *"I was at the IMSS, they gave me an appointment with the oncologist and then he told me that he was going to admit me to do studies, but apparently you have to be almost dying for them to tend to one. The doctor told me that I was fine and that there were others that were worse and they only gave me painkillers. I arrived at a very advanced stage and I think that perhaps I could have arrived earlier, although perhaps not. The orthopaedist did not realise that I already had bone metastases. You spend what you don't have because you want to survive. It is both physical and monetary exhaustion"*

Lung cancer journey during COVID-19 pandemic

During the COVID-19 pandemic, cancer care was significantly impacted due to the need to prioritise healthcare resources for COVID-19 patients and to reduce the risk of exposure to the virus in healthcare settings [188]. The epidemic drove healthcare professionals to reduce medical encounters [188]. Hospitals had to establish treatment prioritising strategies such as reduction of immuno-suppressive drugs, treatment breaks, and switching to oral medicines [188]. To minimise in-person visits and reduce the risk of COVID-19 transmission, healthcare providers increasingly turned to telemedicine. [188]. Moreover, beyond the standard cultural barriers, additional fear impacted patients' symptom appraisal and help seeking behaviour.

Many patients despite appraising their symptoms (whichever they were), even after perceiving these were now out of the ordinary and that the severity or chronicity suggested them to seek for care, they preferred to avoid the health-system. In the overall balance of risk, patients preferred to continue living with the symptoms than becoming infected with COVID-19. Similarly, they wouldn't want their caretakers or family members to become at risk of contracting COVID.

> *Emotionally, I'm afraid to bring my parents to the consultations or everywhere else. I only ask that they are well. But I can't do it alone.."*

Patients facing cancer during COVID-19 often experienced a complex emotional struggle. The sense of vulnerability and the fear of the disease created a desire for isolation as a means of self-protection. Patients felt that staying away from social gatherings and limiting contact with others reduced their exposure to potential health risks. Additionally, while the isolation shielded them from the possibility of

emotional distress caused by discussing their illness with others, isolation also led to feelings of loneliness and emotional distress. The disconnection from social circles and activities intensified the emotional toll of cancer even more profound.

> *We are all panicked because we travelled to Mexico City, and we are in contact at a hospital. Therefore, we have more risk of COVID-19. I lost my job, financially because we don't have another income. Also, well, it makes us neurotic because everyone wants to go see you and I don't want to because right now I don't want anyone to get close to me, because I'm vulnerable. It changes your life."*

In other cases, patients were not even given a choice. Medical appointments were suspended, or the clinic was no longer providing care to reach a preliminary diagnosis, so patients did not know how to reach access to healthcare. In one of the interviews, a patient referred to stop seeking for care for up to six months before diagnosis was confirmed. Consequently, the health seeking and appraisal intervals in 2020-2022 became longer.

> *"In the health centre there are no specialists and because of COVID they could not accept us, the doctor referred us to come to INCAN. It was a hot burning pain. I felt that I was going to die, that I had already reached the limits."*

> *"Due to Covid we did not want to or could not find hospitals to follow up. We stopped going to the doctor for about 6 months.."*

> *I thought that, since I was wearing braces, that was the problem. So I went to the dentist to rule it out, but it wasn't, we hadn't gone to the dentist for a year because of COVID. The dentist said that it had nothing to do with it, and that I needed to go to the doctor. The second thing I thought was that it was something neurological, that it was urgent..."*

Moreover, results from this mixed methods study show 28% of patients did not know which clinic or hospital was open and available to provide care for them and reach a diagnosis. Some patients refer to even call the hospital and nobody answered. Once they arrived at the INCAN 20% of patients reported experiencing prolonged intervals in setting appointments and changes in their care. Nonetheless, fear was also prevalent: 26% of the patients interviewed referred to be afraid of COVID-19 and not wanting to be return to the INCAN.

> *"My relatives came for the treatment, and I stopped coming (to the INCAN)."*

> *"November came and the COVID-19 pandemic was at its peak, so we looked for a doctor in private care. We sent everything digitally because as things were I wasn't able to see anyone. He ordered another study to be done, and he already said that there was a pleural effusion and that it had to be removed."*

6.3.3 Discussion (qualitative stream)

This comprehensive understanding of the patient journey and the factors affecting it can serve as a foundation for designing targeted interventions and improving LC care in the country. The study's results emphasise the importance of early diagnosis,

education about LC symptoms, and improved healthcare access for timely and effective LC care.

Integrating Quantitative and Qualitative Data

Cancer research has traditionally focused on quantitative data but incorporating narratives into the analysis can humanise the research process, making it more relatable and impactful. This study aimed to explore the patient journey, using both qualitative and quantitative methodologies to provide a comprehensive understanding of the challenges faced by patients and identify opportunities for research, intervention, and policy improvement.

In this case, narrative profiles inspire patient advocacy efforts, raise awareness about challenges faced by patients, and drive positive changes in care [189, 190]. The case of Juan humanises the research process, reminding researchers and policymakers of the individuals behind the statistics and clinical data [189, 190].

Similarly, quantifying qualitative data in this study allows results to be compared across different populations, identifying patterns and correlations, and enriching the evidence base for cancer care improvement [150, 191]. Thus, it is equally important to delve into the complexity of cancer care through both quantitative and qualitative methodologies [174].

Identifying patterns: patient journey typologies

The identification of typologies through the interviews conducted in the 46 LC patients provides valuable insights into the different healthcare-seeking behaviours and preferences of patients. Understanding these patterns will help researchers, healthcare providers and policymakers develop targeted interventions and support strategies for each typology, ensuring that patients receive appropriate and patient-centred care based on their healthcare utilisation patterns and needs.

Additionally, these typology results can inform discussions around healthcare access and equity, and aid in improving the overall LC care experience for patients across different healthcare settings.

Chain of risk

Overall this Chapter sustains the "chain of risk model" represents a valuable framework to examine prolonged cancer care intervals, as it elucidates a sequence of interconnected factors influencing such timeliness [175, 176, 192]. This model offers a comprehensive understanding of the multiple stages and determinants that contribute to the occurrence of delayed cancer care, allowing for a holistic analysis of the underlying causal factors. For instance, let us consider a hypothetical scenario involving a patient facing untimely cancer care:

1. Socioeconomic Deprivation: Lower socioeconomic status emerges as the initial link in the chain of risk, potentially limiting the patient's access to essential healthcare services and resources required for timely cancer detection and treatment.

2. Health Literacy Deficiency: Inadequate health awareness among patients may impede early symptom recognition and deter prompt medical consultation, thus exacerbating delays in diagnosis.

3. Accessibility of Primary Care: Restricted access to primary care services might further hinder timely diagnosis, as patients may encounter challenges in promptly accessing healthcare facilities for evaluation.

4. Diagnostic Delays: Upon seeking medical attention, the patient may face delays in diagnostic procedures, including imaging tests or biopsies, due to factors

such as equipment shortages or diagnostic service backlogs.

5. Referral to Specialist Care: Following diagnosis, the patient's referral to a specialist or oncologist can experience delays arising from scheduling issues or insufficient availability of specialists in the vicinity.

It is crucial to acknowledge that not all factors in the chain of risk are inherently interdependent. Some exposures or determinants may independently contribute to prolonged cancer care, irrespective of subsequent exposures [175, 176, 192]. For instance: patients may exhibit delayed help-seeking behaviour owing to fear of a cancer diagnosis or societal stigmatisation associated with cancer, irrespective of their access to healthcare facilities; or patients lacking proficiency in the local language may face delays in cancer care due to communication challenges during medical consultations, leading to misunderstandings and necessitating additional appointments. Otherwise, patients may encounter prolonged time to cancer care if confronted with transportation issues, even when they possess awareness of symptoms and have access to healthcare facilities.

By employing the "chain of risk model," public health practitioners and researchers can undertake a comprehensive analysis of delays in cancer care, elucidating the sequential determinants that contribute to elevated risks and identifying independent factors that directly influence timeliness. This approach can guide targeted interventions and policy initiatives aimed at enhancing cancer care timelines and improving overall health outcomes.

Proximal determinants of health

This study provides valuable insights into the factors that impact patients' decision-making and help-seeking behaviour during LC care. Addressing fear,

work-related concerns, as well as involving family members in the care-seeking process, can potentially reduce delays in diagnosis and improve patient outcomes. Healthcare providers should consider these findings when developing interventions and educational programmes aimed at promoting early detection and timely access to medical care for LC patients.

Additionally, this study highlights the importance of addressing cultural beliefs and misconceptions surrounding symptoms in LC care. Early evidence suggests that interventions that improve symptom awareness result in earlier-stage LC diagnosis, as well as increased numbers of chest X-rays and total LC diagnoses [24].Hence, to reduce delays in diagnosis and treatment initiation, healthcare providers should be aware of patients' cultural backgrounds and perceptions of symptoms [24, 61]. Educating patients and their families about LC symptoms and risk factors, especially in rural and marginalised areas, could lead to earlier diagnosis and improved outcomes [61].

Distal determinants of health

The Mexican system faces many challenges in preventing, diagnosing and treating patients with cancer [1]. These findings shed light on the multifaceted challenges faced by LC patients in Mexico, encompassing barriers related to unequal risk factors, symptom appraisal, healthcare access, insurance coverage, diagnostic and therapeutic processes.

As seen in the literature [1], this study shows the distal determinants of health are commonly the barriers for early diagnosis and treatment of cancer. The fragmented multi-level and multi-healthcare-system in Mexico have prevented effective access to health care and fostered inequality. This is particularly concerning when experiencing chronic conditions such as cancer where complying

with the guidelines for the patients' diagnosis and treatment becomes a complex task.

Structural barriers such as the silos generated by the coexisting health sub-systems and lack of portability of insurance; the malfunctioning referral system between institutions and levels of care [37]; and the lack of universal health coverage [1] negatively impact the LC journeys. As such, some become more difficult than others to navigate. As a result, these "health system" barriers are also responsible for advanced-stage disease and its association with increased morbidity and mortality

Moreover, the health care system infrastructure itself (through the division of healthcare delivery levels across the country) represents a barrier for early diagnosis and treatment of cancer.The first and second level of care usually lack the infrastructure to diagnose a patient with cancer, meanwhile third level hospitals only provide care for patients with a confirmed diagnosis [57], again resulting in a breach in the pathway to treatment. Additionally, diagnostic tests are not always conducted nor covered. These are also reported to come from surrogate services by pharmaceutical companies, which means testing is not done exclusively at centralised laboratories as suggested by some authors [1].

Recent changes in the health system render today's panorama with additional complications in cancer care for the open population. Today it is still unclear whether the new institution replacing the SP (otherwise known as INSABI) will serve the same population group (most unprivileged) and if it will use the same funding scheme for catastrophic and non-catastrophic illnesses; and whether they will continue to not cover LC [48].

More research needs to be done to understand the pathway taken by physicians in Mexico to diagnose LC and whether that leads to a reduced timeliness in care. As a result, capacity building amongst primary care physicians to reduce observer errors in LC identification via X-ray should be conducted. Additionally, instructing primary care about the best and fastest pathway to LC care might also be beneficial in increasing diagnostic and treatment timeliness.

Outstanding circumstances

In cases when the patient is covered by the IMSS, they may choose not to seek diagnostic care or even LC treatment through this public insurance. This highlights an important issue that lies outside the scope of this PhD study, which aims to understand the reasons why patients with health insurance may prefer to consult one or more private doctors for diagnosis and then once the patient becomes aware of their condition, they then navigate the healthcare system to access the INCAN.

Patient referral

Timely and effective referral of patients are key to a national program for the early diagnosis of LC [25]. However, there is no referral protocol, and it is assumed many patients get lost on the cancer journey, rendering the health system a difficult one to navigate. Furthermore, unique identifiers are crucial elements to conduct research on cancer pathways and examine cancer intervals across care and facilities [73]. Thus, the lack of an EHR, national identification number, disconnected levels of care and fragmented system, discontinue the patient's pathway [71–73]. Data linkage between different social security institutions, public or private healthcare sector throughout a cancer pathway is non-existent [46]. For example, if a patient moves from one institution to another there is neither a standard nor an official method to share the patient's information, nor is it possible to transfer the patient without interrupting the cancer care pathway [73]. Consequently, the silos generated by the coexisting health subsystems [46] are strong barriers for the

portability of health services and transferability of clinical information.

Catastrophic LC expenses

Catastrophic expenses and their impact on LC patients are particularly concerning because access to affordable and equitable healthcare are not a fundamental right. This study highlights the need for comprehensive health insurance coverage and financial assistance programmes to support individuals and families facing the financial burden of cancer treatment. Furthermore, efforts to reduce healthcare costs, improve cost transparency, and implement policies that prioritise patient financial well-being are essential in mitigating the impact of catastrophic expenses and reducing hospital dropouts among LC patients.

Unusual symptoms

Healthcare systems could implement risk assessment tools to promote timely access to LC suspected cases, especially for patients with risk factors that are experiencing severe, unusual or changing symptoms that may indicate underlying health issues. By training healthcare providers, the health system might improve LC care and reduce the burden of the disease among patients in Mexico.

Similarly, it is proven that knowledge about cancer symptoms, when combined with a high level of anxiety or fear, led to prolonged intervals to reach care, whereas knowledge with a low level of anxiety led to more timely care [193]. Hence, awareness campaigns focusing on risk factors (other than smoking) and symptom awareness [193] could potentially lead earlier presentation [193].

Median doctor visits and time to arrival

In a previous survey conducted at the INCAN among 490 participants, the median time to arrive to the hospital took 5 hours [194]. This study suggests a shorter period (105 minutes). However, these should be considered as a non-random finding as

patients who were invited to participate were most likely better off and potentially had better outcomes. As a result, these results should not be generalisable to the complete LC population.

In the UK, LC patients experience many general practitioner consultations before hospital referral [167, 168]. Larger numbers are regarded as a less positive experience in cancer-care due to its association with prolonged diagnosis and treatment in primary care [167, 168]. This study sheds light onto how many doctors are visited before arriving to the INCAN where diagnosis is potentially confirmed, and LC patient treated. More research should be done with a larger sample and through quantitative methods to be able to compare results with other types of cancer and with other studies.

In summary, studying the LC patient journey offers a patient-centred approach, providing insights into their experiences (barriers, outcomes, and relevant actors). By combining qualitative and quantitative approaches, a more comprehensive understanding of LC care is drawn. This study elucidates barriers and provides an in-depth exploration of the access-related challenges experienced by patients. Moreover, this study lays the foundation for the subsequent quantitative study, outlining the most important dates to be used for the interval analysis and identifying potential data gaps. Additionally, it establishes the basis for categorising patients into three typologies for evaluating timeliness: patients coming for private, public, or mixed healthcare utilisation backgrounds. Furthermore, this qualitative study establishes the chain of risk framework for developing regression models that will independently evaluate associations with time to care across the cancer continuum. Notably, it also highlights the significance of excluding patients who initiated their pathway through screening or clinical findings from the analysis. These meticulous considerations pave the way for a robust and

insightful exploration of the factors influencing patients' diagnostic journeys and their subsequent impact on healthcare outcomes.

6.3.4 Limitations

Using an unvalidated questionnaire

Throughout the research process, it became apparent that certain questions in the questionnaire were not as effective as anticipated in capturing patient journeys and relevant events crucial to build care intervals. Some of these questions may have been ambiguous, lacked specificity, or were not tailored to address the distinctive experiences and challenges encountered by cancer patients. Consequently, the data obtained from these questions may not have yielded precise or comprehensive insights into the patients' experiences and prolonged intervals in care. In research previously conducted for breast cancer in Mexico, the questionnaire had been previously validated [138]. To address these limitations, it is imperative to generate and utilise a validated questionnaire in future research, thereby bolstering the credibility of the findings and instilling greater confidence in the study results.

Asking about diagnosis and/or treatment dates in the structured interview was very difficult, as the interpretations of these concepts vary for each patient. The patient is unaware of the specific meaning of a diagnosis. Therefore, during the interview, the patient was assisted in elucidating the events that occurred chronologically.

In some instances, the information gathered through interviews did not match the data found in the medical records. In such cases, it was decided to retain the dates obtained from the interviews. While this approach may introduce a higher margin of error due to memory recall, it is worth noting that the collection of

information from medical records also carries the risk of data collection errors or missing data.

Misinterpreting or selecting patient narratives

When conducting a qualitative study that uses patient narratives, potential limitations may arise, for instance: potential biases in data collection and interpretation [189, 190] may lead to oversimplifying or homogenising the narratives, as each patient's experience is unique and multifaceted [189, 190]. Furthermore, patient narratives may not capture the perspectives of all cancer patients, particularly those who may have difficulty articulating their experiences or choose not to participate in the study [189, 190]. This can limit the generalisability of the findings to the broader cancer patient population.

Another limitation is the potential for selectivity in the narratives shared by patients [189, 190]. Some individuals may be more inclined to share positive or negative experiences, leading to an imbalanced representation of their overall journey. Cancer patients may draw upon a diverse range of narrative resources to negotiate and construct their identities, including the process of recounting their own stories. The act of sharing their experiences can be transformative and contribute to their biographical work, helping them make sense of their illness journey and adapt to the changes it brings [189, 190]. Thus, another potential limitation is the subjective nature of narratives, which can be influenced by individual perspectives, emotions, and memories [189, 190].

Despite these limitations, patient narratives offer valuable and rich insights into the human experience of cancer. As researchers, it is essential to approach patient narratives with sensitivity, openness, and a commitment to understanding

the diverse and complex experiences of cancer patients.

Missing data

While not all dates were recorded, some were captured and proved valuable in comprehending the barriers, journeys, and timeliness in care faced by LC patients. The inclusion of three key dates provided a comprehensive overview of the events: the date of symptom awareness, the date of the first medical consultation, and the date of treatment initiation. Therefore, in the event of limited data availability, researchers should prioritise these three dates to effectively capture patient journeys and diagnostic and treatment timeliness.

For instance, patient 28 does not have a treatment date, which consequently prevents the calculation of intervals. An intriguing observation in this specific case is that extra-pulmonary symptoms lead to a shorter patient interval, but it does not necessarily imply that the patient had fewer medical visits. Hence, a swift patient interval does not always correspond to a rapid health system interval. These findings highlight the importance of studying these intervals separately to gain a more comprehensive understanding of the factors influencing diagnosis timeliness.

For patients who did not experience any symptoms, the patient interval is not calculated. Instead, they may have been diagnosed based on a clinical finding during another medical procedure or due to routine screening. As their pathway to diagnosis differs significantly from other patients, it is essential to consider potential exclusion of these cases when studying diagnosis timelines. For instance, in such instances, the total time would be equivalent to the health-system interval. Including these cases could introduce bias when interpreting the "rapidness" of patient intervals and their impact on health-system intervals and outcomes. Therefore,

in the quantitative section (chapter) of the analysis, these patients will be excluded. Future research should focus on comparing the outcomes of different pathway groups in relation to the final outcome.

Some patients have missing data on the date of treatment, making it challenging to calculate the total treatment interval. Additionally, there are cases where information about the date of diagnosis or the first visit to the general practitioner is also absent, leading to further data gaps. To address this issue and improve data completeness, it is suggested to utilise technology that automatically captures relevant dates when a patient's file is opened. The record should be structured with a dedicated section for dates, ensuring that essential information is recorded before finalising the consultation. Implementing such measures will help minimise data discrepancies and enhance the accuracy of research findings.

COVID-19

Data was partially collected during 2020 and 2021. Hence, perhaps the most important limitation in this study is selection bias. Most of these participants were potentially already being treated or worse off than most patients who have limited access. Additionally, these patients could potentially have no desire to go to a hospital during the COVID-19 pandemic. In fact, prolonged time intervals due to the pandemic, both from the patient and the health-system perspective, have been illustrated in the literature [188, 195]. As a result, the patients who were selected for interviews can be biased.

Moreover, the patient journeys described could also be biased, as they tend to describe past events happening before the interview, but also potentially during the pandemic. Hence, when patients describe their set of events, health systems have

already declared alterations in access to health services. Hence, the journeys should all be interpreted in the context of the COVID-19 pandemic and later compared to the literature that arises on patient journeys in the future.

6.4 Quantitative stream

6.4.1 Analytical Methods

Date and framework selection to evaluate outcomes

The main outcome of interest in this study is *time*, particularly time across cancer care. In this thesis, three frameworks from the international and Mexican literature are utilised to determine dates and intervals relevant to this study: Walter et al, and the Aarhus statement [2, 5, 88] and Unger-Saldaña [139].

Using all these frameworks, several dates were identified as relevant and were collected when available as the INCAN did not always capture dates, specifically dates related to the use of primary care. Thus, the next section will describe the relevant dates used for this study and the missing and existing dates across frameworks. The availability of intervals in each one of the frameworks used for this thesis are available in **Appendix A1** in ***Figures F12, F13, F14***.

The date of diagnosis used in this thesis is based on the date on the pathology report. If this was unavailable then the first date of clinical diagnosis in the medical record. Date-of-external-diagnosis meant patients who, before reaching the INCAN, were previously diagnosed in another hospital. Date-of-entry is the first time the patient is registered in the EHR and thus it represents the date of admission. The date-of-treatment is defined as the first time at which a systemic, local, or palliative treatment is provided to the patient i.e., chemotherapy, radiotherapy, immunotherapy, or other. Lastly, date-of-death or date-of-last-visit were used to calculate survival from the date of diagnosis. No data was collected on treatment end-date.

Although most date variables were automatically generated by the EHR

software in each consultation, for participants' whose dates were not captured automatically, dates were extracted from the clinical record narrative. This approach has also been previously employed in an English prospective cohort study [24]. For example, if the record described symptoms in a particular month or year but did not specify when, the mid-month for "a month," mid-year for "a year" is used as a *proxy* for the first-symptom-date [24]. Similarly, if the clinical record said two weeks ago, two weeks were calculated back from the time the record is filled in.

In previous Chapters, the time intervals studied by *Walter et al*, and the modified *"cancer appraisal-to-survival pathway"* developed in this thesis were described. Similarly, the *Aarhus statement* was presented in the background of this Chapter. The aforementioned frameworks found in the literature are similar. However, they do not measure the same intervals. Now ***Figure 6.8*** shows all events, processes, and intervals from all frameworks. This includes cancer care intervals studied by *Unger-Saldaña et al* among breast cancer patients in Mexico.

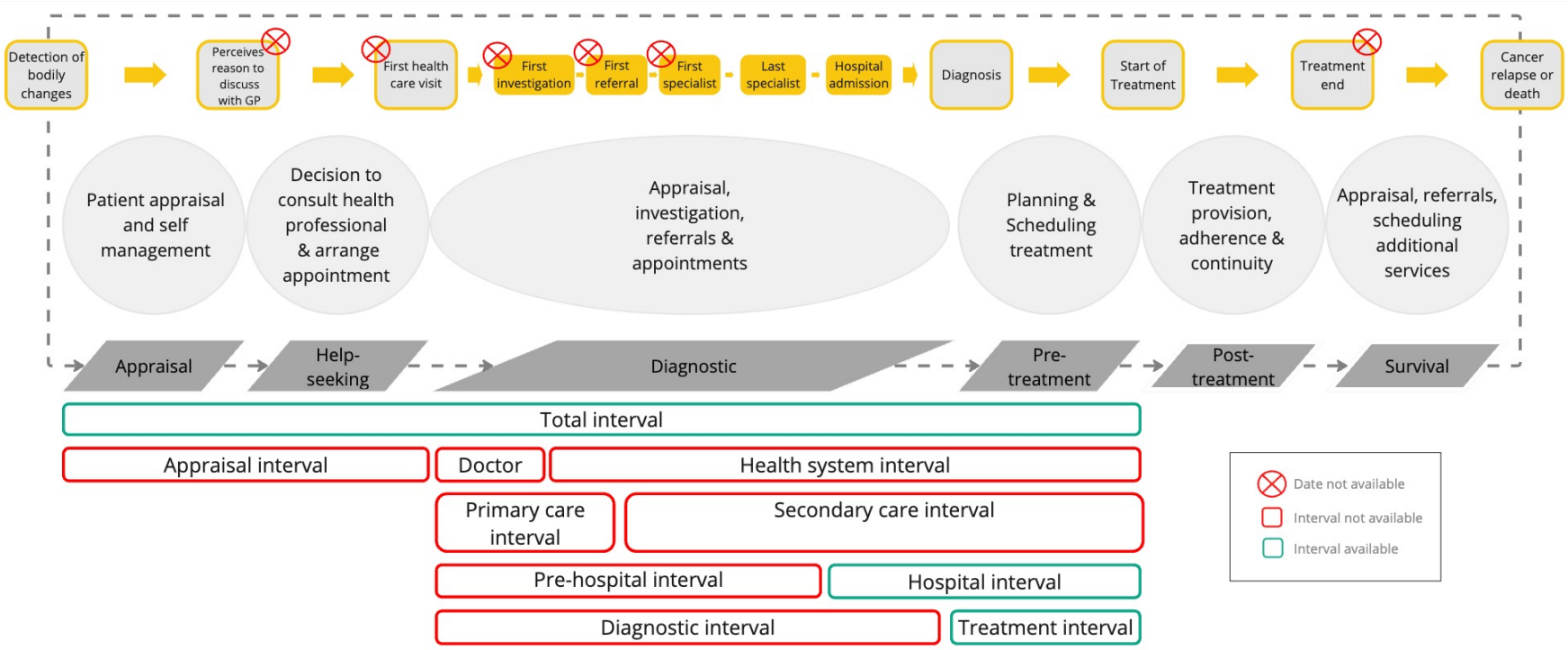
Due to missing date-1st-healthcare-visit and date-of-decision-to-consult-the-GP, the appraisal and help-seeking intervals are not available. The **"primary care interval"**, **"doctor interval"**, and **"secondary care interval"** are not obtainable. The **"patient interval"**, **"pre-hospital"** and **"health system interval"** are not complete due to a lack of 1st-healthcare visit date. Similarly, the full diagnostic interval is unknown. The only fragments of the diagnostic interval available are: **"diagnostic (a)"** (from external diagnosis to diagnosis) and **"diagnostic (b)"** (from arrival to hospital to diagnosis). ***Figure 6.8***, shows the unavailable dates marked with an X. As a result of the missing dates, the unknown intervals are marked in red.

Figure 6.9 shows available and reliable intervals marked in green. From all frameworks, the measurable intervals are the: the **"total interval"**, **"total**

diagnostic interval",**"hospital interval"** and **"treatment interval"**. Diagnosis from external-diagnosis-date (**"diagnostic a"**) and diagnosis from admission-date (**"diagnostic b"**) are available and can therefore build shorter sections of the diagnostic interval. For each one, the sample size is different due to people having different journeys and being directly admitted to the INCAN or being diagnosed beforehand. The length of survival can also be calculated from diagnosis. Lastly, as a function of the time spent from symptom appearance to the time of final diagnosis [24], Total Diagnostic Interval (TDI) is also added to ***Figure 6.9***.

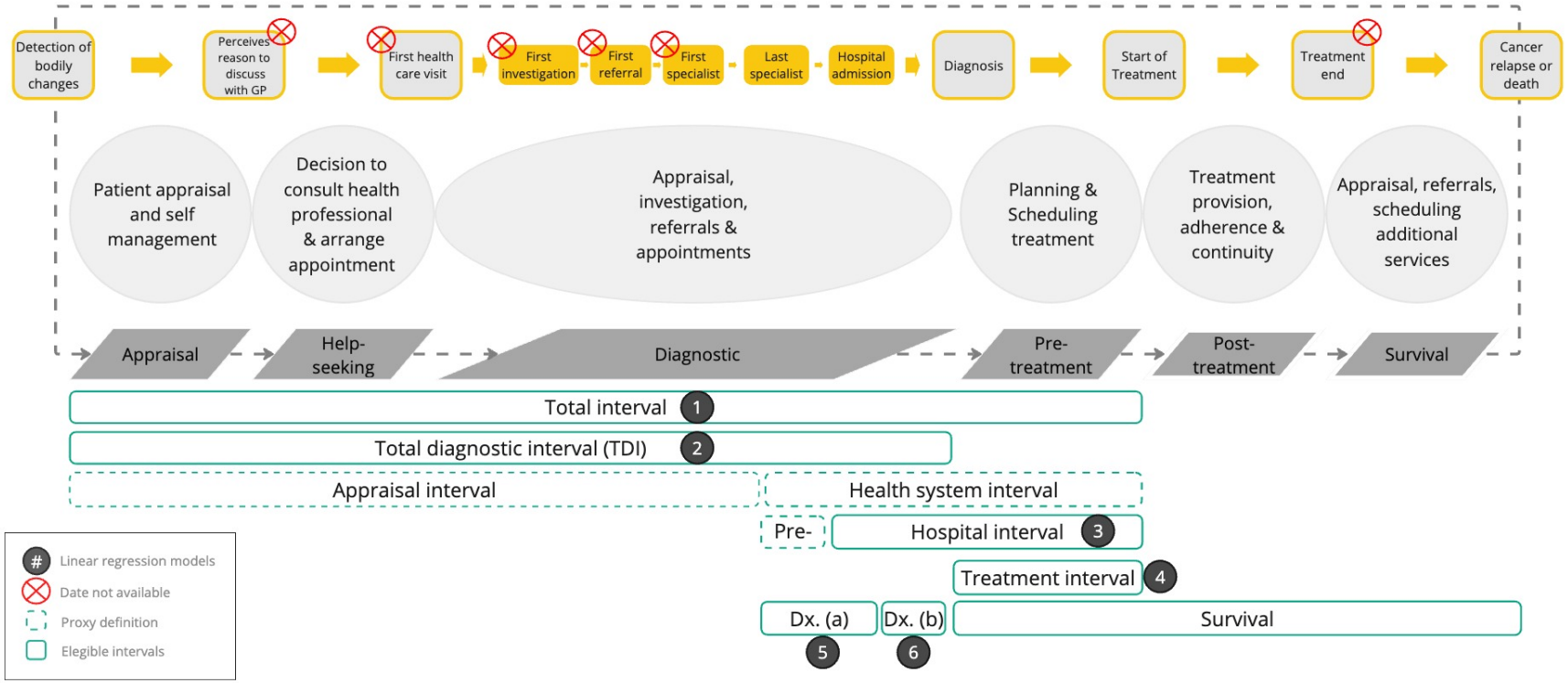
The numbered intervals in ***Figure 6.9*** are the ones selected for inclusion in this thesis. Additionally, it shows the unreliable proxies in a shaded line. Due to the lack of 1st-healthcare visit date, **"appraisal interval"**, **"health system interval"** and **"pre-hospital interval"** can only be partially determined using "external-diagnosis-date" as a *proxy*. However, this could lead to an overall underestimation or overestimation of the intervals. These proxies will not be deeply analysed for this PhD.

Figure 6.8: Framework comparison, date and interval availability



Source: Own work

Figure 6.9: Intervals selected for analysis for this thesis



Source: Own work

Covariates

The independent variables chosen for this analysis encompass a range of clinical, socio-demographic and health system factors. These variables are selected based on their theoretical relevance and prior empirical research in the field.

Similar to other authors [24], relevant clinical, socio-demographic and other data was collected. Gender, age at the time of entry, level of education, marital status, region, are collected from the EHR. Place of referral was also collected and classified into categories private and public (as suggested by findings from the qualitative stream of this Chapter). Mixed was not included in the categories as only one institution was entered in the patient record using binary categories.

The eligible participants are classified into three groups: NSCLC, SCLC, and unspecified LC.[4] [15–19]. Previous authors have kept the "Unspecified LC" type as a separate category. Furthermore, utilising the NSCLC vs. SCLC classification in epidemiological research allows for the differentiation of LC cases based on their clinical features, risk factors, treatment approaches, and prognosis [15]. Hence, this study uses it to standardise case definitions to ensure consistency and comparability of data across different studies and populations.

Primary LC staging was categorised using TNM status at diagnosis [196], and further categorised into early-stage (stages I and II), stages III, IV and unspecified (when stage of diagnosis had not been determined or not noted down in the EHR). As suggested by the literature [24], difficult or unusual diagnoses, are agreed by EBG and an two lung oncologists from the INCAN.

[4]The unknown category was kept under the assumption patients are not yet provided with the pathology diagnosis and they are indeed LC

Additionally, first symptoms and exposure to risks are included in the data extraction sheet. For the purpose of this study, the first self-reported symptom is used for adjustment in the analysis. Furthermore, positive predictive values of symptoms for LC are used to guide the first self-reported symptom categorisation [181]. As a result, first self-reported symptom was categorised into "cough", "dyspnoea", "chest-pain", "haemoptysis", "weight-loss" and "other". ***Figure F15*** in **Appendix A1** describes the positive predictive values and their interaction with symptoms [181]. Additionally, patients with unspecified symptoms are also kept in the analysis to consider those patients who are clinically asymptomatic.

Analytical steps

The initial step involves conducting a general descriptive analysis of the total sample, which comprises 2645 cases. This analysis focuses on various covariates, presenting the counts and percentages of each covariate. Additionally, intervals are then analysed through time from 2004-2021. Moreover, for each time interval, the distribution of the outcome (time) is plotted to validate skewness through a histogram. Next, an examination of intervals takes place, specifically looking at the median number of days for intervals using the full sample in days and in months.

The following steps encompass descriptions of different intervals categorised by covariates using descriptive tables. These include intervals related to the total, TDI patient, health-system, pre-hospital, hospital, diagnostic (a), diagnostic (b), and treatment intervals. Each description is presented through counts and percentages based on the number of cases for each covariate category. Similarly, a detailed analysis is done of the sub-sample of complete interval data (N=832). Similar to the earlier steps, descriptions are provided in terms of counts and percentages by covariate categories. Intervals are further explored using a median days metric and a histogram, both focused on the subset of 832 cases.

Sensitivity analysis

For each time interval, the characteristics of the complete sample vs missing cases are compared. The differences between these two samples are tested using Chi-square if categorical and t-test if continuous; low p-values (large chi-square values) in each covariate will indicate that the characteristics of the two samples are different for that particular variable. By comparing the characteristics of the complete sample with those of the missing cases for each time interval, the analysis aims to determine whether there are systematic differences between the two groups.

Linear regression

A linear regression analysis is conducted to assess the association between covariates (age, sex, education, region, marital status, first symptom, cancer stage, cancer type, diagnosis, institution of referral, political terms) and different time intervals (outcome). The primary statistical method employed in this study is multiple linear regression. The model is specified as:

$$\log(\text{Time}) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_n X_n + \varepsilon$$

where $\log(\text{Time})$ represents the natural logarithm of the outcome variable, and $\beta_0, \beta_1, \ldots, \beta_n$ are the coefficients associated with the selected independent variables [197]. This model allows to explore the relationships between independent variables and time while controlling for potential confounding variables [197].

To ensure the validity of a linear regression model for selected intervals, several key assumptions are tested, including linearity, and the normality of residuals [197]. Each interval in this thesis is drawn to visualise the linearity through residual plots.

However, due to skewness in the data, time intervals are converted into log-scale in order to reduce the dynamic range of the intervals so that the differences are preserved, and the scale is not overly skewed. Once converted, residual plots are drawn, and linearity is once again tested.

The interpretation of the regression coefficients involves understanding the impact of both numerical and categorical independent variables on the natural logarithm of time. Numerical coefficients lead to a change in log(Time) by an amount equal to their respective coefficients, while categorical variables are assessed in comparison to reference categories. The significance of the regression coefficients will be assessed using two-tailed hypothesis tests with a significance level of $\alpha = 0.05$. The goodness of fit of the linear regression model will be evaluated through the R-squared statistic, which quantifies the proportion of variance in the natural logarithm of time explained by the selected independent variables [197].

The intervals selected for linear regression analysis are marked 1-6 in ***Figure 6.9***. Using the previously described time interval frameworks and definitions, associations between "*time intervals*" and covariates (age, sex, education, region, marital status, first symptom, cancer stage, cancer type, diagnosis, institution of referral, political terms) are examined, both in un-adjusted and then adjusted models. Although all intervals are analysed, only six regression models are presented in this Chapter through tables: total interval, total-diagnostic interval TDI , hospital interval, two fragments of the diagnostic interval (diagnostic (a) and diagnostic (b)) and treatment interval. The proxy intervals are available in ***Tables T13 and T14 in Appendix A2***.

Results from linear regression models are presented with [log] coefficients and p-values. After performing multiple linear regression analysis, the coefficients obtained are initially based on a log-transformed version of the time variable. This transformation was done to handle the skewed distribution of the data and ensure that the assumptions of linearity and normality of residuals are met. To make the interpretation of these coefficients more intuitive, they are then transformed back into the original scale of time intervals (measured in days) using an exponential transformation. This process allows us to understand the effect of each independent variable on the actual time intervals experienced.

The mean fitted (predicted) values of this log-transformed dependent variable by categories of your explanatory variables (such as men and women when estimating gender difference), and use exponentiated difference between these fitted values as the estimate of difference in particular time interval of interest between these categories. The goodness of fit of the linear regression model is evaluated through the R-squared statistic, which quantifies the proportion of variance in the natural logarithm of time explained by the selected independent variables.

Survival analysis: Kaplan-Meier

Kaplan-Meier is a non-parametric method used to estimate the survival function from time-to-event data [197]. It calculates the probability of survival at each distinct time point where an event occurs, considering the observed survival times and censoring information. It does so by multiplying the conditional probabilities of surviving beyond each event time, given that the individual has survived up to that point. The product of these probabilities yields the overall estimate of the survival function over the entire study period [197]. Assumptions of Kaplan-Meier analysis are censoring, independence, consistency and homogeneity. Kaplan-Meier assumes

that censoring is non-informative, meaning that the probability of being censored at any given time is unrelated to the true survival time. This assumption implies that individuals who are censored have the same underlying survival probabilities as those who are not censored [197, 198]. It also assumes that survival times for different individuals are independent of each other and that individuals are accurately followed up until the event of interest or censoring occurs, without any errors in recording or classifying event times. Lastly, Kaplan-Meier estimator assumes that the rate at which events occur is constant over time within each group being compared [197, 198].

For this thesis, each individual subject is followed up from the time of admission to the time of last visit. If the patient has date of death recorded in the EHR then the patient is considered to have the event=1. Otherwise, right censoring was applied to account for participants who did not experience the event of interest during the follow-up period (until 2021), no event=0.

A detailed exploration of the survival is drawn to analyse people at risk, deaths and population censured through time. Then a similar comparison of women and men over years 0-5 is conducted, providing valuable insights into the dynamics of the studied events within each group.

Furthermore, stratified analyses are performed using graphs to explore the impact of covariates on survival outcomes using Kaplan-Meier (`stsgraph` command in Stata). The `log-rank test` is used to assess the significance of differences between survival curves. A significant log-rank test implies that there is a statistically significant divergence in survival experiences among the groups under investigation [197, 198].

Survival analysis: Cox regression

In the Cox model survival is adjusted for sex. Results from the Cox-model are presented with Hazard Ratio (HR), 95% Confidence Intervals (CI) and p-values. In Cox hazards regression, interpreting HR involves considering both the magnitude and direction of the effect [197, 198]. A HR greater than 1 indicates that individuals in the exposure group have a higher risk of experiencing the event compared to those in the reference group. Conversely, a HR less than 1 suggests a lower risk of the event in the exposure group compared to the reference group [197, 198]. A hazard ratio of 1 implies no difference in risk between the two groups. The hazard function is expressed as:

$$h(t|\mathbf{X}) = h_0(t) \cdot \exp(\beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_k X_k)$$

Where: - $h(t|\mathbf{X})$ is the hazard at time t for a subject with covariate values $\mathbf{X}$. - $h_0(t)$ is the baseline hazard function. - $\beta_1, \beta_2, \ldots, \beta_k$ are coefficients representing the effect of covariates $X_1, X_2, \ldots, X_k$.

The proportional hazards assumption implies that the ratio of two hazard functions $h_1(t|\mathbf{X})/h_2(t|\mathbf{X})$ remains constant over time for any two sets of covariate values $\mathbf{X}$ and $\mathbf{Y}$. In other words, it implies that the effect of the predictor variables on the hazard of an event is constant over time [197, 198]. If the proportional hazards assumption is met, it indicates that the relationship between the covariates and the hazard is consistent throughout the study period [197, 198].

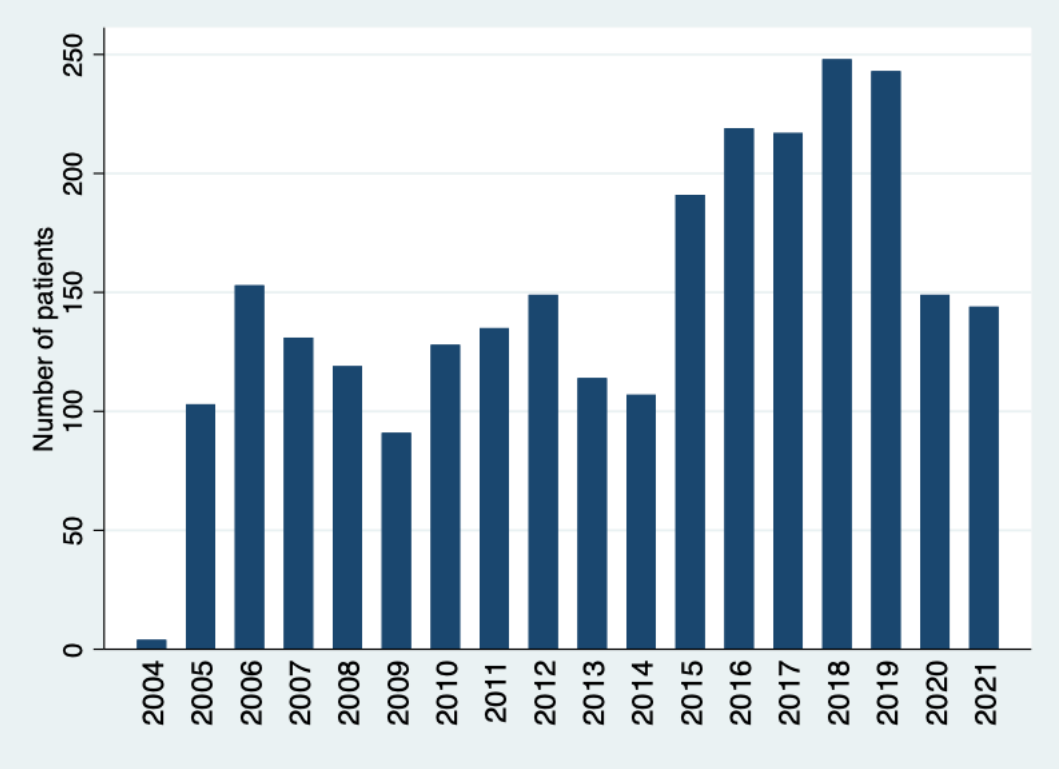
For this thesis the proportional hazards assumption is verified through the `estat phtest` command [197, 198] in Stata and then plotted using the command `stphplot` [197, 198] adjusted for sex and age.

6.4.2 Results

6.4.2.1 General description of the sample

From the initial patient records, 373 were not eligible to be included in the study due to: initially being classified as LC but was later found to be mesothelioma, thymoma or other types of cancer (N=130). Similarly, N=45 observations were dropped due to patients not reaching a LC diagnosis (tuberculosis or other) or was secondary to a primary cancer site (N=198) resulting in a final sample of *N=2645* patient records with a LC diagnosis from 2004-2021. **Figure 6.10** shows that a large portion of the sample comes from years 2015 and over. Very small sample in this study represents data from 2004.

Figure 6.10: Distribution of the lung cancer patient sample per year at the INCAN (N=2645)



The largest proportion of patients from this sample is from 2015 onwards.

From the N=2645 observations in this study, only N=832 held measurement of all intervals (31.4% of the sample). **Figure F17 in Appendix A1** describes the median days in each time interval among the N=832 sub-sample. The largest differences between the full sample and the sub-sample (complete intervals) lies in the TDI increasing the by 21% in the sub-sample. Similarly, a 15% increase in the "*total interval*" among the sub-sample (832 observations) is observed. The rest of the intervals share a difference of 1-3 days (less than 0.5-1.5% difference between the samples).

Table 6.5 describes the sample characteristics. The mean age is 61.2 years (see the distribution of age in **Figure F16 in Appendix A1** and the sample is almost equally divided into men (48.7%) and women (51.3%). More than half of the full sample(N=2645) reported to be married (55.1%). The most frequent level of education amongst the sample is primary school (33.3%) and in terms of Socioeconomic position (SEP), people belong most commonly to the poorest SEP (54.0%). The people from the full sample, most frequently come from Mexico City (45.9%) and a less proportion from the central region (19.7%) and south (19.1%). ***Figures F18 and F19 in Appendix A1*** describe the full list of categories in variables region and education.

Clinically, patients received a diagnosis of NSCLC in 75.8% of the cases and SCLC 2.1%. However, 22.1% of the sample did not have a set diagnosis. Only 8.4% of the samples' stage was diagnosed early (stages I & II), whereas 74.0% in advanced stages. For 17.6% of the population LC stage is unknown.

Table 6.5: General characteristics of the patient sample N=2645

Age	61.3	
Sex	Women	51.3%
	Men	48.7%
Education	>=High-school	44.8%
	Middle school	6.5%
	Elementary	33.3%
	No education	7.0%
	Unknown	8.4%
Socioeconomic position	Lower	54.0%
	Middle	32.8%
	Higher	13.2%
Region	North	6.1%
	Centre	19.7%
	Mexico City	45.8%
	South	19.1%
	Unknown	9.3%
Marital status	Divorced	13.4%
	Married	55.1%
	Single	9.8%
	Widowed	11.8%
	Unknown	10.0%
First symptom	Cough	47.4%
	Dyspnoea	13.2%
	Chest-pain	11.0%
	Haemoptysis	2.4%
	Weight-loss	4.8%
	Other symptoms	21.1%
Cancer stage	I or II	8.4%
	III	7.7%
	IV	66.3%
	Unknown	17.6%
Diagnosis	NSCLC	75.8%
	SCLC	2.1%
	Unspecified	22.1%
Institution of referral	Private hospital	52.1%
	Public hospital	41.9%
	Unknown	6.0%
Period	2019/2021	20.3%
	2013/2018	41.4%
	2007/2012	28.5%
	2004/2006	9.8%

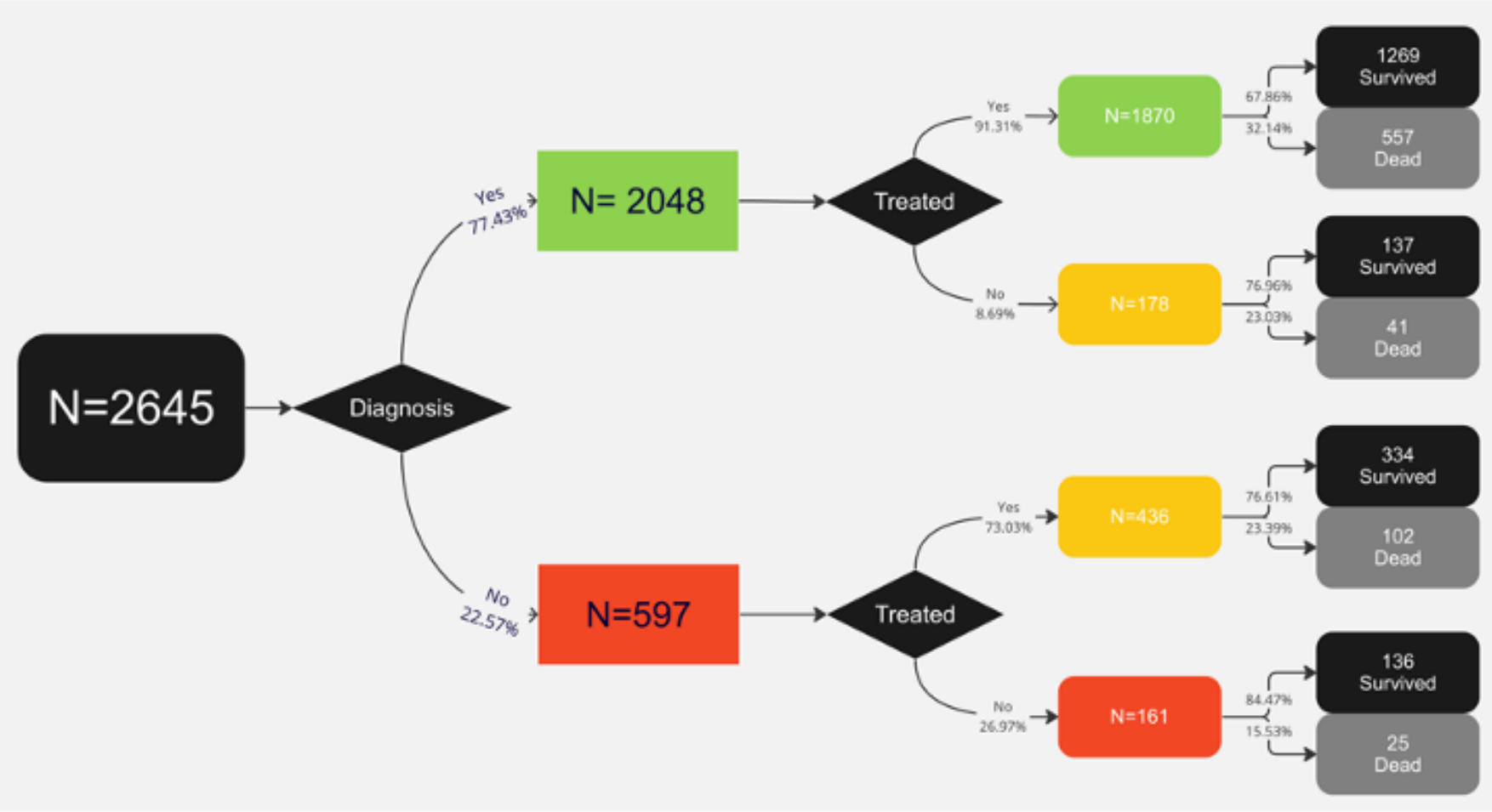
Amongst the most frequent first symptoms experienced by the sample were cough 39.5%, dyspnoea 11.0% and chest pain 9.2%. Only 2.4% of the population experienced haemoptysis. Other symptoms were also mentioned for instance: weight loss, flu-like symptoms, limbs pain, abdominal pain, nodules, loss of appetite, fatigue, seizures, syncope, hemiplegia, hemiparesis and loss of sight. Up to 16.6% of the symptoms were "Unspecified" or "missing" in the EHR. ***Figure F20 in Appendix A1*** describes the samples' full list of symptoms.

The population primarily came from private hospitals 52.6%, 41.9% from public hospitals of the cases. However, 6% of the population was not specified who they were referenced from. ***Figure F21 in Appendix A1*** describes the samples' full list of Institutions that refer patients to the INCAN.

6.4.2.2 Diagnosis and treatment per year

Figure 6.11 suggests there are three different populations trajectories that lead to different patient outcomes. From the total sample (N=2645), 70.7% of patients were diagnosed and treated, 6.7% were diagnosed but not treated, 16.4% were not diagnosed but were indeed treated and 6.0% were not diagnosed nor treated. Marked in red, 161 cases do not have information regarding diagnosis or treatment. Some of the sample was diagnosed but not treated (N=178) or was not diagnosed but was indeed treated (N=436) (these were marked as yellow). The green colour shows the sample that has been both diagnosed and treated (N=1870). After entry to INCAN, 77.4% of the patients (N=2048) were diagnosed and 91.3% of them followed treatment (N=1870). In parallel, 22.6% of the sample was not diagnosed (N=597) and 27.0% of them were left untreated (N=161) (see **Figure 6.11**). From the survival point of view, N=1876 patients survived or were censored, whereas N=725 patients died from 2004-2021.

Figure 6.11: Distribution of the lung cancer patient sample (N=2645) by diagnosis, treatment, and survival status at the INCAN



Source: Own work

From the original sample 2645 observations, a total amount of 161 cases do not have information regarding diagnosis or treatment, and thus no intervals are generated (red). Otherwise Some of the sample was diagnosed but not treated (N=178) (yellow). Additionally, some of the sample was not diagnosed but was indeed treated (N=436) (yellow). The green colour shows the sample that has been both diagnosed and treated (N=1870).

Figure F22 in Appendix A1 shows the variation in the percentage of patients being treated per term, with a significant decline in period 2019 to 2021. Based on the sample of patients treated (N=2306), this represents the percentage of treated patients according to the different political parties governing Mexico: 2019/2021, 2013/2018, 2007/2012, 2004/2006.

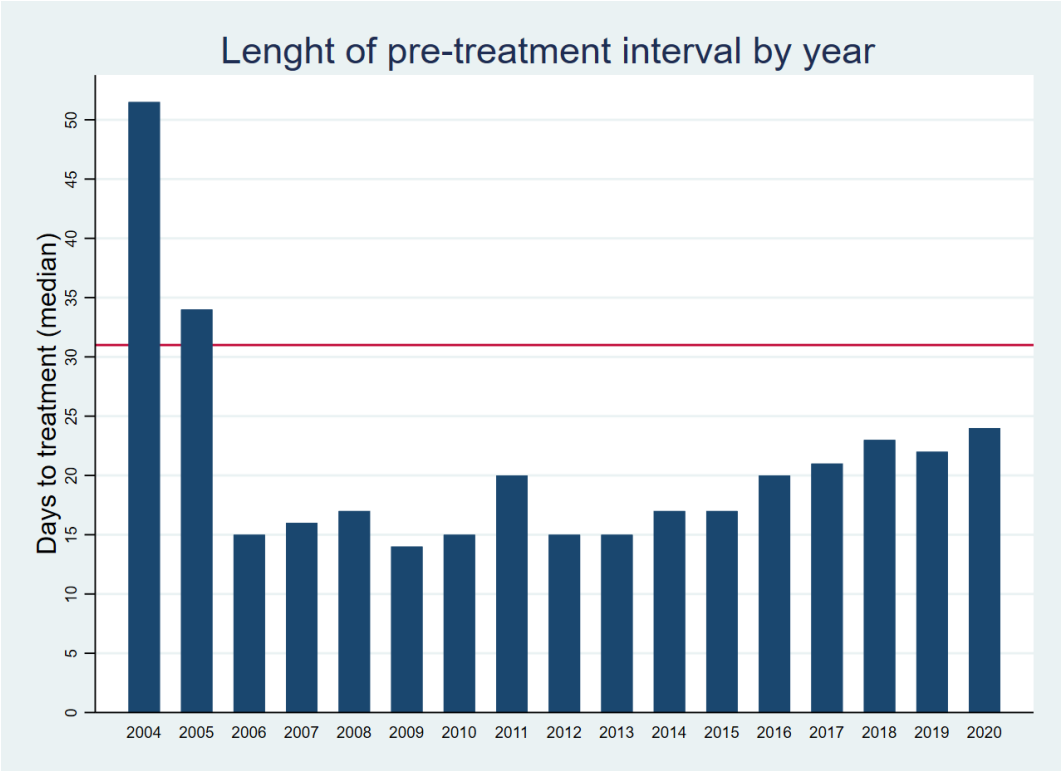
6.4.2.3 All intervals sample, median days, and distribution

The distribution of each outcome (interval) is described in **Figure F23 in Appendix A1**; all of which show a skewed distribution with a long tail to the right. Additionally, the median days to event per year from 2004-2021 for each outcome (interval) is drawn. For example, ***Figure 6.12*** shows the median days to treatment (from diagnosis to treatment) per year, and it shows a steady increase in the days to treatment after a steep drop from 2005 to 2006.

Median days to event from other time intervals are available in ***Figure F24 in Appendix A1***. Results show slow increase in the median days in the total, total diagnostic, appraisal, *hospital interval* and diagnostic interval (b) interval. Meanwhile, the median days to event in intervals: health system, pre-hospital, and diagnostic interval (a) seem to have a bimodal shape.

The median days across the cancer continuum for the full sample is described in **Figure 6.13**. These results show different medians days for each time interval using the theoretical frameworks previously described by Walter et al and Unger-Saldaña et al [88, 139]. The median length for each interval is: "*total interval*"=192 days, TDI=160 days, patient interval=107 days, health system interval= 77 days, diagnostic interval (from external diagnosis)= 52 days, diagnostic interval (from entry)= 7 days, pre-hospital interval=41 days, hospital interval=26

Figure 6.12: Median days (from diagnosis to treatment) per year at the INCAN

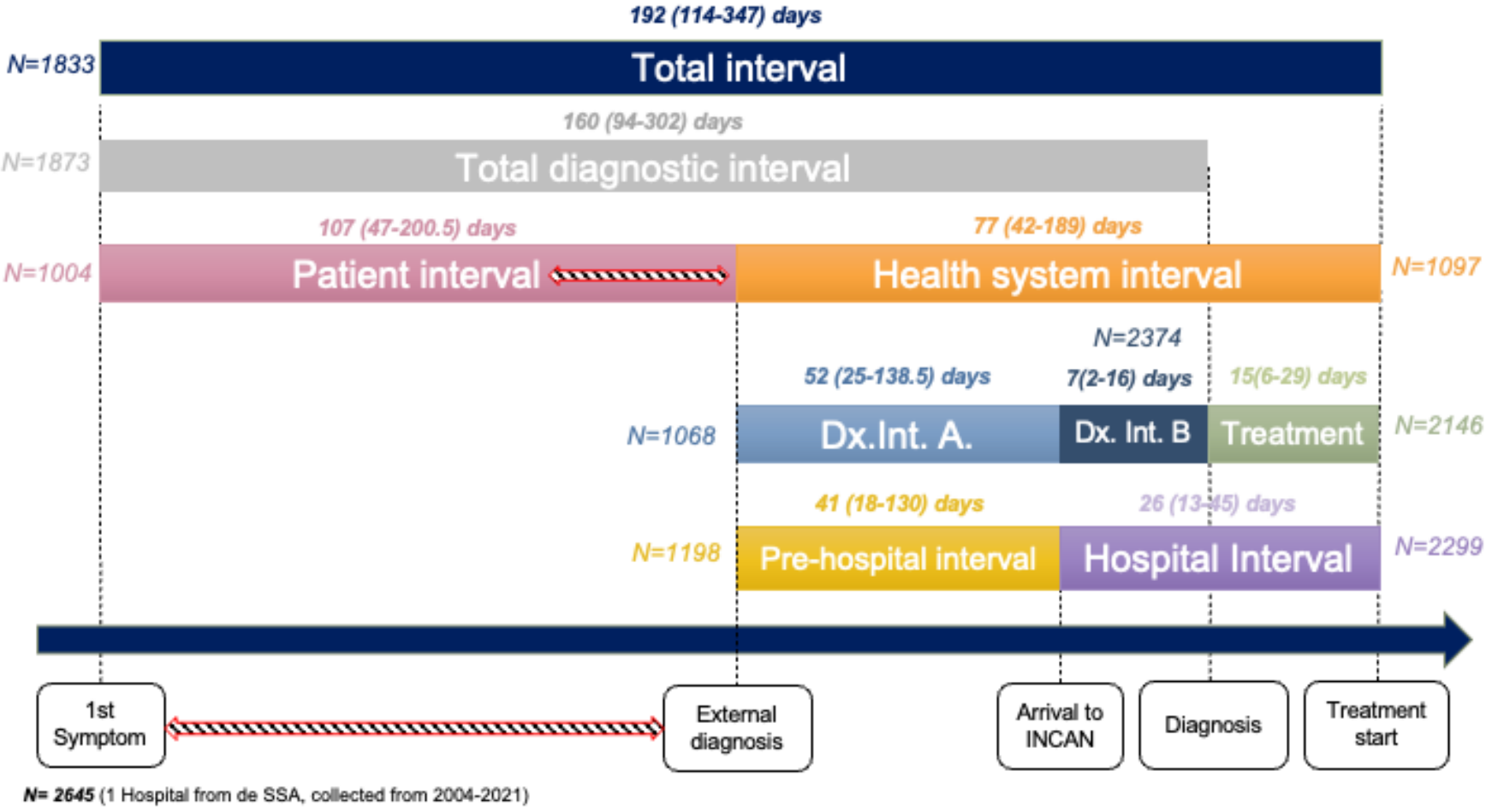


Source: Own work

days, treatment interval=15 days.

Due to the sample being studied in-hospital, dates from the *hospital interval* are the ones that are most available: dates of entry (N:2645), date of internal diagnosis (N:2048), date of treatment (N:2306). In contrast, date of first symptoms was somewhat available in 78.6% of the cases (N:2080) and external diagnosis only in 45.7% of the cases (N:1211). As a result of these variations, differences exist in the samples for each interval.

Figure 6.13: Lung cancer care intervals across the full sample of patients studied at the INCAN (median days)



Source: Own work.
Dx. Int A= Diagnostic interval (a) ; Dx. Int. B = Diagnostic interval (b).

6.4.2.4 Total interval by covariates

Results slightly show younger generations have longer "*total interval*" (see **Figure F26 in Appendix A1**). Furthermore, some differences were found in the median "*total interval*" by region: North=214 days, Centre= 201 days, Mexico City= 185 days and South= 195 days (see **Figure F27 in Appendix A1**). Data seems to have longer "*total interval*" in the more educated groups (see **Figure F28 in Appendix A1**). Moreover, according to institution of referral the most relevant differences were found in the "*total interval*" in: SEDENA=355 days (longer) and Other SSA hospitals= 143 days (shorter), compared to ISSSTE= 184 days, IMSS= 195 days, National SSA hospitals= 196 days and private healthcare services/practices= 197 days (see **Figure F29 in Appendix A1**).

Patients with loss of appetite as the first symptom take longer to be treated than other symptoms categories and patients with hemiplegia are the ones that take longer to reach diagnosis compared to other categories. In contrast, syncope, visual loss and other neurological symptoms were amongst the ones with fastest diagnostic resolution. The percentage of the symptoms in the population was previously described in ***Figure F20 in Appendix A1*** and the median days in the "*total interval*" per symptom are shown in ***Figure F30 in Appendix A1.***

6.4.2.5 All interval outcomes by covariates in missing and complete cases

"Complete" refers to a group of data where the outcome is available, and "Missing" are cases where data on the "*interval*" outcome is missing. For each time interval (outcome) a comparison is made for the complete vs the missing cases.

Total interval (missing vs complete)

Table 6.6 compares the population characteristics by each outcome for the complete case sample and the missing data sample. The characteristics of the "Complete" and "Missing" groups, particularly in age, sex, SEP, region, marital status, cancer stage, LC type and political terms were different. For instance, in the "Cancer stage" variable, the "Complete" observations group has a higher percentage of individuals with a higher stage at diagnosis compared to the "Missing" group. If cancer stage is related to the "*total interval*" outcome, this could introduce bias. Similarly, almost double the amount of the missing "*total interval*" group has unspecified cancer type.

The highest percentage of people missing "*total interval*" arise from period 2013-2018 (with 49% vs complete 38.1%). All three variables (cancer stage, diagnosis, and term) are statistically significant (< 0.001), thus suggesting differences in the population can introduce bias into the analysis of the "*total interval*" outcome.

Table 6.6: Total interval by covariates (missing vs complete data)

Variable	Categories	Complete (N=1833)	Missing (N=812)	p-value
Age		60.6 (13.4)	61.9 (12.8)	< 0.001
Sex	Women	50.8%	52.2%	0.52
	Men	49.2%	47.8%	
Education	>=High-school	44.5%	45.6%	0.087
	Middle school	6.9%	5.5%	
	Elementary	34.3%	31.0%	
	No education	6.6%	8.0%	
	Unspecified	7.7%	9.9%	
SEP	Lower	56.4%	49.0%	0.006
	Middle	31.1%	36.5%	
	Higher	12.6%	14.6%	
Region	North	6.2%	5.9%	0.015
	Centre	21.0%	16.9%	
	Mexico City	44.7%	48.3%	
	South	19.6%	17.7%	
	Unspecified	8.4%	11.2%	
Marital status	Divorced	12.1%	16.4%	0.002
	Married	56.6%	51.6%	
	Single	10.6%	8.0%	
	Widowed	11.1%	13.2%	
	Unspecified	9.6%	10.8%	
First symptom	cough	47.4%	47.6%	0.42
	dyspnoea	13.6%	11.8%	
	chest-pain	11.0%	11.0%	
	haemoptysis	2.3%	2.7%	
	weight-loss	4.4%	6.6%	
	other symptoms	21.3%	20.3%	
Cancer stage	I & II	5.4%	15.3%	< 0.001
	III	8.4%	6.2%	
	IV	72.4%	52.5%	
	Unspecified	13.8%	26.1%	
Diagnosis	Unspecified LC	17.8%	31.8%	< 0.001
	NSCLC	79.8%	66.7%	
	SCLC	2.4%	1.5%	
Institution of referral	Private hospital	52.4%	51.4%	0.35
	Public hospital	42.1%	41.6%	
	Unspecified	5.6%	7.0%	
Period	2019/2021	23.1%	13.8%	< 0.001
	2013/2018	38.1%	49.0%	
	2007/2012	31.8%	20.9%	
	2004/2006	7.0%	16.3%	

Total diagnostic interval (missing vs complete)

The median TDI was 160 days. However, the population missing the TDI were not at random. In fact, people missing the TDI were older, from higher SEP, more widowed or divorced and less married compared to the complete group. The missing group had 1.6 times more prevalence of stage I disease. People missing TDIheld 4.6 times more prevalence of an unspecified cancer stage and 3 times more prevalence of an unspecified LC type. Lastly, patients in the missing group were also more prone to enter the INCAN during 2004-2006 or 2013-2018 rather than the rest of the political terms. Further comparisons of the sample characteristics of these two groups are available in ***Table T5 in Appendix A2***.

Appraisal interval (missing vs complete)

The median *appraisal interval* (patient interval) was 107 days. However, only 1004 observations had this interval (1641 missing) and the missingness seems to not be at random. The population missing the patient interval is older, less educated, had a lower SEP, from Mexico City and more were not married. The missing group held less prevalence of cough as a primary symptom and experienced dyspnoea, chest-pain, haemoptysis, weight-loss, or other symptoms instead. Missing patients held 2.8 times more prevalence of stage I disease and were less frequently were coded as unspecified LC type. Lastly, the missing group held more prevalence of observations entering the INCAN during 2013-2018 rather than the rest of the political terms. Further comparisons of the two groups are available in ***Table T6 in Appendix A2***.

Health system interval (missing vs complete)

The median health system interval was 77 days. Similar to the health system interval, missingness was not found to be at random. Patients without a health

system interval (1548 observations, either because they did not have the treatment date, the external diagnosis date or both), were also older, less educated, had a lower SEP, from Mexico City and less prevalence of category married. Similar to the patient interval, these patients experienced less prevalence of cough as a primary symptom and experienced dyspnoea, chest-pain, haemoptysis, weight-loss, or other symptoms instead. Missing group patients were 2.9 times more prevalent to have a stage I disease, less frequently to have an unspecified LC type and more commonly to come to the INCAN from an unspecified institution. Lastly, these patients were also more commonly entering the INCAN during 2013-2018 or 2004-2006 rather than the rest of the political terms. Further comparisons of the two groups are available in ***Table T7 in Appendix A2***.

Pre-hospital interval (missing vs complete)

The median pre-hospital interval was 41. The characteristics of the patients missing a pre-hospital interval (1447 observations, due to either missing hospital entry date and date of external diagnosis) were like the patient and health system interval, these patients were less frequently experienced cough as a primary symptom and experienced dyspnoea, chest-pain, haemoptysis, weight-loss, or other symptoms instead. They were also older, less educated, had a lower SEP, from Mexico City and more commonly not be married. Patients from the missing group were 2.3 times more prevalence of stage I disease, were less likely to have an unspecified LC type and more frequently arrived to the INCAN via an unspecified institution. Lastly, these patients were also more commonly entering the INCAN during 2013-2018 or 2004-2006 rather than the rest of the political terms. Further comparisons of the two groups are available in ***Table T8 in Appendix A2***.

Hospital interval (missing vs complete)

The median *hospital interval* was 26 days. The characteristics of the patients missing a *hospital interval* (346 observations, due to either missing hospital entry date and/or date of treatment) were: were older and more commonly divorced, compared to the complete group. Regarding cancer stages, a significant disparity was evident. Stage I cancer was notably less prevalent in the complete data group, comprising 7.0% of cases, as opposed to the missing data group, where it accounted for 17.6%. Unspecified LC was more frequent in the missing data group, making up 46.2% of cases, in contrast to the complete data group, where it constituted 18.4% ($p < 0.001$). Lastly, these patients were also more commonly entering the INCAN during 2013-2018 or 2004-2006 rather than the rest of the political terms. Further comparisons of the two groups are available in ***Table T9 in Appendix A2***.

Diagnostic interval (a) -from external diagnosis- (missing vs complete)

The median diagnostic interval (a) was 52 days. Notably, the group with complete data exhibited statistically significant differences in mean age, with the missing data group being older. The complete data group had a higher representation of women at 55.0%, in contrast to the missing data group where women accounted for 48.8%. Both educational attainment and SEP was lower in the missing data group. Regional variations added another layer of distinction, with the Mexico City region being more prevalent in the missing data group. Marital status also displayed a discernible difference, with the complete data group having a higher proportion of married individuals. First symptom revealed significant disparities, with cough being more prevalent in the complete data group at 52.3%, as opposed to 44.0% in the missing data group. Stage I cancer was less common in the complete data group at 5.5%, compared to 10.4% in the missing data group. Unspecified LC was more

common in the missing data group at 25.6% vs 16.9%. Finally, the distribution of political terms demonstrated significant variations, with the 2019/2021 period being more frequently observed in the complete data group at 29.1%, in contrast to 14.3% in the missing data group. Further comparisons of the two groups are available in ***Table T10 in Appendix A2***.

Diagnostic interval (b) -from hospital admission- (missing vs complete)

The median diagnostic interval (b) was 7 days. The characteristics of the patients missing diagnostic interval (b) (271 observations) was not at random. For instance, men were more prevalent in the missing group; these were also from higher Socioeconomic position and had higher education than the complete group. The missing group had more prevalence of people who were divorced and widowed compared to married. Observations among the missing group have zero prevalence of patients being diagnosed at stage I and sure enough 93% of them have an unknown cancer stage and 94% of them are also missing LC type. Lastly, patients in the missing group were more prevalent during 2004-2006 compared to 8.8%. Further comparisons of the two groups are available in ***Table T11 in Appendix A2***.

Treatment interval (missing vs complete)

The median "*treatment interval*" was 15 days. The characteristics of the patients missing the "*treatment interval*" (N=499) were not at random. For instance, men were more prevalent in the missing group; a higher proportion of missing data is found among individuals aged 70/max. The missing observations were also from higher Socioeconomic background and more frequently divorced. Observations among the missing group have a higher prevalence of patients being diagnosed at stage I (12% vs 7.5% in the complete *treatment interval* group) or belonging to the "unspecified" category (53% vs 9.1%) and thus was less frequently found in

stages III and IV. Furthermore, observations missing the "*treatment interval*" were more frequently "unspecified" LC (60% vs 13%) (p <0.0001). Lastly, patients in the missing group were more prevalent during 2004-2006. Further comparisons of the two groups are available in ***Table T12 in Appendix A2***.

6.4.2.6 Log linear regression

These log-scale linear regressions examine the relationship between the natural logarithm of the outcome (time) and several independent variables. Distribution of residuals and [log] residuals for each interval are visible in ***Figure F25 in Appendix A1***.

After conversion these are more closely distributed to the diagonal line, suggesting linear regression is a good method for analysis. Results from each interval are presented below. The linear regression for patient, pre-hospital and health system interval are available in **Appendix A2** in **Tables T13, T14, T15** .

Total interval

Table 6.7 describes a [log] linear regression of a sample of 1821 observations. In the unadjusted model, age, sex, first symptom, SCLC diagnosis, and term were associated with the outcome. Once adjusted, the "*total interval*" analysis suggests that age, sex, unspecified marital status, certain symptoms (dyspnoea, chest-pain, other symptoms, and unspecified category), an SCLC diagnosis, cancer stage IV and some terms, have statistically significant associations with the natural logarithm of the outcome variable. Other variables, such as education, region, institutional reference, and term 2013/2018 do not appear to be significant predictors of "*total interval*". The R-squared value of the adjusted model is 0.0742, indicating that the model explains 7.42% of the variance in "*total interval*".

The coefficient for age after adjustment with the rest of the variables is -0.0047. It has a negative association, meaning that as age increases, "*total interval*" decreases. The p= 0.002, indicating that age is statistically significant in predicting "*total interval*". The coefficient for women is -0.1472, suggesting that being female is associated with lower "*total interval*" compared to being male. The confidence interval ranges from 0.2230 to 0.0714, thus the p-value=<0.0001, indicating that there is a statistically significant association between sex and "*total interval*" length.

None of the education categories show a statistically significant association with "*total interval*" compared to the reference group "no education" (p >0.05). These categories include "No education", "High-school", Middle school", "Elementary", and "Unspecified." For marital status, only the "unspecified" category the coefficient was -0.31 and p-value of 0.029, indicating a reduced association with "*total interval*" compared to those "married". When using Mexico City as a reference category, none of the region categories ("north", "centre", "south" and "Unspecified") show a statistically significant association with "*total interval*".

Several symptom categories have statistically significant negative associations with outcome "*total interval*" compared to "cough", including "dyspnoea" (p=<0.0001), "chest-pain" (p=0.044), "other symptoms" (p=<0.0001) and "Unspecified symptoms" (p=0.018), suggesting that the presence of these symptoms is associated with lower "*total interval*" compared to having symptom "cough". Furthermore, for the variable diagnosis, SCLC has a statistically significant negative association with "*total interval*" (p=0.010) compared to NSCLC, meaning that patients with SCLC tend to have shorter "Total intervals" than people with a NSCLC diagnosis. Moreover, among cancer stages, IV has a statistically significant

negative association with "*total interval*" (p=0.034) compared to cancer stages I-I. This indicates that patients with stage IV cancer tend to have lower "*total interval*", compared to the reference stages I-II.

The institution from which the patients originally were referred from (institution previously visited by the patients) did not show statistically significant association with "*total interval*". Lastly, terms 2007/2012 and 2004/2006 have statistically significant negative associations with "*total interval*" compared to reference category 2019/2021. In comparison to term 2019-2021 (206 days), the "*total interval*" for term 2007/2012 and 2004/2006 was 179 days and 151 days respectively.

Practical considerations in days in statistically significant categories: The median total interval days in this full sample is 192 days (114-348). As a result of back transformation from [log] coefficients into days for each category, from symptom onset to treatment women experience longer "*total interval*" than men (210 days vs 179 days). In comparison to the married people (196 days), the people with missing marital status had a shorter "*total interval*" (183 days). Compared to people with cough (221 days), other symptoms experienced reduced "*total interval*": dyspnoea (175 days), chest-pain (190 days), other symptoms (164 days) and unspecified symptoms (169 days). Patients with SCLC (138 days) tend to have shorter "Total intervals" than people with a NSCLC diagnosis (192 days). Patients with stage IV cancer tend to have lower "*total interval*" (188 days), compared to the reference stages I-II (212 days). These results are all statistically significant.

Table 6.7: Total interval unadjusted and adjusted [log] linear regression

Total interval					
Variable	**Categories**	*N=1821*		*N=1821*	
		Unadjusted	p-value	**Adjusted**	p-value
Age		-0.0033	0.019	-0.0047	0.002
Sex	Male	*Reference*		*Reference*	
	Female	0.1688	<0.0001	0.1472	<0.0001
Education	No education	*Reference*		*Reference*	
	>=High-school	0.0963	0.226	0.0596	0.465
	Middle school	0.0847	0.414	0.0096	0.927
	Elementary	0.0619	0.444	0.0725	0.363
	Unspecified	0.0509	0.617	0.2275	0.427
Marital status	Married	*Reference*		*Reference*	
	Divorced	0.0250	0.678	-0.0024	0.967
	Single	-0.0672	0.290	-0.1103	0.080
	Widowed	0.0606	0.330	0.0688	0.284
	Unspecified	-0.0672	0.317	-0.3130	0.029
Region	Mexico City	*Reference*		*Reference*	
	North	0.0446	0.583	0.0072	0.928
	Centre	0.0632	0.209	0.0412	0.409
	South	0.0528	0.305	0.0348	0.495
	Unspecified	0.0135	0.852	0.0451	0.845
Symptom	cough	*Reference*		*Reference*	
	dyspnoea	-0.2345	<0.0001	-0.2231	<0.0001
	chest-pain	-0.1583	0.015	-0.1295	0.044
	haemoptysis	-0.1046	0.427	-0.0446	0.732
	weight-loss	-0.1579	0.101	-0.1215	0.202
	other symptoms	-0.3086	<0.0001	-0.2979	<0.0001
	Unspecified	-0.2727	0.002	-0.2201	0.018
Diagnosis	NSCLC	*Reference*		*Reference*	
	SCLC	-0.3392	0.006	-0.3128	0.010
	Unspecified	0.0863	0.084	0.0816	0.297
Cancer stage	I-II	*Reference*		*Reference*	
	III	-0.0063	0.951	-0.0209	0.839
	IV	-0.1278	0.130	-0.1774	0.034
	Unspecified	0.0123	0.898	-0.0442	0.701
Institution	Public	*Reference*		*Reference*	
	Private hospital	0.0801	0.42	0.027	0.512
	Unspecified	-0.0014	0.987	-0.0018	0.984
Term	2019/2021	*Reference*		*Reference*	
	2013/2018	0.0243	0.624	-0.0314	0.562
	2007/2012	-0.1419	0.006	-0.2329	<0.0001
	2004/2006	-0.3072	<0.0001	-0.4237	<0.0001

In addition to the un-adjusted and fully adjusted model for "*total interval*", an intermediate model was built. Intermediate models help in understanding the relative importance of variables. By observing how variables affects the model's performance, these gauge the importance of each variable in explaining the variation in the outcome. For this thesis, the intermediate model used sex, age, education level and diagnosis. After adjustment, the intermediate model showed positive association with sex (p=<0.0001) and cancer type (p=0.012), which remained statistically significant. Age however, after being significant in the univariate analysis model, age is not significant in this intermediate model. Education remains unassociated with the outcome both in the unadjusted and adjusted models. Results can be seen in **Appendix A2** in **Table T16**.

Total diagnostic interval

The linear regression model in **Table 6.8** is used to predict the natural logarithm of *TDI* based on a set of independent variables with a total of N=1863 observations. The R-squared value for the model is 0.0748, indicating that the model explains approximately 7.48% of the variability in *TDI*.

Looking at the adjusted model, the coefficient for age is -0.0063. This negative coefficient suggests that as age increases, *TDI* tends to decrease. The p-value for age is <0.0001, indicating that age is statistically significant in predicting *TDI*. The coefficient for sex is 0.1933, indicating that being male is associated with lower *TDI* compared to being female (p=<0.0001). Neither education nor region was statistically associated with *TDI*. The coefficients for being single is -0.1359 and category "unspecified marital status" (p=0.009) indicate negative associations with *TDI* compared to the married population. Several symptom categories have statistically significant associations with *TDI*. Coefficients for "dyspnoea" -0.3183

(p=<0.0001), -0.3264 "other symptoms" (p=<0.0001) and -0.3088 "Unspecified" (p=0.002) are negatively associated with *TDI* after keeping the rest of the variables constant, with reference category "cough"; meaning that the presence of these symptoms is associated with shorter *TDI*. Furthermore, diagnosis, cancer stage and Institution do not show statistically significant associations with *TDI*. The coefficient for terms "2007/2012" -0.1952 (p=0.003) and "2004/2006" -0.5470 (p=<0.0001) have statistically significant negative associations with *TDI* (reference category 2019-2021), suggesting that these terms are associated with shorter *TDI*. Other term categories are not statistically significant.

Practical considerations in days in statistically significant categories: The median TDIis 160 days to diagnosis. As a result of back transformation from [log] coefficients into days for each category, results suggest being a man is associated with shorter *TDI* compared to being a woman (145 days vs 179 days). Compared to reference category married (162 days), people with unspecified marital status experienced shorter *TDI* (151 days). Compared to cough as first symptom (188 days), people with dyspnea (134 days), other symptoms (134 days) and unspecified symptoms (138 days), experience shorter *TDI*. These results are all statistically significant.

Table 6.8: Total diagnostic interval unadjusted and adjusted [log] linear regression

TDI interval					
Variable	**Categories**	*N=1863*		*N=1863*	
		Unadjusted	p-value	**Adjusted**	p-value
Age	Age	-0.0049	0.002	-0.0063	<0.0001
Sex	Male	*Reference*		*Reference*	
	Female	0.2094	<0.0001	0.1933	<0.0001
Education	No education	*Reference*		*Reference*	
	>=High-school	0.0684	0.416	0.0052	0.951
	Middle school	0.0684	0.541	-0.0274	0.808
	Elementary	0.0523	0.542	0.0500	0.554
	Unspecified	0.05161	0.628	0.2565	0.422
Marital status	Married	*Reference*		*Reference*	
	Divorced	0.0345	0.598	0.0148	0.819
	Single	-0.0833	0.237	-0.1359	0.052
	Widowed	0.0469	0.493	0.0456	0.516
	Unspecified	-0.0663	0.348	-0.4001	0.009
Region	Mexico City	*Reference*		*Reference*	
	North	0.0278	0.755	0.0030	0.972
	Centre	0.0511	0.353	0.0253	0.642
	South	0.0556	0.321	0.0311	0.576
	Unspecified	0.02577	0.736	0.0592	0.823
Symptom	cough	*Reference*		*Reference*	
	dyspnoea	-0.3357	<0.0001	-0.3183	<0.0001
	chest-pain	-0.1414	0.042	-0.1186	0.086
	haemoptysis	-0.2174	0.137	-0.1531	0.290
	weight-loss	-0.1926	0.056	-0.1462	0.145
	other symptoms	-0.3361	<0.0001	-0.3264	<0.0001
	Unspecified	-0.3135	<0.0001	-0.3088	0.002
Diagnosis	NSCLC	*Reference*		*Reference*	
	SCLC	-0.2107	0.107	-0.1747	0.173
	Unspecified	0.0093	0.877	0.0728	0.366
Cancer stage	I-II	*Reference*		*Reference*	
	III	0.0785	0.451	0.0461	0.653
	IV	-0.0688	0.395	-0.1374	0.090
	Unspecified	-0.0214	0.839	-0.0783	0.514
Institution	Public hospital	*Reference*		*Reference*	
	Private hospital	0.0492	0.253	0.0115	0.799
	Unspecified	-0.0066	0.939	0.0322	0.732
Term	2019/2021	*Reference*		*Reference*	
	2013/2018	-0.0002	0.996	-0.0657	0.264
	2007/2012	-0.0937	0.097	-0.1952	0.003
	2004/2006	-0.4211	<0.0001	-0.5470	<0.0001

Diagnostic interval (a) (from external diagnosis)

The linear regression analysis aimed to explore the factors associated with the natural logarithm of *"Diagnosis (from external diagnosis) interval"* in a sample of 1063 observations (see **Table 6.9**). The model explained approximately 4.79% of the variance in *"Diagnosis (from external diagnosis) interval"* (R-squared = 0.0479).

Age showed no significant association with *"Diagnosis (from external diagnosis) interval"*. However, females had a statistically significant positive association with *"Diagnosis (from external diagnosis) interval"* compared to males (coefficient = 0.1972, p = 0.015), indicating that, on average, females had a longer *"Diagnosis (from external diagnosis) interval"*. Education, marital status and region did not have statistically significant associations with *"Diagnosis (from external diagnosis) interval"*. Only the presence of "weight-loss" and the "Unspecified" symptom category are significantly associated with the *"Diagnosis (from external diagnosis) interval"*. "Weight-loss" is linked to a shorter interval (coefficient = -0.5019, p = 0.022), while "unspecified" symptoms are associated with a longer interval compared to patients with "cough" (coefficient = 0.3876, p = 0.001). Other symptom categories do not exhibit significant associations with the *"Diagnosis (from external diagnosis) interval"*. Cancer stage categories III and IV, were not significantly associated with *"Diagnosis (from external diagnosis) interval"*. In contrast, the "Unknown" category had a statistically significant negative association with *"Diagnosis (from external diagnosis) interval"*(coefficient = -0.5223, p = 0.028), implying that individuals with "unspecified" cancer stages had shorter *"Diagnosis (from external diagnosis) interval"* compared to the reference category (Stage I-II). Institution and term were not significantly associated with *"Diagnosis (from external diagnosis) interval"*.

Table 6.9: Diagnostic interval (a) (from external diagnosis) unadjusted and adjusted [log] linear regression

Diagnosis interval (a)					
Variable	**Categories**	*N=1063*		*N=1063*	
		Unadjusted	p-value	**Adjusted**	p-value
Age	Age	-0.0005	0.860	-0.0022	0.483
Sex	Male	*Reference*		*Reference*	
	Female	0.2249	0.004	0.1972	0.015
Education	No education	*Reference*		*Reference*	
	>=High-school	0.2641	0.148	0.1695	0.378
	Middle school	0.2234	0.325	0.1354	0.567
	Elementary	0.2940	0.120	0.2523	0.188
	Unspecified	0.0869	0.691	0.0605	0.911
Marital status	Married	*Reference*		*Reference*	
	Divorced	-0.0056	0.966	-0.0183	0.891
	Single	-0.0371	0.776	-0.0838	0.524
	Widowed	0.0525	0.696	0.0036	0.979
	Unspecified	-0.1253	0.342	0.1098	0.725
Region	Mexico City	*Reference*		*Reference*	
	North	0.1256	0.401	0.0768	0.610
	Centre	0.0372	0.730	-0.0178	0.871
	South	0.0333	0.755	0.0315	0.773
	Unspecified	-0.1338	0.336	-0.1698	0.664
Symptom	Cough	*Reference*		*Reference*	
	Dyspnoea	-0.1257	0.366	-0.0957	0.493
	Chest-pain	-0.0355	0.804	-0.0289	0.840
	Haemoptysis	-0.2660	0.424	-0.2476	0.460
	Weight-loss	-0.4850	0.023	-0.5019	0.022
	Other symptoms	-0.1591	0.149	-0.1659	0.137
	Unspecified	0.3877	0.001	0.3876	0.001
Diagnosis	NSCLC	*Reference*		*Reference*	
	SCLC	-0.2667	0.334	-0.2679	0.334
	Unspecified	-0.0867	0.412	0.3323	0.038
Cancer stage	I-II	*Reference*		*Reference*	
	III	-0.0311	0.886	0.0756	0.731
	IV	-0.2022	0.241	-0.1609	0.362
	Unknown	-0.4310	0.028	-0.5223	0.028
Institution	Public hospital	*Reference*		*Reference*	
	Private hospital	0.2025	0.012	0.1557	0.083
	Unspecified	-0.0755	0.683	-0.2132	0.257
Term	2019/2021	*Reference*		*Reference*	
	2013/2018	0.1921	0.046	0.0692	0.515
	2007/2012	-0.0228	0.824	-0.0445	0.717
	2004/2006	-0.2868	0.172	-0.2425	0.284

Practical considerations in days in statistically significant categories: The median days to diagnosis from external diagnosis were 52 days. As a result of back transformation from [log] coefficients into days for each category, results suggest significant differences were seen between men and women in the diagnostic (a) interval (54 days in men vs 67 days in women). Compared to cough as first symptom (62 days), people with weight-loss had shorter *"Diagnosis (from external diagnosis) interval"* (38 days), whilst unspecified symptoms had longer *"Diagnosis (from external diagnosis) interval"* (91 days). Compared to NSCLC (62 days), patients with unspecified LC experienced shorter *"Diagnosis (from external diagnosis) interval"* (57 days). Lastly, patients with unspecified stage of the disease also experienced shorter *"Diagnosis (from external diagnosis) interval"* (49 days) vs stages I-II (75 days).

Diagnostic interval (b) (from hospital admission)

The linear regression analysis aimed to explore the factors associated with the natural logarithm of *Diagnosis (from admission) interval* in a sample of 2,361 observations (see ***Table 6.10***). The model explained only approximately 4.79% of the variance in *Diagnosis (from admission) interval* (R-squared = 0.0479).

Age showed a statistically significant positive association with *Diagnosis (from admission) interval* (coefficient = 0.0046, p = 0.043). This suggests that, on average, each additional year of age was associated with a slight increase in the duration of *Diagnosis (from admission) interval*. The variable "Sex" did not demonstrate a statistically significant association with *Diagnosis from admission interval* (coefficient = -0.0561, p = 0.334). This implies that, within the scope of this analysis, there was no significant difference in the length of *Diagnosis (from admission) interval* between men and women. On the contrary, education and

Table 6.10: Diagnostic interval (b) (from hospital entry/admission) unadjusted and adjusted [log] linear regression

Diagnosis interval (b)					
Variable	**Categories**	*N=2361*		*N=2361*	
		Unadjusted	p-value	**Adjusted**	p-value
Age	Age	0.0081	<0.0001	0.0046	0.043
Sex	Male	*Reference*		*Reference*	
	Female	-0.0321	0.569	-0.0561	0.334
Education	No education	*Reference*		*Reference*	
	>=High-school	-0.1280	0.260	-0.1056	0.372
	Middle school	0.0767	0.619	0.0525	0.739
	Elementary	0.0284	0.807	0.0437	0.707
	Unspecified	0.2483	0.081	0.5820	0.153
Marital status	Married	*Reference*		*Reference*	
	Divorced	0.1310	0.145	0.1158	0.198
	Single	-0.1643	0.090	-0.1374	0.158
	Widowed	0.1384	0.125	0.0616	0.513
	Unspecified	0.3072	0.001	0.1586	0.484
Region	Mexico City	*Reference*		*Reference*	
	North	-0.5387	<0.0001	-0.5543	<0.0001
	Centre	-0.0041	0.957	-0.0302	0.689
	South	-0.1132	0.138	-0.1324	0.084
	Unspecified	0.1688	0.091	-0.5794	0.065
Symptom	cough	*Reference*		*Reference*	
	dyspnoea	0.0147	0.881	-0.0089	0.927
	chest-pain	0.02994	0.771	0.0542	0.594
	haemoptysis	0.3807	0.071	0.4352	0.037
	weight-loss	0.0416	0.777	0.0115	0.937
	other symptoms	-0.0657	0.413	-0.0608	0.444
	Unspecified	0.0921	0.258	0.0951	0.253
Diagnosis	NSCLC	*Reference*		*Reference*	
	SCLC	0.2525	0.171	0.2802	0.127
	Unspecified	-0.3232	<0.0001	-0.1573	0.140
Cancer stage	I-II	*Reference*		*Reference*	
	III	-0.1456	0.271	-0.1452	0.276
	IV	-0.2286	0.018	-0.2580	0.009
	Unspecified	-0.6689	<0.0001	-0.4197	0.006
Institution	Public hospital	*Reference*		*Reference*	
	Private hospital	0.0968	0.098	-0.0131	0.834
	Unspecified	-0.1253	0.295	-0.1877	0.125
Term	2019/2021	*Reference*		*Reference*	
	2013/2018	-0.0006	0.993	0.0537	0.519
	2007/2012	-0.3216	<0.0001	-0.2478	0.008
	2004/2006	-0.2442	0.029	-0.1927	0.120

marital status were not associated with diagnosis from admission (diagnosis b). The "North" region displayed a statistically significant negative association with *Diagnosis (from admission) interval* implying that individuals in this region spent fewer days in the hospital compared to those in "Mexico City". The "Centre" and "South" regions did not exhibit statistically significant associations compared to the "Mexico City" region, while the "Unspecified" region category had a marginally significant association, similar in magnitude to the "north region".

The symptom "haemoptysis" stands out with a statistically significant positive association (coefficient = 0.4353, p = 0.037), suggesting that patients with this first symptom have longer *Diagnosis (from admission) interval* compared to those with cough. Other symptom categories do not exhibit significant associations with *Diagnosis (from admission) interval* compared to cough. The diagnosis categories SCLC and "Unspecified" do not demonstrate significant associations with *Diagnosis (from admission) interval* ($p > 0.05$) when compared to NSCLC. Moreover, cancer stage "IV" and "Unspecified" categories both displayed statistically significant negative associations with *Diagnosis (from admission) interval* ($p < 0.05$), suggesting that, on average, individuals in these stages spent fewer days in the hospital compared to the reference category Stage I-II. Stage "III" exhibited a non-significant negative association. The institution was not associated with *Diagnosis (from admission) interval*. Term category 2007/2012 compared to 2019-2021 exhibited statistically significant associations in the *Diagnosis (from admission) interval*. This implies that this term led to differences in the time spent from admission to diagnosis.

Practical considerations in days in statistically significant categories: The median time to diagnosis (from admission) was: 7 days. As a result of back transformation from [log] coefficients into days for each category, results show that

compared to the youngest group (min/49) patients ages 70/max spend 2 additional days being diagnosed after being admitted. People from the northern region have shorter time to diagnosis that the people from Mexico City (4 vs 6 days). Compared to cancer stages I-II(8 days), patients with cancer stage IV is delayed by one day, whereas the patients without a specified cancer stage have a shorter time to diagnosis (4 days). Patient with haemoptysis spend 3 more days waiting for diagnosis after admission compared to patients only debuting with cough. Patients wait for 7 days to be diagnosed in 2019/2021 vs 5 days in 2007/2012.

Hospital interval

The linear regression model in **Table 6.11** is used to predict the natural logarithm of *Hospital interval* based on a set of independent variables in a sample of 2284 observations. The model explained approximately 9.26% of the variance in *Hospital Interval* (R-squared = 0.0926).

Age did not exhibit a statistically significant association with *Hospital Interval* (coefficient = -<0.0001, p-value = 0.650), suggesting that, on average, each additional year of age was not associated with a significant change in *Hospital Interval*. Similarly, sex showed no statistically significant association with *Hospital Interval* (coefficient = -0.0054, p-value = 0.914). Educational attainment, did not display statistically significant associations with *Hospital Interval* meaning that different education levels did not lead to significant differences in *Hospital Interval*, when compared to the reference category "No education". Marital status, however, yielded mixed results. Divorced individuals had a statistically significant positive association with *Hospital Interval* (coefficient = 0.1596, p = 0.042), suggesting that, on average, divorced individuals spent more days in the hospital compared to the reference category "married". Similarly, widowed individuals also exhibited a

Table 6.11: Hospital interval unadjusted and adjusted [log] linear regression

Hospital interval					
Variable	**Categories**	*N=2284*		*N=2284*	
		unadjusted	**p-value**	**Adjusted**	**p-value**
Age	Age	0.0004	0.817	-0.0009	0.650
Sex	Male	*Reference*		*Reference*	
	Female	-0.0527	0.295	0.0054	0.914
Education	No education	*Reference*		*Reference*	
	>=High-school	0.0980	0.344	0.0650	0.536
	Middle school	0.0737	0.592	0.0567	0.679
	Elementary	0.0784	0.459	0.0837	0.417
	Unspecified	0.4819	<0.0001	0.4927	0.159
Marital status	Married	*Reference*		*Reference*	
	Divorced	0.1796	0.025	0.1596	0.042
	Single	0.0791	0.351	0.0585	0.482
	Widowed	0.1854	0.020	0.1702	0.037
	Unspecified	0.3744	<0.0001	-0.0043	0.982
Region	Mexico City	*Reference*		*Reference*	
	North	-0.4761	<0.0001	-0.4572	<0.0001
	Centre	-0.1491	0.026	-0.1326	0.044
	South	-0.2118	0.002	-0.1668	0.012
	Unspecified	0.2390	0.009	-0.0832	0.752
Symptom	cough	*Reference*		*Reference*	
	dyspnoea	-0.0401	0.637	-0.0279	0.734
	chest-pain	-0.0404	0.663	-0.0604	0.501
	haemoptysis	0.1302	0.483	0.1062	0.553
	weight-loss	0.1021	0.454	0.0486	0.712
	other symptoms	0.0077	0.914	-0.0225	0.746
	Unspecified	0.0916	0.212	0.0102	0.888
Diagnosis	NSCLC	*Reference*		*Reference*	
	SCLC	-0.2697	0.115	-0.2781	0.102
	Unspecified	-0.7147	<0.0001	-0.3562	<0.0001
Cancer stage	I-II	*Reference*		*Reference*	
	III	-0.2195	0.080	-0.2406	0.058
	IV	-0.2695	0.005	-0.2991	0.002
	Unspecified	-1.0906	<0.0001	-0.8011	<0.0001
Institution	Public hospital	*Reference*		*Reference*	
	Private hospital	0.0851	0.102	-0.0085	0.875
	Unspecified	0.254	0.026	0.1646	0.144
Term	2019/2021	*Reference*		*Reference*	
	2013/2018	0.0211	0.754	0.1084	0.134
	2007/2012	-0.1430	0.047	0.0512	0.523
	2004/2006	-0.1871	0.062	0.1103	0.305

significant positive association (coefficient = 0.1702, p = 0.037), indicating a longer duration of *Hospital Interval* compared to those married.

Individuals residing in the North, Centre, and South regions displayed statistically significant negative associations with *Hospital Interval* ($p < 0.05$), indicating that, individuals in these regions spent fewer days in the hospital compared to the reference category (Mexico City). The "Unspecified" region category, did not show a statistically significant association.

Symptoms did not exhibit statistically significant associations with *Hospital Interval* suggesting that different symptoms did not significantly impact the *Hospital Interval* when compared to the reference category cough. In terms of diagnosis, individuals with "Unspecified" diagnoses had a statistically significant negative association with *Hospital Interval* (coefficient = -0.3562, $p < 0.001$), indicating that, on average, they spent fewer days in the hospital compared to the patients diagnosed with NSCLC. There was no such association for individuals with SCLC diagnosis.

Cancer stage was also relevant. "IV" and "Unspecified" cancer stages both displayed statistically significant negative associations with *Hospital Interval* ($p < 0.05$), suggesting that, individuals in these stages spent fewer days in the hospital compared to the reference category. "III" stage exhibited a marginally significant negative association with *Hospital Interval* duration.

Institution type, whether "Private hospital" or "Unspecified," did not show statistically significant associations with *Hospital Interval* indicating that the type of institution did not significantly impact the *Hospital Interval* compared to the reference category "Public hospital". Lastly, the term categories (2013/2018,

2007/2012, 2004/2006) did not exhibit statistically significant associations with *Hospital Interval* suggesting that different political terms did not lead to significant differences in *Hospital Interval* 2019-2021.

Practical considerations in days in statistically significant categories: The median time to treatment from hospital admission was: 26 days. As a result of back transformation from [log] coefficients into days for each category, results suggest that compared to the people who were married (20 days), patients who were divorced or widowed had longer hospital intervals (24 days each). Geographical region played a notable role: compared to Mexico City (24 days), patients in other regions experience shorter *hospital interval*: North: 15 days, Centre: 20 days, South: 19 days. Compared to cancer stages I-II(34 days), patients with cancer stage IV experience shorter hospital intervals (14 days) , whereas the patients without a specified cancer stage have even shorter time to treatment (10 days). Patient with "unknown" cancer type wait 12 days for treatment, unlike people with NSCLC who wait 25 days for treatment.

Treatment interval

In this multiple linear regression analysis, the purpose was to dissect the factors affecting medical treatment timeliness, denoted as *Treatment interval* in a sample of 2284 observations. The model's explanatory power was limited, as it explained only approximately 3.46% of the variance in *Treatment interval*.

In **Table 6.12** the age of the individuals did not show a statistically significant association with the *Treatment interval*(coeff -0.0021, p = 0.399). Similarly, the sex of individuals also did not appear to be a significant predictor of the *Treatment interval* (coeff 0.0611, p = 0.331). Education and marital status were not associated

with *Treatment interval*.

Table 6.12: Treatment interval unadjusted and adjusted [log] linear regression

Treatment interval					
Variable	**Categories**	*N=2133*		*N=2133*	
		Unadjusted	p-value	**Adjusted**	p-value
Age	Age	-0.0006	0.791	-0.0021	0.399
Sex	Male	*Reference*		*Reference*	
	Female	0.1327	0.028	0.0611	0.331
Education	No education	*Reference*		*Reference*	
	>=High-school	0.1053	0.396	0.0642	0.621
	Middle school	0.0777	0.639	0.0368	0.829
	Elementary	0.0489	0.701	0.0438	0.732
	Unspecified	0.4433	0.005	0.2171	0.624
Marital status	Married	*Reference*		*Reference*	
	Divorced	0.2057	0.034	0.1696	0.083
	Single	0.2354	0.022	0.1969	0.058
	Widowed	0.2110	0.028	0.1955	0.054
	Unspecified	0.3714	<0.0001	-0.0144	0.952
Region	Mexico City	*Reference*		*Reference*	
	North	-0.4446	0.001	-0.4861	<0.0001
	Centre	-0.136	0.092	-0.122	0.133
	South	-0.1050	0.201	-0.0724	0.382
	Unspecified	0.2713	0.013	0.1447	0.672
Symptom	cough	*Reference*		*Reference*	
	dyspnoea	0.1335	0.201	0.1127	0.278
	chest-pain	-0.0691	0.534	-0.0661	0.550
	haemoptysis	0.063	0.778	0.0280	0.900
	weight-loss	0.1040	0.527	0.1034	0.528
	other symptoms	-0.0040	0.962	-0.0290	0.735
	Unspecified	0.0720	0.416	0.0124	0.891
Diagnosis	NSCLC	*Reference*		*Reference*	
	SCLC	-0.6936	0.001	-0.6727	0.001
	Unspecified	-0.3240	<0.0001	-0.2527	0.035
Cancer stage	I-II	*Reference*		*Reference*	
	III	-0.3240	0.396	-0.1207	0.428
	IV	-0.1040	0.366	-0.1221	0.296
	Unspecified	-0.422	0.005	-0.1836	0.293
Institution	Public hospital	*Reference*		*Reference*	
	Private hospital	0.1727	0.006	0.1100	0.104
	Unspecified	0.2656	0.048	0.2211	0.107
Term	2019/2021	*Reference*		*Reference*	
	2013/2018	-0.0258	0.747	0.0210	0.813
	2007/2012	-0.2376	0.006	-0.1075	0.280
	2004/2006	-0.0783	0.524	0.0888	0.511

The geographic region did show some significant association with *Treatment interval*. Notably, individuals from the "North" region had a lower *Treatment interval* length (coefficient= -0.4862, $p < 0.001$), suggesting that the *Treatment interval* tended to be shorter for this region compared to the reference group.

Symptoms were not associated with the *Treatment interval* outcome. The diagnosis, particularly SCLC and the "Unspecified" category, had a significant association with *Treatment interval* compared to NSCLC category. Patients diagnosed with SCLC had a significantly shorter outcome (coefficient = -0.6728, p = 0.001, 6 days) compared to the reference group NSCLC. Similarly, those with "Unspecified diagnoses" had a shorter outcome (coefficient = -0.2528, p = 0.035). Although in the univariate analysis they were statistically significant, the stage of cancer, institution and term did not show a significant association with *Treatment interval* outcome.

Practical considerations in days in statistically significant categories: The median *Treatment interval* in this sample is: 15 days. As a result of back transformation from [log] coefficients into days for each category, results suggest people from the "North" experiences shorter time to treatment (8 days) compared to the people in Mexico City (12). Patients diagnosed with NSCLC: experienced longer time to treatment (13 days), versus 6 days among both SCLC and "Unspecified diagnoses".

6.4.2.7 Interval results summary

Overall, in LC care intervals among patients at the INCAN are associated with age, sex, region, symptom, cancer type, cancer stage and term. In contrast, institution from referral and education were not associated with untimely care in any of the

intervals studied. Each one of these covariates' role changes depending on the interval in question. For instance, sex is only relevant in three of the intervals studied and portray significant lags in women compared to men. Similarly, the unspecified categories seem to be relevant in some cases and not in others.

The intermediate model conducted only for the "Total interval" showed robust association with sex and cancer type, but not for age or education. Once adjusted for the complete set of variables the association between the outcome, sex and cancer type persisted with almost no change in coefficients.

The back-transformation from coefficients shows wide differences in some cases, but small differences in other that might be clinically negligible. Results from the other (proxy) intervals can be seen in **Appendix A2**.

6.4.2.8 Survival analysis

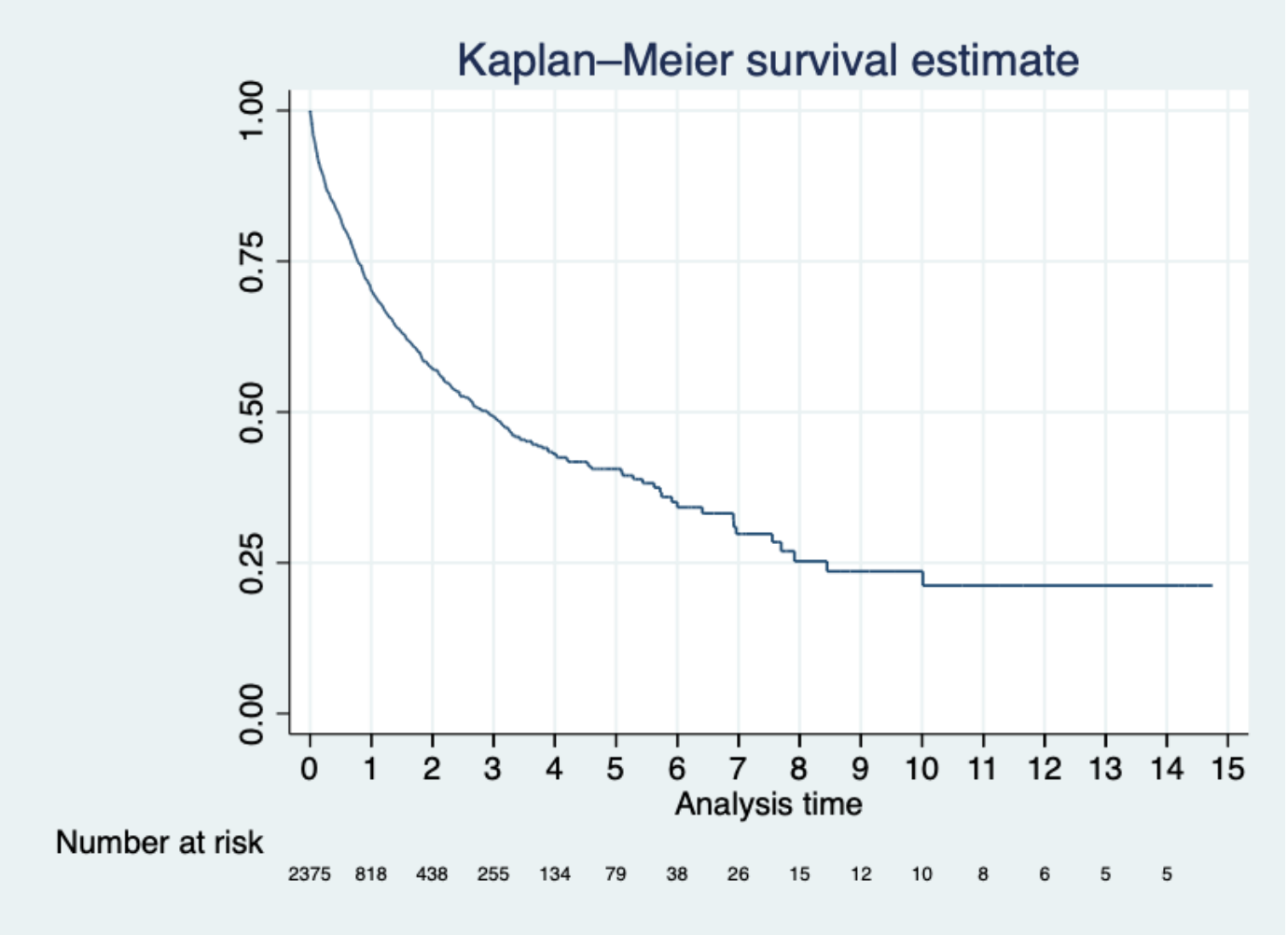
From the full sample, only 270 subjects did not have data for survival analysis. The total number of subjects with available survival data was N=2375. Entry time, representing the starting point of observation, was uniformly set at 0, using the date of diagnosis. Meanwhile the exit time was set as last visit or date of death and ranged from 1 to 5383 days, with a median exit time of 191 days. The overall time at risk for the cohort was 978997 days. The mean time at risk was 412 days. Within this sample 717 deaths were observed, and 1668 patients were right censored. Hence, approximately 17.00% of the total population experienced death over the observed period (2004-2021). Moreover, results revealed that approximately 39.49% of the population was lost to follow-up during the study period. This substantial proportion of individuals no longer under observation suggested various reasons, including dropout, withdrawal from the study, or loss to follow-up.

The Kaplan-Meier survivor function is presented in ***Table 6.13***. This table explains the survivor function value that ranged from 1 to 15 years. For instance, in Year 1 the probability of an individual surviving beyond is 0.7015. In other words, it indicates that 70.15% of the individuals in the study population did not experience the event of interest (death) up to time. Furthermore, a Kaplan-Meier plot shown through ***Figure 6.14*** illustrates the death estimates in the sample in years 1-15. The number of patients at risk at the start is N=2375 and rapidly goes down in the first year, leaving only 819 patients at risk in the sample. Additionally, ***Figure 6.15*** shows the survival Kaplan-Meier curves for years one 1-5 only. The survival probability differences between groups are illustrated across various Kaplan-Meier curves using years 1-5 only. ***Figures 6.16, 6.17*, and 6.18**.

Table 6.13: Detail of Kaplan-Meier Survivor Function

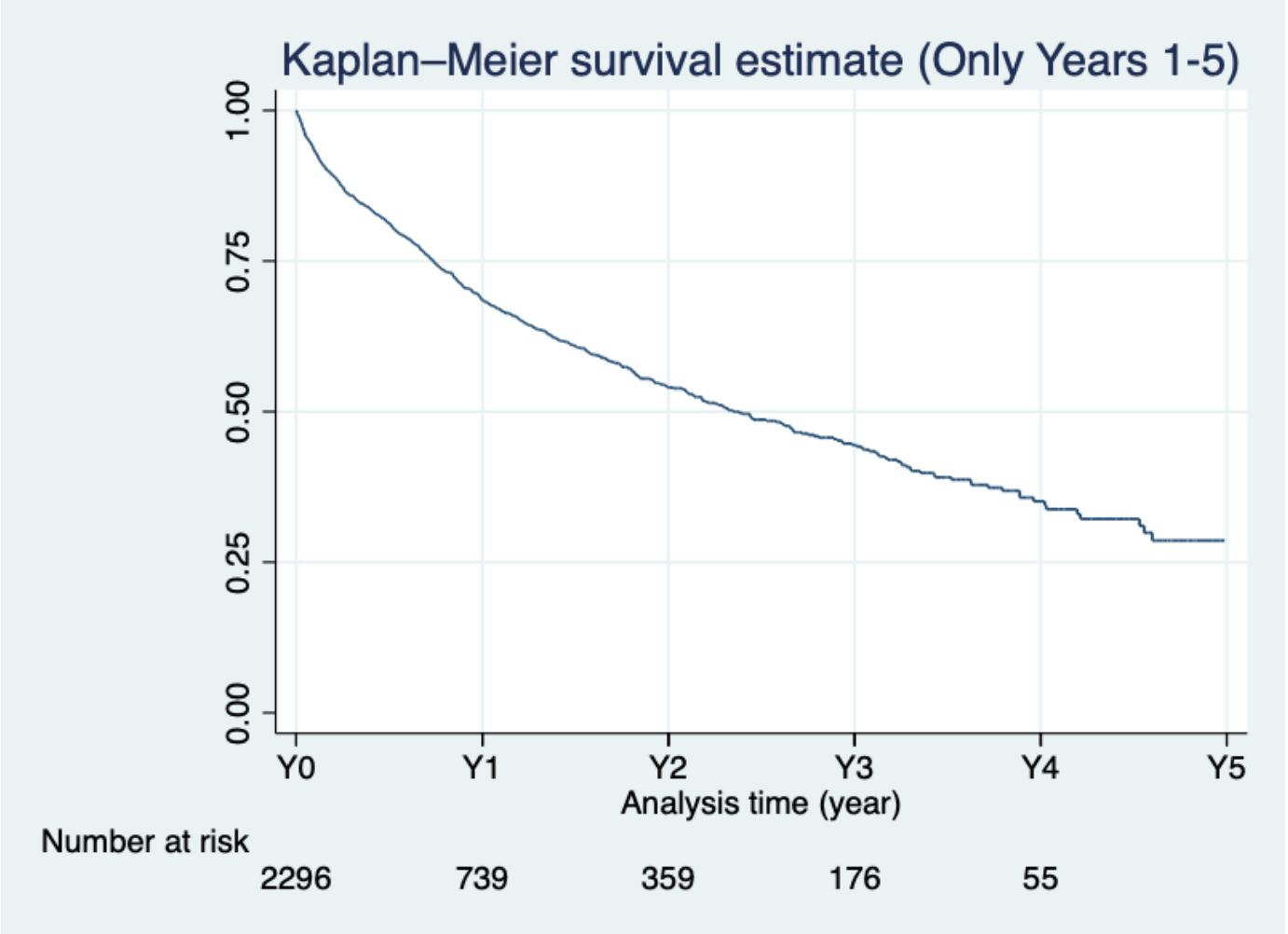
Year	People at risk	Deaths	Censored	Survivor function	95% Conf. Int.
Year 0	2375	490	1066	0.9958	(0.9922, 0.9977)
Year 1	819	126	255	0.7015	(0.6777, 0.7238)
Year 2	438	50	133	0.5711	(0.5425, 0.5986)
Year 3	255	26	95	0.4926	(0.4605, 0.5238)
Year 4	134	7	48	0.4310	(0.3951, 0.4664)
Year 5	79	8	31	0.4056	(0.3672, 0.4437)
Year 6	40	5	9	0.3420	(0.2918, 0.3927)
Year 7	26	3	8	0.2979	(0.2395, 0.3585)
Year 8	15	1	2	0.2526	(0.1862, 0.3242)
Year 9	12	0	2	0.2357	(0.1675, 0.3108)
Year 10	10	1	1	0.2357	(0.1675, 0.3108)
Year 11	8	0	2	0.2122	(0.1397, 0.2949)
Year 12	6	0	1	0.2122	(0.1397, 0.2949)
Year 13	5	0	0	0.2122	(0.1397, 0.2949)
Year 14	5	0	5	0.2122	(0.1397, 0.2949)
Year 15	0	0	0	-	-

Figure 6.14: Kaplan-Meier survival graph years 1-15 (N= 2375)



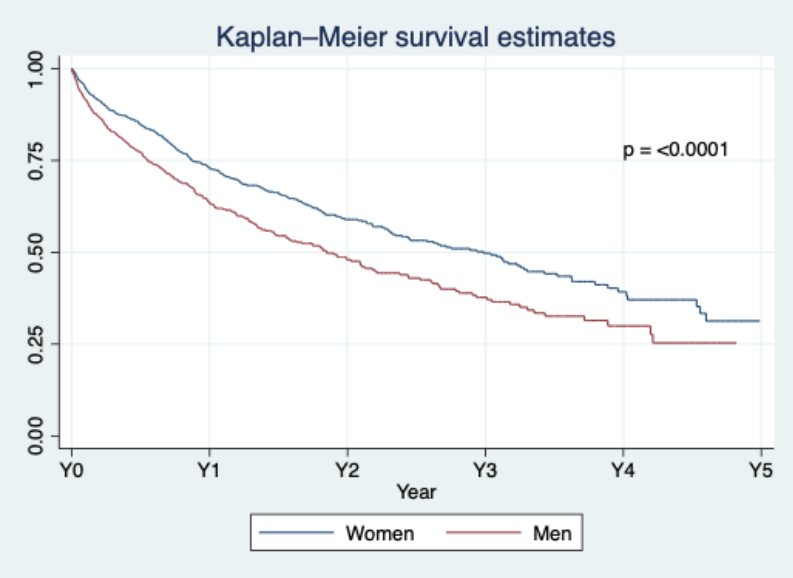
Source: Own work.

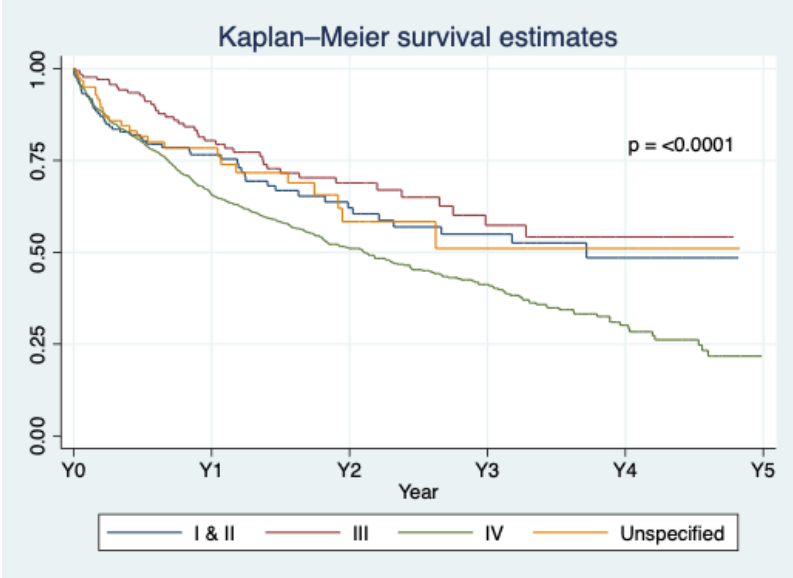
Figure 6.15: Kaplan-Meier survival graph years 1-5 (N= 2296)

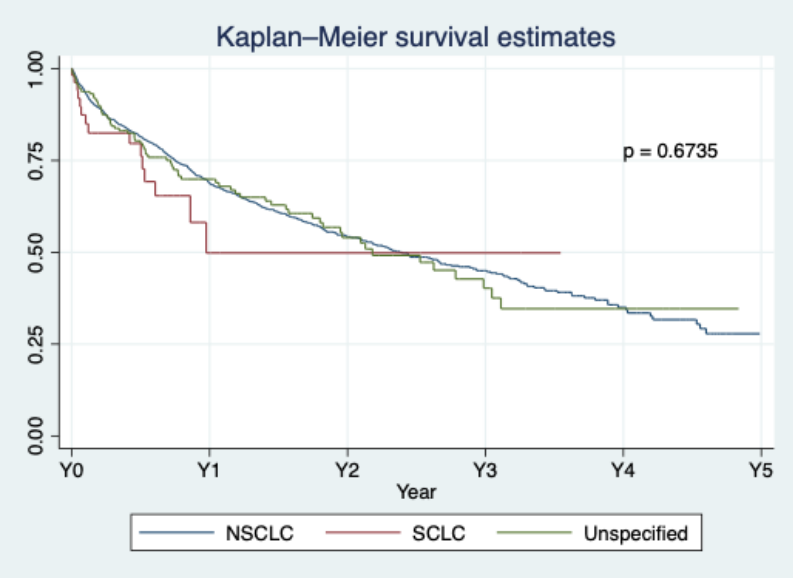


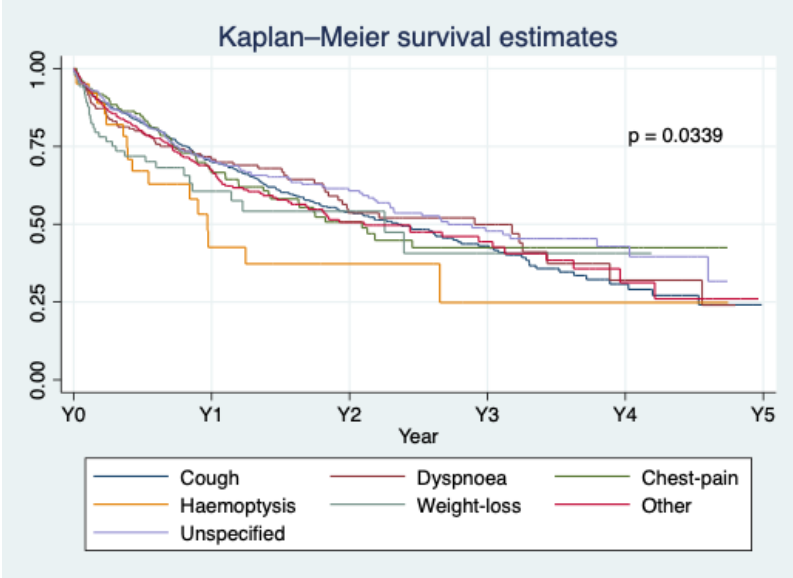
Source: Own work.

Figure 6.16: Kaplan-Meier survival graphs and Log-rank test results for covariates sex, cancer stage, lung cancer type, symptom



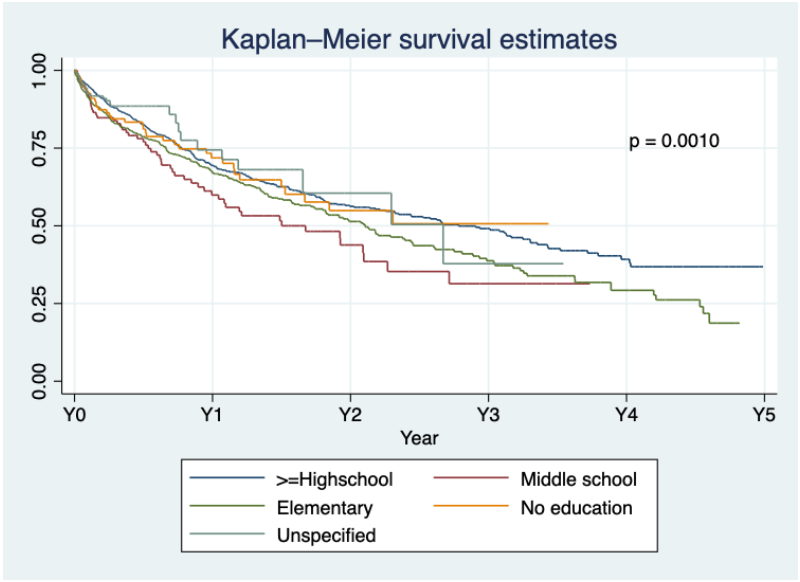


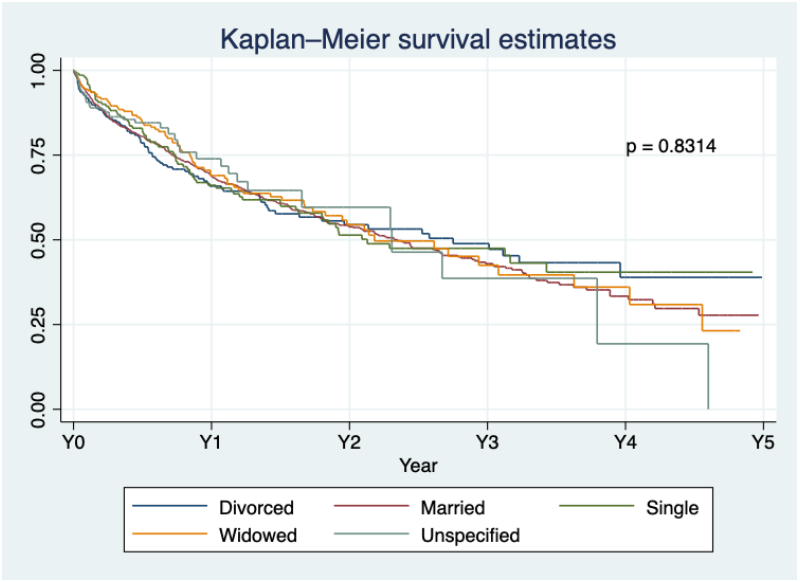


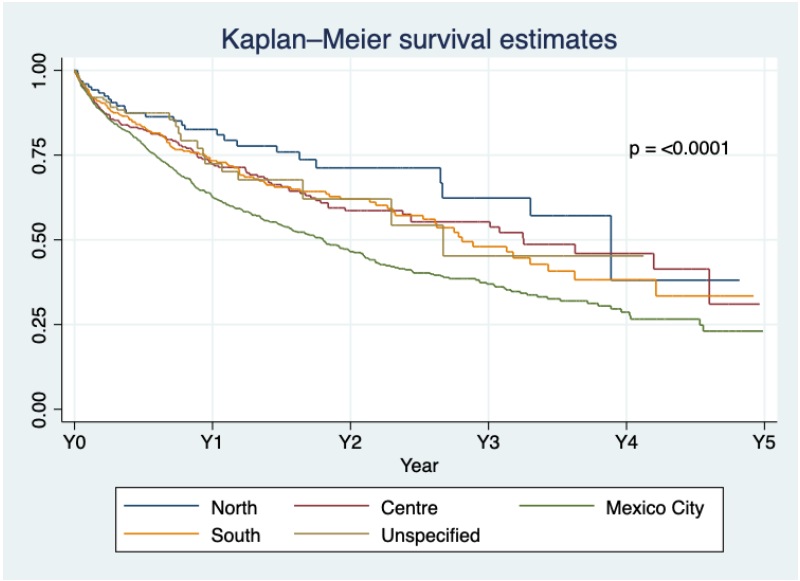


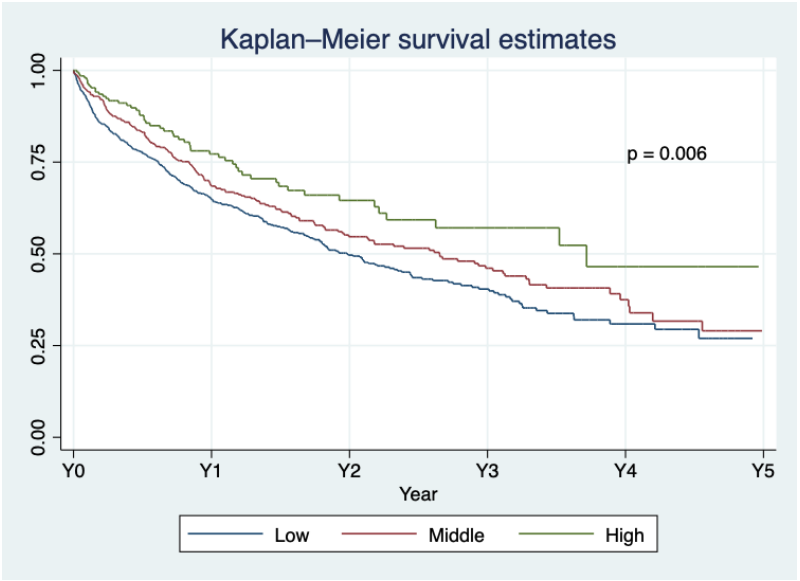
Source: Own work

Figure 6.17: Kaplan-Meier survival graphs and Log-rank test results for covariates education, region, marital status and socioeconomic position



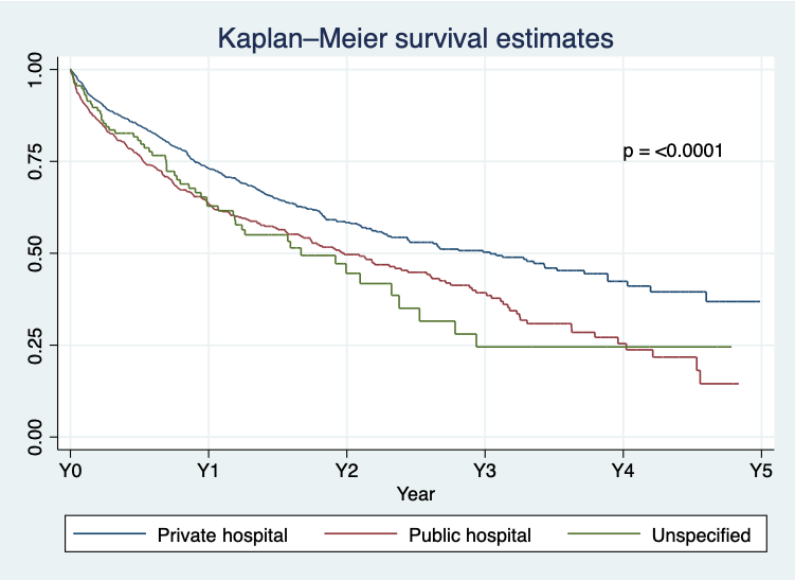


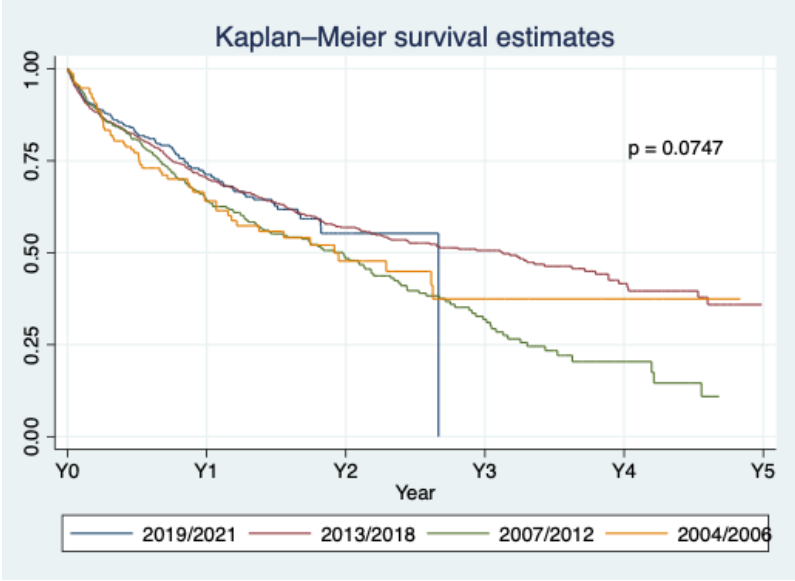




Source: Own work.

Figure 6.18: Kaplan-Meier survival graphs and Log-rank test results for covariates institution form referral and political terms





Source: Own work.

Results from the log-rank test are presented in ***Figures 6.16, 6.17*, and 6.18**. The p-values are presented inside the graph environment. Variables sex, cancer stage, first symptom, education, socioeconomic position, region, and place from referral show differences in survival curves that are statistically significant *(p-value <0.05)*. Whilst lung cancer type, term and marital status show the differences in categories are not statistically significant.

Moreover, results from ***Table 6.14*** present detailed information on the survival analysis conducted for women and men, over survival years 1-5. For instance, in the women group, at the initial time point (0 days), all individuals were at risk, but over the subsequent time intervals, the number at risk decreases due to deaths or censoring.

Table 6.14: Description of time at risk and survival from years 1-5 by sex

Time	At risk	Censored	Deaths	Survivor function	95% CI
Women					
Year 0	1235	224	525	0.9976	(0.925 - 0.9992)
Year 1	486	70	139	0.7445	(0.7133 - 0.7728)
Year 2	277	28	89	0.6180	(0.5800 - 0.6536)
Year 3	160	17	59	0.5416	(0.4988 - 0.5825)
Year 4	84	5	33	0.4706	(0.4214 - 0.5182)
Year 5	46	11	35	0.4380	(0.3845 - 0.4902)
Men					
Year 0	1140	266	541	0.9939	(0.9872 - 0.9971)
Year 1	333	56	116	0.6506	(0.6135 - 0.6850)
Year 2	161	22	44	0.5136	(0.4697 - 0.5556)
Year 3	95	9	36	0.4311	(0.3825 - 0.4787)
Year 4	50	2	15	0.3820	(0.3294 - 0.4342)
Year 5	33	7	26	0.3653	(0.3105 - 0.4203)

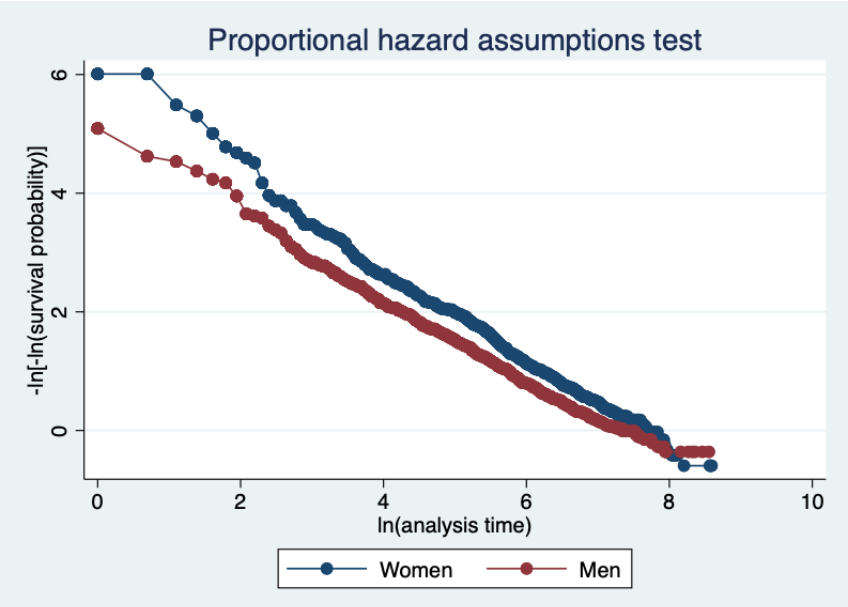
Lastly, the Cox regression analysis indicates a statistically significant association between sex and the hazard of experiencing the event of interest. ***Table 6.15*** evidence women experience 28% lower hazard of dying in the time studied compared to men (p-value= <0.0001) and 95% confidence interval ranging from 0.622 to 0.834, indicating a statistically significant association between the variable "sex" and the outcome (death). The proportional-hazards assumption for sex is met (p-value 0.0349), suggesting that the effect of sex on the hazard remains constant over time [197, 198]. See ***Figure 6.19***.

Table 6.15: Stata Cox Regression Results

Variable	**Haz. ratio**	**P>|z|**	**Confidence Interval**
Women	0.7209064	<0.0001	0.622 - 0.834
Proportional-Hazards Test	**Chi2**		
Global test	4.45	0.0349	

This analysis involved 2,375 subjects, with 717 failures observed during a total time at risk of 978,997 units.

Figure 6.19: Proportional hazards assumptions test



Source: Own work.

6.4.3 Discussion (quantitative stream)

Population and generalisability

Previously in ***Figure 2.5***, the population from the INCAN was explained to hold more accessibility to cancer care. In consequence, these uninsured patients are suggested to have better outcomes that their counterparts not diagnosed nor treated at the INCAN. Results from this thesis potentially show the best scenario amongst LC patients and the rest are expected to be longer intervals.

Prolonged Breast cancer vs Lung cancer care intervals in Mexico

With the purpose of comparing the time intervals with previous literature published on breast cancer in Mexico [139], **Figure F31** in the Appendix describes the LC intervals in median months [5].

In the background section of this chapter, **Figure** 6.2 illustrates the results obtained in breast cancer research [139]. It reveals a 7-month delay in the "*total interval*", compared to a 6.3-month delay in LC. Notably, the median interval time appears to be somewhat similar.

The *hospital interval* shows shorter time (2 months versus 0.8 median months in LC), and the *treatment interval* is also briefer (1 month versus 0.4 median months in LC). The diagnosis duration in this study, as determined through external diagnoses, was 1.7 months, which is notably shorter than the 4 months observed in breast cancer cases. However, it's important to note that these findings might underestimate the actual time spent in the diagnostic process. This is because they do not take into account the time from the initial medical consultation to the medical

[5] Among the total sample the median length for the "*total interval*" was 6.3 months, TDI=5.2 patient interval=3.5 months, health system interval=2.5 months, diagnostic interval (a)=1.7 months, diagnostic interval (b) 0.2months, pre-hospital interval=1.3 months, hospital interval=0.8 months, pre-treatment interval=0.4 months

institution responsible for the external diagnosis, which is separate from INCAN. Furthermore, to obtain a more comprehensive picture of the diagnostic interval, the additional 0.2 months identified in "Diagnosis b" (from hospital admission) must also be considered and added. Consequently, the time to diagnosis can only interpreted from the results that derive from "Diagnosis a" and "Diagnosis b" as partial segments of the complete diagnostic timeline.

In this case, the *appraisal interval* (patient interval) reveals more significant differences between breast cancer and LC. The results indicate a 3.5-month median in LC, while the breast cancer study found only a 0.3-month median. However, it's important to note that these disparities can be attributed to the way the patient interval is estimated. In this study, the patient interval considers external diagnosis as the final moment when the interval ends, whereas the breast cancer research concludes it with the first medical consultation.

Further research is needed to determine whether these differences are due to underestimation or overestimation of patient interval or if they genuinely reflect longer patient intervals in LC and shorter health system intervals compared to breast cancer.

Lung cancer care intervals in Mexico vs the literature

Literature uncovers striking distinctions in LC care intervals between Mexico and other nations [24, 63, 165, 199–207]. Particularly in the "pre-hospital interval" and "total interval", targeted improvements are needed in Mexico's healthcare system to mitigate untimely LC care (see ***Table 6.16***).

In the context of LC care intervals, Mexico stands out with the highest *appraisal interval* at 107 days, in stark contrast to Germany's mere 3 days [202],

highlighting significant disparities in how swiftly patients recognise symptoms and seek medical attention. Furthermore, Mexico's pre-hospital interval extends to 41 days, surpassing that of many nations, including the Finland [200] and Germany [202], indicating potential issues in timely referral and evaluation within the Mexican healthcare system. Interestingly, despite of untimely care in the earlier stages of the continuum, Mexico manages a relatively short *hospital interval* of 26 days, possibly indicating efficient in-hospital processes. However, an important data gap emerges in the form of the diagnostic interval, which Mexico does not provide, in contrast to numerous other countries, thus hindering an understanding of the diagnostic interval within Mexico's healthcare system. Overall, Mexico's total diagnostic interval reaches 160 days, suggesting room for improvement in the diagnostic process itself. Regarding the treatment interval, Mexico's 15-day timeline is similar to Finland [200] and Germany [202]. Lastly, Mexico's "*total interval*" surpasses all countries (192 days). This indicates that, overall, lung cancer care intervals in Mexico may be on par with or even longer than those encountered in other countries, depending on which interval is being observed.

Table 6.16: Lung cancer intervals in the literature compared to this study

Country	*N*	Appraisal interval	Health system interval	Pre hospital interval	Hospital interval	Diagnostic interval	Treatment interval	Total diagnostic interval	Total interval	Author
Mexico	2645	107 days	77 days	41 days	26 days	52 days (from external unconfirmed diagnosis) 7 days (from admission)	15 days	160 days	192 days	Own work
Finland	132	14 days		15 days			15 days		121 days	[199]
Finland	221						27 days		130 days	[200]
France	355			30 days		10 days	9 days		62 days	[201]
Germany	50	3 days		8 days		8 days	17 days		85 days	[202]
Poland	3479								78 days	[203]
India	265					23 days	24 days			[204]
Spain	415						27 days		87.5 days	[205]
Sweden	466				49 days				140 days	[206]
Turkey	101					16.4 days	24.7 days			[63]
UK								112 days		[165]
UK		21 days						91 days		[24]
USA	129								84 days.	[207]

Yearly increases in the diagnostic and treatment intervals have been previously described in the literature due to staging procedures, molecular testing, and imaging [126]. For instance, in the USA [207], the median day to treatment increased from 26 days in 2004 to 34 days in 2013. In this study, an increase of approximately a week is observed in the *treatment interval* from 2014 onwards. This is relevant as, each week of treatment delay results in a 3.2% drop in survival for stage I NSCLC [126]. In the advanced stages of the disease, untimely care's toll on survival is expected to be even higher [126].

Total interval

LC care intervals increased from 2004 to 2021 in the "total interval" (147 vs 212 median days). These differences can be due to the COVID-19 pandemic in the most recent years [53, 188, 195] but also, due to potential policies being instrumented during those political terms [46, 48]. More research is needed to comprehend the nature of the untimely care in years 2004-2012. Future efforts should be done to compare all intervals per year or use other terms as a reference to evaluate the effect term has in the "total interval".

Compared to the literature, Mexico has the highest "total interval" among patients with LC compared to other countries (see ***Table 6.16***). Younger women seem to be the group that is most at risk for being treated later. In the literature, untimely care among women has also been found (65 days vs 18 days in men) [202]. In Mexico particularly, increased intervals among young women with breast cancer were confirmed [143, 208]. These have been reported to be due to occupation or duties as a carer [202]. Women compared to men might experience many diseases differently due to differences in education, self-efficacy and economic autonomy might also take a toll on the timeliness women have in their LC

journey [64, 143, 209–212]. Hence, so far, this study finds similar results to the ones found in a similar breast cancer population in Mexico.

Highly specialised cancer services are concentrated in Mexico City [46, 48]. This study, like others in Mexico [143], indeed evidence patients from the full sample come from other regions and travelling to Mexico City to receive care. A case in the qualitative stream even mentions travelling by plane from other regions to achieve care. Moreover, the quantitative analysis shows that people from the "North" (N=162) are being treated earlier and have better survival outcomes than people in Mexico City. One potential hypothesis that can explain the differences might be that the INCAN is speeding up care for people who live farthest. However, the same is not happening for the people who also come from far away from the "South". Hence, further analysis was conducted to understand differences in the "total interval" outcome and in fact, people from the "North" hold higher SEP than people from Mexico City (3.5 vs 2.7 in a 1-6 SEP scale). Furthermore, 71% of the patients from the "North" have a high-school degree or higher vs the population from Mexico City 53%. These results imply that in fact the INCAN is receiving patients from other northern states but generally these have higher SEP, potentially broadening health inequalities. Efforts to reduce the gaps in healthcare between regions should be prioritised.

This study shows, depending on the symptom, a patient has a completely different outcome. For instance, among the patients that held a recorded symptom, only 2.4% experienced haemoptysis; they experienced timely care but worse survival. In the literature, this symptom is present in 4.6%- 21% of LC patients [24, 56, 181, 213], haemoptysis holds a highly predictive value for malignancy [164, 181] and it is more commonly associated with NSCLC. The negative association with the "total interval" in this study suggests this symptom

is related to shorter time to treatment compared to cough. This seems likely as cough might be initially studied as a respiratory infection and holds little positive predictive value compared to haemoptysis [181]. Worse survival can possibly be explained by the higher stage of the disease at the time of symptomatic presentation.

A similar effect is found in other symptoms such as dyspnoea, chest-pain, other symptoms, and unspecified symptoms. This is further supported by the qualitative study that mentions acute more worrisome symptoms spark an immediate search response compared to cough. In theory, differences in symptoms should not generate any difference in cancer outcomes. However, in Mexico and other countries patients have been previously described to have lack of awareness of cancer [54, 143]. Additionally, GP's might not recognise a high-risk patient and/or might be unaware of the referral guidelines [63, 171]. In consequence, the implementation of RAT in Mexico could guide GP's and aid them in understanding their patients' symptoms, expediting diagnosis [181] and reducing healthcare inequalities.

Compared to NSCLC, shorter "total interval" were experienced by SCLC in this study (191 days vs 127 days). More timely care amongst patients with SCLC has been previously described in the literature [79, 199, 202, 214]. A potential explanation can be due to reduced access for targeted therapies and immunotherapies amongst the population diagnosed with NSCLC. Nonetheless, SCLC shows worse survival compared to NSCLC. This has also been described in the literature as SCLC has higher stages of the disease at the time of diagnosis [15, 16].

Cancer stage is statistically significant and shows a negative association with *"total interval"*. This can be potentially a result of higher stages being treated

earlier. This has been widely addressed by the literature as the sicker quicker paradox [56, 215]. In this case, it refers to the rapid response the healthcare system has when the disease is more symptomatic. Furthermore, this becomes even more complex when the paradox also takes place in the patient's home with family members and carers.

Total diagnostic interval

Terms were found to be relevant in the *Total diagnostic interval*. Compared to 2019-2021, from 2004-2012 there were shorter diagnostic intervals. This suggests that in the macro of things, policies taking place in those years (i.e., Seguro Popular, INSABI, etc. [46, 48]) might have had an impact, leading to a shortened *total diagnostic interval*. More research should be done to understand what type of interventions were done then and if it coincides with these results.

In the literature, the TDI in the UK was 91 days and 112 days in USA [165, 202]. In this case, Mexico has a TDI of 160 days. Due to the fact this interval excludes the time from diagnosis to treatment but includes the total time from symptom onset to diagnosis, this interval roughly explains the appraisal interval. In the literature the appraisal intervals has been previously described to be the one that causes prolonged intervals in LC [63]. Longer TDI in this case might be attributable to in longer appraisal intervals taken in the account. Hence, it might explain the longer intervals compared to breast cancer and compared to other countries.

Like in the literature [202], this study shows women experience longer TDI than men. Furthermore, older people tend to be diagnosed earlier. This is similar to results found in the literature [216, 217]. This shows that before the population begins treatment, younger women are the people at most risk of untimely diagnosis.

This is similar to results found in breast cancer in Mexico [143, 208]. One potential explanation for younger women not reaching diagnosis earlier might be due to lack of awareness of the disease and lack of cancer suspicion at the first health care service consulted [143, 208, 218, 219]. Women perceiving themselves as not being at risk seek care later [218, 219]. Another explanation for this might be due to lack of empowerment, lower SEP or caring duties [12, 62, 143]. Results from the qualitative stream support this.

Although dyspnoea is not highly predictive of LC [181], this study shows its presence was associated with timely care. This might be explained by the "Código Infarto" programme installed in Mexico, that prompts rapid referrals for myocardial infarction symptomatology [220]. The "other symptoms" category (included neurological symptoms) similarly could raise high concerns in the patient and family member and thus reduce time to diagnosis. Results from the qualitative stream support this. However, it is still unclear why not having a specified symptom could lead to shorter time to diagnosis. Potentially, these patients experienced symptoms that arose worry quite quickly, reaching earlier care. The reason for the symptoms being missing might be due to lack of incentives to write all data in EHR and also the transition to an EHR, potentially leaving out important medical records and a detailed description of symptoms. In the future, data imputation could help identify what symptoms were in this population.

Diagnostic Interval (a) (from external diagnosis)

Results from this thesis suggest that patients have missing data regarding stage and lung cancer type, despite being previously partially diagnosed. Hence, not having a lung cancer type or stage in this thesis does not imply that the patient did not have cancer, but that its missingness might be due to issues in transcribing results into

the EHR.

People with the categories "unspecified symptoms" and "unspecified lung cancer type" were associated with longer intervals from external diagnosis. Whereas "unspecified cancer stage" was associated with shorter intervals. In the literature, patients with SCLC have shorter diagnostic intervals [215]. Hence, this population is behaving like people with NSCLC and in higher stages; but showing more prolonged intervals than cough. In the future, potential data imputation could be useful to reveal who these people are.

The analysis in the diagnostic interval (from external diagnosis to internal diagnosis) shows women tend to be diagnosed later after being partially diagnosed in another hospital. In the literature, women have been found to have longer intervals than men [143, 202] and the reasons for this have been previously described [64, 143, 209–212].

People with weight-loss tend to be diagnosed earlier. This is congruent with the literature, as weight-loss is highly predictive of LC [181] and might help healthcare workers seek a confirmatory diagnosis. However, at this stage, the patients first symptom has already been identified by primary care and somewhat confirmed by secondary care. More research should be done to evaluate when the symptoms should not be adjusted for across the cancer continuum.

Stratifying the full sample into two groups for this particular outcome might be useful in determining whether the population is different (patients that are diagnosed externally and those diagnosed internally might). This might prove that in fact we are dealing with different population groups. Further research using qualitative and quantitative methods could further uncover the differences between these groups.

Unlike results found for breast cancer patients in Mexico in the diagnostic interval [143], the place from referral (medical institution) did not significantly impact *Diagnostic interval a*. However, this study does not capture the full diagnostic interval but rather the time to diagnosis from either admission or external diagnosis.

Diagnostic Interval (b) (from admission)

Unlike other intervals, the analysis revealed that as individuals age, the duration of time required for diagnosis tends to increase after being admitted to the hospital. In the literature, prolonged intervals in the older and younger generations with lung cancer have been both confirmed [166, 215] and dismissed [221]. However, in other intervals, normally the association is inverse; younger patients tend to be diagnosed later when facing a lung cancer [216, 217, 222] and other cancer diagnosis [143, 223, 224]. The observed difference in the Mexican context highlights the possible obstacles faced by elderly individuals within a hospital setting. Upon the patient's admission, the diagnostic procedure should proceed in a straightforward manner. The findings derived from this qualitative investigation further confirms that patients encounter several hurdles of cultural, economic, and other natures, which might contribute to prolonged intervals in diagnosis. These barriers encompass factors such as patients' reluctance to inconvenience a family member, fear, economic struggles, etc. These barriers have been further described in the literature [143, 172, 183, 225, 226].

According to these results, the hospital is apparently providing enhanced access to medical services for patients who live in states in the "North" region, compared to Mexico City. However, as it was previously described in results from the *"total interval"*, "North" hold higher SEP and educational attainment

than people from Mexico City. In this case, understanding the regional variations in *diagnosis b interval (from admission)* is critical for hospital patient navigation interventions and surely an equity indicator of patients being supported by the health system.

Although haemoptysis is highly predictive of LC [181], patients with haemoptysis are diagnosed after patients debuting with cough (8 days vs 3 days after being admitted). In contrast, in the *"total interval"* patients with haemoptysis are treated earlier. However, from a therapeutic perspective, a mere three-day discrepancy may not provide significant implications. Potentially, at the time of diagnosis (after being admitted), the symptom-type might not be as relevant to determining any untimely care, and thus is not important to adjust for it. These contrasting results between haemoptysis' negative vs positive association with timeliness should be further studied across the cancer continuum.

In the qualitative stream, deferrals of care due to affiliation in a similar population were mentioned for breast cancer patients, which further supported the inclusion of it in the quantitative analysis [143]. Hence, in the *diagnosis b interval (from admission)* differences were expected due to institution of referral [143]. Nonetheless, these differences were not statistically significant for lung cancer patients in Mexico. This means that even if you are from the IMSS or any other institution, the time to diagnosis after admission remains unchanged. These results might be explained by how the variable was collected, altering the results of study and the fact that the diagnostic interval is split into smaller pieces rather than the full diagnostic interval. More research will need to prove the association of institution from referral with diagnosis.

Moreover, patients with stages IV and the unspecified stage experience

reduction in the number of days in the *diagnosis b interval (from admission)*. This again supports the sicker quicker paradox [56, 215], with less days in stages IV and in the unspecified category.

Although term seems to hold a more important role in the definition of the *diagnosis b interval (from admission)* during the unadjusted regression; only 2007/2012 remained significant after adjustment. More research should be done to understand why these particular political terms show shorter outcomes and if particular hospital policies defined timeliness in this term.

Hospital interval

There appears to be an association between marital status and hospital interval, with divorced or widowed individuals exhibiting lengthier intervals compared to their married counterparts. This association has been previously evidenced in other types of cancer [183, 227] and in the Mexican population with breast cancer particularly in the appraisal interval [143]. In the literature it is hypothesised spouses, carers or family may have a substantial impact on encouraging the individual to seek medical treatment and act as facilitators in the hospital environment [183]. Conversely, the absence of an additional individual might also result in a delay in receiving care. For instance, in the qualitative stream of this study certain individuals lacking a substantial companion encountered difficulties in independently accessing healthcare facilities. Thus, marital status as a measure for social support seems relevant while studying in LC care intervals.

It is noteworthy that the region of patients' residence exhibits an association with the hospital interval. Specifically, those residing in the "North" region have a *hospital interval* of 15 days, while those in the "Centre" and "South" regions have 20

and 19 days, respectively. In contrast, patients in Mexico City have a longer median *hospital interval* of 24 days. Despite its seeming contradiction, there is a possibility that the INCAN is facilitating expedited access to care for patients residing in other states, particularly those who reside at a greater distance. While this proposition remains purely theoretical in nature, differences across these categories holds little therapeutic relevance. Furthermore, as previously mentioned people from the "North" are better off compared to the rest of the regions. Hence, as previously found in the breast cancer population in Mexico [143], SEP inequalities should be further studied and addressed to mitigate differences and extended waiting times in cancer care.

The unspecified diagnosis category was kept due to patients not reaching diagnosis by the time the data from EHR was extracted. This has been previously observed in the literature and although it suggests bias (attrition) in these data collection methods, the lack of patients' diagnosis in this case was not due to time not being enough to capture the diagnosis itself. Patients from 2004 exhibit the pattern of not having a diagnosis and the data collection happened between 2020-2021. It is noteworthy to mention the *hospital interval* is as short as 12 days for these unspecified patients. Potentially, these patients might have been given palliative treatment and therefore explain the shorter hospital interval. Such effect has been previously described in the literature [3]. Further research should include treatment type and discern if the treatment is rather palliative or curative.

Cancer stage in the *hospital interval* demonstrates the "sicker quicker paradox" [56, 215]. More research needs to be done on the type of treatment provided and if that makes a difference in the hospital interval.

In the future other variables could explain variations in this outcome

further, such as: PET-CT performance, number of pathology samples, number of radiological studies, total studies, time until CT performance, time until histological sample or time until pathology report [228].

Treatment interval

Surprisingly, age and gender appeared to have no substantial impact on the *Treatment interval*. In the literature, differences in the timeliness in treatment between age groups have been found [215]. This suggests that the interval was not influenced by the patients' age or gender. This finding could reassure both patients and healthcare providers that the *Treatment interval* remains consistent across different age groups and sex. Similarly, education and marital status failed to exhibit any meaningful association with *Treatment interval* outcomes. This implies that socioeconomic and marital factors may not significantly influence the *Treatment interval*, eliminating potential sources of health disparities.

The geographic region emerged as a determinant of shorter *Treatment interval* for patients in the "North". However, as previously mentioned region "North" holds higher SEP and educational attainment. Further investigation into regional disparities in healthcare access should be prioritised as this seems to be a constant through-out this study.

The most significant and important association in the treatment *Treatment interval* is type of cancer. Patients diagnosed with SCLC experienced significantly shorter outcomes, as did those with Unspecified diagnoses. Previous literature has found similar results where SCLC patients are treated faster [79, 199, 202, 214]. This underscores the importance of tailoring *treatment interval* approaches and intensifying efforts to improve outcomes for patients with NSCLC.

The stage of cancer did not significantly affect the *treatment interval*. This discovery indicates that the *treatment interval* exhibited similarity across all stages of cancer, hence challenging the notion of the "sicker quicker" paradox in this context. Potentially, once entering the hospital environment, patients are treated within the same timeframe regardless of their stage. This finding could reassure both patients and healthcare providers that the *Treatment interval* remains consistent across patients at the INCAN.

Unlike results found in the international literature for lung cancer [229], or for breast cancer in Mexico in the diagnostic interval [143], the type of medical institution did not significantly impact *Treatment interval* outcomes. This implies that coming from both private provided comparable *Treatment interval* results to public hospitals. Policymakers may find this result reassuring, as it suggests that *Treatment interval* is not strongly contingent on the institution's type. However, it is noteworthy to mention that the sample patients in unspecified category were less treated (78%), compared to the public and private institutions (87% and 88% respectively). Hence, more research should be done to fully understand the role of the referring institution with the treatment outcome and interval.

Political terms had no discernible effect on *Treatment interval*. This indicates that the outcome remained consistent over different terms. However, ongoing monitoring and quality assurance in *Treatment interval* should continue to ensure this consistency.

Survival Analysis

In the literature, prolonged intervals in cancer care have not been fully linked to reductions in survival [200, 230, 231]. Suggesting that fast-track approaches

might not improve lung cancer outcomes [200]. This study adds to the survival literature women are at lower hazard of dying during the period studied compared to men. Results from this thesis further evidence women, despite longer total time to treatment, generally exhibit improved survival rates. In the literature diagnosed with LC often have unique risk factors such as exposure to indoor cooking fumes and secondhand smoke [206]. Despite longer time to treatment, women show improved survival rates across cancer stages and treatment modalities, even when accounting for factors like smoking history and age [206].

Lower socioeconomic position, people from Mexico City, and public institution from referral seemed to experience worse survival. These variables should be used in the future to fully adjust for in a cox model and evaluate the role of these variables in mortality.

Cancer stage being consistent with mortality was expected in the Kaplan-Meier Plots. Although symptoms were significant in the log-rank test, symptoms could potentially be in the causal pathway. The inclusion of these in future cox-models should be further analysed and potentially excluded.

The inclusion of survival in this thesis serves to observe how it behaves across time from 2004 to 2021. The thesis findings underscore the importance of accounting for censoring and dropout in survival analyses, as well as the critical role of rigorous data collection and follow-up procedures in ensuring the validity and reliability of survival analyses.

Surprisingly, the type of cancer was not significant in the survival analysis using the Kaplan-Meier curves. This was not expected as there is literature on the differences in survival posed by the different cancer types. Thus, this suggests that

the third variable: unspecified cancer poses some noise that creates the illusion of non-significance and overlap with NSCLC. This is again one of the many challenges that the Mexican system will keep on facing when not collecting data routinely through the electronic record and using data extraction from the medical narrative as a means to collect diagnosis. Nonetheless, it will remain an issue in the case that the pathology report is not provided because the patient is lost to follow-up. Further research needs to be done to be able to define a clear strategy on how to handle data and how to conduct these types of analysis.

While the Kaplan-Meier estimator is robust and widely used, violations of these assumptions can affect the accuracy and reliability of the results. Potential issues with this method are individuals were not accurately followed up until the event of interest. Some patients were lost to follow-up, and no data was recorded on the EHR about the date of death. This was exemplified since **Figure 6.11** explained not all patients are diagnosed, treated and many are lost to follow-up. Potentially, those who are censored have different socio-demographic characteristics to the patients who are followed up throughout the cancer continuum. More efforts should be placed by health professionals collecting data on their day-to-day consultations, in gathering information from the patient's last visit or death.

In the past, survival was evaluated in the same population [232]. Results showed increased survival among the patients that were enrolled in clinical trials. In the future, adding the RCT as a covariate, might prove interesting to validate results.

6.4.4 Limitations

The data was collected retrospectively using the EHR. As described in the methods section, some calculations had to be done to be able to generate intervals. This might

render incomplete outcome elicitation and incomplete recording, thus introducing biases [54]. Although this approach will not render exact dates, overall, the potential margin-error is expected to be distributed across the full data-set. Moreover, this study did not employ double entry of these dates, thus preventing systematic assessment of the margin of error.

In our exploration of patient journeys, a significant limitation arises from the exclusive focus on continuous dates in our methodology. By adopting a linear approach, it is inherently assumed that one date follows another, providing a sequential representation of the patient's medical trajectory. While this methodology offers valuable insights into the progression of a patient's condition over time, it inadvertently neglects crucial aspects of the healthcare experience.

One notable omission in our linear analysis pertains to events characterised by repeating treatment dates. In the realm of medical research, patients often undergo periodic or recurrent treatments that do not conform to a straightforward chronological sequence. These interventions may span varying intervals and possess unique patterns, challenging the linear narrative we've chosen to dissect. Consider a scenario where a patient undergoes a series of rehabilitation sessions or periodic diagnostic tests. These recurring events are essential components of the patient journey, contributing significantly to their overall healthcare experience. Unfortunately, our current methodology fails to capture the nuances associated with these repetitive yet critical interventions. To address this limitation, future research endeavours could explore alternative methodologies that incorporate a more comprehensive representation of patient journeys. This might involve integrating data on repeating treatment dates, implementing innovative modelling techniques, or considering the development of a hybrid approach that combines both linear and non-linear perspectives.

Furthermore, the "patient delay" analysis is retrospective in this thesis, relying on patients who have already sought care [64]. Thus, to fully understand the appraisal interval, prospective studies on symptom interpretation are suggested [64]. Also, this thesis leaves out patients who did not reach care in the first place.

Cancer stage, type of cancer and term were significantly associated with differences between the complete and the incomplete sample. Thus, patients left out of the analysis are different from the population included in the regression analysis. Similarly, in the context of missing-not-at-random in time intervals, data is missing in a way that depends on the unobserved values. In other words, the probability of data being missing is potentially related to the value of the unobserved data itself. This introduces bias into the analysis because the "missing interval" group might be different from the "complete data" group. Nonetheless, it is possible that the social determinants of health explain why some patients have less data than others. For instance, missingness of interval data was more prevalent among the lower Socioeconomic and low educational attainment group. Similarly, people not belonging to category "married" seemed to be more frequently missing the interval data. This might be explained for instance due to the support system patients had through family members, particularly their partners in remembering dates.

Another particularity of "missing interval" data group is the fact that most had increased recorded stage I cancer. In fact 55% (124 observations) of the patients with stage I cancer are missing the *"total interval"*. This raises the following questions: why would stage I cancer be associated to "missing interval" data? and is it due to not having the first symptoms date or the treatment date? Taking *"total interval"* as an example, 58% of patients did not have a first symptom date but had treatment at the INCAN (471 observations), meanwhile 30% of the population

missing the "*total interval*" was due to not having a treatment date but having specific symptom date. Only 94 observations had none of the dates that compose this interval. Hence, a potential hypothesis for this is that patients did not have a particular symptom and potentially that is why a date is missing in the EHR. In the literature asymptomatic patients make up to 7-13% of LC [233]. If this was the case, these people would have been left out of the study anyway, due to having a different pathway of diagnosis, for instance screening or a clinical finding. In any case, as not much data exists on EHR that describe these unique situations, one takeaway from this result is EHR should capture whether or not this was a patient diagnosed through a screening programme or whether the presentation of the patient was due to clinical finding during another procedure or in fact due to active symptoms. This would render the analysis much easier and without bias.

Overall, in the "missing interval" groups across intervals there was a tendency for patients to not be experiencing "cough" as their primary symptom. Hence, beyond the patients that did not have a symptom or a symptom date, these patients surely had a symptom in their EHR. This raises the question of whether the patients had a significant clinical difference due to having different symptoms and whether these were potentially in higher or lower stages of the disease. More research needs to be done to understand the differences from the missing and the complete interval data groups across intervals. By continuing to compare the population groups, research will be able to adjust how data is collected and overcome barriers that might lead to selection bias.

Perhaps one of the most important limitations in this study is the fact that many dates were not collected due to being originally not captured by the oncologists at the time of the medical visits through the EHR. This then limits the time intervals being analysed in this research and compared to the international literature.

Nonetheless, these findings serve as a basal measurement of the "*treatment interval*" and "*total interval*" in Mexico.

Previous studies have demonstrated that patients often made multiple visits to their primary care physician before additional investigation was initiated [3]. For the same reason as before, this study unfortunately couldn't capture more data on the number nor type of previous medical visits. This is mainly due to the fragmented healthcare system and the inability for them to share information between them. However, through the qualitative study in this thesis, the number of visits pointed out were 2.5 ranging from 1-13 amongst the patients interviewed. In the future, more data should be collected on dates and number of GPs if research is to be conducted on this topic and compared to the literature in the UK.

Although data was missing due to health system factors, proxies were generated in this thesis to be able to capture "proxy intervals". ***Figures F13, F12, F14*** described the interval availability for the PhD according to previous frameworks and ***Figure 6.13*** also showed the median days for the "proxy intervals": patient, health system, diagnostic and pre-hospital intervals. All of these "proxy intervals" assume the date the patient enters the health system starts with the date of external diagnosis, ignoring the date of first healthcare visit. This is biased because patients started their pathway to care before reaching a diagnosis outside of the INCAN. This means the current results presented through ***Figure 6.13*** of the "proxy intervals" could all be under or overestimating the time spent in each one. ***Figure F13*** explains the under or overestimation concept using the red arrows.

For instance, this study does not exactly point out how much time is spent in appraisal and how much in the health system interval (107 and 77 median respectively in each "proxy interval"), but rather is an approximate of the time spent

in each. There are patients who, before entering the INCAN did not visit another institution and those who did, rendering mixed results. Nonetheless, this research provides a foundation for assessing LC care intervals and is valuable for identifying gaps in data and determining the kind of databases that need be developed within the healthcare system to facilitate such investigations.

The analytical and reporting approaches were robust and performed according to the methodological approaches and definitions recommended in the Aarhus statement [2]. Nonetheless, due to the lack of an EHR in primary care in Mexico, unlike the UK, there is no General Practice Research Database [165] to collect first symptoms from. Hence, symptoms from this database were self-reported and captured from the patients' narrative by medical doctors. Moreover, 93% of them were symptoms that initiated less than a year of the first health visit captured by the EHR at the INCAN. However, this patient interval is a proxy, as the EHR does not capture what happened in primary care, but rather what institution or hospital was visited before the INCAN.

Furthermore, literature suggests that symptoms from such distant past are unlikely to be related to LC [165, 181]. This study did not use first medical encounter to filter these symptoms. As a result, some patients have an *appraisal interval* of over two thousand days. Moreover, other authors propose that the symptom may indeed be the same but might have changed in form or frequency over time [181]. This could be a limitation of our study, as it only captures the primary symptom for which the patient seeks medical attention and the symptom that causes the most concern, but it does not collect data on whether the symptom changed or the date of any such change. Gathering information on symptom changes and their corresponding dates might be challenging to recall and captured through qualitative and methods.

In further studies a new categorisation of symptoms might be useful to use all the symptoms categories that have been found to be associated with a LC diagnosis [68]. For example, chest and shoulder pain, fatigue and weight-loss might be paired together [68]. This would reduce the number of patients pilled-up together in the "other" category and might be useful to further analyse the role symptoms have in prolonges intervals of care. Furthermore, in this study all the symptoms were kept despite the time they appeared. This could render the study with some bias.

When studying "patient delay" or the "appraisal interval", individuals are asked to define the evolution of symptoms related to their cancer, establishing a connection between bodily sensation, symptom, and cancer diagnosis [64]. Notably, symptoms do not emerge solely as physiological realities; their recognition as symptoms depends on social confirmation, influenced by an individual's social position. Gender roles also play a role, with studies indicating that traditional female roles may affect symptom interpretation [64]. However, a challenge in investigating *appraisal interval* lies in the lack of a validated measure, hindering the understanding of its causes and impact on morbidity and mortality. Current studies on patient delay often overlook existing theories on symptom interpretation, adopting a simplistic view [64]. To enhance measures of patient delay, it is essential to consider the complexity of how people interpret symptoms [64].

Cancer stage was not captured at the time of treatment but rather at the time of diagnosis. Therefore, studying associations between the length of the intervals and the stage at which a patient is treated is not viable due to only having the stage of the disease captured at the time of diagnosis.

This study assumes the patients in the "unknown diagnosis "category indeed have LC and have not and will not change to other disease. This however is unlikely in patients from the early 2000's, but is highly possible in recent years when diagnosis is still underway.

Another limitation is diagnosis is considered the same, regardless if it was extracted from a pathology report than from the clinical narrative in the EHR.

Data was collected from EHR during 2020 and 2021. Unlike the qualitative streams of this research, LC care intervals in care are evaluated from 2004 onwards and thus capture more than just intervals during the COVID19 pandemic. Nonetheless, data from observations being collected during these years are potentially different to the patients that came before 2020. Thus, the period of reference was 2019-2021 to potentially notice differences between these periods.

In the literature, wide inequalities in completion rates have been found in LC. Particularly black communities in the USA have been compared to outcomes amongst the white community [125]. This study does not investigate ethnic differences per outcome. Although a question was included in ethnicity, none of the patients included in the study self-declared as indigenous. As a result, these findings are not generalisable to the full Mexican population and thus might not capture the outcomes of patients who are most deprived and potentially the ones most experiencing untimely care. More efforts need to be placed to be able to capture patient outcomes in the indigenous population.

The treatment modality was captured in the data extraction sheet. However, when collecting, there was uncertainty about whether it was palliative treatment or not in cases where the EHR did not explicitly mention it. Thus, although the

data can be analysed by the treatment type, this was not conducted for this thesis. Further research should aim to analyse the impact treatment type has in LC care intervals, particularly by cancer type as treatment modalities might differ.

Once the institution from referral was included in the regression analysis, it did not make a difference in the model. Therefore, although the three themes from the qualitative section of this study suggested three types of health-services users, they were not associated with the outcomes. Nonetheless, these results could be biased by the fact that only the last place from referral was considered instead of the subsequent stakeholders the patients navigated through. More research should be conducted to capture the journey's impact on LC care intervals. The use of "three-type-user" typologies is suggested.

As a result of missingness, not all patients had survival times available. Additionally, almost 40% of patients were censored. Hence, the results from this analysis should be considered as exploratory, due to the lack of linkage to mortality records or census.

Different dates to measure survival introduce different bias. Measuring survival from the preliminary diagnosis may introduce uncertainty as the final diagnosis might change after further tests, potentially affecting the accuracy of survival estimates. In contrast, measuring survival from the final diagnosis provides more certainty and accuracy in survival estimates, but considers only confirmed cancer cases. Measuring survival from treatment initiation may not account for delays in diagnosis and the potential influence of earlier disease stages on patient outcomes. In this thesis survival is calculated from diagnosis.

Several prior investigations have aimed to assess the relationship between

LC care intervals and overall survival. However, this specific exploration was not undertaken within the scope of the present thesis. Future research endeavours could benefit from a comprehensive examination of this aspect to elucidate potential associations and contribute to a more thorough understanding of the topic.

6.5 Discussion

The qualitative stream of this thesis presented insights of the patient journey surrounding cancer care. Conversely, the quantitative data, drawn from a larger sample of patient records, offered a broader perspective on trends and patterns of LC. Together, they revealed concrete figures on LC care intervals. Each stream independently discussed validity and trustworthiness; however, the legitimacy of these results is discussed in this section [179, 180]. **Table 6.17** displays the study results through a Side-by-side table and depicts the convergent mixed-methods research design in which qualitative and quantitative data are integrated, following separate analyses to draw meta-inferences and assess legitimacy [179, 234]. In this process, both quantitative and qualitative findings are compared by assessing confirmation, complementarity, expansion, and discordance [177, 179].

Meta-inferences confirmed results presented by either stream, enriching the overall understanding of LC care. For instance, this study stresses the importance of establishing local screening programmes by confirming through both streams of work the lack of screening practices and the prevalence of high stages at diagnosis. Similarly, qualitative findings on family support aligns with quantitative data showing being married helps the LC patient navigate the hospital environment and thus reduce the hospital interval. This alignment legitimises the findings and underscores the interconnectedness of individual contexts and timeliness in cancer care.

Table 6.17: Side by Side inferences and meta-inferences of: Barriers in lung cancer care, journeys and timeliness in lung cancer care

Barriers in lung cancer care & how these influence journeys and affect access and timeliness in care in Mexico		
QUALITATIVE	**QUANTITATIVE**	**META-INFERENCES**
Screening practices: 76% of patients had never gotten their lungs checked before diagnosis	Only 8.4% of the sample was diagnosed in early stages.	**Expanded**: Lack of screening interventions and advanced stage at diagnosis.
Misdiagnosis: 52% were given other diagnoses after first appointment (disease of infectious origin, allergy, asthma, musculoskeletal issues, pulmonary oedema, etc.)	45 patients from the original sample (N= 3018) were found not to have cancer at all (infectious or inflammatory diseases).	**Confirmed**: Lung cancer misdiagnosis represents a barrier to early care in the Mexican context.
The most common pathway to care is through **symptomatic patients** (89%).	From the original sample 2207 patients were symptomatic	**Confirmed**: The patients most commonly were diagnosed through symptoms and not screening or medical finding.
Cough was the most common symptom	Cough 47%, Dyspnoea 13.2%, Chest-pain 11.0%, Haemoptysis 2.4%, Weight-loss 4.8%, Other symptoms 21.1%	**Confirmed:** cough is the most common symptom.
Symptom "normalisation"; cultural beliefs influence appraisal.	Longer lung cancer care intervals	**Expanded:** These are barriers to early LC care, particularly during the appraisal interval.
The **most common journey** towards the INCAN is through private care.	52% of patients were referred from private hospital, 42% public hospital, 6% Unknown.	**Divergent:** only half of the patients reaching the INCAN is via the private route.

QUALITATIVE	QUANTITATIVE	META-INFERENCES
Intervals *"Total interval"* = (49-2378 days) *"health system interval"* = (31-685 days) *"patient interval"* = (1-1963 days)	**Intervals:** *"Total interval"* = 192 days (4-2222) *"health system interval"* = 77 days (2-1915) *"patient interval"* = 107 days (1-1362)	**Expanded:** usage of quantitative methods is best to calculate more precise time intervals (medians and ranges).
Untimely lung cancer care is described in the patient narrative and differences in intervals across the continuum are visible in the sample of interviewed patients (N=46). These attributable delays could be due to the proximal and distal determinants of health	Care intervals varied by: sex, age, region, cancer type and stage, marital status, institution type of symptoms and year (N=2645).	**Complementary:** Differences in intervals varied by clinical and socio-demographic characteristics. Depending on the interval studied, these have less/more statistical significance and similar or reversed effect.
Age impacts timeliness in LC care	**Age:** Younger population experience lengthier *"Total interval"* and *"total diagnostic interval"*; Older population experiences longer *"diagnostic (b) interval"* (after admission)	**Complementary:** The effect of age is not always the same. Sometimes age shortens intervals and sometimes lengthens intervals.

QUALITATIVE	QUANTITATIVE	META-INFERENCES
Sex impacts timeliness in LC care	**Sex:** *"Total interval"*: Men: 179 days vs Women 210 days; *"total diagnostic interval"*: Men: 145 days vs Women 179 days; *"Diagnostic (a) interval"*: Men: 54 days vs Women 67 days	**Complementary:** Sex is relevant only in certain intervals, but there is no difference in the outcomes between sexes after admission to the INCAN.
Cancer type impacts timeliness in LC care	**Cancer type:** SCLC has shorter *"Total interval"* compared to NSCLC (192 vs 138 days); Unspecified lung cancer type has shorter *"diagnostic (a) interval"* compared to NSCLC (62 vs 57 days); Unspecified lung cancer type has shorter *"hospital interval"* compared to NSCLC (25 vs 12 days) ; SCLC has shorter *"treatment interval"* compared to NSCLC (13 vs 6 days); Unspecified lung cancer type has shorter*"treatment interval"* compared to NSCLC (13 vs 6 days)	**Complementary:** Lung cancer type plays a role in certain intervals. SCLC show shorter intervals than NSCLC. However, the unspecified cancer changes from positive to negative associations.

QUALITATIVE	QUANTITATIVE	META-INFERENCES
Cancer stage impacts timeliness in LC care	**Cancer stage:** Cancer stage IV has shorter *"total interval* compared to stages I-II (188 vs 212 days); Cancer stage IV has shorter *"diagnostic (b) interval"* compared to stages I-II (3 vs 7 days); Cancer stage IV has shorter *"Hospital interval"* compared to stages I-II (24 vs 34 days) Unspecified cancer stage has shorter *"diagnostic (a) interval"* compared to stages I-II (40 vs 75 days); Unspecified cancer stage has shorter *"diagnostic (b) interval"* compared to stages I-II (3 vs 7 days); Unspecified cancer stage has shorter *"Hospital interval"* compared to stages I-II (10 vs 34 days)	**Complementary:** The sicker-quicker paradox is confirmed in the Mexican population. However, it does not stand from diagnosis to treatment. **Complementary** The population in the unspecified category always have shorter time-to-event than early stages I-II.
Insurance status influences differences in LC care intervals	Private, public or unknown institution from referral is not significantly linked to the length of LC care intervals.	**Divergent:** Referral from private or public institutions are not associated with the length of LC care intervals.
Unequal access to healthcare and treatment in the population	There is heterogeneity in prevalence of diagnosis and treatment reached by insurance status.	**Expanded:** After entering the INCAN, lung cancer patients experience differences in reaching diagnosis and treatment.

QUALITATIVE	QUANTITATIVE	META-INFERENCES
Unequal distribution of resources some regions defer LC care	**Region:** is significantly associated with longer LC care intervals after adjustment in particular outcomes: 1) Region is relevant for the "Diagnostic (b)" interval (from admission to diagnosis). Compared to people from Mexico City (6 days), people from the North are diagnosed earlier (3 days). 2) Region is relevant for the "hospital" interval. Compared to people from Mexico City (24 days), people from the North, Centre and South are treated earlier (15, 20 and 19 days respectively). 3) Region is relevant for the "treatment" interval. Compared to people from Mexico City (12 days), people from the North are diagnosed earlier (8 days).	**Expanded:** Region is particularly relevant during the search for hospital-care and during the diagnostic and treatment interval. Regional differences in infrastructure do not play a role in the pre-hospital environment.
Symptom signature plays a role in health-care seeking.	Symptoms are significant in fully adjusted models of outcome: "appraisal/patient", "health system", "pre-hospital", "total", "total diagnostic", "diagnostic (a)" and "diagnostic (b)", but not in "hospital" or "treatment" interval.	**Complementary:** Symptom type does impact timeliness in care, but not during the hospital or treatment interval.
Lack of awareness or inadequate knowledge of lung cancer risks;	Longer lung cancer care intervals	**Expanded:** These are barriers to early LC care, particularly during the appraisal interval.

QUALITATIVE	QUANTITATIVE	META-INFERENCES
Caregiving duties and work commitments hinder timely healthcare seeking	Longer lung cancer care intervals	**Expanded:** These are barriers to early LC care, particularly during the appraisal interval.
Fear about disease hinders timely healthcare seeking	Longer lung cancer care intervals	**Expanded:** These are barriers to early LC care, particularly during the appraisal interval.
Worry about covering expenses	Longer lung cancer care intervals	**Expanded:** These are barriers to early LC care throughout the cancer continuum.
Family plays a crucial role in urging patients to seek care	**Marital status** People who are widowed or divorced have longer intervals than those who are married (in the "hospital interval").	**Expanded:** As a proxy of family, marital status impacts timeliness in LC care.
Financial constraints impacts LC care intervals and/or lead to drop-out of care.	**Drop-outs:** Higher drop-outs in higher socioeconomic groups and higher levels of education. **Delays:** Education level was not significantly associated with longer intervals after adjustment.	**Expanded:** Financial constraints may lead to drop-outs particularly in higher socioeconomic groups. **Expanded:** LC care intervals are not associated with the education level.
Navigating the **fragmented system** and informal referral pathways cause longer intervals.	Longer lung cancer care intervals	**Expanded:** These are barriers to early LC care across the continuum of care.
Insufficient diagnostic infrastructure longer LC care intervals	Longer lung cancer care intervals	**Expanded:** These are barriers to early LC care, particularly during the diagnostic interval.

QUALITATIVE	QUANTITATIVE	META-INFERENCES
Poor-quality specimens contribute to longer LC care intervals	Longer lung cancer care intervals	**Expanded:** These are barriers to early LC care, particularly during the diagnostic interval.
Journey during COVID-19: pandemic impacted cancer care; fear of infection led to delayed seeking and disruptions in care.	Reduced number of admitted patients from 2019-2021 Decrease in LC care intervals in *"Total interval"* and *"total diagnostic interval"* from 2020-2021. Increase in LC care intervals in *"hospital interval"* and *"treatment interval"* from 2019-2021.	**Complementary:** COVID-19 had a mixed impact in outcomes from 2020-2021

In some cases, the qualitative stream expanded on the interplay between individual patient experiences and broader healthcare system challenges. Through the patient narrative derived from in-depth patient interviews, qualitative results expanded knowledge by providing a detailed understanding of the cancer journey, including the influence of informal referral pathways, barriers in LC care and the impact of external factors such as the COVID-19 pandemic.

Other results are complementary. For instance, the population interviewed described financial constraints may lead to lengthier LC care intervals and drop-outs. In addition, catastrophic expenditures are mentioned in the literature. However, in this study expenses derived from care were not systematically collected nor were financial constrains properly assessed. Patients who dropped out and did not reach diagnosis or treatment were most commonly in higher socioeconomic groups. Additionally, the qualitative stream found most patients are referred by or visit a private hospital just before the INCAN. In contrast, the quantitative study actually finds only half of the patients reach the INCAN via the private route. In the future, research should aim to analyse the economic impact the disease has in the patients journey and if the education level or economic position in fact leads to untimely care and drop-outs.

Meta-inferences from streams were sometimes also discordant. For instance, although qualitative analysis suggested categorising patients based on their private or public place of referral, such distinctions did not yield discernible differences in the regression modelling outcomes. Hence, while qualitative narratives provided intricate insights into individual journeys and generated distinct patient typologies, these may not encapsulate the broader trends observed at the population level. This can be potentially explained by limitations found in capturing only the institution last visited instead of the full list of institutions. Future data collection efforts should

include information on the mix of institutions utilised for diagnosis and treatment to better understand journey differences and outcomes. Potentially stratifying by different institutions might help shed light on difference by insurance status instead of by the classification proposed in this thesis. Divergent findings such as these should be further explored.

Side-by-side **Table 6.17**, helps not only compare the results that emerge from each study, but also drafts the research agenda from the gaps identified were no quantitative data was collected. Although concepts like risk perception or misdiagnosis arose during the interviews these were not directly measured in the quantitative section. As a result, further research could strive to formally introduce covariates for these measures, i.e., for catastrophic expenditures, including economic variables that define spending. Nonetheless, in some cases measuring data through quantitative methods might not be useful. For example, measuring the effect of fragmented health systems is challenging due to not being able to appropriately collect data from all the institutions that patients visit throughout their journey. In limited contexts such as LMIC, health systems are fragmented, and data is not routinely collected through the same methods and electronic tools. In consequence, qualitative methods might remain useful to capture these barriers in the short and medium terms.

From the literature, it was expected age would have an effect in timeliness in cancer care [143, 208]. In this case, the qualitative stream identified differences in the timeliness to care associated to different age, sex and other socio-demographic characteristics. Through quantitative analysis each variables association with LC care intervals was properly evaluated. Results show the older population experience shorter LC care intervals except during the time from admission to diagnosis. This can be due to older patients having a harder time navigating the hospital

environment than younger patients and younger patients having less awareness of chronic diseases and less visits to the doctor that would facilitate earlier diagnosis. This is an interesting discovery as it portrays how patient characteristics play a role in different intervals in the pathway to cancer care. Hence, in the future, more research should be done to identify if the regression models studying LC care intervals should adjust for the full set of variables or tailor each interval with specific covariates. Identifying and comparing the differences in younger versus older lung cancer patients might be due as a new qualitative research project.

Overall, this mixed methods study demonstrates the importance of bringing together the qualitative and quantitative methods. Due to the sequential analytical design of this Chapter, the qualitative stream informed the quantitative. However, if the order of the analytical approach would have been inverted, potentially the results could have been different. For instance, the place from referral was relevant in the patient narrative and seemed to define differences in the patient journey. The approach taken to define the type of patient journeys (public, private or mixed) was done taking into account inferences from the literature, in addition to the results from the qualitative study. However, once the quantitative data was analysed this classification did not show any relevance in the study. Breaking down the journey types into three types instead of keeping the long list of institutions from referral potentially hindered the regression models to capture the effect the IMSS had in the patient journey. Hence, in the future, the long list of institution from referral should be used instead of the journey classification proposed by the qualitative stream in the quantitative analysis.

6.6 Summary

- There are atypical and typical cancer LC journeys. The most common journey is through a private system user.
- **Symptom Appraisal:** Patients normalise symptoms like cough, delaying seeking care; cultural beliefs influence appraisal.
- **Access to Care:** Fear, work commitments, and care-giving duties hinder timely healthcare seeking; varied ease in access reported.
- **Risks and Medical Education:** Lack of awareness on lung cancer risks; delayed seeking due to inadequate knowledge and symptom interpretation.
- **Family Support and Guilt:** Family plays a crucial role in urging patients to seek care; guilt and fear of burdening family delay seeking.
- **Treatment Inequalities:** Unequal access to healthcare due to insurance disparities; navigating the fragmented system causes longer LC care intervals .
- **Informal Referral Pathways:** Varied and complex patient journeys influenced by informal referrals; lack of consolidated pathways leads to longer LC care intervals.
- **Unequal Distribution of Resources:** Insufficient diagnostic infrastructure, unequal distribution of resources, and poor-quality specimens contribute to longer LC care intervals .

- **Catastrophic Expenses:** Financial constraints lead to worries about covering expenses; catastrophic expenses can force patients to drop out of treatment.
- **Lung Cancer Journey during COVID-19:** COVID-19 impacts cancer care; fear of infection leads to delayed seeking and disruptions in care.
- Compared to the literature, the Mexican context shows the highest time from first symptom to treatment 192 days.
- Intervals in breast and LC care in Mexico seem relatively similar.
- The most important difference between breast cancer and LC in Mexico, lies in the appraisal interval (3.5 months vs 0.3 month).
- Cough is the most common symptom. But leads to lower survival estimates.
- Older patients reach treatment and diagnosis faster than younger patients. However, once admitted into the hospital, older patients with age increasingly delay their care.
- Women experience longer "total interval" than men but have better survival outcomes.
- Educational level is not significantly associated with the outcomes.

- Regional disparities are significantly associated with longer LC care intervals, but health institutions are not. However, public institutions have worse survival outcomes.
- Once admitted to the hospital, being married serves as a protective factor against untimely care.
- SCLC experience shorter LC care intervals compared to NSCLC.
- The sicker quicker paradox remains in the Mexican context for LC.
- Results from this research show changes in the number of patients and time intervals during the years 2020-2021.

This study reveals patients are more commonly symptomatic and diagnosed in higher stages of the disease. From 2004 to 2021, N=2645 patients had a LC diagnosis; 66% in stage IV, 7.7% stage III and 8.4% in stages I or II. The rest of the patients (17%) did not have a stage on their EHR. Similarly, 22% of the patients did not have a LC type diagnosis. Thus, 75.8% were classified as NSCLC and 2.1% as SCLC. Cough is the most common symptom and haemoptysis has lower survival estimates.

LC care intervals in the Mexican context are much worse (192 days), compared to the international literature. Intervals in breast and LC care in Mexico seem relatively similar. The most important difference between breast cancer and LC in Mexico, lies in the appraisal interval (3.5 months vs 0.3 month).

Only 31% of the sample had complete interval measurements. Missing data was closely related to cancer stages I and II. Ongoing monitoring and data collection

efforts are essential to track changes in healthcare delivery and their impact on timeliness. Ultimately, addressing these issues can contribute to better outcomes for LC patients in Mexico and serve as a foundation for further research and policy interventions in cancer care.

This study has provided valuable insights into the factors influencing LC care intervals in Mexico. The analysis revealed several important findings related to the patient interval, health system interval, and treatment interval, as well as the impact of various demographic and clinical factors on these intervals. One key finding of this study is the significant impact of socio-demographic factors on cancer care timeliness. Women experience longer total intervals. Older people are treated earlier, and the sicker quicker paradox is confirmed in the Mexican population. SCLC is also associated with shorter LC care intervals. However, all of these associations vary depending on the interval studied. Thus, this study demonstrates why studying different time intervals is very important, indicating a potential need for targeted interventions to address unique and interval-specific challenges. For instance, efforts should focus on reducing health inequalities and improving access to timely care, especially for women across the continuum particularly from symptom onset to treatment or external diagnosis to internal diagnosis; NSCLC across the hospital interval; etc.

The health-care system fragmentation, regional disparities, and gaps in infrastructure, in addition to predominant private spending, private care usage and catastrophic expenditures are all important barriers found in LC care that render an unequal patient pathway from the start. The "North" region experiences shorter total and diagnosis intervals. However, this advantage is linked to higher socioeconomic status, highlighting the need to address health inequalities across different regions.

Symptom interpretation and self-appraisal is challenging for patients in Mexico. When experiencing ambiguous symptoms such as loss of appetite, fatigue, or limb pain they think of them as "normal", "momentary" or "non-serious", as a result this leads to increased time to treatment. Hence, the findings emphasise the importance of tailoring approaches to facilitate the patients understanding of the disease, its risks and severity. Lung cancer campaigns delivered at the community level might raise awareness of the symptoms associated with LC.

This study also shows additional efforts need to be placed in building capacity amongst primary care health care workers to communicate risks, assess symptoms using positive predictive values and if necessary, effectively refer to imaging for follow-up. Similarly, misdiagnosis and the use of antibiotic also demonstrate the need for health professionals to be more equipped to handle a LC suspicion. More research should be done to understand why patients are more frequently being sent for a CT instead of an X-ray or why patients had never had their lungs checked before despite the risks.

This thesis outlines patients experience typical and atypical journeys when searching for care. On average patients took 18 days to speak to someone about their symptoms. Family or carers in this context indirect and directly both push and prevent the patients to search for care. On average 2.5 doctors are visited before reaching a diagnosis. Amongst the most prevalent journeys, patients search for treatment in the private sector (52%), eventually leading to economic strain. Regardless of the journey type: public, mixed, or private care only, patients experience longer LC care intervals across the cancer continuum. Patients discontinue treatment and make use of informal referral pathways. The role caregivers and family members these have in timeliness should be further studied as results from the quantitative arm from this study shows marital status

plays a role in some of the time intervals found. Understanding patient journeys and the available infrastructure can help develop guidelines to generate standardised pathways that lead the patient to diagnosis and treatment earlier.

Women compared to men live longer with the disease after the diagnosis, despite having longer total intervals. This has been previously described in the literature. However, this does not disregard the need for the disparities experienced by women in the cancer care continuum in the Mexican context to be tackled through early cancer care interventions.

The number of patients admitted to the INCAN has increased over time. However, results from this research show reduced number of admitted patients and increase in the hospital interval and diagnosis (from admission) throughout 2020 and 2021. More research could be done to compare it to the rest of the cohort to be able to capture LC care intervals pertaining to the COVID-19 pandemic.

The study outlines the importance of conducting mixed-methods research to expand our knowledge of barriers in cancer care, identify research gaps that can be addressed by qualitative or quantitative methods particularly or discard methods to answer specific research questions.

Chapter 7

Conclusion

Through qualitative analysis of patient journeys, and examination of electronic health records, this thesis presents a significant contribution to the understanding of LC care intervals in Mexico, especially at the INCAN and valuable insights into the complex factors influencing the timeliness of care. Additionally, through a systematic review and case studies of PNP, the potential role of PNP in addressing untimely care was assessed using both international and local examples.

The systematic review evidenced no effect on increasing timely diagnosis or treatment in LC. Although contrasting results were seen between experimental and non-experimental studies, the lack of strong evidence to support the implementation of PNP can be explained by heterogeneity in PNP design and evaluation, low sample sizes, bias in reporting the intervention effect, and precision of the estimates. Moreover, at the local level, PNP in Mexico do not monitor time intervals but rather gather patient feedback through satisfaction surveys or other administrative indicators, ultimately hindering understanding of their local impact on early diagnosis and treatment. Consequently, evidence today does not support the implementation of PNP for LC in Mexico, particularly for the use of increasing LC care timeliness. Nonetheless, results from this thesis show the majority of LC patients are diagnosed with advanced stage disease, with a median duration

from first symptom to treatment of 192 days. This is higher than results from the international literature, indicating significant challenges in accessing timely care in the Mexican context. Thus, despite the non-supporting findings to implement PNP, this thesis reaffirms the need to intervene in the patient's journey to improve health outcomes and reduce the consequences prolonged time to care has on patients' lives and healthcare system costs.

The typical and atypical cases of LC patients illustrated in this thesis explain the patient's difficult navigation through the system and potential explanations for longer intervals, i.e., challenges related to symptom recognition, limited access to healthcare facilities, disparities in treatment availability, and financial constraints. Similarly, key findings emerging from the calculation of intervals highlight the influence of socio-demographic factors such as age, sex, type of symptom, cancer stage and cancer type. These findings underscore the need for targeted interventions to address prolonged intervals in LC care, among specific socio-demographic groups in particular segments of the cancer continuum.

Although there are many challenges in LC care in Mexico, this research illuminates paths for positive change. By leveraging insights from this study, stakeholders can work collaboratively to implement targeted interventions, enhance PNP and their research, and ultimately ensure timely access to care, leading to improved outcomes for individuals affected by LC in Mexico.

Recommendations for Patient Navigation Programmes

Table 7.1: Recommendations for Patient Navigation Programmes - Part 1

Recommendation	Description
Patient Navigation Services	Policymakers should not consider implementing patient navigation programmes for Lung cancer until further research is done to support cost/benefit.
Standardisation of Patient Navigation Research	Both the systematic review and case studies demonstrate that navigation is heterogeneous. The diversity underscores the need for standardisation in programme design and outcome measurement to enable rigorous evaluation and evidence-based decision-making.
Establish Consensus Guidelines for PNP outcome measurement	Develop consensus guidelines for selecting and applying outcome measures consistently across studies to enhance methodological rigour and comparability.
Integrate Evaluation Methods and Time-to-Event Intervals	PNP should adopt rigorous evaluation methods, focusing particularly on time-to-event intervals, to gauge impact over time and promote effective evaluation strategies.
Elucidate Specific Time Intervals of Interventions	It's essential to clarify the temporal aspects of interventions to understand their impact on patient outcomes and inform the development of targeted navigation strategies.
Single vs Multiple Cancer Navigation	Evaluate the comparative effectiveness of navigation across single versus multiple cancer types to optimise navigation strategies for diverse populations.
Define Healthcare Levels Involved in Navigation	Research efforts should delineate specific healthcare tiers involved in navigation to enhance the standardised implementation of programmes.
Inclusion of Patients in PNP Development	Conduct comprehensive needs assessments involving community stakeholders in the PNP planning process to provide a holistic understanding of barriers to care.
Systematic Follow-Up and Evaluation of PNP	Implement systematic follow-up procedures to monitor progress along the healthcare continuum and ensure ongoing attention to barriers.
Embed a Research Agenda Addressing Health Inequalities	Embed a research agenda focused on health disparities within patient navigation efforts to promote health equity among marginalised communities.

Table 7.2: Recommendations for Patient Navigation Programmes - Part 2

Recommendation	Description
Foster Funding Opportunities	Employ theoretical frameworks, logic models, and rigorous evaluation methods to effectively communicate the value of PNP to potential funders.
Technology Access, Literacy and Usage	Investigate the adoption and effectiveness of technology in PNP, while preserving the integrity of patient-navigator relationships, considering digital literacy and device availability among patients, and develop guidelines for proper utilisation of digital tools.
Organisational Dynamics and Resource Challenges	Future studies should explore operational challenges in PNP, including the influence of administrative procedures and funding streams, as well as the impact of international vs. domestic funding sources.
Prevalence of Patient Navigation in LMIC	Understand factors influencing the prevalence of PNP across different income settings to address global disparities in cancer care access and outcomes.
Enhanced Dissemination of Findings	Actively disseminate findings through platforms like Cochrane and the International Clinical Trials Registry Platform by WHO and provide DOIs of results on websites.
Maintaining Accessibility of Trial Information	Ensure trial information remains easily accessible for reference to facilitate comprehensive understanding of navigation programmes and their outcomes.
Incorporate Minorities in Trials	Future trials should prioritise the inclusion of minority groups to understand unique barriers and tailor navigation interventions accordingly.
Consolidation of Published Literature	Integrate previously published literature into subsequent articles to provide a cohesive narrative and aid in synthesising the evolution of navigation programmes and outcomes.

Recommendations for the Evaluation of the Lung Cancer Journey

Table 7.3: Recommendations for the Evaluation of Lung Cancer Journey - Part 1

Recommendation	Description
Mixed-Methods Approach	Embrace a mixed-methods approach in cancer research to enrich the evidence base and provide a comprehensive understanding of patient journeys and care barriers, spanning patient, system, and provider domains,
Comprehensive Data Collection and Analysis	Develop standardised electronic health record systems to capture comprehensive patient information and enhance data infrastructure for assessing cancer care intervals.
Addressing Missing Data	Standardise data collection procedures and consider socioeconomic factors influencing data quality to ensure equitable representation in research and analysis.
Exclusion of Asymptomatic Patients	Exclude screened patients from analysis to avoid bias in interpreting diagnostic timelines.
Questionnaire Validation and Improvement	Prioritise the validation and enhancement of questionnaires used to capture patient journeys and care delays to bolster research findings and policy recommendations.
Improving Healthcare Access	Address structural barriers within the healthcare system, such as fragmented service delivery and inadequate coverage, to enhance access and quality of care.
Financial Assistance and Comprehensive Health Insurance Coverage	Roll out comprehensive health insurance coverage and financial aid programmes to alleviate the financial strain of treatment and improve health outcomes.
Investment in Healthcare Infrastructure	Invest in healthcare infrastructure, including diagnostic facilities, to improve timely diagnosis and treatment.
Referral Protocols and Data Standardisation	Establish referral protocols and standardise data collection methods to enhance care coordination and facilitate research on care intervals.
Rapid Referral and Diagnostic Processes	Streamline referral and diagnostic processes to expedite lung cancer diagnosis, with guidelines for recognising high-risk symptoms.

Table 7.4: Recommendations for the Evaluation of Lung Cancer Journey - Part 2

Recommendation	Description
Quality Assurance and Intervals Monitoring	Establish quality assurance mechanisms to ensure consistency in cancer care intervals and identify areas for improvement through continuous evaluation.
Symptom and risk awareness campaigns	Implement public awareness campaigns to educate about lung cancer symptoms and risk factors, targeting under-served communities and addressing symptom normalisation and cultural misconceptions.
Targeted Interventions to Address Health Disparities	Implement targeted interventions to reduce disparities in lung cancer care intervals, focusing on under-served populations and socioeconomic factors.
Enhancing Treatment Completion Rates	Address structural inequities in access to care to improve treatment completion rates through culturally tailored interventions and financial assistance.
Improving Survival Analysis	Invest in cancer registries and collaborative partnerships to enhance survival analysis and outcomes research.
COVID-19 Pandemic Response and Policy Adaptation	Develop policies to address the impact of the COVID-19 pandemic on lung cancer care delivery and ensure continuity of care during future health crises.

Research and policy recommendations in line with the findings can be seen in **Figure 7.1** below. By addressing these policy and research recommendations, stakeholders can collaborate to improve the LC care journey.

Figure 7.1: Summary of PhD thesis results and recommendations

The Lung Cancer Patient Journey	The potential solution		Alternatives to PNP
	PNP Systematic Review (lung cancer)	PNP Case Studies (Mexico)	
The time from first symptom to treatment 192 days (the highest in the literature)= Advanced stage at diagnosis. Usage of quantitative methods is best to calculate more precise time intervals (medians and ranges). Differences in intervals varied by clinical and socio-demographic characteristics. Depending on the interval studied, these have less/more statistical significance and similar or reversed effect. COVID-19 had a mixed impact on outcomes from 2020-2021.	Experimental studies show that Patient Navigation Programs (PNP) do not increase timeliness in Lung Cancer (LC) care.	PNP in Mexico vary widely in activities and scopes, but do not focus on increasing timeliness in cancer care.	
Cough is the most common symptom. Symptom type does impact timeliness in care, but not during the hospital or treatment interval. However, cough is usually normalised.	Quasi-experimental and observational studies suggest that PNP can reduce intervals in LC care. - Bias arises in areas such as blinding, reporting of intervention effects, and precision of estimates. - Sample size, study design, and evaluation methods limit the strength of evidence. - 55% of studies pair LC with other diseases. PNP for lung cancer more frequently focuses on researching the treatment interval.	Lack of data on time-to-diagnosis or treatment intervals hinders understanding of their impact on early diagnosis and treatment.	**Risk awareness campaigns directed to patients and family members**
The patients most commonly were diagnosed through symptoms and not screening or medical finding.	General population, low income or other minorities.	Population focus: uninsured, insured and publicly insured.	
The sicker-quicker paradox is confirmed in the Mexican population. However, it does not stand from diagnosis to treatment.	Three major activities being conducted by navigators: emotional support, infrastructure navigation, and advanced navigation activities (legal support).	PNP in Mexico address administrative, logistical, emotional needs, and provide resources.	
Family plays a crucial role in urging patients to seek care; guilt and fear of burdening family delay seeking.	Patient navigators can be health professionals, lay navigators, or social workers. Sometimes they are not specified.	Patient navigators with varied backgrounds, including a taxi driver, demonstrate the importance of community expertise.	
Lung cancer misdiagnosis at the primary care level	Health inequalities are not the primary scope of analysis in PNP articles.	Health inequalities are not the primary scope of analysis in PNP case studies.	**Capacity building among general practitioners**
Unequal access to healthcare due to insurance disparities; navigating the fragmented system causes longer LC care intervals.	Different models of navigational care are found in PNP studies, limiting direct comparisons of interventions.	The adapted framework reveals navigation programs are different navigation models, focused on different time intervals across the cancer continuum.	**Universal Health Coverage**
There are atypical and typical cancer LC journeys. Patients can enter the INCAN through a private informal pathway. Varied and complex patient journeys influenced by informal referrals; lack of consolidated pathways leads to longer LC care intervals. Referral from private or public institutions are not associated with the length of lung cancer care intervals.	Administrative outcomes are the most frequently used measures in PNP studies.	Mexico's tiered healthcare system poses challenges; navigation intensity varies based on healthcare levels traversed.	**Consolidate patient pathways and referral mechanisms**
Insufficient diagnostic infrastructure, unequal distribution of resources, and poor-quality specimens contribute to longer LC care intervals.	Not enough evidence to suggest PNP adapt to newly identified barriers over time.	PNP adapt to healthcare landscape changes, focusing on access to evolving treatments and shifting healthcare coverage.	**Increase diagnostic and therapeutic infrastructure according to population density and needs.**
Financial constraints lead to worries about covering expenses; catastrophic expenses can force patients to drop out of treatment.	Stakeholders and roles are not transparent in the literature	Diverse funding sources impact PNP dynamics; public and private sectors collaborate to connect patients with external resources.	**Allocate funds to support people who have caregiving duties or work commitments to seek for health early**
Fear, work commitments, and caregiving duties hinder timely healthcare seeking; varied ease in access reported.	Rigorous and standardized research is needed to evaluate the effects of PNP across the LC continuum.	Heterogeneous evaluation methods for PNP require standardization and use of logic model.	
-	The "cancer appraisal-to-survival pathway" can guide the establishment of standardized outcome measurements in PNP studies.	The "cancer appraisal-to-survival pathway" can guide the establishment of standardized outcome measurements in PNP studies.	**Use the typology to conduct research and implement PNP**

Future directions

In the pursuit of addressing critical gaps in cancer care delivery, the doctoral journey catalysed the inception and evolution of "Código Cáncer." Commissioned by FUNSALUD, this project emerged from the PhD research insights, expanding its scope to encompass four additional cancer types beyond the initial focus on lung cancer care interval measurement at the National Cancer Institute and other cancer centre.

"Código Cáncer" epitomises a multi-phase project, orchestrating seven distinct studies spanning economic research to infrastructure mapping. This collaborative effort, nurtured by insights gained from navigating patients through healthcare institutions during the COVID-19 pandemic, endeavours to streamline cancer care delivery through the implementation of a rapid patient referral system.

"Código Cáncer" has gained considerable support from stakeholders, including FUNSALUD. Collaborative efforts with governmental bodies and healthcare institutions have allowed the project to more forward. As "Código Cáncer" embarks on its implementation phase, the commitment to ongoing learning, stakeholder engagement, and collaborative partnership remains steadfast. The ultimate aim is to foster equitable and expeditious access to cancer care services for all individuals, transcending geographical and socioeconomic barriers.

Future research will endeavour to develop systematic reviews for other types of cancer using the established framework for PNP. Lastly, according to the recommendations arising from this thesis, publications addressing some research gaps might be followed.

Bibliography

1. Goss PE, Lee BL, Badovinac-Crnjevic T, Strasser-Weippl K, Chavarri-Guerra Y, St Louis J, Villarreal-Garza C, Unger-Saldaña K, Ferreyra M, Debiasi M, Liedke PER, Touya D, Werutsky G, Higgins M, Fan L, Vasconcelos C, Cazap E, Vallejos C, Mohar A, Knaul F, Arreola H, Batura R, Luciani S, Sullivan R, Finkelstein D, Simon S, Barrios C, Kightlinger R, Gelrud A, Bychkovsky V, Lopes G, Stefani S, Blaya M, Souza FH, Santana Santos F, Kaemmerer A, de Azambuja E, Cardona Zorilla AF, Murillo R, Jeronimo J, Tsu V, Carvalho A, Gil CF, Sternberg C, Dueñas-Gonzalez A, Sgroi D, Cuello M, Fresco R, Reis RM, Masera G, Gabús R, Ribeiro R, Knust R, Ismael G, Rosenblatt E, Roth B, Villa L, Lara Solares A, Leon MX, Torres-Vigil I, Covarrubias-Gomez A, Hernández A, Bertolino M, Schwartsmann G, Santillana S, Esteva F, Fein L, Mano M, Gomez H, Hurlbert M, Durstine A. Planning cancer control in Latin America and the Caribbean. Lancet Oncol. 2013 Apr;14(5):391-436.

2. Weller D, Vedsted P, Rubin G, Walter FM, Emery J, Scott S, Campbell C, Andersen RS, Hamilton W, Olesen F, Rose P, Nafees S, van Rijswijk E, Hiom S, Muth C, Beyer M, Neal RD. The Aarhus statement: improving design and reporting of studies on early cancer diagnosis. Br J Cancer. 2012 Mar;106(7):1262-1267.

3. Olsson JK, Schultz EM, Gould MK. Timeliness of care in patients with lung cancer: a systematic review. Thorax. 2009 Sep;64(9):749-756.

4. Hamilton M, Hodgson O, Dai D, McDonnell P. Waiting times for suspected and diagnosed cancer patients: 2017-18 annual report. 2018 Jun.

5. Olesen F, Hansen RP, Vedsted P. Delay in diagnosis: the experience in Denmark. Br J Cancer. 2009 Dec;101 Suppl 2

6. Freeman HP, Rodriguez RL. History and principles of patient navigation. Cancer. 2011 Aug 1;117(15 Suppl):3539-3542.

7. Krok-Schoen JL, Brewer BM, Young GS, Weier RC, Tatum CM, DeGraffinreid CR, Paskett ED. Participants' barriers to diagnostic resolution and factors associated with needing patient navigation. Cancer. 2015 Aug 15;121(16):2757-2764.

8. Gorin SS, Haggstrom D, Han PKJ, Fairfield KM, Krebs P, Clauser SB. Cancer care coordination: a systematic review and meta-analysis of over 30 years of empirical studies. Ann Behav Med. 2017 Aug;51(4):532-546.

9. Guadagnolo BA, Dohan D, Raich P. Metrics for evaluating patient navigation during cancer diagnosis and treatment: crafting a policy-relevant research agenda for patient navigation in cancer care. Cancer. 2011 Aug 1;117(15 Suppl):3565-3574.

10. Bukowski A, Chávarri-Guerra Y, Goss PE. The potential role of patient navigation in low- and middle-income countries for patients with cancer. JAMA Oncol. 2016 Aug 1;2(8):994-995.

11. Lairson DR, Dicarlo M, Deshmukh AA, Fagan HB, Sifri R, Katurakes N, Cocroft J, Sendecki J, Swan H, Vernon SW, Myers RE. Cost-effectiveness of a standard intervention versus a navigated intervention on colorectal cancer screening use in primary care. Cancer. 2014 Apr 1;120(7):1042-1049.

12. Tan CHH, Wilson S, McConigley R. Experiences of cancer patients in a patient navigation program: a qualitative systematic review. JBI Database System Rev Implement Rep. 2015 Mar;13(2):136-168.

13. Miranda-Filho A, Piñeros M, Bray F. The descriptive epidemiology of lung cancer and tobacco control: a global overview 2018. Salud Publica Mex. 2019 Jun;61(3):219-229.

14. Cheng TYD, Cramb SM, Baade PD, Youlden DR, Nwogu C, Reid ME. The international epidemiology of lung cancer: latest trends, disparities, and tumor characteristics. J Thorac Oncol. 2016 Jun;11(10):1653-1671.

15. Yang P. Epidemiology of lung cancer prognosis: quantity and quality of life. Methods Mol Biol. 2009;471:469-486.

16. Grossman R, Haim O, Abramov S, Shofty B, Artzi M. Differentiating small-cell lung cancer from non-small-cell lung cancer brain metastases based on MRI using EfficientNet and transfer learning approach. Technol Cancer Res Treat. 2021;20:15330338211004919.

17. American Cancer Society. Lung cancer signs symptoms. [Internet]. Atlanta: American Cancer Society; c2024 [cited 2024 Jan].
Available from: https://www.cancer.org/cancer/lung-cancer.html

18. Moffitt Cancer Center. Differences between small cell and non-small cell lung cancer. [Internet]. Tampa: Moffitt Cancer Center; c2024 [cited 2024].
Available from: https://moffitt.org/cancers/lung-cancer/types/

19. Cancer Research UK. Types of lung cancer. [Internet]. London: Cancer Research UK; c2022 [cited 2022 Dec].
Available from: https://www.cancerresearchuk.org/about-cancer/lung-cancer/

20. Arrieta O, Zatarain-Barrón ZL, Aldaco F, Barrón F, Báez-Saldaña R, Campos-Gómez S, Trejo R, De la Garza J. Lung cancer in Mexico. J Thorac Oncol. 2019 Oct;14(10):1695-1700.

21. Bychkov A. Pathologic TNM staging of carcinomas of the lung, AJCC 8th edition. 2019 Jan.

22. Detterbeck FC, Boffa DJ, Kim AW, Tanoue LT. The eighth edition lung cancer stage classification. Chest. 2017 Jan;151(1):193-203.

23. National Institute for Health and Care Excellence. Lung cancer: diagnosis and management. [Internet]. London: NICE; c2019 [cited 2019 Mar]. Available from: https://www.nice.org.uk/guidance/ng122

24. Walter FM, Rubin G, Bankhead C, Morris HC, Hall N, Mills K, Dobson C, Rintoul RC, Hamilton W, Emery J. Symptoms and other factors associated with time to diagnosis and stage of lung cancer: a prospective cohort study. Br J Cancer. 2015 Mar;112 Suppl 1

25. Arroyo-Hernández M, Zinser-Sierra JW, Vázquez-García JC. [Lung cancer screening program in Mexico]. Salud Publica Mex. 2019 Jun;61(3):347-351.

26. Lozano P, Arillo-Santillán E, Barrientos-Gutiérrez I, Zavala-Arciniega L, Reynales-Shigematsu LM, Thrasher JF. E-cigarette use and its association with smoking reduction and cessation intentions among Mexican smokers. Salud Publica Mex. 2019 Jun;61(3):276-285.

27. Guerrero-López CM, Serván-Mori E, Rodríguez-Franco R, Montañez-Hernández JC, Gómez-Dantés H. Lung cancer in Mexico: findings from the Global Burden of Disease Study, 1990-2016. Salud Publica Mex. 2019 Jun;61(3):240-248.

28. Comisión Nacional de Población (CONAPO). Conciliación demográfica de México 1950-2015. 2017 Apr.
Available from: http://www.conapo.gob.mx/

29. Organisation for Economic Co-operation and Development (OECD). Fertility rates (indicator). 2016.
Available from: https://data.oecd.org/pop/fertility-rates.htm

30. Organisation for Economic Co-operation and Development (OECD). Life expectancy at 65 (indicator). 2017.
Available from: https://data.oecd.org/healthstat/life-expectancy-at-65.htm

31. Instituto Nacional de Estadística y Geografía (INEGI). Estimaciones y proyecciones de la población total, 2018-2050. 2020 Jan.
Available from: https://www.inegi.org.mx/programas/proyecciones/Default

32. Organisation for Economic Co-operation and Development (OECD). Infant mortality rates (indicator). 2016.
Available from: https://data.oecd.org/healthstat/infant-mortality-rates.htm

33. Organisation for Economic Co-operation and Development (OECD). Health spending (indicator). 2017.
Available from: https://data.oecd.org/healthres/health-spending.htm

34. Organisation for Economic Co-operation and Development (OECD). Life expectancy at birth (indicator). 2017.
Available from: https://data.oecd.org/healthstat/life-expectancy-at-birth.htm

35. Organisation for Economic Co-operation and Development (OECD).
Available from: https://www.oecd.org/

36. Organisation for Economic Co-operation and Development (OECD). Gross

national income (indicator). 2017.
Available from: https://data.oecd.org/gdp/gross-national-income.htm

37. Global health research center at the University of Washington. Institute for Health Metrics and Evaluation. Measuring what matters. [Internet].
Available from: URL:https://www.healthdata.org/ Accesed: [19/01/2020].

38. Mohar-Betancourt A, Reynoso-Noverón N, Armas-Texta D, Gutiérrez-Delgado C, Torres-Domínguez JA. Cancer trends in Mexico: essential data for the creation and follow-up of public policies. J Glob Oncol. 2017 Dec;3(6):740-748.

39. Arrieta O, Quintana-Carrillo RH, Ahumada-Curiel G, Corona-Cruz JF, Correa-Acevedo E, Zinser-Sierra J, de la Mata-Moya D, et al. Medical care costs incurred by patients with smoking-related non-small cell lung cancer treated at the National Cancer Institute of Mexico. Tob Induc Dis. 2014;12(1):25.

40. Hu H, Zhao L, Yong Y, Nicholas S, Maitland E, Zhao W, Yan H, et al. Medical insurance payment schemes and patient medical expenses: a cross-sectional study of lung cancer patients in urban China. BMC Health Serv Res. 2023 Jan;23(1):89.

41. Organisation for Economic Co-operation and Development (OECD). Hospital beds (indicator). 2016.

42. Organisation for Economic Co-operation and Development (OECD). Computed tomography (CT). 2016.

43. Organisation for Economic Co-operation and Development (OECD). MRI (indicator). 2017.

44. Organisation for Economic Co-operation and Development (OECD). Doctors (indicator). 2017.

45. Organisation for Economic Co-operation and Development (OECD). Nurses (indicator). 2017.

46. Instituto Nacional de Geografía y Estadística (INEGI). Principales resultados de la encuesta intersensal 2015. Estados Unidos Mexicanos. XI:122, 2015.

47. Becerril VM, Knaul FM, Arreola H, et al. Sistema de salud de México. Salud Publica Mex. 2011;53(2) Centro de Investigación Económica y Presupuestaria (CIEP). Sistema universal de salud: retos de cobertura y financiamiento. 2018.

48. Knaul FM, Arreola-Ornelas H, Touchton M, McDonald T, Blofield M, Avila Burgos L, et al. Setbacks in the quest for universal health coverage in Mexico: polarised politics, policy upheaval, and pandemic disruption. Lancet. 2023 Aug; 402(10403):731-746.

49. Frenk J, Gómez-Dantés O. Health system in Mexico. In: Levy A, Goring S, Gatsonis C, Sobolev B, van Ginneken E, Busse R, editors. Health Services Evaluation, Health Services Research. Springer US; 2019. p. 849-859.

50. Gómez-Dantés O, Frenk J. Crónica de un siglo de salud pública en México: de la salubridad pública a la protección social en salud. Salud Publica Mex. 2019 Mar-Apr;61(2):202.

51. Gobierno de México. El Seguro Popular. 2019.

52. Gerson R, Zatarain-Barrón ZL, Blanco C, Arrieta O. Access to lung cancer therapy in the Mexican population: opportunities for reducing inequity within the health system. Salud Publica Mex. 2019 Jun;61(3):352-358.

53. Bautista-González E, Werner-Sunderland J, Pérez-Duarte Mendiola P, Esquinca-Enríquez-de-la Fuente CJ, Bautista-Reyes D, Maciel-Gutiérrez MF, et al. Health-care guidelines and policies during the COVID-19 pandemic in Mexico: A case of health inequalities. Health Policy OPEN. 2021 Dec;2:100025.

54. Koo MM, Unger-Saldaña K, Mwaka AD, Corbex M, Ginsburg O, Walter FM, Calanzani N, et al. Conceptual framework to guide early diagnosis programs for symptomatic cancer as part of global cancer control. JCO Glob Oncol. 2021 Jan;7:35–45.

55. Lim C, Tsao MS, Le LW, Shepherd FA, Feld R, Burkes RL, Liu G, et al. Biomarker testing and time to treatment decision in patients with advanced nonsmall-cell lung cancer. Ann Oncol. 2015 Jul;26(7):1415-1421.

56. Koo MM, Zhou Y, Lyratzopoulos G. Delays in diagnosis and treatment of lung cancer: Lessons from US healthcare settings. Cancer Epidemiol. 2015 Dec;39(6):1145-1147.

57. Chavarri-Guerra Y, Soto-Perez-de Celis E, Ramos-López W, San Miguel de Majors SL, Sanchez-Gonzalez J, Ahumada-Tamayo S, Viramontes-Aguilar L, et al. Patient navigation to enhance access to care for underserved patients with a suspicion or diagnosis of cancer. Oncologist. 2019 Sep;24(9):1195-1200.

58. Charvel S, Cobo-Armijo F, Hernández-Ávila M, Reynales-Shigematsu LM, Salas J, Arrieta O, Santillán-Doherty P, Roldán-Xopa J., Pérez-Cuevas R., Escudero-de Los Ríos P.M., Segú-Tolsa J.L. Needs in coverage and care for lung cancer in Mexico. Salud Publica Mex. 2019 Jun;61(3):339-346.

59. Neal RD, Allgar VL. Sociodemographic factors and delays in the diagnosis

of six cancers: analysis of data from the "National Survey of NHS Patients: Cancer". Br J Cancer. 2005 Jun;92(11):1971-1975.

60. Malalasekera A, Nahm S, Blinman PL, Kao SC, Dhillon HM, Vardy JL. How long is too long? A scoping review of health system delays in lung cancer. Eur Respir Rev. 2018 Sep;27(149).

61. Lubuzo B, Ginindza T, Hlongwana K. Exploring barriers to lung cancer patient access, diagnosis, referral and treatment in KwaZulu-Natal, South Africa: the health providers' perspectives. Transl Lung Cancer Res. 2019 Aug;8(4):380-391.

62. Natale-Pereira A, Enard KR, Nevarez L, Jones LA. The role of patient navigators in eliminating health disparities. Cancer. 2011 Aug;117(15 Suppl):3543-3552.

63. Sulu E, Tasolar O, Berk Takir H, Yagci Tuncer L, Karakurt Z, Yilmaz A. Delays in the diagnosis and treatment of non-small-cell lung cancer. Tumori. 2011 Nov-Dec;97(6):693-697.

64. Andersen RS, Vedsted P, Olesen F, Bro F, S. J. Patient delay in cancer studies: a discussion of methods and measures. BMC Health Serv Res. 2009 Oct;9:189.

65. Antonovsky A, Hartman H. Delay in the detection of cancer: A review of the literature. Health Educ Monogr. 1974 Jun;2(2):98-128.

66. Marmot M. Inclusion health: addressing the causes of the causes. Lancet. 2018 Jan;391(10117):186-188.

67. Marmot M, Friel S, Bell R, Houweling TAJ, Taylor S, Commission on Social Determinants of Health. Closing the gap in a generation: health

equity through action on the social determinants of health. Lancet. 2008 Nov;372(9650):1661-1669.

68. Hamilton W, Green T, Martins T, Elliott K, Rubin G, Macleod U. Evaluation of risk assessment tools for suspected cancer in general practice: a cohort study. Br J Gen Pract. 2013 Jan;63(606)

69. Jianrong, IJzerman MJ, Oberoi J, Karnchanachari N, Bergin RJ, Franchini F, Druce P, et al. Time to diagnosis and treatment of lung cancer: A systematic overview of risk factors, interventions and impact on patient outcomes. Lung Cancer. 2022 Apr;166:27-39.

70. Moguel-Ancheita A, Valdés-Olmedo C, González-Pier C, Martínez-González PE, Barraza-Llorens G, Aguilera-Aburto M, Trejo-Rayón N, et al. Universalidad de los servicios de salud en México. Salud Publica Mex. 2013;55:1-64.

71. Dirección General de Información en Salud. Manual del expediente clínico electrónico 2011. 2011.

72. Ochoa-Moreno JA. El expediente clínico electrónico universal en México: ¿Cómo se puede definir el expediente clínico electrónico? 2018;3(2).

73. Brouwers MC, Vukmirovic M, Tomasone JR, Grunfeld E, Urquhart R, O'Brien MA, Walker M, et al. Documenting coordination of cancer care between primary care providers and oncology specialists in Canada. Can Fam Physician. 2016 Oct;62(10)

74. Molina A. A México le urge el expediente clínico electrónico universal. 2017 Sep.

75. Hunnibell LS, Rose MG, Connery DM, Grens CE, Hampel JM, Rosa M,

Vogel DC. Using nurse navigation to improve timeliness of lung cancer care at a veterans hospital. Clin J Oncol Nurs. 2012 Feb;16(1):29-36.

76. Soto-Perez-de Celis E, Chavarri-Guerra Y, Ramos-Lopez WA, Alcalde-Castro J, Covarrubias-Gomez A, Navarro-Lara Á, Quiroz-Friedman P, et al. Patient navigation to improve early access to supportive care for patients with advanced cancer in resource-limited settings: A randomized controlled trial. Oncologist. 2021 Feb;26(2):157-164.

77. Neal CD, Weaver DT, Raphel TJ, Lietz AP, Flores EJ, Percac-Lima S, Knudsen AB, Pandharipande PV. Patient navigation to improve cancer screening in underserved populations: Reported experiences, opportunities, and challenges. J Am Coll Radiol. 2018 Nov;15(11):1565-1572.

78. Percac-Lima S, Ashburner JM, Zai AH, Chang Y, Oo SA, Guimaraes E, Atlas SJ. Patient navigation for comprehensive cancer screening in high-risk patients using a population-based health information technology system: A randomized clinical trial. JAMA Intern Med. 2016 Jul;176(7):930-937.

79. Vinas F, Ben Hassen I, Jabot L, Monnet I, Chouaid C. Delays for diagnosis and treatment of lung cancers: a systematic review. Clin Respir J. 2016 May;10(3):267-271.

80. Gabitova G, Burke NJ. Improving healthcare empowerment through breast cancer patient navigation: A mixed methods evaluation in a safety-net setting. BMC Health Serv Res. 2014 Sep;14:407.

81. Gunn CM, Clark JA, Battaglia TA, Freund KM, Parker VA. An assessment of patient navigator activities in breast cancer patient navigation programs using a nine-principle framework. Health Serv Res. 2014 Oct;49(5):1555-1577.

82. McBrien KA, Ivers N, Barnieh L, Bailey JJ, Lorenzetti DL, Nicholas D, Tonelli M, et al. Patient navigators for people with chronic disease: A systematic review. PLoS One. 2018 Feb;13(2)

83. Freund KM. Implementation of evidence-based patient navigation programs. Acta Oncol. 2017 Feb;56(2):123-127.

84. Crane-Okada R. Evaluation and outcome measures in patient navigation. Semin Oncol Nurs. 2013 May;29(2):128-140.

85. Paskett ED, Harrop JP, Wells KJ. Patient navigation: an update on the state of the science. CA Cancer J Clin. 2011 Aug;61(4):237-249.

86. Freeman HP. The origin, evolution, and principles of patient navigation. Cancer Epidemiol Biomarkers Prev. 2012 Oct;21(10):1614-1617.

87. Freund KM, Battaglia TA, Calhoun E, Dudley DJ, Fiscella K, Paskett E, Raich PC, et al. National Cancer Institute patient navigation research program: methods, protocol, and measures. Cancer. 2008 Dec 15;113(12):3391-3399.

88. Walter F, Webster A, Scott S, Emery J. The Andersen model of total patient delay: a systematic review of its application in cancer diagnosis. J Health Serv Res Policy. 2012 Apr;17(2):110-118.

89. Jean-Pierre P, Hendren S, Fiscella K, Loader S, Rousseau S, Schwartzbauer B, Sanders M, et al. Understanding the processes of patient navigation to reduce disparities in cancer care: perspectives of trained navigators from the field. J Cancer Educ. 2011 Mar;26(1):111-120.

90. A summary of the American Cancer Society report to the nation: cancer in the poor. CA Cancer J Clin. 1989 Oct;39(5):263-265.

91. Tejeda S, Darnell JS, Cho YI, Stolley MR, Markossian TW, Calhoun EA. Patient barriers to follow-up care for breast and cervical cancer abnormalities. J Womens Health (Larchmt). 2013 Jun;22(6):507-517.

92. Institute of Medicine. Unequal treatment: confronting racial and ethnic disparities in health care. Washington, D.C.: National Academies Press; 2003.

93. Hou SI, Roberson K. A systematic review on US-based community health navigator (CHN) interventions for cancer screening promotion–comparing community- versus clinic-based navigator models. J Cancer Educ. 2015 Mar;30(1):173-186.

94. Coughlin SS, Matthews-Juarez P, Juarez PD, Melton CE, King M. Opportunities to address lung cancer disparities among African Americans. Cancer Med. 2014 Dec;3(6):1467-1476.

95. Dohan D, Schrag D. Using navigators to improve care of underserved patients: current practices and approaches. Cancer. 2005 Aug 15;104(4):848-855.

96. Villarreal-Garza C, Castro-Sanchez A, Platas A, Miaja M, Mohar-Betancourt A, Barragan-Carrillo R, Fonseca A, Vega Y, Martinez-Cannon BA, Aguilar D, Bargalló-Rocha E, Cardona-Huerta S, Peña-Curiel O, Matus-Santos J. "Joven Fuerte": program for young women with breast cancer in Mexico - initial results. Rev Invest Cualit. 2017 Jul;69(4).

97. Molina Y, Glassgow AE, Kim SJ, Berrios NM, Pauls H, Watson KS, Darnell JS, Calhoun EA. Patient navigation in medically underserved areas study design: a trial with implications for efficacy, effect modification, and full continuum assessment. Contemp Clin Trials. 2017;53:29-35.

98. Psooy BJ, Borgaonkar J, Caines JS. Patient navigation: improving timeliness in the diagnosis of breast abnormalities. Can Assoc Radiol J. 2004;55(3):145-150.

99. Charlot M, Santana MC, Chen CA, Bak S, Heeren TC, Battaglia TA, Egan AP, Kalish R, Freund KM. Impact of patient and navigator race and language concordance on care after cancer screening abnormalities. Cancer. 2015 May 1;121(9):1477-1483.

100. Fink RM, Kline DM, Siler S, Fischer SM. Apoyo con cariño: a qualitative analysis of a palliative care-focused lay patient navigation intervention for Hispanics with advanced cancer. J Hosp Palliat Nurs. 2020 Aug;22(4):335-346.

101. Ell K, Vourlekis B, Lee PJ, Xie B. Patient navigation and case management following an abnormal mammogram: a randomized clinical trial. Prev Med. 2007 Jan;44(1):26-33.

102. Wells KJ, Battaglia TA, Dudley DJ, Garcia R, Greene A, Calhoun E, Mandelblatt JS, Paskett ED, Raich PC, Patient Navigation Research Program. Patient navigation: state of the art or is it science? Cancer. 2008 Oct 15;113(8):1999-2010.

103. Tho PC, Ang E. The effectiveness of patient navigation programs for adult cancer patients undergoing treatment: a systematic review. JBI Database System Rev Implement Rep. 2016;14(2):295-321.

104. Mireles-Aguilar T, Tamez-Salazar J, Muñoz-Lozano JF, Lopez-Martinez EA, Romero C, Platas A, Villarreal-Garza C. Alerta rosa: novel alert and navigation breast cancer program in Nuevo Leon, Mexico, for reducing health system interval delays. Oncologist. 2018 Dec;23(12):1461-1466.

105. Loskutova NY, Tsai AG, Fisher EB, LaCruz DM, Cherrington AL, Harrington TM, Turner TJ, Pace WD. Patient navigators connecting patients to community resources to improve diabetes outcomes. J Am Board Fam Med. 2016 Feb;29(1):78-89.

106. Markossian TW, Darnell JS, Calhoun EA. Follow-up and timeliness after an abnormal cancer screening among underserved, urban women in a patient navigation program. Cancer Epidemiol Biomarkers Prev. 2012 Oct;21(10):1691-1700.

107. Hendren S, Chin N, Fisher S, Winters P, Griggs J, Mohile S, Fiscella K. Patients' barriers to receipt of cancer care, and factors associated with needing more assistance from a patient navigator. J Natl Med Assoc. 2011 Aug;103(8):701-710.

108. Dudley DJ, Drake J, Quinlan J, Holden A, Saegert P, Karnad A, Ramirez A. Beneficial effects of a combined navigator/promotora approach for Hispanic women diagnosed with breast abnormalities. Cancer Epidemiol Biomarkers Prev. 2012 Oct;21(10):1639-1644.

109. Battaglia TA, Roloff K, Posner MA, Freund KM. Improving follow-up to abnormal breast cancer screening in an urban population. A patient navigation intervention. Cancer. 2007 Jan 1;109(2 Suppl):359-367.

110. Battaglia TA, Bak SM, Heeren T, Chen CA, Kalish R, Tringale S, Taylor JO, Lottero B, Egan AP, Thakrar N, Freund KM. Boston patient navigation research program: the impact of navigation on time to diagnostic resolution after abnormal cancer screening. Cancer Epidemiol Biomarkers Prev. 2012 Oct;21(10):1645-1654.

111. Herazo-Maya F, Garcia H, Yepes A, Ossa CA, Angel G, Borrero M, Jimenez JA, Montoya ME, Suarez LD, Reyes P, Gutierrez Restrepo EV, Ortiz LD,

Mesa G, Abad JM, Gomez LR. Navigation programs' impact in a Colombian breast cancer patients cohort. J Clin Oncol. 2015 May 33 (15) e17553-e17553

112. Carroll JK, Humiston SG, Meldrum SC, Salamone CM, Jean-Pierre P, Epstein RM, Fiscella K. Patients' experiences with navigation for cancer care. Patient Educ Couns. 2010 Aug;80(2):241-247.

113. Lee T, Ko I, Lee I, Kim E, Shin M, Roh S, Yoon D, Choi S, Chang H. Effects of nurse navigators on health outcomes of cancer patients. Cancer Nurs. 2011 Oct;34(5):376-384.

114. Wagner EH, Ludman EJ, Aiello Bowles EJ, Penfold R, Reid RJ, Rutter CM, Chubak J, McCorkle R. Nurse navigators in early cancer care: a randomized, controlled trial. J Clin Oncol. 2014 Jan 1;32(1):12-18.

115. Bensink ME, Ramsey SD, Battaglia T, Fiscella K, Hurd TC, McKoy JM, Patierno SR, Raich PC, Seiber EE, Warren-Mears V, Whitley E, Paskett ED, Mandelblatt S, Patient Navigation Research Program. Costs and outcomes evaluation of patient navigation after abnormal cancer screening: evidence from the Patient Navigation Research Program. Cancer. 2014 Feb 15;120(4):570-578.

116. De Mil R, Guillaume E, Guittet L, Dejardin O, Bouvier V, Pornet C, Christophe V, Notari A, Delattre-Massy H, De Seze C, Peng J, Launoy G, Berchi C. Cost-effectiveness analysis of a navigation program for colorectal cancer screening to reduce social health inequalities: a French cluster randomized controlled trial. Value Health. 2018 Jun;21(6):685-691.

117. Tian L, Huang L, Liu J, Li X, Ajmal A, Ajmal M, Yao Y, Tian L. Impact of patient navigation on population-based breast screening: a systematic review and meta-analysis of randomized clinical trials. J Gen Intern Med. 2022 Aug;37(11):2811-2820.

118. Chai Y, Li L, Wu YL, Wang T, Jia YM, Lin XL, Chen X, Zhong H, Liu LX, Tao LD. The effects of case management for breast cancer patients: A protocol for systematic review and meta-analysis. Medicine (Baltimore). 2022 Mar;101(9)

119. Yin YN, Wang Y, Jiang NJ, Long DR. Can case management improve cancer patients quality of life?: A systematic review following PRISMA. Medicine (Baltimore). 2020 Oct 2;99(40)

120. Wulff CN, Thygesen M, S J, Vedsted P. Case management used to optimize cancer care pathways: a systematic review. BMC Health Serv Res. 2008 Nov 5;8:227.

121. Bush ML, Kaufman MR, Shackleford T. Adherence in the cancer care setting: a systematic review of patient navigation to traverse barriers. J Cancer Educ. 2018 Dec;33(6):1222-1229.

122. Shusted CS, Barta JA, Lake M, Brawer R, Ruane B, Giamboy TE, Sundaram B, Evans NR, Myers RE, Kane GC. The case for patient navigation in lung cancer screening in vulnerable populations: a systematic review. Popul Health Manag. 2019 Aug;22(4):347-361.

123. Miller CJ, Smith SN, Pugatch M. Experimental and quasi-experimental designs in implementation research. Psychiatry Res. 2020 Jan;283:112452.

124. Munn Z, Peters MDJ, Stern C, Tufanaru C, McArthur A, Aromataris E. Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. BMC Med Res Methodol. 2018 Nov;18(1):143.

125. Cykert S, Eng E, Manning MA, Robertson LB, Heron DE, Jones NS, et al. A multi-faceted intervention aimed at black-white disparities in the treatment

of early stage cancers: The ACCURE pragmatic quality improvement trial. J Natl Med Assoc. 2020 Oct;112(5):468-477.

126. Charlot M, Stein JN, Damone E, Wood I, Forster M, Baker S, et al. Effect of an antiracism intervention on racial disparities in time to lung cancer surgery. J Clin Oncol. 2022 Jun;40(16):1755-1762.

127. Fleisher L, Miller SM, Crookes D, Kandadai V, Wen KY, Slamon RE, et al. Implementation of a theory-based, non-clinical patient navigator program to address barriers in an urban cancer center setting. J Oncol Navig Surviv. 2012 Jun;3(3):14-23.

128. Pitter JG, Moizs M, Ezer ÉS, Lukács G, Szigeti A, Repa I, et al. Improved survival of non-small cell lung cancer patients after introducing patient navigation: A retrospective cohort study with propensity score weighted historic control. PLoS One. 2022 Oct;17(10)

129. Zibrik K, Laskin J, Ho C. Integration of a nurse navigator into the triage process for patients with non-small-cell lung cancer: creating systematic improvements in patient care. Curr Oncol. 2016 Jun;23(3)

130. Battaglia TA, Gunn CM, Bak SM, Flacks J, Nelson KP, Wang N, et al. Patient navigation to address sociolegal barriers for patients with cancer: A comparative-effectiveness study. Cancer. 2022 Jul;128 Suppl 13:2623-2635.

131. Berezowska A, Passchier E, Bleiker E. Professional patient navigation in a hospital setting: a randomized controlled trial. Support Care Cancer. 2021 Apr;29(4):2111-2123.

132. Lorhan S, Cleghorn L, Fitch M, Pang K, McAndrew A, Applin-Poole J, et al. Moving the agenda forward for cancer patient navigation:

understanding volunteer and peer navigation approaches. J Cancer Educ. 2013 Mar;28(1):84-91.

133. Langballe R, Dalton SO, Jakobsen E, ValbjKarlsen R, Iachina M, Freund KM, et al. NAVIGATE: improving survival in vulnerable patients with lung cancer through nurse navigation, symptom monitoring and exercise - study protocol for a multicentre randomised controlled trial. BMJ Open. 2022 Oct;12(10)

134. Gödde K, Fügemann H, Goerling U, Grittner U, Kohl R, Meisel A, et al. Feasibility of a patient-oriented navigation programme for patients with lung cancer or stroke in Germany: Protocol of the CoreNAVI study. PLoS One. 2023 Jun;18(6)

135. Koller M, Warncke S, Hjermstad MJ, Arraras J, Pompili C, Harle A, et al. Use of the lung cancer-specific quality of life questionnaire EORTC QLQ-LC13 in clinical trials: A systematic review of the literature 20 years after its development. Cancer. 2015 Dec;121(24):4300-4323.

136. Koller M, Hjermstad MJ, Tomaszewski KA, Tomaszewska IM, Hornslien K, Harle A, et al. An international study to revise the EORTC questionnaire for assessing quality of life in lung cancer patients. Ann Oncol. 2017 Nov;28(11):2874-2881.

137. Glaser BG, Strauss AL. The Discovery of Grounded Theory. 1st ed. New Brunswick, NJ: AldineTransaction; 1967 Jan.

138. Unger-Saldaña K, Peláez-Ballestas I, Infante-Castañeda C. Development and validation of a questionnaire to assess delay in treatment for breast cancer. BMC Cancer. 2012 Dec;12:626.

139. Unger-Saldaña K, Miranda A, Zarco-Espinosa G, Mainero-Ratchelous F, Bargalló-Rocha E, Lázaro-León JM. Health system delay and its effect

on clinical stage of breast cancer: Multicenter study. Cancer. 2015 Jul;121(13):2198-2206.

140. Battaglia TA, Freund KM, Haas JS, Casanova N, Bak S, Cabral H, et al. Translating research into practice: Protocol for a community-engaged, stepped wedge randomized trial to reduce disparities in breast cancer treatment through a regional patient navigation collaborative. Contemp Clin Trials. 2020 Jun;93:106007.

141. Bautista-González E, Soto-Pérez-de Celis E, Hasselkus-Sánchez GA, Muñoz Rocha TV, Gay-Molina JG, Ortiz-Blas LA, et al. Código cáncer: resultados preliminares. Gac Med Mex Oncol. 2023 Sep.

142. Unger-Saldaña K. Challenges to the early diagnosis and treatment of breast cancer in developing countries. World J Clin Oncol. 2014 Aug;5(3):465-477.

143. Unger-Saldaña K, Ventosa-Santaulària D, Miranda A, Verduzco-Bustos G. Barriers and explanatory mechanisms of delays in the patient and diagnosis intervals of care for breast cancer in Mexico. Oncologist. 2018 Apr;23(4):440-453.

144. Tashakkori A, Teddlie C. SAGE Handbook of Mixed Methods in Social Behavioral Research. 2nd ed. Thousand Oaks, CA: SAGE Publications, Inc.; 2010.

145. Collins KMT, Onwuegbuzie AJ, Jiao QG. Prevalence of mixed-methods sampling designs in social science research. Eval Res Educ. 2006 May;19(2):83-101.

146. Palinkas LA, Horwitz SM, Green CA, Wisdom JP, Duan N, Hoagwood K. Purposeful sampling for qualitative data collection and analysis in

mixed method implementation research. Adm Policy Ment Health. 2015 Sep;42(5):533-544.

147. Curry LA, Nembhard IM, Bradley EH. Qualitative and mixed methods provide unique contributions to outcomes research. Circulation. 2009 Mar;119(10):1442-1452.

148. Baxter P, Jack S. Qualitative case study methodology: study design and implementation for novice researchers. Qual Rep. 2015 Jan.

149. Stake RE. The Art of Case Study Research. 1st ed. Thousand Oaks, CA: Sage Publications; 1995.

150. Creswell JW. Qualitative Inquiry and Research Design: Choosing Among Five Approaches. 2nd ed. Thousand Oaks, CA: SAGE Publications, Inc.; 2006.

151. Clarke V, Braun V. Thematic analysis. In: Teo T, editor. Encyclopedia of Critical Psychology. New York, NY: Springer New York; 2014. p. 1947-52.

152. Hendren S, Griggs JJ, Epstein RM, Humiston S, Rousseau S, Jean-Pierre P, et al. Study protocol: a randomized controlled trial of patient navigation-activation to reduce cancer health disparities. BMC Cancer. 2010 Oct;10:551.

153. Gilbert J, Veazie S, Joines K, Winchell K, Relevo R, Paynter R, et al. Patient navigation models for lung cancer. AHRQ rapid evidence products. Rockville, MD: Agency for Healthcare Research and Quality (US); 2018.

154. Myers RE, Sifri R, Daskalakis C, DiCarlo M, Geethakumari PR, Cocroft J, et al. Increasing colon cancer screening in primary care among African Americans. J Natl Cancer Inst. 2014 Dec;106(12).

155. Corbett CM, Somers TJ, Nuñez CM, Majestic CM, Shelby RA, Worthy VC, et al. Evolution of a longitudinal, multidisciplinary, and scalable patient navigation matrix model. Cancer Med. 2020 May;9(9):3202-3210.

156. Grimes C, Dankovchik J, Cahn M, Warren-Mears V. American Indian and Alaska Native cancer patients' perceptions of a culturally specific patient navigator program. J Prim Prev. 2017;38(1-2):121-135.

157. Lee JH, Fulp W, Wells KJ, Meade CD, Calcano E, Roetzheim R. Patient navigation and time to diagnostic resolution: results for a cluster randomized trial evaluating the efficacy of patient navigation among patients with breast cancer screening abnormalities, Tampa, FL. PLoS One. 2013 Sep;8(9)

158. American Cancer Society. Navigation metrics toolkit. 2020 Aug.

159. Phillips S, Nonzee N, Tom L, Murphy K, Hajjar N, Bularzik C, et al. Patient navigators' reflections on the navigator-patient relationship. J Cancer Educ. 2014 Jun;29(2):337-344.

160. Ward PR, Meyer SB, Verity F, Gill TK, Luong TC. Complex problems require complex solutions: the utility of social quality theory for addressing the social determinants of health. BMC Public Health. 2011 Aug;11:630.

161. Masseria C, Hernández-Quevedo C, Allin S. Health inequality: what does it mean and how can we measure it? Expert Rev Pharmacoecon Outcomes Res. 2010 Apr;10(2):177-186.

162. Asada Y, Hurley J, Norheim OF, Johri M. A three-stage approach to measuring health inequalities and inequities. Int J Equity Health. 2014 Nov;13:98.

163. Alleyne GAO, Castillo-Salgado C, Schneider MC, Loyola E, Vidaurre M. Overview of social inequalities in health in the region of the Americas,

using various methodological approaches. Rev Panam Salud Publica. 2002 Dec;12(6):388-397.

164. Koo MM, Hamilton W, Walter FM, Rubin GP, Lyratzopoulos G. Symptom signatures and diagnostic timeliness in cancer patients: A review of current evidence. Neoplasia. 2018;20(2):165-174.

165. Neal RD, Din NU, Hamilton W, Ukoumunne OC, Carter B, Stapley S, et al. Comparison of cancer diagnostic intervals before and after implementation of NICE guidelines: analysis of data from the UK general practice research database. Br J Cancer. 2014 Feb;110(3):584-592.

166. Nadpara P, Madhavan SS, Tworek C. Guideline-concordant timely lung cancer care and prognosis among elderly patients in the United States: A population-based study. Cancer Epidemiol. 2015 Dec;39(6):1136-1144.

167. Lyratzopoulos G, Neal RD, Barbiere JM, Rubin GP, Abel GA. Variation in number of general practitioner consultations before hospital referral for cancer: findings from the 2010 national cancer patient experience survey in England. Lancet Oncol. 2012 Apr;13(4):353-365.

168. Lyratzopoulos G, Abel GA, McPhail S, Neal RD, Rubin GP. Measures of promptness of cancer diagnosis in primary care: secondary analysis of national audit data on patients with 18 common and rarer cancers. Br J Cancer. 2013 Feb;108(3):686–690.

169. Di Girolamo C, Walters S, Gildea C, Majano SB, Rachet B, Morris M. Can we assess cancer waiting time targets with cancer survival? a population-based study of individually linked data from the national cancer waiting times monitoring dataset in England, 2009-2013. PLoS One. 2018 Aug;13(8)

170. Hansen F, Rosvold Berntsen GK, Salamonsen A. Patient pathways as social drama: a qualitative study of cancer trajectories from the patient's perspective. Int J Qual Stud Health Well-being. 2019 Dec;14(1):1639461.

171. Malalasekera A, Dhillon HM, Blinman PL, Kao SC, Vardy JL. Delays to diagnosis and treatment of lung cancer in Australia: healthcare professional perceptions of actual versus acceptable timeframes. Intern Med J. 2018 Sep;48(9):1063-1071.

172. Malalasekera A, Dhillon HM, Shunmugasundaram C, Blinman PL, Kao SC, Vardy JL. Why do delays to diagnosis and treatment of lung cancer occur? a mixed methods study of insights from Australian clinicians. Asia Pac J Clin Oncol. 2021 Apr;17(2)

173. Llewellyn H, Higgs P, Sampson EL, Jones L, Thorne L. Topographies of 'care pathways' and 'healthscapes': reconsidering the multiple journeys of people with a brain tumour. Sociol Health Illn. 2018 Mar;40(3):410-425.

174. Bravi F, Di Ruscio E, Frassoldati A, Cavallesco GN, Valpiani G, Ferrozzi A, et al. Patient and health care professional perspectives: A case study of the lung cancer integrated care pathway. Int J Integr Care. 2018 Oct;18(4):7.

175. Lynch J, Hallqvist J, Power C, Kuh D, Ben-Shlomo Y. Lifecourse epidemiology. J Epidemiol Community Health. 2003;57:778-783.

176. Lynch J, Davey Smith G. A life course approach to chronic disease epidemiology. Annu Rev Public Health. 2005;26:1-35.

177. Younas A, Fàbregues S, Creswell JW. Generating metainferences in mixed methods research: A worked example in convergent mixed methods designs. Methodol Innov. 2023 Jul. 16(3), 276-291

178. Dawadi S, Shrestha S, Giri RA. Mixed-methods research: A discussion on its types, challenges, and criticisms. J Pract Stud Educ. 2021 Feb;2(2):25-36.

179. Perez A, Howell Smith MC, Babchuk WA, Lynch-O LI. Advancing quality standards in mixed methods research: extending the legitimation typology. J Mix Methods Res. 2023 Jan;17(1):29-50.

180. Fàbregues S, Molina-Azorín JF. Addressing quality in mixed methods research: a review and recommendations for a future agenda. Qual Quant. 2016 Oct; 51(6):2847–2863

181. Hamilton W, Peters TJ, Round A, Sharp D. What are the clinical features of lung cancer before the diagnosis is made? a population based case-control study. Thorax. 2005 Dec;60(12):1059-1065.

182. Dinos S, Ascoli M, Owiti JA, Bhui K. Assessing explanatory models and health beliefs: an essential but overlooked competency for clinicians. BJPsych Adv. 2017 Mar;23(2):106-114.

183. Pati S, Hussain MA, Chauhan AS, Mallick D, Nayak S. Patient navigation pathway and barriers to treatment seeking in cancer in India: a qualitative inquiry. Cancer Epidemiol. 2013 Dec;37(6):973-978.

184. Rodrigues A, Chauhan J, Sagkriotis A, Aasaithambi S, Montrone M. Understanding the lived experience of lung cancer: a European social media listening study. BMC Cancer. 2022 Apr;22(1):475.

185. Biswas B, Talwar D, Meshram P, Julka PK, Mehta A, Somashekhar SP, et al. Navigating patient journey in early diagnosis of lung cancer in India. Lung India. 2023;40(1):48-58.

186. Castro MA, Guerra YC, Ramos-Lopez WA, Covarrubias-Gómez A, Sanchez S, Quiroz P, et al. Diagnostic and prognostic awareness among patients with

metastatic solid cancer in a public cancer center in Mexico. J Clin Oncol. 2018 Dec;36 (34):42-42.

187. Zhang JM, Zhang MR, Yang CH, Li Y. The meaning of life according to patients with advanced lung cancer: a qualitative study. Int J Qual Stud Health Well-being. 2022 Dec;17(1):2028348.

188. Chow MC, Chambers P, Singleton G, Patel J, Cooper S, Mythen C, et al. Global changes to the chemotherapy service during the COVID-19 pandemic. J Oncol Pharm Pract. 2021 Jul;27(5):1073-1079.

189. Frank AW. The Wounded Storyteller: Body, Illness, and Ethics. Chicago (IL): University of Chicago Press; 1995.

190. Atkinson S, Rubinelli S. Narrative in cancer research and policy: voice, knowledge and context. Crit Rev Oncol Hematol. 2012 Dec;84 Suppl 2

191. Fakis A, Hilliam R, Stoneley H, Townend M. Quantitative analysis of qualitative information from interviews. J Mix Methods Res. 2014 Apr;8(2):139-161.

192. Ben-Shlomo Y, Kuh D. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. Int J Epidemiol. 2002 Apr;31(2):285-293.

193. McCutchan GM, Wood F, Edwards A, Richards R, Brain KE. Influences of cancer symptom knowledge, beliefs and barriers on cancer symptom presentation in relation to socioeconomic deprivation: a systematic review. BMC Cancer. 2015 Dec;15:1000.

194. Silvia AP, Nieves AP, Gonzalez LG, Carrillo EM, Aviles EV. Reality, delays, and challenges within pain prevalence and treatment in palliative care

patients: A survey of first-time patients at the national cancer institute in Mexico. J Palliat Care. 2021 Jul;36(3):181-187.

195. Arrieta O, Lara-Mejía L, Bautista-González E, Heredia D, Turcott JG, Barrón F, et al. Clinical impact of the COVID-19 pandemic in Mexican patients with thoracic malignancies. Oncologist. 2021 Dec;26(12):1035-1043.

196. Travis WD, Asamura H, Bankier AA, Beasley MB, Detterbeck F, Flieder DB, et al. The IASLC lung cancer staging project: Proposals for coding T categories for subsolid nodules and assessment of tumor size in part-solid tumors in the forthcoming eighth edition of the TNM classification of lung cancer. J Thorac Oncol. 2016 Apr;11(8):1204-1223.

197. Kirkwood BR. Essential medical statistics. Malden (MA): Blackwell Science; 2003.

198. Cleves M, Gould W, Marchenko Y. An introduction to survival analysis using Stata. 3rd ed. College Station (TX): Stata Press; 2010 Sep.

199. Salomaa ER, Sällinen S, Hiekkanen H, Liippo K. Delays in the diagnosis and treatment of lung cancer. Chest. 2005 Oct;128(4):2282-2288.

200. Alanen V, Koivunen JP. Association of diagnostic delays to survival in lung cancer: single center experience. Acta Oncol. 2019 Jul;58(7):1056-1061.

201. Virally J, Choudat L, Chebbo M, Sartene R, Jagot JL, Elhadad A, et al. Épidémiologie et délais de prise en charge de 355 patients atteints de cancer bronchique. Rev Mal Respir. 2006 Feb;23(1):43-48.

202. Brueckl WM, Wagner H, Wagner M, Wiest GH, Ficker JH. Delays in the diagnosis and treatment of women with lung cancer: A systematic analysis. J Clin Oncol. 2015 May;33(15) e17740-e17740

203. Radzikowska E, Roszkowski-Sliz K, Chabowski M, Glaz P. Influence of delays in diagnosis and treatment on survival in small cell lung cancer patients. Adv Exp Med Biol. 2013;788:355-362.

204. Garg A, Iyer H, Jindal V, Vashistha V, Chawla G, Tiwari P, et al. Evaluation of delays during diagnosis and management of lung cancer in India: A prospective observational study. Eur J Cancer Care. 2022 Sep;31(5)

205. González-Barcala FJ, García-Prim JM, Alvarez-Dobaño JM, Moldes-Rodríguez M, García-Sanz MT, Pose-Reino A, et al. Effect of delays on survival in patients with lung cancer. Clin Transl Oncol. 2010 Dec;12(12):836-842.

206. Myrdal G, Lambe M, Hillerdal G, Lamberg K, Agustsson T, Stahle E. Effect of delays on prognosis in patients with non-small cell lung cancer. Thorax. 2004 Jan;59(1):45-49.

207. Gould MK, Ghaus SJ, Olsson JK, Schultz EM. Timeliness of care in veterans with non-small cell lung cancer. Chest. 2008 May;133(5):1167-1173.

208. Unger-Saldaña K, Fitch-Picos K, Villarreal-Garza C. Breast cancer diagnostic delays among young Mexican women are associated with a lack of suspicion by health care providers at first presentation. J Glob Oncol. 2019 Jul;5:1-12.

209. Salgado-de Snyder VN, Wong R. Género y pobreza: determinantes de la salud en la vejez. Salud Publica Mex. 2007, vol.49, suppl.4, pp.s515-s521

210. Fuentes MU. Los determinantes Sociales de la Salud y de la equidad en Salud. Colección de Aniversario: 150 años de la Academia Nacional de Medicina. Mexico: Intersistemas Sa de CV; 2016. ISBN: 978-607-443-633-4

211. Silberman M., Moreno Altamirano L., Kawas Bustamante V., González Almada E.. Determinantes sociales de la salud en los usuarios de atención

sanitaria del distrito federal: una experiencia desde los centros de salud pública. Rev Fac Med UNAM. aug 2013; 56(4): 24-34.

212. Banik A, Schwarzer R, Pawlowska I, Boberska M, Cieslak R, Luszczynska A. Women with family cancer history are at risk for poorer physical quality of life and lower self-efficacy: a longitudinal study among men and women with non-small cell lung cancer. Health Qual Life Outcomes. 2017 Apr;15(1):62.

213. Hamilton W. The CAPER studies: five case-control studies aimed at identifying and quantifying the risk of cancer in symptomatic primary care patients. Br J Cancer. 2009 Dec;101 Suppl 2

214. Guirado M, Fernández Martín E, Fernández Villar A, Navarro Martín A, Sánchez-Hernández A. Clinical impact of delays in the management of lung cancer patients in the last decade: systematic review. Clin Transl Oncol. 2022 Aug;24(8):1549-1568.

215. Forrest LF, Adams J, White M, Rubin G. Factors associated with timeliness of post-primary care referral, diagnosis and treatment for lung cancer: population-based, data-linkage study. Br J Cancer. 2014 Oct;111(9):1843-1851.

216. Venuta F, Diso D, Onorati I, Anile M, Mantovani S, Rendina EA. Lung cancer in elderly patients. J Thorac Dis. 2016 Nov;8(Suppl 11)

217. Potter A, Senthil P, Mansur A, Mathey-Andrews C, Auchincloss H, Yang CFJ. OA05.06 early diagnosis of lung cancer among younger vs. older adults: widening disparities in the era of lung cancer screening. J Thorac Oncol. 2022 Sep;17(9)

218. Tagliacozzo R, Vaughn S. Women's smoking trends and awareness of health risk. Prev Med. 1980 May;9(3):384-387.

219. Sarna L. Lung cancer: the overlooked women's health priority. Cancer Pract. 1995; 3(1): 13-18.

220. Robledo-Aburto ZA, Duque-Molina C, Lara-Saldaña GJ, Borrayo-Sánchez G, Avilés-Hernández R, Reyna-Sevilla A. [Infarction code care protocol, towards the federalization of IMSS bienestar]. Rev Med Inst Mex Seguro Soc. 2022 Dec;60(Suppl 2):49-53.

221. Giroux Leprieur E, Labrune S, Giraud V, Gendry T, Cobarzan D, Chinet T. Delay between the initial symptoms, the diagnosis and the onset of specific treatment in elderly patients with lung cancer. Clin Lung Cancer. 2012 Sep;13(5):363-368.

222. Dale DC. Poor prognosis in elderly patients with cancer: the role of bias and undertreatment. J Support Oncol. 2003 Dec;1(4 Suppl 2):11-17.

223. Rydbeck D, Asplund D, Bock D, Haglind E, Park J, Rosenberg J, et al. Younger age at onset of colorectal cancer is associated with increased patient's delay. Eur J Cancer. 2021 Sep;154:269-276.

224. Castelo M, Sue-Chue-Lam C, Paszat L, Scheer AS, Hansen BE, Kishibe T, et al. Clinical delays and comparative outcomes in younger and older adults with colorectal cancer: A systematic review. Curr Oncol. 2022 Nov;29(11):8609-8625.

225. Morris NS, Field TS, Wagner JL, Cutrona SL, Roblin DW, Gaglio B, et al. The association between health literacy and cancer-related attitudes, behaviors, and knowledge. J Health Commun. 2013;18 Suppl 1:223-241.

226. Herb J, Friedman H, Shrestha S, Kent EE, Stitzenberg K, Haithcock B, et al. Barriers and facilitators to early-stage lung cancer care in the USA: a qualitative study. Support Care Cancer. 2022 Dec;31(1):21.

227. Facione NC. Delay versus help seeking for breast cancer symptoms: a critical review of the literature on patient and provider delay. Soc Sci Med. 1993 Jun;36(12):1521-1534.

228. Leiro-Fernández V, Mouronte-Roibás C, García-Rodríguez E, Botana-Rial M, Ramos-Hernández C, Torres-Durán M, et al. Predicting delays in lung cancer diagnosis and staging. Thorac Cancer. 2019 Feb;10(2):296-303.

229. Gould MK. Delays in lung cancer care: time to improve. J Thorac Oncol. 2009 Nov;4(11):1303-1304.

230. Vinod SK, Chandra A, Berthelsen A, Descallar J. Does timeliness of care in non-small cell lung cancer impact on survival? Lung Cancer. 2017 Jul;112:16-24.

231. Abrao FC, de Abreu IRB, Rocha RO, Munhoz FD, Rodrigues JHG, Batista BN. Interaction between treatment delivery delay and stage on mortality from non-small cell lung cancer. J Thorac Dis. 2018 May;10(5):2813-2819.

232. Arrieta O, Carmona A, Ramírez-Tirado LA, Flores-Estrada D, Macedo-Pérez EO, Martínez-Hernández JN, et al. Survival of patients with advanced non-small cell lung cancer enrolled in clinical trials. Oncology. 2016 Jul;91(4):185-193.

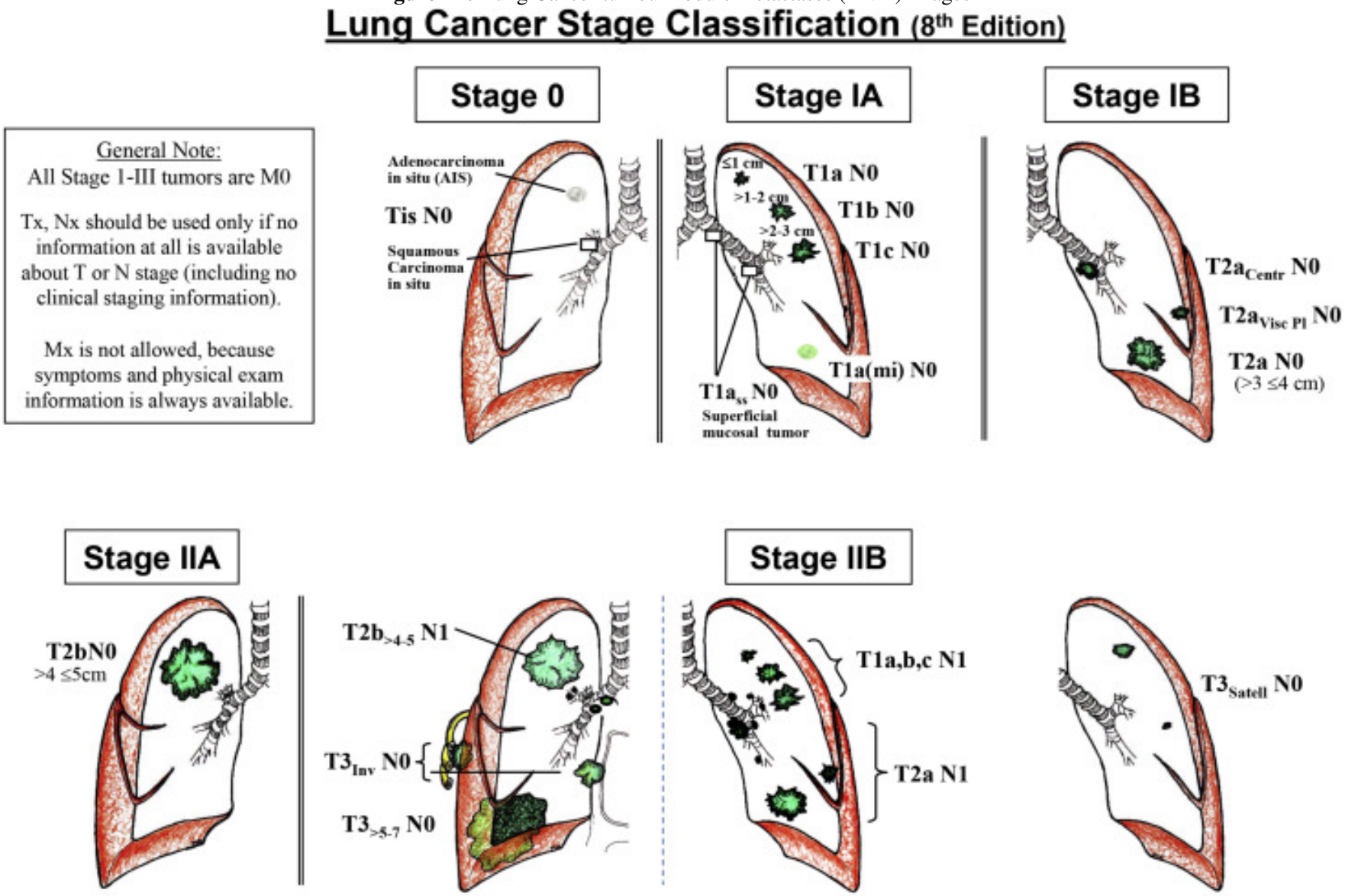
233. Hamilton W, Sharp D. Diagnosis of lung cancer in primary care: a structured review. Fam Pract. 2004 Dec;21(6):605-611.

234. Guetterman TC, Fetters MD, Creswell JW. Integrating quantitative and qualitative results in health science mixed methods research through joint displays. Ann Fam Med. 2015 Nov;13(6):554-561.

Appendix

A1: Supplementary Figures

Figure F2: Lung Cancer tumour nodule metastases (TNM) images



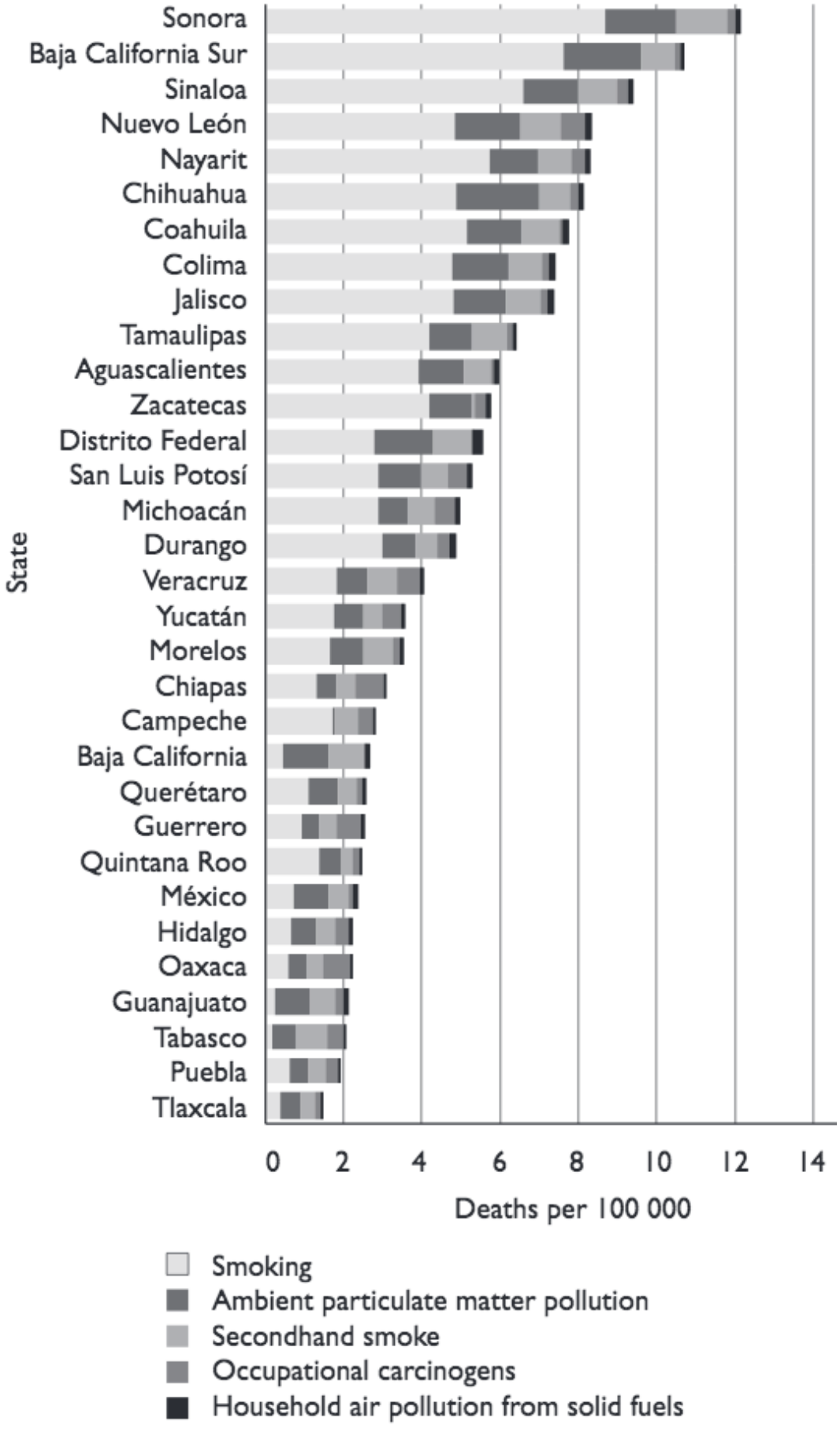
Source: Detterbeck et al., 2017 [22]

Figure F3: Lung Cancer tumour nodule metastases (TNM) classification

TNM 8th - Primary tumor characteristics	
T_x	Tumor in sputum/bronchial washings but not be assessed in imaging or bronchoscopy
T_0	No evidence of tumor
T_{is}	Carcinoma in situ
T_1	≤ 3 cm surrounded by lung/visceral pleura, not involving main bronchus
$T_{1a(mi)}$	Minimally invasive carcinoma
T_{1a}	≤ 1 cm
T_{1b}	> 1 to ≤ 2 cm
T_{1c}	> 2 to ≤ 3 cm
T_2	> 3 to ≤ 5 cm *or* involvement of main bronchus without carina, regardless of distance from carina or invasion visceral pleural *or* atelectasis or post obstructive pneumonitis extending to hilum
T_{2a}	>3 to ≤4cm
T_{2b}	>4 to ≤5cm
T_3	>5 to ≤7cm in greatest dimension *or* tumor of any size that involves chest wall, pericardium, phrenic nerve *or* satellite nodules in the same lobe
T_4	> 7cm in greatest dimension *or* any tumor with invasion of mediastinum, diaphragm, heart, great vessels, recurrent laryngeal nerve, carina, trachea, oesophagus, spine *or* separate tumor in different lobe of ipsilateral lung
N_1	Ipsilateral peribronchial and/or hilar nodes and intrapulmonary nodes
2	Ipsilateral mediastinal and/or subcarinal nodes
3	Contralateral mediastinal or hilar; ipsilateral/contralateral scalene/ supraclavicular
M_1	Distant metastasis
M_{1a}	Tumor in contralateral lung or pleural/pericardial nodule/malignant effusion
M_{1b}	Single extrathoracic metastasis, including single non-regional lymphnode
M_{1c}	Multiple extrathoracic metastases in one or more organs

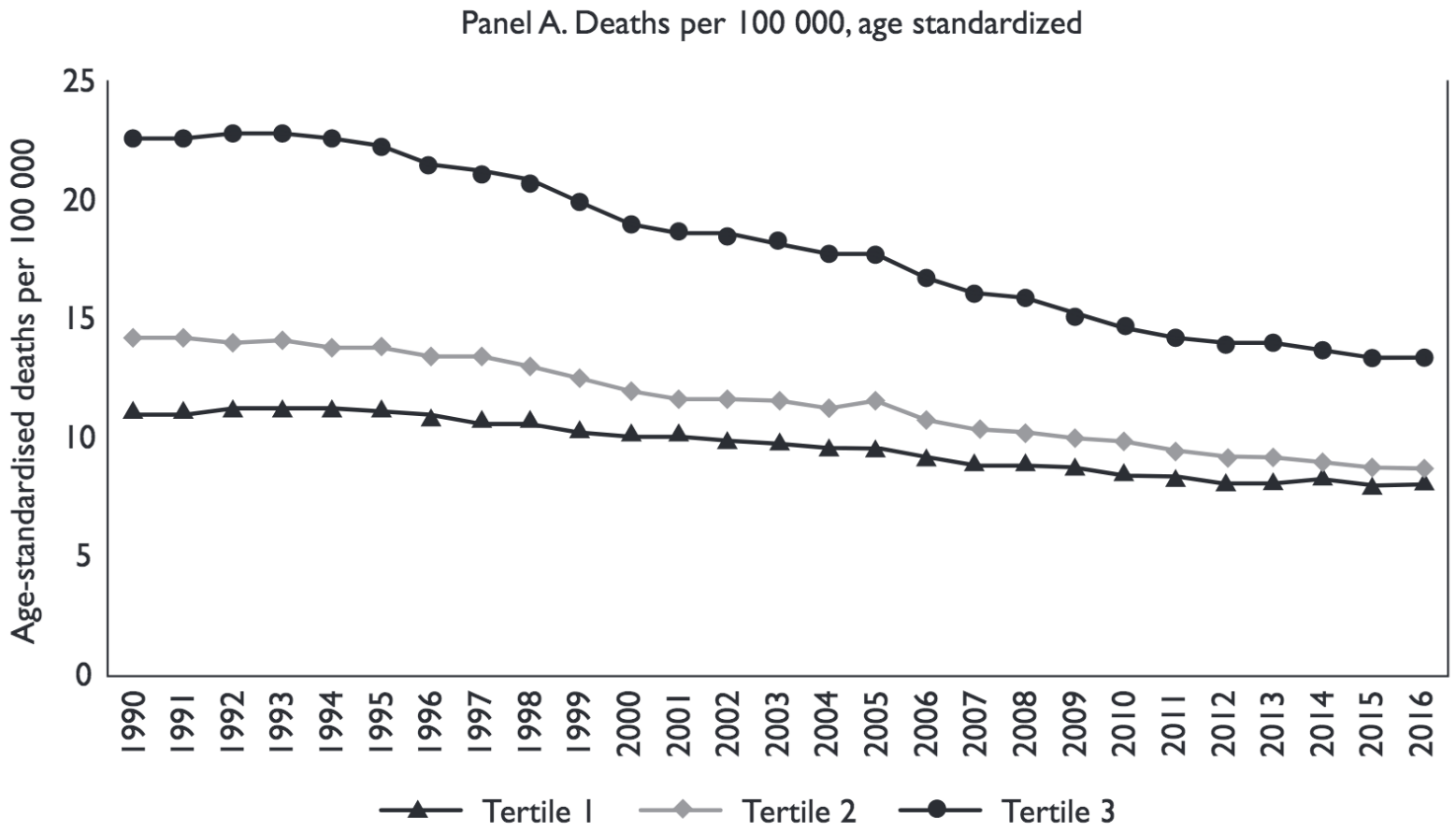
Source: Detterbeck et al., 2017 [22]

Figure F4: Deaths due to lung cancer by risk factor & region in Mexico



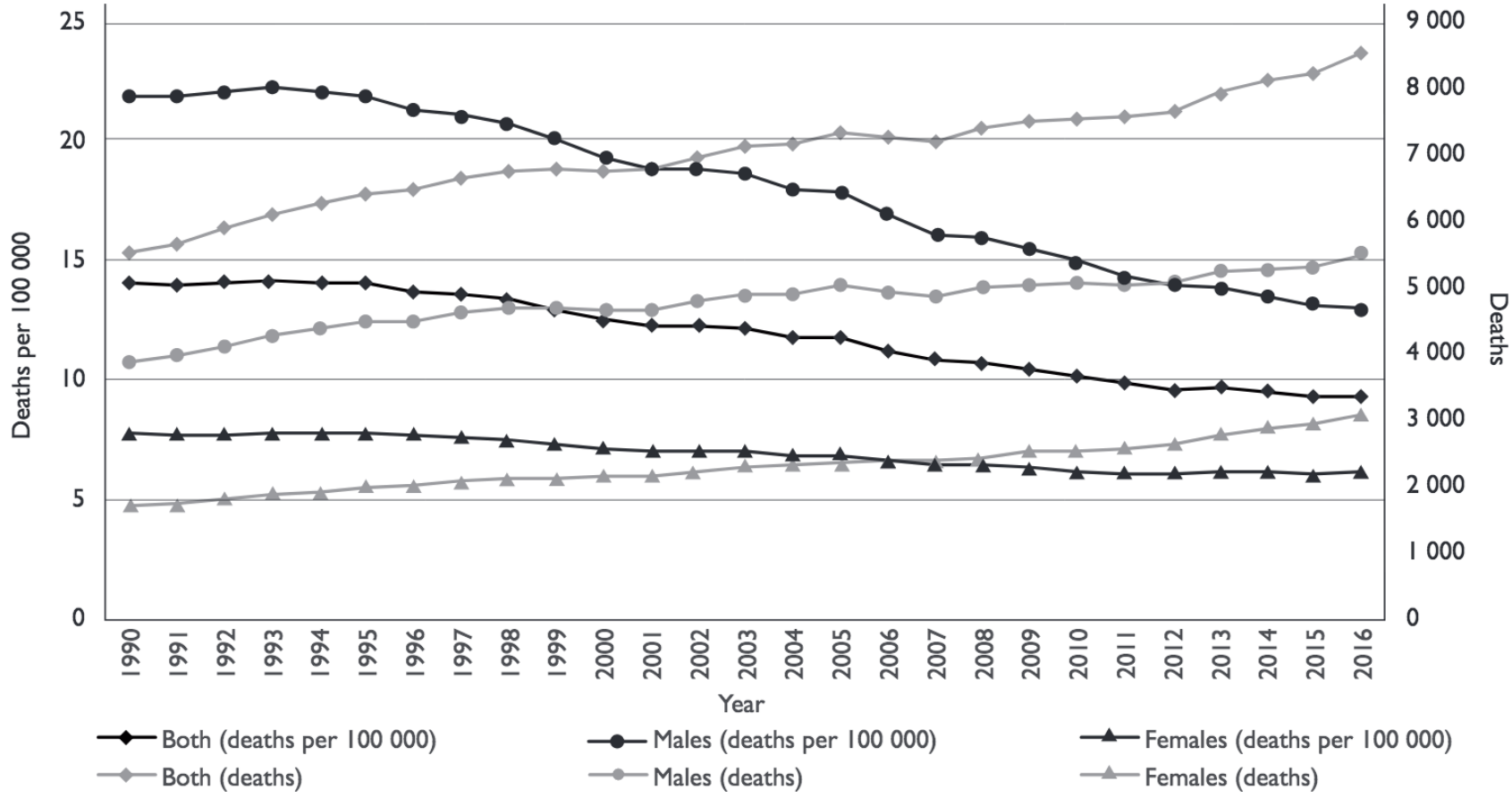
Source: Guerrero-Lopez CM et al., 2019 [27]

Figure F5: Age-standardised lung cancer mortality rate and deaths by deprivation tertiles in Mexico



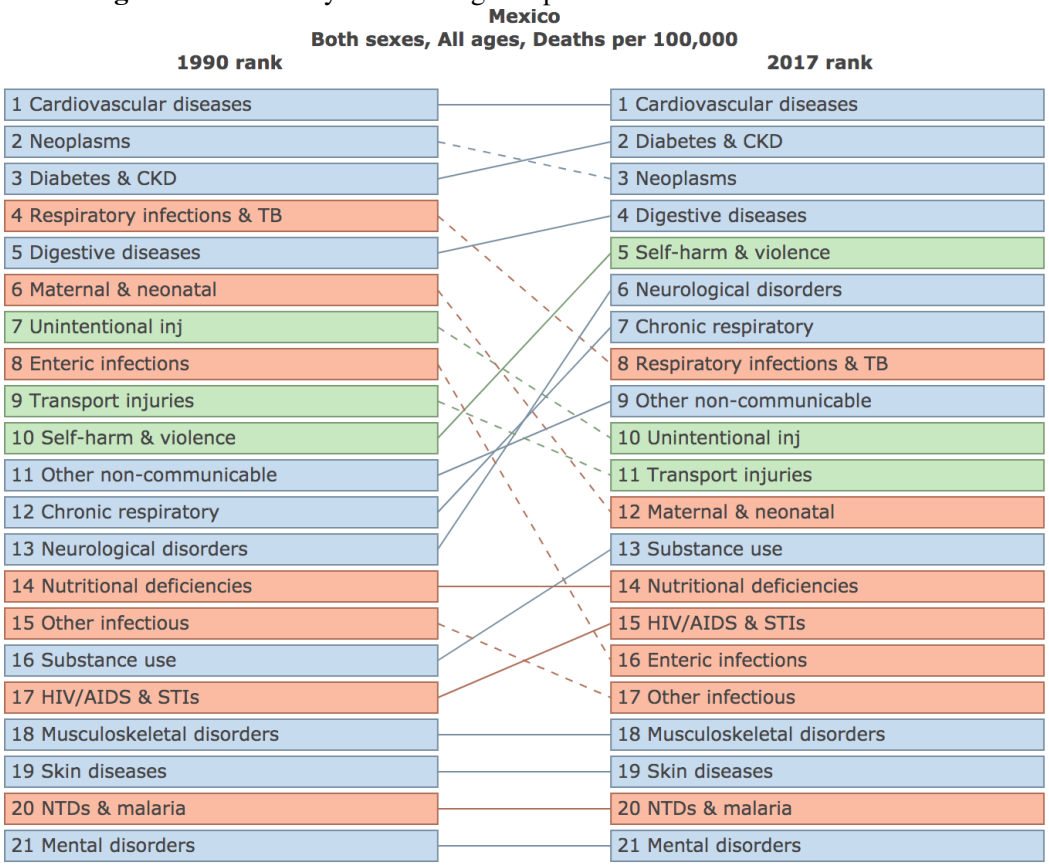
Source: Guerrero-Lopez CM et al., 2019 [27]

Figure F6: Age-standardised lung cancer mortality rate and deaths by sex in Mexico



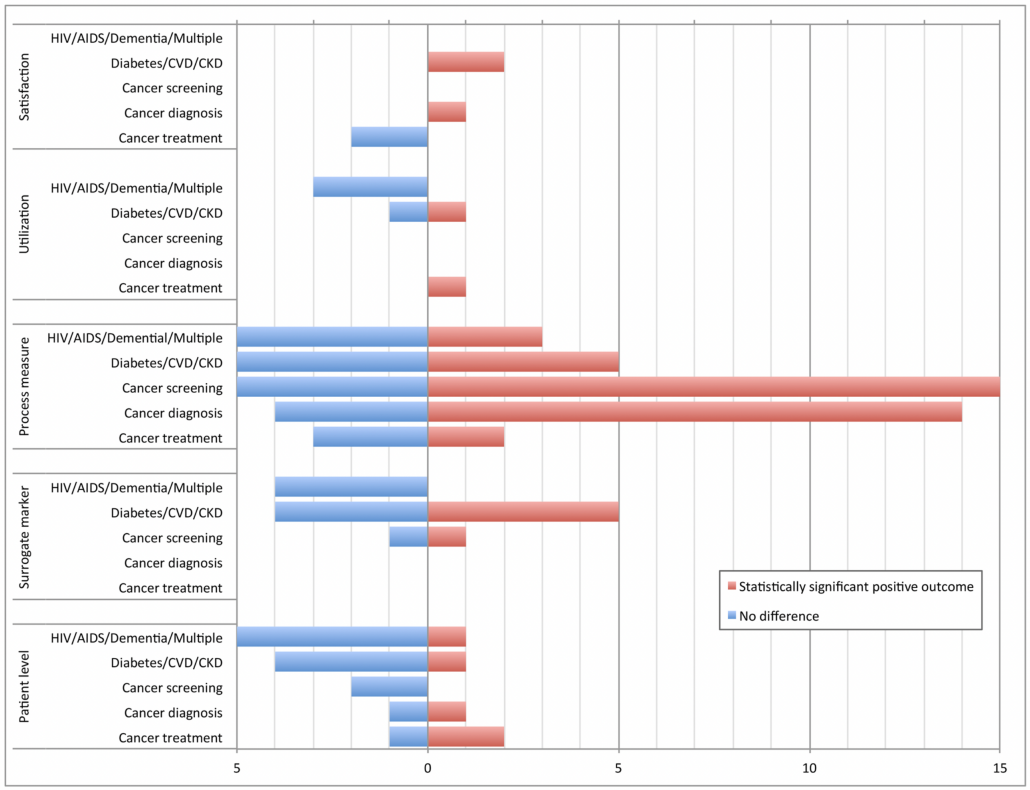
Source: Guerrero-Lopez CM et al., 2019 [27]

Figure F7: Mortality rate ranking comparison in Mexico from 1990 to 2017



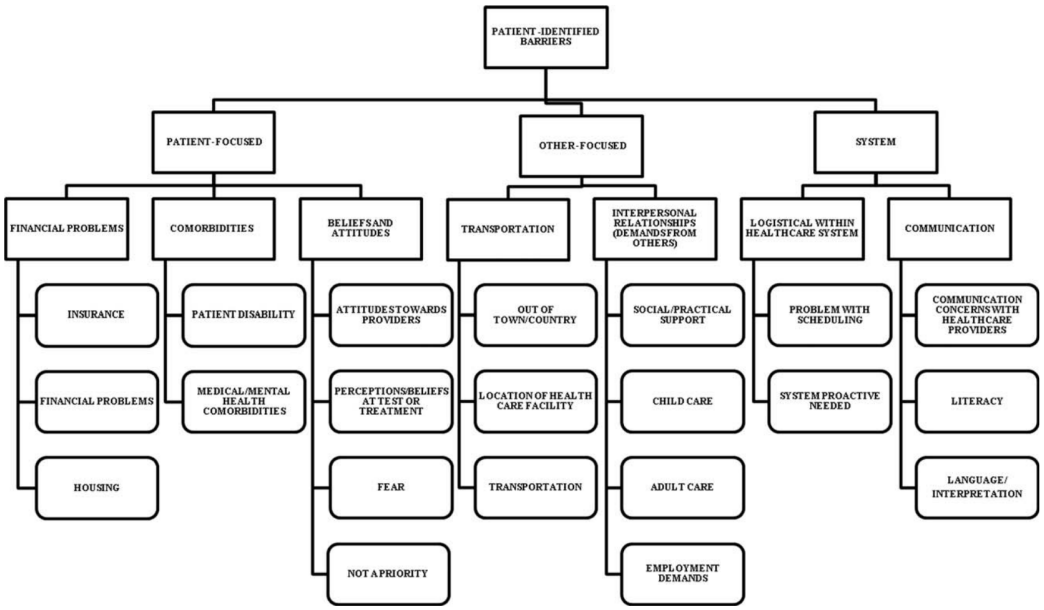
Source: Institute of Health Metrics, 2019 [36]

Figure F8: Evidence of the effect of patient navigation programmes: results from a systematic review in 2018



Source: McBrien et al. 2018
Significant positive outcomes in red and no difference marked in blue [82]

Figure F9: Framework of patient identified barriers to health-care



Source: Krok-Schoen JL, et al. 2015 [7]

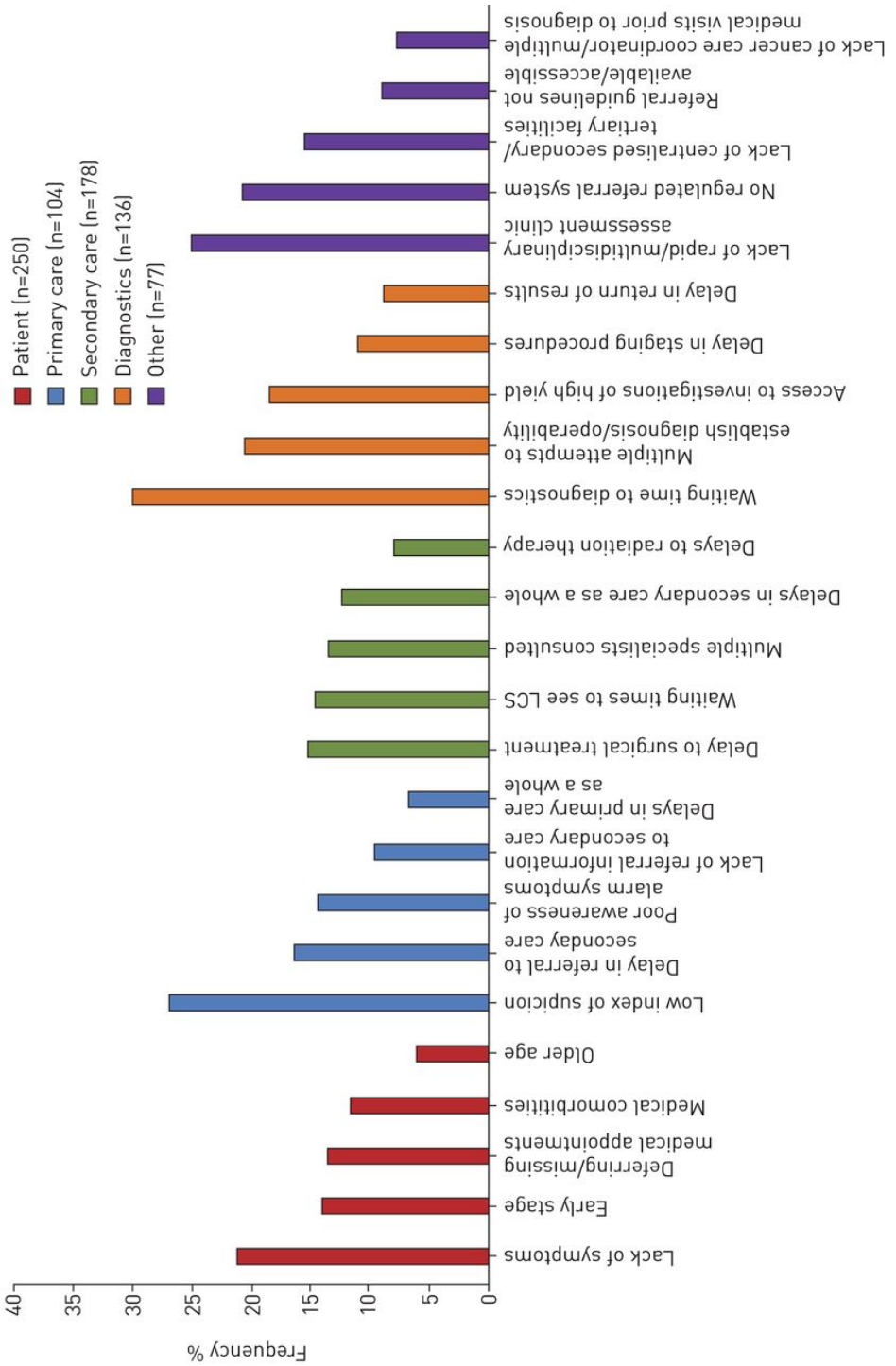


Figure F10: Classification of barriers to early lung cancer care

Source: Malalasekera A, et al. 2018 [60]

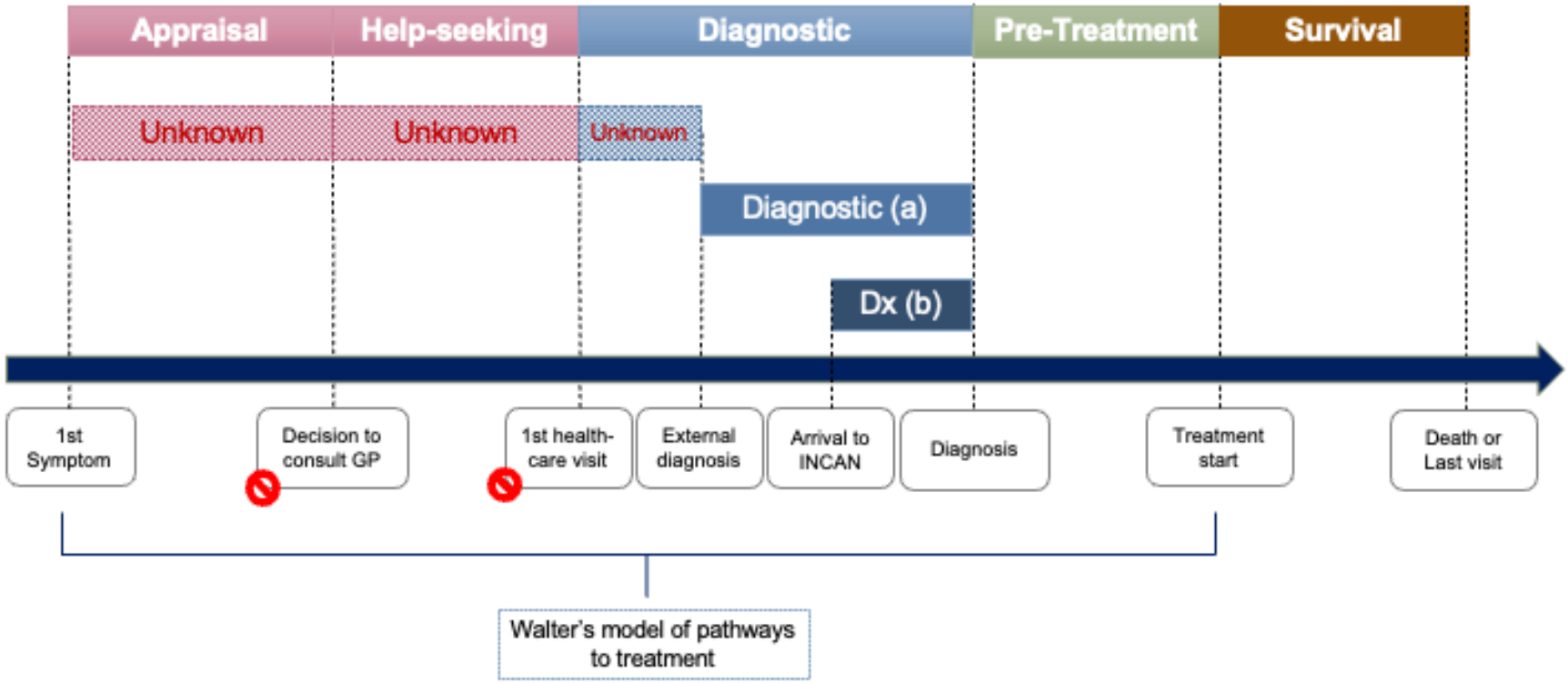
Figure F11: Summary of previous evidence to support Patient navigation programmes to reduce delays in Lung Cancer

Title	*N=*	*Design*	*Multi-center?*	*Metrics*	*Navigated patients' outcome*	*Significance of outcomes*
Patient Navigation for Lung Cancer Screening among Current Smokers in Community Health Centers: A Randomized Controlled Trial[28]	1200	Randomized controlled trial	Yes	Screening rate	• Higher uptake of screening	• $P<0.001$
Impact of Nurse Navigation on Timeliness of Diagnostic Medical Services in Patients with Newly Diagnosed Lung Cancer[41]	460	Retrospective chart review	No	Time to treatment initiation	• Suspicion of cancer to treatment (45 vs 64 days)	• $P<0.001$
Implementation of a Lung Cancer Nurse Navigator Enhances Patient Care and Delivery of Systemic Therapy at the British Columbia Cancer Agency, Vancouver[25]	408	Retrospective chart review	No	Time to treatment initiation and number of patients receiving systemic therapy	• More patients receiving therapy • Undergoing molecular testing (91% vs 62%) • Referral to oncology consult (15.5 vs 18 days) • Referral to systemic treatment (38 vs 48 days) • Referral to radiation (8 vs 10 days) • Referral to radiotherapy (11.5 vs 18 days)	• Number of patients in therapy ($P=0.05$) • Patients undergoing molecular testing ($P<0.001$) • Reduction in time from referral to oncology consult ($P=0.11$) • Reduction in time from referral to treatment ($P=0.016$) • Reduction in time from referral to radiation ($P=0.005$) • Reduction in time from referral to radiotherapy ($P<0.001$)
The Effect of a Lung Cancer Care Coordination Program on Timelines of Care[42]	352	Retrospective chart review		Time to treatment initiation and number of patients diagnosed early	• 25-day reduction from abnormal finding to treatment • Stage I/II diagnoses (48% vs 32%)	• Time to treatment initiation ($P=0.015$) • Number of patients diagnosed early ($P=0.006$)

Shusted et al 2019 [122]

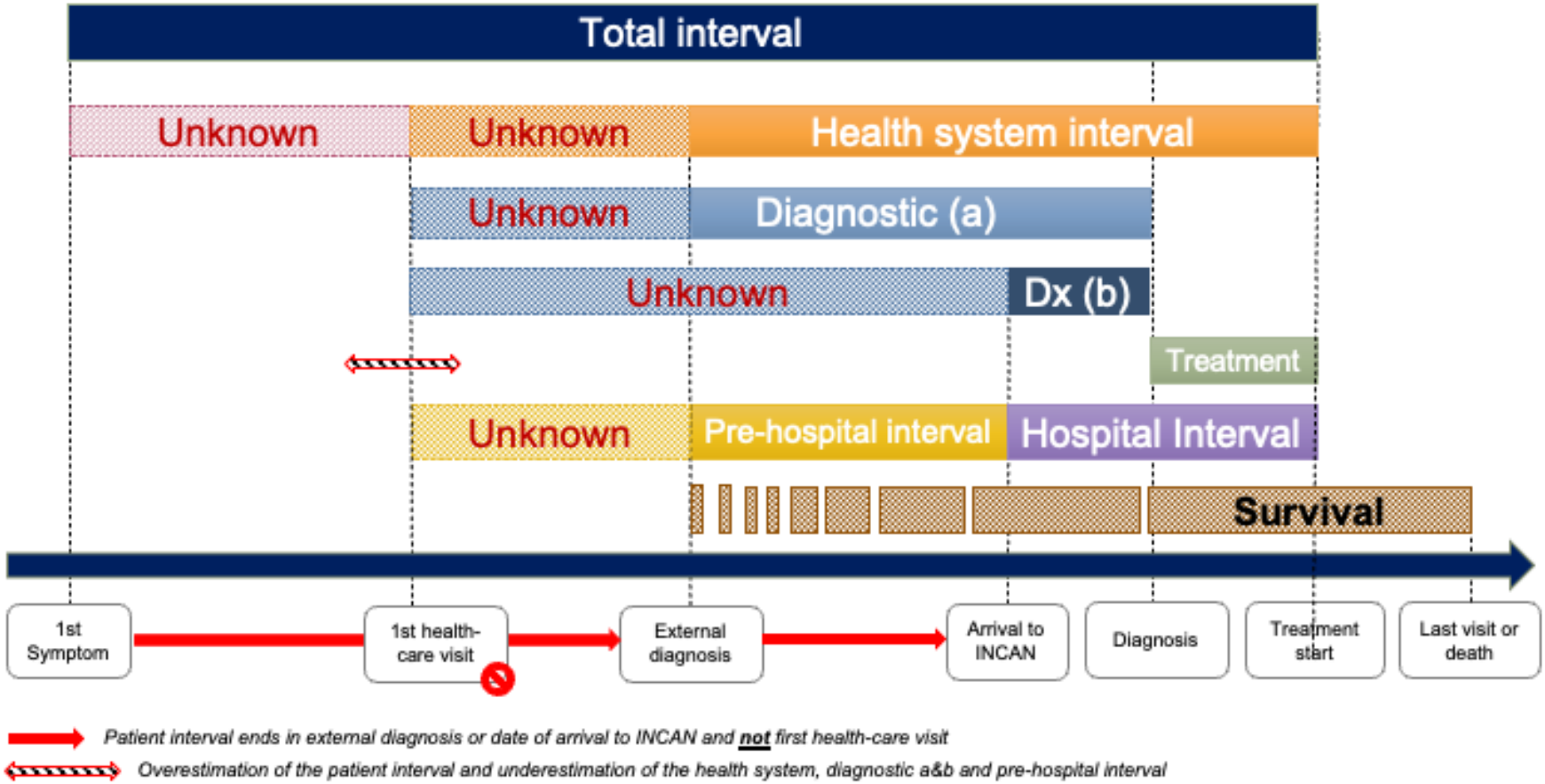
Effects in Lung cancer PNP by Shusted et al. This image shows only the results focused on Lung cancer particularly. Studies paired with other types of cancer were not included in this summary.

Figure F12: Interval availability in the PhD according to modified Walter's framework: The cancer appraisal-to-survival pathway



Source: Adapted from Walter et al "Pathway to cancer treatment framework" [88]
The red icons mark the unavailable dates in the electronic health records at the INCAN. The unknown intervals are marked "Unknown".

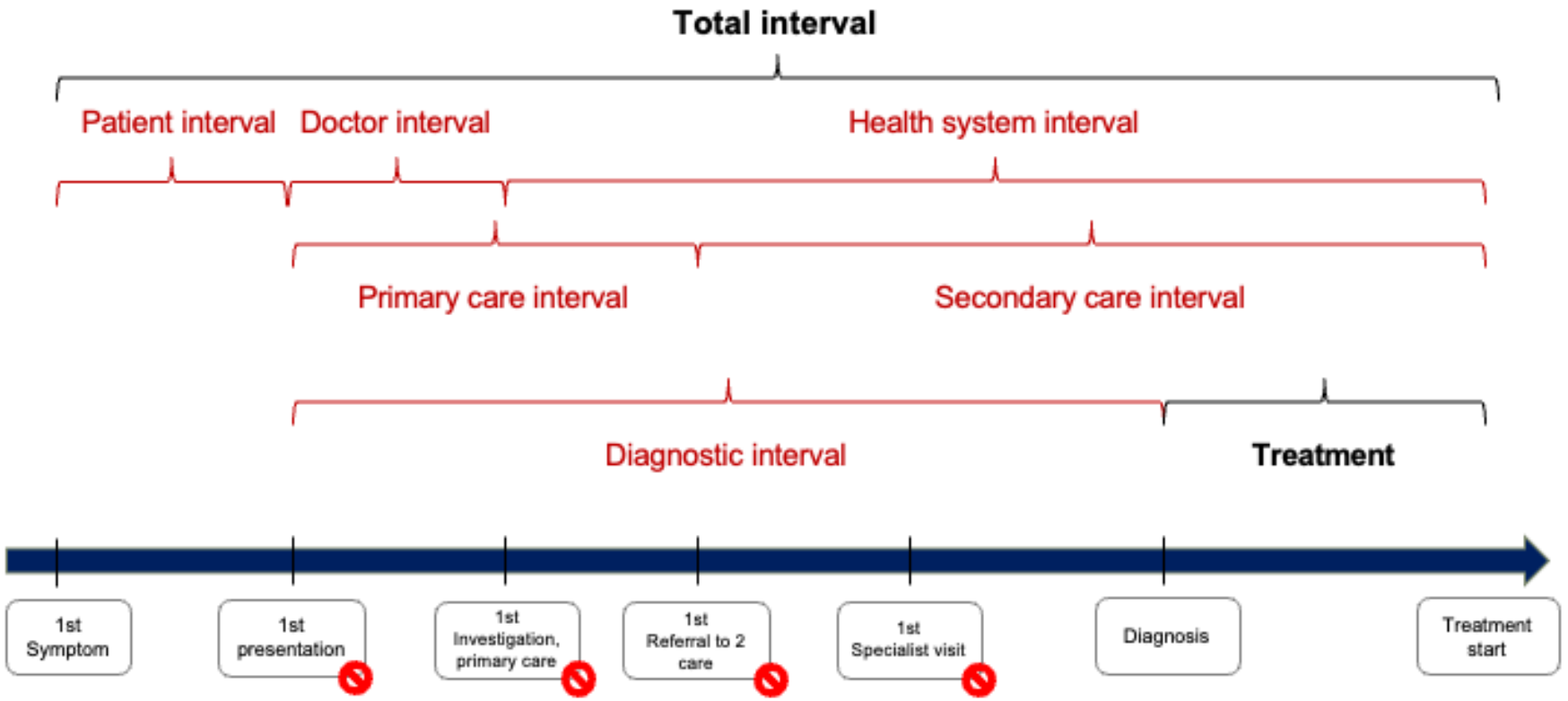
Figure F13: Interval availability in the PhD according to Unger's framework and the concept of over or underestimation of "proxi intervals"



Source: Adapted from Unger-Saldaña et al "Interval definitions in the Mexican context" [139]

The red icons mark the unavailable dates in the electronic health records at the INCAN. As a result of the missing dates, the unknown intervals are marked "Unknown". Survival is exemplified in (brown).

Figure F14: Interval availability in the PhD according to the Aarhus statement



Source: Adapted from Olesen et al "Interval definitions" [2, 5]

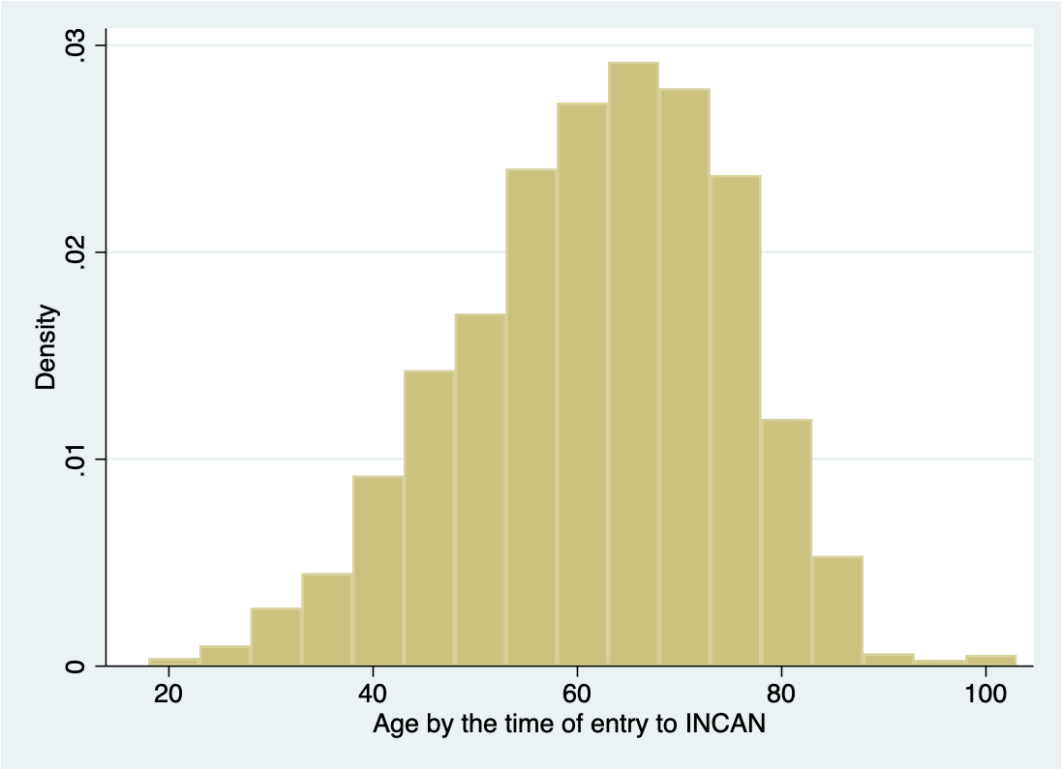
The red icons mark the unavailable dates in the electronic health records at the INCAN. As a result of the missing dates, the time intervals marked in red are not available for analysis. ***Treatment interval*** *and* ***total interval*** *are the only ones available for analysis.*

Figure F15: Positive predictive values for symptoms linked to Lung Cancer

Cough	Fatigue	Dyspnoea	Chest pain	Loss of weight	Loss of appetite	Thrombo-cytosis	Abnormal spirometry	Haemoptysis	
0.40 0.3, 0.5	**0.43** 0.3, 0.6	**0.66** 0.5, 0.8	**0.82** 0.6, 1.1	**1.1** 0.8, 1.6	**0.87** 0.6, 1.3	**1.6** 0.8, 3.1	**1.6** 0.9, 2.9	**2.4** 1.4, 4.1	PPV as a single symptom
0.58 0.4, 0.8	**0.63** 0.5, 0.9	**0.79** 0.6, 1.0	**0.76** 0.6, 1.0	**1.8** 1.1, 2.9	**1.6** 0.9, 2.7	**2.0** 1.1, 3.5	**1.2** 0.6, 2.6	**2.0** 1.1, 3.5	Cough
	0.57 0.4, 0.9	**0.89** 0.6, 0.3	**0.84** 0.5, 1.3	**1.0** 0.6, 1.7	**1.2** 0.7, 2.1	**1.8**	**4.0**	**3.3**	Fatigue
		0.88	**1.2** 0.9, 1.8	**2.0** 1.2, 3.8	**2.0** 1.2, 3.8	**2.0**	**2.3**	**4.9**	Dyspnoea
			0.95 0.7, 1.4	**1.8** 1.0, 3.4	**1.8** 0.9, 3.9	**2.0**	**1.4**	**5.0**	Chest pain
				1.2 0.7, 2.3	**2.3** 1.2, 4.4	**6.1**	**1.5**	**9.2**	Loss of weight
					1.7	**0.9**	**2.7**	**>10**	Loss of appetite
							3.6	**>10**	Thrombocytosis
								>10	Abnomal spirometry
								17	Haemoptysis

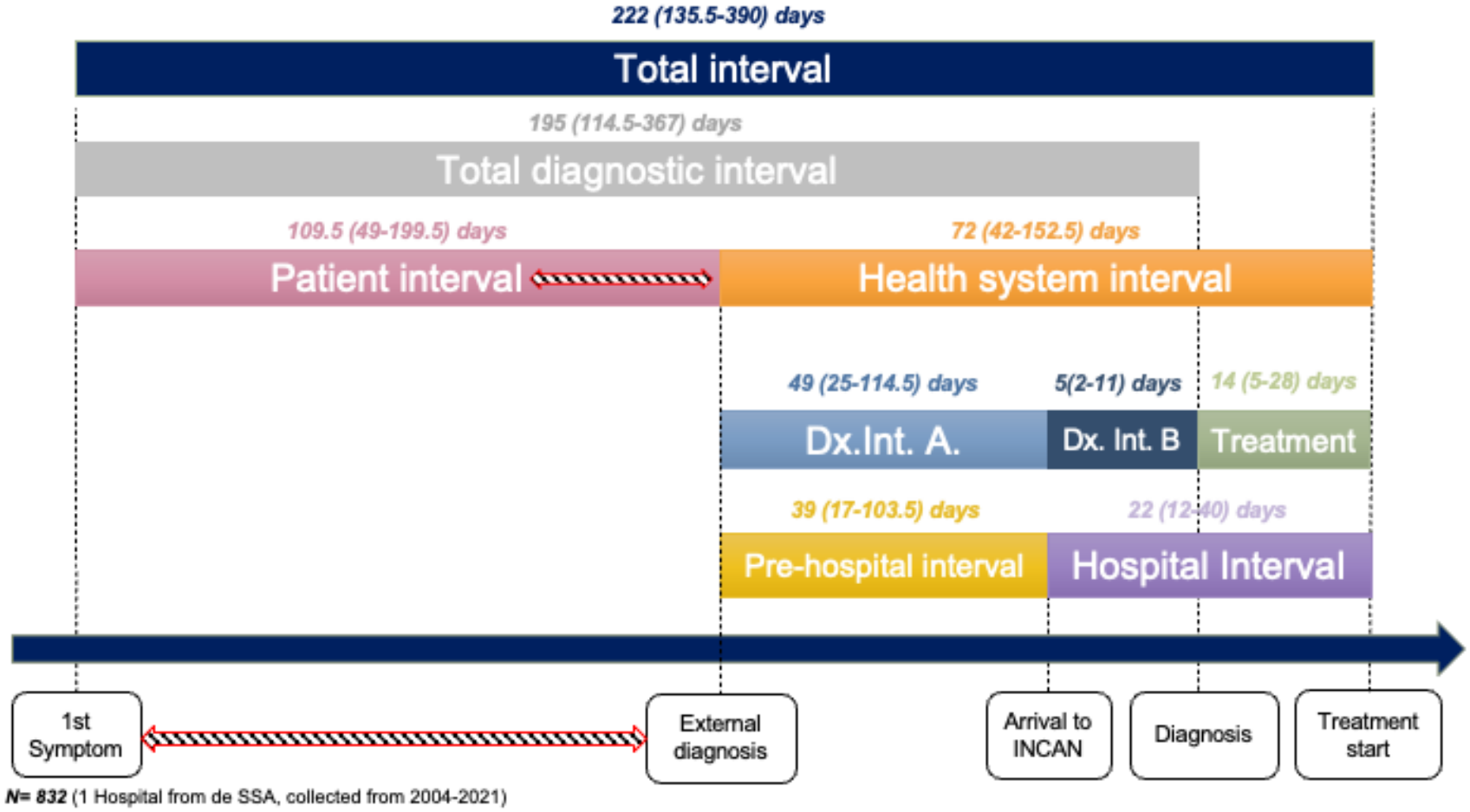
Source: Hamilton et al., 2005 [181]

Figure F16: Distribution of the sample's age (N:2645)



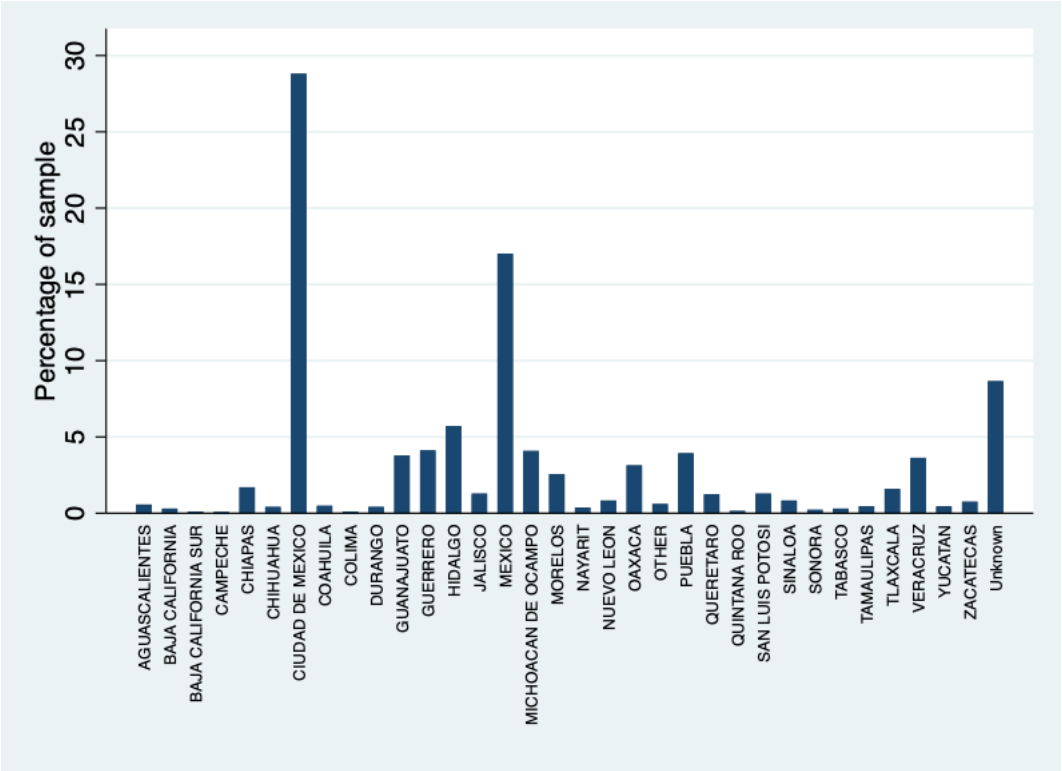
Source: Own work

Figure F17: Intervals description using days in the complete case lung cancer sub-sample (median days)



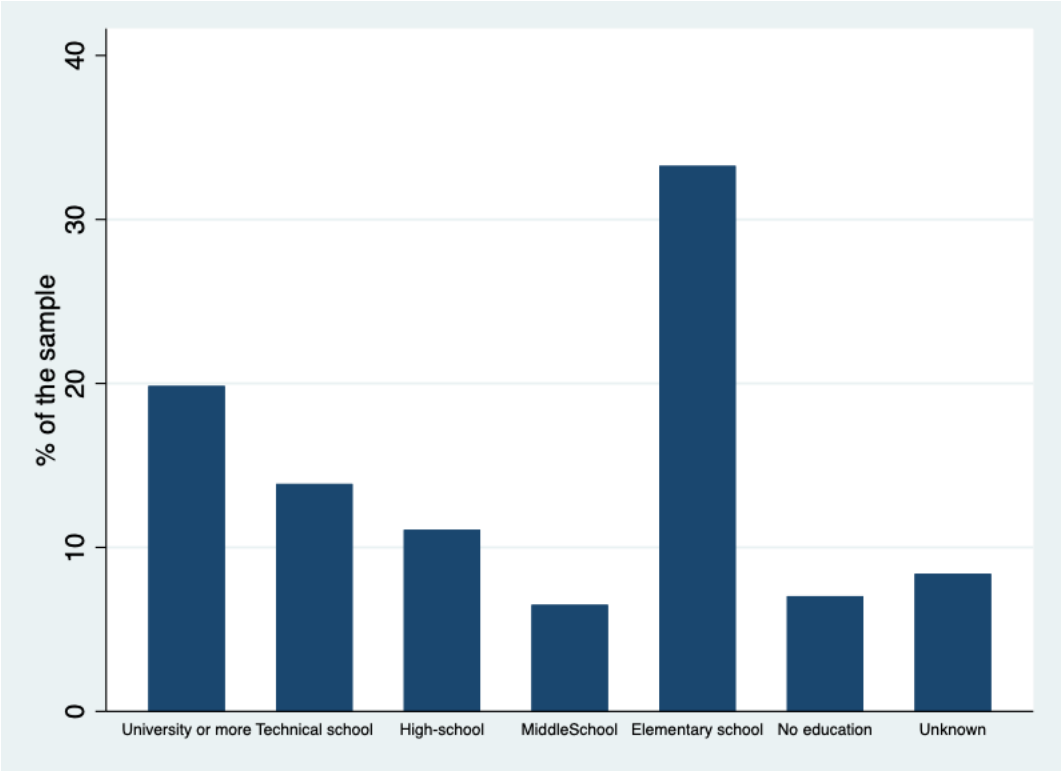
Source: Own work

Figure F18: Distribution of the sample by state (N:2645)



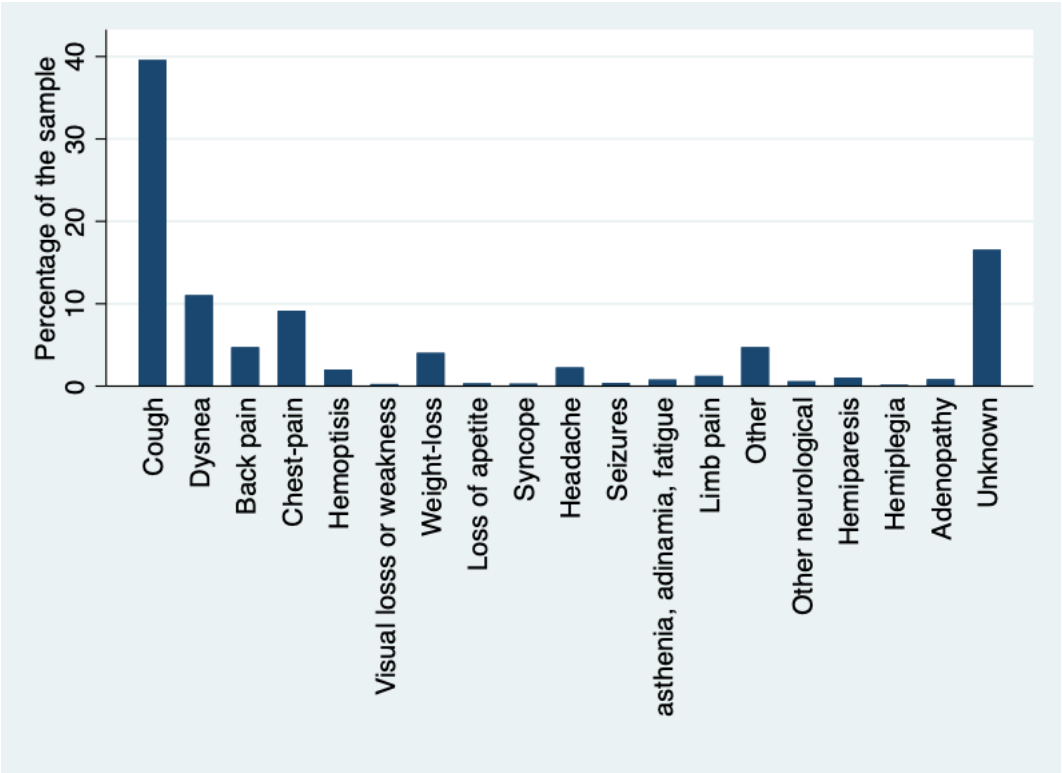
Source: Own work

Figure F19: Distribution of the sample by education (N:2645)



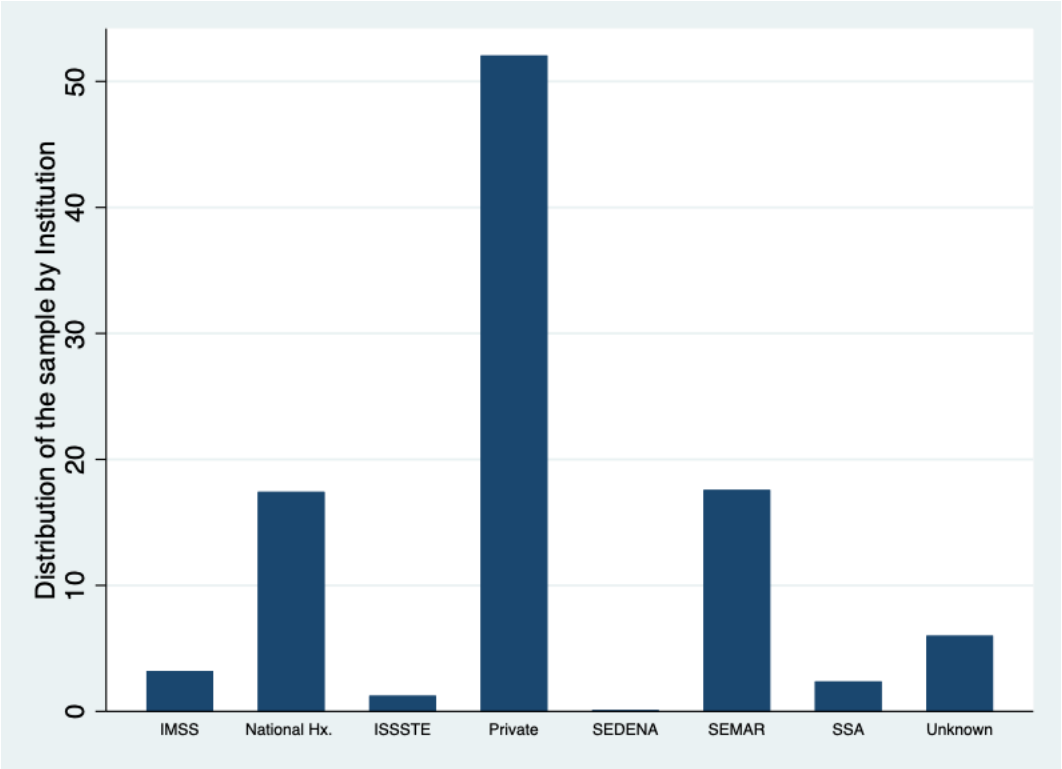
Source: Own work

Figure F20: Distribution of the sample by first symptom (N:2645)



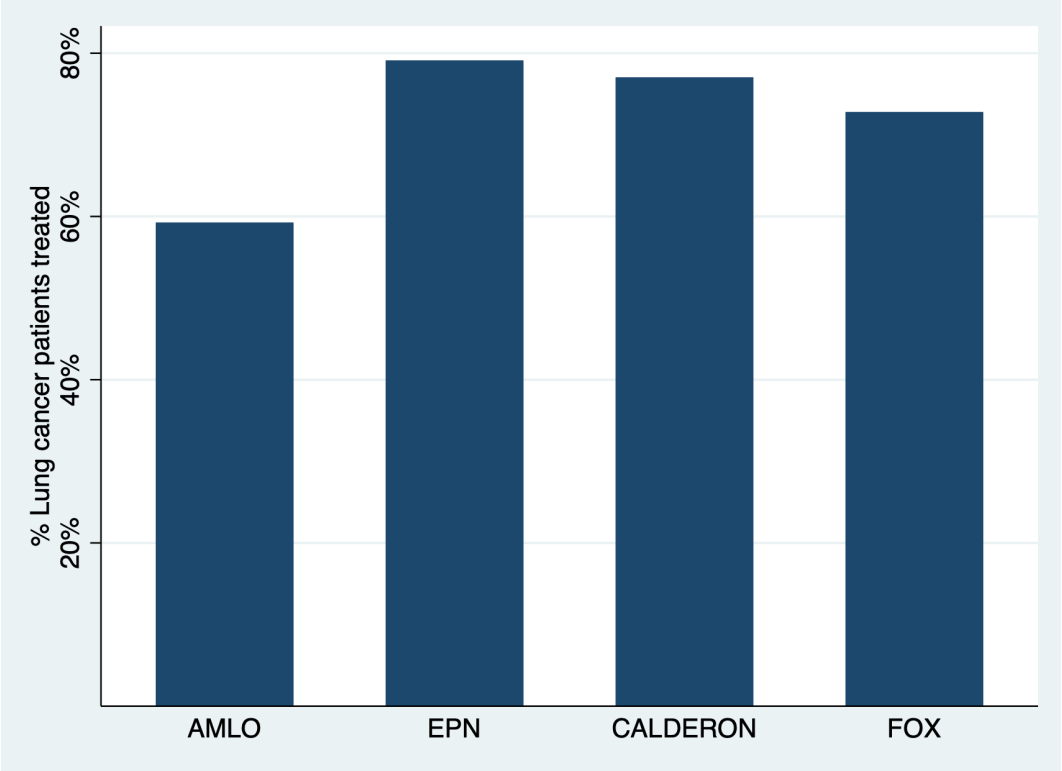
Source: Own work

Figure F21: Distribution of the sample by Institution (N:2645)



Source: Own work

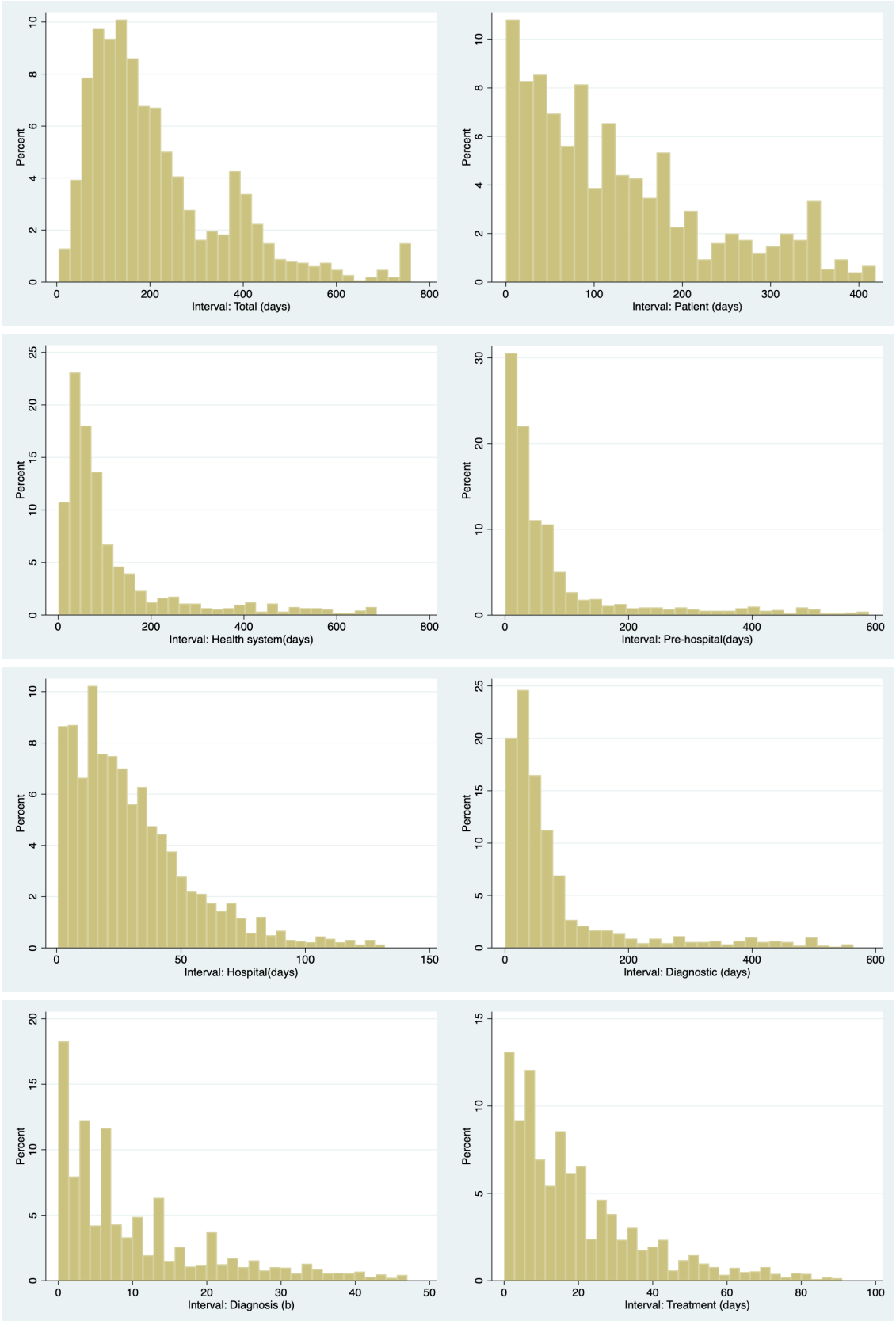
Figure F22: Comparison of lung cancer patients treatment prevalence per term



Source: Own work

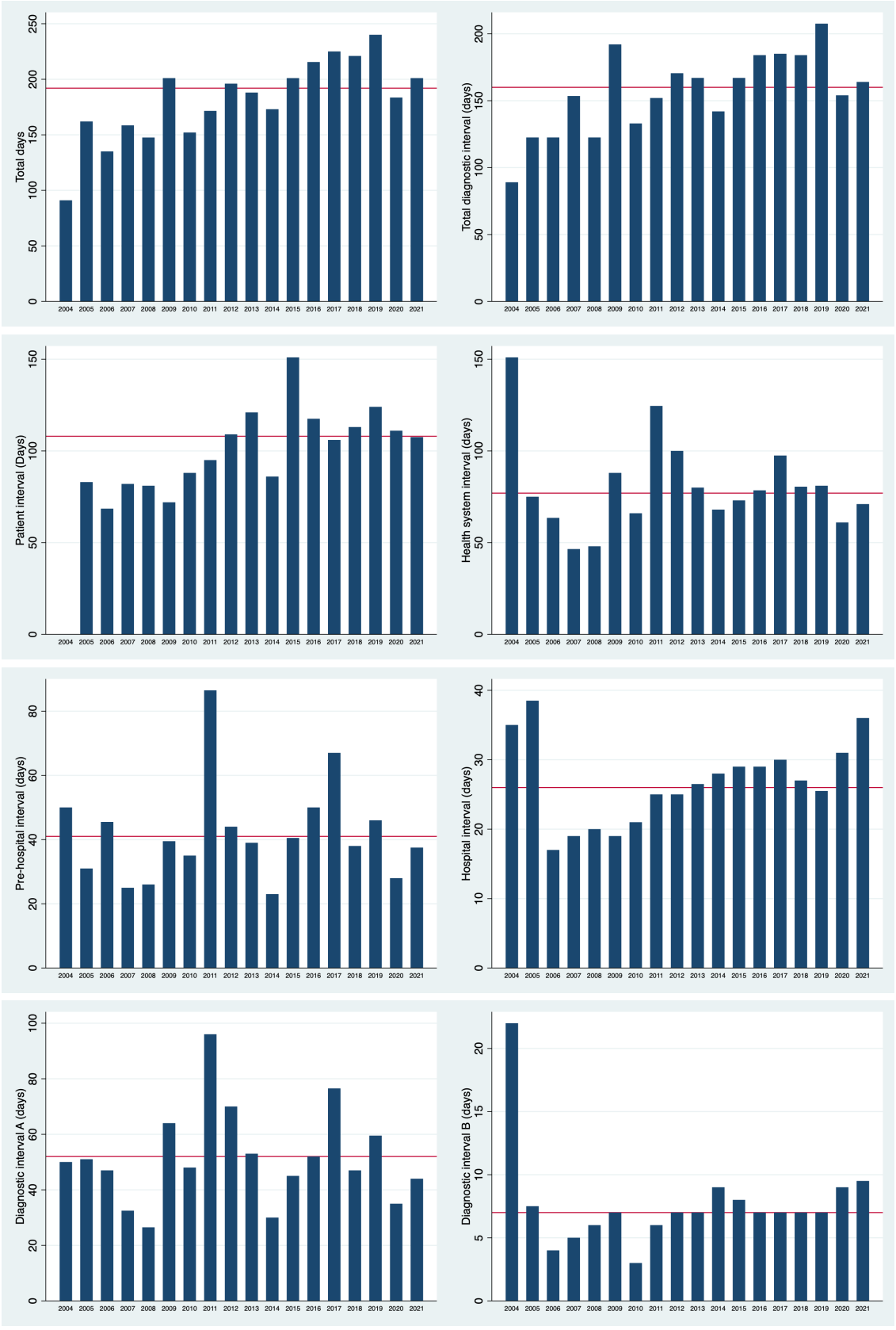
This represents presidential terms of different political parties: 2019/2021, 2013/2018, 2007/2012, 2004/2006.

Figure F23: Distribution of outcomes in 95% of the sample (days in each interval)



Source: Own work

Figure F24: Median days per interval from 2004-2021



Source: Own work

Figure F25: [Log] Distribution of residuals

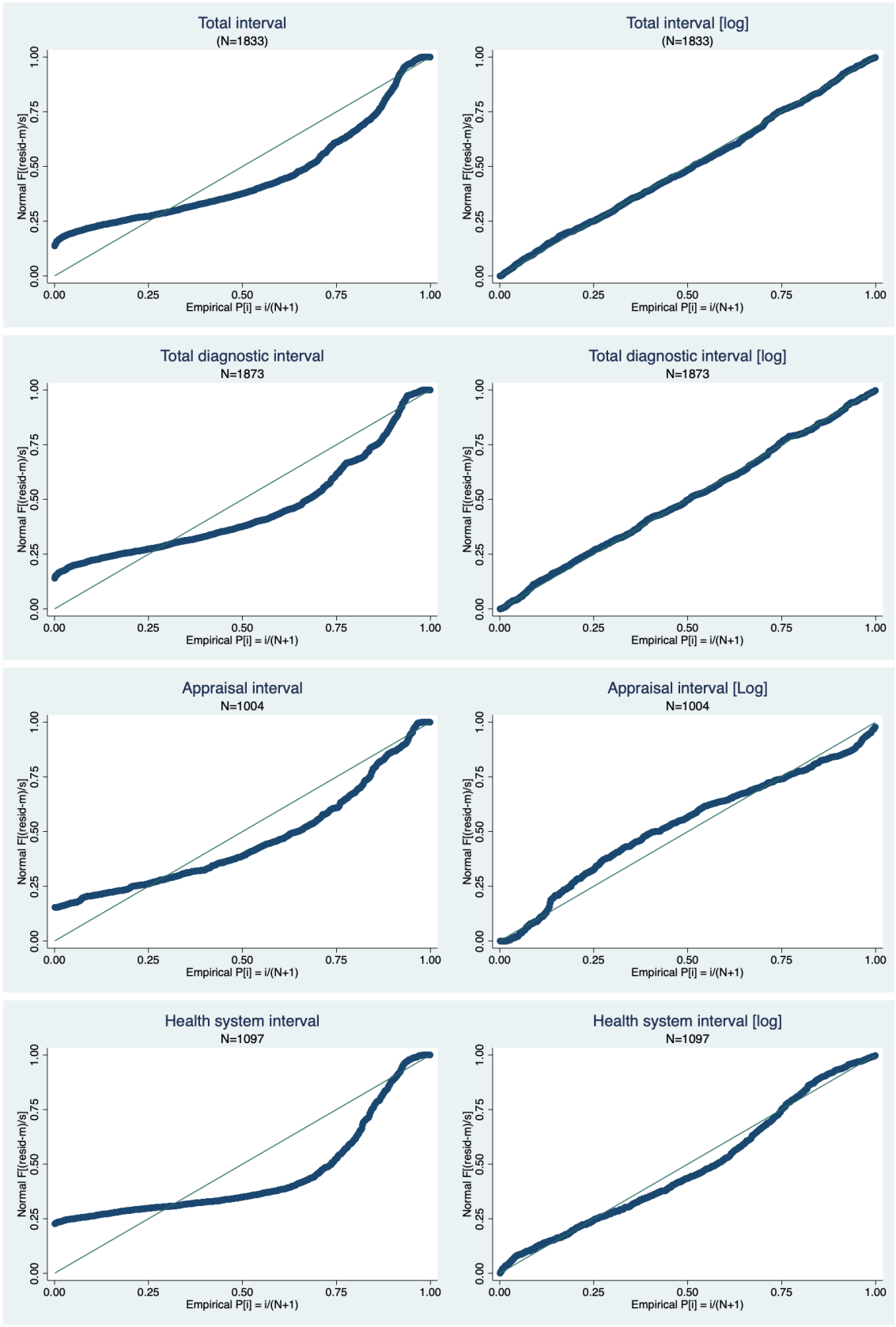


Figure I of III

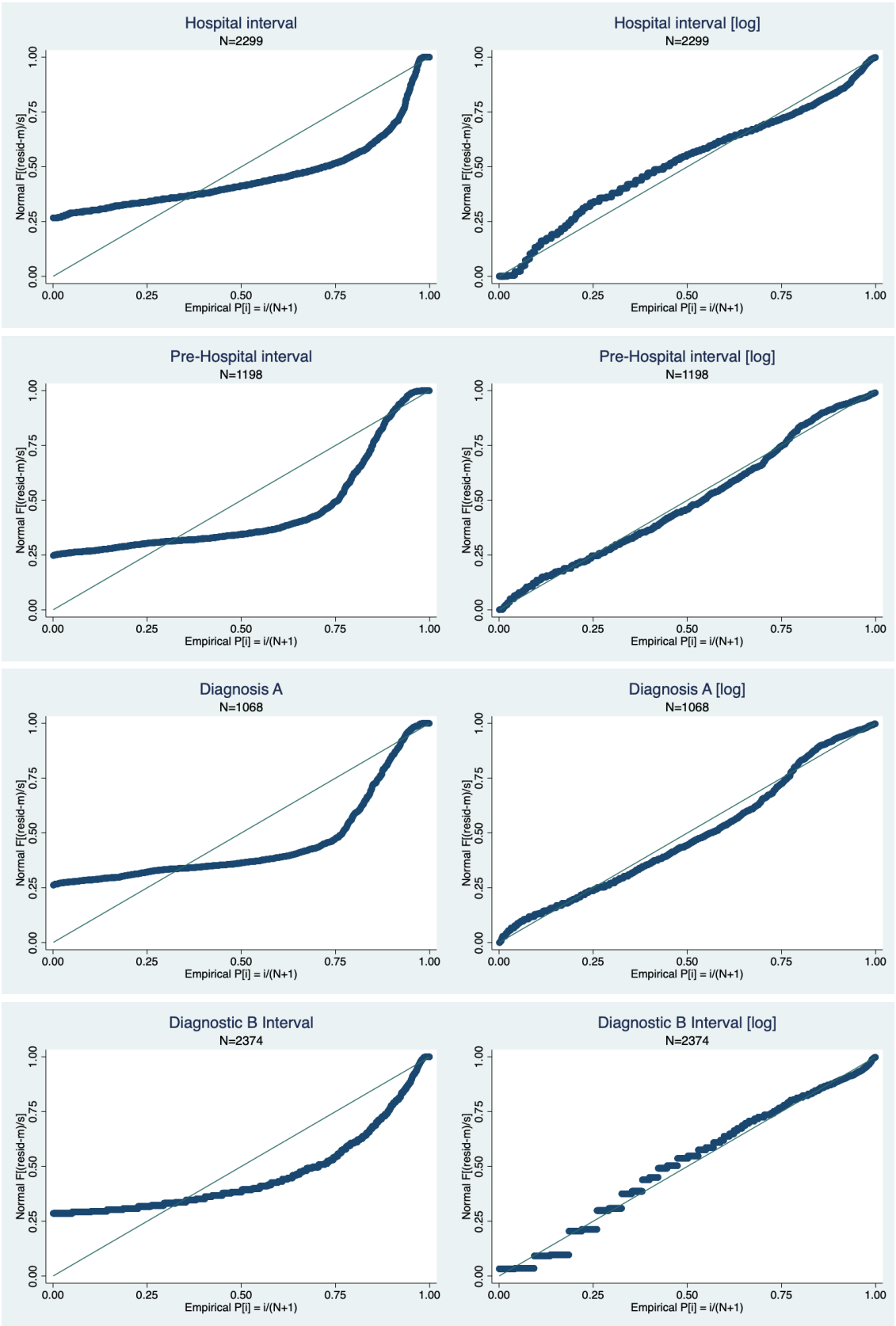


Figure II of III

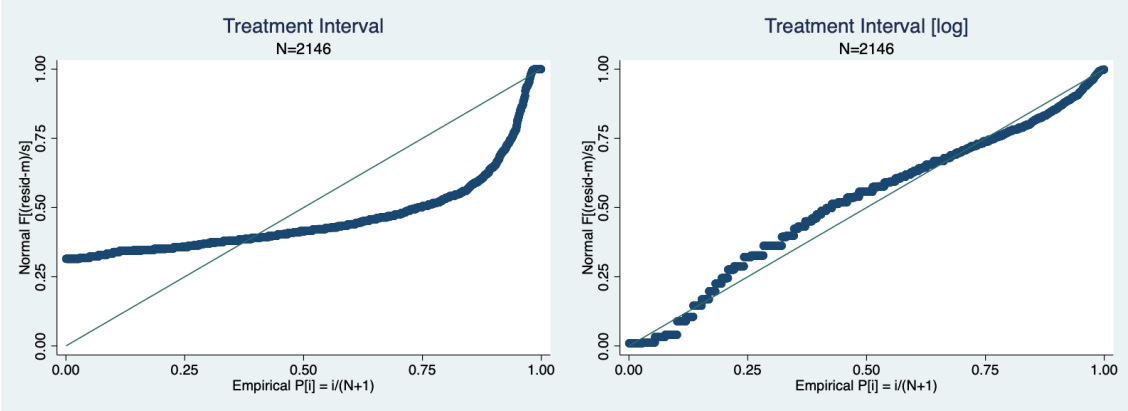
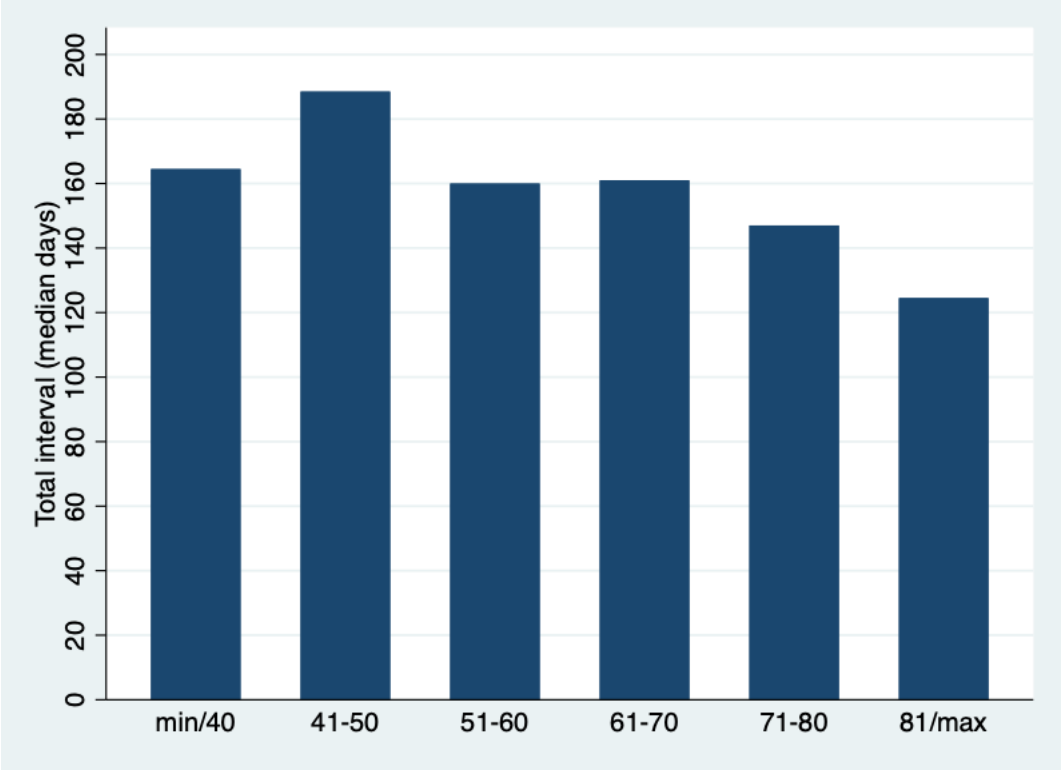


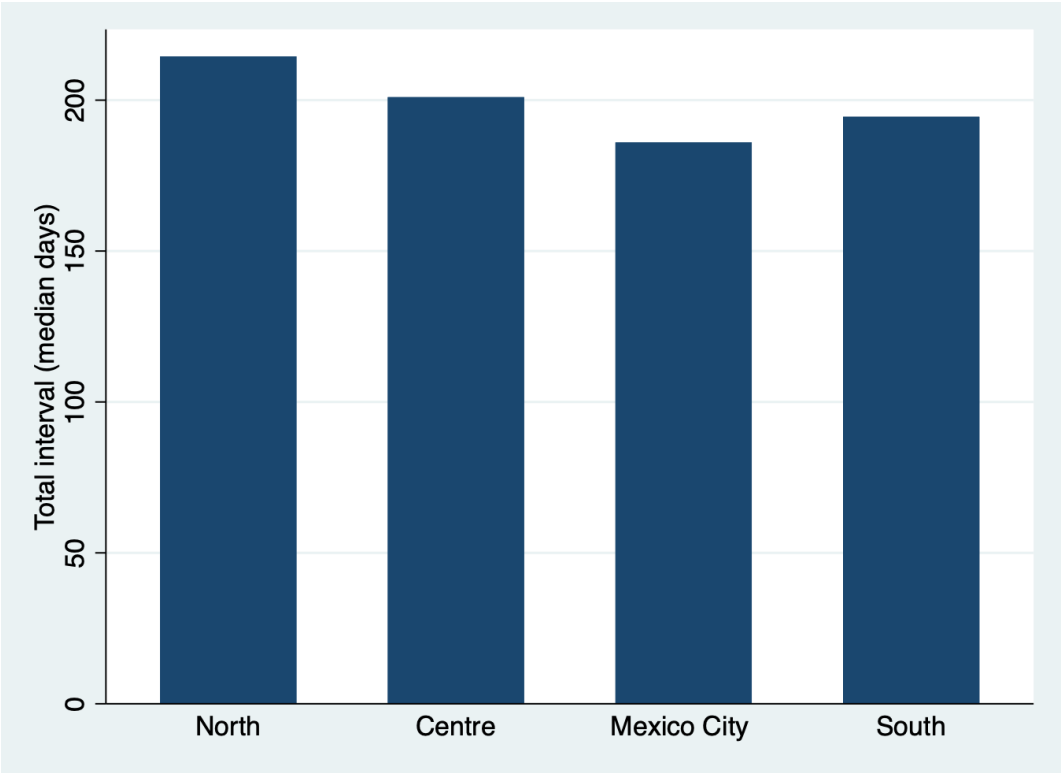
Figure III of III
On the left, the original non-log-transformed figure illustrates the relationship between time intervals (X) and the variable of interest (Y). On the right, the log-transformed figure shows the same relationship after applying a logarithmic transformation to Y. The linear regression line on the log scale is fitted to capture a potentially more linear relationship. Residuals, depicted as vertical distances between observed and predicted values, are presented on both sides. The log transformation aims to address non-linearity and heteroscedasticity, providing a visual representation of improved linearity and variance stabilisation.

Figure F26: Total interval median days by age



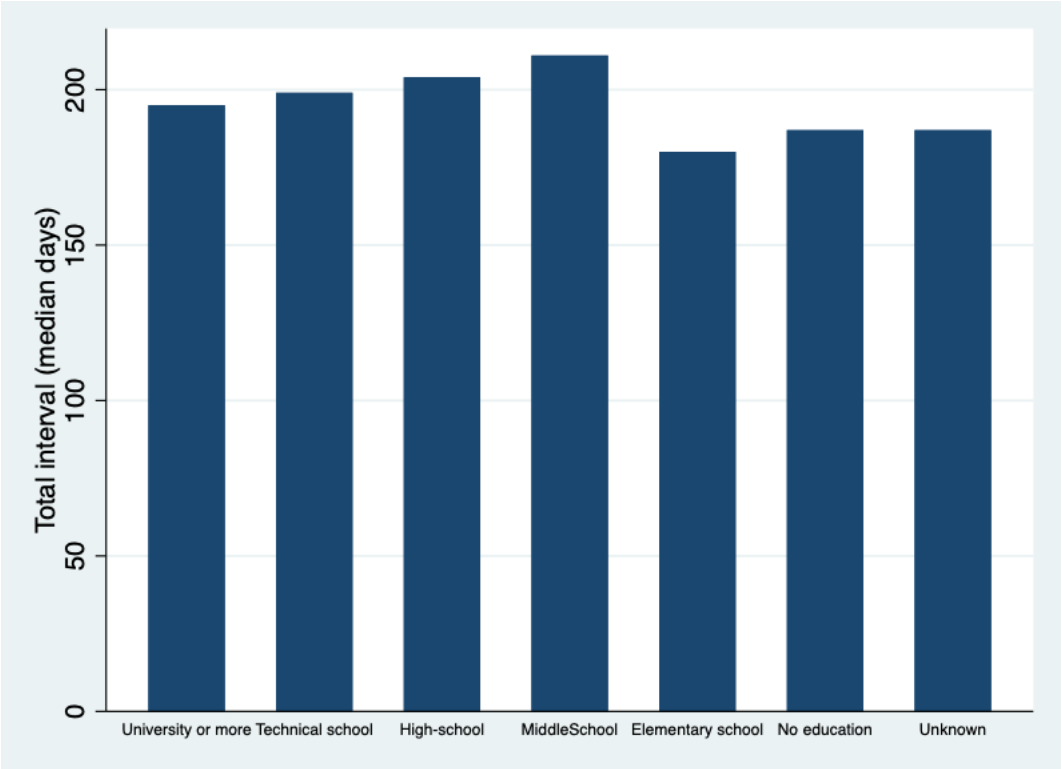
Source: Own work

Figure F27: Total interval median days by region



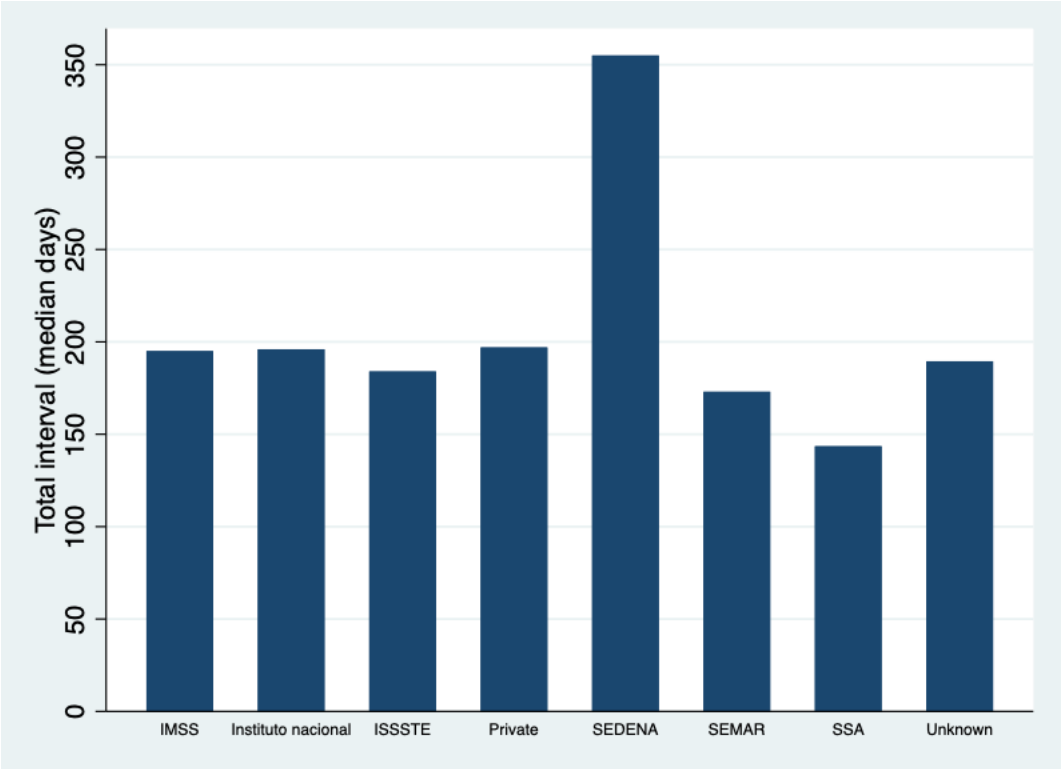
Source: Own work

Figure F28: Total interval median days by education



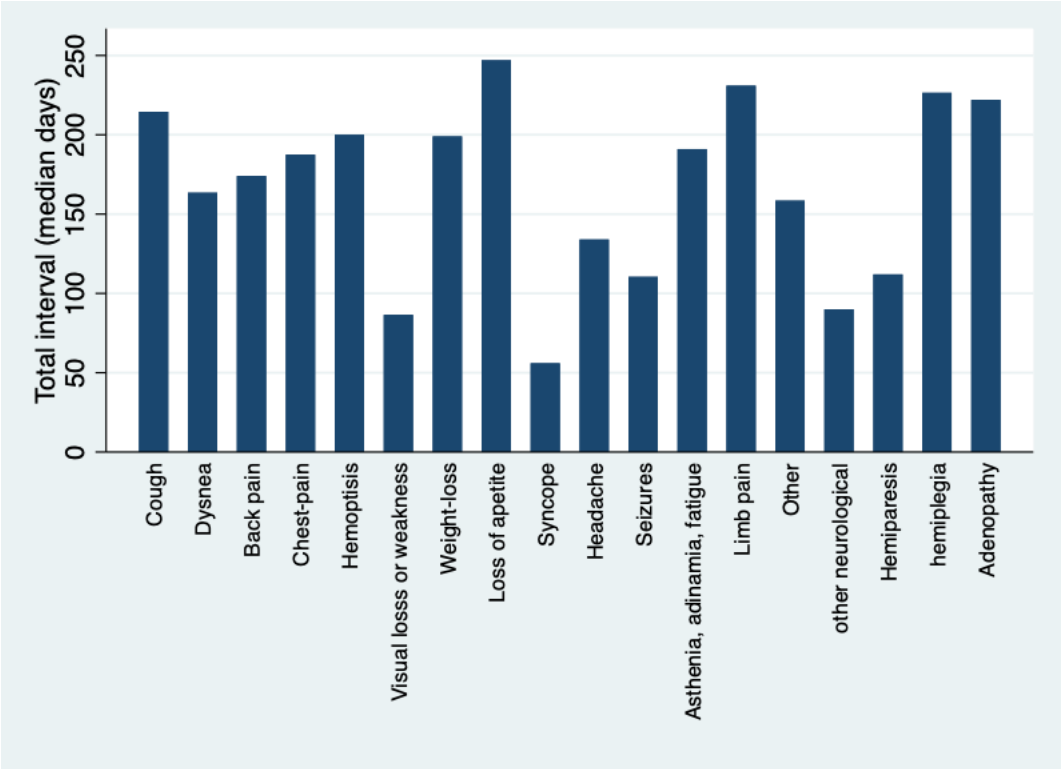
Source: Own work

Figure F29: Total interval median days by Institution



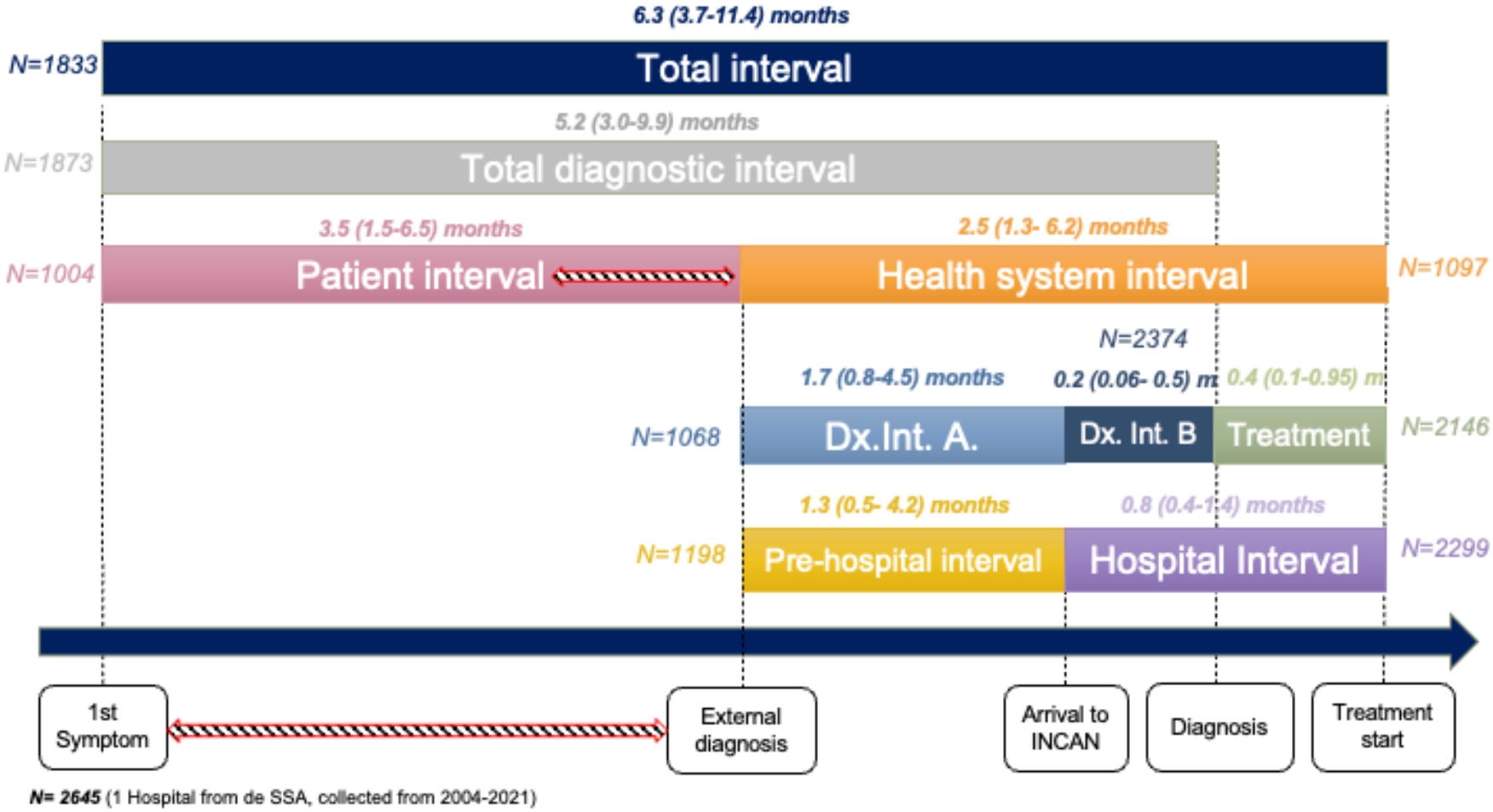
Source: Own work

Figure F30: Total interval median days by symptoms



Source: Own work

Figure F31: Lung cancer interval description using median months (N=2645)



Source: Own work

The red arrow describes the under and overestimation this study described. Total, total diagnostic, treatment and hospital interval are the only comparable intervals with Unger Saldaña's research on breast cancer.

A2: Supplementary Tables

Table T5: Total diagnostic interval by covariates (missing vs complete data)

Variable	Categories	Complete (N=1873)	Missing (N=772)	p-value
		61.0 (13.1)	62.1 (13.0)	0.041
Age	min/49	19.3%	17.3%	0.10
	50/59	23.0%	22.4%	
	60/69	29.6%	27.4%	
	70/103	28.1%	32.9%	
Sex	Women	51.0%	51.8%	0.72
	Men	49.0%	48.2%	
Education	>=High-school	44.3%	46.0%	0.94
	Middle school	6.7%	6.1%	
	Elementary	33.6%	32.5%	
	No education	7.0%	7.0%	
	Unknown	8.4%	8.4%	
SEP	Lower	57.1%	47.1%	< 0.001
	Middle	31.1%	36.5%	
	Higher	11.8%	16.4%	
Region	North	6.1%	6.2%	0.20
	Centre	20.7%	17.4%	
	Mexico City	44.7%	48.4%	
	South	19.5%	18.0%	
	Unknown	9.0%	10.0%	
Marital status	Divorced	12.1%	16.6%	0.002
	Married	56.7%	51.2%	
	Single	10.1%	9.1%	
	Widowed	10.8%	14.0%	
	Unknown	10.3%	9.2%	
First symptom	Cough	47.6%	47.0%	0.36
	Dyspnoea	12.6%	15.7%	
	Chest-pain	11.3%	9.6%	
	Haemoptysis	2.2%	3.1%	
	Weight-loss	4.8%	5.1%	
	Other symptoms	21.5%	19.5%	
Cancer stage	I	7.1%	11.7%	< 0.001
	III	8.8%	5.1%	
	IV	75.5%	43.8%	
	Unknown	8.5%	39.5%	
Diagnosis	Unspecified lung cancer	13.6%	42.6%	< 0.001
	NSCLC	83.8%	56.3%	
	SCLC	2.6%	1.0%	
Institution of referral	Private hospital	51.9%	52.5%	0.23
	Public hospital	41.6%	42.7%	
	Unknown	6.5%	4.8%	
Period	2019/2021	23.6%	12.2%	< 0.001
	2013/2018	39.2%	46.8%	
	2007/2012	30.3%	24.0%	
	2004/2006	6.8%	17.1%	

Table T6: Patient interval by covariates (missing vs complete data)

Variable	Categories	Complete (N=1004)	Missing (N=1641)	p-value
		59.8 (13.3)	62.2 (12.9)	< 0.001
Age	min/49	22.1%	16.7%	< 0.001
	50/59	24.5%	21.8%	
	60/69	28.0%	29.5%	
	70/103	25.3%	32.1%	
Sex	Women	52.8%	50.3%	0.22
	Men	47.2%	49.7%	
Education	>=High-school	49.2%	42.1%	< 0.001
	Middle school	7.9%	5.7%	
	Elementary	30.0%	35.3%	
	No education	5.4%	8.0%	
	Unknown	7.6%	8.9%	
SEP	Lower	52.5%	54.9%	< 0.001
	Middle	29.6%	34.5%	
	Higher	17.9%	10.5%	
Region	North	8.1%	4.9%	0.009
	Centre	19.7%	19.7%	
	Mexico City	43.8%	47.0%	
	South	20.0%	18.5%	
	Unknown	8.4%	9.8%	
Marital status	Divorced	10.8%	15.0%	< 0.001
	Married	60.0%	52.1%	
	Single	10.6%	9.3%	
	Widowed	9.3%	13.3%	
	Unknown	9.5%	10.3%	
First symptom	Cough	51.7%	44.2%	0.020
	Dyspnoea	12.2%	14.1%	
	Chest-pain	10.1%	11.6%	
	Haemoptysis	1.9%	2.8%	
	Weight-loss	4.3%	5.3%	
	Other symptoms	20.0%	22.0%	
Cancer stage	I	3.9%	11.2%	< 0.001
	III	7.4%	7.9%	
	IV	65.5%	66.7%	
	Unknown	23.2%	14.1%	
Diagnosis	Unspecified lung cancer	26.2%	19.6%	< 0.001
	NSCLC	71.9%	78.2%	
	SCLC	1.9%	2.3%	
Institution of referral	Private hospital	51.9%	52.2%	0.25
	Public hospital	43.0%	41.3%	
	Unknown	5.1%	6.6%	
Period	2019/2021	30.2%	14.2%	< 0.001
	2013/2018	35.0%	45.4%	
	2007/2012	31.3%	26.8%	
	2004/2006	3.6%	13.7%	

Table T7: Health system interval by covariates (missing vs complete data)

Variable	Categories	Complete (N=1097)	Missing (N=1548)	p-value
		59.7 (13.3)	62.4 (12.9)	< 0.001
Age	min/49	21.9%	16.5%	< 0.001
	50/59	25.0%	21.2%	
	60/69	27.5%	29.9%	
	70/103	25.5%	32.3%	
Sex	Women	54.3%	49.1%	0.008
	Men	45.7%	50.9%	
Education	>=High-school	49.5%	41.5%	< 0.001
	Middle school	7.8%	5.6%	
	Elementary	29.5%	35.9%	
	No education	5.1%	8.4%	
	Unknown	8.0%	8.7%	
SEP	Lower	52.4%	55.1%	< 0.001
	Middle	30.6%	34.2%	
	Higher	17.0%	10.7%	
Region	North	8.3%	4.6%	0.001
	Centre	19.8%	19.7%	
	Mexico City	43.0%	47.8%	
	South	19.9%	18.5%	
	Unknown	9.0%	9.4%	
Marital status	Divorced	10.2%	15.6%	< 0.001
	Married	59.3%	52.1%	
	Single	10.7%	9.2%	
	Widowed	10.1%	12.9%	
	Unknown	9.7%	10.2%	
First symptom	Cough	51.9%	44.2%	0.003
	Dyspnoea	12.4%	13.8%	
	Chest-pain	10.3%	11.5%	
	Haemoptysis	1.6%	3.0%	
	Weight-loss	3.7%	5.7%	
	Other symptoms	20.1%	21.9%	
Cancer stage	I	3.9%	11.6%	< 0.001
	III	7.1%	8.1%	
	IV	66.5%	66.1%	
	Unknown	22.5%	14.1%	
Diagnosis	Unspecified lung cancer	24.4%	20.4%	0.023
	NSCLC	73.9%	77.1%	
	SCLC	1.6%	2.5%	
Institution of referral	Private hospital	52.0%	52.1%	0.013
	Public hospital	43.6%	40.8%	
	Unknown	4.5%	7.1%	
Period	2019/2021	28.1%	14.7%	< 0.001
	2013/2018	37.2%	44.4%	
	2007/2012	30.8%	26.8%	
	2004/2006	3.9%	14.0%	

Table T8: Pre-hospital interval by covariates (missing vs complete data)

Variable	Categories	Complete (N=1198)	Missing (N=1447)	p-value
		60.0 (13.2)	62.4 (12.9)	< 0.001
Age	min/49	21.3%	16.6%	< 0.001
	50/59	25.2%	20.8%	
	60/69	27.4%	30.2%	
	70/103	26.1%	32.3%	
Sex	Women	53.6%	49.3%	0.030
	Men	46.4%	50.7%	
Education	>=High-school	50.3%	40.3%	< 0.001
	Middle school	7.3%	5.8%	
	Elementary	28.9%	36.9%	
	No education	5.3%	8.5%	
	Unknown	8.3%	8.5%	
SEP	Lower	51.1%	56.3%	< 0.001
	Middle	30.9%	34.2%	
	Higher	18.0%	9.5%	
Region	North	8.3%	4.3%	< 0.001
	Centre	19.4%	20.0%	
	Mexico City	43.1%	48.1%	
	South	19.9%	18.4%	
	Unknown	9.3%	9.2%	
Marital status	Divorced	10.8%	15.5%	< 0.001
	Married	58.8%	52.0%	
	Single	10.4%	9.3%	
	Widowed	10.2%	13.1%	
	Unknown	9.9%	10.0%	
First symptom	Cough	52.0%	43.4%	0.001
	Dyspnoea	11.9%	14.4%	
	Chest-pain	9.7%	12.0%	
	Haemoptysis	1.8%	3.0%	
	Weight-loss	4.1%	5.5%	
	Other symptoms	20.5%	21.7%	
Cancer stage	I	4.8%	11.5%	< 0.001
	III	7.0%	8.3%	
	IV	64.4%	67.9%	
	Unknown	23.9%	12.4%	
Diagnosis	Unspecified lung cancer	26.0%	18.8%	0.023
	NSCLC	72.1%	78.9%	
	SCLC	1.8%	2.3%	
Institution of referral	Private hospital	51.9%	52.2%	0.16
	Public hospital	43.0%	41.1%	
	Unknown	5.1%	6.8%	
Period	2019/2021	27.6%	14.2%	< 0.001
	2013/2018	38.1%	44.2%	
	2007/2012	30.2%	27.0%	
	2004/2006	4.1%	14.6%	

Table T9: Hospital interval by covariates (missing vs complete data)

Variable	Categories	Complete (N=2299)	Missing (N=346)	p-value
		61.0 (13.1)	63.4 (12.6)	< 0.001
Age	min/49	19.5%	13.9%	0.013
	50/59	23.0%	21.4%	
	60/69	28.9%	28.9%	
	70/103	28.5%	35.8%	
Sex	Women	52.0%	46.2%	0.045
	Men	48.0%	53.8%	
Education	>=High-school	45.2%	41.9%	0.44
	Middle school	6.6%	6.1%	
	Elementary	33.3%	33.2%	
	No education	6.8%	8.7%	
	Unknown	8.1%	10.1%	
SEP	Lower	54.9%	48.6%	0.096
	Middle	32.4%	35.2%	
	Higher	12.7%	16.2%	
Region	North	6.3%	4.9%	0.49
	Centre	20.0%	17.9%	
	Mexico City	45.5%	48.0%	
	South	19.2%	18.2%	
	Unknown	9.0%	11.0%	
Marital status	Divorced	11.7%	24.3%	< 0.001
	Married	56.2%	47.4%	
	Single	10.3%	6.6%	
	Widowed	12.0%	10.1%	
	Unknown	9.7%	11.6%	
First symptom	Cough	47.3%	48.3%	0.16
	Dyspnoea	13.6%	11.0%	
	Chest-pain	10.8%	12.0%	
	Haemoptysis	2.3%	2.7%	
	Weight-loss	4.4%	7.5%	
	Other symptoms	21.5%	18.5%	
Cancer stage	I	7.0%	17.6%	< 0.001
	III	8.0%	5.8%	
	IV	70.2%	39.9%	
	Unknown	14.7%	36.7%	
Diagnosis	Unspecified lung cancer	18.4%	46.2%	< 0.001
	NSCLC	79.5%	51.4%	
	SCLC	2.1%	2.3%	
Institution of referral	Private hospital	52.2%	50.9%	0.006
	Public hospital	42.3%	39.3%	
	Unknown	5.4%	9.8%	
Period	2019/2021	20.9%	15.9%	< 0.001
	2013/2018	40.5%	47.4%	
	2007/2012	29.6%	20.8%	
	2004/2006	8.9%	15.9%	

Table T10: Diagnostic interval (a) by covariates (missing vs complete data)

Variable	Categories	Complete (N=1068)	Missing (N=1577)	p-value
		59.8 (13.2)	62.3 (12.9)	< 0.001
Age	min/49	21.5%	16.8%	< 0.001
	50/59	25.3%	21.1%	
	60/69	27.6%	29.9%	
	70/103	25.6%	32.2%	
Sex	Women	55.0%	48.8%	0.002
	Men	45.0%	51.2%	
Education	>=High-school	50.5%	41.0%	< 0.001
	Middle school	7.2%	6.0%	
	Elementary	28.3%	36.7%	
	No education	5.2%	8.2%	
	Unknown	8.8%	8.1%	
SEP	Lower	52.4%	55.0%	0.001
	Middle	31.0%	33.8%	
	Higher	16.5%	11.1%	
Region	North	8.2%	4.7%	0.002
	Centre	19.0%	20.2%	
	Mexico City	43.4%	47.5%	
	South	19.6%	18.7%	
	Unknown	9.8%	8.9%	
Marital status	Divorced	10.4%	15.4%	< 0.001
	Married	58.4%	52.8%	
	Single	10.7%	9.2%	
	Widowed	10.0%	12.9%	
	Unknown	10.5%	9.6%	
First symptom	Cough	52.3%	44.0%	0.002
	Dyspnoea	11.1%	14.7%	
	Chest-pain	10.4%	11.3%	
	Haemoptysis	1.6%	2.9%	
	Weight-loss	4.2%	5.3%	
	Other symptoms	20.3%	21.7%	
Cancer stage	I	5.5%	10.4%	< 0.001
	III	7.8%	7.7%	
	IV	72.2%	62.3%	
	Unknown	14.5%	19.7%	
Diagnosis	Unspecified lung cancer	16.9%	25.6%	< 0.001
	NSCLC	81.0%	72.3%	
	SCLC	2.1%	2.2%	
Institution of referral	Private hospital	51.7%	52.3%	0.12
	Public hospital	43.4%	41.0%	
	Unknown	5.0%	6.7%	
Period	2019/2021	29.1%	14.3%	< 0.001
	2013/2018	37.8%	43.9%	
	2007/2012	29.1%	28.0%	
	2004/2006	3.9%	13.8%	

Table T11: Diagnostic interval (b) by covariates (missing vs complete data)

Variable	Categories	Complete (N=2374)	Missing (N=271)	p-value
		61.2 (13.1)	61.8 (12.8)	0.051
Age	min/49	18.8%	17.8%	0.60
	50/59	22.8%	23.0%	
	60/69	29.2%	26.4%	
	70/103	29.1%	32.7%	
Sex	Women	52.0%	45.0%	0.030
	Men	48.0%	55.0%	
Education	>=High-school	45.0%	42.8%	0.040
	Middle school	6.2%	8.9%	
	Elementary	32.8%	37.3%	
	No education	7.1%	6.6%	
	Unknown	8.8%	4.4%	
SEP	Lower	55.4%	43.4%	< 0.001
	Middle	32.6%	33.9%	
	Higher	12.0%	22.7%	
Region	North	6.1%	6.6%	0.38
	Centre	19.7%	19.9%	
	Mexico City	45.7%	47.2%	
	South	18.9%	20.3%	
	Unknown	9.6%	5.9%	
Marital status	Divorced	11.7%	28.0%	< 0.001
	Married	56.3%	44.6%	
	Single	9.8%	9.6%	
	Widowed	11.7%	12.2%	
	Unknown	10.5%	5.5%	
First symptom	Cough	47.7%	45.0%	0.092
	Dyspnoea	12.5%	18.9%	
	Chest-pain	11.1%	9.7%	
	Haemoptysis	2.3%	3.4%	
	Weight-loss	4.8%	5.0%	
	Other symptoms	21.5%	18.1%	
Cancer stage	I	9.4%	0.0%	< 0.001
	III	8.5%	0.7%	
	IV	73.2%	5.5%	
	Unknown	8.9%	93.7%	
Diagnosis	Unspecified lung cancer	13.8%	94.8%	< 0.001
	NSCLC	83.9%	5.2%	
	SCLC	2.4%	0.0%	
Institution of referral	Private hospital	52.0%	52.8%	0.14
	Public hospital	41.7%	43.9%	
	Unknown	6.3%	3.3%	
Period	2019/2021	21.4%	10.7%	< 0.001
	2013/2018	41.7%	38.7%	
	2007/2012	28.1%	32.1%	
	2004/2006	8.8%	18.5%	

Table T12: Treatment interval by covariates (missing vs complete data)

Variable	Categories	Complete (N=2146)	Missing (N=499)	p-value
		60.9 (13.1)	62.8 (12.8)	0.004
Age	min/49	19.4%	15.9%	0.019
	50/59	23.3%	20.5%	
	60/69	29.0%	28.8%	
	70/103	28.3%	34.8%	
Sex	Women	52.6%	45.5%	0.004
	Men	47.4%	54.5%	
Education	>=High-school	45.3%	42.7%	0.80
	Middle school	6.5%	6.4%	
	Elementary	32.9%	34.9%	
	No education	6.8%	7.8%	
	Unknown	8.4%	8.2%	
SEP	Lower	56.0%	46.1%	< 0.001
	Middle	32.2%	34.9%	
	Higher	11.8%	19.0%	
Region	North	6.2%	5.6%	0.93
	Centre	20.0%	18.6%	
	Mexico City	45.6%	46.9%	
	South	19.0%	19.4%	
	Unknown	9.2%	9.4%	
Marital status	Divorced	11.6%	20.8%	< 0.001
	Married	56.1%	50.9%	
	Single	10.2%	8.2%	
	Widowed	12.0%	10.6%	
	Unknown	10.1%	9.4%	
First symptom	Cough	47.6%	46.9%	0.17
	Dyspnoea	12.8%	14.9%	
	Chest-pain	10.9%	11.1%	
	Haemoptysis	2.3%	2.6%	
	Weight-loss	4.4%	6.7%	
	Other symptoms	21.9%	17.8%	
Cancer stage	I	7.5%	12.2%	< 0.001
	III	8.5%	4.2%	
	IV	74.8%	29.7%	
	Unknown	9.1%	53.9%	
Diagnosis	Unspecified lung cancer	13.0%	60.9%	< 0.001
	NSCLC	84.7%	37.5%	
	SCLC	2.2%	1.6%	
Institution of referral	Private hospital	52.1%	51.7%	0.33
	Public hospital	42.2%	40.9%	
	Unknown	5.7%	7.4%	
Period	2019/2021	21.5%	14.8%	< 0.001
	2013/2018	40.9%	43.7%	
	2007/2012	29.2%	25.3%	
	2004/2006	8.3%	16.2%	

Table T13: Patient interval unadjusted and adjusted [log] linear regression

Patient interval					
Variable	Categories	*N=999*		*N=999*	
		Unadjusted	**p-value**	Adjusted	**p-value**
Age	Age	-.0019496	0.540	-0.0042902	0.217
Sex	Male	*Reference*		*Reference*	
	Female	-.1789465	0.035	-0.1730475	0.048
Education	No education	*Reference*		*Reference*	
	>=High-school	-.2323451	0.231	-0.2916435	0.155
	Middle school	-.1814412	0.447	-0.3222735	0.194
	Elementary	-.2624043	0.190	-0.2938557	0.146
	Unspecified	-.374286	0.121	-0.6712827	0.280
Marital status	Married	*Reference*		*Reference*	
	Divorced	-.051944	0.711	-0.0123663	0.931
	Single	-.137321	0.332	-0.1541062	0.280
	Widowed	-.0337325	0.822	-0.0983768	0.526
	Unspecified	-.0796249	0.595	0.2481363	0.438
Region	Mexico City	*Reference*		*Reference*	
	North	.1331285	0.411	0.1184851	0.468
	Centre	.2403509	0.036	0.1782043	0.132
	South	.1637915	0.153	0.116507	0.324
	Unspecified	-.0519923	0.747	-0.0441587	0.926
Symptom	Cough	*Reference*		*Reference*	
	Dyspnoea	-.4516063	0.001	-0.4125325	0.003
	Chest-pain	.0530603	0.720	0.0512485	0.732
	Haemoptysis	-.0092578	0.977	0.0594648	0.853
	Weight-loss	.1809481	0.401	0.2350571	0.287
	Other symptoms	-.48423	0.000	-0.4780341	0.000
	Unspecified	.0980469	0.645	0.214122	0.352
Diagnosis	NSCLC	*Reference*		*Reference*	
	SCLC	-.1515227	0.627	-0.1783597	0.569
	Unspecified	-.1034448	0.287	0.2292946	0.204
Cancer stage	I-II	*Reference*		*Reference*	
	III	-.0902741	0.733	-.0840303	0.753
	IV	-.2363127	0.285	-.1830584	0.421
	Unspecified	-.3984119	0.086	-.4649428	0.097
Institution	Public hospital	*Reference*		*Reference*	
	Private hospital	.0841334	0.337	0.0110536	0.909
	Unspecified	-.0011478	0.995	-0.1382304	0.507
Term	2019/2021	*Reference*		*Reference*	
	2013/2018	.0229628	0.827	-0.0293681	0.796
	2007/2012	-.2079699	0.055	-0.2844127	0.027
	2004/2006	-.2368401	0.316	-0.3658525	0.149

Table T14: System interval unadjusted and adjusted [log] linear regression

System interval					
Variable	Categories	*N=1090*		*N=1090*	
		Unadjusted	**p-value**	Adjusted	**p-value**
Age	Age	-.0014589	0.565	-0.0039399	0.151
Sex	Male	*Reference*		*Reference*	
	Female	-.1205652	0.074	-0.0767854	0.270
Education	No education	*Reference*		*Reference*	
	>=High-school	.24523	0.122	0.1636394	0.324
	Middle school	.1302064	0.499	0.0389268	0.845
	Elementary	.2124561	0.193	0.1834727	0.264
	Unspecified	.0408369	0.832	0.1693474	0.720
Marital status	Married	*Reference*		*Reference*	
	Divorced	.0649841	0.567	0.0451618	0.695
	Single	-.0864744	0.438	-0.1457385	0.196
	Widowed	.1232227	0.282	0.1260226	0.292
	Unspecified	-.14484	0.217	0.0168611	0.950
Region	Mexico City	*Reference*		*Reference*	
	North	.0361863	0.777	-0.0523961	0.685
	Centre	-.0237503	0.795	-0.0728485	0.438
	South	-.0424669	0.642	-0.0560004	0.550
	Unspecified	-.1736533	0.161	-0.2254043	0.506
Symptom	Cough	*Reference*		*Reference*	
	Dyspnea	-.1627138	0.152	-0.1563805	0.173
	Chest-pain	-.1100852	0.372	-0.1094247	0.378
	Haemoptysis	-.1657639	0.567	-0.1955541	0.501
	Weight-loss	-.3809619	0.049	-0.3807542	0.052
	Other symptoms	-.1240035	0.192	-0.141615	0.141
	Unspecified	.2831254	0.005	0.2732855	0.010
Diagnosis	NSCLC	*Reference*		*Reference*	
	SCLC	-.5486345	0.038	-.5656382	0.034
	Unspecified	-.029981	0.704	.2167142	0.119
Cancer stage	I-II	*Reference*		*Reference*	
	III	-.0753771	0.721	0.0014521	0.995
	IV	-.173712	0.319	-0.1476597	0.405
	Unspecified	-.2375277	0.197	-0.2912324	0.188
Institution	Public hospital	*Reference*		*Reference*	
	Private hospital	.187938	0.006	0.1301396	0.091
	Unspecified	-.0702927	0.672	-0.1932819	0.252
Term	2019/2021	*Reference*		*Reference*	
	2013/2018	.223799	0.007	0.132754	0.146
	2007/2012	-.026074	0.766	-0.083467	0.422
	2004/2006	-.1250384	0.487	-0.1751237	0.364

Table T15: Pre-hospital interval unadjusted and adjusted [log] linear regression

Pre-hospital interval					
Variable	Categories	*N=1191*		*N=1191*	
		Unadjusted	**p-value**	Adjusted	**p-value**
Age	Age	-.0032577	0.306	-0.0048688	0.157
Sex	Male	*Reference*		*Reference*	
	Female	-.2217285	0.008	-0.2011285	0.021
Education	No education	*Reference*		*Reference*	
	>=High-school	.3402385	0.080	0.2228763	0.274
	Middle school	.2948345	0.221	0.1426169	0.567
	Elementary	.3713806	0.065	0.3135804	0.122
	Unspecified	.0443801	0.851	0.3773467	0.511
Marital status	Married	*Reference*		*Reference*	
	Divorced	.1295615	0.350	0.1333227	0.342
	Single	-.0509063	0.718	-0.0929771	0.514
	Widowed	.0034123	0.981	-0.0012555	0.993
	Unspecified	-.237585	0.101	-0.019527	0.954
Region	Mexico City	*Reference*		*Reference*	
	North	.3356755	0.034	0.2578492	0.109
	Centre	.2403041	0.035	0.1948718	0.096
	South	.13483	0.235	0.1011619	0.385
	Unspecified	-.180225	0.235	-0.3380532	0.406
Symptom	Cough	*Reference*		*Reference*	
	Dyspnea	-.083905	0.563	-0.0477967	0.742
	Chest-pain	-.037205	0.814	-0.0093516	0.953
	Haemoptysis	-.331594	0.338	-0.3169554	0.359
	Weight-loss	-.4510486	0.051	-0.4089188	0.081
	Other symptoms	-.1394214	0.238	-0.120186	0.311
	Unspecified	.2760628	0.030	0.3257719	0.013
Diagnosis	NSCLC	*Reference*		*Reference*	
	SCLC	-.2459839	0.431	-0.2410639	0.443
	Unspecified	.081706	0.396	0.4166893	0.017
Cancer stage	I-II	*Reference*		*Reference*	
	III	.0575881	0.817	0.1966502	0.433
	IV	-.1190702	0.549	-0.0622759	0.759
	Unknown	-.0990457	0.638	-0.2892199	0.266
Institution	Public hospital	*Reference*		*Reference*	
	Private hospital	.21108	0.015	0.1384554	0.151
	Unspecified	-.0912764	0.641	-0.2131872	0.285
Term	2019/2021	*Reference*		*Reference*	
	2013/2018	.2329761	0.026	0.0923062	0.418
	2007/2012	-.0852054	0.440	-0.1778736	0.174
	2004/2006	-.1638578	0.458	-0.2261284	0.338

Table T16: Total interval unadjusted, intermediate and fully adjusted [Log] linear regression

Total interval							
Variable	**Categories**	*N=1821*					
		Unadjusted	**p-value**	**Intermediate**	**p-value**	**Adjusted**	**p-value**
Age		-.0033798	0.019	-.002	0.085	-.0047895	0.002
Sex	Male	*Reference*		*Reference*		*Reference*	
	Female	.1688046	<0.0001	.162443	<0.0001	.1472388	<0.0001
Education	No education	*Reference*		*Reference*		*Reference*	
	>=High-school	.096338	0.226	.095126	0.235	.0596258	0.465
	Middle school	.0847009	0.414	.081562	0.432	.009648	0.927
	Elementary	.0619756	0.444	.068813	0.393	.0725776	0.363
	Unspecified	.0509085	0.617	.036649	0.718	.227509	0.427
Marital status	Married	*Reference*		*Reference*		*Reference*	
	Divorced	.0250182	0.678			-.0024414	0.967
	Single	-.0672753	0.290			-.11036	0.080
	Widowed	.060693	0.330			.0688188	0.284
	Unspecified	-.0672613	0.317			-.3130457	0.029
Region	Mexico City	*Reference*		*Reference*		*Reference*	
	North	.0446332	0.583			.0072072	0.928
	Centre	.0632258	0.209			.0412253	0.409
	South	.0528982	0.305			.0348487	0.495
	Unspecified	.0135788	0.852			.0451142	0.845
Symptom	cough	*Reference*		*Reference*		*Reference*	
	dyspnoea	-.234595	<0.0001			-.2231695	<0.0001
	chest-pain	-.158339	0.015			-.1295138	0.044
	Haemoptysis	-.1046023	0.427			-.0446872	0.732
	weight-loss	-.1579765	0.101			-.1215609	0.202
	other symptoms	-.3086754	<0.0001			-.2979587	<0.0001
	Unspecified	-.272706	0.002			-.2201305	0.018
Diagnosis	NSCLC	*Reference*		*Reference*		*Reference*	
	SCLC	-.3392539	0.006	-.312774	0.012	-0.3128614	0.010
	Unspecified	.0863383	0.084	.094044	0.059	.081627	0.297
Cancer stage	I-II	*Reference*		*Reference*		*Reference*	
	III	-.0063998	0.951			-.0209834	0.839
	IV	-.1278982	0.130			-.1774248	0.034
	Unspecified	.0123379	0.898			-.0442251	0.701
Institution	Public	*Reference*		*Reference*		*Reference*	
	Private hospital	.0801	0.42			.027223	0.512
	Unspecified	-.0014245	0.987			-.0018526	0.984
Term	2019/2021	*Reference*		*Reference*		*Reference*	
	2013/2018	.0243691	0.624			-.0314109	0.562
	2007/2012	-.141938	0.006			-.2329795	<0.0001
	2004/2006	-.3072679	<0.0001			-.4237538	<0.0001

This intermediate models adjusts for age, sex, education and type of lung cancer. Results show only sex (female) and SCLC are statistically significant.

A3: Ethical Approval and data sharing agreements with INCAN

SALUD
SECRETARÍA DE SALUD

Instituto Nacional de Cancerología

UCL ETHICAL COMMITTEE

Mexico City, September 19, 2019

TO WHOM IT MAY CONCERN,

Hoping this letter finds you well. I am writing you to confirm the Thoracic Oncology Unit and Personalized Medicine Laboratory at the Instituto Nacional de Cancerología in Mexico (INCan) are satisfied with the research protocol: "***Lung cancer in Mexico: patient trajectories, barriers to health-care and the effect of a patient navigation model on delays to health-care, patient satisfaction, quality of life, health-literacy and self-efficacy"***, elaborated by Elysse Bautista Gonzalez (PhD student at the Epidemiology and Public Health Department in University College London (UCL)) under the supervision of Hynek Pikhart, Anne Peasey, Cecilia Vindrola and Sir Michael Marmot. As a result, we will proceed to submit the research protocol into our internal ethical committee and support Dr. Elysse Bautista Gonzalez with the internal administrative and procedural tasks to take on the project from January 2020 to January 2023.

The extent of the intervention is yet to be determined after the initial phase of Elysse's research. Hence, results from this initial research will then inform decision makers on the budget expenses required for the secondary phase. Nonetheless, support from grants and non-profit organisations will be sought for throughout this period.

Please, feel free to contact me if you have any further queries.

Kind regards,

Oscar Gerardo Arrieta Rodríguez, MD MSc
Head of the Thoracic Oncology Unit
National Cancer Institute, Mexico City-Mexico
Avenida San Fernando 22, Belisario Domínguez Secc 16, 14080 Mexico City, Mexico.
Email: ogarrieta@gmail.com Tel: 01 55 5628 0400 Ext: 71101 (Office)

SALUD
SECRETARÍA DE SALUD

INSTITUTO NACIONAL DE CANCEROLOGÍA

Comité de Ética en Investigación
Gestión 2019-2022
Registrado ante COFEPRIS 12 CEI 09 014 11
Registrado ante CONBIOETICA-09-CEI-002-20160413
Office For Human Research Protections (OHRP)
IORG0006100
IRB00007348
FWA00019235

No protocolo: CEI/1493/20
No. Ref. INCAN/CEI/1267/20
DÉCIMA SEXTA SESIÓN ORDINARIA
10 de diciembre, 2020.

Dr. Oscar G. Arrieta Rodríguez.
Investigador Principal

P r e s e n t e.

En relación al protocolo: **"Retrasos en el acceso a servicios de salud durante la trayectoria del paciente con cáncer de pulmón" (020/043/ICI) (CEI/1493/20).** El Comité de Ética en investigación revisó y aprobó los siguientes documentos:

- Formato único del protocolo (versión 3, 03 noviembre 2020)
- En el anexo se encuentran:
  - A1. Descripción de la colaboración
  - A2. Guía temática (entrevistas estructuradas)
  - A3. Variables recolectadas (expediente electrónico)
  - A4. Consentimiento informado (versión III-03 noviembre 2020)
  - A5. Acuerdo de intercambio de datos entre instituciones
  - A6. Seguro de responsabilidad pública

Esta documentación cumple con todos los requisitos por lo que el Comité de Ética en Investigación puede proceder con la aprobación. Esta aprobación tiene una vigencia hasta el 10 de diciembre del 2021. Por lo que en caso necesario le solicitamos atentamente someter su renovación anual antes de esta fecha, junto con un informe de los resultados obtenidos. También será necesario informar al comité cualquier información derivada del estudio que deba ser informada a los participantes. De acuerdo con los lineamientos de regulación interno, buenas prácticas clínicas y políticas de operación del Comité de Ética en Investigación del INCan, es indispensable hacer de su conocimiento que cualquier miembro de los comités que participa en un proyecto de investigación NO tiene VOZ ni Voto en las resoluciones acerca del estudio. (Se requiere informe de los avances "status" de eventos adversos y enmiendas de manera semestral).

Atentamente

[redacted]

Dra. Myrna G. Candelaria Hernández
Presidente del Comité de Ética en Investigación.

SALUD
SECRETARÍA DE SALUD

INSTITUTO NACIONAL DE CANCEROLOGÍA

Comité de Ética en Investigación
Gestión 2019-2022
Registrado ante COFEPRIS 12 CEI 09 014 11
Registrado ante CONBIOETICA-09-CEI-002-20160413
Office For Human Research Protections (OHRP)
IORG0006100
IRB00007348
FWA00019235

No protocolo: CEI/1493/20
No. Ref. INCAN/CEI/1267/20
DÉCIMA SEXTA SESIÓN ORDINARIA
10 de diciembre, 2020.

Dr. Oscar G. Arrieta Rodríguez.
Investigador Principal

Presente.

En relación al protocolo: **"Retrasos en el acceso a servicios de salud durante la trayectoria del paciente con cáncer de pulmón" (020/043/ICI) (CEI/1493/20).** El Comité de Ética en Investigación, le reitera que en su carta de aprobación fechada 10 de diciembre del 2020. Se señala que es necesario, presente informes semestrales y renovación anual dúrate el tiempo que su proyecto esté vigente por lo anterior para dar **seguimiento continuo** a su protocolo.

Atentamente

[redacted]

Dra. Myrna G. Candelaria Hernández
Presidente del Comité de Ética en Investigación.

SALUD
SECRETARÍA DE SALUD

INSTITUTO NACIONAL DE CANCEROLOGÍA

Comité de Ética en Investigación
Gestión 2019-2022
Registrado ante COFEPRIS 12 CEI 09 014 11
Registrado ante CONBIOETICA-09-CEI-002-20160413
Office For Human Research Protections (OHRP)
IORG0006100
IRB00007348
FWA00019235

No protocolo: CEI/1493/20
No. Ref. INCAN/CEI/1267/20
DÉCIMA SEXTA SESIÓN ORDINARIA
10 de diciembre, 2020.

Dr. Oscar G. Arrieta Rodríguez.
Investigador Principal

P r e s e n t e.

En relación al protocolo: **"Retrasos en el acceso a servicios de salud durante la trayectoria del paciente con cáncer de pulmón" (020/043/ICI) (CEI/1493/20).** Se extiende la presente donde se hace constar que el Comité de Ética en Investigación de Instituto Nacional de Cancerología se rige bajo los lineamientos estipulados por la Comisión Nacional de Bioética, los criterios de armonización Internacional y las **guías de buenas prácticas clínicas**.

Atentamente

[redacted]

Dra. Myrna G. Candelaria Hernández
Presidente del Comité de Ética en Investigación.

SALUD
SECRETARÍA DE SALUD

INSTITUTO NACIONAL DE CANCEROLOGÍA

Comité de Ética en Investigación
Gestión 2019-2022
Registrado ante COFEPRIS 12 CEI 09 014 11
Registrado ante CONBIOETICA-09-CEI-002-20160413
Office For Human Research Protections (OHRP)
IORG0006100
IRB00007348
FWA00019235

No protocolo: CEI/1493/20
No. Ref. INCAN/CEI/1267/20
DÉCIMA SEXTA SESIÓN ORDINARIA
10 de diciembre, 2020.

Dr. Oscar G. Arrieta Rodríguez.
Investigador Principal

P r e s e n t e.

En relación al protocolo: **"Retrasos en el acceso a servicios de salud durante la trayectoria del paciente con cáncer de pulmón" (020/043/ICI) (CEI/1493/20).** Los miembros del Comité de Ética en Investigación, certificamos que los siguientes miembros del Comité de Ética en Investigación participaron en la evaluación de los aspectos éticos, comprometiéndose guardar la confidencialidad relacionada con su protocolo. Asimismo, señalaron no tener conflicto de interés en esta evaluación.

Dra. Myrna Gloria Candelaria Hernández (presidente)	[redacted]
Psic. María del Carmen Lizeth León Castillo (Vocal secretario)	
Dra. María Teresa Ramírez Ugalde (vocal)	
Dr. Bernardo Cacho Díaz (vocal)	
Dr. José Antonio Bahena González (vocal)	
Dra. Alejandra Monroy López (vocal)	
Sr. Rene Aragón Ramírez (representante del núcleo afectado o usuarios de servicios de salud)	

UCL RESEARCH ETHICS COMMITTEE
OFFICE FOR THE VICE PROVOST RESEARCH

03/03/2021

Professor Hynek Pikhart
Institute of Epidemiology and Health Care
UCL

Cc: Elysse Bautista Gonzalez

Dear Prof Pikhart,

Notification of Ethics Approval
Project ID/Title: 16607/001 Lung cancer in Mexico: patient trajectories, barriers to health-care and the effect of a patient navigation model on delays to health-care, patient satisfaction, quality of life, health-literacy and self-efficacy

Further to your satisfactory responses to the reviewer's comments, I am pleased to confirm that your study has been ethically approved until **31/12/2022.**

Ethical approval is subject to the following conditions:

Notification of Amendments to the Research
You must seek Chair's approval for proposed amendments (to include extensions to the duration of the project) to the research for which this approval has been given. Each research project is reviewed separately and if there are significant changes to the research protocol you should seek confirmation of continued ethical approval by completing an 'Amendment Approval Request Form'
http://ethics.grad.ucl.ac.uk/responsibilities.php

Adverse Event Reporting – Serious and Non-Serious
It is your responsibility to report to the Committee any unanticipated problems or adverse events involving risks to participants or others. The Ethics Committee should be notified of all serious adverse events via the Ethics Committee Administrator (ethics@ucl.ac.uk) immediately the incident occurs. Where the adverse incident is unexpected and serious, the Joint Chairs will decide whether the study should be terminated pending the opinion of an independent expert. For non-serious adverse events the Joint Chairs of the Ethics Committee should again be notified via the Ethics Committee Administrator within ten days of the incident occurring and provide a full written report that should include any amendments to the participant information sheet and study protocol. The Joint Chairs will confirm that the incident is non-serious and report to the Committee at the next meeting. The final view of the Committee will be communicated to you.

Office of the Vice Provost Research, 2 Taviton Street
University College London
Tel: +44 (0)20 7679 8717
Email: ethics@ucl.ac.uk
http://ethics.grad.ucl.ac.uk/

Final Report
At the end of the data collection element of your research we ask that you submit a very brief report (1-2 paragraphs will suffice) which includes in particular issues relating to the ethical implications of the research i.e. issues obtaining consent, participants withdrawing from the research, confidentiality, protection of participants from physical and mental harm etc.

In addition, please:

- ensure that you follow all relevant guidance as laid out in UCL's Code of Conduct for Research: www.ucl.ac.uk/srs/governance-and-committees/research-governance
- note that you are required to adhere to all research data/records management and storage procedures agreed as part of your application. This will be expected even after completion of the study.

With best wishes for the research.

Yours sincerely

[redacted]

Professor Michael Heinrich
Joint Chair, UCL Research Ethics Committee

LONDON'S GLOBAL UNIVERSITY

UCL

Data Sharing Agreement

between

University College London

and

Instituto Nacional de Cancerología (INCan)

Date this Agreement comes into force: [19/09/2019]

1. Parties to this Agreement

(a) **UNIVERSITY COLLEGE LONDON** a body corporate established by Royal Charter with company number RC000631 of Gower Street, London, WC1E 6BT (**UCL**); and

(b) Instituto Nacional de Cancerología in Mexico City, Mexico a body of the ministry of health at Avenida San Fernando 22, Belisario Domínguez Secc 16, 14080 Mexico City , México .

2. Purpose

(a) This Agreement establishes the terms and conditions under which the parties will share personal data in connection with the project *Lung cancer in Mexico: patient trajectories, barriers to health-care and*

[redacted]

the effect of a patient navigation model on delays to health-care, patient satisfaction, quality of life, health-literacy and self-efficacy.

(b) The parties shall share the personal data described in 2(a) above only in accordance with the terms of this Agreement.

3. Term and termination

(a) This Agreement shall commence on the date set out at the beginning of it and shall continue until 19/09/2019 unless terminated earlier in accordance with its terms.

(b) Either party may terminate this Agreement with immediate effect by giving written notice to the other party if that other party commits a material breach of any term of this Agreement which breach is irremediable or (if such breach is remediable) fails to remedy that breach within a period of 30 days after being notified in writing to do so;

(c) Clause 3 (Term and termination) and Clause 4 (Data protection) shall survive the termination or expiry of this Agreement, as shall any other Clause which, by its nature, is intended to survive termination or expiry.

(d) Termination or expiry of this Agreement shall not affect any rights, remedies, obligations or liabilities of the parties that have accrued up to the date of termination or expiry, including the right to claim damages in respect of any breach of the Agreement which existed at or before the date of termination or expiry.

4. Data protection

(a) In this Clause, the following terms have the following meanings:

(i) **Controller** means a person which, alone or jointly with others, determines the purposes and means of the Processing of Personal Data;

(ii) **Data Protection Laws** means all applicable statutes and regulations in any jurisdiction pertaining to the processing of Personal Data, including but not limited to the privacy and security of Personal Data;

(iii) **Data Subject** means the individual to whom the Personal Data relates;

(iv) **Personal Data** means any information relating to an identified or identifiable living individual;

(v) **Processing** means any operation or set of operations which is performed on Personal Data or on sets of Personal Data, whether or not by automated means, and Process, Processes and Processed shall be construed accordingly; and

(vi) **Personal Data Breach** means a breach of security leading to the accidental or unlawful destruction, loss, alteration, unauthorised disclosure of, or access to, Personal Data transmitted, stored or otherwise processed.

(b) The parties acknowledge and agree that where a party Processes Personal Data under or in connection with this Agreement it alone determines the purposes and means of such processing as a Controller.

(c) In respect of the Personal Data a party Processes under or in connection with this Agreement, the party shall:

(i) comply at all times with its obligations under the Data Protection Laws;

(ii) notify the other party without undue delay after becoming aware of a Personal Data Breach; and

(iii) assist and co-operate fully with the other party to enable the other party to comply with their obligations under Data Protection Law, including but not limited to in respect of keeping Personal Data secure, dealing with Personal Data Breaches, complying with the rights of Data Subjects and carrying out data protection impact assessments.

(d) The parties shall work together to ensure that each of them is able to Process the Personal Data it Proc under or in connection with this Agreement for the purposes contemplated by this Agreement lawfully, f and in a transparent manner and in compliance with the Data Protection Laws. This shall include but no

[redacted]

limited to entering into such other written agreements as may be required from time to time to enable each party to comply with the Data Protection Laws.

5. Miscellaneous

(a) No variation of this Agreement shall be effective unless it is in writing and signed by the parties (or their authorised representatives).

(b) A failure or delay by a party to exercise any right or remedy provided under this Agreement or by law shall not constitute a waiver of that or any other right or remedy, nor shall it prevent or restrict any further exercise of that or any other right or remedy. No single or partial exercise of any right or remedy provided under this agreement or by law shall prevent or restrict the further exercise of that or any other right or remedy.

(c) If any provision or part-provision of this Agreement is or becomes invalid, illegal or unenforceable, it shall be deemed modified to the minimum extent necessary to make it valid, legal and enforceable. If such modification is not possible, the relevant provision or part-provision shall be deemed deleted. Any modification to or deletion of a provision or part-provision under this Clause shall not affect the validity and enforceability of the rest of this Agreement.

(d) This Agreement constitutes the entire agreement between the parties and supersedes and extinguishes all previous agreements, promises, assurances, warranties, representations and understandings between them, whether written or oral, relating to its subject matter.

(e) Each party agrees that it shall have no remedies in respect of any statement, representation, assurance or warranty (whether made innocently or negligently) that is not set out in this Agreement.

(f) Nothing in this Agreement is intended to, or shall be deemed to, establish any partnership or joint venture between any of the parties, constitute any party the agent of another party, or authorise any party to make or enter into any commitments for or on behalf of any other party.

(g) This Agreement does not give rise to any rights under the Contracts (Rights of Third Parties) Act 1999 to enforce any term of this Agreement.

(h) This Agreement may be executed in any number of counterparts, each of which when executed shall constitute a duplicate original, but all the counterparts shall together constitute the one Agreement.

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

(j) Each party irrevocably agrees that the courts of England and Wales shall have exclusive jurisdiction to settle any dispute or claim (including non-contractual disputes or claims) arising out of or in connection with this Agreement or its subject matter or formation.

Signed for and on behalf of **University College London**

Name (print):

Job title:

Date:

Signed [redacted] r Arrieta, Head of the Tho [redacted] stituto Nacional de Cancer [redacted] y, Mexico.

Name ([redacted] ez

Job title: Head of the Thoracic Oncology Unit and Personalized Medicine Laboratory.

Date: September 19th of 2019.

A4: Patient information sheets and consent forms

Epidemiology and Public Health Department

CONSENT FORM

Please complete this form after you have read the Information Sheet and/or listened to an explanation about the research

Title of Study: ***Delays in timely access to lung cancercare and the role of patient navigation programmes s in secondary cancer prevention***

Department: Department of Epidemiology and public Health
Name and Contact Details of the Researcher(s): Elysse Bautista-Gonzalez
Name and Contact Details of the Principal Researcher: Hynek Pikhart (UCL) & Oscar Arrieta (National Cancer Institute)
Name and Contact Details of the UCL Data Protection Officer: Ms Alexandra Potts , data-protection@ucl.ac.uk
This study has been approved by the UCL Research Ethics Committee: Project ID number: 16607/001

Thank you for considering taking part in this research. The person organising the research must explain the project to you before you agree to take part. If you have any questions arising from the Information Sheet or explanation already given to you, please ask the researcher before you decide whether to join in. You will be given a copy of this Consent Form to keep and refer to at any time.

I confirm that I understand that by ticking/initialling each box below I am consenting to this element of the study. I understand that it will be assumed that unticked/initialled boxes means that I DO NOT consent to that part of the study. I understand that by not giving consent for any one element that I may be deemed ineligible for the study.

		Tick Box
1.	*I confirm that I have read and understood the Information Sheet for the above study. I have had an opportunity to consider the information and what will be expected of me. I have also had the opportunity to ask questions which have been answered to my satisfaction *and would like to take part in an individual interview*	
2.	*I understand that I will not be able to withdraw data *collected in my audio recordings*	
3.	*I consent to participate in the study. I understand that my personal information will be used for the purposes explained to me. I understand that according to data protection legislation, 'public task' will be the lawful basis for processing.	
4.	**Use of the information for this project only** *I understand that all personal information will remain confidential and that all efforts will be made to ensure I cannot be identified I understand that my data gathered in this study will be stored pseudo-anonymously and securely. It will not be possible to identify me in any publications.	
5.	*I understand that my information may be subject to review by responsible individuals from the University, CONACYT or the National Cancer Institute in Mexico for monitoring and audit purposes.	
6.	*I understand that my participation is voluntary and that I am free to withdraw at any time without giving a reason, [*without the care I receive or my legal rights being affected*]. I understand that if I decide to withdraw, any personal data I have provided up to that point through interviews will be deleted.	
7.	I understand the potential risks of participating and the support that will be available to me should I become distressed during the course of the research.	
8.	I understand there are no direct benefits of participating.	
9.	I understand that the data will not be made available to any commercial organisations but is solely the responsibility of the researcher(s) undertaking this study.	
10.	I understand that I will not benefit financially from this study or from any possible outcome it may result in in the future.	
11.	I understand that I will not be compensated for the portion of time spent in the study	
12.	I agree that my pseudonymised research data may be used by others for future research. [No one will be able to identify you when this data is shared.]	

13.	I understand that the information I have submitted will be published as a report or used in conferences.	
14.	I consent to my interview being audio recorded and understand that the recordings will be stored anonymously, using password-protected software and will be used for training, quality control, audit and specific research purposes. It will be destroyed immediately following transcription.	
15.	I hereby confirm that I understand the inclusion criteria as detailed in the Information Sheet and explained to me by the researcher.	
16.	I hereby confirm that: (a) I understand the exclusion criteria as detailed in the Information Sheet and explained to me by the researcher; and	
	(b) I do not fall under the exclusion criteria.	
18.	I have informed the researcher of any other research in which I am currently involved or have been involved in during the past 12 months.	
19.	I am aware of who I should contact if I wish to lodge a complaint.	
20.	I voluntarily agree to take part in this study.	
21.	Use of information for this project and beyond I would be happy for the data I provide to be archived for 20 years at Data Safe Haven. I understand that other authenticated researchers will have access to my pseudonymised data.	
22.	**Overseas Transfer of Data** I understand that my personal data will be transferred to a safe location (Data Safe Haven) in the United Kingdom and the following safeguards will be put in place: data encryption. Identifiable data will not be sent back to Mexico.	

If you would like your contact details to be retained so that you can be contacted in the future by UCL researchers who would like to invite you to participate in follow up studies to this project, or in future studies of a similar nature, please tick the appropriate box below.

	Yes, I would be happy to be contacted in this way	
	No, I would not like to be contacted	

_____	_____	_____
Name of participant	Date	Signature
_____	_____	_____
Name of witness (If applicable)	Date	Signature
_____	_____	_____
Name of witness (If applicable)	Date	Signature
_____	_____	_____
Researcher	Date	Signature

Epidemiology and Public Health Department

Participant information sheet

Title of Study: Delays in timely access to lung cancer care and the role of patient navigation programs in secondary cancer prevention
Department: Epidemiology and public health research department
Researchers:
Hynek Pikhart, h.pikhart@ucl.ac.uk (PI in the UK), Oscar Arrieta, ogarrieta@gmail.com (PI in Mexico) and Elysse Bautista Gonzalez, elysse.bautista.16@ucl.ac.uk (PhD student)
UCLData Protection Officer: Alexandra Potts, data-protection@ucl.ac.uk

This study has been approved by the UCL Research Ethics Committee
Project ID number: 16607/001

You are being invited to take part in a research project. Before you decide to participate it is important for you to understand why the research us being done and what participation will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

1. **What is the project's purpose?**
   Lung cancer patients experience delays in health-care. Thus, the general aim of this study is to understand what prevents lung cancer patientsto receive care. Particular focus is placed on what prevents early diagnosis and treatment of lung cancer. Results from this study will serve to generate interventionS to reduce delays in cancer-care. The duration of the project is 12 months for each individual and requires approximately one hour interview.

2. **Why have I been chosen?**
   You have been invited to participate in this study as you have a lung cancer diagnosis and fulfill the eligibility criteria.
   Inclusion criteria: Patients with a lung cancer diagnosis, who a**re** above the legal age to vote (18 years old) are considered to participate in this study. Patients have to be within 0-3 points in the Eastern Cooperative Oncology Group (ECOG) Performance Status scale at the time of participation. Having a COVID19 diagnosis does not mean the patients are ineligible for the study. All genders are eligible to enter the protocol. **Exclusion criteria:** Patients without a confirmed a lung cancer diagnosis, below the age of 18 or with ECOG >=4.

3. **Do I have to take part?**
   It is up to you to decide whether or not to take part in this research. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. You can withdraw at any time without giving a reason. If you decide to withdraw no more data will be asked of you from that point onwards. However audios from the interviews will not be erased as they are recorded without identification number and will not be traceable. Additionally, data from electronic health records will be kept (due to previous consent). in contrast, data collected from structured interviews will be deleted permanently.

4. **What will happen to me if I take part?**

    - One hour interview conducted by one of the researchers, after the interview patients will **not** be contacted in the future.

5. **What are the possible disadvantages and risks of taking part?**
   There are no physical identifiable risks in patients taking part in this research. However, you may become distressed due to sensible questions during the interview. If needed you can skip questions and a mental health team is in continuous aid of patients in distress throughout the research.

6. **What are the possible benefits of taking part in this research?**
   Whilst there are no immediate benefits for those people participating in the project, it is hoped that this work will help inform future cancer policies in Mexico

7. **What if something goes wrong?**
   In the case of a complaint or any serious adverse event you can contact contact Dr. Oscar Arrieta (head of department at the INCAN) in Mexico or Dr. Hynek Pikhart. In Second instance you can contact Alexandra Potts, a.potts@ucl.ac.uk If you feel that your issue has not been handled to your satisfaction you can also contact the Chair of the UCL Research Ethics Committee –ethics@ucl.ac.uk. In addition,

8. **Will my taking part in this research be kept confidential ?**
   'All the information that we collect about you during the course of the research will be kept strictly confidential. You will not be able to be identified in any ensuing reports or publications.

9. **Limits to confidentiality**
    - Please note that confidentiality will be maintained as far as it is possible, unless during our conversation I hear anything which makes me worried that someone might be in danger of harm, I might have to inform relevant agencies of this.

11. **What will happen to the results of the research project?**

The data collected will be used as part of PhD thesis. In addition, it might be used for other or subsequent research. This will be un-identifiable at all times. Results from the study will be published at the end of the research through a conference in the hospital. Medical staff and patients are encouraged to attend.

12. **Data Protection Privacy Notice**

The data controller for this project will be UCL. The UCL Data Protection Office provides oversight of UCL activities involving the processing of personal data, and can be contacted at data-protection@ucl.ac.uk. UCL's Data Protection Officer can also be contacted at data-protection@ucl.ac.uk.

Further information on how UCL uses participant information can be found here: *www.ucl.ac.uk/legal-services/privacy/participants-health-and-care-research-privacy-notice*

Your personal data will be used for the purposes outlined in this notice. The categories of personal data used will be

- Place of residence
- Gender
- Ethnicity
- Education
- Marital status

The legal basis that would be used to process your personal data will be performance of a task in the public interest. The legal basis used to process special category personal data will be for statistical purposes detailing differences in the population.

Your personal data will be processed so long as it is required for the research project. If we are able to anonymise or pseudonymise the personal data you provide we will undertake this, and will endeavour to minimise the processing of personal data wherever possible.

You have certain rights under data protection legislation in relation to the personal information that we hold about you. These rights apply only in particular circumstances and are subject to certain exemptions such as public interest (for example the prevention of crime). They include:

- The right to access your personal information;
- The right to rectification of your personal information;
- The right to erasure of your personal data;
- The right to restrict or object to the processing of your personal data;

- The right to object to the use of your data for direct marketing purposes;
- The right to data portability;
- Where the justification for processing is based on your consent, the right to withdraw such consent at any time; and
- The right to complain to the Information Commissioner's Office (ICO) about the use of your personal data.

If you are concerned about how your personal data is being processed, or if you would like to contact us about your rights, please contact UCL in the first instance at data-protection@ucl.ac.uk.

If you remain unsatisfied, you may wish to contact the ICO. Contact details, and further details of data subject rights, are available on the ICO website at: https://ico.org.uk/for-organisations/data-protection-reform/overview-of-the-gdpr/individuals-rights/

Data will be safely transferred outside of Mexico and will be shared with other researchers in University College London. The researchers with access to this information are:

(a) Elysse Bautista

(b) Anne Peasey

(c) Cecilia Vindrola

(d) Hynek Pikhart

13. **Who is organising and funding the research?**

This research is a collaboration between UCL and the National Cancer Institute.

Elysse Bautista is partially funded by Consejo Nacional de Ciencia y Tecnologia (CONACYT) and the National Cancer institute.

14. **Contact for further information**

Elysse Bautista Gonzalez

elysse.bautista.16@ucl.ac.uk

Thank you for reading this information sheet and for considering to take part in this research study.

CONSENTIMIENTO INFORMADO

Versión III-3 Noviembre 2020.

Título del estudio: Retrasos en el acceso a servicios de salud durante la trayectoria del paciente con cáncer de pulmón.

Departamento: Unidad funcional de Pulmón, INCAN y Departamento de investigación en epidemiología y salud pública, University College London

Investigador principal: Oscar Arrieta, oscararrietaincan@gmail.com

Estudiante de doctorado: Elysse Bautista González, elysse.bautista.16@ucl.ac.uk

Supervisores en University College London (UCL): Hynek Pikhart, Cecilia Vindrola, Anne Peasey, Sir Michael Marmot

Presidente y Secretario del comité de ética en investigación del INCAN: Dra. Myrna G. Candelaria y/o Psic. María del Carmen Lizeth León Castillo.

Oficial de protección de datos de UCL: Hitakshi Tailor, hitakshi.tailor@UCL.ac.uk

Por favor, complete este formulario después de haber leído la información sobre el estudio de investigación y/o haber escuchado una explicación sobre la investigación.

Sección de información

1. ¿Cuál es el propósito del proyecto?

Los pacientes con cáncer de pulmón experimentan retrasos en la atención médica. Por lo tanto, el objetivo general de este protocolo de investigación es comprender las barreras en la atención médica que experimentan los pacientes con cáncer de pulmón que condicionan retrasos en la atención de su enfermedad. Aproximadamente tomará 20 minutos el cuestionario, sin embargo se dará seguimiento al paciente por medio del expediente electrónico hasta diciembre del 2021.

2.¿Por qué he sido elegido?

Usted ha sido invitado a participar en este estudio ya que cuenta con un diagnóstico de cáncer, tiene más de 18 años y ha ingresado al INCAN. Aproximadamente se invitarán a 400 pacientes a participar en entrevistas y se revisarán entre 1200-3000 expedientes clínicos de los pacientes con cáncer de pulmón en el archivo historico del INCAN (2005-2021).

3.¿Tengo que participar?

Depende de usted decidir si participa o no en esta investigación. Si decide participar, se le entregará esta hoja de información para conservar y se le pedirá que firme un formulario de consentimiento. Puede retirarse en cualquier momento del estudio sin dar una razón y sin que eso afecte los servicios a los que tiene derecho. Si decide retirar, no se le solicitarán más datos a partir de ese momento y los datos almacenados serán anonimizados.

4.¿Qué me pasará si participo?

-Cuestionario de 20-30 minutos realizado por Mtra. Elysse Bautista Gonzalez
-Recolección de información clínica y sociodemográfica desde el expediente electrónico del INCAN
-Después del estudio, los pacientes no serán contactados en el futuro. En el caso de que se retire del estudio, ya no se recopilarán datos. Sin embargo, si los datos de las entrevistas ya se han procesado, no se borrarán y se registran sin número de identificación y no serán rastreables.

5.¿Seré grabado y cómo se utilizarán los medios grabados?

Las grabaciones de audio realizadas durante esta investigación se utilizarán sólo para análisis de sus respuestas abiertas. No se hará ningún otro uso de ellos sin su permiso por escrito, y nadie fuera del proyecto tendrá acceso a las grabaciones originales.

6.¿Cuáles son las posibles desventajas y riesgos de participar?

No hay riesgos en participar en esta investigación.

7.¿Cuáles son los posibles beneficios de participar?

Si bien no hay beneficios inmediatos para las personas que participan en el proyecto, se espera que este trabajo ayude a informar futuras políticas públicas sobre la detección, diagnóstico y tratamiento temprano del cáncer de pulmón en México.

8. ¿Qué pasa si algo sale mal o tengo una queja?

En el caso de una queja o cualquier evento adverso grave, puede comunicarse con el Dr. Oscar Arrieta oscararrietaincan@gmail.com. Si considera que su problema no se ha solucionado satisfactoriamente, también puede comunicarse con la Dra. Myrna G. Candelaria (Presidente del comité de ética de investigación del INCAN) al teléfono 56280400 extensión 37015 o con el comité de investigación de UCL ethics@ucl.ac.uk.

9.¿Mi participación en este proyecto se mantendrá confidencial?

Toda la información que recopilamos sobre usted durante el curso de la investigación se mantendrá estrictamente confidencial. No podrá ser identificado en ningún informe o publicación posterior.

10.Límites a la confidencialidad

Tenga en cuenta que la confidencialidad se mantendrá, a menos que durante nuestra conversación escuche algo que me haga preocuparme de que alguien pueda estar en peligro de sufrir daños por ejemplo: aspectos clínicos que requieras seguimiento, violencia intra-familiar, riesgo de suicidio etc. En tal caso, será notificado el Dr. Arrieta de tales riesgos y se le dará seguimiento por parte de la Unidad de toráx.

11. ¿Qué pasará con los resultados del proyecto de investigación?

Los datos recopilados se utilizarán como parte de la tesis doctoral de la Mtra. Elysse Bautista Glez. La información personal no será identificable en todo momento. Los resultados del estudio se publicarán al final de la investigación a través de una conferencias, publicaciones y presentaciones nacionales e internacionales. Se alienta al personal médico y a los pacientes a asistir a la presentación de resultados.

INSTITUTO NACIONAL DE CANCEROLOGÍA
CON VALIDEZ
DEL AL
10 DIC 2020 10 DIC 2021
COMITÉ DE ÉTICA EN INVESTIGACIÓN
COFEPRIS 12 CEI 09 014 11
CONBIOÉTICA-09CEI-002-20160413
(OHRP) FWA00019235
GESTIÓN 2019-2022

El estudio se conducirá bajo los lineamientos de las buenas prácticas clínicas y los lineamientos de la Secretaría de salud. La base legal utilizada para procesar datos personales será para fines de interés público y estadísticos que detallen las diferencias en la población en los retrasos en la atención en el cáncer de pulmón.

Sus datos personales se utilizarán para los fines descritos en este aviso. Las categorías de datos personales utilizadas serán genero, etnicidad, educación, nivel socio-económico. Sus datos personales serán procesados siempre que sean necesarios para el proyecto de investigación. Se minimizará el procesamiento de los datos personales siempre que sea posible.

Usted tiene ciertos derechos bajo la legislación de protección de datos en relación con la información personal que tenemos sobre usted. Estos derechos incluyen:
- El derecho a acceder a su información personal;
- El derecho a la rectificación de su información personal;
- El derecho a borrar sus datos personales;
- El derecho a restringir u oponerse al procesamiento de sus datos personales;
- El derecho a oponerse al uso de sus datos con fines de marketing directo;
- El derecho a la portabilidad de datos;
- Cuando la justificación para el procesamiento se basa en su consentimiento, el derecho a retirar dicho consentimiento en cualquier momento; y
- El derecho a presentar una queja ante la Oficina del Comisionado de Información (ICO) sobre el uso de sus datos personales.

Si le preocupa cómo se procesan sus datos personales, o si desea comunicarse con nosotros sobre sus derechos, comuníquese con UCL en primera instancia a data-protection@ucl.ac.uk. Si sigue insatisfecho, puede comunicarse con el ICO. Los detalles de contacto y más detalles sobre los derechos de los sujetos de datos están disponibles en el sitio web de ICO en: https://ico.org.uk/for-organisations/data-protection-reform/overview-of-the-gdpr/individuals-rights.

Los datos personales se transferirán de manera segura fuera de México y se compartirán con otros investigadores en el University College London. Los investigadores con acceso a esta información son:
(a) Elysse Bautista
(b) Anne Peasey
(c) Cecilia Vindrola
(d) Hynek Pikhart
(e) Oscar Arrieta
(f) Michael Marmot

12.¿Quién está organizando y financiando la investigación?

Esta investigación es una colaboración entre UCL y el INCAN. Elysse Bautista está parcialmente financiada por Consejo Nacional de Ciencia y Tecnologia (CONACYT).

13.Para más información comuníquese con:

Elysse Bautista Gonzalez al correo elysse.bautista.16@ucl.ac.uk o al 5551030556

Gracias por leer la sección informativa y por considerar participar en este estudio de investigación.

Consentimiento informado

Gracias por considerar participar en esta investigación. La persona que organiza la investigación debe explicarle el proyecto antes de que acepte participar. Si tiene alguna pregunta que surja de la sección de información o la explicación que ya se le dio, pregúntele al investigador antes de decidir si desea participar. Se le entregará una copia de este Formulario de consentimiento para que conserve y consulte en cualquier momento.

Confirmo que entiendo que marcando / iniciando cada cuadro a continuación, doy mi consentimiento para este elemento del estudio. Entiendo que se supondrá que las casillas sin marcar / con iniciales significan que NO doy mi consentimiento para esa parte del estudio. Entiendo que al no dar mi consentimiento para ningun elemento, se me puede considerar no elegible para el estudio.

INSTITUTO NACIONAL DE CANCEROLOGÍA
CON VALIDEZ
DEL AL
10 DIC 2020 10 DIC 2021
COMITÉ DE ÉTICA EN INVESTIGACIÓN
COFEPRIS 12 CEI 09 014 11
CONBIOÉTICA-09CEI-002-20160413
(OHRP) FWA00019235
GESTIÓN 2019-2022

Marque con X o una	si está de acuerdo con cada punto	
	Acepto	No acepto
) Confirmo que he leído y entendido la hoja de información para el estudio anterior. He tenido la oportunidad de considerar la información y lo que se espera de mí. También tuve la oportunidad de hacer preguntas que fueron respondidas a mi satisfacción y estoy de acuerdo en que me gustaría participar en las encuestas o cuestionarios involucrados en el protocolo.	☐	☐
) Entiendo que toda la información personal permanecerá confidencial y que se harán todos los esfuerzos para garantizar que no pueda ser identificado. Entiendo que mis datos recopilados en este estudio se almacenarán de forma anónima y segura	☐	☐
) Entiendo que mi información puede estar sujeta a revisión por parte de personas responsables del University College London y el INCAN para fines de monitoreo y auditoría.	☐	☐
) Entiendo que la información que he presentado será analizada y los resultados serán publicados, utilizados como un informe y en conferencias en México y en el extranjero	☐	☐
) Entiendo que los datos no estarán disponibles para ninguna organización comercial y que es de uso exclusivo de los investigadores que realizan este estudio.	☐	☐
)		

INSTITUTO NACIONAL DE CANCEROLOGÍA
CON VALIDEZ
DEL 10 DIC 2020 AL 10 DIC 2021
COMITÉ DE ÉTICA EN INVESTIGACIÓN
COFEPRIS 12 CEI 09 014 11
CONBIOÉTICA-09CEI-002-20160413
(OHRP) FWA00019235
GESTIÓN 2019-2022

Doy mi consentimiento para que mi entrevista se grabe en audio y entiendo que las grabaciones se almacenarán de forma anónima, utilizando un software protegido con contraseña y se utilizarán para capacitación, control de calidad, auditoría y fines de investigación específicos.	☐	☐
') Entiendo que mi participación es voluntaria y que soy libre de retirarme en cualquier momento sin dar una razón. Entiendo que si decido retirarme del estudio, cualquier información personal que haya proporcionado hasta ese momento no se eliminará	☐	☐
9) Entiendo los riesgos potenciales de participar y el apoyo que estará disponible para mí en caso de tener una queja durante el curso de la investigación.	☐	☐
) Entiendo que no hay beneficios directos de participar.	☐	☐
10) Entiendo que no me beneficiaré financieramente de este estudio o de cualquier posible resultado que pueda tener en el futuro.	☐	☐
11) Entiendo que no se me compensará la parte del tiempo que pase en el estudio.	☐	☐
12) Por la presente confirmo que entiendo los criterios de inclusión que se detallan en la Hoja de información y que me explicó el investigador.	☐	☐
13) Por la presente confirmo que entiendo los criterios de exclusión que se detallan en la sección de información y que me explica el investigador; y que no estoy bajo los criterios de exclusión	☐	☐
14)		

INSTITUTO NACIONAL DE CANCEROLOGÍA
CON VALIDEZ
DEL AL
10 DIC 2020 10 DIC 2021
COMITÉ DE ÉTICA EN INVESTIGACIÓN
COFEPRIS 12 CEI 09 014 11
CONBIOÉTICA-09CEI-002-20160413
(OHRP) FWA00019235
GESTIÓN 2019-2022

Soy consciente de a quién debo contactar si deseo presentar una queja.	☐	☐
15) Estoy de acuerdo con que los datos que proporciono se archiven de manera segura durante el protocolo de investigación en Data Safe Haven y que éstos serán transferidos al extranjero.	☐	☐
16) Entiendo que otros investigadores tendrán acceso a mis datos pero que no podré ser identificado en los mismos	☐	☐
17) Acepto voluntariamente participar en este estudio.	☐	☐

INSTITUTO NACIONAL DE CANCEROLOGÍA
CON VALIDEZ
DEL 10 DIC 2020 AL 10 DIC 2021
COMITÉ DE ÉTICA EN INVESTIGACIÓN
COFEPRIS 12 CEI 09 014 11
CONBIOÉTICA-09CEI-002-20160413
(OHRP) FWA00019235
GESTIÓN 2019-2022

Firma del participante

18) Nombre del participante

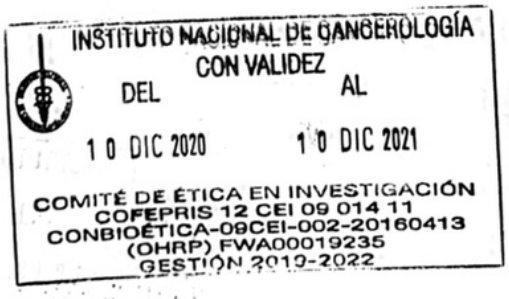
19) Correo electrónico

20) Dirección del participante

21) Teléfono del participante

22) Fecha de nacimiento del participante (día/mes/año)

23) Fecha de firma (dd-mm-aa)



Firma del testigo (1)

24) Nombre del testigo

25) Parentesco del participante

26) Dirección del testigo

27) Teléfono del testigo

28) Fecha de nacimiento del testigo (día/mes/año)

29) Fecha de firma (dd-mm-aa)

INSTITUTO NACIONAL DE CANCEROLOGÍA
CON VALIDEZ
DEL 10 DIC 2020 AL 10 DIC 2021
COMITÉ DE ÉTICA EN INVESTIGACIÓN
COFEPRIS 12 CEI 09 014 11
CONBIOÉTICA-09CEI-002-20160413
(OHRP) FWA00019235
GESTIÓN 2019-2022

Firma del testigo (2)

30) Nombre del testigo

31) Parentesco del participante

32) Dirección del testigo

33) Teléfono del testigo

34) Fecha de nacimiento del testigo (día/mes/año)

35) Fecha de firma (dd-mm-aa)

Dr. Oscar Arrieta Rodriguez
Nombre del investigador principal

FIRMA

Fecha de firma (dd-mm-aa)

INSTITUTO NACIONAL DE CANCEROLOGÍA
CON VALIDEZ
DEL AL
10 DIC 2020 10 DIC 2021
COMITÉ DE ÉTICA EN INVESTIGACIÓN
COFEPRIS 12 CEI 09 014 11
CONBIOÉTICA-09CEI-002-20160413
(OHRP) FWA00019235
GESTIÓN 2019-2022

A5: Data management plan, risk assessments and public liability insurance

Data Impact Assessment

UCL DATA IMPACT ASSESSMENT TEMPLATE FOR RESEARCH

Step 1 – DPIA team			
	Name	Job Title	Email Address (as contact point for future privacy concerns)
Principal Investigator owning DPIA	Hynek Pikhart	Professor	h.pikhart@ucl.ac.uk
Third Part(y/ies) assisting with DPIA (if any)			
Step 2 – Research summary			
Project Name	Lung cancer: barriers and delays in health care		
Department /entity	Epidemiology and Health Care, Dpt. Epidemiology and Public Health		
Date	August 6th 2019		
Step 3 – Identify the need for a DPIA			
Describe the purpose/aims of the research. In your description set out the benefits to: i. UCL ii. individuals iii. the wider public	To reduce delays in health-care among lung cancer patients through a patient navigation intervention that seeks the reduction of barriers and delays in cancer care. As result, this research will provide rigorous evidence on the effect of patient navigation models as early detection and treatment public health tools in the Mexican context. These results will help inform future public policies on the detection, diagnosis and treatment of lung cancer in Mexico.		
Please explain: - the role of personal data in the project; - the risks to privacy there are in your project (please list), and - why the processing of personal data is necessary and proportional for the purposes of your project.	Personal data such as hospital identification number, gender, ethnicity, education, socio-economic position and health-care affiliation will help differentiate the barriers and delays in health-care between different social groups. The identification and measurement of inequalities at this level is important to directly link barriers to delays. Interviews will also allow patients share their experience while navigating the health system. Moreover, this study also requires the collection of time-to-care individual data to be able to capture the effect of the intervention between the intervention and control group. Additionally the effect on patient satisfaction, quality of life, self-efficacy and health literacy will also be measured.		
Step 4 - Please describe the information flows. If this is described in another document, please attach it to this DPIA			
Information Flows: means the collection, retention, use, transfer and deletion – i.e. all types of data processing as part of the project's lifecycle - of personal data should be described here. 'Transfers' would include emails between the team members. If information is sent outside the EU/EEA, you should state that here. It would also be helpful to produce and refer to a flow diagram or another way of explaining data flows.	Data will be collected in Mexico and then accessed from Mexico or the UK. Hence, international access and transfer of data will be contingent on having the individual's explicit consent expressed in the consent form. Data will be processed lawfully, fairly and in a transparent manner and will not be further processed in a way that is incompatible with our research purposes. Data will be stored for the duration of the research project. The computers used to open the data will have anti-virus software. Data will be stored in the Data Safe Haven network. In case data breach data will be encrypted and anonymous. Data will be encrypted in email and attachments. For the qualitative data, such as transcribed interviews, a person's name is replaced with a pseudonym or with a tag that typifies the person. De-identifying quantitative data may involve removing or aggregating variables or reducing the precision the indirect identifiers. Direct identifiers will not be collected. Data transfers or sharing are allowed through UCL One drive contingent on prior de-identification and security of cloud storage.		

Data Impact Assessment

UCL DATA IMPACT ASSESSMENT TEMPLATE FOR RESEARCH

Step 5 – What steps or controls are you taking to minimise risks to privacy?

Please tick

a. Risks to individual privacy are minimal	✓	j. Special category personal data is not used	
b. Personal data is pseudonymised	✓	k. Randomisation	
c. Encryption of data at rest, i.e. when stored	✓	l. Participant opt out at any stage of the research	✓
d. Encryption used in transfers	✓		
e. Total number of participants is less than 50		m. Personal data kept in the EEA	
f. Information compliance training for staff has been completed - data protection, information security, FOI	✓	n. Research is not used to make decisions directly affecting individuals	✓
		o. De-identification	✓
g. Hashing or salting employed		p. Short retention limits	
h. Adherence to privacy by design principles	✓	q. Restricted access controls	✓
i. Probalistic risk management		r. Other (please specify)	

Step 6 – What steps have you taken to make sure the research is as accurate as possible and there are minimal unintended consequences? Please tick

a. data management plan in place	✓	d. this study builds on a pilot study	
b. data management plan is peer reviewed		e. an extension to a previous similar study registered by DPO, if there is, please provide the number	
c. PI experience levels - no experience;			
some experience;	✓		
very experienced			

Step 7 – How have you assessed what participants will think of the research? What have you done to address concerns raised? Please tick

a. pilot project	b. use of focus group	c. information sheet/consent form	d. experience drawn from previous study
		✓	✓

Step 8 – For the controls/steps specified in Step 5, who will make sure the controls are put in place? Please tick

a. PI	b. Head of School	c. other body (please specify)
✓		The hospital will hire 2 nurses to collect data on electronic health records (EHR). Despite data in EHR not being anonymous, data will be transcribed using hospital ID code.

Data management plan

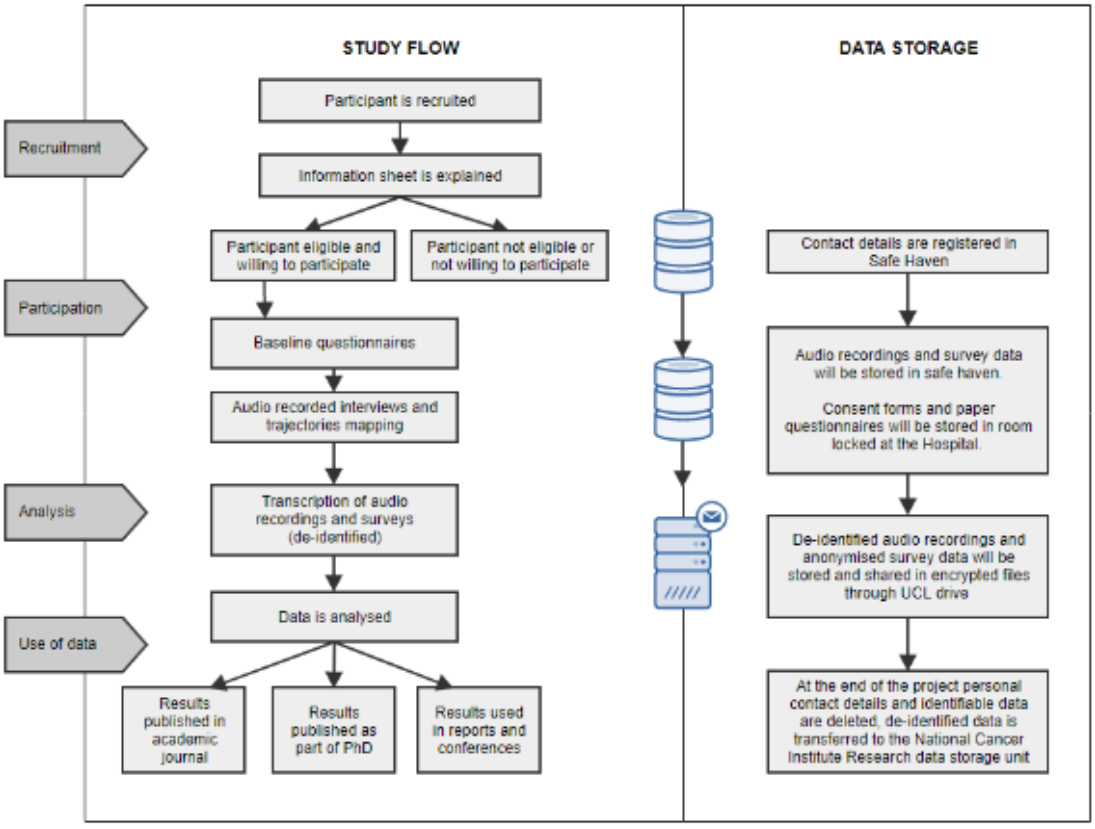
All data will be processed lawfully, fairly and in a transparent manner and will not be further processed in a way that is incompatible with our research purposes.

Primary data will be collected in Mexico and then accessed from Mexico or the UK. Data will be stored for the duration of the research project. The computers used to open the data will have anti-virus software. Data will be stored in the Data Safe Haven network. Data transfers or sharing are allowed through Data-Safe-Haven contingent on prior de-identification and authorisation from data administrator. No identifiable data will be sent back to Mexico.

In case of a data breach, data will be anonymous or pseudo-anonymous. For the qualitative data, such as transcribed interviews, a person's name is replaced with a pseudonym or with a tag that typifies the person and thus becomes anonymous. Although direct identifiers will not be collected, quantitative methodologies used in this protocol will require personal data to be included. Thus, de-identifying quantitative data may involve removing or aggregating variables or reducing the precision the indirect identifiers.

Moreover, secondary data will be transferred securely through Data Safe Haven. Data will have the individual's explicit consent expressed in the consent form to transfer data beyond the national boundaries. No identifiable data will be sent back to Mexico.

Figure 2.1: Primary data flow throughout the research protocol



Risk Assessment

Ref: RA031571/1 RA042706/1 & RA044169/1
Status: Authorised
Risk Level: B Tolerable

Risk Assessment

Summary

Reference: **RA031571/1** **Sign-off Status:** **Authorised**

Date Created:	11/11/2019	**Confidential?**	No
Assessment Title:	Risk assessment for field work to conduct mixed methods protocol in a middle income country.		
Assessment Outline:	Risk assessment for semi-structured interviews and questionnaires capturing clinical, administrative and patient reported outcomes in middle income countries. This risk assessment is made to comply with UCL's regulations and requirements for the registry of a NEW research protocol aiming to achieve ethical approval.		

Area Responsible (for management of risks)		**Location of Risks**	Off-Site
Division, School, Faculty, Institute:	Faculty of Pop Health Sciences	**Building:**	
Department:	Institute of Epidemiology & Health	**Area:**	
Group/Unit:	All Groups/Units	**Sub Area:**	

Further Location Information:	Study protocol is to be conducted in Mexico at the National Cancer Institute. Avenida San Fernando 22, Belisario Domínguez Secc 16, Tlalpan, 14080 Ciudad de México, CDMX, México
RISK_HE_FORMA_COUNTRYLABEL:	**RISK_HE_FORMA_COUNTRY_HEADER**
	UNITED KINGDOM

Assessment Start Date:	11/11/2019	**Review or End Date:**	11/11/2020

Relevant Attachments:

Description of attachments:

Location of non-electronic documents:

All documents will be electronic Paper-based documents in a secure drawer with the lung cancer clinic office.

Assessor(s):	BAUTISTA, ELYSSE PEASEY, ANNE PIKHART, HYNEK VINDROLA, CECILIA
Approver(s):	SYDONNIE HYMAN
Signed Off:	SYDONNIE HYMAN (19/11/2019 16:15)
Distribution List:	HYNEK PIKHART (h.pikhart@ucl.ac.uk) - 30/10/2019 Anne Peasey (a.peasey@ucl.ac.uk) - 11/11/2019 Cecilia Vindrola (c.vindrola@ucl.ac.uk) - 18/11/2019

PEOPLE AT RISK (from the Activities covered by this Risk Assessment)

CATEGORY
Post-Graduates

Risk Assessment

Reference: **RA031571/1** **Sign-off Status:** **Authorised**

1. Field work - environmental assessment	
Description of Activity:	This risk assessment applies to field work conducted in Mexico at the National Cancer Institute. Data collection methods will include: semi-structured interviews with patients, extracting data from electronic health records and interviewing stakeholders and health professionals.

These activities will involve conducting a mixed methods protocol by doctoral student EB. Data collection will be conducted from February to June 2020 (approximately).
 |

Hazard 1. Transportation security	
Injury during transportation to and from the national cancer institute. (Minor injury-unlikely)	**Existing Control Measures** Traveling to and rom the National Cancer Institute will be done so in recognized transportations systems (UBER or certified Taxis).

Hazard 2. Security (off-site)	
General researcher security: Mexico is flagged in the Foreign & Commonwealth Office. However, the risk of violence off site is minor as violence is within tolerable levels in Mexico City. Violence could include robbery, armed robbery or any other minor violence-related issues. (Minor injury-possible)	**Existing Control Measures** Check the foreign & Commonwealth Office (FCO) consulted to determine the current political situation and to determine whether it is safe to travel to location. Be familiarized with the areas in Mexico city that the researcher should not visit. (Researcher EB has lived in Mexico city before for over 10 years). Not wear jewelry when using public transportation. Not cary large electronic devices (laptop, printer, etc) with them when using the public transportation.

UCL

Risk Assessment

Hazard 3. Security (in-site)	
Security within the hospital: The researcher will be interviewing patients and due to the nature of their disease they might be express themselves in a violent manner. (Minor injury-possible)	**Existing Control Measures** Researchers are instructed to carry their National Cancer Institute ID card. There is a security guard at the hospital and people who do not carry a hospital ID are not able to enter. The researcher will inform the lung cancer team of the location and times of the interviews. The researcher will be assigned a room to conduct the interviews and will have access to internet and a phone line within the hospital. A second person will be asked to accompany the researcher during the interviews. Additionally, participants are trained in good interview techniques: covering suitable locations, awareness of delicate issues and the importance of body language. Immunisation advice should be sought and fulfilled if required. Travel/medical insurance cover note obtained from Mexican NHS for the period of activity.
Hazard 4. Fire (In and Off site)	
Fire is a minor risk for the doctoral researcher. Places of risk: accommodation and National Cancer Institute. (Minor injury-unlikely)	**Existing Control Measures** Evacuation plans understood and undertaken in fire or earthquake drills. Researcher has been provided with information and instruction on checking the escape routes and familiarization with the layout of the building.

Risk Level
With Existing Controls: Risk Level **B - Low / Tolerable**

Risk Assessment

Summary

Reference: **RA042706/1** **Sign-off Status:** **Authorised**

Date Created:	11/11/2020	**Confidential?**	No

Assessment Title:	Obtaining secondary data from hospital library
Assessment Outline:	The PhD student will obtain data from library at the cancer hospital in Mexico. This will take approximately 3 months and the student is expected to finish by february 1st 2021.

Area Responsible (for management of risks)		**Location of Risks**	Off-Site
Division, School, Faculty, Institute:	Faculty of Pop Health Sciences	**Building:**	
Department:	Institute of Epidemiology & Health	**Area:**	
Group/Unit:	Epidemiology & Public Health	**Sub Area:**	

Further Location Information:	Data obtaining will take place in a Mexican Cancer Hospital at the library building. This building is separate from the patients wards.Therefore there is no contact with patients.
Is this a GMM Class 1 Risk Assessment?:	MEXICO

Assessment Start Date:	11/11/2020	**Review or End Date:**	11/11/2021

Relevant Attachments:

Description of attachments:

Location of non-electronic documents:

hospital library

Assessor(s):	Bautista Gonzalez, ELYSSE
Approver(s):	SYDONNIE HYMAN
Signed Off:	SYDONNIE HYMAN (11/12/2020 09:16)
Distribution List:	Cecilia Vindrola (c.vindrola@ucl.ac.uk) - 11/11/2020 Anne Peasey (a.peasey@ucl.ac.uk) - 11/11/2020

PEOPLE AT RISK (from the Activities covered by this Risk Assessment)

CATEGORY
Post-Graduates

UCL

Risk Assessment

Reference: **RA042706/1** **Sign-off Status:** **Authorised**

1. Obtain secondary data from hospital library

Description of Activity:	Obtaining data from the hospital through a library-based computer.

Hazard 1. Infection transmission at work site

Members of the UCL community may contract COVID-19, as a result of contact with infected individuals and/or contaminated surfaces. In addition, you have the potential to transmit the virus yourself and pose a hazard to susceptible individuals you may encounter. Note that, as stated in Government guidance, the risk of infection increases the closer you are to another person with the virus and the amount of time you spend in close contact.	**Existing Control Measures** The PhD student will enter hospital facilities and avoid entering the building were cancer patients are being treated. There is a separate building were the library is based. This library only allows 3 people to be inside obtaining data. All hospital facilities, including the library are properly sanitized every day. In addition, people in the library are far away from each other and they are asked to use PPE and gloves during their time at the library. - Quarantine and Self-isolation recommendations remain. Staff and students are individually responsible for accepting their share of responsibility, including personal safety and checking work or travel advice - Those who are unwell with symptoms of COVID-19 must not travel to or attend the workplace. Anyone who develops symptoms of COVID-19 must be sent home and stay at home in line with National Healthcare guidance. If someone lives in a household where someone else is unwell with symptoms of COVID-19, then they must also stay at home in line with the National Healthcare guidance. - Be aware of the surfaces you or others touch and wash or sanitise your hands before and after a journey. - Wear a face covering (fabric covering your nose and mouth) - make changes to enable social distancing on pavements and cycle routes. - If you have to travel with people outside your household, try to share the transport with the same people each time and keep to small groups of people at any one time. - Consider seating arrangements to optimise distance between people in the vehicle. - Be aware of the surfaces you or others touch and wash or sanitise your hands before and after a journey.

Risk Level
With Existing Controls:

UCL

Risk Assessment

Risk Level	B - Low / Tolerable

2. Travel from house to hospital

Description of Activity:	Travel in a private car to the hospital (located 10 min away from the students house)

Hazard 1. Car accident

Minor injuries	**Existing Control Measures** The student holds car insurance. The streets are very small so it is unlikely that there will be an accident.

Risk Level

With Existing Controls:

Risk Level	A - Very Low / Trivial

Risk Assessment

Summary

Reference: **RA044169/1** **Sign-off Status:** **Authorised**

Date Created:	11/01/2021	**Confidential?**	No

Assessment Title:	General risk assessment to support OVERSEAS fieldwork
Assessment Outline:	Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered coronavirus, SARS-CoV-2. The virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes. Droplets fall on people in the vicinity and can be directly inhaled or picked up on the hands and transferred when someone touches their face. A risk assessment must be undertaken and approved before any fieldwork takes place in a non-UCL setting. This is to ensure the safety of staff and students. This risk assessment documents the principles adopted by UCL at an institutional level. Whilst considering a range of personal and activity profiles, it is necessarily general. THIS RISK ASSESSMENT APPLIES ONLY TO OVERSEAS FIELDWORKS (ACTIVITY/LOCATIONS OUTSIDE OF U.K.). It does not cover specific work activities which must have their own risk assessment. Departments must use and customise this risk assessment to document local variations, method statements and specific local arrangements. This risk assessment documents key risks to support a return to OVERSEAS fieldworks. Departments must use and complete a separate return to on site working at UCL risk assessment. This will help verify that appropriate risk control measures are in place. Departments should revise any existing risk assessments. Fieldwork risk assessments should to be revised and approved by line managers/supervisors to include suitable control measures for COVID-19 using this generic risk assessment for reference only. Note: 1. Due to current restrictions in place, it is highly encouraged to avoid any non-essential fieldwork. 2. Staff and students are individually responsible for accepting their share of responsibility, including personal safety. 3. Please check the current Government guidance whether any planned travel falls within one of the exemptions: - https://www.gov.uk/government/publications/higher-education-reopening-buildings-and-campuses/higher-education-reopening-buildings-and-campuses#travel-and-transport - https://www.gov.uk/guidance/travel-advice-novel-coronavirus 4. Review and update Fieldwork and any associated risk assessments. 5. Review if ongoing / planned work should be suspended or must continue. 6. Consider other risks that may be impacted as a result of the government and local changes. 7. If it is not possible to maintain a 2 metre distance in a specific environment or for a specific task, a risk assessment must be used to determine if it should take place / if the area should be closed. Record either in a new assessment or by reviewing your existing assessments. ANY SUCH RISK ASSESSMENT MUST BE SIGNED-OFF AS PER THE PROCESS IN BELOW POINT 8. 8. A Dean is responsible for approving the risk assessment of any fieldwork at a non-UCL setting led by a researcher or doctoral student in their faculty. The Dean may appoint one or more delegated authorities within the faculty to handle any requests for approval. A delegated authority could be a committee or Head of Department / Division Director. Existing local arrangements for approving risk assessments (especially for those requiring specialist knowledge of lower- and middle-income countries) should continue as before with final approval by the Dean (or the delegated authority). Anyone working in the field on the project (including any UCL staff or student) needs to acquaint themselves with the approved risk assessment. They must report any change in circumstances to the researcher or doctoral supervisor as appropriate. This assessment will be reviewed regularly and significant changes communicated to stakeholders.

Area Responsible (for management of risks)		**Location of Risks**	Off-Site
Division, School, Faculty, Institute:	Faculty of Pop Health Sciences	**Building:**	
Department:	Institute of Epidemiology & Health	**Area:**	
Group/Unit:	Epidemiology & Public Health	**Sub Area:**	

Further Location Information:	This risk assessment documents the principles adopted by UCL at an institutional level. Departments must use and customise this risk assessment to document local variations, method statements and specific local arrangements. Departments should revise any existing risk assessments. Where controls are mandatory ("must do"), these must not be relaxed locally. Note: Staff and students are individually responsible for accepting their share of responsibility, including personal safety.
Is this a GMM Class 1 Risk Assessment?:	UNITED KINGDOM

Assessment Start Date:	11/01/2021	**Review or End Date:**	11/07/2021

Relevant Attachments:

Description of attachments:

Location of non-electronic documents:

Working Safely During a Pandemic: https://www.ucl.ac.uk/safety-services/working-safely-during-pandemic Fieldwork: https://www.ucl.ac.uk/safety-services/policies/2020/sep/fieldwork Covid-19 individual health assessment tool for managers: https://www.ucl.ac.uk/human-resources/health-wellbeing/workplace-health/what-we-do/covid-19-individual-health-assessment-tool-managers Travel on UCL Business: https://www.ucl.ac.uk/finance/expenses-insurance/travel-ucl-business Foreign Travel Advice: https://www.gov.uk/foreign-travel-advice List of departments assigned by Lead Safety Advisor: https://www.ucl.ac.uk/safety-services/staff

Assessor(s):	Bautista Gonzalez, ELYSSE
Approver(s):	SYDONNIE HYMAN
Signed Off:	SYDONNIE HYMAN (29/01/2021 10:29)

PEOPLE AT RISK (from the Activities covered by this Risk Assessment)

CATEGORY
Post-Graduates

Risk Assessment

Reference: **RA044169/1** **Sign-off Status:** **Authorised**

1. Return to OVERSEAS fieldworks - to be adapted by each department.

Description of Activity:	Staff and students who travel to fieldwork or other outdoor working must follow the risk control measures as outlined in this assessment. There are 5 priority controls for all to follow: (1) If you are classed as vulnerable or extremely vulnerable (at increased risk of severe illness) - you must not travel at all and stay home. (2) Do not attend work if you think you may be unwell or if someone in your household is unwell. Keep in mind the symptoms of COVID-19 and adhere to government guidelines on self-isolation as appropriate. Symptoms include a new, continuous cough, high temperature and/or loss of taste or smell. (3) Strictly follow government guidelines on social distancing, hand washing and respiratory hygiene. (4) Where possible, reduce the number of people carrying out fieldwork and outdoor working. (5) Line managers/Supervisors must keep in contact with their teams and constantly review any work being conducted. Task specific protocols and risk assessments must be kept up to date, in response to new hazards or changes in risk level. Once a decision to undertake some site or field work has been taken and justified, a full risk assessment should be carried out. The risk assessment and management approach should demonstrate that the individual(s) can depart, arrive, work and return to base with negligible effect on themselves or on any third parties. This approach needs to address both risks to the health and safety of the individual(s) and anyone the individual(s) might foreseeably come into contact with, and also risks to the reputation of the practice and profession.

Hazard 1. Infection transmission when travelling to and from fieldwork or other outdoor working.

Members of the UCL community may contract COVID-19, as a result of contact with infected individuals and/or contaminated surfaces. In addition, you have the potential to transmit the virus yourself and pose a hazard to susceptible individuals you may encounter. Note that, as stated in Government guidance, the risk of infection increases the closer you are to another person with the virus and the amount of time you spend in close contact.	**Existing Control Measures** PRIMARY CONTROLS: - Stay at home (only where it is not possible to meet the objectives of the fieldwork) - staff/students should work from home unless it is not possible to do so. This includes continuation of remote teaching and assessment. - Where possible, any/all interviews must be carries out virtually. - Where possible, any/all samples must be sent to UCL locations rather to avoid any travelling. - A risk-based approach will be taken to UCL staff and students, with an individual health assessment tool available. This tool recognises clinically vulnerable and extremely vulnerable groups. It also recognise those caring for vulnerable and extremely vulnerable people. - Quarantine and Self-isolation recommendations remain. Staff and students are individually responsible for accepting their share of responsibility, including personal safety and checking work or travel advice both national and international. - Those who are unwell with symptoms of COVID-19 must not travel to or attend the workplace. Anyone who develops symptoms of COVID-19 must be sent home and stay at home in line with National Healthcare guidance (for example NHS in UK). If someone lives in a household where someone else is unwell with symptoms of COVID-19, then they must also stay at home in line with

UCL
Risk Assessment

	the National Healthcare guidance (for example NHS in UK). - Line managers/Supervisors must ensure individual staff and students who need to travel are authorised, competent and where necessary, qualified. - Staff and students are encouraged to avoid overnight stays and complete all fieldwork in one day trip where possible. - Where overnight stay is required such arrangements (including accommodation) must meet social distancing guidelines. - For short field trips, staff and students are encouraged to walk, cycle or use cars/taxis to travel to and from fieldworks. Avoid using public transport wherever possible. - Line managers/Supervisors must review start and end times as people return. If staff will use public transport, consideration must be given to avoidance of peak times and known busy periods wherever possible. An individual member of staff may still chose a busier period because of individual circumstances, but the impact of this should be discussed. - Where possible, Fieldwork group should travel as a social-bubble to minimize the number of external interactions. When travelling, following steps should be considered: - Follow any/all local rules and government guidelines. - Walk or cycle. - Plan ahead and use a direct route - Depending upon location/activities, travel at 'off peak' times. - Take hand sanitiser and a face covering - Wash or sanitise your hands before beginning your journey - and when you arrive - Try to maintain social distancing, for example when approaching or passing other pedestrians or waiting at crossings and traffic lights. - Use a face covering when you will be close to others. Only use public transport if you have to. If you must use public transport, take the following additional precautions: - Check with your provider for the latest travel advice before you leave. - Plan ahead and use a direct route. - Depending upon location/activities, travel at 'off peak' times. - Take hand sanitiser and a face covering. - Wash or sanitise your hands before beginning your journey - and when you arrive. - Try to maintain social distancing, for example when approaching or passing other people, waiting on platforms or at stops. - Use a face covering when you will be close to others. - If you can't stay away from people (e.g. when boarding or alighting, on busier services, at busier times of day) try to face away from other people, and keep the time you spend near others as short as possible. - Be aware of the surfaces you touch. Be careful not to touch your face. - Use contactless payment where possible. - Always follow instructions from transport and regulatory authorities. If using private vehicles to travel, take the following steps:

Risk Assessment

	- If you normally share a vehicle with people from other households, you should find a different way to travel if possible. - Plan your route, including any breaks, before setting out. Routes may be different as local areas make changes to enable social distancing on pavements and cycle routes. - If you have to travel with people outside your household, try to share the transport with the same people each time and keep to small groups of people at any one time. Consider seating arrangements to optimise distance between people in the vehicle. - Be aware of the surfaces you or others touch and wash or sanitise your hands before and after a journey. - If sharing the journey, wear a face covering (fabric covering your nose and mouth) inside the car.
Hazard 2. Stress and poor mental health.	
UCL staff and students may experience mental health problems caused by unfamiliar working conditions or anxiety over infection. Stress may increase vulnerability to infection, because of lowered immune response.	**Existing Control Measures** - Line managers/Supervisors are asked to actively support their staff. Staff and students are encouraged to contact their line manager and supervisor if they have concerns. - Line managers/Supervisors must ensure provision of adequate and competent on-site support, instruction, information, training (where applicable) and supervision. - All on-site activities must be supervised by a competent person at all times – check/discuss specific details with your Head of Department/ Dean of Faculty. - For staff; Care First can be contacted 24/7 for confidential, impartial support. Call for free on 0800 197 4510. - For students; support is provided by Student Psychological and Counselling Services (SPCS) during 'office hours'. Care First can be contacted outside office hours (5pm to 9am) by calling for free on 0800 197 4510. - Care First also offer support through a one-to-one online messaging service, in which you can speak to a counsellor in real time. - Where appropriate, adjustments to working times or hours should be made, to account for staff or students experiencing poor mental health. If confidential advice and assessment would be helpful, please contact Workplace Health using the management referral process. - A wide range of other resources and guidance is available via the 'Remote not distant' website, Student Support and Wellbeing website and UCL Health and Wellbeing website. - In addition, UCL Parents and Carers Together (PACT) network has a MS Teams site to support colleagues with caring responsibilities.

UCL

Risk Assessment

Hazard 3. Emergency response.	
It may not be possible to maintain social distancing and other COVID-19 related risk control measures during an emergency.	**Existing Control Measures** - Line managers/Supervisors must ensure that details of the Fieldtrip Fire Safety and Emergency Safety Plan, and relevant contact numbers are included in the risk assessment. - All field trips must have designated first aider(s) who is responsible for the first aid provision. - In emergencies such as supporting a seriously injured colleague or responding to a chemical spill, people do not have to stay 2 metres apart if it would be unsafe to do so. - If you need to provide assistance to others, you must pay particular attention to sanitation measures immediately afterwards including washing hands. - All staff/students must remain aware of the local emergency numbers. - All returning staff must have completed the Basic Fire Safety eLearning course and use fire safety form TN086 to ensure familiarisation with emergency escape routes. - In the event of a fire alarm sounding, all people must evacuate as normal. Wherever possible, observe 2 metre social distancing whilst evacuating. This is particularly important on stairs, at final exits and moving to the fire assembly point or muster point. - Use every fire escape route to reduce congestion and bunching on stairs and exits. - If there is a conflict between social distancing and rapid evacuation, focus on getting out quickly as the priority. - Once outside move to assemble by the Fire Assembly Points or muster points, observing social distancing. - When given the 'all clear' to return to work areas, make sure to re-enter by staggering the return. - When re-entering a building (e.g. porta-cabin), wash or sanitise your hands. Even after checking with foreign office, there must be emergency plans that include: - How to quarantine the group upon return. - Getting the group back safely if the flight is grounded. - Find suitable accommodation at the fieldwork location if the group is told to self-isolate by the local authorities.
Hazard 4. Generic Return to fieldworks - applies to all people	
It is strongly recommended that members consider thoroughly if alternative methods of working would allow progress with the project to be made at a lower risk. This could for example be subcontracting some of the work to a more locally-based contractor or consultant (obviating travel), using Internet-based information as far as possible to minimise time required on site, and agreeing to postpone as much site and field work with clients as possible. These will all reduce the scale of operation requiring novel risk management.	**Existing Control Measures** General - Each site and work operation will generate its own risk profile and should be considered as an individual case; risk assessments should not be copied across instances. Thorough preparation ahead is required. - The current Government (national and local) and Regulatory bodies' guidance/ recommendations for outdoor working must be followed. This is rapidly evolving and is found in different places. - If applicable, the guidance issued to other professionals and contractors should be referred to as necessary and certainly if different practitioners will be working together. - Consideration needs to be given on how equipment and PPE will be cleaned or disposed of safely and how safe re-entry to the site area, office workspace (e.g. porta cabin) will be handled.

UCL
Risk Assessment

PPE & Hygiene
- Employees should be provided with appropriate PPE including hand sanitisers and gloves (and possibly face coverings/masks) as indicated by government guidance.
- Having strong measures in place to promote good hygiene is paramount. It is widely accepted that all staff and students should wash their hands with soap and water for 20 seconds or more and more frequently than normal.
- Review the provisions for access to adequate water supply.
- Allow frequent breaks to attend to hygiene requirements.
- The capacity to sanitise site and countryside furniture (e.g. gates/stiles) and equipment (especially where laid down for other workers to pick up) may be necessary before and after use.

Travel and Accommodation

Travel
- Public transport should be avoided where possible.
- Vehicles used must be in a good state of repair and maintenance.
- Where possible, Fieldwork group should travel as a social-bubble to minimize the number of external interactions. If this involves hire cars these should be intensively cleaned before and after use.
- If applicable, staff should travel equipped with shareable copies of written authorisations which clearly justify the need for the travel and the work being undertaken. Where relevant these should include information from the client which explains the commission being undertaken. The authorisation will need to detail the work site and the company/contractor involved and be specific to the individual and the work location.

Accommodation
- Staff and students travelling on fieldtrips must stay in accommodation which is accessible to them, appropriate and safe.
- Third party accommodation providers, such as Airbnb, are encouraged not be used, as properties are unknown and unchecked which poses a potential risk to staff and students health and safety.
- Staff and students may wish to stay in home from home type accommodation rather than hotels when away on longer trips must refer to UCL's approved Travel Management Company.

On-site or In-field
- Staff may need to travel equipped with signage which explains the work being undertaken to the public.
- Review local and national rules for social-bubble, two weeks self-isolation and 2metres.
- On site staff must maintain the specified social distance from other staff and members of the public at all times (typically 2m but may be different in different countries). Where this distance absolutely cannot be secured then other relevant government guidance should be followed (e.g. staff should work side by side, or facing away from each other, rather than face to-face).
- Consideration should be given as to how any disturbance/interruption from local community will be dealt with.
- If workers have to share enclosed spaces, they should keep the window open for ventilation and

wash hands on leaving.
- Staff will need to be equipped for the work and with spare equipment. This includes items such as food and water.
- Additional investment in equipment which can capture site data rapidly and comprehensively and hygienically for viewing offsite may be appropriate.

UCL Insurance
- UCL has a Business Travel Insurance policy that will insure UCL employees, students, and persons assisting UCL with its business who are normally resident in the UK. When travelling on UCL business you'll need to register your trip. Please refer to Travel on UCL Business webpage for further information: https://www.ucl.ac.uk/finance/expenses-insurance/travel-ucl-business
- UCL personnel are covered, subject to financial limits, for Personal Accident, Medical Expenses (this includes COVID), Personal property, Money, Kidnap and Ransom, Personal Liability/Legal Expenses"
- UCL costs of travel aren't. Any booked flights and hotels that need to be cancelled while the FCO guidance remains "against all but essential travel", are not covered under the insurance policy. Do assess whether the travel could be delayed until the FCO guidance is relaxed.
- UCL insurer will require assurance that all government advice and guidelines are being followed, hence it is vital to complete specific risk assessments, and both the FCO's guidance and the national or regional guidance must be followed. This should include considering the availability and standard of medical assistance available to travels in the destination country, and the ability to repatriate travels.

Note - UCL does not have any cover in force for Afghanistan, Colombia, Iraq, Mexico, Nigeria, Pakistan, Philippines, Somalia, Venezuela or Yemen. This should be flagged to RSA via the UCL insurance team.

UCL Insurance
If an individual is resident in an overseas country, they may not be covered by UCL travel insurance. This should be checked on a case by case basis with the UCL insurance team. For staff resident in, or on long term secondment, current overseas policy is:
- All UCL staff and students are covered under UCL's Personal Injury insurance when working on UCL business.
- This policy applies to staff and students' resident overseas, or seconded (defined as staff who are contracted to work overseas for a period over 12 months).
- Where overseas resident and seconded individual are required to travel as part of their role (either in-country of internationally), additional travel insurance should be requested here https://www.ucl.ac.uk/staff/task/arrange-travel-insurance, this also allows the secondee to have a health insurance policy in place for GP and pre-existing medical treatment.
- UCL insurer will require assurance that all government advice and guidelines are being followed, hence it is vital to complete specific risk assessments, and both the FCO's guidance and the national or regional guidance must be followed.
- Where staff are resident in the country, and are not a secondee, then they are responsible for their own medical and insurance cover when not on UCL business.

Note - UCL does not have any cover in force for Mexico. This should be flagged to RSA via the UCL insurance team.

Risk Assessment

Risk Level
With Existing Controls:
Risk Level **C - Medium / Moderate**

2. Vulnerable groups.	
Description of Activity:	There may be heightened risks faced by individuals from exposure to COVID 19 in community settings or the workplace. This includes people more at risk due to their ethnicity, age, disability or status as new or expectant mothers.

Risk Assessment

Hazard 1. Heightened risk to vulnerable groups.

- Emerging evidence suggests there are three key characteristics that can affect vulnerability. These are Age, Gender and Ethnicity. Older people, men, and people from BAME communities seem to be at greater risk from COVID-19.
- Those with underlying health conditions may also be particularly vulnerable.
- Disabled people may face additional challenges returning to UCL. Some disabled staff members may have a weak immune system, leaving them more vulnerable to getting an infection. There may be issues associated with access to hand washing facilities, application of protective equipment and those with a mental health condition may feel increased levels of anxiety and stress.
- Pregnant individuals, particularly those in their 3rd trimester may be at higher risk from COVID-19. Those returning from maternity leave must also be considered.

Existing Control Measures

- All staff and students are encouraged to regularly follow Government guidance (national and local).

- Clinically Extremely Vulnerable must stay at home in line with current Government guidance.
- All staff and students are encouraged to speak to their line managers/supervisors/personal tutors for any concerns.

- UCL is taking a risk-based approach to UCL staff and students who may be ask to return to working in UCL buildings. An individual health assessment tool must be used by line managers.
- Refer to Workplace Health if there is doubt as to the relevant risk factors that may apply to you. Workplace Health can also support in instances where an individual and their manager may disagree on an individual assessment.

- All staff and students are encouraged to disclose in confidence any health condition that might compromise their health to their line manager, Workplace Health or Student Support and Wellbeing. This will help ensure you are protected.
- However, individuals should not feel they must disclose underlying health conditions if they do not wish to do so.

- Line managers/supervisors/personal tutors must have sensitive and comprehensive conversations with their staff who may be vulnerable or at higher risk. They should identify any existing underlying health conditions that may increase the risks for people in undertaking their roles, in any capacity. Most importantly, the conversations must also consider the feelings of colleagues, particularly with regard to their mental health.
- Line managers/supervisors must listen carefully to staff concerns and provide support. Also consider adjustments for staff. This may include moving to a lower-risk work area, undertaking lower risk tasks, limiting exposure (for example through reducing working times) and working from home.

- If vulnerable staff are to continue working from home, line managers/supervisors should ensure the quality of work required does not disadvantage these colleagues, in terms of appraisals, or the prospect of future promotion.
- Support is available for line managers and staff through Workplace Health. Students should contact Student Support and Wellbeing.
- All members of the UCL community can access support through Care First.

Risk Level

With Existing Controls:

Risk Assessment

Risk Level	B - Low / Tolerable

3. Fieldsites entrances, exits, circulation spaces, on-site accommodation, shared and welfare areas - applies to all people.	
Description of Activity:	Staff and students who travel to fieldwork or other outdoor working must follow the risk control measures as outlined in this assessment.

Risk Assessment

Hazard 1. Infection transmission in the workplace.	
Members of the UCL community may contract COVID-19, when there is more than one person working within a department / area at the same time (including contractors and staff from other organisations). Note that, as stated in Government guidance, the risk of infection increases the closer you are to another person with the virus and the amount of time you spend in close contact.	**Existing Control Measures** Follow controls as described in activity 1 above, in addition to those below. Follow controls as described in activity 1 above, in addition to those below. - Create a social-bubble and self-isolate before going to field trips. - Minimise contact with people outside of the social-bubble or fieldwork group. - Follow good infection control principles – see GOOD HABITS below. INFORMATION AND TRAINING: - Clear Information/guidance on working arrangements and control measures is available and communicated, via the UCL Coronavirus website. - The control measures and new ways of working must be communicated to all staff and students before returning to their workplace, or within their first day back. GOOD HABITS - Everyone must practice good hand hygiene. This means washing hands with soap and water regularly for at least 20 seconds. Hand sanitiser should be used where hand washing is not convenient. - Hands should be washed or sanitised after entering a site or moving between site areas, before and after eating and drinking, after using communal facilities, after touching high contact surfaces such as door handles and when arriving home. - Everyone should protect their skin by applying hand moisturising cream regularly, after hand washing. - Paper towels will be provided in place of air dryers where possible. Paper towels can be more effective than air dryers for removing microbes when still-contaminated hands are dried. - Everyone must practice good respiratory hygiene. This means catching coughs and sneezes in tissues (catch it, bin it, kill it). - Tissues will be provided at welcome stations. - Everyone must avoid touching their face without washing hands first. No-one should shake hands. - All shared areas must be kept clear of personal items to prevent transmission by contaminated items. Use lockers or your dedicated workspace to store personal items. Shared hooks or coat stands should not be used. PRECAUTIONARY EQUIPMENT - All staff, students and visitors are expected to wear face coverings when moving around site areas, and maintain 2 metres social distancing. - Adhere to UCL Face covering policy regardless of location.

Risk Level

Risk Assessment

With Existing Controls:

Risk Level **C - Medium / Moderate**

Public liability insurance

ZURICH
MUNICIPAL

To Whom It May Concern

Our ref: KM/IND 24 May, 2019

Zurich Municipal Customer: **University College London and Subsidiary Companies**

Zurich Municipal
Zurich House
1 Gladiator Way
Farnborough
Hampshire
GU14 6GB

Telephone: 0800 335500
E-mail:
claire.cripps@uk.zurich.com

This is to confirm that University College London and Subsidiary Companies has in force with this Company until the policy expiry on 31 July 2020 Insurance incorporating the following essential features:

Policy Number: **NHE-01CA06-0023**

Limit of Indemnity:		
Public Liability:	£ 50,000,000	any one event
Products Liability:	£ 50,000,000	for all claims in the aggregate during any one period of insurance
Pollution:		
Employers' Liability:	£ 50,000,000	any one event inclusive of costs

Excess:	
Public Liability/Products Liability/Pollution:	£ 250 any one event
Employers' Liability:	Nil any one claim

Indemnity to Principals:
Covers include a standard Indemnity to Principals Clause in respect of contractual obligations.

Full Policy:
The policy documents should be referred to for details of full cover.

Yours faithfully

[redacted]

Underwriting Services
Zurich Municipal

ZURICH MUNICIPAL

To Whom It May Concern

Our ref: NK/IND 17 May, 2020

Zurich Municipal Customer: **University College London and Subsidiary Companies**

This is to confirm that University College London and Subsidiary Companies has in force with this Company until the policy expiry on 31 July 2021 Insurance incorporating the following essential features:

Policy Number:	**NHE-01CA06-0023**	
Limit of Indemnity:		
Public Liability:	£50,000,000	any one event
Products Liability:	£50,000,000	for all claims in the aggregate during any one period of insurance
Pollution:		
Employers' Liability:	£50,000,000	any one event inclusive of costs

Excess:

Public Liability/Products Liability/Pollution:	£250 any one event
Employers' Liability:	Nil any one claim

Indemnity to Principals:
Covers include a standard Indemnity to Principals Clause in respect of contractual obligations.

Full Policy:
The policy documents should be referred to for details of full cover.

Yours faithfully

[redacted]

Underwriting Services
Zurich Municipal

Zurich Municipal
Zurich House
1 Gladiator Way
Farnborough
Hampshire
GU14 6GB

Telephone: 0800 335500
E-mail: claire.cripps@uk.zurich.com

A6: Systematic review data extraction forms

Systematic review data extraction sheet

Systematic review tool for article selection

Study ID	_____
ID Number	_____
Is this a systematic review or meta-analysis?	◯ Yes ◯ No
Is the main focus of the article about cancer?	◯ Yes ◯ No

The MAIN objective of the paper was around:

	Yes	No
Theory (non-interventional)	◯	◯
Design	◯	◯
Evaluation methodology	◯	◯
Results	◯	◯
Educational resources	◯	◯
Patient-navigator relationship	◯	◯
Types of navigator	◯	◯
Cost-effectiveness	◯	◯

Is there another objective of this paper?	_____
What is the main focus of the navigation model?	☐ Navigating patients: cancer screening ☐ Navigating patients: cancer diagnosis ☐ Navigating patients: cancer treatment ☐ Navigating patients: cancer palliative-care ☐ Navigating patients: cancer rehabilitation ☐ Navigating patients: other ☐ NA
Which organisations were involved in the navigation of cancer patients?	☐ Ministry of health (specialized hospitals) ☐ Ministry of health (primary health-care clinics) ☐ Private hospitals or insurance companies ☐ Non-governmental organisations
What study population is it focused on?	◯ Ethnic minorities ◯ Minorities (without a particular ethnicity) ◯ Patients at risk of a disease ◯ General population ◯ Not mentioned

Please mark if the study focuses on any of these population groups	☐ Pediatric patients with cancer ☐ People with mental or psychiatric illness with cancer ☐ People with disabilities and cancer ☐ People who are or have been in prison with cancer ☐ Multi-morbidity patients (i.e. cancer and other diseases) ☐ People who want to quit smoking and with cancer
How many people were involved in the intervention group?	_____
Is a power calculation considered?	◯ Yes ◯ No ◯ Cant tell
Describe the type of navigator?	☐ Peer to peer navigator ☐ lay person navigator ☐ health-professional ☐ social worker ☐ other ☐ not specified
What kind of activities did the patient navigation model hold?	☐ Clinical activities ☐ Emotional Support (focus groups, mental health services, support groups, etc) ☐ Legal support ☐ Administrative and logistical support (i.e schedule appointments, linkage with external resources) ☐ Patient education and empowerment (i.e. Q&As, informative sessions, videos, etc) ☐ Referrals (inter or intra institutional referrals) ☐ Lobbying (i.e. for treatment and resource allocation) ☐ Infrastructure navigation (i.e. navigating the hospital infrastructure itself) ☐ Research ☐ Others ☐ Not specified
What kind of other activities?	_____
What kind of referral is it?	☐ Primary health-care clinic to specialized hospital ☐ NGO to specialized hospital ☐ Inter-hospital referrals ☐ Intra-hospital referrals
Is this an RCT?	◯ No ◯ Yes
What kind of study is it?	_____

What kind of clinical outcomes were studied?	☐ Clinical (i.e. timeliness of care, adherence, survival, mortality,) ☐ Non-clinical (i.e. patient satisfaction, quality of life). ☐ Administrative (cost-effective etc)
Describe the main outcome measurement:	_____
Describe the periodicity of measurement of the primary outcome:	_____
Please describe the secondary outcome	_____
Describe the periodicity of measurement of the secondary outcomes:	_____
How large was the treatment effect? (Include C.I. and measurement of effect)	_____

Critical Appraisal of RCTs

	Yes	No	Can't tell
Trial addresses the issue?	○	○	○
Randomisation of treatment and control	○	○	○
All patients in trial are properly accounted for at the end	○	○	○
Blinding methods	○	○	○
Participants similar at the start of trial	○	○	○
Participants treated equally (aside from intervention)	○	○	○
Measure of effect is mentioned	○	○	○
Results are relevant	○	○	○
Are the benefits worth the harms and costs	○	○	○

Methods for randomisation	☐ Simple randomisation ☐ Quasi-randomisation ☐ Computer generated random number
What type of blinding was used?	○ Single blinding ○ double blinding ○ triple blinding ○ No blinding
Was there use of technology during the intervention?	○ Yes ○ No

A7: Electronic health records data extraction forms

EHR Socio-demographic data Extraction sheet

Record ID	_____ (hospital identification number)
Birth date	_____
Gender	◯ Female ◯ Male
Was your first language spanish?	◯ Yes ◯ No
What is your first language?	_____
State of residence	◯ Aguascalientes ◯ Baja California ◯ Baja California Sur ◯ Campeche ◯ Chiapas ◯ Chihuahua ◯ Ciudad de México ◯ Coahuila ◯ Colima ◯ Durango ◯ Estado de México ◯ Guanajuato ◯ Guerrero ◯ Hidalgo ◯ Jalisco ◯ Michoacán ◯ Morelos ◯ Nayarit ◯ Nuevo León ◯ Oaxaca ◯ Puebla ◯ Querétaro ◯ Quintana Roo ◯ San Luis Potosí ◯ Sinaloa ◯ Sonora ◯ Tabasco ◯ Tamaulipas ◯ Tlaxcala ◯ Veracruz ◯ Yucatán ◯ Zacatecas
Type of residence:	◯ Urban ◯ Rural

Level of education	◯ Primaria ◯ Secundaria ◯ Preparatoria/Bachillerato ◯ Universidad ◯ Maestria/Doctorado
Marital status	◯ Single ◯ Married ◯ Widowed
What is the socio-economic position assigned by the INCAN?	_____
Laboral status	◯ Employed ◯ Self-employed ◯ Not employed

EHR Clinical data Extraction Sheet

Record ID

_____
(hospital identification number)

Lung cancer stage

_____

Histological type of cancer

_____

Risk factors associated to lung cancer

	Yes	No
History of smoking	○	○
Exposure to asbetos	○	○
Exposure to wood combustion	○	○

Smoking index

_____

EHR Date Extraction sheet

Record ID

_____
(hospital identification number)

When did the patient get to the INCAN?

_____
(dd-mm-yyyy)

When did the patient get the pathology results?

_____
(dd-mm-yyyy)

When did the patient get the genetic results?

_____
(dd-mm-yyyy)

When did the patient start treatment?

_____
(dd-mm-yyyy)

What is the date of this last visit?

_____
(dd-mm-yyyy)

Has the patient died?

◯ Yes
◯ No

When did the patient die?

_____
(dd-mm-yyyy)

A8: Interview data extraction forms

Date in which you first noticed your symptoms	_____ (dd-mm-yyyy)
Date in which the you decided when to seek for medical advice?	_____ (dd-mm-yyyy)
Date of the first interaction with a medical unit	_____ (dd-mm-yyyy)
Please indicate the transportation methods you used to get to all the places you selected above	☐ Car ☐ Metro ☐ Combi ☐ Bus ☐ Taxi ☐ Uber ☐ Walking
How many referrals did you go through before being sent to the INCAN?	_____
How many hospitals did you visit before coming to the INCAN?	_____
Did you get any other diagnosis before you were told you had cancer?	◯ Yes ◯ No

Record ID	_____ (hospital identification number)
When did you initially identify that you had a problem with your lungs?	_____ (dd-mm-yyyy)
How did you realise that you had a problem in your lungs?	◯ Symptoms ◯ Routine health check ◯ Lung cancer screening program
What was the first symptom you noticed?	◯ Hemoptysis ◯ Chest pain ◯ Dyspnea ◯ Cough ◯ Loss of appetite ◯ Weight-loss
When you first noticed your symptom, how serious did you think it was?	◯ Not serious at all ◯ Somewhat serious ◯ Moderately serious ◯ Serious ◯ Very serious ◯ Doesn't answer
How worried did you become over this symptom back then?	◯ Not worried at all ◯ A little worried ◯ Somewhat worried ◯ Very worried ◯ Doesn't answer
When you first noticed this symptom did you think it could be related to cancer?	◯ Yes ◯ No ◯ Doesn't answer
I'm going to read some of the following symptoms and I want you to tell me if you've experienced them	☐ Chest pain ☐ Shoulder pain ☐ Cough ☐ Cough with blood ☐ Tiredness ☐ Weight loss ☐ Loss of appetite
Which one of the aforementioned symptoms were you worried about the most?	◯ Chest pain ◯ Shoulder pain ◯ Cough ◯ Cough with blood ◯ Tiredness ◯ Weight loss ◯ Loss of appetite

What made you decide to look for medical attention?	◯ That the symptoms mentioned before could reappear ◯ That the symptoms mentioned before could worsen ◯ That the symptoms mentioned before could interfere with your usual activities ◯ Family advice or social network ◯ Something else* ◯ Doesn't answer
What other things?	_____
How long did you feel was the time that passed between the time you got your first symptom (for the first time) to the time you first went to the doctor?	◯ Immediately ◯ Soon, but not immediately ◯ Took a while ◯ Took a long time ◯ Doesn't answer
How long did you feel was the time from the first medical consultation to the time you got to the INCAN?	◯ Very little time ◯ Little time ◯ Regular ◯ A long time ◯ Doesn't answer

Why didn't you seek for medical attention sooner?

	Yes	No
I thought the problem was going to disappear	◯	◯
I thought I didn't have any health insurance that would cover me	◯	◯
I didn't have money to use the health system	◯	◯
Because I didn't want to stop working	◯	◯
Because I have to take care of a family member (kids, elderly or other)	◯	◯
Because I was lazy	◯	◯
Because I was afraid	◯	◯
Because I didn't want to be examined	◯	◯
For another reason* (describe)	◯	◯

What reason? _____

Which of these reasons didn't allow you to get there sooner?

	Yes	No
I didn't have the information on which services I could have access to	○	○
I didn't have money to pay for the medical consultation or the diagnostic studies	○	○
The scheduling of the appointments did not match my needs	○	○
That initially a wrong diagnosis was made	○	○
That I couldn't leave my job to come to get care	○	○
That I was afraid	○	○
That I had to take care of a family member, elderly or sick person	○	○
Something else*	○	○

What else?

_____

Please indicate ALL the actors you have encountered before being admitted to the INCAN

- ☐ Health clinic (A)
- ☐ National Institute (B)
- ☐ Other public third level hospital (C)
- ☐ Other private hospital (D)
- ☐ Pharmacy (E)
- ☐ Private laboratory (F)
- ☐ Primary health-care clinic (G)
- ☐ IMSS (I)
- ☐ ISSSTE (J)
- ☐ Other*

What other health institution?

_____

Please order the actors you selected in a sequential order. (The actors can repeat themselves and not all actors have to be included if not visited i.e. A-> E->E->B)

_____

Date in which the 1st services were used

_____
(dd-mm-yyyy)

Whit the first health professional you encountered, what did he/she say about your lungs?

- ○ Benign tumor
- ○ Suspicious tumor
- ○ Malign tumor
- ○ Other*

What did they say?

_____

What studies were first asked by your first general practicioner?

◯ Biopsy
◯ Tomography
◯ X-ray
◯ Sputum cytology
◯ None of the above

Was an anti-inflammatory or antibiotic prescribed during your first consultation?

◯ Yes
◯ No

Have you had a bronchoscopy?

◯ Yes
◯ No

Who sent you here?

◯ Primary health care
◯ Health clinic
◯ General hospital
◯ National Institute
◯ Private medical services
◯ Pharmacy
◯ IMSS
◯ ISSSTE
◯ Other*

Specify the other:

_____

Why did you come here?

◯ Through my own initiative
◯ Through the advice of a friend or family member

Have you used any alternative methods to medicine or a remedy to alleviate any of your symptoms?

◯ Yes
◯ No

Have you had to stop doing any of the following activities?

	Yes	No
Home work	◯	◯
Taking care of children or grandchildren	◯	◯
Work	◯	◯
Activities outside the house	◯	◯
Personal favourite activity	◯	◯

Has someone helped you continue with these activities now that you've been ill?

◯ Yes
◯ No

Who helps you with these activities now?

_____
(Relationship)

Who is the person you spoke to first about your illness?

_____
(Relationship)

How much time went by between the time you first noted symptoms to the time to spoke about them?	_____ (mm or dd)
Did someone recommend you to get medical attention for your symptoms?	◯ Yes ◯ No
If so who? and what is their relationship to you?	_____ (Up to three people, please just state the relationship, divided by commas)
Until now the payments for your medical consultations and treatment	◯ Have been payed by me ◯ Have been payed by me and someone ◯ Has been payed by someone else
In total, how much have you spent to pay for consultations, medicines or other until now?	_____ (In mexican pesos. If not answered mark doesn't know)
Who has helped you pay your treatment or medical consultations	◯ Husband or wife ◯ Other family member ◯ Non-for-profit (NGO) ◯ Children ◯ Nobody
Who will be available to come with you to the medical consultations?	☐ Husband or wife ☐ Children ☐ Parent(s) ☐ Friend(s) ☐ Work colleagues ☐ Other community groups ☐ Nobody

Guía temática (entrevista estructurada)

Número identificador de paciente (número de expediente)	_____ (Número de identificación)
Por favor declare el ECOG del paciente durante la entrevista	○ 0 ○ 1 ○ 2 ○ 3 ○ 4
Fecha de nacimiento	_____ ((dd/mm/aa))
Número de teléfono del paciente	_____ ((número de casa o celular))
Sexo	○ Mujer ○ Hombre
¿El español fue su primer idioma?	○ Yes ○ No
¿Cual es su lengua materna?	_____ ((dialecto o otro idioma))
¿Sabe usted leer y escribir?	○ Yes ○ No
¿Cual es su nivel educativo?	○ Sin educación formal ○ Primaria incompleta ○ Primaria completa ○ Secundaria incompleta ○ Secundaria completa ○ Preparatoria/Bachillerato incompleto ○ Preparatoria/Bachillerato completo ○ Universidad incompleta ○ Universidad completa ○ Maestria/Doctorado

¿Cuál es el estado donde reside actualmente?

- ○ Aguascalientes
- ○ Baja California
- ○ Baja California Sur
- ○ Campeche
- ○ Chiapas
- ○ Chihuahua
- ○ Ciudad de México
- ○ Coahuila
- ○ Colima
- ○ Durango
- ○ Estado de México
- ○ Guanajuato
- ○ Guerrero
- ○ Hidalgo
- ○ Jalisco
- ○ Michoacán
- ○ Morelos
- ○ Nayarit
- ○ Nuevo León
- ○ Oaxaca
- ○ Puebla
- ○ Querétaro
- ○ Quintana Roo
- ○ San Luis Potosí
- ○ Sinaloa
- ○ Sonora
- ○ Tabasco
- ○ Tamaulipas
- ○ Tlaxcala
- ○ Veracruz
- ○ Yucatán
- ○ Zacatecas

¿Se encuentra usted afiliado a alguna de los siguientes instituciones?

- ☐ INSABI
- ☐ ISSSTE
- ☐ IMSS
- ☐ PEMEX
- ☐ SEDEÑA
- ☐ SEMAR
- ☐ Ninguno
- ☐ Otro

(Asegurar al paciente que ésto no afecta el tratamiento que se le va a otorgar)

Estado civil

- ○ Soltero(a)
- ○ Casado(a)
- ○ Divorciado(a)
- ○ Viudo(a)

Estado laboral

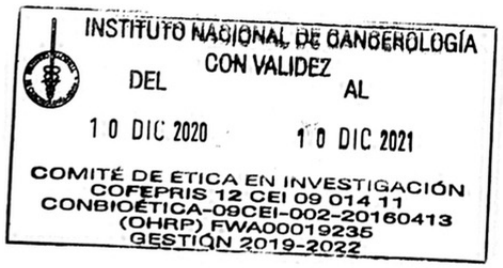
- ○ Empleado
- ○ Desempleado
- ○ No trabaja
- ○ Jubilado
- ○ Desempleo por COVID19

¿Cuánto gana al mes en pesos mexicanos?

_____

(Si es recientemente desempleado, utilizar el último de sus recibos. Si no trabaja, poner 0. NO poner simbolos)

¿Actualmente usted fuma?	○ Si ○ No, pero he fumado en el pasado ○ Nunca he fumado
¿De qué material está construido el techo de su casa?	☐ Lamina de metal ☐ Concreto ☐ Ladrillo ☐ Lamina de asbesto ☐ Tejas ☐ Otro material
¿De qué material están construidas las paredes de su casa?	☐ Tabique ☐ Block ☐ Madera ☐ Lámina de asbesto ☐ Lámina de metal ☐ Otro material
¿Desde su infancia, recuerda usted haber cocinado o calentado su casa con humo de leña?	○ Si ○ No
Índice tabáquico	_____



Por favor, cuénteme de manera ordenada/cronológica ¿como es que empezó todo?

¿Cómo se dió cuenta que tenía un problema en sus pulmones?	◯ síntomas pulmonares y/o extrapulmonares ◯ control de salud de rutina ◯ programa de detección de cáncer de pulmón ◯ hallazgo durante otro procedimiento o diagnóstico
¿Cuál fue el primer síntoma que notó?	◯ hemoptisis ◯ dolor en el pecho ◯ dolor en la espalda ◯ dolor en el hombro ◯ disnea ◯ tos ◯ pérdida de apetito ◯ pérdida de peso ◯ Otro(s) (Anotar sólo el primer sintoma)
*¿Qué otros síntomas?	_____ ((utilizar comas si es necesario))
¿Qué otros síntomas ha tenido después del primero? (Sintomatología adicional)	☐ dolor en el pecho ☐ dolor de hombro ☐ dolor en la espalda ☐ tos ☐ tos con sangre ☐ cansancio ☐ pérdida de peso ☐ pérdida de apetito ☐ disnea (falta de aire) ☐ otros síntomas pulmonares ☐ otros síntomas extra-pulmonares
Otros*	_____
¿Cuál de los síntomas mencionados previamente le preocupaba más?	◯ dolor en el pecho ◯ dolor de hombro ◯ tos ◯ tos con sangre ◯ cansancio ◯ pérdida de peso ◯ pérdida de apetito ◯ disnea ◯ otros pulmonares ◯ otros extra-pulmonares
¿En que fecha identificó inicialmente el primer síntoma?	_____ (dd-mm-aaaa)
Platiqueme, ¿que pensaba usted de éstos síntomas/dolencias/molestias?	_____

¿Quién es la persona con la que habló primero sobre su enfermedad?	○ Padre ○ Madre ○ Hijo(a) ○ Esposo(a) ○ Amigo(a) ○ Colega ○ Hermano(a) ○ Otro ○ Médico (Relationship)
¿Cuánto tiempo transcurrió entre la primera vez que notó los síntomas y la hora de hablar sobre ellos (en días)?	_____ (Especificar cuantos días o meses)
Cuándo notó por primera vez su síntoma, ¿creía que su síntoma era grave?	○ nada grave ○ algo grave ○ moderadamente grave ○ grave ○ muy grave
¿Estaba preocupado por este síntoma en ese entonces?	○ no preocupado en absoluto ○ un poco preocupado ○ algo preocupado ○ muy preocupado ○ no responde
Cuando notó éste síntoma por primera vez, ¿pensó que podría estar relacionado con el cáncer?	○ sí ○ no
¿Cuántos hospitales/médicos visitó ántes de llegar al INCAN?	_____
Indique TODOS los hospitales/médicos que ha encontrado el paciente (antes de ser admitido en el INCAN por la misma enfermedad)	☐ UMF del IMSS (A) ☐ Instituto Nacional (B) ☐ otro hospital público de segundo o tercer nivel de SSA (C) ☐ otro hospital privado (D) ☐ consultorio de farmacias privadas (E) ☐ laboratorio privado (F) ☐ Clínica de primer nivel (SSA) (G) ☐ IMSS (segundo o tercer nivel) (I) ☐ ISSSTE (segundo o tercer nivel) (J) ☐ Otro * (K)
¿Qué otra institución de salud?	_____
Por favor ordene los hospitales/médicos que seleccionó en un orden cronológico i.e. A-> E-> E-> B (Los actores pueden repetirse)	_____
¿Cuando acudió por primera vez al médico?	_____ (dd-mm-aaaa)

INSTITUTO NACIONAL DE CANCEROLOGÍA
CON VALIDEZ
DEL AL
10 DIC 2020 10 DIC 2021
COMITÉ DE ÉTICA EN INVESTIGACIÓN
COFEPRIS 12 CEI 09 014 11
CONBIOÉTICA-09CEI-002-20160413
(OHRP) FWA00019235
GESTIÓN 2019-2022

Con el primer profesional de la salud con el que se encontró ¿Qué dijo él / ella sobre tus pulmones?	○ tumor benigno ○ tumor sospechoso ○ tumor maligno ○ otro *
*¿Que otro diagnóstico le dieron?	_____
¿Qué estudios le solicitó el primer médico con el que habló de su primer síntoma o hallazgo?	☐ biopsia ☐ tomografía ☐ rayos X ☐ citología del esputo ☐ ninguno de los anteriores ☐ El paciente fue referido a otro médico ☐ Ningún estudio
¿Le recetaron un antiinflamatorio o antibiótico durante su primera consulta?	○ Si ○ No
Anotar: a) Fecha de visita b) distancia de su casa a los actores c) marcar donde se realiza el diagnóstico	_____ (Por ejemplo: E, 01/01/20, 15 minutos)
¿Qué piensa usted de esta trayectoria (ir y venir) de médico en médico?	_____
¿Qué fue lo que le hizo decidir buscar atención médica?	☐ que los síntomas mencionados anteriormente podrían reaparecer ☐ que los síntomas mencionados anteriormente podrían empeorar ☐ que los síntomas mencionados anteriormente podrían interferir con sus actividades habituales ☐ asesoramiento familiar o red social ☐ algo más*
*¿Que más le hizo buscar atención médica?	_____
¿Siente que fue fácil ir al médico esa primera vez?	○ Mucho ○ Algo ○ Más o menos ○ Poco ○ Nada

Sección: INCAN

¿Cuando llegó por primera vez al INCAN?

_____

¿Por qué vino aquí (al INCAN)?

- ○ por mi propia iniciativa
- ○ a través del consejo de un amigo o familiar
- ○ me envió un doctor(a)/hospital
- ○ otro

INSTITUTO NACIONAL DE CANCEROLOGÍA
CON VALIDEZ
DEL AL
10 DIC 2020 10 DIC 2021
COMITÉ DE ÉTICA EN INVESTIGACIÓN
COFEPRIS 12 CEI 09 014 11
CONBIOÉTICA-09CEI-002-20160413
(OHRP) FWA00019235
GESTIÓN 2019-2022

¿Cuál institución lo envió aquí (al INCAN)?

- ○ atención primaria de salud
- ○ clínica de salud
- ○ hospital general
- ○ instituto nacional
- ○ servicios médicos privados
- ○ farmacia
- ○ IMSS
- ○ ISSSTE
- ○ otras*

*Especifique que otra institución:

_____

¿Fue usted diagnosticado PREVIO a su ingreso al INCAN?

- ○ Si
- ○ No

¿Cual es la fecha de su diagnóstico (institución externa)?

_____
(utilizar el señalado por la institución que lo envía)

¿Fue usted tratado(a) por la institución externa?

- ○ Si
- ○ No

¿Cual es la fecha de inicio de tratamiento (institución externa)?

_____
(utilizar el señalado por la institución que lo envía)

Tipo de tratamiento otorgado (institución externa)

- ☐ Cirugía
- ☐ Quimio
- ☐ TKI
- ☐ Inmunoterapia
- ☐ Radioterapia

((tratamiento de primera vez))

¿Qué tan fácil considera que fue el proceso para lo recibieran en el INCAN?

- ○ Mucho
- ○ Algo
- ○ Más o menos
- ○ Poco
- ○ Nada

En caso de identificar dificultades, ¿por qué cree que tuvo esas dificultades para llegar al INCAN?

_____

	_____
¿Cuántas horas tarda en llegar al INCAN?	_____
¿Qué métodos de transporte utilizó para llegar a todos los lugares que visitó anteriormente?	☐ Car ☐ Metro ☐ Combi ☐ Bus ☐ Taxi ☐ Uber ☐ Caminando ☐ ADO, Estrella Blanca, u otro bus inter-estatal
¿Ha tenido que buscar albergues para usted o sus familiares durante este proceso?	○ Yes ○ No
Hasta ahora los pagos por sus consultas médicas y tratamiento.	☐ han sido pagados por mí ☐ han sido pagados por mí y alguien de mi familia ☐ ha sido pagado por otro ☐ Pagado por servicios médicos ☐ Otro

¿Quién lo ha ayudado a pagar su tratamiento o consultas médicas?	○ esposo o esposa ○ otro miembro de la familia ○ sin fines de lucro (ONG) ○ hijo(a) ○ nadie ○ otro
En total, ¿cuánto ha gastado para pagar consultas, medicamentos, transporte u otros hasta ahora?	_____ (En pesos mexicanos)
¿Habrá alguien disponible para acompañarlo a las consultas médicas?	☐ esposo o esposa ☐ hijo(as) ☐ padre (s) ☐ amigo (s) ☐ otro familiar ☐ compañeros de trabajo ☐ otros grupos comunitarios ☐ nadie
¿Alguna vez le ofrecieron un examen de detección de cáncer de pulmón?	○ Si ○ No
¿Qué tipo de información le han dado los médicos o profesionales de salud que lo han atendido?	☐ información sobre mi enfermedad (cancer de pulmón) ☐ información sobre los servicios prestados por los hospitales o clínicas para mi enfermedad ☐ información sobre los horarios para los hospitales o clínicas ☐ información sobre el tratamiento de la enfermedad ☐ información sobre costos de la enfermedad ☐ Otro tipo de información NO relacionada con mi enfermedad ☐ Ningún tipo de información
En caso de que le hayan dado información ¿considera que la información fue útil para usted?	○ Si ○ No
¿Qué información le hubiera gustado que le hubieran dado?	☐ Enfermedad ☐ Pronóstico ☐ Tratamiento ☐ Servicios disponibles ☐ Información sobre albergues ☐ Información sobre apoyo económico ☐ Otros
Otro	_____
¿Se le han acercado alguna organización o programa para brindarle ayuda durante su enfermedad p.ej. ayudarle a obtener su diagnóstico y/o tratamiento?	○ Si ○ No
¿Antes de llegar al INCAN, confiaba en que le estaban dando el mejor tratamiento/la mejor atención/estaba en buenas manos?	○ Yes ○ No ○

INSTITUTO NACIONAL DE CANCEROLOGÍA
CON VALIDEZ
DEL 10 DIC 2020 AL 10 DIC 2021
COMITÉ DE ÉTICA EN INVESTIGACIÓN
COFEPRIS 12 CEI 09 014 11
CONBIOÉTICA-09CEI-002-20160413
(OHRP) FWA00019235
GESTIÓN 2019-2022

¿Ahora que está en el INCAN?¿cómo se siente?

_____

¿Qué sabe usted del COVID19?

_____

¿Cómo considera que le ha afectado a usted el COVID-19?

- ☐ Acceso a servicios de diagnóstico
- ☐ Acceso a servicios de tratamiento
- ☐ Miedo a contagiarme
- ☐ Otro*
- ☐ No me ha afectado el COVID-19
- ☐ No responde

Otro*

_____

INSTITUTO NACIONAL DE CANCEROLOGÍA
CON VALIDEZ
DEL AL
10 DIC 2020 10 DIC 2021
COMITÉ DE ÉTICA EN INVESTIGACIÓN
COFEPRIS 12 CEI 09 014 11
CONBIOÉTICA-09CEI-002-20160413
(OHRP) FWA00019235
GESTIÓN 2019-2022

Hoja de extracción de datos del expediente

Número identificador del paciente (número del expediente)	_____ (número del expediente)
Fecha de nacimiento	_____
Sexo	○ Hombre ○ Mujer
¿Qué institución de salud envía al paciente?	○ IMSS ○ ISSSTE ○ SSA/INSABI ○ PEMEX ○ SEDENA ○ SEMAR ○ Privado ○ Ninguno de los anteriores ○ INER u otro instituto ○ Se desconoce la institución emisora

INSTITUTO NACIONAL DE CANCEROLOGÍA
CON VALIDEZ
DEL 10 DIC 2020 AL 10 DIC 2021
COMITÉ DE ÉTICA EN INVESTIGACIÓN
COFEPRIS 12 CEI 09 014 11
CONBIOÉTICA-09CEI-002-20160413
(OHRP) FWA00019235
GESTIÓN 2019-2022

OJO:
LOS SIGUIENTES DATOS CORRESPONDEN A LOS EVENTOS PREVIOS AL INGRESO AL INCAN

Riesgos asociados a cáncer de pulmón	☐ Humo de leña ☐ Tabaquismo ☐ Asbesto ☐ Ninguno ☐ Se desconoce
Índice tabáquico	_____
Indice de humo de leña	_____
¿Cómo se dieron cuenta de que tenía afectación pulmonar?	○ Sintomatología pulmonar o extrapulmonar ○ Hallazgo clínico ○ No se encontró información en expediente ○ Otro
¿Por qué otro motivo se dió cuenta que tenía algo en los pulmones?	_____

Confidential

Primer síntoma	○ Tos ○ Hemoptisis ○ Dolor en pecho ○ Dolor en espalda ○ Disnea ○ Pérdida de peso ○ Pérdida del apetito ○ Otro
¿Cuál otro síntoma?	_____
¿Cuenta con fecha del primer síntoma?	○ Yes ○ No
Fecha de primer síntoma	_____ (dd-mm-aaaa)
¿Paciente es diagnosticado PREVIO a su ingreso al INCAN?	○ Yes ○ No
Fecha de diagnóstico (institución externa) (dd-mm-aaa)	_____ (dd-mm-aaa) utilizar el señalado por la institución que lo envía)
Tipo de cáncer de pulmón (institución externa)	○ Cáncer de pulmón de células pequeñas ○ Cáncer de pulmón de células NO pequeñas ○ Cáncer de pulmón no especificado ○ Sin dx de cáncer (utilizar el señalado por la institución que lo envía)
Tipo histológico	○ Adenocarcinoma ○ Squamous cell carcinoma ○ Small cell carcinoma ○ Adenosquamous ○ Large Cell ○ Neuro-endocrine tumours ○ Pleomorphic carcinoma ○ Pulmonary blastoma ○ Salivary gland carcinoma ○ Other types of lung cancer ○ Not lung cancer ○ Not specified
Estadio de Ca Pulmón (institución externa)	○ Estadio I ○ Estadio II ○ Estadio IIIa ○ Estadio IIIb ○ Estadio IV ○ No especificado (utilizar el señalado por la institución que lo envía)

INSTITUTO NACIONAL DE CANCEROLOGÍA
CON VALIDEZ
DEL 10 DIC 2020 AL 10 DIC 2021
COMITÉ DE ÉTICA EN INVESTIGACIÓN
COFEPRIS 12 CEI 09 014 11
CONBIOÉTICA-09CEI-002-20160413
(OHRP) FWA00019235
GESTIÓN 2019-2022

Confidential

Metástasis (institución externa)	○ SI ○ No (utilizar el señalado por la institución que lo envía)
Tipo de metástasis (institución externa)	_____
¿El/la paciente fue tratado por la institución externa?	○ Si ○ No
Fecha de inicio de tratamiento (institución externa)	_____ (dd-mm-aaa) utilizar el señalado por la institución que lo envía)
Tipo de tratamiento otorgado (institución externa)	☐ Cirugía ☐ Quimio ☐ TKI ☐ Inmunoterapia ☐ Radioterapia ☐ Se desconoce ((tratamiento de primera vez))
OJO: DATOS CORRESPONDIENTES AL INCAN	
Fecha de primer cita (en el INCAN)	_____ (dd_mm_aaaa)
Por qué servicio entra al INCAN	○ Urgencias ○ Consulta externa ○ Otro ○ No especificado
Se obtuvo diagnóstico patología en el INCAN	○ Si ○ No
Fecha diagnóstico por patología (en el INCAN)	_____ ((dd-mm-aaa))
Tipo de cáncer de pulmón	○ Cáncer de pulmón de células pequeñas ○ Cáncer de pulmón de células NO pequeñas ○ Cancer de pulmón no especificado ○ Otro (no pulmonar) ○ Otro (no cancer) (utilizar el señalado por la institución que lo envía)

Confidential

Page 4

Tipo histológico	○ Adenocarcinoma ○ Squamous cell carcinoma ○ Small cell carcinoma ○ Adenosquamous ○ Large Cell ○ Neuro-endocrine tumours ○ Pleomorphic carcinoma ○ Pulmonary blastoma ○ Salivary gland carcinoma ○ Other types of lung cancer ○ Not lung cancer ○ Se desconoce
Estadio de Cáncer	○ Estadio I ○ Estadio II ○ Estadio III ○ Estadio IIIb ○ Estadio IV ○ Se desconoce
Metastasis	○ Si ○ No ○ Se desconoce
Lugar de metástasis	_____ Si se desconoce, poner (.)
¿El diagnóstico del paciente cambió al ingresar al INCAN?	○ SI ○ No
¿Qué cambió?	☐ El estadio clínico ☐ El tipo histológico ☐ Metástasis
Por favor, describa los cambios en el estadio o el tipo histológico o en metástasis	_____
¿Se realizó inmuno-histoquímica?	○ SI ○ No
Tipo de mutación encontrada (en el INCAN)	☐ EGFR ☐ ALK ☐ PDL-1 ☐ Otras ☐ Ninguna mutación ☐ Se desconoce
Paciente inicia tratamiento en INCAN	○ Si ○ No
Fecha de inicio de tratamiento (en el INCAN)	_____ ((dd-mm-aaa))

Tipo de tratamiento otorgado (en el INCAN)	☐ Cirugía ☐ Quimio ☐ TKI ☐ Inmunoterapia ☐ Radioterapia ☐ Paliativos ☐ Sin tratamiento ☐ Se desconoce ☐ otro no relacionado con cancer ((tratamiento de primera vez))
Fecha de última visita	_____ (dd-mm-aaaa)
Status actual	○ Vivo ○ Muerto
Fecha de muerte	_____ (dd-mm-aaaa)