Defining lung cancer pre-diagnostic pathways in primary care: an explanatory sequential mixed-methods study

Satya Rashi Khare, PhD (c)

Department of Family Medicine

Faculty of Medicine, McGill University, Montreal, Quebec, Canada

December 2020

A thesis submitted to McGill University, Faculty of Graduate Studies and Research in partial fulfilment of the requirements of the degree of Doctor of Philosophy (PhD).

Dedication

This thesis is dedicated to my husband, Desmond Joanes. The reasons why would require another thesis to list.

I further dedicate this work to my daughters, Ila and Maia. One day when you are little adults, I hope you will feel inspired by our example to do what you need to do when you need to do it. Everything is possible – maybe not recommended, but possible.

Abstract

Lung cancer is the most common cancer diagnosed in Canada and the leading cause of cancer-related deaths. Lung cancer survival is highly associated with the stage at which it is diagnosed. The cumulative probability that lung cancer patients survive at least three years (i.e. 3-year net survival) is 71% for those diagnosed at the earliest stage (stage 1) and 5% for those diagnosed at the latest stage (stage 4). In Canada, about 70% of lung cancer patients are diagnosed with late stage disease (stages 3 and 4) emphasizing a need to detect lung cancer earlier. Studies investigating delays in lung cancer diagnosis have shown delays in primary care largely contribute to overall diagnostic delays. In Canada, there is a poor understanding of what transpires in primary care from first patient presentation with signs and symptoms suggestive of lung cancer to referral to a respiratory specialist – otherwise known as the primary care interval. Furthermore, Québec has been shown to have the highest lung cancer mortality rate across Canada yet there are no studies focused in primary care in Québec. In order to reduce unnecessary diagnostic delays in lung cancer, a solid understanding of the primary care interval is needed to inform targeted improvement strategies.

The overall objective of my thesis was to gain an in-depth understanding of the primary care interval of the lung cancer diagnostic pathway (first presentation to referral), referred to as pre-diagnostic pathways, to inform potential improvement strategies aligned with sources of unnecessary delay in the local context of Québec. This was accomplished in five specific objectives – one methods objective (objective 1) and four study objectives (objectives 2-5) – described in four manuscripts.

In the first manuscript (objective 1, Chapter 3), I identified strategies to reduce recall bias in patients' self-reported healthcare utilization in primary care. This was a methodological concern

in my study methods for the next objective where I collected healthcare utilization data in structured patient interviews. I conducted a literature review that resulted in several effective strategies, like memory aids and forward recall, that were incorporated into the next phase of work.

In the second manuscript, I identified the different lung cancer pre-diagnostic pathways in primary care (objective 2, Chapter 4) based on healthcare utilization data collected from 50 structured patient interviews and chart reviews and analyzed using latent class analysis. I then described the pathways based on patient- and tumor-related characteristics, and sequence of healthcare utilization activities (objective 3, Chapter 4). 68% of patients followed a pathway where family physician (FP) visits were dominant (FP group) and 32% followed a pathway where walk-in clinic and emergency department (ED) visits were dominant (ED group). Time spent in the primary care interval (i.e. from first presentation to referral) in the FP group was double that of the ED group [45 days (IQR 12-111) vs 22 (IQR 5-69)] with more late stage disease (65% vs 50%). In the FP group, 29% of patients saw their FP 3 times or more before being referred and 41% had an ED visit. These findings suggested challenges with diagnosing lung cancer in primary care, missed opportunities for earlier diagnosis, and a lack of integration between primary and specialist care.

In the third manuscript (objective 4, Chapter 5), I explored the role of factors that can influence the timeliness of cancer diagnosis – patient, disease, and system factors – on the pre-diagnostic pathways identified (FP group and ED group). Data was collected from 12 semi-structured patient interviews and analyzed using thematic analysis with a focus on similarities and differences between the pathways. Key similarities included the importance of symptoms, the notion of self-awareness, emotional distress, and for those who used it, an appreciation for

the efficiency of care at the ED. A key difference was easy access to, and prompt attention received by, a FP for the FP group that was contrasted with a lack of responsiveness at walk-in clinics for the ED group where several aspects of care were unsatisfactory. This difference primarily reflected perceived quality of care which was highly dependent on quality of the patient-physician relationship. These findings supported the importance of improved access to FP's where an established patient-physician relationship led to the experience of seamless pathways.

In the fourth manuscript (objective 5, Chapter 6), I identified potential sources of pre-diagnostic delay based on merged findings from the previous two manuscripts. This resulted in supporting evidence for four sources of delay in primary care: missed opportunities for earlier referral, lack of integration between primary and secondary care, ineffectiveness of walk-in clinics, and lack of standardization in the pre-diagnostic process. Finally, I suggested the following coupled improvement strategies: significant event audits, a new diagnostic strategy focused on supporting FP access to respiratory specialists and diagnostic imaging, expansion of the primary care workforce with other healthcare professionals (e.g. nurse practitioners) who can provide care continuity, quality improvement programs at walk-in clinics focused on continuous evaluation of the patient experience, and standardized care pathways.

This PhD thesis provides an in-depth understanding of lung cancer pre-diagnostic pathways from first presentation to referral to inform potential improvement strategies aligned with sources of unnecessary delay. This work supports timely referral, and ultimately timely diagnosis, of patients with suspected lung cancer – a cancer that kills more Canadians than any other cancer.

Résumé

Le cancer du poumon est le cancer le plus fréquemment diagnostiqué au Canada et la première cause de décès liée au cancer. La survie du cancer du poumon est fortement associée au stade auquel il est diagnostiqué. La probabilité cumulative que les patients atteints d'un cancer du poumon survivent au moins trois ans (i.e., une survie nette de trois ans) est de 71 % pour ceux qui sont diagnostiqués au stade le plus précoce (stade 1) et de 5 % pour ceux qui sont diagnostiqués au stade le plus tardif (stade 4). Au Canada, environ 70 % des patients atteints d'un cancer du poumon sont diagnostiqués à un stade avancé de la maladie (stades 3 et 4), ce qui souligne la nécessité de détecter le cancer du poumon plus tôt. Des études portant sur les retards de diagnostic du cancer du poumon ont montré que les retards en première ligne contribuent largement aux retards de diagnostic globaux. Au Canada, on comprend mal ce qui se passe dans les soins de première ligne, depuis la première présentation du patient avec des signes et symptômes évocateurs d'un cancer du poumon, jusqu'à la référence vers un spécialiste des maladies respiratoires - autrement dit, l'intervalle de temps passé en première ligne. En outre, il a été démontré que le Québec a le taux de mortalité de cancer du poumon le plus élevé au Canada, mais aucune étude n'est consacrée aux soins de première ligne au Québec. Afin de réduire les retards inutiles dans le diagnostic du cancer du poumon, il est nécessaire de bien comprendre l'intervalle de temps passé première ligne pour pouvoir élaborer des stratégies d'amélioration ciblées.

L'objectif général de ma thèse était d'acquérir une compréhension approfondie de l'intervalle de temps passé première ligne avant le diagnostic définitif de cancer du poumon (de la première présentation à la référence au spécialiste), appelée parcours pré-diagnostic, afin d'informer des stratégies d'amélioration potentielles alignées sur les sources de retards inutiles dans le contexte

du Québec. Cela a été réalisé en cinq objectifs spécifiques - un objectif de méthode (objectif 1) et quatre autres objectifs (objectifs 2-5) décrits dans quatre manuscrits.

Dans le premier manuscrit (objectif 1, chapitre 3), j'ai identifié des stratégies visant à réduire le biais de rappel dans l'utilisation des soins de santé de première ligne déclaré par les patients. Il s'agissait d'une préoccupation méthodologique pour l'objectif suivant où j'ai recueilli des données sur l'utilisation des soins de santé dans le cadre d'entretiens structurés avec les patients. J'ai effectué une analyse de la littérature qui a débouché sur plusieurs stratégies efficaces, comme les aide-mémoires et le rappel direct, qui ont été intégrées dans la phase suivante du travail.

Dans le deuxième manuscrit, j'ai identifié les différents parcours pré-diagnostics du cancer du poumon dans les soins de première ligne (objectif 2, chapitre 4) en me basant sur les données d'utilisation des soins de santé recueillies lors de 50 entretiens structurés avec les patients et par une revue de dossiers employant l'analyse des classes latentes. J'ai ensuite décrit les parcours en fonction des caractéristiques des patients et des tumeurs, et de la séquence des activités d'utilisation des services de santé (objectif 3, chapitre 4). 68 % des patients ont suivi un parcours où les visites chez le médecin de famille (MF) étaient majoritaires (groupe MF) et 32 % ont suivi un parcours où les visites dans les cliniques sans rendez-vous et les services d'urgence étaient majoritaires (groupe Urgence). Le temps passé en première ligne dans le groupe des médecins de famille était le double de celui du groupe Urgence [45 jours (IQR 12-111) contre 22 (IQR 5-69)], la maladie étant plus avancée (65 % contre 50 %). Dans le groupe des médecins de famille, 29 % des patients ont vu leur médecin de famille trois fois ou plus avant d'être orientés et 41 % ont eu une visite à l’urgence. Ces résultats suggèrent que le diagnostic du cancer du poumon est difficile en première ligne, que des occasions de diagnostic précoce ont été manquées et qu'il y a un manque d'intégration entre les soins de première ligne et les soins spécialisés.

Dans le troisième manuscrit (objectif 4, chapitre 5), j'ai exploré le rôle des facteurs qui peuvent influencer la rapidité du diagnostic de cancer - facteurs liés au patient, à la maladie et au système - sur les parcours pré-diagnostic identifiés (groupe MF et groupe Urgence). Les données ont été collectées à partir d'entretiens semi-structurés avec des patients (n=12) et analysées à l'aide d'une analyse thématique en mettant l'accent sur les similitudes et les différences entre les parcours. Les similitudes principales comprennent l'importance des symptômes, la notion de conscience de soi, la détresse émotionnelle et, pour ceux qui l'ont utilisée, une appréciation de l'efficacité des soins à l'urgence. Une différence essentielle est la facilité d'accès et la rapidité de l'attention reçue par un médecin de famille pour le groupe MF, qui contraste avec le manque de réactivité des cliniques sans rendez-vous pour le groupe Urgence, où plusieurs aspects des soins sont insatisfaisants. Cette différence reflète principalement la perception de la qualité des soins, qui dépend fortement de la qualité de la relation patient-médecin. Ces résultats confirment l'importance d'un meilleur accès aux médecins de famille puisqu'une relation patient-médecin bien établie permet un expérience des parcours sans heurts.

Dans le quatrième manuscrit (objectif 5, chapitre 6), j'ai identifié des sources potentielles de retard dans les parcours pré-diagnostic en me basant sur les résultats intégrés des deux manuscrits précédents. Les résultats montrent quatre sources de retard en première ligne : occasions manquées de référence plus précoce, manque d'intégration entre les soins de première ligne et secondaires, inefficacité des cliniques sans rendez-vous et manque de standardisation du parcours pré-diagnostic. Enfin, j'ai suggéré les stratégies d'amélioration combinées suivantes : audits des événements significatifs, amélioration de l'accès aux spécialistes des maladies respiratoires et à l'imagerie diagnostique pour les médecins de famille, augmentation du personnel de soins de première ligne avec d'autres professionnels de la santé (par exemple, les

infirmières praticiennes) qui peuvent assurer la continuité des soins, programmes d'amélioration de la qualité dans les cliniques sans rendez-vous axés sur l'évaluation continue de l'expérience du patient, et parcours de soins standardisés.

Cette thèse de doctorat permet de comprendre en profondeur les parcours pré diagnostic du cancer du poumon, de la première présentation à la référence, afin d'éclairer les stratégies d'amélioration potentielles en fonction des sources de retards inutiles. Ce travail peut favoriser la référence en temps utile, et en fin de compte le diagnostic en temps utile, des patients chez qui l'on suspecte un cancer du poumon - un cancer qui tue plus de canadiens que tout autre cancer.

Table of Contents

Dedication ..... ***II***

Abstract ..... ***III***

Résumé ..... ***VI***

Table of Contents ..... ***X***

List of Figures ..... ***XIV***

List of Tables ..... ***XIV***

Acknowledgments ..... ***XV***

Acknowledgement of financial support ..... **XVII**

Preface that states format of the thesis ..... ***XVIII***

Statement of Originality ..... ***XIX***

Contribution of Authors ..... ***XXI***

Manuscript 1 (Chapter 3); Methods Brief; Published: ..... **XXI**

Manuscript 2 (Chapter 4); Original Research Article; Submitted: ..... **XXI**

Manuscript 3 (Chapter 5); Original Research Article; Submitted: ..... **XXII**

Manuscript 4 (Chapter 6); Commentary; In preparation for submission: ..... **XXIII**

1. Chapter 1: Introduction ***24***

1.1. Background **24**

1.2. Objectives **26**

2. Chapter 2: Literature Review ***29***

2.1. Lung cancer incidence and mortality **29**

2.2. Lung cancer classification by histology **31**

2.3. Lung cancer classification by stage **32**

2.4. Lung cancer stage distribution in Canada **33**

2.5. Association of lung cancer stage and survival **34**

2.6. Further rationale for diagnosing lung cancer as early as possible **35**

2.7. Components of the lung cancer diagnostic interval **36**

2.8. Causes of primary care delay in the lung cancer diagnostic pathway **38**

2.8.1. Harder-to-suspect 38

2.8.2. Multiple consultations 39

2.8.3. Issues with diagnostic tests 40

2.8.4. Misdirected referrals 40

2.9. The knowledge gap in Canada **41**

2.10. Summary of knowledge gaps and research needs 42
2.11. Thesis objectives 43
3. Chapter 3: Recall bias and reduction measures: an example in primary health care service utilization (Manuscript 1) 44
3.1. Preamble 44
3.2. Title Page 45
3.3. Introduction 45
3.4. Sources of recall bias 47
3.5. How to reduce recall bias 49
3.6. An example in practice 51
3.7. Question/interview design 51
3.8. Memory aids 52
3.9. Forward recall 52
3.10. Mode of data collection 53
3.11. Concluding remarks 53
3.12. Declaration 55
3.13. References 55
4. Chapter 4: Lung cancer pre-diagnostic pathways from first presentation to specialist referral (Manuscript 2) 60
4.1. Preamble 60
4.2. TITLE PAGE 62
4.3. ABSTRACT 64
4.4. INTRODUCTION 65
4.5. METHODS 66
4.5.1. Study design and population 66
4.5.2. Data collection 67
4.5.3. Statistical analysis 70
4.5.4. Ethics approval 70
4.6. RESULTS 71
4.6.1. Identifying pre-diagnostic pathways 72
4.6.2. Characteristics of patients by pre-diagnostic pathway 74
4.6.3. Sequence of events within pre-diagnostic pathways 75
4.7. DISCUSSION 76
4.7.1. Strengths and limitations 79
4.8. CONCLUSION 80
4.8.1. Acknowledgements 80

4.8.2. Conflict of Interest Disclosure 80
4.9. REFERENCES 81
4.10. Supplemental File 1: Structured interview guide 86
5. Chapter 5: How patient, disease, and system factors influence lung cancer pre-diagnostic pathways (Manuscript 3) 90
5.1. Preamble 90
5.2. TITLE PAGE 92
5.3. ABSTRACT 93
5.4. INTRODUCTION 94
5.5. METHODS 95
5.5.1. Setting 95
5.5.2. Design 95
5.5.3. Participants 96
5.5.4. Data collection 96
5.5.5. Data analysis 97
5.5.6. Ethics approval 98
5.6. RESULTS 98
5.6.1. Patient factors 100
5.6.2. Disease factors 103
5.6.3. System factors 104
5.7. DISCUSSION 108
5.7.1. Strengths and limitations 110
5.8. CONCLUSION 111
5.8.1. Acknowledgements 112
5.8.2. Conflict of Interest Disclosure 112
5.9. REFERENCES 113
5.10. Supplemental File 1: Semi-structured interview guide 119
6. Chapter 6: Defining lung cancer pre-diagnostic pathways in primary care: an in-depth understanding and suggested improvements (Manuscript 4) 123
6.1. Preamble 123
6.2. TITLE PAGE 124
6.3. ABSTRACT 125
6.4. INTRODUCTION 126
6.4.1. STEP 1: QUANTITATIVE RETROSPECTIVE COHORT STUDY 127
6.4.2. STEP 2: QUALITATIVE MULTIPLE CASE STUDY 127
6.5. A DEEPER UNDERSTANDING TO INFORM IMPROVEMENT STRATEGIES 128
6.5.1. Missed opportunities for earlier referral 128

6.5.2. Lack of integration between primary and secondary care 129
6.5.3. Ineffectiveness of walk-in clinics 130
6.5.4. Lack of standardization in the pre-diagnostic process 131
6.6. CONCLUSION 133
6.7. REFERENCES 133
7. CHAPTER 7: DISCUSSION 135
7.1. Summary of research results 135
7.2. Discussion with current evidence 137
7.2.1. Common lung cancer pre-diagnostic pathways 138
7.2.2. Sources of pre-diagnostic delay 139
7.3. Strengths and limitations 144
7.4. Implications for practice 145
7.5. Future study 147
8. CHAPTER 8: CONCLUSION 148
9. REFERENCES 149
10. Appendix 1: Ethics Approval Documents 154
10.1. Ethics Approval 154
10.2. Study Advertisement Flyer 157
10.3. Study Script to Introduce Study 159
10.4. Consent Forms: Patient 161
10.5. Consent Forms: Caregiver 171
10.6. Study Closure 179
11. Appendix 2: French Interview Guides 180
11.1. Guide d'entrevue structurée pour la phase quantitative 180
11.2. Guide d'entrevue semi-structurée pour la phase qualitative 182

List of Figures

Figure 2.1 Age-standardized lung cancer mortality rates (2013-2017) by geographic region, Canada 30
Figure 2.2 Percent distribution of lung cancer cases in Canada by histologic type (2012-2016). 31
Figure 2.3 Percent distribution of lung cancer cases in Canada by stage (2012-2016) 33
Figure 2.4 Three-year predicted net survival estimates for lung cancer by stage in Canada (2012-2014) 34
Figure 2.5 Components of the cancer diagnostic pathway, including the diagnostic interval 36
Figure 3.1 Calendar data illustrating event recall around a routinely scheduled activity 52
Figure 3.2 Modifiable attributes as per Bhandari & Wagner (12) and specific measures to improve data accuracy using the example of Khare et al. (31) 54
Figure 4.1 Chart review conducted on a patient from one year prior to their referral date to one month after their diagnosis date. 68
Figure 4.2 Cue card given to patients and caregivers in advance of the interview 69
Figure 4.3 Summary of interview data shown as number of healthcare utilization activities by month 69
Figure 4.4 Flow of participant recruitment from the Peter Brojde Lung Cancer Centre 71
Figure 4.5 Class conditional probabilities for the final 2-class model from the latent class analysis 74
Figure 4.6 Sequence of utilization activities for each patient showing the order of specific events within the pathway, stratified by group 76
Figure 5.1 Main themes according to the three categories of the Model of Pathways to Treatment 100
Figure 6.1 Methods for each step of the two-step explanatory sequential mixed-methods study 127
Figure 6.2 Potential sources of lung cancer pre-diagnostic delay and associated improvement strategies 132

List of Tables

Table 2.1 Lung cancer stage group according to the 8th edition TNM staging system 33
Table 4.1 Characteristics of patients included in the study 72
Table 4.2 Statistical comparison of latent class models 73
Table 4.3 Characteristics of patients stratified by FP centric and ED centric groups 75
Table 5.1 Characteristics of patients 99
Table 5.2 Quotes from patients by theme 105

Acknowledgments

I would like to start by thanking Gillian Bartlett. I met Jill during my career and was impressed with the knowledge and skillset she brought to a project I was working on. Jill encouraged me to apply to this doctoral program, and because I wanted the same research know-how she exemplified, I jumped at the chance. The experiences I have had in this program – both educational and personal – have been nothing short of enlightening. Jill, I have you to thank for that.

As I formulated my research protocol, I had the absolute pleasure and good fortune to align my work with the portfolio of Isabelle Vedel. In all honesty, I was not sure what to expect when Isabelle became my thesis supervisor, however, within a very short time her expertise, mentorship, and support in all aspects of life were overwhelmingly apparent. Isabelle, thank you for treating me with respect, for always discussing my work with me as opposed to telling me what to do, and most of all, for prioritizing my well-being over everything else. Your leadership is what made me more productive than I could have ever imagined during stressful and challenging times. My journey in this program may be coming to an end, but I will forever aspire to demonstrate the kindness and compassion you embodied during our supervisor-student relationship. You are truly extraordinary.

Another extraordinary individual who greatly supported this work in every possible way was Gerald Batist. I met Gerry during my previous career where he supported virtually every idea I had – even the ones that failed. His unwavering support followed me through this doctoral program from beginning to end. Gerry, thank you for always making time for me, for bringing a sense of humility to every conversation we have (despite your incredible brilliance), and for

always making me feel like everything is within my reach. I am not convinced you are aware of the impact your support has had in my successes.

This thesis would have been a pile of data if not for the wisdom and guidance from Sreenath Madathil whose wealth of knowledge as an epidemiologist, and what I call 'the data guy,' was remarkable. Sreenath, thank you for being so patient with me as I struggled to learn and understand what was statistically possible. I learned so much from you about data analyses, and even began to appreciate your passion for Bayesian statistics – maybe not with the same enthusiasm, but with some enthusiasm.

Importantly, this thesis would not have had any data if not for the support of the clinicians and administrative staff at the Peter Brojde Lung Cancer Centre, particularly Goulnar Kasymjanova. As an oncology researcher in the clinic, Goulnar had answers to all my questions in record time. Goulnar, thank you for helping me navigate every obstacle – of which there were many – and ensuring that nothing stood in the way of this work. Perhaps more importantly, thank you for nurturing my soul during all our 'hangouts' in your office where I felt I could tell you anything. Your friendship was, and continues to be, a major support.

Another true friend who offered support in so many ways during this work was Maud Mazaniello-Chezol. Though I met her late in my thesis work, Maud made everything easier and better. Maud, thank you for imparting your admirable knowledge of qualitative research, for being so engaged in this work, and for bringing your whole self to every encounter we had. I will never forget the deep thought-provoking conversations with you – along with the not so deep, borderline juvenile, ones. I also think I can say you are the single best resource for all things technology to make life simpler. Thank you for so many things.

Speaking of making life simpler, this thesis may not have ever materialized if not for the help of Mary Henein. Mary, thank you for accepting the arduous task of amalgamating and formatting sections of my thesis to create this beautiful document. Without your assistance – well, I cannot fathom such a scenario.

On a more personal note, I would like to thank my husband without whom the thought of completing a doctorate would have always remained a thought. Desmond, thank you for your sacrifices, your encouragement, your love, and most importantly, your regular paycheck that paid our bills. Who would have thought the outcomes of this doctorate would include a thesis AND two children! With all that we have been through in these past six years, this thesis is as much yours as it is mine – in which case, you should read it.

Finally, I would like to extend my heartfelt thanks to all the patients and their families who participated in this research. Their willingness to recount specific events that led up to a life-changing moment for the sake of improving care delivered to others is an act of altruism that we can all learn from. Thank you to each and every participant for your generosity, your honesty, and your expertise. This work is a product of your strength.

Acknowledgement of financial support

My doctoral research was funded by the Fonds de recherche Québec – Santé, the Strategy for Patient-Oriented Research, and the Lady Davis Institute for Medical Research.

In addition, I received financial support to disseminate my findings from the Canadian Institutes of Health Research, Canadian Centre for Applied Research in Cancer Control, Réseau Québécois de Recherche sur le Vieillissement, the Strategy for Patient-Oriented Research, and the McGill Department of Family Medicine.

Preface that states format of the thesis

This thesis is manuscript-based, an alternative to the traditional format accepted by Graduate and Postdoctoral studies at McGill University. It is presented as four linked scholarly papers of which I am the first author. One manuscript has been published in Family Practice, two have been submitted to Current Oncology, and one is being prepared for submission to Canadian Family Physician.

Manuscripts in this thesis are identical to the published, submitted, or preparation for submission versions, including the reference list. They were however formatted in the following ways as per requirements stipulated by McGill University in 'Guidelines for Preparation of a Thesis': 1) uniform font, line spacing, and margins, and 2) addition of text connecting each manuscript in a logical progression to present a single program of research. This was done to produce a consistent, unified, logically coherent thesis representing detailed scholarly work as opposed to a collection of manuscripts.

Each chapter of the thesis that represents a manuscript is clearly labeled as such. Each of these chapters end with a reference list specific to the manuscript. At the end of the thesis, a master reference list is included and lists all references cited in non-manuscript-based chapters such as introduction, literature review, and discussion.

Statement of Originality

This PhD thesis is the first in Canada to provide an in-depth understanding of lung cancer pre-diagnostic pathways in primary care. Currently in Canada there is a poor understanding of how lung cancer patients move through primary care to get to specialist care, including where unnecessary delays in timely referral occur. In this thesis, I present 1) the first study in Canada to identify and describe lung cancer pre-diagnostic pathways and identify potential sources of delay, 2) the first study in Canada to explore the role of patient, disease, and system factors on common lung cancer pre-diagnostic pathways and elicit an understanding of key similarities and differences between pathways, and 3) the first study in Canada to combine quantitative and qualitative evidence in support of sources of unnecessary delay in primary care and suggest associated improvement strategies. Importantly, this work was conducted in a province with the highest lung cancer mortality rate across all Canadian provinces and has the potential to improve the pre-diagnostic process in lung cancer towards timely referral, and ultimately, timely diagnosis.

Beyond these contributions to practice, this PhD thesis further provides a key methodological contribution in demonstrating how a mixed-methods study design can provide in-depth knowledge on a research topic with inherent complexity. Purely quantitative or qualitative study designs may not have fully captured the intricacies of lung cancer pre-diagnostic pathways resulting in insufficient evidence to guide practical action. The quantitative component, qualitative component, and merging of components I describe in this thesis offer an innovative approach to studying topics that are complex, nonlinear, and multifactorial.

The knowledge gained from this PhD thesis is a significant original contribution to a notably under-researched area of the lung cancer diagnostic pathway. With a focus on primary care, this

work sheds light on how timely referral of patients with suspected lung cancer can be improved. Without this knowledge, interventions aimed at reducing unnecessary delays in lung cancer diagnosis would be at best incomplete and at worst completely ineffective.

Contribution of Authors

As a doctoral candidate, I am the first author of each manuscript included in this thesis. I conducted the literature review, identified a pertinent topic, developed the research questions and study design, conducted or supervised all data collection, conducted or supervised all data analyses, interpreted findings, and wrote the manuscripts and thesis. This work was supported by my supervisors, my advisory committee members, my co-authors, and clinicians and researchers with subject matter expertise. Below is the contribution of authors for each manuscript included in this thesis.

Manuscript 1 (Chapter 3); Methods Brief; Published:

Khare SR, Vedel I. Recall bias and reduction measures: an example in primary health care service utilization. Family Practice. 2019;36(5):672-6

I developed the original idea and corresponded with journal editors to gauge interest. I conducted the literature review and wrote the manuscript draft, including visualization/data presentation in the figures. Dr. Isabelle Vedel critically reviewed the manuscript and participated in revisions. I finalized the manuscript and was responsible for journal submission.

Manuscript 2 (Chapter 4); Original Research Article; Submitted:

Khare SR, Madathil SA, Batist G, Peter Brojde Lung Cancer Group, Vedel I. Lung cancer pre-diagnostic pathways from first presentation to specialist referral. Submitted to Current Oncology in December 2020.

I developed the research questions and study design with key input from Dr. Isabelle Vedel (IV), Dr. Gerald Batist and the Peter Brojde Lung Cancer Group – a group of specialist clinician

researchers from the lung cancer clinic. I developed all study materials, including the structured interview guide, and was responsible for obtaining ethics approval. I recruited and supervised two research assistants who participated in patient recruitment and data collection. I collated all data and prepared it for analysis. I supervised data analyses performed by Dr. Sreenath Madathil. I interpreted the data with input from all co-authors. I drafted the manuscript, including all tables and figures, and all co-authors provided critical review to inform revised versions. I finalized the manuscript and was responsible for journal submission. IV supported each activity described above.

Manuscript 3 (Chapter 5); Original Research Article; Submitted:

Khare SR, Mazaniello-Chezol M, Vedel I. How patient, disease, and system factors influence lung cancer pre-diagnostic pathways. Submitted to Current Oncology in December 2020.

I developed the research questions and study design with key input from Dr. Isabelle Vedel (IV). I developed all study materials, including the semi-structured interview guide, and was responsible for obtaining ethics approval. I recruited and supervised one research assistant, Maud Mazaniello-Chezol (MM). I selected the patient sample based on specific sampling criteria and MM contacted patients to confirm interest in participating and conducted most patient interviews. MM and I collated all data and co-conducted the analyses. MM and I co-interpreted findings with key input from IV. I drafted the manuscript, including all tables and figures, and all co-authors provided critical review to inform revised versions. I finalized the manuscript and was responsible for journal submission. IV supported each activity described above.

Manuscript 4 (Chapter 6); Commentary; In preparation for submission:

Khare SR, Vedel I. Defining lung cancer pre-diagnostic pathways in primary care: an in-depth understanding and suggested improvements. To be submitted to Canadian Family Physician in 2021.

I developed the original idea in collaboration with Dr. Isabelle Vedel (IV). I collated all findings and prepared them for interpretation. I interpreted findings with input from IV. I wrote the manuscript draft, including visualization/data presentation in the figures. IV critically reviewed the manuscript and participated in revisions. I finalized the manuscript and will be responsible for journal submission.

1. Chapter 1: Introduction

1.1. Background

Canadians are more likely to be diagnosed with, and die from, lung cancer than any other type of cancer.(1) As the leading cause of cancer-specific deaths in Canada, lung cancer accounts for 26% of all cancer deaths in both men and women.(2) In 2020, it is projected that 29 800 Canadians will be diagnosed with lung cancer, of whom 21 200 will die from the disease.(3) Although lung cancer incidence rates have been declining due to decreases in smoking prevalence, lung cancer continues to kill more men and women than all other common cancers combined.(1, 3) Across Canada, Québec has been shown to have one of the highest lung cancer incidence and mortality rates in the country.(1, 2, 4)

Survival in lung cancer is strongly associated with the stage at which it is diagnosed as stage is a main consideration in treatment options.(5) Surgical resection with curative intent is the most optimal treatment option but can only be offered to patients with early (stages 1 and 2) disease. Patients who are diagnosed with late (stages 3 and 4) disease are more difficult to treat as the cancer has now spread to other parts of the body.(6) In Canada, three-year net survival decreases from 71% for stage 1 lung cancer to 5% for stage 4 lung cancer with an overall five-year net survival of only 19% - among the lowest of all cancer types.(2, 7) This poor survival rate is primarily because approximately 70% of lung cancer patients in Canada are diagnosed with late stage disease when survival probabilities are much lower.(1-3, 8) In fact, about 50% of lung cancers are diagnosed at stage 4, at which point the three-year net survival is only about 5%.(2) Therefore, early detection and diagnosis of lung cancer is key to improving patient outcomes.

Opportunities for early detection and diagnosis can occur anytime within the diagnostic interval from first patient presentation in primary care to definitive diagnosis by a specialist in secondary care.(9) Accordingly, there are two main components of the diagnostic interval: the primary care interval – first presentation in primary care with signs and symptoms suggestive of lung cancer to referral to a respiratory specialist, and the secondary care interval – referral to definitive diagnosis.(10) Studies investigating delays in each interval have shown that delays in primary care largely contribute to overall diagnostic delays in lung cancer.(11-14) This supports the need to focus early lung cancer diagnosis research in primary care.

Primary care delays have been shown to be caused by a mix of patient, disease, and system level factors, some of which are modifiable and can be reduced with appropriate improvement strategies.(13, 15, 16) However, in order to inform improvement strategies, there must be a solid understanding of the primary care interval, including causes of delay, in the local context.

Most research on the primary care interval of the lung cancer diagnostic pathway has been conducted in European countries. In Canada, research has been more targeted towards secondary care and time to definitive diagnosis.(17, 18) As such, the primary care interval in Canada is severely understudied and poorly understood. Furthermore, despite its high lung cancer mortality rate, Québec has no studies on the primary care interval of the lung cancer diagnostic pathway and consequently limited knowledge about where unnecessary delays occur and how delays can be reduced.

In order to design targeted interventions that address specific causes of unnecessary diagnostic delay in lung cancer, there is an urgent need for extensive research in primary care in Canada, especially Québec. Without an in-depth understanding of the primary care interval, practice improvements will be difficult to inform and will run the risk of being ineffective. Given

the high burden of lung cancer in Canada, and more specifically in Quebec, the importance of early lung cancer detection in patients with suspicious signs and symptoms cannot be understated.

1.2. **Objectives**

The overall objective of my thesis was to gain an in-depth understanding of the primary care interval of the lung cancer diagnostic pathway in Québec, otherwise referred to as pre-diagnostic pathways, to inform potential improvement strategies aligned with sources of unnecessary delay so that timely referral, and ultimately timely diagnosis, can be improved. To ensure all pre-diagnostic pathways were considered, the primary care setting referred to any first-line care in the healthcare system including family physician offices, walk-in clinics, and emergency departments.(12)

The overall objective of my thesis was broken down into five specific objectives: one methods objective (objective 1) and four study objectives (objectives 2-5). These were as follows:

1) To identify mitigation strategies for reducing recall bias in patients' self-reported healthcare utilization (e.g. visits to walk-in clinics, family physicians, emergency departments, etcetera) (methods objective, Chapter 3)
2) To identify groups of lung cancer patients with similar pre-diagnostic pathways based on healthcare utilization patterns in the primary care interval (i.e. from first presentation in primary care with signs and symptoms suspicious of lung cancer to referral to a respiratory specialist) (Chapter 4)

3) To describe each pre-diagnostic pathway group by demographic, patient-, and tumor-related characteristics as well as sequence of healthcare utilization activities (Chapter 4)
4) To understand how patient, disease, and system factors play a role in the pre-diagnostic pathway groups identified (Chapter 5)
5) To identify potential sources of pre-diagnostic delay and suggest associated improvement strategies (Chapter 6)

For objective 1, I conducted a literature review to uncover strategies for reducing recall bias to inform methodological decisions pertinent to study methods in the next objective. One of my study methods involved structured interviews with patients where I asked them to self-report on their healthcare utilization in primary care, leading to potential recall bias in the data. Learnings were published in a Methods Brief in the journal Family Practice (see Manuscript #1 in Chapter 3).(19)

For objectives 2-5, I used an explanatory sequential mixed-methods design employed in three phases: a quantitative phase (objectives 2 and 3), a qualitative phase (objective 4), and a merging of findings phase (objective 5).

In the quantitative phase (objectives 2 and 3), I conducted a retrospective cohort study. To achieve objective 2, I used latent class analysis to cluster lung cancer patients into similar pre-diagnostic pathway groups based on common healthcare utilization activities in primary care. To achieve objective 3, I described each pathway group based on the distribution of demographic, patient-, and tumor-related characteristics, and used event sequence analysis to describe the order of utilization activities. This work has been submitted to the journal Current Oncology (see Manuscript #2 in Chapter 4).

In the qualitative phase (objective 4), I conducted a multiple case-study where each pre-diagnostic pathway group was treated as a case. To achieve objective 4, I used thematic analysis of data collected from semi-structured patient interviews along with data from the previous quantitative phase. I further conducted a within-case analysis followed by a cross-case analysis to explore similarities and differences between the pathway groups. This work has been submitted to the journal Current Oncology (see Manuscript #3 in Chapter 5).

In the final phase, to achieve objective 5, all quantitative and qualitative findings were merged to provide supporting evidence for four potential sources of delay in primary care coupled with suggested improvement strategies. This work will be submitted to the journal Canadian Family Physician (see Manuscript #4 in Chapter 6).

In the following chapters I present a detailed explanation of the research problem and knowledge gap (Chapter 2), then a methods brief addressing the concern of recall bias in patient self-reported data (Chapter 3, Objective 1, Manuscript #1), common lung cancer pre-diagnostic pathways and their characteristics (Chapter 4, Objectives 2&3, Manuscript #2), as well as the role of patient, disease, and system factors in common lung cancer pre-diagnostic pathways (Chapter 5, Objective 4, Manuscript #3), followed by evidence for four potential sources of pre-diagnostic delay along with suggested improvement strategies (Chapter 6, Objective 5, Manuscript #4), and finally, an overall discussion of findings and implications (Chapter 7).

2. Chapter 2: Literature Review

In this chapter, I discuss lung cancer incidence and mortality in Canada, the distribution of stage at diagnosis, the association of stage and survival, and components of the diagnostic interval. Here, I focus on the importance of the primary care interval from first patient presentation in primary care to referral to a respiratory specialist and highlight where gaps in knowledge exist. I conclude with the objectives of my PhD thesis.

2.1. **Lung cancer incidence and mortality**

Lung cancer is the leading cause of cancer related death in the world.(7, 20) In 2018, lung cancer accounted for approximately 2.1 million diagnoses and 1.8 million deaths globally.(21)

In Canada, lung cancer represents 13% of new cancer cases and 26% of cancer deaths making it the **most common cancer diagnosed and the leading cause of cancer-specific mortality**.(2) In 2020, it is projected that 29 800 Canadians will be diagnosed with lung cancer, of whom 21 200 will die from the disease.(3) This translates to an estimated 1 in 15 Canadians diagnosed with lung cancer and 1 in 17 Canadians dying from lung cancer.(1)

Lung cancer incidence rates peak at 75-84 years of age,(2) with 98% of lung cancers expected to occur in people 50 years of age or older.(1) In males, lung cancer incidence rates have been decreasing since 1990 with a steep decline after 2011.(1, 22) In females, lung cancer incidence rates did not start decreasing until 2011 after sharp increases between 1984 and 1993.(1) These trends reflect sex differences in cigarette smoking where a decrease in smoking prevalence started in the mid-1960's among males but not until the mid-1980's among females.(23) Changes in smoking trends impact lung cancer incidence around the 20-year mark.(24) Across Canada,

Québec has one of the highest lung cancer incidence rates largely due to a history of high smoking prevalence.(2, 4)

Despite overall declining incidence of lung cancer among males and females, lung cancer is the most common cause of cancer death in Canada accounting for 25% of cancer-related deaths in males and 26% in females.(1) For comparison, prostate cancer accounts for 10% of cancer-related deaths in males and breast cancer accounts for 13% of cancer-related deaths in females.(1) In fact, lung cancer kills more Canadians than all other common cancers combined.(1, 3) Largely attributed to changes in smoking prevalence, lung cancer mortality rates among males have been decreasing since the late 1980's.(24) Among females, mortality rates started decreasing in 2006 but at a reduced annual percent change that was not statistically significant.(24) According to the most recent age-standardized mortality rates for lung cancer across Canada, Québec has the highest mortality rate among all Canadian provinces (Figure 2.1).(1, 2) **This makes lung cancer the deadliest cancer in the province.**

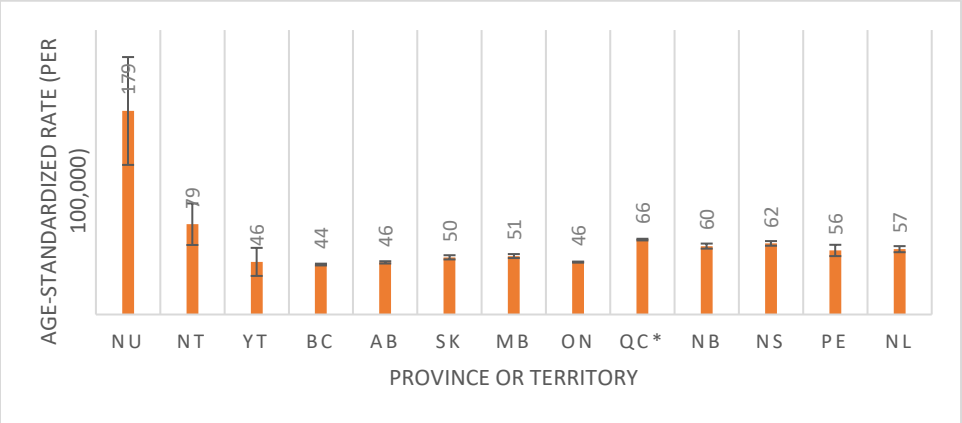

Figure 2.1 Age-standardized lung cancer mortality rates (2013-2017) by geographic region, Canada

Canadian Cancer Statistics Advisory Committee. Canadian Cancer Statistics: A 2020 special report on lung cancer. Toronto, ON: Canadian Cancer Society; 2020. Available at: cancer.ca/Canadian-Cancer-Statistics-2020-EN (accessed November 11, 2020).

2.2. **Lung cancer classification by histology**

Lung cancer generally refers to malignant tumors of the bronchus and lung and excludes malignancies in the trachea and pleura.(25) Lung cancer is broadly classified into two histologic types: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC).

NSCLC is the most common type of lung cancer representing 88% of all lung cancer cases.(2, 26) NSCLC is further divided into three main histologic subtypes: adenocarcinoma, squamous cell carcinoma, and large cell carcinoma (Figure 2.2). Adenocarcinoma is the most common subtype overall and particularly in non-smokers, women, and those who are younger.(26, 27) This is followed by squamous cell carcinoma which is almost always diagnosed in smokers and ex-smokers.

SCLC, also known as oat cell carcinoma, is a more aggressive lung cancer type compared to NSCLC. SCLC represents 12% of all lung cancer cases and occurs almost exclusively in smokers.(2, 28)

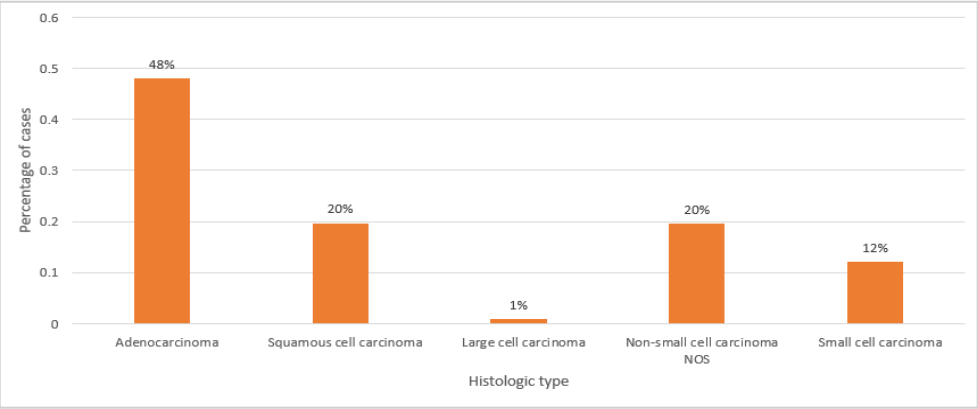

Figure 2.2 Percent distribution of lung cancer cases in Canada by histologic type (2012-2016)

Note: NOS = not otherwise specified

Canadian Cancer Statistics Advisory Committee. Canadian Cancer Statistics: A 2020 special report on lung cancer. Toronto, ON: Canadian Cancer Society; 2020. Available at: cancer.ca/Canadian-Cancer-Statistics-2020-EN (accessed November 11, 2020).

2.3. **Lung cancer classification by stage**

Cancer staging reflects the extent of cancer at the time of diagnosis and increases in severity from stage 1 to stage 4 (often written as Roman numerals; I to IV). When there is not enough information to determine stage, the cancer is classified as 'stage unknown'.

Lung cancer is staged using the anatomically based tumor-node-metastasis (TNM) classification system. The T descriptor (Tis-T4) refers to the size, location, and extent of the primary tumor, the N descriptor (N0-N3) refers to the presence and location of lymph node involvement, and the M descriptor (M0-M1) refers to the presence or absence of distant metastases (spread to other parts of the body).(29) Each descriptor informs treatment options and prognosis. Based on emerging evidence, the TNM staging system for lung cancer is periodically revised by the International Association for the Study of Lung Cancer (IASLC); the 8th edition was recently released.(30)

Lung cancer can also be broadly classified as early (cancer is only in the lung), locoregional (cancer has spread to lymph nodes or other parts of the chest on the same side of the body as the cancer), and advanced (cancer has spread to other parts of the body).(29, 31) Table 2.1 shows each stage group based on TNM descriptors and indicates which are considered early, locoregional, or advanced. **Locoregional and advanced disease are often referred to as late stage disease**.

Table 2.1 Lung cancer stage group according to the 8th edition TNM staging system

EARLY	Stage IA	T1	N0	M0
	Stage IB	T2a	N0	M0
	Stage IIA	T2b	N0	M0
	Stage IIB	T1a-c, T2a,b T3	N1 N0	M0 M0
LOCOREGIONAL	Stage IIIA	T1a-c, T2a,b T3 T4	N2 N1 N0,N1	M0 M0 M0
	Stage IIIB	T1a-c, T2a,b T3, T4	N3 N2	M0 M0
	Stage IIIC	T3, T4	N3	M0
ADVANCED	Stage IV	Any T	Any N	M1
	Stage IVA	Any T	Any N	M1a,b
	Stage IVB	Any T	Any N	M1c

2.4. **Lung cancer stage distribution in Canada**

Most lung cancer patients in Canada are diagnosed with late stage disease. About half of all lung cancer cases are diagnosed at stage 4 (advanced) when the cancer has already metastasized or spread to other parts of the body.(1-3, 8) Another 20% are diagnosed at stage 3 (locoregional) when the cancer has spread to nearby tissue or distant lymph nodes.(1-3) Only about 21% of lung cancers in Canada are diagnosed at stage 1 when the cancer has not spread outside the lung.(2, 8) This stage distribution is presented in Figure 2.3.

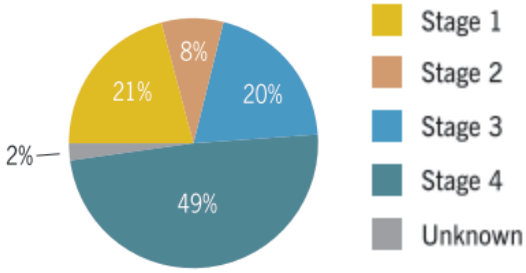

Figure 2.3 Percent distribution of lung cancer cases in Canada by stage (2012-2016)

Canadian Cancer Statistics Advisory Committee. Canadian Cancer Statistics: A 2020 special report on lung cancer. Toronto, ON: Canadian Cancer Society; 2020. Available at: cancer.ca/Canadian-Cancer-Statistics-2020-EN (accessed November 11, 2020).

2.5. **Association of lung cancer stage and survival**

The five-year net survival for lung cancer is 19%, among the lowest of all cancer types.(2, 7) **Lung cancer survival is highly associated with the stage at which it is diagnosed** as stage is a main consideration in treatment options.(5) Lung cancer patients diagnosed with early stage disease can be offered treatment options with curative intent. The optimal treatment is surgical resection; advances in the delivery of radiation therapy has offered another potentially curative treatment option for those not well enough to undergo surgery.(2) However, once lung cancer spreads to other parts of the body (i.e. stage 4) it is more difficult to treat and is associated with lower survival probabilities.(6)

Recent Canadian data on survival by stage showed that three-year net survival decreased from 71% for stage 1 lung cancer to 5% for stage 4 lung cancer (Figure 2.4).(2) Meanwhile about 50% of lung cancers in Canada are diagnosed at stage 4.(2) Stage data is not available for Québec, however, given that Québec has the highest lung cancer mortality rate among all Canadian provinces,(1) it is likely that the percent of cases diagnosed at stage 4 is the same or more compared to other provinces.

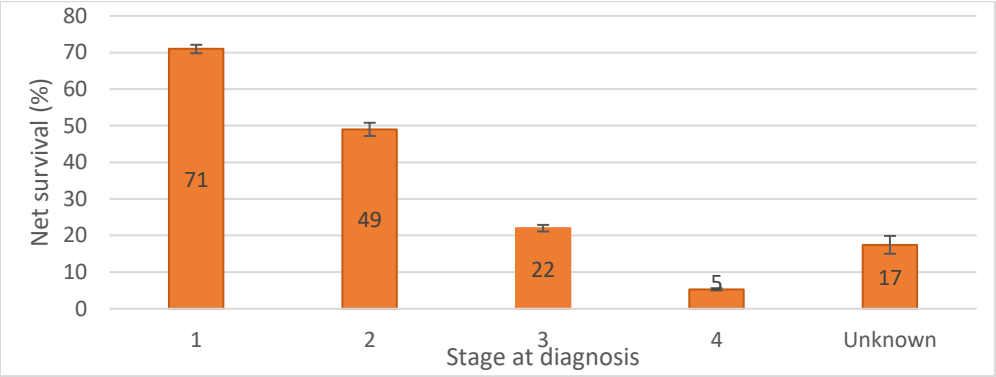

Figure 2.4 Three-year predicted net survival estimates for lung cancer by stage in Canada (2012-2014)

Canadian Cancer Statistics Advisory Committee. Canadian Cancer Statistics: A 2020 special report on lung cancer. Toronto, ON: Canadian Cancer Society; 2020. Available at: cancer.ca/Canadian-Cancer-Statistics-2020-EN (accessed November 11, 2020).

Combining stage distribution data with survival data shows that only about 21% of Canadians diagnosed with lung cancer have a three-year predicted net survival over 70%, and about 50% of Canadians diagnosed with lung cancer have a three-year predicted net survival of only 5%.(2) These grim statistics underscore a **need to diagnose lung cancer at the earliest stage possible when survival probabilities are higher**.

2.6. **Further rationale for diagnosing lung cancer as early as possible**

Beyond the goal of diagnosing lung cancer in its earliest stages when survival is much higher, there are several rationales to diagnosing lung cancer as early as possible. For instance, the treatment landscape for lung cancer has changed dramatically over the past decade with newer, more effective agents now available for all stages of disease.(32) In particular, targeted therapy and immunotherapy have led to improved survival rates in many patients, even those with advanced disease where the cancer has metastasized.(33) For example, a recent study showed a 27% reduction in risk of death for advanced lung cancer patients taking nivolumab, an immunotherapy medication, compared to docetaxel, a chemotherapy medication.(34) Another treatment option that has been shown to be more effective when started early is palliative care. This can dramatically improve quality of life, and even survival, through symptom control.(35) Finally, and importantly, lung cancer patients diagnosed quickly can benefit from reduced anxiety associated with not knowing what is wrong or waiting for a definitive diagnosis.

Essential to promoting early lung cancer diagnosis is reducing unnecessary delays in the diagnostic process from when the patient first presents in primary care to when they receive a

definitive lung cancer diagnosis by a specialist in secondary care, otherwise known as the diagnostic interval.(9)

2.7. **Components of the lung cancer diagnostic interval**

The diagnostic interval is divided into two main components: **a primary care interval** that starts at first presentation in primary care with signs and symptoms suggestive of lung cancer and ends at referral to a respiratory specialist, and a **secondary care interval** that starts at referral and continues to definitive diagnosis (Figure 2.5).(10) In countries that operate under a gatekeeping system, like Canada, patients must present in primary care before they can access a specialist in secondary care.(36) As such, **most lung cancer patients initially present to their family physician with symptoms** and are then referred to a respiratory specialist for definitive diagnosis.(37, 38)

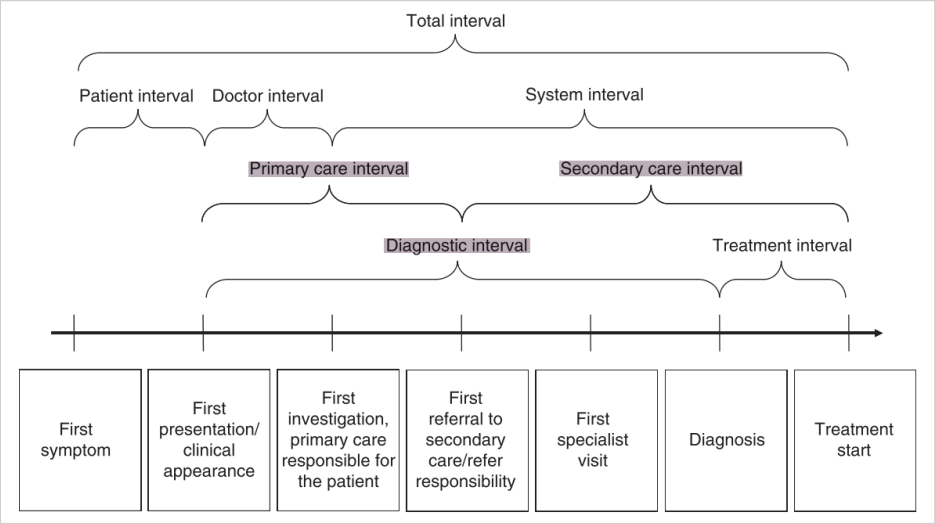

Figure 2.5 Components of the cancer diagnostic pathway, including the diagnostic interval

Olesen F, Hansen RP, Vedsted P. Delay in diagnosis: the experience in Denmark. Br J Cancer 2009; 101 (suppl 2): S5-8.

Studies investigating time spent in each interval, otherwise referred to as primary care delay and secondary care delay, have shown that lung cancer patients spend significantly more time (days) in primary care compared to secondary care. In other words, **primary care delay has been shown to be significantly longer than secondary care delay**. For example, a Swedish study showed that lung cancer patients had a median primary care delay of 33 days compared to 9 days in secondary care.(14) Similarly, a UK study showed a median primary care delay of 51 days verses 29 days in secondary care.(12) In a study conducted in Denmark where only the primary care interval time was reported, median delay was again found to be 33 days with over half of the delay attributed to waiting for diagnostic investigations.(13) Another population-based UK study found that primary care delays contributed to larger proportions of total diagnostic delay among lung cancer patients than did secondary care delays.(11) These findings support the **need to focus early lung cancer diagnosis research in the primary care interval** to ensure early detection and timely referral of patients with suspected lung cancer.(16)

Although these studies stress delay as a function of time, it is important to note that short time intervals are not necessarily synonymous with diagnosis at an early stage. Known as the waiting time paradox, advanced disease may present more serious symptoms that makes the diagnosis easier and/or leads to quicker investigation. This could result in a short primary care interval time but also late stage diagnosis and poor patient outcomes.(39, 40) This suggests that **time to diagnosis may not be as important as the pathway to diagnosis which should be without unnecessary delays**.

Delays in the primary care interval are likely not due to clinical incompetency or poor performance. In fact, delays have been shown to have complex and multifactorial causes that

highly reflect the diagnostic difficulty associated with lung cancer in the primary care setting.(41)

2.8. **Causes of primary care delay in the lung cancer diagnostic pathway**

Studies have identified **a mix of patient, disease, and system level factors that play a role in primary care delays**.

2.8.1. Harder-to-suspect

Once the patient presents to a physician, a major source of delay is related to signs and symptoms.(13) Due to the absence of a clear symptom signature, physicians may not recognize signs and symptoms as suggestive of lung cancer.(15, 42, 43) Though many studies have focused on how well certain symptoms predict lung cancer, the positive predictive values (PPV's) in primary care are generally quite low.(16, 44) The QCancer study – a prospective study using large primary care databases aimed at developing algorithms that estimate risk of a current cancer – showed the following to be independent predictors of lung cancer: hemoptysis, appetite loss, weight loss, cough, smoking, history of chronic obstructive pulmonary disease, increased body mass index, and high material deprivation (measured by the Townsend deprivation index).(45) Hemoptysis had the highest PPV but patients infrequently present with this symptom.(42, 46) On the other hand, cough is a common presenting symptom among lung cancer patients but has a PPV in primary care of only 0.4%.(47) Multiple symptoms, persistent symptoms, and presence of risk factors such as age and smoking history tend to improve prediction.(47)

Diagnosing lung cancer in patients with comorbidities can also pose challenges as symptoms of other illnesses, especially existing respiratory disease, can be similar to lung cancer and confuse the cause of signs and symptoms.(48) Given that lung cancer incidence rates peak at 75-84 years of age, many patients with suspected lung cancer in primary care will likely have comorbidities. Alternatively, patients may present in primary care with non-respiratory or atypical symptoms that suggest a non-cancerous diagnosis,(16, 49) or with signs and symptoms related to metastatic disease and/or paraneoplastic syndromes (e.g. syndrome of inappropriate antidiuretic hormone in SCLC).(50) As a result, lung cancer has been categorized as 'harder-to-suspect' on a relative difficulty of diagnosis scale.(41)

2.8.2. Multiple consultations

As indicated in the previous section, presenting signs and symptoms of lung cancer are common and not cancer specific. Furthermore, most patients presenting in primary care with signs and symptoms that could indicate lung cancer suffer from benign disorders that are self-limiting.(16) In fact, a family physician may only see one lung cancer case per year in their practice despite a high volume of patients presenting with respiratory symptoms.(16, 51)

Accordingly, all differential diagnoses (e.g. pneumonia, bronchitis, etc.) must be considered, along with the risk profile of the patient, before deciding on whether specialist referral is necessary. Consequently, many patients will have multiple consultations with their family physician before being referred.(18) These multiple visits may be to assess changes in symptoms over time or assess for resolution of symptoms after pharmacological management of presumed non-cancerous disease. For example, one study showed significantly higher diagnostic delays in lung cancer patients who initially received antitubercular treatment.(52)

2.8.3. *Issues with diagnostic tests*

When there is suspicion for lung cancer in primary care, the principal diagnostic test is a chest radiograph (CXR).(53) An over-reliance on CXR results has been shown to delay referral owing to low sensitivity, especially for small (<2-3 cm) or central tumors, and resulting high rates of false negatives.(13, 15) Two case series showed that initial CXR results were normal in 20%-25% of people who were subsequently diagnosed with lung cancer.(54) Moreover, two systematic reviews also pointed to a high likelihood of false negative CXR's.(55, 56) A positive CXR showing a nodule can also create uncertainty as many pulmonary nodules are indeterminate for malignant versus benign origin and require repeat testing to assess changes in size over time.

Relatedly, multiple consecutive investigations in primary care have been attributed to delays, as has a failure to follow-up on imaging results.(15) Patient-mediated delays can also occur when the patient refuses to undergo further investigation or has certain beliefs about the changes in their health,(15, 57) while system-related delays can occur when there are excessive waiting times for diagnostic tests in primary care.(13)

2.8.4. *Misdirected referrals*

In addition to the sources of delay described above, referral to appropriate secondary care can be further delayed by initial referrals to non-respiratory specialists.(39, 58) One UK study looking at various pathways to a lung cancer diagnosis found the longest interval from first symptom to diagnosis to be in those with misdirected referrals.(12)

Another complicating factor is the risk threshold for referral, which remains elusive.(16, 59) If the threshold is set too high, then diagnosis can be severely delayed with detrimental patient

outcomes. Conversely, if the threshold is set too low, then the system can be over-burdened and patients may experience unnecessary psychological distress.

Some of these sources of delay are non-modifiable, such as absence of a clear symptom signature, but other sources of delay like over-reliance on CXR results or excessive waiting times for diagnostic tests can be reduced with appropriate improvement strategies. However, **in order to inform targeted improvement strategies, there must be a solid understanding of the primary care interval, including causes of delay, in the local context.**

2.9. **The knowledge gap in Canada**

Most of the aforementioned studies have been conducted in European countries with minimal research from Canada. Among Canadian studies, the focus has been on time to definitive diagnosis with little data specific to the primary care interval.(18) For example, a study conducted in Manitoba emphasized time between first physician visit and lung cancer diagnosis, reporting a median wait time of almost 5 months.(17) This study called for more efficient healthcare service delivery in the lung cancer diagnostic pathway but lacked specifics about where delays occurred or what contributed to diagnostic delay within the pathway.

Despite the important role of primary care in the lung cancer diagnostic pathway, **the primary care interval in Canada is severely understudied**. Moreover, despite having the highest lung cancer mortality rate among Canadian provinces, **Québec has no studies on the primary care interval in the lung cancer diagnostic pathway**. Consequently, there is a poor understanding of where unnecessary delays occur and how delays can be reduced.

2.10. Summary of knowledge gaps and research needs

In Canada, lung cancer is the most common cancer diagnosed and the leading cause of cancer-specific mortality. Québec has the highest mortality rate among all Canadian provinces making it the deadliest cancer in the province.

Most lung cancer patients in Canada are diagnosed with late stage disease (locoregional and advanced disease) when survival probabilities are low. Given that lung cancer survival is highly associated with stage at diagnosis, there is a need to diagnose lung cancer at the earliest stage possible when survival probabilities are higher.

Essential to promoting early lung cancer diagnosis is reducing unnecessary delays in the diagnostic process, or diagnostic interval. This interval has two main components: a primary care interval and a secondary care interval. Studies have shown that delays in the primary care interval are significantly longer than delays in the secondary care interval. These primary care delays are due to a mix of patient, disease, and system level factors, some of which can be reduced with appropriate improvement strategies. However, in order to inform targeted improvement strategies, there must be a solid understanding of the primary care interval, including causes of delay, in the local context.

In Canada, the primary care interval is severely understudied and in Québec where the highest mortality rate is reported, there are no studies on the primary care interval in the lung cancer diagnostic pathway. Consequently, there is insufficient knowledge to guide improvements.

In order to inform how delays in primary care can be reduced, it is imperative to understand how patients move through primary care (i.e. pathways) and where unnecessary delays occur. This knowledge can then be used to inform targeted improvement strategies aimed at ensuring early detection and timely referral of patients with suspected lung cancer.

2.11. Thesis objectives

The overall objective of this thesis was to gain an in-depth understanding of the primary care interval of the lung cancer diagnostic pathway, herein referred to as the pre-diagnostic pathway, to inform potential improvement strategies aligned with sources of unnecessary delay in the local context of Québec.

This was broken down into five specific objectives – one methods objective (objective 1) and four study objectives (objectives 2-5) – as follows:

1) To identify mitigation strategies for reducing recall bias in patients' self-reported healthcare utilization (e.g. visits to walk-in clinics, family physicians, emergency departments, etcetera) (Chapter 3)
2) To identify groups of lung cancer patients with similar pre-diagnostic pathways based on healthcare utilization patterns in the primary care interval (i.e. from first presentation in primary care with signs and symptoms suspicious of lung cancer to referral to a respiratory specialist) (Chapter 4)
3) To describe each pre-diagnostic pathway group by demographic, patient-, and tumor-related characteristics as well as sequence of healthcare utilization activities (Chapter 4)
4) To understand how patient, disease, and system factors play a role in the pre-diagnostic pathway groups identified (Chapter 5)
5) To identify potential sources of pre-diagnostic delay and suggest associated improvement strategies (Chapter 6)

3. Chapter 3: Recall bias and reduction measures: an example in primary health care service utilization (Manuscript 1)

3.1. **Preamble**

In this chapter, I address objective 1 of my thesis: To identify mitigation strategies for reducing recall bias in patients' self-reported healthcare utilization (e.g. visits to walk-in clinics, family physicians, emergency departments, etc.).

I used structured patient interviews as a data collection method for addressing objective 2 of my thesis (described in Chapter 4). In these interviews, patients were asked to self-report on their healthcare utilization in the primary care interval (i.e. from first presentation in primary care with signs and symptoms suspicious of lung cancer to referral to a respiratory specialist). As these data were prone to recall bias, an important precursor was to identify strategies from the literature to reduce recall bias. Identified strategies were then incorporated into the next phase of work described in the next chapter.

In this chapter, I present the results of a literature review including sources of recall bias in self-reported healthcare utilization data, measures that can be instituted to reduce such bias, and how these measures were used in my study. This manuscript was published in a Methods Brief in the journal Family Practice.

Khare SR, Vedel I. Recall bias and reduction measures: an example in primary health care service utilization. Family Practice. 2019;36(5):672-6

3.2. **Title Page**

Running head: Reducing recall bias in primary care studies

Article category: CASFM Methods Brief

Authors: Satya Rashi Khare[a], Isabelle Vedel[a]

a. Department of Family Medicine, McGill University, Montreal, Canada

Corresponding author:

Ms. S.R. Khare

Department of Family Medicine, McGill University

5858, Chemin de la Côte-des-Neiges, Suite 300

Montreal, Canada

H3S 1Z1

satya.khare@mail.mcgill.ca

Keywords: Health-services utilization, patient recall, primary care services, recall bias, self-report

3.3. **Introduction**

There are many primary care studies in which the research question aims to discern the frequency of health-care service utilization, or the frequency of visits to a clinical provider. Some examples include evaluating comparative use of services,(1) building typologies based on utilization patterns,(2) and health economic evaluations.(3) Often, data on the use of health services are collected retrospectively from large administrative databases, patient medical records, self-reported health care service utilization, or a combination of these strategies.(4)

Utilization data sourced from administrative databases and patient medical records is often considered the gold standard given that data is collected at the time of encounter with the health care system. However, in some situations, use of administrative data can be time consuming, costly, and labour intensive,(4) and is not without concerns regarding quality and comprehensiveness.(5) For example, use of services in the private sector may not be reflected in primarily 'public' data sources,(6) and services rendered by health care professionals under capitation payments may not be reflected as individual visits. When such challenges arise, self-reported data can offer a feasible and comprehensive alternative.

In self-reported health care service utilization, the service user (e.g. study sample participants) directly reports on their service use. The most common method in this context is a study-specific survey that is either self-administered or administered by an interviewer.(7) An example of self-administration is the Canadian Community Health Survey used by Statistics Canada to gather data on health care service utilization across the country.(8) This survey is mailed to households on an annual basis and depends on a large sample of respondents who are geographically dispersed, thus necessitating a low cost, low resource option. Interviewer-administration may be more suitable in difficult to reach, complex or marginalized populations. An example is a study where accessibility and quality of health care services was evaluated in female prisoners at a detention centre through face-to-face interviews conducted by specially trained research assistants.(9)

Regardless of the mode of data collection, reliance on participant recall of past utilization events results in data that are prone to recall error – inaccurate or incomplete recollection – which can lead to recall bias if there is a systematic under- or over-reporting of events.(10, 11) In the case of random recall error, all participants are equally affected hence precluding any

important bias. However, when recall error is not random and only certain participants are affected based on some characteristic, this can lead to an important bias that can threaten the reliability of results.

In this article, we present sources of recall bias in self-reported health care service utilization data, as well as measures that can be instituted to reduce such bias. We conclude with a specific example in the context of a study conducted in primary care on lung cancer pre-diagnostic pathways.

3.4. **Sources of recall bias**

Systematic errors in self-report stem from a number of different but related causes. When asking about utilization events that occurred in the past, participants may fail to remember the event entirely, otherwise known as memory decay.(12) The extent to which this error manifests is, in part, related to the length of the recall period. Although a longer period of recall (i.e. utilization over a 12-month period versus a 6-month period) can yield a greater quantity of information, the accuracy of the information decreases as the recall period increases.(11) This inverse relationship means that quantity and quality must always be balanced, especially when the type of utilization activities differs among participants in the study sample. For instance, salient and less frequent utilization events, such as hospitalizations and specialist visits, have been shown to be more accurately self-reported,(13, 14) compared to more typical and frequent events, such as general practitioner visits.(15, 16) Therefore, if some participants in the study sample had more visits to a general practitioner and other participants had more specialist visits, event recall may not be as accurate in the former as compared to the latter. Validation studies of self-reported health care utilization have shown under-reporting to be more common than over-

reporting, especially with recall periods of 12 months or more.(15) For type of utilization activities, under-reporting is especially evident in the context of primary care visits(10, 12) and stigmatized visits like those related to mental health.(4) Although the focus of this paper is not on recall bias by design type, the extent of self-reported data accuracy, including the possibility of under- or over-reporting may also be affected by study design. For example, in case-control designs participant recall of exposure may be affected by whether or not the outcome of interest is present.

Memory decay can be further exacerbated in elderly populations where cognitive ability, such as memory impairment, can lead to inaccurate reporting of events.(12, 17) It should be noted, however, that the literature is somewhat conflicted on this as several studies have found no relationship between demographics and self-report accuracy.(18, 19) For studies that have shown a relationship, under-reporting has been more commonly found among the elderly.(20, 21)

A recall bias related to the frequency of utilization events is rounding where events with large values are rounded up by the participant. The extent of rounding tends to increase as the number of events increase – visits up to five may be reported as raw values but then rounded by five's up to about 20 visits, and then rounded by ten's after that.(22) This may further be the case in temporal ordering of utilisation events where participants are asked to place events in order of when they occurred – 1 year ago, 5 years ago, 10 years ago, etc. Frequency of events can also be overestimated in a recall bias known as forward telescoping where events that occurred *before* the period of interest are remembered to have occurred *within* the period of interest.(23, 24) Conversely, events occurring *after* the period of interest can be reverse telescoped within the period of interest as well.(12)

Finally, confusion that results from ambiguous or poor-quality questions, and poor communication between the interviewer and interviewee can promote recall bias.(11) These factors can be compounded by participant stress, motivation, and interview dynamics, all of which can have profound impacts on data accuracy and be quite variable within a study sample.(25, 26)

3.5. **How to reduce recall bias**

Recall bias cannot be eliminated and should therefore always be acknowledged in the limitations of a study that involves self-reported health care service utilization. To maintain the highest level of data accuracy, however, there are several measures that can be incorporated to minimize its impact.

Bhandari and Wagner (2006) present a conceptual model highlighting modifiable and fixed attributes that can affect the accuracy of self-reported data.(12) Modifiable attributes include questionnaire/interview design, mode of data collection (e.g. phone, mail, face-to-face, online) and memory aids. In the same model, recall timeframe (i.e. recall period), utilization type and utilization frequency are also presented as modifiable; however, it can be argued that these attributes are simply a reflection of the health care utilization activities of interest and the optimal recall window (i.e. the research objective), and thus cannot be modified. Fixed attributes include cognitive and psychosocial differences within the sample that can lead to variability in the interpretation of questions presented in a survey or asked by an interviewer.

The modifiable attributes offer opportunities to improve accuracy and validity of utilization data.

With respect to the questionnaire/interview design, valid and reliable data can be obtained by formulating questions that are clear and precise to reduce variation in comprehension.(27) In addition, backwards recall can facilitate memory recall by following an ordered sequence of events; start with the present and think backwards to a point in time.(28) The more recent events are easier to recall and help with the recall of previous, less recent, events.(25) The opposite of this would be forward recall where a causal sequence of events is followed; go back to a point in time and think forward to the present. Memory aids, such as personal diaries, and probes, such as follow-up questions on a specific utilization event, can also enhance recall and reduce the risk of under-reporting.(29) In terms of mode of collection, in-person interviews have been speculated to lead to more accurate recall data.(10, 30)

As the length of the recall period can affect data accuracy, this should be considered during the development of study methods. Primary importance should be given to meeting research objectives but with a careful balance regarding the optimal recall window and data integrity. Long recall periods of 12 months or more could be justified in a study focused on inpatient visits (i.e salient and infrequent events), whereas a study focused on primary care visits (i.e typical and frequent events) would ideally be limited to a 6 month, or less, recall period.(12, 19) In cases where the utilization events of interest are regular and predictable, such as consumption of prescription drugs, monthly utilization data could be used to infer annual utilization.(11) However, this would introduce substantial estimation error with utilization activities that are irregular or subject to seasonal variation, like physician visits.

In addition, if time and availability of resources permit, the level of recall bias could be quantified and the self-reported data could then be inflated or deflated accordingly. For example, Brusco and Watts (2015) quantified the level of under-reporting of self-reported visits to a

general practitioner by comparing with national claims data, leading to the recommendation to inflate such visits by 16%.(10)

3.6. **An example in practice**

Many of the techniques described earlier were used in a study aimed at identifying groups of lung cancer patients with similar pre-diagnostic pathways in the primary care interval – from first presentation in primary care with signs and symptoms suggestive of lung cancer to specialist referral.(31) The grouping of patients was based on health care service utilization patterns with a focus on visits to general practitioners, hospitalizations and imaging tests.

A major issue in relation to recall bias in this study was the length of the recall period. Although this was set at a maximum of 1 year, the uniqueness of each patient's pathway led to a large variation of recall timeframes within the sample. For example, some patients were referred the same day they presented in primary care, whereas others had long delays before referral. Moreover, recruited patients were already diagnosed with lung cancer meaning that the time between the utilization activities and the interview may have been up to three years. For patients diagnosed much earlier, this led to difficulties in grounding them in the specific recall period.

Accordingly, the following measures were used to reduce recall bias.

3.7. **Question/interview design**

In the preparation phase, the interview guide was pilot tested and revised to ensure questions were clear and precise. This was done to reduce variation in comprehension and allowed practice and evaluation of interviewer technique to ensure consistency across interviews.

3.8. **Memory aids**

Approximately 1 week before the interview, patients were asked to think about past visits and have their personal agenda or other helpful items with them at the time of the interview. This served to enhance recall and reduce the risk of under-reporting, especially in patients who were older.

3.9. **Forward recall**

During the interview, patients were asked to self-report their health care utilization starting with their first presentation in primary care with signs and symptoms suspicious of lung cancer and working forward month by month to the date of specialist referral. In addition, the interviewer brought a large calendar to record the data in a collaborative manner with the patient. This allowed a visual of the causal sequence of events and facilitated event recall around landmark events such as birthdays, or routine activities. An example of this is shown in Figure 3.1 where the patient recalls an appointment with their family physician the day after a regularly scheduled bridge game.

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
	1	2	3	4	5	6
7	8	9	10 Chest radiograph (CXR)	11	12 *Bridge game – could not see family physician so went the next day*	13 Saw family physician to discuss CXR results
14	15	16	17	18 Referred to respirologist	19	20
21	22	23	24	25	26	27
28	29					

Figure 3.1 Calendar data illustrating event recall around a routinely scheduled activity

3.10. Mode of data collection

These measures necessitated a face-to-face interview where we were also able to include a caregiver/companion who was knowledgeable about the patient's health care utilization during the period of interest. This helped to improve data accuracy, especially in cases where there may have been mild cognitive impairment.

3.11. Concluding remarks

Self-reported health care utilization is a viable method that can be used in a range of studies; however, the potential for recall bias must be acknowledged and reduction measures to address it must be incorporated. We have presented various types and sources of recall bias and have provided measures that can be easily incorporated into a study to promote data accuracy. The example in primary care presents several challenges, such as length of the recall period, and offers concrete strategies to offset such challenges. We have summarized these points in Figure 3.2 as a helpful guide towards measures that can be taken when trying to reduce recall bias.

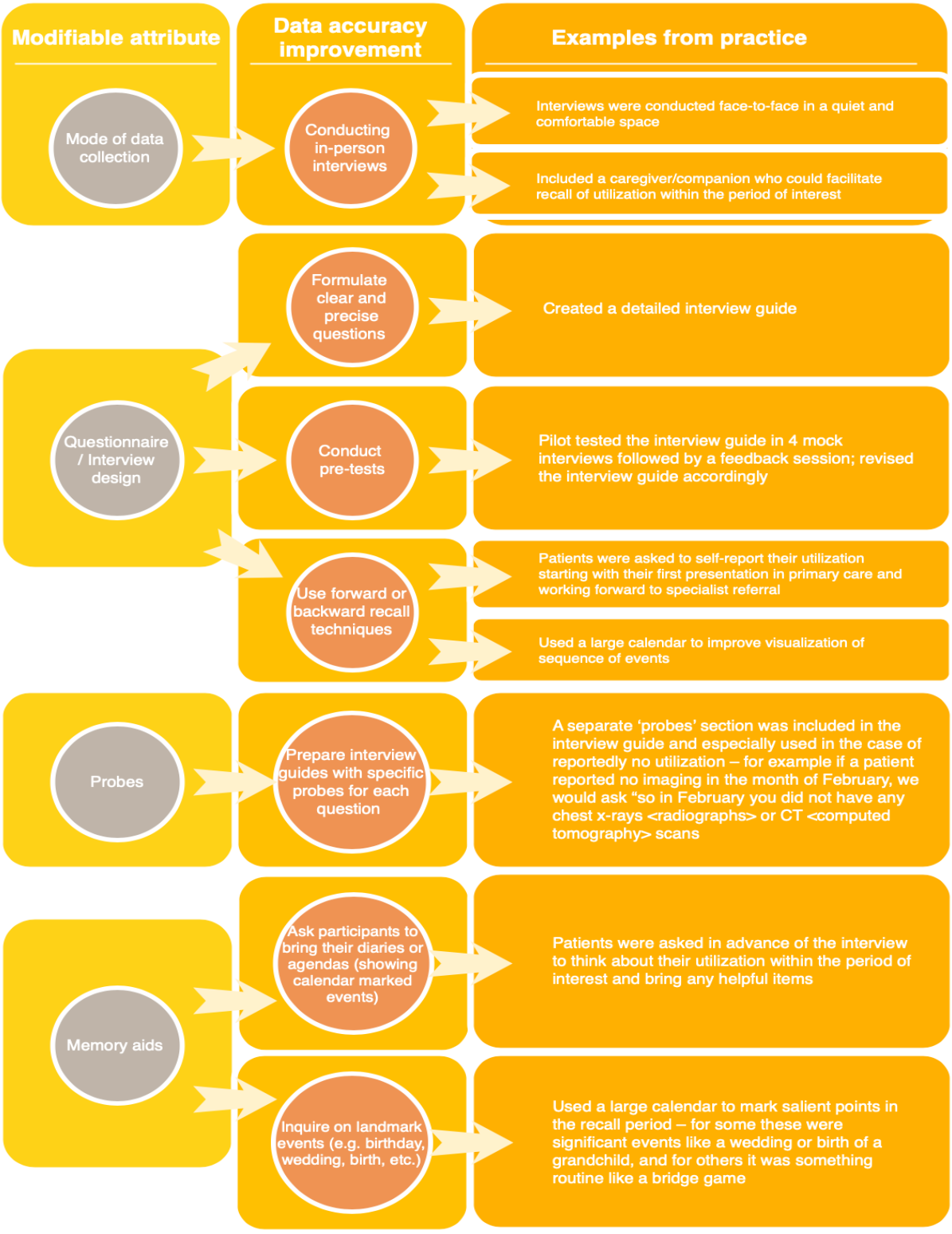

Figure 3.2 Modifiable attributes as per Bhandari & Wagner (12) and specific measures to improve data accuracy using the example of Khare et al. (31)

3.12. **Declaration**

Funding: The study discussed in this article was supported by the Fonds de recherche du Québec -Santé (FRQS) and the Unité de soutien à la stratégie de recherche axée sur le patient (SRAP).

Ethical approval: The study discussed in this article received approval from the Research Review Office of the Integrated Health and Social Services University Network for West-Central Montreal.

Conflict of interest: The authors have no conflicts of interest to declare.

3.13. **References**

1. Bath B, Lawson J, Ma D, Trask C. Self-reported use of family physician, chiropractor and physiotherapy services among adult Canadians with chronic back disorders: an observational study. BMC Health Services Research. 2018;18(1):970.

2. Willis JR, Doan QV, Gleeson M, Haskova Z, Ramulu P, Morse L, et al. Self-reported healthcare utilization by adults with diabetic retinopathy in the United States. Ophthalmic Epidemiology. 2018;25(5-6):365-72.

3. Petrou S, Murray L, Cooper P, Davidson LL. The accuracy of self-reported healthcare resource utilization in health economic studies. International journal of technology assessment in health care. 2002;18(3):705-10.

4. Killeen TK, Brady KT, Gold PB, Tyson C, Simpson KN. Comparison of self-report versus agency records of service utilization in a community sample of individuals with alcohol use disorders. Drug and Alcohol Dependence. 2004;73(2):141-7.

5. Leggett LE, Khadaroo RG, Holroyd-Leduc J, Lorenzetti DL, Hanson H, Wagg A, et al. Measuring Resource Utilization: A Systematic Review of Validated Self-Reported Questionnaires. Medicine. 2016;95(10):e2759.

6. Guzmán J, Peloso P, Bombardier C. Capturing Health Care Utilization after Occupational Low-Back Pain: Development of an Interviewer-Administered Questionnaire. Journal of Clinical Epidemiology 1999;52(5):419–27.

7. Dillman DA, Smyth JD, Christian LM. Internet, mail, and mixed-mode surveys : the tailored design method. 3rd ed. / ed. Hoboken, N.J.: Wiley & Sons; 2009.

8. Canada S. Canadian Community Health Survey - Annual Component (CCHS) 2018 [cited 2019 April 15]. Available from: http://www23.statcan.gc.ca/imdb/p2SV.pl?Function=getSurvey&SDDS=3226.

9. Geitona M, Milioni SO. Health status and access to health services of female prisoners in Greece: a cross-sectional survey. BMC Health Services Research. 2016;16:243.

10. Brusco NK, Watts JJ. Empirical evidence of recall bias for primary health care visits. BMC Health Serv Res. 2015;15:381.

11. Clarke PM, Fiebig DG, Gerdtham UG. Optimal recall length in survey design. J Health Econ. 2008;27(5):1275-84.

12. Bhandari A, Wagner T. Self-reported utilization of health care services: improving measurement and accuracy. Med Care Res Rev. 2006;63(2):217-35.

13. Seidl H, Meisinger C, Kirchberger I, Burkhardt K, Kuch B, Holle R. Validity of self-reported hospital admissions in clinical trials depends on recall period length and individual characteristics. J Eval Clin Pract. 2016;22(3):446-54.

14. Ungar WJ, Coyte PC, Pharmacy Medication Monitoring Program Advisory Board. Health Services Utilization Reporting in Respiratory Patients. Journal of Clinical Epidemiology. 1998;51(12):1335–42.

15. Schmitz MF, Russell DW, Cutrona CE. The validity of self-reports of physician use among the older population. Journal of Applied Gerontology. 2002;21(2):203-19.

16. Bellon JA, Lardelli P, Luna J, Delgado A. Validity of self reported utilisation of primary care services in an urban population in Spain. Journal of Epidemiology and Community Health. 2000;54:544-51.

17. Daly JM, Levy BT, Joshi M, Xu Y, Jogerst GJ. Patient clock drawing and accuracy of self-report compared with chart review for colorectal cancer (CRC) screening. Arch Gerontol Geriatr. 2010;50(3):341-4.

18. Reijneveld SA, Stronks K. The validity of self-reported use of health care across socioeconomic strata: A comparison of survey and registration data. International Journal of Epidemiology. 2001;30:1407-14.

19. Ritter PL, Stewart AL, Kaymaz H, Sobel DS, Block DA, Lorig KR. Self-reports of health care utilization compared to provider records. Journal of Clinical Epidemiology. 2001;54:136-41.

20. Hunger M, Schwarzkopf L, Heier M, Peters A, Holle R, KORA Study Group. Official statistics and claims data records indicate non-response and recall bias within survey-based estimates of health care utilization in the older population. BMC Health Services Research 2013;13(1).

21. Raina P, Torrance-Rynard V, Wong M, Woodward C. Agreement between Self-reported and Routinely Collected Health-care Utilization Data among Seniors. Health Services Research 2002;37(3):751-74.

22. Huttenlocher J, Hedges LV, Bradburn NM. Reports of elapsed time: bounding and rounding processes in estimation. Journal of Experimental Psychology. 1990 16(2):196-213.

23. Bradburn NM, Rips LJ, Shevell SK. Answering Autobiographical Questions: The Impact of Memory and Inference on Surveys. Science 1987;236(4798):157-61.

24. Sudman S, Bradburn NM. Effects of Time and Memory Factors on Response in Surveys. Journal of the American Statistical Association. 1973;68(344):805-15.

25. Jobe JB. Cognitive psychology and self-reports: Models and methods. Quality of Life Research. 2003;12(3):219-27.

26. Knauper B, Turner PA. Measuring health: Improving the validity of health assessments Quality of Life Research. 2003;12(Suppl. 1):81-9.

27. Roberts R, Bergstrulh EJ, Schmidt L, Jacobsen SJ. Comparison of Self-Reported and Medical Record Health Care Utilization Measures. Journal of Clinical Epidemiology. 1996;49(9):989-95.

28. Loftus EF, Fathi DC. Retrieving multiple autobiographical memories. Social Cognition 1985;3:280-95.

29. Kashner TM, Suppes T, Rush AJ, Altshuler KZ. Measuring use of outpatient care among mentally ill individuals: Acomparison of self reports and provider records. Evaluation and Program Planning. 1999;22:31-9.

30. Norrish A, North D, Kirkman P, Jackson R. Validity of self-reported hospital admission in a prospective study. American Journal of Epidemiology. 1994;140(10):938-42.

31. Khare S, Vedel I, Bartlett G. Defining lung cancer diagnostic pathways in the primary care setting in Montréal , Québec. Innov Aging. 2017;1(Suppl 1):462.

4. Chapter 4: Lung cancer pre-diagnostic pathways from first presentation to specialist referral (Manuscript 2)

4.1. Preamble

In the previous chapter, I identified strategies to reduce recall bias which was the first objective of my thesis. To address the remaining four objectives of my thesis, I used an explanatory sequential mixed-methods design employed in three phases: a quantitative phase (objectives 2 and 3, Chapter 4), a qualitative phase (objective 4, Chapter 5), and a merging of quantitative and qualitative findings phase (objective 5, Chapter 6).

In this chapter, I address objectives 2 and 3 of my thesis:

- To identify groups of lung cancer patients with similar pre-diagnostic pathways based on healthcare utilization patterns in the primary care interval (i.e. from first presentation in primary care with signs and symptoms suspicious of lung cancer to referral to a respiratory specialist) (objective 2),
- To describe each pre-diagnostic pathway group by demographic, patient-, and tumor-related characteristics as well as sequence of healthcare utilization activities (objective 3).

I present a retrospective cohort study where I identify two groups of lung cancer patients with similar pre-diagnostic pathways (objective 2). I further describe each group based on the distribution of several characteristics and sequence of utilization activities (objective 3), findings that suggest several potential sources of delay. This is the first study in Canada to identify and describe lung cancer pre-diagnostic pathways and identify potential sources of delay. This manuscript has been submitted to the journal Current Oncology.

Khare SR, Madathil SA, Batist G, Peter Brojde Lung Cancer Group, Vedel I. Lung cancer pre-diagnostic pathways from first presentation to specialist referral. Submitted to Current Oncology in December 2020.

All ethics documents and approval are in thesis Appendix 1. This study involved patient interviews to collect self-reported healthcare utilization data; the structured interview guide is included as supplemental material at the end of this chapter (in English) and in thesis Appendix 2 (in French).

4.2. **TITLE PAGE**

TITLE:

Lung cancer pre-diagnostic pathways from first presentation to specialist referral

AUTHORS:

1. S.R. Khare* MScN, MBA
2. S.A. Madathil[†] BDS, PhD
3. G. Batist[‡] MD
4. Peter Brojde Lung Cancer Group[§]

G. Kasymjanova MD, F. Manceau RN BScN, T. Jesion RN MScN, C. Pepe MD, L. Sakr MD, D. Small MD, V. Cohen MD, T. Jagoe MD PhD, J. Agulnik MD

5. I. Vedel*[‖] MD, PhD

* Department of Family Medicine, Faculty of Medicine, McGill University, Montreal, QC, Canada

[†] Division of Oral and Maxillofacial Surgery, Faculty of Dentistry, McGill University, Montreal, QC, Canada

[‡] Department of Oncology, Segal Cancer Centre, Jewish General Hospital, Montreal, QC, Canada

[§] Peter Brojde Lung Cancer Centre, Jewish General Hospital, Montreal, QC, Canada

[‖] Lady Davis Institute, Jewish General Hospital, Montreal, QC, Canada

RUNNING HEADER:

LUNG CANCER PRE-DIAGNOSTIC PATHWAYS

CORRESPONDING AUTHOR:

Satya Rashi Khare

5858 Chemin de la Côte-des-Neiges, Suite 300, Montreal, QC, Canada, H3S 1Z1

satya.khare@mail.mcgill.ca

(tel) 514-243-4322

(fax) 514-398-4202

FUNDING SUPPORT:

This study received funding support from the Fonds de recherche du Québec -Santé (FRQS) and the Strategy for Patient-Oriented Research (SPOR).

WORD COUNT: 3118

FIGURES AND TABLES: 9

4.3. **ABSTRACT**

Background: Lung cancer is often diagnosed at a late stage with high associated mortality. Timely diagnosis depends on timely referral to a respiratory specialist however in Canada little is known about how patients move through primary care to get to a respiratory specialist. Accordingly, we aimed to identify and describe lung cancer pre-diagnostic pathways in primary care from first presentation to referral.

Methods: In this retrospective cohort study patients with primary lung cancer were recruited using consecutive sampling (n=50) from a lung cancer centre in Montréal, Québec. Data on healthcare service utilization in primary care were collected from chart reviews and structured patient interviews and analyzed using latent class analysis to identify groups of patients with similar pre-diagnostic pathways. Each group was described based on patient- and tumor-related characteristics, and sequence of utilization activities.

Results: 68% of patients followed a pathway where family physician (FP) visits were dominant ('FP centric') and 32% followed a pathway where walk-in clinic and emergency department (ED) visits were dominant ('ED centric'). Time to referral in the FP group was double that of the ED group [45 days (IQR 12-111) vs 22 (IQR 5-69)] with more advanced disease (65% vs 50%). In the FP group, 29% of patients saw their FP 3 times or more before being referred and 41% had an ED visit.

Conclusions: Our findings may reflect the challenge of diagnosing lung cancer in primary care, missed opportunities for earlier diagnosis, and a lack of integration between primary and specialist care.

Keywords: primary care, lung cancer, diagnostic pathways, early diagnosis, delay

4.4. **INTRODUCTION**

In Canada, lung cancer represents 13% of new cancer cases and 26% of cancer deaths making it the most commonly diagnosed cancer and the leading cause of cancer related mortality.(1) With a 5-year survival of 17%, lung cancer kills more people than all other common cancers combined.(2) The most important prognostic factor is stage at diagnosis with treatment being more successful in early stage disease. However, 70% of Canadians with lung cancer are diagnosed with late stage disease(3) emphasizing a need to improve timely diagnosis.

Most lung cancer patients initially present to their family physician with symptoms(4, 5) making the primary care interval – first presentation with signs and symptoms suggestive of lung cancer to referral to a respiratory specialist – a key component of the diagnostic interval.(6) Despite this, Canadian research on reducing time to diagnosis has been concentrated in secondary care – from referral to definitive diagnosis – leading to an evidence gap on delays in timely referral.(7) This is concerning as studies in countries with similar healthcare systems (i.e. gatekeeper systems) have shown longer delays in primary care,(5) some as much as four times greater than those observed in secondary care.(8) A major reason is that common presenting symptoms in primary care, like cough, have low positive predictive values for lung cancer while symptoms with high positive predictive values, like hemoptysis, are rare.(9, 10)

Importantly, rapid diagnosis can be associated with worse survival. Known as the waiting time paradox, late stage disease may present serious symptoms that lead to quicker investigation and shortened diagnostic times but also poor outcomes.(11) This complicated association between timely diagnosis and survival suggests time to diagnosis may not be as important as the path to diagnosis which should be without unnecessary delays. In fact, variation in how patients

are managed in primary care has been suggested to contribute to international cancer survival differences.(12)

Among Canadian provinces, Québec has the highest lung cancer incidence and mortality rates(13) yet there are no studies on lung cancer pre-diagnostic pathways in primary care and, as a result, no province wide primary care initiatives aimed at reducing unnecessary delays. The lack of knowledge in Canada, especially Québec, on how lung cancer patients move through primary care has made it difficult to inform practice improvements. In order to ground improvement initiatives in local contexts, extensive research in primary care is needed.

In this study, we aimed to gain an in-depth understanding of lung cancer pre-diagnostic pathways in primary care in Québec in order to inform potential improvement initiatives. First, we identified different pathways by clustering patients with similar patterns of healthcare utilization in the primary care interval into distinct groups. Second, we examined patient and clinical characteristics of each group as well as sequence of healthcare utilization activities. This detailed understanding was then used to suggest several improvement strategies.

4.5. **METHODS**

4.5.1. Study design and population

This retrospective cohort study took place at the Peter Brojde Lung Cancer Centre (PBLCC) located in a large teaching hospital in Montréal. The clinic serves approximately 200 new lung cancer patients annually and maintains a detailed patient registry. We included patients diagnosed with primary lung cancer between May 1, 2015 and October 31, 2017. We excluded patients if they were actively followed in pulmonology for another respiratory condition at the time of referral or if their cancer was discovered incidentally; in both scenarios the pre-

diagnostic pathway generally does not involve primary care. We also excluded patients who were presenting for a second opinion due to incomplete data within the study setting.

We recruited patients by consecutive sampling. A list of eligible patients was pulled from the PBLCC registry and contacted by trained research assistants and nurses during a clinic appointment or by phone to ensure the most exhaustive sample. Two research assistants were present at every clinic (five per week) to approach patients in person and two nurses made several attempts to contact patients by phone. For patients who agreed to participate, we further extended the invite to a family member who was knowledgeable about use of healthcare services during the primary care interval.

4.5.2. Data collection

In accordance with methodological recommendations for early cancer diagnosis research,(6) we used three data sources: the PBLCC registry was used to collect demographic and tumor-related data, patient charts were used to collect documented healthcare service utilization data during the primary care interval, and patient interviews were used to complete the account of pre-diagnostic activities.

We collected the following data from the registry: age at diagnosis, sex, referral source, referral date, diagnosis date, and stage of disease. Stages I and II were categorized as early, stage III as locoregional, and stage IV as advanced.(14) Additionally, postal codes were used to convert to an area-based deprivation score for each patient.(15)

We collected the following utilization data from chart reviews and structured patient interviews: number of family physician visits, walk-in clinic visits, emergency department visits, hospitalizations, chest radiographs, computed tomography scans, and non-respiratory specialist

visits. Additionally, presenting symptoms, comorbidities, and smoking history were abstracted from charts. Date of first presentation in primary care, set at a maximum of one year prior to the date of referral, was collected at the interview. The purpose of using multiple data sources was twofold. First, secondary care charts do not have complete data on primary care visits nor are they detailed enough to discern complex time points such as date of first presentation.(6) This necessitated patient interviews. Second, validation studies of self-reported healthcare utilization emphasize under-reporting especially in the context of primary care visits.(16) By cross-verifying chart and interview data, under-reporting was mitigated and data were more complete.

Patient charts were comprehensively reviewed from one year prior to the referral date to one-month post-diagnosis by a researcher with extensive chart review experience in the study setting (SK). Information pertaining to the primary care interval was documented as a timeline in ascending order (Figure 4.1). All data from the chart review were verified during the interviews.

CHART REVIEW – <PATIENT IDENTIFIER>

Date of referral: Aug 28, 2017
Date of diagnosis: Sept 13, 2017

July 21, 2017: CXR (ordered by FP) – right pleural effusion + nodularity right upper lobe, CT recommended

Aug 25, 2017: CT chest, upper abd (ordered by FP) – significant neoplastic process arising from right lung + associated right pleural effusion +/- obstructive pneumonitis

Aug 28, 2017: Referred from FP to respirology

Sept 3, 2017: Respirology consult note states 'persistent dry cough since Dec 2016 initially attributed to URTI + renovation work at home – SOBOE (while playing tennis) almost a month ago – also mentions intermittent nightsweats and low energy for the past few months + 8 pound weight loss in the last 6 months

Past Medical History = Glaucoma
Medications = Travoprost - timolol
Smoking history = 15 pack-years

CXR: chest x-ray; FP: family physician; CT: computed tomography; abd: abdomen; URTI: upper respiratory tract infection; SOBOE: shortness of breath on exertion; pack-years: packs per day x number of years smoked

Figure 4.1 Chart review conducted on a patient from one year prior to their referral date to one month after their diagnosis date.

Patient interviews were conducted in a private room at the clinic or the patient's home by two trained research assistants who pilot tested the interview guide (Supplemental File 1: Structured interview guide) to ensure clarity and precision of questions. Before the interview, we gave patients a cue card (Figure 4.2) with information on the data that would be collected.

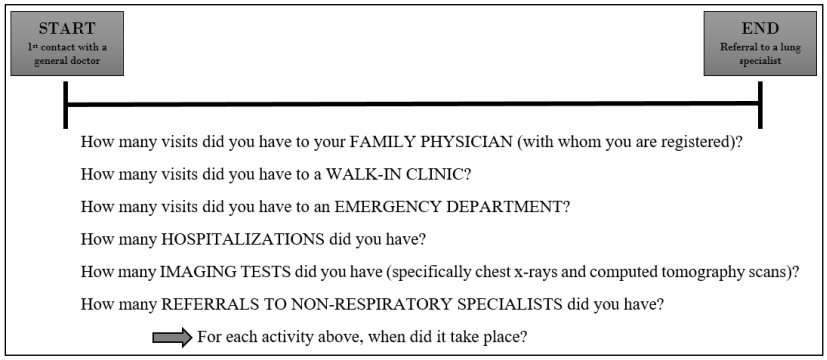

Figure 4.2 Cue card given to patients and caregivers in advance of the interview

During the interview, imaging data (date and time stamped documents) from the chart review were used to ground patients in the time period of interest. Several measures were used to improve event recall including memory aids, forward recall, and use of large calendar sheets for collaborative data recording. These measures have been described in detail elsewhere.(17) As an example of the additional data provided, Figure 4.3 shows a summary of interview data for the patient whose chart review is shown in Figure 4.1.

STRUCTURED INTERVIEW – <PATIENT IDENTIFIER>

Date of first presentation: Dec 15, 2016
Presenting symptom: cough

Dec, 2016: 1 FP visit – dry cough

<no visits in Jan & Feb, 2017>

March, 2017: 1 FP visit – persistent cough

April, 2017: 1 FP visit – persistent cough

May, 2017: 1 FP visit – persistent cough, FP suggested cough syrup

June, 2017: 1 FP visit, Rx budesonide/formoterol

July, 2017: CXR + 1 FP visit for CXR f/u

Aug, 2017: CT + 1 FP visit for CT f/u (referred Aug 28)

Utilization summary: 7 FP visits, 1 CXR, 1 CT

FP: family physician; Rx: prescription; CXR: chest x-ray; f/u: follow-up; CT: computed tomography

Figure 4.3 Summary of interview data shown as number of healthcare utilization activities by month

4.5.3. Statistical analysis

We analyzed healthcare utilization data using latent class analysis (LCA), a model-based approach to clustering that statistically partitions a heterogeneous population (lung cancer patients) into homogeneous subgroups (pre-diagnostic pathways) according to response patterns to observed variables (utilization activities).(18) The subgroups are latent classes that represent unobservable categorical constructs inferred indirectly through observed variables. Therefore, this analysis is most useful when the construct of interest is unobservable, unmeasurable, and unknown, as is the case with pre-diagnostic pathway groups.(19)

As the distribution of utilization variables ranged from 0-2, we dichotomized them as none (0) verses any (1+). In the modeling process, we started with a one-class solution and added classes in a progressive fashion up to four classes. We evaluated the resulting models statistically (model fit) using the Akaike information criterion (AIC) and substantively (model usefulness) according to knowledge of the construct being modelled.(20) This was completed by family medicine researchers, cancer researchers, an oncologist, and a cancer epidemiologist over several workshops. We then described each class in the final model based on the distribution of demographic, patient-, and tumor-related characteristics. Finally, we performed an event sequence analysis where utilization activities were presented as events occurring at a given position thus showing their order.(21) All analyses were conducted using R Version 3.5.

4.5.4. Ethics approval

The Research Review Office of the Integrated Health and Social Services University Network for West-Central Montréal granted ethics approval.

4.6. **RESULTS**

We recruited 62 patients between June and December 2017; 12 were later found to be ineligible leaving a total of 50 patients included in the study (Figure 4.4).

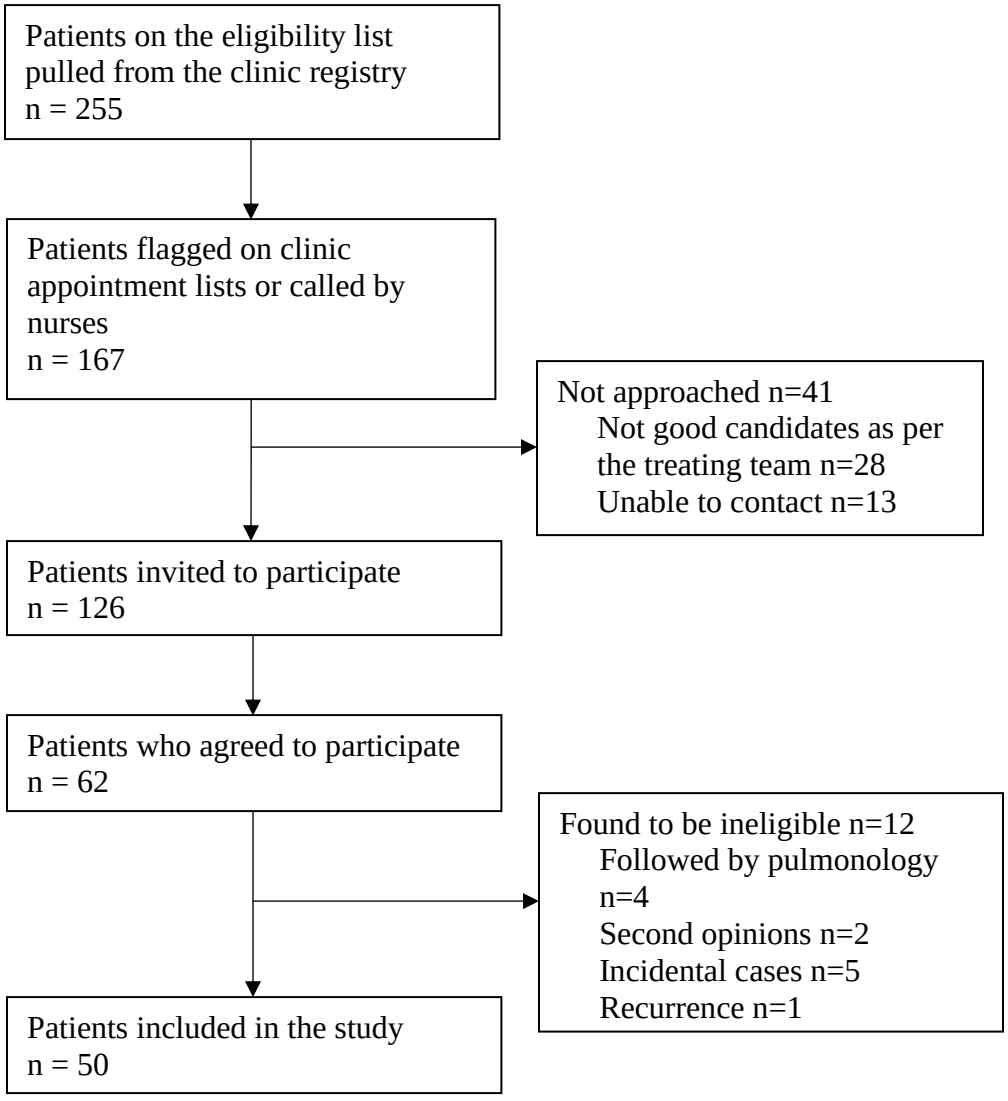

Figure 4.4 Flow of participant recruitment from the Peter Brojde Lung Cancer Centre

Patient characteristics are reported in Table 4.1. 90% of cases were non-small cell lung cancer, 36% had no comorbid conditions, 28% were never-smokers, and 60% were advanced

stage. Characteristics of the study sample were similar to registry patient characteristics except for smoking status where the study sample had almost double the number of never-smokers.(14)

The total diagnostic interval was a median of 82 days (IQR 37-180). The primary care interval was a median of 35 days (IQR 9-101) and the secondary care interval was a median of 27 days (IQR 11-65).

Table 4.1 Characteristics of patients included in the study

Characteristic	**Total median (IQR) of patients* n = 50**
Age at diagnosis, yr	66 (57.2-76.7)
Sex, female, no. (%)	28 (56)
Smoking history, pack-yr	20.7 (0-42)
No. of comorbidities	1 (0-2)
Material deprivation index score†	2 (1-4)
Social deprivation index score†	4 (2-5)
Primary care interval time, d	35 (9-100.7)
Referral source, no. (%)	
Family physician	18 (36)
Emergency department	26 (52)
Non-respiratory specialist	6 (12)
Presenting symptoms, no. (%)	
Cough	21 (42)
Shortness of breath	11 (22)
Hemoptysis	3 (6)
Chest pain	3 (6)
Back pain	4 (8)
Other‡	8 (16)
Stage of disease, no. (%)	
Early	8 (16)
Locoregional	12 (24)
Advanced	30 (60)

Note: IQR = interquartile range
*Unless stated otherwise
†Classified in quintiles from least deprived (1) to most deprived (5)
‡Includes weight loss, general weakness, paresthesia, abdominal pain, sinusitis, jugular vein thrombosis, and hoarseness

4.6.1. Identifying pre-diagnostic pathways

We identified a 2-class model as the best fit model according to statistical and substantive criteria.(20) AIC pointed to a 2- or 3-class model as optimal (Table 4.2). Upon interpretation for

meaning, the 3-class model contained both classes found in the 2-class model with a small third class (n=6) that was not found to be meaningful after expert review.

Table 4.2 Statistical comparison of latent class models

Latent class models	AIC
1-class	334.5149
2-class	323.4714
3-class	322.1228
4-class	329.7299

The final class conditional probabilities are presented in Figure 4.5. With a 68% (n=34) prevalence, class 1 had 0.95 probability of family physician visits, 0.42 probability of emergency department visits, 0.04 probability of walk-in clinic visits, and zero probability of hospitalization. Given the high probability of at least one family physician visit, we labelled this class as a "Family Physician (FP) Centric" pre-diagnostic pathway group.

With a 32% (n=16) prevalence, class 2 had 0.28 probability of family physician visits, 1.0 probability of emergency department visits, 0.5 probability of walk-in clinic visits, and 0.17 probability of hospitalization. Given the high probability of at least one emergency department visit, we labelled this class as an "Emergency Department (ED) Centric" pre-diagnostic pathway group.

Probability of imaging and non-respiratory specialist visits did not meaningfully differentiate the classes.

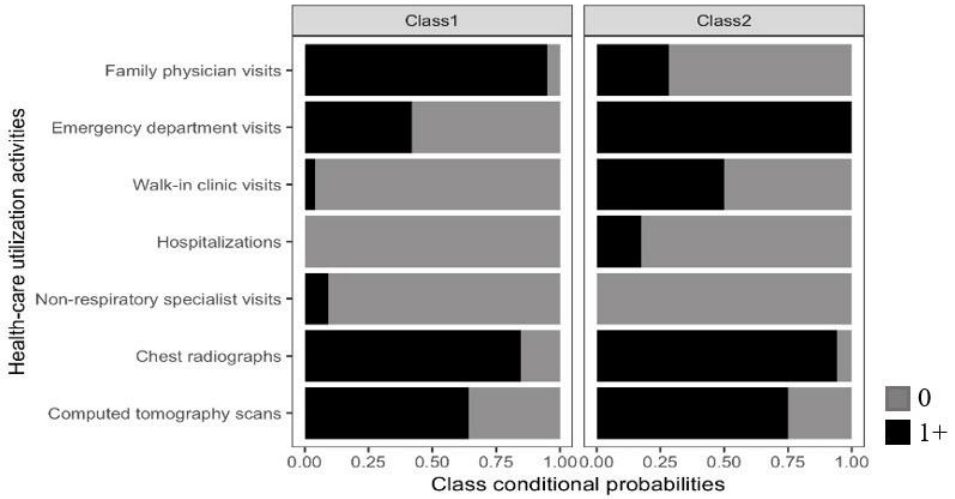

Figure 4.5 Class conditional probabilities for the final 2-class model from the latent class analysis

4.6.2. Characteristics of patients by pre-diagnostic pathway

Patient characteristics by group are reported in Table 4.3.

The FP centric group had a primary care interval time of 45 days (IQR 12-111) and 65% of patients had advanced stage disease. In this group, 50% of patients were referred to a respiratory specialist by their FP and 38% were referred from the ED. The most common presenting symptoms were cough and shortness of breath.

The ED centric group had a primary care interval time of 22 days (IQR 5-69)] and 50% of patients had advanced stage disease. In this group, 6% of patients were referred to a respiratory specialist by their FP and 81% were referred from the ED. The most common presenting symptoms were cough and those categorized as ‘other’ including hoarseness and weight loss. Other demographic and patient related characteristics were similar between the groups.

Table 4.3 Characteristics of patients stratified by FP centric and ED centric groups

Characteristic	FP centric; median (IQR) of patients* n=34	ED centric; median (IQR) of patients* n=16
Age at diagnosis, yr	65 (58.5-76.7)	67.5 (56.5-72)
Sex, female, no. (%)	18 (52.9)	10 (62.5)
Smoking history, pack-yr	20 (0.4-35)	27.5 (0-49.2)
No. of comorbidities	1 (0.2-2)	0 (0-2)
Material deprivation index score†	2 (1-3.7)	1 (1-3.5)
Social deprivation index score†	4 (2-5)	4 (1.5-5)
Primary care interval time, d	45 (11.7-111.2)	22 (4.7-69.5)
Referral source, no. (%)		
Family physician	17 (50)	1 (6.2)
Emergency department	13 (38.2)	13 (81.2)
Non-respiratory specialist	4 (11.6)	2 (12.4)
Presenting symptoms, no. (%)		
Cough	16 (47.1)	5 (31.2)
Shortness of breath	8 (23.5)	3 (18.8)
Hemoptysis	2 (5.9)	1 (6.2)
Chest pain	2 (5.9)	1 (6.2)
Back pain	3 (8.8)	1 (6.2)
Other‡	3 (8.8)	5 (31.2)
Stage of disease, no. (%)		
Early	5 (14.7)	3 (18.8)
Locoregional	7 (20.6)	5 (31.2)
Advanced	22 (64.7)	8 (50)

Note: IQR = interquartile range
*Unless stated otherwise
†Classified in quintiles from least deprived (1) to most deprived (5)
‡Includes weight loss, general weakness, paresthesia, abdominal pain, sinusitis, jugular vein thrombosis, and hoarseness

4.6.3. Sequence of events within pre-diagnostic pathways

The sequence of utilization activities within each patient's pathway is shown in Figure 4.6 by group. In the FP centric group, 88% of patients started their pathway with a visit to their FP. 62% of patients had imaging after 1-2 FP visits. Throughout their entire pathway, 29% of patients saw their FP 3 times or more before being referred and 41% of patients had an ED visit. In this group, 68% of pathways had a sequence of events that differed from all other pathways (i.e. they were unique).

In the ED centric group, 50% of patients started their pathway with a visit to the ED and 44% of patients started their pathway with a visit to a walk-in clinic. All patients had imaging after 1-

2 visits to the ED or walk-in clinic and all patients had at least 1 ED visit in their pathway. In this group, none of the pathways shared the same sequence of events.

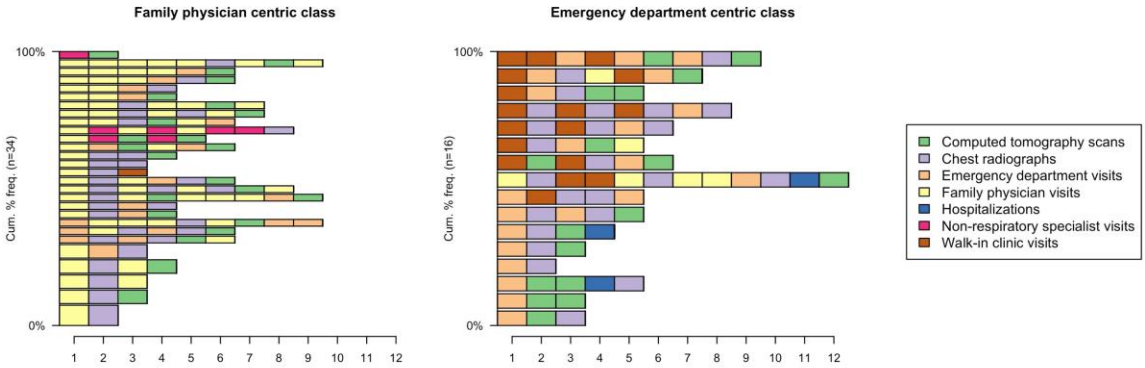

Figure 4.6 Sequence of utilization activities for each patient showing the order of specific events within the pathway, stratified by group

4.7. **DISCUSSION**

This study presents findings on how lung cancer patients move through primary care in a province with high lung cancer incidence and mortality rates in order to inform early diagnosis initiatives. Median time in the primary care interval was not much greater than the secondary care interval (35 days vs 27) however there was large variation (9-101 days). Over 2/3 of patients followed a pathway where FP visits were dominant (FP centric) and less than 1/3 followed a pathway where walk-in clinic and ED visits were dominant (ED centric). The FP centric group had a primary care interval time that was double that of the ED centric group [45 days (IQR 12-111) vs 22 (IQR 5-69)] and more advanced stage disease (65% vs 50%).

A large UK study similarly showed that patients who saw their FP's prior to diagnosis had significantly longer diagnostic intervals than those who did not.(22) In our study we found that while 62% of patients in the FP centric group had imaging after 1-2 FP visits, 29% visited their FP 3 times or more before being referred to a respiratory specialist. Given that patients in this

group mostly presented with cough and shortness of breath, this may be a reflection of the diagnostic difficulty associated with lung cancer(23) owing in part to non-specific symptoms.(24) Additionally, chest radiograph is the principal diagnostic test in primary care but has been shown to have a high false negative rate for lung cancer.(25) Alternatively, this could represent missed opportunities for earlier diagnosis with disease progression over time leading to the higher proportion of advanced stage disease found in this group.(26) In either case, more education in primary care on common presentations of lung cancer patients, including the risk threshold for referral, may contribute to reduced delays. One method could be significant event audits where performance feedback is used to prompt FP's to review their diagnostic practice and identify improvement opportunities.(27) Lessons learned could also be shared between primary care practices.

Despite the FP centric group being dominated by FP visits, there was still moderate use of the ED. In this group, 38% of patients were referred to a respiratory specialist from the ED with 41% of patients visiting the ED at least once in their pathway. This could be linked to higher symptom severity or FP's may be using the ED as a means for quicker access to a specialist due to a lack of integration between primary and specialist care.(28) Rapid investigation clinics were implemented in Québec to fast-track diagnosis of patients with suspected lung cancer however our study suggests that these are not being used as intended.(29) Québec also recently implemented an electronic referral system to improve access to specialists. While an impact evaluation has not yet been done, electronic consultation services where FP's can discuss cases with respiratory specialists before referral could further promote integration and reduce delays.(30)

The ED centric group in our study likely represents patients without a FP who use walk-in clinics and ED's for their primary care needs. Nationally, Québec has the highest number of persons without a FP.(31) Walk-in clinics were intended to reduce ED burden, however, our study found that all patients in this group had an ED visit. This suggests that walk-in clinics may be ineffective at reducing ED visits and supports the need for improved access to a regular source of care. More nurse practitioners in the primary care setting could help fill the gap as Québec currently employs the lowest number in Canada.(32)

Importantly, increasing the number of primary care practitioners alone will likely not resolve access issues. We found a considerably shorter primary care interval time in the ED centric group that suggests greater care efficiency among patients who present at the ED. In accordance with the waiting time paradox,(11) reduced time to referral could also reflect more advanced disease however patients in this group had more early/locoregional disease. As such, there is a greater likelihood that direct access to diagnostic imaging and consultative services in the ED led to more timely referral. To decrease the primary care interval time in the community, primary care practitioners should have more direct and timely access to these services.

Lastly, we found that in both groups most pre-diagnostic pathways were unique. Although it can be argued that pathways will vary depending on clinical presentation and medical history, this may also indicate a need for standardization. Given there are no referral guidelines in Québec for suspected lung cancer in primary care, an evidence-based guideline developed by Cancer Care Ontario could be adapted for local use.(33)

To further inform improvement initiatives, qualitative inquiry to understand what contributes to the emergence of these pathways will be an important next step.

4.7.1. Strengths and limitations

We present a single centre study based on a small sample of lung cancer patients from an urban setting. Given these constraints, we acknowledge generalizability concerns. Although provincial administrative healthcare databases would have allowed a broader sample, they lacked clinical data pertinent to our study (e.g. smoking history, presenting symptoms, disease stage) as well as granular data necessary to capture the complexity of cancer diagnostic pathways. As such, we used alternative data sources (clinic charts and patient self-report) – reasonable methods for any jurisdiction where administrative data may be incomplete or inaccessible. Additionally, we followed international standardized guidelines both in our study design and definitions (date of first presentation, date of referral, date of diagnosis, primary care interval) to ensure consistency with early cancer diagnosis literature.(6)

Our sample demographics were similar to registry patient characteristics except for an over-representation of never-smokers which may have been due to survival bias; patients diagnosed in 2015 had to survive two years to participate and better lung cancer survival has been reported among never-smokers compared to ever-smokers.(34) There may have also been selection bias as the participation rate was 30% of the eligible sample despite efforts to contact patients in clinic and by phone. Similar recruitment challenges among lung cancer patients have been widely reported.(35, 36) Despite this, model convergence was reached indicating good model-data fit and characteristics of the pre-diagnostic pathway groups coincided with the literature. Finally, recall periods varied depending on length of the primary care interval and diagnosis date leading to potential recall bias. Several measures were used to mitigate this including triangulation of data.

Notwithstanding these limitations, our study provides important evidence in an under-researched area of understanding cancer pathways in primary care.

4.8. **CONCLUSION**

Our study is the first in-depth look at the primary care interval of the lung cancer diagnostic pathway in Québec and contributes to a dearth of evidence in Canada on lung cancer diagnostic delays. We present several potential sources of delay and suggest associated initiatives to reduce avoidable delays in primary care. These include significant event audits, electronic consultation services, and referral guidelines.

4.8.1. Acknowledgements

This study received funding support from the Fonds de recherche du Québec -Santé (FRQS) and the Strategy for Patient-Oriented Research (SPOR). Funding sources were not involved in any aspect of the work.

4.8.2. Conflict of Interest Disclosure

We have read and understood Current Oncology's policy on disclosing conflicts of interest and declare that we have none.

4.9. **REFERENCES**

1. Canadian Cancer Society. Lung cancer statistics Toronto, ON: Canadian Cancer Society 2019 [cited 2019 May 14]. Available from: http://www.cancer.ca/en/cancer-information/cancer-type/lung/statistics/?region=qc.

2. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2017 Toronto, ON: Canadian Cancer Society; 2017 [cited 2019 March 11]. Available from: cancer.ca/Canadian-CancerStatistics-2017-EN.pdf.

3. Canadian Cancer Statistics Advisory Committee. Canadian Cancer Statistics 2018 Toronto, ON: Canadian Cancer Society; 2018 [cited 2019 May 14]. Available from: cancer.ca/Canadian-Cancer-Statistics-2018-EN.

4. Allgar VL, Neal RD. General practictioners' management of cancer in England: secondary analysis of data from the National Survey of NHS Patients-Cancer. Eur J Cancer Care (Engl). 2005;14(5):409-16.

5. Barrett J, Hamilton W. Pathways to the diagnosis of lung cancer in the UK: a cohort study. BMC Fam Pract. 2008;9:31.

6. Weller D, Vedsted P, Rubin G, Walter FM, Emery J, Scott S, et al. The Aarhus statement: improving design and reporting of studies on early cancer diagnosis. British journal of cancer. 2012;106(7):1262-7.

7. Rankin NM, McGregor D, Stone E, Butow PN, Young JM, White K, et al. Evidence-practice gaps in lung cancer: A scoping review. Eur J Cancer Care (Engl). 2018;27(2):e12588.

8. Koyi H, Hillerdal G, Branden E. Patient's and doctors' delays in the diagnosis of chest tumors. Lung Cancer. 2002;35(1):53-7.

9. Rubin G, Berendsen A, Crawford SM, Dommett R, Earle C, Emery J, et al. The expanding role of primary care in cancer control. The Lancet Oncology. 2015;16(12):1231-72.

10. Shim J, Brindle L, Simon M, George S. A systematic review of symptomatic diagnosis of lung cancer. Family Practice. 2014;31(2):137-48.

11. Olsson JK, Schultz EM, Gould MK. Timeliness of care in patients with lung cancer: a systematic review. Thorax. 2009;64(9):749-56.

12. Rose PW, Rubin G, Perera-Salazar R, Almberg SS, Barisic A, Dawes M, et al. Explaining variation in cancer survival between 11 jurisdictions in the International Cancer Benchmarking Partnership: a primary care vignette survey. BMJ open. 2015;5(5):e007212.

13. Canadian Partnership Against Cancer. The 2015 Cancer System Performance Report. System Performance Reports Jun ed. Toronto, ON: Canadian Partnership Against Cancer; 2015. p. 1-161.

14. Kasymjanova G, Small D, Cohen V, Jagoe RT, Batist G, Sateren W, et al. Lung cancer care trajectory at a Canadian centre: an evaluation of how wait times affect clinical outcomes. Current oncology (Toronto, Ont). 2017;24(5):302-9.

15. Pampalon R, Hamel D, Gamache P. Health inequalities in urban and rural Canada: comparing inequalities in survival according to an individual and area-based deprivation index. Health & Place. 2010;16(2):416-20.

16. Brusco NK, Watts JJ. Empirical evidence of recall bias for primary health care visits. BMC Health Services Research [Internet]. 2015; 15(1):[381 p.].

17. Khare SR, Vedel I. Recall bias and reduction measures: an example in primary health care service utilization. Family Practice. 2019;36(5):672-6.

18. Flaherty BP, Kiff CJ. Latent class and latent profile models. In: Cooper H, editor. APA Handbook of Research Methods in Psychology: Vol 3 Data Analysis and Research Publication: American Psychological Association; 2012. p. 391-404.

19. UCLA: Statistical Consulting Group. Latent Class Analysis in Mplus California, Los Angeles: Statistical Computing Seminars 2016 [cited 2020 March 15]. Available from: http://www.ats.ucla.edu/stat/mplus/seminars/lca/.

20. Hagenaars JA, McCutcheon AL, (eds). Applied Latent Class Analysis. Cambridge: Cambridge University Press; 2002.

21. Brzinsky-Fay C, Kohler U. New Developments in Sequence Analysis. SMR/Sociological Methods & Research. 2010;38(3):359-64.

22. Allgar VL, Neal RD. Delays in the diagnosis of six cancers: analysis of data from the National Survey of NHS Patients: Cancer. Br J Cancer. 2005;92(11):1959-70.

23. Lyratzopoulos G, Wardle J, Rubin G. Rethinking diagnostic delay in cancer: how difficult is the diagnosis? BMJ. 2014;349:g7400.

24. 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;60(12):1059-65.

25. Stapley S, Sharp D, W. H. Negative chest X-rays in primary care patients with lung cancer. Br J Gen Pract. 2006;56:570-3.

26. Yap S, Goldsbury D, Yap ML, Yuill S, Rankin N, Weber M, et al. Patterns of care and emergency presentations for people with non-small cell lung cancer in New South Wales, Australia: A population-based study. Lung Cancer. 2018;122:171-9.

27. Mitchell ED, Rubin G, Macleod U. Understanding diagnosis of lung cancer in primary care: qualitative synthesis of significant event audit reports. The British journal of general practice : the journal of the Royal College of General Practitioners. 2013;63(606):37-46.

28. Grunfeld E. It takes a team: CanIMPACT: Canadian Team to Improve Community-Based Cancer Care along the Continuum. Canadian family physician Medecin de famille canadien. 2016;62(10):781-2.

29. Ezer N, Navasakulpong A, Schwartzman K, Ofiara L, Gonzalez AV. Impact of rapid investigation clinic on timeliness of lung cancer diagnosis and treatment. BMC pulmonary medicine. 2017;17(1):178.

30. Keely E, Liddy C. Transforming the specialist referral and consultation process in Canada. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2019;191(15):E408-E9.

31. Statistics Canada. Health fact sheet: Primary health care providers, 2016: Government of Canada 2017 [cited 2019 Dec 19]. Available from: https://www150.statcan.gc.ca/n1/pub/82-625-x/2017001/article/54863-eng.htm.

32. Canadian Institute for Health Information. Canada's Health Care Providers: Provincial Profiles, 2008 to 2017 - Data Tables: CIHI; 2019 [cited 2020 Feb 13]. Available from: https://www.cihi.ca/en/access-data-reports/results?f%5B0%5D=field_primary_theme%3A2047&f%5B1%5D=field_professions%3A2010.

33. Del Giudice ME, Young SM, Vella ET, Ash M, Bansal P, Robinson A, et al. Guideline for referral of patients with suspected lung cancer by family physicians and other primary care providers. Can Fam Physician. 2014;60(8):711-6, e376-82.

34. Casal-Mouriño A, Valdés L, Barros-Dios JM, Ruano-Ravina A. Lung cancer survival among never smokers. Cancer Letters. 2019;451:142-9.

35. Kjær TK, Mellemgaard A, Stensøe Oksen M, Andreassen Rix B, Karlsen R, Johansen C, et al. Recruiting newly referred lung cancer patients to a patient navigator intervention (PACO): lessons learnt from a pilot study. Acta oncologica (Stockholm, Sweden). 2017;56(2):335-41.

36. Spiro SG, Gower NH, Facchini FM, Rudd RM, Evans MT. Recruitment of patients with lung cancer into a randomised clinical trial: experience at two centres. Thorax. 2000;55(6):463-5.

4.10. Supplemental File 1: Structured interview guide

PART I

Note: Although this is a structured interview with specific data points, the interview itself will be conversational to facilitate recall of prior activities by 'talking-through' the pre-diagnostic pathway. The specific technique will be forward recall – start with first presentation in primary care and think forward to date of referral. A large calendar will be used to facilitate the interview and document the data.

The specific activities of interest include: *1) family physician visits (with whom the patient is registered), 2) visits to a walk-in clinic, 3) visits to an emergency department, 4) hospitalizations, 5) imaging tests (specifically CXR and CT), and 6) referrals to non-respiratory specialists.*

INITIATION:

1. Remind the participant(s) of the goals of the interview, projected length, and general topics of the interview.
    a. Suggested preamble: You were referred to a lung specialist on <REFERRAL DATE>. I am interested in what health care services you used – such as doctor appointments and tests – from when you had symptoms of lung cancer that made you see a doctor to the time you were referred to a lung specialist on <REPEAT DATE>. I have brought a calendar where we can record this information and hopefully make it a bit easier to remember the appointments you had.

2. Ask the participant(s) if he/she has their diary, appointment book, calendar, or anything else that could help remember appointments and activities.

3. Ask the participant if he/she has any questions before you start.

INTERVIEW START:

I would like to start with the first signs and symptoms of lung cancer that made you see a doctor. What were they and when did you see a doctor? <NOTE SIGNS AND SYMPTOMS ON THE CALENDAR ON THE DATE OF FIRST PRESENTATION, NOT MORE THAN 1 YEAR BEFORE THE REFERRAL DATE>

<IF THE PARTICIPANT HAS DIFFICULTY UNDERSTANDING THE QUESTION OR REMEBERING THEIR PRESENTING SIGNS AND SYMPTOMS, THEN USE THOSE LISTED IN THE CANCER CARE ONTARIO GUIDELINE AS A GUIDE>

Now, can you tell me what other appointments, tests, hospital visits, etcetera you had in this month (i.e. month of first presentation)? If an appointment or test was missed or cancelled, please tell me so I can put that on the calendar too. <NOTE ALL ACTIVITY ON THE CALENDAR ON THE DATES THEY OCCURRED – IF EXACT DATES ARE NOT KNOWN, USE AN APPROXIMATE DATE AND PLACE A QUESTION MARK BESIDE IT – USE THE SIDE COLUMNS FOR ADDED NOTES>

<CONTINUE THIS FOR EVERY MONTH UNTIL YOU REACH THE DATE OF REFERRAL>

PROBES (if needed):

1. FAMILY PHYSICIAN VISITS

a. Did you have a family doctor during this time? *IF YES*: How many times did you see your family doctor in this month?

2. WALK-IN CLINIC VISITS

    a. How many times did you go to a walk-in clinic in this month?

<if the participant is unsure whether the clinic is considered a walk-in, ask if it is a clinic where they normally see their family physician if they have one>

3. EMERGENCY ROOM VISITS

    a. How many times did you go to an emergency room in this month?

4. HOSPITALIZATIONS

    a. Were you ever hospitalized in this month? *IF YES*: How many times?

5. IMAGING TESTS

    a. Did you have any chest x-rays or CT scans in this month? *IF YES*: How many?

< if the participant is unsure what these tests are, show pictures and briefly explain how the tests are done>

6. REFERRALS TO NON-RESPIRATORY SPECIALISTS

    a. In this month, were you referred to see another specialist besides a lung specialist? *IF YES*: How many and what was their specialty (e.g. cardiology specialist, geriatric specialist, etcetera)? *<just to be certain it was a non-respiratory specialist>*

PART II

I have two final questions about your medical history.

1. What medications do you take for illnesses other than lung cancer and what do you take the medications for? *<ex. diabetes, hypertension, etc>*

2. Do you, or did you ever, smoke? *IF YES*: How many packs did you smoke per day and for how many years?

CONCLUSION:

1. Thank the participant for their contribution.
2. Explain how the project will proceed and how their information will be used.
3. Ask the participant if he/she has any questions before you conclude.

5. Chapter 5: How patient, disease, and system factors influence lung cancer pre-diagnostic pathways (Manuscript 3)

5.1. Preamble

In the previous chapter, I identified two groups of lung cancer patients with similar pre-diagnostic pathways based on healthcare service utilization patterns in primary care: one where patients were mainly managed by their family physician (FP) before being referred to a respiratory specialist for definitive diagnosis (FP group), and one where patients were managed by the emergency department (ED) with some use of walk-in clinics before being referred to a respiratory specialist (ED group). In addition, I identified several potential sources of delay in each group based on their patient- and tumor-related characteristics, and sequence of healthcare utilization activities.

In this chapter, I address objective 4 of my thesis: To understand how patient, disease, and system factors play a role in the pre-diagnostic pathway groups identified (FP group and ED group).

I present a multiple case-study where each pre-diagnostic pathway group is treated as a case. Key similarities and differences between the groups are presented along with modifiable factors that can reduce delay in the pre-diagnostic process. This is the first study in Canada to explore the role of patient, disease, and system factors on common lung cancer pre-diagnostic pathways and elicit an understanding of key similarities and differences between pathways. This manuscript has been submitted to the journal Current Oncology.

Khare SR, Mazaniello-Chezol M, Vedel I. How patient, disease, and system factors influence lung cancer pre-diagnostic pathways. Submitted to Current Oncology in December 2020.

All ethics documents and approval are in thesis Appendix 1. This study involved semi-structured patient interviews; the semi-structured interview guide is included as supplemental material at the end of this chapter (in English) and in thesis Appendix 2 (in French).

5.2. **TITLE PAGE**

TITLE:

How patient, disease, and system factors influence lung cancer pre-diagnostic pathways

AUTHORS:

6. S.R. Khare* MScN, MBA
7. M.M. Mazaniello-Chezol* MA, M.Mgt
8. I. Vedel*† MD, PhD

*Department of Family Medicine, Faculty of Medicine, McGill University, Montreal, QC, Canada

† Lady Davis Institute, Jewish General Hospital, Montreal, QC, Canada

RUNNING HEADER:

FACTORS INFLUENCING LUNG CANCER PRE-DIAGNOSTIC PATHWAYS

CORRESPONDING AUTHOR:

Satya Rashi Khare

5858 Chemin de la Côte-des-Neiges, Suite 300, Montreal, QC, Canada, H3S 1Z1

satya.khare@mail.mcgill.ca

(tel) 514-243-4322

(fax) 514-398-4202

FUNDING SUPPORT:

This study received funding support from the Fonds de recherche du Québec -Santé (FRQS) and the Strategy for Patient-Oriented Research (SPOR).

WORD COUNT: 3970

FIGURES AND TABLES: 3

5.3. **ABSTRACT**

Background: Lung cancer has high mortality largely due to advanced disease at diagnosis. Most lung cancer patients present in primary care first where delayed referral to a respiratory specialist can delay diagnosis. In Canada, little is known about what influences timeliness of care from first presentation to referral. We aimed to understand how patient, disease, and system factors influence lung cancer pre-diagnostic pathways in primary care.

Methods: This multiple case-study was conducted at a lung cancer centre in Québec. We conducted semi-structured interviews with 12 patients from two common pre-diagnostic pathways – one focused on use of family physicians (FP group) and one focused on use of walk-in clinics and emergency departments (ED group). We used the Model of Pathways to Treatment framework to guide data collection and thematic analysis.

Results: Key similarities between the two groups included the importance of symptoms, the notion of self-awareness, emotional distress, and for those who used it, an appreciation for the efficiency of care at the emergency department. A key difference was easy access to, and prompt attention received by, a family physician for the FP group that was contrasted with a lack of responsiveness at walk-in clinics for the ED group where several aspects of care were unsatisfactory. This difference primarily reflected perceived quality of care which was highly dependent on quality of the patient-physician relationship.

Conclusions: We highlight an important modifiable factor that supports improved access to family physicians where an established patient-physician relationship leads to the experience of seamless pathways.

Keywords: primary care, lung cancer, diagnosis, delay, qualitative research, delivery of health care

5.4. **INTRODUCTION**

Worldwide, lung cancer is the commonest type of cancer and the leading cause of cancer-specific mortality.(1) In Canada, lung cancer is responsible for 26% of all cancer deaths.(2) Outcomes are highly associated with stage at diagnosis with one-year net survival ranging from 86% for early (stage I) disease to 17% for advanced (stage IV) disease.(3) Unfortunately, 70% of Canadians with lung cancer are diagnosed with advanced stage disease.(4) This underscores a need to reduce diagnostic delays and increase the proportion of patients diagnosed at an earlier stage.

Most lung cancer patients present symptomatically in primary care (e.g. family physician clinics, walk-in clinics, emergency departments) and are then referred to a specialist for definitive diagnosis.(5) Thus, one major component of time to diagnosis is the primary care interval starting at first presentation in primary care with signs and symptoms suggestive of lung cancer and ending at referral to a respiratory specialist. As lung cancer symptoms are generally non-specific, timely investigation and referral in this interval is challenging(6) and considerable delays have been demonstrated.(7, 8)

There are two pre-diagnostic pathways commonly found in primary care. In the first, patients predominantly rely on their family physicians for timely investigation of symptoms, suspicion of lung cancer, and specialist referral.(9) In the second, patients rely more on emergency departments for investigation, suspicion, and referral.(10) Despite their pervasiveness, little is known about how these pathways emerge and what influences pre-diagnostic activities within them.

To inform how avoidable diagnostic delays can be reduced, there is a need to understand how cancer symptoms are managed in common lung cancer pre-diagnostic pathways and how such

management ultimately influences timely referral to a respiratory specialist. As patient (e.g. social context), disease (e.g. symptom acuity), and system (e.g. healthcare access) factors can influence the timeliness of cancer diagnosis,(11) we aimed to understand how these factors influence the two pre-diagnostic pathways commonly found in primary care – one focused on use of family physicians and one focused on use of emergency departments. To better inform improvement strategies, we concentrate on similarities and differences between these pathways.

5.5. **METHODS**

5.5.1. Setting

We conducted this study at a lung cancer centre located in a large teaching hospital in Québec. The clinic population is diverse in age, ethnicity, and socioeconomic status, and patients are geographically dispersed as the clinic attracts people outside the hospital catchment area. All patients are broadly covered under a provincial universal healthcare plan.

5.5.2. Design

This multiple case-study(12) was nested within an explanatory sequential mixed-methods design: this study followed a quantitative study to explain the quantitative results.(13)

In the quantitative study, we used clustering methods to identify groups of lung cancer patients with similar pre-diagnostic pathways based on healthcare service utilization patterns in primary care. We found two distinct groups.

The first group represented patients who were mainly managed by their family physician (FP) before being referred to a respiratory specialist for definitive diagnosis (FP group). This group comprised two-thirds of patients and had a much longer primary care interval time (i.e.

from first presentation to referral) and more advanced disease (stage IV) compared to the second group. Of note, almost half of the patients in this group visited the emergency department before referral to a respiratory specialist.

The second group represented patients who were all managed by the emergency department (ED) with some use of walk-in clinics before being referred to a respiratory specialist (ED group). This group comprised one-third of patients and had more early/locoregional disease (stages I, II and II) and half the primary care interval time than the previous group.

In this study, each group was treated as a case.

5.5.3. Participants

We recruited patients from each group – FP and ED – using maximum variation and purposive sampling until data saturation was reached.(13) Maximum variation was based on stage of disease to ensure perspectives of patients with early/locoregional and advanced disease were represented. We then purposefully selected patients based on typical pathways within each stage category. For patients who were not able to participate, we used opportunistic sampling to replace them with patients who had similar pathways.(14)

Patients were selected from the quantitative study sample where consent had already been obtained for this study. We contacted patients by phone to confirm willingness to participate.

5.5.4. Data collection

We used three data sources for triangulation. The main data source was semi-structured patient interviews conducted in this study. Two additional data sources were from the quantitative study: structured patient interviews that resulted in calendars depicting all patient

contacts with the healthcare system during the primary care interval (i.e. utilization), and medical charts that resulted in sociodemographic and tumor related data.

Semi-structured interviews were guided by the Model of Pathways to Treatment, a cancer diagnostic pathway adapted from the Andersen model of total patient delay.(15) This framework outlines contributing factors to the diagnostic process categorized into patient, disease, and system factors – all of which influence processes within the pathway and thus duration.(11) Patient factors include demographics, comorbidities, psychological aspects, social context, cultural context, and previous experience; disease factors include tumor site, size, and growth rate; system factors include access, policy, and delivery. These categories formed the general topics of our interview guide (Supplemental File 1: Semi-structured interview guide). Additionally, calendars were brought to the interview to stimulate discussion on factors influencing the pathways and assist recall of the time period and associated events.

Semi-structured interviews were conducted at the lung cancer clinic, patient's home, or over the phone from February to May 2019 by two of the study authors (MM & SK). Neither had prior interaction with the patients being interviewed and were not involved in their care. Each interview started with a recap of the study purpose and a general overview of the patient's diagnostic journey. All interviews were digitally recorded and transcribed verbatim. This was completed shortly after each interview and allowed both interviewers to get familiar with the data.

5.5.5. Data analysis

We followed Braun & Clarke's framework for thematic analysis to identify and make sense of emerging patterns in the data.(16) After familiarization with the data, M.M. and S.K.

independently generated codes from the verbatim using a hybrid approach.(17) We started with the three categories of the Model of Pathways to Treatment framework and inductively identified themes for each category. Independent coding was done for each transcript to minimize individual bias. In an iterative process, individual coding was gradually compared to inform the analysis. Data from other sources (chart data and calendar data) complemented the analysis by allowing a better understanding of patient context (e.g. sociodemographic) and how they made sense of their contacts with the healthcare system (e.g. which utilization activities were emphasized). We then categorized codes into themes, defined the themes, and synthesized the findings. To ensure trustworthiness, team meetings were held to cross-check the findings and explore alternative interpretations.(18) Finally, we conducted a within-case analysis followed by a cross-case analysis(19) where we explored similarities and differences between groups (FP vs ED).

5.5.6. Ethics approval

Study approval was granted by the Research Review Office of the Integrated Health and Social Services University Network for West-Central Montréal.

5.6. **RESULTS**

A total of 12 interviews were conducted (6 per group). All but 2 interviews were face-to-face and interview length was 60 minutes on average. Patient characteristics are reported in Table 5.1. Patients were a mean of 66.7 years of age and 75% were women.

Table 5.1 Characteristics of patients

Pre-diagnostic pathway		**Stage of disease**	
		Early/Locoregional	Advanced
ED* group	Gender	1 woman, 2 men	1 man, 2 women
	Age (mean)	64.6	59
	Area-based deprivation index (score)†	3.3	1
	Registered with a FP‡	33% (N=1)	100% (N=3)
	Marital status	Married (N=2) Single (N=1)	Widow (N=1) Married (N=1) Common-law partner (N=1)
FP‡ group	Gender	3 women	3 women
	Age (mean)	66.3	77
	Area-based deprivation index (score)†	1.7	3.3
	Registered with a FP‡	100% (N=3)	100% (N=3)
	Marital status	Married (N=2) Single (N=1)	Widow (N=3)

*ED = emergency department
†Classified in quintiles from least deprived (1) to most deprived (5)
‡FP = family physician

We grouped our findings according to the three categories of contributing factors outlined in the Model of Pathways to Treatment: patient factors, disease factors, and system factors. Each theme and associated sub-themes are described in detail below and summarized in Figure 5.1. Supporting patient quotes are shown in Table 5.2. Many themes represented similarities between the two groups; differences, where found, are clearly highlighted under the relevant theme.

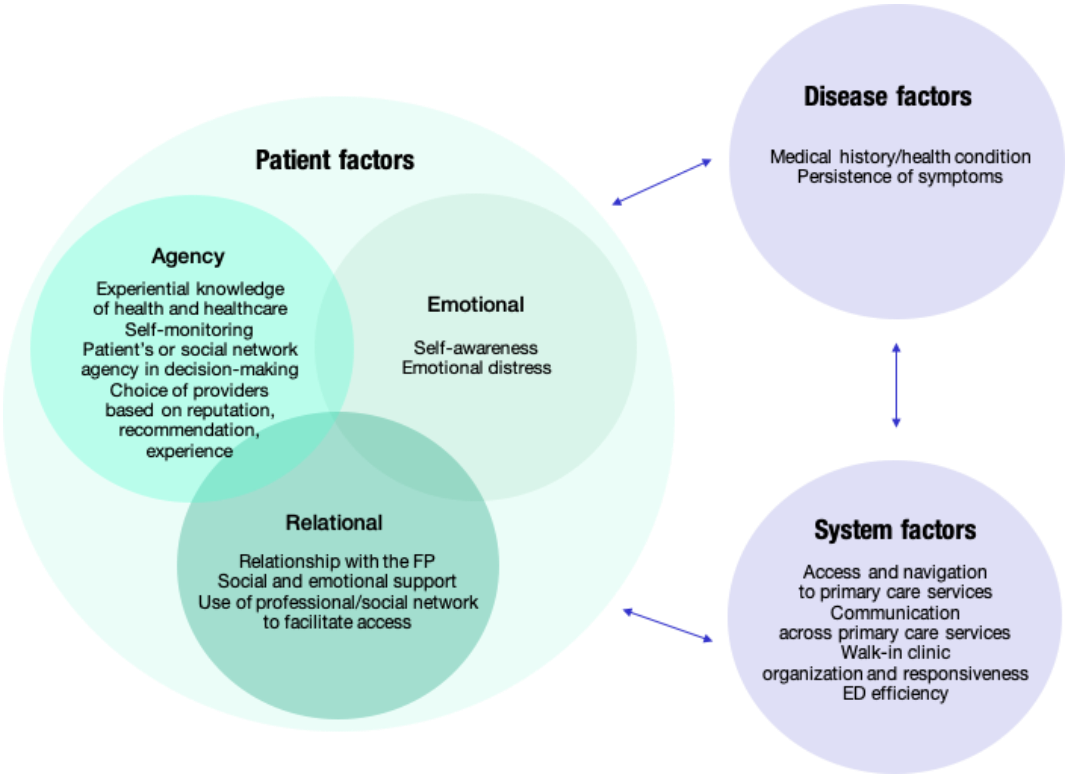

Figure 5.1 Main themes according to the three categories of the Model of Pathways to Treatment

5.6.1. Patient factors

Agency

This theme encompassed how patients perceived their active input in the pre-diagnostic pathway and the impact it had on facilitating or preventing investigation and suspicion of lung cancer in primary care. Patients used their experience and knowledge to self-monitor, make decisions, and seek help.

Experiential knowledge of health and healthcare. Previous experiences with illness and the healthcare system were used to inform reasoning for help-seeking and to facilitate the pathway. For example, patients with a history of recurrent pneumonia sought care when similar symptoms occurred and if treatment did not result in symptom resolution – as it did in the past – they

sought care elsewhere, often an ED. Knowledge of how the appointment system in primary care works also determined the ability to consult a physician in a timely manner. For example, one patient recounted the specific steps to get a same day appointment like calling at exactly 6h00.

Self-monitoring. Patients paid attention to the evolution of their condition leading to a practice of self-monitoring. This entailed consideration of their usual state of health in the context of new or worsening symptoms and observation of symptoms on a regular basis. For example, an asthmatic patient noted increase use of her bronchodilator as she became more short of breath over time. She then used this information to decide where was the best place to seek care (e.g. FP, ED, pharmacist, etc.).

Patient's or social network agency in decision-making. Decisions to consult other physicians allowed advancement of clinical investigations. This was facilitated either by the patient's own motivation or influence by their social network (family and friends). This was primarily the case when patient expectations were not met at previous clinical encounters leading to walk-in clinic or ED visits. For example, after 3 visits to her FP and "no results", one patient decided to present at the ED where further investigations were promptly conducted.

Choice of providers based on reputation/recommendation/experience. Based on their network's endorsement and shared beliefs regarding reputation, patients went to great lengths to seek care at their preferred healthcare centre. For example, one patient travelled almost an hour to a hospital of his choosing instead of presenting to one near his home. This was motivated by a sense of security in terms of care expectations being met and a sense of trust in the healthcare team and their clinical decisions. No matter what transpired before, once patients were at their preferred healthcare centre the pathway was perceived as very efficient.

Relational

This theme encompassed relationships used by patients to facilitate navigation within the healthcare system. Relationships with FP's, along with professional and social networks, played an important role in reaching appropriate services.

Relationship with the FP. A positive relationship with their FP led patients to have more trust, feel guided through their pathway, and improve their well-being during such an uncertain time. Patients attributed seamless pathways and early stage diagnosis in part to their FP's caring attitude towards them. One patient made a parallel to his profession as a lawyer and the importance of knowing how to talk to, and guide, his clients toward the right action.

Social and emotional support. Social support was important in managing symptoms and emotional distress experienced by patients as they navigated through clinical encounters and tests during their pathway. This was especially evident among patients in the FP group.

Use of professional/social network to facilitate access. Patients felt the need to exploit their professional and social networks to secure access to physicians (FP's or specialists) and clinical investigations. This was especially evident among advanced stage patients who perceived their symptoms as severe but unaddressed with prior care leading to emotional distress. For example, one patient sought care from a distant family member who was an emergency physician after feeling "discouraged" with the lack of care from her FP. Notably, this sub-theme did not emerge from patients in the FP group with early stage disease.

Emotional

This theme encompassed intertwined notions of self-awareness and emotional distress that affected how patients further investigated changes in their health.

Self-awareness. Patients described being aware of odd symptoms without necessarily knowing "something is wrong" which made it difficult to articulate in a clinical encounter. For example, one particularly active patient noticed several things that limited her activity but did not attribute her symptoms to something as serious as lung cancer. This was especially evident among patients in the FP group with advanced stage disease who did not feel "sick or unhealthy" but noticed something "unusual". This was in large part because symptoms did not interfere with regular daily activities.

Emotional distress. Although emotional distress was felt by most patients with persistent symptoms, this was emphasized among those with a smoking history who did not feel their symptoms were being taken seriously despite repeat presentations with the same complaint. This led to a sense of hopelessness that forced patients to seek care at the ED; therefore, this was especially evident among patients in the ED group.

5.6.2. Disease factors

This theme encompassed the role of symptom persistence and medical history on the length of the pre-diagnostic pathway. When presenting symptoms could be attributed to a pre-existing condition or health behaviour, the pathway was perceived to be prolonged. In addition, disease, patient, and system factors were interconnected. For instance, a trusting relationship with a FP factored into how patients perceived their symptoms were managed.

Medical history and health condition. Many patients reported a history of respiratory illness or relevant health behaviour (e.g. smoking) that became the focus of clinical encounters. FP's (with whom patients were registered or those seen at walk-in clinics) and, to a certain extent, patients continued to make sense of presenting symptoms in the context of pre-existing conditions even

when prescribed medications were ineffective. For example, one patient with a history of asthma kept being prescribed different bronchodilators despite worsening symptoms. Given her FP's confidence in the diagnosis of asthma, the patient also believed it was asthma until her pharmacist showed concern regarding excessive use of her pump. This led the patient to present at the ED.

Persistence of symptoms. Patients with persistent or worsening symptoms initiated follow-up appointments with their FP's. Depending on the level of trust in their physician, which was associated with relationship, patients either felt heard or unheard irrespective of how the FP responded to their symptoms. For example, one patient with a persistent cough initiated several follow-ups with her FP over a 3-month period before a chest radiograph showing a lung mass was ordered. Despite the time it took to get an "answer," the patient very much "liked" her FP and felt she was probably just following protocol.

5.6.3. System factors

This theme encompassed different layers of the healthcare system, from access and responsiveness of FP clinics to perceived efficiency of ED's. In most layers, having a FP facilitated the pre-diagnostic pathway.

Access and navigation to primary care services. Independent of patients social and professional network, access to, and navigation within, primary care services were related to whether patients were registered with a FP. Patients without a FP felt the need to rely on ED's to access care, even after consulting at walk-in clinics. Therefore, this aspect of access had an influence over agency and help-seeking behaviour of patients.

Communication across primary care services. The perceived efficiency of information

exchange, especially related to test results, was dependent on whether the patient had a FP or was seeking care at walk-in clinics. When a patient required imaging, those with a FP were referred to healthcare centres known to their FP (i.e. centres on-site or in close proximity) and results were communicated back to the FP, and ultimately the patient, relatively quickly. Conversely, patients who used walk-in clinics reported delayed communication of results. Thus, information exchange either facilitated (for those with a FP) or hindered (for those without a FP) follow-up and decision making in the pathway.

Walk-in clinic organization and responsiveness. Patients who sought care at walk-in clinics experienced lack of promptness, trust, autonomy, dignity, and choice of healthcare professional, all of which equated a perceived lack of responsiveness that forced patients to seek care elsewhere, often an ED.

ED efficiency. Despite long wait times to see a physician, patients who used the ED described it as the "best" option to facilitate the pathway owing to its efficiency and effectiveness. This was true regardless of whether the patient had a FP or not. For patients without a FP, the ED was perceived as their only feasible option for accessing care. For patients with a FP, the ED was a practical option to ensure quick investigations and referral. For these patients, some self-presented to the ED for quicker access while others were referred by their FP for quicker access.

Table 5.2 Quotes from patients by theme

PATIENT FACTORS
- Agency: Experiential knowledge of health and healthcare *"But beware, you have to be equipped to get an appointment at a walk-in clinic. You have to call at six o'clock sharp, 6:00, actually, the night before. If you don't get a line there and you get there at 6:10, forget it, there'll be no more appointments. And if you call a minute before that, they'll tell you-it won't work either [laughing]. So it's really… it's almost nervousness. It's like, "It's like entering the scene, you know." – translation from French by the authors* (JB18; ED group; early-locoregional disease)

Self-monitoring
"When I was well, at the beginning, I was barely taking [Ventolin for asthma]-that's how I used to feel in the summer, I need a pump, if necessary. Do you know what I mean? But then, it was not only when I needed it, it was all the time." – translation from French by the authors
(JB10; FP group; advanced disease)

Patient's or social network agency in decision-making
"I went there and then he [her family physician] checked me out again and then he said the same thing to me. And then, it was the third time I went, three times, it was the third time I was there, when I really saw «there is no result», I went to the emergency room." ... "He [the family doctor] never sent me to, like, go for a scan, go for something. When I saw something was really wrong, I went myself. In the emergency room right away I was well received, in [the hospital], right away, right away, right away." – translation from French by the authors
(JB10; FP group; advanced disease)

Choice of providers based on reputation/recommendation/experience
"I decided to come to [this hospital] because of its reputation. So we drove all the way to [this hospital], we told them he had a mass. Downstairs here at the emergency, right away, they did the scan, they kept him overnight, they said yes and in fact the next day they confirmed it was, um, a cancer and therefore they referred us to the oncology here."
(JB19; ED group; early-locoregional disease)

- Relational:

Relationship with the family physician
"…[my family physician] paid attention to what I said, you know? I mean, she listened to my chest, it sounded clear, you know, she wrote a requisition for an X-ray, so, I mean, that, that was it….I probably had it on a Wednesday. And, uh, Saturday—I got a phone call on Friday to say come and see her Saturday morning."
(CS11; FP group; early-locoregional disease)

Social and emotional support
"…whoever was able to come came to the hospital, and the communication to others, like, you know, you felt the caring, you felt the support behind you, you know? And I wasn't even scared over there, you know? At the hospital, like, I was fine, I was gonna come out of this fine, you know?"
(DL3; FP group; advanced disease)

Use of professional/social network to facilitate access
"So he called his brother-in-law, who was an emergency doctor at [the hospital], and said, «Listen, [name of the emergency doctor], I don't like asking you this, but you know, [patient's name], uh, [patient's name], is not well, and uh, it's not working at all, and she's walking around from doctor to [doctor]...», he said, «It's okay! I'm going to see her», he says «I'm in the emergency room, so come tomorrow, tomorrow morning, at any time, and, uh, tell her I know you're going to show up»" – translation from French by the authors
(JB4; ED group; advanced disease)

- Emotional:

Self-awareness
"Because physically I was, you know, still felt strong enough. I didn't feel sick except for the coughing, and that was every morning…I went about my usual duties, you know, like normal. I didn't feel that anything was wrong."
(CS8; FP group; advanced disease)

Emotional distress

"The first doctor I saw there, I told you, she-she had such a strong prejudice [against smokers]." [...]
"The third doctor, she didn't even put her stethoscope on to listen to my lungs there. That's something, you're prescribing, wouldn't you like to listen, a bit?" – translation from French by the authors
(JB18; ED group; early-locoregional disease)

DISEASE FACTORS

Medical history and health condition
"I went to see my family doctor, and then he- he checked me out, he said «Ah, it's asthma, it's asthma», he gave me a puffer and then I went back again, the puffer had no effect. I went to see him again, he gave me a pump and I said «Well, it doesn't work», I took the pump 20 minutes ago, it takes 30 minutes, you see?.... in the evening I have trouble breathing, not a little bit, I have to get up two or three times to take the pump! So they [the pharmacist] said, «[patient's name], you're taking too much, what's going on? It hasn't been long since you bought the pumps»" – translation from French by the authors
(JB10; FP group; advanced disease)

Persistence of symptoms
"I was coughing, then February I went to my family doctor and she said I had bronchitis and she gave me antibiotics…and then a month later I went back to see her, it was still the same thing. Again I got antibiotics in March and [the cough] was still persisting and I wasn't getting any better. April, I go back and now she sent me for an X-ray, after three months…I don't know if another doctor would have sent me earlier, for the X-ray, I don't know, but I mean, I still see her, I like her, and uh, I can't say anything else."
(CS8; FP group; advanced disease)

SYSTEM FACTORS

Access and navigation to primary care services
"...there's a system I don't know, and I find it a little complicated, and all we've been hearing for years and years and years is that we're not able to access services... we need to know about the system, but I find the system very complicated." – translation from French by the authors
(JB4; ED group; advanced disease)

Communication across primary care services
"I couldn't stop coughing, that's why I went to see him [the family doctor], but he gave me X-rays. That's the way it is, I got a call the next morning to say I had to take another one, another test because they saw things on my x-ray, and they weren't sure what it was...Wednesday morning, I went to see him, and I had my scan. And Thursday morning, that's when he told me I had cancer." – translation from French by the authors
(JB9; FP group; early-locoregional disease)

Walk-in clinic organization and responsiveness
"…well the walk-in clinic couldn't do anything: they're a walk-in clinic, I know that much. You got to go in the morning, put your name in, maybe they'll take you, maybe not, it's never the same doctor, it's a total waste of time, I don't even know why they have that system…To see the doctor, you have to be practically on your death bed. And then that doctor, her hands are tied, she cannot follow you. So, what did I do there? I wasted my time."
(JB19; ED group; early-locoregional disease)

Emergency department efficiency
"I went up to the emergency department, and the [hospital] being what it is, it was extraordinary, there, I didn't wait at all, and as soon as the lady heard me, she immediately put me in a stretcher and they brought me from there, […] When I sat down on that stretcher, I thought, «Phew, finally. Someone's going to take care of me»." – translation from French by the authors
(JB18; ED group; early-locoregional disease)

5.7. **DISCUSSION**

This multiple case-study provides insight into contextual factors that frame lung cancer pre-diagnostic pathways in primary care with a focus on two common pathway groups: a FP group where patients are mainly managed by their FP before referral to a respiratory specialist, and an ED group where patients are mainly managed by walk-in clinics and the ED before referral.

We found key similarities between the groups included the importance of symptoms (e.g. shortness of breath), the notion of self-awareness (e.g. noticing something unusual), and emotional distress (e.g. not being taken seriously). We further found an appreciation for the prompt attention received at the ED for patients who used the ED in their pathway.

We found a key difference between the two groups was promptness of care. Easy access to, and prompt attention received by, a FP for the FP group was contrasted with a lack of responsiveness at walk-in clinics for the ED group where several aspects of care were unsatisfactory. This difference primarily reflected perceived quality of care which was highly dependent on the quality of relationship between the patient and physician.

The importance of relationship quality in lung cancer pre-diagnostic pathways has been found elsewhere(20) with attributes such as confidence and trust being associated with improved cancer detection in primary care.(21) In our study, for patients who sought care from their FP (FP group) a positive relationship led to feelings of trust and well-being that facilitated the experience of a seamless pathway independent of the timeliness of care or stage at diagnosis. Patients in this group felt heard, taken care of, and guided through a process that was foreign and uncertain. Here, the patient-physician relationship resembled a partnership that likely helped patients adeptly navigate the system(22) and provide assurance that the patient's best interest

was at the core of clinical decisions.(23) This supported the emergence of a FP pathway as patients relied on their FP during the pre-diagnostic process.

Patients reporting no FP or a poor relationship with their FP relied on ED's and walk-in clinics. Patients who sought care from walk-in clinics (ED group) felt their symptoms and feelings were not taken seriously leading to a lack of trust and dignity. This was especially evident among patients with a smoking history who experienced high levels of distress and hopelessness after multiple visits with persistent symptoms. This may have been due to poor communication during the clinical encounter leading to insufficient diagnostic information(24) or uncertainty about next steps(25) perhaps further complicated by stigmatization. This can lead to a sense of blame and pose a barrier to lung cancer diagnosis(26-28) and high-quality care.(29) In our study, patients in this group felt forced to eventually seek care at an ED, supporting the emergence of an ED pathway.

Regardless of where a patient initially sought care (FP or walk-in clinics), rapid diagnosis was often achieved through the ED. This represented a key similarity in our study where patients in both groups described the ED as their 'best' option for efficient and effective care, a finding endorsed by others.(30, 31) However, we found an important difference within this similarity was related to choice, or lack thereof. For patients with a FP, the ED was a *practical* option to expedite investigations and access to specialty care; some patients self-presented while others were sent by their FP. For patients without a FP, the ED was their *only* option.

Our findings further demonstrate that the patient experience is influenced more by relationship quality than actual efficacy. For example, in both groups symptoms were often attributed to benign conditions, not uncommon among patients ultimately diagnosed with lung cancer.(32, 33) However patients who reported a positive relationship with their FP in the FP

group experienced seamless pathways whereas patients who used walk-in clinics in the ED group experienced a minimization of symptoms.

These findings highlight important modifiable factors. The patient experience suggests walk-in clinics compromise quality of care – a sentiment shared among many FP's(34, 35) – and can lead to diagnostic delays in lung cancer. This supports the need for improved access to FP's. Also, the ED efficiency experienced by patients with and without a FP points to a need to reduce system barriers related to diagnostics and specialty care especially given that some patients were referred to the ED by their FP for quicker access to investigations and specialists. This may include greater access to computed tomography scans in primary care,(36) decision-support tools,(37) or rapid access routes.(38) Further qualitative study with FP's would better inform how they can be supported.

5.7.1. Strengths and limitations

Our study is based on a small sample of lung cancer patients. Despite this, we reached data saturation with no new emerging themes. Data richness was facilitated by triangulating interview data with chart data from a previous study and using a theoretical framework – Model of Pathways to Treatment – to ensure consistency and structure across interviews.(15) Data triangulation was also important in establishing credibility of findings which was further established through triangulation of analysts with a range of scientific and clinical expertise.(39) This was particularly important in our study as the declining health of some patients hindered respondent validation, a challenge reported by others in lung cancer qualitative research.(40)

Our sample was selected from a single centre located in an urban setting in Canada which could compromise transferability of results. Given that timely referral can be influenced by

location (i.e. urban vs rural areas), future studies would benefit from a broader geographical range.(41)

Finally, interviews were not conducted at the time of referral as patients were selected from a previous study sample. Given the passage of time between the pre-diagnostic pathway and the interview, there may have been recall bias. This was minimized by including data from other sources, particularly calendars that portrayed an overview of the patient's journey in primary care. There may have also been bias in our sample of patients; all patients in the FP group were female. This may have influenced the emphasis on relationship quality, especially if the FP was also female.(42, 43) Future studies should explore the role of physician gender in the patient experience of pre-diagnostic pathways.

Despite these limitations, our study provides vital knowledge to a poorly understood area of lung cancer diagnostic pathways where improvements can lead to earlier diagnosis. Importantly, our study ensured a wider representation of perspectives by including an equal number of early/locoregional and advanced stage patients. Furthermore, we captured experiences of patients presenting to their FP, walk-in clinics, and ED's. This wider inclusion represents a major strength as it goes beyond other studies that only include patients seen and referred by their FP.(44) This allowed for sound improvement recommendations that were grounded in a more holistic patient experience.

5.8. **CONCLUSION**

Our study is the first to examine common lung cancer pre-diagnostic pathways in primary care and elicit an understanding of key similarities and differences to better inform improvement strategies. We report a rich contextualization of the pathways derived from lived patient

experiences and organized according to patient, disease, and system factors. Based on our findings, we suggest modifiable factors that can improve the pre-diagnostic process towards timely referral. These include improved access to patients own FP's where an established patient-physician relationship leads to the experience of seamless pathways, and greater support for FP's so that efficiency experienced at ED's in terms of access to tests and specialists can be emulated in the community.

5.8.1. Acknowledgements

This study received funding support from the Fonds de recherche du Québec -Santé (FRQS) and the Strategy for Patient-Oriented Research (SPOR). Funding sources were not involved in any aspect of the work.

5.8.2. Conflict of Interest Disclosure

We have read and understood Current Oncology's policy on disclosing conflicts of interest and declare that we have none.

5.9. **REFERENCES**

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. International Journal of Cancer. 2015;136(5):E359-E86.

2. Canadian Cancer Society. Lung cancer statistics Toronto, ON: Canadian Cancer Society 2019 [cited 2019 May 14]. Available from: http://www.cancer.ca/en/cancer-information/cancer-type/lung/statistics/?region=qc.

3. Walters S, Maringe C, Coleman MP, Peake MD, Butler J, Young N, et al. Lung cancer survival and stage at diagnosis in Australia, Canada, Denmark, Norway, Sweden and the UK: a population-based study, 2004-2007. Thorax. 2013;68(6):551-64.

4. Canadian Cancer Statistics Advisory Committee. Canadian Cancer Statistics 2018 Toronto, ON: Canadian Cancer Society; 2018 [cited 2019 May 14]. Available from: cancer.ca/Canadian-Cancer-Statistics-2018-EN.

5. Macleod U, Mitchell ED, Burgess C, Macdonald S, Ramirez AJ. Risk factors for delayed presentation and referral of symptomatic cancer: evidence for common cancers. British journal of cancer. 2009;101(Suppl 2):S92-S101.

6. Lyratzopoulos G, Wardle J, Rubin G. Rethinking diagnostic delay in cancer: how difficult is the diagnosis? BMJ. 2014;349:g7400.

7. Allgar VL, Neal RD. Delays in the diagnosis of six cancers: analysis of data from the National Survey of NHS Patients: Cancer. Br J Cancer. 2005;92(11):1959-70.

8. Barrett J, Hamilton W. Pathways to the diagnosis of lung cancer in the UK: a cohort study. BMC Fam Pract. 2008;9:31.

9. Goulart BHL, Reyes CM, Fedorenko CR, Mummy DG, Satram-Hoang S, Koepl LM, et al. Referral and treatment patterns among patients with stages III and IV non-small-cell lung cancer. J Oncol Pract. 2013;9(1):42-50.

10. Newsom-Davis T. The route to diagnosis: emergency presentation of lung cancer. Lung cancer manag. 2017;6(2):67-73.

11. Scott SE, Walter FM, Webster A, Sutton S, Emery J. The model of pathways to treatment: conceptualization and integration with existing theory. Br J Health Psychol. 2013;18(1):45-65.

12. Yin RK. Case study research : design and methods. Thousand Oaks: Sage Publications; 1994.

13. Creswell JW, Plano Clark VL. Designing and conducting mixed methods research 2nd ed. California, US: SAGE Publications Inc. ; 2011.

14. Pope C, Mays N. Qualitative research in health care. Fourth edition. ed. Hoboken: Wiley-Blackwell; 2020. pp. 272. (p. 49) p.

15. 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;17(2):110-8.

16. Braun V, Clarke V, Hayfield N, Terry G. Thematic Analysis. In: Liamputtong P, editor. Handbook of Research Methods in Health Social Sciences. Singapore: Springer Singapore; 2019. p. 843-60.

17. Fereday J, Muir-Cochrane E. Demonstrating Rigor Using Thematic Analysis: A Hybrid Approach of Inductive and Deductive Coding and Theme Development. International Journal of Qualitative Methods. 2006;5(1):80-92.

18. Nowell LS, Norris JM, White DE, Moules NJ. Thematic Analysis : Striving to Meet the Trustworthiness Criteria. International Journal of Qualitative Methods. 2017;16(1).

19. Ayres L, Kavanaugh K, Knafl KA. Within-Case and Across-Case Approaches to Qualitative Data Analysis. Qualitative Health Research. 2003;13(6):871-83.

20. Cassim S, Chepulis L, Keenan R, Kidd J, Firth M, Lawrenson R. Patient and carer perceived barriers to early presentation and diagnosis of lung cancer: a systematic review. BMC Cancer. 2019;19(1):25.

21. Rogers S, Gildea C, Meechan D, Baker R. Access, continuity of care and consultation quality: which best predicts urgent cancer referrals from general practice? Journal of public health (Oxford, England). 2014;36(4):658-66.

22. Rankin NM, York S, Stone E, Barnes D, McGregor D, Lai M, et al. Pathways to Lung Cancer Diagnosis: A Qualitative Study of Patients and General Practitioners about Diagnostic and Pretreatment Intervals. Ann Am Thorac Soc. 2017;14(5):742-53.

23. Malmstrom M, Rasmussen BH, Bernhardson BM, Hajdarevic S, Eriksson LE, Andersen RS, et al. It is important that the process goes quickly, isn't it?" A qualitative multi-country study of colorectal or lung cancer patients' narratives of the timeliness of diagnosis and quality of care. European Journal of Oncology Nursing. 2018;34:82-8.

24. Sheringham J, Sequeira R, Myles J, Hamilton W, McDonnell J, Offman J, et al. Variations in GPs' decisions to investigate suspected lung cancer: a factorial experiment using multimedia vignettes. BMJ Qual Saf. 2017;26(6):449-59.

25. MacArtney J, Malmström M, Nielsen TO, Evans J, Bernhardson BM, Hajdarevic S, et al. Patients' initial steps to cancer diagnosis in Denmark, England and Sweden: What can a

qualitative, cross-country comparison of narrative interviews tell us about potentially modifiable factors? BMJ Open. 2017;7(11).

26. Murray SR, Kutzer Y, Habgood E, Murchie P, Walter FM, Mazza D, et al. Reducing barriers to consulting a General Practitioner in patients at increased risk of lung cancer: a qualitative evaluation of the CHEST Australia intervention. Fam Pract. 2017;34(6):740-6.

27. Chapple A, Ziebland S, McPherson A. Stigma, shame, and blame experienced by patients with lung cancer: qualitative study. BMJ: British Medical Journal. 2004;328(7454):1470-3.

28. Scott N, Crane M, Lafontaine M, Seale H, Currow D. Stigma as a barrier to diagnosis of lung cancer: patient and general practitioner perspectives. Prim Health Care Res Dev. 2015;16(6):618-22.

29. Hatzenbuehler ML, Phelan JC, Link BG. Stigma as a fundamental cause of population health inequalities. American journal of public health. 2013;103(5):813-21.

30. Black G, Sheringham J, Spencer-Hughes V, Ridge M, Lyons M, Williams C, et al. Patients' experiences of cancer diagnosis as a result of an emergency presentation: A qualitative study. PLoS ONE. 2015;10(8).

31. Brousselle A, Breton M, Benhadj L, Tremblay D, Provost S, Roberge D, et al. Explaining time elapsed prior to cancer diagnosis: patients' perspectives. BMC Health Services Research. 2017;17(1):448.

32. Caswell G, Seymour J, Crosby V, Hussain A, Manderson C, Farnan S, et al. Lung cancer diagnosed following an emergency admission: exploring patient and carer perspectives on delay in seeking help. Support Care Cancer. 2017;25(7):2259-66.

33. Mitchell ED, Rubin G, Macleod U. Understanding diagnosis of lung cancer in primary care: qualitative synthesis of significant event audit reports. Br J Gen Pract. 2013;63(606):e37-46.

34. Brown JB, Bouck LM, Ostbye T, Barnsley JM, Mathews M, Ogilvie G. Walk-in clinics in Ontario. An atmosphere of tension. Can Fam Physician. 2002;48:531-6.

35. Jones D. BC walk-in clinics warned. CMAJ: Canadian Medical Association Journal. 2006;175(12):1512-.

36. Wagland R, Brindle L, James E, Moore M, Esqueda AI, Corner J. Facilitating early diagnosis of lung cancer amongst primary care patients: The views of GPs. European Journal of Cancer Care. 2017;26(3).

37. Moffat J, Ironmonger L, Green T. Clinical Decision Support Tool for Cancer (CDS) Project: evaluation report to the Department of Health 2014.

38. Prades J, Espinàs JA, Font R, Argimon JM, Borràs JM. Implementing a Cancer Fast-track Programme between primary and specialised care in Catalonia (Spain): a mixed methods study. British Journal of Cancer. 2011;105(6):753-9.

39. Cope DG. Methods and meanings: Credibility and trustworthiness of qualitative research. Oncology Nursing Forum. 2014;41(1):89-91.

40. Cattaneo SM, II, Geronimo MCM, Putscher TMJ, Brady-Copertino C, Meisenberg BR. Improved coordination of care for patients with abnormal chest imaging: The rapid access chest and lung assessment program. J Clin Outcomes Manage. 2014;21(10):453-8.

41. Verma R, Pathmanathan S, Otty ZA, Binder J, Vangaveti VN, Buttner P, et al. Delays in lung cancer management pathways between rural and urban patients in North Queensland: a mixed methods study. Intern Med J. 2018;48(10):1228-33.

42. García JA, Paterniti DA, Romano PS, Kravitz RL. Patient preferences for physician characteristics in university-based primary care clinics. Ethnicity & disease. 2003;13(2):259-67.

43. Hall JA, Irish JT, Roter DL, Ehrlich CM, Miller LH. Gender in medical encounters: an analysis of physician and patient communication in a primary care setting. Health psychology : official journal of the Division of Health Psychology, American Psychological Association. 1994;13(5):384-92.

44. Birt L, Hall N, Emery J, Banks J, Mills K, Johnson M, et al. Responding to symptoms suggestive of lung cancer: A qualitative interview study. BMJ Open Respir Res. 2014;1(1).

5.10. **Supplemental File 1: Semi-structured interview guide**

INITIATION:

1. Re-introduction.
2. Explain what was done in the previous phase of work and why they were selected.
3. Remind the participant of the goals of the interview, projected length, and general topics of discussion. Also inform the participant that the interview can be continued at a later time if they feel the need to stop.
4. Remind the participant that they are being interviewed as an expert who can help the researcher better understand the phenomenon.
5. Ask the participant if he/she has any questions before you start.

INTERVIEW QUESTIONS:

Patient factors

In this first part of the interview, I would like to understand how individual, social, and cultural aspects played a role in your pathway from when you had symptoms of lung cancer that made you see a doctor to being referred to a lung specialist. They may not have played a role at all, so I just want to explore that with you.

1. Can you describe your thoughts as you went through your experience of first seeing a doctor to being referred to a lung specialist?
    a. *Probes*: I would like you to try and focus on…
        i. Previous experiences you may have had
        ii. Influences from your social situation, for example, competing priorities or advice from family and friends

iii. Cultural influences

iv. Your mental or emotional state – your spiritual state

v. Influence of other illnesses you have

vi. Influence of your so-called demographic – for example, age, gender, income, education

<Others = marital status, employment status, occupation, geographical location>

Health-care provider and system factors

In this second part of the interview, I would like to understand how the health care providers and health care system played a role in your pathway.

1. Can you tell me about challenges or barriers/obstacles you had during your experience, if any, that were related to how the heath-care system operates?
    a. *Probe 1*: Perhaps issues related to accessing the health-care system…
        i. How did you go about seeing a doctor?
        ii. What was your experience during the appointment?
        iii. What was your experience after seeing the doctor for the first time?
    b. *Probe 2*: Thoughts on how health-care policy affected your experience…
        i. Is there any health-care policy that played a role in your experience, and if so, how? <examples: gatekeeper system, catchment areas, insurance, community services>
    c. *Probe 3*: Thoughts on how health-care delivery affected your experience…

i. Once you saw a doctor, how did you feel about how you were medically treated after in terms of follow-up, timely appointments, tests, and finally referral?

2. Can you tell me about things within the health-care system that made your experience easier, if any?

Disease factors

In this last part of the interview, I would like to understand how the disease itself played a role in your pathway.

1. Can you describe how the evolution of your symptoms impacted your pathway from when you first saw a doctor to when you got a referral? My notes from the first time we spoke says that <SIGNS AND SYMPTOMS> made you go see a doctor.
    a. *Probe 1*: How quickly did your symptoms progress and how did that affect your pathway?
    b. *Probe 2*: Is there anything else specific to your cancer that you feel affected your pathway – perhaps where the tumor was located, the size of the tumor, or the specific type of cancer (i.e. non-small cell vs small cell)?

Anything else

I do not have any remaining questions. Is there anything else you would like to add about what played a role or influenced your pathway from first presenting to a doctor to getting a referral to a lung specialist – something we may have missed or not discussed?

CLARIFYING QUESTIONS:

1. Can you expand a little on that?

2. Can you give me some examples?
3. That is very interesting – can you tell me more?

CONCLUSION:

1. Thank the participant for their contribution.
2. Explain how the project will proceed and how their information will be used.
3. Ask the participant if he/she has any questions before you conclude.

6. Chapter 6: Defining lung cancer pre-diagnostic pathways in primary care: an in-depth understanding and suggested improvements (Manuscript 4)

6.1. **Preamble**

In the previous two chapters, I identify and describe common lung cancer pre-diagnostic pathways in primary care, and explore the role of patient, disease, and system factors in these common pathways.

In this chapter, I address objective 5 of my thesis: To identify potential sources of pre-diagnostic delay and suggest associated improvement strategies.

I present merged findings from the previous two manuscripts as supporting evidence for four potential sources of delay in primary care coupled with suggested improvement strategies. This is the first study in Canada to combine quantitative and qualitative evidence in support of sources of unnecessary delay in primary care and suggest how delays can be reduced. This manuscript will be submitted to the journal Canadian Family Physician.

Khare SR, Vedel I. Defining lung cancer pre-diagnostic pathways in primary care: an in-depth understanding and suggested improvements. To be submitted to Canadian Family Physician in 2021.

6.2. **TITLE PAGE**

TITLE:

Defining lung cancer pre-diagnostic pathways in primary care: an in-depth understanding and suggested improvements

AUTHORS:

1) Satya Rashi Khare MScN, MBA

   Department of Family Medicine, Faculty of Medicine, McGill University, Montreal, QC, Canada

   satya.khare@mail.mcgill.ca

2) Isabelle Vedel MD, PhD

   Department of Family Medicine, Faculty of Medicine, McGill University, Montreal, QC, Canada

   isabelle.vedel@mcgill.ca

CORRESPONDING AUTHOR:

Satya Khare

5858 Côte-des-Neiges, Suite 300

Montréal, QC H3S 1Z1

(Tel) 514-243-4322

(Fax) 514-398-4202

satya.khare@mail.mcgill.ca

WORD COUNT: 1715

COMPETING INTERESTS:

The authors have no conflicts of interest to declare.

6.3. **ABSTRACT**

Lung cancer is the leading cause of cancer-related mortality largely due to advanced disease at diagnosis. This underscores a need to reduce unnecessary diagnostic delays which requires an understanding of how patients move through the healthcare system to get their diagnosis. The critical time period from when the patient first presents in primary care to when they are referred to a respiratory specialist is poorly understood in Canada. We conducted a two-step explanatory sequential mixed-methods study to address this knowledge gap; first we identified and described common pre-diagnostic pathways in primary care and second, we explored how various factors influenced the pre-diagnostic process within each common pathway. In this article, we present our combined findings that support four potential sources of delay in primary care: missed opportunities for earlier referral, lack of integration between primary and secondary care, ineffectiveness of walk-in clinics, and lack of standardization in the pre-diagnostic process. Based on this, we recommend several improvement strategies to support timely diagnosis through timely referral from primary care.

KEYWORDS: Early diagnosis, lung cancer, primary care, pre-diagnostic pathway, interventions

6.4. **INTRODUCTION**

Lung cancer is the leading cause of cancer-related mortality.(1) A large proportion of patients, 70% in Canada,(2) are diagnosed when their disease is advanced partly due to unnecessary delays in diagnosis. In order to improve the proportion of patients diagnosed at an earlier stage, it is important to have a detailed understanding of how patients move through the healthcare system to get a diagnosis to inform targeted improvement strategies aimed at reducing diagnostic delay.

Once a patient presents in the healthcare system, there are two time intervals that contribute to time to diagnosis: the primary care interval that spans first presentation to specialist referral and the secondary care interval that spans referral to diagnosis.(3) In Canada, much attention has been paid to the secondary care interval even though most lung cancer patients first present in primary care where delay in referral can exacerbate delays in diagnosis;(4) accelerated diagnosis in secondary care is less impactful if there is considerable referral delay. Consequently, reducing referral delay in primary care is an extremely important aspect of early lung cancer diagnosis but severely understudied in Canada.

We sought to fill this knowledge gap by conducting a two-step explanatory sequential mixed-methods study in Québec, a province with the highest lung cancer incidence and mortality rates of all Canadian provinces.(5) In the first step, we identified and described common pre-diagnostic pathways in primary care. In the second step, we explored how various factors influenced the pre-diagnostic process within each pathway with a focus on similarities and differences between pathways. Methods for each step are presented in Figure 6.1. In both steps, findings were used to inform how unnecessary diagnostic delays in primary care could be reduced and how timely referral could be supported. Here, we present our combined findings and

improvement suggestions.

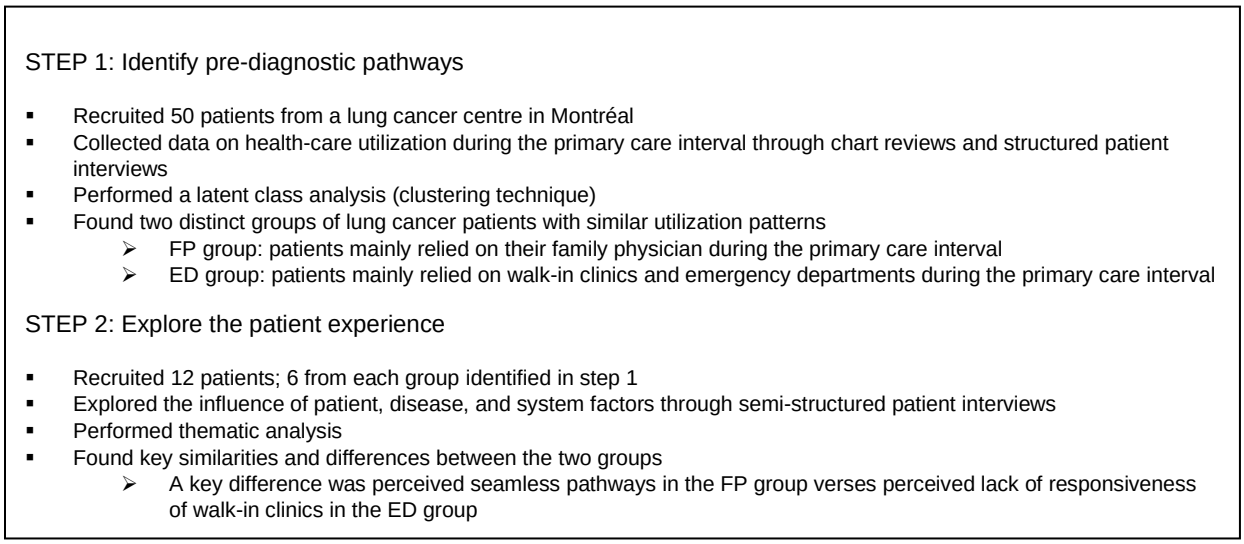

Figure 6.1 Methods for each step of the two-step explanatory sequential mixed-methods study

6.4.1. STEP 1: QUANTITATIVE RETROSPECTIVE COHORT STUDY

High-level findings: Two distinct pre-diagnostic pathways

We found two distinct pre-diagnostic pathways during the primary care interval (first presentation to referral). In the first, patients predominantly relied on their family physicians (FP) for investigation of symptoms (FP group) and referral. In the second, patients predominantly relied on emergency departments (ED) and walk-in clinics (ED group). Objectively, the FP group fared worse with double the time to referral compared to the ED group [45 days (IQR 12-111) vs 22 (IQR 5-69)] and more advanced stage disease (65% vs 50%).

6.4.2. STEP 2: QUALITATIVE MULTIPLE CASE STUDY

High-level findings: Distinct patient experiences in each pathway

A key difference was uncovered between the two pathways: patients in the FP group reported positive experiences with perceived seamless pathways while patients in the ED group reported a

sense of hopelessness and perceived overall lack of responsiveness. These experiences were reflective of perceived relationship quality between patients and physicians. More positive relationships were reported by those seen by their FP in the FP group and more negative relationships were reported by those seen at walk-in clinics in the ED group.

6.5. A DEEPER UNDERSTANDING TO INFORM IMPROVEMENT STRATEGIES

In step 1, each pathway was described by patient and tumor characteristics and sequence of utilization activities from first presentation in primary care to referral to a respiratory specialist (e.g. FP visit – chest radiograph – ED visit – computed tomography scan – referral). This revealed potential sources of delay that were further illuminated by a rich description of the patient experience in step 2 where a complex interplay of patient, disease, and system factors was demonstrated. Below we present merged quantitative and qualitative findings for each potential source of delay coupled with recommendations on improvement strategies; a summary is presented in Figure 6.2.

6.5.1. Missed opportunities for earlier referral

In the FP group, 29% of patients had 3 or more visits to their FP before being referred to a respiratory specialist. We hypothesized that this represented missed opportunities for earlier referral. This was supported by the patient experience in that patients with a history of respiratory issues (e.g. asthma) or risk factors (e.g. smoking) perceived their time to referral to be prolonged because of the focus that was placed on these pre-existing conditions. According to patients, despite persistent or worsening symptoms lung cancer was not considered in multiple visits. Some advanced stage patients who felt their symptoms were not being addressed by their

FP went through their own professional and social networks to access appropriate care while other patients presented to the ED or kept seeing their FP until a referral was made.

Given that many patients presented with non-specific symptoms, an alternative hypothesis for multiple FP visits prior to referral was the challenging nature of suspecting lung cancer in primary care. This also had support from advanced stage patients in the FP group who reported unusual symptoms that did not interfere with their day-to-day activities. These odd symptoms were reportedly difficult to communicate to the FP and were not perceived to be serious by patients.

Recommended improvement strategy: We suggest a quality improvement initiative where FP's can learn from specific lung cancer cases where time to referral was prolonged. This could be in the form of significant event audits (SEA's);(6) interrogate untimely cases to discern what went wrong and what could have been done differently. This may reveal issues with clinical reasoning or uncover systemic issues that act as barriers to timely referral. We further suggest that learnings be widely shared across FP clinics given that FP's may only see one lung cancer case per year.(7) In this way, exposure to varying presentations and management decisions could be increased.

6.5.2. Lack of integration between primary and secondary care

In the FP group, 41% of patients had at least one ED visit and 38% of patients were referred to a respiratory specialist from the ED. We hypothesized that this represented a lack of integration between primary and specialist care compelling FP's to use the ED for quicker access to a specialist. This was supported by the patient experience in that the ED was often used for its perceived efficiency, however some patients self-presented to the ED while others were referred

by their FP. In both scenarios the reason for ED presentation was quicker access to investigations and specialists. Of note, 'quicker access' through the ED was quantitatively suggested in the ED group where time to referral was half that of the FP group. This finding was not explained by advanced disease patients being prioritized for quicker investigation; the ED group had less advanced stage patients compared to the FP group.

Recommended improvement strategy: Priority access to diagnostic imaging and specialist consult in the ED needs to be mirrored, to some extent, in community settings. We suggest a new diagnostic strategy focused on supporting FP access to respiratory specialists and diagnostic imaging, specifically more sensitive diagnostics like computed tomography. Although rapid investigation clinics (RIC's) were implemented in Québec to fast-track investigation of patients with suspected lung cancer,(8) it is unclear whether these are being used. Further study with FP's should be conducted to assess if this is the case and why. To complement RIC's in improving access to respiratory specialists, electronic consultation services could be implemented to discuss cases that are concerning but ambiguous before a referral decision is made.(9) This may be particularly helpful given that a clear threshold for referral does not currently exist.

6.5.3. Ineffectiveness of walk-in clinics

In the ED group, 44% of patients first presented at a walk-in clinic but all patients eventually sought care at the ED. We hypothesized that walk-in clinics were ineffective at making care more convenient for patients and reducing ED burden. This was greatly supported by the patient experience in that many felt emotionally distressed and hopeless after presenting at walk-in clinics. This was generally due to a perceived lack of responsiveness to patient symptoms and concerns, a sentiment that was most felt by patients with a smoking history – particularly

worrisome in the case of timely lung cancer diagnosis. Consequently, patients who used walk-in clinics inevitably felt forced to use the ED to get the care they needed. Similar to the FP group, once patients presented at the ED, care was perceived as prompt and effective.

Additionally, compared to patients who sought care from their FP, patients who used walk-in clinics reported delayed communication of results from imaging tests that was believed to have delayed further management.

Recommended improvement strategy: FP access has been a long-standing issue in Canada but is especially dire in Québec despite many improvement initiatives.(10) We suggest other healthcare professionals who can provide care continuity be expanded in primary care to support FP's. This could include nurse practitioners who are employed in greater numbers with wider scopes of practice in Canadian provinces outside Québec.(11)

Walk-in clinics will likely remain a complementary source of care. Accordingly, walk-in clinics should be equipped with a strong quality improvement program that focuses on continuous evaluation of the patient experience to understand where and how improvements need to be made, and if improvements are having the desired impact. One component of quality improvement should be continuous training on patient-centered care and reflection on how personal beliefs may interfere with clinical decision-making. The intent would be to reduce stigmatization of patients with risky or unhealthy behaviours while improving overall quality of care.

6.5.4. Lack of standardization in the pre-diagnostic process

In the FP group, 68% of patients had a unique sequence of utilization activities (i.e. they differed from the rest) and in the ED group, all patients had a unique sequence of activities. As

this suggested wide variability in the pre-diagnostic process, we hypothesized that this represented a lack of standardization.

Recommended improvement strategy: We suggest the design and implementation of standardized care pathways that can support FP's in their clinical decision-making by outlining who should receive what care when. Not only are these pathways based on best available evidence and expert opinion, they also promote uniform harmonized care with clear care expectations. Further study with FP's should be conducted to formally assess variation in symptom management when presented with an identical patient case.

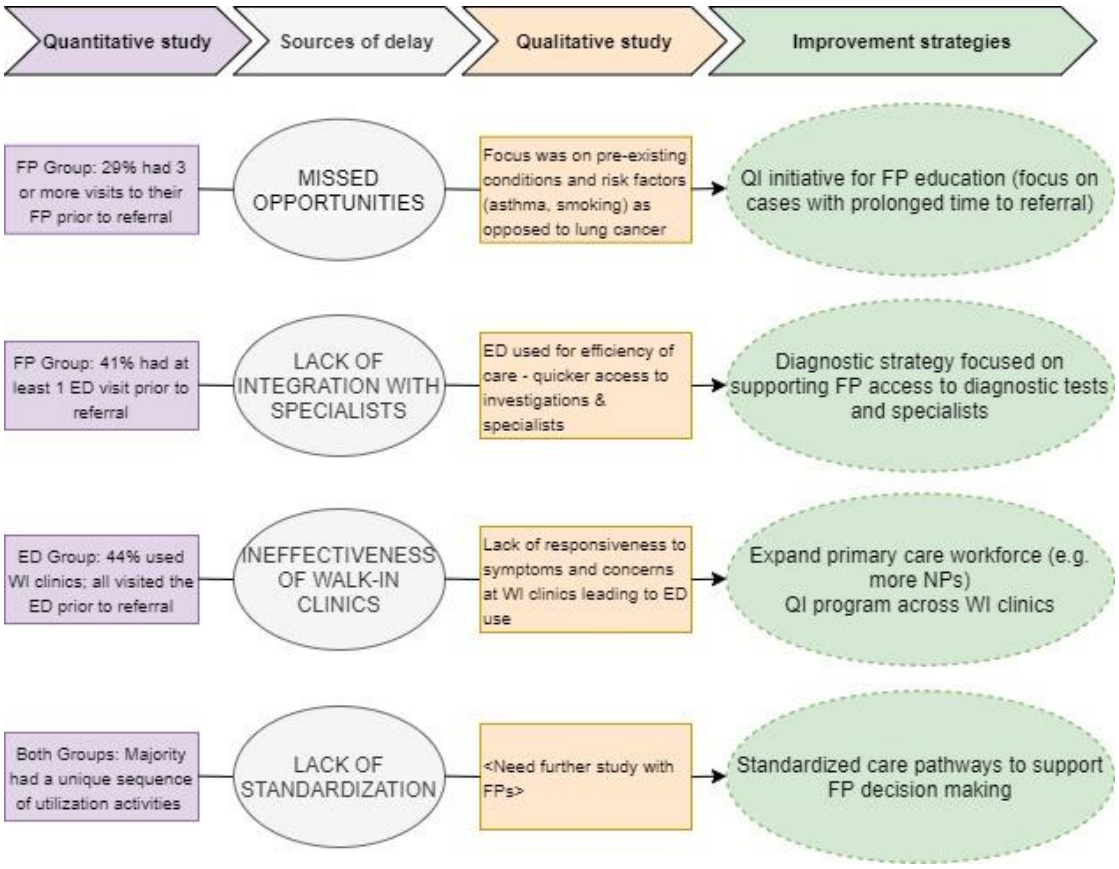

Figure 6.2 Potential sources of lung cancer pre-diagnostic delay and associated improvement strategies

FP = family physician; QI = quality improvement; ED = emergency department; WI = walk-in; NP = nurse practitioner

6.6. **CONCLUSION**

We provide the first comprehensive evaluation of lung cancer pre-diagnostic pathways in Canada with evidence-informed recommendations to reduce diagnostic delay. We hope these recommendations can be further evaluated for use in local contexts across Canada, and that best practices can be shared for national improvement of early lung cancer diagnosis through timely referral.

6.7. **REFERENCES**

1. Canadian Cancer Society. Lung cancer statistics Toronto, ON: Canadian Cancer Society 2019 [cited 2019 May 14]. Available from: http://www.cancer.ca/en/cancer-information/cancer-type/lung/statistics/?region=qc.
2. Canadian Cancer Statistics Advisory Committee. Canadian Cancer Statistics 2018 Toronto, ON: Canadian Cancer Society; 2018 [cited 2019 May 14]. Available from: cancer.ca/Canadian-Cancer-Statistics-2018-EN.
3. Weller D, Vedsted P, Rubin G, Walter FM, Emery J, Scott S, et al. The Aarhus statement: improving design and reporting of studies on early cancer diagnosis. British journal of cancer. 2012;106(7):1262-7.
4. Rankin NM, McGregor D, Stone E, Butow PN, Young JM, White K, et al. Evidence-practice gaps in lung cancer: A scoping review. Eur J Cancer Care (Engl). 2018;27(2):e12588.
5. Canadian Partnership Against Cancer. The 2015 Cancer System Performance Report. System Performance Reports Jun ed. Toronto, ON: Canadian Partnership Against Cancer; 2015. p. 1-161.

6. Mitchell ED, Rubin G, Macleod U. Understanding diagnosis of lung cancer in primary care: qualitative synthesis of significant event audit reports. The British journal of general practice : the journal of the Royal College of General Practitioners. 2013;63(606):37-46.

7. Rubin G, Berendsen A, Crawford SM, Dommett R, Earle C, Emery J, et al. The expanding role of primary care in cancer control. The Lancet Oncology. 2015;16(12):1231-72.

8. Ezer N, Navasakulpong A, Schwartzman K, Ofiara L, Gonzalez AV. Impact of rapid investigation clinic on timeliness of lung cancer diagnosis and treatment. BMC pulmonary medicine. 2017;17(1):178.

9. Keely E, Liddy C. Transforming the specialist referral and consultation process in Canada. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2019;191(15):E408-E9.

10. Statistics Canada. Health fact sheet: Primary health care providers, 2016: Government of Canada 2017 [cited 2019 Dec 19]. Available from: https://www150.statcan.gc.ca/n1/pub/82-625-x/2017001/article/54863-eng.htm.

11. Canadian Institute for Health Information. Canada's Health Care Providers: Provincial Profiles, 2008 to 2017 - Data Tables: CIHI; 2019 [cited 2020 Feb 13]. Available from: https://www.cihi.ca/en/access-data-reports/results?f%5B0%5D=field_primary_theme%3A2047&f%5B1%5D=field_professions%3A2010.

7. CHAPTER 7: DISCUSSION

In Canada, lung cancer kills more men and women than all other common cancers (breast, prostate, and colorectal) combined.(3) Most lung cancer patients are diagnosed when their disease is advanced(60) and this has underscored a need to reduce unnecessary delays in the diagnostic pathway in hopes to catch the disease at an earlier stage. As lung cancer patients must present in primary care to access a specialist where their diagnosis is confirmed, the time from first presentation to specialist referral – what is called the primary care interval – is a critical period of the pre-diagnostic pathway.(16) It is therefore imperative to understand how patients move through the primary care interval, where delays may occur, and what can be done to reduce delay.

7.1. **Summary of research results**

The aim of this PhD thesis was to examine lung cancer pre-diagnostic pathways in the primary care interval to inform potential improvement strategies aimed at timely referral to a respiratory specialist and, in turn, timely lung cancer diagnosis. This work was conducted in Québec which has one of the highest lung cancer incidence and mortality rates among Canadian provinces.(61) The work resulted in four manuscripts.

In the first manuscript (methods brief; Chapter 3),(19) I addressed a methodological concern in my thesis regarding recall bias. One of my data collection methods was structured interviews with patients to collect data on healthcare utilization during the primary care interval (e.g. visits to walk-in clinics, family physicians, emergency departments, etcetera). Within the study sample, there was a large variation in the length of the recall period that was dependent on how much time was spent in the primary care interval (i.e. how long it took to get referred) and when the

diagnosis was made (i.e. recent vs non-recent date of diagnosis) which may have led to recall bias. A review of the literature uncovered several strategies for reducing recall bias. In a manuscript titled 'Recall bias and reduction measures: an example in primary health care service utilization' I summarized what was found in the literature and used my work on identifying groups of lung cancer patients with similar pre-diagnostic pathways (described next) as an example of how these strategies could be applied. Use of memory aids and forward recall were particularly helpful measures for reducing recall bias in my study.

In the second manuscript (original research article; Chapter 4) titled 'Lung cancer pre-diagnostic pathways from first presentation to specialist referral,' I identified the different lung cancer pre-diagnostic pathways in primary care. Patients with similar patterns of healthcare utilization in the primary care interval were clustered into distinct groups using latent class analysis. Two pre-diagnostic pathways were identified: one where family physician (FP) visits were dominant (FP group) with 68% prevalence and one where walk-in clinic and emergency department (ED) visits were dominant (ED group) with 32% prevalence. The FP group had a primary care interval time that was double that of the ED group [45 days (IQR 12-111) vs 22 (IQR 5-69)] and more advanced stage disease (65% vs 50%). I further described each pathway group by various patient and clinical characteristics as well as sequence of utilization activities to generate hypotheses on potential sources of delay.

In the third manuscript (original research article; Chapter 5) titled 'How patient, disease, and system factors influence lung cancer pre-diagnostic pathways,' I explored the patient experience to gain an in-depth understanding of factors that influenced delay within each pathway group. In semi-structured interviews, patients were asked about patient, disease, and system specific factors that may have played a role in their pathway. In the thematic analysis, similarities and

differences between the two groups were uncovered. A key similarity was an appreciation for the efficiency of care received at the ED for patients who used the ED in their pathway. A key difference was related to promptness of care; patients in the FP group experienced easy access and prompt attention whereas patients in the ED group experienced lack of responsiveness that was reflective of care received at walk-in clinics. This was driven by relationship quality between the patient and physician that highly impacted perceived quality of care.

In the fourth manuscript (commentary article; Chapter 6), I merged findings from the previous two articles to provide supporting evidence for four potential sources of pre-diagnostic delay in primary care: missed opportunities for earlier referral, lack of integration between primary and secondary care, ineffectiveness of walk-in clinics, and lack of standardization in the pre-diagnostic process. These are discussed in more detail in the next section. I then suggested correlated improvement strategies to support timely referral of patients with suspected lung cancer. This final manuscript was titled 'Defining lung cancer pre-diagnostic pathways in primary care: an in-depth understanding and suggested improvements' and represented a culmination of my PhD work.

7.2. **Discussion with current evidence**

In this section I will place my findings in the context of what is known in the literature. First, I will discuss my results related to common lung cancer pre-diagnostic pathways and second, I will discuss my results related to potential sources of lung cancer diagnostic delay in primary care. For both aspects, I will focus on literature from countries that have similar healthcare systems, specifically strong primary care systems with a gatekeeping role to secondary specialist care.

7.2.1. Common lung cancer pre-diagnostic pathways

Much of the research on lung cancer pre-diagnostic pathways in primary care has been conducted in European countries, namely the United Kingdom and Denmark. Although study methodology and definition of time intervals vary between studies, the pre-diagnostic pathways found in my study – FP dominant and ED dominant pathways – have been found in several other studies with similar prevalence.(12, 62-68)

FP pathway to lung cancer diagnosis

Most lung cancer patients present to their FP's with symptoms,(69-72) so it is not surprising that the FP pathway where patients mainly rely on their FP's for timely investigation and referral often emerges.(62-64) Relatedly, this pathway has a relatively higher prevalence than others. For example, a UK study with a similar aim of identifying lung cancer diagnostic pathways found that 61% of patients were referred to specialist care by their FP implying a FP pathway (comparable to 68% found in my study).(12) Studies have also indicated longer diagnostic times for patients who see their FP prior to diagnosis compared to those who do not.(11) My study similarly found longer time to referral, as well as more advanced disease, in the FP group however the qualitative exploration added an interesting dimension. Despite poor objective measures, patients in the FP group – all of whom sought care from their own FP with whom they were registered – had overall positive experiences that translated into perceived seamless pathways. This supports the complexity that is inherent in cancer diagnostic pathways and suggests that future research in early cancer diagnosis should incorporate measures of patient experience alongside clinical measures.

ED pathway to lung cancer diagnosis

Besides the FP pathway, many studies have supported an ED pathway as another common pathway to lung cancer diagnosis,(65, 66) albeit with a lower prevalence. For example, separate studies in England and Canada found that approximately 35% of lung cancer patients were diagnosed as a result of emergency presentation (comparable to 32% found in my study).(67, 68) The ED pathway to diagnosis has been shown to be associated with poorer outcomes owing to more serious symptoms and relatedly, more advanced disease.(64, 73-75) In my study, some patients in the ED group indeed presented to the ED with potentially serious symptoms, however, my findings showed an opposite trend of less advanced disease among patients in the ED group. A likely explanation for this came from the qualitative exploration which suggested that ED presentation in my study was driven by access issues and lack of responsiveness among walk-in clinics as opposed to severity of symptoms or disease. This was reflective of the lack of a regular source of primary care which has been shown to be associated with ED use among patients with suspected lung cancer.(76) With a higher proportion of patients registered with a FP in other countries and Canadian jurisdictions where similar studies have been conducted,(77) these important dissimilar findings are underrepresented in the literature. This supports the need for considering the local context in early cancer diagnosis research as different conditions can point to very different improvement strategies.

7.2.2. Sources of pre-diagnostic delay

Next, I will discuss the four potential sources of pre-diagnostic delay suggested by the collective findings of my PhD thesis.

Missed opportunities for earlier referral

In my study, 29% of patients in the FP group had three or more visits to their FP before being referred to a respiratory specialist. Multiple FP visits in the pre-diagnostic pathway has been widely reported elsewhere. For example, an Australian study showed that 60% of patients had four or more visits to their FP in the three months prior to their lung cancer diagnosis,(64) and a study in England showed 1/3 of patients saw their FP three or more times for symptoms related to their lung cancer prior to diagnosis.(78) These studies, along with my findings, suggest missed opportunities for earlier referral.

Reasons for this was offered in the qualitative exploration of my study. According to patients, their FP focused on pre-existing conditions (mostly respiratory conditions like asthma) and health behaviours (like smoking) to explain patient symptoms even when symptoms persisted or worsened leading to multiple visits. These pre-existing conditions seemed to preclude consideration of lung cancer.

The common and non-specific nature of lung cancer symptoms makes lung cancer suspicion difficult in primary care,(79) especially when there are pre-existing conditions that can explain presenting symptoms.(80) FP's also lack clinical experience with lung cancer as most will only see one new case of lung cancer per year.(81) As positive findings on physical examination are rare,(79) FP's often rely on diagnostic imaging to support the need for referral which may not be readily available or accurate. In the local context of this study, a further complicating issue is the lack of a clear referral threshold so FP's may not feel empowered to refer until the risk level is very high.(82)

Lack of integration between primary and secondary care

In my study, 41% of patients in the FP group had at least one ED visit and time to referral in the ED group was half that of the FP group. In the qualitative exploration, patients experienced high efficiency of care at the ED with quicker access to investigations and specialist care. These findings suggest a lack of integration between primary and secondary care with patients presenting at the ED for quicker access to diagnostics and specialists.

This is an important finding as there is evidence of improved lung cancer survival in settings with wider access to diagnostic investigations.(83) Improved direct access to computed tomography scans for FP's could assist in more timely referral(84) especially given the sensitivity issues with first-line investigation in primary care, chest radiography.(54) However, it should be noted that such a change in clinical practice would require high levels of engagement with FP's to ensure uptake.(85)

Notably, in the local context of this study there are no national or provincial recommendations on acceptable time limits between first patient presentation and specialist referral (i.e. wait time targets). This may be impeding specific initiatives to reduce wait times. For example, England has a 2-week-wait suspected lung cancer referral pathway where patients get a specialist appointment within 2 weeks when certain signs, symptoms, or abnormal investigations are present.(86) An equivalent urgent referral pathway does not exist locally, though other clinics have been designed for rapid diagnostic investigations with priority access to imaging and radiology guided biopsies if necessary. These clinics were designed to reduce the need for ED visits by offering an alternative expedited care option. However, my findings suggested quite the opposite where the ED was reported to be the best option for prompt investigation and specialist access. This implies that rapid investigation clinics are not having their intended impact.

Ineffectiveness of walk-in clinics

In my study, 44% of patients in the ED group first presented at a walk-in clinic but all patients eventually sought care at the ED. Walk-in clinics were intended to be an alternate source of care so that patients without a regular source of care did not have to visit the ED. My findings did not support this to be the case. Reasons for this was offered in the qualitative exploration of my study where patients experienced a lack of responsiveness to their symptoms and concerns that forced them to seek care at the ED. This was more strongly reported among patients with a smoking history. These findings suggest an ineffectiveness of walk-in clinics.

The perceived stigmatization of smokers is an important finding that needs addressing given that the lifetime risk of lung cancer is extremely high in smokers compared to never-smokers(87) as is the relative risk of death due to lung cancer.(88) As mentioned previously, lung cancer symptoms are often common and non-specific and when they can be attributed to something pre-existing, like smoking, a more serious disease like lung cancer can be easily overlooked. Nonetheless, positive predictive values for any given lung cancer symptom are higher in those with a smoking history.(89) That being said, suspicion of lung cancer should not be reserved for those with a smoking history as the proportion of never-smokers diagnosed with lung cancer is still high at 10-15%.(90)

My findings suggest that there was little safety-netting at walk-in clinics where patients are advised to re-present if symptoms persist or new symptoms develop; basically a clear follow-up plan. Not only has safety-netting been suggested as an important strategy to reduce diagnostic delays,(49) it may have also improved the patient experience by acknowledging the importance of their symptoms. Despite the lack of responsiveness, patients in my study recognized that something was wrong and sought further care at the ED where they were eventually diagnosed

with lung cancer. This is an interesting finding as it has been suggested that patient (and physician) intuition is more important than results of clinical investigations in early lung cancer diagnosis.(91, 92)

Lack of standardization in the pre-diagnostic process

In my study, most patients – 68% in the FP group and 100% in the ED group – had a unique sequence of utilization activities and thus unique pre-diagnostic pathways within their pathway group. This finding suggests a lack of standardization in the pre-diagnostic process.

The gatekeeping role of primary care has been suggested to contribute to poor survival in lung cancer(93) presumably because it can act as a barrier to timely access to specialists. Referral guidelines and standardized cancer care pathways can help to streamline access by harmonizing care and taking some of the guess work out of referral decisions. An important consideration in guideline development is ensuring that less serious symptoms like persistent cough are equally prioritized for investigation as more serious symptoms like hemoptysis. The reason is two-fold. First, less serious symptoms may be associated with less advanced disease and would have the most to gain from early diagnosis.(71, 94) Second, more serious symptoms with high positive predictive values are relatively uncommon. For example, hemoptysis has the highest positive predictive value but is reported by only a fifth of lung cancer patients.(47, 48)

Referral recommendations for suspected lung cancer have been developed internationally(86) and within some Canadian provinces.(95) However, in the local context of this study there are no provincial referral guidelines for suspected lung cancer in primary care and no standardized lung cancer care pathway. This may be contributing to variability in how lung cancer patients are managed in the pre-diagnostic pathway.

7.3. **Strengths and limitations**

A major strength of my PhD thesis was the study design; an explanatory sequential mixed-methods design. Here, a quantitative study to identify and describe lung cancer pre-diagnostic pathways was followed by a qualitative study to explore how patient, disease, and system factors influenced the pathways identified. Given the complexity of cancer diagnostic pathways, this design allowed an in-depth understanding that would not have been possible with purely quantitative or qualitative designs. Not only did the qualitative results build upon the quantitative results, the quantitative results also guided purposeful sampling in the qualitative study to ensure that the sample was representative of common pre-diagnostic pathways in primary care. The explanatory sequential mixed-methods design had the added strength of simplicity and straightforwardness that facilitated research planning and communication of results. Overall, this is a robust design for researchers who want to form groups based on quantitative results and follow up with the groups through subsequent qualitative research.(96)

Additionally, my study design and methods were chosen to enhance generalizability even though this study was conducted in a limited geographical area. Indeed, design and methods are in accordance with the guidelines outlined in the Aarhus Statement on improving design and reporting of studies on early cancer diagnosis,(9) thus ensuring consistency with the literature and enhancing generalizability. I also used the theoretical Model of Pathways to Treatment,(97) a cancer specific diagnostic pathway, to underpin the qualitative exploration in my study.

However, a key limitation in my study remains related to generalizability of results. Given my results were based on a small sample of lung cancer patients from a single urban lung cancer clinic, broad extension of the results to other settings would need to be cautioned. For example, generalizability may be limited to countries that have similar healthcare systems, particularly a

gatekeeping system, as well as the absence of an organized lung cancer screening program. Additionally, my findings may not be generalizable to rural areas as pre-diagnostic pathways and referral practices may differ in these locations.(98) Nonetheless, despite a small sample in the quantitative study (n=50), sample demographics were similar to patient characteristics of the lung cancer clinic and study results coincided with the literature.

Other limitations included possible recall bias in the self-reported healthcare utilization data gathered from patients which was minimized using several strategies found in the literature (see Chapter 3). In the quantitative study, there was possible survival bias and selection bias (see Chapter 4). In the former, patients diagnosed between 2015 and 2017 were included in the study but recruitment was in 2017 meaning some patients had to survive two years to participate. In the latter, the participation rate was 30% of the eligible sample despite significant recruitment efforts. Finally, in the qualitative study, there was no respondent validation due to the declining health of study participants, however, data triangulation and triangulation of analysts were used to establish credibility (see Chapter 5). These limitations would have been reduced or eliminated in a prospective study design however this was not feasible within a PhD timeline given the relatively low number of incident lung cancer cases in primary care.

7.4. **Implications for practice**

The aim of this PhD thesis was to examine lung cancer pre-diagnostic pathways in primary care to inform potential improvement strategies aimed at timely referral to a respiratory specialist. As such, I prepared a commentary (see Chapter 6) that outlined four potential sources of diagnostic delay based on my study findings and coupled each with suggested improvement strategies for practice.

These strategies include the following: a quality improvement initiative where FP's can learn from cases with prolonged time to referral (e.g. significant event audits), a new diagnostic strategy focused on supporting FP access to respiratory specialists and diagnostic imaging (e.g. computed tomography), electronic consultation services where FP's can consult with respiratory specialists prior to referral decisions, expansion of the primary care workforce to improve patient access to a regular source of care (e.g. nurse practitioners), a robust quality improvement program for walk-in clinics focused on evaluating the patient experience, and standardized care pathways for suspected lung cancer in primary care. These strategies have been shown to promote timely referral practices in other jurisdictions and could have a positive impact, either alone or in combination, in the local context of this study.

In addition, knowledge translation activities were embedded in my PhD thesis and began with extensive consultations among clinicians (e.g. nurses, family physicians, oncologists) and researchers to inform the research question and study design. Other knowledge translation activities included oral and poster presentations at several primary care and oncology conferences as well as oral presentations in research seminars, family medicine grand rounds, and lung cancer clinician meetings. I also organized a film screening event showcasing the cancer journey of a young Albertan patient to brainstorm ideas on system improvements towards earlier cancer diagnosis. This event was well attended by a diverse crowd of students, clinicians, researchers, policy makers, and patients and led to several potential ideas. Unfortunately, the Covid 19 pandemic hit shortly after forcing a pause on further work.

7.5. **Future study**

My PhD thesis, though comprehensive, is missing the vital perspective of FP's in the pre-diagnostic process. As such, I plan to co-supervise, along with Dr. Isabelle Vedel (my PhD supervisor), an MSc student thesis focused on the FP perspective in lung cancer pre-diagnostic pathways. With a goal to understand challenges and needs faced by primary care providers, this would likely be a qualitative study involving in-depth interviews or a series of focus groups with representation of FP's from different settings (i.e. community practices, hospital-based clinics, walk-in clinics, emergency). This work will build on my PhD thesis and serve to further refine suggested improvement strategies aimed at timely referral to a respiratory specialist. I hope to start this work within the next year, or as soon as is feasible with respect to the current Covid 19 pandemic.

During this work the knowledge translation plan will be updated to ensure findings are applied in the form of effective practice changes. In fact, I have been approached by senior leadership from the Centre intégré universitaire de santé et de services sociaux (CIUSSS) du Centre-Ouest-de-l'Île-de-Montréal and the Rossy Cancer Network. There is an interest among executive leadership to spearhead initiatives aimed at better integrating hospital and primary care specifically towards timely lung cancer diagnosis; this may open opportunities for supported pilot projects in a healthcare network that serves a diverse patient population.

Lastly, I have started a position with the Canadian Partnership Against Cancer leading early diagnosis initiatives in the cancer control division. While my work will be guided by national priorities, I have already started discussing the importance of primary care in these initiatives and have cited the evidence, including my own, in this regard.

8. CHAPTER 8: CONCLUSION

Lung cancer is the leading cause of cancer-specific deaths in Canada with most patients diagnosed at an advanced stage of disease. In order to promote earlier diagnosis, unnecessary delays in the diagnostic process must be understood and reduced, particularly during the primary care interval from first presentation to specialist referral. In Canada, the primary care interval is understudied and poorly understood. Furthermore, Québec is known to have high lung cancer incidence and mortality rates yet there has been no research on pre-diagnostic pathways in primary care to understand how timely referral to a respiratory specialist can be supported.

My study is the first in Québec to examine lung cancer pre-diagnostic pathways and offer an in-depth understanding of how patients move through the primary care interval from first presentation to referral. In addition to identifying and describing common pre-diagnostic pathways, I present a rich contextualization of the pathways based on lived patient experiences and propose several sources of diagnostic delay based on quantitative and qualitative evidence. To promote improvement practices, I further suggest associated improvement strategies that are informed by the literature but grounded in the local context.

Beyond provincial contributions, my work is the first comprehensive evaluation of lung cancer pre-diagnostic pathways in Canada. My study adds to a dearth of evidence on primary care delays and provides a vital stepping-stone to furthering our knowledge in the primary care interval. Not only are my findings novel, the methodological backbone of my study could be replicated across Canada to facilitate the development of national early diagnosis initiatives in primary care. As such, my work represents a first and crucial step towards building a solid evidence base in primary care where improvements can lead to earlier cancer diagnosis.

9. REFERENCES

1. Canadian Cancer Statistics Advisory Committee. Canadian Cancer Statistics 2019 Toronto, ON: Canadian Cancer Society; 2019 [cited 2020 October 11]. Available from: cancer.ca/Canadian-Cancer-Statistics-2019-EN
2. Canadian Cancer Statistics Advisory Committee. Canadian Cancer Statistics: A 2020 special report on lung cancer Toronto, ON: Canadian Cancer Society; 2020 [cited 2020 November 4]. Available from: cancer.ca/Canadian-Cancer-Statistics-2020-EN.
3. Canadian Cancer Society. Lung cancer statistics Toronto, ON: Canadian Cancer Society 2019 [cited 2019 May 14]. Available from: http://www.cancer.ca/en/cancer-information/cancer-type/lung/statistics/?region=qc.
4. Lung Cancer Canada. The Faces of Lung Cancer: Fighting Disease, Fighting Disparity. . Toronto, ON; 2014.
5. Dean AG, Kreis R. Understanding Lung Cancer: Presentation, Screening, and Treatment Advances. Journal for Nurse Practitioners. 2018;14(4):316-22.
6. Latimer KM. Lung Cancer: Clinical Presentation and Diagnosis. FP essent. 2018;464:23-6.
7. Bray F, Colombet M, Mery L, Piñeros M, Znaor A, Zanetti R, et al. Cancer Incidence in Five Continents, Vol. XI (electronic version). Lyon: International Agency for Research on Cancer; 2017 [cited 2020 October 26]. Available from: http://ci5.iarc.fr.
8. System Performance. Distribution of cases by stage at diagnosis for non-small cell lung cancer – 2013 diagnosis year.: Canadian Partnership Against Cancer [cited 2016 February 5]. Available from: https://www.systemperformance.ca/cancer-control-domain/diagnosis/stage-distribution/.
9. Weller D, Vedsted P, Rubin G, Walter FM, Emery J, Scott S, et al. The Aarhus statement: improving design and reporting of studies on early cancer diagnosis. British journal of cancer. 2012;106(7):1262-7.
10. Olesen F, Hansen RP, Vedsted P. Delay in diagnosis: the experience in Denmark. BRITISH JOURNAL OF CANCER. 2009;101(SUPP/2):S5-S8.
11. Allgar VL, Neal RD. Delays in the diagnosis of six cancers: Analysis of data from the National Survey of NHS Patients: Cancer. British Journal of Cancer. 2005;92(11):1959-70.
12. Barrett J, Hamilton W. Pathways to the diagnosis of lung cancer in the UK: a cohort study. BMC Fam Pract. 2008;9:31.
13. Bjerager M, Palshof T, Dahl R, Vedsted P, Olesen F. Delay in diagnosis of lung cancer in general practice. Br J Gen Pract. 2006;56(532):863-8.
14. Koyi H, Hillerdal G, Branden E. Patient's and doctors' delays in the diagnosis of chest tumors. Lung Cancer. 2002;35(1):53-7.
15. Singh H, Sethi S, Raber M, Petersen LA. Errors in cancer diagnosis: current understanding and future directions. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2007;25(31):5009-18.
16. Rubin G, Berendsen A, Crawford SM, Dommett R, Earle C, Emery J, et al. The expanding role of primary care in cancer control. The Lancet Oncology. 2015;16(12):1231-72.
17. Cheung WY, Butler JR, Kliewer EV, Demers AA, Musto G, Welch S, et al. Analysis of wait times and costs during the peri-diagnostic period for non-small cell lung cancer. Lung Cancer. 2011;72(1):125-31.
18. Rankin NM, McGregor D, Stone E, Butow PN, Young JM, White K, et al. Evidence-practice gaps in lung cancer: A scoping review. Eur J Cancer Care (Engl). 2018;27(2):e12588.
19. Khare SR, Vedel I. Recall bias and reduction measures: an example in primary health care service utilization. Family Practice. 2019;36(5):672-6.
20. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. International Journal of Cancer. 2015;136(5):E359-E86.
21. Ferlay J, Ervik M, Lam F, Colombet M, Mery L, M P. Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer; 2018 [cited 2020 October 3]. Available from: https://gco.iarc.fr/today.
22. Statistics Canada. Lung cancer, age-standardized incidence rates per 100,000, by year and sex, Canada, 1992 to 2007. 2011 [cited 2016 February 10]. Available from: http://www.statcan.gc.ca/pub/82-624-x/2011001/article/chart/11596-02-chart2-eng.htm.

23. Canadian Institute for Health Information. Benchmarking Canada's Health Care Systems: International Comparisons, 2017. 2017 [cited 2020 February 11]. Available from: https://www.cihi.ca/en/benchmarking-canadas-health-care-systems-international-comparisons-2017.
24. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2017. Toronto, ON: Canadian Cancer Society; 2017 [cited 2019 March 11]. Available from: cancer.ca/Canadian-CancerStatistics-2017-EN.pdf.
25. Public Health Agency of Canada. Canadian Cancer Incidence Atlas - Volume 2, 2000-2006. In: Centre for Chronic Disease Prevention, editor. Ottawa, ON: Public Health Agency of Canada; 2014.
26. Yoder LH. An overview of lung cancer symptoms, pathophysiology, and treatment. Medsurg Nurs. 2006;15(4):231-4.
27. Beckles MA, Spiro SG, Colice GL, Rudd RM. Initial evaluation of the patient with lung cancer: symptoms, signs, laboratory tests, and paraneoplastic syndromes. Chest. 2003;123(1 Suppl):97S-104S.
28. Ganti AK, Gerber DE. Lung Cancer New York, NY: Oxford University Press 2013.
29. Canadian Cancer Society. Stages of non–small cell lung cancer. Toronto, ON: Canadian Cancer Society; 2020 [cited 2020 July 21]. Available from: https://www.cancer.ca/en/cancer-information/cancer-type/lung/staging/?region=qc.
30. Feng SH, Yang S-T. The new 8th TNM staging system of lung cancer and its potential imaging interpretation pitfalls and limitations with CT image demonstrations. Diagn Interv Radiol. 2019;25(4):270-9.
31. Kasymjanova G, Small D, Cohen V, Jagoe RT, Batist G, Sateren W, et al. Lung cancer care trajectory at a Canadian centre: an evaluation of how wait times affect clinical outcomes. Current oncology (Toronto, Ont). 2017;24(5):302-9.
32. Howlader N, Forjaz G, Mooradian MJ, Meza R, Kong CY, Cronin KA, et al. The Effect of Advances in Lung-Cancer Treatment on Population Mortality. The New England journal of medicine. 2020;383(7):640-9.
33. Dawe DE, Harlos CH, Juergens RA. Immuno-oncology-the new paradigm of lung cancer treatment. Current oncology (Toronto, Ont). 2020;27(Suppl 2):S78-S86.
34. Huang Q, Zhang H, Hai J, Socinski MA, Lim E, Chen H, et al. Impact of PD-L1 expression, driver mutations and clinical characteristics on survival after anti-PD-1/PD-L1 immunotherapy versus chemotherapy in non-small-cell lung cancer: A meta-analysis of randomized trials. Oncoimmunology. 2018;7(12):e1396403.
35. Temel JS, Greer JA, Muzikansky A, Gallagher ER, Admane S, Jackson VA, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. The New England journal of medicine. 2010;363(8):733-42.
36. Velasco Garrido M, Zentner A, Busse R. The effects of gatekeeping: a systematic review of the literature. Scand J Prim Health Care. 2011;29(1):28-38.
37. Macleod U, Mitchell ED, Burgess C, Macdonald S, Ramirez AJ. Risk factors for delayed presentation and referral of symptomatic cancer: evidence for common cancers. British journal of cancer. 2009;101(Suppl 2):S92-S101.
38. Allgar VL, Neal RD. General practictioners' management of cancer in England: secondary analysis of data from the National Survey of NHS Patients-Cancer. Eur J Cancer Care (Engl). 2005;14(5):409-16.
39. Olsson JK, Schultz EM, Gould MK. Timeliness of care in patients with lung cancer: a systematic review. Thorax. 2009;64(9):749-56.
40. Lovgren M, Levealahti H, Tishelman C, Runesdotter S, Hamberg K. Time spans from first symptom to treatment in patients with lung cancer--the influence of symptoms and demographic characteristics. Acta Oncol. 2008;47(3):397-405.
41. Lyratzopoulos G, Wardle J, Rubin G. Rethinking diagnostic delay in cancer: how difficult is the diagnosis? BMJ. 2014;349(dec09 3):g7400.
42. Shim J, Brindle L, Simon M, George S. A systematic review of symptomatic diagnosis of lung cancer. Family Practice. 2014;31(2):137-48.
43. Del Giudice ME, Young SM, Vella ET, Ash M, Bansal P, Robinson A, et al. Systematic review of guidelines for the management of suspected lung cancer in primary care. Can Fam Physician. 2014;60(8):e395-404.
44. Hamilton W. The CAPER studies: five case-control studies aimed at identifying and quantifying the risk of cancer in symptomatic primary care patients. British Journal of Cancer [Internet]. 2009; 101:[S80-S6 pp.].
45. Hippisley-Cox J, Coupland C. Identifying patients with suspected lung cancer in primary care: derivation and validation of an algorithm. The British Journal of General Practice. 2011;61(592):e715-e23.
46. Ades AE, Biswas M, Welton NJ, Hamilton W. Symptom lead time distribution in lung cancer: natural history and prospects for early diagnosis. International journal of epidemiology. 2014;43(6):1865-73.
47. 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;60(12):1059-65.

48. Walter FM, Rubin G, Bankhead C, Morris HC, Hall N, Mills K, et al. Symptoms and other factors associated with time to diagnosis and stage of lung cancer: a prospective cohort study. British Journal of Cancer. 2015;112 Suppl 1:S6-13.
49. Mitchell ED, Rubin G, Macleod U. Understanding diagnosis of lung cancer in primary care: qualitative synthesis of significant event audit reports. The British journal of general practice : the journal of the Royal College of General Practitioners. 2013;63(606):37-46.
50. Collins LG, Haines C, Perkel R, Enck RE. Lung cancer: diagnosis and management. American family physician. 2007;75(1):56-63.
51. Abel G, Saunders CL, Mendonca SC, Gildea C, McPhail S, Lyratzopoulos G. Variation and statistical reliability of publicly reported primary care diagnostic activity indicators for cancer: a cross-sectional ecological study of routine data. BMJ quality & safety. 2018;27(1):21-30.
52. Chandra S, Mohan A, Guleria R, Singh V, Yadav P. Delays during the diagnostic evaluation and treatment of lung cancer. Asian Pac J Cancer Prev. 2009;10(3):453-6.
53. Beckles, Spiro MA, Colice SG, Rudd GL. Initial Evaluation of the Patient With Lung Cancer : Symptoms, Signs, Laboratory Tests, and Paraneoplastic Syndromes. Chest: Supplement. 2003;123(1 Supplement):97S-104S.
54. Stapley S, Sharp D, Hamilton W. Negative chest X-rays in primary care patients with lung cancer. Br J Gen Pract. 2006;56(529):570-3.
55. Kvale PA. Chronic cough due to lung tumors: ACCP evidence-based clinical practice guidelines. Chest. 2006;129(1 Suppl):147S-53S.
56. Scottish Intercollegiate Guidelines Network. Management of patients with lung cancer: a national clinical guideline. Edinburgh, SCT: Scottish Intercollegiate Guidelines Network (SIGN); 2005.
57. Carlsson L, Håkansson A, Nordenskjöld B. Common cancer-related symptoms among GP patients. Opportunistic screening in primary health care. Scand J Prim Health Care. 2001;19(3):199-203.
58. Corner J, Hopkinson J, Fitzsimmons D, Barclay S, Muers M. Is late diagnosis of lung cancer inevitable? Interview study of patients' recollections of symptoms before diagnosis. Thorax. 2005;60(4):314-9.
59. Banks J, Hollinghurst S, Bigwood L, Peters TJ, Walter FM, Hamilton W. Preferences for cancer investigation: a vignette-based study of primary-care attendees. The Lancet Oncology. 2014;15(2):232-40.
60. Canadian Cancer Statistics Advisory Committee. Canadian Cancer Statistics 2018 Toronto, ON: Canadian Cancer Society; 2018 [cited 2019 May 14]. Available from: cancer.ca/Canadian-Cancer-Statistics-2018-EN.
61. Canadian Partnership Against Cancer. The 2018 Cancer System Performance Report. System Performance Reports Nov ed. Toronto, ON: Canadian Partnership Against Cancer; 2018. p. 1-63.
62. Baughan P, O'Neill B, Fletcher E. Auditing the diagnosis of cancer in primary care: The experience in Scotland. British Journal of Cancer. 2009;101:S87-S91.
63. Guldbrandt LM, Fenger-Gron M, Rasmussen TR, Jensen H, Vedsted P. The role of general practice in routes to diagnosis of lung cancer in Denmark: a population-based study of general practice involvement, diagnostic activity and diagnostic intervals. BMC Health Serv Res. 2015;15:21.
64. Purdie S, Creighton N, White KM, Baker D, Ewald D, Lee CK, et al. Pathways to diagnosis of non-small cell lung cancer: a descriptive cohort study. npj Primary Care Respiratory Medicine. 2019;29(2).
65. Elliss-Brookes L, McPhail S, Ives A, Greenslade M, Shelton J, Hiom S, et al. Routes to diagnosis for cancer - determining the patient journey using multiple routine data sets. British journal of cancer. 2012;107(8):1220-6.
66. Maringe C, Pashayan N, Rubio FJ, Ploubidis G, Duffy SW, Rachet B, et al. Trends in lung cancer emergency presentation in England, 2006-2013: Is there a pattern by general practice? BMC Cancer. 2018;18(1).
67. National Cancer Intelligence Network. Routes to Diagnosis: Tumours Diagnosed 2006-2016. London: Public Health England; 2019 [cited 2020 October 6]. Available from: https://data.healthdatainsight.org.uk/apps/routes_to_diagnosis/routes_subbreakdowns/.
68. Suhail A, Crocker CE, Das B, Payne JI, Manos D. Initial presentation of lung cancer in the emergency department: a descriptive analysis. CMAJ open. 2019;7(1):E117-E23.
69. Demagny L, Holtedahl K, Bachimont J, Thorsen T, Letourmy A, Bungener M. General practitioners' role in cancer care: a French-Norwegian study. BMC research notes. 2009;2:200.
70. Ewing M, Naredi P, Nemes S, Zhang C, Mansson J. Increased consultation frequency in primary care, a risk marker for cancer: a case-control study. Scand J Prim Health Care. 2016;34(2):205-12.
71. Hamilton W. Five misconceptions in cancer diagnosis. The British journal of general practice : the journal of the Royal College of General Practitioners. 2009;59(563):441-5.
72. Torring ML, Frydenberg M, Hansen RP, Olesen F, Vedsted P. Evidence of increasing mortality with longer diagnostic intervals for five common cancers: a cohort study in primary care. Eur J Cancer. 2013;49(9):2187-98.

73. Beckett P, Tata LJ, Hubbard RB. Risk factors and survival outcome for non-elective referral in nonsmall cell lung cancer patients—analysis based on the National Lung Cancer Audit. Lung Cancer. 2014;83(3):396–400.
74. Laudicella M, Walsh B, Burns E, Li Donni P, Smith PC. What is the impact of rerouting a cancer diagnosis from emergency presentation to GP referral on resource use and survival? Evidence from a population-based study. BMC Cancer. 2018;18(1):394.
75. McPhail S, Elliss-Brookes L, Shelton J, Ives A, Greenslade M, Vernon S, et al. Emergency presentation of cancer and short-term mortality. British journal of cancer. 2013;109(8):2027-34.
76. Mitchell ED, Pickwell-Smith B, Macleod U. Risk factors for emergency presentation with lung and colorectal cancers: a systematic review. BMJ Open [Internet]. 2015; 5(4).
77. Statistics Canada. Health fact sheet: Primary health care providers, 2016: Government of Canada 2017 [cited 2019 Dec 19]. Available from: https://www150.statcan.gc.ca/n1/pub/82-625-x/2017001/article/54863-eng.htm.
78. 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. British journal of cancer. 2013;108(3):686-90.
79. Bradley SH, Kennedy MPT, Neal RD. Recognising Lung Cancer in Primary Care. Adv Ther. 2019;36(1):19-30.
80. Guldbrandt LM, Moller H, Jakobsen E, Vedsted P. General practice consultations, diagnostic investigations, and prescriptions in the year preceding a lung cancer diagnosis. Cancer Med. 2017;6(1):79-88.
81. Neal RD, Hamilton W, Rogers TK. Lung cancer. BMJ. 2014;349(nov06 2):g6560.
82. Barraclough K. New NICE guidance on referral for cancer. BMJ (Clinical research ed). 2015;351:h3640.
83. Rose PW, Rubin G, Perera-Salazar R, Almberg SS, Barisic A, Dawes M, et al. Explaining variation in cancer survival between 11 jurisdictions in the International Cancer Benchmarking Partnership: a primary care vignette survey. BMJ open. 2015;5(5):e007212.
84. Millett D. Why GPs need better access to diagnostic cancer scans: GP; 2014 [cited 2020 October 6]. Available from: https://www.gponline.com/why-gps-need-better-access-diagnostic-cancer-scans/cancer/article/1322828.
85. Guldbrandt LM, Rasmussen TR, Rasmussen F, Vedsted P. Implementing direct access to low-dose computed tomography in general practice--method, adaption and outcome. PLoS ONE. 2014;9(11):e112162.
86. NICE guideline [NG12]. Suspected cancer: recognition and referral 2015 [Internet]. 2017. Available from: https://www.nice.org.uk/guidance/ng12
87. Villeneuve PJ, Mao Y. Lifetime Probability of Developing Lung Cancer, by Smoking Status, Canada. Canadian Journal of Public Health / Revue Canadienne de Sante'e Publique. 1994;85(6):385-8.
88. Doll R, Peto R, Boreham J, Sutherland I. Mortality from cancer in relation to smoking: 50 years observations on British doctors. British Journal of Cancer. 2005;92(3):426-9.
89. Hamilton W. Towards earlier diagnosis of cancer in primary care: a population-based case-control study of colorectal, lung and prostate cancer. Bristol2005.
90. Pelosof L, Ahn C, Gao A, Horn L, Madrigales A, Cox J, et al. Proportion of Never-Smoker Non-Small Cell Lung Cancer Patients at Three Diverse Institutions. Journal of the National Cancer Institute. 2017;109(7).
91. Hamilton W. Cancer diagnosis in primary care. The British Journal of General Practice. 2010;60(571):121-8.
92. Ingeman ML, Christensen MB, Bro F, Knudsen ST, Vedsted P. The Danish cancer pathway for patients with serious non-specific symptoms and signs of cancer-a cross-sectional study of patient characteristics and cancer probability. BMC Cancer. 2015;15(1).
93. Vedsted P, Olesen F. Are the serious problems in cancer survival partly rooted in gatekeeper principles? An ecologic study. The British journal of general practice : the journal of the Royal College of General Practitioners. 2011;61(589):508-12.
94. Jensen H, Torring ML, Fenger-Gron M, Olesen F, Overgaard J, Vedsted P. Tumour stage and implementation of standardised cancer patient pathways: a comparative cohort study. Br J Gen Pract. 2016;66(647):E434-E43.
95. Del Giudice ME, Young SM, Vella ET, Ash M, Bansal P, Robinson A, et al. Guideline for referral of patients with suspected lung cancer by family physicians and other primary care providers. Can Fam Physician. 2014;60(8):711-6, e376-82.
96. Tashakkori A, Teddlie C. Mixed methodology : combining qualitative and quantitative approaches. Thousand Oaks, Calif.: Sage; 1998.

97. 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;17(2):110-8.
98. Verma R, Pathmanathan S, Otty ZA, Binder J, Vangaveti VN, Buttner P, et al. Delays in lung cancer management pathways between rural and urban patients in North Queensland: a mixed methods study. Intern Med J. 2018;48(10):1228-33.

10. Appendix 1: Ethics Approval Documents

10.1. Ethics Approval

Centre intégré universitaire de santé et de services sociaux du Centre-Ouest-de-l'Île-de-Montréal

Québec

Hôpital général juif

BUREAU DE L'EXAMEN DE LA RECHERCHE
RESEARCH REVIEW OFFICE

CENTRE GÉRIATRIQUE DONALD BERMAN MAIMONIDES GERIATRIC CENTRE

CENTRE D'HÉBERGEMENT FATHER-DOWD RESIDENTIAL CENTRE

CENTRE D'HÉBERGEMENT HENRI-BRADET RESIDENTIAL CENTRE

CENTRE D'HÉBERGEMENT ST-ANDREW RESIDENTIAL CENTRE

CENTRE D'HÉBERGEMENT ST-MARGARET RESIDENTIAL CENTRE

CENTRE MIRIAM HOME AND SERVICES

CENTRE DE RÉADAPTATION CONSTANCE-LETHBRIDGE REHABILITATION CENTRE

CENTRE DE RÉADAPTATION MAB-MACKAY REHABILITATION CENTRE

CHSLD JUIF DE MONTRÉAL JEWISH ELDERCARE CENTRE

CLSC DE BENNY FARM

CLSC DE CÔTE-DES-NEIGES

CLSC MÉTRO

CLSC DE PNBC-EXTENSION

CLSC RENÉ-CASSIN

HÔPITAL CATHERINE BOOTH HOSPITAL

HÔPITAL GÉNÉRAL JUIF JEWISH GENERAL HOSPITAL

HÔPITAL MOUNT SINAI HOSPITAL

HÔPITAL RICHARDSON HOSPITAL

Integrated Health and Social Services University Network for West-Central Montreal

Dr. Vasiliki Bessy Bitzas, N, PhD, CHPCN (C)
Présidente, Comité d'éthique de la recherche Médical/biomedical
CIUSSS Centre-Ouest-de-L'Île-de-Montréal
3755 Côte-Ste-Catherine, A-925
Montréal, Québec, H3T 1E2
514-340-8222 local 22445
cer@jgh.mcgill.ca
jgh.ca/rec

Me. Alain Klotz, L...M.
Président, Comité d'éthique de la recherche Première ligne & psychocial
CIUSSS Centre-Ouest-de-L'Île-de-Montréal
3755 Côte-Ste-Catherine, A-925
Montréal, Québec, H3T 1E2
514-340-8222 local22445
cer@jgh.mcgill.ca
jgh.ca/rec

Amended: May 8, 2017

May 3, 2017

Dr. Isabelle Vedel
Dept. of Family Medicine
McGill University
CIUSSS-CODIM

SUBJECT: Ethics Protocol #: CODIM-FLP-17-031
Title: "Defining Lung Cancer Diagnostic Pathways in the Primary Care Setting in Montreal, Quebec: An Exploratory Sequential Mixed Methods Study"
Funding: FRQS & PDSI
Contact: Sayta Rashi Khare: rashi.khare@gmail.com

Dear Dr. Vedel,

Thank you for submitting the following documents pertaining to the above-mentioned protocol the above-mentioned documents to the Research Review Office for review:

- Protocol (April 11, 2017)
- Budget (April 11, 2017)
- Proof of Scientific Review: Final Report for the PhD Comprehensive Examination
- Patient Consent Document English Version (April 11, 2017)
- Patient Consent Document French Version (April 11, 2017)
- Caregiver Consent Document English Version (April 11, 2017)
- Caregiver Consent Document French Version (April 11, 2017)
- Script for Determining patients' capacity to consent English version (February 8, 2017)
- Lay Summary of research (February 8, 2017)
- Data capture form

The Research Ethics Committees of the West-Central Montreal Health (Federalwide Assurance Number: 0796) are designated by the province (MSSS) and follows the published guidelines of the TCPS 2 - Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (2014), in compliance with the "Plan d'action ministériel en éthique de la recherche et en intégrité scientifique" (MSSS, 1998), and acts in conformity with standards set forth in the

Centre intégré universitaire de santé et de services sociaux du Centre-Ouest-de-l'Île-de-Montréal
Québec

Hôpital général juif

CENTRE GÉRIATRIQUE DONALD BERMAN MAIMONIDES GERIATRIC CENTRE

CENTRE D'HÉBERGEMENT FATHER-DOWD RESIDENTIAL CENTRE

CENTRE D'HÉBERGEMENT HENRI-BRADET RESIDENTIAL CENTRE

CENTRE D'HÉBERGEMENT ST-ANDREW RESIDENTIAL CENTRE

CENTRE D'HÉBERGEMENT ST-MARGARET RESIDENTIAL CENTRE

CENTRE MIRIAM HOME AND SERVICES

CENTRE DE RÉADAPTATION CONSTANCE-LETHBRIDGE REHABILITATION CENTRE

CENTRE DE RÉADAPTATION MAR-MACKAY REHABILITATION CENTRE

CHSLD JUIF DE MONTRÉAL JEWISH ELDERCARE CENTRE

CLSC DE BENNY FARM

CLSC DE CÔTE-DES-NEIGES

CLSC MÉTRO

CLSC DE PARC-EXTENSION

CLSC RENÉ-CASSIN

HÔPITAL CATHERINE BOOTH HOSPITAL

HÔPITAL GÉNÉRAL JUIF JEWISH GENERAL HOSPITAL

HÔPITAL MOUNT SINAI HOSPITAL

HÔPITAL RICHARDSON HOSPITAL

Integrated Health and Social Services University Network for West-Central Montreal

United States Code of Federal Regulations governing human subjects research, and functions in a manner consistent with international, federal and provincial accepted principles of good clinical practice.

As this study involves no more than minimal risk in accordance with TCPS 2 article 6.12, this protocol received a delegated research ethics review. The revised documents were reviewed by the Chair and deemed acceptable. We are pleased to inform you that the above-mentioned documents are granted Delegated Approval for the period of one year. For quality assurance purposes, you must use the approved "Research Ethics Approval" stamped consent forms when obtaining consent by making copies of the enclosed ones. For information purposes, the proposal will be presented the full board FLP committee meeting to be held on May 10, 2017

Please note that it is the Investigator's responsibility to ensure that all necessary final approval letters (Science and Feasibility) are granted before the study can be initiated at our site.

Approval Date:	**DATE: May 3, 2017**
Expiration date of Approval:	**DATE: May 2, 2018**

Your "Continuing Review Application" must be received by the Research Review Office one month prior to the expiration date mentioned above in order to ensure timely review. Otherwise, the study will be terminated. If any modification to the study occurs (amendment) over the next twelve months, or should this study be completed during this period, please submit appropriate documentation to the Research Review Office. Visit our website for information www.jgh.ca/rec and to access our downloadable forms, or contact us.

Please note that in the future, we request that you include the additional clause in the "Statement of Consent" that has been sent to you, electronically, for this and other studies submitted to the FLP committee.

Respectfully,

Me Alain Klotz, LL.M.
Chair, First-Line/Psychosocial & Geriatrics Research Ethics Committee

Resource person for this project:

Resource for this project:
Linda Furlini, PhD
Clinical Activity Specialist
Telephone: 514 340-8222, ext. 28475
e-mail: linda.furlini.ccomtl@ssss.gouv.qc.ca

3755, chemin de la Côte-Sainte-Catherine Road
Montréal (Québec) H3T 1E2
T. 514-340-8222
ciusss-centreouestmtl.gouv.qc.ca

Centre intégré
universitaire de santé
et de services sociaux
du Centre-Ouest-
de-l'Île-de-Montréal
Québec

Hôpital général juif

CENTRE GÉRIATRIQUE
DONALD BERMAN
MAIMONIDES GERIATRIC
CENTRE

CENTRE D'HÉBERGEMENT
FATHER-DOWD
RESIDENTIAL CENTRE

CENTRE D'HÉBERGEMENT
HENRI-BRADET
RESIDENTIAL CENTRE

CENTRE D'HÉBERGEMENT
ST-ANDREW RESIDENTIAL
CENTRE

CENTRE D'HÉBERGEMENT
ST-MARGARET
RESIDENTIAL CENTRE

CENTRE MIRIAM HOME
AND SERVICES

CENTRE DE RÉADAPTATION
CONSTANCE-LETHBRIDGE
REHABILITATION CENTRE

CENTRE DE RÉADAPTATION
MAB-MACKAY
REHABILITATION CENTRE

CHSLD JUIF DE MONTRÉAL
JEWISH ELDERCARE
CENTRE

CLSC DE BENNY FARM

CLSC DE CÔTE-DES-
NEIGES

CLSC MÉTRO

CLSC DE PARC-
EXTENSION

CLSC RENÉ-CASSIN

HÔPITAL CATHERINE
BOOTH HOSPITAL

HÔPITAL GÉNÉRAL JUIF
JEWISH GENERAL HOSPITAL

HÔPITAL MOUNT SINAI
HOSPITAL

HÔPITAL RICHARDSON
HOSPITAL

*Integrated Health
and Social Services
University Network
for West-Central
Montreal*

3755, chemin de la Côte-Sainte-Catherine Road
Montréal (Québec) H3T 1E2
T. 514-340-8222
ciusss-centreouestmtl.gouv.qc.ca

10.2. **Study Advertisement Flyer**

Hôpital général juif
Jewish General Hospital

RESEARCH STUDY

Defining lung cancer diagnostic pathways in the primary care setting in Montréal, Québec

During your visit with your doctor at the lung cancer clinic, you may be invited to participate in a research study that is focused on pathways to a lung cancer diagnosis and things that cause delays in these pathways.

This study will involve:

- An approximate 60-minute interview done at a time and location that is most convenient for you, and
- *Possibly* an approximate 60-90 minute interview done within 12 months, at a time and location that is most convenient for you

Your doctor will ask you if a researcher can talk to you about the study. If you agree, the researcher will explain the study to you and answer any questions you may have. You may then choose to participate or not participate in the study.

Information learned from this research may lead to changes in how health care is delivered so that delays in lung cancer diagnosis can be reduced.

For any questions or concerns, please page Rashi Khare at 514-413-0112.

THANK YOU

This study has been reviewed and approved by the Research Ethics Review Board of the Jewish General Hospital

Hôpital général juif
Jewish General Hospital

ÉTUDE DE RECHERCHE

Définir les cheminements diagnostiques du cancer du poumon dans un contexte de première ligne à Montréal (Québec)

Durant votre visite chez le médecin à la clinique du cancer du poumon, vous pourriez être invité à participer à une étude portant sur les cheminements diagnostiques du cancer du poumon et les éléments qui causent des retards dans ces cheminements.

Cette étude comprendra :

- Une entrevue d'environ 60 minutes qui aura lieu à une heure et dans un lieu qui vous conviennent.
- Une *possible* entrevue d'environ 60 à 90 minutes réalisée dans les 12 mois, à l'heure et à l'endroit qui vous conviennent le mieux.

Votre médecin vous demandera si un chercheur peut vous parler au sujet de l'étude. Si vous êtes d'accord, le chercheur vous expliquera l'étude et répondra à vos questions. Vous pourrez ensuite choisir de participer ou non à l'étude.

L'information recueillie par cette recherche pourrait conduire à des changements dans la façon dont les soins de santé sont dispensés et faire en sorte que les retards dans le diagnostic du cancer du poumon soient réduits.

Pour toute question ou si vous avez des préoccupations, veuillez contacter Rashi Khare au 514-413-0112.

MERCI

Cette étude a été examinée et approuvée par le Comité d'éthique de la recherche de l'Hôpital général juif

10.3. Study Script to Introduce Study

Introducing the study to the patient:

Hello. My name is <NAME>. I'm part of a research team that is studying pathways to a lung cancer diagnosis. We're trying to understand how patients move through first-line, primary care to get to a specialist where the diagnosis is confirmed. For this, we're asking patients if they would be willing to be interviewed for about 60 minutes about the health care services they used before being referred to a lung specialist – things like doctor appointments and tests. The interview would take place at a time and location that is convenient for you and if someone else also knows about the health care services you used, then they can join the interview too.

Then, as a second part to the study, we want to understand factors that may lead to delays in diagnosis from the perspective of patients. This will give us a deeper understanding of pathways to a lung cancer diagnosis. For this, we will be asking some patients if they would be willing to do a 60-90 minute interview at a later time.

You can choose to participate in only the first part of the study if you want, or you can choose to participate in both parts of the study and withdraw later if you change your mind. You can also choose not to participate without any impact on the care you receive.

We're hoping that the results of this study will allow us to figure out how things can be done better and faster to avoid diagnostic delays.

Would you be interested in hearing more about the study, either now or later?

<IF YES AND IN PERSON, GO OVER CONSENT FORM>

<IF YES AND OVER THE PHONE, SCHEDULE A TIME AND PLACE TO GO OVER CONSENT FORM>

Version date: February 8, 2017

Présentation de l'étude au patient :

Bonjour. Je m'appelle <NOM>. Je fais partie d'une équipe de recherche qui étudie les cheminements vers le diagnostic de cancer du poumon. Nous essayons de comprendre comment les patients progressent dans les soins primaires de première ligne pour avoir accès à un spécialiste qui confirmera le diagnostic. À cette fin, nous demandons aux patients s'ils acceptent d'être interrogés pendant environ 60 minutes sur les services de soins de santé qu'ils utilisaient avant d'être recommandés à un spécialiste du poumon, par exemple les rendez-vous et les examens médicaux. L'entrevue aura lieu à un moment et à un endroit qui vous conviennent et si une autre personne de votre entourage connaît également les services de soins de santé que vous avez utilisés, celle-ci peut également se joindre à l'entrevue.

Ensuite, pour la seconde partie de l'étude, nous voulons comprendre les facteurs qui peuvent entraîner des retards dans le diagnostic du point de vue des patients. Cela nous permettra de mieux comprendre les cheminements vers un diagnostic de cancer du poumon. À cette fin, nous demanderons à certains patients s'ils acceptent de se livrer à un entretien de 60 à 90 minutes à un moment ultérieur.

Vous pouvez choisir de participer uniquement à la première partie de l'étude si vous le souhaitez, ou vous pouvez choisir de participer aux deux parties de l'étude et vous retirer plus tard si vous changez d'avis. Vous pouvez également choisir de ne pas participer, sans que cela n'ait d'incidence sur les soins que vous recevez.

Nous espérons que les résultats de cette étude nous permettront de comprendre comment les choses pourraient être faites de façon plus efficace et plus rapidement afin d'éviter les retards de diagnostic.

Souhaitez-vous en savoir plus sur l'étude, soit maintenant ou plus tard?

<SI OUI ET EN PERSONNE, PASSEZ AU FORMULAIRE DE CONSENTEMENT>

<SI OUI ET AU TÉLÉPHONE, PRÉVOYEZ UNE HEURE ET UN LIEU POUR PASSER EN REVUE LE CONSENTEMENT POUR M>

Date de la version : 8 février 2017

10.4. Consent Forms: Patient

Jewish General Hospital
Peter Brojde Lung Cancer Centre
Principal Investigator: Dr. Isabelle Vedel
Co-investigators: Drs. Gillian Bartlett, Gerald Batist, François Béland, and Jean-Louis Denis

3755 chemin de la Côte-Ste-Catherine
Montreal, Quebec, Canada
H3T 1E2

PATIENT CONSENT FORM
Defining lung cancer diagnostic pathways in the primary care setting in Montréal, Québec

Study supported by: Fonds de recherche du Québec – Santé (FRQS)
***Projet de développement stratégique innovant* (PDSI)**

INTRODUCTION

You are invited to participate in a research project. This research is focused on pathways to a lung cancer diagnosis. You are being asked to participate because you have been diagnosed with lung cancer and we would like to know more about your experience. You have the right to know about the purpose of this study and the procedures that will be used. You also have the right to be informed about the potential benefits, risks, compensation, and discomfort of this study.

Before you agree to take part in this study, it is important that you read the information in this consent form. You should ask as many questions as you need to in order to understand what you will be asked to do. **You do not have to take part in this study if you do not want to**.

WHAT IS THE PURPOSE OF THIS STUDY?

Patients with lung cancer are often diagnosed at a late stage of disease. In Canada, patients must be seen in primary care to access a specialist where the diagnosis is confirmed and treatment is started. In other countries that operate in the same way, major delays in diagnosis have been shown to take place in primary care, with many complex factors involved.

There are two parts to this study with two different purposes. In the first part of this study, the purpose is to identify lung cancer diagnostic pathways in the primary care setting, or in other words, identify how patients get from primary care to specialist care. For this part of the study, we will recruit about 261 participants.

In the second part of this study, the purpose is to understand patient, disease, and health-care system factors that play a role in the diagnostic pathways. From those who participated in the first part of the study, we will ask about 24 people to further participate in this second part of the study.

The results of this study will be used to create ways to avoid delays to a lung cancer diagnosis and allow for diagnosis at earlier stages of disease.

WHAT WILL MY PARTICIPATION INVOLVE?

PART 1: In the first part of this study, you will be interviewed by a member of the research team for **about 60 minutes**. In the interview, you will be asked about the health care services you used before being referred to a lung specialist, as well as your health history. Based on your preference, the interview will be done at the clinic before or after your next appointment (or during a treatment session), or at another location that is most convenient for you. This part of the study will take place between April and September of 2017. If someone else (e.g. caregiver or companion) was also knowledgeable about your appointments and tests before your referral to a specialist, they will be asked to participate in the interview with you, with your permission. In addition to the interview, the research team will collect information on use of health care services, health history, and demographics (e.g. age, sex) from your medical records at the Jewish General Hospital. Your medical record will not be accessed until you have provided written consent.

PART 2: In the second part of this study, you ***may be selected*** to be interviewed for **about 60-90 minutes** by a member of the research team. In the interview, you will be asked about things that affected your pathway to a lung cancer diagnosis. The interview will be audio-recorded to help the analysis later. Based on your preference, the interview will be done at the clinic or any other location that is most convenient for you. Once the interview has started, if it is difficult for you to continue for whatever reason, you will be able to stop whenever you feel like it and schedule another time to continue. This part of the study will take place between December, 2017 and March, 2018.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS OF PARTICIPATION?

There is a risk that the interview questions may bring up some negative or difficult emotions about your diagnosis. Should you feel unwell during the interview, or experience any distress, you will be referred to your primary nurse. The length of the interview may also cause some discomfort. Should this occur, you can stop at any time and continue at a later date, or you can withdraw from the study.

WHAT ARE THE POSSIBLE BENEFITS OF PARTICIPATION?

You may not receive any direct benefits from participating in this study. However, information learned from this research may lead to changes in how health care is delivered so that delays in lung cancer diagnosis can be reduced.

IS MY PARTICIPATION VOLUNTARY?

Yes, your participation in this study is voluntary. **You may choose to participate now and decide to stop your participation at any time.** Your future medical care and your patient-doctor relationship will not be affected in any way.

If you withdraw from this study, any information collected up to the point of withdrawal for the purpose of this research may still be used in order to protect the scientific integrity of the study.

HOW WILL MY INFORMATION BE KEPT CONFIDENTIAL?

While you take part in this research study, the research team will collect and store personal identifiable information about you in a file for the purpose of the study. Only information necessary for the research study will be collected.

All the information collected about you during the study will remain confidential within the limits of the Law. To protect your identity, your name and identifying information will be replaced with a numeric code that will not contain any identifiers. The link between the code and your identity will be held in a locked filing cabinet in a locked office at the Jewish General Hospital and will only be accessible by the research team. All paper-based research documents will also be kept in a locked filing cabinet in a locked office. Electronic data will be encrypted and kept on a password-protected computer in a locked office. No information that discloses your identity will be allowed to leave the Jewish General Hospital. A copy of this consent form will not be placed in your medical record but a copy will be given to you. The study researcher will only share coded information about you with her study supervisors. This information will not include your name or address. The study supervisors will use the information collected about you only to reach the study goals as they are explained in this Consent Form. Your study information will be kept for 10 years at the Jewish General Hospital and then destroyed. All paper documents will be shredded and electronic documents will be permanently deleted using an advanced security tool called Eraser. The study information could be printed/published in medical journals or shared with other people at scientific meetings, but your identity will not be revealed. The study information may also be used to help in the development of future studies.

WHAT ARE THE COSTS AND COMPENSATION FOR THIS STUDY?

You will not be paid for your participation in this study and there will be no costs to you for participating.

STUDY SUPPORT

This study is being financially supported by the Projet de développement stratégique innovant (PDSI) fund at the Lady Davis Institute for Medical Research, provided by the Fonds de recherche du Québec – Santé (FRQS). The researcher in charge of the study is Dr. Isabelle Vedel who can be reached at 514-399-9107.

WHO DO I CONTACT IF I HAVE QUESTIONS?

If you have any questions about the study or if you feel you have a problem related to taking part in the study, you can communicate with **Rashi Khare at 514-340-8222 ext. 26585**. For any questions concerning your rights as a person taking part in this study, or if you have comments or wish to file a complaint, you can communicate with the Jewish General

Hospital's Local Commissioner of Complaints & Quality of Services, **Rosemary Steinberg, at (514) 340-8222 ext. 25833**.

For purposes of monitoring this research, your research study file as well as your medical records identifying you could be checked by a person authorized by the Research Ethics Committee of the Jewish General Hospital. This person is obliged to respect your privacy.

STATEMENT OF CONSENT

Defining lung cancer diagnostic pathways in the primary care setting in Montréal, Québec

I have read the above information and my questions were answered to my satisfaction. A copy of this signed consent form will be given to me. My participation is voluntary and I can withdraw from the study at any time without giving reasons, without it affecting my medical care now or later. I do not give up any of my legal rights by signing this consent form. I agree to participate in this study.

I give permission to access my medical records. ☐

Name of Researcher	Signature of Researcher	Date

Name of Participant	Signature of Participant	Date

Hôpital général juif *3755, chemin de la Côte-Ste-Catherine*
Centre d'oncologie pulmonaire Peter Brojde *Montréal, Québec, Canada*
Chercheuse principale : D^re^ Isabelle Vedel *H3T 1E2*
Co-chercheuses: D^re^ Gillian Bartlett, Gerald Batist, François Béland, and Jean-Louis Denis

DÉCLARATION DE CONSENTEMENT DU PATIENT
Définir les cheminements diagnostiques du cancer du poumon dans un contexte de première ligne à Montréal (Québec)

Étude soutenue par : Fonds de recherche du Québec — Santé (FRQS)
***Projet de développement stratégique innovant* (PDSI)**

INTRODUCTION

Vous êtes invité à participer à un projet de recherche. Cette recherche est axée sur les cheminements diagnostiques du cancer du poumon. On vous demande de participer à cette étude, car vous avez reçu un diagnostic de cancer du poumon et parce que nous aimerions en connaître davantage sur votre expérience. Vous avez le droit de connaître le but de cette étude et les procédures qui y seront suivies. Vous avez également le droit d'être informé des bénéfices, des risques, des dédommagements et des inconforts potentiels liés à cette étude. Avant d'accepter de participer à la présente étude, il est important que vous lisiez les informations contenues dans le présent formulaire de consentement. Vous devez poser autant de questions qu'il vous faut pour comprendre ce qu'on vous demandera de faire. **Vous n'avez pas à participer à cette étude si vous ne le voulez pas**.

QUEL EST LE BUT DE CETTE ÉTUDE?

Les patients atteints d'un cancer du poumon reçoivent souvent leur diagnostic alors que la maladie se trouve à un stade avancé. Au Canada, les patients doivent être examinés dans un contexte de première ligne pour avoir accès à un spécialiste. C'est dans ce contexte que le diagnostic est confirmé et que le traitement est commencé. Dans les pays qui opèrent de la même manière, des retards majeurs dans le diagnostic — qui impliquent de nombreux facteurs complexes — ont été mis en évidence dans les soins de première ligne.

La présente étude est divisée en deux parties, chacune d'elles ayant des objectifs différents.

La première partie de cette étude a pour objectif d'identifier les cheminements diagnostiques du cancer du poumon dans le contexte de première ligne, c'est-à-dire de déterminer comment les patients passent des soins de première ligne aux soins spécialisés. Pour cette partie de l'étude, nous recruterons environ 261 participants.

La seconde partie de cette étude a pour objectif de comprendre les facteurs relatifs au patient, à la maladie et au système de soins de santé qui jouent un rôle dans les cheminements diagnostiques. Nous demanderons à 24 personnes qui auront participé à la première partie de l'étude de prendre également part à ce second volet de l'étude.

Les résultats de cette étude seront utilisés pour créer des moyens d'éviter les retards dans le diagnostic du cancer du poumon et de permettre le diagnostic à des stades précoces de la maladie.

QU'EST-CE QUE MA PARTICIPATION IMPLIQUERA?

PREMIÈRE PARTIE : Dans la première partie de cette étude, vous serez interviewé par un membre de l'équipe de recherche pendant **environ 60 minutes**. Lors de l'entrevue, on vous posera des questions sur les services de santé que vous avez utilisés avant d'être recommandé à un spécialiste du poumon, ainsi que sur vos antécédents de santé. Selon vos préférences, l'entrevue sera effectuée à la clinique avant ou après un rendez-vous (ou pendant une séance de traitement), ou à un autre endroit qui vous convient davantage. Cette partie de l'étude se déroulera entre avril et septembre 2017. Si quelqu'un d'autre (par exemple, un soignant ou un compagnon) est également au courant des rendez-vous et des examens qui ont eu lieu avant votre recommandation auprès d'un spécialiste, il ou elle sera invité(e) à participer à l'entrevue avec vous, avec votre permission. En plus de l'entrevue, l'équipe de recherche recueillera des renseignements sur l'utilisation des services de soins de santé, les antécédents médicaux et les données démographiques (par exemple l'âge et le sexe) à partir de vos dossiers médicaux à l'Hôpital général juif. Votre dossier médical ne pourra pas être consulté tant que vous n'y aurez pas consenti par écrit.

SECONDE PARTIE : Dans la seconde partie de cette étude, vous ***pourriez être sélectionné*** pour être interviewé **environ 60 à 90 minutes** par un membre de l'équipe de recherche. Lors de cette entrevue, on vous posera des questions sur les éléments qui ont eu une incidence sur votre cheminement vers un diagnostic de cancer du poumon. L'entrevue sera enregistrée pour aider à l'analyse ultérieure. Selon vos préférences, l'entrevue sera effectuée à la clinique ou à tout autre endroit qui vous convient davantage. Si vous avez de la difficulté à poursuivre l'entretien pour une quelconque raison une fois l'entrevue commencée, vous pourrez arrêter à tout moment et demander de continuer à moment ultérieur. Cette partie de l'étude se déroulera entre décembre 2017 et mars 2018.

QUELS SONT LES RISQUES ET LES MALADIES QUI PEUVENT DÉCOULER DE MA PARTICIPATION?

Il est possible que les questions d'entrevue soulèvent certaines émotions négatives ou difficiles quant à votre diagnostic. Si vous vous sentez mal pendant l'entretien ou que vous éprouvez un sentiment de détresse, vous serez recommandé à votre infirmière principale. La durée de l'entrevue peut également causer un certain inconfort. Si cela se produit, vous pouvez vous arrêter à tout moment et continuer à une date ultérieure, ou vous pouvez vous retirer de l'étude.

QUELS SONT LES BÉNÉFICES POSSIBLES LIÉS À LA PARTICIPATION?

Vous pourriez ne retirer aucun bénéfice direct à la suite de votre participation à cette étude. Cependant, l'information recueillie par cette recherche pourrait conduire à des changements

dans la façon dont les soins de santé sont dispensés et faire en sorte que les retards dans le diagnostic du cancer du poumon soient réduits.

MA PARTICIPATION EST-ELLE VOLONTAIRE?

Oui, votre participation à cette étude est volontaire. **Vous pouvez choisir de participer maintenant et décider de mettre fin à votre participation à tout moment.** Vos futurs soins médicaux et votre relation patient-médecin ne seront en aucun cas affectés.
Si vous vous retirez de cette étude, toute information recueillie jusqu'au moment du retrait aux fins de cette recherche pourra encore être utilisée afin de protéger l'intégrité scientifique de l'étude.

COMMENT LA CONFIDENTIALITÉ DE MES RENSEIGNEMENTS PERSONNELS SERA-T-ELLE ASSURÉE?

Pendant que vous participerez à cette étude, l'équipe de recherche recueillera des renseignements personnels permettant de vous identifier et les consignera dans un fichier aux fins de l'étude de recherche. Seule l'information nécessaire à l'étude sera collectée.
Toute l'information recueillie à votre sujet au cours de l'étude restera confidentielle dans les limites de la loi. Pour protéger votre identité, votre nom et vos renseignements d'identification seront remplacés par un code numérique ne contenant aucun identifiant. Le lien entre le code et votre identité sera conservé dans un classeur verrouillé, dans un bureau fermé à clé, à l'Hôpital général juif et seule l'équipe de recherche y aura accès. Tous les documents de recherche en format papier seront également conservés dans un classeur verrouillé dans un bureau fermé à clé. Les données électroniques seront chiffrées et conservées sur un ordinateur protégé par mot de passe dans un bureau fermé à clé. Aucune information révélant votre identité ne sera autorisée à quitter l'Hôpital général juif. Une copie du présent formulaire de consentement signée sera ajoutée à votre dossier médical, mais une copie vous sera remise.
Le chercheur de l'étude ne partagera que de l'information codée à votre sujet avec les superviseurs de son étude. Ces renseignements ne comprendront pas votre nom ou votre adresse. Les superviseurs de l'étude utiliseront les renseignements recueillis à votre sujet seulement pour atteindre les objectifs de l'étude tels qu'ils sont expliqués dans le présent formulaire de consentement. L'information à votre sujet relative à l'étude sera conservée 10 ans à l'Hôpital général juif, puis sera détruite. Tous les documents papier seront déchiquetés et les documents électroniques seront supprimés de façon permanente à l'aide d'un outil de sécurité avancé appelé Eraser. L'information de l'étude pourrait être imprimée ou publiée dans des revues médicales, ou partagée avec d'autres personnes lors de réunions scientifiques, mais votre identité ne sera pas révélée. L'information de l'étude pourra également être utilisée pour aider au développement d'études futures.

QUELS SONT LES COÛTS ET LES DÉDOMMAGEMENTS PRÉVUS DANS LE CADRE DE CETTE ÉTUDE?

Vous ne serez pas rémunéré pour votre participation à cette étude et il n'en coûte rien pour y participer.

SOUTIEN À L'ÉTUDE

Cette étude est soutenue financièrement par le fonds du Projet de développement stratégique innovant (PDSI) de l'Institut Lady Davis pour la recherche médicale, fourni par le Fonds de recherche du Québec — Santé (FRQS). Le chercheur responsable de l'étude est D^{re} Isabelle Vedel, que l'on peut joindre au 514-399-9107.

À QUI DOIS-JE M'ADRESSER SI J'AI DES QUESTIONS?

Si vous avez des questions au sujet de l'étude ou si vous jugez avoir un problème lié à votre participation à celle-ci, vous pouvez communiquer avec **Rashi Khare au 514-340-8222 poste 26585**. Pour toute question concernant vos droits en tant que personne participant à cette étude, ou si vous avez des commentaires ou souhaitez déposer une plainte, vous pouvez communiquer avec Rosemary Steinberg, commissaire aux plaintes et à la qualité du service de l'Hôpital général juif au 514-340-8222 poste 25833.

À des fins de surveillance, de contrôle, de protection, de sécurité, votre dossier de recherche ainsi que vos dossiers médicaux pourront être consultés par une personne mandatée par l'établissement ou du comité d'éthique de la recherche. Ces personnes adherent à une politique de confidentialité.

DÉCLARATION DE CONSENTEMENT

Définir les cheminements diagnostiques du cancer du poumon dans un contexte de première ligne à Montréal (Québec)

J'ai lu l'information ci-dessus et on a répondu à mes questions de manière satisfaisante. Une copie du présent formulaire de consentement signé me sera remise. Ma participation est volontaire et je peux me retirer de l'étude à tout moment, sans justifications, sans que cela n'affecte les soins médicaux que je reçois actuellement ou que je recevrai. Je ne renonce à aucun de mes droits légaux en signant le présent formulaire de consentement. J'accepte de participer à la présente étude.

J'accepte qu'on ait accès et qu'on consulte mes dossiers médicaux. ☐

Nom du chercheur (en lettres moulées)	Signature du chercheur	Date
Nom du participant (en lettres moulées)		
	Signature du participant	Date

10.5. Consent Forms: Caregiver

Jewish General Hospital *3755 chemin de la Côte-Ste-Catherine*
Peter Brojde Lung Cancer Centre *Montreal, Quebec, Canada*
Principal Investigator: Dr. Isabelle Vedel *H3T 1E2*
Co-investigators: Drs. Gillian Bartlett, Gerald Batist, François Béland, and Jean-Louis Denis

CAREGIVER CONSENT FORM
Defining lung cancer diagnostic pathways in the primary care setting in Montréal, Québec

Study supported by: Fonds de recherche du Québec – Santé (FRQS)
***Projet de développement stratégique innovant* (PDSI)**

INTRODUCTION

You are invited to participate in a research project. This research is focused on pathways to a lung cancer diagnosis. You are being asked to participate because you are knowledgeable about the health care services used by a lung cancer patient who has agreed to participate in this study. You have the right to know about the purpose of this study and the procedures that will be used. You also have the right to be informed about the potential benefits, risks, compensation, and discomfort of this study.

Before you agree to take part in this study, it is important that you read the information in this consent form. You should ask as many questions as you need to in order to understand what you will be asked to do. **You do not have to take part in this study if you do not want to**.

WHAT IS THE PURPOSE OF THIS STUDY?

Patients with lung cancer are often diagnosed at a late stage of disease. In Canada, patients must be seen in primary care to access a specialist where the diagnosis is confirmed and treatment is started. In other countries that operate in the same way, major delays in diagnosis have been shown to take place in primary care, with many complex factors involved.

There are two parts to this study with two different purposes. In the first part of this study, the purpose is to identify lung cancer diagnostic pathways in the primary care setting, or in other words, identify how patients get from primary care to specialist care. For this part of the study, we will recruit about 261 participants. In the second part of this study, the purpose is to understand patient, disease, and health-care system factors that play a role in the diagnostic pathways. From those who participated in the first part of the study, we will ask about 24 people to further participate in this second part of the study. The results of this study will be used to create ways to avoid delays to a lung cancer diagnosis and allow for diagnosis at earlier stages of disease.

You are being asked to participate in the first part of this study only.

WHAT WILL MY PARTICIPATION INVOLVE?

In this study, you will be interviewed by a member of the research team for **about 60 minutes**, along with the participating patient. In the interview, you will be asked about the health care services that were used by the participating patient (e.g. appointments and tests) before being referred to a lung specialist. The location of the interview will depend on the preference of the participating patient. The options include the clinic before or after an appointment (or during a treatment session), or at another location that is most convenient. This part of the study will take place between April and September of 2017.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS OF PARTICIPATION?

There is a risk that the interview questions may bring up some negative or difficult emotions about the lung cancer diagnosis. The length of the interview may also cause some discomfort. Should this occur, you can stop at any time and continue at a later date, or you can withdraw from the study.

WHAT ARE THE POSSIBLE BENEFITS OF PARTICIPATION?

You may not receive any direct benefits from participating in this study. However, information learned from this research may lead to changes in how health care is delivered so that delays in lung cancer diagnosis can be reduced.

IS MY PARTICIPATION VOLUNTARY?

Yes, your participation in this study is voluntary. **You may choose to participate now and decide to stop your participation at any time.** The future medical care of yourself or the participating patient will not be affected in any way.

If you withdraw from this study, any information collected up to the point of withdrawal for the purpose of this research may still be used in order to protect the scientific integrity of the study.

HOW WILL MY INFORMATION BE KEPT CONFIDENTIAL?

While you take part in this research study, only information necessary for the research study will be collected. A copy of this consent form will be given to you for your records.

WHAT ARE THE COSTS AND COMPENSATION FOR THIS STUDY?

You will not be paid for your participation in this study. There may be travel costs for participating if the interview is done at a location where you did not plan to be.

STUDY SUPPORT

This study is being financially supported by the Projet de développement stratégique innovant (PDSI) fund at the Lady Davis Institute for Medical Research, provided by the Fonds de recherche du Québec – Santé (FRQS). The researcher in charge of the study is Dr. Isabelle Vedel who can be reached at 514-399-9107.

WHO DO I CONTACT IF I HAVE QUESTIONS?

If you have any questions about the study or if you feel you have a problem related to taking part in the study, you can communicate with **Rashi Khare at 514-340-8222 ext. 26585**. For any questions concerning your rights as a person taking part in this study, or if you have comments or wish to file a complaint, you can communicate with the Jewish General Hospital's Local Commissioner of Complaints & Quality of Services, **Rosemary Steinberg, at (514) 340-8222 ext. 25833**.

STATEMENT OF CONSENT

Defining lung cancer diagnostic pathways in the primary care setting in Montréal, Québec

I have read the above information and my questions were answered to my satisfaction. A copy of this signed consent form will be given to me. My participation is voluntary and I can withdraw from the study at any time without giving reasons, without it affecting any medical care now or later. I do not give up any of my legal rights by signing this consent form. I agree to participate in this study.

Name of Researcher	Signature of Researcher	Date

Name of Participant	Signature of Participant	Date

Hôpital général juif *3755, chemin de la Côte-Ste-Catherine*
Centre d'oncologie pulmonaire Peter Brojde *Montréal, Québec, Canada*
Chercheuse principale : D^re^ Isabelle Vedel *H3T 1E2*
Co-chercheuses : D^re^ Gillian Bartlett, Gerald Batist,
François Béland, and Jean-Louis Denis

FORMULAIRE DE CONSENTEMENT DE L'AIDANT
Définir les cheminements diagnostiques du cancer du poumon dans un contexte de première ligne à Montréal (Québec)

Étude soutenue par : Fonds de recherche du Québec — Santé (FRQS)
***Projet de développement stratégique innovant* (PDSI)**

INTRODUCTION

Vous êtes invité à participer à un projet de recherche. Cette recherche est axée sur les cheminements diagnostiques du cancer du poumon. On vous demande d'y participer parce que vous êtes familier avec les services de soins de santé auquel a recours un patient atteint de cancer du poumon ayant accepté de participer à cette étude. Vous avez le droit de connaître le but de cette étude et les procédures qui y seront suivies. Vous avez également le droit d'être informé des bénéfices, des risques, des dédommagements et des inconforts potentiels liés à cette étude.

Avant d'accepter de participer à la présente étude, il est important que vous lisiez les informations contenues dans le présent formulaire de consentement. Vous devez poser autant de questions qu'il vous faut pour comprendre ce qu'on vous demandera de faire. **Vous n'avez pas à participer à cette étude si vous ne le voulez pas**.

QUEL EST LE BUT DE CETTE ÉTUDE?

Les patients atteints d'un cancer du poumon reçoivent souvent leur diagnostic alors que la maladie se trouve à un stade avancé. Au Canada, les patients doivent être examinés dans un contexte de première ligne pour avoir accès à un spécialiste. C'est dans ce contexte que le diagnostic est confirmé et que le traitement est commencé. Dans les pays qui opèrent de la même manière, des retards majeurs dans le diagnostic — qui impliquent de nombreux facteurs complexes — ont été mis en évidence dans les soins de première ligne.

La présente étude est divisée en deux parties, chacune d'elles ayant des objectifs différents. La première partie de cette étude a pour objectif d'identifier les cheminements diagnostiques du cancer du poumon dans le contexte de première ligne, c'est-à-dire de déterminer comment les patients passent des soins de première ligne aux soins spécialisés. Pour cette partie de l'étude, nous recruterons environ 261 participants. La seconde partie de cette étude a pour objectif de comprendre les facteurs relatifs au patient, à la maladie et au système de soins de santé qui jouent un rôle dans les cheminements diagnostiques. Nous demanderons à 24 personnes qui auront participé à la première partie de l'étude de prendre également part à ce second volet de l'étude. Les résultats de cette étude seront utilisés pour créer des moyens

d'éviter les retards dans le diagnostic du cancer du poumon et de permettre le diagnostic à des stades précoces de la maladie.

On vous demande de participer à la première partie de cette étude seulement.

QU'EST-CE QUE MA PARTICIPATION IMPLIQUERA?

Dans cette étude, vous serez interviewé par un membre de l'équipe de recherche pendant **environ 60 minutes**, en présence du patient participant. Lors de l'entrevue, on vous posera des questions sur les services de santé qui ont été utilisés par le patient participant (p. ex. rendez-vous et examens) avant d'être recommandé à un spécialiste du poumon. Le lieu de l'entrevue dépendra de la préférence du patient participant. Les options possibles comprennent la clinique avant ou après un rendez-vous (ou pendant une séance de traitement), ou à un autre endroit qui est plus commode. Cette partie de l'étude se déroulera entre avril et septembre 2017.

QUELS SONT LES RISQUES ET LES MALADIES QUI PEUVENT DÉCOULER DE MA PARTICIPATION?

Il est possible que les questions d'entrevue soulèvent certaines émotions négatives ou difficiles quant au diagnostic de cancer du poumon. La durée de l'entrevue peut également causer un certain inconfort. Si cela se produit, vous pouvez vous arrêter à tout moment et continuer à une date ultérieure, ou vous pouvez vous retirer de l'étude.

QUELS SONT LES BÉNÉFICES POSSIBLES LIÉS À LA PARTICIPATION?

Vous pourriez ne retirer aucun bénéfice direct à la suite de votre participation à cette étude. Cependant, l'information recueillie par cette recherche pourrait conduire à des changements dans la façon dont les soins de santé sont dispensés et faire en sorte que les retards dans le diagnostic du cancer du poumon soient réduits.

MA PARTICIPATION EST-ELLE VOLONTAIRE?

Oui, votre participation à cette étude est volontaire. **Vous pouvez choisir de participer maintenant et décider de mettre fin à votre participation à tout moment.** Les futurs soins médicaux que vous-même ou le patient participant recevrez ne seront en aucun cas affectés. Si vous vous retirez de cette étude, toute information recueillie jusqu'au moment du retrait aux fins de cette recherche pourra encore être utilisée afin de protéger l'intégrité scientifique de l'étude.

COMMENT LA CONFIDENTIALITÉ DE MES RENSEIGNEMENTS PERSONNELS SERA-T-ELLE ASSURÉE?

Pendant que vous participerez à cette étude, seule l'information nécessaire à l'étude sera collectée. Une copie du présent formulaire de consentement signée vous sera remise pour vos dossiers.

QUELS SONT LES COÛTS ET LES DÉDOMMAGEMENTS PRÉVUS DANS LE CADRE DE CETTE ÉTUDE?

Vous ne serez pas rémunéré pour votre participation à cette étude. Des frais de déplacement pourront s'avérer nécessaires pour participer si l'entrevue est réalisée dans un lieu où vous n'aviez pas prévu vous rendre.

SOUTIEN À L'ÉTUDE

Cette étude est soutenue financièrement par le fonds du Projet de développement stratégique innovant (PDSI) de l'Institut Lady Davis pour la recherche médicale, fourni par le Fonds de recherche du Québec — Santé (FRQS). Le chercheur responsable de l'étude est D^{re} Isabelle Vedel, que l'on peut joindre au 514-399-9107.

À QUI DOIS-JE M'ADRESSER SI J'AI DES QUESTIONS?

Si vous avez des questions au sujet de l'étude ou si vous jugez avoir un problème lié à votre participation à celle-ci, vous pouvez communiquer avec **Rashi Khare au 514-340-8222 poste 26585**. Pour toute question concernant vos droits en tant que personne participant à cette étude, ou si vous avez des commentaires ou souhaitez déposer une plainte, vous pouvez communiquer avec Rosemary Steinberg, commissaire aux plaintes et à la qualité du service de l'Hôpital général juif au 514-340-8222 poste 25833.

DÉCLARATION DE CONSENTEMENT

Définir les cheminements diagnostiques du cancer du poumon dans un contexte de première ligne à Montréal (Québec)

J'ai lu l'information ci-dessus et on a répondu à mes questions de manière satisfaisante. Une copie du présent formulaire de consentement signé me sera remise. Ma participation est volontaire et je peux me retirer de l'étude à tout moment, sans justifications, sans que cela n'affecte les soins médicaux, quels qu'ils soient, que je reçois actuellement ou que je recevrai. Je ne renonce à aucun de mes droits légaux en signant le présent formulaire de consentement. J'accepte de participer à la présente étude.

Nom du chercheur (en lettres	Signature du chercheur	Date
Nom du participant (en lettres		
	Signature du participant	Date

10.6. Study Closure

Centre intégré universitaire de santé et de services sociaux du Centre-Ouest-de-l'Île-de-Montréal
Québec
Integrated Health and Social Services University Network for West-Central Montreal

2019-10-31

Dr. Isabelle Vedel
c/o: Satya Rashi Khare
email: rashi.khare@gmail.com

Object: Project 2018-690, 17-031 - Closure of study
Defining Lung Cancer Diagnostic Pathways in the Primary Care Setting in Montreal, Quebec: An Exploratory Sequential Mixed Methods Study

---

Dear Dr. Vedel,

Thank you for submitting the study completion report (**F10-11724**) for the above-mentioned study to the Research Review Office.

The completion of the study will be reported at the Psychosocial Research Ethics Committee meeting to be held on 2019-11-08 and recorded into the minutes of the meeting.

Respectfully,

Me Alain Klotz, LL.B., LL.M.
Chair, Psychosocial Research Ethics Committee

FWA 00000796

11. Appendix 2: French Interview Guides

11.1. Guide d'entrevue structurée pour la phase quantitative

PREMIÈRE PARTIE :

Remarque : Bien qu'il s'agisse d'une entrevue structurée avec des points de données précis, l'entrevue elle-même se fera sur un ton plus familier pour faciliter le souvenir des activités antérieures et la remémoration du cheminement diagnostique. La technique spécifique sera celle du rappel vers l'avant — en commençant par la présentation en soins primaires, puis en passant ensuite à la date de recommandation. Un grand calendrier sera utilisé pour faciliter l'entrevue et documenter les données.

Les activités qui présentent un intérêt sont les suivantes : *1) visites chez le médecin de famille (chez qui le patient est inscrit), 2) visites à une clinique sans rendez-vous, 3) visites à un service d'urgence, 4) hospitalisations, 5) tests d'imagerie (en particulier radiographie pulmonaire et tomodensitométrie) et 6) recommandations à des spécialistes non respiratoires.*

DÉBUT :

4. Rappelez au participant les objectifs de l'entrevue, la longueur prévue de celle-ci et les thèmes généraux qui y seront abordés.
    a. Préambule suggéré : Vous avez été recommandé à un spécialiste du poumon le <DATE DE RÉFÉRENCE>. Je m'intéresse aux services de soins de santé que vous avez utilisés — tels que les rendez-vous et les examens médicaux — du moment où les symptômes de cancer du poumon sont apparus et vous ont poussé à consulter un médecin, jusqu'à ce qu'on vous recommande à un spécialiste des poumons le <DATE DE RÉPÉTITION>. J'ai apporté un calendrier où nous pourrons consigner cette information ce qui, nous l'espérons, vous aidera à vous souvenir des rendez-vous que vous aviez.

5. Demandez au participant s'il a son journal, son carnet de rendez-vous, son calendrier ou tout autre objet qui pourrait l'aider à se rappeler des rendez-vous et des activités.

6. Demandez-lui s'il a des questions avant de commencer.

DÉBUT DE L'ENTRETIEN :

Je voudrais commencer par les premiers signes et symptômes du cancer du poumon qui vous ont fait voir un médecin. Quels étaient-ils et quand avez-vous vu un médecin? <NOTEZ LES SIGNES ET SYMPTÔMES SUR LE CALENDRIER À LA DATE DE PREMIÈRE PRÉSENTATION, PAS PLUS DE 1 AN AVANT LA DATE DE RECOMMANDATION>

<SI LE PARTICIPANT A DE LA DIFFICULTÉ À COMPRENDRE LA QUESTION OU À SE RAPPELER DES PREMIERS SIGNES ET SYMPTÔMES, UTILISEZ COMME GUIDE CEUX QUI SONT INDIQUÉS DANS LES DIRECTIVES DE CANCER CARE ONTARIO>

Maintenant, pouvez-vous me dire quels autres rendez-vous, tests, visites à l'hôpital, etc., vous avez eu durant ce mois (c'est-à-dire le mois de la première présentation)? Si vous avez manqué ou annulé un rendez-vous, veuillez me le dire afin que je puisse l'indiquer sur le calendrier aussi. <NOTEZ TOUTES LES ACTIVITÉS SUR LE CALENDRIER AUX DATES AUXQUELLES

ELLES ONT EU LIEU — SI LES DATES EXACTES NE SONT PAS CONNUES, UTILISEZ UNE DATE APPROXIMATIVE ET AJOUTEZ UN POINT D'EXCLAMATION À CÔTÉ — UTILISEZ LES COLONNES LATÉRALES POUR LES NOTES ADDITIONNELLES>
<PROCÉDEZ AINSI POUR CHAQUE MOIS JUSQU'À CE QUE VOUS ATTEIGNIEZ LA DATE DE RECOMMANDATION>

QUESTIONS (au besoin) :

7. VISITES AU MÉDECIN DE FAMILLE
    a. Aviez-vous un médecin de famille pendant cette période? *SI OUI* : Combien de fois avez-vous vu votre médecin de famille durant ce mois?

8. VISITES À DES CLINIQUES SANS RENDEZ-VOUS
    a. Combien de fois êtes-vous allé dans une clinique sans rendez-vous durant ce mois?

<Si le participant ne sait pas si la clinique est considérée comme une clinique sans rendez-vous, demandez le nom de la clinique et indiquez-le sur le calendrier – il sera googlé plus tard>

9. VISITES À L'URGENCE
    a. Combien de fois vous êtes-vous présenté à l'urgence durant ce mois?

10. HOSPITALISATIONS
    a. Avez-vous déjà été hospitalisé durant ce mois? *SI OUI* : Combien de fois?

11. TESTS D'IMAGERIE
    a. Avez-vous passé des radiographies pulmonaires ou des tomodensitométries durant ce mois? *SI OUI* : Combien?

<Si le participant n'est pas sûr de ce que sont ces tests, montrez-lui des images et expliquez-lui brièvement comment les tests sont effectués>

12. RECOMMANDATIONS AUX SPÉCIALISTES NON RESPIRATOIRES
    a. Durant ce mois, avez-vous été recommandé à un autre spécialiste en plus d'un spécialiste du poumon? *SI OUI* : À combien de spécialistes avez-vous été recommandé et quelle était leur spécialité (par exemple, spécialiste en cardiologie, spécialiste en gériatrie, etc.)? *<pour s'assurer qu'il s'agit d'un spécialiste non respiratoire>*

SECONDE PARTIE :

Remarque : Si l'information suivante se trouve dans l'examen du dossier effectué avant l'entrevue, cette partie sera omise.

J'ai deux dernières questions sur vos antécédents médicaux.

3. Quels médicaments prenez-vous pour les maladies autres que le cancer du poumon et pour quelle(s) affection(s) prenez-vous ces médicaments? *<ex. diabète, hypertension, etc.>*

4. Fumez-vous ou avez-vous déjà fumé? *SI OUI* : Combien de paquets avez-vous fumés par jour et pendant combien d'années?

CONCLUSION :

4. Remerciez le participant pour sa contribution.

5. Expliquez-lui comment le projet se déroulera et comment l'information fournie sera utilisée.
6. Demandez au participant s'il a des questions avant que vous ne terminiez.

11.2. Guide d'entrevue semi-structurée pour la phase qualitative

DÉBUT :

6. Réintroduction.
7. Expliquez ce qui a été fait dans la phase précédente et pourquoi le patient a été sélectionné.
8. Rappelez au participant les objectifs de l'entrevue, la longueur prévue de celle-ci et les thèmes généraux qui y seront abordés. Informez-le également que l'entretien peut se terminer plus tard s'il souhaite y mettre fin à un quelconque moment.
9. Rappelez-lui qu'il est interviewé en tant qu'expert qui peut aider le chercheur à mieux comprendre le phénomène étudié.
10. Demandez-lui s'il a des questions avant de commencer.

QUESTIONS D'ENTRETIEN

Facteurs liés au patient

Dans cette première partie de l'entrevue, j'aimerais comprendre comment les aspects individuels, sociaux et culturels ont joué un rôle dans votre cheminement, c'est-à-dire du moment où les symptômes de cancer du poumon sont apparus et vous ont poussé à consulter un médecin, jusqu'à ce que l'on vous recommande à un spécialiste du poumon. Il est possible qu'ils n'aient joué aucun rôle : je veux simplement explorer ce volet avec vous.

2. Pouvez-vous décrire vos pensées pendant votre expérience de consultation d'un médecin pour être ensuite recommandé à un spécialiste du poumon?
    a. *Questions* : J'aimerais que vous essayiez de vous concentrer sur...
        i. Des expériences antérieures que vous avez pu vivre
        ii. Des influences liées à votre situation sociale, par exemple, des priorités concurrentes ou des conseils reçus de la famille et des amis
        iii. Des influences culturelles
        iv. Votre état mental ou émotionnel, votre état spirituel
        v. L'influence d'autres maladies que vous avez
        vi. L'influence de votre profil démographique, par exemple, l'âge, le genre, le revenu, l'éducation

        <Autres = état matrimonial, statut professionnel, profession, emplacement géographique>

Facteurs liés aux fournisseurs de soins de santé et au système

Dans cette deuxième partie de l'entrevue, j'aimerais comprendre comment les fournisseurs de soins de santé et le système de soins de santé ont joué un rôle dans votre cheminement.

3. Pouvez-vous me parler des défis ou des obstacles ou barrières que vous avez rencontrés au cours de votre expérience, le cas échéant, relativement à la façon dont fonctionne le système de soins de santé?
    a. *Question 1* : Cela peut être des problèmes liés à l'accès au système de santé...
        i. Comment avez-vous obtenu une consultation auprès d'un médecin?
        ii. Quelle a été votre expérience lors du rendez-vous?

iii. Quelle a été votre expérience après avoir consulté le médecin pour la première fois?

b. *Question 2* : Avez-vous des réflexions à partager sur la façon dont la politique en matière de soins de santé a eu des conséquences sur votre expérience...
   i. Y a-t-il une politique en matière de soins de santé qui a joué un rôle dans votre expérience et si oui, comment? <Exemples : système de contrôle d'accès, circonscriptions hospitalières, assurance, services communautaires>

c. *Question 3* : Avez-vous des réflexions à partager sur la façon dont la prestation des soins de santé a eu des conséquences sur votre expérience...
   i. Une fois que vous avez vu un médecin, qu'avez-vous pensé de la façon dont vous avez été traité médicalement par la suite sur les plans du suivi, des rendez-vous en temps opportun, des tests et enfin de la recommandation?

4. Pouvez-vous me nommer des éléments au sein du système de soins de santé qui ont facilité votre expérience, le cas échéant?

Facteurs liés à la maladie

Dans cette dernière partie de l'entrevue, j'aimerais comprendre comment la maladie a joué un rôle dans votre cheminement.

2. Pouvez-vous décrire comment l'évolution de vos symptômes a eu une incidence sur votre cheminement, du moment où vous avez vu un médecin au tout début jusqu'à ce que vous receviez une recommandation? Mes notes de notre premier entretien indiquent que <SIGNES ET SYMPTÔMES> vous ont fait voir un médecin.
   a. *Question 1* : À quelle vitesse vos symptômes ont-ils progressé et comment cela a-t-il affecté votre cheminement?
   b. *Question 2* : Y a-t-il un élément, propre à votre cancer, qui a selon vous eu incidence sur votre cheminement : par exemple, l'endroit où la tumeur était située, la taille de la tumeur ou le type de cancer (c'est-à-dire non à petites cellules ou à petites cellules)?

Y a-t-il quoi que ce soit d'autre?

Je n'ai pas d'autres questions. Y a-t-il autre chose que vous souhaitez ajouter sur ce qui a joué un rôle ou influencé votre cheminement depuis votre première visite chez un médecin pour obtenir une recommandation à un spécialiste du poumon — quelque chose que nous avons oublié ou dont nous n'avons pas discuté?

QUESTIONS DE CLARIFICATION :

4. Pouvez-vous m'en dire un peu plus à ce sujet?
5. Pouvez-vous me donner quelques exemples?
6. C'est très intéressant, pouvez-vous m'en dire plus?

CONCLUSION :

4. Remerciez le participant pour sa contribution.
5. Expliquez-lui comment le projet se déroulera et comment l'information fournie sera utilisée.
6. Demandez au participant s'il a des questions avant que vous ne terminiez.