Stigma as a barrier to treatment and adoption of innovation

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Abstract

Diseases such as mental illnesses, HIV, or certain cancer types carry a stigma that may deter patients from seeking treatment and, in turn, hinder the diffusion of innovative therapies. We investigate the link between social stigma as a barrier to access treatment and the adoption of innovation using the population of patients diagnosed with advanced lung cancer in Ontario (Canada) over the last decade: among all cancers, lung cancer suffers most from stigma because of its association with smoking behavior. Thanks to the rich information on patients at the geographic level, we are able to incorporate social stigma in a model of patient's utility for pursuing treatment. We find that patients face significant stigma acting as a barrier to treatment participation, which in turn slows down the adoption of innovative lung cancer treatment. Removing social stigma would increase the use of innovative treatment by 4%, with benefits in survival outweighing the additional treatment costs.

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But I think that's how you associate it. Because the first thing they ask—even me, the first thing I would ever ask somebody was, "Did you smoke?" (Female lung cancer patient, recent quitter)

But I feel really guilty, and it's as though—well, like I said, I'm not sure if I'm not blaming myself for having it. Although I don't know what I did to do it, I feel guilty. I feel guilty. And it's—it's—it's strange. I don't think I would feel that guilty with anything else. (Male lung cancer patient, never smoker)

Quotes from Hamann et al. (2013).

1 Introduction

Lung cancer is the most commonly diagnosed cancer and the leading cause of cancer-related deaths worldwide: it accounts for 13% of all new cancer cases and its five-year survival rate of 17.8% is the lowest among leading cancers (Ferlay et al. (2014), Wong et al. (2017)). However, in the past decade, innovation in cancer treatment, a result of cheaper genetic sequencing, has revolutionized our understanding of the disease: targeted therapies exploit genetic changes that cause the cancer (mutations) to find the right match between patients and treatment. Figure 1 offers a graphical illustration of the therapeutic revolution in lung cancer, with the number of targeted drugs greatly expanding over the last decade. Those therapies present both health and economic advantages, especially when compared to the standard of care, based on aggressive and toxic chemotherapy: they significantly improve patient survival; they are often administered in tablets, with potential cost savings compared to intravenous drugs; and they tend to imply fewer side effects: see Djalalov et al. (2014) for a cost effectiveness analysis.

Recent medical literature shows that up to 70% of lung cancer patients have an alteration that is targetable by existing drugs or drugs currently under development (Suh et al. (2016)), so the potential for these new therapies is huge. However, several years after the introduction of targeted treatments, their potential has not been fully exploited: systemic therapy (chemotherapy and targeted therapy) is administered to significantly fewer patients than in other cancers at comparable stages, despite evidence that treatment is effective (Davidoff et al. (2010), Sacher et al. (2015)). One reason for these low treatment rates is the presence of barriers to access treatment for patients, with stigma being one of them. Lung cancer is a stigmatized disease because of its association with smoking behavior: the majority of lung cancer patients (about 85%) have a history of smoking, although most of them are non-smokers by the time of the diagnosis. Stigma is defined as the patients' feeling of shame

or guilt connected with having lung cancer and conferred by the social representation of lung cancer as a self-inflicted disease with poor prognosis; such stigma does not only affect smokers, as research shows that non-smokers may feel stigma even more acutely because they are automatically assumed to be blamed for their cancer (Dunn et al. (2016)). Stigma has been associated with a variety of negative outcomes: diagnostic delays, reluctance to seek treatment or limited use of it, and under-prioritization of research funding (Gillum et al. (2011), Chambers et al. (2012), Aggarwal et al. (2016)). Lung cancer patients access treatment less than patients affected by cancers with similar survival: treatment rates are around 25% for stage IV lung cancer, but reach 60% for stage IV colorectal patients, 55% for stage IV stomach cancer, and 62% for stage IV ovarian cancer (Coburn et al. (2010), Meyer et al. (2016)). Interestingly, while lung cancer is responsible for 32% of cancer deaths, it only receives 10% of cancer research funding (Kamath et al. (2019)).[1]

As stigma constitutes a barrier to access treatment, it is likely to impact the adoption and diffusion of innovative therapies for cancer patients. In this paper we explicitly tackle the question: to which extent may social stigma hinder the adoption of innovation? While the current literature has explored a variety of motives to investigate heterogeneity in adoption patterns, from learning and uncertainty about side effects (Gong (2019), Crawford and Shum (2005)), to healthcare culture (Cutler et al. (2019)), we are the first to explore the connection between disease stigmatization and adoption of innovative therapies.

We combine a unique collection of micro-level datasets, including treatment modalities, health and socio-demographic information for the population of patients diagnosed with lung cancer in the Canadian province of Ontario between 2008 and 2016. We model treatment choices as a nested sequence of joint decisions between a patient and their physician: at the top level, the choice is between pursuing treatment or not; at the bottom level, the choice is between the different treatment options, including the innovative targeted therapies. Our measure of social stigma exploits the granular geographic information available in the data, capturing the role of a patient's reference group in the decision to seek treatment. Social stigma is hard to identify empirically, in particular because of the difficulty in distinguishing between situations in which a patient truly behaves according to the prevalence of that behavior in their reference group (endogenous effects) and situations where such correlation arises because of some shared attributes (correlated social effects). We explicitly tackle these issues in our empirical strategy. First, to avoid the reflection problem (Manski (2000)), we focus on the choice of newly diagnosed patients and how those patients are influenced by

[1] Kamath et al. (2019) reports an average spending of $2,229 in research per lung cancer death, compared to $24,442 for breast cancer, and $922 in research per person year life lost for lung cancer, compared to $1,299 for breast cancer.

untreated patients from the same neighborhood diagnosed in the previous year. Second, to tackle correlated effects, we follow Aizer and Currie (2004) and include a rich set of individual and neighborhood characteristics. Finally, we use another cancer type for which stigma is less of a concern, colorectal cancer, as a falsification test to confirm the robustness of our findings.

Model estimates support and provide a quantification of the hypothesis of social stigma as a deterrent to treatment participation. After controlling for a very rich set of individual's socio-demographic, health, and neighborhood attributes, we find that a patient is less likely to pursue treatment if a higher share of recent patients in the same neighborhood is left untreated. Patient's socio-demographic characteristics also affect treatment participation, in line with findings from the literature: higher income patients and those coming from areas where households are more stable and less deprived are more likely to access treatment. Finally, age and health status are, as expected, important drivers of the decision of whether to pursue treatment. Social stigma represents one fifth of the variation in utility attributable to other socio-demographic characteristics that affect treatment participation. Hence, while it is not the sole barrier to access treatment, it is a substantial one, which should be taken into account by policy makers when designing policies to mitigate disparities in access to care.

While comprehensive tobacco control efforts, including smoking restrictions and media campaigns, have been successful in reducing tobacco use, some "hard-hitting" messages may have also unintentionally increased social stigma toward lung cancer patients (Riley et al. (2017)). Readdressing public messages can mitigate the issue. We therefore illustrate the value of a policy designed to change the way lung cancer is perceived. We find that removing social stigma increases treatment rates for all patients, and in particular by 4% for innovative/targeted therapy. Following a cost-effectiveness approach that typically guides policy decisions when evaluating a given therapy, we compare the costs from additional treatment with its benefit, measured by the incremental quality-adjusted life year (QALY): we find that abating stigma would imply an additional overall cost of CAD 1.13 million in innovative therapies. However, the gain in survival is also high, which clearly justifies the use of innovative therapies: each additional patient would imply an additional annual cost of CAD 25,000 compared to the "no treatment" option, which is much lower than CAD 65,000 (USD 50,000) per year of longer quality life, which has been the de facto standard used by the Canadian medicine agency to decide on public coverage of drugs or medical procedures.

All in all, the results provide strong evidence that the patients face accessibility problems linked to stigma, which in turn slow down the adoption of innovative treatments and are likely to lower the incentives to invest in R&D. While we focus on lung cancer, our findings are of

interest for other stigmatized diseases in which scientific knowledge has produced important therapeutic advances, such as mental illnesses and HIV, but social stigma may hinder the diffusion of those innovations and, in turn, discourage further investments in R&D.

This paper relates to three main strands of literature. First, the medical literature has sought to examine stigma and the negative attitude towards lung cancer and its effects on care: Chapple et al. (2004), Chambers et al. (2012), Hamann et al. (2013), Dunn et al. (2016), Riley et al. (2017). Some economic studies have related social stigma to the limited use of welfare programs, as in Moffitt (1983), Stuber et al. (2000), and Bertrand et al. (2000). Recent works have investigated the role of stigma in learning and reporting the status of stigmatized diseases such as HIV (Thornton (2008), Yu (2019)) or mental health (Bharadwaj et al. (2017), Cronin et al. (2020)). However, neither the medical nor the economic literature has explicitly investigated the link between stigma and adoption of innovation.

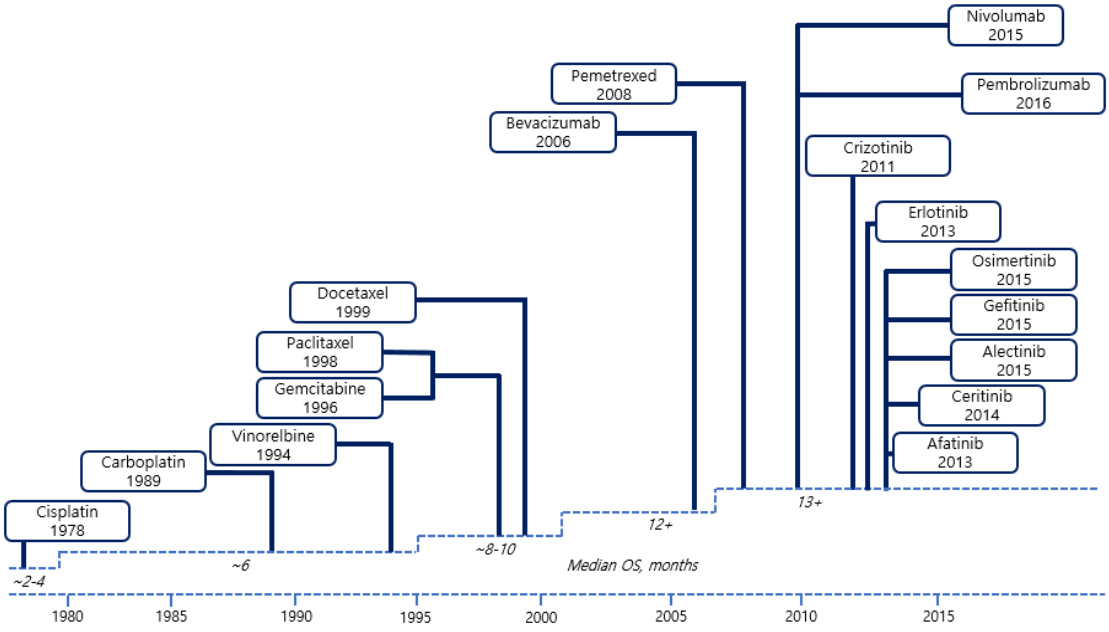
Second, we relate to the literature investigating the role played by physician and patient characteristics in the treatment decision: Coscelli (2000); Hellerstein (1998). More recently, the literature has focused on the determinants of physicians' heterogeneous response to different types of information shocks (Avdic et al. (2019)) or the adoption of innovative treatment (Gong (2019), Crawford and Shum (2005)), trying to disentangle the role of preferences versus skills (Currie and MacLeod (2018); Chan et al. (2019)).

Third, we relate to the empirical literature on social networks and their impact in a variety of contexts: program participation (Moffitt (1983), Bertrand et al. (2000), Duflo and Saez (2002), Aizer and Currie (2004), Chetty et al. (2013), Grossman and Khalil (2020)), crime (Bayer et al. (2009)), and labor markets (Bayer et al. (2008)). Manski (1993) and Manski (2000) warn about the difficulties of separately identifying endogenous, exogenous, and correlated social effects and explain the conditions under which such identification is possible. We specifically contribute to the strand of this literature emphasizing the role of social interactions on the diffusion of innovation: since the seminal work by Granovetter (1978), several studies have shown the importance of social learning in technology adoption in different contexts, from medical innovation (Agha and Molitor (2018), Burke et al. (2007)) to agriculture in developing countries (Munshi (2004), Bandiera and Rasul (2006), Conley and Udry (2010), Beaman et al. (2020)). Most of these works emphasize how social networks facilitate the adoption and diffusion of technology via the acquisition or transmission of information. Social interactions in our context may also operate through the information channel, but predominantly emerge as a specific form of social norms, namely stigma. With the exception of the recent work applied to sanitation investment by Guiteras et al. (2019), we are not aware of any other work highlighting this mechanism.

The remainder of the paper is organized as follows. Section 2 describes the empirical

setting, identifying the factors that influence barriers to access and stigma, and the data. Section 3 outlines the treatment choice model and section 4 provides details on the empirical estimation strategy and the identification issues. Section 5 presents the main results and their interpretation. Section 6 presents policy counterfactuals, and in particular a scenario in which we investigate the implications on adoption of innovative drugs when access barriers attributable to social stigma are removed and the implied gains for patients. Section 7 concludes.

Figure 1: FDA approvals in advanced lung cancer - First line only



The figure shows a timeline with FDA drug approvals for stage IV lung cancer - first line - since 1980. OS = overall survival (in months). Source: fda.gov.

2 Data and Institutional Details

2.1 Data and Cohort Definition

We use administrative data held at the Institute for Clinical Evaluative Sciences (ICES), a data repository consisting of record-level, linkable health data sets encompassing much of the publicly funded administrative health services records for the Ontario population. The main dataset used in this analysis is the Ontario Cancer Registry (OCR), which reports the diagnosis date, stage, and tumor characteristics for each patient diagnosed with cancer in

Ontario. We select all patients diagnosed with stage IV (metastatic) non-small cell lung cancer with known disease stage from 2007 to 2015, with follow-up to the end of 2016. Lung cancer accounts for 14% of all new cancer cases in Ontario and contributes to most cancer-related deaths for both sexes (Cancer Care Ontario (2013)). Our cohort comprises 14,238 patients. The cohort selection is motivated by two reasons: first, this population presents a desirable setting for our study because the treatment decisions for this cancer-stage are made by one main physician, while in non-metastatic stages there may be other variables at play, including complementarities between radiology/surgical interventions and systemic therapy. Second, many innovative cancer drugs introduced in recent years were initially approved only for the metastatic stage of the disease and only later approved for the treatment of earlier stages.

We also select the cohort of stage IV colorectal cancer during the same years. Colorectal cancers account for 13% of all new cancer cases in Ontario, with around 900 patients diagnosed each year, for a total of 8,015 patients in our sample period. Colorectal cancer patients are unlikely to face the same social stigma hindering access to treatment when presented with the cancer diagnosis. Similarly to lung cancer patients, therapeutic decisions at this cancer-stage are taken only by the oncologist. We therefore perform our empirical analysis on the population of colorectal cancer patients, in parallel with the main one, as a falsification check, with the expectation that social stigma is irrelevant in the context of colorectal cancer.

We merge the OCR using anonymized patients' identifiers with a number of ICES datasets, including Cancer Activity Level Reporting, Discharge Abstracts Database, National Ambulatory Care Reporting System, Ontario Health Insurance Plan Claims, Registered Person Database, New Drug Funding Program, Physician Database. In sum, we have access to detailed health information on these patients, including measures of utilization (treatment, hospitalization, spending), outcomes (mortality, disability), patient and disease characteristics (tumor morphology and histology, stage, patient sex, age, and income), and physician characteristics (sex, age, specialty, hospital of practice, and experience). Table B.1 in Appendix A provides an overview of the datasets and the relevant variables we extract from each of them.

To measure patients' health status at the time of the diagnosis, we follow the medical literature and use International Classification of Diseases-9 (ICD-9) diagnosis codes to retrieve all claims for each patient's episode of care from the Ontario Health Insurance Plan to calculate the Charlson comorbidity index for each patient, adapted for cancer patients (Klabunde et al. (2007)). The index uses information on patients' medical history with a look-back period of 2 years to categorize comorbidities and pre-existing medical conditions known to

increase the risk of death and, therefore, good predictors of the likelihood of treatment. We also extract information on whether the patient received any cancer-related surgery. While only less than 3% of lung cancer patients in our sample undergo a surgery, the procedure places a strong physiologic demand on the cardiovascular and respiratory system, so we use it as a control to proxy for the current health status of the patient, complementing the Charlson index.

Combining hospital claims for systemic treatment from the New Drug Funding Program database and the Activity Level Reporting System, we are able to reconstruct the treatment plans (denominated regimens), if any, administered to each patient. Details on how we construct the regimens administered to each patient are reported in Appendix A. The Activity Level Reporting System also reports information on the administration of radiation therapy, which helps achieving palliation and symptom controls in patients with metastatic disease. Finally, we match patients' records with physicians' claim records to identify the main physician treating the patient around the time of diagnosis. Details on the matching algorithm are presented in Appendix A.

One feature of the data makes it ideal for exploring barriers to access: the data reports the patient's place of residence at a very granular level, the three-digit zip code (FSA, Forward Sortation Area), which is more refined or equivalent to a census block. We can therefore geocode the FSA to the census block level and add socio-demographic information combining the census and other surveys administered by StatCan, the Canadian Statistical Institute. In particular, we supplement our data with the following information at the FSA level: unemployment rate, share of immigrants, education level, and rurality. We also include the Ontario marginalization index. The index measures multiple axes of deprivation in Ontario, including economic, ethno-racial, age-based and social marginalization. It was developed by researchers at the Centre for Urban Health Solutions at St. Michael's Hospital in Toronto to explicitly capture inequalities in various measures of health and social well-being, either between population groups or between geographical areas (Matheson et al. (2012)). It combines a wide range of demographic indicators from the census into four distinct dimensions of marginalization: residential instability (percent of renters and living alone); material deprivation (percent of low income and lone parent families); dependency (percent of seniors and employment); ethnic concentration (percent of recent immigrants and visible minority).

Finally, we exploit the geographic dimension of our data to compute the distance between the geographical unit of residence of the patient and both the nearest regional cancer center (should the patient decide not to be treated) and the one of choice of the patient.[2]

[2]The vast majority of patients in the data (80%) are treated at the nearest hospital. Half of the patients

We perform the same work on the data for colorectal cancer patients. We use this population to verify the robustness of our results.

2.2 Descriptive statistics

Column 1 of table 1 reports the summary statistics for our sample of patients. After excluding patients with missing stage or incomplete records, as well as those only diagnosed via an autopsy, we observe 14,238 patients and more than 2,000 physicians. Only 5,578 patients (39% of our sample) receive treatment; 61% of the patients do not receive any systemic therapy, one third receive the standard of care, while only 6% receive innovative treatment (targeted therapy). We identify as standard of care both platinum doublet chemotherapy regimens based on combinations of cytotoxic agents (cisplatin or carboplatin) and third-generation agents (such as gemcitabine and pemetrexed), as well as single agents: for a complete list see Table B.2 in Appendix A.[3] Innovative targeted therapy includes all approved oral agents for first-line treatment (afatibib, crizotinib, erlotinib, and gefitinib), which steadily gain market share during the period: less than 2% of the patients receive targeted treatment in 2010 (almost entirely gefitinib) and this share increases to reach 17% in 2016, after the entry of afatinib and crizotinib. At the same time, the share of patients treated with standard chemotherapy decreases slightly from 33% to 30%. The majority of patients does not receive any treatment, despite an increase in treatment rates over time (from 37% in 2008 to 45% in 2016).

Columns 2-4 of table 1 compare the characteristics of patients that do not receive treatment to patients receiving standard of care and targeted treatment and the last 3 columns report the results of a Wilcoxon test on the equality of distribution of the variables for each subsample. The figures in the table uncover interesting heterogeneity in the characteristics of patients that receive different treatment options. Patients who do not receive any systemic treatment tend to be male, older, more likely to present a tumor with squamous morphology, have more comorbidities and are less likely to undergo surgery than patients that receive any systemic therapy. They also have lower income and live further away from a regional cancer center. Differences exist even among patients that are treated: those receiving targeted therapy are more urban, live closer to a regional cancer center, are healthier beyond cancer (usually adenocarcinoma), and more likely to be women. As expected, geographic variation

choosing otherwise seek care at a hospital in a neighboring region. The remaining 10% are treated in one of the two Toronto regional cancer centers, which are considered the best providers of cancer care in Ontario.

[3] Our definition of a patient who does not receive any systemic therapy is conservative: we could also consider patients receiving only one or two cycles of treatment as untreated. We prefer our conservative approach as we do not know whether the patients dropped because of toxicities caused by those treatments, or because of economic difficulties in carrying out treatment.

matters, with lower rates of treatment systematically observed in some regions, which tend to be more marginalized, deprived, and with higher rates of low-educated and unemployed population.

Table 2 reports summary statistics for physicians. We observe a large number of doctors in our sample, with medical and radiation oncologists representing the majority and almost entirely responsible for patients who receive treatment. While referral to oncologists is very high, around 10% of patients are not matched to a specialist as their main physician, which explains the figure on family doctors we observe. Even within oncologists that prescribe some treatment, heterogeneity is substantial: those choosing innovative therapies tend to be younger, more female and more specialized (in terms of the number of lung cancer patients seen both by year and in total).

In parallel, we report the same set of summary statistics in Table B.4, Appendix B for colorectal cancer patients. We have 8,015 colorectal patients patients. Compared to lung cancer, they are more likely to receive treatment (63% of our sample), despite a similar age and sex profile. They also tend to be healthier than lung cancer patients and exhibits longer survival. However, after controlling for a host of health characteristics, for those who are left untreated the prognosis is similar to lung cancer, as highlighted by the survival curves reported in Figures 1 and 2, Appendix B.

Table 1: Sample Summary Statistics: Patients

	Cohort	Treatment type			$p-value$		
		untreated	SOC	innovative	1=2	0=2	0=1
		0	1	2			
			Patient demographics				
Male (%)	0.53	0.54	0.53	0.39	0.000	0.000	0.190
Age	53.99	57.68	49.00	47.83	0.000	0.000	0.000
Charlson index	0.62	0.72	0.46	0.36	0.000	0.000	0.000
			Cancer characteristics				
Adenocarcinoma	0.69	0.63	0.76	0.92	0.000	0.000	0.000
Squamous cell	0.20	0.23	0.18	0.03	0.000	0.000	0.000
Large cell carcinoma	0.02	0.02	0.02	0.01	0.005	0.003	0.717
Multiple cancers	0.01	0.01	0.02	0.03	0.033	0.000	0.001
1-year survival prob.	0.21	0.09	0.39	0.42	0.000	0.000	0.000
			Health care utilization				
Surgery	0.04	0.03	0.04	0.03	0.168	0.331	0.000
Palliative radiotherapy	0.63	0.56	0.74	0.72	0.172	0.012	0.000
Treated by oncologist	0.70	0.54	0.97	0.95	0.004	0.000	0.000
			3-digit zipcode characteristics				
Rural	1.13	1.13	1.14	1.10	0.001	0.005	0.091
Distance hospital (km)	31.24	31.10	32.92	24.14	0.000	0.553	0.000
Income quintile	2.85	2.78	2.94	3.02	0.089	0.000	0.000
% immigrant population	0.27	0.26	0.26	0.33	0.000	0.000	0.883
% population no education	0.18	0.18	0.18	0.18	0.007	0.000	0.099
Unemployment rate	8.25	8.28	8.18	8.27	0.059	0.774	0.002
Marginalization index (quintile):							
1. instability	3.07	3.16	2.98	2.70	0.000	0.000	0.000
2. deprivation	3.28	3.33	3.20	3.26	0.229	0.124	0.000
3. dependency	3.18	3.21	3.18	2.89	0.000	0.000	0.111
4. ethnic concentration	3.00	2.98	2.97	3.46	0.000	0.000	0.651
Total number of patients	14,248	8,660	4,731	847			

The table reports summary statistics of the main variables in our sample related to patients. The first column includes demographics, tumor attributes, health care utilization measures, and a set of characteristics related to the three-digit zip code of the patient's residence for the whole sample. Column 2-4 compare those characteristics between (i) untreated patients; (ii) patients treated with standard of care (SOC, chemotherapy); (iii) patients treated with innovative therapies (targeted treatment). Columns 5-7 report the results of a Wilcoxon test on the equality of distribution of the variables for each subsample.

Table 2: Sample Summary Statistics: Physicians

	Cohort	Treatment type			$p-value$		
		untreated	SOC	innovative	1=2	0=2	0=1
				Physician demographics			
Male	0.67	0.70	0.64	0.52	0.000	0.000	0.000
Age	49.06	49.87	48.30	45.29	0.000	0.000	0.000
Tenure (# years)	14.80	15.30	14.40	11.40	0.000	0.000	0.000
				Specialty			
Oncologist	0.70	0.53	0.97	0.95	0.004	0.000	0.000
Radiation oncologist	0.20	0.31	0.02	0.05	0.001	0.000	0.000
Other	0.01	0.02	0.00	0.00	0.719	0.000	0.000
Family doctor	0.08	0.13	0.00	0.00	0.274	0.000	0.000
				Workload			
Lung cancer patients/year	10.46	8.92	12.42	14.91	0.000	0.000	0.000
Lung cancer patients (full period)	67.00	54.36	85.93	91.36	0.039	0.000	0.000

The table reports summary statistics of the main variables in our sample related to physicians. The first set of columns include demographics, specialty, where "other" refers to thoracic surgeon and respirologist. Column 2-4 compare those characteristics between (i) untreated patients; (ii) patients treated with standard of care (chemotherapy); (iii) patients treated with innovative therapies (targeted treatment). Columns 5-7 report the results of a Wilcoxon test on the equality of distribution of the variables for each subsample.

2.3 Lung cancer in Ontario

Regional differences Lung cancer is the most common cause of cancer death among men and women in Ontario, accounting for 6,580 deaths in 2011 and a quarter of all cancer deaths. The reason for such a sobering figure is that it is both highly common (it is the second most diagnosed cancer in Ontario) and highly fatal. Of the four most common cancers, lung cancer has the lowest 5-year survival at every stage, only 60.8% at stage I, declining to 3.3% at stage IV. This is especially concerning as more than half of all lung cancer cases in Canada are diagnosed when they are at an advanced stage and the cancer has spread beyond the lungs (metastatic).

The burden of cancer, however, is not equally spread across geography (Chafe et al. (2011)). The average mortality rate in Ontario is 224 deaths per 100,000 cases, with important regional differences: the death rate ranges from 186 in the Central region to 268 in the North-East. This figure reflects heterogenous incidence rates, due to different risk factors (mostly smoking rates) and socio-demographic profiles (sex, age, health status) across regions. Notable differences are visible even at finer geographic levels. Figures 3 and 4

in Appendix B report the incidence rates for stage IV non-small cell lung cancer from our sample computed both at the administrative health region (LHIN, Local Health Integration Network, capturing a cancer center's catchment area) and at the three-digit postal code level.[4] The maps show that variation in incidence is large both across and within regions: zip codes in the 75th percentile of the regional incidence distribution display up to four times the incidence rates of FSAs in the 25th percentile.

Heterogeneous incidence rates and risk factors do not tell the whole story: access to cancer treatment plays a major role. Socio-demographic characteristics drive access to care, with racial and ethnic disparities deterring healthcare use even in the absence of discriminatory motives: see Balsa and McGuire (2001), Baicker et al. (2004). In the context of cancer, extensive work in health policy and the medical literature has emphasized the relationship between certain socio-demographic characteristics and the likelihood of receiving cancer care, especially income, rurality and remoteness, sex, ethnicity and immigration status (Ahmed and Shahid (2012), Borkhoff et al. (2013), Canadian Partnership Against Cancer (2014), Iqbal et al. (2017), Mackillop et al. (1997), Jembere et al. (2012)). Hospitalization rates are higher in higher income areas (CIHI (2008)) and, at the same time, risk factors such as smoking and obesity are more prevalent in rural areas, which are characterized by less access to primary care, higher unemployment rates, lower levels of formal education, and higher distance to specialized health care services: see Gillan et al. (2012).

Lung cancer stigma The above mentioned socio-demographic factors relate to late diagnosis and lower rates of treatment for any cancer. Treatment rates for lung cancer remain the lowest among leading cancers and only 39% of the patients in our sample receive any systemic therapy, compared to 60% of metastatic colorectal cancer patients. This is not specific to our sample and a large medical literature has documented similar patterns across countries (Davidoff et al. (2010), Sacher et al. (2015)). The aggressiveness of lung cancer compared to other tumors, the fact that most patients are old and cannot tolerate toxic treatment, or the diagnosis at an advanced stage only partially explain such striking differences (Sacher et al. (2015)). Unfortunately, lung cancer carries a unique social stigma due to its association with cigarette smoking, and hence is often seen as a smoker's disease, self-inflicted, and preventable. Smoking is estimated to account for over 70% of new lung cancer cases in Ontario, but between 15% and 20% of those diagnosed with lung cancer never smoked and 35% quit long before the diagnosis. Stigma arises when a patient is held responsible for the disease, irrespective of whether or not the patient is a smoker and the

[4] Figures are smaller than the Ontario's average because of our cohort definition: only stage IV patients, excluding patients with multiple cancers on different sites.

exact etiology of the disease is actually unknown for the individual patient. A 2010 survey by the Global Lung Cancer Coalition found that 22% of Canadians admitted to have less sympathy for a person with lung cancer than other tumors (Ipsos MORI (2010)). Lung cancer stigma has been frequently documented in the medical literature and the internalization of such guilt and shame has been linked to reluctance and delay in seeking care (Chapple et al. (2004)). Widespread clinical evidence exists that even patients with significant comorbidities can receive curative therapy that preserves quality of life while offering cure or prolonging survival. Metastatic (stage IV) lung cancer is generally incurable, but treatable: clinical studies have demonstrated clear survival benefits of chemotherapy (Davidoff et al. (2010), Arenberg (2012), Sacher et al. (2015)). Cancer Care Ontario evidence-based guidelines, which strictly follow the recommendations issued by the American Society of Clinical Oncology, clearly indicate that metastatic patients should be offered systemic therapy and that therapeutic options exist even for patients that may not be fully active. Treatment decisions should not be based on age alone and should strike a balance between improving survival, increased toxicity, and patient preference: Ellis et al. (2016).

Innovation in lung cancer Lung cancer survival has historically been and still remains among the lowest across all cancers (Canadian Cancer Statistics Advisory Committee (2018), Lichtenberg (2015), Honoré and Lleras-Muney (2006)). However, in recent years, lung cancer experienced one of the highest growth in survival, from 13.6% to 19.6% between 2008 and 2012; early detection is crucial to increase survival, but screening programs for lung cancer are not common, so the observed increase in survival is mainly attributable to therapeutic innovation.[5] Despite the low research funding compared to other areas of oncology, major innovations were introduced in the past two decades. In the 1990s, many new chemotherapeutic agents (paclitaxel, docetaxel, vinorelbine, gemcitabine, pemetrexed) were discovered and used in patients with advanced disease either as single-agents, or combined with platinum compounds (cisplatin or carboplatin). The use of platinum doublets led to increases in median survival to 9 months (1-year survival of 30%-35%), up from median survival of 3-4 months for untreated patients (1-year survival of approximately 15%, Danesh et al. (2019), Sacher et al. (2015)). In the 2000s, improved understanding of the molecular basis of cancer led to treatments exploiting specific molecular abnormalities (targeted therapy). Treatment has become more complex over time, in part because of recognition of tumor-specific and patient-specific traits that predict a greater likelihood of success, or lack of success, with specific drugs. Though epidermal growth factor receptor (EGFR) mutations are only present

[5] Cancer Care Ontario. Cancer Fact: Lung cancer mortality differences between men and women influenced by smoking trends. April 2015. Available at cancercareontario.ca/cancerfacts.

in nearly 15% of lung cancer patients, they are strong predictors of the efficacy of specific inhibitors of EGFR such as erlotinib or gefitinib. Patients with EGFR-mutated tumors can achieve response rates higher than 70% and, most importantly, they can achieve an overall survival longer than two years, never seen before in lung cancer (de Castro-Carpeño et al. (2011)). Following a similar research path, discovery of fused proteins based on anaplastic lymphoma kinase (ALK) rearrangements has opened up the possibility of blockage by specific inhibitors such as crizotinib. All of these targeted agents improve survival to up to 2 years in metastatic patients with relevant mutations. At the same time, they present a side effect profile that is milder and more manageable than standard platinum-based chemotherapy, making them good candidate treatments even for older patients with comorbidities. CCO guidelines recommend targeted agents even for patients with poor performance status, a measure of cancer patients' ability to tolerate therapy.[6]

A common critique to these survival figures is that they may be overestimated, since they come from clinical trials, where patients are highly selected and may not be representative of the population of metastatic lung cancer patients. We confirm these findings in our sample, using our data to estimate a flexible parametric survival model. Following Danesh et al. (2019), we include gender, age group, treatment modality (no treatment, chemotherapy, innovative therapy), histology of tumor, year of diagnosis, and cancer care centre of treatment or catchment area (if untreated), and interaction terms between age group and histology, and treatment modality and year of diagnosis. In addition, age group, treatment modality, and year of diagnosis are included as time-dependent variables. Based on the model, we plot the survival curves for each treatment modality. The curves all refer to a hypothetical female patient with adenocarcinoma, aged 65-69 and with low Charlson index (healthy), receiving palliative radiation but no surgery, diagnosed in year 2012 and treated at Toronto Central. Figure 1 shows that a patient left untreated has a significantly worse expected survival. Receiving treatment improves survival, especially for patients administered innovative treatment: the survival of the hypothetical patient at one year from the diagnosis is 0.16 if untreated, 0.55 if treated with chemotherapy, and 0.79 if treated with innovative therapy.

3 The Model

We develop a model of treatment choice for metastatic lung cancer. Individuals choose the hospital where they are treated, but the allocation to physicians is random: this assumption allows us to abstract from issues of matching between patients and physicians and stems

[6] Targeted therapy is allowed even for patients who are capable of only limited self-care and confined to bed for up to 50% of their time (Ellis et al. (2016)).

from the rules governing patient referral by family doctors to oncologists in Ontario, which only allow for the choice of the cancer center.[7] In other contexts, patients with certain characteristics may pursue physicians with a higher propensity to treat (Dubois and Tuncel (2014)), or the physicians may actively seek a certain kind of patient (Chang and Obermeyer (2020)). While the specific institutional features of the Ontario healthcare system reassure us about the appropriateness of this assumption, in table B.3 in Appendix B, we test for this type of selection and regress a set of patients' characteristics on individual physician fixed effects, controlling for the year of diagnosis and the cancer care centre. We then run a joint test of physicians' fixed effects and find no statistically significant difference across physicians for most observable characteristics: proportion of female patients, health status, type of cancer (adenocarcinoma vs. others), additional malignancies, income quintile; we cannot reject that some selection exists for age, but the effect is nevertheless small. Finally, to abstract from dynamic considerations of learning patients' reactions through usage, we focus on the first treatment choice at the time the disease is diagnosed (first line regimens).[8]

The treatment decision is a joint decision of the patient and their physician.[9] In our setting each patient is matched to one main physician, so we suppress the physician-specific subscript in the utility specification to keep the notation clean. Let there be $i = 1, ..., I$ patients with stage IV lung cancer diagnosed at year t. For each patient i, the choice is between treating or not treating the disease: $g = 0, 1$. Conditional on treating, there are four treatment options: $j = 1, .., 4$: cisplatin-based chemotherapy, carboplatin-based chemotherapy, single agent chemotherapy, and targeted therapy (the innovative treatment). The nesting tree is depicted in Figure 2. The first three options fall under the category of standard of care, but differ in the drugs used and their toxicity profile. Cisplatin doublets (combination of cisplatin and another chemoterapic agent) are considered more effective than carboplatin doublets, but are more toxic and less tolerated and hence not recommended for older or sicker patients. Single agent regimens are used for patients who cannot tolerate any platinum-based therapy.

We assume that the indirect utility of each patient i from pursuing treatment j, as perceived and maximized by the physician, is additively separable into a component that is specific to the treatment choice j (V_{ijt}) and a component that varies with the decision to

[7] Ontario's guidelines for GP do not allow for referral to one specific oncologist within the chosen cancer center. Conversations with medical oncologists also confirm that direct referral is not possible.

[8] Only 2,366 patients in our sample receive second-line treatment.

[9] CCO and ASCO guidelines recommend a shared decision making between the doctor and the patient and treatment decisions should balance survival and toxicity and directly incorporate patient preferences (Ellis et al. (2016)).

treat g (W_{igt}) but does not vary across the treatment choices:[10]

$$u_{ijt} = V_{ijt} + W_{igt} + \varepsilon_{ijt.} \tag{1}$$

The random component of utility follows the distributional assumptions of a two-level nested logit model (McFadden (1978)), which allows valuations to be correlated across alternatives in the same nest. At the top level, there are two nests: the "treatment" nest $g = 1$, which includes the treatment options, and the "no-treatment" nest $g = 0$, which is a degenerate nest with only alternative $j = 0$. Individual i's utility for the no-treatment option is:

$$u_{i0t} = W_{i0t} + \varepsilon_{i0t.}$$

At the bottom level, the treatment nest consists of the J treatment options. The distribution of ε_{ijt} and ε_{i0t} contains the nesting parameter λ, with $0 < \lambda \leq 1$. The parameter proxies for the degree of dissimilarity of treatment options belonging to the "treatment" nest. As λ goes to one, the distribution of the error terms ε_{ijt} approaches an i.i.d. extreme value distribution, so correlation in the error between treatment options is weak; as it tends to zero, the error terms become perfectly correlated and patients/physicians choose the alternative with the highest observable utility. The nested logit results in simple expressions for the choice probabilities. The probability of choosing treatment option j is the product of the conditional probability that treatment option j is chosen in the "treatment" nest (the bottom-level logit), and the marginal probability that patient i chooses to be treated (the top-level logit):

$$s_{ijt} = s_{ijt|g} \cdot s_{igt}.$$

Choice between treatment options The bottom-level choice probabilities are:

$$s_{ijt|g} = \frac{\exp\left(V_{ijt}/\lambda\right)}{\sum_{l \in J} \exp\left(V_{ilt}/\lambda\right)}.$$

[10] We assume that the physician acts in the best interest of their patient, i.e. is a perfect agent. In Ontario all medical oncologists are on alternative funding plans and the choice of treatment regimens has no effect on their compensation: this feature mitigates concerns about agency issues.

We define the inclusive value term I_{i1t} as a measure of the expected aggregate utility of all options in the nest "treatment" ($g = 1$):

$$I_{i1t} = \log \left[\sum_{j \in J} \exp \left(V_{ijt} / \lambda \right) \right].$$

Choice of whether to pursue treatment The top-level choice probability that a patient chooses to pursue treatment ($g = 1$) is:

$$s_{i1t} = \frac{\exp \left(W_{i1t} + \lambda I_{i1t} \right)}{\exp(W_{i0t}) + \exp \left(W_{i1t} + \lambda I_{i1t} \right)}.$$

At the top-level, all patients' and treatments' characteristics included at the bottom-level indirectly enter the decision of accessing treatment through the inclusive value term I_{it}.

The probability that patient i chooses the no-treatment option s_{i0t} is simply:

$$s_{i0t} = 1 - s_{i1t} = \frac{\exp \left(W_{i0t} \right)}{\exp(W_{i0t}) + \exp \left(W_{i1t} + \lambda I_{i1t} \right)}$$

Indirect utility specification We now specify the deterministic components of utility $(V_{ijt} + W_{igt})$. The first component, which depends on variables that describe each treatment option, is specified as follows:

$$V_{ijt} = \beta_j + x'_{it} \gamma_j,$$

where x'_{it} is a vector of characteristics related to: (i) the patient, at the time of diagnosis: sex, age group (nine dummies), health status proxied by the Charlson index (two dummies), tumor histology (adenocarcinoma and squamous), the presence of synchronous malignancies in the lungs, whether the patient has undertaken a surgery or not; (ii) the physician: specialty, age, sex, annual workload. All treatment-specific characteristics are absorbed by the constant β_j**.** We do not include the price of each regimen: from the point of view of the patient, all drugs included in the regimens are publicly funded, including the supportive ones. Physicians are on alternative funding plans and the choice of therapy has no impact on their compensation, as well as the choice of whether to treat the patient at all.

The second component, which depends on variables describing the nest "treatment" against the "no-treatment" nest, is specified as follows:

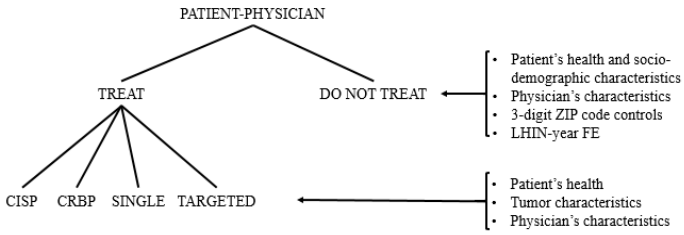
$$W_{igt} = z'_{it} \gamma_g + \alpha_g b_{it}, \tag{2}$$

where z'_{it} denotes a vector of: (i) patient-specific health attributes at the time of diagno-

sis: sex, age group and health status proxied by the Charlson index; (ii) physician-specific characteristics: specialty, age, sex, annual workload; (iii) patient- and neighborhood-specific socio-demographic characteristics: the patient's income, the four components of the Ontario marginalization index (residential instability, material deprivation, dependency, ethnic concentration), rurality, share of immigrants, unemployment rate and distance to the closest cancer care center. We also control for the year of diagnosis interacted by the regional cancer centre of choice of the patient, or the centre belonging to the catchment area according to patients' residence, should the patient decide not to get treated (111 dummies). The socio-demographic characteristics are common to all patients in the same geographic location except for income, which is individual-specific.

The second term in (2), b_{it}, captures social barriers, or social stigma, namely the social disapproval or discrimination against lung cancer patients. Manski (1993) warns about the importance of correctly identifying the reference group. Previous works have emphasized the role of geographical proximity in the prevalence of social norms, including social stigma. Most of the literature on social norms uses an individual's community as the relevant reference group (Bertrand et al. (2000), Aizer and Currie (2004), as well as the medical and health policy literature Stewart et al. (2015), Elliot et al. (2018)), often identified at the neighborhood level. Following this approach, we treat members of the same neighborhood in which the patient resides as a likely reference group. Patients from the same community are likely to be subject to similar degrees of social discrimination, hence fellow patients may play a role on an individual's choice to seek treatment. We define social stigma as a function of decision indicators for all other lung cancer patients in a certain neighborhood. We detail below how we construct this variable to deal with simultaneity and unobserved heterogeneity in identifying social stigma in our model.

Figure 2: Regimen choice model



The figure depicts the nesting tree. CISP: cisplatin-based chemotherapy; CRBP: carboplatin-based chemotherapy; SINGLE: single agent chemotherapy; TARGETED: targeted treatment. For the full list of regimens in each group, see Appendix B, Table B.2.

4 Identification

Our variable to proxy for social stigma as a barrier to access treatment (b_{it}) is the share of patients living in the same small geographic area who were diagnosed in the previous period and did not access treatment. In particular, we specify the stigma barrier variable b_{it} as follows:

$$b_{it} = \frac{1}{N} \sum_{k \neq i} d_{kt-1} \text{ if } j = 0,$$

where N denotes the number of patients in the same zip code (three-digit level); d_{it} is a vector of decision indicators equal to 1 if patient k is *not* treated ($j = 0$) in period $t - 1$.

This specification leverages the rich information in our data on the geographical proximity between patients diagnosed with the same disease and exploits variation in treatment rates that we observe at this granular level. Figure 5 in Appendix B reports the share of patients that receive systemic therapy by administrative health region (LHIN): regional differences are striking and the share of treatment ranges from one third to one half across areas. Significant heterogeneity is present also within the same region: treatment rates more than double in some cases moving from a zip code in the 25^{th} percentile of the regional distribution to one in the 75^{th} percentile (see Figure 6 Appendix B). To understand whether such variation may be observed in the absence of any correlation in treatment choices, we follow Duflo and Saez (2002) and compare the empirical variance in the data with the variance under the hypothesis that choices are independent. We find that the 0.96 variance in treatment choices across zip codes cannot be generated by independent behavior, which would give rise to a

variance of only 0.24 in the province of Ontario.

We think of social stigma as a form of endogenous social interaction, in the spirit of Manski (1993) and Manski (2000), where individual behavior varies with the prevalence of that behavior in the reference group to which the individual belongs. Empirically identifying endogenous social effects is challenging, as they may be indistinguishable from two other types of social effects, which would lead to the same observational outcomes: exogenous effects, where individual behavior varies with exogenous characteristics of the group; and correlated effects, where similar behaviors from members of the same group depend on similar characteristics or similar institutional environments. In our context, the main challenge is to distinguish social stigma from correlated effects. We explain below how these would materialize and the method we use to mitigate such identification concerns.

Simultaneity: the reflection problem A patient may choose whether to access treatment on the basis of their peers; their peers' choices may in turn be affected by the individual's choice. Interdependence in patients' decisions (i) generates simultaneity bias; (ii) impedes the use of standard maximum likelihood methods to estimate the parameters of interests, as independence in individual choice probabilities may be violated. We solve the issue by focusing on the choices of newly diagnosed patients: in our setting, the social stigma effect is naturally unidirectional as new patients can be affected by the decisions of previously diagnosed patients, but not vice versa. Following Manski (1993) and much of the recent literature, we use the no treatment decisions for patients from the same neighborhood diagnosed the year before.

Unobserved heterogeneity: correlated effects Patients in the same reference group may behave similarly because they share similar characteristics or face similar institutional environments, some of which may be unobserved by the researcher. Correlation in the treatment decisions among patients in the same neighborhood may therefore not necessarily arise from social stigma, but, for example, from similar socio-demographic factors or from sharing the same doctors or visiting the same hospital. To disentangle the effect of social stigma on lung cancer patients from common characteristics, we follow Aizer and Currie (2004) and run the following regression:

$$\begin{aligned} treat_{ait} &= \alpha_0 + \alpha_1 treat\_own_{ait-1} + \alpha_2 treat\_other_{ait-1} \\ &\quad + \alpha_3 x_{ait} + \alpha_4 zip_{at} + LHIN \cdot year_t + \varepsilon_{ait}, \end{aligned} \tag{3}$$

where $treat_{ait}$ is a binary variable indicating whether the patient i in area a at time of diagnosis t is treated, x_{ait} denotes patient's characteristics at the time of diagnosis, mainly related to their health as listed above, zip_{at} denotes characteristics of the neighborhood, $LHIN \cdot year_t$ are administrative health region (LHIN) by year fixed effects that control for trends in treatment at the level of the catchment area of the hospital.[11] The parameters of interest are the coefficients of $treat\_own_{ait-1}$ and $treat\_other_{ait-1}$. The variable $treat\_own_{ait-1}$ measures the impact of other patients of the same neighborhood on the probability of receiving treatment and is computed as the fraction of patients diagnosed in the previous year $(t-1)$ that receive treatment in the same neighborhood (three-digit zip code); the variable $treat\_other_{ait-1}$ measures instead the impact on the probability of receiving treatment of patients who are *not* in the reference group of patient i: it is computed as the share of patients receiving treatment the previous period in contiguous three-digit zip codes.[12] A positive coefficient on $treat\_other_{ait-1}$, after controlling for geographic characteristics, would suggest that at least some of the effects captured by $treat\_own_{ait-1}$ may actually be effects stemming from correlated geographic characteristics.

Columns 1 to 4 of Table B.6 report the results of specification 3 where the reference group is the share of recently diagnosed patients receiving treatment in the same neighborhood. Pursuing treatment is highly correlated within a neighborhood: the coefficient of $treat\_own_{ait-1}$ is positive and significant (column 1); importantly, the coefficient remains positive and significant after controlling for neighborhood characteristics, including the average health and socio-demographic profile of resident patients (column 2). More importantly, such magnitude is barely affected by the inclusion of $treat\_other_{ait-1}$, which is never significant (column 3 and 4). These results reassure us that the effect of social stigma is not merely a neighborhood effect but an endogenous social effect à la Manski (1993). It also confirms the appropriateness of our definition of the reference group as the three-digit zip code, for the influence of neighbors tends to dissipate quickly with distance.[13]

We also look at patterns within subgroups of our reference group: in particular, we restrict the reference group to the patients residing in the same three-digit zip code in the same income bracket (above or below the median), while controlling for neighborhood characteristics, including the socio-demographic profile, population size, and marginalization measures. As long as social interactions tend to happen between individuals of similar social status, we expect correlation in treatment decisions within the subgroup of neighbors,

[11] Unfortunately, neighborhood fixed effects cannot be used because of overfitting concerns given the limited sample size.

[12] We use all zip codes sharing the same first two digits.

[13] A specification where we compute $treat\_other_{ait-1}$ at the level of the hospital catchment area (LHIN) provides qualitatively similar results.

with less influence of other subgroups. Columns 5-8 of table B.6 report the results of this regression. We find that most of the effect identified in our main specification stems indeed from the influence of neighbors in the same subgroup on a patient's behavior, suggesting that zip code-specific common unobservables are not the sole drivers of our findings.[14]

We finally conduct a falsification test and run the same set of regressions using the sample of stage IV colorectal cancer patients. As social stigma is less of a concern for this cancer, we do not expect the treatment decisions of patients in the same reference group to affect the treatment decision of an individual patient after controlling for neighborhood characteristics. Table B.7 reports the parameter estimates, which confirm our intuition: the coefficient of $treat\_own_{ait-1}$ is positive and significant in the specifications without controls at neighborhood level (column 1 and 5). As soon as we control for neighborhood characteristics, the coefficient of $treat\_own_{ait-1}$ becomes insignificant, suggesting the presence of correlated social effects and confirming the importance of neighborhood characteristics to control for them; the variable $treat\_other_{ait-1}$ does not have a significant coefficient in any of the specifications.

5 Estimation Results

Preliminary evidence To first explore the determinants of treatment, focusing on the potential influence of stigma as a barrier to access, we estimate a linear probability model in which access to treatment is regressed on the share of recently diagnosed patients left untreated in the same neighborhood b_{it}, three-digit zip code controls z_{it} (the four components of the marginalization index, rurality, distance to the closest cancer center), patient and physician controls, including patients' income, cancer characteristics and patient's health. We flexibly control for a full set of geographic and temporal dummies, the administrative health region (LHIN) interacted by year fixed effects. Results are reported in column 1 of Table 3. The resulting parameter estimates indicate a negative and statistically significant deterring effect of the share of untreated neighbors diagnosed in the previous year on the individual's probability of being treated: each additional percentage point in the share of untreated neighbors is associated with a 0.03 percentage point decrease in the individual probability of receiving treatment, conditional on patient's and neighborhood attributes. To verify the reliability of this result, we run the same regression on the sample of colorectal cancer patients, for which we do not expect a significant role of social stigma in pursuing

[14] We run an additional specification in which we estimate a separate coefficient for social stigma barrier in high income and low income subgroups. We find that the coefficients are not significantly different, suggesting that the two income groups respond similarly to the behavior of their peers.

treatment. The estimates reported in column 2 of Table 3 confirm that the coefficient of social barrier b_{it} is small in magnitude and statistically insignificant for colorectal cancer patients.

Table 3: Linear Probability Model of Treatment

	(1) Lung	(2) Colorectal
	Treatment (0/1)	
Share of untreated patients b_{it}	-0.031	-0.012
	(0.014)	(0.014)
Cancer characteristics	Yes	Yes
Patient health status	Yes	Yes
Patient socio-demographics	Yes	Yes
Zip-code controls (w_{it})	Yes	Yes
Physician controls	Yes	Yes
LHIN by year	Yes	Yes
Observations	13,129	7,021
R-squared	0.302	0.446

The table reports the parameter estimates and standard errors for a linear probability modelling patient's access to treatment. Standard errors (in brackets) are clustered at zip code level. All these specifications are weighted by the total number of patients in each year/FSA combination. The total number of observations is 13,129 for lung cancer and 7,021 for colorectal cancer.

Main specification We now move beyond correlations and estimate the discrete choice model represented in equation (1). At the bottom level, we have a full set of alternative-specific intercepts β_j and slope vectors γ_j, which are interacted with the individual characteristic vector x_{it} : the total number of parameters to be estimated is $23 \cdot 3 = 69$. At the top level, thanks to the rich set of neighborhood-specific controls and fixed effects, we have 156 parameters to be estimated. Given the large number of parameters, we use sequential maximum likelihood; we correct the standard errors of the top model, which are biased downward, using a bootstrap procedure.

We first discuss the determinants of the choice of a specific regimen. Table 4 reports the bottom level results, in which we investigate those determinants as a function of (i) patient; (ii) tumor; and (iii) physician characteristics. The base treatment option is CISP, which is part of the standard of care and tends to be quite aggressive compared to the other options. Age and health conditions (a higher value of the Charlson index indicates worse health) are, intuitively, important drivers of the decision of the type of treatment. Patients whose health conditions are worse tend to be administered single agents. People with squamous cancer are

very unlikely to receive innovative regimens, which aligns with the indications of those drugs. Concerning physicians, parameter estimates indicate that their annual workload, which we interpret as a proxy for experience, is an important determinant of the type of treatment chosen.

We now discuss the determinants of participation to treatment. Table 5 reports the maximum likelihood estimates of the top level. The coefficient of the main variable of interest, stigma barrier, is negative and precisely estimated: after conditioning for a host of observable characteristics related to (i) the patient, (ii) the physician, and (iii) the neighborhood, we find that a patient is less likely to pursue treatment if recent fellow patients in their immediate neighborhood did not receive treatment. Patient's socio-demographic characteristics affect treatment participation as well: higher-income patients and those coming from areas where households are more stable and less deprived are more likely to access treatment. Finally, age and health status are, as expected, important drivers of treatment participation.

To compare the importance of social stigma to other patient's socio-demographic characteristics, which also act as critical barriers to access treatment, we compute the ratio of the standard deviation of their contribution to a patient's utility. The socio-demographic component includes a patient's income and distance to the closest cancer centre, the four components of the Ontario marginalization index and other neighborhood attributes such as percent of non-educated residents, immigrants, unemployment, rurality. The average ratio of the variance reveals that variation in the social stigma component is around 19% of the magnitude of utility variation due to socio-demographic attributes. Stigma is therefore an influential driver to treatment participation, which should be taken into account by policy makers when reflecting on strategies to mitigate disparities in access to care.

Table 4: Regimen choices - A disaggregate nested logit model

	CRBP	SINGLE	TARGETED
Age 45-49	0.549	-0.294	-0.359
	(0.323)	(0.382)	(0.299)
Age 50-54	0.451	-0.162	-0.541
	(0.291)	(0.321)	(0.257)
Age 55-59	0.903	-0.332	-0.461
	(0.282)	(0.316)	(0.248)
Age 60-64	1.018	-0.345	-0.526
	(0.278)	(0.309)	(0.243)
Age 65-69	1.230	-0.193	-0.470
	(0.278)	(0.308)	(0.246)
Age 70-74	1.635	0.159	0.0892
	(0.281)	(0.313)	(0.247)
Age 75-79	2.138	0.918	0.653
	(0.292)	(0.320)	(0.262)
Age 80-84	2.738	1.942	1.863
	(0.366)	(0.397)	(0.345)
Age 85+	3.036	3.066	3.156
	(0.671)	(0.682)	(0.648)
Male (0/1)	0.0414	0.264	-0.453
	(0.0689)	(0.102)	(0.0906)
Charlson medium	0.128	0.146	-0.107
	(0.0801)	(0.117)	(0.108)
Charlson high	0.672	0.588	0.131
	(0.142)	(0.192)	(0.200)
Adenocarcinoma	0.351	-0.193	0.0893
	(0.158)	(0.207)	(0.194)
Squamous	0.210	-0.289	-1.945
	(0.173)	(0.232)	(0.289)
Oncologist	0.786	0.208	1.742
	(0.605)	(0.638)	(1.121)
Radiologist	0.811	0.664	3.099
	(0.654)	(0.698)	(1.148)
Age physician	0.0114	0.0250	-0.00594
	(0.00355)	(0.00504)	(0.00475)
Workload	0.0199	-0.0244	0.0333
	(0.00376)	(0.00633)	(0.00472)
Observations		20,732	
Individuals		*5,183*	
Alternatives		*4*	
Log likelihood		-6081.71	

The table reports the parameter estimates and standard errors for the bottom level of the nested logit model where the choice of the specific regimen is modelled, where the base regimen is CISP. The excluded age is the youngest category, the excluded health status category is the lowest Charlson (most healthy individual). The model also controls for the presence of multiple cancers, whether the patient underwent surgery, physician's other specialty and sex, and a constant for each option. The total number of observations is 5,183.

Table 5: Treatment participation - A disaggregate nested logit model

	Treatment (0/1)
Inclusive Value	0.491
	(0.354)
Share of untreated patients b_{it}	-0.162
	(0.079)
Income quintile 2	0.072
	(0.065)
Income quintile 3	0.250
	(0.070)
Income quintile 4	0.319
	(0.072)
Income quintile 5	0.307
	(0.077)
Age 45-49	-0.481
	(0.264)
Age 50-54	-0.608
	(0.237)
Age 55-59	-0.927
	(0.231)
Age 60-64	-0.889
	(0.227)
Age 65-69	-1.312
	(0.238)
Age 70-74	-1.667
	(0.292)
Age 75-79	-2.209
	(0.411)
Age 80-84	-3.436
	(0.658)
Age 85+	-4.512
	(2.264)
Charlson medium	-0.203
	(0.061)
Charlson high	-0.889
	(0.169)
Oncologist	3.674
	(0.282)
Observations	13,118
Log likelihood	-6349.37

The table reports the parameter estimates and standard errors for the upper level of the nested logit model where the choice of whether pursuing treatment or not is modelled. The excluded age is the youngest category, the excluded health status category is the lowest Charlson (most healthy individual), the excluded quintile category of income is the lowest. Standard errors (in brackets) are bootstrapped. The model includes instability, deprivation, dependency, and ethnicity quintiles, rurality, population, percent of immigrants, uneducated and unemployed inhabitants by three-digit zip code, physician's sex, age, specialty (oncologist, radiation oncologist, other), workload, and 111 dummy variables resulting from the interaction of LHIN (administrative health regions) and years of patients' diagnosis. The total number of observations is 13,118.

Misspecified reference group As a robustness check, we estimate the model in equation (1) using the choices of other patients from a randomly assigned zip code. We find that, as expected, the impact of those patients is irrelevant for the choice of pursuing treatment: the mean of the parameter α is -0.008 and the standard deviation, as estimated from 100 random permutations, is 0.070.

The role of physicians Our results confirm our hypothesis that stigma associated to lung cancer can act as a barrier to access treatment. An alternative or additional explanation of our finding is that the variable b_{it} does not merely capture the patient's reluctance to get treatment attributable to social stigma, but also the physician's attitude toward lung cancer treatment. Spatial correlation in choices would arise as patients that live nearby are treated by the same doctors, who share a certain preference for different types of treatment (including no treatment at all). Unfortunately, due to the large number of doctors in our sample, some of whom with few patients associated to them, we cannot use physician fixed effects to control for this. We use instead all the available physician-level information in our data and control for physician's sex, age, specialty, and annual workload as predictors of treatment and treatment type. To further distinguish between patients' and physicians' attitude towards treatment, we re-run the analysis on a subsample of the patients for whom we observe their performance status (PS). This variable is an index summarizing a patient's level of functioning in terms of their ability to care for themselves, daily activity, and physical ability (walking, working, etc.).[15] Observing the PS and treatment decision for each patient would allow us to separately identify a patient's reluctance to receive treatment (a consequence of stigma) and a doctor's reluctance to treat: a low PS (high ability to tolerate therapy) assigned to a patient that is never treated would suggest an intention to treat by the physician and likely a refusal of pursuing treatment by the patient. Unfortunately, the index is reported for only a small fraction of the patients in our sample (around 10%), making the inclusion of this variable unfeasible in our main specification. Nevertheless, some patterns in the data confirm our intuition. We restrict our analysis to the sample of 1,439 lung cancer patients with a non-missing PS either in the days preceding the start of the first treatment (for those who are treated) or right after the diagnosis (for those who do not receive treatment). Out of the 847 untreated patients, only 211 have a PS of 3 or 4, 207 have a PS of 2 and 429 (more

[15] In its Eastern Cooperative Oncology Group (ECOG) scale, the one reported in the ICES data, it ranges from 0 (fully active) to 5 (dead). This index should be assigned by the doctor to the patient upon each visit, to assess their ability to tolerate treatment and choose the most appropriate therapy. For example, as per CCO and ASCO guidelines (Ellis et al. (2016)), patients with PS 0-1 can tolerate aggressive and more toxic treatment, while those with PS 2 or above should be offered less aggressive options (single agents or targeted therapy in lieu of platinum doublets).

than half) have a PS of 0 or 1, and are hence good candidates for treatment despite never receiving any. We run the same linear regression of individual treatment reported in Table 3 on this sample, including the PS as an additional control. Table 6 reports that, as expected, the PS is a strong predictor of treatment; its inclusion does not reduce the effect of b_{it}, but makes it even stronger. We experiment with various definitions of weights to account for the representativeness of this subsample vis à vis the lung cancer patient population in our data: our results are robust to those alternative specifications. We repeat the analysis for the sample of colorectal cancer patients. We find, again, that performance status is a predictor of treatment, but the coefficient on stigma barrier b_{it} is unchanged by its inclusion and still practically zero. These results reassure us that the effect of the lagged share of untreated neighbors on treatment is indeed capturing social stigma and is not severely affected by the physician's attitude towards treatment.

Table 6: Linear Probability Model of Treatment including Performance Status

	Treatment (0/1)
Share of untreated patients b_{it}	-0.070
	(0.041)
Performance status	-0.075
(ECOG)	(0.011)
Cancer characteristics	Yes
Patient health status	Yes
Patient socio-demographics	Yes
Zip-code controls	Yes
Physician controls	Yes
LHIN by year	Yes
Observations	1,428
R-squared	0.390

The table reports the parameter estimates and standard errors for a linear probability modelling patient's access to treatment estimated on a subsample of patients for which the performance status index is available. Standard errors (in brackets) are clustered at zip code level. Calibration weights by raking are based on the following variables: sex, income quintile, age group, Charlson index, adenocarcinoma, surgery dummy, and distance to the cancer centre. The total number of observations is 1,428.

6 Removing stigma

We now consider what would happen to lung cancer treatment rate, and in particular to the adoption of innovative therapies, if the stigma barrier could be removed. Intuitively, absent

social stigma, treatment rates increase, with an additional 215 patients (4% increase) as a whole and 35 patients accessing innovative treatment, as reported in Table 7. The majority (133) of the additional patients come from unstable areas (above median instability), compared to 82 from stable areas (instability below median).

We use information on (i) median survival by treatment type; (ii) regimen prices, including the price of the drug (per tablet for orals and per mg. for intravenous) and accessory costs[16]; (iii) average dose and frequency of administration to calculate the average treatment cost for each patient and the total amount of extra spending that is required to treat the counterfactual patients by regimen type. Those average costs by regimen are reported in Table B.8 Appendix B and align with estimates from the literature (de Oliveira et al. (2013)) and pCODR, the Canadian review board for the approval of oncological drugs. Following a cost-effectiveness approach that typically guides policy decisions when evaluating a given therapy, we compare these treatment costs with the incremental quality-adjusted life year (QALY). Abating stigma would imply an additional overall cost of CAD 1.13 million (USD 900,000) for innovative treatment, which is much higher than the increase in costs attributable to the incremental patients treated under the standard of care. However, the gain in survival is also higher, which clearly justifies the use of innovative therapies with respect to the "no treatment" current scenario: the additional annual cost amounts to CAD 25,000 (USD 20,000) per patient, which is much lower than the gain of CAD 65,000 (USD 50,000) per year of quality life, which has been the de facto standard used by the Canadian medicine agency to determine whether to cover drugs or medical procedures.

If we treat those incremental patients using standard of care, for example under the most optimistic regimen type in term of survival, CISP, we would obtain a cost saving equal to CAD 24,000 per patient, but a loss in terms of survival equal to 102 days, or CAD 18,164 QALY. Costs-benefits are more or less aligned in this scenario, with benefits from the use of innovative therapy becoming even clearer when comparing it to other types of standard of care with lower survival. In addition, when comparing cisplatin-based regimens to innovative therapy, we need to remember that cisplatin-based therapy tends to be quite aggressive: it can be administered only to healthy patients, it implies a lower quality of life and a more frequent use of urgent care facilities. Our data show that patients under a cisplatin-based therapy are 30% to 50% more likely to use urgent and emergency care with respect to patients under a targeted therapy, resulting in additional costs for the health system. Keeping these

[16] Those costs include, for each regimen: the number of chemotherapy suite visits, the number of ambulatory clinic visits during treatment; nursing and pharmacy workload time to prepare and administer the specific regimen; drugs not included in the New Drug Funding Program and supportive drugs; manager and clerical time for managing and scheduling in the cancer centre; other supplies and costs, including medical/surgical supplies.

considerations in mind, it is clear that removing social stigma stimulates the adoption of innovative treatment which would be cost-effective while benefitting patients.

Table 7: The effect of removing stigma

	Untreated	CISP	CRBP	SINGLE	Targeted
Number of patients - Base	7935	1690	2086	567	840
Number of patients - Counterfactual	7720	1754	2165	604	875
Δ number of patients	-215	64	79	37	35
Median survival (days)	81	366	294	264	468
Avg cost per patient ($ thousand)	n/a	7.73	8.07	4.78	32.33
Δ cost ($ million)	n/a	0.49	0.64	0.18	1.13

The table reports the change in number of patients and related costs implied by the removal of stigma barrier, based on the parameter estimates reported in Table 5.

7 Conclusion

We develop a model of treatment participation and therapy choice to investigate to which extent social stigma acts as a barrier to access treatment and deters the adoption of innovation in lung cancer. We use administrative data on the population of patients diagnosed with advanced lung cancer in Ontario (Canada) over the last decade and exploit the unique level of geographic detail to incorporate social stigma in a model of patient's utility for pursuing treatment. We think of stigma as a form of endogenous social effect and measure it as the share of patients in the neighborhood who were diagnosed the year before and did not receive treatment. While social stigma is hard to identify empirically, we follow Aizer and Currie (2004) and include a rich set of characteristics at individual and neighborhood level to tackle correlated effects. Finally, we use another cancer type for which stigma is less of a concern, colorectal cancer, as a falsification test to confirm the robustness of our findings. After controlling for individual's socio-demographic, health, and neighborhood attributes, we find that a patient affected by lung cancer is less likely to pursue treatment if a higher share of recent patients in the same neighborhood is left untreated. Social stigma represents one fifth of the variation in utility attributable to other socio-demographic characteristics that affect treatment participation. Hence, while not the sole barrier to access treatment, it is a substantial one, which should be taken into account by policy makers when designing policies to mitigate disparities in access to care. Removing social stigma would increase treatment rates and result in a 4% increase in the use of innovative therapy, with benefits in survival outweighing the additional treatment costs. Our empirical results inform the policy

debate on considering lung cancer stigma in the development of messaging for anti-tobacco media campaigns and promoting societal understanding of lung cancer.

Our paper is the first to explore the link between stigma and adoption of innovation. Future research on other stigmatized diseases in which scientific knowledge has produced important therapeutic advances, such as mental illnesses and HIV, will be helpful to understand to which extent social stigma hinders the diffusion of those innovations and, in turn, discourage further investments in R&D.

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A Appendix A: Sample and variable construction

ALR Merging datasets

Retrieved missing information in ALR

Matching patient - physician Matching algorithm patient-physician

Checks on the algorithm

B Appendix B: Additional Figures and Tables

Table B.1: Overview of ICES Databases

Dataset	Data and variables
Ontario Cancer Registry	Diagnoses date, stage, tumor histology
Registered Person Database	Birth/death dates, residence, income
New Drug Funding Program	List of specific, expensive intravenous drugs
Activity Level Reporting	Reporting of systemic therapy services (date and specific regimens) and radiation
Ontario Health Insurance Plan	Billing and reporting of all physician services, diagnostic tests and visits
Ontario Drug Benefit	Oral systemic therapy drugs covered by the
Discharge Abstract Database	Inpatient admissions to hospital cancer-related surgeries and other admissions
National Ambulatory Care Reporting	ER/Urgent Care Centre visits
ICES Physician Database	Physician characteristics (age, sex, tenure)

The table reports the list of databases and the main variables contained in those databases available through the Institute for Clinical Evaluative Sciences.

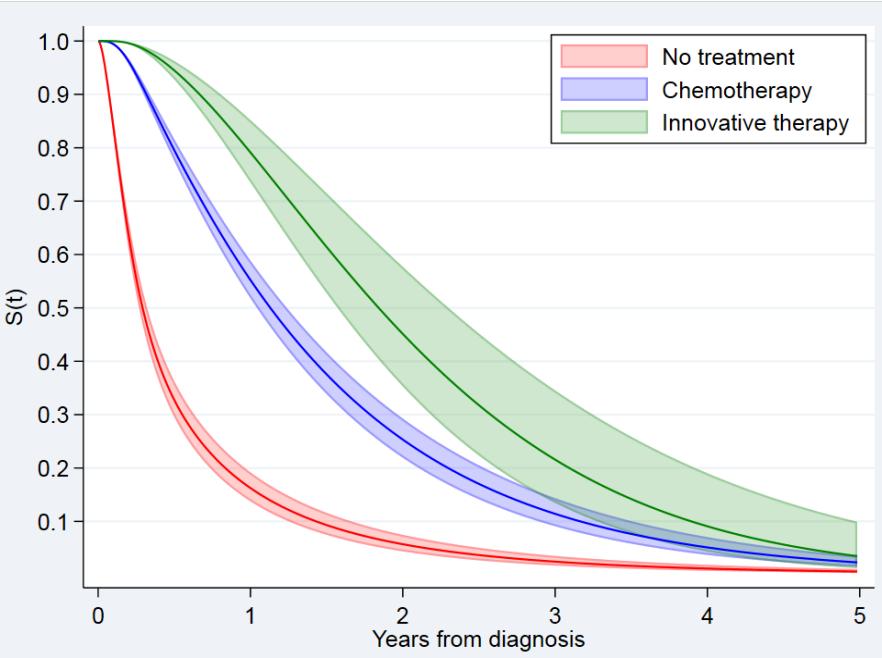
Table B.2: Overview of Regimens

Standard of care	Regimen Group	Regimen	Drugs
	CISP	CISPDOCE	docetaxel; cisplatin
		CISPETOP	etoposide; cisplatin
		CISPGEMC	gemcitabine ; cisplatin
		CISPPEME	pemetrexed; cisplatin
		CISPVINO	vinorelbine; cisplatin
		CISPVNBL	vinblastine; cisplatin
	CRBP	CRBPDOCE	docetaxel; carboplatin
		CRBPETOP	etoposide; carboplatin
		CRBPGEMC	gemcitabine ; carboplatin
		CRBPPACL	paclitaxel; carboplatin
		CRBPPEME	pemetrexed; carboplatin
		CRBPVINO	vinorelbine; carboplatin
		CRBVNBL	vinblastine; carboplatin
	SINGLE	DOCE	docetaxel
		GEMC	gemcitabine
		PEME	pemetrexed
		VINO	vinorelbine
Innovative	TARGETED	AFAT	afatinib
		GEFI	gefitinib
		ERLO	erlotinib
		CRIZ	crizotinib

The table reports the list of regimens approved for first-line treatment of stage IV lung cancer classified as standard of care (chemotherapy) and innovative (targeted therapy).

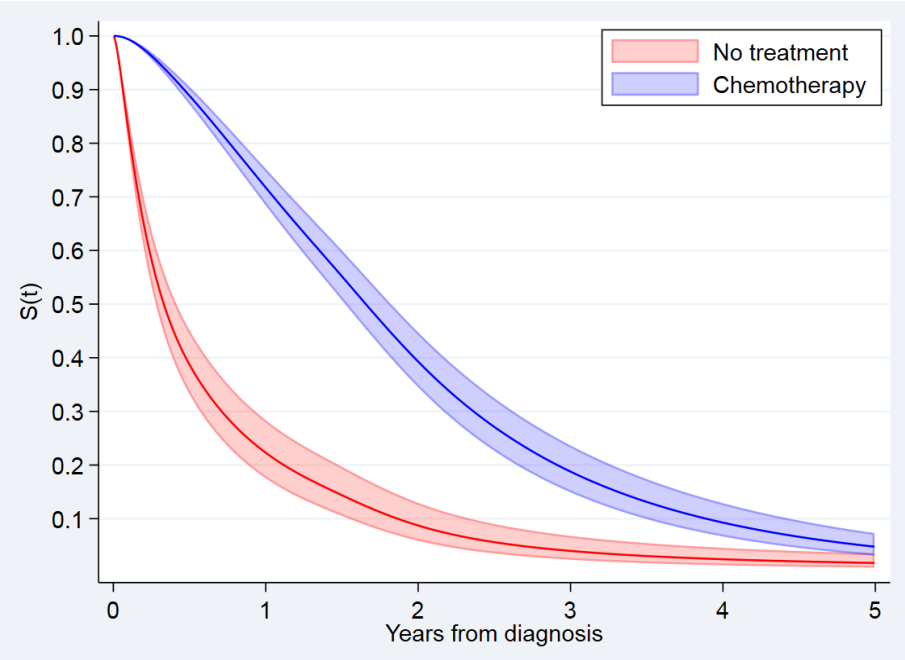
B.1 Survival Analysis

Figure 1: Survival Curves by Treatment Type - Lung



Adjusted Kaplan–Meier survival curves based on the treatment classification we use in our work: no treatment, chemotherapy (standard of care), and innovative therapy. This graph is the based on the estimates of a flexible parametric survival model which includes sex, age group, treatment modality, histology of tumor, Charlson index, surgery dummy, the use of palliative radiology, and year of diagnosis. On the basis of Danesh et al. (2019), the model also includes interaction terms between age group and histology, treatment modality and year of diagnosis. In addition, age group, treatment modality, and year of diagnosis are included as time-dependent variables. The curves all refer to an hypothetical female patient, receiving palliative radiotherapy, no surgery, histology adenocarcinoma, age between 65-69, low Charlson index (healthy), diagnosed in year 2012 and treated at Toronto Central, treated according to the three treatment modes.

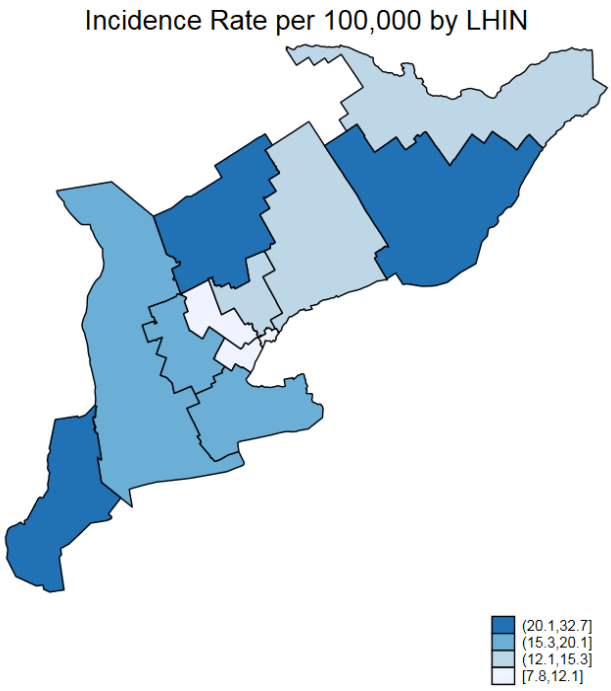
Figure 2: Survival Curves by Treatment/No treatment - Colon



Adjusted Kaplan–Meier survival curves for colorectal cancer patients based on whether they are treated or not. This graph is the based on the estimates of a flexible parametric survival model which includes sex, age group, treatment modality, histology of tumor, Charlson index, surgery dummy, the use of palliative radiology, and year of diagnosis. On the basis of Danesh et al. (2019), the model also includes interaction terms between age group and histology, treatment modality and year of diagnosis. In addition, age group, treatment modality, and year of diagnosis are included as time-dependent variables. The curves all refer to an hypothetical female patient, receiving palliative radiotherapy, no surgery, histology adenocarcinoma, age between 65-69, low Charlson index (healthy), diagnosed in year 2012 at Toronto Central.

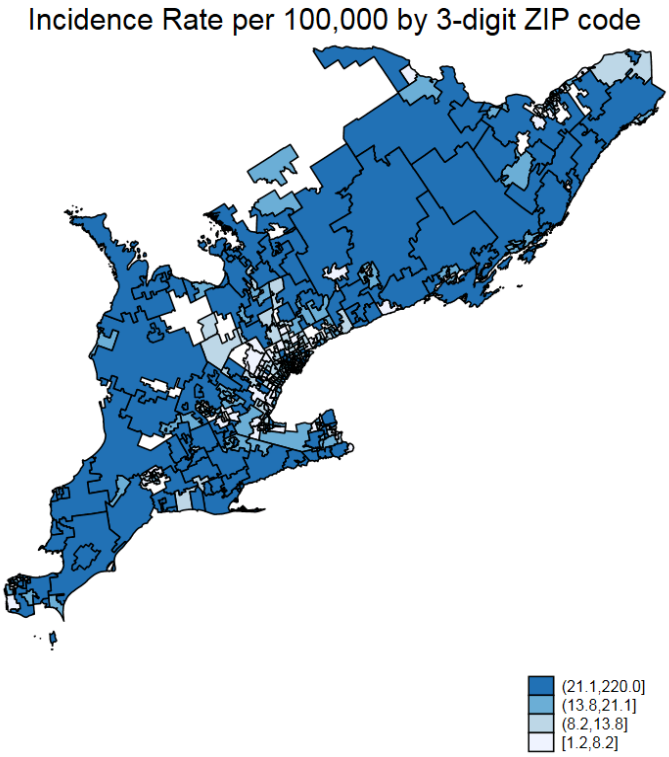
B.2 Incidence and treatment rates

Figure 3: Incidence of Lung Cancer - LHIN



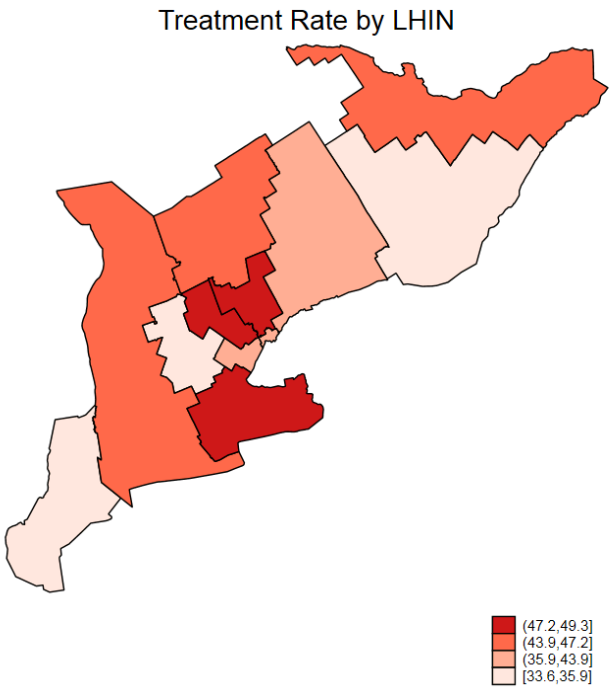
Number of Lung Cancer Patients per 100,000 inhabitants at Local Health Integration Network Area.
Source: authors' calculations from 2014 ICES data.

Figure 4: Incidence of Lung Cancer - ZIP code



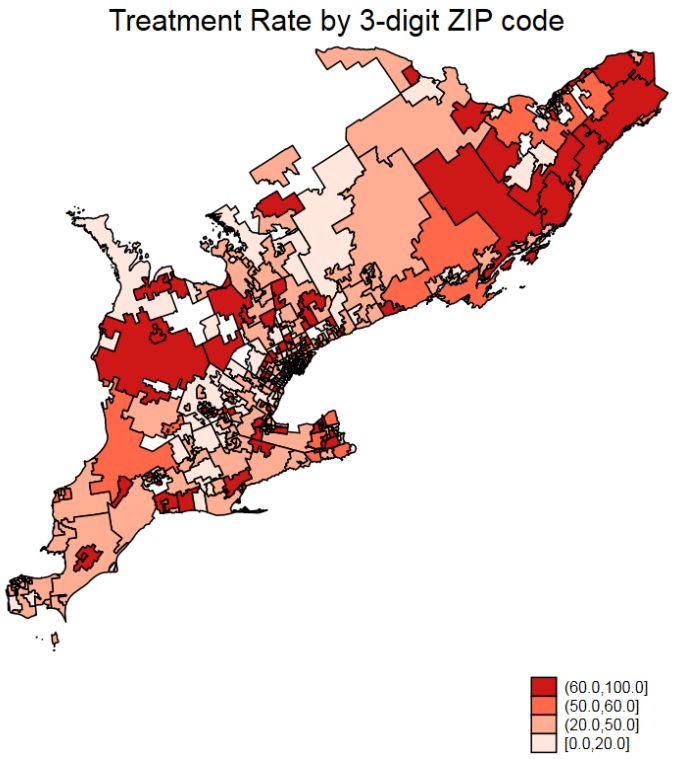
Number of Lung Cancer Patients per 100,000 inhabitants at three-digit ZIP code. Source: authors' calculations from 2014 ICES data.

Figure 5: Treatment Rate of Lung Cancer - LHIN



Treatment Rate of Lung Cancer Patients at Local Health Integration Network Area. Source: authors' calculations from 2014 ICES data.

Figure 6: Treatment Rate of Lung Cancer - LHIN



Treatment Rate of Lung Cancer Patients at three-digit ZIP code. Source: authors' calculations from 2014 ICES data.

B.3 Physician-Patient matching

Table B.3: Preference variation for observable patient characteristics across physicians

Variables	Gender	Charlson index	Adeno carcinoma	Multiple cancers	Income quintile	Age
F-test	1.278	0.877	1.701	1.194	1.429	6.203
Prob > F	0.191	0.608	0.0320	0.256	0.106	0.000
Year controls	Yes	Yes	Yes	Yes	Yes	Yes
Hospital area controls	Yes	Yes	Yes	Yes	Yes	Yes
Observations	8,295	8,295	8,295	8,295	8,268	7,922
R-squared	0.027	0.030	0.038	0.029	0.069	0.177

The table reports the results of the F-test on physician fixed effects after regressing a set of observed patients' characteristics (share of females, Charlson index, share of patients with adenocarcinoma, share of patients by income quintile) on individual physician fixed effects controlling for diagnosis year and cancer care centre.

B.4 Colorectal Cancer

Table B.4: Sample Summary Statistics: Colorectal Patients

	Cohort	Treatment type		$p-value$
		untreated	treated	untreated=treated
		Patient demographics		
Male (%)	0.56	0.52	0.59	0.000
Age	52.28	58.42	48.80	0.000
Charlson index	0.40	0.62	0.27	0.000
		Cancer characteristics		
Adenocarcinoma	0.91	0.91	0.91	0.502
Mucinous	0.07	0.07	0.07	0.853
Signet ring cell	0.02	0.02	0.02	0.206
Multiple cancers	0.05	0.03	0.07	0.000
1-year survival probability	0.49	0.20	0.66	0.000
		Health care utilization		
Surgery	0.57	0.45	0.65	0.000
Palliative radiotherapy	0.26	0.14	0.33	0.000
Treated by oncologist	0.81	0.53	0.98	0.000
		3-digit zipcode characteristics		
Rural	0.13	0.13	0.14	0.153
Distance hospital (km)	30.66	28.61	31.89	0.000
Income quintile	2.98	2.86	3.06	0.000
% immigrant population	0.26	0.26	0.26	0.008
% population no education	0.18	0.18	0.18	0.532
Unemployment rate	8.12	8.26	8.04	0.000
Marginalization index (quintile):				
1. instability	3.04	3.19	2.95	0.000
2. deprivation	3.22	3.32	3.16	0.000
3. dependency	3.17	3.24	3.13	0.000
4. ethnic concentration	2.98	3.03	2.95	0.023

The table reports summary statistics of the main variables in our sample related to patients for colorectal patients. The first column includes demographics, tumor attributes, health care utilization measures, and a set of characteristics related to the three-digit zip code of the patient's residence for the whole sample. Column 2-3 compare those characteristics between (i) untreated patients; (ii) treated patients. Columns 4-5 report the results of a Wilcoxon test on the equality of distribution of the variables for each subsample.

Table B.5: Sample Summary Statistics: Physicians of Colorectal Patients

	Cohort	Treatment type		$p-value$
		untreated	treated	untreated=treated
		Physician demographics		
Male	0.66	0.72	0.63	0.000
Age	48.78	51.10	47.40	0.000
Tenure (# years)	14.53	16.39	13.58	0.000
		Specialty		
Oncologist	0.81	0.53	0.98	0.000
Radiation oncologist	0.04	0.09	0.01	0.000
Other	0.06	0.16	0.01	0.000
Family doctor	0.08	0.22	0.00	0.000
		Workload		
Colorectal cancer patients/year	6.05	3.85	7.37	0.000
Colorectal cancer patients (full period)	38.38	21.66	48.40	0.000

The table reports summary statistics of the main variables in our sample related to physicians treating colorectal patient. The first set of columns include demographics, specialty, where "other" refers to surgeons and gastroenterologists. Column 2-3 compares those characteristics between (i) untreated patients; (ii) treated patients. Columns 4 report the results of a Wilcoxon test on the equality of distribution of the variables for each subsample.

B.5 Aizer and Currie test

Table B.6: The effect of social stigma on accessing treatment - Lung

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
	Treatment (0/1)				Treatment (0/1)			
	Reference group: 3-digit ZIP				Reference group: 3-digit ZIP & income			
$treat\_own_{ait-1}$	0.049	0.029	0.047	0.030	0.043	0.029	0.041	0.028
	(0.013)	(0.014)	(0.015)	(0.015)	(0.013)	(0.012)	(0.012)	(0.012)
$treat\_other_{ait-1}$			0.016	-0.020			0.012	0.004
			(0.031)	(0.028)			(0.014)	(0.012)
Patient controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Zip code controls	No	Yes	No	Yes	No	Yes	No	Yes
Observations	13,162	13,162	13,162	13,162	13,162	13,162	13,162	13,162
R-squared	0.28	0.30	0.28	0.30	0.28	0.30	0.28	0.30

The table reports the parameter estimates and standard errors for specification 3 using the sample of lung cancer patients. Standard errors (in brackets) are clustered at zip code level. All these specifications are weighted by the total number of patients in each year/FSA combination. The total number of observations is 13,162.

Table B.7: The effect of social stigma on accessing treatment - Colorectal

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
	Treatment (0/1)				Treatment (0/1)			
	Reference group: 3-digit ZIP				Reference group: 3-digit ZIP & income			
$treat\_own_{ait-1}$	0.025	0.008	0.019	0.015	0.024	0.010	0.021	0.010
	(0.013)	(0.012)	(0.014)	(0.011)	(0.011)	(0.010)	(0.011)	(0.010)
$treat\_other_{ait-1}$			0.022	0.006			0.009	-0.006
			(0.026)	(0.013)			(0.012)	(0.011)
Patient controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Zip code controls	No	Yes	No	Yes	No	Yes	No	Yes
Observations	7,038	7,038	7,038	7,038	7,038	7,038	7,038	7,038
R-squared	0.44	0.45	0.44	0.45	0.44	0.45	0.44	0.46

The table reports the parameter estimates and standard errors for specification 3 using the sample of colorectal cancer patients. Standard errors (in brackets) are clustered at zip code level. All these specifications are weighted by the total number of patients in each year/FSA combination. The total number of observations is 7,038.

B.6 Treatment costs by regimen

Table B.8: Estimated total treatment cost by regimen

Regimen group	Regimen	Total cost per patient
		CAD
CISP	CISPDOCE	3,879
	CISPETOP	14,835
	CISPGEMC	6,939
	CISPPEME	8,709
	CISPVINO	6,076
	CISPVNBL	6,746
CRBP	CRBPDOCE	5,523
	CRBPETOP	10,235
	CRBPGEMC	9,017
	CRBPPACL	5,115
	CRBPPEME	6,620
	CRBPVINO	6,015
	CRBPVNBL	6,079
SINGLE	DOCE	6,049
	GEMC	7,224
	PEME	9,346
	VINO	4,051
Targeted	AFAT	32,934
	CRIZ	52,100
	ERLO	11,357
	GEFI	31,111

The table reports the estimated total treatment cost by regimen/patient accounting for median survival, cost per cycle of treatment and average number of cycles in the lifetime of a patient. Source: authors' calculations on the basis of ICES data.