Social environment as a barrier to treatment and innovation adoption

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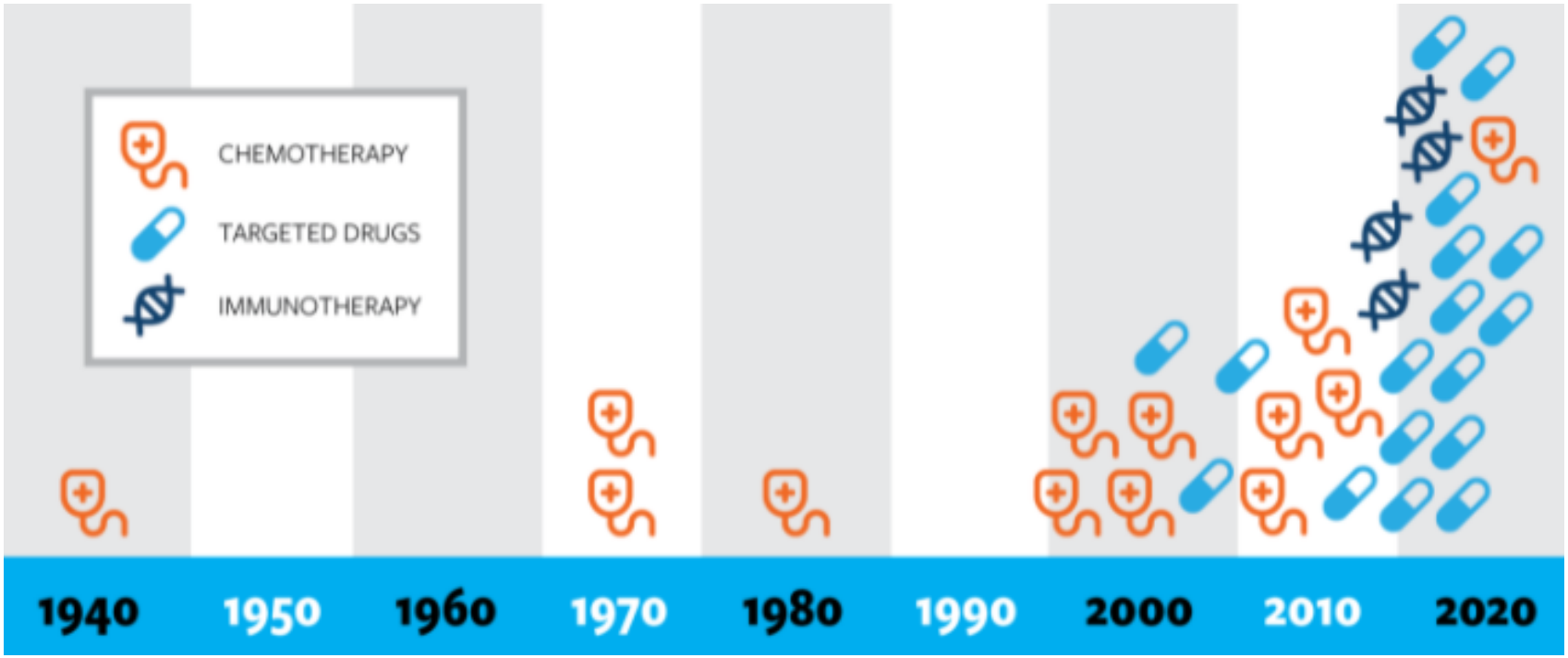
The burden and hope of lung cancer

- Most common and most deadly cancer worldwide
  - 2.1 mln cases, 1.8 mln deaths in 2018
- Lowest 5-year survival among leading cancers (18%)
- Scientific revolution: innovative targeted and immunotherapy drugs
  - health + economic advantages
  - $\uparrow$ survival, $\downarrow$ toxicity, easier administration (oral vs IV)

The therapeutic revolution in lung cancer



History of lung cancer treatment advances: FDA approvals

Low treatment

However, their potential not fully exploited

- Lower treatment rate vis à vis comparable cancer-stage

Stage IV Lung	30%
Stage IV Colorectal	60%
Stage IV Stomach	55%
Stage IV Ovarian	62%

  - if left untreated, similar survival
  - cancer and patient char. only partial explanation (*Sacher et al. 2015*)

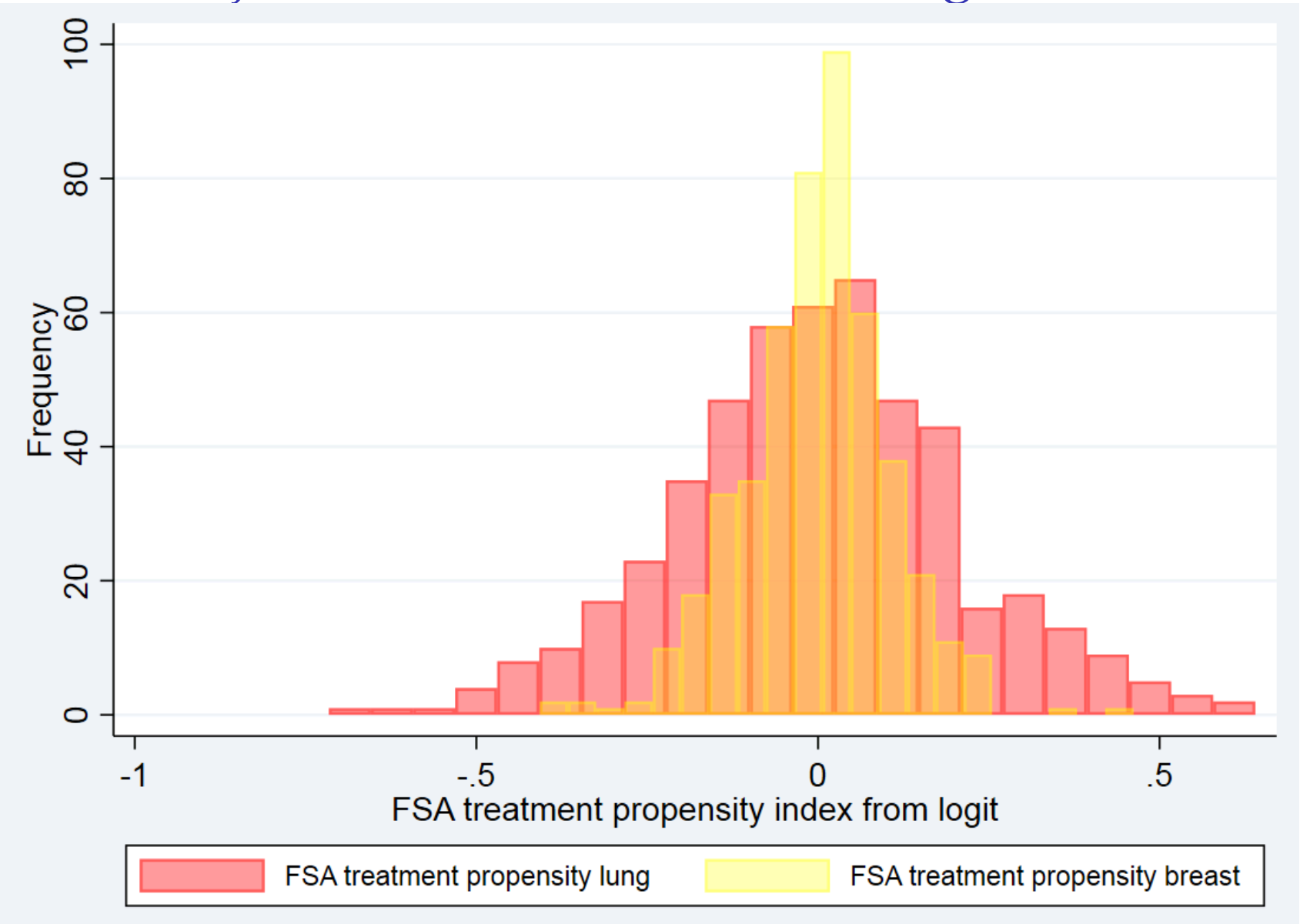
Low R&D spending

- lung: 32% of cancer deaths, 10% cancer research funding
- average spending in R&D per cancer death (*Kamath et al. 2019*):
  - lung: \$ 2,229
  - breast: \$24,442
- higher number of treated patients stimulates R&D spending and innovation (*Dubois et al. 2015*)

Negative Social Environment around Lung Cancer

- Lung cancer = smoker's disease
  - 80-85% patients have history of smoking (incl. passive)
  - 15-20% patients never smoked
  - 35-45% quit before diagnosis
- Social environment: range mechanisms
  - Biased beliefs: hopeless disease
  - Stigma: feeling of shame or guilt linked to having lung cancer: unworthy of treatment
- Specific mechanism has no effect on counterfactual/policy
- 22% of Canadians less sympathy for lung cancer than other tumors (*Ipsos MORI 2010*)

FSA risk-adjusted treatment rates: lung vs breast



This paper

Do social factors hinder access to treatment and adoption of innovation?

Data: stage IV lung cancer patients, Ontario 2008-2018

- treatment, health, socio-demo, geographic info

Model: 2-level nested logit

- top: treatment/no treatment
- bottom: specific therapy

Social environment

- Share of untreated patients in the same neighborhood diagnosed in recent years
  - patients same community subject to similar degrees of social discrimination/shared biased beliefs
- Identification:
  - rich set of individual and neighborhood characteristics
  - IV exogenous shifter treatment rate: average (risk-adjusted) treatment propensity of physicians treating reference group in previous years
  - placebo tests confirm effectiveness identification strategy
  - account for supply (physicians)

Findings

- Social environment: deterrent to treatment
  - $\uparrow$ 1 pp in share of untreated associated to $\downarrow$ 0.2 pp prob accessing treatment
    - from 90th to 10th prcntle share untreated (72% to 45% untreated): +3 pp prob.treatment
    - from low to high-income quint: +7 pp
    - age group 80-84 to 45-49: +32 pp prob. treatment
  - stronger effect for smokers: smoker stigma
- Role social environment on innovation
  - $\approx$ 2% lower R&D spending for lung cancer (USD 7 mln; NCI funding for lung cancer in 2018: 350mln)
- Complementary evidence: survey
  - elicited stigma positively correlated with proxy in data

Related literature

No explicit link social norms - adoption of innovation

- Medical literature
  - under treatment in lung cancer
  - stigma, low adherence to guidelines (survey)
    Davidoff 2010, Sacher 2015, Chambers et al. 2004; Chambers et al. 2012; Dunn et al. 2016
- Econ literature: Stigma as a social conformity effect
  - use of welfare programs *Bertrand et al. 2000; Stuber et al. 2000*
  - learning and reporting stigmatized diseases *Bharadwaj et al. 2017; Cronin et al. 2020*
- Social networks and their impact
  Manski 1993, 2000; Aizer&Currie 2004; Guiteras et al. 2019
  (sanitation adoption)
- Elasticity of innovation to market size
  Dubois et al. 2015; Acemoglu 2004

Data

ICES (Institute for Clinical Evaluative Science)

- All patients with cancer diagnoses Ontario 2008-2018
- Stage IV non-small cell lung cancer and colorectal cancer
- Patients:
  - age, sex, income quint, education, employment status
  - cancer char, comorbidities, drug and healthcare utilization at diagnosis
- Physicians: age, sex, specialty, experience, workload
- Match patient to main care provider (medical and radio oncologists)

3-digit zip code statistics:

- StatCan: income, employment, immigration, education, rurality, smoking and drinking habits, pollution
- Ontario Marginalization Index: disparity in access to health care (*Matheson & van Ingen, 2016*)

Patients and treatment

- Lung: 17,584 patients
- Restrict sample to address concerns of estimation error:
  - physicians with minimum 5 patients (oncologists)
  - Neighborhoods with minimum 10 patients in previous 3 years
- Colorectal: 9,948 patients
  - untreated: 37% $\rightarrow$ stable over time

Lung cancer patients: health and demo

	Cohort	**Treatment type**		
		untreated	chemo	innov
		Patient demographics		
Male	0.53	0.54	0.53	0.41
Age	70-74	70-74	65-69	65-69
Charlson index	2.17	2.30	2.02	1.87
		Cancer characteristics		
Adenocarcinoma	0.74	0.71	0.77	0.91
Squamous cell carcinoma	0.21	0.24	0.18	0.04
Large cell carcinoma	0.02	0.02	0.02	0.01
Multiple cancers	0.01	0.01	0.02	0.03
1-year survival probability	0.27	0.11	0.45	0.68
		Health care utilization		
Surgery	0.03	0.02	0.04	0.03
Palliative radiotherapy	0.62	0.56	0.73	0.68
Preventive care	0.47	0.42	0.5	0.6
Treated by oncologist	0.74	0.57	0.98	0.98

A linear specification

LPM:

$$y_{it} = \beta_1 \bar{d}_{it} + x_{it}\beta_2 + z_{it}\beta_3 + \eta_{r(i)t} + \eta_{p(i)} + \varepsilon_{it}, \quad (1)$$

- y_{it}: 1/0 decision to pursue treatment
- $\bar{d}_{it}$: share untreated patients same neighborhood diagnosed before i
- x_{it}, z_{it}: individual health and socio-dem charact
- $\eta_{r(i)t}$: contextual effects reference group (neighborhood)
- $\eta_{p(i)}$: physician fixed effect (supply)

Identification

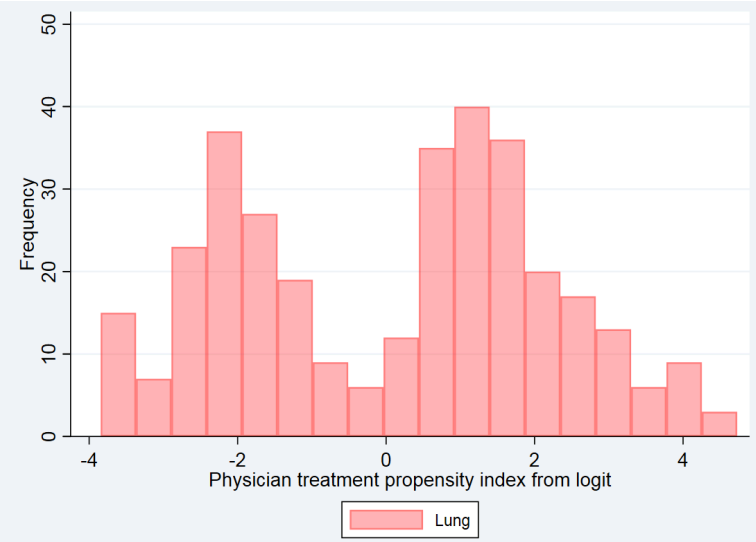
Challenges to identification:

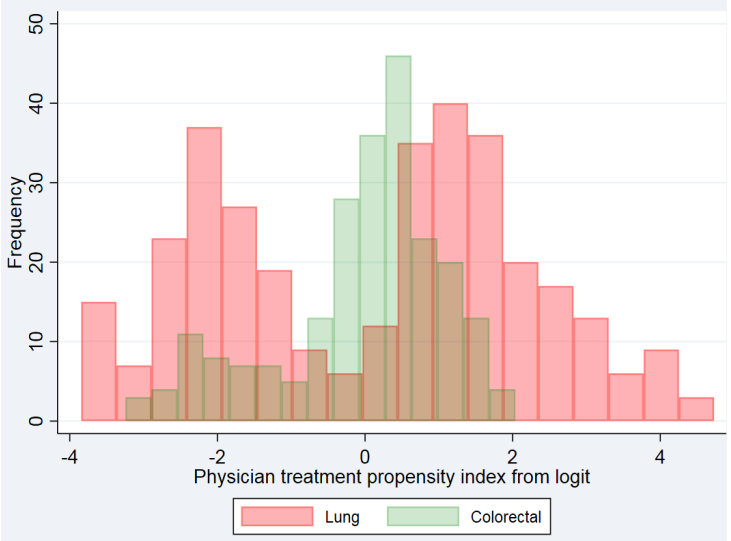
1. Reflection problem: simultaneity: choice of *newly* diagnosed patients influenced by untreated patients from same neighborhood diagnosed *in the past*
2. Correlated effects: same behavior due to shared attributes: IV strategy

IV: strategy

- IV: average treatment propensity of physicians in neighborhood: exogenous shifter of treatment rates (*Angrist 2014*) →
  - no direct referral to physician for patients (quasi-random allocation)
  - specialists work in regional cancer centers: neighbors share same doctor only 7% of the time
  - team decisions or group practices are uncommon
  - patients choose hospital but >70% closest cancer center (no sorting)
- Identification assumption: past treatment propensity of physicians does not influence patient treatment decision (after controlling for patient's own physician)

Variation in physician treatment propensity

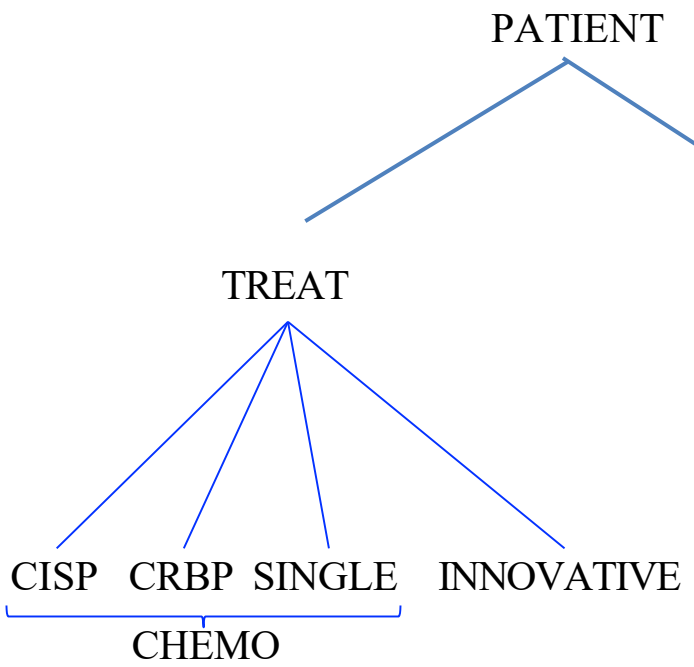




The effect of social environment on treatment

	Baseline			'Shrunk' share untreated		
	(1) OLS	(2) IV	(3) First stage	(4) OLS	(5) IV	(6) First stage
Share untreated	-0.072	-0.167		-0.033	-0.379	
	(0.033)	(0.073)		(0.051)	(0.133)	
Phys treat prop			-0.150			-0.130
			(0.010)			(0.011)
Controls:						
Patient health	Yes	Yes	Yes	Yes	Yes	Yes
Patient socio-demo	Yes	Yes	Yes	Yes	Yes	Yes
3-digit zip code	Yes	Yes	Yes	Yes	Yes	Yes
Fixed effects:						
Physician	Yes	Yes	Yes	Yes	Yes	Yes
Year	Yes	Yes	Yes	Yes	Yes	Yes
Two-digit zip code	Yes	Yes	Yes	Yes	Yes	Yes
Observations	7,882	7,882	7,882	7,882	7,882	7,882
F-statistic			98.27			89.57

Model: 2-level nested logit



- **Social factors (share untreated)**
- Patient's health, tumor & socio-demographic char
- 3-digit ZIP code controls
- 2-digit ZIP FE
- Year + Physician FE

- Patient's health
- Tumor characteristics
- Physician's characteristics

Mitigation of negative social environment

- Move patients to 10th prcntle share untreated (risk-adj): 45% untreated ($\approx$ colon)

	Untreated	Cisplatin	Carboplatin	Single-agent	Innov
Nb. patients - Base	3,630	936	1,396	206	956
Nb. patients - CF	3,487	973	1,462	216	986
Δ patients	-143	37	66	10	30
Estimated cost of treatment					
Estimated survival (dd)	142	522	438	355	682
Avg. cost per patient	-	7,364	5,562	3,211	42,835
Δ cost (100,000$)	-	2.72	3.67	0.32	12.85

Estimated total healthcare spending

- Additional benefits innovative: less frequent hospital visits, lower ER use

	Untreated	Cisp	Carbo	Single	Innov
Inpatient	22,138	25,598	23,116	25,536	25,601
Outpatient	6,820	43,258	34,105	27,310	36,964
Emergency	1,133	2,006	1,938	1,941	1,917
Drugs	1,645	23,394	20,168	11,301	54,499
Long term care	6,473	9,042	8,982	8,486	10,225
Physician	7,554	18,160	15,180	13,757	19,898
Total	45,763	121,459	103,489	88,331	149,104
Estimated survival	142	522	438	355	682

R&D investment and market size

- US public funding data 2004-2018 for 12 cancer sites (NCI)
- Nb patients treated and not (American College of Surgeons)
  - National Cancer Database: 70% of all newly diagnosed patients
  - first course of treatment
- reverse causality innovation $\leftrightarrow$ mkt size
  $\rightarrow$ IV: diagnoses for treated
  - R&D should not affect nb diagnosed patients
  - R&D may affect timing of diagnosis
- Estimates: 10% increase in market size: 3.4 to 5.6% increase R&D spending

Conclusion

- Social environment as barrier to access treatment and deterrent to innovation adoption
- Model: treatment participation and therapy choice
  - social environment as endogenous effect
- Data: population of lung cancer patients in Ontario
- Result: negative social environment substantial barrier to access treatment
  - Mitigation of negative social factors $\uparrow$ treatment, +3% use innovative therapy
  - benefits in survival $>>$ treatment costs
- Future research on other stigmatized diseases
  - does the social environment hinder the diffusion of innovation and discourage further investments in R&D?
  - 2% lower R&D research funding

Test random assignment ←

	Physician treatment propensity
Share heavy smokers	-2.160
	(1.159)
Share heavy drinkers	-0.521
	(0.635)
Pollution (pm 2.5)	6.34e-05
	(0.000260)
Observations	15,761
R-squared	0.097
Year FE	Yes
Joint $p-$value	0.103

p-value from an F-test of joint significance of variables

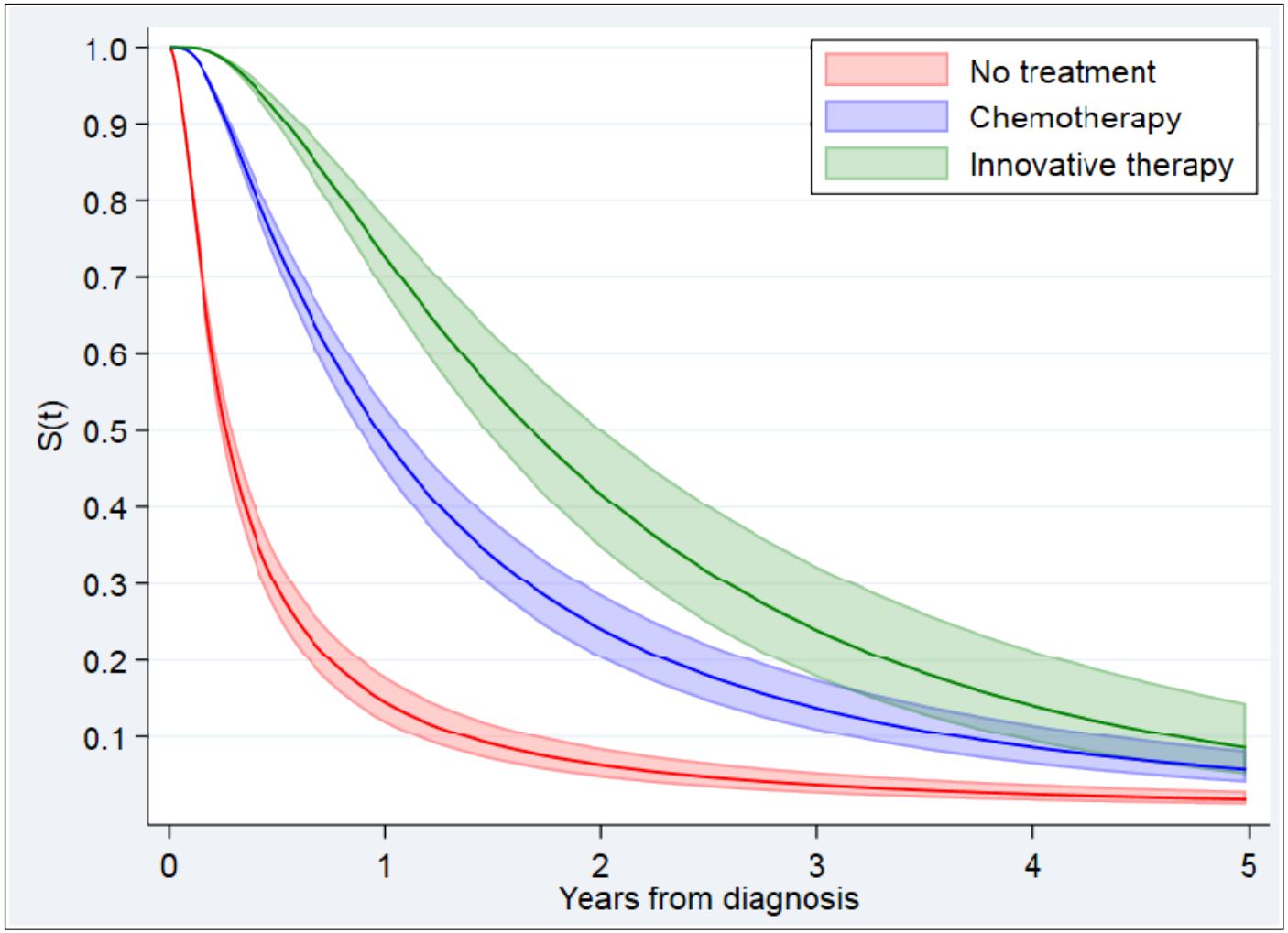
List of regimens

	Regimen Group	Regimen	Drugs
Standard of care	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

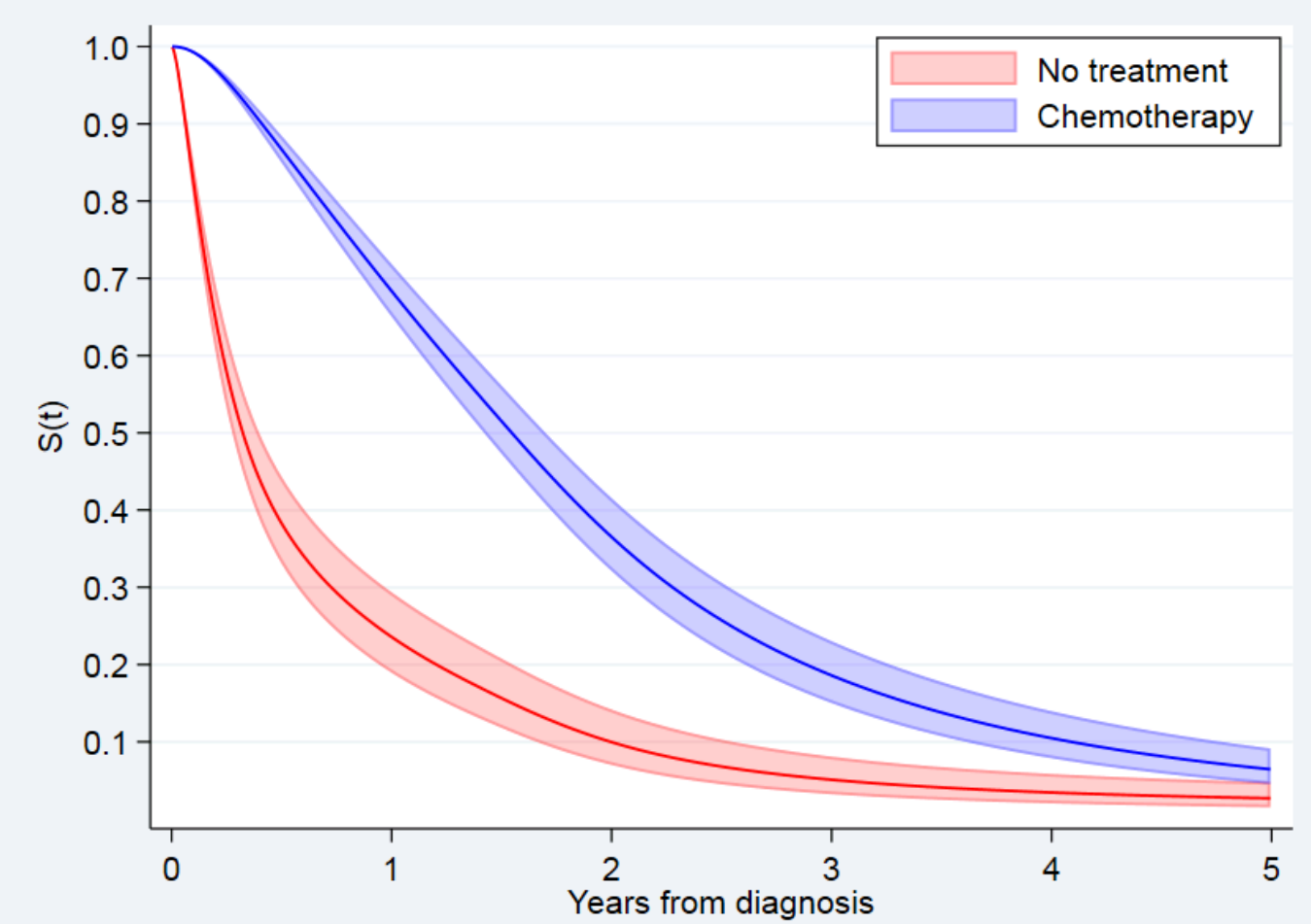
Colorectal cancer patients: health and demo

	Cohort	**Treatment type**	
		untreated	treated
	Patient demographics		
Male	0.56	0.53	0.59
Age	70-74	75-80	65-69
Charlson index	2.11	2.46	1.91
	Cancer characteristics		
Adenocarcinoma	0.91	0.91	0.91
Mucinous adenocarcinoma	0.07	0.07	0.07
Signet-ring carcinoma	0.02	0.02	0.02
Multiple cancers	0.06	0.03	0.08
1-year survival probability	0.52	0.16	0.73
	Health care utilization		
Surgery	0.57	0.44	0.64
Palliative radiotherapy	0.26	0.15	0.32
Preventive care	0.43	0.33	0.47
Treated by oncologist	0.83	0.55	0.99

Survival: lung cancer patients



Survival: colorectal cancer patients



Lung cancer patients: geography

	Cohort	Treatment type		
		untreated	chemo	innov
	3-digit zipcode characteristics			
Rural	0.13	0.13	0.14	0.1
Distance to hospital	31.66	31.55	33.84	24.71
Income quintile	2.81	2.72	2.92	2.97
% immigrant popul	0.26	0.26	0.26	0.32
% popul no educ	0.18	0.18	0.18	0.18
Unemployment rate	8.25	8.29	8.18	8.25
Smoking rate	0.18	0.19	0.18	0.16
% heavy drinkers	0.36	0.37	0.36	0.34
pollution (pm10)	29.49	28.74	33.09	21.66
Marginalization index (quintile):				
1. instability	3.06	3.16	2.97	2.81
2. deprivation	3.28	3.34	3.2	3.23
3. dependency	3.18	3.22	3.17	2.93
4. ethnic concentr.	3.00	2.96	2.94	3.41

Side effects: lung vs. colorectal

	Lung cancer				**Colorectal cancer**	
	chemo		targeted		chemo	
Side effect	frequent	severe	frequent	severe	frequent	severe
Myelosuppression	✓	✓			✓	✓
Neurotoxicity	✓	✓	✓		✓	✓
Nausea, vomiting	✓✓		✓		✓✓	✓
Metabolic disorders	✓		✓		✓✓	
Fatigue	✓✓		✓		✓✓	
Rash, alopecia	✓✓	✓	✓	✓	✓	

Robustness

	(1) Baseline	(2) Controls for metastases	(3) Control for survival past patients
Share untreated	-0.167	-0.163	-0.179
	(0.073)	(0.074)	(0.095)
Controls:			
Patient health	Yes	Yes	Yes
Patient socio-demo	Yes	Yes	Yes
3-digit zip code	Yes	Yes	Yes
Fixes effects:			
Physician	Yes	Yes	Yes
Year	Yes	Yes	Yes
2-digit zip code	Yes	Yes	Yes
Observations	7,882	6,245	7,882

Neighborhood FE and Social Connectness

	(1) 3-digit zip code	(2) High social connectedness	(3) Low social connectedness
Share untreated	-0.193	-0.344	0.160
	(0.078)	(0.105)	(0.132)
Controls:			
Patient health	Yes	Yes	Yes
Patient socio-demo	Yes	Yes	Yes
3-digit zip code	Yes	Yes	Yes
Past patient characteristics	Yes	Yes	Yes
Fixes effects:			
Physician	Yes	Yes	Yes
Year	Yes	Yes	Yes
Three-digit zip code	Yes	Yes	Yes
Observations	7,882	4,710	3,172

Placebo tests: lung vs colon

	(1)	(2)	(3)	(4)
	Lung		Colon	
	OLS	IV	OLS	IV
Share untreated	-0.086	-0.239	0.022	0.346
	(0.043)	(0.088)	(0.081)	(0.246)
Controls:				
Patient health	Yes	Yes	Yes	Yes
Patient socio-demo	Yes	Yes	Yes	Yes
Physician characteristics	Yes	Yes	Yes	Yes
3-digit zip code	Yes	Yes	Yes	Yes
Fixed effects:				
Physician	No	No	No	No
Year	Yes	Yes	Yes	Yes
2-digit zip code	Yes	Yes	Yes	Yes
Hospital	Yes	Yes	Yes	Yes
Observations	7,882	7,882	1,490	1,493

Estimation results: therapy choice

	(1) Carboplatin therapy	(2) Single-agent therapy	(3) Innovative therapy
Adenocarcinoma	0.508	0.0682	0.732
(0/1)	(0.258)	(0.562)	(0.307)
Squamous cell	0.308	0.058	-0.980
(0/1)	(0.274)	(0.591)	(0.354)
Charlson index	0.0982	0.274	-0.158
medium	(0.104)	(0.204)	(0.121)
Charlson index	0.431	0.709	-0.148
high	(0.130)	(0.236)	(0.157)
Controls:			
Patient health	Yes	Yes	Yes
Patient socio-demo	Yes	Yes	Yes
3-digit zip code	No	No	No
Physician characteristics	Yes	Yes	Yes
Fixed effects:			
Physician	No	No	No
Year	Yes	Yes	Yes
Hospital	Yes	Yes	Yes
Observations		14,592	

Estimation results: treatment decision

	Logit
Share untreated	-1.194
	(0.606)
Inclusive value	0.256
	(0.189)
Controls:	
Patient health	Yes
Patient socio-demo	Yes
3-digit zip code	Yes
Past patient characteristics	Yes
Fixed effects:	
Physician	Yes
Year	Yes
FS2	Yes
Observations	7,127

Spending-Survival ratio

	$\frac{\text{Additonal spending}}{\text{Additional suvival}}$
Innovative vs untreated	68,073
Innovative vs Cisp	63,145
Innovative vs Carbo	64,970
Innovative vs Single	64,605

Complementary evidence

- Survey 404 respondents across Ontario (Omnibus survey, Canadian Hub for Applied and Social Research)
- Direct measure of attitude towards lung cancer
  - 21.4% feel less sympathy for lung cancer patients
  - 14.2% feel that treating lung cancer is not worthwhile
  - 13.4% prefer supporting research on other cancer types
- Variation in degree of elicited stigma across zipcodes positively correlated with share untreated in our data (0.52)