



Geographic impact on access to care and survival for non-curative esophagogastric cancer: a population-based study

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Abstract

Background Among patients not undergoing curative-intent therapy for esophagogastric cancer, access to care may vary. We examined the geographic distribution of care delivery and survival and their relationship with distance to cancer centres for non-curative esophagogastric cancer, hypothesising that patients living further from cancer centres have worse outcomes.

Methods We conducted a population-based analysis of adults with non-curative esophagogastric cancer from 2005 to 2017 using linked administrative healthcare datasets in Ontario, Canada. Outcomes were medical oncology consultation, receipt of chemotherapy, and overall survival. Using geographic information system analysis, we mapped locations of cancer centres and outcomes across census divisions. Bivariate choropleth maps identified regional outcome discordances. Multivariable regression models assessed the relationship between distance from patient residence to the nearest cancer centre and outcomes, adjusting for demographic, clinical, and socioeconomic factors.

Results Of 10,228 patients surviving a median 5.1 months (IQR: 2.0–12.0), 68.5% had medical oncology consultation and 32.2% received chemotherapy. Certain distances (reference ≤ 10 km) were associated with lower consultation [relative risk 0.79 (95% CI 0.63–0.97) for ≥ 101 km], chemotherapy receipt [relative risk 0.67 (95% CI 0.53–0.85) for ≥ 101 km], and overall survival [hazard ratio 1.07 (95% CI 1.02–1.13) for 11–50 km, hazard ratio 1.13 (95% CI 1.04–1.23) for 51–100 km].

Conclusion A third of patients did not see medical oncology and most did not receive chemotherapy. Outcomes exhibited high geographic variability. Location of residence influenced outcomes, with inferior outcomes at certain distances > 10 km from cancer centres. These findings are important for designing interventions to reduce access disparities for non-curative esophagogastric cancer care.

Keywords Esophagus · Stomach · Cancer · Outcomes · Geography

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Introduction

Esophagogastric cancers rank among the highest cancers for years of life lost globally [1]. Though cure at early stages is possible via resection or chemoradiation, patients often present with late-stage disease and most are unable to undergo curative-intent treatment [2–4]. Nevertheless, non-curative systemic therapy can improve survival while reducing symptom burden and slowing disease progression [5–10].

It is unknown whether patients are able to consistently access systemic therapy for non-curative esophagogastric cancer should they choose to do so. Geography may play an important role in access to cancer care [11]. Much of the existing literature concerning geography in cancer has focused on surgically treatable cancers [12–17]. Prior work has shown that investigations, treatment, and survival vary with geography for metastatic gastric cancer [18, 19]. Community material deprivation was found to be associated with lower rates of oncology assessment and cancer-directed therapy among patients with non-curative gastrointestinal cancers [20]. For patients with non-curative pancreatic cancer, place of residence in relation to cancer facilities was specifically shown to impact access to care and survival [21]. This potential relationship is important to understand to better care delivery and outcomes but has yet to be explored for non-curative esophagogastric cancer.

To characterise how gaps in care for non-curative esophagogastric cancer may be related to geography, we performed a population-based study investigating the association between distance from cancer facilities and rates of medical oncology consultation, receipt of cancer-directed therapy, and survival. We also sought to describe regional trends in these outcomes. We hypothesised that outcomes vary with geography, and that patients living further from cancer facilities have worse outcomes.

Methods

Study design and setting

We performed a population-based retrospective cohort study using data from linked administrative datasets from ICES (formerly known as the Institute for Clinical Evaluative Sciences) in Ontario, Canada. As of 2016, the province of Ontario had a population of 13,448,494 and a land area of 908,669 km². Ontario's population receives publicly funded universal healthcare through the Ontario Health Insurance Plan (OHIP) as per the Canada Health Act [22]. This study was approved by the Research Ethics Board of Sunnybrook Health Sciences Centre. Results

were reported according to the REporting of studies Conducted using Observational Routinely collected health Data (RECORD) statement [23]. The design of this study was adapted from that of a previous study of pancreatic cancer [21].

Study population and cohort

The study population comprised all patients in Ontario with a valid OHIP number diagnosed with esophagogastric cancer, defined as esophageal or gastric adenocarcinoma or squamous cell carcinoma, who did not receive curative-intent treatment, defined as esophagectomy, gastrectomy, or non-palliative chemoradiation therapy (eTable 1 in the Supplement) [4, 24–28]. Patients with diagnoses from January 1, 2005 to December 31, 2017 were included.

Data sources

Information about data sources is summarised in eTable 2 in the Supplement. Using each patient's unique Identification Key Number, we linked administrative healthcare datasets from ICES. Demographic and vital status data are contained in the Registered Persons Database (RPDB) [29]. Information about all patients in Ontario diagnosed with cancer, excluding non-melanoma skin cancer, is contained in the Ontario Cancer Registry (OCR) [30]. Information about health services provided to patients is contained in the National Ambulatory Care Reporting System (NACRS) and the Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD) and Same Day Surgery (CIHI-SDS) Database [31]. The OHIP Claims Database contains information about provider billing for healthcare services. The Cancer Activity Level Reporting (ALR) database contains information about in-hospital chemotherapy, supportive medication, and radiotherapy.

The Postal Code Conversion File (PCCF) links postal codes to census geographic regions in Canada [32]. One such region is the census division, of which there are 49 in Ontario (eFigure 1 in the Supplement) [33]. Geospatial data pertaining to Ontario's census divisions as of the 2016 census were obtained from Statistics Canada [34]. Centres providing systemic cancer therapy were identified from a list maintained by Cancer Care Ontario [35]. These cancer centres are classified hierarchically into 4 levels based on complexity of care and services provided. Level 1 and Level 2 centres are regional cancer centres, with Level 1 centres maintaining teaching and research responsibilities. Level 3 centres are affiliate sites, and Level 4 centres are satellite sites with no onsite medical oncologists. The point location of each cancer centre with

onsite medical oncology (Levels 1–3) was determined with latitude and longitude using Google Maps 3.35 (Google, Mountainview, CA, USA).

Exposure

The exposure of interest was the straight-line distance from the centroid of each patient's postal code of residence to the nearest Level 1, 2 or 3 cancer centre, which served as a patient-level measure of access to care [36]. Straight-line distance has been used extensively in studies of geographic access to care [14, 15, 21, 37–42]. Distance was categorised as ≤ 10 km, 11–50 km, 51–100 km, and ≥ 101 km based on the distribution of distances across the study population, which demonstrated clustering consistent with residence in communities of varying urbanicity and remoteness. For this reason, as well as to facilitate the clinical applicability of results, the distance variable was categorical rather than linear.

Outcomes

The outcomes of interest were medical oncology consultation, receipt of chemotherapy, and overall survival as previously described [4, 21, 43]. Definitions are detailed in eTable 1 in the Supplement. Medical oncologists were defined as physicians submitting OHIP billing codes for chemotherapy during the study period. Consultations were defined by consultation billing codes from medical oncologists from date of diagnosis to end of follow-up. Receipt of chemotherapy was defined by billing codes for two or more cycles of chemotherapy from date of diagnosis to end of follow-up. Overall survival was defined from date of diagnosis until date of death in the RPDB. The end of follow-up was defined as the earliest of date of death or date of end of study, defined as March 31, 2018, providing the opportunity for a minimum of 3 months of follow-up for all included patients.

Covariates

Covariate definitions and data sources are described in eTable 1 in the Supplement. Age and sex were abstracted from the RPDB. Year of diagnosis was abstracted from the OCR. Material Deprivation Quintile, a subset of the Ontario Marginalization Index (ON-Marg), is an ecologic measure of material socioeconomic status and was assigned to each patient according to postal code [44]. The Elixhauser comorbidity index was used to assign each patient's comorbidity burden, and high comorbidity burden was defined as Elixhauser index ≥ 4 [25, 26].

Statistical analysis

Descriptive analyses described baseline cohort characteristics stratified by category of distance from place of residence to the nearest cancer centre. Continuous variables were reported as median with interquartile range (IQR) and categorical variables as absolute number (n) with proportion (%). Comparison testing was performed by the Kruskal–Wallis and Chi-square tests for continuous and categorical variables, respectively. Risks of medical oncology consultation and receipt of chemotherapy were estimated by Modified Poisson regression with robust error variance and reported as relative risk (RR) with 95% confidence interval (95%CI). Risk of death was estimated by Cox Proportional Hazards regression and was reported as hazard ratio (HR) with 95%CI. RR and HR were reported using the ≤ 10 km distance category as the reference.

Adjusted multivariable regression models assessed the relationship between distance and the outcomes of interest. Models were adjusted for the following covariates, which were identified a priori as potential confounders based on existing literature and clinical relevance: age (categorical), sex, year of diagnosis (2005–2011 vs. 2012–2017), comorbidity burden (dichotomous), and Material Deprivation Quintile [21, 45–48]. Data for Material Deprivation Quintile were missing in 0.9% of the cohort. A complete case analysis approach was used such that cases with missing data were excluded.

Patients were linked to their census divisions of residence using the PCCF. Univariate choropleth maps of the primary outcomes across census divisions were created to visualise geographic trends in outcomes in relation to the locations of cancer centres [37]. Bivariate choropleth maps of pairs of primary outcomes were then created. Whereas a univariate choropleth map displays only one variable, a bivariate approach allows for the visualisation of two variables in a single map by representing each with a distinct colour gradient, whereby the tonally additive result of the overlapping gradients can describe each areal unit's degree of concordance or discordance between the variables [49–51]. All maps were created with the geographic information system (GIS) software QGIS 2.12 (QGIS Geographic Information System, Open Source Geospatial Foundation Project).

A subgroup analysis was performed to assess the relationship between distance to the nearest cancer centre and receipt of chemotherapy among patients who received medical oncology consultation and thereby had realised entry into the cancer care system. To distinguish potential differences in care delivery and outcomes between esophageal and gastric cancer, a sensitivity analysis was then performed in which the relationship between distance and each of the primary outcomes was assessed separately for each cancer.

Table 1 Characteristics of included patients, stratified by distance from place of residence to nearest cancer centre

Characteristics	≤ 10 km <i>n</i> = 6381	11–50 km <i>n</i> = 2764	51–100 km <i>n</i> = 651	≥ 101 km <i>n</i> = 432	All patients <i>n</i> = 10,228	<i>p</i> value
Age (years old)						
≤ 60	1447 (22.7%)	685 (24.8%)	162 (24.9%)	118 (27.3%)	2412 (23.6%)	< .001
61–70	1405 (22.0%)	706 (25.5%)	173 (26.6%)	107 (24.8%)	2391 (23.4%)	
71–80	1674 (26.2%)	744 (26.9%)	171 (26.3%)	131 (30.3%)	2720 (26.6%)	
≥ 81	1855 (29.1%)	629 (22.8%)	145 (22.3%)	76 (17.6%)	2705 (26.4%)	
Female sex	2286 (35.8%)	816 (29.5%)	153 (23.5%)	113 (26.2%)	3368 (32.9%)	< .001
Year of diagnosis						
2005–2011	3269 (51.2%)	1,318 (47.7%)	320 (49.2%)	211 (48.8%)	5118 (50.0%)	0.017
2012–2017	3112 (48.8%)	1,446 (52.3%)	331 (50.8%)	221 (51.2%)	5110 (50.0%)	
High comorbidity burden (Elixhauser index ≥ 4)	796 (12.5%)	347 (12.6%)	90 (13.8%)	52 (12.0%)	1285 (12.6%)	0.778
Material deprivation quintile						
Missing	33 (0.5%)	24 (0.9%)	11 (1.7%)	24 (5.6%)	92 (0.9%)	< .001
1st—least deprived	905 (14.2%)	596 (21.6%)	58 (8.9%)	32 (7.4%)	1591 (15.6%)	
2nd	1069 (16.8%)	647 (23.4%)	113 (17.4%)	67 (15.5%)	1896 (18.5%)	
3rd	1116 (17.5%)	642 (23.2%)	166 (25.5%)	106 (24.5%)	2030 (19.8%)	
4th	1412 (22.1%)	533 (19.3%)	156 (24.0%)	119 (27.5%)	2220 (21.7%)	
5th—most deprived	1846 (28.9%)	322 (11.6%)	147 (22.6%)	84 (19.4%)	2399 (23.5%)	

Statistical significance was defined as $p \leq 0.05$ and all analyses were two sided. All statistical analysis was performed with SAS Enterprise Guide 6.1 (SAS Institute, Cary, NC, USA).

Results

Description of cohort

10,228 patients were included in the study cohort (eFigure 2 in the Supplement). 3623 (35.4%) had esophageal cancer and 6605 (64.6%) had gastric cancer. Demographic and clinical characteristics of the cohort stratified by distance are presented in Table 1. The oldest patients were less likely to live further from cancer centres.

Outcomes

7011 (68.5%) patients consulted medical oncology and 3297 (32.2%) patients received chemotherapy. The most common first-line regimens used were cisplatin monotherapy in 45.6% ($n = 1,503$), 5-FU monotherapy in 29.0% ($n = 957$), and cisplatin combination therapy in 19.5% ($n = 643$). Median survival for the entire cohort was 5.1 months (IQR 2.0–12.0). Median survival was 5.2 months (IQR 2.1–11.0) for patients with esophageal cancer and 5.1 months (IQR 1.9–12.8) for patients with gastric cancer.

Geographic mapping analysis

Univariate choropleth maps exhibit regional variation in medical oncology consultation, receipt of chemotherapy, and survival (eFigures 3–5 in the Supplement). Across census divisions, medical oncology consultation ranged from 45 to 81%, receipt of chemotherapy from 0 to 47%, and median survival from 1.2 to 14.9 months. Cancer centres clustered heavily in the southern part of Ontario and were most concentrated in and around Toronto, the province's largest metropolitan region.

Bivariate choropleth maps exhibit regions of concordance and discordance between outcomes. Census divisions with concordantly high medical oncology consultation and receipt of chemotherapy clustered in the southern metropolitan regions of Ontario, whereas concordantly low oncology consultation and receipt of chemotherapy predominated in northern regions (Fig. 1). Census divisions with high survival, respectively, overlapping high oncology consultation and high receipt of chemotherapy were associated with metropolitan regions, with some distribution in more northern regions (Figs. 2 and 3). Pairs of outcomes had distinct patterns of discordance. The northernmost part of the province exhibited adjacent census divisions with high survival despite low oncology consultation (Fig. 2). Scattered census divisions demonstrated low receipt of chemotherapy despite high oncology consultation and high receipt of chemotherapy despite low oncology consultation (Fig. 1), low survival despite high oncology consultation (Fig. 2), and low survival

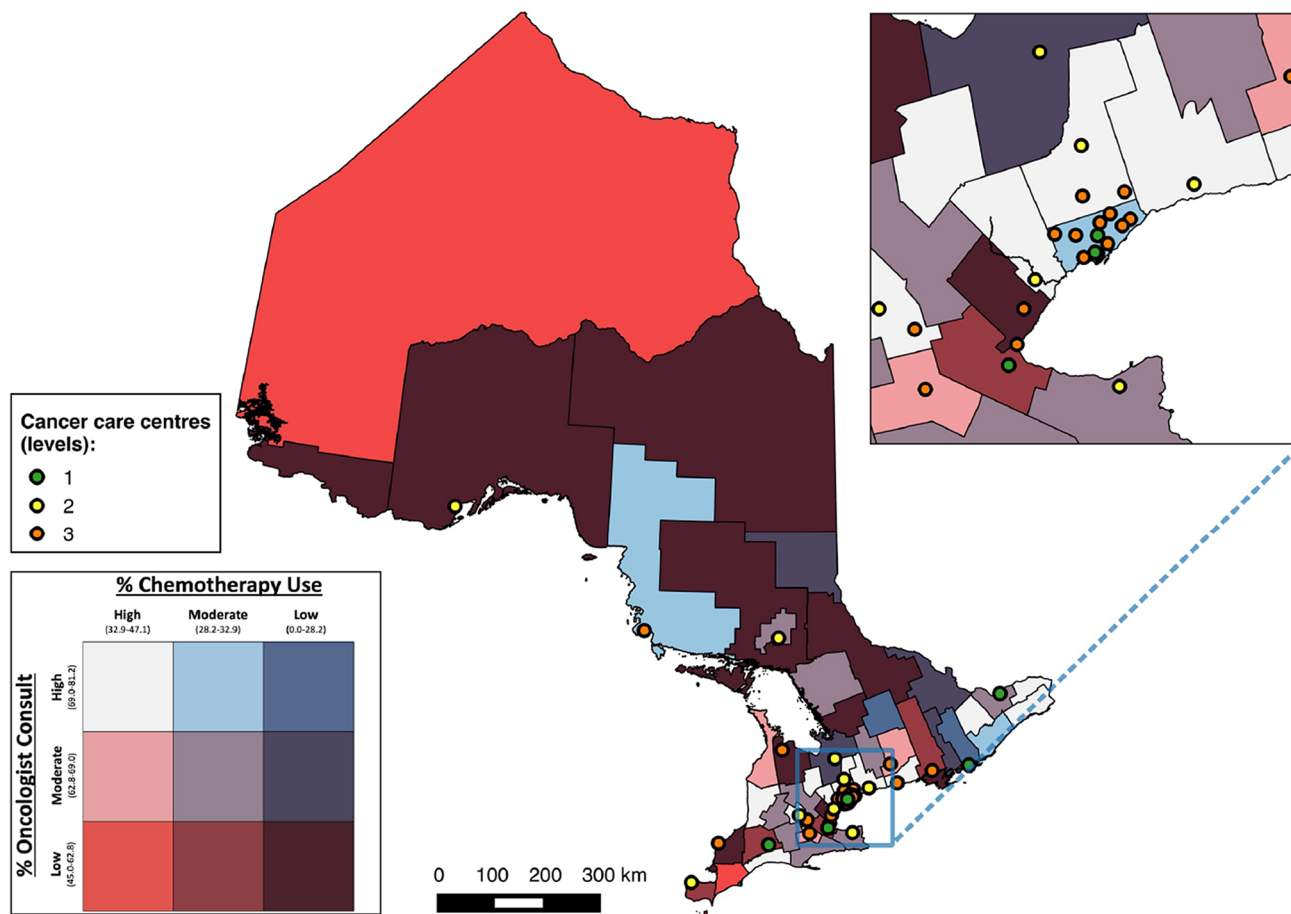


Fig. 1 Bivariate choropleth map of the distribution of medical oncology consultation and receipt of chemotherapy by Census Division in Ontario, Canada. Low, moderate, and high values, respectively, denote the 1st, 2nd, and 3rd tertiles for each variable

despite high receipt of chemotherapy and high survival despite low receipt of chemotherapy (Fig. 3).

Association between distance to nearest cancer centre and outcomes

Adjusted effect estimates of the association between distance from place of residence to the nearest cancer centre and each of oncology consultation, receipt of chemotherapy, and overall survival are presented in Table 2. Compared to patients living ≤ 10 km from the nearest centre, residence ≥ 101 km was significantly associated with lower oncology consultation [RR 0.79 (95% CI 0.63–0.97)] and lower receipt of chemotherapy [RR 0.67 (95% CI 0.53–0.85)]. Residence 11–50 km and 51–100 km from the nearest centre was significantly associated with worse overall survival [HR 1.07 (95% CI 1.02–1.13) and HR 1.13 (95% CI 1.04–1.23), respectively]. Residence ≥ 101 km was not significantly associated with worse overall survival.

In a subgroup analysis of the 7011 patients who consulted medical oncology, distance ≥ 101 km remained significantly

associated with lower receipt of chemotherapy [RR 0.85 (95% CI 0.74–0.97)], albeit with a reduced magnitude (RR 0.85 vs. RR 0.67).

In a sensitivity analysis of distance–outcome relationships for each of esophageal and gastric cancer, trends for each cancer were consistent with those of the combined cohort, albeit with fewer significant associations in the context of fewer patients within each distance category. Results of this sensitivity analysis are summarised in eTable 3 in the Supplement.

Discussion

In this geography-based study, we evaluated the impact of physical location on care delivery and survival for non-curative esophagogastric cancer. Using choropleth maps, we identified high interregional variability in rates of oncology consultation, receipt of chemotherapy, and overall survival, and also identified regional discordances between pairs of outcomes. We additionally demonstrated that patients living

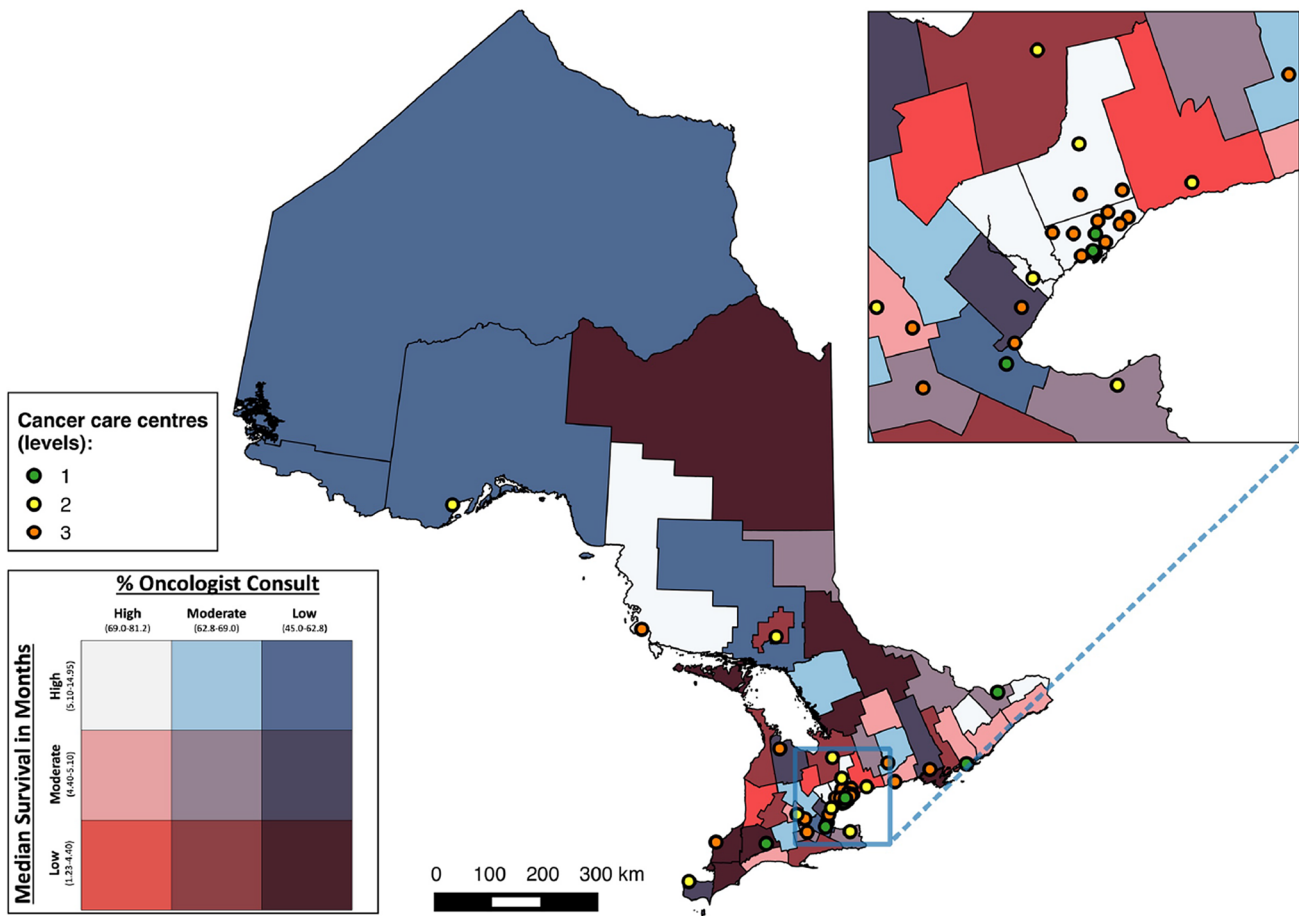


Fig. 2 Bivariate choropleth map of the distribution of medical oncology consultation and median survival by Census Division in Ontario, Canada. Low, moderate, and high values, respectively, denote the 1st, 2nd, and 3rd tertiles for each variable

the furthest from cancer centres have lower rates of oncology consultation and receipt of chemotherapy, and that patients living at moderate distances have worse overall survival.

The present study contributes to an emerging body of geography-based research on non-curative cancers and to our knowledge is the first application of such methods for non-curative esophagogastric cancer [18, 19, 21, 52]. This approach has unique strengths. Combining distance analysis with choropleth mapping reveals patterns of care access at the patient and regional levels, thereby informing both clinical and administrative decision-making to reduce disparities in care and outcomes [21]. A non-curative cancer population is ideal for examining the impact of distance on care delivery in that systemic therapy can be delivered at a single location. Additionally, the setting of this study within a universal healthcare system ensured that insurance status did not confound access to care, thereby providing an ideal context to examine “physical accessibility” as defined by the World Health Organization [53]. Our findings are nevertheless generalisable to other healthcare systems owing to Ontario’s diverse geography of both metropolitan and

remote communities, which was captured by the distance categories used in our analysis. For instance, the distribution of oncology services across rural and urban regions in the United States similarly exhibits high geographic variability [54].

The negative impact of distance on outcomes is consistent with prior research in cancer care [12, 13, 16, 17, 21, 38, 55–57]. Specific trends within this distance–outcome relationship carry important implications for clinicians and policymakers. The reduced impact of distance on receipt of therapy among patients who first received oncology consultation suggests that much of the distance burden lies in entering the cancer care system via oncologist assessment. Similar findings have previously been reported, including by our group for pancreatic cancer [21, 38, 52]. In the present study, this could be due to patients accessing chemotherapy at nearby satellite centres so long as they have first consulted a medical oncologist [21, 35]. That survival was worst at moderate distance (11–100 km) is also consistent with our group’s findings for pancreatic cancer. Although our analysis may have been underpowered to detect a distance–survival

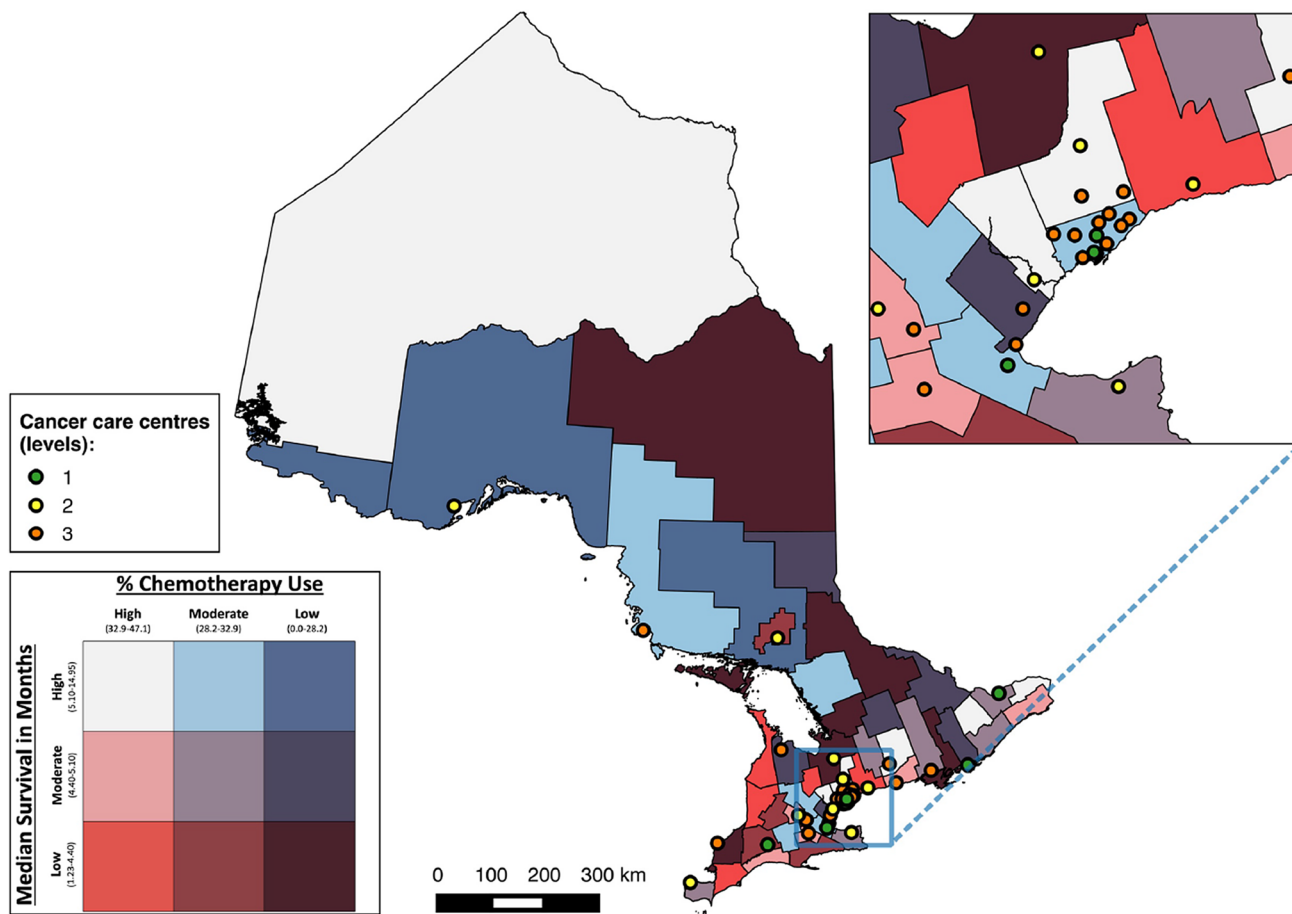


Fig. 3 Bivariate choropleth map of the distribution of receipt of chemotherapy and median survival by Census Division in Ontario, Canada. Low, moderate, and high values, respectively, denote the 1st, 2nd, and 3rd tertiles for each variable

Table 2 Adjusted risk estimates for the association between distance from residence to the nearest cancer centre and outcomes

Distance to nearest cancer centre (km)	Medical oncology consultation		Receipt of chemotherapy		Overall survival	
	Relative risk*	95%CI	Relative risk*	95%CI	Hazard ratio*	95%CI
≤ 10 (Ref)						
11–50	0.97	0.90–1.05	0.97	0.87–1.08	1.07	1.02–1.13
51–100	0.95	0.81–1.12	0.99	0.76–1.29	1.13	1.04–1.23
≥ 101	0.79	0.63–0.97	0.67	0.53–0.85	1.09	0.98–1.21

* Adjusted for age, sex, year of diagnosis, comorbidity burden, and material deprivation quintile

relationship at ≥ 101 km given the small size of this category ($n=432$), this trend could also reflect beneficial social and behavioural factors among the most remote patients as previously described, such as stronger social networks and greater propensity to travel further for more effective treatment [21, 58, 59]. In designing accessible cancer care systems, policymakers should remain cognizant that access to care and survival are sensitive to proximity to cancer centres, and that such opportunities for even modest improvements in survival could hold great importance for patients with non-curative esophagogastric cancer given its poor prognosis [1, 4].

The regional outcome discordances revealed by our mapping analysis suggest unique opportunities for focused investigations. Regions with poor outcomes despite favourable access to consultation and treatment may benefit from evaluation of unaddressed system-level inefficiencies in care delivery, whereas regions with favourable outcomes despite poor access could provide insight into protective community-level programmes not yet adopted by other regions [21]. Such programmes have been described in the United States and could serve to facilitate regional access to the cancer care system through community outreach,

cancer education, and involvement in clinical trials [54]. Outcome disparities seen across the entire jurisdiction under study nevertheless necessitate widespread intervention to improve access to care and survival for non-curative esophagogastric cancer.

We propose three areas that interventions should target. First, equitable access to care should be established across regions. This would require facilitating entry into the cancer care system via medical oncology consultation for the most geographically disadvantaged patients. Established telemedicine infrastructure offers a potential solution [54, 60, 61]. How telemedicine services may be optimised to best serve remote patients with non-curative esophagogastric cancer is therefore an important area for future research. Second, geographic variation in outcomes should be addressed. Provision of care by high-volume providers has long been associated with superior outcomes for cancer surgery [62–64]. More recently, care by high-volume medical oncologists has been associated with superior receipt of chemotherapy and overall survival [4, 65]. In non-curative esophagogastric cancer, high-volume medical oncologists have also been associated with lower healthcare costs [66]. Ensuring widespread geographic access to high-volume medical oncology services is, therefore, an economically viable approach to improving outcomes for this disease. Third, access to high-volume medical oncology care should be established in a way that minimises distance to cancer centres, given the potential for high-volume care to be less geographically accessible [42, 67, 68]. Recent work using GIS analysis has demonstrated that existing cancer centres can be reorganised to provide high-volume care without increasing travel distance for patients undergoing pancreaticoduodenectomy [69]. Applied to non-curative esophagogastric cancer, such an approach could improve care delivery and survival without exacerbating geographic barriers.

This study has some limitations. The datasets we used were not designed specifically for this study, and thus, certain patient characteristics, such as cancer stage, could not be accounted for. Similarly, we were unable to capture care delivery that may have occurred outside of Ontario, though this would be unusual. Although we cannot comment on treatment patterns as they pertain to palliative care or allied health services, we acknowledge the critical role these services play in end-of-life care for the population under study. Inferences drawn from our choropleth maps alone are potentially subject to bias by the modifiable areal unit problem, whereby apparent geographic trends are influenced by the locations of administrative boundaries [70]. Additionally, although our straight-line distance analysis was a simplification of how patients travel for cancer care, no single measure of distance can perfectly capture the multiple modes of transportation and routes of travel that individual patients use.

Conclusion

We identified regional variation in medical oncology consultation, receipt of chemotherapy, and overall survival for patients with non-curative esophagogastric cancer. These outcomes are negatively impacted by increasing distance from patient place of residence to the nearest cancer centre. Much opportunity exists to reduce barriers to care access and improve survival for non-curative esophagogastric cancer, both between individual patients and across geographic space. Future research and policy changes should take aim at improving entry into cancer care systems, improving the availability of high-volume providers, and ensuring that access to optimal assessment and treatment is improved without worsening the burden of distance.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s10120-021-01157-w>.

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Compliance with ethical standards

Conflict of interest Julie Hallet has received speaking honoraria from Ipsen Biopharmaceuticals Canada and Novartis Oncology. Natalie G. Coburn receives salary support from Cancer Care Ontario as the Clinical Lead for Patient Reported Outcomes.

Ethical standards All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. For the conduct of this retrospective population-based study, informed consent was waived by the Research Ethics Board of Sunnybrook Health Sciences Centre.

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