A POPULATION-BASED STUDY OF HEALTHCARE RESOURCE UTILIZATION BY METASTATIC GASTRIC CANCER PATIENTS IN ONTARIO

by

Alyson Lindsay Mahar

A thesis submitted to the Department of Community Health & Epidemiology

In conformity with the requirements for

the degree of Master of Science

Queen's University

Kingston, Ontario, Canada

(August, 2012)

Abstract

Background: Gastric cancer is the fourth most common cancer in the world. Non-curative, metastatic disease is frequent in low incidence countries; management strategies for relief of symptoms include surgery, chemotherapy and radiotherapy. The resource utilization of metastatic gastric cancer patients is unstudied in the Canadian system, and predictors of major cost drivers and end-of-life care unknown. Our purpose was to describe the resource utilization of metastatic gastric cancer patients in Ontario, compare resource utilization among Local Health Integration Networks (LHINs) and examine predictors of inpatient hospital days and receipt of homecare.

Methods: This is a retrospective cohort study of metastatic gastric adenocarcinoma patients registered in the Ontario Cancer Registry between April 1, 2005 and March 31st, 2008. Chart review and administrative healthcare data were linked to describe non-therapeutic endoscopic, radiologic and surgical investigations and treatment strategies from the healthcare system perspective, using a two-year and two month time horizon. Chi square tests were used to compare proportions of resource utilization, and non-parametric one-way ANOVA compared mean per patient usage. Negative binomial regression was used to model the number of inpatient hospital days. Modified Poisson regression was used to model receipt of homecare.

Results: The cohort consisted of 1433 patients with metastatic disease. Less than half of the patients received chemotherapy (43%), gastrectomy (37%) or radiotherapy (28%). Geographic variation existed in the type of health services consumed and in the frequency of their use among LHINs. Location of the primary tumour, resource utilization band, receipt of a gastrectomy and care from a high volume physician were independent predictors of inpatient hospital days. Home care use was predicted by location of the primary tumour, receipt of care from a high volume physician and the number of days survived within the study period.

Conclusion: Variation in healthcare resource utilization exists between LHINs in Ontario for the care of metastatic gastric cancer patients. Whether these differences reflect differential access to

resources, patient preference or physician preference is not known. Further research needs to examine differences and how they impact on clinical disease outcomes. Next steps include incorporating predictors of resource utilization measures into clinical and policy-level decision-making.

Co-Authorship

This thesis was the product of Alyson Mahar in collaboration with her supervisors Dr. Ana P. Johnson, Dr. Natalie G. Coburn and Dr. Raymond Viola. This study was designed by Alyson Mahar, Dr. Johnson, Dr. Coburn and Dr. Viola. Data linkage was performed by Ms. Marlo Whitehead, Institute of Clinical Evaluative Sciences Senior Programmer & Biostatistician. TNM cancer staging and statistical analyses were performed by Alyson Mahar, with insight and guidance provided by Drs. Johnson, Coburn and Viola. This thesis was written by Alyson Mahar with contributions and suggestions from the supervisory committee.

Acknowledgements

Thank you to everyone who answered a question, offered their opinion, provided insight or made me laugh.

Ana, Natalie and Ray- Thank you for your belief that I would one day complete this degree, for your patience and for providing much needed guidance. A special thank you to Natalie for providing me with invaluable mentorship and both supporting me and putting up with me through my journey from Research Assistant to Master of Science.

To my family- I am now the expert, I've definitely read more than two books on it ☺ Thank you for listening to my crazy, reminding me that ice cream isn't the ideal breakfast food and loving me while I ate it anyway.

Table of Contents

List of Figures

List of Tables

Chapter 1

Introduction

1.1 Rationale and Purpose

Gastric cancer is the second leading cause of cancer-related mortality in the world and the costs of treatment rank highly among cancer types. Within the public payer system, the costs of care are generally not the primary focus of providing the clinically appropriate treatment; however, current budget constraints and funding models require a description of the impact of a disease on the healthcare system. Without this knowledge, it is difficult to plan fiscally sustainable care for patients, while maintaining optimal clinical outcomes.

Advanced, non-curative disease represents the largest and potentially most costly proportion of gastric cancer care provided in North America. Little is known about healthcare resource consumption by these patients within the Canadian healthcare system and the independent, potentially modifiable factors that influence the use of health services. This thesis will describe the resource utilization associated with metastatic gastric cancer in Ontario, compare resource utilization across healthcare regions in the province, and investigate the impact of disease, patient, and health system factors on the number of inpatient hospital days and receipt of home care, in a retrospective cohort of metastatic gastric cancer patients.

1.2 Overview of Study Design

A retrospective cohort study was performed to explore the resource utilization of patients with metastatic gastric cancer, investigate regional variation in resource utilization, and identify predictors of two resource utilization measures. All metastatic gastric cancer patients in Ontario with a diagnosis registered to the Ontario Cancer Registry between April 1, 2005 and March 31, 2008 were included. The perspective of the healthcare system was taken, and resource utilization was measured for each patient from two months prior to diagnosis, to two years following diagnosis. This study required the linkage of several administrative healthcare datasets housed at the Institute for Clinical Evaluative Sciences with the results of a province-wide chart review. Measures of resource utilization included physician visits, medical imaging (e.g. computed tomography scans), hospitalizations, oncology treatment modalities (e.g. chemotherapy) and end-of-life care (e.g. home care). Two resource utilization outcomes were studied in detail (inpatient hospital days, receipt of at least one home care visit) given their important contributions to the costs of healthcare.

1.3 Study Objectives

In a population-based, retrospective cohort of metastatic gastric cancer patients in Ontario, the study objectives were to:

1. describe disease, patient, and healthcare system factors and healthcare resource utilization;
2. compare disease, patient, and healthcare system factors and healthcare resource utilization among Local Health Integration Networks; and
3. identify disease, patient, and healthcare system predictors of inpatient hospital days and home care use.

1.4 Thesis Outline

This thesis is divided into five sections, with an additional six appendices. Chapter 2 provides background for the study objectives, including information about the disease of gastric cancer, measuring healthcare resource utilization, and geographic variation in the provision of gastric cancer care, and rationale for choosing the number of inpatient hospital days and home care use as the two outcomes for multivariate predictor analysis. Chapter 3 describes the objectives of the thesis and the methods used to achieve those objectives. Chapter 4 provides the results associated with each objective and Chapter 5 discusses these results in the context of the literature, study limitations, strengths, and contributions.

Chapter 2

Literature Review

2.1 Introduction

The following chapter provides the setting and context for this thesis project. Section 2.2 begins with an introduction to gastric cancer, that includes information on the biology and pathology (2.2.1); incidence (2.2.3); detection and diagnosis (2.2.4); staging (2.2.5); clinical management of gastric cancer in general (2.2.6); non-curative management of metastatic gastric cancer (2.2.7); and prognosis. Background on healthcare resource utilization follows in Section 2.3, which includes an introduction to health economics and measuring resource use (2.3.1); a review of the literature on measuring resource utilization for gastric cancer (2.3.2); and a review of the literature regarding predictors of resource utilization (2.3.3). Section 2.4 briefly describes the Canadian and Ontario healthcare systems. Background on regional variation in resource utilization is presented in Section 2.5, followed by sections on predictors of inpatient hospital days (Section 2.6) and predictors of home care use (Section 2.7). The final section is a summary of the reviewed literature, identifying gaps and providing a rationale for the thesis project (Section 2.8).

2.2 An Overview of Gastric Cancer

2.2.1 Biology and Pathology

Gastric cancer encompasses all malignancies that originate from the anatomical organ, including tumours located at the gastroesophageal junction to the duodenal cap. The current International Classification of Diseases (ICD)-10 system organizes primary tumours of the gastroesophageal junction to just above the duodenal cap as having a primary site in the stomach.[1]

Determining the primary origin of tumours that cross the gastroesophageal junction may be difficult, and tumours of the lower esophagus may erroneously be classified as gastric cancer.

The majority (90-95%) of gastric cancers are adenocarcinomas that originate in the mucous-producing cells in the lining of the stomach wall.[2] In the literature, unless otherwise specified, using the term gastric cancer or carcinoma or gastric cancer refers to adenocarcinoma. Other tumours that originate in the stomach include gastrointestinal stromal tumours (GIST), endocrine tumours (carcinoids), lymphomas, leiomyomas and leiomyosarcomas. GISTs arise from the interstitial cells of Cajal in the nervous tissue in the stomach and make up less than 2% of all gastrointestinal tumours.[3] Gastric carcinoids are rare tumours that grow from endocrine cells and account for 8% of all gastrointestinal malignancies.[4] Lymphomas, leiomyomas and leiomyosarcomas represent 5-10% of gastric cancers; lymphomas originate from beta cells in the tissues of the immune system and leiomyomas/sarcomas, very rarely found in the stomach, develop from muscle cells.[5,6]

All adenocarcinomas do not behave similarly; classification is according to Lauren type: instestinal, diffuse, and mixed type tumours.[7,8] The diffuse type is more aggressive and infiltrative than the intestinal type.[7] Similarly, tumours located at the cardia or proximal section of the stomach, behave differently than tumours located in the distal stomach and are influenced by different risk factors than distal or non-cardia tumours.[2,9,10] Distal tumours are more likely to be associated with a previous *Helicobacter pylori* infection than proximal tumours, which are thought to be influenced by alcohol intake and tobacco use.[2,9,10] Proximal tumours are generally associated with a worse prognosis than distal tumours.

2.2.2 Descriptive Epidemiology

Gastric cancer is the fourth most common cancer worldwide and the second leading cause of cancer-related mortality; however global incidence has been decreasing steadily since the 1930s and has only recently dropped from being the second most common cancer worldwide.[11] Gastric cancer incidence varies geographically (between countries and among provinces), as well as by sex and age.[2,10-13] World data from 2002 estimated the age-adjusted incidence of gastric cancer for men at 22 per 100,000 and for women at 10.3 per 100,000,[11] with two-thirds of all cases occurring in developing countries. Japan has the highest-incidence in the world, reporting 2002 age-adjusted incidence rates of 62.1 in men and 26.1 in women.[11] Overall, gastric cancer is responsible for approximately 700 000 deaths annually world-wide, although with decreasing incidence, this number is expected to decrease as well.[11]

North America is considered a low-incidence continent, and Canada a low-incidence country.[11] The Canadian age-adjusted incidence rate estimate for men and women combined in 2012, was 7 per 100 000, well below the global rates.[14] Gastric cancer cases were expected to represent 2.1% of new cancer cases in men and 1.3% of new cases in women. The estimated number of Canadian deaths due to gastric cancer in 2012 was expected to be 2100, or 4 per 100,000.[14]

Variation in incidence is demonstrated on a smaller scale within Canada.[14] Manitoba (11 per 100,000), Quebec (11 per 100,000), and Newfoundland and Labrador (15 per 100,000) all report higher age-standardized rates for males than the national average (10 per 100,000). Newfoundland and Labrador reports a higher incidence for females (8 per 100,000) than the national average (5 per 100,000). The age-standardized incidence rate for Ontario in 2012 was estimated to be 9 per 100 000 for males and 5 for females.[14]

Mortality also varies inter-provincially,[14] ranging from an age-standardized rate of 5 per 100 000 in Saskatchewan and Prince Edward Island for men to 12 per 100,000 in Newfoundland and Labrador (double the national average). For women, age-standardized mortality rates range from 2 deaths per 100,000 in British Columbia and Saskatchewan, to 7 deaths per 100,000 in Newfoundland and Labrador (more than double the national average).[14]

Men are twice as likely to develop gastric cancer as women and this trend appears to be uniform around the globe.[2,10,11,15] Hypotheses exist to explain this gender effect, as differences in exposure to risk factors are not sufficient to explain such a large difference in risk. One hypothesis is that women benefit from a protective effect of estrogen, which has been explored in animal models, in studies of men who have received hormone replacement therapy and of women who have received hormone therapy that blocks estrogen binding. These studies have not yet definitively explained the protective mechanism of estrogen in gastric cancer, but they do highlight a possible protective role of the hormone.[16]

Incidence and mortality also vary by age. Two-thirds of gastric cancer cases occur after 65 years of age. Canadian data from 2005 reported the incidence rate increasing in males from 26.7 in the 60-64 age group to 128.5 in the 85 and older age group and from 10.4 in women aged 60-64 to 51.3 in the oldest age group.[17] This trend is mirrored across the globe in both low and high incidence countries.

2.2.3 Detection and Diagnosis

Gastric cancer is usually asymptomatic in its early stages and typically not detected until it has advanced, causing symptoms. The doubling time of early stage gastric cancer has been estimated at 16.6 months.[18-20] High incidence countries such as Japan and Korea provide screening programs for high risk populations, often using routine endoscopy.[21,22] The disease is an excellent candidate for screening procedures because of the presence of precursor lesions and the potential for substantial improvement in outcomes when diagnosed early. In North America and other low incidence countries, the number of cases is not large enough to support a cost-effective population-level screening program;[23-25] therefore, gastric cancer is most often detected when patients present with problems such as pain, bleeding, obstruction or malnutrition,[26-28] indicating the disease has reached an advanced, non-curable stage. Abdominal ultrasound or computed tomography (CT scan) is used to investigate general gastrointestinal symptoms, while endoscopy is generally the method used for diagnosis, by directly visualizing and/or biopsying the tumour or suspicious areas of the stomach and adjacent organs, with subsequent pathologic examination. Biopsies may also be taken during laparoscopy, a procedure that involves making a small incision to allow passage of an instrument to view inside the abdomen, and through percutaneous biopsy of the primary tumour or suspected metastases. Diagnosis is also possible from cytology, examining cells taken from esophageal brushings or gastric washings.[26,29] In less than 5% of cases, the gastric cancer may go undetected until the primary tumour perforates the stomach and the diagnosis made during an emergency operation.[30]

2.2.4 Staging

After the diagnosis of gastric adenocarcinoma is made, the cancer is staged most often using the tumour/lymph nodes/metastasis (TNM) staging system, developed by the Union for International Cancer Control/American Joint Committee on Cancer (UICC/AJCC).[31,32] This system describes the depth of penetration of the tumour in the T category, ranging from T0 to T4 with a higher T stage indicating greater tumour depth. Gastric cancer may be confined to the organ or may penetrate the serosa and extend into adjacent organs. The organ invaded depends on the location of the primary tumour, and may include the pancreas, colon, spleen, liver, or esophagus.

Lymph node involvement is described using the N category and ranges from N0 (no nodal involvement) to N3 (involvement of 16 or more regional lymph nodes). Distant metastases are summarized as being absent (M0) or present (M1). The most common site of spread is to the peritoneum (clinically presenting as peritoneal carcinomatosis or with ascites), followed by distant metastases to the liver.[26] Confirmation of the presence or absence of distant metastases and lymph node involvement may be made using a variety of radiologic methods, such as computed tomography (CT) scans of the chest, abdomen and pelvis, plain film x-rays, bone scans, or, less commonly, magnetic resonance imaging (MRI) or positron emission tomography (PET) scans.[33] The National Comprehensive Cancer Network (NCCN) recommends that all patients have a CT scan of the abdomen and pelvis to determine disease spread and all curative-intent patients undergo laparoscopy prior to tumour resection to evaluate for distant metastasis.[26,29]

Advanced, non-curative disease is categorized as stage IV using the 7th Edition of the (UICC/AJCC) staging system and is defined as the presence of metastatic disease.[32] Previous versions of the UICC/AJCC staging manuals included patients with large tumours or extensive nodal disease in the absence of metastases as stage IV; however, this was at odds with the majority of other tumour sites,[31] and the most recent version considers only patients with distant metastases as having stage IV disease.[32] Another classification system used for the staging of gastric cancer was developed by the Japanese Gastric Cancer Association (JGCA).[34] Although the two systems (UICC/AJCC and the JGCA) were divergent in the past, they are now congruent to better facilitate sharing knowledge and research efforts.[32,34]

Data from Surveillance, Epidemiology and End Results in the United States provides evidence that only 25% of tumours of the stomach are diagnosed with disease confined to the primary organ.[35] In Canada, population-based staging for gastric cancer in national or provincial registries does not exist, and data describing the burden of gastric cancer by stage of disease are lacking; however, recent estimates from administrative data in Ontario estimate that 50% of disease is metastatic at diagnosis.[36]

2.2.5 Clinical Management of Gastric Cancer

A number of international professional associations provide recommendations for care, including the NCCN, the European Society for Medical Oncology (ESMO), and the JGCA.[29,34,37] In all cases in which the cancer has not metastasized, surgery is the cornerstone of curative therapy. Complete excision of the tumour with margins free of tumour and microscopic tumour cells (R0), combined with adequate lymphadenectomy (the removal of more than 15 lymph nodes), is necessary to achieve optimal outcomes. This may be performed through a number of surgical procedures, the choice of which depends on the location and size of the tumour. Adjuvant chemoradiotherapy or peri-operative chemotherapy in addition to surgery is associated with an increase in overall survival for curatively resected patients. Both are considered appropriate curative regimens and have become the standard of care.[38,39]

2.2.6 Management of Non-Curative, Metastatic Disease

Patients with metastatic gastric cancer experience symptoms ranging from minor (mild anemia, reflux, poor appetite) to those that significantly impact quality of life (weight loss, early satiety, pain, bloating, severe anemia) to life-threatening problems (bleeding or obstruction).[26,27,40] Accordingly, the management of non-curative disease is driven by symptoms and goals of symptom palliation and improving quality of life.

Non-curative management options for advanced cancer patients include surgery (partial or total gastrectomy, bypass), chemotherapy, radiotherapy, and stent placement.[26,29,34,37,40] Debate surrounding the role of surgery for non-curative management is long-standing in the literature.[41-43] Two randomized controlled trials have been initiated in North America and Asia to address the lack of high quality evidence.[44,45] The aim of these studies is to quantify the risks and benefits of non-curative surgical resection compared to chemotherapy alone. Only one study includes quality of life endpoints in this palliative setting, and neither explicitly documents relief of symptoms as a primary or secondary outcome.[44,45]

Chemotherapy is widely recommended for metastatic disease management, for improved survival and not for alleviation of symptoms.[46] Median survival in a meta-analysis of patients managed with chemotherapy was reported to be 11 months, a significant improvement compared to best supportive care alone (Hazard Ratio: 0.37; 95% confidence interval: 0.24-0.55).[46] Recently, a randomized controlled trial exploring the role of trastuzumab, a molecular targeted therapy for HER2 positive, advanced gastric cancer patients, compared management with trastuzumab and chemotherapy versus chemotherapy alone and concluded a significant survival benefit could be gained with the new targeted therapy agent.[47] This expensive regimen has not yet been approved for reimbursement by Canadian healthcare systems.

Both surgery and chemotherapy are associated with life-threatening adverse events[26,46,48,49] and more invasive surgical procedures are associated with high rates of procedure-related mortality. [48,49] Recently, an international expert panel examining processes of care for gastric cancer agreed that surgery (resection or bypass) was inappropriate for the care of most metastatic cancer patients.[50] Uncertainty remains around the role of surgery for patients with a minimal burden of metastatic disease, and the identification of the optimal candidates to receive best supportive care alone.[50]

2.2.7 Prognosis

Five year survival for gastric cancer in North America is very poor, with median survival for stages III and IV disease reported to be 12 months and 3 months, respectively, in Canada.[51] Recent Ontario data indicates adjusted 5-year survival of 37% for curative intent patients and 3 % for patients with metastatic disease, or who were managed palliatively.[36] The care of metastatic cancer patients is a frequent focus in the literature, and improving the dismal survival prognosis for these patients through the development of new treatments and techniques has been a primary goal. Unfortunately, little progress has been made, and the prognosis for patients presenting with metastatic disease has changed very little in the past several decades, with the exception of a moderate survival gain with intensive chemotherapy.

2.3 Resource Utilization

2.3.1 Introduction to Health Economics and the Measurement of Resource Utilization

Health economics is the study of the optimal allocation of limited resources within the medical and/or healthcare setting, generally aiming to evaluate both the efficiency and effectiveness of a medical treatment, healthcare program or healthcare system.[52] The study of health economics includes the investigation and monetary valuation of resource utilization directly or indirectly related to a medical treatment or procedure, healthcare program or healthcare system for a target population (e.g. individuals with a specific illness, the general population in a given timeframe, individuals susceptible to a specific illness), from a stated evaluation perspective (e.g. patient, healthcare system, societal).[52] The healthcare system perspective is often used to determine the economic burden of an illness, or to compare the cost-effectiveness or cost-utility of a treatment.[53] From the perspective of the healthcare system, resource utilization refers to the health system contacts, investigations and procedures that the system is financially responsible for funding, either as the service provider or service contractor. For example, in Canada these may include physician visits, emergency room admissions, operations, radiologic investigations or operational costs of a hospital or system-funded healthcare facility. Conversely, from a patient perspective, measures of resource utilization may include time off work, travel time and cost for travel to and from doctor and clinic appointments or procedures related to an illness, or the cost of medical supplies not covered by a public or private insurance carrier.[52,53] Studies of healthcare costs go further and assign a monetary value to each measure of resource utilization, describing or comparing the costs of medical procedures, programs or the course of an illness or disease, in a formal economic evaluation.

It is useful to study measures of resource utilization, in addition to the costs of healthcare, because they provide granular information on elements of healthcare use related to the disease or procedure of interest and offer a means of comparing the costs of an illness, treatment or program between healthcare systems or institutions that is not possible with dollar amounts. For example, because the cost of a physician visit may vary among healthcare systems, according to negotiated contracts or standard pay schedules, comparing the costs of care may be less informative than describing the number of visits to a physician. The number of visits is a more accurate measure to compare among systems, as it reflects practice patterns and differences between systems, as well as the burden to the system related to the treatment or disease.

Information on specific measures of resource utilization may be used by healthcare policy decision-makers to forecast use of a service or program, to plan for future resource allocation needs and to help with overall budgeting, rationing and allocation of resources. Resource utilization measures may be used by clinicians to compare the efficacy of treatments or procedures that have similar clinical outcomes and to aid in the decision-making between treatment choices to offer patients. The information may also be used by clinicians and decision-makers simultaneously, to assess the quality or appropriateness of specific measures of resource utilization in a target population, or to ensure that funding is in place for particular investigations or programs that have the most effective outcomes. These data also provide insight for public health officials aiming to ensure that healthcare resources are accessible to all individuals in a population, by identifying differences in utilization that cause inequities which may be modifiable. Finally, these data may be used by healthcare policy decision-makers to develop financial incentives to guide clinical practice toward appropriate use of services and to lower costs associated with a treatment, program or disease; the ethical and moral ramifications of this practice are debated.[54]

2.3.2 Measurement of Resource Utilization in Gastric Cancer Management

Gastric cancer has been identified as one of the most expensive cancers to treat in the United States;[55] recent data suggests that this may also be true in Canada (Krahn, unpublished). An analysis of the United States Surveillance, Epidemiology and End Results (SEER)-Medicare linked database estimated the mean net cost of managing metastatic gastric cancer patients in the last year of life to be $78,430 in 2004 US dollars, ($74,416 to $82,444).[55] Differences in primary treatment strategy have been identified as explaining the largest amount of variance in models predicting the costs of gastric cancer management.[56] The majority of costs however, may be attributed to inpatient hospital days, with approximately 75% of costs derived from this resource.[56,57] Few studies have explored specific measures of resource utilization related to the management of gastric cancer, to explain why the costs for caring for this population may be so high.

The impact of resource utilization on the healthcare system in cancer care includes diagnostic healthcare contacts, investigations and procedures; tests and medical imaging for accurate staging of the disease for prognosis and determination of treatment options, treatment modalities, hospitalizations, emergency department admissions and additional procedures and investigations associated with complications of treatments; as well as end-of-life care. For example, complications arising from receipt of chemotherapy, such as febrile neutropenia, may require different care and resource utilization than the complications associated with bowel obstruction from the primary tumour, necessitating a gastrectomy, feeding tube placement or placement in palliative care. Theburden to the healthcare system among the primary modalities for addressing symptoms and end-of-life needs are undocumented.

Kuwabara et al.[58] described the number of patients receiving gastrectomy, chemotherapy, radiation therapy, and supportive therapies (total parenteral nutrition, ventilation, hemodialysis) in a cohort of Japanese patients. Less than 2% received a palliative surgical procedure and the majority underwent either partial gastrectomy (29%) or endoscopic mucosal resection (16%), reflecting early stage disease management.[58] Blood transfusions have been measured in patients receiving surgery for gastric cancer in a series of Japanese patients.[59] Of the 57 patients included in the series, 15% (9/57) required a blood transfusion and 90% (8/9) of these patients had either advanced disease or underwent a multivisceral resection (removal of more than one organ).[59] While these reports provide an outline of resources accessed by gastric cancer patients in Asia, these patients have an earlier stage of cancer at diagnosis than in North America due to screening programs and undergo more curative-intent treatments. The experience in Japan may not accurately reflect resource use in the Canadian system.

One Canadian study described measures of resource utilization in gastric cancer treatment, but was limited by a lack of information on stage of disease.[36] Treatment intent was inferred from administrative data codes for advanced disease; 10% of patients underwent non-curative gastrectomy or surgical bypass, while 11% had a non-curative, non-resectional surgery, and 35% of patients did not receive an operation. Pre-treatment investigations included endoscopy, computed-tomography (CT) scans, ultrasound, laparoscopy and endoscopic ultrasound. The majority of patients had an endoscopy (90%) and/or a CT scan (81%). Less than half of patients received chemotherapy (40%) and/or radiotherapy (40%). [36] Existing studies have not reported on the number of emergency room admissions, hospitalizations, physician services, and the admitted hospital days per patient. The picture of resource utilization, including major cost drivers, is therefore incomplete for gastric cancer patients and especially for the metastatic cancer population, who may require the largest proportion of resources among all gastric cancer patients.

2.3.3 Predictors of Healthcare Resource Utilization

A number of predictors of healthcare resource utilization and costs have been identified in oncology care, end-of-life care and other illness-specific literature.[60] Prognostic factors in cancer research have been classified into disease, host and environmental factors, to acknowledge factors aside from the tumour itself that influence clinical outcomes.[60] This approach may be used to categorize predictors of healthcare resource utilization into disease-level (cancer stage,[61-64] tumour location[58,65]); patient-level (age,[62-64,66-72] sex,[67-69,72,73] socioeconomic status indicators,[64,67-69] co-morbidities,[62-64,66,70,72-78]; rurality[79]); and healthcare system-level (the type of treatment provided,[66,71,74,76-78] physician volume and/or experience,[69,75,80] hospital type[67,69,76,81]).

Disease predictors are not easily modified; however, they provide information for healthcare planning and may be of importance when evaluating the cost-effectiveness or cost-utility of different treatment strategies. *Patient* predictors of resource utilization and cost may not be modifiable at the level of the patient, but their interaction with the healthcare system may be influenced by changes in public health policy or clinical guidelines for appropriate medical care. For examples, disparities among measures of socioeconomic status may warrant targeted interventions at the policy-level to ensure equal access to healthcare. *Healthcare system* predictors likely represent the class that includes the most modifiable factors responsible for influencing resource utilization in cancer care.

Research investigating predictors of resource utilization in the setting of gastric cancer do not exist. A few studies have been done to identify predictors of costs specific to the treatment or management of gastric cancer. Kuwabara et al.[58] explored predictors of costs of gastric cancer in the Japanese healthcare system and determined that age, gender, emergent status of an operation, severity of disease (defined as metastatic disease or not), Dartmouth-Manitoba co-morbidity index score, presence of post-operative complications and the type of surgical procedure received predicted costs.[58]

Yabroff et al.[55] determined phase of disease costs of cancer treatment by matching cancer patients with controls and subtracting total costs to determine the net costs of cancer care by primary tumour site. The control group was comprised of Medicare beneficiaries without a cancer diagnosis during the study period and these patients were matched to the malignancy cohot on factors such as sex, 5-year age group and SEER registry area.[55] After stratifying by sex, they concluded that the costs of treatment for gastric cancer did not vary significantly between males and females at any of the phases of disease treatment.[55] Bachmann et al.[56] investigated the effect of hospital and physician volume on costs per day survived in a multiple linear regression model, adjusting for such factors as age, gender, socioeconomic status, indicators of disease severity and treatment. Neither hospital nor surgeon volume were statistically significant as explanatory variables in the model after adjusting for covariates and neither explained a large portion of the model variance.[56]

Burden of Metastatic Disease

The association between the number of metastatic sites and measures of resource utilization has not been studied; however, advanced stage of disease at diagnosis has been associated with both higher and lower resource utilization.[61,63] Within the advanced cancer population, the number of metastatic disease sites influences recommendations for treatment and response to treatment.[48] In a current randomized controlled trial to investigate the role of gastrectomy in non-curative disease, more than one site of metastatic disease is an exclusion criterion.[45] Patients with differing burdens of metastatic disease may therefore also be managed with different treatments, creating differences in the majority of measures of resource utilization.

Tumour Location

Kuwabara et al.[58] described the mean costs and standard errors (SE) of gastric cancer treatment (for all stages of disease) by anatomic site of the primary gastric tumour. Costs of treating tumours of the gastric body were lowest at $12,891 (SE: $244) compared to tumours of the fundus, which cost $17,306 (SE: $652); however, statistical comparisons for differences in costs were not performed, and the costs for treating tumours of the cardia were not included.[58] Patients with tumours in an unknown location were in the mid-range of the most expensive and least expensive primary sites. Tumour location plays an important role in the types and extent of treatment provided to a gastric cancer patient, especially in the metastatic population, where tumour location likely influences symptoms. Different investigations, treatment modalities and follow-up care warranted by the primary locations may result in differences in resource utilization among patients. In esophageal cancer, the site of the primary tumour has also been identified as an independent predictor of costs in patients with.[65] Tumours located at the gastroesophageal junction were significantly more expensive to manage than tumours at any other location in the esophagus.

Sex

Sex has been identified as predicting healthcare resource utilization across many diseases.[67-69,72,73] For example, studies have documented that females dying of cancer are more likely to access homecare in the last 6 months of life (OR 1.15, 95% CI 1.12-1.18).[68] Yabroff et al.[55] reported that the costs of treating gastric cancer were not significantly different between men and women; however, the impact of gender on gastric cancer resource utilization has not been studied.

Age

Age has been established as a predictor of resource utilization, and has been shown to both increase and decrease resource utilization as age increases.[62-64,66-72] Age is associated with the choice of treatment strategy, procedure-related complications and survival, all of which are associated with resource utilization.[62-64,66-72,82] Specifically in end-of-life care, younger, dying patients incur higher costs and increased utilization in comparison with older, dying patients.[68,70]

Co-morbidity

The number and type of co-morbid diseases a patient has predicts their level of healthcare resource utilization.[62-64,66,70,72-78] The Charlson score, a well established measure of severity of co-co-morbid disease for predicting in-hospital mortality, has been validated to predict resource utilization and costs.[83] Individuals with higher scores, indicating more severe burdens of co-morbid disease, have higher illness or treatment-related costs.[83] Another measure of co-morbidity has been created at Johns Hopkins University to specifically predict resource utilization.[84] Resource utilization bands are used in an algorithm to estimate an individual's pattern of healthcare use to predict use of services in a multivariate model.[84] These tools allow for control of other diseases in the prediction of resource use related to a separate illness or procedure, and allow healthcare decision-makers to forecast the potential increased burden of a treatment or procedure, related to a patient's overall health status.

Socioeconomic Status

Indicators of socioeconomic status have been identified as possibly impacting on healthcare resource utilization.[85] Gastric cancer patients who did not receive adjuvant radiotherapy (standard of care) in the United States were less likely to have completed high school education and more likely to have an income below the poverty line than those who received adjuvant radiotherapy.[86] However, in Ontario receipt of adjuvant radiotherapy was not significantly associated with median community income quintiles.[36] Another Ontario study concluded that patients dying of cancer in the lowest median income quintile are more likely to die in an acute care hospital bed and less likely to receive house calls in the last two weeks of life or to receive home care in the last 6 months of life than patients in higher median income quintiles.[68]

Rurality

Patients living in a rural or remote setting and receiving end-of-life care in Saskatchewan for respiratory illnesses have been documented as visiting a physician significantly fewer times in the last year of life than those in urban dwellings.[79] Trends toward increased utilization of healthcare services, such as the emergency department visits and hospitalizations, have been documented for rural patients in comparison with urban patients.[79] An increased distance between a patient's residence and their regional cancer centre has also been associated with increased lengths of hospital stay for lung cancer operations.[64] These differences may not relate only to the rurality of a patient's residence, but also of the treating institution. Patients undergoing bariatric surgery at rural institutions have longer hospital lengths of stay and per patient costs than those operated on at urban centres.[67] A lack of availability of services, decreased access to specialized services and increased geographic and social distances from appropriate places of care may potentially explain the differences in resource utilization.

Gastrectomy

Receipt of surgery is associated with different rates and types of complications and these are known to influence resource utilization.[58,66,71,74,76-78] The costs of elective liver, gastric, colorectal and pancreatic surgery were 2.3 times lower if there were no complications, and the type and severity of complications further influenced the costs.[78] Additionally, in the metastatic population where surgery is non-curative, physicians may select younger and healthier patients for gastrectomy and more aggressive treatment of the primary tumour. These patients may use healthcare resources similar to curatively treated patients and have subsequently different resource use. Patients undergoing gastrectomy in the metastatic setting may be doing so to address severe symptoms, such as bleeding or obstruction, which may portend heavier resource use in the future.

Physician Volume

The role of physician volume in the prediction of resource utilization for gastric cancer treatment is unclear. Increased physician volume has not been shown to be significantly associated with costs of care.[56,58] In some cancer sites, such as the esophagus and oral cavity, overall institution volume has been identified as a significant predictor of healthcare resource utilization and costs.[75,87] High volume physicians may assign treatment strategies for non-curative patients more appropriately, leading to fewer complications and less days admitted to hospital; however, this relationship has yet to be investigated.

2.4 Ontario Healthcare System

The Canadian healthcare system operates within a public, single payer framework; the majority of direct medical costs are paid by the provincial or territorial government.[88] The primary role of the federal government in healthcare is to regulate adherence to the principles of the Canada Health Act, through financial incentives, and to ensure that the key features of public administration, comprehensiveness, universality, portability and accessibility are met for all medically necessary treatments.[88] While some inter-provincial and territorial differences exist in the extent of public coverage and how healthcare services are delivered, the majority of provinces and territories further de-centralize the planning and provision of health services to smaller, regional governing bodies.

In Ontario, the provincial healthcare structure is headed by the Ministry of Health and Long Term Care, the ultimate organization with financial culpability for the provision of healthcare to Ontarians. All persons residing in Ontario for greater than three months are provided, at no charge, health insurance coverage through the Ontario Health Insurance Plan (OHIP). Healthcare contacts, services and interventions covered under this plan are billed by physicians to the Ministry at a negotiated rate.[89] While this is considered the primary method of reimbursement for medical services provided, alternate funding plans, such as team-based practices and salaried physicians, also exist; however, the primary payer is still the province.

In addition to the reimbursement of physician services, the Ministry is responsible for funding other medically necessary services, including emergency health services, non-cosmetic surgery, cancer care, hospital care and home care. The provision of health services was separated into 14 Local Health Integration Networks (LHINs) in 2006,[90] to better target regional health needs and to plan and organize targeted health services for community members. LHINs have local authority over hospitals, community health centres and services provided by Community Care Access Centres (which coordinate home care services in each LHIN).[90] The largest LHIN geographically is the North West region, which also has the smallest proportion of the population. The smallest geographic LHIN is Toronto Central, which is also the most densely populated and the only completely urban region.[91]

Cancer health services, such as the delivery of chemotherapy and radiotherapy, are under the leadership of Cancer Care Ontario (CCO) and are provided to the Ontario population through collaboration with the Local Health Integration Networks. The scope of priority areas for CCO ranges from active prevention and screening efforts, to palliation at end of life, to the system-wide monitoring and improvement of the quality of care provided to cancer patients and their families across the province.[88,91] Through interaction with regional cancer programs and their affiliated hospitals, CCO directly oversees the provision of cancer care in Ontario. A separate, specialized, overseeing organization for the delivery of cancer health services has existed in Ontario for over 50 years.

2.5 Geographic Variation in Patient and Disease Characteristics and Resource Use

Geographic variation in the attributes of patients treated for gastric cancer has been documented.[92] A medical centre treating patients with curative-intent gastrectomy in Poland, performed resectional surgery on more females ($p=0.019$), patients with less severe comorbidity status ($p <0.001$), patients with different histopathology ($p<0.001$), and patients with different levels of tumour invasion ($p<0.001$) and less often on patients with metastatic disease ($p=0.009$) than a similar centre in Germany.[92] Variations in patient and disease characteristics have also been documented in gastric cancer cases across institutions and in studies investigating the impact of high and low volume institutions on surgical outcomes for gastric cancer.[93] Low volume physicians are more likely to treat older, sicker, more emergent gastric cancer patients than high volume physicians, and are less likely to perform a gastrectomy as the primary care strategy.[93]

Non-randomized evidence currently makes up the bulk of information available for the creation of practice guidelines for advanced gastric cancer management. A lack of high-level evidence is known to be associated with increased institution level variation in care.[94-97] Despite attempts to standardize practices, variations in the provision of gastric cancer care have been demonstrated across healthcare system variables, especially across geographic regions and centres of care.[92,98-106] Patients in Poland were more likely to receive a total gastrectomy than patients at a similar facility in Germany, and more likely to simultaneously undergo removal of the spleen during their resectional procedure ($p<0.001$).[92] A study of the uptake of adjuvant radiotherapy following the publication of a seminal randomized controlled trial that demonstrated a significant clinical benefit with the addition of radiotherapy to curative gastrectomy documented significant variation within a single country, across Surveillance, Epidemiology, and End Result healthcare regions in the United States.[98] Rates of adjuvant radiotherapy usage ranged from 24.5% of patients in the Los Angeles region to 44.2% of patients in the San Jose/Monterey region.[98]

Regional variation in the provision of palliative and end-of-life care for both cancer and non-cancer patients has been documented across numerous healthcare systems and geographic regions. There is consistent evidence of variation in the rates of hospitalization among geographic regions in the last weeks to months of life of cancer patients in Ontario.[68,68,91,107-109] Similarly, differences in the number of emergency room admissions in the last six months of life, the proportion of patients with cancer dying in hospital, and the aggressiveness of cancer care at end-of-life (e.g. receipt of chemotherapy within two weeks of death) have been documented across the province.[110-113]

Cancer Care Ontario has also documented a number of discrepancies across the province in both treatment and end-of-life care for cancer patients as part of their Cancer Quality Council of Ontario, an offshoot of CCO that monitors the quality of cancer care provided to Ontarians. The differences among LHINs in the indicators they measure may be related to inequalities in access to palliative care and/or the availability of resources between regions.[91] For example, the median acute-care length of stay per hospitalization for cancer patients varies among LHINs, from 10 days in the Hamilton Niagara Haldimand Brant region and the South East region, to 15 days in the Central West, Mississauga Halton, Central and Champlain regions. Explanations for differences in the availability of hospice care and advanced care planning have been proffered; however, the province has yet to undertake an analysis to further understand these regional differences in end-of-life practices.[91] In the last two weeks of life, admissions to the emergency department are tracked as a quality indicator by the province. Differences in the proportion of patients presenting to the emergency room ranged from 34% in Champlain to 49% in the North East.[91]

Provincial data investigating trends in the treatment of gastric cancer, but without stage information, suggest that the use of treatment modalities (surgery, chemotherapy, radiotherapy) for gastric cancer do not differ among LHINs.[36] Coburn et al. (2010) reported the proportion of patients receiving potentially non-curative surgery was similar among LHINs. The most common treatment modalities (chemotherapy, radiotherapy) for metastatic gastric cancer were not investigated to see if they differed among LHINs and neither were any measures of end-of-life care, such as use of home care.[36] A detailed, stage-specific investigation of gastric cancer specific utilization, comparing resource use among regions, is necessary. Variations in treatment patterns and resource use have the potential to increase the costs incurred by the healthcare system, to increase patient wait times and to cause delays for necessary, limited access investigations or procedures. This could impact patient-related outcomes negatively, such as survival and quality of life. Given the universal, open-access infrastructure of the Canadian healthcare system, differences in resource utilization that reflect inequitable access to care among regions require targeted interventions at the federal and provincial levels.

2.6 Major Cost Driver- Inpatient Hospital Days

Admissions to the emergency department and hospitalizations at the end of life are potential indicators of uncontrolled symptoms, resulting in misuse of acute care for the management of non-emergent complaints. A study of cancer patients presenting to the emergency room in Ontario documented the thirty most common complaints from the hospital charts of almost 200,000 patients. Symptoms, such as pain and constipation, which could be managed through other healthcare contacts were among the top twenty complaints.[114] Admission to the emergency department at end-of-life is often a gateway to hospitalization. Inpatient stay related to palliative care is a costly use of limited hospital beds, while both patients and the system may be better serviced by the provision of alternate places of care such as long-term care or hospice care facilities.

Within healthcare spending, hospital-related costs make up almost one quarter of all expenditures.[115] Inpatient hospital days related to malignancy have been estimated to represent almost 10% of all hospitalization costs in Canada, costing the system approximately $600 million dollars between 2004-2005. Hospital-based cancer care ranks fourth in contributing to inpatient costs, behind diseases related to the circulatory system, poisoning and other external causes of illness, and respiratory diseases.[116] The average cost of an inpatient oncology stay was estimated to be $250,000 CAN per patient in the same report from the Canadian Institute for Health Information.[116] The average cost per patient in palliative and/or end-of-life care in Ontario is estimated to include 39% of costs from intensive care unit or acute care hospital days[117,118] and a similar figure has been quoted for palliative care provided to cancer patients in Alberta.[118] Another report from the Canadian Institute of Health Information indicated that the number of hospitalizations per patient has decreased over the last ten years, with a shift toward out-patient services noted.[115] An increased length of stay per patient was also documented;[115] however, these figures are across all diseases and large improvements in clinical pathways for such common procedures as hip or knee replacements, or the use of minimally invasive surgeries in other domains may mask increases or stagnancy within terminal illnesses, such as metastatic cancer.

The number of days spent in hospital is a quality indicator of appropriate end-of-life care, an indicator of potentially aggressive end-of-life cancer care, and a major driver of the costs of oncology care in Canada and abroad, including costs to the healthcare system in Ontario.[117-119]

Identifying predictors of the length of time a patient spends in hospital at the end-of-life may uncover avenues for decreasing costs, while also improving the patient experience in palliative care.

2.7 Home Care Use at End-of-Life

In early 2000, the Government of Canada sanctioned an investigation into the sustainability and quality of Canada's healthcare system.[120] The original healthcare recommendations proposed in the Romanow report, which was the end product of this federal government commission, included increasing the use and availability of home care services,[120] since decreased use of acute healthcare services, such as emergency room admissions and hospitalizations, requires increased access to home care services.[68,121,122] Use of home care to off-set hospital admissions and use of acute healthcare services in providing palliative care for individuals dying in Ontario was a major focus of the provincial End-of-Life strategy, initiated in 2005 by the Ministry of Health and Long-Term Care.[91] In an evaluation of the provision of end-of-life care following the roll-out of this program, the use of home care and acute care services did not change, although the evaluation was self-criticized as not having given enough time for changes to take place or improvements to become evident. [108] Rates of home care use specifically among cancer patients were documented to be lower than home care use among non-cancer patients at end of life in Ontario.[108] This may be the result of more aggressive cancer care provided at end-of-life in lieu of palliation, which has been documented for both lung cancer and ovarian cancer in Ontario.[110,113]

Recently, a Commission on the Reform of Ontario's Public Services was undertaken, to review how to improve the efficiency of provincial services, including the healthcare sector.[123] The Drummond recommendations for improvement in public healthcare were released in 2012, stressing the importance of increasing the utilization of home care services to decrease costs to the public healthcare provider.[123] Home care use has never been studied specifically in patients dying of gastric cancer, but with the emphasis in the last twenty years to improve access to and use of these services, it warrants further research.

While the typical time period to study home care use has been the last six months following a diagnosis of cancer,[68,110,114,117,118,121,122] metastatic gastric cancer patients survive for less time following diagnosis than many other cancers. This may limit the ability to understand the use of this resource. Studying potential predictors of home care use in the metastatic gastric cancer population would allow us to understand potential modifiable barriers to the receipt of home care, as well as to provide insight into differences in rates of home care use. Healthcare policy makers could use this information to target non-users of home care, if these patients were also those with the greatest rates of hospitalization at end-of-life, to both decrease the burden to the healthcare system and optimize use of in-home services for palliative care.

2.8 Summary of the Evidence, and Rationale

Although the majority of gastric cancer presents as non-curative disease without hope for cure, little is known about the metastatic gastric cancer population in North America and its impact on the Canadian healthcare system. Guidelines directing the care of metastatic gastric cancer patients rely on low quality evidence and choices of management strategy are driven by symptom relief and addressing quality of life. Geographic variation in the availability and use of investigations, procedures and treatments are expected for metastatic gastric cancer and differences in the end-of-life care of these patients are possible. This thesis describes the burden of caring for metastatic gastric cancer patients to the public healthcare system and investigates geographic variation to determine if policy-level interventions are necessary.

While a complete picture of the costs of caring for metastatic gastric cancer does not exist, developing an understanding of predictors of major cost drivers will provide information for health policy decision-makers to reduce costs and improve efficiencies. Days spent in hospital are a major driver of costs in oncology, end-of-life and palliative care. This project identifies predictors of the costs of inpatient hospital days, and home care use, a service touted by the government and authors of healthcare reform that could reduce burden to the healthcare system while providing optimal palliative care.

This project provides a description of who is diagnosed with metastatic gastric cancer in Ontario, and what and how much healthcare services they use and identifies predictors of two important health resource utilization outcomes, to generate explanations as to why differences in healthcare utilization exist. Ultimately, the results of this thesis will need to be combined with an understanding of relevant clinical outcomes to determine targets for improvements in appropriate patient care with accompanying benefits to the healthcare system.

Chapter 3

Methods

3.1 Introduction

This project is a population-based, retrospective cohort study that describes disease, patient, and healthcare system factors, as well as the resource utilization of metastatic gastric cancer patients in Ontario. The results provide a picture of who is diagnosed with metastatic gastric cancer in Ontario; describe what and how much healthcare services they consume; explore regional variation in healthcare resource use; investigate predictors of major cost drivers of healthcare; and explore appropriate end-of-life care. Data from a provincial chart review linked to national and provincial administrative healthcare databases housed at the Institute for Clinical Evaluative Sciences were used to achieve the study objectives.

This chapter begins with the study objectives and hypotheses (Section 3.1); describes the study design (Section 3.2); provides background on the parent study (Section 3.3); delineates the study population and inclusion and exclusion criteria (Section 3.4); provides the study's timeframe (Section 3.5); describes the data sources and data linkage process (Section 3.6); describes the study variables (disease, patient and healthcare system factors, resource utilization) (Section 3.7); and outlines the analytic strategies (Section 3.8) and study power (Section 3.9).

3.1.1 Study Objectives

In a population-based, retrospective cohort of metastatic gastric cancer patients in Ontario, to:

1) Describe disease, patient, and healthcare system factors and healthcare resource utilization, and

2) Compare disease, patient, and healthcare system factors and healthcare resource utilization among Local Health Integration Networks.

3) Identify disease, patient, and healthcare system predictors of admitted inpatient hospital days, and home care use.

3.1.2 Hypotheses

A review of the literature informed a number of hypothesized relationships between disease, patient and healthcare systems factors and healthcare resource utilization: (1) Significant geographic variation in disease, patient, physician and healthcare system factors exists among Local Health Integration Networks; (2) Significant geographic variation in healthcare resource utilization exists among Local Health Integration Networks; (3) Variables describing disease severity (increased burden of metastatic cancer), disease anatomy (tumour location), less healthy patients (increased age, high co-morbidity scores) or potential inequality in access to healthcare services (age, sex, socioeconomic status, rural residence, not seeing a high volume physician, Local Health Integration Network) will predict healthcare resource utilization (the number of inpatient hospital days and home care use).

3.2 Study Design

A population-based, retrospective cohort design was followed for this study. It was designed to describe who is diagnosed with metastatic gastric cancer in Ontario, to describe the impact of this disease on the healthcare system and to investigate regional variation in disease, patient, healthcare system characteristics and healthcare resource utilization. It also evaluated predictors of admitted inpatient hospital days and home care use. This study was performed from the healthcare system perspective, specifically the Ontario Ministry of Health and Long-Term Care. As such, only measures of healthcare resources that would pose a burden to the healthcare system were considered in this project.

3.3 Existing Clinical Dataset

This investigation of healthcare resource utilization is part of a larger retrospective cohort study titled *Improving Gastric Cancer Survival: Development and Measurement of Quality Indicators using the RAND/UCLA Appropriateness Method and Population-Based Data Analysis* (Canadian Cancer Society grant # 019325). The parent study was designed to examine the clinical management and outcomes of gastric cancer patients in Ontario (Principal Investigator- Dr. Natalie Coburn). Eligible patients for the study were identified using the Ontario Cancer Registry (OCR). The population for the parent study was all cases of gastric adenocarcinoma in Ontario registered to the OCR between April 1, 2005 and March 31, 2008, in patients 18-99 years of age, with a valid Ontario Health Insurance Plan (OHIP) number, excluding those with a diagnosis made on autopsy. Overall, the parent study included 2516 gastric cancer patients from across the province. Province-wide chart review data for the parent study were abstracted by a trained physician and included the results of pre-operative staging (radiologic and endoscopic investigations), pathology reports, details of surgical procedures and additional clinical patient information (symptomology). Staging was performed using the abstracted information, following a standard Collaborative Staging methodology for TNM staging, combining radiological, pathological, surgical and clinical findings. Stage was categorized using the International Union Against Cancer (UICC)/American Joint Committee on Cancer (AJCC) 7th Edition staging system.[32]

3.4 Study Population

The target population of this study is individuals diagnosed with and treated for metastatic gastric adenocarcinoma in Ontario. Patients with a registered diagnosis of gastric cancer in the Ontario Cancer Registry between April 1, 2005 and March 31, 2008 were included if they had evidence of metastatic disease. According to the UICC/AJCC staging criteria, metastatic gastric cancer is any size or depth of tumour (T_{any}), any lymph node status of involvement (N_{any}), with evidence of cancer spread to other organs or areas of the body outside the primary tumour (M1). This may include metastases to the liver, lung, bone, brain, distant lymph nodes or carcinomatosis. The study included only patients with UICC/AJCC stage IV M1 gastric adenocarcinoma ($T_{any}N_{any}M1$) identified in the parent study described in section 3.3.

3.4.1 Inclusion and Exclusion Criteria

Patients were eligible for inclusion in this study if they were between 18 and 99 years old, had a valid Ontario Health Insurance Plan number, had a valid Institute for Clinical Evaluative Sciences key number (IKN), had an IKN traceable in the Registered Persons Database, had a confirmed diagnosis of gastric adenocarcinoma, and had at least one site of metastatic disease recorded on pathology or radiology, or a clinical diagnosis of metastatic (M1) disease in the chart abstraction notes. Patients were excluded if they were missing stage information, had a UICC/AJCC diagnosis of Stage 0-IV M0 or MX (metastatic status unknown) disease, had a tumour location identified as being in the upper, middle or entire esophagus on endoscopy or were missing information on their Local Health Integration Network of residence.

3.5 Study Horizon and Timeframe

The study time horizon in an economic evaluation is the time constraint imposed on the collection of resource utilization for an individual patient in the cohort.[52,53] This time period should be clinically meaningful to the research question, and be long enough to include relevant outcomes.[52,53] Given the estimated median survival for metastatic gastric cancer is between 5 and 20 months,[124] and the short time period between diagnosis, clinical management and death, resource utilization related to staging is difficult to disentangle from that related to treatment planning, active treatment and end-of-life care. Because of this, the time horizon included two months prior to the date of diagnosis and up to two years following the date of diagnosis to accommodate resource utilization related to staging, treatment planning, clinical management and end-of-life care (**Error! Reference source not found.**).

The timeframe for data collection refers to the inclusive time constraints on the entire study, including the time periods of patient accrual to the study, look-back windows of data collection related to descriptive characteristics of the cohort and the follow-up period for each patient from the time of entry into the study. The timeframe of this study will be from April 1, 2003- Dec 1, 2010 (Figure 3). Patients will enter the cohort on their OCR date of diagnosis between April 1, 2005- and March 31, 2008 (as determined by the parent study). Data will be collected from two years prior to the date of diagnosis until the date of diagnosis to collect information pertaining to disease presentation (e.g., symptoms) and patient characteristics (e.g., co-morbidity). Data will be collected on resource utilization from two months prior to the date of diagnosis until two years following the date of diagnosis. To calculate median survival of the cohort, survival data will be collected from the date of diagnosis until Dec 1, 2010, for a minimum follow-up period of two years and eight months for those patients diagnosed March 31, 2008.

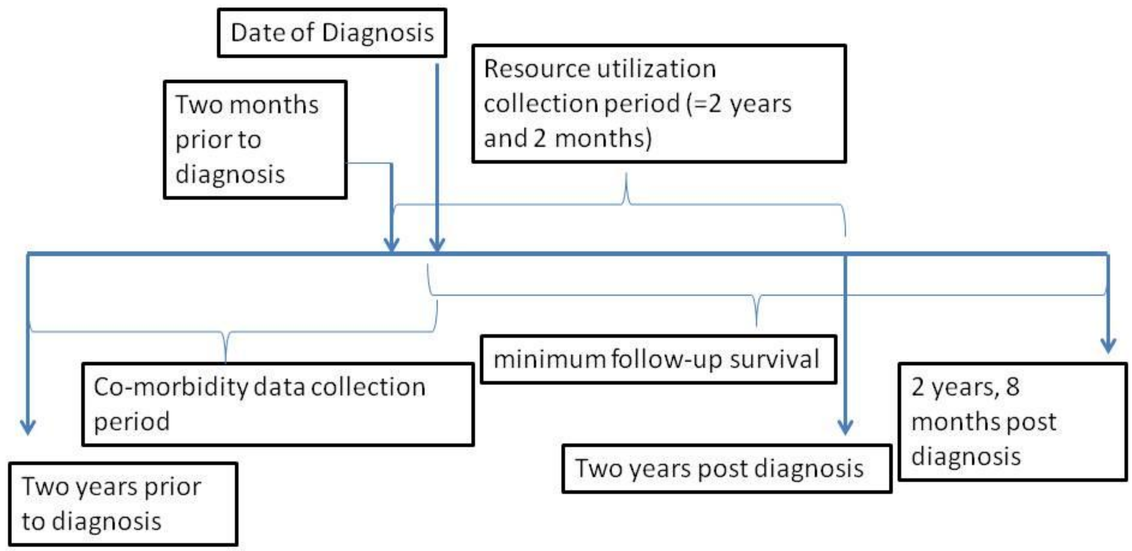

Figure 1: Description of study timeframe

3.6 Data Sources

3.6.1 Data Linkage

The clinical variables in the chart review dataset were linked to national and provincial administrative healthcare databases held at the Institute for Clinical Evaluative Sciences. Examples of the variables accessed from the chart review database are provided in Appendix A. Deterministic linkage was performed by an Institute for Clinical Evaluative Sciences Senior Biostatistician using each individual's unique IKN. The following databases were linked for this project.

3.6.2 Canadian Institute for Health Information- Discharge Abstract Database & Same-Day Surgery

The Canadian Institute for Health Information (CIHI)- Discharge Abstract Database (DAD) & Same Day Surgery (SDS) holdings are updated annually and are a national source of patient and facility-level data on all acute, chronic, rehabilitation and same-day surgery facilities in the country.[125] Information from CIHI-DAD & SDS were used to identify hospital admissions, the number of admitted inpatient hospital days, blood transfusions and the following procedures: endoscopy, chest, abdominal, and pelvic computed tomography (CT) scans, ultrasounds (US), plain film x-rays, magnetic resonance imaging (MRI) scans, positron emission tomography (PET) scans, gastrectomy, surgical bypass, and feeding tube placement. Data to assign a Charlson-Deyo co-morbidity score and the Johns Hopkins Resource Utilization Band for each patient to provide a measure of co-morbid illness (described further in Section 3.7) were also accessed from this database.[126,127]

3.6.3 CIHI: National Ambulatory Care Reporting System

The National Ambulatory Care Reporting System (NACRS) is updated annually and is a national database that includes patient and facility-level information on emergency department visits, day surgery, and outpatient clinic visits.[125] NACRS was used to identify emergency room admissions, and was another source of information on blood transfusions.

3.6.4 Home care Database

The Home Care Database (HCD) is updated annually and consists of the records of in-home services provided to residents of Ontario.[125] These services are coordinated by Community Care Access Centres and include such services as personal-support work, nursing and social work. This database was used to identify the receipt of home care, including the number and type of visits.

3.6.5 Ontario Health Insurance Plan

The Ontario Health Insurance Plan (OHIP) database is a provincial dataset, updated bi-monthly and contains information claims submitted by health care providers who can claim under OHIP (physicians both in and out of province, and laboratories) for financial reimbursement from the Ministry of Ontario Health and Long-Term Care.[125] Data from the OHIP dataset were used to determine physician volume, identify physician visits (general practice, medical oncologist, radiation oncologist, surgeon), and identify procedures (endoscopy, CT scans, US, MRI scans, PET scans, gastrectomy, surgical bypass, stent placement, chemotherapy use, radiotherapy use, feeding tube placement, laparoscopy, exploratory laparotomy, and incisional biopsies).

3.6.6 Registered Person Database

The Registered Persons Database (RPDB) is updated bi-monthly, is coordinated by the Ontario Ministry of Health and provides basic demographic information about anyone who has ever received an Ontario health card number.[125] Data are enriched with geographic, contact and death information from other Institute for Clinical Evaluative Sciences-held administrative datasets. This database provides patient-level information on demographics (described in Section 3.7), Local Health Integration Network of residence and aggregate-level data on socioeconomic status (described in Section 3.7).

3.7 Study Variables

The variables described in the following sections were collected to describe the metastatic disease patient population, compare characteristics among Local Health Integration Networks, to describe the healthcare resource utilization of the cohort, compare measures of utilization among Local Health Integration Networks, and understand predictors of two resource utilization measures. The list of disease, patient, physician and healthcare system variables to describe the cohort and for evaluation as predictors of resource utilization was developed *a priori* by the thesis team based on the gastric cancer, general cancer, and health economics literature. The variables in this list were restricted to those collected in the parent study or accessible from the administrative data. The variables described in Section 3.7.1 have been categorized into disease (number of metastatic sites, tumour location), patient (age, gender, co-morbidity, rurality, socioeconomic status), and healthcare system (physician volume, treatment , Local Health Integration Network) level categories to reflect potential modifiable and non-modifiable targets for health policy interventions and planning decision-making. The resource utilization outcomes described in Section 3.7.2 were chosen because they are directly involved in cancer and end-of-life care for gastric cancer patients. The number of inpatient hospital days was evaluated as a resource utilization outcome because it is a major contributor to the costs of treating cancer. Home care use was investigated as a resource utilization outcome because the vast majority of the cohort was predicted to die within the two year and two month timeframe outlined in the analysis, and receipt of home care is considered an indicator of appropriate end-of-life care in Ontario. Figure 2 provides an overview of the hypothesized study relationships between the predictor variables and the outcomes of interest. Table 1 provides a summary list of study predictor variables, definitions and sources.

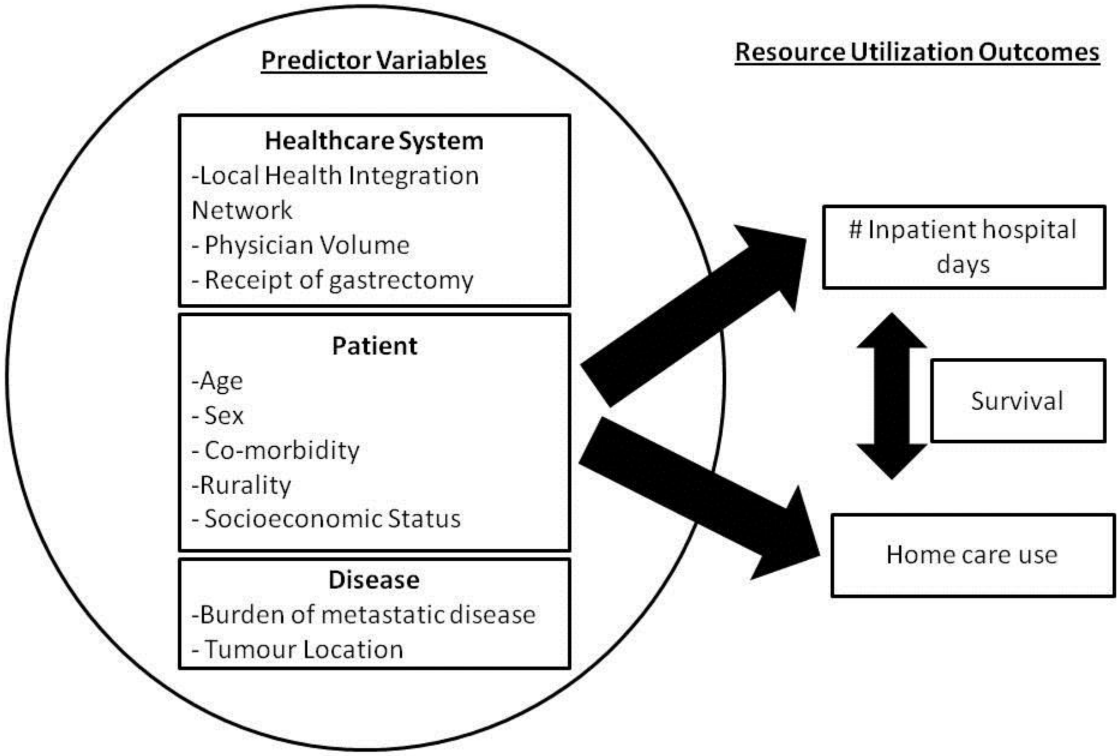

Figure 2: Conceptual model linking disease, patient, and healthcare system predictor variables with resource utilization outcomes

3.7.1 Disease Characteristics

Variables describing the extent of metastatic disease and the primary tumour location were categorized as disease-level characteristics that may contribute to resource utilization and are characterized by their non-modifiable nature after disease presentation. The extent of metastatic disease was defined as the number of metastatic disease sites and categorized into a binomial variable, corresponding to 1 site and >1 site of metastatic disease. Data abstracted from radiology and pathology reports, as well as from clinical consult notes from the chart review were used (Appendix A). The number of sites was calculated as the number of distant sites of cancer, which were not involved through direct invasion of the primary tumour. These included such sites as the liver, lung, bone, brain, distant lymph nodes, and carcinomatosis (peritoneal seeding of the tumour in the abdominal cavity or malignant fluid in the abdomen). Cancer found in more than one lobe of the lungs or liver, more than one distant lymph node, both kidneys or multiple bones were counted only once for each organ (e.g. cancer found in the sacrum, pelvic bone and spine would count once as bone metastasis). Patients who were described in pathology, radiology or clinical consult notes as having metastatic disease, but for whom the specific sites of metastatic disease were not indicated, were categorized as having only one site of metastatic disease. An example of such a patient would be one who had a report that indicated the patient was M1, but did have any supplementary information or report describing the location of metastases.

The tumour location variable describes the anatomic site of the primary tumour in the stomach. Location was categorized into the gastroesophageal junction, proximal stomach, middle stomach, distal stomach, entire stomach or unknown. Primary tumour locations have different risk factors, behave differently, and require different technical approaches by treatment modalities. Their different symptomatology may explain receipt of different management strategies. Tumour location was determined from the tumour location variables taken from upper endoscopy reports in the chart review. A maximum of two upper endoscopy reports performed prior to diagnosis or initial treatment was abstracted per patient. Reports may not have been complete or may not have included information on tumour location. Patients who did not receive an endoscopy or whom did not have the tumour location recorded in the report, or whose report stated explicitly that the tumour was not visualized during endoscopy, were classified as unknown. The tumour location of patients with two endoscopy reports was determined by combining the locations mentioned in one or both reports.

Table 1: Definitions and sources of disease, patient, and healthcare variables

Variable	Type	Source	Operational Definition
Disease Characteristic			
Burden of metastatic disease	Categorical	Chart review	1/>1 site of metastatic disease
Tumour Location	Categorical	Chart review	Gastroesophageal Junction/

			Proximal/ Middle/ Distal/ Entire Stomach/ Unknown
Patient Characteristic			
Age	Categorical	RPDB	<65 years/ 65-74 years/ >74 years
Sex	Categorical	RPDB	Male/Female
Charlson score	Categorical	CIHI-DAD	0/ 1/ >1
Hopkins Resource Utilization Band	Categorical	CIHI-DAD, OHIP	0/1/2/3/4/5
Rurality	Categorical	RPDB	Rural/Urban
Socioeconomic Status	Categorical	RPDB	Lowest/2/3/4/Highest
Healthcare System Characteristic			
Gastrectomy	Categorical	Chart review, OHIP, CIHI-DAD	Yes/No
High Volume Physician	Categorical	OHIP	Yes/No
Local Health Integration Network	Categorical	RPDB	1-14

RPDB= Registered Persons Database; CIHI-DAD= Canadian Institute of Health Information-Discharge Abstract Database; OHIP= Ontario Health Insurance Plan

3.7.2 Patient Characteristics

Variables related to an individual that contribute to their unique clinical and demographic profile are categorized into patient-level characteristics. These variables are characterized by their tendency to represent non-modifiable factors that may cause or be related to modifiable barriers to resource utilization and the healthcare system. Age (at diagnosis) and sex were assigned from the RPDB. Age was measured in years, and analyzed as a variable using three categories: less than 65 years old, 65-74 years old, and greater than 74 years old. Previous studies in Ontario have used this categorization to study gastric cancer and home care use. [36,68]

Co-morbid illnesses that may contribute to resource utilization were measured using two scoring systems: the Charlson-Deyo score and the Johns Hopkins Resource Utilization Band (Hopkins RUB). The Charlson-Deyo score is a method of measuring an individual's burden of co-morbidities originally designed and validated to predict in-patient mortality using medical records.[126,127] It requires the use of data on previous hospitalizations and out-patient visits. Records of hospitalizations and out-patient visits (excluding family physician visits) are compared to a list of diseases with accompanying point values (Table 2) and the patient receives a final score. The scores range from 0 (no history of co-morbidity) to 29 (most severe burden of co-morbid illness), but may also be documented as 'missing', indicating the patient has not had an interaction with the healthcare system within the disease and data source constraints defined in the scoring system. The Charlson-Deyo score has also been validated to predict resource utilization and costs in administrative cohort studies.[83] Standard Institute for Clinical Evaluative Sciences methodology using a SAS macro was used to calculate the scores for this project, and followed the validated, Deyo adaptation of the Charlson score (Charlson-Deyo).[127] The Deyo adaptation allows for the conversion of the algorithm to use administrative healthcare record International Classification of Disease codes (9th version). Scores were calculated for the cohort using hospitalization data for the two years prior to the date of diagnosis (not including the diagnosis of gastric cancer). Patients with missing scores in our analysis were considered to have no co-morbid illnesses and included with the 0 score patients for reporting and analysis. These scores were further categorized into: 0, 1 and >1 for our analysis; categorization of Charlson-Deyo scores has been done elsewhere in the cancer resource utilization literature.[128,129]

Table 2: Co-morbid diseases and scoring system used to calculate the Charlson score

Co-morbidity	**Score**
Acute Myocardial Infarction	1
Congestive Heart Failure	1
Peripheral Vascular Disease	1
Dementia	1
Chronic Obstructive Pulmonary Disease or other Respiratory Diseases	1
Ulcers of the Digestive System	1
Liver Disease- Mild	1
Diabetes- No Chronic Complications	1
Hemiplegia or Paraplegia	2
Renal Disease	2
Cancer (No secondary found)	2
Liver Disease- Moderate or Severe	3

Cancer (Metastatic- secondary)	6
HIV/AIDS	6
Total Charlson score= weighted sum of number of co-morbid diseases	

The Hopkins RUB is a measure of co-morbid illness that was originally developed and validated to predict healthcare resource utilization and was calculated for each patient using data from OHIP and CIHI-DAD.[84,130-132] The Hopkins RUB is a multi-step algorithm that assigns International Disease Classification codes into 32 Aggregated Diagnostic Groups, which are then combined with age, gender, duration and severity of disease and the number of diseases to categorize patients into one of 102 clinically similar disease groups called Adjusted Clinical Groups (ACGs) to describe the patient in terms of the totality of their previous disease history. The system then categorizes patients into quintiles of predicted healthcare resource utilization that may not be clinically similar, but are expected to have a similar burden to the healthcare system. Categories of RUB are 0 (no co-morbidity or only invalid diagnoses), 1 (Healthy Users), 2 (Low), 3 (Moderate), 4 (High), 5 (Very High).[84] The Hopkins system differs from the Charlson score because it includes all physician contacts, regardless of the location/setting of care provided, while the Charlson score system is restricted to hospital-based contacts.

Socioeconomic status was measured as a community-level variable using data from the Canadian census and reported as median household income quintile (Lowest, 2, 3, 4, Highest).[133] Geographic areas were first categorized into quintiles based on their community income. Data holdings at the Institute for Clinical Evaluative Sciences allow patients to be linked to a median community income level via their postal code. Because categorizations are made within a pre-defined geographic area, the highest income quintile in one community is not representative of the highest income quintile in a neighbouring area.

The rurality variable was measured using an Institute for Clinical Evaluative Sciences algorithm that updates each patient's geographical residence information annually within the

Institute for Clinical Evaluative Sciences from a variety of data sources (the RPDB, OHIP, CIHI-DAD and SDS, NACRS, HCD, the Continuing Care Reporting System, and the National Rehabilitation System) and then uses this postal code information to apply the Rurality Index of Ontario system.[134] This system involves ranking communities in Ontario based on 10 facets of a definition of rurality that pertains to the delivery of healthcare services. Each patient's postal code is linked to the community rurality score and defines each individual's residence code as being urban or rural.[134]

3.7.3 Healthcare Characteristics

Variables that potentially affected resource utilization outside of the disease biology and patient characteristics were considered to exist at the healthcare system level. These variables represented those interactions between the patient and the healthcare system that may be modified at the health policy level. Receipt of care or consultation with a high volume physician (surgeon, medical oncologist or radiation oncologist) experienced in gastric cancer treatment was categorized into having received a consultation (yes) or not having received a consultation (no). Medical oncologist was defined as physicians billing for gastric cancer related chemotherapy consults in OHIP. Surgeon was defined as physicians billing for total gastrectomy or subtotal gastrectomy in OHIP as the primary surgeon. Billings for the same procedures, where the surgeon was the assistant on the procedure were not counted toward their annual volume. Radiation Oncologist was defined as physicians billing for radiotherapy related consults or planning in OHIP directed at patients with a diagnosis of gastric cancer. Gastric cancer patient volume for each physician within each specialty was calculated over a 7 year time period (April 1, 2003-March 31, 2010) and physicians were categorized into volume terciles (Low, Medium, High) by specialty. Volume classifications were created such that one third of patients fell into each category. If a patient saw a physician of any of the three specialties in the high volume category during the study timeframe, the variable value was "yes"; and the value was "no" if none of the affiliated treating physicians were considered high volume. To be considered a “yes” for the high volume surgeon variable, patients had to have received a gastrectomy (total or subtotal), bypass or exploratory laparotomy. Patients who received more than one surgery were assessed for exposure to a high volume surgeon for the most complicated surgery only. A high volume surgeon performed an average of at least 2.3 gastrectomies per year (range 2.3-6.8 per year, over the seven year period); a high volume medical oncologist saw at least an average of 5 gastric cancer patients per year (range 5-15 patients per year); and a high volume radiation oncologist saw on average at least 8 gastric cancer patients per year (range 8-34 patients per year).

A gastrectomy is the complete (total) or partial (subtotal, proximal, distal) removal of the stomach. This procedure may be performed in combination with removal of nearby organs invaded by the primary tumour. Patients who had an administrative data code for having undergone a multi-visceral resection of the esophagus, colon, spleen or liver in combination with a gastrectomy (during the same procedure), or a gastrectomy (total, distal or proximal) within the timeframe were a “yes” for the gastrectomy variable. Those patients who did not receive resective surgery for their gastric cancer tumour received a “no”.

Local Health Integration Network of residence was defined using postal code data mapped onto the Ministry of Ontario Health and Long-Term Care designated geographic health regions (Figure 3). These regions represent independent regions within the province that provide, coordinate and fund healthcare services for the encompassed communities. The province has been sub-divided into 14 unique healthcare regions (the numbers correspond to the figure below): Erie St. Clair (1), South West (2), Waterloo Wellington (3), Hamilton Niagara Haldimand Brant (4), Central West (5), Mississauga Halton (6), Toronto Central (7), Central (8), Central East (9), South East (10), Champlain (11), North Simcoe Muskoka (12), North East (13) and North West (14) (Figure 3).

Figure 3: Map of the geographic location of Ontario's 14 Local Health Integration Networks

3.8 Confounders

The number of days a patient lived from the time of diagnosis influences the amount of resource utilization captured in the time horizon. Patients who lived longer within the time horizon may have increased exposure to accumulate resource utilization. They may appear to have increased utilization in some areas (e.g., related to regular follow-up, more aggressive management), but less utilization for those associated with death (e.g., receipt of home care, admitted hospital days). It was important to record the number of days alive to describe the survival of the cohort, and for consideration in the multivariate analysis. The number of days each patient lived from the time of diagnosis to death or the end of the time horizon was recorded using information in the RPDB. The patient had a date of diagnosis (date of entry into the cohort) which was subtracted from the date of death (if recorded in the RPDB) to get the number of days alive. Patients who did not die within the two year period following diagnosis were assigned the maximum allowable value of days alive in this study (730 days).

3.8.1 Resource Utilization Outcomes

Measures of healthcare resource utilization were the outcomes of interest for this project, for both the descriptive and analytic portions. The aim was to include any and all outcomes that were likely to be involved in both direct cancer-related care and end-of-life care for the patients for the two year and two month time horizon, or until death. Specific ICD codes to identify procedures and events associated with a diagnosis of gastric cancer were not required. The assumption was made in the analysis that even if gastric cancer was not indicated as the diagnosis related to the procedure or event, it was likely that having metastatic cancer was in some way related to use of that healthcare resource. Investigative procedures (radiology, endoscopy), interventions such as surgery, chemotherapy and radiotherapy, blood transfusions, general practitioner visits, specialist visits (medical oncologist, surgeon, radiation oncologist), emergency room visits, hospitalizations, the number of admitted inpatient hospital days, and receipt of home care were described. Data for these variables came from the chart review, CIHI-DAD & SDS, OHIP, NACRS and the HCD. The chart review data was considered the best source of information of whether or not an investigation was performed for the following variables: endoscopy, computed tomography scans (CT), abdominal ultrasound (US), plain film x-ray, magnetic resonance imaging (MRI), positron emission tomography (PET) and stent placement. These variables were measured categorically (yes/no) and endoscopy, CT, US, and x-rays were also measured as count variables. If the chart review indicated that a patient had received any of these investigations, the patient was counted as having had at least one of these procedures. If a patient did not have a record of receiving these procedures in the chart review, but a record existed in OHIP, the patient was counted as having had at least one of these procedures. The count for endoscopy, CT, US, and x-rays was determined using the number of OHIP billing codes for each procedure during the two year and two month time period or until death. If the patient did not have a record of these procedures in OHIP, the maximum count they could have recorded for a procedure was dictated by the number of reports abstracted during the chart review (2 X endoscopy, 3 X CT scan, 2 X US, 1 X x-ray). OHIP billing data is more complicated for MRI and PET, recording each imaging slice by anatomic area per code, rather than the entire procedure as one billing code. This makes it very difficult to determine the number of unique procedures actually received by a patient, so only the proportion of patients receiving either of these procedures at least once was recorded.

Surgical procedures were tracked using OHIP billing codes and CIHI-DAD & SDS. OHIP billing codes were considered the most accurate and valid codes for describing the type of surgery that occurred. Surgical procedures of interest were total gastrectomy, proximal gastrectomy, distal gastrectomy, multi-visceral resection (gastrectomy with one of the following: esophagectomy, colectomy, splenectomy, hepatectomy), surgical bypass (gastrojejunostomy-reconnecting the stomach to the intestine while bypassing the tumour), other intestinal obstruction surgery, incisional biopsy, and laparoscopy (small incision in the abdomen and passing a scope to view the primary tumour and/or metastases in the abdomen). Using these two data sources, whether or not a patient received each procedure was recorded.

Receipt of chemotherapy or radiotherapy was measured as categorical variables using OHIP billing codes. OHIP billing codes provide information on whether or not a patient received chemotherapy by proxy, as the physician bills for the provision of chemotherapy, but does not provide information on the regimen, dose or the number of cycles. This includes chemotherapy provided at regional cancer centres, as well as chemotherapy provided at other hospital settings. Receipt of radiotherapy is restricted to provisions at regional cancer centres only, at specially equipped buildings for the safe delivery of nuclear radiation targeted to either the primary tumour or metastatic sites. Radiation oncologists are salaried employees of the regional cancer centres and do not bill for services rendered the same way that surgeons or medical oncologists do; however, hospitals require that radiation oncologists “shadow” bill for their time so that they are reimbursed for radiation oncologist salaries appropriately by the Ministry of Ontario Health and Long-Term Care. Radiation Oncologists bill for the planning of radiation separately from consultations with patients, and while both may occur, this does not mean that the patient actually received the therapy. The assumption was made that if a patient had a consult with a radiation oncologist only, this did not contribute to the proportion of patients who received radiotherapy. If a patient also had a billing code for treatment planning, the assumption was made that they received the treatment. OHIP billing codes do not contain information on the dose or number of doses received by the patient.

The proportion of patients who received at least one blood transfusion and the number of blood transfusions per patient were measured using variables from CIHI-DAD & SDS and NACRS. Reporting blood transfusions is mandatory while hospitalized, during a surgery or during a visit to the emergency room or any other out-patient facility contributing to CIHI-DAD & SDS or NACRS. The number of units of blood, and the type of blood product are not mandatory variables and are infrequently reported; therefore, only whether or not a patient received a blood transfusion and the number of times the patient had a blood transfusion recorded in the administrative data were included as outcomes. The number of times a blood transfusion was recorded was summed over the time horizon to provide the total number of blood transfusions required.

Whether or not a patient was hospitalized (yes/no), the number of hospitalizations and the cumulative number of admitted inpatient hospital days were measured using CIHI-DAD. To calculate the number of admitted inpatient hospital days, the number of days between each admission date and discharge date during the time horizon were summed. This would include each unique admission, as well as re-admissions and hospital or facility transfers. Only whole numbers were considered- a patient could not have a fraction of a day reported in this project, even if they were admitted on the morning of one day and discharged at noon the following day (e.g. this would count as two days, not 1.5).

Emergency department (ED) visits were recorded categorically (yes/no) and as a count (number of visits) for each patient using records in NACRS. Each ED record in NACRS counted as one visit and these visits were summed over the time horizon.

Physician visits were recorded categorically (yes/no) and as a count (number of visits) using billing codes in OHIP. Billing codes related to general practitioner visits and billing codes for specialists (surgeons, medical oncologists and radiation oncologists) were counted. While billing codes exist for palliative care, any physician may bill those codes and, palliative care physicians may bill general visit codes, so these were captured under general practitioner visits. Any contact with a physician (e.g. face-to-face visit, telephone consult, in-hospital visit, home visit) was considered a visit.

Receipt of home care was collected as a categorical variable (yes/no) and as a count (number of visits) and was measured using data in the HCD. Home care may be provided for a number of services (e.g. physiotherapy, speech pathology, personal care) and by a number of different caregivers (e.g. nurses, personal support workers). Information on the visit includes the type of service provided and the number of hours (for nursing); however, only the visit record itself, indicating that home care was provided, is considered reliable.[125] Each record of home care for a patient in the system was counted as a visit for this project.

3.9 Statistical Analysis

The analysis of this project included describing the disease, patient and healthcare system characteristics of patients in the cohort, and their resource utilization and exploring if regional variation in characteristics and utilization exists. The analysis also included investigating significant predictors of the number of inpatient hospital days (major cost driver) and receipt of home care (indicator of appropriate palliative care). Section 3.8.1 outlines the descriptive analysis and exploration of regional variation, and Section 3.8.2 describes the multivariate analytic process for identifying independent predictors of the dependent outcomes. Cell sizes containing < 6 patients are suppressed due to privacy and confidentiality regulations of the Institute for Clinical Evaluative Sciences and the Ontario Privacy Commissioner. All analyses were performed at the ICES@Queen's Health Services Research Facility using SAS 9.2 Copyright 2008 (Cary, North Carolina, USA).

3.9.1 Descriptive analysis and comparison among Local Health Integration Networks

Frequencies of disease, patient, and healthcare system characteristics were reported for the cohort. Ranges of these characteristics were reported for Local Health Integration Networks (LHINs) to describe geographic variation. Frequencies, means and standard deviations, and inter-quartile ranges of per patient and total cohort resource utilization were reported. Ranges of resource utilization measures were reported for LHINs. Chi square tests for independence were used to compare proportions of resource utilization between LHINs. Non-parametric ANOVA and Kruskal-Wallis tests were used to compare mean measures of resource utilization among LHINs. Median survival was calculated using Kaplan-Meier methods and compared using Log-Rank tests. Two-sided hypothesis testing was performed and an alpha of 0.05 was used to establish statistical significance.

3.9.2 Identifying predictors of inpatient hospital days

The goal of this objective was to identify disease, patient and healthcare system predictors of inpatient hospital days, to determine if any predictors are potentially modifiable to the benefit of the patient and/or the healthcare system.

Potential predictors of the number of inpatient hospitals days over the two year and two month time horizon were investigated using two different methods. First, non-parametric

Analysis of Variance (ANOVA) methods were used to compare the mean number of hospital days accumulated in each predictor category overall, to understand if an association between the predictor and outcome existed. Incidence rates of inpatient hospital days were then calculated per 100 days alive for each predictor category, to describe utilization in the context of the length of time survived during the data collection period. The potential relationship between the number of days survived and the predictor variables was explored, using Kaplan-Meier methods and Log-Rank tests. Median survival in days and corresponding 95% confidence intervals were reported for each predictor variable strata. The relationship between the number of days survived and the number of inpatient days was explored using non-parametric ANOVA, to compare the mean number of inpatient hospital days among categories of survival time. This relationship was also graphed to explore the likelihood of a linear trend.

Multivariate Poisson regression for count data was initially used to model the relationship between the predictors and the outcome and to produce estimates of the relative risk. Large ratios of overdispersion from the Poisson regression model indicated that the mean and variance were not equal, meaning a lack of fit to the data. To account for this situation, multiple negative binomial regression was used, and modified Poisson methods with robust error estimation to confirm the acceptability of the negative binomial estimates. This method to deal with the over-dispersion of healthcare resource utilization data has been used previously in the literature.[135-137] Because each patient had a different observation period (length of survival in days from the date of diagnosis), the number of inpatient hospital days was modeled using an offset variable. The offset variable was included as the log of the number of days survived (up to 730 days). This method was chosen because logically, the longer a patient survived, the greater the opportunity to accumulate inpatient hospital days and the assumption that each patient had the same observation period was violated. Inclusion of an offset variable calculated incidence rate ratios, comparing the cumulative number of inpatient hospital days per cumulative days alive for each predictor variable category with respect to the referent. Backward elimination predictor selection method was used to identify independent predictors of the outcome, and an alpha of 0.05 was used to keep predictors in the model. Model fit was further assessed through the visual inspection of deviance statistics; smaller deviance values and scaled deviance close to one indicated better model fit. Alternate models were developed using an alpha of 0.2; however, the addition of non-statistically significant predictors into the model did not improve the model fit and these results are not reported.

3.9.3 Identifying predictors of the receipt of home care

The goal of this objective was to identify disease, patient and healthcare system predictors of the receipt of at least one home care visit, to determine if any predictors may be modifiable to the benefit of the patient and/or the healthcare system, and not to create a predictive model. Potential associations between predictors and the receipt of at least one home care visit were investigated using the chi square test for independence. Proportions of home care users were compared to describe whether or not usage was significantly different among predictor variable categories using an alpha of 0.05. Potential confounding between the number of days survived and the receipt of at least one home care visit was explored in two different ways. First, a continuous form of the number of days alive variable was modeled to predict home care use. Then, the number of days survived was broken into small time periods and the proportion of home care users was compared among these 14 categories to understand if a linear relationship existed. Finally, days alive were modeled as a categorical variable, splitting the data into three categories: 0-30 days, 31-729 days and 730 days, to reflect the different likelihoods of receiving home care if the patient died quickly, or lived longer than the study period. Modified Poisson regression with robust standard error variance estimation was used to model the multivariate relationship between the predictors and the outcome. This is an established method used to model relative risks for a common outcome (>10%),[138,139] where logistic regression cannot be used, because the odds ratio no longer approximates the relative risk. Backward elimination was used to identify independent predictors of home care use, using an alpha of 0.05. Model fit was visually inspected using the Quasi-likelihood Information Criterion (QIC); smaller values indicate better model fit. Alternate models were developed using an alpha of 0.2; however, the addition of non-statistically significant predictors into the model did not improve the model fit.

3.10 Study Power

A minimum detectable effect size difference for age categories and gender was calculated for their ability to predict home care use prior to analysis. The estimations were based on the assumption that 1000 patients (half of the *predicted* number of patients in the parent study cohort) would have metastatic disease. This estimation was based on a previous study of gastric cancer patients in Ontario that used administrative codes for metastasis to estimate the number of patients who had metastatic disease [36]. Study power was set at 0.9 and alpha at 0.05. The number of patients who would fall into each age category was estimated using the same study, as was the expected number of males and females in the cohort. We estimated that the minimum increased relative risk of receiving home care that could be detected by this study was 1.17 (comparing the middle age category to the lowest age category) and 1.16 (comparing the highest age category to the lowest age category).

A study power calculation was calculated to determine the ability of this project to detect a difference in likelihood of receiving home care between females and males using data from the Ontario study of gastric cancer mentioned previously and a study of home care use during end-of-life for all cancer patients in Ontario.[36,68] Alpha was set at 0.05. We estimated that the study had 93% power to detect a relative risk of 1.15 for the likelihood of receiving home care for females compared with males.

3.11 Ethical Considerations

Ethics approval for the parent study was provided by the Sunnybrook Health Sciences Centre Research Ethics Board; internal review of the parent study was also performed and approved by the Institute for Clinical Evaluative Sciences. Health Science Research Ethics Board approval for this project was obtained through Queen's University. Internal review and approval of this project were provided by the Institute for Clinical Evaluative Sciences. The policies and mandate of the Tri-Council Policy- Ethical Conduct for Research Involving Humans were upheld. All project data was stored and analyzed at the Institute for Clinical Evaluative Sciences, a provincial non-profit organization that houses national and provincial administrative healthcare datasets for the improvement of Ontario health systems and outcomes. The Institute for Clinical Evaluative Sciences holds prescribed entity status under Ontario's privacy law. The Person Health Information Protection Act (PHIPA) (s.45) provides the statutory authority for the collection and use of administrative healthcare data for statistical and evaluative purposes without individual consent. As a prescribed entity under PHIPA, the Institute for Clinical Evaluative Sciences' policies, practices and procedures for privacy protection and data security are routinely reviewed and approved triannually. Individual-level demographic and clinical data for Ontario residents with a valid Ontario Health Insurance Plan (OHIP) number are anonymized using an Institute for Clinical Evaluative Sciences key number. Data may be linked to physician-level information, hospital-level information or healthcare system level information through these unique identifiers to answer research questions relevant to the health of the Ontario population. In Kingston, the ICES @Queen's-Health Services Research Facility allows access to the data for Institute for Clinical Evaluative Sciences scientists, their students and staff at Queen's University through a secure server.

Chapter 4

Results

4.1 Introduction

The main objectives of this study were to describe the healthcare resource utilization of metastatic gastric cancer patients in Ontario, investigate potential geographic variation in resource use, and identify predictors of the number of inpatient hospital days and receipt of home care. The results are described in this chapter. Section 4.1 presents the cohort selection process and the final study population after application of the exclusion criteria. The results of Objective 1 (to describe disease, patient, and healthcare system factors and healthcare resource utilization of the study population) are presented in Section 4.2 and 4.3. Sections 4.4 and 4.5 contain the findings of Objective 2 (to compare disease, patient, and healthcare system factors and healthcare resource utilization among Local Health Integration Networks in the study population). Finally, Sections 4.6 and 4.7 present the results from Objective 3 (to identify disease, patient, and healthcare system predictors of inpatient hospital days, and home care use).

4.2 Cohort Selection

Using the Ontario Cancer Registry, 2516 potentially eligible patients with a diagnosis of gastric cancer registered between April 1, 2005 and March 31, 2008 were identified. Patients were excluded for the following reasons: missing chart review and/or stage data (n=25); no confirmed diagnosis of gastric adenocarcinoma following the chart review (n=44); no evidence of metastatic disease on pathology, radiology or clinical consult notes (n=989); tumour located in the upper, middle or entire esophagus (n=23); or missing Local Health Integration Network (LHIN) of residence (N=2) (see Figure 4).The final study population consisted of 1433 patients with UICC/AJCC stage IV disease (Tany Nany M1)[32]. Overall, 59% of new cases of gastric adenocarcinoma in Ontario between 2005 and 2008 were diagnosed with metastatic disease.

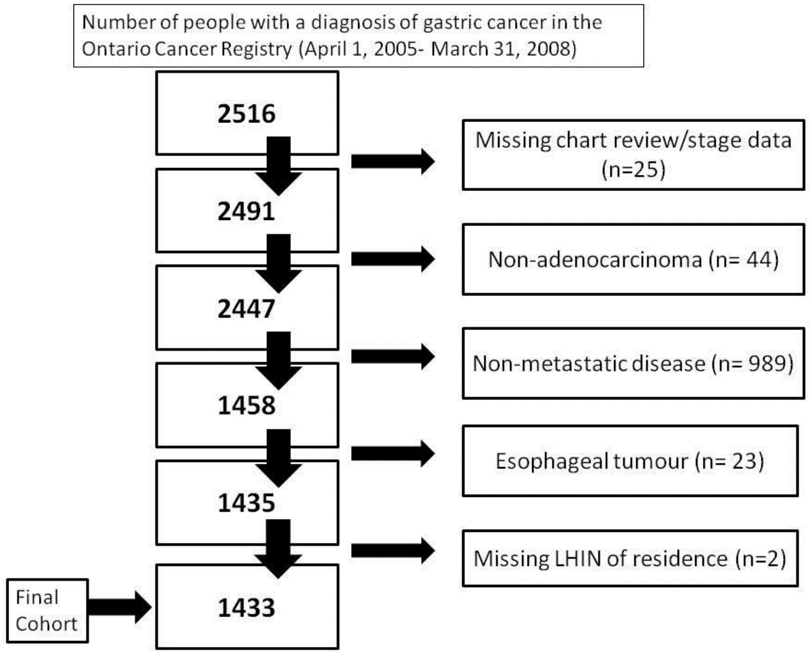

Figure 4: Cohort selection process

4.3 Objective 1: Describe patient, disease, and healthcare system characteristics of metastatic gastric cancer patients in Ontario

Patient, disease, and healthcare system characteristics for the entire cohort are presented in Table 3. Almost two thirds of the patients were male (934). The mean age at diagnosis was 67.5 years with individual ages ranging from 20 to 97 years. The burden of metastatic disease was split almost evenly, with 747 (52.2%) having one site of metastatic disease and 685 (47.8%) having more than one site. The vast majority of patients had a Charlson-Deyo score of 0 or missing (89.3%) and a Johns Hopkins Resource Utilization Band (RUB) of ≥ 3 (93.8%), most lived in an urban area (89.0%). The distribution of patients at each level of median income ranged from 18-23% across quintiles. One third of patients were seen by a high volume physician (32.1%). The smallest number of metastatic gastric cancer patients resided in the North West and North Simcoe Muskoka LHINs and the largest number lived in the Hamilton Niagara Haldimand Brant LHIN, and Central LHIN; however, the overall proportion of metastatic cases compared to non-metastatic cases was similar among LHINs (p=0.2756; Appendix B). The proportion of patients with metastatic disease ranged from 51.2% in the North West region to 65.3% in Erie St. Clair. Median survival was 6.2 months (95% confidence interval (CI) 5.6-6.9), and mean survival was 13.3 months (standard error 0.48). Overall, 231 patients (16%) contributed the maximum number of days alive to the time period (730 days) and were still alive 24 months from their date of diagnosis.

Table 3: Patient, disease, and healthcare system characteristics of metastatic gastric cancer patients in Ontario (n=1433)

Patient Characteristics	**Number of patients (%)**
Gender	
Male	934 (65.2)
Age	
<65	534 (37.3)
65-74	404 (28.2)
>74	494 (34.5)
Charlson-Deyo score	
0	1279 (89.3)
1	82 (5.7)
≥2	71 (5.0)
John Hopkins ACG Resource Utilization Bands (RUB)	
0	12 (0.8)
1	15 (1.0)
2	63 (4.4)
3	658 (46.0)
4	386 (27.0)
5	298 (20.8)
Socioeconomic status (n=1432)	
Lowest Income	296 (20.7)
2	329 (23.0)
3	284 (19.8)
4	268 (18.7)
Highest Income	255 (17.8)
Rurality	
Urban	1274 (88.9)
Disease Characteristics	
Metastatic Sites	
1	747 (52.2)
>1	686 (48.8)
Tumour Location	
Gastroesophageal Junction	390 (27.2)

Proximal Stomach	139 (9.7)
Middle Stomach	229 (16.0)
Distal Stomach	476 (33.2)
Entire Stomach	134 (9.4)
Unknown	65 (4.5)
Health Care System Characteristics	
Gastrectomy	
Yes	527 (37)
High Physician Volume	
Yes	460 (32)
Local Health Integration Network (LHIN)	
Erie St. Clair	81 (6)
South West	79 (5)
Waterloo Wellington	77 (5)
Hamilton Niagara Haldimand Brant	167 (12)
Central West	72 (5)
Mississauga Halton	122 (9)
Toronto Central	151 (11)
Central	211 (15)
Central East	152 (11)
South East	53 (4)
Champlain	127 (9)
North Simcoe Muskoka	41 (3)
North East	78 (5)
North West	22 (2)

ACG= adjusted clinical group

4.4 Objective 1: Describe the healthcare resource utilization of metastatic gastric cancer patients in Ontario

A number of healthcare services were accessed by patients in the cohort over the time horizon, including a variety of non-therapeutic procedures and non-curative management options. All patients had enough healthcare contacts to receive a diagnosis of metastatic gastric cancer (either radiologic, pathologic or clinical) and thus none had zero healthcare utilization. The healthcare resource utilization for the entire cohort, and the average per patient usage are described in Table 4 and Table 5. Both the total usage for the cohort and the average per patient usage correspond to the two year and two month time horizon. Almost all individuals had at least one upper endoscopy (98.3%), computed tomography (CT) scan (99.1%) or x-ray (96.2%) in the two months preceding or in the two years following diagnosis of gastric cancer, while fewer patients had an ultrasound (76.8%) (Table 4). On average, patients incurred x-ray imaging most often (mean 9.3 per patient) and ultrasounds least often (mean 4.6 per patient). Overall, the cohort obtained over 12,500 x-ray images, and over 12,000 CT scans, and a total of 34,556 of these 4 types of investigations. On the other hand, few patients (13.7%) underwent magnetic resonance imaging (MRI) scanning and less than one third (26.2%) had a positron emission tomography (PET) scan. Not only was upper endoscopy a common investigational procedure, but each patient scoped had an average of 3.4 procedures. A laparoscopy, to assist in operative planning, was performed in less than 10% of patients.

Most individuals visited a general practitioner (98.4%), or saw a specialist --medical oncologist, surgeon or radiation oncologist-- (99.8%). For individuals who visited a general practitioner, the average number of visits was 15.4 per patient; in comparison, the average number of specialist visits was 62.6 per patient. Overall, the cohort visited a general practitioner or specialist a total of 111,159 times. Visits to the emergency department were common (86.6%), and for those who visited an emergency department at least once, the average number of visits was 3.0 per patient. Admissions to hospital were also common (95.3%) in this time period. Individuals who were hospitalized spent an average of 30.2 days in hospital over the time horizon, for a total of 41,239 days overall, averaging 2.4 admissions per patient. Over two thirds of patients received at least one home care visit (77.5%). A home care service was provided a total of 70,045 times to patients in this cohort, and for patients who received home care, each received on average 63.1 visits, with many receiving more than one type of visit.

Palliative or non-curative surgical management of the primary tumour was provided to over half of patients (51.3%), with 14.5% of patients undergoing a non-resectional operation (surgical bypass) and 36.8% undergoing a gastrectomy. A subtotal gastrectomy without the removal of additional organs was most commonly performed (16.6% of patients). A total gastrectomy without resection of additional organs was performed the least often (7.2%). A multivisceral resection accompanied either a subtotal or total gastrectomy in 15.4% of patients, and included removal of a segment of the esophagus in 57.7% of cases, removal of part of the colon in 44% of cases and less often included removal of the pancreas (4.1%) or the spleen (3.2%). Exploratory laparatomy (a non-therapeutic procedure that involves opening the abdomen, often with the intent of carrying out a therapeutic procedure, then closing without carrying out a therapeutic procedure) was performed in nearly 10% of patients. Almost half of all patients were managed with chemotherapy (42.9%), one quarter received radiotherapy (27.8%) and one quarter required placement of a feeding tube (26.7%). Stent placement for relief of obstruction at either the gastroesophageal junction or the pylorus was performed for only 5.4% of the cohort.

Table 4: Description of resource utilization in metastatic gastric cancer in Ontario - Visits, hospitalizations, home care use, investigations, and non-surgical palliative procedures (n= 1433)

Variable	Number of patients (%)	Per patient w/use (mean ± SD)	Interquartile Range	Cohort Total Count	Per patient total cohort (mean ± SD)
Healthcare Visits					
General Practitioner Visits	1410 (98.4)	15.4 ± 14.4	6-20	21662	15.12 ± 14.43
Specialist Visits	1430 (99.8)	62.6 ± 51.4	25-85	89497	62.45 ± 51.37
Emergency Room Visits	1236 (86.6)	3.0 ± 3.6	1-3	3700	2.58 ± 3.48
Hospitalizations					
Hospitalizations	1366 (95.3)	2.4 ± 1.6	1-3	3240	2.26 ± 1.67
Hospital Days	1366 (95.3)	30.2 ± 29.7	10-37	41239	28.78 ± 29.66
Home care Use					
Home care visits (all)	1110 (77.5)	63.1 ± 93.3	1-62	70045	48.88 ± 86.25
Nursing visits	1007 (70.3)	40.2 ± 54.0	0-44	44565	31.10 ± 50.39
PSW visits	461 (32.2)	37.9 ± 77.4	0-3	17486	37.93 ± 77.40
Investigations					
Upper Endoscopy	1409 (98.3)	3.4 ± 2.2	2-4	4690	3.27 ± 2.29
Computed Tomography	1420 (99.1)	8.5 ± 7.1	3-11	12033	8.40 ± 7.11
X-ray	1379 (96.2)	9.3 ± 9.1	3-12	12774	8.91 ± 9.07
Ultrasound	1101 (76.8)	4.6 ± 5.1	1-5	5059	3.53 ± 4.83
MRI*	196 (13.7)	--	--	--	--
PET*	376 (26.2)	--	--	--	--
Non-surgical Palliative Procedure					
Blood Transfusions	861 (60.1)	3.1 ± 6.3	0-2	2655	1.85 ± 5.09

SD= standard deviation; PSW= personal support worker; CT= computed tomography; MRI= magnetic resonance imaging; PET= positron emission tomography; *because of the way MRI and PET scans are billed compared to other investigations, it is not reliable to report the number of scans per patient or the total number of scans

Table 5: Non-therapeutic investigations, surgical management and non-surgical palliative procedures for metastatic gastric cancer patients in Ontario (n= 1433)

Non-therapeutic Investigations		**Number of patients (%)**
Incisional Biopsy		6 (0.4)
Laparoscopy		125 (8.7)
Exploratory Laparotomy		127 (8.9)
Surgical Management		**Number of patients (%)**
Bypass or Intestinal Obstructive Surgery		208 (14.5)
Gastrectomy		527 (36.8)
Total Gastrectomy		103 (7.2)
Subtotal Gastrectomy		238 (16.6)
Multivisceral Resection		220 (15.4)
	Colectomy	97 (44.1)
	Esophagectomy	127 (57.7)
	Pancreatectomy	9 (4.1)
	Spleen	7 (3.2)
Non-Surgical Palliative Procedures		**Number of patients (%)**
Stent Placement		78 (5.4)
Stent Location	Gastroesophageal Junction	61 (78.2)
	Pylorus	17 (21.8)
Specialist	Radiologically Placed	21 (26.9)
	Endoscopically Placed	57 (73.1)
Chemotherapy		615 (42.9)
Radiotherapy		398 (27.8)
Feeding Tube		382 (26.7)

4.5 Objective 2: Comparison of disease, patient, and healthcare system factors among Local Health Integration Networks

Individuals with metastatic gastric cancer residing across Local Health Integration Networks (LHINs) were not significantly different on most of the disease, patient and healthcare system factors that were hypothesized to potentially influence healthcare resource utilization (Table 6). The burden of metastatic disease, distributions of primary tumour location, age, sex, Charlson-Deyo score and Johns Hopkins RUB did not vary significantly between LHINs. Although not statistically significant, considerable variation in the primary tumour location was documented: in one LHIN less than 15% of patients had tumours in the distal stomach, while in another LHIN 47.6% had primary tumours in this location; similarly, the proportion of patients with primary tumours located at the gastroesophageal junction ranged from 19.4% to 41.8% among LHINs.

As would be expected, the proportion of patients living in a rural setting and the distribution of median community income levels differed significantly between LHINs. In more than one LHIN, none of the patients were associated with a rural postal code, while in other LHINs, up to 42.9% of patients were considered to live in a rural area ($p<0.0001$). The proportion of patients living in areas with the highest median community income quintile ranged from 5.6% to 42.9% among LHINs ($p<0.0001$).

Whether or not an individual received a gastrectomy as part of their non-curative management strategy was not associated with LHIN of residence ($p=0.4823$); however, a 20% variation in receipt of a gastrectomy existed and ranged from 31.7% in the North Simcoe Muskoka region, to 52.8% in the Central West LHIN. Although this difference was not statistically different, it is still an interesting amount of variation observed across healthcare regions. Receipt of care from a high volume physician experienced in treating gastric cancer was highly dependent on LHIN of residence ($p<0.0001$). Within each LHIN, the proportion of patients receiving consultation with or care from a high volume gastric cancer specialist ranged from 0% in the North Simcoe Muskoka LHIN to 38.2% in the Toronto Central region.

Table 6: Variation of characteristics of metastatic gastric cancer patients among Local Health Integration Networks in Ontario (n=1433)

Characteristic	Variation by LHIN		p-value
	Lowest %	Highest %	

Disease Factors			
Burden of Metastatic Disease			
1 site	43.1	66.7	0.1694
> 1 site	33.3	57.0	
Tumour Location			
Distal	14.6	47.6	0.1131
Entire	4.1	17.0	
GEJ	19.4	41.8	
Middle	7.6	29.3	
Proximal	5.1	13.9	
Unknown	0	7.6	
Patient Factors			
Age Category			
<65	17.1	47.5	0.1724
65-75	9.1	41.5	
>74	25.0	54.6	
Sex			
Male	58.0	76.0	0.2227
Charlson-Deyo Score			
0	85.8	92.2	0.7542
≥ 1	7.8	14.2	
Rurality			
Rural	**0**	**42.9**	**<0.0001**
Median Community Income (n=1432)			
Lowest	**7.4**	**35.9**	**<0.0001**
2	**4.8**	**31.9**	
3	**13.2**	**36.1**	
4	**9.3**	**27.1**	
Highest	**5.6**	**42.9**	
Resource Utilization Band			
<3	2.4	13.9	0.3926
3	36.7	54.5	
4	22.0	35.4	
5	9.1	28.0	
Healthcare System Factors			
Treatment Strategy			
Gastrectomy (Yes)	31.7	52.8	0.4823
High Volume Gastric Cancer Specialist			
Consult/Treatment	**0**	**38.2**	**<0.0001**

LHIN= Local Health Integration Network; GEJ= gastroesophageal junction

4.6 Objective 2: Comparison of healthcare resource utilization among Local Health Integration Networks

Significant regional variation existed among LHINs with respect to the use of healthcare services, (Table 7) and the number of times each service was provided to individuals (Table 8). Use of ultrasound and x-ray imaging varied significantly among LHINs. Differences of 20% in utilization of ultrasound (p=0.0022) and almost 15% for x-rays (p=0.0205) were noted. Although rates of PET and MRI scan usage ranged considerably among LHINs, from 18.9 to 35.4% for PET (p=0.1090) and from 4.9 to 27.3% for MRI (p=0.2357), these regional differences were not statistically significant. These differences may not be statistically different given the overall low utilization rates for these imaging modalities in combination with the small sample sizes among LHINs.

The proportion of patients who visited an emergency department at least once was associated with LHIN of residence, ranging from 77.8 to 95.5% (p=0.0233). The smallest proportion of patients accessing emergency department services was recorded in the largely urban, densely populated Hamilton Niagara Haldimand Brant region (77.8%) and the largest proportion was in the largely remote North East region (95.5%). Of those who were seen in emergency rooms, the average number of emergency department visits also varied significantly among LHINs, ranging from 2.4 per patient in the Waterloo Wellington region of southwestern Ontario to 5.7 visits per patient in the North East region (p=0.0039). While the proportion of patients visiting a specialist (medical oncologist, surgeon, radiation oncologist) showed little variation from 98.8-100%, the average number of visits varied significantly, ranging from 43.6 visits in the lowest-use LHIN (North Simcoe Mukoka) to 83.9 visits per patient in the highest-use LHIN (Central West). Considerable variation in the number of home care visits was evident among LHINs, although not statistically significant (p=0.5528). Home care users in Toronto

Central received an average of 48.8 visits per patient, while users in the North East region received an average of 80.4 per patient.

Hospitalization was common for patients in all LHINs (ranging from 90.6-100%); however, the number of inpatient hospital days showed significant regional variation ($p=0.0040$). Individuals residing in the Hamilton Niagara Haldimand Brant region had the lowest average number of inpatient hospital days per patient (23.6 days) while patients in the North East had the highest average per patient (40.1 days). Receipt of at least one blood transfusion showed significant regional variation, ranging from 49.7% of patients in Hamilton Niagara Haldimand Brant to 68.8% of those in Waterloo Wellington ($p= 0.0266$) and the average number of blood transfusions also demonstrated significant variation by region ($p<0.0001$) - 1.6 transfusions per patient in the South East LHIN to 6.1 transfusions per patient in Toronto Central.

Rates of chemotherapy use among LHINs showed variation (less than one quarter in North Simcoe Muskoka to over half in the Central West LHIN), but differences were not statistically significant ($p=0.2349$). Use of gastrectomy as part of the non-curative management of patients was least common in the Erie St. Clair and South East regions (32.1% of patients) and most common in the Central West region (52.8% patients) ($p=0.4726$). Radiotherapy use varied significantly among LHINs ($p<0.0001$). It was used least often in the Erie St. Clair region (18.5%) and most often in the North West region (40.9%). Use of stent placement ranged from less than 2% of patients in some LHINs to 12.5% of patients in others ($p=0.0017$). Central East LHIN had the highest use of stent placement, followed by Mississauga Halton Peel region (11.5%). Due to cell sizes of less than six patients, the lowest use LHINs cannot be identified.

Table 7: Variation in the proportion of metastatic gastric cancer patients utilizing specific healthcare resources among Local Health Integration Networks in Ontario

Resource	**Variation by LHIN (%)**		**P-value**
	Lowest Use	**Highest Use**	
General Practitioner Visits	93.6	100	--
Specialist Visits	98.8	100	--
Emergency Room Visits	**77.8**	**95.5**	**0.0233**
Hospital Visits	90.6	100	0.8560
Receipt of Home care	65.9	84.7	0.2124
Upper Endoscopy	94.9	100	--
Computed Tomography	97.6	100	--
Xrays	**85.4**	**98.8**	**0.0205**
Ultrasound	**60.5**	**84.4**	**0.0022**
MRI	4.9	27.3	0.2357
PET	18.9	35.4	0.1090
Blood Transfusions	**49.7**	**68.8**	**0.0266**
Gastrectomy	32.1	52.8	0.4726
Chemotherapy	24.4	51.4	0.2349
Radiotherapy	**18.5**	**40.9**	**0.0001**
Stent Placement	**1.9**	**12.5**	**0.0017**

LHIN= Local Health Integration Network; PET= positron emission tomography; MRI= magnetic resonance imaging

Table 8: Variation in the average per patient resource utilization for healthcare resource users among Local Health Integration Networks

Resource	**Variation by LHIN (mean use per patient)**		**P-value**
	Lowest Use	**Highest Use**	
General Practitioner Visits	12.8	16.5	0.1494
Specialist Visits	**43.6**	**83.9**	**0.0025**
Emergency Room Visits	**2.4**	**5.7**	**0.0039**
Hospital Visits	**2.1**	**3.4**	**0.0024**
Inpatient Days	**23.6**	**40.1**	**0.0040**
Home Care Visits	48.8	80.4	0.5528
Endoscopy	**2.7**	**4.0**	**0.0002**
Computed Tomography	**6.5**	**10.0**	**0.0052**
Ultrasound	**3.3**	**6.3**	**0.0060**
Xrays	**6.7**	**11.9**	**0.00151**
Blood Transfusions	**1.6**	**6.1**	**<0.0001**

LHIN= Local Health Integration Network

4.7 Objective 3: Identify disease, patient, and healthcare system predictors of the number of admitted inpatient hospital days in a cohort of metastatic gastric cancer patients in Ontario.

4.7.1 Exploring the association between predictor variables and the number of inpatient hospital days

Potential associations between each variable and the number of inpatient hospital days were explored by calculating the rate of inpatient hospital days (per 100 days alive) for each category of variables (Table 9). Patients with more than one site of metastatic disease were admitted to hospital 2.2 days longer per 100 days alive than patients with one site of metastatic disease. Patients with tumours involving the entire stomach had the highest rate of inpatient hospital days across tumour locations, and were admitted for 1.69 days longer per 100 days alive than patients with a tumour in the mid-stomach, and 3.37 days longer per 100 days alive than patients with a tumour at the gastroesophageal junction.

Patients older than 74 years were admitted to hospital 1.61 days longer per 100 days alive than patients younger than 65. Similarly, patients with a greater burden of co-morbid disease (Charlson-Deyo score of >1) had a higher rate of inpatient hospital days, and were admitted to hospital for 1.72 days more per 100 days alive than patients with a score of zero. Patients in the heavy resource consumption Johns Hopkins Resource Utilization Band (RUB) group (11.33 inpatient days per 100 days alive) were in hospital 2.99 days longer per 100 days alive than those in the lowest use category. Individuals in the lowest socioeconomic quintile had the highest rate of inpatient hospital days (10.68 days per 100 days alive) among income quintiles; however, this translated into less than one additional day in comparison with the highest income quintile. Individuals living in a rural area were admitted to hospital for 2.87 days longer per 100 days alive than urban residents.

Local Health Integration Networks with the highest rates of admitted inpatient hospital days included the North Simcoe Muskoka region, with 14.99 admitted inpatient days per 100 days alive, and the North East region, with 14.35 admitted inpatient days per 100 days alive. This resulted in an additional 7.95 days in hospital for patients in the North Simcoe Muskoka region in comparison with the region with the lowest rate, and an extra week of inpatient days in the North East region (7.31 days). Patients who received a gastrectomy as part of their non-curative management strategy stayed 3.72 fewer days in hospital per 100 days alive than patients who did not undergo a gastrectomy. Patients who received care from a high volume physician experienced in the care of gastric cancer were admitted to hospital for 4.08 fewer days than patients who did not receive care from a high volume specialist.

Table 9: Rates of inpatient hospital stay per 100 days alive by category of predictor variable for metastatic gastric cancer patients in Ontario (n= 1433)

Predictor Variable	Category	Rate of inpatient hospital days (per 100 days alive)
Disease Characteristics		
Metastatic Sites	1 site	9.4
	>1 site	11.2
Tumour Location	Distal Stomach	9.8
	Gastroesophageal Junction	9.3
	Proximal Stomach	10.1
	Middle Stomach	11.0
	Entire Stomach	12.8
	Unknown	9.2
Patient Characteristics		
Sex	Male	9.06
	Female	10.55
Age Category	< 65 years	8.46
	65-74 years	9.84
	>74 years	11.07
Charlson Score	0	9.35
	1	12.59
	>1	11.02
Resource Utilization Band	0	4.89
	1	8.34

	2	7.07
	3	8.87
	4	10.36
	5	11.33
Socioeconomic Status	Lowest Income	10.68
	Quintile 2	9.90
	Quintile 3	9.17
	Quintile 4	8.36
	Highest Income	9.74
Rurality	Urban	9.31
	Rural	12.18
Health Care System Characteristics		
Local Health Integration Network	Erie St. Clair	9.91
	South West	12.16
	Waterloo Wellington	7.91
	Hamilton Niagara Haldimand Brant	7.04
	Central West	7.39
	Mississauga Halton	10.41
	Toronto Central	9.92
	Central	9.75
	Central East	8.65
	South East	11.34
	Champlain	9.80
	North Simcoe Muskoka	14.99
	North East	14.35
	North West	9.49
Treatment Strategy	No Gastrectomy	11.64
	Gastrectomy	7.92
High Volume Gastric Cancer Specialist	No consult/treatment	11.42
	Consult/treatment	7.34

4.7.2 Identifying predictors of the number of inpatient hospital days

Bivariate models were first fit for each variable, to estimate the crude association between the predictor and the number of inpatient hospital days. One patient was missing information on median community income and was excluded from this stage in analysis. The unadjusted relative risks and their 95% confidence intervals (95% CI) are reported in Table 10. Burden of metastatic disease (p= 0.0273), tumour location (p= 0.0004), sex (p=0.0162), age (p <0.0001), RUB (p= 0.0107), treatment by gastrectomy (p <0.0001) and care from a high volume gastric cancer specialist (p<0.0001) were all significantly associated with the number of inpatient hospital days. Individuals with a greater burden of metastatic disease spent significantly more days in hospital (RR= 1.19; 95% CI: 1.02-1.38). Compared to individuals with tumours in the distal stomach, people with tumours at the gastroesophageal junction spent significantly fewer days in hospital (RR= 0.81; 95% CI: 0.67-0.99) and individuals with unknown tumour locations spent 1.7 times more days in hospital (95% CI: 1.14-2.55).

Females spent significantly more time in hospital (RR=1.21; 95% CI: 1.04-1.42), as did patients 75 years and older, who spent 1.48 times as many days in hospital compared to those younger than 65 years (95% CI: 1.24-1.77). Hopkins RUB was significantly associated with the number of admitted hospital days; however, the sample sizes in the low-user categories were quite small, resulting in wide confidence intervals for the effect estimates. A pattern of increased use was not observed comparing the categories of RUB to the lowest use (score of 1); however, a statistically significant association existed.

Local Health Integration Networks were not associated with the number of inpatient hospital days. It should be noted that the Central West LHIN had significantly fewer inpatient hospital days in comparison with the reference LHIN (Hamilton Niagara Haldimand Brant), with a relative risk of 0.60 (95% CI: 0.40-0.91); however, small sample sizes in the high-user LHINs may explain the wide confidence intervals, as well as the lack of statistical association between LHIN and number of inpatient hospital days.

The other two healthcare system predictors were highly significant in their relationship with the outcome. Receipt of gastrectomy had a significant protective effect on the number of days spent in hospital (RR 0.59, 95% CI: 0.51-0.69), as did receipt of care from a high volume gastric cancer specialist (RR 0.47, 95% CI: 0.40-0.55).

Table 10: Association between predictor variables and the number of inpatient hospital days for metastatic gastric cancer patients in Ontario (n= 1433)

Predictor	Inpatient Hospital Days		p-value
	Unadjusted RR*	95% CI	
Disease Characteristics			
Metastatic Sites			
1	reference		**0.0273**
>1	**1.19**	**1.02-1.38**	
Tumour Location			
Distal Stomach	reference		**0.0004**
Gastroesophageal Junction	**0.81**	**0.67-0.99**	
Proximal Stomach	0.87	0.66-1.14	
Middle Stomach	1.14	0.91-1.43	
Entire Stomach	1.25	0.95-1.65	
Unknown	**1.71**	**1.14-2.55**	
Patient Characteristics			
Male	reference		**0.0162**
Female	**1.21**	**1.04-1.42**	
Age Category			
<65	reference		**<0.0001**
65-74	1.14	0.95-1.37	
>74	**1.48**	**1.24-1.77**	
Resource Utilization Band			
0	0.85	0.28-2.60	**0.0107**
1	reference		
2	0.44	0.19-1.03	
3	0.70	0.33-1.51	
4	0.78	0.36-1.70	
5	0.91	0.42-1.98	
Socioeconomic status (n=1432)			
Lowest Income	reference		0.2348
Quintile 2	0.85	0.67-1.06	
Quintile 3	0.91	0.72-1.15	
Quintile 4	0.96	0.75-1.23	
Highest Income	**0.77**	**0.60-0.98**	
Rurality			
Urban	reference		0.3265
Rural	1.13	0.89-1.43	
Health Care System Characteristics			
Local Health Integration Network			
Erie St. Clair	1.21	0.82-1.80	0.5118
South West	0.98	0.66-1.45	
Waterloo Wellington	0.95	0.64-1.43	
Hamilton Niagara Haldimand Brant	reference		

Central West	**0.60**	**0.40-0.91**	
Mississauga Halton	1.09	0.77-1.54	
Toronto Central	0.95	0.69-1.32	
Central	1.02	0.75-1.39	
Central East	1.08	0.78-1.50	
South East	1.09	0.69-1.71	
Champlain	0.94	0.67-1.33	
North Simcoe Muskoka	1.23	0.74-2.04	
North East	1.13	0.76-1.68	
North West	0.83	0.43-1.61	
Treatment Strategy			
No Gastrectomy	reference		**<0.0001**
Gastrectomy	**0.59**	**0.51-0.69**	
High Volume Gastric Cancer Specialist			
No consult/treatment	reference		
Consult/treatment	**0.47**	**0.40-0.55**	**<0.0001**

RR= relative risk; CI= confidence interval; *Univariate negative binomial regression with an offset

To assess the possibility of confounding by the number of days survived within the time period, associations were also investigated between the predictors of interest and the number of days alive within the time horizon, and the full results are presented in Appendix C. Sex, RUB and socioeconomic status were the only predictor variables not significantly associated with number of days alive in the time horizon. A relationship between the proportion of admitted inpatient hospital days and the number of days alive was also investigated (Appendix D), and a significant difference in the mean number of inpatient hospitals days was observed ($p<0.0001$) between categories. As a patient lived longer, they spent a smaller proportion of their days alive, admitted to hospital. Patients who died more quickly spent a larger proportion of their time following diagnosis admitted to hospital ranged from 80% of days alive spent in hospital for those surviving 30 days or less, to 3% for those surviving 730 days or more.

Multivariate analysis using negative binomial regression was performed. Model fit statistics leading to the choice of negative binomial for the model building and final model are provided in Table 11. The deviance statistics and the overdispersion parameters in the negative binomial model were dramatically lower than those observed when the Poisson distribution was performed. The final values of the deviance statistics were lower in the final model than the null model, and the dispersion parameter was close to one, approximating an acceptable fit of the model. The potential for missing predictors from the model may explain the remaining unexplained variance.

Table 11: Model selection and fit statistics comparing the null and full models, for those created using general linear modeling with Poisson and negative binomial distributions

Model[1]	Distribution	Deviance[2]	Deviance/DF[3]	Scale/Dispersion[4]
Null	Poisson Log	1726366.4685	1206.4056	34.7212
Final	Poisson Log	1701449.6515	1199.0484	34.67
Null	Negative binomial Log	1762.6082	1.2317	1.6086
Final	Negative binomial Log	1733.7470	1.2218	1.4743

1= an offset variables was included in both the null and final models; 2= smaller is better; 3= close to 1 is better; 4= close to 1 is better: values higher than one indicates overdispersion and values lower than one indicate underdispersion

On multivariate analysis, tumour location (p<0.0001), RUB (p=0.0270), treatment strategy (p<0.0001) and whether an individual received care from a high volume gastric cancer specialist (p<0.0001) remained independent predictors of the number of inpatient hospital days (Table 12), implying that disease, patient and healthcare system factors contribute to explaining variation in the number of days patients with metastatic gastric cancer spend in hospital. Having a tumour located at the gastroesophageal junction or in the proximal stomach, undergoing gastrectomy or having care from a high volume gastric cancer specialist, all predicted spending significantly fewer days admitted to hospital. Compared to patients with a distal tumour, patients with a gastroesophageal tumour spent fewer days in hospital (RR= 0.76; 95% CI: 0.63-0.92), as did patients with tumours in the proximal stomach (RR= 0.74; 95%CI: 0.57-0.97). Patients with unknown tumour locations had an increased risk of spending more days in hospital in comparison with patients with a distal tumour location (RR 1.48; 95%CI: 1.00-2.19); although, this did not reach statistical significance. It should be noted that the Unknown category of tumour location contained the smallest number of patients. Patients categorized in the second (RR= 0.95; 95% CI: 0.42-0.83) and third (RR= 0.81; 95% CI: 0.68-0.96) RUB (medium consumers of healthcare resources) had a significantly lower risk of accumulating inpatient hospital days than the highest quintile. This trend was also observed in the lowest RUB categories; however, they were not significantly different, likely due to the small numbers of patients in each low use category. Undergoing a gastrectomy and receipt of care from a high volume specialist both remained strongly protective against spending more days in hospital ($p<0.0001$) after adjustment for all variables in the model. Patients who underwent a gastrectomy were almost 35% less likely to accumulate inpatient hospital days (RR 0.66; 95% CI: 0.56-0.77). Patients who received care from a high volume specialist experienced in gastric cancer care were 44% less likely to spend days admitted to hospital (RR 0.54; 95%CI: 0.46-0.63).

Table 12: Predictors of number of inpatient hospital days for metastatic gastric cancer patients in Ontario (n= 1433)

Predictor	Inpatient Hospital Days		p-value
	Adjusted RR*	**95% CI**	
Disease Characteristics			
Tumour Location			
Distal Stomach	reference		**<0.0001**
Gastroesophageal Junction	**0.76**	**0.63-0.92**	
Proximal Stomach	**0.74**	**0.57-0.97**	
Middle Stomach	1.04	0.84-1.30	
Entire Stomach	1.15	0.88-1.51	
Unknown	1.48	1.00-2.19	
Patient Characteristics			
Hopkins Resource Utilization Band			
0	0.88	0.42-1.84	**0.0270**
1	1.06	0.54-2.07	
2	**0.95**	**0.42-0.83**	
3	**0.81**	**0.68-0.96**	
4	0.92	0.76-1.11	
5	reference		
Health Care System Characteristics			
Treatment Strategy			
No Gastrectomy	reference		**<0.0001**
Gastrectomy	**0.66**	**0.56-0.77**	
High Volume Gastric Cancer Specialist			
No consult/treatment	reference		**<0.0001**
Consult/treatment	**0.54**	**0.46-0.63**	

RR= relative risk; CI= confidence interval; *Negative binomial regression adjusting for all variables in the model with an offset

4.8 Objective 3: Identify disease, patient, and healthcare system predictors of the receipt of at least one home care visit in a cohort of metastatic gastric cancer patients in Ontario.

4.8.1 Exploring the association between predictor variables and receipt of at least one home care visit

Overall, 77.5% of patients with metastatic gastric cancer were recipients of at least one home care service. Comparing proportions of patients who received at least one home care visit among disease-related predictors, the burden of metastatic disease was not associated with receipt of a home care visit (p=0.8619); however, the proportion of patients receiving a home care visit was significantly different among tumour locations (p=0.0032), and ranged between 68% of patients who had an unknown tumour location to 84% of patients with a tumour located at the gastroesophageal junction (Table 13).

The proportion of patients receiving at least one home care visit did not differ by the majority of patient factors, including sex (p= 0.8682), burden of co-morbid disease (p= 0.3391), socioeconomic status (p= 0.3767), and rural residence (p= 0.9791). The proportion of patients receiving home care did vary significantly between the age categories (p=0.0006). Eighty-two percent of patients aged 65-74 received home care, while only 72% of patients 75 and older and 77% of patients 64 and younger used a home care service. Home care use among Hopkins RUB categories was also significantly different (p=0.0182). A trend towards increased use was observed across the low to heavy usage categories; 47% of patients in the lowest user group (RUB=1) received home care versus 79% in the highest user group (RUB=5).

The only healthcare system factor that varied significantly in the proportion of patients who received home care, was care from a high volume specialist experienced in gastric cancer care (p <0.0001). Patients who received care from a high volume specialist were more likely to receive home care (88%) than patients who did not (72%). Use of home care was similar among Local Health Integration Networks (p=0.2124) and not different based on whether or not the patient received a gastrectomy (p= 0.0937).

Table 13: Association between predictor variables and receipt of at least one home care visit for metastatic gastric cancer patients in Ontario (n=1433)

Predictor	Receipt of home care (%)		p-value
	Yes	No	
Disease Characteristic			
Metastatic Sites			
1	78	22	0.8619
>1	77	23	
Tumour Location			
Gastroesophageal Junction	**84**	**16**	**0.0032**
Proximal Stomach	**78**	**22**	
Middle Stomach	**78**	**22**	
Distal Stomach	**74**	**26**	
Entire Stomach	**76**	**24**	
Unknown	**68**	**32**	
Patient Characteristics			
Gender			
Female	78	22	0.8682
Male	77	23	
Age			
<65	**77**	**23**	**0.0006**
65-74	**82**	**18**	
>74	**72**	**28**	
Charlson-Deyo Score			
0	78	22	0.3391
1	72	28	
>1	82	18	
Hopkins Resource Utilization Band			
0	**58**	**42**	**0.0182**
1	**47**	**53**	
2	**84**	**16**	
3	**76**	**24**	
4	**79**	**21**	
5	**79**	**21**	
Median Community Income			
Lowest Median Income	76	24	0.3767
Quintile 2	80	20	
Quintile 3	77	23	

Quintile 4	74	26	
Highest Median Income	80	20	
Rurality			
Rural	77.4	22.6	0.9741
Urban	77.5	22.5	
Health Care System Characteristics			
Local Health Integration Network			
Erie St. Clair	84	16	0.2124
South West	82	18	
Waterloo Wellington	79	21	
Hamilton Niagara Haldimand Brant	83	17	
Central West	85	15	
Mississauga Halton	72	28	
Toronto Central	76	24	
Central	73	27	
Central East	78	22	
South East	81	19	
Champlain	77	23	
North Simcoe Muskoka	66	34	
North East	74	26	
North West	73	27	
Treatment Strategy			
No Gastrectomy	76	24	0.0937
Gastrectomy	80	20	
High Volume Gastric Cancer Specialist			
No consult/treatment	**72**	**28**	**<0.0001**
Consult/treatment	**88**	**12**	

4.8.2 Identifying predictors of the receipt of home care

Bivariate unadjusted modified Poisson models were fit for each disease, patient and healthcare predictor variable, to estimate the crude relative risk of receiving at least one home care visit (Table 14). Individuals with one site of metastatic disease had a similar likelihood of receiving home care as individuals who had more than one site of metastatic disease. Tumour location was a significant disease-level predictor of receipt of home care. Patients with a tumour in the gastroesophageal junction were more likely to receive home care (RR 1.15, 95%CI: 1.07-1.23) than patients with a distal tumour.

Females and males had a similar likelihood of receiving a home care visit (RR 1.00; 95%CI: 0.95-1.06). Similarly, RUB was not significantly associated with receipt of home care. The three higher use categories did demonstrate an increased likelihood of receiving home care, although this was not statistically significant. This may be a reflection of small sample sizes in the low use categories, rather than a true lack of association. Compared with individuals in the lowest income quintile, individuals in all other income categories had a similar likelihood of receiving home care. Similarly, individuals residing in a rural residence did not have a significantly different likelihood of receiving home care than individuals residing in an urban residence.

LHIN of residence was not significantly associated with receipt of home care (p=0.2240), nor was receipt of a gastrectomy (p=0.0955). Individuals who received care from a high volume gastric cancer specialist were 22% more likely to receive a home care visit (95%CI: 1.16-1.29) than patients who did not receive care from a high volume specialist.

Table 14: Associations between predictor variables and the receipt of at least one home care visit for metastatic gastric cancer patients in Ontario (n=1433)

Predictor	**Receipt of home care**		**p-value**
	Unadjusted RR*	**95% CI**	
Disease Characteristics			
Metastatic Sites			
1	reference		0.9021
>1	1.00	0.94-1.05	
Tumour Location			
Distal Stomach	reference		**0.0016**
Gastroesophageal Junction	**1.15**	**1.07-1.23**	
Proximal Stomach	1.06	0.95-1.17	
Middle Stomach	1.06	0.97-1.15	
Entire Stomach	1.04	0.93-1.15	
Unknown	0.92	0.77-1.10	
Patient Characteristics			
Male	reference		0.8697
Female	1.00	0.95-1.06	

Age Category			
<65	reference		**0.0007**
65-74	0.94	0.88-1.00	
>74	**0.88**	**0.82-0.94**	
Resource Utilization Band			
0	1.25	0.61-2.57	0.1134
1	reference		
2	1.80	1.04-3.13	
3	1.64	0.95-2.82	
4	1.69	0.98-2.92	
5	1.69	0.98-2.91	
Socioeconomic status			
Lowest Income	reference		0.3813
Quintile 2	1.06	0.97-1.15	
Quintile 3	1.02	0.94-1.12	
Quintile 4	0.98	0.89-1.08	
Highest Income	1.06	0.97-1.15	
Rurality			
Urban	reference		0.9147
Rural	1.00	0.92-1.10	
Health Care System Characteristics			
Local Health Integration Network			
Erie St. Clair	1.02	0.90-1.14	0.2240
South West	1.00	0.88-1.13	
Waterloo Wellington	0.96	0.84-1.10	
Hamilton Niagara Haldimand Brant	reference		
Central West	1.02	0.91-1.16	
Mississauga Halton	0.87	0.77-0.99	
Toronto Central	0.92	0.82-1.03	
Central	0.88	0.79-0.98	
Central East	0.94	0.84-1.05	
South East	0.98	0.85-1.14	
Champlain	0.93	0.83-1.05	
North Simcoe Muskoka	0.80	0.63-1.00	
North East	0.90	0.78-1.04	
North West	0.92	0.72-1.18	
Treatment Strategy			
No Gastrectomy	reference		0.0955
Gastrectomy	1.05	0.99-1.11	
High Volume Gastric Cancer Specialist			
No consult/treatment	reference		
Consult/treatment	**1.22**	**1.16-1.29**	**<0.0001**

RR= relative risk; CI= confidence interval; *Univariate modified Poisson regression

A possible relationship between the number of days a patient lived within the two year horizon following diagnosis, and receipt of home care was investigated to determine whether or not it should be included as a covariate in the multivariate analysis. Patients who received home care survived a median of 228 days (95% CI: 206-246), while those who did not receive home care survived a median of 66 days (95% CI: 55-75). A breakdown of home care use across survival times is presented in Appendix E. Individuals who lived longer had an increasing chance of receiving home care, and the results of the Cochran-Armitage test for trend confirmed a positive linear relationship ($p<0.0001$); therefore, the number of days survived in the time frame was modeled as a continuous variable in the multivariate regression.

Final multivariate analysis was performed using modified Poisson regression with robust error variance estimation. Using logistic regression, the same variables were identified as being significant independent predictors, at similar p-values. When Poisson regression was used, the same independent predictors emerged as expected, and the odds ratios calculated in the logistic regression systematically overestimated the true relative risks. On final multivariate analysis, disease, patient and healthcare system variables were all significant contributors in predicting a home care visit (Table 15). Individuals with a tumour at the gastroesophageal junction were significantly more likely to receive home care than individuals with a distal tumour (RR=1.12; 95% CI: 1.05-1.19). Patients seeing a high volume specialist were 15% more likely to receive home care than those who did not see a high volume specialist (RR 1.15; 95% CI: 1.09-1.20). Patients who died less than one month after diagnosis were 58% less likely to receive a home care visit (RR=0.42; 95% CI: 0.33-0.53) than those patients who lived between 31 and 729 days. Details of the model selection process and presentation of the quasilikelihood criteria statistics for model fit for the null and final model are provided in Table 16.

Table 15: Predictors of receipt of at least one home care visit for metastatic gastric cancer patients in Ontario (n=1433)

Predictor	Receipt of home care Adjusted RR*	95% CI	p-value
Disease Characteristics			
Tumour Location			
Distal Stomach	reference		**0.0133**
Gastroesophageal Junction	**1.12**	**1.05-1.19**	
Proximal Stomach	1.06	0.96-1.16	
Middle Stomach	1.07	1.00-1.18	
Entire Stomach	1.04	0.94-1.16	
Unknown	0.96	0.88-1.13	
Patient Characteristics			
Health Care System Characteristics			
High Volume Gastric Cancer Specialist			
No consult/treatment	reference		
Consult/treatment	**1.15**	**1.09-1.20**	**<0.0001**
Covariates			
Days alive			
per 180 days	**1.04**	**1.02-1.06**	**0.0001**
≤ 30 days	**0.42**	**0.33-0.53**	
31-730 days	reference		

RR= relative risk; CI= confidence interval; *Modified Poisson regression adjusting for all variables in the model

Table 16: Model selection and fit statistics comparing the null and full models, for those created using modified Poisson regression with robust error variance

Model	QIC[1,2]	QICu[3]
Null	12358.0328	12358.0342
Final	12249.5814	12249.7744

1= Quasilikelihood criterion; 2= smaller is better; 3= adjusted Quasilikelihood criterion; 4= smaller is better

Chapter 5

Discussion and Conclusions

5.1 Introduction

A summary and discussion of study findings, limitations, strengths, and contributions, and the direction of further research follow in this chapter. A summary of the study objectives and key findings are outlined in Section 5.2, and a discussion of the key findings in the context of existing research is presented in Section 5.3. Study limitations (Section 5.4) and strengths (Section 5.5) are reviewed, followed by a summary of the study contributions (Section 5.6) and a discussion of future research directions (Section 5.6).

5.2 Summary of Study Objectives and Key Findings

Patients with metastatic disease made up almost 60% of gastric cancer cases recorded in the Ontario Cancer Registry between April 1, 2005 and March 31, 2008 (n=2516). Prognosis in these patients was poor, with median survival of only 6 months. The majority of patients with metastatic disease presented with the primary tumour in the distal stomach; just under half of patients presented with more than one site of metastatic disease. Geographic variation exists among Local Health Integration Networks (LHINs) with respect to the distribution of patients in the five median income quintiles, the proportion of patients with a rural residence and the proportion of patients who visit a high volume surgeon, medical oncologist or radiation oncologist. The remainder of disease, patient and healthcare system characteristics described in this study did not demonstrate significant geographic variation.

Healthcare resource utilization was measured in a two year, two month time frame that captured the two months preceding diagnosis and the two years following diagnosis, or until death, whichever was earliest. Medical imaging, physician contacts, emergency room visits, hospitalizations, home care, treatment modalities (e.g. surgery, chemotherapy, radiotherapy) and other relevant clinical outcomes (e.g. upper endoscopy, blood transfusions) were measured during this time frame. None of the patients had zero health system contacts. Geographic variation in the use of most healthcare services and the frequency of use was demonstrated, with significant variation in the proportion and frequency of emergency room visits, receipt of imaging, blood transfusions, use of stent placement and radiotherapy. Rates of home care use, chemotherapy use and gastrectomy were not significantly different, although a large degree of variation still existed. Statistically significant variation in the average number of all radiological scans, number of specialist, emergency room, and hospital visits, as well as the average number of upper endoscopies per patient existed.

Disease, patient and healthcare system factors were identified as being predictive of both inpatient hospital days and the receipt of at least one home care visit, within the time horizon, after controlling for the confounding affect of individual patient survival within the time period. Primary tumour location was a significant predictor of the length of time spent as an inpatient. Patients with a tumour located at the gastroesophageal junction were at a significantly reduced risk of spending time admitted to hospital (RR= 0.76; 95% CI: 0.63-0.92), and were significantly more likely to receive at least one home care visit (RR= 1.15; 95% CI: 1.07-1.23).

Receipt of care from a high volume specialist experienced in gastric cancer management (seeing either a high volume surgeon, medical oncologist or radiation oncologist) was significantly associated with fewer days spent admitted to hospital (RR= 0.54; 95% CI: 0.46-0.63) and with a higher likelihood of receiving at least one home care visit (RR= 1.15; 95% CI: 1.09-1.20). Patients who underwent a gastrectomy as part of their non-curative management had a significantly lower risk of accumulating inpatient hospital days (RR= 0.66; 95% CI: 0.56-0.77), but this did not translate into a significant association with use of home care services. Similarly, Hopkins Resource Utilization Band (RUB) was a significant predictor of the number of inpatient hospital days, but not for the receipt of home care. None of the other disease, patient or healthcare system factors were independent predictors of the number of inpatient hospital days or receipt of home care, although significant bivariate associations were documented.

5.3 Discussion of Key Findings

Regional Variation in Healthcare Resource Utilization

Resource utilization associated with the care of metastatic gastric cancer patients varied across Local Health Integration Networks (LHINs) in Ontario. Geographic variation in practice patterns is common when clear standards of care do not exist for treatment of a disease, or if resources are limited or unavailable and alternative measures are required.[94,97,105,140-143] Even in the presence of clear recommendations for clinical care, rates of uptake of clinical guidelines may be greatly influenced by geographic location and system characteristics.[95,143] Cancer Care Ontario tracks and compared a number of quality care indicators related to surgery, chemotherapy and radiotherapy utilization, as well as emergency room use and inpatient stay at the end of life for healthcare regions across the province.[91] Initiatives exist to decrease variation between LHINs that results from barriers to access to treatment modalities or to specialists and to improve the quality of cancer care provided in Ontario.[91] In this study, utilization rates differed more than 10% for the majority of measures, including emergency room visits, receipt of home care, blood transfusions, use of x-ray, ultrasound, MRI and PET imaging and the major classes of treatment modalities (gastrectomy, chemotherapy and radiotherapy), even if not all reached statistical significance. Defining variation that is clinically significant or important at the policy-level, and separating it from non-meaningful differences that may be statistically significant or variation that results from small numbers in one geographic area is necessary to set at the policy-level, to better understand what these differences mean for patients in the numerous healthcare regions.

The cohort is entirely stage IV disease, meaning almost all patients will die quickly and without hope of curative treatment. The relationship between practice variation and differences in healthcare resource utilization is important if these differences are related to clinical outcomes for the patient. The differences in utilization identified in this project may indicate areas to investigate and if negative health outcomes are the product of these differences, approaches may be needed to improve the quality of care and to make access to effective treatment equal across the province. An understanding of why variations exist (e.g. patient preferences, physician preferences, and barriers to accessing care) and how they impact on quality of life, symptom relief and survival for the metastatic gastric cancer population is necessary. This population-based description of differences that exist is hypothesis-generating, leaving room for the exploration of factors predicting both differences in healthcare utilization and clinical outcomes.

Predictors of Inpatient Hospital Days and Home Care Use

Inpatient hospital days are a major cost driver to the healthcare system. Hospitalization and inpatient stay in the six months preceding death from cancer has been suggested as an indicator of aggressive end of life care,[110-113,144] and may be a greater economic burden to the healthcare system than the use of other sites for the provision of palliative care services.[119] Insight into the predictors of hospital inpatient bed use may help formulate policy to improve the efficiency of the healthcare system, if these factors do not negatively impact patient outcomes when modified. Home care use has been advocated as a more effective and efficient means of addressing patient symptoms and needs at end-of-life, while decreasing the number of hospitalizations and days spent in hospital.[108,109,122,123] Similarly, understanding the predictors of home care use may help decision-makers target areas for further efficiency at the healthcare system level, or interventions aimed at reducing barriers to accessing care at the patient level.

Primary Tumour Location

The location of the primary tumour when the patient presents with metastatic disease is not a modifiable factor to reduce inpatient hospital stay, but was a significant predictor of both the number of inpatient hospital days and the receipt of at least one home care visit. Tumours at the gastroesophageal junction predicted a lower rate of admitted hospital days and an increased likelihood of home care use, in comparison with tumours in the distal stomach. Differences in the cost of gastric cancer treatment by primary tumour location have been described. Kuwabara et al. reported the mean costs of treating primary gastric cancers in Japan, for tumours located in the fundus (15,612.41US$: year unavailable), in the body (11,629.71 US$: year unavailable) and in the antrum (12,985.75US$: year unavailable).[58] Differences in the mean costs per patient were not compared statistically, although tumours in the fundus (higher in the stomach) appeared to be more costly than tumours in the mid- (body) and distal (antrum) stomach.

These differences in healthcare resource utilization may be logical, since tumour location and associated symptoms dictate the clinical management of gastric cancer.[40] Patients with tumours higher in the stomach (at the gastroesophageal junction or proximal stomach) may be more likely to receive radiotherapy or have stent placement (congruent with management of unresectable esophageal cancer) and less likely to be considered candidates for surgery. Tumours of the distal stomach may be more amenable to subtotal gastrectomy and chemotherapy, with the complications associated with these treatments.[29,145] Furthermore, surgical resection of tumours involving the esophagus should involve a thoracic surgeon and should be performed within a designated institution meeting the minimum requirements for thoracic oncologic surgery mandated by Cancer Care Ontario. The involvement of a highly experienced thoracic surgeon, within these optimal settings may reduce the occurrence of complications during the procedure and the length of stay.

Measures of Co-morbidity: Hopkins and Charlson-Deyo Scores

Incorporation of a measure of co-morbidity has been well documented as being important in the prediction of resource utilization and costs,[146,147] although the optimal scoring system or measure is undetermined. A review of the literature supporting the available measures of co-morbidity for the prediction of clinical and economic outcomes indicated that the Charlson-Deyo score was overall better at predicting mortality than costs, and the Hopkins Resource Utilization Band was better at predicting resource utilization and costs than other morbidities; but also concluded that either method would be acceptable for predicting clinical and economic outcomes.[148] Accordingly, both of these measures have been used often in studies evaluating predictors of economic endpoints.

The Charlson-Deyo scores for this cohort did not measure comorbidity in a way that categorized of patients into separate, useful categories and it lacked predictive power in the models built to predict the number of inpatient hospital days or home care use. While the Charlson-Deyo score has been used successfully to predict costs in other studies, the lack of differentiation between levels of morbidity in the gastric cancer population may be at fault. Within an advanced cancer, hospice-using population, Charlson-Deyo score has been identified as an independent predictor of hospitalizations, emergency department visits and intensive care unit admissions.[149] In this study however, 33% of patients fell into the severe co-morbidity category (score of ≥ 2), while in this thesis, only 5% of the cohort fell into that category.[149]

The Hopkins RUB model categorized half of the metastatic gastric cancer population in this thesis into moderate to heavy user categories, and we considered it a better measure of the differences in multimorbidity as it relates to resource utilization. Resource utilization bands adjust for differences in healthcare utilization that relate to the extent of co-morbidity, incorporating predicted differences in resource utilization that would occur between genders and across age categories.[147] In this study, if RUB was a significant predictor of an outcome, age and sex would not be expected to be independent predictors of the outcomes. Models built to predict cost have demonstrated that when RUB is included, adding age and sex only marginally increase the amount of explained variation.[146] While dividing patients into quintiles based on their predicted resource utilization does indeed predict some measures of healthcare use, understanding the contribution of burden of co-morbid illness, age and sex separate from one another may identify targets for interventions to improve access to specific healthcare services for specific subpopulations, or to reduce the amount of inappropriate services. Further work may consider building separate models without the RUB measure, to understand the independent effects of age and gender on resource utilization.

Resource utilization quintiles did predict the cumulative length of stay in hospital over the time period, but not receipt of a home care visit. Home care use may have been largely influenced by hospitalization rates and survival time, as patients who survived longer were more likely to receive home care, and spent a smaller proportion of their time alive, in hospital. Therefore, the influence of other predictors that traditionally predict resource utilization use may have become less important. If the analysis had been performed to predict the number of home care visits, rather than receipt of care, other predictors such as the RUB measure may have emerged as independent predictors. Furthermore, RUB categories were developed to predict low to heavy usage of services, rather than whether or not a service was used, and this difference in outcome may also explain why RUB was not a independent predictor of the receipt of a home care visit. Future analysis should include the number of inpatient hospitals days in the model, to see if hospitalizations predict use of home care in this population.

Receipt of Gastrectomy

Patients who received a gastrectomy had a reduced risk for spending time as an inpatient, after controlling for the effects of primary tumour location, RUB, care from a high volume physician and survival. While receipt of gastrectomy is an independent, modifiable predictor of inpatient hospital days, it does not mean that providing this management strategy to all patients will reduce the number of days spent in hospital. The decision to resect the primary tumour is likely related to a number of patient, disease and physician factors. Patients must first be healthy enough to withstand surgery and its risks must not outweigh its possible benefits. Additionally, in patients with carcinomatosis, a large burden of metastases and/or multiple sites of metastatic disease, surgery may not be a safe option. Non-curative resection is still commonly debated in the literature for its utility. Although data do show that patients who receive a gastrectomy have better survival, all studies are retrospective, and heavily influenced by selection bias. Confounding by underlying patient characteristics not captured by administrative data, likely explain this benefit – patients undergoing gastrectomy likely have fewer sites of metastatic disease, sites of metastatic disease more amenable to surgical resection and better performance status. These factors may also predict fewer days in hospital subsequently.

High Volume Specialist in Gastric Cancer Management

Receipt of care from a high volume physician is a potentially modifiable factor that was a significant independent predictor of both the number of inpatient hospital days and receipt of home care. Patients who received care from either a surgeon, medical oncologist or radiation oncologist who treated a high volume of gastric cancer patients each year were much less likely to spend time admitted to hospital than individuals who did not, after adjustment for primary tumour location, whether or not they received a gastrectomy, their RUB quintile and the number of days they survived within the time horizon.

Volume is considered to be a proxy measure of physician experience and knowledge of a procedure or disease.[150,151] To categorize a high volume practitioner, patients were categorized by physician volume such that equal terciles of patients were created. Each high volume category contained one third of patients treated in that specialty for gastric cancer over the seven year period. This method of classifying institution and physician volume has been used previously in the gastric cancer surgical literature.[93] Other methods include creating quartiles or quintiles of patients to further discriminate volume categories, or plotting patient volumes for physicians or institutions and inspecting the data for natural cut-points.

One third of gastric cancer patients in Ontario were operated on by physicians who performed 2.3-6.8 gastrectomies per year. This categorization of high volume is not congruent with other low incidence countries, which consider high volume surgeons to perform anywhere from 6 or more procedures a year, to 13 or more procedures per year.[93] However, this category of physicians still treated one third of gastric cancer patients in Ontario, which is an interesting point of discussion—two thirds of gastric cancer patients are operated on by a surgeon who performs fewer than 2.3 operations as a primary surgeon, per year. While these numbers reflect practice patterns in Ontario, it is possible that this wide classification of high volume has attenuated the association identified between receipt of care from a high volume physician (surgeon, medical oncologist or radiation oncologist) and the number of inpatient hospital days and home care use.

The classification of surgeons into the high volume category would not have happened differentially between outcomes, and biased the potential effect of physician volume toward the null. Because physician volume still emerged as an independent predictor of resource use, it is possible that applying a more strict definition of surgeon volume (e.g. using quintiles instead of terciles) may result in a greater magnitude of effect. Future work will include re-conceptualizing this variable to better understand the role of truly high volume surgeons on resource utilization outcomes.

Length of hospital stay and subsequent costs of gastric cancer surgery have been associated with high hospital volume in the literature. Lee et al.(2011) performed a study in South Korea to compare the costs and length of stay associated with gastrectomy for gastric cancer between very high volume institutions (defined as >652 gastrectomies per year) and very low volume institutions (<95 gastrectomies per year).[152] Higher volume hospitals had shorter mean lengths of stay in hospital following subtotal and total gastrectomies than lowest volume hospitals (p<0.0001) and high hospital volume remained a significant predictor of length of stay after adjustment for patient case-mix.[152] The components of how a surgeon's annual operative volume influences resource utilization outcomes has not been elucidated, and requires further research.

Care from any specialist experienced in gastric cancer management, as evidenced by billing for a high volume of gastric cancer related treatments and consults, may be indicative of the appropriate involvement of a multidisciplinary team. Centralization of gastric cancer care has been debated, stemming from the complexity of its surgical treatment and the potential improvements in clinical outcomes if care was provided at high volume institutions.[93] While an inconsistent reduction in surgical mortality has been documented along with possible improvements in long-term survival, the argument has not resulted in a similar healthcare policy reform as has occurred with thoracic and pancreatic cancer surgery in Ontario. Provincial policy-makers have set minimum case-loads and institutional requirements for approved performance of operations for lung, esophageal and pancreatic cancer patients.[91] While centralization is one potentially modifiable way to address differences in healthcare resource utilization and clinical outcomes, the inclusion of a high volume physician in decision-making may also be achieved through the use of video-assisted consults or other methods utilizing information technology to avoid barriers such as large geographic regions, rare cancers and patient preferences.

5.4 Study Limitations and Strengths

Data Quality

Administrative data captured at the national and provincial levels are vulnerable to issues in coding and reporting that may influence the validity of study results. Acknowledging potential limitations with the validity and reliability of data sources used for administrative data analyses is important when interpreting results from studies using these data. The Canadian Institute for Health Information, in partnership with hospitals across the country and province, has been active in monitoring and improving national data quality.[153-157] Since 2005, yearly reports have been produced on the National Ambulatory Care Reporting System (NACRS) and the Discharge Abstract Database (DAD), documenting the results of re-abstraction studies (where the original charts are re-coded by a separate set of professionals and their results compared). Across the board, improvements have been documented in the DAD over time.[153] For example, since 2005 the reporting of interventions has improved from a national average of 85% of interventions captured in the DAD being confirmed in the chart, to 96% in 2008.[153] In Ontario specifically, the rate of improvement is even greater, with only 80% of interventions coded in the DAD being confirmed on chart review in 2005, increasing to 95% in 2008.[153]

Data elements with the highest agreement include demographic and institution-related variables, in both the NACRS and DAD.[156] In Ontario, gender was recorded reliably in the DAD in 100% of cases examined in a re-abstraction project lead by the Institute for Clinical Evaluative Sciences, and birth date 99.9% of the time.[157]

The reliability of reporting diagnostic and therapeutic interventions and procedures has been studied in the DAD.[153,154] Diagnostic digestive procedures specifically are not well reported in Ontario, with only 81% of procedures in the DAD being found in the chart on re-abstraction. Examining the situation in the reverse direction, 87% of diagnostic digestive procedures that were documented in the chart were also found in the DAD. These data indicate that the capture of diagnostic digestive procedures in the DAD may not be consistent, and that alternate sources may be required to ensure that procedures are not over- or under-reported.[153,154] For therapeutic digestive procedures captured in the DAD, there was 93% agreement with chart re-abstraction; however, of those captured from the original charts, only 78% were in the DAD.[153,154] These figures indicate that the DAD reporting is incomplete and may underestimate the true number and types of procedures performed.[153,154] For this project, data for endoscopy and radiology investigations were taken only from the chart review and Ontario Health Insurance Plan (OHIP) billing codes, because the capture of these diagnostic procedures is incomplete in the DAD. Therapeutic digestive procedures related to cancer-directed treatments, such as gastrectomy were primarily identified using OHIP billing codes as well, for the same reason.

Variation in capturing procedures and interventions may influence the number and types of procedures documented as being used by the metastatic gastric cancer population in this thesis.

While the degree of over and under reporting was dependent on the individual hospital sampled, it is unlikely that systematic differences in reporting occurred by LHIN that would bias the comparison of resource utilization outcomes among regions.[153,154,157,158]

Factors thought to influence the reporting of investigations and interventions include the following: the procedures in place for training employees, the workload burden and the methods of data abstraction. These are unlikely to be clustered at the LHIN level.[153,154,157,158] The capture of procedures and investigations is unlikely to be related to any other disease, patient or healthcare system characteristic of interest and we anticipate that any misclassification of the number of hospital days or the use of home care would be non-differential, biasing differences towards the null. Admission dates and discharge dates, which were used in this thesis project to determine the number of inpatient hospital days, also demonstrated near perfect (99.9%) reliability in re-abstraction studies.[153,154,157] Additionally, the incorporation of multiple sources (DAD, OHIP billing and chart review) into a hierarchy of data collection to ensure complete reporting of receipt and frequency of procedures, as was performed for this project, decreases the likelihood that measures were underreported and practice patterns underestimated or explained by variation in reporting methods. Overall, the use of administrative data to study the resource utilization of cancer care is generally limited by lack of staging data. Despite this, much may still be learned from this study. The administrative data holdings were augmented by a province-wide chart review that provided information on cancer stage and biological details, such as primary tumour location, that would have been otherwise unavailable.

In addition, the processes behind treatment decision-making cannot be understood using administrative data, leading to treatment selection bias if resource utilization is attributed to a treatment itself, and treatments compared.[159,160] The selection bias of individuals into different management streams (gastrectomy, chemotherapy) prohibited the comparison of healthcare utilization between primary treatment strategies, and means that the resource utilization of patients who received one strategy or another cannot be compared, because there were underlying differences in the disease or patient that prompted the receipt of a specific treatment and they are not truly equal. Although comparisons based on treatment received would have added interesting information, this is the first study to present information on healthcare utilization and practice patterns in the metastatic gastric cancer population in North America.

Measuring Predictor Variables and Outcomes

Post Hoc Power Calculation

Post hoc power calculations were performed to better understand the ability of the study to compare patient characteristics among Local Health Integration Networks (Table 17). A lack of statistical power available in this study to compare regional differences was evident and limited the ability for conclusions to be made about variation in these characteristics. The number of metastatic gastric cancer patients diagnosed in the northern regions was very small, and as a result the power to make comparisons was reduced. Although the comparisons made in Objective 2 infer that the patients appear to be statistically similar, we lack the confidence to accept the null hypothesis that a difference in characteristics does not truly exist. This retrospective study did report on all metastatic gastric cancer patients with a registered diagnosis during the study period. Collapsing the Local Health Integration Network regions to increase the sample sizes in each category was not appropriate, because the purpose of the comparison is based on the assumption that each region caters the planning and provision of healthcare services differently to best meet the needs of their communities.

The range in variation between the healthcare regions is still of interest to policy decision-makers performing surveillance of disease indicators across healthcare regions, even though the differences were not statistically significant. The Ontario Health Quality Council uses both statistical significance and pre-determined clinical significance to understand regional variation in a number of healthcare outcomes.[161] In addition to statistical differences, 5% variation from the provincial average was considered a meaningful difference in the uptake of best practices or in patient satisfaction, and 25% was considered meaningful variation in wait times or in the rate of serious adverse outcomes.[161] Future studies should attempt to ensure *a priori* that an adequate time horizon for accrual of patients is used to have the statistical power necessary to make relevant comparisons. They should also stipulate clinically meaningful variations separate from statistically significant differences, to contextualize the results for making health policy decisions.

Table 17: Post-hoc power calculations for differences in patient characteristics and treatment strategies between Local Health Integration Networks (alpha=0.05, two-sided tests)

Variable	Probability of Outcome		Sample Sizes		Absolute Difference in Outcome	Power
	Lowest LHIN	Highest LHIN	Lowest LHIN	Highest LHIN		
Burden of Metastases >1	36	57	22	151	21	36%
Tumour Location-Distal	15	45	41	22	30	62%
Tumour Location-GEJ	19	34	211	41	15	46%
Age <65 years	17	43	41	77	26	78%
Age >74 years	25	55	77	22	30	67%
Sex- Male	58	76	81	79	18	62%
Charlson-Deyo Score ≥1	8	14	77	167	6	18%
Resource Utilization Band =3	37	55	79	22	18	25%
Receipt of Gastrectomy	31	53	41	72	22	54%
Receipt of Chemotherapy	24	51	41	72	27	38%

LHIN=Local Health Integration Network; GEJ= gastroesophageal junction

Misclassification

Misclassification of study participants as having non- metastatic disease, and the exclusion of these eligible patients from the cohort may have occurred during the cohort creation phase. Patients were included in the cohort if radiologic or pathologic documentation of metastatic disease existed in the results from the chart review. An additional mode of being classified as having metastatic disease could have been through operative reports, but these documents were not available at the time of analysis. Patients may appear to be free of metastases prior to surgery; however, if a patient was found to have metastatic disease at the time of laparotomy (surgical opening of the abdomen), and if the newly identified sites of metastases were not biopsied, the documentation of metastatic status may only exist in the operative note. If the operative note was the only indication of metastatic disease, the patient would have been incorrectly classified as having M0 (non-metastatic disease), resulting in exclusion from this study. A thorough review of all gastric cancer patients' clinical, radiology and pathology notes was performed, making it less likely that any patients with metastases were missed.

Conceptualizing the burden of metastases may also have been incorrect and biased the results toward the null. Categorization of the burden of disease into 1 and >1 site of disease was based on a study that indicated that patients with 1 non-curative factor had a significantly better prognosis than patients with more than one non-curative factor.[48] This understanding can be further refined, to demonstrate that the number of metastatic sites (modeled as count data) is a significant predictor of prognosis, as are specific sites of metastatic disease.[162,163] It is reasonable to assume that the more sites of metastatic disease a patient has, the more resources they may consume as the result of an increased burden of symptoms, until a plateau for accessing care within the system is reached, or death occurs. There may be a spectrum of health care needs even for patients with one site of metastasis - a patient with one, small liver metastasis may require fewer health care services than a patient with multiple liver metastases. The simplistic approach may have underestimated a relationship between burden of metastatic disease and resource utilization.

Residual Confounding

The investigation of predictors of inpatient hospital stay and home care use was limited to the data existing in administrative healthcare datasets and the additional variables collected from the chart review. Ideally, patient preference,[164,165] ethnicity/race,[98,102,166-169] marital status (as an example of a measure of social support), [168,170-172] and access to alternative care (e.g. hospice use), all of which are known predictors of palliative care resource utilization, home care use and inpatient hospital stay, would have been included in the analysis. These variables are not available in national or provincial datasets and were not collected during the chart review; therefore, not all relevant predictors could be explored. Residual confounding likely exists and may potentially explain all or some of the associations identified in the multivariate analysis.

Differences in the provision of cancer and palliative end-of-life care have been documented to be significantly associated with ethnicity/race.[98,102,166-169] Non-white race has been associated with increased intensity of services provided at end-of-life (increased number of hospitalizations, increased length of hospital stay, lack of hospice care),[166,169] increased frequency of inpatient hospital death,[168] and continued cancer treatment in the palliative setting.[166] In addition, in gastric cancer, non-Asian race has been associated with differences in the cancer treatment options provided as well as in worse gastric cancer specific-survival.[98,102,173] The inclusion of race as a predictor of both inpatient hospital stay and home care use may have explained remaining variation among individuals or the relationships of predictors with these measures of end-of-life care utilization. Receipt of care from a high volume physician was identified as a significant predictor of home care use in this study of gastric cancer patients. Racial differences have also been documented in the receipt of services from high volume specialists and hospitals for gastric cancer surgery and for other cancer sites-[174,175] this residual confounding may explain the association documented in this study.

Marital status is also a known predictor of home care use and hospitalization at end-of-life.[168,170-172] Individuals with cancer who are married, are more likely to receive home care than single or widowed individuals,[171,172] more likely to die at home and are less likely to die in-hospital.[168,170] Marital status has also been identified as a significant predictor of a recommendation for gastrectomy for stage IV gastric cancer patients, while non-married patients were less likely to undergo surgery than married patients and more likely to have worse survival.[176] The relationship of marital status to survival, treatment strategies and home care use may confound the associations identified in this study and is an area for further research.

Future research may require a mixed-methods approach, enriching utilization data with an understanding of patient preferences, support networks and ethnic background to better understand differences in end-of-life care use. To date, studies have focused on one aspect or another, but none have comprehensively explored these relationships and their interactions with the appropriate delivery of palliative care.

Statistical Methods

Multiple methods exist to outline the inclusion criteria for which resource utilization measures collected and assigned to a disease, procedure or healthcare program, and how to differentiate unrelated resource use. This project made the assumption, that because the majority of patients are at end-of-life, almost all resource consumption will be related to palliation of the disease and related complications. This “collect all” approach has been used in other cancer care and palliative care literature.[68,110,117,118,177,178] Other authors have attempted to further specify resource use only related to the primary cancer or metastases through the use of non-cancer control populations, these cancers generally have a longer survival period and an increased likelihood that co-morbid conditions may be the underlying factor behind utilization.[61,62] If the assumption that all resource use is not related to the cancer or dying from the cancer is false, it would lead to the overestimation of the resource utilization attributed to the disease. This could potentially mediate the relationship between comorbidity and the prediction of resource utilization, with patients with higher comorbidities being misclassified as having increased resource use related to their cancer. It is unlikely that this potential overestimation would interfere with comparisons of resource utilization among Local Health Integration Networks, as the misclassification would be more likely to be non-differential. This is assumption is further supported by similar levels of comorbid disease measured across the healthcare regions.

Methodologies for modeling predictors of health resource utilization outcomes and costs are relatively new and still in development. The best methods for addressing the non-linear distributions of resource utilization and cost outcomes, addressing common outcomes, and dealing with issues of censoring and assigning relevant resource use and costs to an illness or procedure are still being refined and debated in the literature.[52,136] A one-size-fits-all approach to analysis has yet to be described, and much work is being done to focus on the specific needs and methods for the economic evaluation of cancer care and palliative care services data.[179-181]

Count data describing resource utilization outcomes have been modeled using a number of generalized linear models and/or generalized estimating equations. Poisson regression models, modified-Poisson, zero-inflated Poisson, negative binomial and hurdle models have all been commonly applied to resource utilization data,[135-137] to identify predictors and to build predictive models. Models predicting the number of emergency room department visits have been developed and compared using Ontario administrative healthcare data for the general population.[137] For their data, where many were non-users given they were not an illness-specific cohort, the hurdle model was determined to be the best fit to predict the number of emergency room visits. Hurdle models separately model the probability of being a non-user compared to a user, and then model the number of visits for users. Some advocate the use of this modeling technique as being the most informative for healthcare decision-makers, because it allows the prediction of non-users, in addition to heavy users, where accessing care and frequency of use may be related to separate factors. Had we used this type of informative model, we would have been able to describe both predictors of hospitalization and the number of days accrued once admitted at least once, and predictors of at least one home care visit as well as the number of times a home care service was accessed. The second best fitting model to the data however, was the negative binomial model, which we used to identify predictors of the number of inpatient hospital days.

Generalizability of Results

Generalizability of these results to the healthcare resource utilization of other metastatic gastric cancer populations may not be possible. Differences in the prevalence of predictors, such as tumour location, vary between high and low incidence countries, as do treatment benefits and approaches to palliation. While the associations between the predictors and the measures of resource utilization themselves may be generalizable to populations with similar disease biology and presentation, differences in how individuals interact with the healthcare system may exist across healthcare infrastructures (e.g. private health insurance for end-of-life care in private payer systems) and may better predict outcomes than those identified in a public payer system. Comparing measures of resource utilization is easier and more accurate than comparing overall costs between systems, given differences in currency valuation, purchase prices and whether or not a service is charged to the patient for a profit. Differences in geographic variation, and the predictors identified in this project are likely worth investigating in other metastatic gastric cancer populations, or other metastatic cancer populations in general. Overall, this study provides a picture of how patients are managed, as well as geographic differences in healthcare resource utilization. It also provides an in-depth look at disease, patient and healthcare system predictors of two major end-of-life care quality indicators.

5.5 Contributions, Conclusions, and Future Directions

This study is the first population-based description of the health resource utilization of metastatic gastric cancer patients in North America or Europe, and the first population-based investigation of metastatic gastric cancer treatment patterns using administrative data. Population-based information on which healthcare services being accessed, their frequency of use, and where these resources were being consumed was provided. Geographic variation in management practices and by extension, the costs of management, identified potentially modifiable predictors of a major cost driver (inpatient hospital days) that warrants further research, as well as an important quality of end-of-life care indicator (home care) in the metastatic gastric cancer population.

Next steps in end-of-life care research for metastatic gastric cancer in Ontario, include incorporating clinical data to understand if variations in resource utilization result in variations in clinical outcomes. If differences in resource use are associated with worse outcomes, they may identify targets for intervention to improve the effectiveness and efficiency of the healthcare system. If differences in clinical outcomes do not result in worse health outcomes, work may be done to decrease unnecessary usage and spending where possible.

Valuing the measures of resource utilization with cost data to further this work would also be a logical next step, to provide both a description of the financial burden of metastatic gastric cancer in Ontario, which currently does not exist in North America or Europe, and to understand if differences in costs exist from the differences in resource utilization among the LHINs. Identifying predictors of costs could also point decision-makers toward modifiable factors to reduce costs while improving clinical outcomes.

Trends in resource utilization and costs over time would also aid decision-makers in forecasting resource allocation and needs of their communities. Examining specific time periods to identify peak periods of use of specific certain resources used, such as around the time of diagnosis versus time of death, or use in the last weeks before death would all provide more information on how metastatic gastric cancer patients access and use care at end-of-life. This information could also be used to provide feedback to clinicians on their cost containment or unnecessary use of resources over time.

In summary, this is the first population-based, investigation of the healthcare resource utilization of metastatic gastric cancer patients in North America. This project provided evidence that differences exist in the way that metastatic gastric cancer patients are treated among geographic regions in Ontario. Finally, predictors of two major cost drivers associated with death from malignancy were identified, some of which that may be modifiable at the health system level.

Bibliography (or References)

1. Endres C. Online ICD9/ICD9CM codes. http://icd9cm.chrisendres.com/index.php?action=contents 2011.

2. Crew KD, Neugut AI. Epidemiology of gastric cancer. *World J Gastroenterol*. 2006;12(3):354-362.

3. Reichardt P, Hogendoorn PC, Tamborini E, et al. Gastrointestinal stromal tumors I: Pathology, pathobiology, primary therapy, and surgical issues. *Semin Oncol*. 2009;36(4):290-301.

4. Delle Fave G, Capurso G, Milione M, Panzuto F. Endocrine tumours of the stomach. *Best Pract Res Clin Gastroenterol*. 2005;19(5):659-673.

5. Davis GB, Blanchard DK, Hatch GF,3rd, et al. Tumors of the stomach. *World J Surg*. 2000;24(4):412-420.

6. Al-Akwaa AM, Siddiqui N, Al-Mofleh IA. Primary gastric lymphoma. *World J Gastroenterol*. 2004;10(1):5-11.

7. LAUREN P. The two histological main types of gastric carcinoma: Diffuse and so-called intestinal-type carcinoma. an attempt at a histo-clinical classification. *Acta Pathol Microbiol Scand*. 1965;64:31-49.

8. Flucke U, Monig SP, Baldus SE, et al. Differences between biopsy- or specimen-related Lauren and World Health Organization classification in gastric cancer. *World J Surg*. 2002;26(2):137-140.

9. Kamangar F, Dawsey SM, Blaser MJ, et al. Opposing risks of gastric cardia and noncardia gastric adenocarcinomas associated with Helicobacter pylori seropositivity. *J Natl Cancer Inst*. 2006;98(20):1445-1452.

10. Plummer M, Franceschi S, Munoz N. Epidemiology of gastric cancer. *IARC Sci Publ*. 2004;(157)(157):311-326.

11. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. *CA Cancer J Clin*. 2005;55(2):74-108.

12. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, ed. *Schistosomes, liver flukes and Helicobacter pylori.* Lyon, France: International Agency for Research on Cancer; 1994; No. 61.

13. Parkin DM. The global health burden of infection-associated cancers in the year 2002. *Int J Cancer*. 2006;118(12):3030-3044.

14. Canadian Cancer Society's Steering Committee on Cancer Statistics. Canadian cancer statistics 2012.

15. Canadian Cancer Society's Steering Committee. Canadian cancer statistics 2009.

16. Chandanos E, Lagergren J. Oestrogen and the enigmatic male predominance of gastric cancer. *Eur J Cancer*. 2008;44(16):2397-2403.

17. Public Health Agency of Canada. Cancer surveillance online. http://dsol-smed.hc-sc.gc.ca/dsol-smed/cancer/index_e.html. Updated 2002; Accessed 2010.

18. Maehara Y, Kakeji Y, Oda S, Baba H, Sugimachi K. Tumor growth patterns and biological characteristics of early gastric carcinoma. *Oncology*. 2001;61(2):102-112.

19. Haruma K, Suzuki T, Tsuda T, Yoshihara M, Sumii K, Kajiyama G. Evaluation of tumor growth rate in patients with early gastric carcinoma of the elevated type. *Gastrointest Radiol*. 1991;16(4):289-292.

20. Tsukuma H, Oshima A, Narahara H, Morii T. Natural history of early gastric cancer: A non-concurrent, long term, follow up study. *Gut*. 2000;47(5):618-621.

21. Leung WK, Wu MS, Kakugawa Y, et al. Screening for gastric cancer in Asia: Current evidence and practice. *Lancet Oncol*. 2008;9(3):279-287.

22. Hamashima C, Shibuya D, Yamazaki H, et al. The Japanese guidelines for gastric cancer screening. *Jpn J Clin Oncol*. 2008;38(4):259-267.

23. Rupnow MF, Owens DK, Shachter R, Parsonnet J. Helicobacter pylori vaccine development and use: A cost-effectiveness analysis using the institute of medicine methodology. *Helicobacter*. 1999;4(4):272-280.

24. Xie F, O'Reilly D, Ferrusi IL, et al. Illustrating economic evaluation of diagnostic technologies: Comparing helicobacter pylori screening strategies in prevention of gastric cancer in Canada. *Journal of the American College of Radiology*. 2009;6(5):317-323.

25. Hassan C, Zullo A, Di Giulio E, et al. Cost-effectiveness of endoscopic surveillance for gastric intestinal metaplasia. *Helicobacter*. 2010;15(3):221-226.

26. Catalano V, Labianca R, Beretta GD, Gatta G, de Braud F, Van Cutsem E. Gastric cancer. *Crit Rev Oncol Hematol*. 2009;71(2):127-164.

27. Sandgren A, Fridlund B, Nyberg P, Strang P, Petersson K, Thulesius H. Symptoms, care needs and diagnosis in palliative cancer patients in acute care hospitals: A 5-year follow-up survey. *Acta Oncol*. 2010.

28. Maconi G, Manes G, Porro GB. Role of symptoms in diagnosis and outcome of gastric cancer. *World J Gastroenterol*. 2008;14(8):1149-1155.

29. Ajani J, D'Amico TA, Hayman JA, Meropol NJ, Minsky B, National Comprehensive Cancer Network. Gastric cancer. clinical practice guidelines in oncology. *J Natl Compr Canc Netw*. 2010;1(1):28-39.

30. Mahar AL, Brar SS, Coburn NG, Law C, Helyer LK. Surgical management of gastric perforation in the setting of gastric cancer. *Gastric Cancer*. 2011.

31. Fleming ID, Cooper JS, Henderson DE. *AJCC cancer staging manual.* 5th ed. New York: Springer; 1997.

32. Washington K. 7th edition of the AJCC cancer staging manual: Stomach. *Ann Surg Oncol*. 2010;17(12):3077-3079.

33. Seevaratnam R, Cardoso R, McGregor C, et al. How useful is preoperative imaging for tumor, node, metastasis (TNM) staging of gastric cancer? A meta-analysis. *Gastric Cancer*. 2011.

34. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2010 (ver. 3). *Gastric Cancer*. 2011;14(2):113-123.

35. Howlader N, Noone AM, Krapcho M, et al. SEER cancer statistics review 1975-2008 http://seer.cancer.gov/statfacts/html/stomach.html. Updated 2011; Accessed 2011.

36. Coburn NG, Lourenco LG, Rossi SE, et al. Management of gastric cancer in Ontario. *J Surg Oncol*. 2010;102(1):54-63.

37. Jackson C, Cunningham D, Oliveira J, ESMO Guidelines Working G. Gastric cancer: ESMO clinical recommendations for diagnosis, treatment and follow-up. *Annals of Oncology*. 2009;20(Suppl 4):34-36.

38. Cunningham D, Allum WH, Stenning SP, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. *N Engl J Med*. 2006;355(1):11-20.

39. Macdonald JS, Smalley SR, Benedetti J, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. *N Engl J Med*. 2001;345(10):725-730.

40. Cunningham SC, Schulick RD. Palliative management of gastric cancer. *Surg Oncol*. 2007;16(4):267-275.

41. Miner TJ, Jaques DP, Karpeh MS, Brennan MF. Defining palliative surgery in patients receiving noncurative resections for gastric cancer. *J Am Coll Surg*. 2004;198(6):1013-1021.

42. Mahar AL, Coburn NG, Karinicolas PJ, Viola R, Helyer LK. Effective palliation and quality of life outcomes in studies of surgery for advanced, non-curative gastric cancer: A systematic review. *Gastric Cancer*. 2011;Epub.

43. Mahar AL, Coburn NG, Singh S, Law C, Helyer LK. A systematic review of surgery for non-curative gastric cancer. *Gastric Cancer*. 2011.

44. Kerkar SP, Kemp CD, Duffy A, et al. The GYMSSA trial: A prospective randomized trial comparing gastrectomy, metastasectomy plus systemic therapy versus systemic therapy alone. *Trials*. 2009;10:121.

45. Fujitani K, Yang HK, Kurokawa Y, et al. Randomized controlled trial comparing gastrectomy plus chemotherapy with chemotherapy alone in advanced gastric cancer with a single non-curable factor: Japan clinical oncology group study JCOG 0705 and Korea gastric cancer association study KGCA01. *Jpn J Clin Oncol*. 2008;38(7):504-506.

46. Wagner AD, Unverzagt S, Grothe W, et al. Chemotherapy for advanced gastric cancer. *Cochrane Database Syst Rev*. 2010;(3)(3):CD004064.

47. Bang YJ, Van Cutsem E, Feyereislova A, et al. Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): A phase 3, open-label, randomised controlled trial. *Lancet*. 2010;376(9742):687-697.

48. Hartgrink HH, Putter H, Klein Kranenbarg E, Bonenkamp JJ, van de Velde CJ, Dutch Gastric Cancer Group. Value of palliative resection in gastric cancer. *Br J Surg*. 2002;89(11):1438-1443.

49. Floris G, Pisanu A, Mattana A, Uccheddu A. Indications and limits of palliative resection for gastric cancer: Our experience. *J Chemother*. 1999;11(3):224-226.

50. Mahar AL, Helyer LK, Swallow C, et al. What care is appropriate and necessary for metastatic gastric cancer patients? results of a RAND/UCLA expert panel. *(submitted to ASCO GI 2012)*.

51. de Gara CJ, Hanson J, Hamilton S. A population-based study of tumor-node relationship, resection margins, and surgeon volume on gastric cancer survival. *Am J Surg*. 2003;186(1):23-27.

52. Drummond MF. *Methods for the economic evaluation of health care programmes.* 2nd ed. Oxford ; New York: Oxford University Press; 1997:305.

53. Guidelines for the economic evaluation of health technologies: Canada. 2006.

54. Sulmasy DP. Cancer care, money, and the value of life: Whose justice? which rationality? *J Clin Oncol*. 2007;25(2):217-222.

55. Yabroff KR, Warren JL, Brown ML. Costs of cancer care in the USA: A descriptive review. *Nature Clinical Practice Oncology*. 2007;4(11) (pp 643-656).

56. Bachmann MO, Peters T, Harvey I. Costs and concentration of cancer care: Evidence for pancreatic, oesophageal and gastric cancers in national health service hospitals. *Journal of Health Services Research and Policy*. 2003;8(2):75-82.

57. Yabroff KR, Lamont EB, Mariotto A, et al. Cost of care for elderly cancer patients in the United States. *J Natl Cancer Inst*. 2008;100(9):630-641.

58. Kuwabara K, Imanaka Y, Matsuda S, et al. Profiling of resource use variation among six diseases treated at 82 Japanese special functioning hospitals, based on administrative data. *Health Policy*. 2006;78(2-3):306-318.

59. Hoya Y, Takahashi T, Saitoh R, et al. Blood transfusion requirement for gastric cancer surgery: Reasonable preparation for transfusion in the comprehensive health insurance system. *International Journal Of Surgery*. 2008;6(3):234-237.

60. *Prognostic factors in cancer.* 3rd ed. United: Wiley Liss; 2006.

61. Lang K, Lines LM, Lee DW, Korn JR, Earle CC, Menzin J. Trends in healthcare utilization among older Americans with colorectal cancer: A retrospective database analysis. *BMC Health Serv Res*. 2009;9:227.

62. Krahn MD, Zagorski B, Laporte A, et al. Healthcare costs associated with prostate cancer: Estimates from a population-based study. *BJU Int*. 2010;105(3):338-346.

63. Taplin SH, Barlow W, Urban N, et al. Stage, age, comorbidity, and direct costs of colon, prostate, and breast cancer care. *J Natl Cancer Inst*. 1995;87(6):417-426.

64. Fleming I, Monaghan P, Gavin A, O'Neill C. Factors influencing hospital costs of lung cancer patients in Northern Ireland. *European Journal of Health Economics*. 2008;9(1):79-86.

65. Gordon LG, Eckermann S, Hirst NG, et al. Healthcare resource use and medical costs for the management of oesophageal cancer. *Br J Surg*. 2011;98(11):1589-1598.

66. Gupta PK, Miller WJ, Sainath J, Forse RA. Determinants of resource utilization and outcomes in laparoscopic roux-en-Y gastric bypass: A multicenter analysis of 14,251 patients. *Surg Endosc*. 2011;25(8):2613-2625.

67. Carbonell AM, Lincourt AE, Matthews BD, Kercher KW, Sing RF, Heniford BT. National study of the effect of patient and hospital characteristics on bariatric surgery outcomes. *Am Surg*. 2005;71(4):308-314.

68. Barbera L, Sussman J, Viola R, et al. Factors associated with end-of-life health service use in patients dying of cancer. *Healthc Policy*. 2010;5(3):e125-43.

69. McCavit TL, Lin H, Zhang S, Ahn C, Quinn CT, Flores G. Hospital volume, hospital teaching status, patient socioeconomic status, and outcomes in patients hospitalized with sickle cell disease. *Am J Hematol*. 2011;86(4):377-380.

70. Kaul P, McAlister FA, Ezekowitz JA, et al. Resource use in the last 6 months of life among patients with heart failure in Canada. *Arch Intern Med*. 2011;171(3):211-217.

71. Wilson LS, Tesoro R, Elkin EP, et al. Cumulative cost pattern comparison of prostate cancer treatments. *Cancer*. 2007;109(3):518-527.

72. Cardenas-Turanzas M, Cooksley C, Kamat AM, Pettaway CA, Elting LS. Gender and age differences in blood utilization and length of stay in radical cystectomy: A population-based study. *Int Urol Nephrol*. 2008;40(4):893-899.

73. Soni A, Sonnenberg A. Healthcare resource utilization in the management of oesophageal adenocarcinoma. *Aliment Pharmacol Ther*. 2001;15(7):945-951.

74. Gupta PK, Turaga KK, Miller WJ, Loggie BW, Foster JM. Determinants of outcomes in pancreatic surgery and use of hospital resources. *J Surg Oncol*. 2011.

75. Lee CC, Ho HC, Jack LC, et al. Association between surgeon volume and hospitalisation costs for patients with oral cancer: A nationwide population base study in Taiwan. *Clin Otolaryngol*. 2010;35(1):46-52.

76. Jayadevappa R, Chhatre S, Wein AJ, Malkowicz SB. Predictors of patient reported outcomes and cost of care in younger men with newly diagnosed prostate cancer. *Prostate*. 2009;69(10):1067-1076.

77. Prescott JD, Factor S, Pill M, Levi GW. Descriptive analysis of the direct medical costs of multiple sclerosis in 2004 using administrative claims in a large nationwide database. *J Manag Care Pharm*. 2007;13(1):44-52.

78. Vonlanthen R, Slankamenac K, Breitenstein S, et al. The impact of complications on costs of major surgical procedures: A cost analysis of 1200 patients. *Ann Surg*. 2011.

79. Goodridge D, Lawson J, Rennie D, Marciniuk D. Rural/urban differences in health care utilization and place of death for persons with respiratory illness in the last year of life. *Rural Remote Health*. 2010;10(2):1349.

80. Rosemurgy AS, Bloomston M, Serafini FM, Coon B, Murr MM, Carey LC. Frequency with which surgeons undertake pancreaticoduodenectomy determines length of stay, hospital charges, and in-hospital mortality. *J Gastrointest Surg*. 2001;5(1):21-26.

81. Kelley AS, Ettner SL, Morrison RS, Du Q, Wenger NS, Sarkisian CA. Determinants of medical expenditures in the last 6 months of life. *Ann Intern Med*. 2011;154(4):235-242.

82. Enestvedt CK, Diggs BS, Shipley DK, Thomas CR, Billingsley KG. A population-based analysis of surgical and adjuvant therapy for resected gastric cancer: Are patients receiving appropriate treatment following publication of the intergroup 0116 results? *Gastrointest Cancer Res*. 2009;3(6):233-238.

83. Charlson ME, Charlson RE, Peterson JC, Marinopoulos SS, Briggs WM, Hollenberg JP. The Charlson comorbidity index is adapted to predict costs of chronic disease in primary care patients. *J Clin Epidemiol*. 2008;61(12):1234-1240.

84. The Johns Hopkins University. The Johns Hopkins university adjusted clinical groups (ACG) case-mix system. http://www.acg.jhsph.org/. Updated 2012; Accessed 2012.

85. Shugarman LR, Decker SL, Bercovitz A. Demographic and social characteristics and spending at the end of life. *J Pain Symptom Manage*. 2009;38(1):15-26.

86. Stessin AM, Sherr DL. Demographic disparities in patterns of care and survival outcomes for patients with resected gastric adenocarcinoma. *Cancer Epidemiol Biomarkers Prev*. 2011;20(2):223-233.

87. Kuo EY, Chang Y, Wright CD. Impact of hospital volume on clinical and economic outcomes for esophagectomy. *Ann Thorac Surg*. 2001;72(4):1118-1124.

88. Sutcliffe SB. A review of Canadian health care and cancer care systems. *Cancer*. 2011;117(10 Suppl):2241-2244.

89. Ontario Ministry of Health and Long-Term Care. Schedule of benefits: Physician services under the health insurance act. 2011.

90. Ministry of Ontario Health and Long-Term Care. Ontario's Local Health Integration Networks. http://www.lhins.on.ca/home.aspx. Updated 2012; Accessed 2012.

91. Cancer Care Ontario. Cancer services quality index 2012. http://www.csqi.on.ca/. Updated 2012; Accessed 2012.

92. Jaworski R, Bollschweiler E, Holscher AH, et al. Prognostic relevance of demographics and surgical practice for patients with gastric cancer in two centers: In Poland versus Germany. *Gastric Cancer*. 2011.

93. Mahar AL, McLeod RS, Kiss A, Paszat L, Coburn NG. A systematic review of the effect of institution and surgeon factors on surgical outcomes for gastric cancer. *J Am Coll Surg*. 2012;214(5):860-8.e12.

94. Greenberg CC, Lipsitz SR, Hughes ME, et al. Institutional variation in the surgical treatment of breast cancer: A study of the NCCN. *Ann Surg*. 2011;254(2):339-345.

95. Greenberg CC, Lipsitz SR, Neville B, et al. Receipt of appropriate surgical care for medicare beneficiaries with cancer. *Arch Surg*. 2011.

96. Shugarman LR, Mack K, Sorbero ME, et al. Race and sex differences in the receipt of timely and appropriate lung cancer treatment. *Med Care*. 2009;47(7):774-781.

97. van der Linden Y, Roos D, Lutz S, Fairchild A. International variations in radiotherapy fractionation for bone metastases: Geographic borders define practice patterns?. *Clin Oncol*. 2009;21(9) (pp 655-658).

98. Coburn NG, Guller U, Baxter NN, et al. Adjuvant therapy for resected gastric cancer--rapid, yet incomplete adoption following results of Intergroup 0116 trial. *Int J Radiat Oncol Biol Phys*. 2008;70(4):1073-1080.

99. Coburn NG, Swallow CJ, Kiss A, Law C. Significant regional variation in adequacy of lymph node assessment and survival in gastric cancer. *Cancer*. 2006;107(9):2143-2151.

100. Qureshi AP, Ottensmeyer CA, Mahar AL, et al. Quality indicators for gastric cancer surgery: A survey of practicing pathologists in Ontario. *Ann Surg Oncol*. 2009;16(7):1883-1889.

101. Helyer LK, O'Brien C, Coburn NG, Swallow CJ. Surgeons' knowledge of quality indicators for gastric cancer surgery. *Gastric Cancer*. 2007;10(4):205-214.

102. Bashash M, Hislop TG, Shah AM, Le N, Brooks-Wilson A, Bajdik CD. The prognostic effect of ethnicity for gastric and esophageal cancer: The population-based experience in British Columbia, Canada. *BMC Cancer*. 2011;11:164.

103. Bashash M, Yavari P, Hislop TG, et al. Comparison of two diverse populations, British Columbia, Canada, and Ardabil, Iran, indicates several variables associated with gastric and esophageal cancer survival. *J Gastrointest Cancer*. 2011;42(1):40-45.

104. Booth CM, Li G, Zhang-Salomons J, Mackillop WJ. The impact of socioeconomic status on stage of cancer at diagnosis and survival: A population-based study in Ontario, Canada. *Cancer*. 2010.

105. Al-Refaie WB, Gay G, Virnig BA, et al. Variations in gastric cancer care: A trend beyond racial disparities. *Cancer*. 2010;116(2):465-475.

106. Dudeja V, Habermann EB, Zhong W, et al. Guideline recommended gastric cancer care in the elderly: Insights into the applicability of cancer trials to real world. *Ann Surg Oncol*. 2011;18(1):26-33.

107. Huang J, Boyd C, Tyldesley S, Zhang-Salomons J, Groome PA, Mackillop WJ. Time spent in hospital in the last six months of life in patients who died of cancer in Ontario. *J Clin Oncol*. 2002;20(6):1584-1592.

108. Seow H, Barbera L, Howell D, Dy SM. Did Ontario's end-of-life care strategy reduce acute care service use? *Healthc Q*. 2010;13(1):93-100.

109. Seow H, King S, Vaitonis V. The impact of Ontario's end-of-life care strategy on end-of-life care in the community. *Healthc Q*. 2008;11(1):56-62.

110. Barbera L, Paszat L, Qiu F. End-of-life care in lung cancer patients in Ontario: Aggressiveness of care in the population and a description of hospital admissions. *J Pain Symptom Manage*. 2008;35(3):267-274.

111. Earle CC, Neville BA, Landrum MB, Ayanian JZ, Block SD, Weeks JC. Trends in the aggressiveness of cancer care near the end of life. *Journal of Clinical Oncology*. 2004;22(2) (pp 315-321).

112. Earle CC, Park ER, Lai B, Weeks JC, Ayanian JZ, Block S. Identifying potential indicators of the quality of end-of-life cancer care from administrative data. *J Clin Oncol*. 2003;21(6):1133-1138.

113. Lewin SN, Buttin BM, Powell MA, et al. Resource utilization for ovarian cancer patients at the end of life: How much is too much? *Gynecol Oncol*. 2005;99(2):261-266.

114. Barbera L, Taylor C, Dudgeon D. Why do patients with cancer visit the emergency department near the end of life? *CMAJ*. 2010;182(6):563-568.

115. Hospital cost drivers technical report. 2011.

116. Canadian Institute for Health Information. The cost of acute care hospital stays by medical condition in Canada, 2004-2005. 2008.

117. Walker H, Anderson M, Farahati F, et al. Resource use and costs of end-of-life/palliative care: Ontario adult cancer patients dying during 2002 and 2003. *J Palliat Care*. 2011;27(2):79-88.

118. Fassbender K, Fainsinger RL, Carson M, Finegan BA. Cost trajectories at the end of life: The Canadian experience. *J Pain Symptom Manage*. 2009;38(1):75-80.

119. Johnson AP, Abernathy T, Howell D, Brazil K, Scott S. Resource utilisation and costs of palliative cancer care in an interdisciplinary health care model. *Palliat Med*. 2009;23(5):448-459.

120. Romanow RJ. Building on values:The future of health care in Canada- final report. 2002.

121. Seow H, Barbera L, Howell D, Dy SM. How end-of-life home care services are used from admission to death: A population-based cohort study. *J Palliat Care*. 2010;26(4):270-278.

122. Seow H, Barbera L, Howell D, Dy SM. Using more end-of-life homecare services is associated with using fewer acute care services: A population-based cohort study. *Med Care*. 2010;48(2):118-124.

123. Drummond D, Giroux D, Pigott S, Stephenson C. Commission on the reform of Ontario's public services: Chapter 5: Health. 2012.

124. Mahar AL, Coburn NG, Singh S, Law C, Helyer LK. A systematic review of surgery for non-curative gastric cancer. *Gastric Cancer*. 2011.

125. Williams JI, Young W. A summary of studies on the quality of health care administrative databases in Canada. In: Goel V, Williams JI, Anderson GM, Blackstien-Hirsch P, Fooks C, Naylor CD, eds. *Patterns of health care in Ontario, the ICES practice atlas.* 2nd ed. Ottawa: Canadian Medical Association; 1996.

126. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *J Chronic Dis*. 1987;40(5):373-383.

127. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol*. 1992;45(6):613-619.

128. Chase DM, Fedewa S, Chou TS, Chen A, Ward E, Brewster WR. Disparities in the allocation of treatment in advanced ovarian cancer: Are there certain patient characteristics associated with nonstandard therapy? *Obstet Gynecol*. 2012;119(1):68-77.

129. Devon KM, Urbach DR, McLeod RS. Postoperative disposition and health services use in elderly patients undergoing colorectal cancer surgery: A population-based study. *Surgery*. 2011;149(5):705-712.

130. Reid R, Evans R, Barer M, et al. Conspicuous consumption: Characterizing high users of physician services in one Canadian province. *J Health Serv Res Policy*. 2003;8(4):215-224.

131. Reid RJ, Roos NP, MacWilliam L, Frohlich N, Black C. Assessing population health care need using a claims-based ACG morbidity measure: A validation analysis in the province of Manitoba. *Health Serv Res*. 2002;37(5):1345-1364.

132. Sibley LM, Moineddin R, Agha MM, Glazier RH. Risk adjustment using administrative data-based and survey-derived methods for explaining physician utilization. *Med Care*. 2010;48(2):175-182.

133. Mackillop WJ, Zhang-Salomons J, Groome PA, Paszat L, Holowaty E. Socioeconomic status and cancer survival in Ontario. *J Clin Oncol*. 1997;15(4):1680-1689.

134. Kralj B. Measuring 'rurality' for purposes of health-care planning: An empirical measure for Ontario. *Ontario Medical Review*. 2000:33-52.

135. McCorkle R, Jeon S, Ercolano E, Schwartz P. Healthcare utilization in women after abdominal surgery for ovarian cancer. *Nurs Res*. 2011;60(1):47-57.

136. Diehr P, Yanez D, Ash A, Hornbrook M, Lin DY. Methods for analyzing health care utilization and costs. *Annu Rev Public Health*. 1999;20:125-144.

137. Moineddin R, Meaney C, Agha M, Zagorski B, Glazier RH. Modeling factors influencing the demand for emergency department services in Ontario: A comparison of methods. *BMC Emerg Med*. 2011;11:13.

138. Zou G. A modified poisson regression approach to prospective studies with binary data. *Am J Epidemiol*. 2004;159(7):702-706.

139. McNutt LA, Wu C, Xue X, Hafner JP. Estimating the relative risk in cohort studies and clinical trials of common outcomes. *Am J Epidemiol*. 2003;157(10):940-943.

140. Visser BC, Ma Y, Zak Y, Poultsides GA, Norton JA, Rhoads KF. Failure to comply with NCCN guidelines for the management of pancreatic cancer compromises outcomes. *HPB (Oxford)*. 2012;14(8):539-547.

141. Cree M, Tonita J, Turner D, et al. Comparison of treatment received versus long-standing guidelines for stage III colon and stage II/III rectal cancer patients diagnosed in Alberta, Saskatchewan, and Manitoba in 2004. *Clin Colorectal Cancer*. 2009;8(3):141-145.

142. Chagpar R, Xing Y, Chiang YJ, et al. Adherence to stage-specific treatment guidelines for patients with colon cancer. *J Clin Oncol*. 2012;30(9):972-979.

143. In H, Neville BA, Lipsitz SR, Corso KA, Weeks JC, Greenberg CC. The role of National Cancer Institute-designated cancer center status: Observed variation in surgical care depends on the level of evidence. *Ann Surg*. 2012;255(5):890-895.

144. Grunfeld E, Urquhart R, Mykhalovskiy E, et al. Toward population-based indicators of quality end-of-life care: Testing stakeholder agreement. *Cancer*. 2008;112(10):2301-2308.

145. National Comprehensive Cancer Network, ed. *NCCN clinical practice guidelines in oncology: Non-small cell lung cancer.* v.3 ed. 2012.

146. Engstrom SG, Carlsson L, Ostgren CJ, Nilsson GH, Borgquist LA. The importance of comorbidity in analysing patient costs in Swedish primary care. *BMC Public Health*. 2006;6:36.

147. Weiner JP, Starfield BH, Steinwachs DM, Mumford LM. Development and application of a population-oriented measure of ambulatory care case-mix. *Med Care*. 1991;29(5):452-472.

148. Perkins AJ, Kroenke K, Unutzer J, et al. Common comorbidity scales were similar in their ability to predict health care costs and mortality. *J Clin Epidemiol*. 2004;57(10):1040-1048.

149. Legler A, Bradley EH, Carlson MD. The effect of comorbidity burden on health care utilization for patients with cancer using hospice. *J Palliat Med*. 2011;14(6):751-756.

150. Urbach DR, Baxter NN. Does it matter what a hospital is "high volume" for? Specificity of hospital volume-outcome associations for surgical procedures: Analysis of administrative data. *Quality & Safety in Health Care*. 2004;13(5):379-383.

151. Urbach DR, Bell CM, Austin PC. Differences in operative mortality between high- and low-volume hospitals in Ontario for 5 major surgical procedures: Estimating the number of lives potentially saved through regionalization. *CMAJ Canadian Medical Association Journal*. 2003;168(11):1409-1414.

152. Lee JA, Park JH, Lee EJ, Kim SY, Kim Y, Lee SI. High-quality, low-cost gastrectomy care at high-volume hospitals: Results from a population-based study in South Korea. *Arch Surg*. 2011.

153. Canadian Institute of Health Information. CIHI data quality study of the 2009-2010 discharge abstract database. 2012.

154. Canadian Institute of Health Information. Data quality study of the 2008-2009 discharge abstract database. 2010.

155. Canadian Institute for Health Information. Database background and general data limitations documentation, national ambulatory care reporting system, 2008-2009. 2009.

156. Canadian Institute of Health Information. CIHI data quality study of Ontario emergency department visits for fiscal year 2004-2005- executive summary. 2008.

157. Juurlink D, Preyra C, Croxford R, et al. Canadian institute for health information discharge abstract database- A validation study. 2006.

158. Gibson D, Richards H, Chapman A. The National Ambulatory Care Reporting System: Factors that affect the quality of its emergency data. *Int J Information Quality*. 2008;2(2):97.

159. Bosco JL, Silliman RA, Thwin SS, et al. A most stubborn bias: No adjustment method fully resolves confounding by indication in observational studies. *J Clin Epidemiol*. 2010;63(1):64-74.

160. Salas M, Hofman A, Stricker BH. Confounding by indication: An example of variation in the use of epidemiologic terminology. *Am J Epidemiol*. 1999;149(11):981-983.

161. Health Quality Ontario. LHIN analysis. In: Health Quality Ontario, Institute for Clinical Evaluative Sciences, eds. *Quality monitor: 2011 report on Ontario's health system.* Toronto, Ontario: Queen's Printer for Ontario; 2011:118.

162. Kim JG, Ryoo B, Park YH, et al. Prognostic factors for survival of patients with advanced gastric cancer treated with cisplatin-based chemotherapy. *Cancer Chemother Pharmacol*. 2008;61(2):301-307.

163. Lee J, Lim T, Uhm JE, et al. Prognostic model to predict survival following first-line chemotherapy in patients with metastatic gastric adenocarcinoma. *Ann Oncol*. 2007;18(5):886-891.

164. Loggers ET, Maciejewski PK, Paulk E, et al. Racial differences in predictors of intensive end-of-life care in patients with advanced cancer. *J Clin Oncol*. 2009;27(33):5559-5564.

165. Barnato AE, Herndon MB, Anthony DL, et al. Are regional variations in end-of-life care intensity explained by patient preferences?: A study of the US medicare population. *Med Care*. 2007;45(5):386-393.

166. Smith AK, Earle CC, Mccarthy EP. Racial and ethnic differences in end-of-life care in fee-for-service medicare beneficiaries with advanced cancer. *J Am Geriatr Soc*. 2009;57(1) (pp 153-158).

167. Al-Refaie WB, Tseng JF, Gay G, et al. The impact of ethnicity on the presentation and prognosis of patients with gastric adenocarcinoma. results from the national cancer data base. *Cancer*. 2008;113(3):461-469.

168. Gallo WT, Baker MJ, Bradley EH. Factors associated with home versus institutional death among cancer patients in Connecticut. *J Am Geriatr Soc*. 2001;49(6):771-777.

169. Fairfield KM, Murray KM, Wierman HR, et al. Disparities in hospice care among older women dying with ovarian cancer. *Gynecol Oncol*. 2012;125(1):14-18.

170. Cohen J, Houttekier D, Onwuteaka-Philipsen B, et al. Which patients with cancer die at home? A study of six European countries using death certificate data. *J Clin Oncol*. 2010;28(13):2267-2273.

171. Stoddart H, Whitley E, Harvey I, Sharp D. What determines the use of home care services by elderly people? *Health Soc Care Community*. 2002;10(5):348-360.

172. Goodridge D, Buckley A, Marko J, Steeves M, Turner H, Whitehead S. Home care clients in the last year of life: Is material deprivation associated with service characteristics? *J Aging Health*. 2011;23(6):954-973.

173. Al-Refaie WB, Gay G, Virnig BA, et al. Variations in gastric cancer care: A trend beyond racial disparities. *Cancer*. 2010;116(2):465-475.

174. Epstein AJ, Gray BH, Schlesinger M. Racial and ethnic differences in the use of high-volume hospitals and surgeons. *Archives of Surgery*. 2010;145(2):179-186.

175. Aranda MA, McGory M, Sekeris E, Maggard M, Ko C, Zingmond DS. Do racial/ethnic disparities exist in the utilization of high-volume surgeons for women with ovarian cancer? *Gynecol Oncol*. 2008;111(2):166-172.

176. Smith JK, Hill JS, Ng SC, McDade TP, Shah SA, Tseng JF. Potential benefit of resection for stage IV gastric cancer: A national survey. *J Gastrointest Surg*. 2010;14(11):1660-1668.

177. Coburn N, Przybysz R, Barbera L, et al. CT, MRI and ultrasound scanning rates: Evaluation of cancer diagnosis, staging and surveillance in ontario. *J Surg Oncol*. 2008;98(7) (pp 490-499).

178. Demeter SJ, Jacobs P, Chmielowiec C, et al. The cost of lung cancer in Alberta. *Canadian Respiratory Journal*. 2007;14(2):81-86.

179. Hoch JS. Improving efficiency and value in palliative care with net benefit regression: An introduction to a simple method for cost-effectiveness analysis with person-level data. *J Pain Symptom Manage*. 2009;38(1):54-61.

180. Gomes B, Harding R, Foley KM, Higginson IJ. Optimal approaches to the health economics of palliative care: Report of an international think tank. *J Pain Symptom Manage*. 2009;38(1):4-10.

181. Smith TJ, Cassel JB. Cost and non-clinical outcomes of palliative care. *J Pain Symptom Manage*. 2009;38(1):32-44.

Appendix A

Examples of Chart Review Data Abstraction Forms

METASTATIC BIOPSY EXAMPLE: OTHER BIOPSY PATHOLOGY

How was the biopsy obtained?
❍ Percutaneous abdominal biopsy of Lymph node
❍Percutaneous abdominal biopsy of stomach
❍ Percutaneous abdominal biopsy of liver
❍ Percutaneous abdominal biopsy of carcinomatosis or mass other than primary site/stomach
❍Percutaneous, non-abdominal biopsy
❍ Pleural fluid
❍ EUS
❍ Other:
Location of lymph node biopsy: ___________________________________
Location of carcinomatosis or mass biopsy: _________________________
Location of non-abdominal biopsy: ________________________________
Location of EUS biopsy:____
Location of other biopsy:____

Presence of carcinoma/adenocarcinoma/signet ring carcinoma:
❍ Yes ❍ No ❍ Not Documented ❍ Unclear

Tumor Subtype, check one box for each line:
☐ Papillary
☐ Tubular
☐ Mucinous
☐ Adenosquamous
☐ Adeno NOS
☐ Signet Ring
☐ Not Documented

Lauren Type:
❍ Intestinal ❍ Diffuse ❍ Mixed ❍ Not Documented

Presence of Signet Ring Carcinoma/adenocarcinoma cells:
❍ Yes ❍ No ❍ Not Documented

Grade of tumor:
❍ Well Differentiated ❍ Moderately (well) Differentiated ❍Poorly Differentiated
❍ Undifferentiated ❍ Not Documented

E-cadherin positive: ❍ Yes ❍ No ❍ Not Documented
Is the other biopsy report unclear? ❍ Yes ❍ No

PATHOLOGY EXAMPLE: SURGICAL RESECTION SPECIMENT

Presence of carcinoma/adenocarcinoma/signet ring carcinoma:
❍ Yes ❍ No ❍ Not Documented ❍ Unclear

Please report the following:

Question	Yes	No	Not Documented
Presence of metaplasia	❍	❍	❍
Presence of dysplasia	❍	❍	❍
Presence of H. pylori	❍	❍	❍
Presence of signet ring carcinoma/adenocarcinoma cells	❍	❍	❍
Presence of lymphatic (small vessel) invasion	❍	❍	❍
Presence of venous (large vessel) invasion	❍	❍	❍
Presence of perineural (PNI) invasion	❍	❍	❍
E-cadherin positive	❍	❍	❍

Tumor Subtype:
☐ Papillary
☐ Tubular
☐ Mucinous
☐ Adenosquamous
☐ Adeno NOS
☐ Signet Ring
☐ Not Documented

Lauren Type:
❍ Intestinal ❍ Diffuse ❍ Mixed ❍Not Documented

Grade of tumor:
❍ Well Differentiated ❍ Moderately (well) Differentiated ❍Poorly Differentiated ❍ Undifferentiated ❍ Not Documented

Tumor description:
❍ Primary tumor cannot be assessed
❍ No evidence of primary tumor
❍ Carcinoma in situ
❍ Intraepithelial tumour without invasion of the lamina propria
❍ Tumour invades lamina propria or submucosa
❍ Tumour invades muscularis propria
❍ Tumour invades subserosa
❍ Tumour penetrates serosa (visceral peritoneum) without invasion of adjacent structures
❍ Tumour invades adjacent structures
❍ Not documented

Direct, local invasion of the:

☐ colon
☐ adrenal
☐ head of pancreas
☐ tail of pancreas
☐ spleen
☐ abdominal wall
☐ liver
☐ small bowl
☐ kidney ☐ other
Specify other structure(s):____

AJCC T-stage
❍ TX (unknown tumour stage)
❍ T0/Tis
❍ T1
❍ T2
❍ T3
❍ T4
❍ Not Documented

Total Number of Positive Nodes:____________ ❍ N/A
Total Number of Nodes Assessed:____________ ❍ N/A

Nodal Status as stated in the pathology report:
❍ NX (unknown nodal status)
❍ N0
❍ N1
❍ N2
❍ N3
❍ indicated "node positive" but exact nodal status not given
❍ Not Documented

What was the distance for the gross proximal margin (cm)? _____ ❍ N/A

What was the distance of the gross distal margin (cm)? ___ ❍ N/A

Were the following assessed:

Question	Yes	No	Not Documented
Intraoperative/frozen proximal margins	❍	❍	❍
Intraoperative/frozen distal margins	❍	❍	❍
Final proximal margins	❍	❍	❍
Final distal margins	❍	❍	❍
Final radial margins	❍	❍	❍

Intraoperative/frozen proximal margin results:

❍ Positive ❍ Negative ❍ Not Documented

Intraoperative/frozen distal margin results:
❍ Positive ❍ Negative ❍ Not Documented

If either margin was positive, was additional operative resection performed?
❍ Yes ❍ No ❍ Not Documented ❍N/A- margins were negative or not assessed

What was the final proximal margin result?
❍ Negative ❍ Positive ❍ Not Documented

The final proximal margin was:
☐ Grossly Positive
☐ Microscopically Positive, submucosal
☐ Microscopically Positive, mucosal
☐ Microscopically Positive, lymphatic channels
☐ Microscopically Positive, vascular spaces
☐ Microscopically Positive, perineural invasion
☐ Microscopically Positive, on IHC (immunohistochemistry)
☐ Microscopically Positive, not otherwise specified
☐ Unclear

What was the final distal margin result?
❍ Negative ❍ Positive ❍ Not Documented

The final distal margin was:
☐ Grossly Positive
☐ Microscopically Positive, submucosal
☐ Microscopically Positive, mucosal
☐ Microscopically Positive, lymphatic channels
☐ Microscopically Positive, vascular spaces
☐ Microscopically Positive, perineural invasion
☐ Microscopically Positive, on IHC (immunohistochemistry)
☐ Microscopically Positive, not otherwise specified
☐ Unclear

What was the final radial margin result?
❍ Negative ❍ Positive ❍ Not Documented

The final radial margin was:
☐ Grossly Positive

☐ Microscopically Positive, submucosal
☐ Microscopically Positive, mucosal
☐ Microscopically Positive, lymphatic channels
☐ Microscopically Positive, vascular spaces
☐ Microscopically Positive, perineural invasion
☐ Microscopically Positive, on IHC (immunohistochemistry)
☐ Microscopically Positive, not otherwise specified
☐ Unclear

Was omentum included in specimen?

- ❍ Yes
- ❍ No
- ❍ Not Documented

Metastasis:

- ❍ M X
- ❍ M0
- ❍ M1
- ❍ Not Documented

Were the following stated in the report:

Question	Positive	Negative	Not Performed	Not Documented
Biopsy of liver	❍	❍	❍	❍
Biopsy of omentum	❍	❍	❍	❍
Biopsy of distant node	❍	❍	❍	❍
Biopsy of peritoneal deposit	❍	❍	❍	❍
Biopsy of other tissue	❍	❍	❍	❍

Location of distant lymph node:_______________________________________
Location of additional tissue:____

Is the original surgical pathology report unclear?
❍ Yes ❍ No

RADIOLOGY EXAMPLE: COMPUTED TOMOGRAPHY SCAN (ABDOMEN/PELVIS)

Diagnosis/suspicion of gastric cancer discussed in request/reasoning for ordering the scan:

❍ Yes
❍ No

Diagnosis/suspicion of gastric cancer discussed in interpretation/findings of the scan:

❍ Yes
❍ No

Stated evidence of:

Question	Yes	Prob Yes	ND	Prob No	No	Unclear
Ascites	❍	❍	❍	❍	❍	❍
Direct local invasion	❍	❍	❍	❍	❍	❍
Metastasis	❍	❍	❍	❍	❍	❍

<u>Direct local invasion of:</u>

☐ liver
☐ head of pancreas
☐ tail of pancreas
☐ colon
☐ spleen
☐ adrenal
☐ abdominal wall
☐ kidney
☐ aorta
☐ celiac axis
☐ hepatic artery
☐ SMA (superior mesenteric artery)
☐ other structure

Specify other structure:_________________________

Site(s) of metastatic disease:

☐ ovary(ies)
☐ liver
☐ omentum
☐ carcinomatosis/diffuse peritoneal involvement/nodularity
☐ evidence of other metastatic disease
☐ Not documented

Specify site(s) of other metastatic disease: _____________________________

<u>Please describe the status of the lymph nodes:</u>

❍ Unremarkable, not involved <u>or</u> normal
❍ The nodal status is unclear
❍ Enlarged, suspicious, pathologic, >1 cm <u>or</u> “involved”
❍ Not Documented

Which nodes are enlarged/suspicious/pathologic/etc.?

☐ perigastric	☐ mediastinal
☐ periaortic	☐ iliac
☐ celiac	☐ peripancreatic
☐ gastroduodenal	☐ omental
☐ hepatic artery	☐ portal
☐ other	☐ Not Documented

Location of other lymph node: ____

Appendix B

Comparing the proportion of gastric cancer cases diagnosed with metastatic disease across Local Health Integration Networks in Ontario

Table 18: Proportion of patients diagnosed with metastatic gastric cancer among Local Health Integration Networks (n=1433)

Local Health Integration Network	**Stage of Disease**		**p-value***
	M1 (%)	**Mnot (%)**	
Erie St. Clair	65.3	34.7	p=0.2756
South West	52.7	47.3	
Waterloo Wellington	61.1	38.9	
Hamilton Niagara Haldimand Brant	61.9	38.1	
Central West	60	40	
Mississauga Halton	51.9	48.1	
Toronto Central	62.7	37.3	
Central	57.7	42.4	
Central East	58.7	41.3	
South East	63.1	36.9	
Champlain	62.3	37.8	
North Simcoe Muskoka	60.3	39.7	
North East	62.9	37.1	
North West	51.2	48.8	

*Chi square test for independence

Appendix C

Association between predictors and the number of days survived

Table 19: Unadjusted associations between the length of time alive from diagnosis in the time horizon and disease, patient and healthcare system predictors for metastatic gastric cancer patients in Ontario (n= 1433)

Predictor Variable	Category	Median Survival in days (95% CI)	Log-rank test p-value
Disease Characteristics			
Metastatic Sites	1 site	254 (227-287)	**<0.0001**
	>1 site	139 (125-155)	
Tumour Location	Distal Stomach	221 (180-246)	**0.0124**
	Gastroesophageal Junction	208 (169-245)	
	Proximal Stomach	197 (143-258)	
	Middle Stomach	151 (118-178)	
	Entire Stomach	128 (94-169)	
	Unknown	227 (113-324)	
Patient Characteristics			
Sex	Male	181 (158-206)	0.1461
	Female	190 (162-229)	
Age Category	< 65 years	256 (225-288)	**<0.0001**
	65-74 years	203.5 (157-234)	
	>74 years	122 (102-143)	
Resource Utilization Band	0	201 (23-NR)	0.0655
	1	107 (11-230)	
	2	246 (129-319)	
	3	205 (177-227)	
	4	183 (158-237)	
	5	136.5 (112-172)	

Median Community Income	Lowest Income	165.5 (141-206)	0.7522
	Quintile 2	186 (157-227)	
	Quintile 3	196 (144-238)	
	Quintile 4	177.5 (145-223)	
	Highest Income	209 (169-244)	
Rurality	Urban	187 (171-211)	**0.0405**
	Rural	155 (126-217)	
Health Care System Characteristics			
Local Health Integration Network	Erie St. Clair	180 (116-273)	**0.0108**
	South West	150 (106-239)	
	Waterloo Wellington	182 (103-259)	
	Hamilton Niagara Haldimand Brant	219 (154-266)	
	Central West	272 (156-389)	
	Mississauga Halton	190 (142-249)	
	Toronto Central	175 (146—215)	
	Central	175 (136-228)	
	Central East	228 (169-307)	
	South East	155 (73-206)	
	Champlain	198 (138-304)	
	North Simcoe Muskoka	103 (65-143)	
	North East	201.5 (128-261)	
	North West	140 (86-563)	
Treatment Strategy	No Gastrectomy	126.5 (116-140)	**<0.0001**
	Gastrectomy	398 (318-403)	
High Volume Gastric Cancer Specialist	No consult/treatment	128 (118-141)	**<0.0001**
	Consult/treatment	356.5 (318-444)	

CI= confidence interval

Appendix D

Association between the number of days survived and the number of admitted hospital days

Table 20: Exploring the relationship between days survived and the number of admitted hospital days through the mean number of days in hospital per survival period, and the proportion of days alive spent admitted to hospital

Survival Time Period (days)	Sum of inpatient hospital days	Sum of days survived	Mean # days in hospital	p-value	Proportion of days alive spent in hospital (%)
0-30 (n= 130)	1835	2270	14.1	p<0.0001	81
31-60 (n= 152)	3622	6878	23.8		53
61-90 (n= 153)	4286	11281	28.0		38
91-120 (n= 98)	2722	10283	27.8		26
121-150 (n= 101)	3309	13516	32.8		24
151-180 (n=76)	2247	12540	29.6		18
181-210 (n= 51)	1820	9975	35.7		18
211-240 (n= 57)	2390	12869	41.9		19
241-270 (n= 47)	1889	11939	40.2		16
271-300 (n= 67)	1096	10605	16.6		10
301-330 (n= 45)	1406	14155	31.2		10
331-360 (n= 23)	690	7981	30		9
361-729 (n=232)	8393	116113	36.2		7
730 or censored (n=231)	5526	168630	23.4		3

Appendix E

Association between the number of days survived and receipt of at least one home care visit

Table 21: Exploration into the association between the number of days survived and home care usage

Survival Time Period (days)	Home Care Use		
	No (%)	**Yes (%)**	**p-value***
0-30 (n= 130)	66.9	33.1	<0.0001
31-60 (n= 152)	43.4	56.6	
61-90 (n= 153)	21.6	78.4	
91-120 (n= 98)	14.3	85.7	
121-150 (n= 101)	17.8	82.2	
151-180 (n=76)	10.5	89.5	
181-210 (n= 51)	5.7	84.3	
211-240 (n= 57)	10.5	89.5	
241-270 (n= 47)	2.1	97.9	
271-300 (n= 67)	11.0	89.0	
301-330 (n= 45)	4.4	95.6	
331-360 (n= 23)	8.7	91.3	
361-729 (n=232)	6.0	94.0	
730 or censored (n=231)	16.0	74.0	

*Cochran-Armitage test for linear trend

Appendix F

Research Ethics Board Approval

QUEEN'S UNIVERSITY HEALTH SCIENCES & AFFILIATED TEACHING HOSPITALS RESEARCH ETHICS BOARD-DELEGATED REVIEW

December 06, 2011

Ms. Alyson Mahar
Department of Community Health and Epidemiology
Queen's University

Dear Dr. Mahar

Study Title: EPID-369-11 An Exploratory Study of the Resource Utilization and Costs of Non-Curative Gastric Cancer Management
File # 6006445
Co-Investigators: A. Johnson, R. Viola and N. Coburn

I am writing to acknowledge receipt of your recent ethics submission. We have examined the protocol for your project (as stated above) and consider it to be ethically acceptable. This approval is valid for one year from the date of the Chair's signature below. This approval will be reported to the Research Ethics Board. Please attend carefully to the following listing of ethics requirements you must fulfill over the course of your study:

Reporting of Amendments: If there are any changes to your study (e.g. consent, protocol, study procedures, etc.), you must submit an amendment to the Research Ethics Board for approval. Please use event form: HSREB Multi-Use Amendment/Full Board Renewal Form associated with your post review file # **6006445** in your Researcher Portal (https://eservices.queensu.ca/romeo_researcher/)

Reporting of Serious Adverse Events: Any unexpected serious adverse event occurring locally must be reported within 2 working days or earlier if required by the study sponsor. All other serious adverse events must be reported within 15 days after becoming aware of the information. Serious Adverse Event forms are located with your post-review file **6006445** in your Researcher Portal (https://eservices.queensu.ca/romeo_researcher/)

Reporting of Complaints: Any complaints made by participants or persons acting on behalf of participants must be reported to the Research Ethics Board within 7 days of becoming aware of the complaint. Note: All documents supplied to participants must have the contact information for the Research Ethics Board.

Annual Renewal: Prior to the expiration of your approval (which is one year from the date of the Chair's signature below), you will be reminded to submit your renewal form along with any new changes or amendments you wish to make to your study. If there have been no major changes to your protocol, your approval may be renewed for another year.

Yours sincerely,

Albert J. Clark

Chair, Research Ethics Board
December 06, 2011

Investigators please note that if your trial is registered by the sponsor, you must take responsibility to ensure that the registration information is accurate and complete