Original Article

Patient-Reported Symptoms Improve Performance of Risk Prediction Models for Emergency Department Visits Among Patients With Cancer: A Population-Wide Study in Ontario Using Administrative Data

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Abstract

Context. Prior work shows measurements of symptom severity using the Edmonton Symptom Assessment System (ESAS) which are associated with emergency department (ED) visits in patients with cancer; however, it is not known if symptom severity improves the ability to predict ED visits.

Objectives. To determine whether information on symptom severity improves the ability to predict ED visits among patients with cancer.

Methods. This was a population-based study of patients who were diagnosed with cancer and had at least one ESAS assessment completed between 2007 and 2015 in Ontario, Canada. After splitting the cohort into training and test sets, two ED visit risk prediction models using logistic regression were developed on the training cohort, one without ESAS and one with ESAS. The predictive performance of each risk model was assessed on the test cohort and compared with respect to area under the curve and calibration.

Results. The full cohort consisted of 212,615 unique patients with a total of 1,267,294 ESAS assessments. The risk prediction model including ESAS was superior in sensitivity, specificity, accuracy, and discrimination. The area under the curve was 73.7% under the model with ESAS, whereas it was 70.1% under the model without ESAS. The model with ESAS was also better calibrated. This improvement in calibration was particularly noticeable among patients in the higher deciles of predicted risk.

Conclusion. This study demonstrates the importance of incorporating symptom measurements when developing an ED visit risk calculator for patients with cancer. Improved predictive models for ED visits using measurements of symptom severity may serve as an important clinical tool to prompt timely interventions by the cancer care team before an ED visit is necessary. J Pain Symptom Manage 2019;58:745–755.

Key Words

Emergency department, Symptom severity, Risk prediction models, Logistic regression, Area under curve, Calibration

Introduction

The burden of emergency department (ED) visits can be high particularly for patients with cancer.[1,2] In addition to trying to cope with symptoms of cancer and toxicity due to treatments, long and uncomfortable ED waits for care can make visits a difficult experience.[2–5] An as example, unplanned ED visits and/or hospitalizations are expected to occur in as many as 42-60% of women receiving adjuvant

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chemotherapy.[6] Reasons for ED visits in the cancer population have been studied,[2,7,8] and recent research has focused on the relationship between symptomatology and emergency care usage showing that worsening of symptoms also contribute to ED visits.[9] Specific physical symptoms such as pain, nausea, and shortness of breath, along with constitutional symptoms such as well-being, fatigue, and appetite are associated with ED visits in the cancer population.[1]

Starting in 2007, Cancer Care Ontario implemented a province-wide program to screen for common cancer symptoms using the Edmonton Symptom Assessment System (ESAS), which is a patient-reported outcome measure. Based on evidence that this symptom screening tool improves symptom identification, symptom monitoring and management, patient-provider communication, and quality of life,[10–13] it is being widely incorporated into routine clinical care.[14,15] All regional cancer centers and nearly 80 non–regional cancer health centers in the province of Ontario, Canada, systematically collect ESAS scores at cancer outpatient visits. Other jurisdictions including Dartmouth, The Netherlands, United Kingdom, and Sweden also collect patient-reported outcome measures on various patient populations[16–19]; however, the program at Cancer Care Ontario remains one of the largest, most comprehensive patient-reported outcome programs in existence.[20]

Although existing research using ESAS has established there is an association between symptom scores and ED visits, to our knowledge there has been no work demonstrating the ability of symptom scores to predict ED visits. An improved predictive algorithm for ED visits using measurements of symptom severity at the time of assessment may serve as an important clinical tool to prompt further detailed assessments and to encourage timely interventions by the cancer care team, depending on the patient's predicted level of risk. This may lead to decreased ED use.

Methods

Study Design and Population

This was a population-based retrospective cohort study using linked administrative health-care databases. The cohort consisted of patients who were newly diagnosed with a primary cancer and had at least one ESAS assessment completed between January 1, 2007 and December 31, 2015 in Ontario, Canada. Ontario is Canada's largest and most ethnically diverse province, with a population of 14 million, and provides universal health-care coverage to its residents. Patients had to be eligible for the Ontario Health Insurance Plan (OHIP) and at least 18 years of age at the time of diagnosis. The OHIP is Ontario's universal health-care insurance program, which is essentially available to all Ontario residents. Confirmation of OHIP eligibility was obtained from the OHIP administrative database, and the Ontario Cancer Registry which captures all incident cases of cancer in Ontario was used to determine the diagnosis date.[21] To capture an ambulatory cohort, patients were included only if their ESAS assessments occurred in a regional cancer center or partner hospital. Administrative databases were linked using unique encoded identifiers and analyzed at the ICES (historically known as the Institute for Clinical Evaluative Sciences). The ICES is an independent, nonprofit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyze health-care and demographic data, without consent, for health system evaluation and improvement. All databases used in this study are regularly checked for validity and have been used extensively in research.

Index Dates

Starting from diagnosis, every patient was observed until one of the following occurred: a subsequent cancer diagnosis, loss of OHIP eligibility, entry into home-care facility, death, or study end date on December 31, 2015. All ESAS assessments occurring over the course of observation, provided there was at least a seven-day gap between consecutive assessments, were retrieved for each patient. The index dates for each individual were the dates of their ESAS assessments; the data were structured at the ESAS level. The ESAS assessment dates were retrieved from the Symptom Management Reporting Database held by Cancer Care Ontario.

Outcome

The outcome was defined as the occurrence of at least one ED visit within seven days after an ESAS assessment. This seven-day window was chosen a priori based on clinical reasoning; the window was long enough for the provider to potentially respond to the symptom screen and short enough that the screening could be attributed to the ED visit.[1] The outcome was treated as a binary variable and was measured after each ESAS assessment for every patient. All ED visits were captured by mandatory reporting in the Canadian Institute for Health Information's National Ambulatory Care Reporting System (CIHI-NACRS) database.[22]

Covariates

At every ESAS assessment, the corresponding ESAS scores for each of the nine symptoms were retrieved from the Symptom Management Reporting Database. Symptoms included anxiety, appetite, depression, drowsiness, nausea, pain, shortness of breath, fatigue, and well-being. The score for each symptom ranged from 0 to 10, with 0 being symptom absence and 10

being most severe. As common in prior work, symptom scores were categorized in the regression model as none (score 0), mild (score 1-3), moderate (score 4-6), or severe (score 7-10).The number of months since diagnosis and the number of prior ESAS assessments were recorded as continuous measures and updated at each ESAS assessment.[23]

Sex and date of birth were captured from the Registered Persons Database, which is a population-based registry maintained by the provincial Ministry of Health to manage publicly funded health-care services. It contains sociodemographic information on all residents of Ontario eligible for the universal government-funded health-care plan.[24] Age was determined at each ESAS assessment and was treated as a continuous covariate. Year of cancer diagnosis (continuous covariate), type of cancer diagnosis (categorical covariate), and stage at cancer diagnosis (categorical covariate) were obtained from the Ontario Cancer Registry. Types of cancer diagnoses were grouped into following categories: lung, breast, lung, gastrointestinal, genitourinary, hematology, and other. Stage categories ranged from one to four, or unknown. Neighborhood median income quintile representing socioeconomic status was captured at the time of diagnosis by linking residential postal codes in the Registered Persons Database to Census dissemination areas based on the 2006 Canada Census.[25] Rurality was also determined at the time of diagnosis by postal code and was recorded as a binary variable representing whether a patient lived in a rural area (versus an urban area) in Ontario. The total number of ED visits and total number of hospitalizations in the two years before cancer diagnosis were obtained from CIHI-NACRS database and Canadian Institute for Health Information's Discharge Abstract Database (CIHI-DAD), respectively.[26] They were each treated as continuous measures.

Receipt of chemotherapy and receipt of radiation within 30 days before an ESAS assessment were each treated as binary covariates. The receipt of surgery before an ESAS assessment (looking back at the date of diagnosis) was also treated as a binary covariate. Dates of chemotherapy and radiation were retrieved from CIHI-NACRS database, and surgery dates were extracted from CIHI-DAD. The total number of clinic visits to a radiation oncologist, medical oncologist, or family physician within 30 days before an ESAS assessment was obtained from OHIP and treated as a continuous measure. Information on all these covariates was updated at every available ESAS assessment for each patient.

To determine the burden of comorbidity for each patient, we identified all diagnoses in the two years before an ESAS assessment using CIHI-DAD, CIHI-NACRS, OHIP, and the Same Day Surgery database. For each subject, we then used the Johns Hopkins Adjusted Clinical Groups® software program to collapse these diagnoses to the 32 Aggregated Diagnosis Groups (ADGs).[27] Specifically, we determined whether an *International Classification of Diseases* diagnosis code within each of the 32 ADGs had occurred in the two years before an ESAS assessment. Every patient, therefore, had 32 ADG indicator variables that were updated at each ESAS assessment.[28] Level of health-care utilization was captured using Resource Utilization Bands, which are quintiles of expected resource use.[29] Resource Utilization Bands were determined via the Johns Hopkins Adjusted Clinical Groups© System, version 10, using data from OHIP and the CIHI-DAD. Levels were updated at each ESAS assessment using a two-year look-back window.

To capture the phase of cancer management at the time of ESAS assessment, phase of care (classified as initial, continuing, or palliative) was determined at each ESAS assessment for every patient, similar to recent work.[30] At the time of diagnosis, a patient with Stage 1, 2, or 3 cancer was considered to be in the initial phase of cancer for the first 12 months and then were considered to be in the continuing phase of care after the 12-month mark. A patient would transition into the palliative phase of care only if they were 1) subsequently diagnosed with metastatic cancer, 2) started chemotherapy or radiation 12 months beyond the date of cancer diagnosis, 3) started chemotherapy or radiation with palliative intent, or 4) started palliative care services. If a patient had Stage 4 cancer at the time of diagnosis, then they were immediately placed in the palliative phase of care. The continuing phase of care captured ongoing monitoring and management of cancer and was thus defined as the time period between the initial and palliative phases of care. Not every patient would have progressed from the initial to the continuing to the palliative phases of care; some started in the initial phase of care and then progressed directly to the palliative phase of care, and others started in the palliative phase of care from diagnosis.

Statistical Analyses

Descriptive Analyses. The distributions of the cohort characteristics were explored; continuous measures were described with medians and interquartile ranges, and categorical measures were described using frequencies and percentages. Before initiating any modeling, we randomly divided our population into two mutually exclusive cohorts: 80% of patients comprised the training cohort and the remaining 20% of patients comprised the test cohort.

Building the Risk Prediction Models (Using the Training Cohort). Logistic regression models to predict an

ED visit within seven days after an ESAS assessment were built using the training cohort. A generalized estimating equations approach under an exchangeable correlation structure was incorporated to account for multiple measurements arising from the same individual because of the longitudinal nature of the data. Since generalized estimating equations are marginal models, predictions correspond to the average estimated risk for a given individual with specific characteristics.[31] Two different regression models were developed: Prediction Model 1—no ESAS model, this contained all covariates listed previously except for the nine symptom measurements (51 covariates); Prediction Model 2—ESAS model, this additionally incorporated all nine symptom measurements to Prediction Model 1 (60 covariates). For each of the two regression models, backwards variable elimination with a significance level of 0.05 for variable retention was used to derive the final parsimonious forms of the models.[27] It should be noted that a third model further incorporating all two-way symptom interactions was implemented—its performance was very similar to Model 2, and thus, for simplicity, we do not discuss this model any further.

Assessing the Performance of the Risk Prediction Models (Using the Test Cohort). The predictive performance of each of the two risk prediction models was assessed and compared using the test cohort. Each model was applied to every individual in the test cohort to obtain their corresponding estimated ED visit probability. Under each model, the predicted number of outcomes was then compared with the actual number of outcomes by composing a confusion matrix. Specifically under each of the two models, we calculated sensitivity (true positive fraction), specificity (true negative fraction), accuracy (true positive or negative fraction), and discrimination. Discrimination was measured using the area under the receiver-operating characteristic curve, in which a value of 0.5 implies a useless model that classifies no better than chance.[32] In theory, a perfectly discriminating model (value of 1.0) would assign a higher event probability to everyone who experienced the event compared to any individual who did not. Calibration plots were also constructed under each of the two models using the test cohort. This was done by grouping patients into deciles based on their predicted risk and then plotting the observed ED visit risk within a decile against the corresponding mean predicted risk within that decile.[33] Points closer to the 45° line indicate better calibration. Characteristics of individuals belonging to the highest predicted risk decile were also described. All analyses were conducted using statistical software R, version 3.2.3.[34]

Results

The distributions of characteristics in our study population are presented in Table 1. For simplicity, as patients could have multiple ESAS assessments during their observation period, only covariate values at the initial ESAS assessment are provided in the table. There was a total of 1,267,294 ESAS assessments conducted among 212,615 unique patients. The median (interquartile range) of the number of ESAS assessments per patient was 3.3 (1.3−7.4). The median (interquartile range) of the number of days from diagnosis to the initial ESAS assessment was 105 (41.9−441.5). Among patients who had at least two ESAS assessments (n = 167,336), the average gap time between consecutive assessments was 93 days. Figure 1 illustrates the trajectory of the mean ESAS score during every month after diagnosis for each of the nine symptoms. The symptom burden trend is consistent over time with fatigue being the most severe, followed by well-being and nausea being the least severe symptom.

Before proceeding with modeling, the study population was randomly divided into two mutually exclusive cohorts: 80% of patients (n = 170,092 undergoing 1,015,125 ESAS assessments) comprised the training cohort and the remaining 20% of patients (n = 42,523 undergoing 252,169 ESAS assessments) were set aside as the test cohort. Among the 1,015,125 ESAS assessments in the training cohort, 31,961 (3.15%) were followed by an ED visit within seven days after assessment. Table 2 provides the final set of odds ratio estimates and P-values from each of the two risk prediction models constructed using the training cohort (Prediction Model 1: no ESAS model, Prediction Model 2: ESAS model). Worsening of appetite, pain, dyspnea, fatigue, or well-being demonstrated a strong significant increase in the risk of going to ED within seven days after the assessment. The risk of ED visits increased slightly as drowsiness or nausea worsened, and there was no significant relationship between anxiety and ED attendance. On the other hand, there was a decrease in ED attendance as the severity of depression increased. The direction and magnitude of the association between the remaining covariates and the risk of ED visits were similar under both risk prediction models. Phase of care at the time of assessment, cancer type, cancer stage, and rurality were the strongest determinants of whether an ED visit would occur within seven days after an assessment.

The predictive performance of each of the two prediction models using the test cohort is shown and compared in Table 3. The test cohort consisted of 42,523 unique patients. These patients collectively had 252,169 ESAS assessments, among which 7812

Table 1

Distributions of Characteristics at Baseline ESAS Assessment Among the Entire Cohort (Before Random Splitting, $N = 212,615$)

Characteristic	Value	Frequency	Percentage	Median	Q1	Q3
Anxiety	None	89,224	42.0			
	Mild	66,849	31.4			
	Moderate	35,498	16.7			
	Severe	21,044	9.9			
Depression	None	125,863	59.2			
	Mild	50,089	23.6			
	Moderate	24,290	11.4			
	Severe	12,373	5.8			
Drowsiness	None	113,199	53.2			
	Mild	55,413	26.1			
	Moderate	28,366	13.3			
	Severe	15,637	7.4			
Appetite	None	120,845	56.8			
	Mild	43,122	20.3			
	Moderate	30,242	14.2			
	Severe	18,406	8.7			
Nausea	None	170,887	80.4			
	Mild	27,165	12.8			
	Moderate	9780	4.6			
	Severe	4783	2.2			
Pain	None	116,676	54.9			
	Mild	55,238	26.0			
	Moderate	26,185	12.3			
	Severe	14,516	6.8			
Dyspnea	None	131,345	61.8			
	Mild	45,202	21.3			
	Moderate	22,403	10.5			
	Severe	13,665	6.4			
Fatigue	None	62,583	29.4			
	Mild	69,451	32.7			
	Moderate	49,110	23.1			
	Severe	31,471	14.8			
Well-being	None	65,747	30.9			
	Mild	75,009	35.3			
	Moderate	49,670	23.4			
	Severe	22,189	10.4			
Months from diagnosis	Continuous			3.5	1.4	14.6
Number of prior ESAS assessments	Continuous			0	0	0
Age at assessment	Continuous			63.8	54.4	72.3
Receipt of chemotherapy within prior 30 days	Yes	25,074	11.8			
Receipt of radiation within prior 30 days	Yes	18,904	8.9			
Receipt of surgery since diagnosis	Yes	105,061	49.4			
Number of radiation oncology visits within prior 30 days	Continuous			0	0	0
Number of medical oncology visits within prior 30 days	Continuous			0	0	0
Number of PCP visits within prior 30 days	Continuous			0	0	0.3
Resource utilization band	0	891	0.4			
	1	1140	0.5			
	2	6214	2.9			
	3	86,459	40.7			
	4	61,889	29.1			
	5	56,022	26.3			
Phase of care	Initial	110,433	51.9			
	Continuing	40,467	19.0			
	Palliative	61,715	29.0			
Sex	Female	114,665	53.9			
Year of diagnosis	Continuous			2011	2008	2013
Cancer type	Breast	46,881	22.0			
	Central nervous system	3073	1.4			
	Gastrointestinal	36,394	17.1			
	Genitourinary	36,626	17.2			
	Gynecologic	17,663	8.3			

(*Continued*)

Table 1
Continued

Characteristic	Value	Frequency	Percentage	Median	Q1	Q3
	Hematology	25,341	11.9			
	Head and neck	11,109	5.2			
	Other	3417	1.6			
	Primary unknown	1303	0.6			
	Skin	6117	2.9			
	Lung	24,691	11.6			
Stage at diagnosis	0	408	0.2			
	1	44,714	21.0			
	2	52,655	24.8			
	3	36,730	17.3			
	4	30,628	14.4			
	Unknown	47,480	22.3			
Income quintile	1	36,259	17.1			
	2	41,218	19.4			
	3	41,950	19.7			
	4	45,956	21.6			
	5	47,232	22.2			
Rural residence	Yes	29,782	14.0			
Number of ED visits 2 yrs before diagnosis	Continuous			0	0	1
Number of hospitalizations 2 yrs before diagnosis	Continuous			0	0	0

Information on 32 Aggregated Diagnosis Group distributions is not shown here due to space restrictions.
ED = emergency department; ESAS = Edmonton Symptom Assessment System; PCP = primary care provider.

(3.10%) were followed by an ED visit within seven days after assessment. The model including patient-reported symptoms (Prediction Model 2: ESAS model) was superior in sensitivity, specificity, accuracy, and discrimination. The area under the receiver-operating characteristic curve was 73.7% (95% CI: 72.9%−74.5%) under the ESAS model, whereas it was 70.1% (95% CI: 68.9%−71.3%) under the model without patient-reported symptoms; CIs were obtained via bootstrapping the test cohort 500 times. This implies that the ESAS model's level of discrimination or ability to correctly classify patients who will

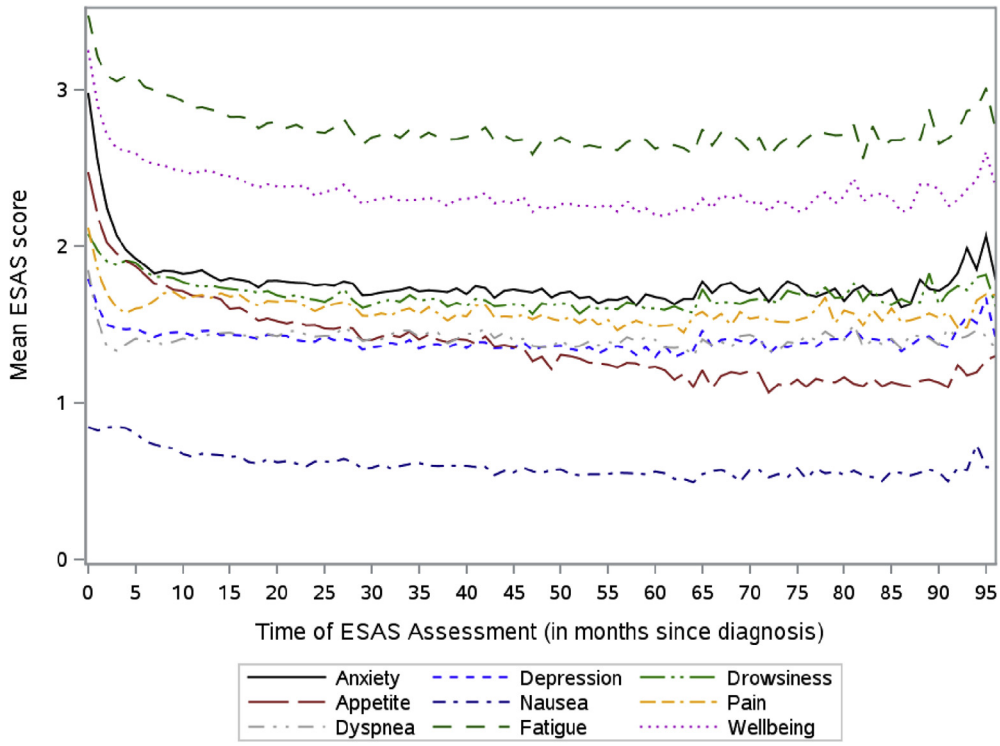

Fig. 1. Trajectory of the mean ESAS score after diagnosis for each of the nine symptoms. ESAS, Edmonton Symptom Assessment System.

Table 2
Results From Each of the Final Two Risk Prediction Models (Using the Training Cohort)

			Prediction Model 1: No ESAS Model		Prediction Model 2: ESAS Model	
Characteristic	Value	Reference	OR Estimate	*P*-value	OR Estimate	*P*-value
Anxiety	Mild	None	na	na	0.97	0.0788
	Moderate	None	na	na	1.04	0.0777
	Severe	None	na	na	1.03	0.2611
Depression	Mild	None	na	na	0.93	<0.0001
	Moderate	None	na	na	0.87	<0.0001
	Severe	None	na	na	0.79	<0.0001
Drowsiness	Mild	None	na	na	1.06	0.0003
	Moderate	None	na	na	1.1	<0.0001
	Severe	None	na	na	1.17	<0.0001
Appetite	Mild	None	na	na	1.2	<0.0001
	Moderate	None	na	na	1.37	<0.0001
	Severe	None	na	na	1.62	<0.0001
Nausea	Mild	None	na	na	1.02	0.2031
	Moderate	None	na	na	1.08	0.0006
	Severe	None	na	na	1.14	<0.0001
Pain	Mild	None	na	na	1.12	<0.0001
	Moderate	None	na	na	1.27	<0.0001
	Severe	None	na	na	1.41	<0.0001
Dyspnea	Mild	None	na	na	1.01	0.3977
	Moderate	None	na	na	1.12	<0.0001
	Severe	None	na	na	1.39	<0.0001
Fatigue	Mild	None	na	na	1.09	<0.0001
	Moderate	None	na	na	1.21	<0.0001
	Severe	None	na	na	1.37	<0.0001
Well-being	Mild	None	na	na	1.11	<0.0001
	Moderate	None	na	na	1.24	<0.0001
	Severe	None	na	na	1.49	<0.0001
Months from diagnosis	Continuous		0.997	<0.0001	1.01	0.0001
Number of prior ESAS assessments	Continuous		0.996	<0.0001	elim	elim
Age at assessment	Continuous		elim	elim	elim	elim
Receipt of chemotherapy within prior 30 days	Yes	No	1.197	<0.0001	1.23	<0.0001
Receipt of radiation within prior 30 days	Yes	No	1.051	0.0132	elim	elim
Receipt of surgery since diagnosis	Yes	No	0.885	<0.0001	0.95	0.0002
Number of radiation oncology visits within prior 30 days	Continuous		1.083	<0.0001	1.06	<0.0001
Number of medical oncology visits within prior 30 days	Continuous		1.244	<0.0001	1.22	<0.0001
Number of PCP visits within prior 30 days	Continuous		1.2	<0.0001	1.17	<0.0001
Resource utilization band	0	5	elim	elim	elim	elim
	1	5	elim	elim	elim	elim
	2	5	elim	elim	elim	elim
	3	5	elim	elim	elim	elim
	4	5	elim	elim	elim	elim
Phase of care	Initial	Continuing	1.514	<0.0001	1.48	<0.0001
	Palliative	Continuing	2.237	<0.0001	1.93	<0.0001
Sex	Female	Male	0.952	0.0005	0.92	<0.0001
Year of diagnosis	Continuous		1.018	<0.0001	1.04	<0.0001
Cancer type	Breast	Lung	0.729	<0.0001	0.8	<0.0001
	Central nervous system	Lung	0.862	0.0015	1.04	0.4495
	Gastrointestinal	Lung	0.863	<0.0001	0.97	0.181
	Genitourinary	Lung	0.66	<0.0001	0.8	<0.0001
	Gynecologic	Lung	0.798	<0.0001	0.87	<0.0001
	Hematology	Lung	0.647	<0.0001	0.77	<0.0001
	Head and neck	Lung	0.646	<0.0001	0.67	<0.0001
	Other	Lung	0.778	<0.0001	0.86	0.0048
	Primary unknown	Lung	0.748	<0.0001	0.8	0.0024
	Skin	Lung	0.773	<0.0001	0.88	0.0054
Stage at diagnosis	2	1	1.157	<0.0001	1.13	<0.0001
	3	1	1.305	<0.0001	1.25	<0.0001
	4	1	1.403	<0.0001	1.34	<0.0001
	Unknown	1	1.481	<0.0001	1.36	<0.0001

(*Continued*)

Table 2
Continued

Characteristic	Value	Reference	Prediction Model 1: No ESAS Model		Prediction Model 2: ESAS Model	
			OR Estimate	*P*-value	OR Estimate	*P*-value
Income quintile	1	5	1.175	<0.0001	1.12	<0.0001
	2	5	1.082	<0.0001	1.05	0.0075
	3	5	1.027	0.1391	1.01	0.5843
	4	5	1.036	0.0479	1.03	0.1053
Rural residence	Yes	No	1.299	<0.0001	1.36	<0.0001
Number of ED visits 2 years before diagnosis	Continuous		1.073	<0.0001	1.07	<0.0001
Number of hospitalizations 2 years before diagnosis	Continuous		elim	elim	0.97	0.001

Information on 32 Aggregated Diagnosis Group results are not shown here due to space restrictions.
elim = implies this variable was eliminated during the backward selection model building process; ED = emergency department; ESAS = Edmonton Symptom Assessment System; na = not applicable for this model; PCP = primary care provider.

experience an ED visit vs patients who will not are higher than the discrimination ability of the model without ESAS. Calibration plots based on each of the two prediction models using the test cohort are given in Figure 2. In each decile of predicted risk, the distance between the point and the 45° line is shorter in the model with ESAS compared with the model without ESAS, indicating that the model with ESAS is better calibrated. Moreover, this improvement in performance for the model with ESAS is particularly noticeable among patients in the higher deciles of predicted risk, as can be seen by the decrease in distances toward the 45° line among these higher risk deciles compared with the corresponding distances under the model without ESAS. It should be noted that majority of patients belonging to the highest decile of predicted ED visit risk had severe scores for drowsiness, appetite, pain, dyspnea, fatigue, and well-being; most had Stage 4 lung or gastrointestinal cancer, were in the palliative phase, and had high prior health-care service use.

Discussion

Not only is symptom severity associated with ED visits, our work demonstrated that information on symptom severity improves the ability to predict ED visits among patients with cancer. Risk prediction models that incorporated symptom measurements were superior with respect to sensitivity, specificity, accuracy, and discrimination, compared with risk prediction models that did not include symptom information. Calibration had also improved implying that we were better able to achieve agreement between predicted and observed ED visit risks by using symptom scores. This study also demonstrated the feasibility of using only administrative data to predict which ambulatory cancer patients are most likely to have an ED visit in the near future. Many of the measures derived from the administrative databases were predictive of ED use, and the inclusion of symptom severity for each patient further improved the prediction tool.

Table 3
Prediction Performance Under Each of the Final Two Risk Prediction Models (Using the Test Cohort)

Performance Measure	Prediction Model 1: No ESAS Model	Prediction Model 2: ESAS Model
Sensitivity	66.0	67.1
Specificity	62.8	67.3
Accuracy	63.0	67.2
Area under the ROC curve (discrimination)	70.1	73.7

ESAS = Edmonton Symptom Assessment System; ROC = receiver-operating characteristic.

Our work showed that worsening of appetite was the strongest symptom predictor of ED visits, and similar to prior findings, worsening of anxiety had no relationship with ED visits.[1] We found that visits to the ED decrease as the severity of depression increases. It is possible that cancer patients with depression are more likely to seek medical support from primary care physicians, rather than attending an ED where the individuals providing care are less familiar to them.[35]

The existing literature on the development of risk prediction models for ED visits is sparse. Recent work focused on building a prediction model for ED use among community-dwelling adults receiving publicly funded and community care in southern Ontario, Canada, using information collected with the Resident Assessment Instrument: Home Care.[36] Similarly, most studies focus on ED visit prediction in the general population, and thus, their derived models may not be applicable to patients diagnosed with cancer. Other risk prediction models for ED visits or hospital admission have been developed for cohorts belonging to a predominantly private health-care system, and these models may not be suitable for prediction in

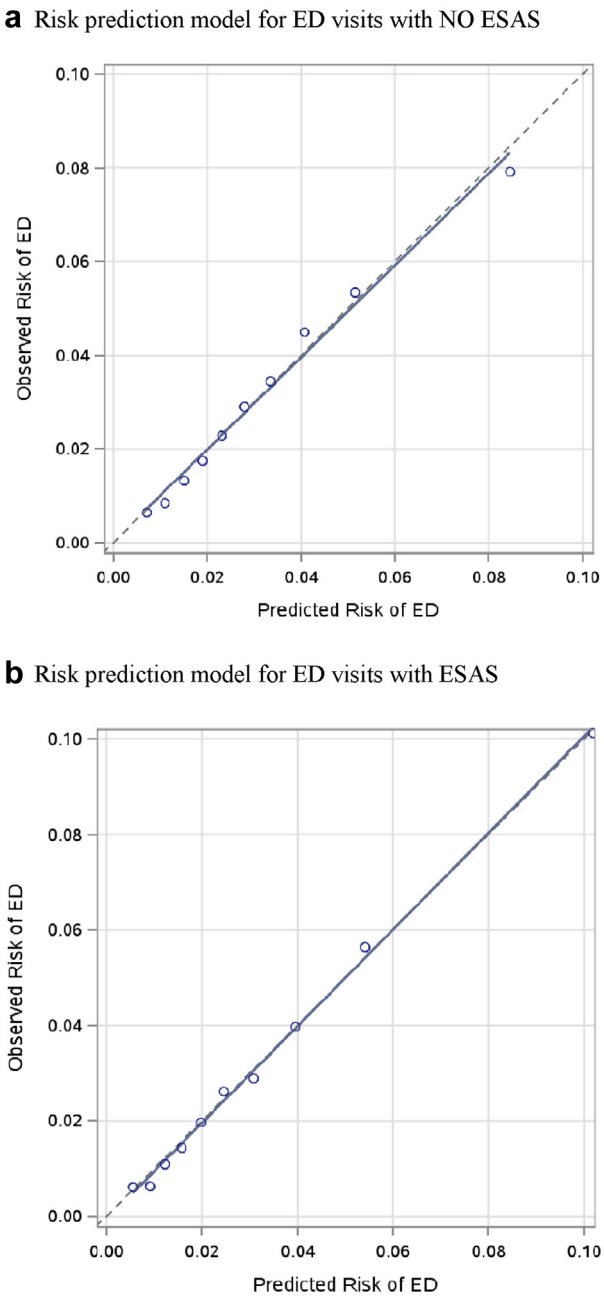

Fig. 2. Calibration plots using the test cohort. (a) Risk prediction model for ED visits with No ESAS; (b) risk prediction model for ED visits with ESAS. ED, emergency department.

populations with single-payer universal health care.[37] A recent systematic review noted poor predictive performance of risk models for hospital readmission (majority of models reported discrimination < 0.7), and it was suggested that information on additional variables collected through patient self-report be included to improve performance.[38,39]

This article has several strengths. This was a population-based study with nine years of data collected on over 200,000 cancer patients with over 1.2 million assessments of symptom severity. The cohort consisted of a broad range of ambulatory patients, including all cancer types, all treatment intents, all phases of care, and from across the entire province of Ontario, Canada. Our risk prediction model for ED visits may thus be generalizable to other ambulatory cancer patient populations belonging to similar single-payer health-care systems. An extensive list of variables was also used to build the prediction model, including both physical and constitutional symptoms; and each variable was recalculated at every assessment for every patient.

There are important limitations to our study. As symptom assessments were only recorded at outpatient visits, our prediction model does not involve any symptom information from patients who were in hospital or hospice or who were otherwise too unwell to visit a cancer clinic. Our risk model may thus not be applicable for predicting ED visits among nonambulatory cancer patients and may not be generalizable to populations without universal health care. We also did not include data on chemotherapy drugs and potentially important clinical prognostic characteristics, such as performance or functional status, which may further improve risk models for predicting ED visits. Future research includes validating our model on cancer patients belonging to similar universal health-care jurisdictions. It is also of interest to examine if the prediction models and their performance vary by type of cancer diagnosis.

This study demonstrates the importance of incorporating symptom measurements when developing a risk calculator for predicting ED visits among patients with cancer. Improved predictive models for ED visits using measurements of symptom severity at the time of assessment may serve as an important clinical tool to prompt timely interventions by the cancer care team before an ED visit is necessary. It is important to note that not all ED visits can be avoided—some are necessary, appropriate, and may lead to further health care (such as those ED visits that result in a hospital admission). Future work may consist of assessing whether an ED visit was necessary by determining if it resulted in a hospital admission—an ED visit followed by hospital stay may be viewed as a necessary ED visit. It is possible to use this tool in several proactive ways. For example, patients at an extremely high risk of experiencing an ED visit may be admitted to hospital proactively to spare long and uncomfortable ED wait times. Other proactive approaches including further detailed assessments and increased attention to symptom management for high-risk patients at the time of clinic assessment may also lead to decreased future ED use.

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Ethical approval: This study involved secondary data analyses only and was, thus, exempt from requiring Research Ethics Board approval because the ICES is a designated "45.1 entity" under the Personal Health Information Protection Act (PHIPA) enabling the use of personal health information.

References

1. Barbera L, Atzema C, Sutradhar R, et al. Do patient-reported symptoms predict emergency department visits in cancer patients? A population-based analysis. Ann Emerg Med 2013;61:427–437.

2. Barbera L, Taylor C, Dudgeon D. Why do cancer patients visit the emergency department near the end of life? CMAJ 2010;182:563–568.

3. Rowe B, Bond K, Ospina M, et al. Frequency, Determinants, and Impact of Overcrowding in Emergency Departments in Canada: A National Survey of Emergency Department Directors. Ottawa, Ontario: Canadian Agency for Drugs & Technologies in Health, 2006.

4. Hwang U, Richardson L, Livote E, et al. Emergency department crowding and decreased quality of pain care. Acad Emerg Med 2008;15:1248–1255.

5. Hassett MJ, O'Malley AJ, Pakes JR, Newhouse JP, Earle CC. Frequency and cost of chemotherapy-related serious adverse effects in a population sample of women with breast cancer. J Natl Cancer Inst 2006;98:1108–1117.

6. Enright K, Grunfeld E, Yun L, et al. Population-based assessment of emergency room visits and hospitalizations among women receiving adjuvant chemotherapy for early breast cancer. J Oncol Pract 2015;11:126–132.

7. Mayer DK, Travers D, Wyss A, et al. Why do patients with cancer visit emergency departments? Results of a 2008 population study in North Carolina. J Clin Oncol 2011;29:2683–2688.

8. Escalante CP, Martin CG, Elting LS, et al. Dyspnea in cancer patients. Etiology, resource utilization, and survival—implications in a managed care world. Cancer 1996;78:1314–1319.

9. Barbera L, Sutradhar R, Howell D, et al. Does routine symptom screening with ESAS decrease ED visits in breast cancer patients undergoing adjuvant chemotherapy? Support Care Cancer 2015;23:3025–3032.

10. Kotronoulas G, Kearney N, Maguire R, et al. What is the value of the routine use of patient-reported outcome measures toward improvement of patient outcomes, processes of care, and health service outcomes in cancer care? A systematic review of controlled trials. J Clin Oncol 2014;32:1480–1501.

11. Chen J, Ou L, Hollis SJ. A systematic review of the impact of routine collection of patient reported outcome measures on patients, providers and health organisations in an oncologic setting. BMC Health Serv Res 2013;13:211.

12. Yang LY, Manhas DS, Howard AF, et al. Patient-reported outcome use in oncology: a systematic review of the impact on patient-clinician communication. Support Care Cancer 2018;26:41–60.

13. Howell D, Liu G. Can routine collection of patient reported outcome data actually improve person-centered health? Healthc Pap 2011;11:42–47; discussion 55-58.

14. Snyder CF, Aaronson NK. Use of patient-reported outcomes in clinical practice. Lancet 2009;374:369–370.

15. Greenhalgh J, Meadows K. The effectiveness of the use of patient-based measures of health in routine practice in improving the process and outcomes of patient care: a literature review. J Eval Clin Pract 1999;5:401–416.

16. Schepers SA, Sint Nicolaas SM, Haverman L, et al. Real-world implementation of electronic patient-reported outcomes in outpatient pediatric cancer care. Psychooncology 2017;26:951–959.

17. Basch E, Barbera L, Kerrigan CL, et al. Implementation of patient-reported outcomes in routine medical care. Am Soc Clin Oncol Educ Book 2018;38:122–134.

18. Patient Reported Outcomes Measures (PROMs). Leeds (UK): National Health Service. Available from https://digital.nhs.uk/data-and-information/data -tools-and-services/data-services/patient-reported-outcome-measures-proms. Accessed September 15, 2018.

19. Nilsson E, Orwelius L, Kristenson M. Patient-reported outcomes in the Swedish National Quality Registers. J Intern Med 2016;279:141–153.

20. Barbera L, Lee F, Sutradhar R. Use of patient-reported outcomes in regional cancer centres over time: a retrospective study. CMAJ Open 2019;7:E101–E108.

21. Clarke EA, Marrett LD, Kreiger N. Cancer registration in Ontario: a computer approach. In: Jensen OM, Parkin DM, MacLennan R, Muir CS, Skeet RG, eds. Cancer Registration Principles and Methods. Lyon, France: IARC Publications, 1991:246–257.

22. Institute for Clinical Evaluative Sciences. ICES Data Dictionary Toronto, ON: Institute for Clinical Evaluative Sciences. Available from https://datadictionary.ices.on.ca/Applications/DataDictionary/Default.aspx. Accessed January 23, 2018.

23. Selby D, Cascella A, Gardiner K, et al. A single set of numerical cutpoints to define moderate and severe symptoms for the Edmonton Symptom Assessment System. J Pain Symptom Management 2010;39:241–249.

24. Iron K, Zagorski BM, Sykora K, Manuel DG. Living and dying in Ontario: an opportunity for improved health information. ICES Investigative Report. Toronto, ON, Canada: Institute for Clinical Evaluative Sciences, 2008.

25. Wilkins R. PCCF + version 3G users guide: automated geographic coding based on the statistics Canada postal code conversion files. Cat. No. 82F0086-XDB. Ottawa, Canada: Statistics Canada, 2001.

26. Canadian Institute for Health Information. Data quality of the discharge abstract database following the first year implementation of ICD-10-CA/CCI-Final Report. Ottawa, ON, Canada: Canadian Institute for Health Information, 2004.

27. Austin PC, van Walraven C, Wodchis WP, et al. Using the John Hopkins Aggregated diagnosis Groups to predict mortality in a general adult population cohort in Ontario, Canada. Med Care 2011;49:932–939.

28. Johns Hopkins University. Johns Hopkins ACG Case-Mix Adjustment System. Available from http://www.acg.jhsph.edu. Accessed July 29, 2010.

29. Martens P, Nickel N, Forget E, et al. The cost of smoking: a Manitoba study. Winnipeg, MB: Manitoba Centre for Health Policy, 2015.

30. Barbera L, Sutradhar R, Seow H, et al. The impact of routine ESAS use on overall survival: results of a population-based retrospective matched cohort analysis. J Clin Oncol 2019. [Under review].

31. Lebenbaum M, Espin-Garcia O, Li Y, Rosella LC. Development and test of a population based risk algorithm for obesity: the Obesity Population Risk Tool (OPoRT). PLoS ONE 2018;13:e0191169.

32. Steyerberg EW, Vickers AJ, Cook NR, et al. Assessing the performance of prediction models: a framework for traditional and novel measures. Epidemiology 2010;21:128–138.

33. Yi M, Meric-Bernstam F, Kuerer HM, et al. Evaluation of a breast cancer nomogram for predicting risk of ipsilateral breast tumor recurrences in patients with ductal carcinoma in situ after local excision. J Clin Oncol 2012;30:600–607.

34. R Development Core Team. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing, 2009. Available from http://www.R-project.org. Accessed July 28, 2014.

35. Lo C, Calzavara A, Kurdyak P, et al. Depression and use of health care services in patients with advanced cancer. Can Fam Physician 2013;59:e168–e174.

36. Jones A, Costa AP, Pesevski A, McNicholas PD. Predicting hospital and emergency department utilization among community-dwelling older adults: statistical and machine learning approaches. PLoS ONE 2018;13:e0206662.

37. Wu J, Grannis SJ, Xu H, et al. A practical method for predicting frequent use of emergency department care using routinely available electronic registration data. BMC Emerg Med 2016;16:12.

38. Wallace E, Stuart E, Vaughan N, et al. Risk prediction models to predict emergency hospital admission in community-dwelling adults: a systematic review. Med Care 2014;52:751–765.

39. Kansagara D, Englander H, Salanitro A, et al. Risk prediction models for hospital readmission: a systematic review. JAMA 2011;306:1688–1698.