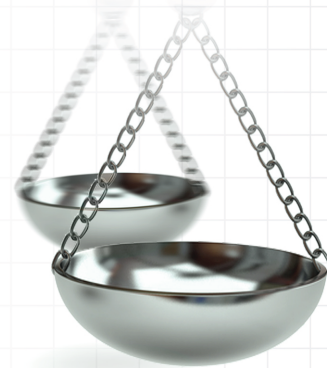




Development and validation of a claims-based approach to proxy ECOG performance status across ten tumor groups

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Aim: To develop a claims-based prediction model of poor performance status (PS) in commercially insured and Medicare supplemental beneficiaries with cancer. **Patients & methods:** Retrospective analysis was conducted of electronic medical records (EMR) from community oncology practices linked to MarketScan claims. Multivariable logistic regression predicted PS scores from the EMR using claims-based diagnostic and procedure codes. **Results:** The study included 8442 patients diagnosed with cancer from 2007 to 2015. Overall, 8.1% of patients had poor EMR-based PS. Bootstrapping results from the final model showed sensitivity and specificity of approximately 75% with a predicted probability cutpoint = 0.078, c-statistic = 0.821 and pseudo-R² = 0.25. **Conclusion:** Patients with poor PS can be identified in claims data. This prediction model enables future studies evaluating cancer treatments and outcomes to account for PS.

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Keywords: cancer • claims data • performance status • validation

High costs of cancer care have stimulated a national conversation and focus on value in oncology [1]. There is considerable interest from payers, providers, industry and academic researchers in ‘real-world’ evidence demonstrating the clinical and economic outcomes associated with cancer treatment. Secondary data sources, such as administrative claims data and electronic medical records (EMR) data, are increasingly used to describe population-based patterns of treatment, assess costs and quality of care and evaluate the comparative effectiveness and safety of different treatments or healthcare processes in oncology [2,3]. These studies may influence clinical decision-making, coverage and reimbursement decisions [4] and clinical treatment guidelines and pathways.

Treatment selection bias and residual unmeasured confounding are key concerns with observational studies examining treatment outcomes in cancer because secondary data sources often lack complete information on factors, such as performance status (PS), that influence treatment selection and health outcomes [2,5,6]. PS is a physician-assessed measure of functional capacity obtained from reports of activity levels and observation of patient mobility during the clinical encounter [7]. Patients may have poor PS due to cancer-related symptoms, age, other chronic conditions unrelated to cancer or some combination of these factors. Patients with poor PS are more likely to experience unacceptable toxicities and reduced survival benefit from aggressive treatment than those with good PS [8–10]. Eastern Cooperative Oncology Group (ECOG) and Karnofsky PS measures are not available in administrative claims data or tumor registries [11], and comorbidity indices based on claims data do not capture functional status [7,12,13]. EMR data from outpatient community or hospital-affiliated oncology practices have PS measures in their structured data, but the field is often underpopulated [11]. Therefore, this dimension of patient

health status remains a gap in most health services research studies using oncology EMR and/or administrative claims data.

The development and use of a claims-based measure of PS may enable partial control for confounding by PS in multivariable analyses or the ability to restrict or stratify a study population based on PS. Previous work in this area led to the development of a claims-based predictor for poor functional status for inclusion in studies of treatment patterns. Davidoff *et al.* [7] developed a multivariate model to predict poor PS in older adults using data from the Medicare Current Beneficiary Survey (MCBS) linked with Medicare claims data. Self-reported functional status information was used to construct a proxy for poor PS. Stepwise regression was used to select variables for model inclusion from a set of healthcare services defined using procedure codes. This claims-based measure of PS was a significant predictor of survival within a validation sample from the MCBS [7], and receipt of cancer-directed treatment in Surveillance, Epidemiology, and End Results Program (SEER)-Medicare patients with breast and lung cancer and myelodysplastic syndromes [14].

There were two key limitations to the prior work. Davidoff *et al.* [7] did not have physician-reported PS, instead constructing a proxy from functional status measures, and the study was limited to older adults enrolled in Medicare. Because younger adults generally start out with better functional status, it is not clear whether the associations between poor PS and claims-based measures of service use are similar across age groups. The purpose of this study is to address these limitations by using physician-reported PS from oncology EMR data and including patients within a broader age spectrum. We developed and internally validated a multivariable prediction model of poor PS using claims data for commercially insured and Medicare supplemental beneficiaries linked with EMR data from outpatient oncology practices. The aim was to produce a model that can predict dichotomized ECOG PS value (PS 0–1 vs PS ≥ 2) using demographic variables, healthcare services indicators and diagnoses from the previous 12 months of claims. A secondary objective was to identify the probability cutpoints that maximize performance of the PS prediction model across tumor types with specific focus in patients with breast, lung, colorectal and pancreatic cancers.

Methods

Data

Patients were identified from the MarketScan oncology claims–EMR-linked database, which contains data records from the Truven Health Analytics MarketScan research databases and the MarketScan oncology EMR database. The MarketScan research databases contain claims data sourced from large employers, health plans and government organizations. The commercial claims database contains claims of patients covered by employer-sponsored health plans, and the Medicare supplemental database contains Medicare supplemental claims and coordination of benefits for employer-sponsored supplemental plans. These databases include integrated enrollment, inpatient, outpatient and prescription drug claims data, as well as carve-out services for eligible beneficiaries and their dependents.

The MarketScan oncology EMR database contains de-identified EMR data from patients seen in 108 community oncology practices in all geographic regions in the USA. The database captures information from contributing practices' EMR systems, including demographics, tumor type, histology, stage, PS and ordered and administered medications. The MarketScan oncology claims–EMR-linked database contains data records from the claims databases and EMR database that were linked using a deterministic methodology. Linkage is conducted by a third-party vendor, and the linked database contains only de-identified records. The resulting linked database contains healthcare and cost data for over 50,000 unique patients who have received cancer treatment in community oncology practices. This study used only de-identified patient records and did not involve the collection, use or transmittal of individually identifiable data, so Institutional Review Board approval was not necessary.

Study cohort

The sample included patients with an encounter in the EMR from 2007 to 2015 with an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis code for breast, colorectal, lung, gastric, bladder, liver, skin (melanoma), hematological/lymphatic, pancreatic or other solid tumor cancers, and at least one additional encounter recorded in the EMR for the same cancer type any time thereafter. Patients were required to have a PS measure recorded in the EMR on or within 30 days of the earliest encounter with a relevant cancer diagnosis. The earliest PS measure during this time window was the index date for the study. Finally, the sample was required to have linkage to the MarketScan claims data and continuous enrollment with medical and pharmacy benefits eligibility during the 12 months prior to the index date. Table 1 shows sample attrition based on selection

Table 1. Attrition table.

Inclusion criteria	Bladder cancer (n)	Breast cancer (n)	Colorectal cancer (n)	Gastric cancer (n)	Liver cancer (n)	Lung cancer (n)	Hematologic/lymph cancers (n)	Other neo-plasms (n)	Pancreatic cancer (n)	Skin cancer (n)
Patients with a cancer diagnosis in the EMR	8288	200,104	61,008	5701	5883	61,693	105,355	135,698	12,107	13,732
And at least two visits/services/encounters recorded in the EMR for the diagnosis	6872	177,977	53,850	4916	4589	53,972	94,671	119,987	10,314	10,568
And a performance status on or within 30 days of cancer diagnosis [†]	2392	54,090	17,313	1663	1713	18,755	30,892	25,551	3906	3375
And linked to MarketScan	201	6094	1658	144	119	1551	3303	2234	375	366
And continuous enrollment in claims 12-month preindex	111	3082	846	71	77	875	1776	1194	219	191

[†]Days measured from first visit in the EMR; this diagnosis is not necessarily the patient's initial diagnosis.
EMR: Electronic medical record.

criteria. Pharmacy benefits were required because previous research has suggested that healthcare utilization and outcomes may differ between patients with and without prescription drug coverage [15].

Variables

PS measures

PS was obtained from the EMR using the earliest ECOG (scored from 0 to 5) [16] or Karnofsky PS (scored from 0 to 100) [17] value recorded within 30 days of the initial cancer encounter. Karnofsky scores were converted to ECOG-equivalent scores using a crosswalk [18]. The ECOG PS measure was then dichotomized into good (ECOG 0–1) and fair/poor (ECOG ≥ 2) because this categorization is clinically meaningful based on prior research. Patients with PS of 2 have been shown to have significantly shorter survival [19,20] and higher rates of serious adverse events compared with patients with PS of 1 [21].

Healthcare services

The claims data were searched to identify diagnoses and indicators for healthcare services received in the 12 months prior to the date of the EMR PS measure. A 12-month preindex period was chosen for consistency with previous research and to provide a sufficient time window in which to observe healthcare services and diagnosis codes. We included all healthcare services indicators as defined by Davidoff *et al.* [7] and used Berenson-Eggers Type of Service codes to group Current Procedural Terminology and Healthcare Common Procedure Coding System codes into clinical categories [22], following their approach while adapting the codes for MarketScan data. Indicators were grouped into the following categories: evaluation and management visits, other visit types, minor or ambulatory procedures, major procedures, imaging, durable medical equipment (DME) use and other (see [Supplementary Tables 1–4](#) for Berenson-Eggers Type of Service groupings and procedure codes). We also tested additional diagnostic and healthcare service indicators identified from the literature as significant positive or negative predictors of functional dependence [23,24]. These additional indicators included diagnoses for rehabilitation services, procedure codes for nursing or personal care services and diagnoses for podiatric care. In contrast with Davidoff *et al.* [7] but consistent with Faurot *et al.* [24], we also included diagnostic codes for arthritis, diabetes mellitus complications, dementias, difficulty walking, fall, heart failure, lipid abnormality, paralysis, Parkinson's disease, psychiatric illness, sepsis, skin ulcer, stroke/brain injury, vertigo and weakness as defined by Faurot *et al.* and Kim and Schneeweiss (see [Supplementary Table 5](#) for ICD-9-CM diagnosis codes) [23].

Patient characteristics

The following patient characteristics were obtained from the EMR, where populated: year of encounter, race/ethnicity, tumor type, stage and advanced stage of disease. Patients were classified as having advanced stage of disease if they had stage IV listed in the EMR or ICD-9 diagnosis codes (196.xx–199.xx) indicating secondary malignant neoplasm of lymph nodes, respiratory and digestive systems and other specified sites in the EMR or in

the claims data within 30 days of PS measurement. Other variables were obtained from the claims data, including age, sex, US geographic region, health plan type, commercial plan or Medicare supplemental beneficiary, urban or rural location and National Cancer Institute adaptation of the Deyo-Charlson Comorbidity Index, excluding claims for malignancies from the score [25,27].

Statistical analysis

Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. The frequency of healthcare service and diagnostic measures were described for the overall study population, as well as by the dichotomized measure of ECOG PS (PS 0–1 vs PS ≥ 2). Bivariate associations between ECOG PS and demographics, healthcare services and diagnostic indicators were evaluated using χ^2 tests.

The aim of the study was to produce a model that can predict the dichotomized PS value (PS 0–1 vs PS ≥ 2) using the available measured demographic and clinical characteristics. A staged approach involving a series of cross-validated stepwise multivariate logistic regressions was used to arrive at a final model consisting only of explanatory variables significantly impacting PS value. The cross-validation of individual stepwise regressions used a training sample of 70% and a validation sample of 30%, representing 5909 and 2533 patients, respectively. Candidate variables for the regressions included demographic variables (age, sex, region and payer) and diagnostic and healthcare services indicators described above. Age was categorized into less than 55 years (reference), 55–64 years, 65–74 years and ≥ 75 years. Region was originally defined according to US Census region; however, it was collapsed into south versus all other regions because these categories provided the most discrimination. Primary payer was categorized as Medicare or commercial. Healthcare services and diagnoses were defined as binary indicator variables, with the exception of the number of evaluation and management office visits (categorized as 0–2, 3–6, ≥ 7 ; see [Supplementary Table 6](#) for the full list of healthcare services and diagnostic variables considered for model inclusion). 92 candidate variables were considered during the stepwise selection process. The stepwise logistic regressions used a 5% significance level for both variable entry and exit. In addition to the main effects only model, pairwise interactions were tested between region and payer type and the significant covariates in the model. Having decided from the series what explanatory variables were in the final model, this model was fitted to all the data to obtain the final coefficients. Further validation of the distributions of the coefficients of the final model was performed by bootstrapping [28]. The bootstrapping to validate the final model from the series of stepwise logistic regressions used 1000 samples with replacement to estimate means and 95% CIs and other distributional statistics for model coefficients, with variables having zero outside the central 95% range of their bootstrap distribution indicated.

Logistic regression model fits were assessed using the available goodness-of-fit test, and C and pseudo- R^2 statistics. Regression coefficients from the final model were used to generate receiver-operating characteristic curves followed by predicted probabilities of poor PS for each patient. The continuous predicted probability was converted to a discrete indicator by selecting a cutpoint that resulted in approximately equal sensitivity and specificity. This cutpoint may be applied in future research that employs this multivariate logistic regression model to categorize patients as having good or poor PS. The concordance between the EMR- (as observed) and claims-based (as predicted by the model) measures of PS was evaluated in terms of sensitivity and specificity in the overall sample. Previous research has shown that sensitivity and specificity may be affected by sources of variation related to the study population, such as demographics or disease severity [29,30]. In this study, demographic characteristics, underlying health status, stage of disease and the prevalence and severity of poor PS are likely to vary across tumor types. For this reason, we also identified cutpoints specific to breast, lung, colorectal and pancreatic cancers to maximize sensitivity and specificity for these subgroups. All analyses were performed using SAS version 9.4 software (SAS Institute Inc., NC, USA).

Results

The study cohort included 8442 patients diagnosed with breast, colorectal, lung, gastric, bladder, liver, skin (melanoma), hematological/lymphatic, pancreatic or other solid tumor cancers. [Table 2](#) shows demographic and clinical characteristics of the eligible study population. Mean age was 64 years (standard deviation = 12.7 years) and 54% of patients ($n = 4526$) were aged less than 65 years. Approximately 65% of patients were female, and the majority was white. Payer type was commercial for 52% of patients and Medicare supplemental for 48%, with Exclusive Provider Organization/Preferred Provider Organization being the most common insurance plan type overall.

Table 2. Demographic and clinical characteristics of cancer patients meeting criteria for study inclusion, n = 8442.

Patient characteristics	n = 8442	
	n or mean	% or SD
Age, years (mean, SD)	64.0	12.7
Age group (n, %):		
– <55 years	1853	21.9%
– 55–64 years	2673	31.7%
– 65–74 years	1992	23.6%
– >74 years	1924	22.8%
Sex (n, %):		
– Male	2917	34.6%
– Female	5525	65.4%
Race (n, %):		
– White	6162	73.0%
– Black	572	6.8%
– Hispanic	62	0.7%
– Other	756	9.0%
– Unknown	890	10.5%
Geographic region (n, %):		
– North-east	2257	26.7%
– North-central	2585	30.6%
– South	2745	32.5%
– West	851	10.1%
– Unknown	4	0.0%
Population density (n, %):		
– Urban	7295	86.4%
– Rural	1145	13.6%
– Unknown	2	0.0%
Insurance plan type (n, %):		
– Fee for service	2192	26.0%
– EPO/PPO	4212	49.9%
– POS (with and without capitation)	496	5.9%
– HMO	680	8.1%
– CDHP/HDHP	447	5.3%
– Unknown	415	4.9%
Payer (n, %):		
– Commercial	4427	52.4%
– Medicare	4015	47.6%
Tumor type (n, %)		
– Breast	3082	36.5%
– Colorectal	846	10.0%
– Lung	875	10.4%
– Gastric	71	0.8%
– Bladder	111	1.3%
– Liver	77	0.9%
– Melanoma	191	2.3%
– Hematologic/lymphatic	1776	21.0%
– Pancreatic	219	2.6%
– Other neoplasms	1194	14.1%

CDHP/HDHP: Consumer-driven health plan/high-deductible health plan; ECOG: Eastern cooperative oncology group; EPO/PPO: Exclusive provider organization/preferred provider organization; HMO: Health maintenance organization; NCI CCI: National Cancer Institute Charlson Comorbidity Index; POS: Point of service; SD: Standard deviation.

Table 2. Demographic and clinical characteristics of cancer patients meeting criteria for study inclusion, n = 8442 (cont.).

Patient characteristics	n = 8442	
	n or mean	% or SD
Performance status ECOG (n, %):		
– 0	5638	66.8%
– 1	2116	25.1%
– 2	542	6.4%
– 3	136	1.6%
– 4	10	0.1%
NCI CCI (mean, SD)	0.84	1.28
NCI CCI categories (n, %):		
– 0	4735	56.1%
– 1	1938	23.0%
– 2	900	10.7%
– 3+	869	10.3%
Disease stage (n, %):		
– Stage 0	101	1.2%
– Stage 1	1192	14.1%
– Stage 2	1062	12.6%
– Stage 3	889	10.5%
– Stage 4	986	11.7%
– Unknown	4212	49.9%
Advanced disease (n, %)		
All cancers:	2611	30.9%
– Breast	632	20.5%
– Colorectal	310	36.6%
– Lung	505	57.7%
– Pancreatic	129	58.9%
– Gastric	46	64.8%
– Bladder	53	47.7%
– Liver	43	55.8%
– Melanoma	57	29.8%
– Hematologic/lymphatic	278	15.7%
– Other neoplasm	558	46.7%

CDHP/HDHP: Consumer-driven health plan/high-deductible health plan; ECOG: Eastern cooperative oncology group; EPO/PPO: Exclusive provider organization/preferred provider organization; HMO: Health maintenance organization; NCI CCI: National Cancer Institute Charlson Comorbidity Index; POS: Point of service; SD: Standard deviation.

In the overall cohort, 8.1% of patients (688/8442) had PS ≥ 2 (poor PS), but the prevalence of poor PS differed by cancer type, ranging from 3.3% for breast cancer (101/3082) to 20.1% for pancreatic cancer (44/219). Stage of disease was not reported in the EMR for 49.9% of patients. However, 30.9% of patients had evidence of advanced disease based on secondary neoplasm ICD-9 codes in the EMR or claims data.

Table 3 shows the frequency counts of EMR ECOG PS category and the levels of the healthcare services and diagnostic indicators that were selected in the stepwise logistic regression model (see [Supplementary Table 6](#) to see frequencies and χ^2 tests for all healthcare services and diagnostic indicators). Patients with poor PS were more likely to have had neurology and pulmonary evaluations, nursing home stays, hospital and emergency room visits, endoscopic procedures (bronchoscopy and upper gastrointestinal), use of wheelchairs, other DME and ambulance services in the 12 months prior to a patient's first EMR oncology diagnosis. Diagnostic codes in the 12 months before EMR oncology diagnosis associated with poor PS included difficulty walking, sepsis, stroke/brain injury and weakness.

Table 4 shows the final multivariable model from the series of stepwise logistic regressions that identified a subset of predictors consistently associated with poor PS. The fit statistics for the final model indicated a reasonable model fit: Hosmer–Lemeshow statistic $\chi^2 = 11.689$, df = 8, p-value = 0.166; $R^2 = 0.245$; c-statistic = 0.821. The bootstrap

Table 3. Frequency of selected healthcare services and diagnostic indicators by electronic medical records Eastern Cooperative Oncology Group performance status category.

Patient characteristics	All patients		ECOG ≤1		ECOG ≥2		p-value
	n = 8442		n = 7754		n = 688		
	n	%	n	%	n	%	
Age group (n, %):							
– <55 years	1853	21.9%	1795	23.1%	58	8.4%	<0.001
– 55–64 years	2673	31.7%	2511	32.4%	162	23.5%	
– 65–74 years	1992	23.6%	1831	23.6%	161	23.4%	
– >74 years	1924	22.8%	1617	20.9%	307	44.6%	
Geographic region (n, %):							
– Northeast	2257	26.7%	2129	27.5%	128	18.6%	<0.001
– North central	2585	30.6%	2385	30.8%	200	29.1%	
– South	2745	32.5%	2450	31.6%	295	42.9%	
– West	851	10.1%	787	10.1%	64	9.3%	
– Unknown	4	0.0%	3	0.0%	1	0.1%	
Healthcare services and diagnostic indicators							
E&M and other visits (n, %):							
– Dermatology	1437	17.0%	1341	17.3%	96	14.0%	0.025
– Neurology	511	6.1%	429	5.5%	82	11.9%	<0.001
– Pulmonary	608	7.2%	519	6.7%	89	12.9%	<0.001
Other visits (n, %):							
– Nursing home visit	422	5.0%	296	3.8%	126	18.3%	<0.001
– Hospital visit – initial	2236	26.5%	1814	23.4%	422	61.3%	<0.001
– Emergency room visit	2653	31.4%	2244	28.9%	409	59.4%	<0.001
BETOS preventive services (n, %):							
– Screenings	2941	34.8%	2794	36.0%	147	21.4%	<0.001
BETOS major procedures (n, %):							
– Cholecystectomy	25	0.3%	17	0.2%	8	1.2%	0.001
BETOS endoscopy (n, %):							
– Bronchoscopy	1021	12.1%	874	11.3%	147	21.4%	<0.001
– Colonoscopy	1483	17.6%	1377	17.8%	106	15.4%	0.120
– Upper gastrointestinal	1069	12.7%	926	11.9%	143	20.8%	<0.001
BETOS durable medical equipment (n, %):							
– Other DME	887	10.5%	755	9.7%	132	19.2%	<0.001
– Wheelchairs	99	1.2%	50	0.6%	49	7.1%	<0.001
BETOS other (n, %):							
– Ambulance	790	9.4%	579	7.5%	211	30.7%	<0.001
– Other tests – cardiovascular stress tests	1018	12.1%	923	11.9%	95	13.8%	0.141
Frailty indicators (n, %):							
– Difficulty walking, abnormality of gait	1267	15.0%	1038	13.4%	229	33.3%	<0.001
– Lipid abnormality	4368	51.7%	4031	52.0%	337	49.0%	0.131
– Sepsis	2179	25.8%	1891	24.4%	288	41.9%	<0.001
– Stroke/brain injury	903	10.7%	735	9.5%	168	24.4%	<0.001
– Vertigo	1308	15.5%	1189	15.3%	119	17.3%	0.173
– Weakness	3015	35.7%	2610	33.7%	405	58.9%	<0.001
BETOS: Berenson-Eggers Type of Service; DME: Durable medical equipment; E&M: Evaluation and management; ECOG: Eastern Cooperative Oncology Group.							

distributions from 1000 resamples had a mean R^2 of 0.250 (95% CI = 0.223, 0.279) and a mean c-statistic of 0.824 (95% CI = 0.808, 0.839). A probability cutpoint of ≥ 0.078 was selected to balance sensitivity and specificity at approximately 75% across all tumors (Figure 1). Supplementary Table 7 shows the values for sensitivity and (1-specificity) for all possible cutpoints.

Table 4. Results of final multivariable logistic regression model predicting poor electronic medical records performance status.

Variable	Coefficient	Odds ratio	95% CI	p-value
Intercept	-4.3599	0.0128	0.0092, 0.0178	<0.0001
Age 55–64	0.7957	2.2160	1.6028, 3.0639	<0.0001
Age 65–74	0.9950	2.7047	1.9376, 3.7756	<0.0001
Age 75+	1.5879	4.8932	3.5433, 6.7575	<0.0001
South region	0.7050	2.0238	1.6973, 2.4132	<0.0001
Dermatology E&M visit	-0.2962	0.7437	0.5820, 0.9503	0.0179
Neurology E&M visit	0.5050	1.6570	1.2435, 2.2080	0.0006
Pulmonary E&M visit	0.3267	1.3864	1.0591, 1.8148	0.0174
Nursing home visit	0.4887	1.6301	1.2317, 2.1575	0.0006
Hospital visit – initial	0.8042	2.2350	1.7884, 2.7931	<0.0001
Emergency room visit	0.3477	1.4158	1.1411, 1.7566	0.0016
Preventive screenings	-0.2568	0.7735	0.6279, 0.9529	0.0158
Major procedure – cholecystectomy	1.3198	3.7426	1.4727, 9.5109	0.0055
Endoscopy – bronchoscopy	0.3699	1.4477	1.1529, 1.8177	0.0014
Endoscopy – sigmoidoscopy, colonoscopy	-0.4190	0.6577	0.5135, 0.8425	0.0009
Endoscopy – upper gastrointestinal	0.3307	1.3920	1.1020, 1.7582	0.0055
Durable medical equipment other	0.3800	1.4623	1.1592, 1.8446	0.0013
Durable medical equipment wheelchair	1.2126	3.3621	2.1130, 5.3496	<0.0001
Ambulance	0.4414	1.5548	1.2276, 1.9693	0.0003
Electrocardiography monitoring and cardiovascular stress tests	-0.5370	0.5845	0.4511, 0.7574	<0.0001
Difficulty walking, abnormality of gait	0.4235	1.5273	1.2387, 1.8832	<0.0001
Lipid abnormality	-0.4604	0.6310	0.5277, 0.7547	<0.0001
Sepsis	0.2230	1.2498	1.0401, 1.5018	0.0173
Stroke/brain injury	0.2778	1.3202	1.0564, 1.6499	0.0146
Vertigo	-0.4097	0.6639	0.5246, 0.8401	0.0007
Weakness	0.3457	1.4129	1.1698, 1.7066	0.0003

E&M: Evaluation and management.

In subgroup analyses, the cutpoint of 0.078 resulted in different estimates of sensitivity and specificity for different cancer types. For example, this cutpoint produced poor specificity for lung and pancreatic cancers, 54.5 and 43.4%, respectively, which have a higher percentage of patients with poor PS. Conversely, the sensitivity was 60.1% for breast cancer, which has a lower percentage of patients with poor PS. We evaluated alternative probability cutpoints to maximize sensitivity and specificity for breast (cutpoint = 0.052; sensitivity and specificity = 75%; [Figure 2A](#)), colorectal (cutpoint = 0.075; sensitivity and specificity = 73.7%; [Figure 2B](#)), lung (cutpoint = 0.115; sensitivity and specificity = 67.5%; [Figure 2C](#)) and pancreatic cancers (cutpoint = 0.152; sensitivity and specificity = 72.2%; [Figure 2D](#)).

The results of the final multivariate logistic regression model in [Table 4](#) are given as logit coefficients to enable calculation of the predicted probability of a PS value ≥ 2 . To illustrate these calculations, consider a patient who is aged ≥ 75 years and only has nonreference levels of 1 or 'yes' (with the reference level being 0 or 'no') for ambulance and vertigo. The coefficients of the intercept, age 75+ years, ambulance and vertigo are added together ($-4.3599 + 1.5879 + 0.4414 + -0.4097$), giving a value of -2.7403 for the log odds. To convert the log odds to the predicted probability of a PS value ≥ 2 , the expression $\exp(-2.7403)/(1 + \exp(-2.7403))$, where $\exp()$ means exponential, is then calculated. The resulting probability value is 0.0606, which being less than 0.078 means that the predicted PS value is greater than 2.

Discussion

The results of this study indicate that cancer patients with an ECOG PS ≥ 2 , as documented in the EMR in an outpatient community oncology setting, can be identified reasonably well using healthcare services indicators

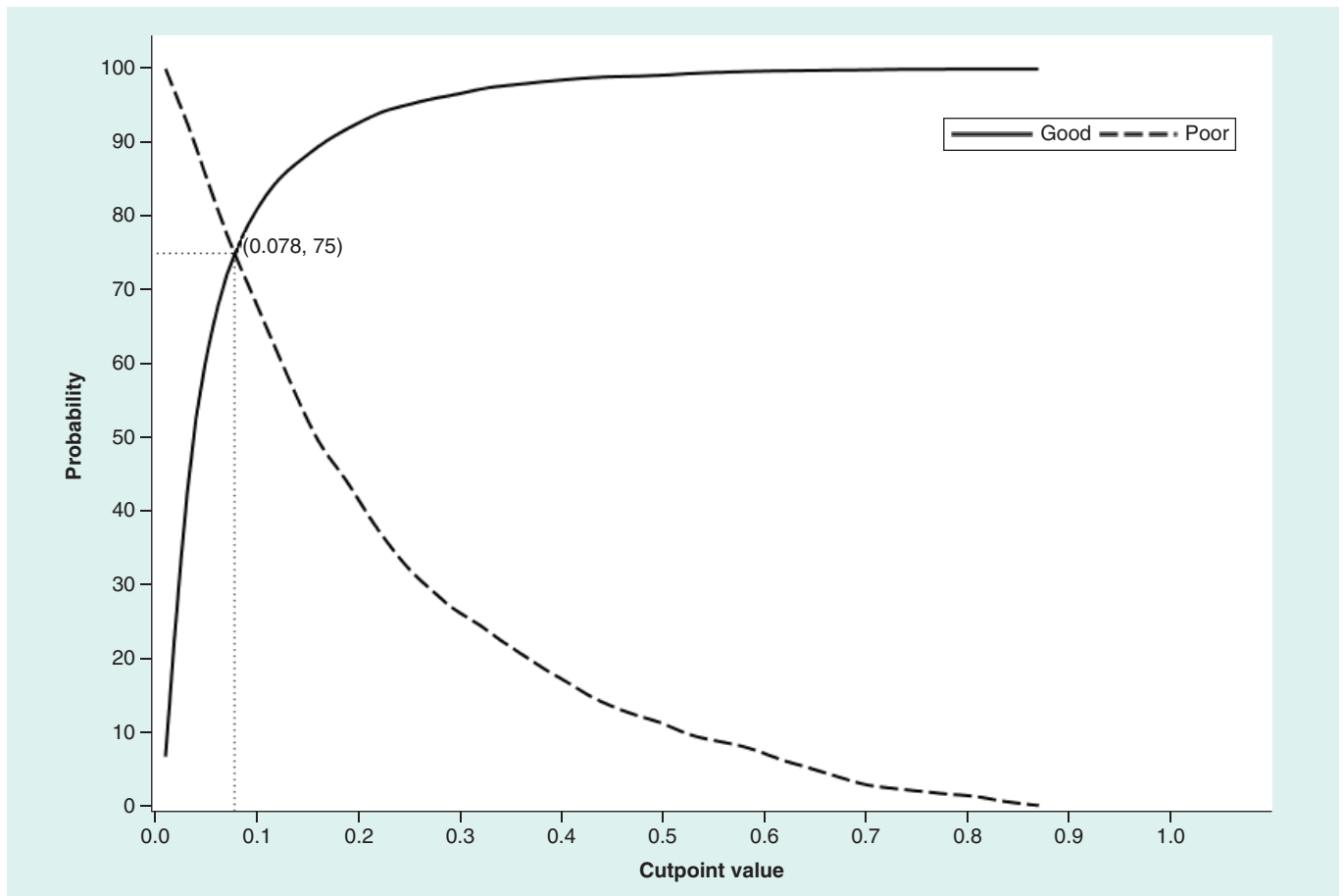


Figure 1. Plot of sensitivity and specificity according to all potential probability cutpoints for the overall cancer sample. The y-axis represents the probability (%) of correct assignment of patients as having a 'good' performance status (specificity, or true negative rate) or a 'poor' performance status (sensitivity, or true positive rate).

and age- and frailty-related diagnoses from commercial and Medicare supplemental insurance claims data. The diagnoses and healthcare service indicators evaluated in this study were identified in previous studies as clinically relevant and significantly predictive of functional dependence in older adults [7,24]. The final predictive model included both positive and negative predictors of PS and demonstrated good discrimination in a general cancer population across a wide age range and in multiple tumor types.

This study sought to extend the work done in two recent studies that developed claims-based models to predict poor functional status in Medicare beneficiaries and in a study that used tumor registry variables and claims-based measures to predict PS in patients with advanced-stage lung cancer. Davidoff *et al.* [7] and Faurot *et al.* [24] used the MCBS to identify indicators of dependence in activities of daily living in fee-for-service Medicare beneficiaries. The predictive models showed good calibration, and poor claims-based functional status was significantly associated with increased hazard of death. However, these studies developed their algorithm using functional status as a proxy for PS and evaluated a general older adult population rather than cancer patients. Salloum *et al.* [11] used claims-based service use measures and an indicator of stage IV disease from a tumor registry to predict physician-reported good PS in patients with lung cancer with Health Maintenance Organization coverage within an integrated health system in Michigan. Our study evaluated patients with cancer using a broader population with commercial or Medicare supplemental insurance coverage who presented to outpatient community oncology practices across the USA. A potential advantage of using this combined commercial and Medicare population is that results may be useful across a broader population of insurance types, tumors and age groups. In addition, this analysis not only provides the algorithm but also estimates for cutpoints specific to common tumors likely subject to future study.

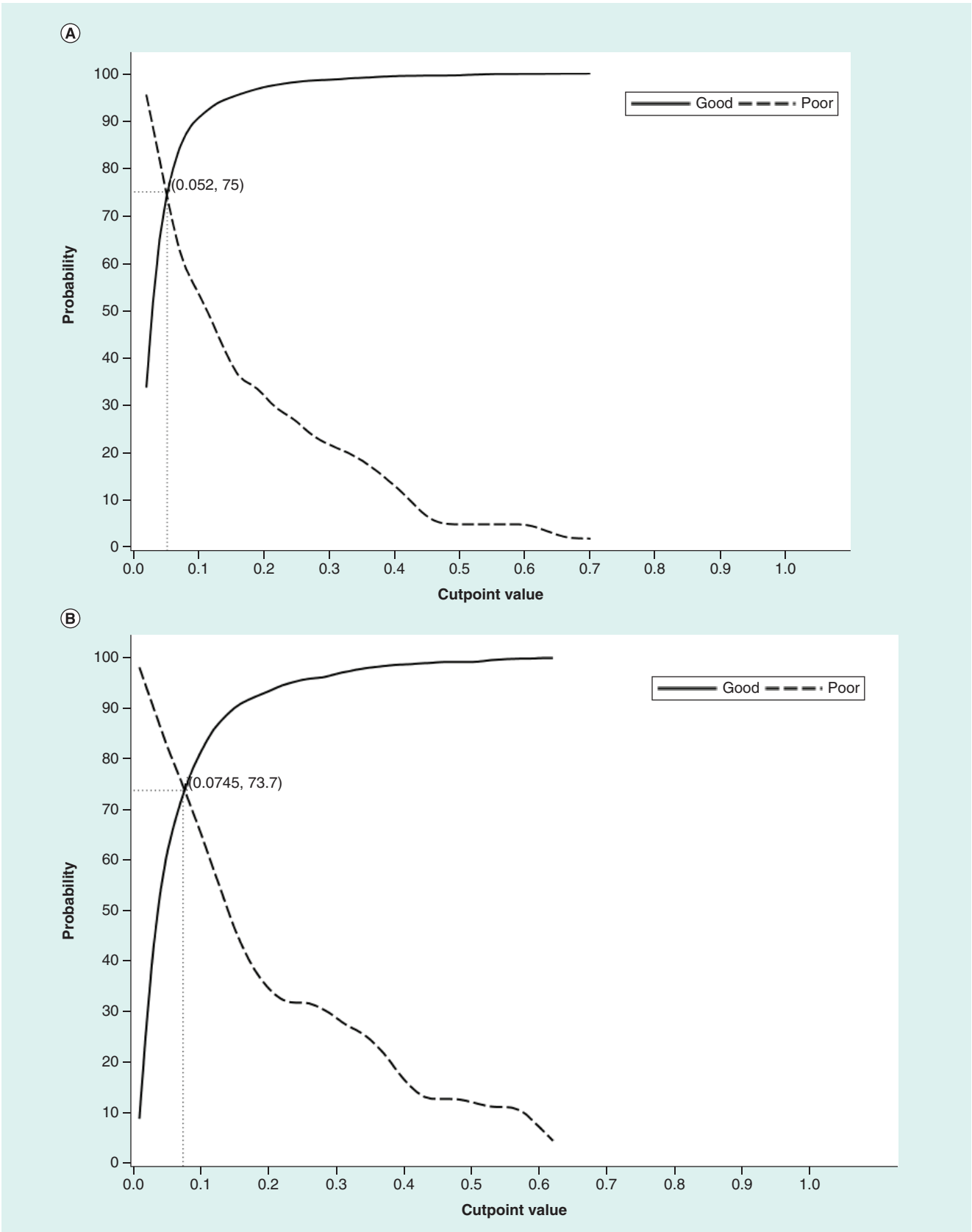


Figure 2. Plots of sensitivity and specificity according to all potential probability cutpoints for four cancer types. (A–D) Plots of sensitivity and specificity according to all potential probability cutpoints for patients with: (A) breast cancer, (B) colorectal cancer, (C) lung cancer and (D) pancreatic cancer. The y-axis represents the probability (%) of correct assignment of patients as having ‘good’ performance status (specificity, or true negative rate) or ‘poor’ performance status (sensitivity, or true positive rate).

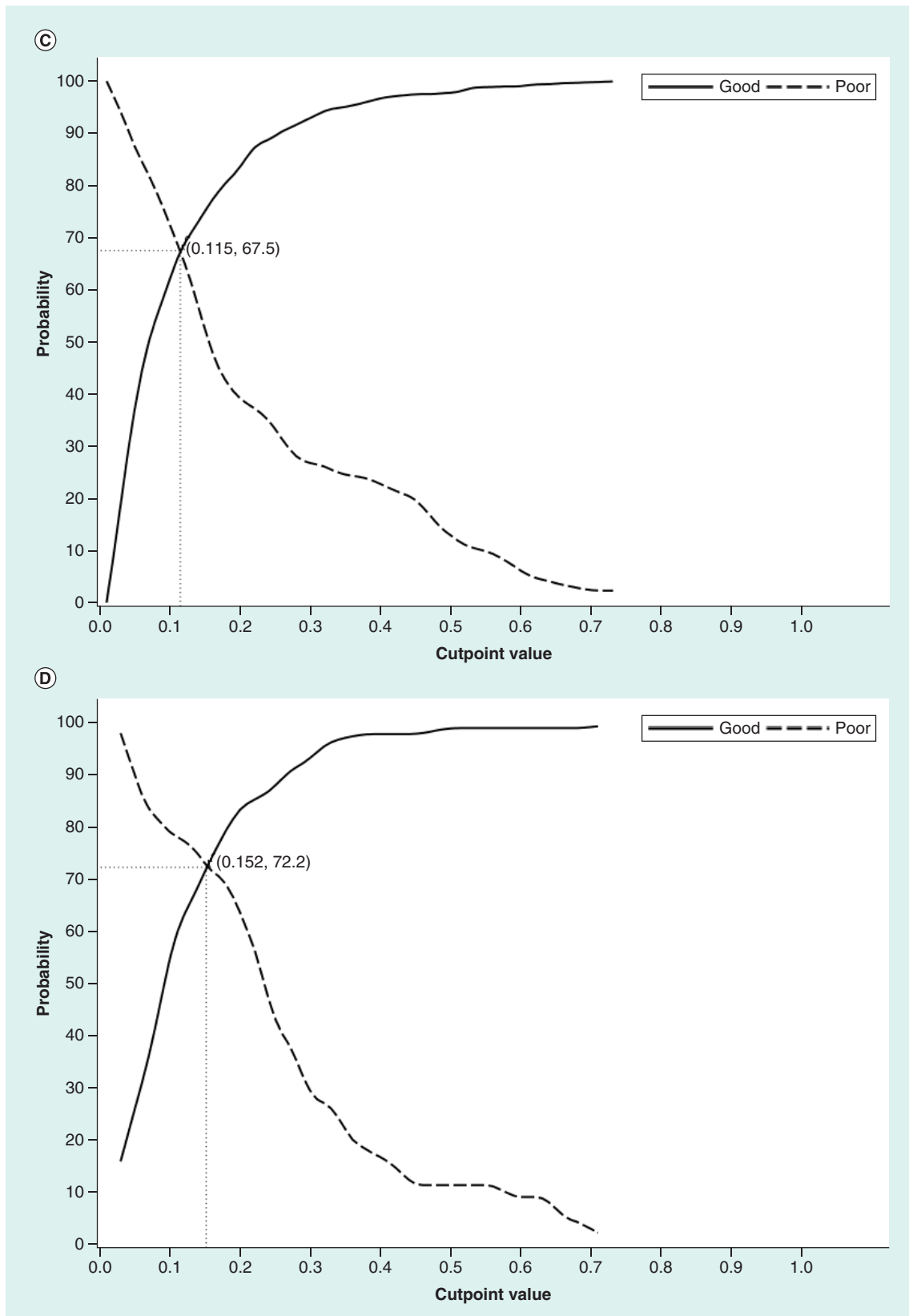


Figure 2. Plots of sensitivity and specificity according to all potential probability cutpoints for four cancer types (cont.). (A–D) Plots of sensitivity and specificity according to all potential probability cutpoints for patients with: (A) breast cancer, (B) colorectal cancer, (C) lung cancer and (D) pancreatic cancer. The y-axis represents the probability (%) of correct assignment of patients as having ‘good’ performance status (sensitivity, or true positive rate) or ‘poor’ performance status (specificity, or true negative rate).

Despite differences in patient populations, data sources and analytic approaches, studies evaluating claims-based measures of PS have identified a number of consistent predictors in their models. For example, the models from Davidoff *et al.* [7], Faurot *et al.* [24] and the current study identified the use of wheelchairs, ambulance services and nursing home visits as positive predictors of poor PS and preventive screenings as a negative predictor. The models from Davidoff *et al.* [7] and the current study also identified other DME, endoscopy of the upper gastrointestinal tract and neurology visits as positive predictors of poor PS and dermatology visits, electrocardiography and sigmoidoscopy or colonoscopy as negative predictors. Both Faurot *et al.* [24] and Davidoff *et al.* [7] identified the use of a home hospital bed as a predictor. In terms of diagnostic indicators, Faurot *et al.* [24] and the current study identified age, stroke/brain injury, weakness, difficulty walking and sepsis as positive predictors, and lipid abnormalities as a negative predictor of poor PS. Previous studies have demonstrated that several of these indicators are associated with lower likelihood of aggressive therapy in patients with breast [31], colon [32] and lung cancers [33,34]. Given the consistency across studies, these diagnoses and healthcare service indicators may be stable predictors of poor PS. However, these indicators are not typically included in multivariable models for studies of comparative clinical or economic outcomes in cancer patients.

Previous cancer outcome studies have provided evidence for confounding due to lack of information on patients' underlying health and PS. In a SEER-Medicare study, active therapy for localized prostate cancer was strongly associated with reduced risk of death from noncancer causes such as pneumonia and cardiovascular disease compared with observation, even after adjusting for age, race, urban residence, marital status, income, education, tumor size, tumor grade and comorbidity [6]. Because it is not plausible that prostate cancer therapy improves survival from causes other than prostate cancer, the authors concluded that these results are an indication that selection biases related to underlying health status of the active therapy and observation groups are responsible for the observed associations. A study using California Cancer Registry data found that breast-conserving therapy plus radiation (compared with mastectomy) was more strongly associated with reduced 3-year mortality rates from heart disease, cerebrovascular disease and respiratory disease than with mortality from breast cancer. The authors believed that these results indicate that women who had mastectomy had a higher burden of comorbidities at presentation that may have influenced surgical decision-making [35]. A similar study using SEER-Medicare data evaluated survival in women who received mastectomy versus breast-conserving therapy with radiation [36]. The authors performed sensitivity analyses to determine the potential impact of unmeasured confounding related to PS, and found that adjusting for potential differences in PS between treatment groups decreased the observed hazard ratio from 1.19 to 1.08. PS is frequently acknowledged as an unmeasured confounder in studies using tumor registry and administrative claims data to evaluate comparative effectiveness or costs of cancer therapies. The use of a claims-based measure of PS may enable partial control for confounding by PS or the ability to restrict or stratify a study population based on PS.

In this study, poor PS was defined as an ECOG score of 2 or greater, and approximately 8% of patients had poor PS according to this definition in our sample of patients from outpatient community oncology practices. Only 1.7% of patients had an ECOG PS score of 3 or 4. For most patients with solid tumors, the standard for chemotherapy use in American Society for Clinical Oncology and National Comprehensive Cancer Network guidelines includes the consideration of use in patients with an ECOG PS of 2 but call for a switch to palliative care in patients with a very poor ECOG PS of 3 or 4, as evidence indicates a less favorable risk–benefit ratio in these patients [37–39]. However, improvements in median overall survival associated with platinum-based combination therapy in patients with an ECOG PS of 2 are variable, ranging from 0.2 to 4 months in a recent meta-analysis [40]. In a recent prospective cohort study of patients with progressive metastatic disease, chemotherapy use was not associated with quality of life improvement near death in those with an ECOG PS of 2 or 3 at study entry [37]. In their claims-based prediction models, Salloum *et al.* [11] evaluated a definition of poor PS that included or excluded an ECOG PS of 2 and found that 'poor' PS can be predicted reasonably well regardless of whether an ECOG PS of 2 is considered 'poor'.

To maximize sensitivity and specificity, the probability cutpoint of 0.078 was selected for the overall study sample. However, the preferred probability cutpoint ultimately depends on research objectives and may be adjusted accordingly in future studies. When applying this algorithm and wishing to maximize sensitivity and specificity in future applications of this predictive model, it will be important to consider the specific cancer type as compared with the broader inclusion in our study. The different probability cutpoints considered in this study reflected different frequencies of poor ECOG PS across cancer types while simultaneously maximizing both sensitivity and specificity. The specificity associated with a cutpoint of 0.078 was better for tumors that were historically screened

(breast, colorectal) than those that were not (lung, pancreas), which might relate to the influence of the patients' stage of disease at diagnosis. When evaluating specific tumors, there will be better algorithm performance if the tumor-specific cutpoints are used for determining which patients are likely $PS \geq 2$. Finally, one might consider a higher probability cutpoint for studies where it is important to identify patients with poor ECOG PS with high specificity, such as those evaluating chemotherapy use in patients for whom it may offer less benefit and more risk [11]. However, in such a case, this study provides no specific guidance for cutpoint determination beyond that for the broad tumor group and the specific tumors analyzed here.

The results of this study should be interpreted in light of the following limitations. The ECOG PS measures are usually physician reported and as such are documented in the EMR. PS scoring by healthcare professionals is subjective in nature, and physicians may overestimate PS [41], either unintentionally or to obtain approval for a specific treatment or clinical trial participation. The study captured patients at the point of presentation to their outpatient oncology practice rather than at the point of initial diagnosis, and as a result, patients may be at different points in the disease trajectory. Patients who were undergoing diagnosis and treatment prior to the PS measurement in the EMR may have different patterns of healthcare services use. Approximately 30% of patients in the study had claims with a cancer diagnosis in the 3–12 months prior to appearance in the EMR. Patients with a prior diagnosis of cancer were not excluded from the study sample. Therefore, the sample may contain patients with a history of cancer as well as a small percentage of patients with another concurrent primary cancer. Only structured documentation of PS was available in the EMR database, and 27% of patients had a PS measurement recorded within 30 days of their earliest encounter. It is unclear which patient, physician or practice factors may influence whether or not a PS measurement is recorded in the EMR. It is possible that patients with PS measurements recorded within 30 days of the earliest encounter represent a select group. Access to the unstructured data (e.g., physician notes) may have increased the completeness of PS measurement [11]. Our study used an internal validation approach. Ideally, this prediction model should be validated in an external sample. There are limitations with a claims-based approach to characterizing PS. For example, medical diagnoses are known to be poorly reported in claims data, resulting in poor sensitivity. DME use varies based on personal preferences as well as restrictions on reimbursement [11]. Finally, the patients included in this study were commercial beneficiaries covered by employer-sponsored health plans and Medicare beneficiaries with employer-sponsored supplemental coverage. These beneficiaries may have better health status and different use patterns of healthcare services because they are younger and qualify for employment-related coverage. A study sample with a combination of commercial and public insurance may produce a more generalizable prediction model.

Future research is needed to evaluate additional subgroups of interest, such as age, gender and cancer stage, because patterns of service use and the associations between diagnoses, health services use and PS may differ across these subgroups. In addition, future research is needed to develop individual models for specific cancer types as well as the other subgroups of interest to determine if predictors are consistent and to identify predictors specific to particular subgroups. Further validation should also be performed to evaluate the ability of this claims-based indicator of poor PS to predict mortality, not available in our dataset. In addition, future work should establish the positive and negative predictive value of this algorithm in populations that have higher prevalence of poor PS.

Conclusion

Administrative claims data are increasingly used in oncology to evaluate treatment patterns and costs, guide insurer decisions and evaluate effectiveness and safety outcomes in many different tumors. To best use these data, health service researchers, policy makers and insurers must understand the potential for selection bias and confounding in treatment comparisons. The ability to approximate PS in these studies will enhance the use of Truven MarketScan databases, for health economics and outcomes research in oncology.

Supplementary data

To view the supplementary data that accompany this paper please visit the journal website at: www.futuremedicine.com/doi/suppl/10.2217/cer-2017-0040

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No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

This study used only de-identified, pre-existing patient records and did not involve the collection, use or transmittal of individually identifiable data, so Institutional Review Board (IRB) approval was not necessary. The exemption from IRB approval, per US Department of Health and Human Services regulations, for studies that use existing information that cannot be used to identify individual patients is contained in 45 CFR [Code of Federal Regulations] 46.101(b)(4).

Summary points

- Administrative claims data are increasingly used to evaluate patient outcomes and costs of care in oncology.
- These studies are susceptible to confounding due to missing variables, such as performance status (PS), a measure of functional capacity used in oncology practice.
- In this retrospective study, we developed a claims-based prediction model of poor PS in commercially insured and Medicare supplemental beneficiaries.
- Electronic medical records (EMR) data from community oncology practices linked to MarketScan commercial claims and Medicare supplemental databases were analyzed for patients with PS scores recorded in the EMR.
- Multivariable logistic regression was used to predict EMR-based PS from diagnostic and procedure codes in the claims data, with split-sampling and bootstrapping performed for internal validation.
- In the overall cohort, 8.1% of patients had Eastern Cooperative Oncology Group PS ≥ 2 , but the percentage ranged from 3.3% for breast to 20.1% for pancreatic cancer.
- Bootstrapping results on the final model showed sensitivity and specificity of approximately 75% with a predicted probability cutpoint of 0.078, c-statistic = 0.821, and pseudo- R^2 = 0.25.
- Patients with poor PS can be identified using diagnostic and procedure codes from claims data, which may enable partial control for confounding by PS or stratification or restriction of the patient sample in future comparative studies.

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