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Validation of a five-year mortality prediction model among US Medicare beneficiaries.

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Abstract

Background/Objectives—A claims-based model predicting five-year mortality (Lund-Lewis) was developed in a 2008 cohort of North Carolina (NC) Medicare beneficiaries and included indicators of comorbid conditions, frailty, disability, and functional impairment. The objective of this study was to externally validate the Lund-Lewis model within a nationwide sample of Medicare beneficiaries.

Design—Retrospective validation study

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Jennifer L. Lund contributed to the conception and design, analysis and interpretation of data, critically revised the article, and provided final approval of the version to be published.

Conflict of Interest

The authors have no conflicts.

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Sponsor's Role

The sponsor played no role in the design, methods, data collection, analysis, or preparation of paper.

Setting—United States Medicare population

Participants (incl sample size)—From a random sample of Medicare beneficiaries, we created four annual cohorts from 2008 to 2011 of individuals aged 66 years and older with an office visit in that year. The annual cohorts ranged from 1.13 to 1.18 million beneficiaries.

Measurements—The outcome was five-year all-cause mortality. We assessed clinical indicators in the 12 months prior to the qualifying office visit and estimated predicted five-year mortality for each beneficiary in the nationwide sample by applying estimates derived in the original NC cohort. Model performance was assessed by quantifying discrimination, calibration, and reclassification metrics compared to a model fit on a comorbidity score.

Results—Across the annual cohorts, five-year mortality ranged from 24.4% to 25.5%. The model had strong discrimination (C-statistics ranged across cohorts from 0.823-0.826). Reclassification measures showed improvement over a comorbidity score model for beneficiaries who died but reduced performance among beneficiaries who survived. The calibration slope ranged from 0.83 to 0.86; the model generally predicted a higher risk than observed.

Conclusion—The Lund-Lewis model showed strong and consistent discrimination in a national US Medicare sample though calibration indicated slight overfitting. Future work should investigate methods for improving model calibration and evaluating performance within specific disease settings.

Keywords

validation; Medicare; predictive model; mortality; older adults

Introduction

Validated risk prediction models are important tools for clinical decision-making and quality measurement. Among older adults, optimizing healthcare is complex and must consider an individual's prognosis. Mortality prediction models can provide information to support individualized treatment planning. For example, such a model may be used to identify patients who are likely or unlikely to benefit from primary prevention-focused healthcare interventions such as cancer screening.[1,2] In quality measurement (e.g. Center for Medicare and Medicaid Services [CMS] Five-Star Quality Rating System and the National Committee for Quality Assurance HEDIS® measures), mortality prediction models can be used for case-mix adjustment for to more accurately compare and benchmark the performance of different providers, institutions, or plans, particularly when sample size constraints do not allow for adjustment of several variables.[3,4]

Lund and colleagues developed a Medicare claims-based risk prediction model for five-year mortality[5] which considered demographics, several comorbid conditions,[6-9] as well as indicators of frailty,[10] disability,[11] and functional impairment[12] (hereafter referred to as the Lund-Lewis model). The model was developed in a 2008 training cohort of North Carolina (NC) Medicare beneficiaries following an office visit at age 66 years or older. The model performed well in a set aside internal validation sample and improved reclassification of five-year mortality risk compared to a previously published comorbidity score model

developed by Gagne *et al.*[13] In contrast to other claims-based mortality prediction models which have predominantly focused on predicting short-term mortality and exclusively included indicators of comorbidity,[7,9] the Lund-Lewis model focused on five-year mortality and included indicators beyond comorbidities. The Lund-Lewis model also differs from other claims-based frailty indices[10,14] as it aims to predict directly mortality as opposed to an intermediate construct, like frailty.

The Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD) statement describes the importance of external validation to identify and address potential overfitting.[15] As the Lund-Lewis model was developed using Medicare data from a single state, the internal validation results[5] may not be applicable to the broader US Medicare population. To that end, we aimed to externally validate the Lund-Lewis model in a nationwide sample of US Medicare beneficiaries.

Methods

Data source and study population

We used a 20% nationwide sample of Medicare beneficiaries. To explore model performance over calendar time, we created four cohorts for each year from 2008 to 2011, allowing at least five years for mortality follow-up. Each cohort included beneficiaries aged 66 years or older with an office visit in that calendar year and at least 12-months continuous Medicare Parts A (hospital) and B (outpatient) enrollment prior to the visit without a hospice claim during that period. Continuous Part D enrollment was not required. The date of the first office visit at which the beneficiary met all inclusion criteria was identified as the index date. We analyzed the cohorts separately (though a single beneficiary could appear in multiple cohorts).

Predicted mortality

The outcome was death due to any cause within five years of the index date obtained from Medicare enrollment files, *i.e.*, five-year all-cause mortality. The predictive model included demographic and beneficiary information (age, sex, race, and dual enrollment eligibility) and clinical indicators (Supplementary Table S1; assessed in the 12 months prior to the index date). See Lund *et al.* for full details of the development of the predictive model.[5] We estimated predicted five-year mortality for each beneficiary in the US Medicare sample by applying the model parameter estimates derived in the original NC training cohort. We compared performance to the comorbidity score model[13] also obtaining mortality predictions using the model parameter estimates from a logistic model including the comorbidity score, age polynomials (linear, quadratic, cubic), and sex fit in the original NC training cohort.

Model performance

We compared the sample demographic characteristics and prevalence of the indicators included in the model of each US Medicare cohort and the original NC training sample. To assess model performance, we compared validation results from the Lund-Lewis model with the comorbidity score model and the original NC internal validation sample. Calibration, the

degree of agreement between predicted and observed event probability, was assessed by plotting the five-year observed versus predicted mortality by decile of the predicted probability.[16] We also calculated the calibration slope by fitting a linear-binomial model of the individual observed versus predicted probabilities of mortality. A slope close to one indicates good calibration.[16] Discriminatory performance, the ability of the model to distinguish beneficiaries who died within five years from those who did not,[17] was measured by C-statistics with 95% confidence intervals (CI). In addition, we calculated C-statistics for shorter term mortality (at 30, 90, 180, and 365 days) in the 2008 cohort. We also assessed reclassification metrics for the Lund-Lewis model compared to the comorbidity score model for the 2008 cohort to evaluate model improvement. We constructed reclassification tables using three risk strata defined by the average prediction from the comorbidity score model among the beneficiaries who survived five years and among the beneficiaries who did not.[18] We calculated the net reclassification improvement (NRI) and the integrated discrimination improvement (IDI) with 95% CIs.[18] The NRI is a measure of the net improved classification and a positive NRI indicates a net improvement in classification by the Lund-Lewis model compared to the comorbidity score model. The IDI is the change in the difference of the average predicted between those who died and those who survived from the Lund-Lewis model and from the comorbidity score model. A positive IDI would reflect that the Lund-Lewis model, on average, predicted greater difference in the average probabilities between those who died and those who survived than the comorbidity score model. We further evaluated model performance by sex, age group (<75 and 75+ years), race (White, Black, Other), and geographic census region (Northeast, Midwest, South, West) for the 2011 cohort, the most recent year. All analyses were conducted using SAS version 9.4 (SAS Institute, Inc., Cary, North Carolina, USA).

Results

The annual US Medicare cohorts ranged in size from 1.13 million in 2010 to 1.18 million in 2011. Supplementary Table S2 includes demographic and outcome risk for each annual cohort compared to the original NC training cohort. The five-year mortality ranged from 24.4% in 2011 to 25.5% in 2008 and was similar to the NC training cohort (24.0%). The proportion of beneficiaries eligible for dual coverage for both Medicare and Medicaid in the nationwide cohorts was higher than the proportion in the NC training population. The prevalence of many of the influential clinical indicators in our US Medicare cohorts differed compared to the NC training cohort (Supplementary Table S1). Generally, the prevalence of chronic conditions and indicators of frailty was higher in the US Medicare population suggesting that these external validation cohorts included a sicker population with more healthcare utilization.

Across the four cohorts, the Lund-Lewis model predicted a probability of death <0.1 for 27.5% of beneficiaries; for the comorbidity score model, this was 25.3%. The Lund-Lewis model predicted a probability >0.8 for 8.5% of beneficiaries; for the comorbidity score model, this was 5.4%. Figure 1 shows the calibration plot as well as the distribution of the predicted probabilities for the 2008 cohort. There was deviation between the predicted and observed mortality at the higher end of the risk-spectrum. For example, among the highest decile of predicted mortality risk using the Lund-Lewis model in 2008, the mean prediction

was 0.88, but the observed risk of death was 0.76 (Figure 1). In the lowest decile of predicted risk, the mean prediction was 0.04 and the observed risk was 0.03. There was also deviation between the predicted and observed mortality risk for the comorbidity score model however the deviation was greater for the Lund-Lewis model. The calibration slope varied little by year (Table 1). Table 1 also includes calibration slopes stratified by sex, age, and race; results did not substantially vary across subgroups. In all strata, the comorbidity score model had a calibration slope closer to 1 than the Lund-Lewis model.

The Lund-Lewis model had improved discrimination measured by the C-statistic compared to the comorbidity score model overall and by subgroup (Table 1). For both models, there was little change by calendar year or region. The Lund-Lewis model C-statistic ranged from 0.823 (95% CI 0.822, 0.824) in 2008 to 0.826 (95% CI 0.825, 0.826) in 2011, and the comorbidity score model C-statistic ranged from 0.795 (95% CI 0.794, 0.796) in 2008 to 0.797 (95% CI 0.796, 0.798) in 2011. Table 1 also includes results stratified by demographics. Stratified results showed a similar pattern. The Lund-Lewis model also had a higher C-statistic than the comorbidity score model for shorter term mortality (at 30, 90, 180 and 365 days) (Supplementary Table S3).

Table 2 presents the reclassification table comparing the Lund-Lewis model to the comorbidity score model for 2008. The cut-offs for risk strata were defined using the average predicted probability of five-year mortality from the comorbidity score model among the beneficiaries who survived and among those who did not (0.22 and 0.47, respectively). The NRI was 10.6% (95% 10.3, 10.8) indicating improved reclassification for the Lund-Lewis model. The Lund-Lewis model had improved reclassification among beneficiaries who died within 5 years (14.3%, 95% CI 14.1, 14.5) but had worse reclassification among beneficiaries who survived (−3.8%, 95% CI −3.7, −3.9). The overall IDI was 0.064 (standard error [SE] 0.0003). The average predicted probability of death from the Lund-Lewis model was higher than that from the comorbidity score model among beneficiaries who died (0.073, SE 0.0003). However, the average predicted probably of death was slightly higher from the Lund-Lewis model than from the comorbidity score model among beneficiaries who survived (0.009, SE 0.0001).

Discussion

In this external validation study using a nationwide sample of Medicare beneficiaries, the Lund-Lewis claims-based prediction model for five-year mortality, which includes indicators of comorbidity and functional impairment, showed strong discrimination and no decline in performance compared to the NC Medicare population where it was developed.[5] Further, the model showed consistent performance over time and by census region, sex, age group, and race indicating strong generalizability. The model also had high discrimination at 30, 90, 180, and 365 days. A model with good discrimination may be particularly beneficial for case-mix adjustment in healthcare quality measurement .[16,19] When used for this purpose, strong calibration is not an important factor.[16] Healthcare payers, including CMS, could utilize the model when benchmarking the use of low-value services (i.e., services where the benefits are unlikely to accrue due to limited life expectancy) as identified by the American Geriatrics Society in the Choosing Wisely initiatives.[20]

In general, the Lund-Lewis model predicted a higher risk of death than observed, particularly at the higher end of the risk spectrum. This overprediction is reflected in the calibration slope of less than one.[19] Despite using a shrinkage (regularization) method during model development,[21] Lund and colleagues observed overfitting, and the finding was still present in this validation. The large number of included indicators (166) may make the model highly susceptible to overfitting, whereas the comorbidity score model with only a few parameters was more robust. Given the calibration performance, the Lund-Lewis model may need refinement including reduction in the number of claims-based indicators and possible augmentation with clinical data from the electronic health record before considering it for clinical uses. Assessment for clinical decision-making should consider both calibration and discrimination, but also the selection of relevant predicted model cut-points that could be used within formal decision analysis to quantify the potential decision harms and benefits and how these vary between people.[19,22]

In conclusion, the Lund-Lewis model demonstrates important improvements in discrimination but not calibration over an existing comorbidity model. Future work should evaluate strategies to improve model calibration and examine predictive performance and application within specific disease settings (e.g., cancer, dementia).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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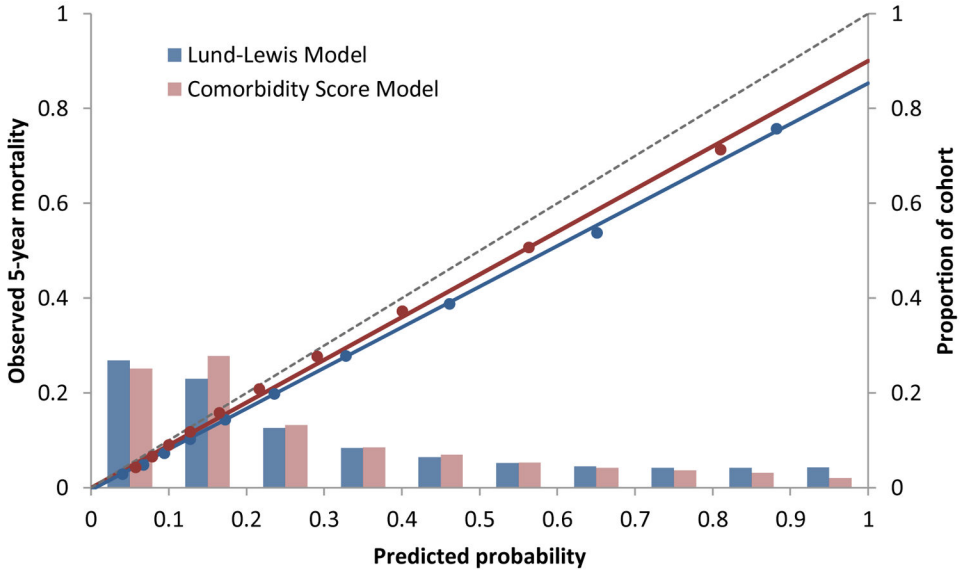

Figure 1.

Calibration plot of Lund-Lewis model and comorbidity score model for predicting five-year mortality in 2008 calendar year cohort. Dashed line is reference line of slope of observed against predicted = 1 (perfect calibration). The solid lines are the estimated calibration slopes (obtained from linear-binomial models fit on the predicted probabilities and observed mortality) for each model. The data points are the observed mortality (left vertical axis) for each predicted probability decile for each model. The bars are the proportion of the cohort (right vertical axis) in each tenth of predicted probability (i.e. <0.1, 0.1 to <0.2, etc…). Black solid line, data points, and bars are the Lund-Lewis model. Gray solid line, data points, and bars are the comorbidity score model.

Table 1.

Calibration and discrimination measures for five-year mortality by calendar year cohort and region

		Calibration[a]		Discrimination	
	Deaths	Lund-Lewis Model	Comorbidity Score Model	Lund-Lewis Model	Comorbidity Score Model
Cohort	n (cumulative incidence)	Slope	Slope	C-statistics[b]	
NC internal validation	36,503 (23.6%)	0.98	0.99	0.83	0.80
Nationwide external validation					
Year					
2008	295,184 (25.5%)	0.86	0.90	0.82	0.79
2009	296,192 (25.1%)	0.85	0.89	0.82	0.80
2010	279,685 (24.9%)	0.84	0.88	0.82	0.80
2011	288,354 (24.4%)	0.83	0.88	0.83	0.80
Region[c]					
Northeast	54,142 (24.8%)	0.80	0.83	0.83	0.80
Midwest	67,797 (25.1%)	0.86	0.91	0.83	0.80
South	118,782 (25.0%)	0.85	0.89	0.82	0.79
West	46,970 (21.9%)	0.80	0.85	0.83	0.80
Sex[c]					
Female	170,347 (22.9%)	0.83	0.87	0.83	0.80
Male	118,007 (27.0%)	0.85	0.88	0.82	0.78
Age[c]					
<75	81,782 (13.7%)	0.82	0.93	0.80	0.76
≥75	206,572 (35.3%)	0.85	0.86	0.79	0.76
Race[c]					
White	248,017 (24.4%)	0.84	0.89	0.83	0.80
Black	23,252 (29.2%)	0.79	0.81	0.80	0.78
Other	17,085 (20.4%)	0.73	0.75	0.82	0.80

Abbreviations: NC, North Carolina

[a] Calibration slopes were estimated from linear-binomials models with observed five-year mortality status as the outcome and the predicted probability as an independent variable.

[b] All standard errors <0.002.

[c] 2011 cohort

Table 2.

Reclassification table for 2008 cohort, Lund-Lewis model and comorbidity score model

		Lund-Lewis model			
	Comorbidity Score Model	**<0.22[a]**	**0.22-0.47**	**>0.47**	**Total**
Beneficiaries who died within 5 years[b]	<0.22[a]	41774	20642	3751	66167
	0.22-0.47	8213	45063	35825	89101
	>0.47	177	9577	130162	139916
	Total	50164	75282	169738	295184
Beneficiaries who survived >5 years[c]	<0.22	503048	62276	4250	569574
	0.22-0.47	49901	116880	35706	202487
	>0.47	760	19239	68828	88827
	Total	553709	198395	108784	860888
All beneficiaries[d]	<0.22	544822	82918	8001	635741
	0.22-0.47	58114	161943	71531	291588
	>0.47	937	28816	198990	228743
	Total	603873	273677	278522	1156072

[a]Predicted probability groupings were defined by the average prediction from the comorbidity score model among the beneficiaries who survived five years (0.22) and among the beneficiaries who did not (0.47).

[b]Among beneficiaries who died, improvement in classification defined: the difference between the number who moved to a higher predicted probability group using the Lund-Lewis model compared to the comorbidity score model (solid gray, 60,218) and the number who moved down to a lower predicted probability group using the Lund-Lewis model compare to the comorbidity score model (hashed, 17,967) divided by the total number of deaths (295,184) = 0.143.

[c]Among beneficiaries who survived, improvement in classification defined: the difference between the number who moved down to a lower predicted probability group using the Lund-Lewis model compared to the comorbidity score model (solid gray, 69,900) and the number who moved up to a higher predicted probability group using the Lund-Lewis model compare to the comorbidity score model (hashed, 102,232) divided by the total number of survivors (860,888) = −0.038.

[d]The net reclassification index (NRI), the net improvement in classification, was 0.143 + (−0.038) = 0.106.