JAMA Network Open

Original Investigation | Health Informatics

Prospective Comparison of Medical Oncologists and a Machine Learning Model to Predict 3-Month Mortality in Patients With Metastatic Solid Tumors

Finly J. Zachariah, MD; Lorenzo A. Rossi, PhD; Laura M. Roberts, MS; Linda D. Bosserman, MD

Abstract

IMPORTANCE To date, oncologist and model prognostic performance have been assessed independently and mostly retrospectively; however, how model prognostic performance compares with oncologist prognostic performance prospectively remains unknown.

OBJECTIVE To compare oncologist performance with a model in predicting 3-month mortality for patients with metastatic solid tumors in an outpatient setting.

DESIGN, SETTING, AND PARTICIPANTS This prognostic study evaluated prospective predictions for a cohort of patients with metastatic solid tumors seen in outpatient oncology clinics at a National Cancer Institute–designated cancer center and associated satellites between December 6, 2019, and August 6, 2021. Oncologists (57 physicians and 17 advanced practice clinicians) answered a 3-month surprise question (3MSQ) within clinical pathways. A model was trained with electronic health record data from January 1, 2013, to April 24, 2019, to identify patients at high risk of 3-month mortality and deployed silently in October 2019. Analysis was limited to oncologist prognostications with a model prediction within the preceding 30 days.

EXPOSURES Three-month surprise question and gradient-boosting binary classifier.

MAIN OUTCOMES AND MEASURES The primary outcome was performance comparison between oncologists and the model to predict 3-month mortality. The primary performance metric was the positive predictive value (PPV) at the sensitivity achieved by the medical oncologists with their 3MSQ answers.

RESULTS A total of 74 oncologists answered 3099 3MSQs for 2041 patients with advanced cancer (median age, 62.6 [range, 18-96] years; 1271 women [62.3%]). In this cohort with a 15% prevalence of 3-month mortality and 30% sensitivity for both oncologists and the model, the PPV of oncologists was 34.8% (95% CI, 30.1%-39.5%) and the PPV of the model was 60.0% (95% CI, 53.6%-66.3%). Area under the receiver operating characteristic curve for the model was 81.2% (95% CI, 79.1%-83.3%). The model significantly outperformed the oncologists in short-term mortality.

CONCLUSIONS AND RELEVANCE In this prognostic study, the model outperformed oncologists overall and within the breast and gastrointestinal cancer cohorts in predicting 3-month mortality for patients with advanced cancer. These findings suggest that further studies may be useful to examine how model predictions could improve oncologists' prognostic confidence and patient-centered goal-concordant care at the end of life.

JAMA Network Open. 2022;5(5):e2214514. doi:10.1001/jamanetworkopen.2022.14514

Key Points

Question How do oncologists and a machine learning model compare in predicting 3-month mortality for patients with advanced solid tumors?

Findings In this prognostic study, the machine learning model significantly outperformed 74 oncologists in predicting 3-month mortality for 2041 patients with metastatic solid tumors overall and in gastrointestinal and breast cancer subpopulations. Findings were not significant in genitourinary, lung, and rare cancer groups.

Meaning The results of this study suggest the potential for a machine learning model trained with electronic health record data to support oncologists in prognostication and clinical decision-making to improve end-of-life care.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

Introduction

Patients and families rely on clinicians to provide transparent and precise prognostic information to make informed, value-based choices about end-of-life care.[1-5] Studies have shown that physicians often overestimate survival or are reticent to discuss prognosis and end-of-life preferences owing to perceived patient distress, rapidly progressive science, and lack of prognostic confidence.[6-16] This overestimation may result in unwanted care and overuse of health care services near the end of life as evidenced by findings that most patients die outside the home and patient preferences are followed completely only about half of the time.[17-19] Within the oncology population, there remains high use of intensive care and chemotherapy and underuse of hospice care near the end of life, costing billions of dollars to the US health care system.[20,21] Improving prognostic confidence and facilitating alignment between patient values and therapeutic delivery represents an important value proposition for patients, caregivers, clinicians, and payers.[22]

Reliable and consistently applied prognostic tools in oncology may enhance prognostic confidence, increase prognostic authority, and improve the clarity and strength of medical recommendations for and against therapies.[23] Many prognostic scales have been studied in oncology, some with more administrative burden.[9,10] A widely and easily implemented prognostic tool is the surprise question (SQ), which asks clinicians whether it would surprise them if a patient died within a particular time frame. The SQ has been used most commonly with a 1-year time frame but also with time frames between 1 week and 6 months with varying performance.[7,9,10,24-41] The SQ has performed better in oncology populations compared with heart failure, kidney failure, and all diagnoses examined in other studies,[7,9,10] albeit modestly, and further research in this area is needed.

Institutions have increasingly used machine learning (ML) to identify patients at high risk of mortality at different points from 30 days to 5 years for activating care teams to conduct goals-of-care discussions and engage palliative care.[42-49] Although there are multiple retrospective evaluations of ML models, there remain few prospective evaluations and even fewer prospective comparisons of clinician and ML predictions.[42,43,46,47,50,51]

We compared the prognostic performance of medical oncologists using an SQ with a supervised model trained to predict the risk of 3-month mortality. A motivator for this analysis was to improve the acceptability of ML for broader scale use in the electronic health record (EHR) and lay the groundwork to potentially increase prognostic confidence, improving discussions on goals of care between patients, families, and clinicians. This pilot study and the consequent evaluation were steps taken to validate the mortality prediction model and facilitate its acceptability among oncologists before integration in our EHR at the City of Hope National Medical Center.

Methods

Setting

This study was a comparison between predictions made by medical oncologists (57 physicians and 17 advanced practice clinicians) and their advanced practice clinicians at the City of Hope academic center and limited community sites and by a custom model running silently (ie, invisible to clinicians) for 20 months. Institutional review board approval was provided, along with a waiver of consent, by the City of Hope. The research needed a waiver of consent because the investigator does not have a reasonable opportunity to obtain consent and the risk inflicting psychological, social, or other harm by contacting participants is greater than the risk of the study procedures. The Standards for Reporting of Diagnostic Accuracy (STARD) reporting guideline was followed.[52]

Background

3-Month Surprise Question

Medical oncologists at City of Hope, a National Cancer Institute–designated cancer center, are adherent in use of a software decision support pathway tool capturing each episode of a patient's

systemic therapy.[53] In a quaternary, highly specialized center for cancer care seeing many patients with advanced cancer, the oncologists believed a 3-month prognostic SQ would be meaningful to introduce in pathways as a trigger for goals-of-care discussions with patients regarding the benefits and burdens of additional therapy. We incorporated a mandatory 3-month surprise question (3MSQ) within the pathway tool for all patients with metastatic solid tumors in December 2019, worded "Would you be surprised if this patient were to die within the next 3 months?" The answer choices are yes or no.

The Machine Learning Model

We trained a gradient-boosted trees binary classifier (via the XGBoost library)[54] with observations from 28 484 deceased and alive patients and 493 features from demographic characteristics, laboratory test results, flowsheets, and diagnoses collected from the EHR between January 1, 2013, and April 24, 2019. In training and retrospective evaluation, we considered 1 observation per patient. For inclusion in training and evaluation sets, patients needed to have at least 2 encounters as a minimal amount of data; living patients needed a completed visit documented in the EHR at least 1 year postprediction date to avoid observations with potential missing death information. To limit the risk of data leakage, we picked dates of prediction to exclude encounters within 7 days of death. We also avoided overrepresenting observations with prediction dates within 30 days of death to not train the model with a disproportionate number of near-term deceased patients. We extracted hand-crafted features from time series of laboratory test results and flowsheet data in the 180-day temporal window preceding each prediction. We imputed missing values for features only in obvious cases because tree-based classifiers can handle missing data. Clinical variables used by the model, including age, sex, race, and body mass index, and other features extracted from laboratory test and flowsheet time series, are listed in eTable 1 in the Supplement. The features associated with the diagnoses consisted of aggregations of publicly available word2vec embeddings[55] of the *International Classification of Diseases, Ninth Revision* codes. A portion of the observations was used for retrospective evaluation based on a temporal split at a single time point to mimic deployment in the real world, in which past observations are used to train a model to predict in the present.

After hyperparameter tuning via cross-validation and retrospective evaluation, we retrained a version of the 90-day mortality model including the evaluation set and deployed it in a silent prospective pilot, inclusive of all City of Hope patients with accessible EHR data. The resulting model consisted of an ensemble of 357 decision trees with a maximum depth of 6. Since October 2019, the model made batches of predictions from observations automatically queried once a day from our enterprise data warehouse. The presence of new results from laboratory tests noted in eTable 2 in the Supplement triggered a prediction.

Study Population

We identified all medical oncologist and advanced practice clinician (oncologist) 3MSQ answers entered into our pathway decision support tool when any new regimen was ordered for metastatic disease between December 6, 2019, and August 6, 2021, from our enterprise data warehouse. After excluding prognostications not associated with outpatient visits and those entered on or after a death date, we defined a cohort inclusive of oncologist prognostications with a model prediction for the same patient within the preceding 30 days. The cohort consisted of 3099 predictions from both the model and oncologists for 2041 patients with advanced cancer. The EHR data in the community network were not yet fully accessible to the model, which limited predictions for the comparison period. Most 3MSQs were associated with encounters at the academic center (2972 [95.9%]) vs community satellites (127 [4.1%]) (**Table 1**). Patient race and ethnicity information was self-reported as part of routine intake and collected from the enterprise data warehouse.

Study Design

This prognostic study compared performance of 3-month mortality predictions made by oncologists and a model for patients with metastatic solid tumors. Oncologists' predictions were made from December 6, 2019, to August 6, 2021, as answers to a 3MSQ. The predictions were paired with the closest model prediction within the preceding 30 days. For the entire study, oncologists and the model were blinded to the predictions of the other. The primary outcome was an in-depth comparison between the performance of oncologists and our model in predicting 3-month mortality for a population of patients with metastatic solid tumors seen in outpatient clinics.

Statistical Analysis

The cohort included 3099 pairs of predictions for 2041 unique patients (Table 1). A prediction from the model comprises a score between 0 and 1 (a value close to 1 indicates high mortality risk). In contrast, oncologist predictions are binary: yes or no. To compare predictions among the model and oncologists, we set a threshold to convert risk scores into decisions (eg, flag patients scoring >0.5 as at risk of 3-month mortality). We set the decision threshold to match model sensitivity to that of the oncologists. Therefore, we compared oncologists and the model on positive predictive value (PPV or precision), which is the ratio of correct predictions over the total number of predictions made. The PPV depends on prevalence; thus, we also included the PPV-to-prevalence ratio to facilitate understanding of the results. In a scenario of pure random guessing, the PPV-to-prevalence ratio asymptotically converges to 1. We computed 95% CIs of the metrics via bootstrapping. For comparisons within disease groups, we computed 95% CIs of the difference between the PPV of the model and clinicians because 95% CIs of the PPV overlapped. A 95% CI of the difference above 0 means the model outperforms oncologists with statistical significance. Moreover, we characterized

Table 1. Patients With Metastatic Solid Tumors Subject to the 3-Month Surprise Question Prognostications and Model Predictions

Variable	Cohort, No. (%)
Encounters/prognostications	3099
Patients	2041
Medical oncologists and advanced practice clinicians	74
Prognostication count per oncologist, mean (range)	41.9 (1-245)
Days between appointment and prognostication, median (SD)	2 (15.5)
Sex	
Male	770 (37.7)
Female	1271 (62.3)
Age, median (range), y[a]	62.6 (18-96)
Disease group	
Breast	482 (23.6)
Gastrointestinal	629 (30.8)
Genitourinary	280 (13.7)
Lung	378 (18.5)
Rare	272 (13.3)
Race	
American Indian/Alaska Native	12 (0.6)
Asian	479 (23.5)
Black/African American	102 (5.0)
White	1322 (64.8)
Other/unknown[b]	126 (6.2)
Ethnicity	
Hispanic or Latino	488 (23.9)
Not Hispanic or Latino	1498 (73.4)
Unknown/declined to answer	55 (2.7)

[a] Age is reported at the encounter level.

[b] Other includes Native Hawaiian and other Pacific Islander (9 [0.4%]), as well as other races not discretely captured within the electronic health record.

performance through sensitivity (or recall), specificity, and median lead days. We defined lead days as the number of days between a correct mortality prediction and the date of death. For the model, we also computed the area under the receiver operating characteristic curve (AUROC) and area under the precision-recall curve. The results for oncologists and the model are summarized in **Table 2** with stratified evaluations over disease groups and changes in systemic therapy in **Table 3**. We also evaluated performance over a larger cohort of 3MSQs including answers without a model prediction (eMethods and eTable 3 in the Supplement).

Table 2. Performance of Oncologists Answering a 3-Month Surprise Question Compared With the 90-Day Mortality Prediction Model

Variable	Oncologists	ML model	Oncologist-ML model concordant decisions
No.	3099	3099	3099
Prevalence (90-d mortality), %	15.2	14.4	15.2
Area under the receiver operating characteristic curve, %	59.8 (57.7-62.0)	81.2 (79.1-83.3)	55.7 (54.2-57.3)
Area under the precision-recall curve, %	NA	46.2 (41.4-51.3)	NA
PPV (precision)	34.8 (30.1-39.5)	60.0 (53.6-66.3)	68.6 (58.2-78.4)
Sensitivity (recall), %	29.7 (25.6-33.8)	29.5 (25.4-34.0)	12.5 (9.6-15.6)
Specificity, %	90.0 (88.9-91.2)	96.7 (96.0-97.3)	99.0 (98.6-99.4)
PPV-to-prevalence ratio	2.3 (2.0-2.6)	4.2 (3.7-4.7)	4.5 (3.8-5.2)
Negative predictive value, %	87.7 (86.4-88.9)	89.1 (87.9-90.2)	86.3 (85.1-87.5)
Median lead days	37.5 (31.5-45.0)	28.5 (25.0-36.0)	30.0 (20.5-32.5)

Abbreviations: ML, machine learning; NA, not applicable; PPV, positive predictive value.

Table 3. Performance of Medical Oncologists With a 3-Month Surprise Question Compared With an ML Model With Stratification by Disease Groups and Presence of Systemic Therapy Changes

Disease group	No.	90-d Mortality, %	AUROC	PPV to prevalence	Sensitivity, %	PPV, %	PPV difference, 95% CI, %[a]
All disease groups							
Oncologists	3099	15.2	NC	2.3 (2.0 to 2.6)	29.7	34.8	18.5 to 31.9
ML model		14.4	81.2 (79.1 to 83.3)	NC	29.5	60.0	
Breast							
Oncologists	697	10.3	NC	3.5 (2.7 to 4.6)	37.5	36.5	1.7 to 32.5
Model		9.9	87.3 (83.0 to 91.1)	NC	36.2	53.2	
Gastrointestinal							
Oncologists	937	15.4	NC	2.1 (1.8 to 2.4)	52.1	32.5	4.1 to 18.5
ML model		14.4	81 (76.8 to 85.0)	NC	52.6	43.8	
Genitourinary (including gynecologic)							
Oncologists	376	12	NC	2.7 (1.4 to 4.2)	20	32.1	−15.7 to 35.6
ML model		11.2	85 (78.8 to 90.5)	NC	19	42.1	
Lung							
Oncologists	639	22.8	NC	2 (1.2 to 2.9)	9.6	46.7	−10.6 to 43.4
ML model		21.6	77.7 (73.2 to 82.2)	NC	10.1	63.6	
Rare							
Oncologists	450	14.4	NC	2.7 (1.7 to 3.8)	23.1	38.5	−1.3 to 45.3
ML model		14	76.4 (69.3 to 82.8)	NC	22.2	60.9	
Patients with no change in therapy							
Oncologists	1333	13.4	NC	2.5 (2.0 to 3.0)	26.8	33.1	5.9 to 26.0
ML model		13.2	80.1 (76.6 to 83.6)	NC	27.3	49	
Patients with changes in therapy							
Oncologists	1766	16.6	NC	2.2 (1.8 to 2.5)	31.4	35.8	19.7 to 37.2
ML model		15.4	82.4 (79.7 to 85.0)	NC	31.7	64.2	

Abbreviations: AUROC, area under the receiving operator characteristic curve; ML, machine learning; NC, not calculated; PPV, positive predictive value.

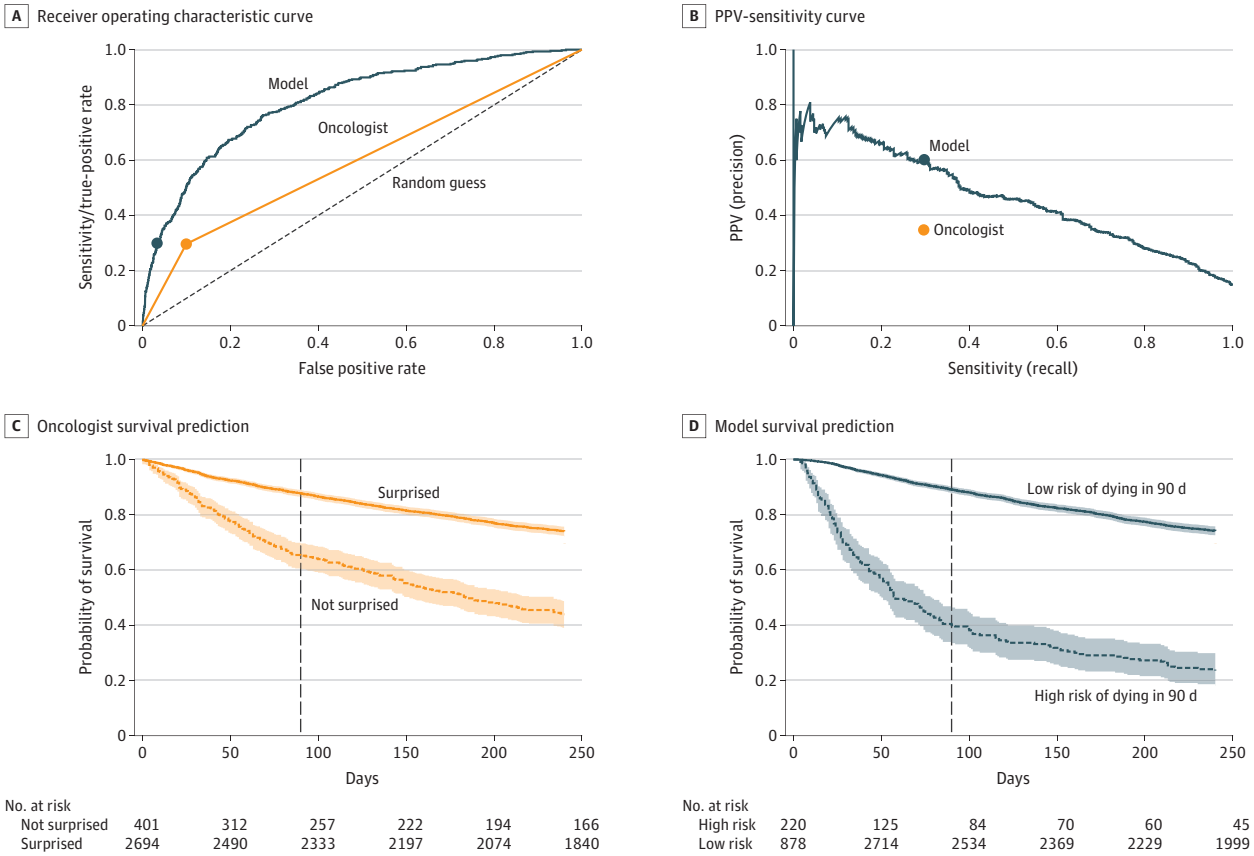
[a] If the 95% CI of the precision difference does not include 0, the precision of the model is statistically significantly better than that of the oncologists.

Results

We evaluated 3099 pairs of 3-month mortality predictions by oncologists and the model for 2041 patients (1271 [62.3%] women; 770 [37.7%] men) with a median age of 62.6 (range, 18-96) years at the time of oncologist prediction. The median lag between a 3MSQ answer and a model prediction was 3 days, with 75% of model predictions made within 8 days from the corresponding answer. We compared model and oncologist performance by setting a decision threshold so that model sensitivity matched the 30% sensitivity of the oncologists. Results showed that the model outperformed oncologists in aggregate (PPV, 60.0%; 95% CI, 53.6%-66.3% vs 34.8%; 95% CI, 30.1%-39.5%; $P < .001$) (Table 2) and within breast (PPV difference, 16.7%; 95% CI, 1.7%-32.5%; $P = .03$) and gastrointestinal (PPV difference, 11.3%; 95% CI, 4.1%-18.5%; $P = .002$) disease subgroups (ie, 95% CI PPV difference >0) (Table 3). The PPV difference was not statistically significant within genitourinary (including gynecologic), lung, and rare cancer groups. For concordant oncologist-model predictions, the PPV of the oncologists increased from 34.8% (95% CI, 30.1%-39.5%) to 68.6% (95% CI, 58.2%-78.4%), with a decrease in sensitivity to 12.5% (Table 2).

Figure 1A and B display ROC and PPV sensitivity curves for the model compared with sensitivity, false-positive rates, and PPV sensitivity for the oncologists. The model AUROC was 81.2% (95% CI, 79.1%-83.3%). The AUROC for the oncologists was 59.8% (95% CI, 57.7%-62.0%). The model operating at the same sensitivity level of the oncologists achieved lower false-positive rates and higher PPVs. Survival curves for oncologists (Figure 1C) and the model (Figure 1D) further show the better discriminative ability of the latter. Scatterplots show PPV and sensitivity for individual

Figure 1. Receiver Operating Characteristic Curve (ROC), Precision Recall Curve (PRC), and Survival Curves for the Model and Oncologists



Receiver operating characteristic curve (A) and positive predictive value (PPV)–sensitivity or PRC (B) for the machine learning model (model) vs oncologists. The model area under the ROC curve was 81%; area under the PRC, 50%; and prevalence, 14.4%. In survival plots for oncologists (C) and the model (D), the continuous curve was associated with a predicted low risk of death and, in the ideal case, would be horizontal for the first 3 months.

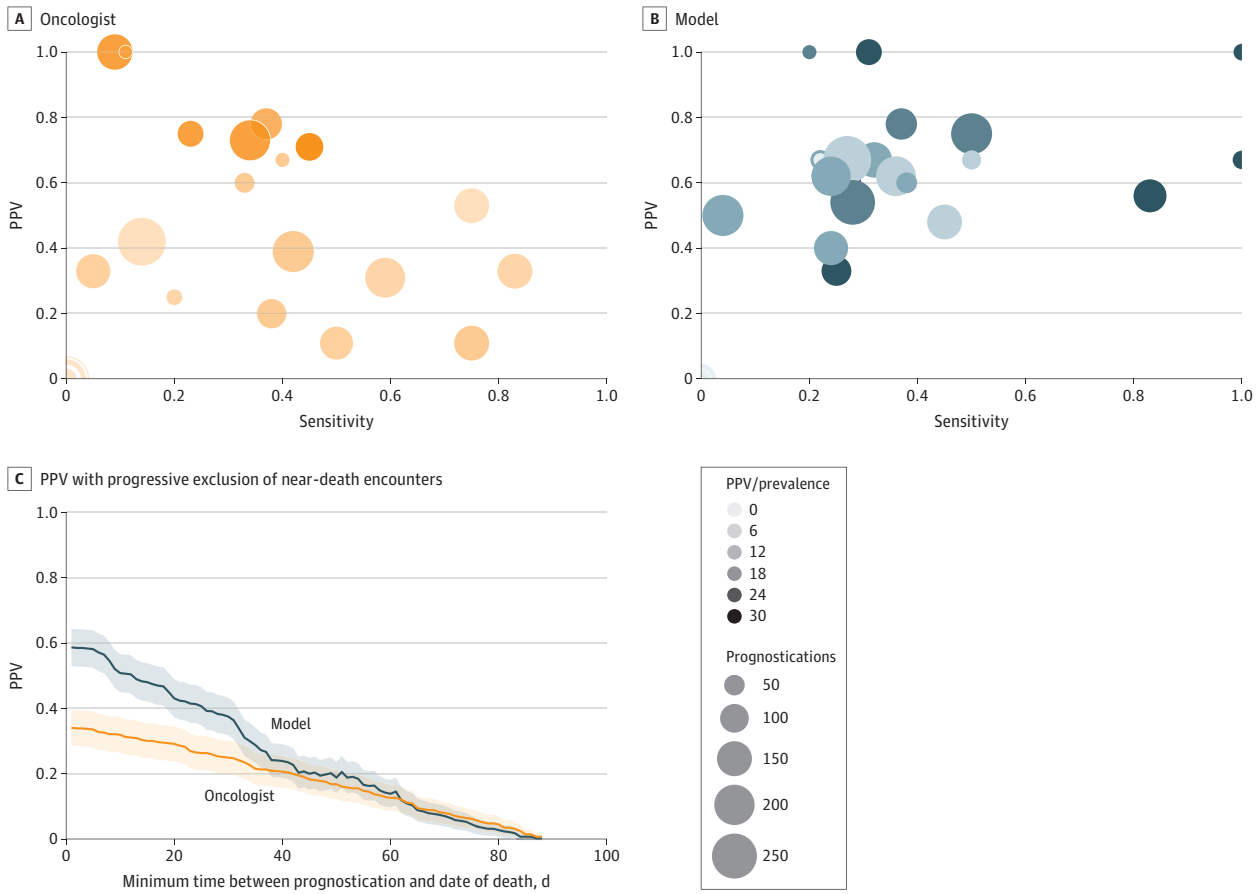
oncologists with at least 20 prognostications (**Figure 2**A) and associated model predictions (Figure 2B). Dots in the origin indicate instances of exclusively incorrect predictions. The plots show higher consistency of the model predictions (ie, the points are less scattered).

Figure 2C displays how the PPV for the model and oncologists varies with progressive exclusion of near-death encounters. For instance, with no encounter within 36 days from death, PPVs of the model and oncologists would be comparable. eFigure 1 in the Supplement shows the most predictive model features over the cohort. eFigure 2 in the Supplement shows that most oncologists predicted risk of death for their patients (ie, answered surprised for a fraction of instances smaller than the related prevalence). This finding could be interpreted as a conservative approach to privilege PPV rather than sensitivity.

Stratification by Changes in Therapy

Because of changes in therapy, 708 patients had multiple (up to 6) SQs answered by clinicians, encompassing 1766 predictions (57.0%). We split the cohort between patients with 1 SQ and patients with multiple SQs and included all SQ answers in our analysis. The difference between the PPV of the model and oncologists was larger for the subpopulation with changes in therapy (PPV difference, 28.4%; 95% CI, 19.7%-37.2%; $P < .001$ vs PPV difference, 15.9%; 95% CI, 5.9%-26.0%; $P = .002$)

Figure 2. Positive Predictive Value (PPV) and Sensitivity Scatterplots in PPV Plots With Exclusion of Near-Death Encounters



A, For oncologists, the PPV was 34.8% and sensitivity was 29.7%. B, For the machine learning model, PPV was 60.0% and sensitivity was 29.5%. Each dot in the scatterplots corresponds to the prognostications of an oncologist (A) and to associated model predictions (B). The size of a dot is proportional to the prediction count, and the hue represents the ratio of PPV over prevalence (darker color indicates better performance). C, Comparison of PPV for the model and oncologists with progressive exclusion of near-death encounters.

(Table 3). We also observed that, for this subpopulation, the oncologists changed predictions for only 31 patients, but the correct prognosis should have changed for 155 patients.

COVID-19

COVID-19 was associated with population shifts in our organization, especially between March and August 2020 when visits were deferred or switched to telehealth if clinically appropriate. The AUROC of the model over the entire patient population (beyond the metastatic solid tumor cohort in this study) decreased during late spring 2020 but then increased in the following summer months. However, in this metastatic cohort, we observed fluctuations in the monthly performance of the model and oncologists without clear temporal patterns, perhaps owing to the homogeneity of the cohort over time. eFigure 3 in the Supplement shows a quarterly comparison of PPV and prevalence between the model and oncologists.

Discussion

In this prognostic study, we compared the performance of medical oncologists and their advanced practice clinicians with an ML model to predict 3-month mortality for a cohort of patients with metastatic solid tumors at City of Hope. At a sensitivity of 30% (matching the oncologists' performance), the model outperformed the oncologists in PPV (60.0% vs 34.8%; $P < .001$) to predict 3-month mortality with 15% prevalence. Stated differently, the model matched the sensitivity of the oncologists but flagged nearly half of the instances (7.7% vs 14.1%). Looking forward, we anticipate tuning the model threshold to increase sensitivity or PPV depending on the clinical application but, more importantly, augmenting oncologists' prognostic capability while tempering overestimation of prognosis.

The model outperformed oncologists across each disease group, with a statistically significant margin for the 2 largest groups: breast ($P = .03$) and gastrointestinal ($P = .002$) cancer. The model AUROC was consistent across all groups (Table 3). To facilitate performance comparison across subpopulations with different prevalence, we evaluated the PPV-to-prevalence ratio. The 95% CIs for the oncologist PPV-to-prevalence ratio were above 1 across all disease groups (Table 3), indicating that oncologist performance was significantly better than random guessing.

In an SQ systematic review by White et al,[7] clinicians with 12-month and 7-day (1 study) SQs in oncology populations achieved an AUROC in the 66% to 82% range, with a 75% mean.[40,50,56] None of the studies limited the population to patients with metastatic solid tumors, and few had oncologists prognosticating. The study most similar to ours was by Vick et al,[40] wherein 81 oncologists answered 4617 twelve-month SQs for a mixed population of patients with metastatic and nonmetastatic cancer, achieving a 74% AUROC. The oncologists in our study achieved a 59.8% (95% CI, 57.7%-62.0%) AUROC, but for a population of patients exclusively with metastatic disease. We believe that for a mixed population, oncologists would have achieved a higher AUROC. The AUROC for evaluation of binary (yes vs no) decisions has limitations because the ROC curve is defined only by 3 points (Figure 1A). After computing the PPV-to-prevalence ratio for the aforementioned oncologic studies,[7,28,31,32,40] we observed that the performance of our clinicians was within range (eTable 4 in the Supplement).

In addition, we compared the model and oncologists' PPVs after progressively excluding predictions associated with near-death encounters. Figure 2C shows that PPVs for the model and oncologists become similar after excluding predictions that are 35 days from the death date. In other words, the model gains in performance over oncologists on near-death cases, which is supported in a study in which higher performance of mortality prediction models occurred in near-death encounters.[57] The consequent higher fraction of correctly predicted near-term deaths results in a lower median of lead days for the model compared with the oncologists.

Contributions

To our knowledge, ours is the first reported prospective comparison of a model with oncology clinician prognostications for patients with metastatic cancer.[42] The most similar prospective study, conducted by Manz et al,[46] reported that a model trained on EHR data from a population of patients with hematologic and oncologic disease could be clinically useful and outperformed Eastern Cooperative Oncology Group and Elixhauser prognostic indices.

We provided insights on how our model outperformed oncologists by stratifying the cohort according to 3 criteria: (1) exclusion of patients near death, (2) different disease group subpopulations, and (3) presence and absence of therapy changes. Besides improved performance in predicting near-term mortality, the model was more consistent in predicting 3-month mortality compared with the widely varying performance seen for individual oncologists (Figure 2B), which is not readily apparent when looking at the oncologists in aggregate (Figure 1B).

We show the PPV-to-prevalence ratio as a potentially helpful metric for comparing the performance of binary predictions (surprised or not surprised) across subpopulations with different prevalence. In a situation of random guessing, the PPV-to-prevalence ratio would tend to 1. Several publications evaluating SQs and even clinical ML did not report prevalence with PPV by omitting it, leaving its extrapolation to the reader or presenting results close to random guessing (ie, with PPV close to prevalence) as instances of good performance.[27-29,49]

Limitations

This study had limitations. The cohort (n = 3099) excluded most prognostications made at clinical network sites because the model was designed to work with laboratory tests performed at the academic cancer center but ordered infrequently at clinical network sites. Model upgrades will enhance coverage of patients receiving care at clinical network sites.

Communication of external deaths may be delayed by up to 6 months, with consequent underestimated prevalence and adjustments of performance results. For instance, the 3-month mortality rate for the cohort increased almost 1% in the span of 1 month. We observed a slow widening of the PPV difference between model and oncologists as death information was updated.

This blinded study evaluated the performance of the model and clinicians separately. To estimate the impact of model predictions in clinical practice, we need to evaluate how clinicians prognosticate once given the model predictions. Even a perfect model would have no benefit if it were not trusted by clinicians.

Conclusions

In this prognostic study, we noted that an ML model trained with EHR data outperformed clinicians in predicting 3-month mortality for a cohort of patients with metastatic solid tumors, with a 95% CI of 18.5%-31.9% for the difference in PPVs at 30% sensitivity. The model was trained on a relatively small population (n = 28 484) and yet achieved an 81.2% AUROC on the cohort. This finding could encourage other centers to develop custom models based on internally available patient data. This study was a step to validate the model before integration in the EHR of our organization.[58] Further evaluation is ongoing to study the performance of oncologists given model prognostications and whether use of the model improves prognostic confidence, patient engagement, and use of resources at the end of life.

ARTICLE INFORMATION

Accepted for Publication: March 24, 2022.

Published: May 31, 2022. doi:10.1001/jamanetworkopen.2022.14514

Corresponding Authors: Finly J. Zachariah, MD (fzachariah@coh.org), and Lorenzo A. Rossi, PhD (lrossi@coh.org), City of Hope National Medical Center, 1500 E Duarte Rd, Duarte, CA 91010.

Author Affiliations: Department of Supportive Care Medicine, City of Hope National Medical Center, Duarte, California (Zachariah); Department of Applied AI and Data Science, City of Hope National Medical Center, Duarte, California (Rossi); Department of Clinical Informatics, City of Hope National Medical Center, Duarte, California (Roberts); Department of Medical Oncology, City of Hope National Medical Center, Duarte, California (Bosserman).

Author Contributions: Dr Rossi had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Drs Zachariah and Rossi contributed equally to the study.

Concept and design: Zachariah, Rossi.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Zachariah, Rossi, Bosserman.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Rossi.

Administrative, technical, or material support: Zachariah, Roberts, Bosserman.

Supervision: Zachariah, Rossi.

Conflict of Interest Disclosures: None reported.

Additional Collaborators: Chi Wah (Alec) Wong, PhD, participated in useful discussion on performance metrics and Deron Johnson, PharmD (City of Hope National Medical Center), provided support in obtaining clinical pathways data. Neither received additional compensation for their assistance.

REFERENCES

1. Kubi B, Istl AC, Lee KT, Conca-Cheng A, Johnston FM. Advance care planning in cancer: patient preferences for personnel and timing. *JCO Oncol Pract*. 2020;16(9):e875-e883. doi:10.1200/JOP.19.00367

2. Bjørk E, Thompson W, Ryg J, Gaardboe O, Jørgensen TL, Lundby C. Patient preferences for discussing life expectancy: a systematic review. *J Gen Intern Med*. 2021;36(10):3136-3147. doi:10.1007/s11606-021-06973-5

3. Lagarde SM, Franssen SJ, van Werven JR, et al. Patient preferences for the disclosure of prognosis after esophagectomy for cancer with curative intent. *Ann Surg Oncol*. 2008;15(11):3289-3298. doi:10.1245/s10434-008-0068-y

4. Ahalt C, Walter LC, Yourman L, Eng C, Pérez-Stable EJ, Smith AK. "Knowing is better": preferences of diverse older adults for discussing prognosis. *J Gen Intern Med*. 2012;27(5):568-575. doi:10.1007/s11606-011-1933-0

5. Hagerty RG, Butow PN, Ellis PA, et al. Cancer patient preferences for communication of prognosis in the metastatic setting. *J Clin Oncol*. 2004;22(9):1721-1730. doi:10.1200/JCO.2004.04.095

6. Parkes CM. Accuracy of predictions of survival in later stages of cancer. *BMJ*. 1972;2(5804):29-31. doi:10.1136/bmj.2.5804.29

7. White N, Kupeli N, Vickerstaff V, Stone P. How accurate is the "surprise question" at identifying patients at the end of life? a systematic review and meta-analysis. *BMC Med*. 2017;15(1):139. doi:10.1186/s12916-017-0907-4

8. Amano K, Maeda I, Shimoyama S, et al. The accuracy of physicians' clinical predictions of survival in patients with advanced cancer. *J Pain Symptom Manage*. 2015;50(2):139-146.e1. doi:10.1016/j.jpainsymman.2015.03.004

9. Hui D, Paiva CE, Del Fabbro EG, et al. Prognostication in advanced cancer: update and directions for future research. *Support Care Cancer*. 2019;27(6):1973-1984. doi:10.1007/s00520-019-04727-y

10. Hui D. Prognostication of survival in patients with advanced cancer: predicting the unpredictable? *Cancer Control*. 2015;22(4):489-497. doi:10.1177/107327481502200415

11. Hofmann JC, Wenger NS, Davis RB, et al; SUPPORT Investigators: Study to Understand Prognoses and Preference for Outcomes and Risks of Treatment. Patient preferences for communication with physicians about end-of-life decisions. *Ann Intern Med*. 1997;127(1):1-12. doi:10.7326/0003-4819-127-1-199707010-00001

12. Bradley EH, Hallemeier AG, Fried TR, et al. Documentation of discussions about prognosis with terminally ill patients. *Am J Med*. 2001;111(3):218-223. doi:10.1016/S0002-9343(01)00798-7

13. Epstein AS, Prigerson HG, O'Reilly EM, Maciejewski PK. Discussions of life expectancy and changes in illness understanding in patients with advanced cancer. *J Clin Oncol*. 2016;34(20):2398-2403. doi:10.1200/JCO.2015.63.6696

14. Committee on Approaching Death; Institute of Medicine. *Dying in America: Improving Quality and Honoring Individual Preferences Near the End of Life*. The National Academies Press; 2015.

15. Han PKJ, Dieckmann NF, Holt C, Gutheil C, Peters E. Factors affecting physicians' intentions to communicate personalized prognostic information to cancer patients at the end of life: an experimental vignette study. *Med Decis Making*. 2016;36(6):703-713. doi:10.1177/0272989X16638321

16. Habib AR, Chen R, Magnavita ES, et al. Prevalence and tolerance of prognostic uncertainty among thoracic oncologists. *Oncologist*. 2021;26(8):e1480-e1482. doi:10.1002/onco.13788

17. Fischer S, Min SJ, Cervantes L, Kutner J. Where do you want to spend your last days of life? low concordance between preferred and actual site of death among hospitalized adults. *J Hosp Med*. 2013;8(4):178-183. doi:10.1002/jhm.2018

18. California Healthcare Foundation. Final chapter: Californians' attitudes and experiences with death and dying. 2012. Accessed April 18, 2022. https://www.chcf.org/publication/final-chapter-californians-attitudes-and-experiences-with-death-and-dying/

19. Kelley AS, Wenger NS, Sarkisian CA. Opiniones: end-of-life care preferences and planning of older Latinos. *J Am Geriatr Soc*. 2010;58(6):1109-1116. doi:10.1111/j.1532-5415.2010.02853.x

20. Miccinesi G, Bianchi E, Brunelli C, Borreani C. End-of-life preferences in advanced cancer patients willing to discuss issues surrounding their terminal condition. *Eur J Cancer Care (Engl)*. 2012;21(5):623-633. doi:10.1111/j.1365-2354.2012.01347.x

21. Wright AA, Mack JW, Kritek PA, et al. Influence of patients' preferences and treatment site on cancer patients' end-of-life care. *Cancer*. 2010;116(19):4656-4663. doi:10.1002/cncr.25217

22. Bhatia V, Geidner R, Mirchandani K, Huang Y, Warraich HJ. Systemwide advance care planning during the Covid-19 pandemic: the impact on patient outcomes and cost. *NEJM Catal Innov Care Deliv*. 2021;2(9). doi:10.1056/CAT.21.0188

23. Hallen SAM, Hootsmans NAM, Blaisdell L, Gutheil CM, Han PKJ. Physicians' perceptions of the value of prognostic models: the benefits and risks of prognostic confidence. *Health Expect*. 2015;18(6):2266-2277. doi:10.1111/hex.12196

24. Barton W, Cohen M, Raker C, et al. The surprise question in gynecologic oncology: an analysis looking at end-of-life care in patients with gynecologic cancer. *Gynecol Oncol*. 2020;159:313. doi:10.1016/j.ygyno.2020.05.565

25. Downar J, Goldman R, Pinto R, Englesakis M, Adhikari NK. The "surprise question" for predicting death in seriously ill patients: a systematic review and meta-analysis. *CMAJ*. 2017;189(13):E484-E493. doi:10.1503/cmaj.160775

26. Edge SB, Liu L, Case AA, et al. Value of oncologist generated "surprise question" in predicting survival in metastatic cancer. *J Clin Oncol*. 2020;38(15)(suppl):12082. doi:10.1200/JCO.2020.38.15_suppl.12082

27. Gade K, Spada N, Ormond E, et al. Prognostic value of the "surprise question" among UPMC Hillman Cancer Center patients with select stage IV cancer diagnoses. *J Clin Oncol*. 2020;38(29)(suppl):25. doi:10.1200/JCO.2020.38.29_suppl.25

28. Hamano J, Morita T, Inoue S, et al. Surprise questions for survival prediction in patients with advanced cancer: a multicenter prospective cohort study. *Oncologist*. 2015;20(7):839-844. doi:10.1634/theoncologist.2015-0015

29. Ikari T, Hiratsuka Y, Yamaguchi T, et al. "3-Day surprise question" to predict prognosis of advanced cancer patients with impending death: multicenter prospective observational study. *Cancer Med*. 2021;10(3):1018-1026. doi:10.1002/cam4.3689

30. Kim SH, Suh SY, Yoon SJ, et al. "The surprise questions" using variable time frames in hospitalized patients with advanced cancer. *Palliat Support Care*. 2021;1-5. Published online June 17, 2021. doi:10.1017/S1478951521000766

31. Lefkowits C, Chandler C, Sukumvanich P, et al. Validation of the "surprise question" in gynecologic oncology: comparing physicians, advanced practice providers and nurses. *J Clin Oncol*. 2015;33(29)(suppl):151. doi:10.1200/jco.2015.33.29_suppl.151

32. Moroni M, Zocchi D, Bolognesi D, et al; the SUQ-P Group. The "surprise" question in advanced cancer patients: a prospective study among general practitioners. *Palliat Med*. 2014;28(7):959-964. doi:10.1177/0269216314526273

33. Moss AH, Lunney JR, Culp S, et al. Prognostic significance of the "surprise" question in cancer patients. *J Palliat Med*. 2010;13(7):837-840. doi:10.1089/jpm.2010.0018

34. Rauh LA, Sullivan MW, Camacho F, et al. Validation of the surprise question in gynecologic oncology: a one-question screen to promote palliative care integration and advance care planning. *Gynecol Oncol*. 2020;157(3):754-758. doi:10.1016/j.ygyno.2020.03.007

35. Rhee J, Clayton JM. The "surprise" question may improve the accuracy of GPs in identifying death in patients with advanced stage IV solid-cell cancer. *Evid Based Med*. 2015;20(2):71. doi:10.1136/ebmed-2014-110114

36. Rice J, Hunter L, Hsu AT, et al. Using the "surprise question" in nursing homes: a prospective mixed-methods study. *J Palliat Care*. 2018;33(1):9-18. doi:10.1177/0825859717745728

37. Singh S, Graham Z, Rodriguez A, et al. Accuracy of the surprise question on an inpatient oncology service: a multidisciplinary perspective. *J Hosp Palliat Nurs*. 2019;21(4):300-304. doi:10.1097/NJH.0000000000000558

38. Singh S, Rodriguez A, Lee D, Min SJ, Fischer S. Usefulness of the surprise question on an inpatient oncology service. *Am J Hosp Palliat Care*. 2018;35(11):1421-1425. doi:10.1177/1049909118777990

39. Verhoef MJ, de Nijs EJM, Fiocco M, Heringhaus C, Horeweg N, van der Linden YM. Surprise question and performance status indicate urgency of palliative care needs in patients with advanced cancer at the emergency department: an observational cohort study. *J Palliat Med*. 2020;23(6):801-808. doi:10.1089/jpm.2019.0413

40. Vick JB, Pertsch N, Hutchings M, et al. The utility of the surprise question in identifying patients most at risk of death. *J Clin Oncol*. 2015;33(29)(suppl):8. doi:10.1200/jco.2015.33.29_suppl.8

41. White N, Oostendorp L, Vickerstaff V, et al. An online international comparison of thresholds for triggering a negative response to the "surprise question": a study protocol. *BMC Palliat Care*. 2019;18(1):36. doi:10.1186/s12904-019-0413-x

42. Gensheimer MF, Aggarwal S, Benson KRK, et al. Automated model versus treating physician for predicting survival time of patients with metastatic cancer. *J Am Med Inform Assoc*. 2021;28(6):1108-1116. doi:10.1093/jamia/ocaa290

43. Avati A, Jung K, Harman S, Downing L, Ng A, Shah NH. Improving palliative care with deep learning. *BMC Med Inform Decis Mak*. 2018;18(suppl 4):122. doi:10.1186/s12911-018-0677-8

44. Wang G, Lam KM, Deng Z, Choi KS. Prediction of mortality after radical cystectomy for bladder cancer by machine learning techniques. *Comput Biol Med*. 2015;63:124-132. doi:10.1016/j.compbiomed.2015.05.015

45. Elfiky AA, Pany MJ, Parikh RB, Obermeyer Z. Development and application of a machine learning approach to assess short-term mortality risk among patients with cancer starting chemotherapy. *JAMA Netw Open*. 2018;1(3):e180926. doi:10.1001/jamanetworkopen.2018.0926

46. Manz CR, Chen J, Liu M, et al. Validation of a machine learning algorithm to predict 180-day mortality for outpatients with cancer. *JAMA Oncol*. 2020;6(11):1723-1730. doi:10.1001/jamaoncol.2020.4331

47. Manz CR, Parikh RB, Small DS, et al. Effect of integrating machine learning mortality estimates with behavioral nudges to clinicians on serious illness conversations among patients with cancer: a stepped-wedge cluster randomized clinical trial. *JAMA Oncol*. 2020;6(12):e204759. doi:10.1001/jamaoncol.2020.4759

48. Thorsen-Meyer HC, Nielsen AB, Nielsen AP, et al. Dynamic and explainable machine learning prediction of mortality in patients in the intensive care unit: a retrospective study of high-frequency data in electronic patient records. *Lancet Digit Health*. 2020;2(4):e179-e191. doi:10.1016/S2589-7500(20)30018-2

49. Gajra A, Zettler ME, Miller KA, et al. Impact of augmented intelligence on utilization of palliative care services in a real-world oncology setting. *JCO Oncol Pract*. 2022;18(1):e80-e88. doi:10.1200/OP.21.00179

50. Flechet M, Falini S, Bonetti C, et al. Machine learning versus physicians' prediction of acute kidney injury in critically ill adults: a prospective evaluation of the AKIpredictor. *Crit Care*. 2019;23(1):282. doi:10.1186/s13054-019-2563-x

51. Jung K, Kashyap S, Avati A, et al. A framework for making predictive models useful in practice. *J Am Med Inform Assoc*. 2021;28(6):1149-1158. doi:10.1093/jamia/ocaa318

52. Cohen JF, Korevaar DA, Altman DG, et al. STARD 2015 guidelines for reporting diagnostic accuracy studies: explanation and elaboration. *BMJ Open*. 2016;6(11):e012799. doi:10.1136/bmjopen-2016-012799

53. Ellis PG. Development and implementation of oncology care pathways in an integrated care network: the Via Oncology Pathways experience. *J Oncol Pract*. 2013;9(3):171. doi:10.1200/JOP.2013.001020

54. Chen T, Guestrin C. Xgboost: a scalable tree boosting system. *arXiv*. Preprint posted online June 10, 2016. https://doi.org/10.48550/arXiv.1603.02754

55. Choi Y, Chiu CYI, Sontag D. Learning low-dimensional representations of medical concepts. *AMIA Jt Summits Transl Sci Proc*. 2016;2016:41-50.

56. Vick J, Pertsch N, Hutchings M, Neville B, Bernacki R. The utility of the surprise question in identifying patients most at risk of death (th360d). *J Pain Symptom Manage*. 2016;51(2). doi:10.1016/j.jpainsymman.2015.12.177

57. Jung K, Sudat SEK, Kwon N, Stewart WF, Shah NH. Predicting need for advanced illness or palliative care in a primary care population using electronic health record data. *J Biomed Inform*. 2019;92:103115. doi:10.1016/j.jbi.2019.103115

58. Rossi LA, Roberts LM, Zachariah F. Prospective evaluation of a 90-day mortality prediction model: from silent pilots to real time deployment in the EHR. Podium abstract presented at: AMIA Informatics Summit; March 21-24, 2022; Chicago, IL.

SUPPLEMENT.