

## Appendix 1: Supplementary methods

### *Candidate predictors and preprocessing*

Candidate variables were defined using registry fields available at diagnosis or during baseline diagnostic/pathological assessment. Missing-data rules were estimated in the training set only and then applied without refitting to the internal and temporal validation sets. Continuous variables were imputed using the training-set median and categorical variables using the training-set mode. Predictors with more than 40% missingness in the training set and predictors with zero variance were removed.

### *Feature selection*

After preprocessing, 11 predictors remained eligible for supervised predictor selection. Predictor selection used a prespecified combined strategy incorporating variable-level univariable logistic regression, least absolute shrinkage and selection operator regression, Boruta selection, and prespecified clinical retention of age at diagnosis, sex, race/ethnicity, and histologic subtype. These approaches were treated as complementary screening procedures, and their results were integrated using a union rule to avoid excluding potentially informative predictors solely because they were not selected by a single statistical procedure. A predictor was retained when it met at least one of these criteria.

### *Model development and evaluation*

Seven algorithms were tuned by fivefold cross-validation in the training set using the area under the receiver operating characteristic curve as the optimization metric. No resampling method was used because the outcome distribution was approximately balanced. Performance was evaluated separately in the held-out internal validation set and the 2018–2023 temporal validation cohort.

### *Secondary prognostic analyses*

The 36-month mortality analysis included patients with distant metastasis diagnosed during 2000–2020 whose 36-month outcome could be determined. Missing tumor size was replaced by the cohort median and accompanied by a missingness indicator; missing surgery status was retained as an unknown category. Treatment variables were interpreted as treatment receipt rather than causal effects. Site-specific metastasis analyses were restricted to complete cases diagnosed during 2016–2020.

**Table S1** Definitions and coding of the outcome and candidate predictors for the distant metastasis model

| Variable                        | Type        | Definition or coding                                                                | Registry source field                                      |
|---------------------------------|-------------|-------------------------------------------------------------------------------------|------------------------------------------------------------|
| Distant metastasis at diagnosis | Categorical | 0 = localized/regional disease; 1 = distant metastasis                              | Derived outcome                                            |
| Age at diagnosis, years         | Continuous  | Continuous, years                                                                   | Age recode with single ages and 90+                        |
| Sex                             | Categorical | 0 = Female, 1 = Male                                                                | Sex                                                        |
| Race/ethnicity                  | Categorical | 0 = non-Hispanic White, 1 = Hispanic, 2 = other race/ethnicity                      | Race and origin recode (NHW, NHB, NHAIAN, NHAPI, Hispanic) |
| Year of diagnosis               | Categorical | 0 = 2000–2007, 1 = 2008–2015, 2 = 2016–2023                                         | Year of diagnosis                                          |
| Primary site                    | Categorical | 0 = adrenal gland, 1 = retroperitoneum/abdomen/pelvis, 2 = thorax/mediastinum/other | Primary site; primary site-labeled                         |

| Variable                             | Type             | Definition or coding                                                                                                                                                                                                                                                                                                                                                                                                                                            | Registry source field                         |
|--------------------------------------|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------|
| Histologic subtype                   | Categorical      | 0 = neuroblastoma NOS, 1 = ganglioneuroblastoma                                                                                                                                                                                                                                                                                                                                                                                                                 | Histologic type ICD-O-3                       |
| Laterality                           | Categorical      | 0 = not paired/bilateral/other, 1 = right, 2 = left                                                                                                                                                                                                                                                                                                                                                                                                             | Laterality                                    |
| Diagnostic confirmation              | Categorical      | 0 = positive histology, 1 = radiography/clinical only, 2 = other/unknown confirmation                                                                                                                                                                                                                                                                                                                                                                           | Diagnostic confirmation                       |
| Tumor size, mm                       | Continuous       | Continuous, mm; unknown or implausible values coded as missing                                                                                                                                                                                                                                                                                                                                                                                                  | Tumor size over time recode (1988+)           |
| Regional lymph nodes examined        | Continuous       | Numeric values from 0 to 90 were retained; special SEER codes were treated as nonnumeric and handled according to the prespecified preprocessing procedure.                                                                                                                                                                                                                                                                                                     | Regional nodes examined (1988+)               |
| Positive regional lymph nodes        | Descriptive only | Numeric values from 0 to 90 were summarized descriptively among patients with available numeric records. Code 98 was treated as a structural non-assessment category associated with no regional lymph nodes examined, while codes 95, 97, and 99 were treated as other special ascertainment codes. This variable was excluded a priori before supervised predictor selection and was not entered as an independent continuous predictor in model development. | Regional nodes positive (1988+)               |
| County-level median household income | Categorical      | 0 = <\$75,000, 1 = \$75,000–\$99,999, 2 = ≥\$100,000                                                                                                                                                                                                                                                                                                                                                                                                            | Median household income inflation adj to 2024 |
| Rural-urban residence                | Categorical      | 0 = Metro ≥1 million, 1 = other metro, 2 = non-metro/rural                                                                                                                                                                                                                                                                                                                                                                                                      | Rural-urban continuum code                    |

Coding values were used for data processing; manuscript tables and figures use the corresponding clinical labels. ICD-O-3, International Classification of Diseases for Oncology, 3rd Edition; NHAIAN, non-Hispanic American Indian/Alaska Native; NHAPI, non-Hispanic Asian or Pacific Islander; NHB, non-Hispanic Black; NHW, Non-Hispanic White; NOS, not otherwise specified.

**Table S2** Missingness, preprocessing decisions, and training-derived imputation rules

| Variable                      | Missingness or special-code status in full cohort, n (%) | Preprocessing decision                    | Training-derived fill value |
|-------------------------------|----------------------------------------------------------|-------------------------------------------|-----------------------------|
| Age at diagnosis, years       | 0 (0.0%)                                                 | Retained for feature-selection assessment | Not required                |
| Sex                           | 0 (0.0%)                                                 | Retained for feature-selection assessment | Not required                |
| Race/ethnicity                | 0 (0.0%)                                                 | Retained for feature-selection assessment | Not required                |
| Year of diagnosis             | 0 (0.0%)                                                 | Retained for feature-selection assessment | Not required                |
| Primary site                  | 0 (0.0%)                                                 | Removed because of zero variance          | Not applicable              |
| Histologic subtype            | 0 (0.0%)                                                 | Retained for feature-selection assessment | Not required                |
| Laterality                    | 0 (0.0%)                                                 | Retained for feature-selection assessment | Not required                |
| Diagnostic confirmation       | 0 (0.0%)                                                 | Retained for feature-selection assessment | Not required                |
| Tumor size, mm                | 747 (19.5%)                                              | Retained for feature-selection assessment | Median: 65 mm               |
| Regional lymph nodes examined | 496 (12.9%)                                              | Retained for feature-selection assessment | Median: 0                   |

| Variable                             | Missingness or special-code status in full cohort, n (%)                                                                                                                                 | Preprocessing decision                                                                                                                                                                                                                                                                     | Training-derived fill value |
|--------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|
| Positive regional lymph nodes        | Numeric values 0–90 available in 1,249 (32.55%); special codes in 2,588 (67.45%), including code 95: 28 (0.73%), code 97: 134 (3.49%), code 98: 2,142 (55.82%), and code 99: 284 (7.40%) | Descriptive only; excluded a priori before supervised predictor selection because its availability was conditional on regional nodal assessment and most nonnumeric records represented special ascertainment categories. It was not used as an independent continuous candidate predictor | Not applicable              |
| County-level median household income | 1 (<0.1%)                                                                                                                                                                                | Retained for feature-selection assessment                                                                                                                                                                                                                                                  | Mode: \$75,000–\$99,999     |
| Rural-urban residence                | 0 (0.0%)                                                                                                                                                                                 | Retained for feature-selection assessment                                                                                                                                                                                                                                                  | Not required                |

Missingness and special-code status are reported for the full primary cohort (n=3,837). For positive regional lymph nodes, the 67.45% nonnumeric proportion should not be interpreted as conventional missingness: code 98 accounted for 55.82% of the cohort and corresponded to records with Regional Lymph Nodes Examined code 00, representing a structural non-assessment pattern. Codes 95, 97, and 99 were treated as other special ascertainment codes. Positive regional lymph nodes were summarized descriptively only and was excluded before supervised predictor selection. For variables requiring imputation, imputation values were estimated using the training set only and applied unchanged to the internal and temporal validation sets.

**Table S3** Evidence used for predictor selection in the distant metastasis model

| Predictor                            | Univariable overall P value | Selected by LASSO | Selected by Boruta | Clinical retention | Recommended |
|--------------------------------------|-----------------------------|-------------------|--------------------|--------------------|-------------|
| Laterality                           | <0.001                      | Yes               | Yes                | No                 | Yes         |
| Histologic subtype                   | <0.001                      | Yes               | Yes                | Yes                | Yes         |
| Tumor size, mm                       | <0.001                      | Yes               | Yes                | No                 | Yes         |
| Diagnostic confirmation              | <0.001                      | Yes               | Yes                | No                 | Yes         |
| Race/ethnicity                       | 0.013                       | Yes               | No                 | Yes                | Yes         |
| Sex                                  | 0.016                       | No                | No                 | Yes                | Yes         |
| Regional lymph nodes examined        | 0.071                       | No                | Yes                | No                 | Yes         |
| Age at diagnosis, years              | 0.092                       | Yes               | Yes                | Yes                | Yes         |
| Year of diagnosis                    | 0.340                       | No                | Yes                | No                 | Yes         |
| Rural-urban residence                | 0.695                       | No                | No                 | No                 | No          |
| County-level median household income | 0.875                       | No                | No                 | No                 | No          |

A predictor was recommended when it was selected by LASSO, selected by Boruta, had a variable-level univariable P value <0.05, or was prespecified for clinical retention. LASSO, least absolute shrinkage and selection operator.

**Table S4** Cross-validated performance and selected hyperparameters

| Model                                           | Best fivefold cross-validation AUC | Selected hyperparameters                                                                            |
|-------------------------------------------------|------------------------------------|-----------------------------------------------------------------------------------------------------|
| Logistic regression                             | 0.754                              | C =1; penalty =l1                                                                                   |
| Decision tree                                   | 0.763                              | ccp_alpha =0.001; max_depth =5;<br>max_features =None; min_samples_split<br>=10                     |
| Random forest                                   | 0.786                              | max_features =sqrt; min_samples_leaf<br>=5; n_estimators =500                                       |
| Support vector machine                          | 0.782                              | C =1; gamma = auto; kernel = rbf                                                                    |
| Multilayer perceptron/artificial neural network | 0.775                              | activation= relu; alpha =0.001;<br>hidden_layer_sizes = [100]                                       |
| XGBoost                                         | 0.794                              | colsample_bytree =0.8; learning_rate<br>=0.05; max_depth =2; n_estimators =200;<br>subsample =0.8   |
| LightGBM                                        | 0.789                              | colsample_bytree =0.8; learning_rate<br>=0.03; n_estimators =100; num_leaves<br>=15; subsample =0.8 |

Hyperparameters were selected in the training set using fivefold cross-validation with receiver operating characteristic AUC as the optimization metric. AUC, area under the curve; LightGBM, light gradient boosting machine; XGBoost, eXtreme Gradient Boosting.

**Table S5** Complete performance of the seven models in the internal validation set

| Model                                           | N/events | AUC (95% CI)        | Brier score (95% CI) | Accuracy | Sensitivity | Specificity | PPV   | NPV   | F1 score |
|-------------------------------------------------|----------|---------------------|----------------------|----------|-------------|-------------|-------|-------|----------|
| LightGBM                                        | 865/446  | 0.775 (0.743–0.804) | 0.193 (0.181–0.206)  | 0.704    | 0.767       | 0.637       | 0.692 | 0.720 | 0.728    |
| Random forest                                   | 865/446  | 0.771 (0.739–0.801) | 0.194 (0.181–0.208)  | 0.697    | 0.753       | 0.637       | 0.689 | 0.708 | 0.719    |
| XGBoost                                         | 865/446  | 0.768 (0.736–0.799) | 0.195 (0.182–0.209)  | 0.701    | 0.742       | 0.656       | 0.697 | 0.705 | 0.719    |
| Multilayer perceptron/artificial neural network | 865/446  | 0.761 (0.727–0.792) | 0.199 (0.186–0.212)  | 0.699    | 0.724       | 0.673       | 0.702 | 0.696 | 0.713    |
| Support vector machine                          | 865/446  | 0.750 (0.718–0.782) | 0.204 (0.190–0.218)  | 0.690    | 0.738       | 0.640       | 0.685 | 0.696 | 0.711    |
| Decision tree                                   | 865/446  | 0.750 (0.717–0.784) | 0.204 (0.189–0.219)  | 0.695    | 0.717       | 0.671       | 0.699 | 0.690 | 0.708    |
| Logistic regression                             | 865/446  | 0.724 (0.689–0.758) | 0.212 (0.199–0.225)  | 0.673    | 0.686       | 0.659       | 0.682 | 0.663 | 0.684    |

Classification metrics were calculated using a probability threshold of 0.5. AUC and Brier-score confidence intervals were obtained from 1,000 bootstrap samples. AUC, area under the curve; CI, confidence interval; LightGBM, light gradient boosting machine; NPV, negative predictive value; PPV, positive predictive value; XGBoost, eXtreme Gradient Boosting.

**Table S6** Complete performance of the seven models in the temporal validation set

| Model                                           | N/events | AUC (95% CI)        | Brier score (95% CI) | Accuracy | Sensitivity | Specificity | PPV   | NPV   | F1 score |
|-------------------------------------------------|----------|---------------------|----------------------|----------|-------------|-------------|-------|-------|----------|
| XGBoost                                         | 953/511  | 0.807 (0.778–0.835) | 0.180 (0.169–0.192)  | 0.743    | 0.730       | 0.758       | 0.777 | 0.708 | 0.753    |
| LightGBM                                        | 953/511  | 0.802 (0.774–0.829) | 0.181 (0.171–0.193)  | 0.740    | 0.750       | 0.729       | 0.761 | 0.716 | 0.755    |
| Random forest                                   | 953/511  | 0.801 (0.772–0.828) | 0.184 (0.174–0.194)  | 0.748    | 0.791       | 0.699       | 0.752 | 0.743 | 0.771    |
| Support vector machine                          | 953/511  | 0.799 (0.771–0.824) | 0.182 (0.170–0.194)  | 0.736    | 0.775       | 0.690       | 0.743 | 0.726 | 0.759    |
| Multilayer perceptron/artificial neural network | 953/511  | 0.797 (0.768–0.824) | 0.185 (0.174–0.197)  | 0.738    | 0.742       | 0.733       | 0.763 | 0.711 | 0.752    |
| Decision tree                                   | 953/511  | 0.794 (0.764–0.821) | 0.180 (0.168–0.193)  | 0.737    | 0.751       | 0.719       | 0.756 | 0.715 | 0.754    |
| Logistic regression                             | 953/511  | 0.782 (0.753–0.812) | 0.192 (0.181–0.204)  | 0.728    | 0.736       | 0.719       | 0.752 | 0.702 | 0.744    |

Classification metrics were calculated using a probability threshold of 0.5. AUC and Brier-score confidence intervals were obtained from 1,000 bootstrap samples. AUC, area under the curve; CI, confidence interval; LightGBM, light gradient boosting machine; NPV, negative predictive value; PPV, positive predictive value; XGBoost, eXtreme Gradient Boosting.

**Table S7** Baseline characteristics of the metastatic cohort according to 36-month mortality

| Characteristic          | Category                            | Overall<br>(n=1,704)  | Alive >36 months<br>(n=1,213) | Death within 36 months (n=491) | P<br>value |
|-------------------------|-------------------------------------|-----------------------|-------------------------------|--------------------------------|------------|
| Age at diagnosis, years | –                                   | 2.00 [0.00, 4.00]     | 2.00 [0.00, 4.00]             | 2.00 [1.00, 4.00]              | <0.001     |
| Sex                     | Female                              | 748 (43.90)           | 531 (43.78)                   | 217 (44.20)                    | 0.917      |
|                         | Male                                | 956 (56.10)           | 682 (56.22)                   | 274 (55.80)                    |            |
| Race/ethnicity          | Non-Hispanic White                  | 920 (53.99)           | 681 (56.14)                   | 239 (48.68)                    | 0.014      |
|                         | Hispanic ethnicity                  | 377 (22.12)           | 261 (21.52)                   | 116 (23.63)                    |            |
|                         | Other racial/ethnic groups          | 407 (23.88)           | 271 (22.34)                   | 136 (27.70)                    |            |
| Year of diagnosis       | 2000–2007                           | 662 (38.85)           | 428 (35.28)                   | 234 (47.66)                    | <0.001     |
|                         | 2008–2015                           | 673 (39.50)           | 500 (41.22)                   | 173 (35.23)                    |            |
|                         | 2016–2020                           | 369 (21.65)           | 285 (23.50)                   | 84 (17.11)                     |            |
| Histologic subtype      | Neuroblastoma                       | 1589 (93.25)          | 1124 (92.66)                  | 465 (94.70)                    | 0.157      |
|                         | Ganglioneuroblastoma histology      | 115 (6.75)            | 89 (7.34)                     | 26 (5.30)                      |            |
| Laterality              | Unpaired, bilateral, or unknown     | 568 (33.33)           | 423 (34.87)                   | 145 (29.53)                    | 0.090      |
|                         | Right-sided primary tumor           | 521 (30.58)           | 358 (29.51)                   | 163 (33.20)                    |            |
|                         | Left-sided primary tumor            | 615 (36.09)           | 432 (35.61)                   | 183 (37.27)                    |            |
| Tumor size, mm          | –                                   | 75.00 [50.25, 109.75] | 72.00 [50.00, 103.00]         | 90.00 [60.00, 117.00]          | <0.001     |
| Tumor-size missingness  | Tumor size observed                 | 1266 (74.30)          | 921 (75.93)                   | 345 (70.26)                    | 0.018      |
|                         | Tumor size missing                  | 438 (25.70)           | 292 (24.07)                   | 146 (29.74)                    |            |
| Primary-site surgery    | No surgery                          | 491 (28.81)           | 327 (26.96)                   | 164 (33.40)                    | 0.001      |
|                         | Less extensive primary-site surgery | 476 (27.93)           | 364 (30.01)                   | 112 (22.81)                    |            |
|                         | More extensive primary-site surgery | 690 (40.49)           | 495 (40.81)                   | 195 (39.71)                    |            |
|                         | Unknown surgery status              | 47 (2.76)             | 27 (2.23)                     | 20 (4.07)                      |            |
| Radiotherapy            | None or unknown                     | 967 (56.75)           | 689 (56.80)                   | 278 (56.62)                    | 0.800      |
|                         | Beam radiotherapy                   | 636 (37.32)           | 455 (37.51)                   | 181 (36.86)                    |            |
|                         | Other radiotherapy                  | 101 (5.93)            | 69 (5.69)                     | 32 (6.52)                      |            |

**Table S7** (continued)

| Characteristic                                | Category              | Overall<br>(n=1,704) | Alive >36 months<br>(n=1,213) | Death within 36 months (n=491) | P<br>value |
|-----------------------------------------------|-----------------------|----------------------|-------------------------------|--------------------------------|------------|
| Chemotherapy                                  | No/Unknown            | 108 (6.34)           | 80 (6.60)                     | 28 (5.70)                      | 0.565      |
|                                               | Chemotherapy received | 1596 (93.66)         | 1133 (93.40)                  | 463 (94.30)                    |            |
| County-level<br>median<br>household<br>income | <\$75,000             | 485 (28.46)          | 340 (28.03)                   | 145 (29.53)                    | 0.492      |
|                                               | \$75,000–\$99,999     | 795 (46.65)          | 577 (47.57)                   | 218 (44.40)                    |            |
|                                               | \$100,000+            | 424 (24.88)          | 296 (24.40)                   | 128 (26.07)                    |            |
| Rural-urban<br>residence                      | Metro ≥1 million      | 1051 (61.68)         | 751 (61.91)                   | 300 (61.10)                    | 0.298      |
|                                               | Other metro           | 648 (38.03)          | 460 (37.92)                   | 188 (38.29)                    |            |
|                                               | Non-metro/rural       | 5 (0.29)             | 2 (0.16)                      | 3 (0.61)                       |            |

Data are median [interquartile range] or n (%). P values were obtained using the Wilcoxon rank-sum test, Chi-squared test, or Fisher's exact test, as appropriate. Missing tumor size was replaced by the cohort median and modeled with a missingness indicator.

**Table S8** Univariable logistic regression for death within 36 months in the full metastatic cohort

| Characteristic                         | OR (95% CI)       | P value |
|----------------------------------------|-------------------|---------|
| Age at diagnosis, per year             | 1.07 (1.04–1.11)  | <0.001  |
| Sex: male                              | 0.98 (0.80–1.21)  | 0.874   |
| Hispanic ethnicity                     | 1.27 (0.97–1.65)  | 0.079   |
| Other racial/ethnic groups             | 1.43 (1.11–1.84)  | 0.006   |
| Diagnosis year: 2008–2015              | 0.63 (0.50–0.80)  | <0.001  |
| Diagnosis year: 2016–2020              | 0.54 (0.40–0.72)  | <0.001  |
| Ganglioneuroblastoma histology         | 0.71 (0.45–1.11)  | 0.130   |
| Right-sided primary tumor              | 1.33 (1.02–1.73)  | 0.035   |
| Left-sided primary tumor               | 1.24 (0.96–1.60)  | 0.105   |
| Tumor size, per 10-mm increase         | 1.08 (1.05–1.12)  | <0.001  |
| Tumor size missing                     | 1.33 (1.06–1.69)  | 0.016   |
| Less extensive primary-site surgery    | 0.61 (0.46–0.81)  | <0.001  |
| More extensive primary-site surgery    | 0.79 (0.61–1.01)  | 0.059   |
| Unknown surgery status                 | 1.48 (0.80–2.71)  | 0.209   |
| Beam radiotherapy                      | 0.99 (0.79–1.23)  | 0.900   |
| Other radiotherapy                     | 1.15 (0.74–1.79)  | 0.537   |
| Chemotherapy received                  | 1.17 (0.75–1.82)  | 0.494   |
| County-level income: \$75,000–\$99,999 | 0.89 (0.69–1.14)  | 0.341   |
| County-level income: \$100,000+        | 1.01 (0.76–1.35)  | 0.924   |
| Rural-urban residence: other metro     | 1.02 (0.82–1.27)  | 0.836   |
| Rural-urban residence: non-metro/rural | 3.75 (0.62–22.59) | 0.148   |

Reference categories were female sex, non-Hispanic White race/ethnicity, diagnosis during 2000–2007, neuroblastoma histology, unpaired/bilateral/unknown laterality, county-level income <\$75,000, and residence in a metropolitan area with at least 1 million population. CI, confidence interval; OR, odds ratio.

**Table S9** Multivariable base model for death within 36 months in the full metastatic cohort

| Characteristic                 | OR (95% CI)      | P value |
|--------------------------------|------------------|---------|
| Age at diagnosis, per year     | 1.06 (1.02–1.10) | 0.002   |
| Sex: male                      | 0.96 (0.77–1.19) | 0.700   |
| Hispanic ethnicity             | 1.32 (1.00–1.74) | 0.046   |
| Other racial/ethnic groups     | 1.45 (1.11–1.89) | 0.006   |
| Diagnosis year: 2008–2015      | 0.60 (0.47–0.77) | <0.001  |
| Diagnosis year: 2016–2020      | 0.51 (0.38–0.68) | <0.001  |
| Ganglioneuroblastoma histology | 0.62 (0.39–1.00) | 0.048   |
| Right-sided primary tumor      | 1.44 (1.10–1.90) | 0.009   |
| Left-sided primary tumor       | 1.32 (1.01–1.72) | 0.043   |
| Tumor size, per 10-mm increase | 1.08 (1.05–1.12) | <0.001  |
| Tumor size missing             | 1.39 (1.08–1.78) | 0.010   |

| Characteristic                         | OR (95% CI)       | P value |
|----------------------------------------|-------------------|---------|
| County-level income: \$75,000–\$99,999 | 0.86 (0.64–1.15)  | 0.306   |
| County-level income: \$100,000+        | 0.93 (0.66–1.31)  | 0.665   |
| Rural-urban residence: Other metro     | 1.04 (0.80–1.36)  | 0.771   |
| Rural-urban residence: Non-metro/rural | 4.23 (0.67–26.57) | 0.124   |

Reference categories were female sex, non-Hispanic White race/ethnicity, diagnosis during 2000–2007, neuroblastoma histology, unpaired/bilateral/unknown laterality, county-level income <\$75,000, and residence in a metropolitan area with at least 1 million population. Tumor size was entered per 10-mm increase, with a separate indicator for missing tumor size. CI, confidence interval; OR, odds ratio.

**Table S10** Treatment-extended multivariable model for death within 36 months in the full metastatic cohort

| Characteristic                         | OR (95% CI)       | P value |
|----------------------------------------|-------------------|---------|
| Age at diagnosis, per year             | 1.06 (1.03–1.10)  | <0.001  |
| Sex: male                              | 0.96 (0.77–1.19)  | 0.686   |
| Hispanic ethnicity                     | 1.28 (0.97–1.69)  | 0.080   |
| Other racial/ethnic groups             | 1.46 (1.12–1.91)  | 0.005   |
| Diagnosis year: 2008–2015              | 0.62 (0.48–0.80)  | <0.001  |
| Diagnosis year: 2016–2020              | 0.51 (0.38–0.70)  | <0.001  |
| Ganglioneuroblastoma histology         | 0.70 (0.43–1.13)  | 0.146   |
| Right-sided primary tumor              | 1.53 (1.15–2.04)  | 0.003   |
| Left-sided primary tumor               | 1.44 (1.09–1.91)  | 0.011   |
| Tumor size, per 10-mm increase         | 1.09 (1.05–1.13)  | <0.001  |
| Tumor size missing                     | 1.26 (0.98–1.63)  | 0.074   |
| County-level income: \$75,000–\$99,999 | 0.86 (0.64–1.16)  | 0.331   |
| County-level income: \$100,000+        | 0.95 (0.68–1.35)  | 0.788   |
| Rural-urban residence: other metro     | 1.05 (0.81–1.38)  | 0.698   |
| Rural-urban residence: non-metro/rural | 3.89 (0.60–25.09) | 0.153   |
| Less extensive primary-site surgery    | 0.58 (0.43–0.80)  | <0.001  |
| More extensive primary-site surgery    | 0.67 (0.50–0.89)  | 0.007   |
| Unknown surgery status                 | 1.24 (0.65–2.35)  | 0.511   |
| Beam radiotherapy                      | 0.95 (0.74–1.22)  | 0.699   |
| Other radiotherapy                     | 1.24 (0.77–2.00)  | 0.380   |
| Chemotherapy received                  | 1.05 (0.65–1.68)  | 0.839   |

Reference categories were female sex, non-Hispanic White race/ethnicity, diagnosis during 2000–2007, neuroblastoma histology, unpaired/bilateral/unknown laterality, county-level income <\$75,000, and residence in a metropolitan area with at least 1 million population. Additional reference categories were no primary-site surgery, no/unknown radiotherapy, and no/unknown chemotherapy. Treatment estimates describe treatment receipt and should not be interpreted causally. CI, confidence interval; OR, odds ratio.

**Table S11** Adjusted site-specific metastasis model for death within 36 months in the modern complete-case cohort

| Characteristic   | OR (95% CI)      | P value |
|------------------|------------------|---------|
| Bone metastasis  | 1.00 (0.55–1.81) | 0.989   |
| Brain metastasis | 2.02 (0.82–4.94) | 0.124   |

| Characteristic                 | OR (95% CI)      | P value |
|--------------------------------|------------------|---------|
| Liver metastasis               | 0.84 (0.45–1.56) | 0.585   |
| Lung metastasis                | 3.09 (1.36–7.04) | 0.007   |
| Distant lymph node metastasis  | 0.73 (0.39–1.38) | 0.335   |
| Other metastasis               | 1.24 (0.73–2.10) | 0.429   |
| Age at diagnosis, per year     | 1.08 (0.99–1.18) | 0.088   |
| Sex: male                      | 1.04 (0.62–1.75) | 0.886   |
| Hispanic ethnicity             | 1.17 (0.61–2.22) | 0.636   |
| Other racial/ethnic groups     | 1.50 (0.81–2.77) | 0.195   |
| Ganglioneuroblastoma histology | 0.31 (0.09–1.14) | 0.078   |

The model included all six site-specific metastasis indicators and was adjusted for age at diagnosis, sex, race/ethnicity, and histologic subtype. The analysis included 361 patients diagnosed during 2016–2020, including 80 deaths within 36 months. Reference categories were absence of the specified metastasis, female sex, non-Hispanic White race/ethnicity, and neuroblastoma histology. CI, confidence interval; OR, odds ratio.

**Table S12** Sensitivity analysis excluding regional lymph nodes examined from the final LightGBM model

| Dataset             | 9-predictor model AUC<br>(95% CI) | 8-predictor model AUC<br>(95% CI) | 9-predictor model Brier<br>score | 8-predictor model Brier<br>score |
|---------------------|-----------------------------------|-----------------------------------|----------------------------------|----------------------------------|
| Internal validation | 0.7746 (0.7430–0.8038)            | 0.7688 (0.7361–0.7994)            | 0.1932                           | 0.1946                           |
| Temporal validation | 0.8021 (0.7744–0.8288)            | 0.8006 (0.7712–0.8286)            | 0.1815                           | 0.1816                           |

The 8-predictor model was constructed by excluding Regional Lymph Nodes Examined from the final 9-predictor LightGBM model and was retuned using the same fivefold cross-validation procedure in the training set. Performance was evaluated using AUC and Brier score in the internal and temporal validation cohorts. AUC, area under the receiver operating characteristic curve; CI, confidence interval; LightGBM, light gradient boosting machine.