Patterns of care and survival for patients with glioblastoma multiforme diagnosed during 2006

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Standard treatment for glioblastoma multiforme (GBM) changed in 2005 when addition of temozolomide (TMZ) to maximal surgical resection followed by radiation therapy (RT) was shown to prolong survival in a clinical trial. In this study, we assessed treatment patterns and survival of patients with GBM in community settings in the United States. Patients with newly diagnosed GBM who were aged ≥20 years in 2006 (n = 1202) were identified as part of the National Cancer Institute’s Patterns of Care Studies. We assessed treatment patterns, and in the subset of patients who received total or partial surgical resection, we used multivariable regression analysis to assess patient, clinical, and health system factors associated with receipt of adjuvant chemotherapy and RT and survival through 2008. Approximately 65% of patients with GBM received total or partial surgical resection, and approximately 70% of these patients received adjuvant TMZ and RT. Receipt of adjuvant therapy was associated with patient age, marital status, health insurance, and tumor location. Median survival in all patients was 10 months (95% confidence interval [CI], 9–11 months). Receipt of adjuvant therapy following resection was associated with a lower risk of dying in adjusted analyses for patients who received TMZ and RT (hazard ratio [HR], 0.25; 95% CI, 0.18–0.35) and other adjuvant therapies (HR, 0.55; 95% CI, 0.37–0.81), compared with no adjuvant therapy. We observed rapid diffusion of a new standard of treatment, adjuvant and concurrent TMZ with RT, among adult patients with newly diagnosed GBM in the community setting following publication of a pivotal clinical trial.

Keywords: brain cancer, glioblastoma, practice patterns, SEER, temozolomide.

In 2010, approximately 22,000 individuals in the United States received a diagnosis of malignant brain and spinal cord cancers, and approximately 13,000 died of their disease.1 Glioblastoma multiforme (GBM) is the most common form of brain cancer,2–4 and incidence rates are increasing, particularly in the older population.5,6 Because the US population is growing and aging, the absolute number of patients with newly diagnosed GBM is expected to increase in the future. Treatment of GBM is constrained by its primary location and infiltrating growth pattern, and median survival is typically short and measured in months, rather than years.1,7 For many years, the standard treatment for GBM consisted of maximum surgical resection, followed by radiation therapy.7 The benefit of adjuvant chemotherapy was not well-established. In 2005, a pivotal randomized trial demonstrated the overall survival advantage of adding adjuvant temozolomide (TMZ) and concurrent TMZ with radiotherapy (RT) following maximal surgical resection.8 Although treatment guidelines have endorsed adding TMZ to surgery and RT,9,10 the extent to which it is used in the community setting is largely unknown. In this study, therefore, we assessed treatment patterns and survival in a population-based sample of patients who received a diagnosis of GBM in 2006.
Methods

Patients who received a diagnosis clinically or pathologically of primary GBM (site codes 710–719 and histology codes 9440–9442) in 2006 were identified from the National Cancer Institute’s (NCI’s) Surveillance, Epidemiology, and End Results program (SEER). SEER collects information on all cancer cases occurring in defined geographic regions and represented approximately 26% of the US population at the time when this study was conducted (http://seer.cancer.gov/registries/data.html). SEER uses Collaborative Staging, the uniform approach to cancer diagnosis and staging registration in the United States (http://training.seer.cancer.gov/collaborative/intro/). Data on tumor characteristics, treatment, and selected demographic characteristics are routinely collected from medical records in hospitals, surgical centers, and radiation therapy facilities. However, because much of the systemic therapies are delivered outside these facilities, in the outpatient setting, this information is under-reported in the SEER data. To obtain information on therapy that is not well collected in the routine registration of patients with cancer, the NCI annually conducts Patterns of Care (POC) studies on selected cancer sites to collect and verify information about treatment provided by each cancer patient’s treating physicians. Each SEER registry obtains institutional review board approval as required prior to initiating the study.

After a central training session attended by the abstractor primarily responsible for the POC study, the 14 participating SEER registries (San Francisco and Oakland, Detroit, Seattle, Atlanta, San Jose and Monterey, Los Angeles County, Connecticut, Iowa, Kentucky, Louisiana, New Jersey, New Mexico, Utah, and the remainder of California) re-abstracted the hospital record of the sampled patients to verify tumor characteristics and demographic information. On the basis of treatment documented in the patient’s charts, each patient’s physician was asked to verify whether radiation or chemotherapy was received and whether the patient participated in a treatment protocol. Each physician was also asked to provide information about other treating physicians, and these physicians were then contacted and asked to provide information about treatment. A total of 5% of patients had their diagnosis and treatment information re-abstracted for quality control. Any discrepancies were used for ongoing quality improvement, and final data for our study reflect the most accurate diagnosis and treatment information.

Patients with a previous diagnosis of cancer other than nonmelanoma skin cancer, a simultaneous cancer diagnosis at another site, or a GBM diagnosis on autopsy or on the death certificate or who were <20 years of age were ineligible for the study. Eligible patients were stratified by registry and racial/ethnic group and randomly sampled within strata. Non-Hispanic black individuals, Hispanic individuals, Asian/Pacific Islanders, American Indians, and Native Alaskans were oversampled to obtain more stable estimates. The study sample consisted of 1202 patients who received a diagnosis of primary GBM during 2006.

Measures

Patient demographic characteristics included age at diagnosis (<55, 55–64, 65–74, or ≥75 years of age), sex (male or female), race and ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, or other), marital status (married or with partner or other), insurance status (private, any Medicaid, Medicare only, no insurance, or other), and area level median income in quartiles (≤$43 463, $43 464–58 500, $58 501–74 559, or ≥$74 560). Clinical characteristics included tumor size, location of tumor (confined to a single lobe, not confined to a single lobe, other, or missing), morphology (glioblastoma, giant cell glioblastoma, or gliosarcoma), and Charlson score measure of comorbidity (0, 1, or ≥2). Hospital characteristics included hospital bed size (<200, 200–299, 300–399, 400–499, or ≥500), ownership (for-profit, not-for-profit, government, or unknown), and residency training (yes or no/unknown).

Treatment included surgical treatment as recorded by SEER (local excision or biopsy only, partial resection, gross total resection, no surgery, surgery not otherwise specified, or unknown whether surgery performed), radiation, and chemotherapy. Specific chemotherapy agents abstracted were Gliadel (carmustine wafer), carmustine, and TMZ; other agents were also identified from records (eg, avastin and cilengitide). Treatment protocol participation, regardless of the sponsorship (yes or no), was also abstracted. Chemotherapy and RT were also defined as (1) TMZ and RT, (2) other chemotherapy or RT (ie, RT only, chemotherapy only, or RT and other chemotherapy), or no/unknown chemotherapy and RT.

Survival following diagnosis was measured through 31 December 2008, up to 36 months following diagnosis. For patients who died during this period, cause of death was also recorded. Because SEER collects the month of cancer diagnosis but not the exact diagnosis day, we assumed that all patients received a diagnosis on the first day of the month. Patients who received a diagnosis of GBM and died during the same month were assumed to have lived 0.5 months following diagnosis.

Statistical Analyses

All descriptive information, including use of surgery and chemotherapy and/or radiation therapy, is presented as observed counts and weighted percentages for the study population. We restricted the sample to the subset of patients who received gross or partial surgical resection in all multivariable analyses to assess the use of adjuvant chemotherapy and RT and the association between adjuvant treatment and survival. By restricting our sample to patients eligible and willing to undergo surgical resection, we were able to identify a more homogenous
group with respect to comorbidity and ability to tolerate subsequent treatments, minimizing the impact of patient selection in our analysis of treatment and survival in an observational cohort. We used multivariable polytomous logistic regression analyses to assess patient, clinical, and health system factors associated with adjuvant chemotherapy and radiation treatment (ie, TMZ and RT, other treatment, or no adjuvant therapy). We used multivariable Cox proportional hazards models to assess the association between adjuvant chemotherapy and RT and survival, controlling for the effects of patient, clinical, health system factors. The proportionality of the survival curves was evaluated with visual inspection. Patients with missing data for covariates ($n = 28$) were excluded from multivariable analyses. Because patient comorbidity, age, and marital status have been reported to influence treatment decisions and prognosis,7,12,13 we decided a priori to include the Charlson comorbidity score, age, and marital status in multivariable models. Other variables with associations with treatment or survival at $P < .20$ in bivariable analysis were retained in the multivariable models. Other variables with associations with treatment or survival were included in multivariable models. Other variables with associations with treatment or survival that were included in multivariable models. Other variables with associations with treatment or survival at $P < .20$ in bivariable analysis were retained in the multivariable models. All tests of significance were 2-sided. We used SAS (SAS Institute) version 9.1.3 and SUDAAN (Research Triangle Park) statistical software14 version 10.0.1 to account for the sampling design in all analyses.

### Results

Most patients with newly diagnosed GBM were aged ≥55 years, male, white non-Hispanic, and married or partnered (Table 1). The majority had private insurance and were treated in larger hospitals with ≥300 beds with residency training programs. Approximately 30% had a Charlson comorbidity score of at least 1. Most tumors were >3.5 cm and located in the frontal lobe (26.0%), temporal lobe (23.0%), or parietal lobe (18.1%) or were overlapping (20.1%). Approximately 70% of the tumors were confined to a single lobe.

Approximately three-fourths of the patients underwent surgical procedures, including gross total resection (38.9%) and partial resection (23.6%) (Table 2). Approximately one-fourth of patients did not undergo any surgical procedures; these patients were less likely
to have their tumor confined to a single lobe than were patients who underwent any surgical procedure (52.4% vs. 76.3%; \(P = 0.0001\) [data not shown]). A higher percentage of patients who did not undergo any surgical procedure were aged \(\geq 75\) years, were not married or partnered, and were treated in smaller hospitals with fewer hospital beds, compared with patients who underwent any surgical procedure (\(P = 0.05\)).

Overall, the majority of patients received some chemotherapy (67.3%), and most received both TMZ and RT (62.7%), with smaller percentages receiving RT without chemotherapy (7.1%) or chemotherapy without RT (1.3%). The proportion receiving TMZ and RT varied by type of surgery; among patients who did not undergo surgery, fewer than half received TMZ and RT (Fig. 1). Among patients who underwent surgery and received chemotherapy, most received chemotherapy after surgery, although some received chemotherapy during surgery (carmustine wafer). Approximately 8.5% of patients participated in treatment protocols, including the phase III trial of adjuvant RT and conventional TMZ versus dose-intensive TMZ (RT0G-0525).

As of 31 December 2008, up to 36 months following diagnosis, 12.6% of the patients were still alive. Median survival was 10 months (95% confidence interval [CI], 9–11 months) for the entire study sample, including patients without treatment. Survival varied significantly by type of surgery, with the shortest survival among patients not receiving surgery and those receiving local excision or biopsy only and the longest survival among patients receiving partial or total resection (Fig. 2). These differences in survival likely reflect differences in patients who underwent surgery, completeness of surgical resection dictated by the location and extent of tumor, and any effects of surgery and adjuvant therapy.

### Table 2. Surgery, chemotherapy and radiation therapy

\(N = 1202\)

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Number</th>
<th>Weighted %</th>
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<tbody>
<tr>
<td>Local excision (biopsy) of lesion or mass</td>
<td>29</td>
<td>2.0</td>
</tr>
<tr>
<td>Partial resection</td>
<td>314</td>
<td>25.6</td>
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<tr>
<td>Gross total resection</td>
<td>461</td>
<td>38.9</td>
</tr>
<tr>
<td>Surgery, NOS</td>
<td>120</td>
<td>8.8</td>
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<tr>
<td>No surgery</td>
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<td>25.5</td>
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<td>Unknown if surgery performed</td>
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<td>0.2</td>
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<table>
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<tr>
<th>Chemotherapy</th>
<th>Number</th>
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<tr>
<td>Any</td>
<td>836</td>
<td>67.3</td>
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<tr>
<td>None given</td>
<td>293</td>
<td>25.8</td>
</tr>
<tr>
<td>Refused</td>
<td>38</td>
<td>3.7</td>
</tr>
<tr>
<td>Recommended, unknown if received/Unknown</td>
<td>35</td>
<td>3.2</td>
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<tr>
<th>Chemotherapy Agents:</th>
<th>Number</th>
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<tr>
<td>Gliadel (carmustine Wafer) only</td>
<td>17</td>
<td>1.7</td>
</tr>
<tr>
<td>Temozolomide (TMZ) only</td>
<td>649</td>
<td>52.0</td>
</tr>
<tr>
<td>Other single agent only</td>
<td>16</td>
<td>1.2</td>
</tr>
<tr>
<td>TMZ and Gliadel</td>
<td>84</td>
<td>6.4</td>
</tr>
<tr>
<td>TMZ and other agent</td>
<td>67</td>
<td>5.8</td>
</tr>
<tr>
<td>Other multiple agent combination</td>
<td>3</td>
<td>0.2</td>
</tr>
<tr>
<td>No chemotherapy</td>
<td>366</td>
<td>32.7</td>
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<table>
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<th>Radiation/Chemotherapy</th>
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<th>Weighted %</th>
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<tr>
<td>Radiation Only</td>
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<td>7.1</td>
</tr>
<tr>
<td>Chemotherapy Only</td>
<td>19</td>
<td>1.3</td>
</tr>
<tr>
<td>Radiation and chemotherapy</td>
<td>811</td>
<td>65.3</td>
</tr>
<tr>
<td>None</td>
<td>201</td>
<td>17.7</td>
</tr>
<tr>
<td>Refused</td>
<td>54</td>
<td>5.0</td>
</tr>
<tr>
<td>Recommended, unknown if received/Unknown</td>
<td>39</td>
<td>3.5</td>
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<th>Treatment protocol participation</th>
<th>Number</th>
<th>Weighted %</th>
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<td>Registered in an open trial</td>
<td>106</td>
<td>8.5</td>
</tr>
<tr>
<td>Not registered in an open trial</td>
<td>1029</td>
<td>84.6</td>
</tr>
<tr>
<td>Refused</td>
<td>5</td>
<td>0.6</td>
</tr>
<tr>
<td>Recommended, unknown if received/Unknown</td>
<td>62</td>
<td>6.3</td>
</tr>
</tbody>
</table>

Fig. 1. Receipt of chemotherapy and radiation therapy among patients who received a diagnosis of glioblastoma multiforme in 2006, by type of surgery (\(N = 1202\)).

Fig. 2. Months of survival among patients who received a diagnosis of glioblastoma in 2006, by type of surgery (\(N = 1082\)).
In multivariable analyses of the subset of patients who underwent total or partial surgical resection, patient age, marital status, type of health insurance, and primary tumor site were significantly associated with receipt of TMZ and RT or receipt of other adjuvant treatment, compared with no adjuvant treatment (Table 3). Compared with younger and married patients, older and unmarried patients were less likely to receive any adjuvant treatment. Compared with patients with private health insurance, patients with Medicare only, any Medicaid, or no insurance were less likely to receive TMZ and RT or other treatment. Patients whose tumor was located in >1 lobe were less likely to receive TMZ and RT or other treatment, compared with patients whose tumor was confined in a single lobe.

Median survival among all patients who received TMZ and RT was 15 months (95% CI, 14–16 months), 7 months (95% CI, 5–8 months) for patients receiving other chemotherapy or RT, and 2 months (95% CI, 2–3 months) for patients not receiving any chemotherapy or RT (Table 4). For the subset of patients with surgical resection followed by TMZ and RT (n = 562), survival was longer among those with total compared with partial resection (median survival, 13 months [95% CI, 11–15 months] and 20 months [95% CI, 18–20 months], respectively) (Fig. 3).

Among the patients who received total or partial surgical resection, survival following diagnosis varied significantly by the type of adjuvant therapy (Fig. 4).

### Table 3. Multivariate associations between patient characteristics and receipt of treatment among adult glioblastoma patients diagnosed in 2006 receiving complete or partial surgical resection (N = 747)

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>TMZ + RT vs. no/unknown chemotherapy and no/unknown RT</th>
<th>Other treatment vs. no/unknown chemotherapy and no/unknown RT</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis</td>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>&lt;55</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>55–64</td>
<td>0.66 (0.33, 1.33)</td>
<td>1.47 (0.53, 4.10)</td>
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</tr>
<tr>
<td>65–74</td>
<td>0.72 (0.31, 1.68)</td>
<td>1.45 (0.48, 4.41)</td>
<td></td>
</tr>
<tr>
<td>≥75</td>
<td>0.22 (0.10, 0.47)</td>
<td>1.43 (0.47, 4.35)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>0.38 (0.22, 0.68)</td>
<td>0.51 (0.25, 1.04)</td>
<td>.005</td>
</tr>
<tr>
<td>Health insurance</td>
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<tr>
<td>Private</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Medicare only</td>
<td>0.38 (0.14, 1.04)</td>
<td>0.46 (0.13, 1.61)</td>
<td>.011</td>
</tr>
<tr>
<td>Any Medicaid</td>
<td>0.35 (0.17, 0.74)</td>
<td>0.71 (0.28, 1.83)</td>
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</tr>
<tr>
<td>No insurance</td>
<td>0.35 (0.14, 0.87)</td>
<td>0.16 (0.03, 0.80)</td>
<td></td>
</tr>
<tr>
<td>Median household income</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1: $≤43 463</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Q2: $43 464–$58 500</td>
<td>1.09 (0.52, 2.30)</td>
<td>0.76 (0.30, 1.90)</td>
<td>.093</td>
</tr>
<tr>
<td>Q3: $58 501–$74 559</td>
<td>1.82 (0.87, 3.84)</td>
<td>0.77 (0.29, 1.99)</td>
<td></td>
</tr>
<tr>
<td>Q4: $≥74 560</td>
<td>1.92 (0.97, 3.81)</td>
<td>0.79 (0.30, 2.12)</td>
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</tr>
<tr>
<td>Charlson comorbidity score</td>
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<tr>
<td>0</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>≥1</td>
<td>1.03 (0.56, 1.90)</td>
<td>1.18 (0.55, 2.49)</td>
<td>.898</td>
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<td>Primary site</td>
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<tr>
<td>Confined to a single lobe</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>More than one lobe/other</td>
<td>0.55 (0.31, 0.97)</td>
<td>0.38 (0.15, 0.97)</td>
<td>.048</td>
</tr>
</tbody>
</table>

**Practice environment and practice patterns**

<table>
<thead>
<tr>
<th>Hospital residency training program</th>
<th>TMZ + RT vs. no/unknown chemotherapy and no/unknown RT</th>
<th>Other treatment vs. no/unknown chemotherapy and no/unknown RT</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>1.00</td>
<td>1.00</td>
<td>.439</td>
</tr>
<tr>
<td>No</td>
<td>0.86 (0.50, 1.49)</td>
<td>1.29 (0.62, 2.71)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: TMZ, temozolomide; RT, radiation therapy; OR, odds ratio; CI, confidence interval.

Note: 28 patients had missing data for one or more covariates and were excluded from the multivariate analysis. *P-values are calculated using the Wald F test statistic.
resection had the longest survival, with median survival of 16 months (95% CI, 15–18 months), whereas median survival for patients who did not receive any adjuvant RT or chemotherapy was 3 months (95% CI, 2–4 months). Controlling for the effects of age, Charlson co-morbidity score, health insurance, marital status, median household income, tumor location, tumor size, and presence of a hospital residency program, receipt of adjuvant therapy was associated with lower risk of dying for patients who received TMZ and RT (hazard ratio, 0.26; 95% CI, 0.19–0.36) and other adjuvant therapies (HR, 0.55; 95% CI, 0.37–0.82), compared with no adjuvant therapy (Table 5). Older patients and those with tumors in >1 lobe had a significantly greater risk of dying than did younger patients with tumor in only a single lobe.

**Discussion**

In this study, we assessed treatment and survival in a population-based sample of patients with newly diagnosed GBM in 2006. To our knowledge, this is one of the largest cohorts of adult patients with GBM with detailed information on current standard of care treatment with surgery, chemotherapy, and RT and survival. Because our study was conducted after completion and publication of the pivotal clinical trial in 2005 that showed the survival advantage of concomitant TMZ and RT compared with RT alone after surgical resection,8 we were able to assess the diffusion of TMZ and RT in a community setting. We found that approximately 65% of patients received partial or total resection of their tumors, and most received at least some chemotherapy and/or RT. Among the patients with resection, approximately 70% received TMZ and RT, suggesting that this standard of care for GBM diffused rapidly in the community setting.

A higher percentage of patients with GBM in our study were treated in hospitals with residency programs.
and a large number of beds, compared with patients with newly diagnosed cancer in other SEER POC studies. Other studies have shown that patients treated at larger hospitals with residency programs and those affiliated with academic institutions are more likely to receive adjuvant chemotherapy and radiation. Referral to larger hospitals may also be associated with rapid diffusion or early adoption of novel treatments. We also found that a slightly higher proportion of patients with newly diagnosed GBM participated in treatment protocols than patients with other cancers in the SEER POC studies and in other studies based in community settings. Clinical trial participation is critical for evaluating the efficacy of novel cancer therapies, particularly for cancer sites, such as GBM, where median survival remains relatively short, even with a new standard therapy. Efforts to improve trial participation, including use of electronic medical records to identify eligible patients, development of clinical trial referral infrastructure, physician education efforts, and patient education and outreach, will be important for improving the quality of care.

Median survival in the entire sample, which included patients who did not undergo cancer-directed surgery, was short (10 months). However, for the subset of patients who received partial or total surgical resection followed by TMZ and RT, median survival was 16 months, more similar to the 14.6 months observed for the patients enrolled in the pivotal clinical trial establishing TMZ and RT as a standard of care. Because clinical trials typically have performance status requirements and other entry criteria related to prior treatment, patients who participate in clinical trials are highly selected, compared with the general population of patients with cancer. Other studies, such as the Glioma Outcomes Project, recruited patients from neurosurgery or neuro-oncology clinics. Patients included in our SEER POC study were identified from cancer registries and included patients who did not undergo any surgery (approximately 25%) and may never have been evaluated in neurosurgery or neuro-oncology clinics. Thus, comparisons of our findings with other studies requires consideration of the methods for identifying patients with newly diagnosed cancer; patient, tumor, and health care system characteristics; and the surgical and adjuvant therapy received. Furthermore, because some patients with newly diagnosed GBM treated in community settings do not have histologic confirmation, they may automatically be ineligible for clinical trials of treatment.

We found that older patients and those who were unmarried were less likely to receive TMZ and RT or any adjuvant radiation or chemotherapy following maximal surgical resection, compared with younger and married patients. Unmarried patients were also less likely to undergo any surgery. Less use of standard therapy for GBM in older and unmarried patients is consistent with earlier studies and is presumably associated with greater frailty and need for caregiving support, both real and perceived, in these patients. Controlling for the effects of patient, tumor, and health system characteristics, we found that older age was associated with poorer survival, a finding that is also consistent with prior studies. Because brain tumor incidence is increasing, particularly in the older

### Table 5. Multivariate associations between treatment and death among adult patients with glioblastoma diagnosed in 2006 who received partial or total resection (N = 755)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>HR (95% CI)</th>
<th>P-value*</th>
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<tr>
<td>Radiation/chemotherapy treatment</td>
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<td></td>
</tr>
<tr>
<td>TMZ + RT</td>
<td>0.26 (0.19, 0.36)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Other treatment</td>
<td>0.55 (0.37, 0.82)</td>
<td></td>
</tr>
<tr>
<td>No/unknown RT and No/unknown chemotherapy</td>
<td>1.00</td>
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</table>

| Patient Characteristics                        |           |          |
| Age at diagnosis                               | 1.00      | .441     |
| <55                                            |           |          |
| 55–64                                          | 1.21 (0.93, 1.57) | <.001    |
| 65–74                                          | 1.84 (1.37, 2.48) |          |
| ≥75                                            | 2.96 (2.08, 4.20) |          |

| Health insurance                               |           |          |
| Private                                        | 1.00      | .226     |
| Medicare only                                  | 1.00      |          |
| Any Medicaid                                   | 1.20 (0.82, 1.76) |          |
| No insurance                                   | 1.10 (0.68, 1.77) |          |
| Unknown/other                                  | 1.93 (0.92, 4.07) |          |

| Median household income                        |           |          |
| Q1: ≤$43 463                                   | 1.00      | .881     |
| Q2: $43 464–$58 500                           | 1.01 (0.75, 1.37) |          |
| Q3: $58 501–$74 559                           | 1.09 (0.80, 1.49) |          |
| Q4: ≥$74 560                                   | 0.97 (0.71, 1.33) |          |

| Marital status                                 |           |          |
| Married or partnered                           | 1.00      | .226     |
| Other                                          | 1.15 (0.92, 1.43) |          |

| Charlson co-morbidity score                    |           |          |
| 0                                              | 1.00      | .345     |
| ≥1                                             | 1.12 (0.89, 1.40) |          |

| Primary site                                   |           |          |
| Confined to a single lobe                      | 1.00      | .025     |
| More than one lobe/other                       | 1.39 (1.04, 1.85) |          |

| Tumor size                                     |           |          |
| ≤3.4 cm                                       | 1.00      | .429     |
| 3.5 cm–4.4 cm                                 | 0.90 (0.65, 1.24) |          |
| 4.5 cm–5.4 cm                                 | 0.95 (0.69, 1.29) |          |
| 5.5+ cm                                       | 1.16 (0.86, 1.56) |          |
| Missing/unknown                               | 1.15 (0.78, 1.70) |          |

| Practice environment and practice patterns      |           |          |
| Hospital residency training program            | 1.00      | .229     |

Abbreviations: TMZ, temozolomide; RT, radiation therapy; HR, hazard ratio; CI, confidence interval.
Note: 20 patients had missing data for one or more covariates and were excluded from the multivariate analysis. *P-values are calculated using the Wald F test statistic.
population, and the US population is aging and increasing, the absolute number of older patients who received a diagnosis of GBM will increase in the future. Increasingly, clinical studies are showing that the benefits from surgery, RT, and chemotherapy treatment can also be realized in older patients. In RT and moderate-dose regimens have been reported to be effective. These benefits have not been shown for patients with GBM, however. In addition to patient preferences for treatment, performance status, and need for social support, physician recommendations for treatment are key components of the complex treatment decision-making process. Understanding and optimizing the GBM treatment decision-making process is important for ensuring optimal care for this increasing population of older patients with GBM.

We also found that sociodemographic factors, such as insurance status and income, were associated with whether patients with GBM who underwent maximal surgical resection also received adjuvant treatment, but not with survival in models controlling for adjuvant treatment. Because survival following diagnosis of GBM is short, the influence of these sociodemographic factors on survival may occur mainly through receipt of treatment. Further evaluation of sociodemographic factors in relation to both treatment and survival will be important in future research.

Despite the strengths of a large population-based sample, our study had several limitations. Although we controlled for comorbid conditions, age, and tumor characteristics in our multivariable analyses, the data in this study were observational and it is possible that unmeasured patient characteristics influenced both treatment selection and survival following diagnosis. We restricted our multivariable analyses of treatment and survival to patients who underwent either partial or total resection. Thus, our subsample was eligible to undergo surgical resection and may be more homogeneous with respect to comorbidity and ability to tolerate subsequent chemotherapy and RT.

We did not have information on mode of diagnosis or initial imaging studies that might more fully inform our measurement of the extent of disease. Because the exact date of diagnosis is not recorded by SEER and, as a result, was not available for this study, we assumed that all patients received a diagnosis on the first day of each month. Although there is some misclassification, it is unlikely that misclassification varied systematically by treatment. Furthermore, differences in survival time by treatment type were >1 month, suggesting that the impact of missing data for exact date of diagnosis is minimal. We did not have information about performance status at diagnosis, patient preferences or physician recommendations for surgery, or chemotherapy and RT, which are important predictors of receipt of treatment and, ultimately, prognosis. Our restriction of the sample for multivariable analysis to patients receiving partial or complete surgical resection and control for age, comorbidity score, and marital status were attempts to address the absence of performance status to some extent. Others have shown that MGMT promoter methylation is associated with greater effectiveness of TMZ, although it was not available for treatment selection at the time of this study. Finally, we did not have detailed data describing the completion of chemotherapy or radiation schedules. Our analysis used an intent-to-treat approach, which is consistent with the approach used in clinical trials, however, all of these patient, physician, and clinical measures will be important for inclusion in future studies of GBM treatment and survival.

In summary, we observed rapid diffusion of a new standard of treatment, TMZ and RT after maximal surgical resection, following the publication of a pivotal clinical trial in a national population of adult patients with newly diagnosed GBM. Patients who received TMZ and RT following surgical resection had longer survival, compared with patients who did not receive any adjuvant therapy following surgery.

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