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QUALITY IMPROVEMENT

Adherence to Prophylactic Anticonvulsant Guidelines for Newly Diagnosed Brain Tumor Patients: A Quality Improvement Study

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Abstract

Background and Purpose: Clinical guidelines suggest that prophylactic antiepileptic drugs (AEDs) should be given to newly diagnosed seizure-naive brain tumor patients for up to 1 week after craniotomy. Yet, data suggest that prophylactic AEDs are used up to 12 months after surgery. A quality improvement project was implemented to improve adherence to evidence-based prophylactic AED guidelines. **Methods:** A quasi-experimental, pre- and post-test intervention design was used to assess the effect of a multiphase intervention on guideline adherence and prophylactic anticonvulsant prescription rates. The 16-week intervention consisted of provider education sessions, provider alerts, documentation templates, and a weekly audit and feedback. Participants included four providers and newly diagnosed seizure-naive brain tumor patients. Measures included guideline adherence rates and AED prescription rates extracted from chart review, and a provider attitude and knowledge survey. Analyses included descriptive statistics, Wilcoxon signed-rank tests, and Chi-square tests. **Results:** Guideline adherence increased significantly ($p < .01$) from 4 months before implementation (15.8%) to 1 year before implementation (27.8%) and then to 93.3% after implementation. Provider knowledge showed clinically meaningful decreases in the likelihood to prescribe prophylactic AEDs (–.5 point) and increased understanding of prophylactic AED side effects (+0.5 point), although these were not statistically significant ($p = .083$). Finally, prophylactic AED prescription rates decreased by 2.2% ($p = .119$) compared with 4 months and 1 year before implementation (2.6%; $p = .072$). **Conclusion:** This project highlights the important role of provider education, provider alerts, a documentation template, and audit and feedback in improving guideline adherence rate. Findings

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suggest that the combination intervention and weekly audit and feedback strategy can improve guideline adherence to prophylactic anticonvulsant use in seizure-naive newly diagnosed brain tumor patients. **Implications:** By following prophylactic AED guideline recommendations, clinicians can avoid the potential side effects of anticonvulsant-induced cognitive, behavioral, and psychiatric issues that can impair patients' quality of life.

Seizures are common initial symptoms among patients with a brain neoplasm (Chandra et al., 2017). It is common practice to administer prophylactic antiepileptic drugs (AEDs) to patients undergoing brain tumor resection to prevent seizure activity during surgery (Chandra et al., 2017; Kong et al., 2015). However, most providers tend to unnecessarily keep their patients on prophylactic AEDs for months and sometimes years after surgery even when patients have not experienced any seizure activity (Lapointe et al., 2015). This unnecessary overprescribing can result in many new problems for patients, such as cognitive impairment and a decrease in overall quality of life due to medication side effects (Akhavan-Sigari et al., 2013; Habets et al., 2017). The American Academy of Neurology (AAN), American Society of Clinical Oncology (ASCO), and Society for Neuro-Oncology (SNO) suggest that AEDs should not be prescribed for more than 1 week following surgery in seizure-naive patients with brain tumors (Glantz et al., 2000; Chang et al., 2019). This guideline is based on multiple studies showing that continuation of prophylactic AEDs does not prevent an initial seizure in this particular patient population (Glantz et al., 2000; Chang et al., 2019). Hence, there is a need for studies examining implementation and adherence to prophylactic AED guidelines for patients undergoing brain tumor resection.

BACKGROUND

Overprescribing prophylactic AEDs is pervasive in the United States and other developed countries (Chen et al., 2014; Dewan et al., 2017; Lwu et al., 2010). International studies show that 46.9% to 70.2% of seizure-free patients continued prophylactic AEDs from 3 months to 5.9 months after their brain tumor resection (de Oliveira et al., 2014; Dewan et al., 2017; Lapointe et al., 2015). In fact, 63% of neurosurgeons prescribe prophylactic AEDs past the recommended duration of 1 week set forth by AAN, ASCO, and SNO guidelines for seizure-free patients with newly diagnosed brain tumors (Chandra et al., 2017; Siminoff, 2013). Fu (2019) found through a retrospective patient chart review at a local academic medical center that the average continuation of prophylactic AEDs was 12 months after craniotomy. Data from this study also indicated that the primary barrier to AED guideline adherence was a lack of awareness about the updated recommendations of prophylactic anticonvulsant use (Fu, 2019). While there are no other studies examining barriers to AED guideline adherence, evidence from cardiovascular disease prevention also indicate that a lack of knowledge is the primary barrier to guideline adherence (Dallongeville et al., 2012; Renier et al., 2010). Therefore, the purpose of this quality improvement project is to implement an educational session on prophylactic AED use and guidelines that target a provider's perceptions and knowledge gaps. "Provider" is defined as any institution or member of the health-care team providing health care (Segen, 2002). In this project, "provider" refers to physicians and advanced practitioners.

This project has the following three aims: (1) to determine if the multiphase approach, including provider education, electronic reminder, and audit and feedback, will improve provider adherence to AAN/ASCO/SNO seizure prophylaxis guidelines in seizure-naive newly diagnosed brain tumor patients from the baseline nonadherence to ≥ 90% in 16 weeks; (2) to determine the impact on providers' knowledge and attitude at this project site after the provider educational sessions at the end of 16 weeks with a pre- and post-survey; and (3) to determine if the prescribing rate of unnecessary anticonvulsants in seizure-naive newly diagnosed brain tumor patients will decrease by 10% at the end of the 16-week project period.

REVIEW OF THE LITERATURE

Adherence to prophylactic anticonvulsant guidelines is crucial to improve care for seizure-naive patients who are newly diagnosed with brain tumors.

However, the continued use of prophylactic AEDs without adhering to AAN guidelines remains a significant problem in the health-care setting (Chandra et al., 2017; Julie et al., 2019). Factors related to guideline nonadherence include time constraints, conflicting opinions between the individual providers, and lack of self-confidence (Cabana et al., 2001; Dallongeville et al., 2012; Julie et al., 2019; Reiner et al., 2010; Salinas et al., 2011). Research also suggests the major contributing factors are the providers' gaps in knowledge and a lack of awareness about the guideline recommendations (Dallongeville et al., 2012; Reiner et al., 2010; Salinas et al., 2011). This review focuses on identifying strategies to improve provider adherence to the evidence-based guidelines on prescribing prophylactic AEDs for seizure-naive individuals who have been newly diagnosed with a brain tumor. The strategies culminated into three major themes: provider education, automated provider alerts, and chart audit and feedback.

Provider Education

The first theme identified was the importance of provider education in increasing adherence to the guidelines (Affronti et al., 2014; Chung et al., 2011; Nelson et al., 2016). Affronti and colleagues (2014) found that implementing an educational session for providers successfully increased provider adherence to antiemetic guideline for patients with malignant brain tumors from 58% to 90%. The education sessions in these studies shared a key characteristic: They focused on summarizing the guidelines and standardizing the training for the providers involved in the implementation process (Affronti et al., 2014; Carey et al., 2009; Chung et al., 2011). In addition, these studies also increased accessibility to the guidelines by displaying them in a short format, flow chart, or poster in the workroom (Carey et al., 2009; Loy et al., 2016; Nelson et al., 2016). Standardizing provider education and increasing accessibility to the guidelines are time-efficient and cost-effective strategies to increase adherence to newly implemented medical guidelines in the inpatient or outpatient settings (Affronti et al., 2014; Carey et al., 2009; Chung et al., 2011).

Automated Provider Alerts

Implementing an automated provider alert into the electronic health record system successfully increased guideline adherence among providers in studies by Carey and colleagues (2009) and Loy and colleagues (2016). Specifically, an automated provider alert in the electronic health record system improved protocol adherence to clinical guidelines on venous thromboembolism prophylaxis (Durieux et al., 2000) and epilepsy follow-up management (Nelson et al., 2016). Another form of an automated provider alert is one that prompts the provider to complete the appropriate documentation template before signing off. In a study by Nelson and colleagues (2016), this specific prompt significantly improved four standardized national quality measures for epilepsy management in both the 2- and 6-month compliance evaluation. Durieux and colleagues (2000) reported that implementing an automated provider alert increased orthopedic physicians' guideline compliance rate from 82.8% to 94.9%. The importance of the alert was further highlighted by the adherence rate dropping to a relative risk of 3.8 after the alert was removed (Durieux et al., 2000). Therefore, the integration of an electronic alert system successfully increased clinical guideline adherence among providers in several medical fields (Carey et al., 2009; Durieux et al., 2000; Loy et al., 2016; Nelson et al., 2016).

Audit-Feedback Strategy

The feedback given to the providers after chart audits, also called the audit-feedback strategy, was essential in improving compliance to newly implemented clinical protocols in studies by Affronti and colleagues (2014) and Carey and colleagues (2009). After giving feedback to the providers regarding adherence to Hepatitis A and B immunization guidelines and best practice guidelines to manage chemotherapy-induced nausea and vomiting, the strategy increased guideline adherence rate to 100% (Chung et al. 2011; Loy et al., 2016).

In addition to the audit-feedback strategy, Affronti and colleagues (2014), Carey and colleagues (2009), and Hysong and colleagues (2006) recommended the provider feedback to be timely, frequent, and nonpunitive. Systemic reviews by Carey and colleagues (2009) and Jamtvedt and colleagues (2006) further indicated that the audit-feedback strategy is particularly effective when baseline adherence is low. Adding timely, frequent, and nonpunitive feedback to the audit-

feedback strategy was shown to be the most effective approach to increasing guideline adherence.

As found among a variety of medical specialties and in both inpatient and outpatient settings, strategies such as standardized provider education (Affronti et al., 2014; Carey et al., 2009; Chung et al., 2011; Nelson et al., 2016), effective patient education (Affronti et al., 2014; Carey et al., 2009; Chung et al., 2011; Nelson et al., 2016), automated provider alerts (Carey et al., 2009; Durieux et al., 2000; Loy et al., 2016; Nelson et al., 2016), and the audit-feedback strategy (Affronti et al., 2014; Carey et al., 2009; Hysong et al., 2006; Jamtvedt et al., 2006; Loy et al., 2016) were found to improve adherence to clinical guidelines among the providers studied. These strategies helped modify the providers' management plans, and perhaps could be translated into enhancing prophylactic anticonvulsant guideline adherence in an academic outpatient setting.

TRANSLATIONAL FRAMEWORK

RE-AIM Framework and Critique

The RE-AIM framework (see Appendix A) is an acronym of five elements in health behavior intervention: reach, effectiveness, adoption, implementation, and maintenance (Gaglio et al., 2013). This RE-AIM framework is considered a gold standard in prevention and disease management research (Glasgow et al., 1999; RE-AIM, 2021). Since its advent in 1999, the framework has been widely adopted and translated into numerous meaningful outcomes (Glasgow et al., 1999). It works exceptionally well when applied in the prevention and disease management field. This framework consists of efforts from multiple levels: participant, setting, and individual. The framework's maintenance element is important to the aims of this project as it supports the sustainment of the evidence-based protocol (RE-AIM, 2021). In addition, the maintenance element is consistent with the organization's mission of maintaining high-quality patient care (RE-AIM, 2021).

A major limitation of the RE-AIM framework lies in the reach element, where the patient's insurance may increase their risk for loss to follow-up. Patients who have health maintenance organization (HMO) insurance are deferred to follow-up with their in-network neurooncologist (Rosenthal et al., 2018). This makes it difficult for the neuro-oncology provider at the operating institution to ensure that the patient follows the recommended prophylactic anticonvulsant management. This is even more troublesome because presently, providers are not consistently translating the guidelines of prophylactic anticonvulsant use into clinical practice despite a strong recommendation to do so (Chang et al., 2019; Glantz et al., 2000). Another limitation is that are only a few published studies that set the precedent for this project by including all five elements of the framework (Gaglio et al., 2013; Harden et al., 2018). This is important to note because the five elements are interdependent and synergistically contribute to achieving the study's intended outcomes (Gaglio et al., 2013).

Additionally, RE-AIM was found to be successful in low-resource settings with patients who are most in need, such as the academic clinical setting of this project (RE-AIM, 2021). Despite the limitations, this framework can still provide a clear direction in translating research into practice regarding guideline adherence for seizure prophylaxis at this outpatient neuro-oncology academic center.

RE-AIM Framework Selection

Through an analysis of the 2,800 publications RE-AIM was cited in, Glasgow and colleagues (2019) found the framework to be most frequently applied to public health and health behavior change research. In the past two decades, RE-AIM has shown its success in these fields. Because the topic of this project is rooted in health behavior change, the RE-AIM framework is uniquely qualified for translating the evidence-based prophylactic AED guidelines into daily clinical practice. Additionally, the RE-AIM framework is valuable for this project because it is consistent with the project site's values of safety and quality patient care. The following will be a discussion of how each of the five elements of RE-AIM relates to this project (Glasgow et al., 2019).

Reach

The reach element centers around recruiting the target population, which in this project includes the providers caring for newly diagnosed seizure-naive patients who are on seizure prophylaxis during their craniotomy. Possible barriers

to obtaining the reach goal are patients' unwillingness to discontinue anti-seizure medications and a lack of fully understanding the risks and benefits of this evidence-based guideline. In addition, restrictions from the COVID-19 pandemic yielded a limited number of elective surgical candidates to enroll in this project.

Effectiveness

The effectiveness element is defined as the impact of the intervention on micro- and macro-level outcomes including potential negative effects (RE-AIM, 2021). The goal of the intervention is to improve providers' adherence to evidence-based prophylactic AED guidelines. Micro-level outcomes include the patients' improved quality of life (QOL), as the AEDs have sedative effects, and decreased medication costs from long-term AED use. Macro-level outcomes include increased quality of patient care in the organization and a reduction of unnecessary medical costs. The effectiveness of the intervention will be measured through chart review.

Adoption

The adoption element is defined as the absolute number, proportion, and makeup of the intervention agents who are adopting the intervention, and why (RE-AIM, 2021). The intervention agents in this project are identified as the neuro-oncology providers and the patients who are seizure-naive and on seizure prophylaxis during their craniotomy. All four providers and 14 out of 15 patients adopted the intervention. However, the remaining one patient was medically exempt due to specific health conditions. Strategies that led to the successful adoption for the providers included reinforcing the updated SNO and ASCO seizure prophylaxis guidelines before launching the intervention, involving the organizational mentors and program directors to get buy-in and support, and continuously monitoring providers' behaviors and providing feedback.

Implementation

The implementation element includes the intervention agents' fidelity to the intervention's key components that include the consistency of delivery, the time and cost of the intervention, and any adaptations that were made (RE-AIM, 2021). The education was delivered consistently across the four providers, which included providing the SNO and ASCO guidelines and team meetings. In addition, seizure prophylaxis guidelines were integrated into an automated provider alert for all the intervention agents. As a result, the intervention's key components were incorporated during the implementation. Additionally, there was no added cost to implement the intervention. Adaptations were made for one patient who was recommended by their provider to continue the prophylactic AEDs.

Maintenance

Maintenance is one of the most critical elements of the RE-AIM framework. It is defined as the long-term outcome after project completion at the individual and organizational level (RE-AIM, 2021). The components of the intervention were developed to ensure sustainment after the implementation process. The template integration and automated provider alerts will continue to be part of the mandatory documentation process. Team meetings to educate the medical staff on updated guidelines and providing the guideline copies at the clinic have now been integrated into the routine of the organization. In addition, ongoing discussion will be encouraged at the team meetings to continually improve on this intervention.

METHOD

Project Design

The project was a quasi-experimental pre/post intervention design that included chart audits from two groups of patients before the intervention and one group of patients after the intervention as well as a survey of providers assessed pre- and post-intervention. The intervention was implemented from September to December 2020. Data for the three-chart audit were collected in pre-test 1 (September–December 2019), pre-test 2 (May–August 2020), and post implementation (September–December 2020).

Setting

This project was conducted at a 300-bed hospital, neuro-oncology outpatient clinic within an academic medical center located on the West Coast. The facility has four providers (three physicians

and one nurse practitioner) who routinely prescribe prophylactic anticonvulsants for newly diagnosed seizure-naive brain tumor patients. Three of the four providers were trained and certified in neurology and neuro-oncology.

Sample

Patient Sample. The project's inclusion criteria were any newly diagnosed seizure-naive brain tumor patients who were started on prophylactic anticonvulsant during the perioperative period. Eligible patients were identified and extracted from the electronic health record system at the project site based on the following ICD-10 codes: C71.9, C75.1, C79.3, C83.3, D18.02, D33.2, D43.2, D44.4, D48.1, G93.0, Z29.8, and CPT codes: 61510, 61512, 61516, 61518, 61519, 61521, 61524, 61304, 61305. Patients with primary or metastatic brain tumors who have a history of seizures and are on anticonvulsants for treatment purposes were excluded from the study. A total of 15 patients met the study inclusion criteria. There are 15 patients identified in this project, including seven males and eight females. The patients had mixed insurance plans, including commercial and government health plans; 27% (4/15) of patients had commercial health insurance with managed care components and 73% (11/15) of patients had government insurance, including Medicare and Medicaid managed care.

Provider Sample. The sample of providers included all four neuro-oncology providers at this outpatient clinic who provide follow-up care for newly diagnosed seizure-naive adult patients post-craniotomy. The facility has four providers (three physicians and one nurse practitioner) who routinely prescribe prophylactic anticonvulsants for newly diagnosed seizure-naive brain tumor patients. Three of the four providers were trained and certified in neurology and neuro-oncology. Because this was a quality improvement project, no recruitment methods were required to obtain provider consent to participate in the project.

Ethical Review

This project was reviewed by the Johns Hopkins School of Nursing (JHSON) Project Ethical Review Committee (PERC) and the project site's Institutional Review Board. It was acknowledged as a quality improvement project.

Intervention

The project assessed the effects of the evidence-based educational sessions, provider alerts, documentation template, and the audit-feedback strategy on providers' practice and attitude toward prophylactic anticonvulsant guideline adherence feedback, guideline adherence rates, and prophylactic anticonvulsant prescription rate.

Provider Educational Session. A week after the pre-survey, each neuro-oncology provider attended one 30-minute educational session about the AAN/ASCO/SNO guidelines on prophylactic anticonvulsants and to introduce the project's interventions. Then, a copy of the prophylactic anticonvulsant guidelines from AAN, ASCO, and SNO was given to the providers.

Audit and Feedback. During the 16-week implementation period, the investigator conducted a daily patient chart review, which identified 15 newly diagnosed seizure-naive brain tumor patients who were started with seizure prophylaxis before their craniotomy. Time was set aside for the investigator weekly chart review and feedback (the audit-feedback strategy) to assess the providers' adherence to guidelines. To reinforce the initial educational session, the weekly team meetings included time to discuss the guidelines and the current patients on prophylactic anticonvulsants.

Provider Alert. The investigator created a "seizure prophylaxis" flag on EPIC so that an alert would appear whenever the patient's electronic chart was opened by a provider.

Documentation Template. During the same week, the neuro-oncology providers started to use a documentation template on EPIC specific to patients with seizure prophylaxis diagnosis that incorporated the suggestions of the providers. Providers used the seizure prophylaxis documentation template for all of these patients.

Measures

Patient Demographics. Basic demographic information was collected by chart review from all patients. These data included age, gender, and diagnosis.

Guideline Adherence Rate. The providers' guideline adherence was determined by chart review to determine if the provider prescribed the newly diagnosed seizure-naive patient prophylac-

tic anticonvulsants with the standard of care being levetiracetam at this specific clinic after the craniotomy. The total number of patients not on seizure prophylaxis during the perioperative period and those who were weaned off seizure prophylaxis vs. the total number of patients with newly diagnosed brain tumors post-craniotomy were used as the measures. The guideline adherence rate was evaluated after intervention based on the patient chart review at 16 weeks. The maximum potential score was 100%, and minimum score was 0%. The adherence rate was then compared to the 1-year and 4-month baseline data.

AED Prescription Rate. "Patients not on seizure prophylaxis" was defined as patients not initially prescribed prophylactic AEDs and those who were initially prescribed but were weaned off after this intervention. AED prescription rates were measured as a proportion of those who were prescribed AEDs (yes = 1, no = 0) out of the total number of patients with a brain tumor diagnosis post craniotomy. The number of prophylactic AED prescriptions given to seizure-naive newly diagnosed brain tumor patients 1 year and 4 months before implementation and after implementation was determined by the seizure prophylaxis diagnosis code of ICD z29.8.

Provider Survey. A survey was created to measure provider knowledge and attitudes about seizure prophylaxis use before and after intervention (see Appendix B). The survey was adapted from the Antimicrobial Stewardship Pre-Post Implementation Provider Survey by the Centers for Disease Control and Prevention (May et al., 2018). The adapted survey consisted of 14 questions about provider attitude, opinion, and preference on the guideline adherence implementation. Two items assessed guideline adherence using a 5-point Likert scale (1= "very unlikely" to 5 = "very likely"). Four questions focused on attitudes about prescribing behaviors and were rated on a 5-item Likert scale (1= "strongly disagree" to 5= "strongly agree"). One item asked the providers "How willing would you be to change your practice based on the audit and feedback?" which was rated on a scale of 1 "being very unwilling" to 10 "being very willing." Finally, providers were asked to respond to the open-ended question, "What additional resources would you like to see available to support practice?" One item asked the providers to rank supporting tools that attribute to implement prophylactic anticonvulsant guidelines in neuro-oncology practice, including published institutional or local guidelines, point-of-care clinical decision support via the electronic health record, continuing education for providers, and individual feedback for providers. One item asked for provider self-reported preferred factors that increase clinical guideline adherence, including preclinical training in medical/advanced practitioner programs, clinical training, established practice guidelines, and established decision support tools.

Data Collection

Patient chart review data were queried from EPIC. Pre-intervention data were gathered on the number of patients who had craniotomy and were on prophylactic anticonvulsants, and the number of patients at the clinic who were prescribed prophylactic anticonvulsants after craniotomy 4 months and 1 year prior to the intervention start date. Data were extracted and entered in Excel, then imported into SPSS for analysis. Patients' names and the identifier number were kept in a separate, password-protected Excel file.

Provider surveys were administered in paper form and returned to the investigator for data entry into Excel. The pre-survey and post-survey (Appendix B) were conducted to assess change in the providers' knowledge and attitudes after the intervention. To match provider pre- and post-surveys, providers used a unique ID consisting of the last four digits of their cell phone number along with a unique letter. All data were stored in a password-protected Excel file on an encrypted computer that only the primary investigator was able to access. The aggregate data findings were shared with the institution leaders and clinical staff at the implementation site after data analysis. The deidentified data for this project were stored on the Johns Hopkins School of Nursing OneDrive.

Statistical Analysis

Data were analyzed using SPSS Version 25 (IBM Corp., 2017). Descriptive statistics (means, standard deviation, counts, percentages) were used to summarize patient and provider demographic information.

Data analysis for aim 1 (guideline adherence rate) included descriptive statistics and a Fisher's exact test to assess the effect of implementing provider education on prophylactic anticonvulsant guideline adherence and prescription rate changes. The average adherence rate was calculated for the total number of compliances vs. the total number of the patients. The maximum potential score was 100%, and minimum score was 0%. The adherence rate was then compared to the 1-year and 3-month baseline data. The desired outcome was to increase the provider guideline adherence rate greater than 90% over 16 weeks.

To determine the impact the intervention had on providers' knowledge and attitudes (aim 2), a Wilcoxon signed-rank test (two-tailed, alpha = .05) evaluated changes pre- and post-intervention. Providers self-reported their prescribing behavior, knowledge, and attitudes, and were also summarized through descriptive statistics before and after the intervention.

Finally, descriptive statistics and a Chi-square test of association (two-tailed, alpha = .05) was used to determine if the prescription rate of prophylactic anticonvulsants in seizure-naive diagnosed brain tumor patients decreased as a result of the intervention (aim 3). The desired outcome was a decrease by 10% of the prophylactic anticonvulsant prescription rate after the intervention.

RESULTS

Sample Summary

The provider sample consisted of four neuro-oncology providers (three physicians and one nurse practitioner). All were female and had a median of 6.5 years of neuro-oncology professional experience (interquartile range = 4.75 years; Table 1).

Among the 15 patients who were included in the study, seven were males and eight were females with an average age of 58 years. Approximately 80% of the patients were diagnosed with primary brain tumors and 20% were diagnosed with metastatic brain tumors. See Table 2 for more patient demographic characteristics.

Table 1. Provider Demographic Data (N = 4)

	No. (%)
Years of experience, median (range)	4.75 (2–18)
Gender	
Female	4 (100)
Years of practice in neuro-oncology	
< 10 years	3 (75)
≥ 10 years	1 (25)
Health-care provider cadre	
Physician	3 (75)
Nurse Practitioner	1 (25)

Aim 1: Guideline Adherence

As displayed in Table 3, the 4-month pre-intervention baseline adherence rate from 5/1/2020 to 8/31/2020 was 15.8% with a 77.5-point increase to 93.3% ($p < .0001$) post-implementation, and the previous 1-year baseline adherence rate from 9/1/2019 to 12/31/2019 was 27.8% with a 65.5-point increase when compared to 93.3% ($p = .0002$) post-implementation from 9/1/2020 to 12/31/2020. A total of 15 patients were recognized as newly diagnosed seizure-naive brain tumor patients who had their first brain tumor resection between 9/1/2020 and 12/31/2020. Of the 15 patients, 10 were not started with prophylactic anticonvulsants during their perioperative period.

Table 2. Patient Demographic Data and Diagnosis (N = 15)

	No. (%)
Age, median	60
Gender	
Male	7 (46.7)
Female	8 (53.3)
Diagnosis	
Primary brain tumors	12 (80)
Glioblastoma	5 (31.6)
Pilocytic astrocytoma	1 (5.3)
Atypical choroid plexus papilloma	1 (5.3)
Meningioma	2 (10.5)
Pituitary adenoma	2 (10.5)
VHL hemangioblastoma	1 (5.3)
Metastatic brain tumors	3 (20)
Metastatic melanoma	2 (10.5)
Metastatic prostate cancer	1 (5.3)

Note. SD = standard deviation.

Table 3. Guideline Adherence Rates of Providers

Date parameters	Total patients	No. of pts not on seizure prophylaxis (% guideline adherence rate)	No. pts on seizure prophylaxis (%)	Fisher's exact test
Comparison of 1 year pre-implementation to post-implementation period				
1 year pre-implementation: 9/1/2019–12/31/2019	18	5 (27.8%)	13 (72.2%)	Reference
Implementation period: 9/1/2020–12/31/2020	15	14 (93.3%)	1 (6.7%)	0.0002[a]
Comparison of 4 months pre-implementation to post-implementation period				
4 months pre-implementation: 5/1/2020–8/31/2020	19	3 (15.8%)	16 (84.2%)	Reference
Implementation period: 9/1/2020–12/31/2020	15	14 (93.3%)	1 (6.7%)	<0.001[a]

Note. [a]Level of significance $p < .05$.

Five patients were initially prescribed prophylactic anticonvulsants. Out of these five patients, four were weaned off per prophylactic anticonvulsant guidelines with varying durations from 7 days to 56 days, with the average being 24.5 days. One patient was a significant outlier because he was weaned off in 56 days due to an unexpected second surgery in 3 weeks after his first surgery. A second patient was also an outlier because he was weaned off in 28 days due to missing several appointments. The last patient was not weaned off due to medical reasons. The patient remained on prophylactic AEDs due to an enormous tumor size and was undergoing radiation and chemotherapy treatment with high risk of seizure. With a previous attempt to wean off the AEDs, the patient developed another tumor progression along with hydrocephalus, which required repeated craniotomy. Therefore, due to his complicated medical condition, the patient remained on prophylactic AEDs.

Compared to the data 1 year before the implementation period, there was a three-fold increase in guideline adherence post-intervention from 27.8% to 93.3%. The two-tailed Fisher's exact test statistic value is 0.0002. The result is significant at $p < 0.05$. When compared to the data 4 months before the implementation period, there was a six-time increase in guideline adherence post-intervention from 15.8% to 93.3%. The two-tailed Fisher's exact test statistic value is 0. The result is significant at $p < 0.05$. In both timeframes where baseline data was pulled, guideline adherence rates substantially increased after the intervention for all four providers.

Aim 2: Provider Knowledge and Attitudes

As displayed in Table 4, there was not a statistically significant increase in provider knowledge or attitudes. However, it was a clinically significant increase. The likelihood of prescribing prophylactic AEDs had a 0.5-point improvement, and provider likelihood of prescribing prophylactic AEDs had a 1.5-point improvement. The score of prophylactic AEDs contributing to cognitive and QOL impairment increased to 0.5 point post-implementation, which indicated provider awareness of the guideline recommendations. The 10-point Likert score on rating the extent of overused prophylactic AEDs increased 1.5 points, reflecting the provider recognition of guideline adherence.

Table 5 shows that all four providers agreed that a lack of access to the guidelines on prescribing prophylactic anticonvulsants was a barrier to guideline adherence. 75% of the providers believed that their medical background and prescribing habits were barriers to guideline adherence. On the other hand, 75% of the providers believed that their clinical training and established practice guidelines would increase their guideline adherence.

Table 6 shows how the providers ranked the importance of the support tools for increasing guideline adherence. 50% of the providers ranked published institutional guidelines as the most important support tool. One provider found EPIC point-of-care clinical decision support to be the

Table 4. Providers' Knowledge and Attitude (Wilcoxon Signed-Rank Test)

Statements	Median (Pre-implementation)	Median (Post-implementation)	Median Δ (Post–Pre)	Z	*p*
1. Likelihood to prescribe AEDs	2.0 (unlikely)	1.5 (↓ to unlikely)	−0.5	−1.732	.083
2. Likelihood of the other providers to prescribe AEDs	3.0 (neutral)	1.5 (↓ to unlikely)	−1.5	−1.890	.059
3. Unnecessary prophylactic AED use contributes to cognitive impairment and jeopardizes quality of life	3.5 (neutral–likely)	4 (likely)	0.5	−1.414	.157
4. Overprescribing prophylactic anticonvulsants is a national and global issue	3.5	3.5 (no change)	0.0	.00	1.00
5. The extent each provider feels prophylactic anticonvulsants are under- or overused	5.5	7	1.5	−.730	.465

Note. AED = antiepileptic drug.

most important support tool. Another provider thought continuing education for providers was the most important support tool. However, no providers ranked individual feedback for providers as the most important support tool. The votes for the least important support tool were split equally among the four choices.

Aim 3: AED Prescription Rate

Table 7 shows that the rate of prophylactic anticonvulsant prescription during the implementation period decreased by 2.2% when compared to the rates 4 months pre-implementation and decreased by 2.6% when compared to the rates 1 year pre-implementation. The association between the prescription rates 1 year before the intervention and post-intervention was not significant, at X^2 (1, N = 693) = 3.2441, p = 0.0716, nor was the association between the prescription rates 4 months before the intervention and post-intervention, X^2 (1, N = 742) = 2.4301, p = 0.1190.

Table 5. Providers' Self-Reported Factors for Guideline Adherence (N = 4)

	No. (%)
Barriers to guideline adherence (multiple responses)	
Lack of access to guidelines on prescribing	4 (100%)
Lack of well-defined supportive evidence	1 (25%)
Provider's medical background and prescribing habits	3 (75%)
Patient's expectations	1 (25%)
Factors that increase guideline adherence	
Pre-clinical training in medical/advanced practitioner program	1 (25%)
Clinical training	3 (75%)
Established practice guidelines	3 (75%)
Established decision support tools	1 (25%)

DISCUSSION

The current practice at this outpatient clinic is that prophylactic AEDs are routinely prescribed to seizure-naive patients post-craniotomy. However, national AAN guidelines on primary brain tumors and ASCO/SNO guidelines on metastatic brain tumors suggest that prophylactic AEDs are not effective in preventing new-onset seizures in patients who are seizure-naive. Despite the extensive evidence, the ASCO/SNO and AAN guidelines have not been adopted in practice due to providers' gap in knowledge and a lack of awareness about the guideline recommendations (Dallongeville et al., 2012; Reiner et al., 2010; Salinas et al., 2011). Utilizing standardized provider education (Affronti et al., 2014; Carey et al., 2009; Chung et al., 2010; Nelson et al., 2016), automated provider alerts (Carey et al., 2009; Durieux et al., 2000; Loy et al., 2016; Nelson et al., 2016), and the audit-feedback strategy (Affronti et al., 2014; Carey et al., 2009; Hysong et al., 2006; Jamtvedt et al., 2006; Loy et al., 2016), the guideline adherence rate was increased in this project.

Findings from this quality improvement project validated that the aforementioned strategies can offset barriers to adoption. The evidence-based prophylactic AED guidelines were success-

Table 6. Providers' Ranking of Support Tools

Statements	Most important	Second choice	Third choice	Least important
EPIC point-of-care clinical decision support	1 (25%)	0	2 (50%)	1 (25%)
Individual feedback for providers	0	1 (25%)	2 (50%)	1 (25%)
Published institutional or local guidelines	2 (50%)	1 (25%)	0	1 (25%)
Continuing education for providers	1 (25%)	2 (50%)	0	1 (25%)

fully translated into the neuro-oncology program. Furthermore, although the decrease in prophylactic anticonvulsant prescribing rate was not statistically significant, the results were clinically significant as the project's purpose was to decrease the unnecessary prescription rate.

Another interesting finding of this project was that there were no clear guidelines on prescribing prophylactic AEDs for medically complex patients with brain tumors. One patient in this project had a metastatic frontal lobe brain tumor and was weaned off in 56 days due to missed appointments and a complex disease course that included repeated craniotomies and a positive *IDH* mutation. The slow wean-off method was supported by findings from a 10-year retrospective review study and a systematic review that showed that gliomas with *IDH1* and *IDH2* mutations located in the frontal and temporal lobes have a high risk of seizures (Easwaran et al., 2021; Huberfeld & Vecht, 2016; Koekkoek et al., 2015; Rudà et al., 2010). There needs to be more research on *IDH* mutation tumors so that standardized guidelines can be developed for use of prophylactic anticonvulsants in seizure-naive patients with newly diagnosed brain tumors.

After analyzing the survey questions from the self-reported providers' knowledge and attitudes, all the providers agreed that a lack of access to the guidelines on prescribing prophylactic anticonvulsants was a barrier to guideline adherence. Half of the providers ranked published institutional guidelines as the most important support tool. The implications for the future are that program directors should make providers aware of updated guidelines and provide them access to it via email or monthly meetings. Ongoing support and education for the patients on their seizure prophylaxis based on the most current guidelines is required for advanced practitioners since advanced practitioners are at the frontline for patients' symptom management every day.

Despite the project's promising findings, the use of prophylactic anticonvulsants in seizure-naive patients continues to be controversial. The national guidelines used in this project state that there lacks evidence that prophylactic anticonvulsants reduce the risk of new-onset seizures in seizure-naive brain tumor patients (Glantz et al., 2000). The *Neuro-Oncology Practice* journal featured an expert panel of neuro-oncologists from

Table 7. Antiepileptic Drug Prophylaxis Prescription Rates in Post-Craniotomy Patients

Date parameters	No. pts prescribed AED prophylaxis	Total no. of pts	% of pts prescribed AED prophylaxis	Chi-square statistic	*p*
Comparison of one year pre-implementation to post-implementation period					
1 year pre-implementation: 9/1/2019–12/31/2019	58	693	8.4%	Reference	
Implementation period: 9/1/2020–12/31/2020	43	746	5.8%	3.2441[a]	.072
Comparison of four months pre-implementation to post-implementation period					
4 months pre-implementation: 5/1/2020–8/31/2020	59	742	8.0%	Reference	
Implementation period: 9/1/2020–12/31/2020	43	746	5.8%	2.4301[a]	0.119

Note. [a]Level of significance $p < .05$.

esteemed health-care institutions nationwide who debated about the benefits of prophylactic anticonvulsants in newly diagnosed seizure-naive brain tumor patients (Stocksdale et al., 2020). Stocksdale and colleagues (2020) argued that no evidence demonstrated a benefit from prophylactic anticonvulsant use in seizure-naive newly diagnosed brain tumor patients. Four randomized control trials and eight cohort studies found that the associated cognitive impairment, behavior, and psychiatric effects from taking prophylactic AEDs can jeopardize the patient's quality of life. Thus, this group of experts supported the national guidelines implemented in this project. However, Stocksdale and colleagues (2020) debated that this claim is unjustified as the clinical studies lacked blinding which increased the risk for bias, had too small of a sample size to generalize findings for dissemination, and did not have a representative sample of each tumor selection and grouped them into a homogeneous group. In light of these controversies, a double-blinded randomized trial would be the best option to assess the efficacy and benefits of long-term prophylactic AED therapy.

Limitations

The first limitation specific to the aim 3 analysis of this QI project was that the reports generated from EPIC could not discriminate between seizure-naive patients with newly diagnosed brain tumors and those with established brain tumors. Therefore, data about the prophylactic anticonvulsant prescription included both newly diagnosed brain tumor patients and recurrent brain tumor patients. Besides, Fisher's exact test was used for the small sample size in this project. Lacking power might be an issue irrespective of a statistically significant test. The second limitation was the small sample size of the neuro-oncology providers, which contributed to the lack of a statistically significant finding. It also inhibited the analysis of resources ranked according to its efficacy in implementing prophylactic anticonvulsant guidelines at this neuro-oncology practice. Since this project occurred during the COVID-19 pandemic when non-emergent surgeries were cancelled or postponed, the third limitation was the small sample size of the patients. We were unable to meet the original power analysis sample size of 44 due to limited elective surgery secondary to the COVID-19 pandemic. The data collection period was extended for an additional 30 days to achieve the targeted sample size due to COVID-19 restrictions on the elective craniotomy surgery. As a result, 15 newly diagnosed seizure-naive patients who had craniotomies were identified during the project period.

Strengths

The strengths of this project included organizational and provider support. The information technology team delivered extensive support to this project. Multicomponent intervention and involvement of stakeholders in the early planning set a successful foundation for this quality improvement project.

CONCLUSION

This project highlights the important role of provider education, provider alerts, documentation templates, and audit-feedback in improving guideline adherence rates. This combination intervention and weekly audit-feedback strategy improved guideline adherence to prophylactic anticonvulsant use in seizure-naive newly diagnosed brain tumor patients. This strategy can be implemented for other clinical sites nationwide that seek to increase guideline adherence to evidence-based protocols. Following the AAN, SNO, and ASCO guideline recommendations can help clinicians avoid the potential side effects of anticonvulsant-induced cognitive, behavioral, and psychiatric issues that can impair patients' quality of life.

Disclosure

The authors have no conflicts of interest to disclose.

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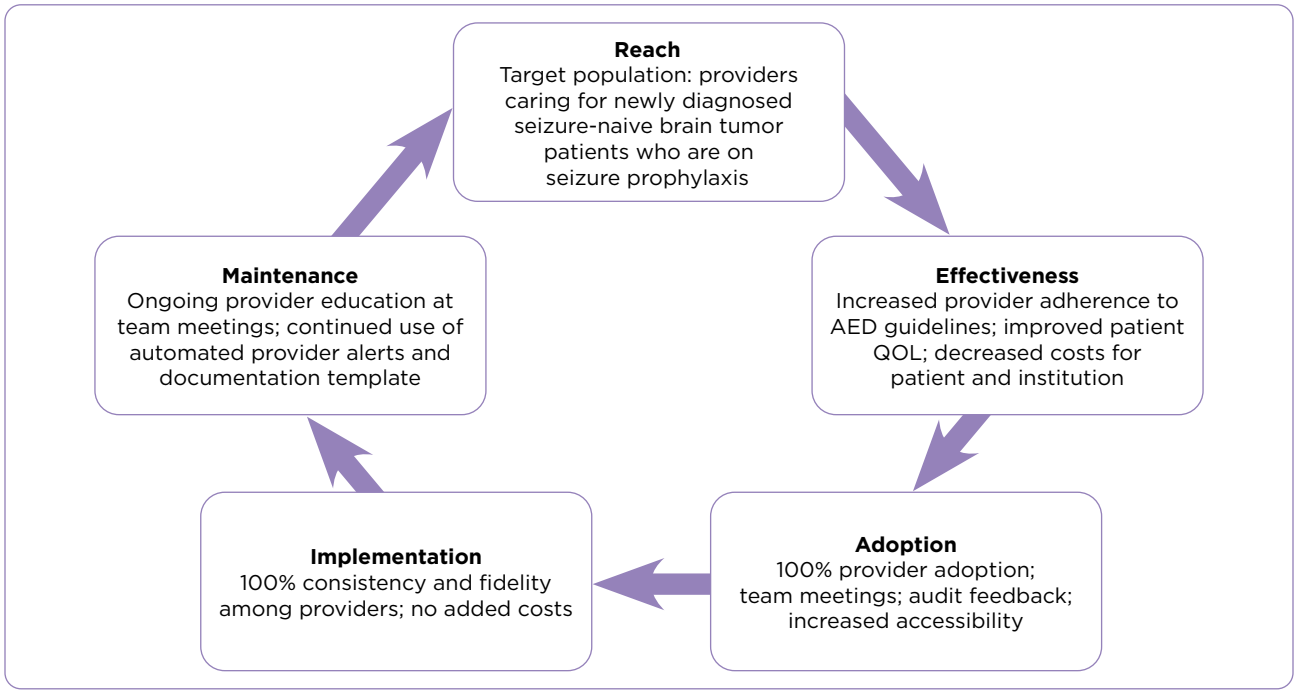

Appendix A. RE-AIM Framework. AED = antiepileptic drug; QOL = quality of life.

Appendix B. Survey Measuring Provider Knowledge and Attitudes on Seizure Prophylaxis Use Pre- and Post-Intervention

How likely are you to prescribe prophylactic anticonvulsant to seizure-naive newly diagnosed brain tumor patients?
❑ Very unlikely ❑ Unlikely ❑ Neutral ❑ Likely ❑ Very likely

How likely do you think other providers in your practice prescribe prophylactic anticonvulsants for seizure-naive newly diagnosed brain tumor patients?
❑ Very unlikely ❑ Unlikely ❑ Neutral ❑ Likely ❑ Very likely

To what extent do you feel prophylactic anticonvulsant is under- or overused in seizure-naive newly diagnosed brain tumor patients (1 being very underused and 10 being very overused)?
❑ 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑ 6 ❑ 7 ❑ 8 ❑ 9 ❑ 10

In your opinion, what are current barriers to appropriate prescribing of prophylactic anticonvulsant for seizure-naive newly diagnosed brain tumor patients? Check all that apply.
❑ Lack of access to guidelines or information on prescribing
❑ Lack of clear evidence and evidence-based recommendations
❑ Providers' background and prescribing habits
❑ Patient expectations
❑ COVID-19 pandemic
❑ Other, please specify _____

How has the current pandemic (SARS CoV-2/COVID-19) impacted or affected your prophylactic anticonvulsant prescribing patterns?

_____

_____

Overprescribing prophylactic anticonvulsants is a national and global issue.
❑ Strongly disagree ❑ Disagree ❑ Neutral ❑ Agree ❑ Strongly Agree

Unnecessary prophylactic anticonvulsant use contributes to patient cognitive impairment and jeopardizes their quality of life.
❑ Strongly disagree ❑ Disagree ❑ Neutral ❑ Agree ❑ Strongly Agree

In your opinion, what are the best strategies to decrease inappropriate use of prophylactic anticonvulsants for seizure-naive newly diagnosed brain tumor patients? Check all that apply.
❑ More education or focus in pre-clinical training (medical/nursing school)
❑ More education in clinical training
❑ Developing rigorous practice guidelines of prophylactic anticonvulsants for seizure-naive newly diagnosed brain tumor patients
❑ Developing more order sets or decision support tools
❑ Other, please specify_____

What resources do you use to stay up to date on current approaches to prophylactic anticonvulsant prescribing?
❑ Lectures at the practice center/Continuing education
❑ Web-based resources (UpToDate or other)
❑ Smart phone app or pocket guide
❑ Other lectures
❑ Other, please specify_____

Based on your preference, please rank the following attributes to implement prophylactic anticonvulsant guidelines in neuro-oncology practice, with 1 being the most preferable.
___ Published institutional or local guidelines
___ Point-of-care clinical decision support via the electronic health record
___ Continuing education for providers
___ Individual feedback for providers
___ Other, please specify _____

What additional resources would you like to see available to support appropriate prescribing of prophylactic anticonvulsants for seizure-naive newly diagnosed brain tumor patients, and why?

_____

_____

Please answer the following questions if you participated in the audit and feedback portion of the program.
Did you find the audit and feedback portion of this program useful?
❑ Not at all ❑ Slightly ❑ Moderately ❑ Greatly

How bothersome was the audit and feedback?
❑ Extremely intrusive ❑ Very intrusive ❑ Somewhat intrusive ❑ A little intrusive ❑ Not at all intrusive

How willing were you to change your practice based on the audit and feedback, with 1 being very unwilling and 10 being very willing?
❑ 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑ 6 ❑ 7 ❑ 8 ❑ 9 ❑ 10