Quality improvement in neurology

Epilepsy Quality Measurement Set 2017 update

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Epilepsy is a common condition in the United States. It is estimated that 1.2% of the population or 3.4 million people have epilepsy. This figure may be underestimated because of potential repercussions and stigma in disclosing epilepsy.¹ Studies have shown that people with epilepsy are more likely to be unemployed or unable to work, have lower annual household incomes, be obese and physically inactive, and be less likely to marry.^{2,3} People with epilepsy can have poor overall health status, impaired intellectual and physical functioning, elevated risk of accidents and injuries, and negative side effects from antiseizure medications.^{2,3} It is estimated the annual direct medical cost of epilepsy in the United States is \$9.6 billion; combined with indirect costs, the total rises to \$15.5 billion yearly.²

The American Academy of Neurology (AAN) created standardized quality measures with the overarching goal to improve the delivery of care for patients with epilepsy for providers, practices, and systems. In 2009, the first set of epilepsy measures were released with an update provided in 2014.^{4,5} Quality measures are not guidelines; however, they are formed using guidelines, evidence-based medicine, and best practice consensus. Quality measures help us understand how often health care services are provided consistent with current medical knowledge. Measures are updated iteratively to reflect evidence and practice changes, as well as to reflect limitations of data collection and analysis.

The AAN reviews each measurement set for updates a minimum of every 3 years. In 2017, the AAN seated a standing multidisciplinary Epilepsy Quality Measurement Set Work Group (work group) charged with updating the measurement set. This work group will revisit the epilepsy measures every 6 months, evaluating new evidence statements and new measures released by other developers. As part of this process, epilepsy measure implementation and performance data review will also occur to nimbly respond to emerging guidelines and evidence.

During this initial review, the work group evaluated new evidence, 2014 epilepsy measure use data, and other new measures released by other development groups that addressed care for patients with epilepsy, such as the AAN's Child Neurology and Universal Neurology Quality Measure projects. The work group approved 6 measures and retired 6 measures from the 2014 update (table 1). Measure retirement occurs if evidence has changed, a gap in performance no longer exists, feasibility concerns exist, or significant edits are needed to the existing measure. It does not mean the topic is no longer important. Full measure specifications are available online at aan.com/practice/quality-measures/ and in appendix e-1, links.lww.com/WNL/A721.

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Glossary

AAN = American Academy of Neurology; CMS = Centers for Medicare & Medicaid Services; ICD-10 = *International Classification of Diseases, Tenth Revision*; MIPS = Merit-based Incentive Payment System; QOL = quality of life; QOLIE-10-P = patient-weighted Quality of Life in Epilepsy Inventory-10.

Table 1 Epilepsy Quality Measurement Set 2017 update

Title	Numerator	Denominator	Exclusions
Counseling for Women of Childbearing Potential with Epilepsy	All females, including all individuals of childbearing potential (aged 12–44 y) with a diagnosis of epilepsy	Patients or caregivers counseled ^a at least once a year about how epilepsy and its treatment may affect contraception and/or pregnancy. Measure is met if patient has documentation they are premenstrual, postmenopausal, surgically sterile, or reproductive organs absent.	None
Comprehensive Epilepsy Care Center Referral or Discussion for Patients with Intractable Epilepsy	Patients with an order for referral to a comprehensive epilepsy care center, who had a discussion of evaluation at a comprehensive epilepsy care center, or who received treatment at a comprehensive epilepsy care center during the measurement period	Patients diagnosed with intractable epilepsy (see appendix of codes) or patients diagnosed with epilepsy who were prescribed 3 or more distinct antiseizure medications in the past 2 y	None
Quality-of-Life Assessment for Patients with Epilepsy	Patients with age-appropriate, condition-specific quality of life assessed ^a at least once in the measurement period	Patients aged 4 y and older diagnosed with epilepsy	Patients who are unable or decline to complete the instrument and for these patients a caregiver is not present to provide proxy report
Quality-of-Life Outcome for Patients with Epilepsy	Patients whose most recent QOLIE-10-P score is maintained or improved from the prior QOLIE-10-P score obtained in the measurement period	Patients aged 18 y and older diagnosed with epilepsy who had 2 office visits during the 2-y measurement period, which occurred at least 4 wk apart	None
Depression and Anxiety Screening for Patients with Epilepsy	Patients aged 12 y and older diagnosed with epilepsy	Patients with epilepsy who were screened for both depression ^a and anxiety ^a at every office visit	<ul style="list-style-type: none"> • Patients who are unable or decline to complete epilepsy-specific screening tool • Patient has a diagnosis of depression or anxiety on active problem list
Seizure Frequency for Patients with Epilepsy	All visits for patients with a diagnosis of epilepsy	Patient visits with current seizure frequency ^a documented for each seizure type	<ul style="list-style-type: none"> • Caregiver is unavailable for a patient who is noncommunicative or has an intellectual disability • Patient or caregiver declines to report seizure frequency

Abbreviation: QOLIE-10-P = patient-weighted Quality of Life in Epilepsy Inventory-10.

The listed measures were approved by the work group. There is no requirement that all measures in the measurement set be used. Providers are encouraged to identify the 1 or 2 measures that would be most meaningful for your patient populations and implement these measures to drive performance improvement in practice.

^a Refer to appendix e-1 (links.lww.com/WNL/A721) for further definitions.

Opportunities for improvement

The work group initially identified 18 concepts for potential measures. The AAN prioritized concepts that are supported by the following criteria: strong evidence and guideline statements, feasible to collect, and have a substantial link to improved health care outcomes. Among the putative concepts, the work group prioritized development of measures

addressing (1) counseling for women of childbearing potential, (2) referral or discussion of referral to a comprehensive epilepsy care center for patients with intractable (treatment-resistant) epilepsy, (3) quality-of-life (QOL) outcome assessments, and (4) depression and anxiety screening.

Counseling for women of childbearing potential

Epilepsy has been linked to reduced fertility, increased pregnancy risks, and risks of malformations and behavioral abnormalities in the infant.⁶ Treatment of seizures with

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antiseizure medications may alter hormone levels, render oral contraceptives less effective, and may interfere with embryonic and fetal development.⁷⁻⁹ In addition, oral contraceptives may lower AED levels thus making them less effective.⁸ Counseling and discussion for women with epilepsy can have important and beneficial effects with the goal of reducing unplanned pregnancies, birth and cognitive deficits among infants, and complications that can occur during pregnancy and delivery for women with epilepsy.¹⁰⁻¹³ Guidelines and interventions are available to assist in conveying this important information as well as initiating interventions once the information is conveyed¹²⁻¹⁶; however, gaps in providing such counseling to women with epilepsy exist.¹⁷⁻¹⁹

Referral or discussion of referral to a comprehensive epilepsy care center for patients with intractable (treatment-resistant) epilepsy

Despite the strong evidence of superior outcomes among those who receive epilepsy surgery and other specialized services at comprehensive epilepsy centers, only a small fraction of patients are referred within 2 years of developing intractable epilepsy (treatment-resistant epilepsy), with years of delay occurring before referral for epilepsy surgery.²⁰⁻²² Contributors to the delay in referral include improper identification of medication treatment resistance (intractability) and gaps in knowledge related to epilepsy surgery guidelines.²³ Evaluation and treatment at comprehensive epilepsy centers can also lead to appropriate diagnosis for patients without epilepsy, but with nonepileptic spells, in addition to the utilization of specialized treatments including, for example, dietary therapy, neurostimulation, medical research trials, and psychosocial supports for those with intractable epilepsy.

Quality-of-life outcome assessments

Maintenance and improvement of QOL is a primary goal in caring for a patient with epilepsy. Given the numerous psychological, cognitive, social, and physical challenges that people with epilepsy face, health-related QOL is an essential patient-centered outcome to assess.²⁴⁻²⁷ Patients and caregivers have signaled that this information is of value to them, and the Centers for Medicare & Medicaid Services (CMS) has recently developed plans to incorporate patient-reported outcome data such as QOL assessments into their Merit-based Incentive Payment System (MIPS). Providers reported that they preferred such instruments be used electronically to collect patient-reported outcome measures on QOL and other important screening areas.²⁸

Depression and anxiety screening

People with epilepsy have high rates of psychiatric disorders, with approximately 20% of patients reporting depression or anxiety.²⁹ Such comorbidities place patients with epilepsy at higher risk of poor QOL,^{30,31} poor adherence to medication,^{32,33} and increased risk of suicide.³⁴ Antiseizure medications can also themselves place patients at risk of

mood-related changes. Screening for symptoms of depression and anxiety in patients with epilepsy using a number of valid, reliable screening instruments has been shown to be effective.^{31,35,36} Screening for depression and anxiety is imperative to identify patients with epilepsy potentially at risk and in need of treatment. For example, treatment of mood disorders can help mitigate the risk of development of mood-related adverse events, including but not limited to loss of work, decreased QOL, and suicide.³⁷

Although measuring seizure frequency was thought to be fraught with feasibility and validity issues, it is being recommended for continued inclusion. The field will need to move toward a more standardized capture of seizure frequency. The work group notes that activity is being done in this area through a Learning Healthcare Collaborative and hopes to utilize these developments to enhance the seizure frequency measure in future updates.

Methods

The AAN Quality and Safety Subcommittee approved a modified, pilot measure development process for this update. Details of the full measure development process are available online.³⁸ The AAN seated a standing work group for a 2-year term, and 2 nonvoting facilitators were seated to provide methodologic support. The work group includes physician, nursing, patient, and caregiver representatives from professional associations and patient advocacy organizations to ensure measures developed included input from all members of the health care team and other relevant stakeholders. All members are required to disclose relationships with industry and other entities to avoid actual, potential, or perceived conflicts of interest. Individuals were instructed to abstain from voting on individual measure concepts if a conflict was present.

The AAN anticipates this work group will revisit measures every 6 months. The work group is charged with updating measures as needed over the 2-year period and developing supporting materials and implementation guides as appropriate.

At the start of the project, existing guidelines, measures, and evidence were identified. A comprehensive literature search was conducted by a medical librarian identifying 852 abstracts relevant to the topic since the last update in 2014. Following review, 10 guidelines were located and became the basis of the evidence for measure development. The AAN measure development process involves a modified Delphi review by the work group to reach consensus on measures to be developed prior to a 21-day public comment period and again following refinement after the public comment period.

The work group reviewed the eight 2014 epilepsy quality measures and proposed 18 new measure concepts. The work

group rated concepts via a modified Delphi review based on the following criteria: impact on improving care, feasibility to collect data, and demonstrated link to improved patient outcomes. The work group removed 5 concepts following these ratings. To further winnow concepts, work group members then ranked new measure concepts. This resulted in 8 additional concepts being dropped from development. Work group discussions were held on the remaining 6 new measure concepts. Two concepts were removed because of feasibility concerns, and the QOL concept was split into process and outcome measures specifications. Seven measures were retired and 5 new concepts approved following work group votes. A 21-day public comment period was held. Following and based on public comment, measure retirement decisions were revisited. Based on public comments, the work group voted to not retire the seizure frequency measure from 2014. Finally, the measure specifications were refined, and the work group, AAN's Quality and Safety Subcommittee, AAN's Practice Committee, and AAN's Board of Directors approved the measurement set.

Results

The work group approved 6 measures (table 1). Full measurement specifications are available online at aan.com/practice/quality-measures/ and in appendix e-1, links.lww.com/WNL/A721. The 6 measures identified have strong guideline statements or evidence to support numerator, denominator, and exclusion criteria. In addition, there are known gaps in care where treatment and outcomes could be improved. For process measures, a link or relationship to improved health care outcomes exists.

Counseling for women of childbearing potential with epilepsy

The women with epilepsy measure remains the one epilepsy-specific measure available for use in CMS's MIPS program. The measure has been implemented in AAN's Axon Registry®. Based on feedback from Axon Registry data, the specifications were updated to clarify which counseling components are required to be compliant with the measure. The measure now requires counseling on at least 2 of 3 topics: (1) need for folic acid supplementation, (2) drug-to-drug interactions with contraception medication, and (3) the potential antiseizure medication effects(s) on fetal/child development and/or pregnancy. The work group discussed a proposal for patients to meet the measure by folic acid prescription alone, but ultimately declined to do so noting the intent of the measure is to increase counseling. Patient representation as well as physician members reported concern that females are often prescribed folic acid without understanding the rationale for the prescription. The work group expanded the definition of female gender to include LGBTQ+ patients who may be at risk of unintended pregnancies. The work group eliminated some exclusions and allowed for providers to meet the

measure by documenting whether a patient is premenstrual, postmenopausal, or surgically sterile, or their reproductive organs are absent. This change was attributable to a low capture rate of exclusions in practice, and it is hoped by moving these to numerator criteria, documentation of these conditions will improve.

Comprehensive epilepsy care center referral or discussion for patients with intractable epilepsy

The 2014 referral to comprehensive epilepsy center measure was retired because of denominator feasibility concerns. Specifically, the denominator required identifying individuals with failure of 2 antiseizure medications, but this is not uniformly documented in the medical record. In addition, some providers have a difficult time identifying these patients because of misunderstanding around the definition of treatment resistance. The work group created a new measure addressing discussion or referral to a comprehensive epilepsy care center. The denominator identified by either (1) an ICD-10 diagnosis of intractable epilepsy (treatment-resistant epilepsy) or (2) a diagnosis of epilepsy and 3 or more distinct antiseizure medications prescribed in the past 2 years will be more feasible to collect. The measurement set includes a list of antiseizure medications that will be updated over time, and excluded rescue medications. The numerator is met by an order for referral, discussion of an evaluation, or receiving treatment during the calendar year at a comprehensive epilepsy care center. By creating a measure ensuring these patient populations are referred or have comprehensive epilepsy care center services discussed, it is anticipated that there will be an increase in appropriate evaluations. Such an evaluation, multidisciplinary in nature, would confirm diagnostic accuracy and result in offering of effective nondrug and nonsurgical treatment options, which may include psychiatric, psychological, and social counseling to address consequences of epilepsy. Difficulty understanding the definition for these patients exists, making the identification of these patients challenging. Validation of the current measure will need to occur to determine whether this is an effective way to identify patients with treatment-resistant epilepsy.

Quality of life

The work group created a process and an outcome measure for QOL for patients with epilepsy. The process measure requires assessment with an age-appropriate, condition-specific QOL assessment tool. A list of multiple assessment tools is provided to meet individual provider and practice needs. The outcome measure assesses maintenance or improvement on patients' Quality of Life in Epilepsy (QOLIE-10-P) scores in the measurement period. The validated QOLIE-10-P was identified to allow comparability in scores and ease of implementation particularly given the low likelihood of respondent fatigue with a brief survey of 10 questions. As noted above, this measure was chosen in part because of its meaningfulness to patients.

Depression and anxiety screening for patients with epilepsy

A quality improvement measure screening annually for depression and anxiety was created. This measure will not be submitted for use in accountability programs or the AAN's Axon Registry, as the measure does not include a follow-up care component. A necessary first step in assessing outcomes is to ensure that patients are screened for anxiety and depression. As such, before implementing an outcome measure, the work group thought that a requisite first step is to routinely screen patients for symptoms of anxiety and/or depression so that proper diagnoses and treatment could be initiated. Future measures may be developed to assess outcomes over time. The work group encourages providers to implement the PHQ-2 (2-item Patient Health Questionnaire) and GAD-2 (2-item Generalized Anxiety Disorder scale) because they are brief, valid, and reliable tools.

The work group reviewed performance data for the entire 2014 epilepsy measurement set, as well as current use in accountability programs. Six measures were retired (table 2). A new measure was created for referral to a comprehensive epilepsy center. The other 5 retired measures are listed below. Retirement decisions should not be viewed to indicate value is lacking in measuring these processes or concepts. The AAN is of the belief no one measurement set can meet the measurement needs of all providers or patients and prioritizes measure concepts based on specificity, feasibility, and

likelihood of improving outcomes. Many lessons on feasibility have been learned since the development of the 2009 measurement set. Some of the prior measures lacked specificity, were infeasible, or were not likely to provide meaningful data to drive improvement in practice. In addition, CMS phased most of the epilepsy measures out of their Physician Quality Reporting System and MIPS programs because of concerns shared by the group including:

1. Seizure intervention was retired because of inability to link documentation to improved outcomes and burdensome process requirements. The work group noted the measure was dropped from use in CMS accountability programs in 2017 because of low-level evidence and failure to link the measure to improved care.
2. Etiology, seizure type, or syndrome was retired because existing specifications had little effect on quality improvement efforts. The work group noted the measure was dropped from use in CMS accountability programs in 2017 because of low-level evidence and failure to link the measure to improved care. The work group could not find evidence to refute the failure to link to improved patient outcomes. The work group noted it is difficult to assess 3 separate components without standardized discrete data fields to ease data collection burdens. If work in the field of epilepsy can overcome this barrier, future measure development in these areas will be considered.

Table 2 Retired epilepsy quality measures

Title	Retirement rationale ^a
Seizure Intervention	Inability to link documentation to improved outcomes and burdensome process requirements. The work group noted the measure was dropped from use in CMS accountability programs in 2017 because of low-level evidence and failure to link the measure to improved care.
Etiology, Seizure Type, or Epilepsy Syndrome	Specifications were not demonstrated to have a meaningful effect on quality improvement efforts. The work group noted the measure was dropped from use in CMS accountability programs in 2017 because of low-level evidence and failure to link the measure to improved care.
Querying and Intervention for Side Effects of Antiseizure Therapy	Feasibility concerns noted as locating uniform data in a medical record was difficult.
Personalized Epilepsy Safety Issue and Education	The broad definition of education affected feasibility of abstraction from the medical record. Potential counseling options were too broad to inform providers on meaningful interventions for quality improvement efforts and because the definition of education was so broad there was no meaningful performance gap to address.
Screening for Psychiatric or Behavioral Health Disorders for Patients with Epilepsy	Specifications were overly broad and inclusive of numerous behavioral health conditions that made abstraction from the medical record difficult. The work group planned to develop an outcome measure addressing depression improvement. However, the work group determined development of an outcome measure on this issue was not feasible given treatment is primarily delivered by psychiatry, primary care physicians, or other treatment team members. The work group developed a refined depression and anxiety screening measure with greater specificity for quality improvement purposes.
Referral to Comprehensive Epilepsy Center	Feasibility concerns noted. The denominator required identifying individuals with failure of 2 antiseizure medications, and this is not uniformly documented in the medical record.

Abbreviation: CMS = Centers for Medicare & Medicaid Services.

These concepts will be retained for consideration in future updates. It is hoped documentation innovation will occur generating greater specificity in patient records that lead to improved opportunities to capture measure specifications and drive change affecting patient outcomes. The American Academy of Neurology prioritizes measure concepts with specificity, feasibility, link to outcomes, and strong evidence. The American Academy of Neurology limits the number of measures released to reduce provider collection burden and to target testing and implementation resources for meaningful measures in practice.

^a Refer to appendix e-1 (links.lww.com/WNL/A721) for further details.

3. Querying and interventions for side effects of antiseizure therapy was retired because of difficulty in locating uniform data in a medical record affecting feasibility without use of a standard and consistent reporting instrument or methodology.
4. Personalized epilepsy safety issue and education provided was retired as potential counseling options were too broad to inform providers on meaningful interventions for quality improvement efforts and because the definition of education was so broad there was no meaningful performance gap to address. The broad definition of education affected feasibility of abstraction from the medical record.
5. Screening for psychiatric or behavioral health was retired to reduce duplicative measures in the field. The measure was overly broad and inclusive of numerous behavioral health conditions that made abstraction from the medical record difficult. The work group planned to develop an outcome measure addressing depression improvement. However, development of an outcome measure on this issue was not feasible at this time given treatment is often delivered outside the field of neurology. The work group developed a refined depression and anxiety screening measure with greater specificity for quality improvement purposes.

Based on information collected during the public comment period, the work group voted again on each individual measure regarding retirement. The work group voted not to retire the seizure frequency measure following further discussion and included the 2014 specification of the measure to meet user needs. The work group noted that the seizure frequency measure has been retired from use in CMS accountability programs because of lack of a gap in care with consistent high-performance rates. Reporting capture of seizure frequency is standard of care, and there is an inability to link documentation of seizure frequency to improved outcomes. The work group also noted there is a lack of specificity and uniformity in collecting quantity of seizures across providers, resulting in feasibility issues. Patient communication on this topic demonstrated that providers rarely inquired what seizure control meant to patients.³⁹ The Axon Registry has implemented the measure through use of a data dictionary and search terms, and the average performance rate for Axon users as of December 2017 is 27.92%. The work group will collaborate with organizational partners and the many current Learning Healthcare Collaborative efforts evaluating this issue to update the specifications during future updates when additional evidence supports standardization in documentation of seizure frequency.

Conclusion

This measure set represents the second update of an ongoing effort to provide individual providers, practices, and systems with tools needed to drive performance improvement in

epilepsy care. There is no requirement that providers use every measure in the set. These measures have been primarily developed to be used in quality improvement projects, and providers are encouraged to identify the 1 or 2 measures that would be most meaningful for their patient population and implement these measures to drive improvement in practice. The work group will be revisiting these decisions over time and anticipates development and release of additional tools to assist in the implementation of these measures into practice. The work group will be able to respond to testing data, performance data, and new evidence such as the planned updates to the AAN's Women with Epilepsy guideline statements.

Select measures will be submitted for consideration in the AAN's Axon Registry, which is proving a useful tool for providers to drive performance improvement in practice while meeting American Board of Psychiatry and Neurology's Maintenance of Certification Part IV requirements. It is anticipated once testing data have been obtained, measures may be submitted for consideration in CMS's MIPS program. In addition, select private payers may utilize these measures to track provider performance. It is important that providers have access to epilepsy measures developed by multidisciplinary treatment team members to ensure that these performance measures are meaningful to providers and patients.

Author contributions

Dr. Patel contributed to concept and design, acquisition of data, analysis and/or interpretation of data, drafting/revising the manuscript, critical revisions of the manuscript for important intellectual content, and supervision including responsibility for conduct and final approval. Dr. Baca contributed to concept and design, acquisition of data, analysis and/or interpretation of data, drafting/revising the manuscript, critical revisions of the manuscript for important intellectual content, and supervision including responsibility for conduct and final approval. Dr. Franklin contributed to acquisition of data, analysis and/or interpretation of data, drafting/revising the manuscript, critical revisions of the manuscript for important intellectual content. Dr. Herman contributed to acquisition of data, analysis and/or interpretation of data, drafting/revising the manuscript, critical revisions of the manuscript for important intellectual content. Dr. Hughes contributed to acquisition of data, analysis and/or interpretation of data, drafting/revising the manuscript, critical revisions of the manuscript for important intellectual content. Ms. Meunier contributed to acquisition of data, analysis and/or interpretation of data, drafting/revising the manuscript, critical revisions of the manuscript for important intellectual content. Dr. Moura contributed to acquisition of data, analysis and/or interpretation of data, drafting/revising the manuscript, critical revisions of the manuscript for important intellectual content. Dr. Munger Clary contributed to acquisition of data, analysis and/or interpretation of data, drafting/revising the manuscript, critical revisions of the manuscript for important intellectual content. Ms. Parker-McFadden contributed to acquisition of data, analysis and/or

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Quality improvement in neurology: Epilepsy Quality Measurement Set 2017 update

Anup D. Patel, Christine Baca, Gary Franklin, et al.

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Disputes & Debates: Editors' Choice

Steven Galetta, MD, FAAN, Editor
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Ariane Lewis, MD, Deputy Editor
James E. Siegler III, MD, Deputy Editor

Editors' Note: Serum Neurofilament Light Association With Progression in Natalizumab-Treated Patients With Relapsing-Remitting Multiple Sclerosis

In "Serum Neurofilament Light Association With Progression in Natalizumab-Treated Patients With Relapsing-Remitting Multiple Sclerosis," Bridel et al. evaluated serum neurofilament light chain (sNfL) levels serially after initiation of natalizumab in patients with relapsing-remitting multiple sclerosis (RRMS) and found that they do not capture or predict clinical/radiologic trajectory. Kropshofer et al. commented that their conclusion that sNfL is not a valid biomarker for disease progression is in opposition to the results from other large studies, noting that the editorial about this article, written by Goldschmidt and Fox, suggested that this may be because prior studies demonstrate natural history, without natalizumab treatment. Nonetheless, Kropshofer et al. noted that they found an association between baseline sNfL and 3-month disability progression in patients treated with siponimod, irrespective of prior disease activity, indicating that baseline sNfL can be used for neuroprognostication, regardless of treatment with anti-inflammatory therapy. Bridel et al. clarified that their conclusion was that sNfL may not be well suited to monitor or predict progression in patients with RRMS on natalizumab. They noted that their results may differ from those from other studies because their patients (1) all had RRMS and (2) were all treated with natalizumab. They also commented that almost half of patients on siponimod in the EXPAND study developed new or enlarging brain lesions on 2-year follow-up imaging, so that is not the ideal population to study the relationship between sNfL and progression. They recommend performance of additional larger studies on the relationship between sNfL and progression in patients on natalizumab and/or ocrelizumab.

Ariane Lewis, MD, and Steven Galetta, MD
Neurology® 2022;98:470. doi:10.1212/WNL.0000000000200131

Reader Response: Serum Neurofilament Light Association With Progression in Natalizumab-Treated Patients With Relapsing-Remitting Multiple Sclerosis

Harald Kropshofer (Basel, Switzerland), Dieter A. Häring (Basel, Switzerland),
Ludwig Kappos (Basel, Switzerland), David Leppert (Basel, Switzerland), and Jens Kuhle (Basel, Switzerland)
Neurology® 2022;98:470–471. doi:10.1212/WNL.0000000000200132

The results of the observational monocentric study by Bridel et al.¹ contrast with those from large phase 3 studies in progressive multiple sclerosis (MS) such as ASCEND, EXPAND, and INFORMS,^{2,3} which suggest association of high baseline serum neurofilament light chain (sNfL) levels with increased risk of disability progression. In the accompanying editorial, Goldschmidt and Fox highlight that these earlier studies included a placebo arm where inflammation followed its natural course,⁴ whereas Bridel et al.¹ studied patients on anti-inflammatory therapy by natalizumab. They hypothesized that the lack of association of sNfL with disability progression may result from suppression of inflammatory activity by natalizumab. They concluded that sNfL is not a valid biomarker for disease progression.

Author disclosures are available upon request (journal@neurology.org).

We addressed this hypothesis in analyses by a treatment group in the EXPAND trial (≤ 5 years follow-up) where patients with confirmed disability progression (CDP) events showed higher sNfL levels.² In the siponimod group ($N = 946$), which controlled for inflammation, high baseline sNfL levels were associated with a higher risk of CDP events at 3 months (HR [95%CI]: 1.30 [1.06; 1.58], $p = 0.0115$). A prognostic association between baseline sNfL and disability progression was also observed for patients with (1.28 [1.01; 1.61], $p = 0.0397$) and without active disease before baseline (1.33 [1.06; 1.58], $p = 0.0149$). In conclusion, increased baseline sNfL is prognostic of disability progression, irrespective of anti-inflammatory therapy.

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Author Response: Serum Neurofilament Light Association With Progression in Natalizumab-Treated Patients With Relapsing-Remitting Multiple Sclerosis

Claire Bridel (Geneva), Joep Killestein (Amsterdam), and Charlotte Teunissen (Amsterdam)

Neurology® 2022;98:471. doi:10.1212/WNL.0000000000200133

We are grateful for the interest in our study.¹ We did not conclude that serum neurofilament light chain (sNfL) is not a valid biomarker for disease progression. Rather, we indicated that it may not be well suited to monitor or predict progression in people with relapsing-remitting multiple sclerosis (RRMS) treated with natalizumab. At least 2 reasons may explain the discrepancy between our findings and those reported by Kropshofer et al.² First, the population we investigated consisted exclusively of people with RRMS, as opposed to people with secondary progressive multiple sclerosis in the EXPAND study.³ The rate of progression differs greatly between these 2 populations, and prediction of progression in people with RRMS may require more sensitive tools. Second, in our study, all patients were treated with natalizumab, which silences acute focal inflammatory disease activity in a vast majority of patients compared with placebo.⁴ In the EXPAND study, 43% of the siponimod-treated patients had new or enlarging T2 lesions during the 24 months follow-up.³ Thus, siponimod-treated patients are less well suited to investigate the biological underpinnings of progression because of residual focal inflammatory disease activity. We contend that larger studies investigating natalizumab and/or ocrelizumab patients are needed to determine the prognostic and monitoring potential of sNfL in terms of progression.

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Quality Improvement in Neurology

Epilepsy Quality Measurement Set 2017 Update

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In the Special Article “Quality Improvement in Neurology: Epilepsy Quality Measurement Set 2017 Update” by Patel et al.,¹ there are several errors in Table 1. The table is republished here. The authors regret the errors.

Table 1 Epilepsy Quality Measurement Set 2017 Update

Title	Denominator	Numerator	Exclusions
Counseling for Women of Childbearing Potential with Epilepsy	All women, including all individuals of childbearing potential (12–44 years) with a diagnosis of epilepsy	Patients or caregivers counseled at least once a year about how epilepsy and its treatment may affect contraception and/or pregnancy. Measure is met if the patient has documentation they are premenstrual, postmenopausal, surgically sterile, or reproductive organs absent.	None
Comprehensive Epilepsy Care Center Referral or Discussion for Patients with Intractable Epilepsy	Patients diagnosed with intractable epilepsy (see Appendix of Codes) OR patients diagnosed with epilepsy who were prescribed 3 or more distinct antiseizure medications in past 2 years	Patients with an order for referral to a comprehensive epilepsy care center, who had a discussion of evaluation at a comprehensive epilepsy care center, OR who received treatment at a comprehensive epilepsy care center during the measurement period.	None
Quality of Life Assessment for Patients with Epilepsy	Patients aged 4 years and older diagnosed with epilepsy	Patients with age-appropriate condition-specific quality of life assessed at least once in the measurement period.	Patients who are unable or decline to complete the instrument and for these patients, a caregiver is not present to provide a proxy report.
Quality of Life Outcome for Patients with Epilepsy	Patients aged 18 years and older diagnosed with epilepsy who had 2 office visits during the 2-year measurement period, which occurred at least 4 weeks apart	Patients whose most recent QOLIE-10-P score is maintained or improved from the previous QOLIE-10-P score obtained in the measurement period.	None
Depression and Anxiety Screening for Patients with Epilepsy	Patients age 12 and older diagnosed with epilepsy	Patients with epilepsy who were screened for both depression and anxiety at every office visit.	<ul style="list-style-type: none"> • Patients who are unable or decline to complete the epilepsy-specific screening tool • Patient has a diagnosis of depression or anxiety on the active problem list.
Seizure Frequency for Patients with Epilepsy	All visits for patients with a diagnosis of epilepsy	Patient visits with current seizure frequency documented for each seizure type.	<ul style="list-style-type: none"> • Caregiver is unavailable for a patient who is noncommunicative or has an intellectual disability. • Patient or caregiver declines to report seizure frequency.

Reference

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