Understandably, a great deal of attention in clinical epilepsyology is focused on the management of patients with treatment-resistant epilepsy. However, the potential impact of epilepsy and treatment on the other two-thirds of patients with epilepsy who are well controlled is not necessarily trivial. For patients who have been seizure free for extended periods of time, adverse drug effects can pose a significant clinical conundrum for both the patient and the physician. The situation largely boils down to a blackjack scenario: 1) do you “stay” on the current anti-epileptic drug(s) (AEDs) and manage the adverse effects as well as possible; 2) do you take a “hit” and switch to an alternative AED to try and maintain seizure freedom without the adverse effects; or 3) do you “fold” on AEDs altogether and taper off the medication to see if seizure freedom is maintained without further treatment.

Complications from longstanding treatment with some AEDs are well described, but relatively few studies exist to establish the risks of tapering AEDs in medically managed seizure-free adults (1–5). A systematic meta-analysis has identified a relapse rate of 29% (5), whereas the prospective studies have identified relapse rates of 27 to 52 percent (1–4).

Literature reviews on this topic have occurred in the past (6–8), and the relative safety of withdrawal of AEDs in the setting of 2 or more years of seizure freedom has been reported. The Italian League Against Epilepsy published guidelines recommending “antiepileptic treatment might be discontinued after a minimum of two years of seizure freedom” (8).

The Q-PULSE panel comprising 146 epilepsy experts from level-4 epilepsy centers in the United States (9) was asked to answer a series of questions about this topic based on the following clinical scenario. “A 50-year-old gentleman presents with a history of focal epilepsy with seizure onset in his 20s, has been on phenytoin monotherapy for over 2 decades, and has been seizure free for the past 12 years. His recent bone density testing shows him to be more than 2 SD below the age- and sex-adjusted normative results. His most recent MRI and EEG (from within the last year) studies are normal”.

A total of 99 panelists responded. Given the scenario above, 49 (50%) said other factors would have to be considered before a decision could be made, 2 (2%) would continue the patient on phenytoin, 18 (18%) would transition to an alternative medication, and 30 (30%) would discontinue medications. The other factors to be considered are summarized in Figure 1. The 18 physicians who said they would transition to an alternative medication were asked to choose up to three medications they would consider. The top three choices were levetiracetam (33%), lamotrigine (16%), and lacosamide (17%).

The scenario was modified for the next question, which asked if the approach would be the same if the patient had an abnormal EEG with focal slowing but no epileptiform abnormalities. The majority (80%) would not change their original response; but 20 changed their response, with 1 choosing to discontinue medications altogether, and 18 (a total of 36 of the 99 respondents including those that kept the same response) choosing to transition to a new medication (one respondent abstained).

The next questions asked respondents whether they had ever experienced negative consequences (a catastrophic result) following discontinuation of a medication. The majority of respondents reported that they had purposes of answering this question that you have counseled him on the risks and benefits of all approaches, and he wishes to follow your recommendation.

Stay, Hit, or Fold? What Do You Do If the Treatment May Be as Bad as the Problem—Results of a Q-PULSE Survey

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FIGURE 1. On what factor(s) does it depend? Note that respondents could choose more than one answer. Total respondents: 47/49.
witnessed a significant bad outcome following withdrawal of anti-epileptic treatment (Figure 2). The majority of those with a catastrophic outcome (69%) reported that it had "a little" impact on how they managed later patients with similar circumstances (Figure 3). Respondents were asked to comment on the nature of the catastrophic response (through free text), and the response categories are shown in Figure 4. Using the anonymous individualized response data, the responses to the initial question were analyzed based upon whether or not a catastrophic occurrence had been reported in the past (Table). Utilizing the $\chi^2$ statistic, a significant difference was seen between those with, versus those without, a previous catastrophic occurrence ($p = 0.03$), with a higher percentage of respondents with a history of a negative outcome choosing either "it depends" or to transition to an alternative AED.

In the fairly common scenario presented here, the initial action for the near majority of Q-PULSE respondents was to evaluate additional information before making a decision. In the Italian guidelines, EEG abnormalities, a known etiology, older age at onset, and focal seizures were identified as potential predictors of a higher likelihood of relapse (8). Among those who would act without additional information, very few respondents (2%) chose to remain on the AED to which the adverse reaction was attributed, and nearly twice as many elected to do a trial off of the AED versus immediately transitioning to an alternative medication. The variability in clinical approach and the large number of clinicians that required additional information in the decision-making process highlight the need for a multi-center study aimed at assessing if and when (as well as how) to taper patients with extended periods of seizure freedom off of medications.

This Q-PULSE panel is meant to stir discussion—what would you do in this scenario? We hope to continue this discussion as part of the new American Epilepsy Society (AES) Web site.

References

### Table. Responses to the Original Case Scenario Based Upon Whether a Catastrophic Occurrence Had Been Reported in the Past*

<table>
<thead>
<tr>
<th>It Depends</th>
<th>Continue PHT or New AED</th>
<th>Discontinue PHT</th>
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<tr>
<td>Catastrophic occurrence</td>
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<td>14</td>
</tr>
<tr>
<td>No catastrophic occurrence</td>
<td>17</td>
<td>6</td>
</tr>
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</table>

Abbreviations: PHT, phenytoin.

Total respondents: 99.
Instructions
The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. The form is in four parts.

1. Identifying information.
   Enter your full name. If you are NOT the main contributing author, please check the box “no” and enter the name of the main contributing author in the space that appears. Provide the requested manuscript information.

2. The work under consideration for publication.
   This section asks for information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The requested information is about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. Checking “No” means that you did the work without receiving any financial support from any third party – that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds with which to pay you. If you or your institution received funds from a third party to support the work, such as a government granting agency, charitable foundation or commercial sponsor, check “Yes”. Then complete the appropriate boxes to indicate the type of support and whether the payment went to you, or to your institution, or both.

3. Relevant financial activities outside the submitted work.
   This section asks about your financial relationships with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. For example, if your article is about testing an epidermal growth factor receptor (DGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer.

   Report all sources of revenue paid (or promised to be paid) directly to you or your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. Please note that your interactions with the work’s sponsor that are outside the submitted work should also be listed here. If there is any question, it is usually better to disclose a relationship than not to do so.

   For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to be affected financially by the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as government agencies, charitable foundations or academic institutions, need not be disclosed. For example, if a government agency sponsored a study in which you have been involved and drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Other relationships
   Use this section to report other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work.
American Epilepsy Society

Epilepsy Currents Journal

Disclosure of Potential Conflicts of Interest

Section #1 Identifying Information

1. Today's Date: 11/12/2014

2. First Name Chad  Last Name Carlson  Degree MD

3. Are you the Main Assigned Author?  ☒ Yes  ☐ No

   If no, enter your name as co-author:

4. Manuscript/Article Title: Stay, Hit, or Fold? What do you do if the treatment may be as bad as the problem – results of a Q-PULSE Survey.

5. Journal Issue you are submitting for: 14.6

Section #2 The Work Under Consideration for Publication

Did you or your institution at any time receive payment or services from a third party for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Complete each row by checking “No” or providing the requested information. If you have more than one relationship just add rows to this table.

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<th>Money to Your Institution*</th>
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* This means money that your institution received for your efforts on this study.

** Use this section to provide any needed explanation.
Section #3 Relevant financial activities outside the submitted work.
Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. Use one line for each entity; add as many lines as you need by clicking the “Add” box. You should report relationships that were present during the 36 months prior to submission.

Complete each row by checking “No” or providing the requested information. If you have more than one relationship just add rows to this table.

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* This means money that your institution received for your efforts.
** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

Section #4 Other relationships
Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

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☐ Yes, the following relationships/conditions/circumstances are present:

Chad Carlson, MD

Thank you for your assistance.
Epilepsy Currents Editorial Board