Multiple steps and prerequisites may cause delay and variability in the recognition and treatment of febrile seizures and febrile status epilepticus. Among the challenges are identification of patients at risk of febrile convulsive status and detection of febrile seizures and febrile status epilepticus. If symptoms are noted by nonmedical personnel, including parents or caretakers, seizures and febrile status epilepticus need to ideally be recognized as such. Families either need to bring the patient to medical attention or may need access to acute treatment options and need to know how to apply treatment, and then contact medical providers to determine further work-up and care as indicated. Medical service providers, be it emergency medical services (EMS), emergency department (ED), primary care, or neurologist, may need to have febrile status rescue medications available and need to be able to give initial treatment, recognize treatment failure, and escalate treatment when initial interventions are not effective.

Seizure Detection and Recognition
While the percentage of parents who do not bring their children with febrile status epilepticus to medical attention for prolonged periods of time may be minimal, there are occasional families who elect to wait. Deterrents and distractors from medical care may vary, including limited awareness of acuity and emergency, access to emergency care, long wait times, or relatively more urgent competing family tasks among others. Mutual collaboration to provide children with better access and families in need with better education of this emergency is crucial. Cardiologists and stroke specialists have demonstrated that time to treatment in myocardial infarct patients (“Time is muscle”) or stroke patients (“Time is brain”) can be improved. This education may also include education regarding varying seizure symptoms and interventions. Despite best intentions and counseling though, seizure onset may occur unwitnessed. To date, there are no clear guidelines regarding the role of novel seizure detection tools, baby monitors, actigraphy sensors, movement sensors, smart clothing, or cameras and other devices detecting seizures, while some of these techniques may benefit patients at risk, allowing easier detection by parents or medical care providers (1).
Febrile Status Epilepticus: Time Is of the Essence

rescue medications, and the indication, type, and route of administration may continue to spark debates. Even if prescribed, medications may not be readily available at the time of the seizure, or families may remain hesitant to give medications. While our perception of “benign” in febrile seizures and febrile status epilepticus shifts, use of rescue medication regimens likely lags behind this perception.

Decision to Treat and Decision to Escalate Treatment
Parents, caretakers, or EMS may decide not to treat because “it is just another brief febrile seizure.” Many febrile status epilepticus episodes present with recurrent convulsive seizures, and not continuous convulsive movements, thereby making it very difficult for bystanders to determine whether a seizure cluster ended, or whether the patient is in-between two convulsive seizures, or may be in nonconvulsive status, and responsiveness may be impaired in all three situations. Additionally, there may be motor movements that are not seizures. At this point, essentially all patients undergoing cardiac resuscitation also undergo minimal EKG lead placement, frequently even in the ambulance. Acute EEG recordings in the setting, despite greater availability of easily placed caps and electrode systems that could at least in part guide treatment, are currently not routinely performed. Remote EEG reading capability and monitoring may make this more feasible. Additionally, electrophysiological recordings and analysis techniques may now provide further insight into whether seizures self-terminate or continue (2), possibly providing additional information regarding treatment choices.

Identification of Patients at Risk
Improving acute seizure care also includes assessing risk prior to the event. With the advent of new biomarkers, be it electrophysiological, proteonomic, or genetic, we may hopefully be able to better identify patients who are more prone to febrile and prolonged seizures. A family history inquiring about familial febrile seizures may open additional genetic testing avenues at this point. Patients at higher risk may require different monitoring, treatment, and prevention strategies than the general population.

Syndi Seinfeld and the FEBSTAT study group set a milestone by providing first benchmarks in febrile status epilepticus, highlighting current acute care practices in pediatric patients with febrile seizures, indicating longer treatment times and greater care variability than some would expect. A common treatment algorithm as suggested by the authors is the first important step to potentially reduce intractability and minimize the percentage of prolonged seizures, in addition to a potential multifactorial intervention at the above-listed febrile status epilepticus prevention, detection, and treatment decision points. The authors show that late-treated seizures lasted longer. While a certain degree of confounding cannot be ruled out, it is conceivable that seizures may be easier to control if treated early. The implications for patients and families, albeit not yet fully known, such as decreased medication application and potentially shortened or no hospital stays, likely fewer complications, improved quality of life, decreased psychological and financial burden on caretakers, and overall decreased cost, make it worthwhile to rethink our current practice. Allow me to not enter the debate over whether seizures beget seizures and cause long-term structural and functional damage, but this thought deserves further mention in the future, considering other findings from the FEBSTAT study team indicating structural hippocampal changes (3). Similar to radiation exposure, there may ultimately not be a safe minimal duration of exposure to febrile seizures and status in susceptible patients. While “time is of the essence” refers to material damage in contract law, it is also conceivable that time to treatment may also be scrutinized by the medicolegal profession.

Raising More Questions
The article raises more questions than answers and is therefore brilliant and thought-provoking at the same time: How do we recognize seizure onset? How do we identify patients at risk? What is our patient and medical care provider education strategy? What is our work-up and treatment algorithm, considering abundant benzodiazepine treatment choices (lorazepam, diazepam, midazolam, clonazepam, clobazam, and chlorazepate, among others) and administration options (intramuscular, rectal, intranasal, sublingual, and intravenous/intraosseous), in addition to other frequently used medications? Who should be allowed to treat and when should treatment be escalated? Which patients are “over-treated”? When do patients need an EEG, a lumbar puncture, or further neuroimaging? Can spot-check EEGs help in the acute care? Do we track time to treatment consistently, and do we monitor outcomes and follow our patients? In whom does febrile status beget febrile status or epilepsy or psychological deficits? What is the psychosocial burden on patients and families? What are the costs for the healthcare system and for society?

Time Is of the Essence
While the FEBSTAT study team may be able to address some of these questions in the near future, other questions may require further investigation. Insurance providers are moving to bundled care reimbursements, and the reduction of medical care interventions in patient groups may soon provide additional financial incentives for healthcare systems to reduce medical expenses. While some of these measures, such as readmission rates, cannot easily be applied to neurologic conditions and febrile seizures or febrile status epilepticus, time to treatment and adherence to treatment paradigms may be measurable. While some may argue that there is not enough time or funds to do this work beyond FEBSTAT at this point, solutions may include putting some responsibility on caretakers. Electronic tools and improved electronic data capture may at some point fulfill the promise of saving time, research data collection, decision support, and improved care. Hopes are that federal funding organizations, institutions and foundations will renew their commitment to these urgent implementation tasks. Some providers and healthcare systems are also working together and delay almost inevitable reduction of expenses by dedicating funds to care improvement during a specified transition time window. But this time window is closing fast, and in a push to evaluate and implement care changes of febrile status epilepticus, and
to improve and to shorten treatment initiation, there is no
time to waste.

by Tobias Loddenkemper, MD

References
1. Ramgopal S, Thome-Souza S, Jackson M, Kadish NE, Sanchez
Fernandez J, Klehm J, Bosl W, Reinsberger C, Schachter S,
Loddenkemper T. Seizure detection, seizure prediction, and
closed-loop warning systems in epilepsy. Epilepsy Behav. 2014
2. Kramer MA, Truccolo W, Eden UT, Lepage KQ, Hochberg LR,
Eskandar EN, Madsen JR, Lee JW, Maheshwari A, Halgren E, Chu
CJ, Cash SS. Human seizures self-terminate across spatial scales
21121.
3. Lewis DV, Shinnar S, Hesdorffer DC, Bagiella E, Bello JA, Chan S, Xu
Y, MacFail J, Gomes WA, Moshé SL, Mathern GW, Pellock JM, Nordli
DR Jr, Frank LM, Provenzale J, Shinnar RC, Epstein LG, Masur D,
Litherland C, Sun S; FEBSTAT Study Team. Hippocampal sclerosis
after febrile status epilepticus: The FEBSTAT study. Ann Neurol
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.
Section #1 Identifying Information

1. Today’s Date: 11/13/14

2. First Name  Tobias  Last Name Loddenkemper  Degree MD

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

   If no, enter your name as co-author:

4. Manuscript/Article Title:

5. Journal Issue you are submitting for:

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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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* 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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<td>No money paid for board membership</td>
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<td>8. Patents (planned, pending or issued)</td>
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<td>10. Payment for development of educational presentations</td>
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<td>11. Stock/stock options</td>
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12. Travel/accommodations/meeting expenses unrelated to activities listed.**
   Academic speaking at academic societies AES, AAN, ACNS, CNS, grand rounds

13. Other (err on the side of full disclosure)
   American Epilepsy Society, the Epilepsy Foundation of America, the Epilepsy Therapy Project, PCORI, the Pediatric Epilepsy Research Foundation, Cure, Danny-Did Foundation, HHV-6 Foundation, Lundbeck, Eisai and Upsher-Smith.
   Research grant funding

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☐ No other relationships/conditions/circumstances that present a potential conflict of interest.
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Tobias Loddenkemper serves on the Laboratory Accreditation Board for Long Term (Epilepsy and Intensive Care Unit) Monitoring, on the Council of the American Clinical Neurophysiology Society, on the American Board of Clinical Neurophysiology, as an Associate Editor for Seizure, as Contributing Editor for Epilepsy Currents, and as an Associate Editor for the Treatment of Epilepsy 6th edition. He performs video electroencephalogram long-term monitoring, electroencephalograms, and other electrophysiological studies at Boston Children's Hospital and bills for these procedures and he evaluates pediatric neurology patients and bills for clinical care. He is part of pending patent applications to detect seizures and to diagnose epilepsy. He may hold health care stocks within retirement funds. He receives research support from the American Epilepsy Society, the Epilepsy Foundation of America, the Epilepsy Therapy Project, PCORI, the Pediatric Epilepsy Research Foundation, Cure, Danny-Did Foundation, HHV-6 Foundation, Lundbeck, Eisai and Upsher-Smith. His wife, Karen Stannard, MD, is a practicing pediatric neurologist who evaluates pediatric neurology patients and bills for clinical care and neurophysiological studies. He has received speaking honorariums from national societies including the AAN, AES and ACNS, and for grand rounds at various academic centers.

Of the listed work, AES/EFA funding and Upsher Smith research funding has the potential to overlap as the work is related to status epilepticus, but overlap/mention was avoided while writing the article. Therefore, none of the listed relationships should interfere.

Thank you for your assistance.

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