Sir,

We thank Dr Grillo for his comments. A growing body of evidence from in vitro studies, animal models, observational studies in critically ill neonates, children and adults supports the hypothesis that electrographic seizures independently contribute to brain injury, whether they are clinically evident or not (Holmes, 2014). However, the relative contribution of seizures to brain injury clearly depends on the underlying aetiology (Hahn and Jette, 2013). In our recent study, the association between seizure burden and outcome was stronger among children with acute seizures and systemic disease than among those with acute brain injury. Therefore, aggressive treatment to reduce seizure burden may be harder to justify among children with acute brain injury. However, even modest improvements in outcome, if sustained, may represent a substantial lifetime benefit to the child, their family and society. Treatment decisions should always be individualized, balancing the potential benefits of reducing seizure burden against the potentially serious complications of antiepileptic drug therapy, particularly when infusions of anaesthetic therapies are being considered.

Clinical trials are urgently needed to address the unanswered question of whether more aggressive seizure treatment can improve outcomes among patients with electrographic seizures of varying aetiologies. Interventional studies on this topic pose ethical and logistical challenges. Current evidence for an association between seizure burden and outcome is a threat to the clinical equipoise required for any trial that proposes to randomize patients to more versus less aggressive seizure treatment. Obtaining informed consent from substitute decision makers with the timeliness required to initiate prompt anti-epileptic drug therapy is difficult. A promising alternative to a classical randomized controlled trial is a comparative effectiveness design, which harnesses the inherent variability of current treatment practice both within and among institutions.

Access to continuous EEG monitoring remains a challenge in both resource-rich and resource-poor settings. Several clinical and EEG factors predictive of seizures among critically ill newborns, children, and adults have been identified (Claassen et al., 2004; McCoy et al., 2011; Abend et al., 2013; Glass et al., 2014), which facilitate allocation of scarce EEG monitoring resources to those most likely to benefit.

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**References**


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