Author's response to reviews

Title: The Vermont Oxford Neonatal Encephalopathy Registry: rationale, methods, and initial results

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Cover Letter

The proposed manuscript represents the rationale, methodology, initial demographic results, and discussion for the Vermont Oxford Network Neonatal Encephalopathy Registry. A previous report detailing solely the rationale, protocol, and analytic plans for our registry was submitted to BMC Pediatrics in 2010 (MS: 3366550613421648). After review of the Registry, the reviewers suggested that our report contain initial demographic results.

Another manuscript is submitted March 5, 2012 to address changes suggested by the editorial team:

The editors have requested confirmation that informed consent was obtained for patient information to be accessed for the study. The Registry has been reviewed and approved by the IRB at the University of Vermont. Additionally, each participating hospital submits the project to their local IRBs for review and each participating site is required to submit a letter of IRB approval from before participation in the Registry.

The editors have also requested confirmation that each infant’s parents’ consent was obtained prior to inclusion in the study. We are unable to make this requested. Consent from the parents of the infants in the VON NER is not sought. All data are de-identified prior to submission and as such identification of parents is not possible. However, as outlined above, institutional consent is obtained from each participating hospital / medical center. The Registry does not dictate patient care, propose any interventions, or endorse any protocols for treatment. Each infant receives care according to the standards of that institution. There is no risk for participation of individual. Since there is no additional risk for individual patients, and only de-identified data are submitted to the Registry, individual patient consent is not required.

The editors have requested a ‘Competing interests’ section which is now included.

The editors have requested that the ‘Authors’ Contributions and Acknowledgements’ section to conform to your formatting requirements. This has been amended as per your request.

Another manuscript is submitted March 7, 2012 to address changes suggested by the editorial team:

The editors have requested a statement in the manuscript detailing that ethical approval was obtained for the particular study detailed in this report, and name the relevant review board, with reference number if applicable. A statement is now included detailing that the University of
Vermont and State Agricultural College Committee on Human Research in the Medical Sciences (CHRMS) Institutional Review Board (IRB) at the University of Vermont granted ethical approval for the methods of the NER (reference number CHRMS 06-100).

Neonatal Encephalopathy is a poorly characterized condition affecting term and late preterm infants that carries a significant risk of death and neurodevelopmental disability. The optimal routine care of these infants is unknown. Recent randomized controlled trials have demonstrated that mild therapeutic hypothermia initiated shortly after birth reduces death and disability for a subset of these infants affected by hypoxic-ischemic injury. Both the National Institute of Child Health and Human Development (NICHD) and the American Academy of Pediatrics (AAP) recommend that if therapeutic hypothermia is implemented outside of a trial, clinicians should follow published trial protocols, ensure systematic follow-up of survivors, and submit patient data to registries.

The Vermont Oxford Network established a Registry for Neonatal Encephalopathy that began enrolling patients in 2006. The Registry currently enrolls newborn infants with encephalopathy and those treated with hypothermia to identify their demographic characteristics, associated perinatal antecedent factors, medical treatments and patterns of care, co-morbidities, and outcomes. Registry participation has been robust, surpassing the randomized trials in terms of numbers infants enrolled. Therefore, it may be the best representation of the care afforded to encephalopathic infants in the “real world” and represent a generalizable view of hypothermia as it occurs outside the academic sector or in a research setting.

We are able to demonstrate gaps between what the evidence from trials shows and what is actually done in practice. Further, we are able to identify variations in the care for treated infants and identify factors associated with differences in survival or adverse events. The registry method is well suited to identify opportunities for improvement in the care of infants affected by neonatal encephalopathy and study interventions such as hypothermia as they are implemented in clinical practice.

This report documents the rationale, methods, and the demographic results of the initial five years of the Registry. Several additional reports detailing affected infant’s antecedent risk factors, seizures and anticonvulsant use, optimal neuromonitoring and imaging use, and the use of hypothermia as it disseminates into routine use are in preparation. These data will be used to define clinical research questions and identify opportunities for improved care.