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# Developmental trajectories of children with birth asphyxia through 36 months of age in low/low-middle income countries



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#### ABSTRACT

*Background:* Resuscitation following birth asphyxia reduces mortality, but may be argued to increase risk for neurodevelopmental disability in survivors.

*Aims:* To test the hypothesis that development of infants who received resuscitation following birth asphyxia is not significantly different through 36 months of age from infants who had healthy births.

*Study design:* Prospective observational cohort design comparing infants exposed to birth asphyxia with resuscitation or healthy birth.

*Subjects:* A random sample of infants with birth asphyxia who received bag-and-mask resuscitation was selected from birth records in selected communities in 3 countries. Exclusion criteria: birth weight < 1500 g, severely abnormal neurological examination at 7 days, mother < 15 years, unable to participate, or not expected to remain in the target area. A random sample of healthy-birth infants (no resuscitation, normal neurological exam) was also selected. Eligible = 438, consented = 407, and  $\geq 1$  valid developmental assessment during the first 36 months = 376.

*Outcome measure(s)*: Bayley Scales of Infant Development-II Mental (MDI) and Psychomotor (PDI) Development Index.

*Results*: Trajectories of MDI (p = .069) and PDI (p = .143) over 3 yearly assessments did not differ between children with birth asphyxia and healthy-birth children. Rather there was a trend for birth asphyxia children to improve more than healthy-birth children.

*Conclusions:* The large majority of infants who are treated with resuscitation and survived birth asphyxia can be expected to evidence normal development at least until age 3. The risk for neurodevelopmental disability should not justify the restriction of effective therapies for birth asphyxia.

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#### 1. Introduction

Of the approximately one million neonatal deaths due to birth asphyxia, or failure to initiate or sustain spontaneous breathing at birth, about 98% occur in low/low-middle income countries (LMIC) [1]. Another one million children who survive birth asphyxia develop neurodevelopmental disorders, which can include learning disability, intellectual disability, and cerebral palsy [2–4]. As a result, 41 million disability adjusted life years (DALYs) are attributed to birth asphyxia

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[5]. Birth asphyxia is therefore among the leading causes of mortality and morbidity in LMIC.

Resuscitation is required to establish normal breathing when asphyxia occurs at birth. About 6–10% of all neonates need some assistance to establish normal breathing [6–8]. Neonatal resuscitation could decrease neonatal mortality or morbidity an estimated 42% in LMIC [9]. If indicated, resuscitation can be applied to almost all newborn infants, including in poor areas of the world, with stimulation and bag and mask ventilation [10,11]. However, neonatal resuscitation training has had limited penetration in many LMIC despite findings that when implemented mortality decreases by 20%–50% [7,12,13].

The concern that infants with birth asphyxia who were resuscitated may be at increased risk for neurodevelopmental impairments may

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contribute to the reduced implementation of resuscitation interventions [4] Survivors with disability would add to the burden of care in resource poor countries and decrease quality of life of these children in subsequent years. Therefore it is important empirically to examine the development of children with birth asphyxia who were treated with resuscitation in LMIC. Results could inform health policy decisions regarding neonatal interventions for birth asphyxia.

We had the opportunity to conduct such an examination using data collected from a multi-national controlled study (FIRST BREATH Trial) in which community birth attendants were trained in bag and mask ventilation with room air as part of essential newborn care training [14]. This intervention reduced 7-day neonatal mortality as well as mortality due to birth asphyxia [15]. Two subgroups of infants from the FIRST BREATH Trial were then followed as part of the randomized controlled trial (RCT) Brain Research to Ameliorate Impaired Neurodevelopment-Home-based Intervention Trial (BRAIN-HIT), including one group with birth asphyxia and resuscitation. As detailed elsewhere [16,17], BRAIN-HIT was designed to determine if a home-based early developmental intervention (EDI) can improve neurodevelopmental outcome compared to a control condition. Indeed, EDI was shown to improve

development at 36 months of age compared to the control condition in both resuscitated and not resuscitated children [16].

In the present study we do not evaluate the RCT. Rather we observe the development of infants exposed to birth asphyxia and resuscitation compared to infants without birth asphyxia and resuscitation, regardless of assigned intervention condition. Moreover, because developmental status was evaluated yearly through 36 months of age, developmental trajectories could be examined in relation to exposure to birth asphyxia and resuscitation, and not just status at the 36 month end point. The current study tests the hypothesis that infants who received resuscitation due to birth asphyxia (without severe encephalopathy during the neonatal period) and those who had healthy births and were not resuscitated would evidence developmental trajectories over the first 36 months that are *not* significantly different from one another.

#### 2. Methods

#### 2.1. Study population

This study was implemented in two populations born from January 2007 through June 2008 in rural communities marked by poverty in



Fig. 1. Participant flow chart of screening, randomization, and completion of developmental assessments, resulting in analysis sample.

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