

# Cost Analysis of Treating Neonatal Hypoglycemia with Dextrose Gel

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**Objective** To evaluate the costs of using dextrose gel as a primary treatment for neonatal hypoglycemia in the first 48 hours after birth compared with standard care.

**Study design** We used a decision tree to model overall costs, including those specific to hypoglycemia monitoring and treatment and those related to the infant's length of stay in the postnatal ward or neonatal intensive care unit, comparing the use of dextrose gel for treatment of neonatal hypoglycemia with placebo, using data from the Sugar Babies randomized trial. Sensitivity analyses assessed the impact of dextrose gel cost, neonatal intensive care cost, cesarean delivery rate, and costs of glucose monitoring.

**Results** In the primary analysis, treating neonatal hypoglycemia using dextrose gel had an overall cost of NZ\$6863.81 and standard care (placebo) cost NZ\$8178.25; a saving of NZ\$1314.44 per infant treated. Sensitivity analyses showed that dextrose gel remained cost saving with wide variations in dextrose gel costs, neonatal intensive care unit costs, cesarean delivery rates, and costs of monitoring.

**Conclusions** Use of buccal dextrose gel reduces hospital costs for management of neonatal hypoglycemia. Because it is also noninvasive, well tolerated, safe, and associated with improved breastfeeding, buccal dextrose gel should be routinely used for initial treatment of neonatal hypoglycemia. (*J Pediatr* 2018;■■■:■■-■■■).

**Trial Registration** Australian New Zealand Clinical Trials Registry: ACTRN12608000623392.

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Neonatal hypoglycemia is a metabolic condition that occurs in approximately 5%-15% of healthy infants, and up to 50% in those with risk factors.<sup>1</sup> It is widespread in developing countries, where access to resources for treatment or monitoring may be limited.<sup>2,3</sup> Neonatal hypoglycemia is frequently asymptomatic and even in the absence of symptoms can be associated with brain injury and poor neurodevelopmental outcomes,<sup>4,5</sup> including cognitive impairment, sensory disability, developmental delay, cerebral palsy, and seizures.<sup>6</sup> Direct costs attributable to the acute management of neonatal hypoglycemia can be large, particularly if the infant is admitted to the neonatal intensive care unit (NICU). Although prompt, early treatment that effectively maintains the blood glucose concentrations >47 mg/dL (2.6 mmol/L) is associated with an absence of developmental impairment at 2 years of age,<sup>7</sup> hypoglycemia may be associated with delays in aspects of development that do not manifest until later, such as executive function and visual-motor performance at 4.5 years<sup>8</sup> and literacy and mathematics achievement at 10 years.<sup>9</sup> Thus, long-term financial and societal costs may accrue from the requirement for ongoing management and support if initial treatment is inadequate, or if covert disease is missed or diagnosed late.

Initial management of neonatal hypoglycemia focuses on increased blood glucose concentration monitoring and the administration of supplemental carbohydrate, traditionally by increased feeding. Admission to NICU for intravenous dextrose is indicated if oral feeding is not tolerated or if the infant does not respond adequately to initial therapy. Both supplemental oral and intravenous administration of carbohydrate may interrupt initiation of breastfeeding,<sup>10</sup> and the latter may also result in separation of the mother and infant.<sup>11</sup> More recently, dextrose gel has been shown to be well tolerated as a treatment for neonatal hypoglycemia in the first 48 hours after birth, and resulted in fewer instances of treatment failure and fewer admissions to the neonatal intensive care unit for hypoglycemia, than feeding alone.<sup>12</sup> However, the overall costs of dextrose gel treatment vs other treatments for neonatal hypoglycemia have not been calculated.

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\*List of additional members of the Children with Hypoglycemia and Their Later Development (CHYLD) Study Team is available at [www.jpeds.com](http://www.jpeds.com) (Appendix).

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NICU Neonatal intensive care unit  
WIESNZ New Zealand Ministry of Health's Weighted Inlier Equivalent Separations

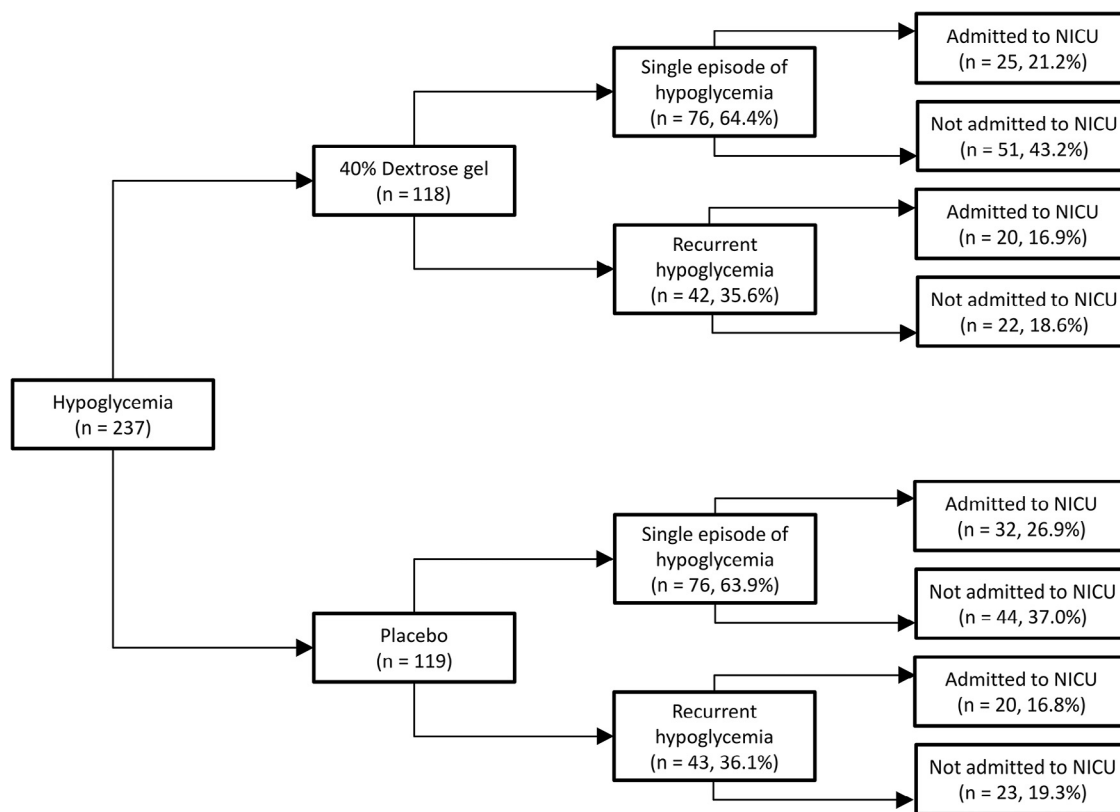
We undertook a cost analysis using a decision tree, comparing the use of dextrose gel for treatment of neonatal hypoglycemia with placebo, with a time horizon limited to the duration of the infants' postnatal hospital stay.

## Methods

A decision tree model was constructed that covered the initial postnatal hospital stay using raw data from the Sugar Babies Study (Australian New Zealand Clinical Trials Registry: ACTRN12608000623392).<sup>12</sup> The Sugar Babies Study was a randomized, double-blind trial comparing 40% dextrose gel with placebo for the treatment of neonatal hypoglycemia in the first 48 hours after birth. Participants were infants at risk of neonatal hypoglycemia (infant of a mother with diabetes, late preterm (35 or 36 weeks of gestation), small (birthweight <2500 g or <10th centile) or large (birthweight >4500 g or >90th centile) or with other risk factors such as poor feeding). Infants who developed hypoglycemia were randomized to a treatment pack containing syringes of either 40% dextrose gel or 2% carboxymethyl cellulose placebo. Of 514 infants enrolled, 242 became hypoglycemic and were randomized, 119 to placebo gel and 118 to dextrose gel. Gel administration (0.5 mL/kg rubbed into the buccal mucosa) was followed by a feed, and, if feeding was poor, infants received supplemental expressed breastmilk or formula. Thus, the comparison

between dextrose and placebo gel groups is effectively a comparison between treatment with dextrose gel and treatment solely with increased feeding. If the infant remained hypoglycemic 30 minutes after treatment, or if hypoglycemia recurred at a later time, the trial protocol allowed for further gel administration from the allocated pack, up to a total of 6 doses over 48 hours. Recurrent hypoglycemia was defined as an infant having a further episode of hypoglycemia after successful treatment, within 48 hours after birth.<sup>12</sup> The primary outcome of treatment failure (blood glucose concentration <47 mg/dL (2.6 mmol/L) after 2 treatment attempts) was observed less frequently in the dextrose gel group (relative risk 0.57, 95% CIs 0.33-0.98,  $P = .04$ ).<sup>12</sup> Infants who met the criteria for treatment failure were then treated according to local clinical protocols, which could include administration of formula, open label dextrose gel and admission to NICU for intravenous dextrose.

For this cost analysis, infants who developed neonatal hypoglycemia were allocated into 8 groups, based on whether they were randomized to receive dextrose gel or placebo, whether their hypoglycemia was a single episode or recurrent, and whether they were admitted to NICU or not, regardless of the reason for admission (Figure). A decision tree modeling approach was selected as each clinical event or disease state forming the branches of the tree are either present or absent, are mutually exclusive at each node in the tree, and occur relatively closely together.<sup>13</sup> The evaluation was undertaken from



**Figure.** Decision tree for treatment of neonatal hypoglycemia.

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