Dose Calculation:

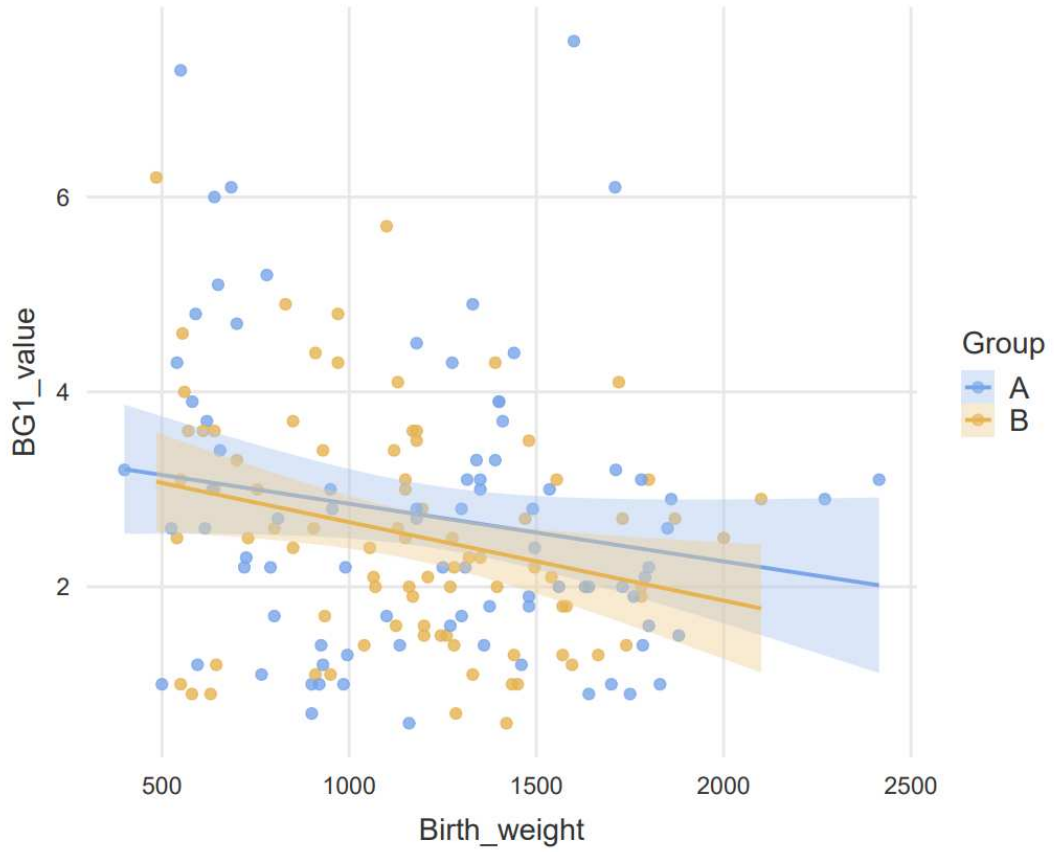
The dose of 40% dextrose gel dose (ml) was decided based upon a need to provide enough exogenous energy (glucose) during the period from birth, through transfer from the delivery suite to the NICU, and until successful intravenous cannula insertion (local data: median 48 mins postnatal age, IQR 15 mins). The literature shows that appropriate for gestational age preterm infants have a glucose oxidation rate (GOR) of 6-8mg/kg/min [1,2]. Estimated birth weights, using the 'INTERGROWTH-21st International Newborn Size References for Very Preterm Infants' [3], necessitated dextrose 40% gel volumes ranging between 0.5ml - 1.4ml (range 24+0/40 to 32+0/40 weeks gestation) to provide enough energy for this early postnatal period. For procedural simplicity (while also providing the appropriate energy requirements), it was decided to stratify this very preterm group into two sub-cohorts, each with a different dose of gel: for newborns ≤ 29+0 weeks GA a total dose of 0.5ml of gel was administered; for newborns ≥ 29+1 weeks GA a total dose of 1ml of gel was administered.

Secondary outcomes – Definitions:

Secondary outcomes included the following: hypoglycaemia <2.6 mmol/L at the time of first intravenous access in the NICU; buccal gel spillage; further hypoglycaemia <1.8 mmol/L (after initial intravenous access but within first 24 hours after birth); further hypoglycaemia <2.6 mmol/L (after initial intravenous access but within first 24 hours after birth); number of episodes of hypoglycaemia <2.6 mmol/L within first 24hrs after birth; need for rescue intravenous dextrose fluids (2ml/kg dextrose 10%) within first 24hrs after birth; hyperglycaemia >10 mmol/L within first 24hrs after birth; death within 12 hours after birth; death prior to discharge home or transfer to another hospital; necrotizing enterocolitis (defined as per Vermont Oxford Network [4]); focal intestinal perforation (defined as per Vermont Oxford Network [4]); early bacterial sepsis and/or meningitis (defined as a positive bacterial

growth in either blood and/or cerebrospinal fluid anytime during first 3 days after birth); intraventricular-germinal matrix haemorrhage (highest grade of IVH from any cranial ultrasound up to postnatal day 28); symptomatic hypoglycaemia, defined by (1) Presence of characteristic clinical manifestations (tremor, lethargy, coma, seizures) (2) coincident with low plasma glucose concentrations measured accurately with sensitive and precise methods, and (3) that the clinical signs resolve within minutes to hours once normoglycaemia has been re-established; retinopathy of prematurity (requiring either anti-VEGF injections or laser therapy); cystic periventricular leukomalacia (defined as per Vermont Oxford Network [4]).

Scatter plot – Admission blood glucose versus birth weight:



Supplemental Figure 1- Scatter plot of admission blood glucose (mmol/L) versus birth weight (grams) (A = control group, B = dextrose group)

Conditional Power:

We calculated the conditional power using the equations in Kundu et al. 2024 [5] (Kundu et al. 2024: binary endpoint, two-arm trial, *Equation 4.7*). The rejection criteria at final analysis used the O'Brien Fleming alpha spending function (two-sided alpha = 0.0492, for final analysis). Conservatively, we assumed that the post-interim trend would be different from the interim result (i.e., we used the original -11% effect) which resulted in a conditional power of 47%. Should we have presumed that the post-interim trend was no different to the interim result, then

the conditional power would have been significantly lower at 2% (Kundu et al. 2024: binary endpoint, two-arm trial, *Equation 4.8* [5]).

Supplemental References:

1 Mesotten D, Joosten K, van Kempen A, *et al.* ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: Carbohydrates. *Clinical nutrition (Edinburgh, Scotland)*. 2018;37:2337–43. doi: 10.1016/j.clnu.2018.06.947

2 Sauer PJ, Van Aerde JE, Pencharz PB, *et al.* Glucose oxidation rates in newborn infants measured with indirect calorimetry and [U-13C]glucose. *Clinical science (London, England : 1979)*. 1986;70:587–93.

3 Villar J, Giuliani F, Fenton TR, *et al.* INTERGROWTH-21st very preterm size at birth reference charts. *Lancet (London, England)*. 2016;387:844–5. doi: 10.1016/s0140-6736(16)00384-6

4 Vermont Oxford Network. Manual of Operations, Part 2, Release 25.0. Vermont Oxford Network. 2021. https://vtoxford.zendesk.com/hc/en-us/articles/360056768093-2021-Manual-of-Operations-Part-2-Release-25-0-PDF (accessed 26 January 2024)

5 Kundu MG, Samanta S, Mondal S. Review of calculation of conditional power, predictive power and probability of success in clinical trials with continuous, binary and time-to-event endpoints. *Health Serv Outcomes Res Method*. 2024;24:14–45. doi: 10.1007/s10742-023-00302-5