

# **Summary Protocol**

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### **Research Question**

To evaluate whether nutritional supplementation with a nutrient blend containing long-chain polyunsaturated fatty acids (LCPUFAs), choline, uridine-5'-monophosphate (UMP), and cytidine-5'-monophosphate (CMP) plus usual care from birth to 12 months post estimated date of delivery (EDD) improves cognitive development at 24 months post EDD, compared to infants receiving a matched control supplement plus usual care (comparator).

# **Trial eligibility**

The trial population are two clearly defined groups:

- All infants born less than 28 weeks of gestation (can be consented up to 3 months post EDD) (preterm)
- All infants born at 35 weeks of gestation or more, receiving therapeutic hypothermia for hypoxic ischaemic encephalopathy (can be consented up to EDD plus 28 days) (HIE)

### **Trial design**

Multicentre blinded randomised placebo-controlled trial of 1,010 infants in approx. 40 UK NHS tertiary neonatal units; 538 infants in the preterm group and 472 infants in the HIE group.

### **Trial Intervention**

Infants will be randomised as soon as possible after consent is obtained, using a 1:1 allocation ratio, to either:

- Active supplement: Micronutrient breast milk/formula milk/food supplement of LCPUFAs, choline, UMP, and CMP, or
- Matched placebo supplement, contains fractions of the active components in the investigational product and no UMP and CMP

Powder supplement is added daily to usual milk feed (breast or formula) on the neonatal unit when infants reach full milk feeds (approx. 120–150ml/kg/day). Supplementation administered on discharge and given by parents at home until 12 months post EDD.

# **Primary outcome**

Non-verbal cognitive scale standardised score of the Parent Report of Children's Abilities-Revised (PARCA-R) questionnaire (parent report) at 24 months post EDD.

#### Secondary outcomes

- Neurodevelopmental outcomes at 24 months post EDD:
  - Language scale standardised score of Parent Report of Children's Abilities-Revised (PARCA-R)
  - Emotional, conduct, hyperactivity and peer problems scale scores and prosocial scale scores of the Strengths and Difficulties Questionnaire (SDQ)
  - Motor Skills using the fine and gross motor scales score of the Ages and Stages Questionnaire (ASQ-3)
- NHS data at discharge and 24 months post EDD for health care received and health conditions diagnosed (for example necrotising enterocolitis, sepsis, chronic lung disease, post discharge hospitalisations, overweight and obesity)
- BMI, weight and head circumference at 24 months post EDD
- · Safety of supplementation throughout the intervention phase
- · Parental adherence to supplementation throughout the intervention phase
- Maternal acceptability of supplementation at 6 and 12 months post EDD
- Bespoke Health Economic questionnaire at 6, 12, 18 and 24 months post EDD
- Parental health-related quality of life using the EuroQol EQ-5D-5L questionnaire at randomisation, 6, 12, 18 and 24 months post EDD
- Supplement tolerance questionnaire (IGSQ-13) at neonatal unit, 3, 6, 12 months post EDD

Number of participants required:	1,010	Number of centres:	40
Planned recruitment start and end dates:	January 2022 to May 2024		
Funding source:	NIHR Health Technology Assessment (HTA) Programme		

#### Flow chart: The DOLFIN Randomised Controlled Trial



DOLFIN flow chart v4.0 26.09.23

# **DOLFIN Contact details**

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