DOLFIN

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NHS The Newcastle upon Tyne Hospitals NHS Foundation Trust

NPEU Clinical Trials Unit

OXFORD POPULATION HEALTH NPEU

By DOLFIN team

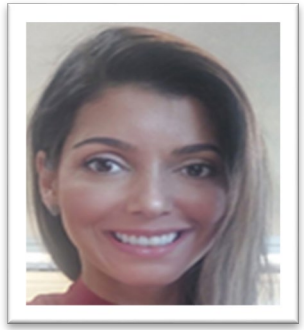
Developmental Outcomes of Long-term Feed Supplementation in Neonates - The DOLFIN randomised controlled trial

DOLFIN TRIAL TEAM

Prof Jeremy Parr
Chief Investigator

Dr Morag Andrew
Co-Chief Investigator

Usharani Wahengbam
Trial Manager



Adriana Francisco
Research Nurse

Hayley Acton
Data Co-ordinator

DOLFIN LOCAL TEAM

Principal Investigator	**Co-Principal Investigator**	**Lead Research Nurse**

✓ *Please include here relevant information from your site*

BACKGROUND

DOLPHIN pilot (2009 to 2013) in 3 UK Neonatal Units

Aim

To investigate whether a micronutrient supplement containing long-chain fatty acids improves neurodevelopment in neonates at risk for neurodevelopmental impairment.

Method

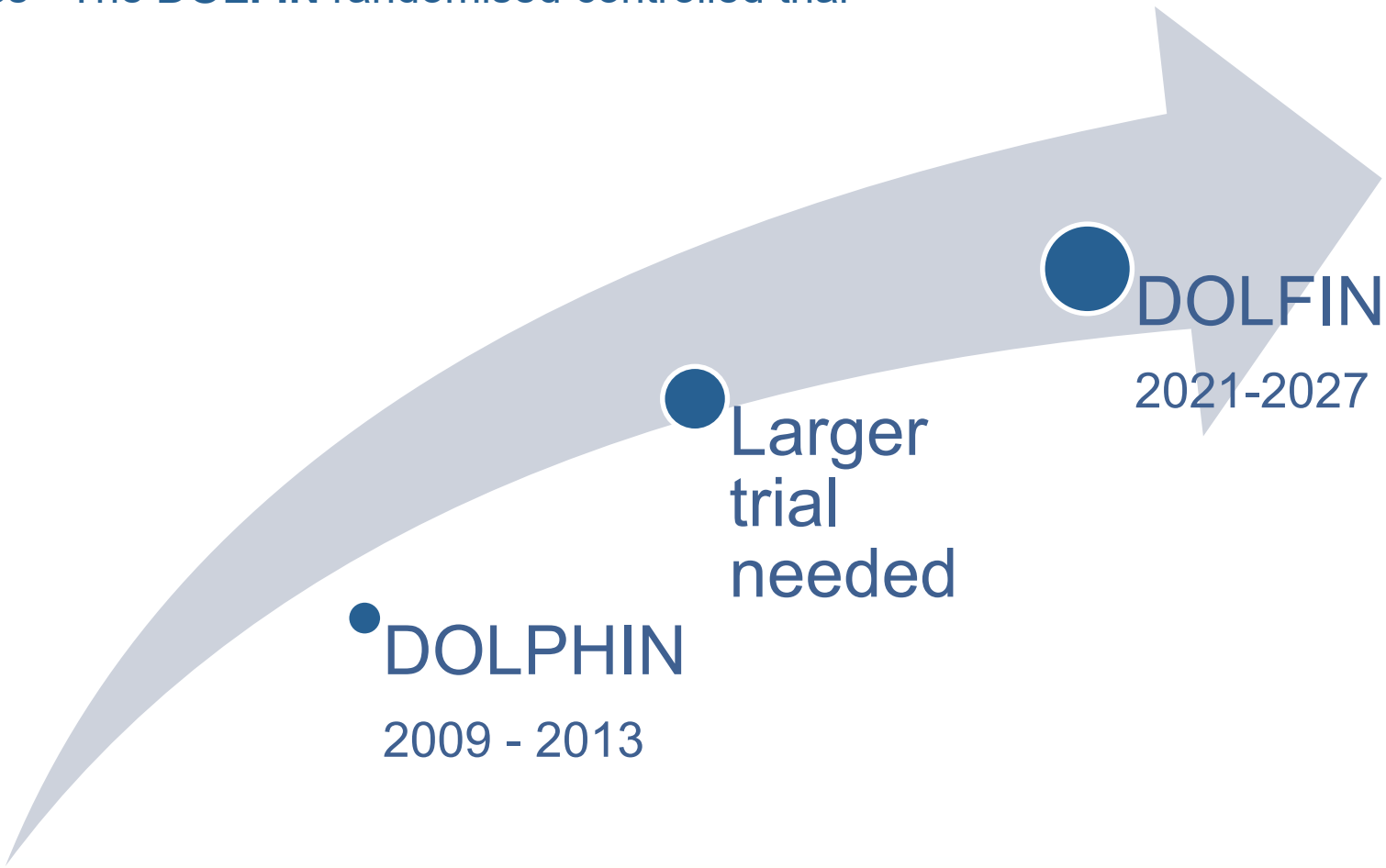
- 62 neonates recruited
- 59 neonates randomised (HIE and preterm)
- 53 neonates started supplementation
- 29 assigned supplement; 24 completed follow up
- 30 were assigned the placebo; 21 completed follow up.

Results

- **Higher mean cognitive scale scores BSID-III**
- **Higher mean language scale scores BSID-III**
- No difference between groups in mean motor scale scores
- Parental reports of neurodevelopmental outcomes showed similar results

DOLPHIN TO DOLFIN

Developmental **O**utcome of **L**ong Term **F**eed Supplementation **i**n **N**eonates - The **DOLFIN** randomised controlled trial



PRIMARY AIM

To evaluate **whether nutritional supplementation** with a nutrient blend LCPUFAs, UMP, CMP **plus usual care from birth to 12 months** post EDD **improves cognitive development at 24 months** post EDD, **compared to** infants receiving a matched **control supplement plus usual care** for:

(1) infants born <28 weeks of gestation (who can be randomised up to 3 months post EDD).

(2) infants born at ≥ 35 weeks of gestation receiving therapeutic hypothermia for HIE (who can be randomised up to EDD plus 28 days).

SECONDARY AIM

To evaluate **whether nutritional supplementation** with a nutrient blend containing LCPUFAs, choline, UMP and CMP **plus usual care from birth to 12 months post EDD alters** the following **outcomes compared** to infants receiving a **matched control supplement plus usual care.**

- **Neurodevelopmental outcomes: language, motor, emotional, conduct, hyperactivity/inattention, peer relationship problems and prosocial behavior at 24 months post EDD.**
- **Infant growth, clinical outcomes, safety, infant tolerability, parental acceptability, maternal quality of life to 24 months post EDD.**
- **Health Economics outcomes**

PRIMARY OUTCOMES

At 24 months post EDD

Non-verbal Cognitive Scale Standardized Score PARCA-R

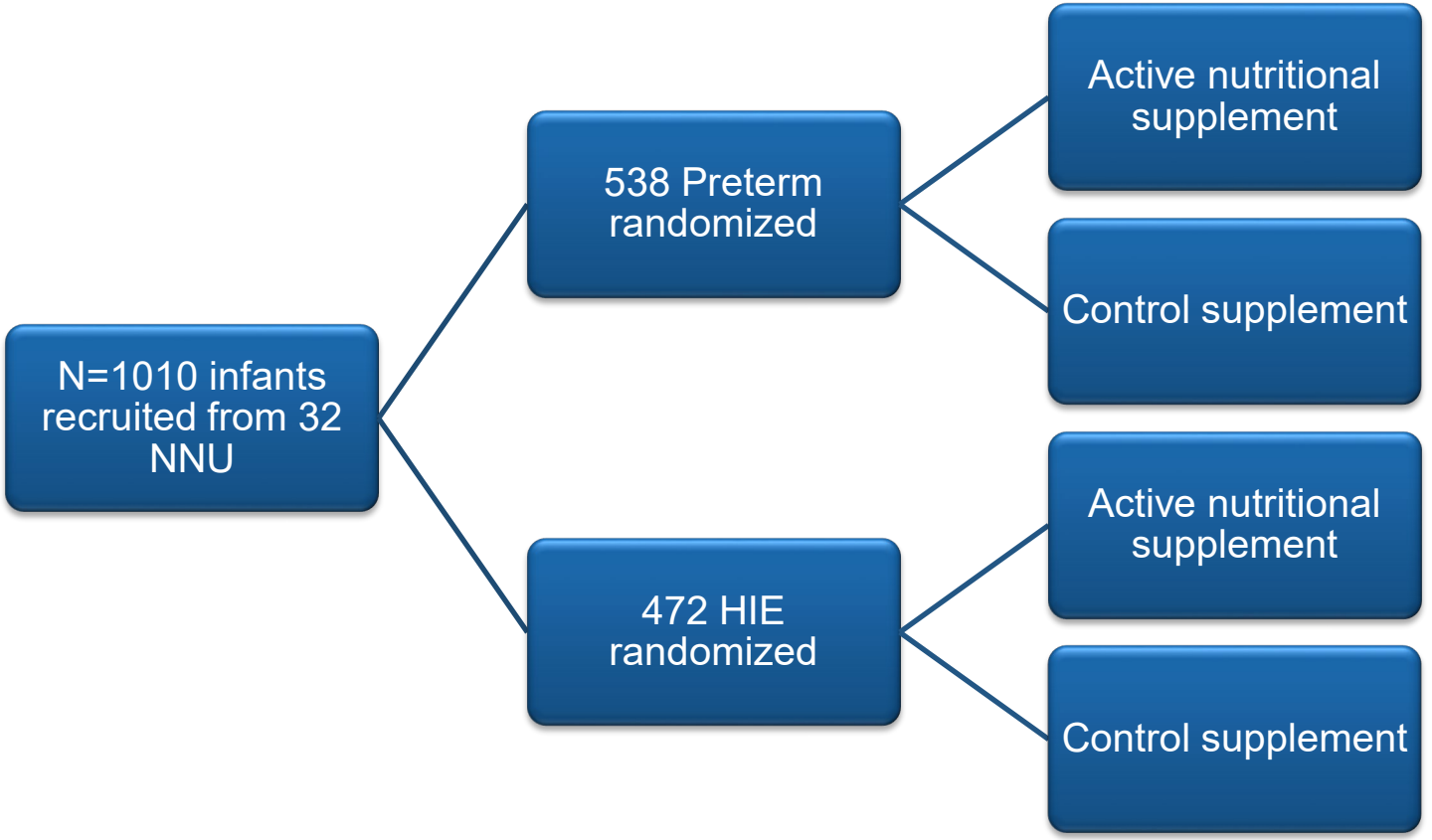
SECONDARY OUTCOMES

At 24 months post EDD (UNLESS OTHERWISE STATED)

- BMI, weight, head circumference
- Language Scale Standardized Score PARCA-R
- Parent acceptability of supplementation (6 and 12 months)
- Safety of supplementation (throughout the intervention phase)
- Motor skills (fine and gross motor scales scores) ASQ-3
- Emotional, conduct, hyperactivity, and peer problems scale scores and prosocial scores SDQ
- NHS data at discharge and 24 months post EDD - health received/diagnosed conditions (NEC, sepsis, CLD, post-discharge hospitalizations, overweight, obesity)

STUDY DESIGN

Multicentre, blinded, stratified, randomized, placebo-controlled trial with economic evaluation



INCLUSION CRITERIA

- ✓ Individual with parental responsibility able to give consent
- ✓ Parents able to comply with the protocol
- ✓ Infants likely to tolerate full enteral feeds
- ✓ Infant has realistic prospect of survival beyond discharge
- ✓ Preterm infants born <28 weeks gestational (can be consented up to 3 months post-EDD)
- ✓ HIE infants born at 35+ weeks gestational age receiving therapeutic hypothermia for HIE (can be consented up to EDD plus 28 days)

EXCLUSION CRITERIA

- ✓ Infants with middle cerebral artery infarcts
- ✓ Infants with major congenital brain malformation, or genetic condition with abnormal brain development
- ✓ Infants with galactosaemia
- ✓ Infants receiving all feeds via jejunal tube, who do not receive any gastric or oral feeds

TRIAL INTERVENTION

Active nutritional supplement

- ✓ Micronutrient breast milk/formula milk/food active supplement powder
- ✓ Contains LCPUFAs, choline, UMP, and CMP
- ✓ Supplied by Nutricia
- ✓ Delivered to sites and parents' homes by IPS
- ✓ Quality and safety tested at the factory
- ✓ Supplied in 13g sachets
- ✓ No Nutricia branding on sachets or trial materials
- ✓ Will be added daily to usual feed (breast/formula/ weaning foods)

OR

Control supplement

- ✓ Similar levels of fat and comparable energy content
- ✓ Contains fractions of the active components in the investigational product and no UMP or CMP
- ✓ Identically packaged
- ✓ Quality and safety tested at the factory
- ✓ Supplied in 13g sachets
- ✓ Delivered to sites and parents' homes by IPS
- ✓ No Nutricia branding on sachets or trial materials
- ✓ Will be added daily to usual feed (breast/formula/ weaning foods)

TRIAL FLOW

SCREENING

- Clinical trial team screen infants admitted to NNU.
- Co-recruitment to other trials is permitted, except for intervention trials with neurodevelopment as primary outcome.

CONSENT

- In-person or remote
- Obtained from parents with legal responsibilities
- **Preterm infants:** remotely in hospital/CCS **prior to discharge home**
- **HIE:** remotely either in hospital/CCS or **post-discharge home**

RANDOMISATION

- ASAP after consent
- Preterm infants: randomized from NNU/CCS or up to 3 months post-EDD prior discharge home
- HIE infants: randomized up to EDD + 28 days. May occur pre-NNU/CCS discharge or post-discharge home
- Allocation ratio: 1:1

TRIAL FLOW

SUPPLEMENTATION

- **INFANTS MUST HAVE REACHED FULL FEED MILK BEFORE STARTING SUPPLEMENT**
- Supplementation lasts 12 months post-EDD
- **Daily basis**

FOLLOW-UP

- Electronic communication to prompt parents to complete and return questionnaires
- 3 , 6, 12, 18 and 24 months post EDD
- Paper copies of the questionnaires.
- Adherence questionnaire completed via APP

DIVERSITY AND INCLUSIVITY

Easy Read PIL and Supplement Leaflets

- Easy Read documents can be offered to families to support participation
- Families must be able to meet post-discharge requirements: (e.g. questionnaires, supplement dosing, adherence reporting); parents must consent using main PIL.


DOLFIN

Parent Information Leaflet

easy read

This Easy Read document has been written in partnership with Sunderland People First. It is an Easy Read version of the DOLFIN Parent Information Leaflet

Sunderland People First
A Voice For Change

The Newcastle upon Tyne Hospitals NHS Foundation Trust | NIHR National Institute for Health and Care Research | NPEU Clinical Trials Unit | Oxford Population Health NPEU


WHY HAVE I BEEN INVITED TO TAKE PART?

You have been invited to take part because you are the parent of a baby who was born early or had difficulties around birth.

Babies born early or who have difficulties around birth have a higher risk of child development problems.

WHAT WILL I HAVE TO DO IF I DECIDE TO TAKE PART?

You will be asked to give the supplement to your baby daily for one year after their original due date.

We will ask you to fill out a questionnaire:
- when your baby joins the study
- when your baby leaves hospital
- at 3, 6, 12, 18 and 24 months after your baby's original due date.

We can send you the questionnaire by text or email. Or you can fill in a paper form. You can choose.

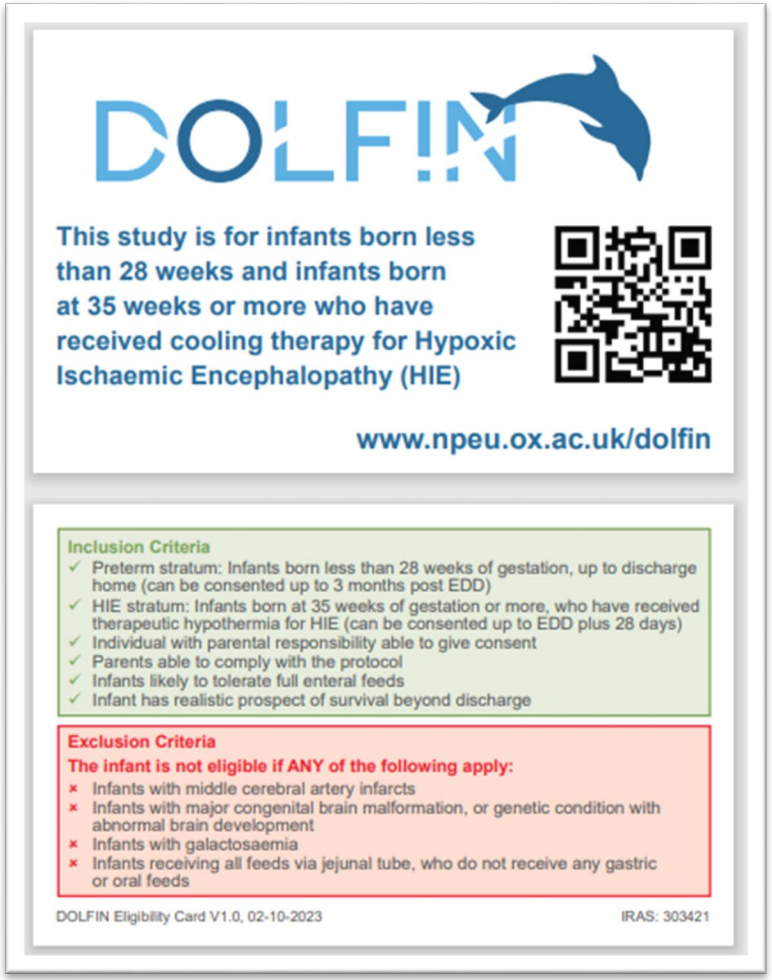

DOLFIN

Parent Information for Supplement Use

easy read

This Easy Read document has been written in partnership with Sunderland People First. It is an Easy Read version of the DOLFIN Supplement Leaflet

PROMOTIONAL ITEMS



Thank you

DOLFIN Study Team Contact details:

NPEU Clinical Trials Unit
University of Oxford
Old Road Campus
Headington
Oxford OX3 7LF

Tel: 01865 617919
Email: dolfin@npeu.ox.ac.uk
Website: www.npeu.ox.ac.uk/dolfin