Health Research Authority

FULL/LONG TITLE OF THE STUDY

Nutritional status of children undergoing treatment for Acute Lymphoblastic Leukaemia: Longitudinal observational study

SHORT STUDY TITLE / ACRONYM

Nutritional status of children undergoing treatment for ALL

PROTOCOL VERSION NUMBER AND DATE

V1 01/01/2024

RESEARCH REFERENCE NUMBERS: ISRCTN13488607

IRAS Number:	**334875**
SPONSORS Number:	23SH18
FUNDERS Number:	

Body Composition and Nutritional Status of Children Undergoing Treatment for Acute Lymphoblastic Leukaemia (ALL)

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the study publically available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor:

Signature:
.....

Date:
...../...../.....

Name (please print):
.....

Position:
.....

Chief Investigator:

Signature:
.....

Date:
...../...../.....

Name: (please print):
.....

Body Composition and Nutritional Status of Children Undergoing Treatment for Acute Lymphoblastic Leukaemia (ALL)

LIST of CONTENTS

Body Composition and Nutritional Status of Children Undergoing Treatment for Acute Lymphoblastic Leukaemia (ALL)

KEY STUDY CONTACTS

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Sponsor	Great Ormond Street Hospital for Children Division of Research & Innovation | Joint R&D Office for GOSH/ICH I UCL Great Ormond Street Institute of Child Health | 30 Guilford Street I London, WC1N 1EH www.gosh.nhs.uk/research-and-innovation research.goverance@gosh.nhs.uk
Joint-sponsor(s)/co-sponsor(s)	NA
Funder(s)	King Abdulaziz University ADDRESS Abdullah Sulayman, Al Ja'amah Dist., Jeddah, Saudi Arabia PHONE NUMBER 02-6952000 02-6400000 FAX02-6952437
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Body Composition and Nutritional Status of Children Undergoing Treatment for Acute Lymphoblastic Leukaemia (ALL)

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Committees	

STUDY SUMMARY

Study Title	Nutritional status of children undergoing treatment for Acute Lymphoblastic Leukaemia
Internal ref. no. (or short title)	Nutritional status of children undergoing treatment for Acute Lymphoblastic Leukaemia
Study Design	Longitudinal prospective observational
Study Participants	Children diagnosed Acute Lymphoblastic Leukaemia
Planned Size of Sample (if applicable)	75
Follow up duration (if applicable)	NA
Planned Study Period	3 years
Research Question/Aim(s)	Observe the pathophysiological impact of Acute Lymphoblastic Leukaemia treatment on the development of sarcopenic obesity in children

Body Composition and Nutritional Status of Children Undergoing Treatment for Acute Lymphoblastic Leukaemia (ALL)

FUNDING AND SUPPORT IN KIND

FUNDER(S) (Names and contact details of ALL organisations providing funding and/or support in kind for this study)	**FINANCIAL AND NON FINANCIALSUPPORT GIVEN**
King Abdulaziz University	

ROLE OF STUDY SPONSOR AND FUNDER

The sponsor (GOSH) will have overall responsibility for the initiation and management of the study,

The protocol explicitly outlines the roles and responsibilities of the sponsor(s) and any funder(s) in study design, conduct, data analysis and interpretation, manuscript writing, and dissemination of results.

ROLES AND RESPONSIBILITIES OF STUDY MANAGEMENT COMMITEES/GROUPS & INDIVIDUALS

Study Steering Groups

PhD Supervisory Team

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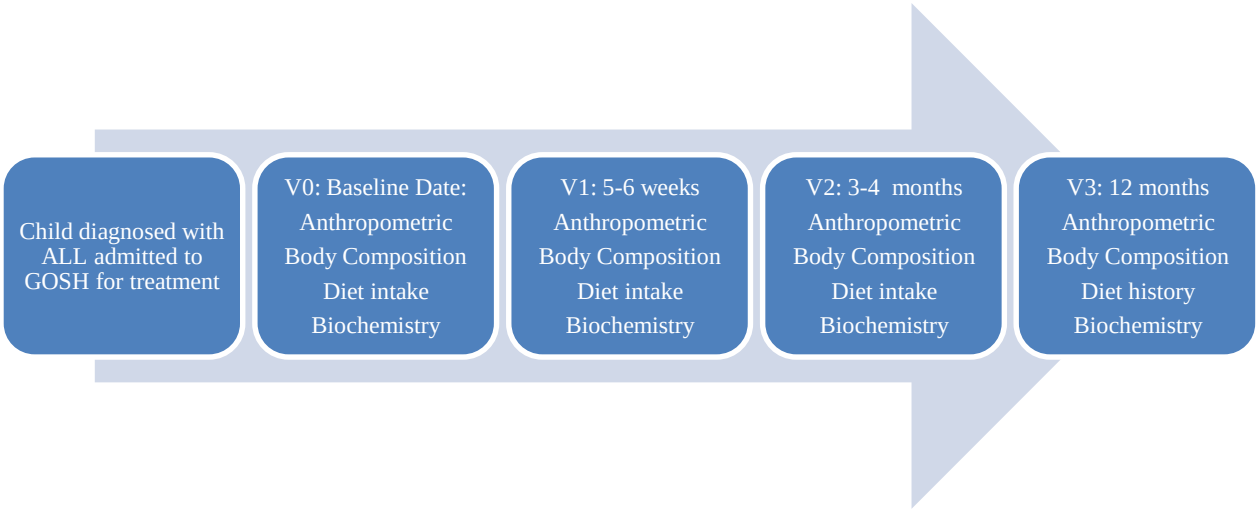
Body Composition and Nutritional Status of Children Undergoing Treatment for Acute Lymphoblastic Leukaemia (ALL)

PROTOCOL CONTRIBUTORS

Dr Graeme O'Connor – lead contributor

KEY WORDS: Children; Acute Lymphoblastic Leukaemia; body composition, sarcopenic obesity

STUDY FLOW CHART



Body Composition and Nutritional Status of Children Undergoing Treatment for Acute Lymphoblastic Leukaemia (ALL)

STUDY PROTOCOL

Nutritional status of children undergoing treatment for Acute Lymphoblastic Leukaemia: Longitudinal observational study

1 BACKGROUND

Acute lymphoblastic leukaemia (ALL) is a malignant transformation and proliferation of lymphoid progenitor cells in the bone marrow, blood and extramedullary sites. Dose intensification strategies have led to a significant improvement in outcomes for paediatric patients, contemporary childhood ALL studies have shown improved 5-year overall survival (OS) rates exceeding 90% (Pieters et al., 2016). The treatment process is classified into phases.

- 1A Remission-induction therapy: consisting corticosteroids, vincristine, and asparaginase administered over 4-6 weeks and induces complete remission in approximately 98% of paediatric patients.
- 1B Consolidation (intensification) therapy 4 to 8 weeks, consisting of cyclophosphamide, cytarabine, and mercaptopurine.
- Interim maintenance. This phase aims to destroy any leukemic cells left in your child's marrow or blood. This phase lasts about 8 weeks.
- Delayed intensification phase: 8 weeks. This phase is important because it can improve a child's event-free survival, which is the period after treatment in which a patient does not experience cancer symptoms or recurrence
- maintenance therapy: Each cycle of maintenance lasts for 84 days. Cycles are repeated until the duration of therapy from the start of interim maintenance is 2 years

Although the 5-year survival rate has significantly increased with improved intensive therapies, many of these survivors experience long-term adverse sequelae of their disease and its treatment. Three-in-four survivors of childhood ALL are at risk of developing chronic diseases such as obesity, type 2 diabetes, and cardiovascular diseases (Wang et al., 2020). Of note, overweight and obesity in ALL is an important prognostic indicator for relapse risk (Gelelete et al., 2011). Corticosteroids are key in the treatment of ALL, and although dexamethasone appears to have benefits in treating ALL, several studies have shown that dexamethasone is more toxic than is prednisolone and that it can cause significantly greater weight gain in ALL (Labar et al., 2010). An increase in weight is seen immediately after the start of Corticosteroids, which are known to be critically involved in regulating energy intake, storage, and mobilization(Zhang et al., 2015). Four days of dexamethasone treatment

significantly increased energy intake, including excessive saturated fat and salt intake, and changed eating behaviour in children with ALL.(Warris et al., 2017)

Preventing early onset of obesity is a priority for improving the care and outcomes for patients with paediatric ALL (Zhang et al., 2015). Children with ALL experience unhealthy weight gain early in treatment and increases in weight are maintained beyond treatment completion (Corella Aznar et al., 2020). A meta-analysis demonstrated a significant increase in mean BMI z-score during treatment in 1,514 patients with paediatric ALL. Importantly, the meta-analysis suggested that patients with paediatric ALL did not return to their pre-treatment weight and were consistently more overweight or obese than their peers beyond treatment completion. (Zhang and Parsons, 2015)

Sarcopenic obesity is an emerging clinical entity characterized by excessive fat mass in the presence of reduced muscle mass (Zembura and Matusik, 2022). Emerging evidence suggests muscle depletion predicts survival of patients with cancer (Martin et al., 2013). Alterations in body composition seen in ALL related sarcopenic obesity carry a burden of morbidity and early mortality (Marriott et al., 2018; Ness et al., 2013). However, the literature predominately focuses on BMI Z-score, BMI underestimates obese childhood leukaemia survivors in comparison with bioelectrical impedance analysis and therefore BMI use could misclassify obese survivors as non-obese (Corella Aznar et al., 2020). Much less attention has been paid to the loss of fat free mass and especially its major component, skeletal muscle mass, which leads to sarcopenia in patients with cancer and contributes to the phenomenon of frailty that has been described in young adult survivors of ALL (Marriott et al., 2018).

Bioelectrical impedance analysis (BIA) is a validated, non-invasive method for assessing body composition (Khalil et al., 2014). It measures the opposition to an alternating current passing through body compartments (resistance) and the delay in conduction by membranes (reactance). BIA uses these measurements to estimate the contribution of various tissues to the (segmental) body weight accurately and provides markers for cellular integrity (phase angle). Bioelectrical impedance analysis-derived phase angle has been gaining attention in the clinical evaluation of nutritional status because it is thought to be a proxy of water distribution and body cell mass; it is also associated to muscle strength and is an effective predictor of different clinical outcomes (Di Vincenzo et al., 2021).

However, body composition changes have not been measured in this cohort. Future studies must include detailed measurements of adiposity such as %Fat Mass and clinical and radiological measures of visceral adiposity (Wang et al., 2020). Furthermore, previous studies focused on the

outcome of now-outdated treatment regimens or have used only simple methods to define body-composition changes (Hunger and Mullighan, 2015).

Total energy expenditure is the amount of energy that individuals use daily (Goran, 2000). The most important contributor to energy expenditure is resting energy expenditure, which is defined as the energy required to maintain physiological homeostasis while fasting and accounts for 50-70% of total energy expenditure (Chima et al., 2020). The other main contributors to energy expenditure are physical activity, linear growth and thermic effects of food intake and digestion (Hall et al., 2012). In individuals with and without obesity, fat-free mass is the most important contributor to resting energy expenditure, accounting for approximately 60-80% of the variation in resting energy expenditure (Browning and Evans, 2015). ALL related sarcopenic obesity manifests due to an increase in fat mass, decrease in skeletal muscle mass which will in turn reduce resting energy expenditure, all culminating in wight gain and increasing the risk of obesity and therefore increasing the risk of ALL relapse (Gelelete et al., 2011).

Concurrently to these pathophysiological changes, lifestyle factors also contribute to obesity in childhood ALL survivors including sedentary behaviours with increased screen time (Ramírez-Coronel et al., 2023). These children may also experience reduced physical activity during and after treatment due to skeletal abnormalities, neuromuscular impairment, reduced cardiopulmonary capacity, fatigue, and imbalance (Coombs et al., 2020). Therefore, lifestyle interventions that aim to alter obesogenic behaviours hold significant promise as a strategy to reduce, delay, or prevent cardiometabolic disorders. Nutritional and behavioural interventions during dexamethasone treatment are recommended to stimulate a healthy lifestyle (Warris et al., 2017).

A systematic review that assessed the effectiveness lifestyle interventions in ALL survivors was unable to draw meaningful conclusions due to a paucity of studies, and the heterogeneity of the studies (Cohen et al., 2016) Future studies should address the best approach to consider nutritional status in their management. (Galati et al., 2022) Although there is low quality evidence for the improvement in health behaviours using health behaviour change interventions, there remains no evidence as to whether this translates into an improvement in dietary intake. There was also no evidence that the studies reduced the risk of cardiovascular and metabolic disorders in childhood cancer survivors, although no evidence of effect is not the same as evidence of no effect. This review highlights the need for further well-designed trials to be implemented in this population (Cohen et al., 2016).

Body Composition and Nutritional Status of Children Undergoing Treatment for Acute Lymphoblastic Leukaemia (ALL)

4 RESEARCH QUESTION/AIM(S)

4.1 Objectives

Research Questions

1. In which period of treatment do changes in body size, body composition, resting energy expenditure and lipidaemia arise?

2. Which factors contribute to those physiological changes in body size, body composition, resting energy expenditure and lipidaemia?

- Measure body composition (fat mass and fat free mass) changes throughout ALL treatment using 4-lead bioelectrical impedance assessment.
- Monitor changes in the nutritional intake using 4-day food diaries throughout the treatment of ALL in children. Compare with changes in body composition
- Review routine bloods for standard clinical monitoring-
- Review routine bloods for standard clinical monitoring Lipid profile (triglycerides/ cholesterol ratio) throughout the treatment of ALL. Compare with changes in body composition and nutritional intake

4.2 Outcome

Aim: observe the pathophysiological impact of ALL treatment on the development of sarcopenic obesity

5 STUDY DESIGN and METHODS of DATA COLLECTION AND DATA ANALYIS

Anthropometry (data collection: T0 baseline; T1 remission induction 6 weeks; T2 Consolidation 4 months; T3 maintenance 12 months)

Weight will be determined to the nearest 0.1 kg, with subjects dressed in light clothing or ward gown among patients, using a Model 880 electronic scale (Seca, Hamburg, Germany) after voiding. Height will be measured to the nearest 0.1 cm without socks or shoes, using a Model 206 wall-mounted stadiometer (Seca). Body mass index (BMI) will calculate using the standard formula (kg m–2). Weight and height will be measured following standard procedures. Body mass index will be calculated as weight in kilograms divided by height in meters squared, and BMI SDS will be obtained from the WHO reference curves. BMI and standard deviations scores (SDS) will be calculated using WHO as reference data.

Obesity will be confirmed when the percentile is higher than 99.9th on the WHO Child Growth Standards Curve, or the z-score was higher than +3 (Cole et al., 2000). Children older than 5 years,

with BMI between the 85th and 97th percentiles on the WHO Child Growth Standards Curve, will be classified as overweight, and as obese when the percentile is higher than the 97th or the z-score is higher than +2.

Circumference (girth) measurements will also be collected, including mid-upper arm circumference (MUAC) and waist circumference, using standardised techniques to provide additional data on body composition and nutritional status.

Mid upper arm circumference (MUAC) will be measured halfway between the tip of the acromion and olecranon process using a non-stretchable measuring tape SECA 212 to the nearest 0.1 cm

Nutrition screening (Strongkids)(104) (**data collection: T0 baseline; T1 remission induction 5 weeks; T2 Consolidation 3-4 months; T3 maintenance 12 months)**

Participants' nutritional status will be assessed using the STrongkids screening tool (see appendix), which evaluates various parameters to identify the risk of malnutrition. Based on this information, each participant's StrongKids score will be generated at every time point.

Body Composition – 4 lead bioelectro impedance (BIA) measurements: (data collection: T0 baseline; T1 remission induction 6 weeks; T2 Consolidation 4 months; T3 maintenance 12 months)

Body composition measurements will be performed with the InBody S10® (InBody Co., Ltd., Seoul, Korea). This multi-frequency, segmental impedance analyser requires height, weight, and sex as input parameters. Measurements will be performed in a seated or supine position with reusable electrodes attached to the left and right thumb and index finger and both ankles. The measurements typically take 3–5 min.

The InBody S10 uses segmental impedance and reactance at multiple frequencies to determine total body water (TBW), (segmental) extracellular water (ECW), and the individual ECW/TBW-ratio. High-frequency currents pass through the TBW, whereas low-frequency currents cannot penetrate cell membranes and flow exclusively through the ECW. Henceforth, it uses validated methods to estimate fat-free mass (FFM), (segmental) soft lean mass (SLM), mineral mass, bone mineral content (BMC), percentage body fat (PBF), visceral fat area (VFA), (segmental) skeletal muscle mass (SMM) and protein mass, in addition to several ratios.

Dietary data collection and instruments: 3 day food history diary (data collection: T0 baseline; T1 remission induction 6 weeks; T2 Consolidation 4 months; T3 maintenance 12 months)

Three-day food records will be used to assess dietary intake and enteral nutrition of children. Parents or caregivers were instructed on how to record the food and beverage consumption of their child using household measures to estimate portion sizes and food type (including brand names of foods, if applicable) in a diary provided. Dietary records will be kept for two weekdays and one weekend day. Analysis of dietary intake will be performed using Nutritics nutritional analysis software (Dublin, Republic of Ireland). Energy and nutrient intake of children will be compared against the SAGN 2017 guidelines.

Vitamin D, and lipid profile (data collection: T0 baseline; T1 remission induction 6 weeks; T2 Consolidation 4 months; T3 maintenance 12 months)

Blood cholesterol concentrations (total, low density lipoprotein and high-density lipoprotein) in plasma will be collected after age appropriate overnight fast. Blood will be centrifuged for 10 min at 1000g and 4°C to separate plasma from RBC stored at −80°C until analysed. HDL, LDL cholesterol and TG efflux capacity (CEC) will be measured by a validated ex vivo system involving the incubation of macrophages with apolipoprotein B-depleted serum from sub

Physical activity (data collection: T0 baseline; T1 remission induction 6 weeks; T2 Consolidation 4 months; T3 maintenance 12 months)

The activity diary is a reliable instrument for measuring physical activity in children, activity for 3 days of activity including a weekend day, recorded as 15 minute activity slots (Bouchard et al., 1983). Categories of activities and the formulas for energy expenditure

Categories of activities for the activity diary

1 = sleeping or resting in bed; 2 = sitting, eating, writing, etc.; 3 = standing, washing, combing, etc.; 4 = walking indoors (< 4 km/h), light home activities; 5 = walking outdoors (4–6 km/h), cleaning bedroom, easy outdoor playing; 6 = recreational sports and leisure time activities with low intensity; 7 = recreational sports and leisure time activities with moderate intensity; 8 = recreational sports and leisure time activities with high intensity; and 9 = sports competitions.

Equations to calculate energy expenditure

Rest time refers to activities that do not increase energy expenditure substantially above resting level, such as sleeping, lying down, and seated activities. These are represented by categories 1 and 2, and the energy costs are 0.98*basal metabolic rate (BMR) and 1.5*BMR, respectively. Intensity thresholds between light physical activity (LPA) and moderate to vigorous physical activity (MVPA) are around 4 metabolic equivalents of tasks25. Therefore, LPA is represented by categories 3, 4, and 5, with an

energy cost of 2.0, 2.8, and 3.3*BMR, respectively. MVPA is category 6 and higher, with an energy cost of 4.4, 6.5, 10.0, and 15.0*BMR, respectively (Ulf et al., 2011).

Other sources of data collection:

Impact of Chemotherapy

- Length of intestinal mucositis
- Length of time of parenteral (intravenous) nutrition
- Length of time on enteral nutrition including nutritional composition of formula
- Infection and antibiotic use
    - Any other significant medical event related to treatment

6 STUDY SETTING

Single centre tertiary haematology centre – Great Ormond Street Hospital.

7 SAMPLE AND RECRUITMENT

7.1 Eligibility Criteria

7.1.1 Inclusion criteria

- Consented to partake in the study
- Aged 2-16 years old
- Diagnosed with ALL and not started treatment
-

7.1.2 Exclusion criteria

- Children who had previously been treated with chemotherapy in another institution age
- <2 years old

7.2 Sampling

7.2.1 Size of sample

In our study, which explores the impact of ALL treatments on body composition and subsequent treatment outcomes, conducting formal power calculations is challenging due to limited prior data. This is particularly

true in exploratory research, where the primary goal is to generate preliminary insights rather than test specific hypotheses. To our knowledge, it is estimated that 60 new ALL admissions occur at GOSH annually. Our recruitment strategy aims to enrol around four participants monthly over 18 months. This approach is projected to yield a robust sample size of approximately 72 participants, ensuring a comprehensive data set of meaningful analyses.

7.2.2 Sampling technique

7.3 Recruitment

The researchers will attend ward rounds and view EPIC (electronic notes) each day to identify new admission with ALL Families will be identified at ward level by their dietitian a member of the patient's existing clinical care team who will check whether they meet the inclusion criteria in light of requiring enteral tube feeding for children who display signs of feed intolerance. An initial approach with a letter of invitation and a participant information sheet will be given to them explaining the study with the details of the research team to discuss the feeding options on the study

7.3.1 Sample identification

7.3.2 Consent

The study's participant information sheet will be offered to the potential participant's family member/carer accompanied by an age-appropriate information sheet describing: the study; its purpose and nature, what it will require for the participant; its risks and burdens, the propositions and limitations of the protocol; the known side effects and any risks involved in taking part. It will be clearly stated that participation is entirely voluntary, be able to make a free choice and the participant is free to withdraw from the study at any time for any reason without affecting or impacting their care, without affecting their rights, and with no requirement to justify withdrawal. This is clearly outlined in the opening paragraphs of PIS.

The participant will be allowed 3 days to consider the information, and the chance to ask any question to the Investigator. Written Informed Consent from the participant's representative will be required and then obtained and the person obtaining the consent must be appropriately qualified, experienced and authorised to do so by the Chief/Principal Investigator.

Informed Consent/Assent Process

A signed copy of the study informed consent /assent form will be given to the participant's legal representative and a copy in the participant's medical records. An original signed form will be retained at the study site in a secure place. Competent Adults (aged 16 at the time of consent)

Upon completion of the above, the patient will then sign and date the informed consent document. Both the person obtaining consent and the participant must personally sign and date the form. A copy of the informed consent document will be given to the patient for their records. The original copy will be filed in the participant's medical notes and a further copy of the signed consent form will be filed in the Investigator Site File. One copy of the consent form should be sent to the YP (aged <16 years at the time of consent) informed consent for a young person under the age of 16 years is provided by a person with parental responsibility or a legal representative.

Children aged 6 years and above will be approached for assent unless the clinical care team deem otherwise, then they will not be entered into the study until assent (in addition to legal consent from an appropriate adult) is provided – an exception to this is made where the minor expresses a wish for the decision to be made solely by the appropriate adult.

Age-appropriate REC-reviewed information Sheets and assent forms, that have been given a favourable opinion, describing (in simplified terms) the details of the study intervention, study procedures and risks will be available for use. The YP should personally write their name and date on the assent form, which is then signed by the parent/legal representative and the researcher.

Young people who were under 16 years old when treatment initially started and turn 16 years old while on the study will be re-consented.

Participants who may have difficulties in an adequate understanding of English will be supported by GOSH Trust interpretation service. 'Thebigword' is the Trust's sole supplier of telephone interpreting, a service which will enable you to help any client who may have limited English language skills. 0800 694 5093

The consent will be recorded in a patient's notes and in the study records.

8 ETHICAL AND REGULATORY CONSIDERATIONS

This protocol and related documents will be submitted for ethics review to Integrated Research Application System (IRAS) and Health Research Authority (HRA).

8.1 Assessment and management of risk

8.2 Research Ethics Committee (REC) and other Regulatory review & reports

- Before the start of the study, a favourable opinion will be sought from a REC
- Before the start of the study, approval from the Health Research Authority (HRA) and Health and Care Research Wales (HCRW) for project-based research taking place in the NHS in England and Wales will be sought.

For NHS REC reviewed research

- Substantial amendments that require review by NHS REC and HRA will not be implemented until that review is in place and other mechanisms are in place to implement at site.
- All correspondence with the REC and HRA will be retained.
- It is the Chief Investigator's responsibility to produce the annual reports as required.
- The Chief Investigator will notify the REC of the end of the study.
- An annual progress report (APR) will be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, and annually until the study is declared ended.
- If the study is ended prematurely, the Chief Investigator will notify the REC, including the reasons for the premature termination.
- Within one year after the end of the study, the Chief Investigator will submit a final report with the results, including any publications/abstracts, to the REC.

Regulatory Review & Compliance

- This is currently a single-centre study
- Before any site[s] can enrol patients into the study, the Chief Investigator/Principal Investigator or designee will ensure that appropriate approvals from participating organisations are in place.
- For any amendment to the study, the Chief Investigator or designee, in agreement with the sponsor will submit information to the appropriate body in order for them to issue approval for the amendment. The Chief Investigator or designee will work with sites (R&D departments at NHS sites as well as the study delivery team) so they can put the necessary arrangements in place to implement the amendment to confirm their support for the study as amended.

Body Composition and Nutritional Status of Children Undergoing Treatment for Acute Lymphoblastic Leukaemia (ALL)

Amendments

For studies involving the NHS:

Amendments are changes made to a research project after approval from a review body has been given.

It is the sponsor's responsibility to decide whether an amendment is substantial or non-substantial.

The sponsor must submit a valid notice of amendment to the REC / HRA for consideration if the sponsor wishes to make a substantial amendment to the REC application or the supporting documents. The REC / HRA will provide a response regarding the amendment within 35 days of receipt of the notice. It is the sponsor's responsibility to decide whether an amendment is substantial or non-substantial for the purposes of submission to the REC or HRA.

If applicable, other specialist review bodies (e.g. Confidentiality Advisory Group (CAG)) need to be notified about substantial amendments in case the amendment affects their opinion of the study.

Amendments also need to be notified to the lead NHS R&D office and communicated where applicable to the participating organisations (R&D office and local research team) departments of participating sites to assess whether the amendment affects the NHS permission for that site.

8.3 Peer review

Great Ormond Street Hospital Clinical Research Adoption Committee reviewed the research study proposal and issued their approval Oct 2023 (letter within IRAS documents)

8.4 Patient & Public Involvement

PPI will continue to be involved in all aspects of this study including:

- The acceptability of the research
- Design of the research
- Management of the research
- Undertaking the research
- Analysis of results
- Dissemination of findings

8.5 Protocol compliance

- Accidental protocol deviations can happen at any time. They must be adequately documented on the relevant forms and reported to the Chief Investigator and Sponsor immediately.

- Deviations from the protocol which are found to frequently recur are not acceptable, will require immediate action and could potentially be classified as a serious breach.
- The end of study will be the date of the last visit of the last participant for data collection as described in the protocol (1 year post baseline). No follow-up has been allocated for this study

8.6 Data protection and patient confidentiality

Investigators and study site staff must comply with the requirements of GCP, the Data Protection Act 2018 and the UK General Data Protection Regulation with regards to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles.

Whereby personal information is collected, kept secure, and maintained. This will involve:

- coded, depersonalised data where the participant's identifying information is replaced by an unrelated sequence of characters.
- Secure maintenance of the data and the linking code in separate locations using encrypted digital files within password protected folders and storage media.
- Limiting access to the minimum number of individuals necessary for quality control, audit, and analysis.
- confidentiality of data will be preserved when the data are transmitted to sponsors and co-investigators
- the data will be stored for 20 years
- the data custodian is the Chief Investigator who will be responsible for the use, security and management of all data generated by the study
- The study may be monitored, or audited in accordance with the current approved protocol, relevant regulations and standard operating procedures. This too is declared in PIS.

8.7 Indemnity

NHS bodies are legally liable for the negligent acts and omissions of their employees. If you are harmed whilst taking part in a clinical research study as a result of negligence on the part of a member of the study team this liability cover would apply.

Non-negligent harm is not covered by the NHS indemnity scheme. Great Ormond Street Child's Hospital, therefore, cannot agree in advance to pay compensation in these circumstances.

In exceptional circumstances, an ex-gratia payment may be offered.

NHS indemnity operates in respect of the clinical treatment that is provided.

8.8 Access to the final study dataset

9 DISSEMINIATION POLICY

9.1 Dissemination policy

The Investigators will be involved in reviewing drafts of the manuscripts, abstracts, press releases and any other publications arising from the study. Authors will acknowledge that the study was funded by. Nestlé HealthCare Nutrition. Authorship will be determined in accordance with the authorship the International Committee of Medical Journal Editors *(*ICMJE) guidelines and other contributors will be acknowledged.

Dissemination process:

GOSH have ownership of data generated in the research project. As per discussion regarding IP as stipulated in agreements

The results of the study will be reported and disseminated as follows:

- Peer reviewed scientific journals

- Internal report

- Conference presentation

-Feedback to families using posters

9.2 Authorship eligibility guidelines and any intended use of professional writers

The International Committee of Medical Journal Editors recommends that authorship be based on the following criteria for manuscripts submitted for publication).

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

ARCHIVING

Archiving will be authorised by the Sponsor following submission of the end of study report.

Essential documents will be retained for a minimum of 20 years after completion of the study. These documents will be retained for longer if required by the applicable regulatory requirements.

10 REFERENCES

References:

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Body Composition and Nutritional Status of Children Undergoing Treatment for Acute Lymphoblastic Leukaemia (ALL)

11. APPENDICIES

11.1 Appendix 1- Required documentation

List here all the local documentation you require prior to initiating a participating site (e.g. CVs of the research team, Patient Information Sheet (PIS) on headed paper etc.).

13.3 Appendix 3 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made

List details of all protocol amendments here whenever a new version of the protocol is produced.

Protocol amendments must be submitted to the Sponsor for approval prior to submission to the REC.