Joint Research Management Office (JRMO) Research Protocol for Research Studies

Full Title	Child growth and development in east London
Short Title	Child growth in east London
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1. Contents

2. Glossary

Linear growth faltering / short stature / stunting

Children are defined as having short stature, otherwise known as linear growth faltering or stunting, if their height-for-age is more than two standard deviations below the population median height.

Linear growth faltering also encompasses reduced growth velocity, which is defined as a growth velocity of less than the 10th percentile, or the growth curve crossing 2 SD lines or centiles on a growth chart.

ASQ-3

Ages and Stages Questionnaire, third edition. Standard instrument used in the Healthy Child Programme to assess early child development in children aged one month to 5 and a half years.

GMDS

Griffiths Mental Development Scale. Development measure administered by child psychologists.

NCMP

National Child Measurement Programme.

3. Signature page

CI Agreement

The study, as detailed within this Research Protocol, will be conducted in accordance with the principles of GCP , the UK Policy Framework for Health and Social Care Research, and the Declaration of Helsinki and any other applicable regulations. I delegate responsibility for the statistical analysis and oversight to a qualified statistician (see declaration below).

CI name: **__Prof Andrew Prendergast_____**

Signature: ____ _____

Date: **_____9Th September 2022_____**

Statistician's Agreement

The study as detailed within this research protocol will be conducted in accordance with the current UK Policy Framework for Health and Social Care Research, the World Medical Association Declaration of Helsinki (1996), Principles of ICH E6-GCP, ICH E9 - Statistical principles for Clinical Trials and ICH E10 - Choice of Control Groups.

I take responsibility for the statistical work in this protocol is accurate and take responsibility for statistical analysis and oversight in this study.

Statistician's name: **___Dr Joanna Orr_____**

Signature: _____ _____

Date: **_____9th September 2022_____**

4. Summary and synopsis

Short title	Child growth in east London
Methodology	Pilot growth screening programme of 630 children recruited from Tower Hamlets, East London
Objectives / aims	The **overarching objective** of this grant is to detect linear growth failure early in childhood by employing an automated growth screening algorithm for pre-school age children. The screening algorithm will be created using national data and piloted for feasibility and acceptability in Tower Hamlets, East London. We have two interlinked aims, with the following hypotheses: **Aim 1:** Pilot an automated growth screening algorithm in a cohort of 630 children in east London. **Hypothesis 1**: Health visitor monitoring of child height using an automated growth-screening algorithm is feasible and is acceptable to health visitors and caregivers. **Hypothesis 2:** Referral of children to a paediatric growth clinic has high uptake and identifies growth problems in pre-school age children. **Hypothesis 3:** An additional height measurement by a health visitor or at the child's preschool booster immunisation appointment at their GP practice is feasible and acceptable. **Hypothesis 4:** Linkage of children's health visitor data to their height measurement as part of the NCMP is feasible and is acceptable to caregivers. **Hypothesis 5:** A smartphone app is feasible and acceptable for caregivers to use to measure their children's height at pre-school age, and there is acceptable inter-test variability between the smartphone measurement and the clinician measurement with a stadiometer.

	Aim 2: Generate pilot data to investigate the best indicators to detect poor school readiness and developmental problems in early childhood. **Hypothesis 1**: The addition of growth and development data to other environmental and socioeconomic variables (including Index of Multiple Deprivation) increases the pick-up rate of children at risk of poor school readiness and/or children with delayed development. **Hypothesis 2:** There is strong correlation between the existing measurement of child development in pre-school age children (ASQ-3) and a gold standard developmental assessment by a child psychologist.
Number of participants	We will enrol a cohort of **630 children** from Tower Hamlets, East London into a pilot screening programme at age 2-2.5 years. A clinical sub-study of 200 children with confirmed diagnosis of a growth disorder will also be analysed.
Inclusion and exclusion criteria	**Aims 1 and 2** (630 children recruited). *Inclusion criteria:* Children aged 2-2.5 years, who live in Tower Hamlets and whose caregiver(s) are willing to provide written informed consent. . *Exclusion criteria:* Children will be excluded if: • The caregiver does not provide written informed consent. • The child is not able to stand for an accurate height measurement. **Clinical sub-study** (200 children) *Inclusion criteria:* Children or young people with confirmed diagnosis of a growth disorder, who are receiving or received treatment at the paediatric endocrinology clinic at the

	Barts NHS Trust, and who's data was collected as part of a clinical effectiveness audit. *Exclusion criteria:* • Parent or carer of the child does not consent to child or parental data to be shared • Patient aged 16 years or over does not consent to his/her data being shared
Statistical methodology and analysis (if applicable)	**Statistical methodology** will be overseen by the study statistician, Dr Joanna Orr. **Aim 1** We will enrol 630 children into the pilot screening programme and acquire measurements of height at three time points. Based on a 95% attendance at the two follow-up appointments, we aim to have three height measurements available on at least 600 children by age 4-5 years. Each child enrolled at age 2.0-2.5 years will have baseline anthropometry (height and weight), demographic data and a developmental assessment conducted by their Health Visitor as part of standard care. In addition to standard data collection, measured or reported parental height will also be recorded. Follow-up anthropometric measurements will be repeated 6-12 months later by the health visitor or at the child's pre-school booster immunisation appointment, which takes place at approximately age 3 years 4 months. Parents' height will also be measured or reported at the follow-up visit if missing. Children will have their height measured by a school nurse at age 4-5 years as part of the National Child Measurement Programme (NCMP). We will link the primary care data to this measurement. This will enable the growth screening algorithm to be applied to these three time points. The algorithm will be used to detect differences in detection of linear growth failure taking into account successive additional datapoints: height at age 2.0-2.5 years, 2.5-3.5 years and 4.0-5.0 years, delta height/growth velocity and distance from parental height. At each measurement, we will identify the 2-3% of children with the poorest growth, in whom prior studies show a high prevalence (30-40%) of medical disorders,

	using the screening algorithm, and refer these children for medical assessment by a paediatric endocrinologist (Prof Storr).[1,2,3,4,5] We estimate in this pilot study that 12 children will be referred for investigations (based on referral of 2% children with the poorest growth) and that 30-40% of these investigated in clinic will have an underlying medical disorder identified (n=4-5) based on the published literature. This pilot study is not designed to evaluate whether the age at diagnosis is significantly reduced using an automated screening approach; rather, our pilot data will inform feasibility and acceptability for a larger NIHR grant application to test the screening programme at scale with a primary outcome of age at diagnosis of medical disorders. We will also investigate the inter-test agreement between the heights measured by caregivers using a smartphone app and heights measured by health professionals using a stadiometer. **Aim 2** **Aim 2** of the pilot study will generate pilot data to investigate the best indicators to detect poor school readiness and/or developmental problems in early childhood. We will investigate whether the addition of growth and development data to other environmental and socioeconomic variables increases the pick-up rate of children at risk of poor school readiness and/or children with delayed development. Growth will be assessed using three height measurements as described above and development assessed as part of standard care by a Health Visitor and practice nurse. As part of routine care, each child's development will be assessed using both the caregiver and health visitor components of the ASQ-3. Following the 2.0-2.5 year contact, a random sample of 150 children will also be invited to enrol in a sub-study to generate pilot data to investigate the correlation between the ASQ-3 and development assessed by a child psychologist using a

	Gold Standard development battery, the Griffiths Mental Development Scale (GMDS). The GMDS will be used to measure gross motor, fine motor, social, language, visual-spatial and practical reasoning skills. These data will inform a larger NIHR grant application to test the sensitivity of the parental and health visitor components of the ASQ-3. We will use the data to conduct analyses to test the hypothesis that linear growth failure either alone or in combination with additional factors identifies children with reduced neurodevelopment, who are therefore at risk of poor school attainment.
Study duration	3 years

5. Introduction

Poor growth in childhood can be due to underlying medical causes or socioeconomic disadvantage.[6] In low- and middle-income countries, poor linear growth (or stunting) affects almost one-quarter of children under 5 years.[7] The prevalence of stunting in high-income countries is less well described and may be clustered sub-nationally in areas of disadvantage. A report in 2017 by the Patients Association suggested there may be a hidden burden of stunting in deprived areas of the UK (including Tower Hamlets) and called for systematic mapping of childhood stunting and consideration of pre-school screening.[8] We have analysed national data (unpublished) and confirmed clusters of high stunting prevalence in east London, particularly in Tower Hamlets, Newham and Hackney, after adjustment for ethnicity. Using longitudinal data from the Millennium Cohort Study for over 10,000 children with height measurements at ages 3, 5, 7, 11, 14 and 17 years, we have found consistent associations between stunting at age 3 and cognitive measures throughout childhood. Regression models adjusted for socio-economic variables showed a robust significant association between stunting and neurodevelopment (unpublished). We therefore believe that linear growth failure may be an important marker of disadvantage and reduced long-term potential among UK children, particularly in regions with substantial deprivation.

A screening programme may be valuable to refer children with severe growth failure to hospital for early investigation, diagnosis and management of serious medical disorders. Screening would also identify a larger group of children with poor growth but no underlying medical cause. We believe short stature in this group of children is a marker of disadvantage and vulnerability that is currently overlooked. We will therefore evaluate whether linear growth failure, either alone or in combination with other social and environmental factors, is a feasible, acceptable and useful marker to detect reduced cognitive development and/or poor school readiness; if so, height screening could enable targeted pre-school education and social interventions, which would be a novel public health approach to improving educational and economic outcomes across the life-course.

5.1. Background

Children with linear growth failure (i.e. low height-for-age or inadequate height velocity) may have an underlying medical cause. Early management of disorders such as growth hormone deficiency (GHD) improves long-term outcomes, but diagnosis is often delayed.[9] In Finland, an automated growth-screening algorithm has been adopted nationwide, leading to a younger age at diagnosis of conditions such as GHD and Turner syndrome.[10] In the UK, children are measured at ages 4-5 and 10-11 years through the National Child Measurement Programme (NCMP) and health visitors measure growth parameters – with weight often prioritised over height - as part of the

Healthy Child Programme. However, there is no systematic national programme to measure and monitor the heights of pre-school children, the systems do not effectively 'join up' data and there is no referral system for linear growth failure if it is identified by the NCMP. Moreover, the NCMP's focus is childhood obesity rather than linear growth, and the current cross-sectional approach of measuring children once on school entry and once on exit has limited utility in the detection of disorders underlying growth failure (99.4% specificity but < 30% sensitivity).

Many UK children with linear growth failure have no identified medical cause after investigations and are discharged from clinical follow-up. A child's dietary intake explains only a small proportion of stunting, and genetics do not account for all the variation in height in the first 5 years of life.[11] Linear growth is a sensitive marker of the overall wellbeing of a child, and impaired growth has multiple social and environmental causes. In low- and middle-income countries, stunting affects almost one-quarter of children, and is associated with higher mortality, impaired neurodevelopment, reduced educational attainment and lower adult economic productivity.[12] Whether these associations are also apparent in children living in high-income countries in the 21st century is less well studied.

We believe there are two situations in which UK children would benefit from linear growth screening. First, an algorithm with high specificity to detect children with medical disorders would lead to earlier referral, diagnosis and targeted treatment to improve clinical outcomes. Second, linear growth failure that is not explained by an underlying medical disorder may be an important marker of vulnerability that should not be ignored. Early identification of these children would ultimately enable tailored pre-school interventions to improve health, education and economic prospects across the life-course. This may be particularly important in areas such as east London where ~50% children are living in poverty, the highest rate in London.[13]

5.2. Rationale

Currently, children with linear growth failure are identified *ad hoc*, if at all, because there is no systematic screening programme in the UK. Several other European countries systematically monitor linear growth in pre-school children, resulting in earlier diagnosis of medical causes of short stature.[14] From parent testimonials, it is apparent that there are often delays in identifying serious medical disorders such as growth hormone deficiency. Developing a screening algorithm for the UK pre-school population would be a major step towards identifying growth failure earlier.

Early identification leads to prompt and appropriate investigation, identification of potential co-morbidities and improves prognosis. Timely initiation of appropriate therapy is critical to minimise the impact of the disease process and maximise general health as well as height gain. Stunting is a sensitive marker of a child's wellbeing, health and educational potential across the life-course. If we generate pilot data

suggesting that growth and development measures in early childhood both improves the early identification of vulnerable children and increases the sensitivity of detecting poor school readiness, it will provide a strong rationale for a new public health approach to identifying vulnerable children in need of pre-school support through simple measurements. Using our algorithm, the screening process would be automated and have potential for adoption at scale.

5.3. Risks / benefits

Benefits: Children in the pilot growth screening programme will benefit from additional pre-school height measurements, parental monitoring of longitudinal growth through use of an app, and feedback of their growth trajectory, which would not usually be undertaken. A subset of 150 children will benefit from a neurodevelopmental assessment prior to school enrolment, which could help inform an Education Health and Care Plan for additional educational support if needed. Any children with substantial developmental delay will be referred for assessment through existing NHS systems. Additionally, 2-3% of children (~12 in total) with the poorest growth will be referred for medical review/investigations at the Royal London Hospital and we anticipate that 4-5 of these children will have a serious, treatable underlying disorder detected, based on previous data.[15,16] The diagnosis of these disorders (such as growth hormone deficiency) is frequently delayed, traumatic for parents, and associated with suboptimal long-term outcomes.

Risks: We will collect sensitive data on household deprivation and social determinants of health on case report forms (CRFs). We are not able to completely de-identify CRFs because we will link the data to the follow-up assessment and (using NHS number) to the NCMP growth data held by Tower Hamlets Local Authority. However, data will be managed to ensure confidentiality as described in section 13. Research staff will undergo Good Clinical Practice and ethics training and the importance of confidentiality when reviewing sensitive clinical documents will be emphasised throughout the study. Child development assessments are potentially sensitive, because they measure cognitive performance, and can be misinterpreted or could be used to disadvantage a child. The results will be discussed in confidence with caregivers; we would seek their permission before sharing any of these findings and would only do so if it were in the best interests of child, for example to inform an Education Health and Care Plan to seek additional educational support for the child.

6. Study objectives

6.1. Primary objective

Pilot an automated growth-screening algorithm in east London.

Within the primary objective we aim to test four hypotheses:

1. Health visitor monitoring of child height using an automated growth-screening algorithm is feasible and is acceptable to health visitors and caregivers.
2. Referral of children to a paediatric growth clinic has high uptake and identifies growth problems in pre-school age children.
3. An additional height measurement by the child's health visitor or at the preschool booster immunisation appointment at the child's GP practice is feasible and acceptable.
4. Linkage of children's health visitor data to their height measurement as part of the NCMP is feasible and is acceptable to caregivers.
5. A smartphone app is feasible and acceptable for caregivers to use to measure their children's height at pre-school age, and there is acceptable inter-test variability between the smartphone measurement and the clinician measurement with a stadiometer.

6.2. Secondary objective

Generate pilot data to investigate the best indicators to detect poor school readiness and/or developmental problems in early childhood.

Within the secondary objective we aim to test the following two hypotheses:

1. The addition of growth and development data to other environmental and socioeconomic variables (including Index of Multiple Deprivation) increases the pick-up rate of children at risk of poor school readiness and/or children with delayed development.

2. There is strong correlation between the existing measurement of child development in pre-school age children (ASQ-3) and a gold standard developmental assessment by a child psychologist.

6.3. Primary endpoint

- Feasibility and acceptability of the screening pilot.

We will assess feasibility using Bowen *et al.*'s '8 areas of focus':[17] acceptability, demand, implementation, practicality, adaptation, integration, expansion and limited-efficacy testing. To achieve this, we will employ a mixed methods evaluation including qualitative data collection using focus groups with caregivers and health visitors as well as questionnaires distributed to all caregiver participants in the study and all health visitors involved in growth and development assessments. We will also collect quantitative data on: uptake of growth measurements; number of successful

growth and development measurements; number of referrals successfully completed (i.e. referred to child growth clinic with participant attending one clinic appointment); number of participants consenting to identification of their child's anthropometric data from NCMP; and uptake of the smartphone app.

6.4. Secondary endpoints

- Linear growth trajectory

This will be assessed by child height measurements at age 2-2.5 years, age 2.5-3.5 years, and age 4-5 years, in combination with target parental height. Parents who make use of the app will provide additional longitudinal growth measurements between age 2-5 years. All measurements will be entered into an algorithm, developed using data from two longitudinal UK cohorts (Millennium Cohort Study and Born in Bradford), which will identify children with poor linear growth based on absolute height, growth velocity and distance from target height.

- Child development at age 2-2.5 years.

This will be assessed using the ASQ-3 questionnaire and the GMDS, as described above.

7. Study population

This study will enrol a cohort of 630 children living in Tower Hamlets into a pilot screening programme at age 2.0-2.5 years and apply a growth-screening algorithm to identify children with poor growth. Children will be selected randomly from health visitor records in Tower Hamlets to ensure a representative sample, based on the inclusion and exclusion criteria outlined in section 7.1 and 7.2. We will include all children whose caregivers are willing to provide written informed consent to i) have a height/weight measurement (+/- a developmental assessment) together with a baseline questionnaire undertaken at age 2.0-2.5 years (by the health visitor) and a repeat weight/height measurement at age 2.5-3.5 years (either by the health visitor as an additional visit or by the GP surgery at the time of pre-school vaccinations); ii) undergo longitudinal growth screening by the parent using an app which measures a child's height; and iii) have the child's identifiers sent to Tower Hamlets Local Authority in order to access their weight/height measurement undertaken at school at age 4.0-5.0 years through the NCMP programme, to prove feasibility of data linkage. We will work in partnership with Tower Hamlets GP Care Group to identify a representative sample of children from the borough based on health visitor lists, to ensure we minimise bias and include even the hardest-to-reach participants.

We will also conduct a secondary analysis of a clinical sample of ~200 children with confirmed growth disorders e.g. Growth Hormone Deficiency, growth failure associated with small for gestational age and Turner syndrome (clinical sub-study).

These children are seen and managed in the paediatric endocrinology clinic at Barts NHS Trust. We will use this sample to test the growth screening algorithm and to identify optimal cut off values to maximize sensitivity and specificity. Retrospective consent will be sought from carers/parents to link the child's diagnosis code, age at diagnosis and parental height to their previously collected NCMP height measurement. When the patient is over 16 years old, consent will be sought from both the parent/carer and the patient, as parental data will also be shared.

7.1. Inclusion criteria

- Aged 2-2.5 years
- Live in Tower Hamlets
- Caregiver willing to provide written informed consent.

7.2. Exclusion criteria

Children will be excluded if:

- The caregiver does not provide written informed consent.
- The child is not able to stand for an accurate height measurement.

7.3 Clinical sub-study inclusion and exclusion criteria

Clinical sub-study children will be included in this analysis if they were part of the clinical sample identified as having a growth disorder at Prof Storr's clinic, and where consent can be obtained from the parent/carer and from the patient if the child patient is now over 16 years old.

8. Study design

We will enrol a longitudinal cohort of 630 children to an observational study in which weight and height will be measured as part of standard care by a Health Visitor in the community. Enrolment and baseline research data collection will be at age 2.0-2.5 years, which coincides with a current contact point with Health Visitors. Parental height will also be measured at this visit (or reported height recorded if measurement is not possible). Prior to the visit, parents will complete the standard pre-school developmental assessment sent to all households by the Health Visitor (Ages and Stages Questionnaire; ASQ-3), and the informed consent form will request

permission to record these data for research purposes. A subgroup of 150 children will be offered a developmental assessment by a psychologist as a gold-standard comparison with the parent-reported ASQ-3. A follow-up height measurement for all children will be conducted by the health visitor approximately 6-12 months later as part of an extra preschool visit which is to be piloted in Tower Hamlets. If this is not operational by the time the study starts, the follow-up measurements will take place at the preschool booster vaccine appointment at the child's GP surgery, which also occurs at age 3.0-3.5 years. If this measurement is missed for any reason, health visitors will attempt to measure the child at a community/ children's centre or at home on a separate occasion. Children will also have their height and weight measured as part of the existing NCMP programme at school entry (age 4-5 years). Additionally, parents will be invited to monitor their child's height through use of an app, if they own a smart phone, which can provide additional data-points between age 2-4 years.

Using this approach, we are maximising opportunities to measure child growth at pre-school ages by using existing contact points with health visitors and GP surgeries, and providing parents with the opportunity to measure their child's height using a novel smartphone app. Longitudinal height measurements, together with data collected on parental height, will be offered up to an automated growth-screening algorithm that we have developed using existing national datasets. Children with the most severe growth faltering (bottom 2-3% of children) will be identified and their caregivers/parents contacted to offer them referral to the paediatric endocrinology service at the Royal London Hospital for investigation of medical disorders of growth (Prof Storr).

9. Study procedures

Children will be identified from the central health visitor lists held by the Health Visiting team at the Tower Hamlets GP Care Group (GPCG), which is a federation of 36 General Practices in Tower Hamlets and a partner in Tower Hamlets Together, a local integrated care partnership. From these lists, children will be randomly selected, with replacement, in two groups: i) the main growth study (N=480), and ii) the growth and development sub-study (N=150), for a total of 630 children. Group 1 will only undergo growth screening, and group 2 will additionally have a gold standard child development assessment conducted at baseline.

9.2 Screening

Prior to the 2.0-2.5 year contact, children's health visitors will contact the family to provide preliminary information about the study and explain that a PIS will be included with the ASQ-3 questionnaire that is routinely sent to families at this age. The health visitor will offer a follow-up phone call, video call or home visit to check the family received the PIS, to address any initial queries and to gauge their interest in the study. They will be offered a screening and consent visit to coincide with the

child's planned 2-2.5 year assessment (section 9.2). At this visit, the child will be screened by a health visitor against the inclusion and exclusion criteria to determine eligibility. Caregivers of eligible children who are interested in joining will be asked to provide written informed consent as outlined in section 9.3. Using demographic information from the primary care platform (EMIS), the information will be communicated in the main language spoken by the caregiver.

9.3 Informed consent

Informed consent will be taken by the study health visitor in a confidential setting (within a children's centre or the child's house) using e-consent on the REDCap database, which includes the questions on the study informed consent form (Form 4). If necessary, consent can be taken on paper using the same form and will still be considered valid. This will take place either prior to the first measurement/development assessment at age 2-2.5 years or on the day of this assessment. An electronic signature will be taken; in addition to a tick box and declaration, permitted forms of electronic signatures will include a stylus or finger drawn signature or a typed name. The health visitor will explain all study procedures, risks and benefits and confidentiality considerations. The study health visitor will explain that the project involves two assessments by health professionals, 6-12 months apart (one at the 2-2.5 year health visitor contact and one undertaken either by the GP surgery at the preschool booster immunisation appointment, or by the health visitor). In addition, as per standard care all children will have their development assessed by the health visitor using the parent-reported ASQ-3 assessment. Parents will also be invited to download a smartphone app and to measure their child's height at 3 timepoints, each time on the same day as the child's height is measured by a health professional (health visitor, GP practice nurse, school nurse). Caregivers will also be asked for consent to health visitors' collection of data on past medical history from children's primary care records and linkage of any relevant diagnoses or medications to the children's study data. It will also be made clear that there will be data linkage with the NCMP programme through Tower Hamlets Local Authority, which involves sharing identifiers (NHS number) if they are happy to provide consent for this to occur. Caregivers can opt out of this data linkage and their child can still be included in the internal study. Caregivers will be made aware that they will be provided with the child's growth measurements and a summary of their growth pattern, and that children with severe growth failure will be contacted and referred to the paediatric endocrinology service, and children with significant developmental concerns will be referred for further assessment through existing NHS referral pathways. In addition to data entry onto the NHS system, the caregivers will be made aware that their child's anthropometric and developmental data, and the parental heights will be recorded in a research database (REDCap) by the health visitor. Caregivers will be asked for consent for routine clinical data collected in the clinic (such as any diagnoses made by the endocrinologist) to be linked with the child's data in the study. Prof Storr is a member of the study team and

leads the paediatric endocrinology clinic to which the children will be referred, and will enter any relevant clinical data onto the REDCap database.

Sub-studies

Development sub-study

A randomly selected subset of 150 children will also be invited to an additional appointment with a child psychologist for a detailed developmental assessment, which is not part of standard care; children in this sub-study will be enrolled using a separate consent form (Form 5). The caregiver will be asked to provide written informed consent and to keep a copy of the PIS. The primary caregiver must have parental responsibility to provide consent. Assent will not be sought since all children will be between 3 and 4 years old.

Where the developmental assessment suggests the child may be experiencing developmental delay, the study psychologist may share the Griffith's report with the child's Health Visitor with the parent's permission. Reports will not be generated for all children and will only be generated when concerns are identified. The Griffith's assessment result is not a formal diagnosis but can provide extra context for a clinician.

Qualitative sub-study

Following the first contact, we will invite a subgroup of participants in the study (caregivers) and health visitors working in Tower Hamlets to take part in focus groups. A total of 16 caregivers will be selected from the sample of children participating in the study to participate in two focus groups of between 6 and 8 participants. Caregivers participating in focus groups will be consented using a separate PIS (PIS 16) and consent form (Form 14).

We will also conduct one focus group with health visitors. A total of eight health visitors currently working within the Healthy Child Programme in Tower Hamlets will be sampled with the help of the health visiting team at the Tower Hamlets GPCG. Separate PIS and consent forms will be used for health visitors (PIS 17, Form 14).

Clinical sub-study secondary analysis

A separate clinical sample of children with diagnosed growth disorders will be analysed to test the algorithm and obtain optimal cut offs for growth screening. In order to obtain a height measurement previous to the child's first attending growth clinic, we will seek to link the children's clinical data to their NCMP height measurement (measured at school and recorded by NHS England at 4 or 5 years old).

We will seek retrospective consent from the child's parent/carer and, in cases where the child is over 16 years old, from the child patient themselves. Consent will be obtained electronically using a e-consent form through REDcap (Forms 22 and 23).

Unique secure links will be sent to patients or their families via email, after first sharing an electronic copy of the PIS (PIS 24 and 25).

9.4 Schedule of study interventions
The study schedule is shown in Table 1.

Baseline (age 2-2.5 years)	Qualitative research sub-study	Development sub-study[2]	Follow-up (age 2.5-3.5 years)[3]	NCMP measurement
Screening for eligibility (Form 3)	Informed consent (Form)	Child development – GMDS	Height measurement (child)	Height measurement
Informed consent (Form 4)	Qualitative interview/ focus group (Form 12)	Informed consent (Form 5)	Height measurement (parental)	Weight measurement
CRF_1 baseline questionnaire			School enrolment information / SENCO input	CRF_2 endline questionnaire
Height measurement				
Weight measurement				
Parental height[1]				
Child development (ASQ-3)				

[1]Attending parent's height (s) measured (where possible) or estimated height documented if not attending

[2]Children in the development sub-study will have all baseline procedures conducted in addition to the developmental assessment conducted by a psychologist

[3]Conducted either by the GP at the time of pre-school vaccinations or the health visitor through a home visit

The following study forms will be used to capture data or provide information:

Form name	Details	Administered by
Patient Information Sheet – growth study (Form 1)	Detailed information about what the study is about and what participation involves	Health visitor
Patient Information Sheet – growth and development study (Form 2)	Detailed information about what the study is about and what participation involves (including additional developmental assessment)	Health visitor
Screening form – inclusion and exclusion (Form 3)	Initial check that child lives in study catchment area and there are no exclusion criteria	Health visitor
Consent form for growth study (Form 4)	Signed by caregiver if informed consent given	Health visitor
Consent form for growth and development sub-study (Form 5)	Signed by caregiver if informed consent given	Health visitor
Baseline form (Form 6)	Baseline data form includes height, weight, development and demographics. No identifiers.	Health visitor

Identifiers/contact form (Form 7)	Form with patient identifiers and contact details	Study team
Follow-up form (Form 8)	Follow-up data form includes height, weight, development. No identifiers.	Health visitor/ psychologist
Exit form (Form 9)	Used if caregiver wishes to withdraw from the study.	Health visitor
Referral form (Form 10)	Template to write to participant's GP asking to refer to paediatric clinic.	PI
NCMP linkage form (Form 11)	Identifiable information to submit to Tower Hamlets Local Authority to link to NCMP data.	Study team
Focus groups – qualitative research sub-study discussion guide – caregivers (Form 12)	Guidance for moderators of the focus groups of caregivers.	Study team
Focus groups – qualitative research sub-study discussion guide – health visitors (Form 13)	Guidance for moderators of the focus groups of health visitors.	Study team
Focus groups – caregivers. Consent form (Form 14)	Signed by caregiver if informed consent given	Study team
Focus groups – health visitors. Consent form (Form 15)	Signed by health visitor if informed consent given	Study team
Focus groups – caregivers. Information sheet (Form 16)	Detailed information on the purpose of the sub-study and what participation involves	Study team

Focus groups – health visitors. Information sheet (Form 17)	Detailed information on the purpose of the sub-study and what participation involves	Study team
Evaluation questionnaire (caregivers) – 2.5-3.5 years (Form 18)	Evaluation questionnaire for all caregivers to be completed after the 2.0-2.5 year and the 2.5-3.5 year contacts	Study team (completed by caregiver)
Evaluation questionnaire (caregivers) – end of study (Form 19)	Evaluation questionnaire for all caregivers at the end of the study (after the 4-5 year contact)	Study team (completed by caregiver)
Evaluation questionnaire – caregivers – smartphone App (Form 20)	Evaluation questionnaire for all caregivers regarding use of the Smartphone App	Study team (completed by caregiver)
Evaluation questionnaire - health visitors (Form 21)	Evaluation questionnaire for all health visitors participating in the main growth study	Study team (completed by health visitor)
Clinical sample linkage consent form for carers/parents (Form 22)	Consent form for clinical sample NCMP linkage	Study team (completed by patient or caregiver)
Clinical sample linkage consent form for patient aged 16 or over (Form 23)	Consent form for clinical sample NCMP linkage	Study team (completed by patient or caregiver)
Clinical sample linkage information sheet for carers/parents (Form 24)	Information leaflet for clinical sample NCMP linkage	Study team
Clinical sample linkage information sheet for patient aged 16 or over (Form 25)	Information leaflet for clinical sample NCMP linkage	Study team

Baseline visit (age 2.0-2.5 years):

At the baseline visit, data will be collected using **CRF1 (Baseline visit).** Demographic data will be collected from the caregiver. Caregivers will be asked to have the personal child health record (Red Book) available, from which will be transcribed: birth weight and length (if available) and any previous measurements of height, weight and head circumference. We will also collect data on gestation and growth on antenatal scans, feeding difficulties including any previous interventions from dietetics or paediatrics, chronic health conditions and any hospital attendances/admissions. The child's height will be measured to the nearest 1mm using a stadiometer according to an SOP. The child's weight will be measured to the nearest 100g using a stand-on scale according to an SOP. The accompanying parents will have height measured using the same methods; if either parent is absent, an estimate will be made of their height based on parental recall. If both parents are not present (i.e. the child is cared for by different family member), we will attempt to contact the parents to record their reported heights. If the child is not in contact with their biological parents, we will not make further attempts to contact family members and will record this as missing data. Health visitors will support caregivers to download a smartphone growth application and demonstrate how to use it. Caregivers will be invited to take the first smartphone measurement at this point. The app converts height data from the camera image to a numerical figure, and this will be transferred to a secure central server with additional relevant demographic data (e.g. gender, ethnicity, weight, date of birth and parents' heights) and an anonymous identifier in GDPR-approved secure space. Each participant will have an anonymised unique identifier. No patient images / names will be transferred. The smartphone app has existing ethical approval (IRAS project ID: 286683; REC reference: 21/WM/0032).

Follow-up visit 2.5-3.5 years

Children will have a further height measurement at approximately 3.0 years by the health visitor. If the preschool health visiting contact is not operational at the time, the child will instead have their height measured by the nurse/healthcare assistant administering the immunisations at the preschool booster appointment at their GP practice, or at a planned research visit appointment Through the health visitor contact at 3.0 years children will have a repeat developmental assessment using the ASQ-3 questionnaire. Data will be collected using **CRF 2 (Follow-up visit).** Child height will be assessed using the same tool as at baseline. If there are any missing parental heights a further attempt will be made to measure or record an estimated height. Families will be occasionally contacted by the study team by phone to improve retention in the study and to remind caregivers about the smartphone app.

School entry measurement (age 4-5 years)

Child height and weight will be recorded as part of the routine NCMP programme at school entry (4-5 years of age). We will provide identifiers to Tower Hamlets Local Authority to enable them to link the NCMP measurement to enrolled children and provide us with their heights and weights recorded at 4-5 years of age. This is a

feasibility piece to see if data could be used from NCMP in a larger screening programme. We will also collect data on school enrolment, and screen for educational concerns by health visitors screening school nursing notes to review if there has been any input from a special educational needs co-ordinator at school. After the NCMP measurement, we will distribute questionnaires for caregivers and health visitors to collect data on feasibility and acceptability of the study procedures. We will also conduct focus groups with small groups of participants (see below).

At each of the 3 measurements of height we will identify the 2-3% of children with the poorest growth, as categorised by the algorithm (based on parental height, child height, and child growth velocity), in whom prior studies show a high prevalence (30-40%) of medical disorders. We will contact parents of these children to offer referral to the paediatric endocrinology clinic at the Royal London Hospital. A member of the study team will call the parents to inform them and will write to the child's GP to request a referral into the Royal London Hospital clinic via the e-referral system. We will evaluate acceptability and feasibility of the screening and referral process, using parental and primary care staff questionnaires. We will evaluate uptake by calculating the proportions screened, referred, investigated in clinic and diagnosed with medical disorders. At the clinic, children will be assessed by a paediatric endocrinologist and will undergo routine medical evaluation for short stature, with appropriate follow-up.

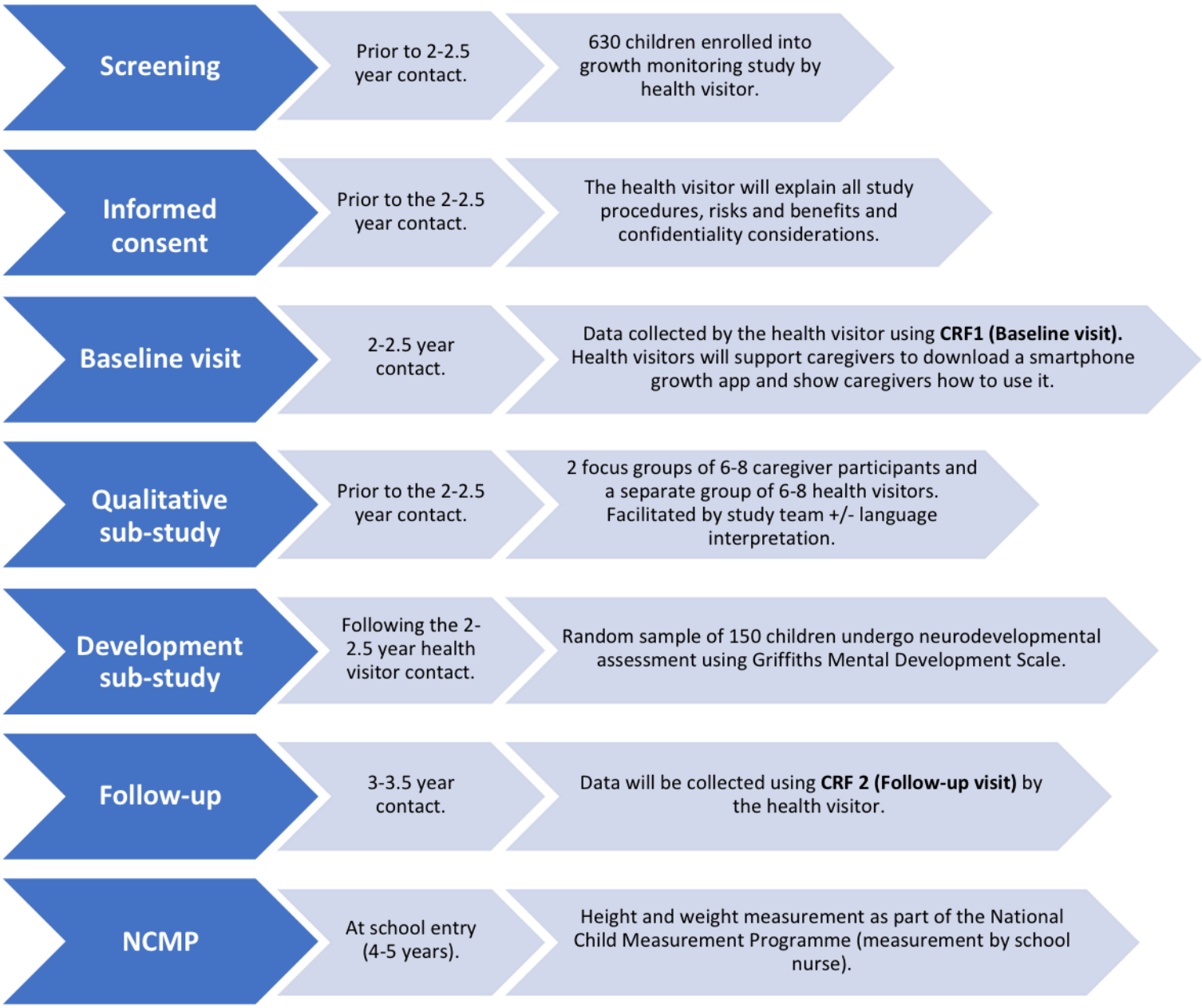
Development sub-study (age 2.0-2.5 years):

A random sample of 150 children will also be invited to enrol in a sub-study to generate pilot data on the sensitivity of the parent-reported ASQ-3 to assess child development compared to a gold standard development battery, the GMDS, undertaken by a psychologist. These children will undergo a neurodevelopmental assessment during their routine health visitor visit of their motor, cognitive, language and social skills using a standardized test battery (GMDS) by a child psychologist. Using data from the ASQ-3 developmental assessments conducted at baseline and follow up visits by the health visitor, we will investigate relationships between growth and development and assess content validity of the ASQ-3 by comparing it with the GMDS.

Qualitative sub-study (following the 2-2.5 year visit)

We will also invite a subgroup of participants in the study (caregivers) and health visitors working in Tower Hamlets to take part in focus groups. We will convenience sample 2 focus groups of 6-8 caregiver participants, with language interpretation if appropriate. With support from the Child Growth Foundation and using our own experience of qualitative research with families of children experiencing stunting in sub-Saharan Africa we will raise and explore generative questions with the focus groups. We will convene the focus groups following the first contact to gather qualitative data on acceptability of the study procedures (in addition to questionnaires). We will also convene a separate group of 6-8 health visitors working in Tower Hamlets to discuss child growth and development monitoring and referral pathways. We will transcribe the data and generate coding categories to analyse with NVivo software.

Flowchart of study procedures



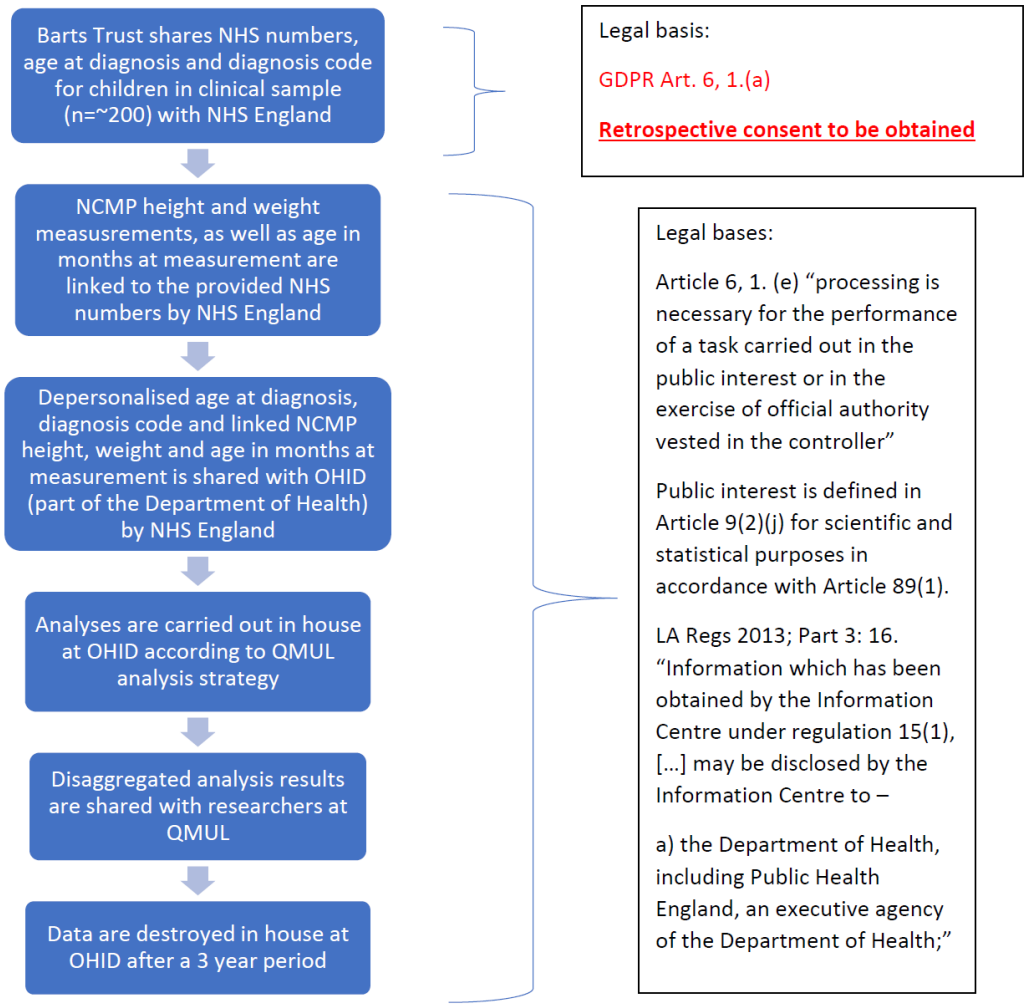
Clinical sample secondary analysis

A sample of ~200 children with diagnosed growth disorders will be linked to NCMP data and used to test the performance, sensitivity and specificity of the growth screening algorithm. Retrospective consent will be sought from the patient and their parent/carer to link their clinical data to their NCMP height measurement. The patients NHS number, diagnosis, age at diagnosis and parental heights will then be shared with NHS England (data controllers for NCMP). Here, data will be linked to NCMP measurements. We will also seek consent to share the patient's first name, surname, postcode and date of birth with NHS England to link the data in cases where the NHS number is missing from the NCMP dataset. Data will be pseudo-anonymised by removing NHS numbers or other identifiers and generating random ID numbers before being shared with the Office for Health Improvement and Disparities (OHID) at the Department of Health and Social Care.

Data will be analysed in-house at OHID according to data sharing agreements between OHID and NHS England, and to minimize the sharing of personal data. The data analysis plan has been developed by researchers at QMUL and analysis will be conducted collaboratively, although data will not be shared outside of OHID at this stage. The growth-screening algorithm will be applied to NCMP data to determine the children's standardized height for age and sex as well as the distance from their mid-parental heights. We will use an age-matched sample of children participating in the Born in Bradford study as controls. We will assess the sensitivity and specificity of using different cut-offs to find children with an underlying growth disorder. We will also estimate the potential improvement in age at diagnosis when using the screening algorithm by calculating the mean of the subtracted age at NCMP measurement from the true age at diagnosis for the children who were correctly identified as having a growth disorder by the algorithm. Analysis will be conducted using Stata 17. Aggregated results will then be shared with researchers at QMUL.

This sub-study will run parallel to the main pilot study, and as it uses a separate dataset is not included in the flowchart of study procedures. A flowchart of the linkage procedure is shown below.

Flow diagram of data sharing and linkage procedure for clinical sample secondary analysis



9.4 Data collection and storage

Data will be handled in accordance with Sponsor protocols to ensure confidentiality and robust data management. Identifiable data will be collected by the research team in order to maintain contact with families to schedule follow-up visits, to allow linkage with the follow-up assessment data, and in order for Tower Hamlets Local Authority to identify the children and link the study data with NCMP data. All identifiable data will be stored separately from any clinical information, with a unique study identifier enabling the NCMP measurements to be added to the clinical data.

The identifiers will be retained for the length of the study as the child may need referring to a paediatric clinical service but will then be destroyed once Aim 2 of the study has been completed.

9.5 Follow-up procedures

Participants who have short stature for their age and parental heights will be identified using the screening algorithm at baseline. These participants will be referred for further clinical investigation. At follow-up, growth velocity will also be included in the screening algorithm, and any children found to have reduced growth velocity will be referred. Children will be followed up in a dedicated research clinic within Barts Health NHS Trust. Prof Storr's clinic is an established paediatric endocrine/growth clinic at the Royal London Hospital. Children will be seen and assessed as per standard clinical practice. They will have auxological assessment (height, weight, head circumference and recording of parental heights), a clinical review (history and physical examination). Patients requiring further investigations for short stature will follow a current best practice guideline investigation protocol. More detailed genetics (if a specific genetic disorder is suspected), Growth Hormone testing (as per standard departmental protocols) or referral to another speciality (e.g. gastroenterology) may be requested if clinically indicated.

9.6 Laboratory and radiological assessments

Laboratory and radiological investigations will not be performed as part of the study, but children who are identified in Aim 1 as having abnormal growth will be investigated in the referral clinic at the Royal London Hospital. This is not part of the study and represents normal clinical care.

9.7 Participant withdrawal

Participants will be able to withdraw from the study at any time and their data will be de-identified. Withdrawals from the study trigger completion of the exit form (Form 9).

9.8 End of Study Definition

The study will end for each child after their follow-up assessment is completed (after their school NCMP measurement at age 4-5 years). All fieldwork will be completed when the target sample of 630 children has been recruited (allowing for 5% loss to

follow up from the cohort of 630), with full measurements of all children on three occasions and developmental assessments on the subset of 150 children. Following the end of clinical assessments, the study will continue until the data have been analysed, linkage to NCMP measurements have been made, and those individuals identified with poor growth have been referred to Prof Storr's paediatric endocrinology clinic.

10. Statistical considerations

10.1. Sample size

The existing literature on growth screening shows that around 30-40% of children identified as having short stature will have an underlying medical disorder. During the course of this study, we estimate we will refer 12 out of 600 children for clinical investigation (based on referral of 2% children with the poorest growth). If the algorithm is successful at identifying children with a high likelihood of an underlying condition we would expect a total of 4 (35%) of the 12 children referred to be diagnosed with a medical condition. The sample size of 12 (2% of 600) gives us 85% power at 5% significance to detect a difference if the algorithm identifies less than 5% of children rather than the expected 35%. Therefore, if fewer than one (5% of 12) child referred to clinic is found to have an underlying medical condition we would be able to conclude that the algorithm had not achieved the goal of identifying children with a higher risk of underlying medical conditions.

10.2. Method of analysis

The overarching goal of this pilot study is to assess the feasibility of a growth screening programme. We are guided by Bowen's framework for feasibility studies, in which three key questions for feasibility are presented.[18] These are: *Can it work? Does it work?* and *Will it work?* In this study we focus largely on the first question, can it work, and seek to provide some preliminary data on the second and third questions. Bowen's areas of focus for feasibility studies informs how we will answer these questions:

Can it work?

Acceptability: Focus groups with parents and health visitors will provide information on the acceptability of growth screening (see Qualitative Analyses, below). We will also examine ongoing study participation (retention rate).

Demand: The uptake of invitations to participate in the study (response rate), as well as uptake of the screening mobile phone app will provide data on demand for growth screening.

Integration: We will test integration into current health visiting systems by assessing the success of data linkage with NCMP, the proportion of parents who consent to NCMP data linkage, and through focus group interviews with health visitors.

Does it work? Will it work?

Below we outline how we seek to provide evidence for limited-efficacy testing, to gain an initial understanding of whether the growth screening algorithm is able to identify children for further clinical investigation. Acceptability, demand and integration are also interwoven into the data analysis strategy throughout.

Aim 1

We will employ an algorithm based on previous methodology, using variables individually and in combination, after checking for co-linearity. Different cut-off values will be chosen and the proportion of the population judged to have linear growth failure estimated for each cut-off. We will then examine the detection rate for each cut-off by applying it to data from ~200 local children treated in the specialist paediatric endocrinology centre with known growth disorders e.g. Growth Hormone Deficiency (GHD), Turner Syndrome (TS) and Small for Gestational Age without catch-up growth (SGA). Consent will be obtained retrospectively from these patients and their parents/carers to link their routinely obtained clinical data (diagnosis, age at diagnosis, height and parental height) to previously height data obtained at school entry via the NCMP. To do this linkage, the hospital clinical data (and the associated NHS number or other identifiers) will be shared with NHS England. This will allow us to calculate sensitivity-and-specificity algorithm cut-offs for the detection of these conditions. This will enable a trade-off between detection rate (sensitivity) and the false positive rate (1-specificity) to be evaluated. Additionally, the time elapsed from the first abnormal screening result until the clinical diagnosis of growth hormone deficiency will be related to the cut-off values.

The outcomes for Aim 1 are age of identification of stunting (which will be reported but the study is not powered to detect age of diagnosis); feasibility of measuring children in the community; the percentage of children referred; the percentage of children found to have underlying medical conditions; and the feasibility, acceptability and inter-test variability of a smartphone app and stadiometer height measures.

The algorithm will be applied to measures collected from each child at each visit, with children who are identified by the algorithm as being in the bottom 2% for height or

growth being referred to clinic for further investigation. The proportion of children with complete observations, including height at three time points and parental height, will be compared to the proportion of children with fewer observation points or missing parental height. Descriptive statistics will be reported: the number and percentage of children found to be stunted and their characteristics (height, gender, age, socio-demographic factors). We will also report the number of children referred to clinic, attending clinic and found to have underlying medical conditions. The age at which each condition is identified will be reported and compared to the average age at diagnosis.

Height data collected by parents using a smartphone app will be analysed. The number of parents consenting to use of the smartphone app and reporting one or more height measurements through the app will be reported. The number of time points at which parent's upload smartphone measured heights will also be reported. Inter-rater reliability between parent-measured height using the smartphone app and Health Visitor measured height using a stadiometer will be assessed using Gwet's Agreement Coefficient.[19]

Aim 2

All children will undergo a developmental assessment in the community, conducted by a health visitor with input from the child's parent, as part of standard care (ASQ-3 questionnaire). A subset of 150 children will, in addition, have a gold standard developmental assessment conducted by a child psychologist using the GMDS, which measures gross motor, fine motor, social, language, visual-spatial and practical reasoning skills.

Data on socioeconomic circumstances will be used to model the probability of a child's risk of developmental delay or sub-threshold delay on the ASQ-3 (n=600) and GMDS (n=150). Poor growth (assessed by the algorithm) will then be included in these models to assess whether model fit is improved, and whether poor growth contributes to the predictive power of socioeconomic variables to predict developmental delay.

Concurrent validity of the ASQ-3 and GMDS will be assessed. Each measure will be used to assess whether the participant has any degree of developmental delay, based on measure-dependent cut offs. The degree of agreement will be assessed using Cohen's kappa, and interpreted using existing guidelines, where a kappa value of >0.4 reflects moderate agreement, and a kappa of >0.6 reflects substantial agreement.[20] The GMDS will also be used as a gold standard child development measure to assess the performance of the ASQ-3. Sensitivity and specificity will be calculated to assess the ability of the ASQ-3 of identifying children identified as having a delay by the GMDS.

The outcomes for Aim 2 are the correlation between the ASQ-3 and the GMDS; and the change in sensitivity with the addition of anthropometric and developmental data to an existing vulnerability index.

Qualitative analyses

To further our understanding of the acceptability of the proposed screening programme, we will conduct two focus groups with parents participating in the study, as well as one focus group with health visitors. The transcribed data from the focus groups with caregivers and health visitors will be used to generate coding categories and will be analysed using NVivo, using thematic analysis.

11. Ethics

Research Ethics Committee approval will be sought. This is not a trial and there is no intervention which could result in direct harm to participants. However, there are potential indirect harms related to the study. We will aim to mitigate these as far as possible and will include detail of these potential harms in the patient information and informed consent procedures.

Firstly, the study will involve collecting sensitive data, which if handled incorrectly could lead to identification of individual children or groups of children. The study procedures to de-identify or pseudo-anonymise children will reduce the risk of identification of individuals. The potential for 'group harm', in which a particular subpopulation (e.g. by area, ethnicity or gender) are stigmatized because of study findings, such as the finding of high prevalence of growth failure, will be minimized in publications and dissemination of study findings, by not releasing results relating to small areas.

An identification of short stature, faltering growth or delayed development (and subsequent referral for specialist care) could result in distress for children and their families and could lead to stigma. We will include information about stigma and discuss this with caregivers as part of the informed consent procedures. Further, if we identify issues with growth and/or development, children will be referred earlier than would have happened without their involvement in the study. Children will be immediately referred to a paediatric growth or community development clinic and as such will be provided care, support and if appropriate treatment for relevant conditions.

We will be providing vouchers worth £15 for the baseline visit as compensation for time spent during participation in the study. These are not intended as rewards for participation, but we are aware of the possibility of these payments leading to coercion. Research staff will undergo Good Clinical Practice and ethics training and will be careful to avoid coercion in recruitment procedures.

11.1. Annual Safety Reporting

N/A

12. Public involvement

The screening algorithm will be created using national data and piloted for feasibility and acceptability in east London, which we have shown is a national hotspot for stunting based on an analysis of NCMP data (currently in review). We have engaged with **the Patients Association**, an independent national charity which campaigns for improvements in health and social care for patients, who stated in a letter to us that in order "to ensure an effective co-production approach to this research bid we welcome the opportunity to work in partnership with Queen Mary, University of London and other local stakeholders to undertake research into child malnutrition which will build on the work we have previously undertaken in 2016/2017."

The **Child Growth Foundation (CGF)** have identified this area of research as one of their key missions / research priorities and provided a letter of support for this work. As Medical Advisor for the CGF, Prof Storr will disseminate and obtain feedback from CGF members via their website, newsletters and annual congress. The CGF are also able to provide individuals for a project advisory board, focus groups and workshops.

As per Section 9.4, we will also engage groups of caregivers in focus groups to develop our understanding of caregivers' experience and understanding of child growth and development, and their thoughts about the current processes for monitoring of these metrics in Tower Hamlets.

13. Data handling and record keeping

13.1. Data management

During Aim 1, we will collect sensitive clinical data including height, weight, developmental information and carer-recalled past medical history. We will also collect sensitive sociodemographic information including data on household deprivation and other social determinants of health. Data from anthropometric assessments, developmental assessments and questionnaires will be entered onto a secure password protected access database (REDCap), and the hard copies of the questionnaires will be stored centrally in a locked cupboard. Two health visitors will double enter the data and resolve any discrepancies.

All data will be linked to an identifier kept separate from the sensitive data. No copies of paper documents will be made. Data will be identifiable only by a unique study ID number and will not display participant identifiable information. A linkage form will be used to link study ID with patient identifiable information (pseudo-anonymisation), which will be stored as a password-protected file on a locked QMUL computer.

The smartphone app we will invite caregivers to use converts height data from the camera image to a numerical figure, and this will be transferred to a secure central server with additional relevant demographic data (e.g. gender, ethnicity, weight, date of birth and parents' heights) and an anonymous identifier in GDPR-approved secure space. Each patient will have an anonymised unique identifier. No patient images / names will be transferred.

Research staff will undergo Good Clinical Practice and ethics training and the importance of confidentiality when reviewing sensitive clinical documents will be emphasised throughout the study. Child development assessments are potentially sensitive, because they measure cognitive performance, and can be misinterpreted or could be used to disadvantage a child. The results will be discussed in confidence with caregivers; we would seek their permission before sharing any of these findings and would only do so if it were in the best interests of child, for example to inform an Education Health and Care Plan to seek additional educational support for the child.

Linkage of the children's data we collect with the pseudo-anonymised national data will contain information such as postcode. Although not a direct identifier, this could lead to identification of groups of children. The potential for 'group harm', in which a particular subpopulation (e.g. by area, ethnicity or gender) are stigmatized because of study findings, such as the finding of high prevalence of growth failure, will be minimized in publications and dissemination of study findings, by not releasing results relating to small areas.

We will also conduct a linkage exercise of previously collected routine clinical data to historic height measurements. Retrospective consent will be sought from patients and parents or carers of a sample of patients who received treatment for growth-related conditions at Professor Helen Storr's paediatric endocrinology clinic at Barts Health NHS Trust. Data on the child's diagnosis, age at diagnosis and parental heights, as well as their NHS number and other identifiers, will be shared with NHS England. NHS England will link these data, using the NHS number, or other identifiers when the NHS number is not available in the NCMP dataset, to the child's first NCMP height measurement, as well as the age of the child when the measurement was taken in months. These data will then be anonymised by removing the NHS number or other identifiers and a new randomly generated identifier assigned to each child. Finally, this pseudo-anonymised dataset will be shared with the Office for Health Improvements and Disparities (OHID), part of the Department of Health and Social Care. Data will be analysed at OHID according to an analysis strategy developed at QMUL, to minimize data sharing. OHID has robust data protection protocols and safe and encrypted sharing pathways with NHS England.

13.1. Source Data

Source data include the anthropometric measurements and developmental assessments and sociodemographic data collected from children and their carers in the community. From experience, it is expected that most children will be brought to their appointment by at least one parent. In this case, the child's parent will also have their height measured, and will be asked about the height of the other parent. We will not apply for approval to access the medical notes of either the child or of the carers/parents, especially since heights entered in medical notes are often recorded from a verbal report from the patient given to the clinician coding the measurement, rather than a direct measurement.

13.2. Confidentiality

Information related to participants will be kept confidential and managed in accordance with the Data Protection Act, the General Data Protection Regulation (GDPR), NHS Caldecott Principles, the UK Policy Framework for Health and Social Care Research, and the conditions of Research Ethics Committee favourable opinion.

13.3. Record retention and archiving

We will keep research records for 20 years after the project has completed, as per the UK Policy Framework for Health and Social Care Research. We will use the Trust Corporate Records Centre as the repository for long-term storage. All research documentation will be archived in physical form.

14. Safety reporting

Given the study design, we do not anticipate adverse events (AE) or adverse reactions (AR). Adverse events could plausibly occur during the face-to-face components of the study. There are two points at which participants will be seen face-to-face. One at age 2-2.5 years, where an anthropometric assessment and developmental assessment will take place on the same day, and an almost identical assessment between 6-12 months later at the GP surgery. The third measurement will take place at the child's school as part of the NCMP, and any children seen in the paediatric endocrinology clinic by Prof Storr will be receiving normal clinical practice. The NCMP measurement and the clinic appointment are not strictly part of the study procedures. There is a very low likelihood of physical injury during the growth and development assessments and/or while the child and caregiver are on the premises.

The research nurses will make an initial assessment of any injury and will seek medical attention as appropriate.

Other contacts will be with the families of children who warrant referral to a paediatric clinical service, which will be in the form of a telephone call and/or letter to the family and to the child's GP. There is potential for distress or psychological harm of the child or family member when being informed of abnormal growth or development or when being referred to the growth clinic. This will be minimized by the breaking of news or discussion of clinical information being undertaken by a senior medically trained member of the research team with advanced training in communication skills.

Any AEs that are plausibly related to the study and which are identified by a member of the research team (including research nurses, psychologist, health visitors or any of the study co-investigators) will be reported to the study CI. The CI or another medically qualified research team member will assess each identified AE for severity and relatedness to establish if it should be classified as a serious adverse event (SAE) and whether the event was related to the study. The assessment will be documented in the participant's study records. The CI or delegate will report any severe AEs or SAEs that are possibly, probably or definitely related to study procedures to the JRMO; a safety reporting form will be completed for each event that requires reporting.

Adverse events or SAEs occurring between visits/questionnaires/sample collections will not be recorded or reported as they are not the aim or focus of this project.

15. Monitoring and auditing

The Sponsor or delegate retains the right to audit any study, study site or central facility. In addition, any part of the study may be audited by the funders where applicable.

Onsite monitoring will be performed as per the study monitoring plan. Monitoring will include source data verification. We will check 100% of consent forms and the CI will undertake spot checks on the quality of recorded data.

16. Study committees

We will form a study management group consisting of the CI, PIs, collaborators, grant holders, statisticians and study coordination team. Since this is a pilot, minimal

risk study, we will not have a Data Monitoring Committee or a Trial Steering Committee.

17. Finance and funding

The project is funded by Barts Charity (12 Cock Ln, Farringdon, London EC1A 9BU); grant number MRC0219).

18. Insurance and indemnity

The insurance that Queen Mary University of London has in place provides cover for the design and management of the study as well as "No Fault Compensation" for participants, which provides an indemnity to participants for negligent and non-negligent harm.

19. Dissemination of research findings

We will disseminate findings through conferences and 2-3 open access peer-reviewed manuscripts. We will produce policy briefs and press releases to communicate findings to policymakers, including Public Health England, the Patients Association and non-governmental organisations such as Save The Children, who have a strong focus on national health and education policy. If we find a substantial hidden burden of stunting, we anticipate drafting a Viewpoint for a journal such as the BMJ or Lancet to highlight the issue, as well as dissemination to the press. There is a need for earlier diagnosis of serious underlying medical disorders in children with growth failure, as is evident from the testimonials we have included with this proposal.

We will leverage the support of the Child Growth Foundation, for whom Prof Storr is a medical advisor, to disseminate the results of the automated growth screening algorithm which has enormous national potential. This would require further evaluation in a follow-on grant, and we plan to apply for NIHR funding following the results of our pilot assessment. We will establish a community advisory board with representation from parents, primary care and local education; this will enable us to gain a range of viewpoints on the proposed work and its implications. We will engage parents through letters prior to the start and end of the project, and through an invited parents' evening to disseminate findings. This work synergizes with ongoing work in sub-Saharan Africa, which focuses on stunting as a marker of poverty, and aims to identify solutions to child linear growth failure. We have an ongoing collaboration with the Centre of the Cell at the Blizard Institute to develop a game and app on undernutrition in Africa; we will use

this as an opportunity to also highlight issues related to local undernutrition for the general public.

We will produce policy briefs and press releases to communicate findings to policymakers, including Public Health England, the Patients Association and non-governmental organisations such as Save The Children, who have a strong focus on national health and education policy.

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