

PErioperAtive CHildhood obesitY (PEACHY): A prospective observational cohort study investigating the proportion of overweight and obese children presenting for a procedure under general anaesthesia in the UK and the incidence of perioperative adverse outcomes in this patient group

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Committees:	Paediatric Anaesthesia Trainee Research Network (PATRN)

#### BACKGROUND

The Lancet Global Burden of Disease Study 2013 showed the prevalence of obesity is increasing in both adults and children worldwide<sup>1</sup>. Children and adolescents in developed countries are particularly affected with 23.8% and 22.6% of boys and girls respectively classed as overweight or obese in 2013. The UK ranks 9<sup>th</sup> for prevalence of overweight and obesity in children aged 2 to 19 years out of the 34 Organisation for Economic Cooperation and Development (OECD) countries<sup>2</sup>.

The UK National Child Measurement Programme (NCMP) mandates measurement of body mass index (BMI) annually amongst reception (4-5 years) and Year 6 (10-11 years) children attending state-maintained schools. The NCMP uses the British 1990 growth reference (UK90) to define the BMI classifications<sup>3</sup>. 2016-17 data show 22.6% of 5-year-olds are overweight (BMI >85<sup>th</sup> centile) and 9.6% are obese (BMI >95<sup>th</sup> centile)<sup>4</sup>. By the age of 11 years, the figures are 34.2% and 20.0% respectively<sup>4</sup>.

Obesity has been shown to track children into adulthood, fuelling the global epidemic<sup>5 6</sup>; the greater the severity of childhood obesity, the greater degree in adulthood. Studies also demonstrate that up to 75% of parents do not appreciate that their child is overweight, or recognise the associated health risks<sup>6 7</sup>.

There is little published data relating to anaesthetic and perioperative implications of childhood obesity, especially in the UK<sup>8</sup>. Previous retrospective single centre studies from the United States have shown that overweight and obesity occur in up to one third of paediatric patients<sup>9 10</sup>. Since approximately half a million children undergo anaesthesia and surgery in England alone every year<sup>11</sup> it is striking that the prevalence of overweight and obesity in this population of children is currently unclear. Whilst an estimate can be extrapolated from playground statistics, the true current prevalence of childhood obesity and the burden of perioperative complications in children presenting to UK hospitals for surgery is largely unknown. An understanding of the prevalence and trends of obesity in this population is vital to develop effective public health interventions and institute appropriate perioperative resource allocation.

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Many anaesthetists classify obese adult patients as American Society of Anesthesiologists (ASA) Grade II, regardless of the presence of any overt comorbidity. Similarly, obese children may have undiagnosed comorbidities such as hypertension, type II diabetes, asthma, obstructive sleep apnoea, fatty liver and gastro-oesophageal reflux<sup>10</sup> <sup>12</sup> which could all increase their perioperative risk. The USA Bogalusa Heart Study showed that 7-22% of obese 5-10 year olds had systolic hypertension, depending on their degree of obesity<sup>13</sup>. Impaired glucose tolerance was detected in 25% of obese 4-10 year olds in a separate US study<sup>14</sup>.

Obese adults are considered to be a high-risk patient group in the perioperative period with a higher incidence of airway complications<sup>15</sup> and perioperative adverse events. There are published national guidelines on the best practice management of these patients in the perioperative period<sup>16</sup>. Similarly, it is perceived that obese children present an increased anaesthetic risk throughout the perioperative period and increased rates of acute perioperative complications are consistently demonstrated in obese children. Previous non-UK studies suggest they require longer in the post-operative anaesthetic care unit (PACU), require more antiemetics and are at greater risk of airway complications<sup>9 12 17</sup>. Since obesity is associated with increased risk of critical airway obstruction such as laryngospasm in the perioperative period<sup>9</sup>, defining prevalence is an important clinical question. This data may indicate that there are adjustments that should routinely be made to anaesthetic technique for such patients. Some of these children may benefit from more formal pre-operative assessment and work-up in advance of surgery.

In addition, obese children are at risk of drug overdose if total body weight is used in dosing calculations. Drug specific adjustments for body weight should be made to take into account the increased proportion of fat to lean mass that complicates the distribution, metabolism and excretion of drugs<sup>18 19</sup>. Local audit and surveys have revealed widespread use of arbitrary unscientific dose reduction in obese children. The exact pharmacokinetics of paracetamol is unclear and most of the established paediatric guidance has been extrapolated from adult studies<sup>20</sup>. Paracetamol-induced hepatic injury is one example of potential harm due to accidental overdose. The appropriate dose adjustment for children according to weight is

unknown and we suspect wide variations in paracetamol prescribing practices<sup>20</sup>. This study would provide an opportunity to explore this variation amongst anaesthetists across the UK.

# AIMS

- To establish the proportion of overweight and obese children aged 2-16 years attending hospitals for procedures under general anaesthesia across the PEACHY registered sites in the UK.
- To establish whether obese children are at increased risk of defined adverse perioperative events as compared to their healthy weight counterparts in this study population.
- 3. To assess variation in perioperative paracetamol dosing for overweight and obese children in the study population.

# Primary outcome

1. The proportion of overweight and obesity in UK children aged 2-16 years attending hospitals for a procedure under general anaesthesia.

# Secondary outcomes

- The proportion of defined adverse events occurring in obese children as compared to healthy weight children attending for a procedure under general anaesthesia.
- 2. The variation in paracetamol dosing in obese children in the UK perioperative setting.
- 3. The proportion of obese children presenting for certain types of surgery compared to their healthy weight counterparts.
- 4. The difference in the proportion of overweight and obesity in the perioperative setting compared to that from the UK National Child Measurement Programme (NCMP).

#### **STUDY OUTLINE**

#### Study Design

A prospective observational 7-day cohort study. Individuals will choose a 7-day study period within a four-week window.

# Pilot study

A pilot study was run over the first week of October 2017 by national co-lead Dr. Zoë Burton at Sheffield Children's Hospital. This was a feasibility study with the aim of providing data for statistical modelling. 244 children attended for surgery. 52 (21.3%) did not have heights and/or weights recorded. 49 were excluded due to age <2yrs (n=38), <12kg (n=7), notes inaccessible (n=3), achondroplasia (n=1). 143 children (58.6%) were included in subsequent analysis. 95 were healthy weight (65.7%) and eight were underweight (5.6%). The remaining 41 (28.7%) were overweight (n = 13, 9.1%), obese (n=18, 12.6%) or severely obese (n = 10, 7.0%). A total of 19.6% of children had a BMI >98<sup>th</sup> centile.

In a separate retrospective study of children aged 4-18 years undergoing general anaesthesia at Great Ormond Street Hospital between 1<sup>st</sup> January 2006 and 2016, 12.2% of children were classified as obese or severely obese. There were a total of 73399 episodes for which BMI data was available for 55170 (75.2%). After data cleaning, 34894 patient episodes were included in the final analysis (47.5%), of which 4271 had a BMI >98<sup>th</sup> centile (12.2%).

# Overview

Date	Time	Task
	allocated	
29 <sup>th</sup> October	1 month	Submission of PEACHY proposal to PATRN Committee and
2017		APAGBI Scientific Committee.
21 <sup>st</sup> November	3 months	Decision regarding successful project made by APAGBI
2017		Scientific Committee. Formulation of draft study proposal
		for review by PATRN Chairs.
20 <sup>th</sup> February	3 months	Initial discussion with Aberdeen statistical analysis and data
2018		management teams. Completion of study proposal
		including data management and statistical plan.
16 <sup>th</sup> May 2018	1 month	Apply for study funding from the Association of
		Anaesthetists of Great Britain and Ireland (to cover
		statistical analysis and data management, PEACHY logo).
June –	4 months	Confirm University Hospital Southampton as study sponsor
September 2018		and lead site. IRAS application, REC approval, NIHR
		portfolio study application.
Date TBC	4 weeks	Invitation to participate in the study sent out by email to all
		PATRN representative trainees and Lead Consultant in each
		hospital on the database (approximately 120 centres).
Date TBC	4 weeks	Registration period for study. Centres to complete
		registration form including short survey regarding hospital
		size and information currently provided to obese children.
Date TBC	4 weeks	Centres to register involvement in study with individual
		R&D departments and send local details to PATRN in order
		to complete registration as participants.
Date TBC	4 weeks	Data collection period (4 week window).
Date TBC	4 weeks	Data to be uploaded to Aberdeen REDCap system by
		individual centres.
	4 weeks	Four weeks contingency for final data upload deadline for
		Aberdeen.
Date TBC	2 months	Certificates for participants to be distributed.
Date TBC	10 months	Write up and present study results.

**Table 1.** Expected timescale of the key components of the study.

#### **Study setting**

All representatives on the Paediatric Anaesthesia Trainee Research Network (PATRN) database will receive an invitation to participate in the study (Appendix 1) which will be accompanied by a study summary information sheet (Appendix 2). We will also advertise via the Research and Audit Federation of Trainees (RAFT) and Association of Paediatric Anaesthetists of Great Britain and Ireland (APAGBI) linkmen coordinators to recruit new sites. The representatives on these databases are trainee and consultant anaesthetists who work in NHS hospitals throughout the UK.

After a four-week invitation to participate window, PEACHY will be launched and centres will have a further four-week window in which to complete registration. This will be an online form that will be stored on Google documents and will incorporate information regarding the size of hospital and whether height and weight are routinely measured prior to a procedure under general anaesthesia (Appendix 3). A total eight-week period from the launch date will be given for centres to return confirmation of local R&D approval to participate in the study and confirmation that the local Principal Investigators have completed the National Institute for Health Research's (NIHR) Good Clinical Practice e-learning. This will complete the registration process.

## **Eligibility criteria**

All children aged 2-16 years and weighing >12kg presenting for a procedure under general anaesthesia.

#### **Inclusion criteria**

- All children aged greater than or equal to two years and less than 16 years presenting for a procedure under general anaesthesia.
- Elective cases, day case and emergency cases will all be included.
- Private cases being undertaken in NHS hospitals will be included.
- MRI, radiology, oncology and dental cases will be included provided the patient receives a general anaesthetic.

# **Exclusion criteria**

- Procedures performed under sedation or local anaesthesia.
- Children aged less than two years since the 0-24 month age group has separate growth charts, which are not currently recommended for interpretation of BMI.
- Children weighing less than 12kg as these are not included on the growth charts for interpretation of BMI.
- Children requiring general anaesthesia purely as part of intensive care treatment.
- Children who are already anaesthetised in the intensive care setting being transferred for a scan or procedure without any intervention to their airway planned.
- Children 16 years or more may be counted as children in some hospitals but not for the purposes of this study.

For the purposes of this study the American Society of Anesthesiologists (ASA) definition of general anaesthesia and sedation will be used<sup>21</sup>. Patients undergoing general anaesthesia will be unrousable even with painful stimulus whereas patients undergoing sedation, a purposeful response following repeated or painful stimulation can be elicited (not just reflex withdrawal from a painful stimulus).

#### Size of sample

Our plan is to recruit as many centres as possible within the UK and for them to recruit all eligible patients in the study within the available time frame. We do not have a specific sample size and statistical models will be adapted to the event rate provided by the sample recruited. Extracting data from PATRN's recent PAediatric unPlanned dAYcase Admissions (PAPAYA) study, it can be estimated that around 90 UK paediatric sites will participate in PEACHY. The mean number of day cases on a weekly basis was 83.5 across all sites that submitted data (range 3 – 230). Since day cases can be considered to account for up to 90-95% of all cases, we may expect a further 5-10% per week in addition. Across 90 sites this would mean we may expect to collect data from the region of 7590 patients. We would expect 20-25% of these patients not to have height and/or weight data available and thus will be excluded from analysis.

#### Recruitment

Local anaesthetic trainee investigators (independent of delivery of anaesthesia but part of the anaesthetic department of the hospital, and therefore members of the direct care team) will identify all children meeting the inclusion criteria from operating department lists during the study period. Additionally, emergency cases added may be identified by the anaesthetist at pre-operative assessment. Data will be collected on all eligible patients during the study period.

#### Data collection

The data collection period for this study is one week (seven consecutive days). This will be confined to a four-week window. Four weeks has been chosen to allow the most feasible seven-day window to be chosen by individual hospitals. This does not have to start on a Monday but should be for seven consecutive days (seven consecutive 24-hour periods). It is perceived that an intensive data collection period will be more likely to capture good quality data compared to a more extended period.

Data will be collected using a single paper case report form (CRF) per patient. This will be initiated by the anaesthetist in the operating theatre and completed by recovery staff in PACU. The CRF is attached as Appendix 4.

To calculate BMI, age (to the nearest month), gender, height and weight are required for each patient. It is anticipated that all hospitals would routinely measure weight but some hospitals may not routinely measure height prior to a procedure under general anaesthesia. NICE guidelines<sup>22</sup> currently recommend that clinical judgement should be used to decide when to measure a person's height and weight, including at routine health checks. The preoperative setting is a specific health check prior to undergoing general anaesthesia and therefore an appropriate time to measure a child's height and weight. The methodology for measuring height and weight should be identical to that used in the NCMP (Appendix 5). Height will be measured with shoes removed to the nearest 0.1cm using a height measure with the child's head positioned so that the Frankfurt plane is horizontal. Body weight will be measured with patients lightly clad, to the nearest 0.1kg using a calibrated electronic weighing scale. **If the local site is unable to collect age, gender, height and weight we will ask for the case to be** 

**logged and uploaded onto REDCap but no other data to be collected.** It will be important to know how many cases we are unable to include in the analysis due to incomplete data, as this will have an impact on the accuracy of the results.

Other information that would routinely be recorded within the clinical notes relating to the patients physical status, surgery, anaesthetic and specific perioperative adverse events will also be collected on the CRF. Patient identifiable data in the form of hospital number and date of birth will be collected on the CRF for traceability in terms of missing data.

Individual sites will be responsible for uploading data directly to REDCap (a secure web application). A unique identifying number will be generated at upload for each case (i.e. the data will be pseudonymised). Date of birth will be inputted onto the REDCap system but this will immediately be digitally converted and stored as age to the nearest month. This is to enable BMI to be calculated and prevent any calculation errors of age by the local site. Gender is also required for BMI calculation. No directly identifiable personal data will be stored on REDCap. There will be a data-uploading deadline four weeks after the close of data collection.

#### Data storage

Data from local sites will be uploaded onto REDCap, which will be managed by the University of Aberdeen. The data is held within the University of Aberdeen and is password protected. Each local investigator will be issued with personal login details to upload their own data to this system. They will not be able to access any data from any other participating sites. All data will be visible to REDCap administrators. Administrators will be members of the Aberdeen data management team, PATRN committee, PEACHY co-ordinators and our consultant advisors. The data will also be accessible to the statistical team via personal login details.

#### **Data analysis**

BMI will be calculated as weight in kilograms divided by the square of the height in meters  $(BMI = kg/m^2)$ .

# Body mass index

BMI is a measure of ideal weight range and used by organisations such as the World Health Organisation (WHO) as a guide to obesity in adults. Identifying the obese child is more difficult as they are still growing. Weight status among children and adolescents is most frequently defined based on BMI percentiles, the most universally accepted method being the use of gender-specific BMI charts developed in 2000<sup>23</sup>. Using BMI percentile identifies children with excess adiposity with acceptable accuracy particularly at the upper end of the sex-specific BMI distribution.

The British 1990 child growth reference (UK90) will be used in this study to assign each child a BMI centile taking into account their height, weight, sex and age. "Clinical" BMI centile thresholds are used for the purposes of individual assessment to place each child in one of four categories: underweight, healthy, overweight or obese (Table 2). This is the approach recommended by the National Institute for Health and Care Excellence (NICE) and Scientific Advisory Committee on Nutrition (SACN)/Royal College of Paediatrics and Child Health (RCPCH) which advises that a child's BMI centile is used to assess their weight status.

Clinical BMI centile category	BMI centile (p-score)	Approximated BMI centile line on growth chart
Obese	0.98	98th
Overweight	0.91	91st
Healthy	>0.02 to <0.91	Between 2 <sup>nd</sup> and 91 <sup>st</sup>
Underweight	0.02	2nd

Table 2. Child BMI centile classifications (clinical cut-offs)

# Population cut-offs

When measuring a population of children such as in the NCMP findings, weight category is defined using UK90 BMI "population" cut-offs. These cut-offs are slightly lower than the "clinical" cut-offs to capture those children already overweight or obese and those at risk of becoming overweight or obese (i.e. those children who may be on the borderline of the clinical definition). This helps ensure that adequate services are planned and delivered. For

this reason, when comparing our data to that of the NCMP, the population cut-offs shown in Figure 1 will be used.



Figure 1. Child BMI centile classifications (population cut-offs)

# **Case definitions**

BMI and weight category will be calculated by the data analysis team from data uploaded to the REDCap system using the appropriate stata add-in zanthro for the UK90 data cut-offs. This will be done in the first instance for all cases using the clinical cut-offs (Table 2) and secondly for children aged 4-5 years and 10-11 years using the population cut-offs (Figure 1) to allow for direct comparison of our data to data from the NCMP, which is collected at these age points.

# Adverse events

Adverse events definitions have largely been derived from the APRICOT study<sup>24</sup> and the PeDi study<sup>25</sup> and are detailed in Appendix 6. Expected incidences from unpublished UK data extracted from APRICOT are shown in Table 3. These will be assessed according to the definitions by the lead anaesthetist for each case.

Complication	Expected incidence
Bronchospasm	0.3%
Laryngospasm	1.1%
Pulmonary aspiration	0.13%
Stridor on emergence	0.3%

**Table 3.** Expected incidences of airway complications

#### Sample size

Assuming we obtain data from 90 hospitals and a total of 7590 children attend for surgery, this will give us a precision of +/- 1% around a mid-point estimate of 15.9% (average of 12.2% and 19.6% from the two pilots) of children with a BMI >98<sup>th</sup> centile.

# Statistical analysis plan

All data will be entered onto an excel database and initial range and logic checks performed. Data will then be transferred into IBM SPSS Statistics version 24 and SAS for statistical analysis. For each variable, appropriate descriptive statistics will be calculated (percentage and n for categorical variables and mean, standard deviation or median interquartile range, plus minimum and maximum for continuous variables).

Using a STATA add-in zanthro, an individual child's BMI will be converted to a z score and centile using the UK90 reference curves. These will be used to define individuals as underweight, healthy, overweight or obese. It may be necessary to combine healthy weight and overweight children and compare with the obese.

The proportion and 95% confidence interval of overweight and obesity in UK children aged 2-16 years attending for surgery will be calculated.

A chi squared test will be used to compare the proportion of defined adverse events, comorbidities, perioperative adverse events and other complications occurring in obese children with that of healthy weight children attending for surgery.

The variation in paracetamol dosing in obese children in the UK perioperative setting will be tabulated and graphed by hospital.

The proportion of obese children presenting for certain types of surgery compared to their healthy weight counterparts will be compared using the chi squared test. A binary logistic regression model will be used to adjust for age and other potential confounders. A mixed effects logistic model will be considered to adjust for the clustering effect of individual patients within hospitals.

The difference in the proportion of overweight and obesity in the perioperative setting compared to that from the UK National Child Measurement Programme will be compared using the chi squared test.

#### Consent

We anticipate that patient consent will not be required for this study as the dataset will include information already recorded as part of routine clinical care, all data will be pseudonymised and no directly identifiable personal data will be stored outside of the individual hospital where each individual patient is treated. The clinicians collecting the data will be part of the anaesthetic department in the hospital where the patient is being treated and can therefore be considered part of the direct care team. No additional tests or interventions are being made as a result of this study and no changes will be made to patient care, with the possible exception of height measurement. Whilst height may not be routinely measured and recorded at all hospitals prior to a procedure under general anaesthesia, this is a non-invasive, low risk test and according to NICE guidelines, this would represent an appropriate time to measure and record this data. Therefore hospitals will be asked to do so for the duration of the study period if they wish to participate.

In order for this study to make accurate, generalisable conclusions to provide future patient benefit, the coverage of the study population at each local site and the total number of sites participating needs to be maximised. By taking consent, we may limit the number of patients recruited. This would prevent accurate determination of the proportion of obese children presenting for general anaesthesia and hence limit the usefulness of the findings. Asking for consent would also be impractical as we anticipate recruiting approximately 7500 patients. For these reasons we do not intend to take consent from patients.

#### **Ethics**

This study will be registered with IRAS and seek REC approval. We believe this is a simple and low risk study both ethically and legally. We plan to collect information relating to general IRAS : 248493 03/10/2018 anaesthesia and basic demographic data in children aged 2-16 years presenting for a procedure under general anaesthesia.

Local investigators will be part of the anaesthetic department in the hospital where the patient is being treated and therefore form part of the direct care team. As no burdensome additional tests, interventions or changes to care will be made (with the possible exception of height measurement), the patients will bear no additional risks. Height measurement is a non-invasive, low risk test and according to NICE guidelines this would be an appropriate time to measure and record this data. All other data being collected is already recorded as part of routine clinical care and will be pseudonymised. Additionally, no decisions affecting an individual patients care will be made based on the information collected by any member of the study team.

Local investigators will collect data from the anaesthesia care record and clinical notes. This information will be entered onto our database via a secure web-based programme (Project REDCap) from password protected NHS desktop computers. The data will be stored securely. No personal identifiable information will be stored outside the local hospital. The central research team will not have access to any directly identifiable personal data. All data will be disposed of securely.

The main issue with project management is achieving data recording consistency across the network. Guidance on measurement methods and definitions will be provided to all local sites. Additionally, all local lead investigators involved in the project will be required to complete the National Institute for Health Research's (NIHR) Good Clinical Practice e-learning, an online resource which aims to ensure that clinical research is conducted ethically and to high standards.

No member of the research team has a conflict of interest.

#### **Data protection**

All information for this study will be held securely and treated as strictly confidential according to NHS policies. Personal data entered onto paper case report forms (CRF) will be stored in a IRAS : 248493 15 03/10/2018

locally arranged secure location, typically a drawer or filing cabinet in a locked anaesthetic department office. Anaesthetic department offices are commonly located in the operating theatre complex, which is itself a secure environment. CRFs will be held locally until a specified time point (five years after the study ends) when they will be destroyed confidentially.

No directly identifiable personal data will be stored outside the local hospital either in paper or electronic format. Pseudonymised data will be collected in REDCap and stored on the University of Aberdeen (UoA) server. The University's primary and secondary data centres are operated as co-hosted services under the North East Scotland Shared Services, with the Robert Gordon University (RGU), and North East Scotland College as partners. The University's primary data centre is on the Old Aberdeen campus and is operated by UoA. The secondary data centre is operated by RGU on the Garthdee campus.

Physical access to the data centres is restricted to essential IT operations personnel, and is only accessible by card controlled locks which log all accesses. Swipe cards to enter the datacentre are kept in a locked digital key safe which only approved personnel can access. All access to the datacentre requires authorisation through a Data Centre & Monitoring team member. All people entering the datacentre must also have completed a safety briefing if they have not done so previously. Access logs are reviewed regularly. RGU and UoA have similar data centre access protocols. RGU staff have no access to UoA data hosted in their data centre.

#### Dissemination

We intend to publish the results of this study in a scientific journal and at a national/international conference by poster or oral presentation. ZB and RL will be joint first authors on any publications. TB will be listed as a second author. ME and PATRN will also be listed as authors. All data collectors will be listed as collaborators. RAFT and any regional networks will also be acknowledged. We will make anonymised data available to all participating hospitals, and they will be able to identify themselves amongst the dataset.

# Study collaborators

Study sponsor & Lead site	University Hospital Southampton (UHS)		
Chief investigators	Zoë Burton (PATRN) Rosie Lewis (PATRN) Mark Edwards (UHS)		
UHS Principal Investigator	Tom Bennett (UHS)		
PATRN	Paediatric Anaesthesia Trainee Research Network committee		
APA Scientific Committee	Tom Engelhardt (Aberdeen) Peter Brooks (Chelsea & Westminster)		
Statistician	Amanda Lee (University of Aberdeen)		
Data management	Katie Wilde (University of Aberdeen)		
Statistical support	Professor Tim Cole (UCL Institute of Child Health)		
Research and Audit	RAFT support our network and allow us to advertise via		
Federation of Trainees (RAFT)	their Basecamp (online platform to communicate with the regional networks)		
Regional networks	PLAN	London	
	OXCCARE	Oxford	
	SWARM	South West	
	SHARC	South Yorkshire	
	SPARC	Wessex	
	West Scotland		
	MAGIQ	Merseyside	
	MERCAT	East Midlands	
	INCARNNET	North East	
	SEQuoIA	East Scotland	
	SQUARES	Scotland	
	AARMY	East and West Yorkshire	

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# APPENDICES

- 1. Invitation to participate
- 2. Study summary
- 3. Registration form
- 4. Case report form (CRF)
- 5. National Child Measurement Programme operational guidance
- 6. Adverse events definitions