Sheffield Children's NHS
NHS Foundation Trust

PAEDIATRIC OXIMETRY ALGORITHMS – NORMATIVE DATA COLLECTION

SHORT STUDY TITLE:
Paediatric Oximetry Algorithms

STUDY NUMBER: 1.0

06/1/2017 VERSION 1.0

Sponsor's Representative …… Dated ……..

Chief Investigator…….. Dated……..

LAY SUMMARY

Children with long-term respiratory conditions such as chronic lung disease of prematurity and muscular dystrophy need frequent monitoring of their blood oxygen concentrations to assess levels of treatment required (e.g. oxygen therapy, ventilation). Such conditions can lead to severe illness or death if oxygen levels are not monitored and appropriate action taken. Currently, blood oxygen levels are monitored at home using pulse oximetry with monitors that are cumbersome and not optimised for movement and paediatric reference values. This leads to inaccurate readings, especially at times when oxygen may be needed most, for example, during feeding and activity. Accurate monitoring will allow targeted treatment when children most need it.

There is no pulse oximeter currently available which can accurately monitor patients able to ambulate and which uses bespoke paediatric algorithms to obtain accurate results from children of different sizes.

At a recent Technology Innovation Transforming Child Health (TITCH) Network meeting the above problems were identified and a collaborative team was set up. This working group consists of Viamed; a medical device company who have worked in the field of pulse oximetry for 40 years, Medilink Yorkshire and Humber; who will provide the project management along with innovation and commercialisation expertise; and the Respiratory and Sleep team at Sheffield Children's Hospital (SCH) who will provide the clinical and research expertise. The team have recently been successful in being awarded £93,318 for 6 month phase 1 funding from the Small Business Research Initiative Scheme (SBRI). The key end point and key output of phase 1 is to design a wearable paediatric oximetry probe.

The first stage of this project is to collect clinical data from children undergoing oximetry monitoring to be able to create bespoke paediatric algorithms. This protocol outlines the normative data collection process of existing clinical algorithms using existing oximetry technology.

GENERAL INFORMATION

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GLOSSARY

AHSN	Academic Health Science Network
BSI	British Standards Institution
CE	Conformite Europeenne
ISO	International Standards Organisation
MEMG	Medical Equipment Management Group
SBRI	Small Business Research Initiative Scheme
SCH	Sheffield Children's Hospital
SpO_2	Arterial haemoglobin oxygen saturation by pulse oximetry
TITCH	Technology Innovation Transforming Child Health
MOOP	Means of Operator Protection
MOPP	Means of Patient Protection

1.0 BACKGROUND

Hypothesis

Obtaining clinical paediatric oximetry data on a wide age range of children undergoing clinical oximetry for respiratory conditions will provide data to determine paediatric software algorithms.

The design of the next phase of the project is to develop a wearable, self-adjustable wireless probe that is supported by clinical evidence (current protocol) to support product claims.

Paediatric Pulse Oximetry

Pulse oximetry is frequently used in clinical practice as a simple, non-invasive measure of oxygen saturation. This technique estimates arterial oxygen saturation with reasonable accuracy. However, this technique can only be used safely if the user is aware of the following limitations[1,2]:

- Motion artefacts
- Poor perfusion
- Irregular pulse rhythms
- Influence of ambient light
- Electromagnetic interference
- Skin pigmentation
- Tissue perfusion
- Nail polish
- Calibration assumptions
- Probe positioning
- Sample rate time
- Intravenous dyes
- Presence of abnormal haemoglobin molecules
- Night to night variability[3]

There are differences in oxygenated (oxyhaemoglobin) and deoxygenated blood (deoxyhaemoglobin) in terms of the amount of red and infrared light absorption. These differences in light absorption ratios are measured by transmission pulse oximeters. Within the microprocessor of an oximeter are stored calibration algorithms. These algorithms are used to calculate the SpO_2. Most oximeters have

algorithms for neonates and adults, however there are no algorithms written specifically for paediatrics.

Within the paediatric community of the South Yorkshire and Humber region, there are over 100 patients who are supported by Sheffield Children's Hospital community paediatric home oxygen and home ventilation team. This team regularly monitor patients with long-term respiratory conditions in terms of pulse oximetry in the home environment. In addition, Sheffield Children's Hospital Sleep Unit and community sleep team undertakes approximately 400 pulse oximetry studies a year to investigate and monitor sleep-disordered breathing in children. Accurate pulse oximetry is required to measure hypoxaemia in all of these paediatric patient groups. Current oximeters are not adapted for accurate continuous perfusion monitoring in patients that are able to ambulate. There remains a gap in the market for a device which can take accurate readings from young children whilst the patient is moving, and which can interpret the data and deliver back to the patient clear indications on when to seek the advice of a medical professional. Such a device would allow these children to live more independently and without the need for the current level of medical care, representing an improvement in overall care provision.

The role of the Phase 1 SBRI study is to

a. explore some of the limitations of current oximetry technology and

b. to develop a wearable paediatric probe and paediatric algorithms.

The data obtained from the study described in this protocol will provide data using existing technology to inform the development of the paediatric algorithm.

2.0 STUDY OBJECTIVES AND PURPOSE

The primary objective of the project will be to obtain oximetry data from our paediatric sleep and respiratory patients to determine normative values with which to develop paediatric oximetry algorithms in children with long-term respiratory conditions.

3.0 STUDY DESIGN

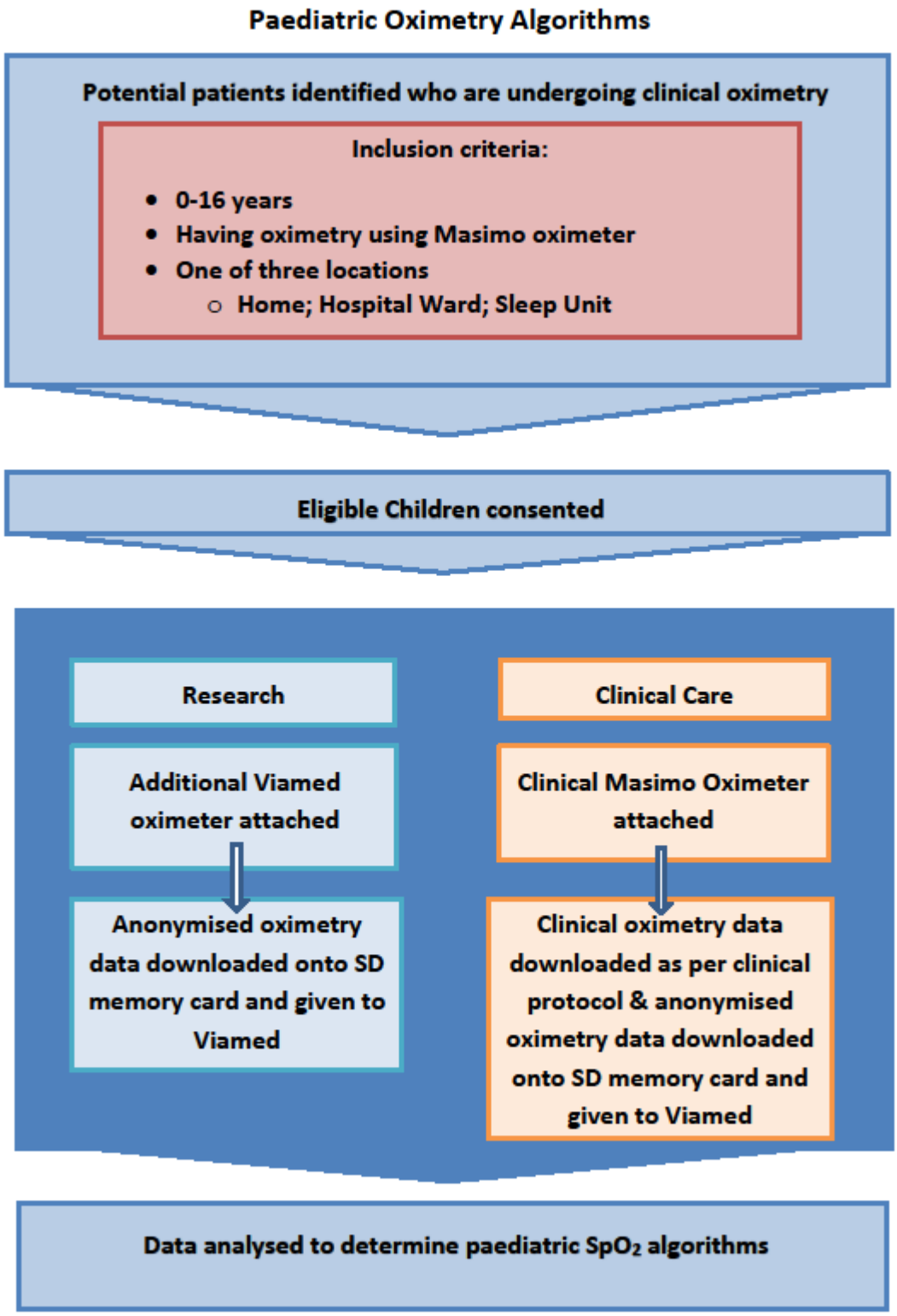
The study design is outlined in Figure 1 and explained below.

Following ethics and HRA approval, we will identify 10-20 suitable children age 1 month – 16 years, who are under the care of the sleep and respiratory team Sheffield Children's Hospital Sleep Unit and are due to undergo an overnight or daytime oximetry recording.

A data collection form of non-identifiable relevant information for the research has been devised [Appendix 1]. This will be completed by RK following consent. This information does not contain any identifiable information. The data collection sheet contains information that will be needed by Viamed to calculate the algorithms: date of test; age; gender; weight; height; ethnicity; comorbidities; the type of saturation probe which was worn; where the probe was attached; the algorithms used.

Each patient will undergo the standard clinical diagnostic / monitoring pulse oximetry recording using a Masimo oximeter. Masimo oximeters are the current oximeter brand used by the respiratory team at the hospital. In this study, we are going to use the Masimo Radical 7 oximeter as the gold standard reference oximeter. In addition to the clinical Masimo oximeter, the participant will also wear a second Viamed oximeter because the data from this oximeter will be used to develop the algorithm. Both oximeters will be connected to a single battery powered data logger. A diagram of the set-up is included in appendix 2. The data logger will allow both oximeters to use the same time stamp and store anonymous clinical data on an SD card. Following on from the oximetry recording, the clinical Masimo oximeter data will be downloaded, interpreted, reported and stored as per usual clinical purposes. In addition, both the anonymous Masimo oximetry and Viamed oximetry data stored on the SD card will be given by hand to Viamed. The data on the SD card consists of voltage numbers and time stamps. There is no patient identifiable information on the SD card. The Masimo data will act as the gold standard reference and allow the team to synchronise the data and compare alarm status and recovery periods. The duration of an oximetry is usually about 8-10 hours, but can occasionally be for a 24 hour period. If the Masimo oximeter failed to work for some reason during the study, the patient would be withdrawn from the study and the Masimo recording repeated alone, in accordance with Trust clinical guidelines.

Figure 1: Schematic Diagram of the Study Design



What is above and beyond standard routine clinical care?

1) The Masimo oximeter will be provided by Viamed so that the same sample rates and existing algorithms can be set up in both oximeters that are going to be worn. This machine is identical to the ones used in clinical practice except for the data logger box attached. This deviation means that the machine will go through MEMG (Medical Equipment Management Group) approval and all relevant indemnity insurance and clinical engineering acceptance testing before patient use.
2) The Viamed oximeter is new to SCH Foundation Trust, as is the data-logger and so will also go to the MEMG committee for approval as a new piece of equipment to the Trust.
3) The anonymous data collected on the SD card from the Viamed and Masimo oximeters into the data-logger will be passed onto Viamed.
4) Anonymous information about the patient (Appendix 1 – Data Collection Form; also see section 5.3) will be passed onto Viamed for algorithm development optimisation.

The research study duration is the duration of the oximetry recording which will be determined by the patient's respiratory clinician.

4.0 SELECTION OF PARTICIPANTS

The participating children will be recruited from Sheffield Children's Hospital (SCH) respiratory and sleep department. All of the patients will be under the medical care of this department with Professor Heather Elphick being the research lead. Patients currently undergo oximetry in three different settings

1) SCH sleep unit
2) SCH wards
3) At home

Patients on the sleep unit attend for overnight oximetry, on average, 2 patients per week. Ward oximetry patient tests occur on average 4 times per week and home oximetry studies occur on average 20 times per week. Therefore, we are confident we will meet the recruitment target of 5-10 patients in hospital and 5-10 patients at home within the study time period of 4 months. The recruited children will include a mix of cases that may or may not have desaturations in their oxygen levels, and include a large age range to give more realistic paediatric algorithms. Suitable participants will be identified by the clinical sleep and respiratory team.

Inclusion Criteria:

- All children who have consented to the study and are undergoing overnight oximetry
- Age 1 month -16 years.

Exclusion Criteria:

- Families who do not understand written or verbal English when no interpreter is available.
- Children who do not attend with their parent /legal guardian and so are therefore unable to give informed consent.
- The research oximetry kit is in use on another patient and so not available for a suitable patient
- Patients deemed too unwell, or unsuitable, by the clinical team

5.0 PARTICIPANT RECRUITMENT

5.1 Recruitment

Patients will be identified and recruited from three different locations:

1) Sheffield Children's Hospital Sleep Unit

Potential participants who are undergoing overnight oximetry using a Masimo oximeter will be identified by specialist sleep nurses on arrival to the sleep unit.

2) Sheffield Children's Hospital Wards

Potential participants who are undergoing overnight oximetry using a Masimo oximeter will be identified by specialist sleep nurses who set up the overnight oximetry studies on the hospital wards.

3) Home oximetry monitoring

Potential participants who are undergoing overnight oximetry using a Masimo oximeter will be identified by specialist home oxygen nurse or specialist home ventilation nurse.

Formal written information will be provided by post along with their appointment to the hospital (for children attending the sleep unit), by the clinical team during a ward round (for children on in-patient wards), or by the child's specialist nurse or consultant during a routine clinical visit (for children being monitored at home). Patients and carers will be given a minimum of 24 hours to read age-appropriate information sheets. The information will be reviewed with the participant/parent by the research physiologist [RK] who has Good Clinical Practice Certification. They will be asked if they understood the content of the information sheets and will be given an opportunity to ask any questions they may have. The study will not include non-English speaking families.

5.2 Consent

Once the child and the legal guardian have verbally agreed to participate, the research physiologist [RK] will obtain written consent and assent where appropriate. A signed copy will be given to the family, a copy will be put in the child's medical case notes and the original securely stored in the research site file at SCH. Patients will be allowed to change their mind after giving consent and can withdraw from the study at any time without it affecting their standard clinical care. For the home oxygen cohort, the research physiologist would attend the home visit with the specialist nurse to obtain consent.

5.3 Data Collection

The participating children will be assigned a unique study number to link their results to their identifiable hospital information. No identifiable data will be collected for the research.

- The oximetry data will be processed at Viamed and stored securely.
- A data collection form of non-identifiable relevant information for the research has been devised [Appendix 1]

6.0 DATA HANDLING AND RECORD KEEPING

The clinical oximetry data recorded on the Masimo pulse oximeter will be handled by clinical staff in the usual manner. In addition, the data from the Masimo oximeter and the Viamed oximeter will be recorded onto an SD card. This data will be time stamped from the Masimo oximeter and contain

overnight values for oxygen saturation levels, artefact and pulse oximetry. The research physiologist [RK] will label the SD card with the research ID that she has allocated to anonymise the data. In addition, RK will complete a data sheet [Appendix 1] that will be given to Viamed along with the SD card. This information does not contain any identifiable information. The data collection sheet contains information that will be needed by Viamed to calculate the algorithms: date of test; age; gender; weight; height; ethnicity; comorbidities; the type of saturation probe which was worn; where the probe was attached; the algorithms used. Rather than obtaining the date of birth, RK will calculate the age in years and months at the time of the oximetry. This means that no identifiable information will be passed onto Viamed. The data collection form will be completed by RK following consent. The data collection sheets form part of the clinical data evidence for the ISO auditors. The data collection sheets and the SD cards will be given to Viamed [SN] at the monthly project meetings for analysis. The consent forms will be stored at Sheffield Children's Hospital in the research site file and a copy in the patient's medical notes. The consent form will contain the patient study ID and be the only data source linking the patient to the oximetry data. Data from the SD cards will be transferred to the technical files at Viamed. These files are stored on Viamed servers with two backups at different locations at Viamed as part of the company disaster management policy. The SD cards will then be erased. Any algorithm enhancements that are taken through to market will be recorded in the ISO technical files. Clinical data has to be present and made available within the CE technical files. Viamed already have full approval from their notified body BSI for adult and neonatal algorithms. This process would be to obtain approval and certification for paediatric algorithms. The anonymous data from the data collection sheets will be inputted into the technical files and then the data collection sheets returned by hand to SCH [RK] at the face-to-face meetings for the SCH research team to store with the research site file.

Clinical oximetry data will be collected and entered into a password protected database (Microsoft Excel) and retained in accordance with the Data Protection Act 1998. Study documents (paper and electronic) will be retained in a secure location during and after the study has finished. All source documents will be archived by the Clinical Research Facility once the study has been completed and these records will be retained for 5 years after the last patient visit.

7.0 ACCESS TO SOURCE DATA

The sponsor will permit monitoring and audits by the relevant authorities, including the Health Research Authority and Research Ethics Committee. The investigator will also allow monitoring and audits by these bodies and the sponsor, and they will provide direct access to source data and documents.

8.0 STATISTICAL ANALYSIS

This is an equipment validation project. The Viamed oximetry data on oxygen saturation and pulse rate will be analysed to look at the age specific ranges of these variables. In addition, comparisons of the current gold standard oximeter will be made. Comparisons of alarm status and recovery periods will also be assessed.

There is a limited time frame for this study and so for the sample size we have chosen a convenience sample of 10-20 children depending on the availability of the oximeters and potential patient availability. We are aiming for 5-10 patients from within the hospital and 5-10 within the home environment.

9.0 SAFETY ASSESSMENTS

The Viamed oximeter which is being used to collect the oximetry data is new to the trust but is used in clinical practice in paediatrics throughout the UK and has full approval from the notified body and is CE marked. There will be a small battery powered data logger attached to the Viamed and Masimo oximeters to record the data onto a SD card. This data logger will be attached via the oximeter's isolated USB ports. New clinical equipment to Sheffield Children's Hospital is reviewed by the medical equipment management group (MEMG) and given approval. In addition, as this equipment is loan equipment it will be acceptance tested by the clinical engineering department and indemnity insurance will be provided by Viamed. This is standard hospital practice for loan kit and new devices to the hospital trust. The Masimo oximeter is used as standard in the hospital, sleep unit and home environment for clinical purposes, however as the one in the research is (1) being loaned by Viamed

and (2) will be attached to the data logger then again the piece of equipment will have to go through MEMG applications. In the home environment, it is standard practice for the oximetry sensor to be attached to the toe and the cable threaded to the waist and then the oximeter is placed on the child's bedroom floor near the feet end of the bed. This minimises the risk of cable strangulation or the machine being pulled onto the child from a bedside cabinet.

The study will be monitored and audited in accordance with the Monitoring Standard Operating Procedures of the Directorate of Research & Innovation at Sheffield Children's NHS Foundation Trust. All study related documents will be made available on request for monitoring and audits by the Sponsor, the Health Research Authority and the relevant Research Ethics Committee.

10.0 ETHICAL CONSIDERATIONS

All data recorded into an oximeter is anonymous. When the oximeter data is downloaded to a PC, this is the point that information about the patient is added. So in the case of this validation work, no identifiable information will be added, just a study ID number.

The study will be conducted in compliance with the NHS Research Ethics Committee favourable opinion, Health Research Authority approval and Confirmation of Capacity & Capability at all participating sites.

The study will also be conducted in accordance with the International Conference for Harmonisation of Good Clinical Practice (ICH GCP), and the Research Governance Framework for Health and Social Care (2nd Edition). The study will also be submitted to the Research Ethics Committee at Sheffield Hallam University for review.

11.0 FINANCE AND INDEMNITY

There will be no payments given to any participants who take part in this study.

This is an NHS sponsored study. For NHS sponsored research HSG (96) 48 reference no. 2 refers. If there is negligent harm during the study when the NHS body owes a duty of care to the person harmed, NHS Indemnity will cover NHS staff, medical academic staff with honorary contracts and those conducting the study. NHS Indemnity does not offer no-fault compensation and is unable to agree in advance to pay compensation for non-negligent harm. Ex-gratia payments may be considered in the case of a claim.

13.0 JUSTIFICATION OF FINANCE AND RESOURCES

Total funding received from the Small Business Research Initiative was £93,318. A small proportion of this funding has been allocated for the research physiologist [RNK] at Sheffield Children's Hospital to undertake the current validation work in this protocol. Funding has been allocated for RNK to identify suitable patients and undergo informed consent. Attend the location where they are having their clinical oximetry and attach the additional oximeter and then download the data following oximetry and giving to Viamed. In addition, some of the awarded funds have been allocated to Viamed for this validation work to analyse the data and determine paediatric algorithms. Viamed will provide the hospital with our gold standard oximeter, Masimo oximeter, for the validation work, along with their Viamed oximeter on loan for the duration of the study.

14.0 REPORTING AND DISSEMINATION

Results will be presented at clinical conferences and published in a journal. The results will also be published on the research and development website and in the Trust communications newsletter. The results will make up part of the funding application for the SBRI Phase 2 development of the paediatric oximeter.

15.0 IMPACT

Developing paediatric oximetry software algorithms will allow more accurate monitoring of paediatric oximetry. This will benefit our patients locally, but also nationally as paediatric oximetry is used

throughout hospitals and in the community UK wide. There is extensive research development work associated with this study that will lead to publication in reputable journals and will further enhance the standing of SCH as a centre of research excellence. Improved paediatric oximetry techniques have the potential to allow some of the monitoring currently performed at hospital to be carried out at home. This will reduce NHS cost and allows the child to be in their own normal environment.

16.0 OUTCOMES

The collected oximetry data will inform our grant application for Phase 2 of the project to clinically evaluate the new paediatric oximetry prototype developed in Phase 1.

The algorithm will be taken through to market by Viamed using appropriate ISO technical files.

17.0 Authorisations

Finance Department Representative:

Finance Department Signature: Date:

Applicant's Manager:

Applicant Manager's Signature: Date:

REFERENCES

1. Fouzas S, Priftis KN, Anthracopoulos MB. Pulse Oximetry in Pediatric Practice. *Pediatrics*. 2011:128;740.
2. Fouzas S, Politis P, Skylogianni E, et al. Knowledge on pulse oximetry among pediatric health care professionals: a multicenter survey. *Pediatrics.* 2010:126(3).
3. Burke RM, Maxwell B, Hunter C, Graham D, O'Donoghue D, Sheilds MD. Night-to-night variation of pulse oximetry in children with sleep-disordered breathing. *Arch Dis Child* 2016 101:1095-1099

APPENDICES

Appendix 1: Data Collection Form

Study ID: _ _ _ _ _ _ _

Oximetry Data Collection Form – Information to be shared with Viamed

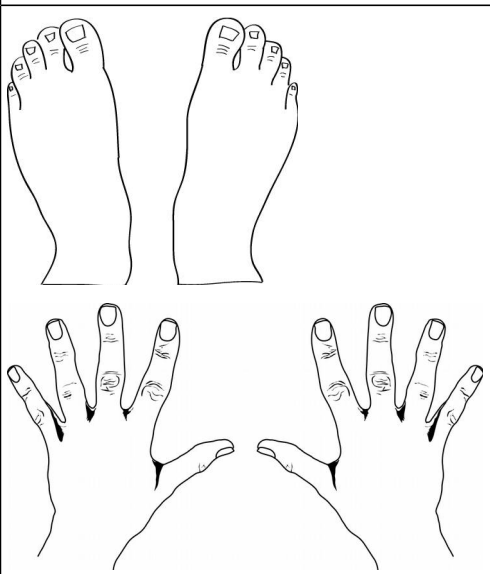
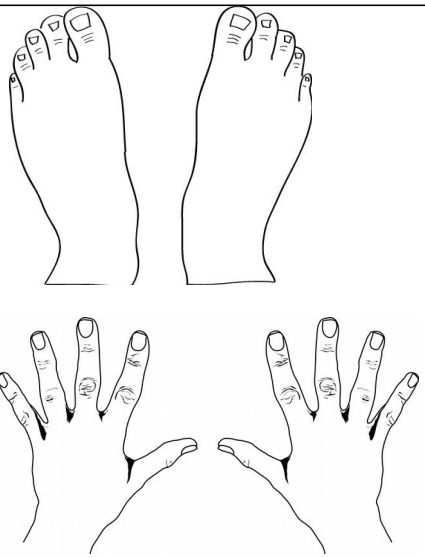
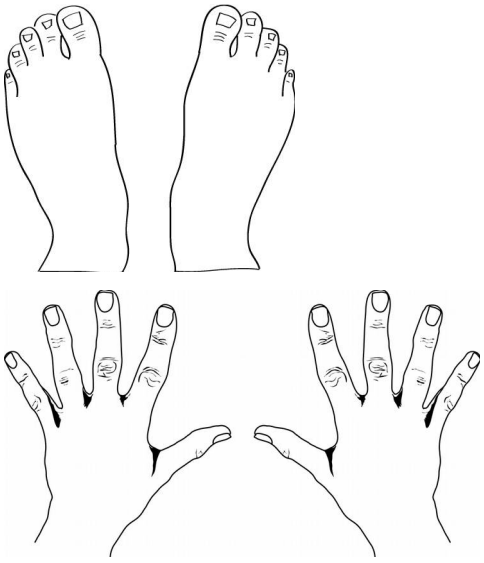
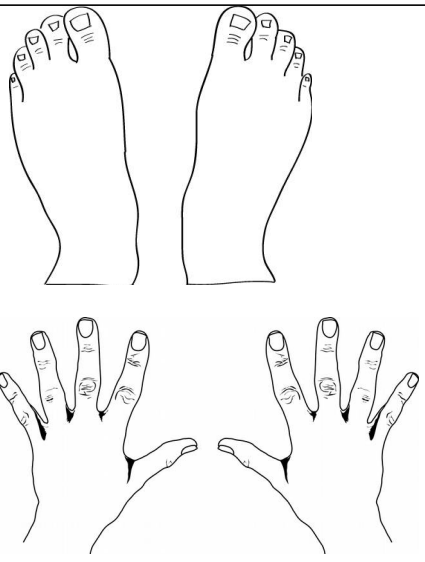
Variable	Value
Date of oximetry	
Age (2dp) at time of oximetry (yrs)	
Height	
Weight	
Gender	
Reason for oximetry	
Co-morbidities	
Ethnicity	
Is this their first oximetry?	

Appendix 1: Data Collection Form

Sheffield Children's NHS
NHS Foundation Trust

Study ID: _ _ _ _ _ _ _

Oximetry Data Collection Form – Information to be shared with Viamed

Variable	Viamed oximeter	Masimo oximeter
Sensor type and model number		
Algorithm used		
Monitoring time started		
Site of sensor (please circle sensor site on diagram)		
Time of sensor repositioning (if appropriate)		
New site of sensor (please circle sensor site on diagram)		
Time monitoring stopped		

Appendix 2: Diagram of oximeter and data-logger set-up.