
Perioperative Comparison of the Agreement between a Portable Fingertip Pulse Oximeter vs. a Conventional Bedside Pulse Oximeter in Adult Patients (COMFORT Trial)

Dr Reuben Nathanael Smith

MBChB (Stell), DA (SA), FCA (SA)
Department of Anaesthesia & Perioperative Medicine
University of Cape Town
SMTREU003

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Supervisor:

Associate Professor Ross Hofmeyr
MBChB (Stell), DipPEC (SA), DA (SA), FCA (SA), MMED (UCT), FAWM
Department of Anaesthesia & Perioperative Medicine
University of Cape Town



DEPARTMENT OF ANAESTHESIA
& PERIOPERATIVE MEDICINE

UNIVERSITY OF CAPE TOWN

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Abstract

Background

Low-cost, portable fingertip pulse oximeters are widely available to health professionals and the public. They are often not tested to ISO standards or undergo accuracy studies in healthy volunteers under ideal laboratory conditions. This study aims to pragmatically evaluate the agreement between one such device and a conventional bedside pulse oximeter in a clinical setting, in patients with varied comorbidities and skin pigmentations.

Methods

A single-centre equipment comparison study was conducted. Simultaneous measurements were obtained in 220 patients with both a Contec CMS50D Portable Fingertip Pulse Oximeter and a Nihon Kohden Life Scope MU-631 RK conventional bedside monitor. Peripheral oxygen saturations (SpO₂) and pulse rates were documented, and patient skin tone was recorded using the Fitzpatrick scale. Data was assessed using a Bland-Altman analysis with bias, precision and limits of agreement (LOA) calculated with 95% confidence intervals. *A priori* acceptability for LOA was determined to be 3%, in keeping with international standards.

Results

Mean difference (bias) between the conventional and portable fingertip oximeters for all data was -0,55% (95% CI -0,73 to -0,36%). Upper and lower limits of agreement (95% CI) were 2,16 (1,84 to 2,47) and -3,25 (-3,56 to -2,94) %. Regression analysis demonstrated worsening agreement with decreasing SpO₂. When samples were separated into “normal” (SpO₂ ≥ 93%) and “hypoxaemic” (SpO₂ < 93%) groups, the normal range displayed acceptable agreement between the two oximeters (bias -0,20 with LOA 2,20 to -2,27%), while the hypoxaemic group fell outside the study’s *a priori* limits. Heart rate measurements had mean difference (LOA) of -0,43 (-5,61 to 4,76) beats per minute. The study was not powered to detect difference among the skin tones, but demonstrated no trend for this parameter to alter the SpO₂ measurements.

Conclusions

During normoxia, portable fingertip pulse oximeters are reliable indicators of SpO₂ and pulse rates in patients with various comorbidities in a pragmatic clinical context. However, they display worsening agreement with conventional pulse oximeters during hypoxaemia. Skin tones do not appear to adversely affect measurements.

What questions this study addressed

This pragmatic, prospective study compared the agreement between the measured arterial oxygen saturation levels and pulse rates using a portable fingertip versus a conventional bedside pulse oximeter in adult patients, presenting for elective and emergency surgery, in a clinical setting.

What this study adds to our knowledge

This study found that there is sufficient agreement between the arterial oxygen saturations and pulse rates measured by a portable fingertip and conventional bedside pulse oximeters amongst adult (surgical) patients who are not hypoxaemic in the clinical setting. However, as saturations dropped into the hypoxaemic range (less than 93%), agreement between the devices worsened. Additionally, it found no significant influence by skin tone on the measurements, although the study was not powered to convincingly detect this outcome.

How this study might change clinical practice

Low-cost portable fingertip pulse oximeters marketed for non-medical use are often not tested in humans under clinical conditions. The measurements obtained by these portable and affordable items of equipment have therefore been regarded with skepticism by medical staff. This study demonstrates that one such pulse oximeter is sufficiently as accurate as a far more expensive bedside pulse oximeter when used to exclude hypoxia. Similar studies can be done using other similar equipment to promote access to these vital medical instruments in resource limited areas.

Keywords: perioperative, portable, monitoring, plethysmography, pulse oximetry, oxygen

Additional relevant MeSH terms: Hypoxia, Signs and Symptoms, Respiratory Signs and Symptoms

Abbreviations: SpO₂, oxygen saturation measured by pulse oximetry; SaO₂, arterial oxygen saturation; WHO, World Health Organization

Declaration

I, Reuben Smith, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

I empower the university to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

Signature:

Signed by candidate

Date: 16 August 2018

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Part A - Research Protocol

University of Cape Town

Department of Anaesthesiology & Perioperative Medicine

*Perioperative Comparison of the Agreement between a
Portable Fingertip Pulse Oximeter vs. Conventional Bedside
Pulse Oximeter in Adult Patients*

Research Proposal

For MMed Dissertation in

Anaesthesiology & Perioperative Medicine

MMed Candidate: Dr Reuben Smith

MP0621919

Supervisor: Associate Professor Ross Hofmeyr

MP0640182

Summary

Background/ Literature review:

Perioperative accurate and non-invasive measurement of a patient's arterial oxygen saturation has become an accepted standard of care endorsed by anaesthetists and their regulatory bodies throughout the world. Pulse oximeters are an integral item on the World Health Organization's Surgical Safety Checklist which is performed prior to the commencement of every surgical procedure. They are also utilised by other medical professionals and patients in various scenarios.

When compared to conventional bedside pulse oximeters, the portable fingertip devices have the advantages of cost-effectiveness, high portability, ease of use and battery operation.

A review of recent literature reveals a paucity of accuracy studies in adult patients with various comorbidities in the clinical setting. Most data has been obtained under ideal laboratory conditions utilizing healthy adult volunteers.

This study aims to be among the first that investigates the performance of a portable fingertip pulse oximeter in adult patients in a hospital setting.

Research questions, hypothesis, objectives:

The purpose of this prospective, quantitative study is to compare the agreement between the measured arterial oxygen saturation levels using a portable fingertip versus a conventional bedside pulse oximeter in adult surgical patients, presenting for elective and emergency surgery to Groote Schuur Hospital over a four-week period.

Methods including all the major aspects:

All adult surgical patients, not meeting any exclusion criteria, who present for elective or emergency surgery will be recruited by convenience sampling. 200 data pairs (SpO₂, heart rate and skin tone) will be recorded in the perioperative period (operating rooms, recovery room and intensive care unit). Existing monitoring devices will not be disturbed. The agreement between the two devices will be compared using a Bland-Altman plot, Microsoft Excel and SPSS software. A root mean square difference value will also be calculated from these values.

Ethical considerations:

No personal patient information will be recorded and pulse oximetry is essential harmless. Potential cross-infection will be avoided by excluding patients with known communicable diseases or open wounds/ bodily fluids in the area to have the oximeter probe inserted. The study devices will be disinfected after each use. Recruitment will not affect clinical care.

Study significance:

The significance of this study into the performance of portable fingertip pulse oximeters in adult surgical patients will result in the availability of cheaper devices, deemed as vital anaesthetic equipment by the WHO and various anaesthetic regulatory bodies, in lower income medical facilities. It will also give anaesthetists and other medical personal the confidence to make clinical decisions based on these highly portable devices, thereby making pulse oximeters more available in resource limited areas. It will also add further data to existing studies and help assess whether darker skin pigment affects the performance of these devices in the clinical setting, which is highly relevant in an African country like South Africa.

Background & Significance

The ability to accurately and non-invasively assess a patient's arterial oxygen saturation has become an accepted standard of care in the perioperative period (1). Pulse oximetry is considered an essential item of equipment for providing safe anaesthesia by various regulatory bodies throughout the world, including the South African Society of Anaesthesiologists (2,3). Subsequent to the World Health Organisation's (WHO) Safe Surgery Saves Lives (SSSL) program in 2007, pulse oximeters were included in the WHO Surgical Safety Checklist (SSC), which was launched in 2008. Following the introduction of the WHO SSC, studies have demonstrated that patients' likelihood of receiving proven standards of surgical care nearly doubled, and that there was a substantial reduction in complications and deaths (4). This checklist is currently utilised in Groote Schuur hospital and other health facilities throughout the country, prior to the commencement of a surgical procedure.

The WHO's Global Pulse Oximetry Project aims to "improve the safety of anaesthesia care throughout the world by providing affordable, robust pulse oximetry devices for every operating room in the developing world that does not have one" (5,6).

The World Federation of Societies of Anaesthesiologists (WFSA) adopted the International Standards for a Safe Practice of Anaesthesia since 1992, which lists pulse oximeters as "highly recommended" for the monitoring of tissue oxygenation and heart rate both during anaesthesia, and post-operatively until the patient has recovered consciousness (7). Pulse oximetry is non-invasive, safe and currently performed routinely on surgical patients during admission, intra-operatively and post-operatively, without requiring specific consent.

Portable fingertip oximeters have the additional benefits of being cost-effective and highly portable. The apparatus could potentially save time in diagnosing an acute episode of hypoxemia in the preoperative ward, or postoperative recovery room, if the conventional bedside oximeters are in use or unavailable. They are also invaluable for periods during which patients are being transported between care locations (e.g. theatre and recovery, or recovery and the ward), and in the case of failure of conventional bedside equipment. In disaster scenarios or remote settings, they may provide lifesaving information without being a burden to transport. Furthermore, their application extends beyond anaesthesia to personnel working

in the fields of emergency medicine, general practice, paramedics, mobile clinics, nursing staff, expedition medicine and many others.

Applications of pulse oximetry:

These vital items of equipment have a wide range of applications, including individual oxygen saturation readings, such as during a pre-operative anaesthetic assessment, or in any clinical situation where hypoxaemia may be a causative factor.

In the primary care setting, pulse oximeters can be utilised to aid assessment and management of various respiratory conditions, including; asthma, chronic obstructive pulmonary disease, community acquired pneumonia and bronchiolitis (8,9).

Pulse oximetry is more cost-effective, less painful, easier to perform and more readily available than invasive arterial blood gas analysis. It has largely replaced this method in many clinical situations, unless carbon dioxide or acid-base status is specifically required.

Neonates and premature babies are vulnerable to certain conditions (e.g. retinopathy of prematurity, bronchopulmonary dysplasia etc.) if exposed to high concentrations of oxygen. Pulse oximeters are helpful in adjusting the inspired oxygen concentration to safer levels. It avoids wastage of oxygen by allowing the titration of oxygen flow to predetermined peripheral arterial oxygen saturation values, depending on the clinical condition and the patient's requirements.

Pulse oximeters continuously record oxygenation, which aids the safe conduct of anaesthesia or sedation, and recovery thereafter. Studies have shown that pulse oximeters allow the early detection of hypoxaemia, aiding appropriate intervention to avoid related disastrous complications, and possibly reduce the frequency of cardiac ischaemia and arrest. There was also more frequent detection of endobronchial intubation and hypoventilation (8). As outlined above, their use during anaesthesia is considered mandatory by most anaesthesia organisations around the world, and they are included on the WHO SSC ((12).

After nausea and vomiting, the second most frequently encountered complication in the post anaesthesia care unit (recovery room) is respiratory-related (13). The early detection of hypoxemia by pulse oximetry leads to early recognition of this complication and helps avoid related adverse outcomes.

Despite a 1993 pulse oximetry trial by Moller et al., involving 20 802 patients and a 2002 Cochrane review failed to demonstrate a difference in postoperative mortality nor in cardiovascular, respiratory, neurologic or infectious complications with the perioperative use of pulse oximeters, there is some intense debate on these findings (11,14,15). A 2009 editorial in *Anaesthesia*, questioned the methods of the Cochrane review and highlighted that the Moller study was underpowered to detect a reduction mortality or myocardial infarction (16).

Despite these findings, the routine perioperative use of pulse oximetry is overwhelmingly supported by healthcare organisations and anaesthesia practitioners worldwide.

How a pulse oximeter functions (17–20):

Pulse oximeters noninvasively measure and display the heart rate and estimated arterial haemoglobin oxygen saturation (SpO_2) derived from photoplethysmographic measurements at two rapidly alternating different wavelengths of light. Oxygenated blood (oxyhaemoglobin) and deoxygenated blood (deoxyhaemoglobin) differ in their absorption of red and infrared light. Measurement is accomplished by utilising the Beer-Lambert Law, which states that absorption at a specific wavelength is proportional to the distance through the specific medium traversed by the light rays. A sensor containing a light emitting diode and a light detecting photodiode is typically placed on a cutaneous vascular bed, such as a fingertip or earlobe, which can be transilluminated. Arterial pulsations are identified by plethysmography, allowing corrections for light absorption by non-pulsating venous blood and tissue. The ratio of the absorptions at the red and infrared wavelengths is analysed by a microprocessor and SpO_2 estimated from a stored calibration curve.

These curves are based on experimental measurements in healthy young volunteers, after induction of hypoxemia, with subsequent determination of oxygen saturation of haemoglobin by both the pulse oximeter (SpO_2) and in vitro laboratory multi-wavelength co-oximeter (SaO_2),

considered as the gold standard for measurement of arterial oxygen saturation). Each manufacturer's exact calibration curve is proprietary. Pulse oximeters are inaccurate at low blood oxygen saturations because researchers are limited in the degree of hypoxaemia inducible in volunteers (approximately 75 to 80%). The shape of the calibration curves must be extrapolated at oxygen saturations below these levels.

Accuracy of Pulse Oximeters:

Oxygen saturation measurement of an arterial blood sample using a blood gas analyser is considered the "gold standard" (17,21–26). This method is invasive (requires a needle puncture of an artery to obtain a blood sample), expensive and slow in comparison to a pulse oximeter. Repeated sampling is necessary, and there is a consequent delay in obtaining the result, which may range from minutes to significantly longer, if the machine is not in close proximity to the patient, and is not helpful in monitoring for an acute episode of hypoxaemia.

Numerous studies have confirmed sufficient accuracy of pulse oximeters when compared to the gold standard in the clinically relevant range of arterial oxygen saturation (21,27,28). Their accuracy progressively deteriorates below a SaO₂ of 90%.

Rational & Justification:

There are numerous advantages of pulse oximeters, which include: cost-effective, non-invasive (thereby less painful than methods which utilise arterial blood sampling), easier to perform, fast and continuous.

Portable fingertip pulse oximeters are highly compact and transportable, battery operated, easy to use and affordable.

When pulse oximeters are manufactured, they are tested for accuracy against blood gas analysis in healthy volunteers. There are published standards from the USA Food and Drug Administration (FDA) on how this should be performed, including statistical methods that feature Bland-Altman analysis.

Conventional bedside pulse oximeters are currently utilised in the hospital setting as a reliable estimate of arterial oxygenation, as outlined above.

This study aims to test the agreement between conventional and portable fingertip devices in the perioperative setting, in terms of clinical decision making. This will allow us to judge the clinically usefulness of the devices. We will use a similar level of agreement (within 3%) as is used for accuracy testing, as this also reflects what would be considered a clinically meaningful difference in oxygen saturation (between, for instance, 94 and 91%).

If this study shows that there is poor agreement between our established (conventional) bedside and portable fingertip saturation monitors, it will discourage the use of portable fingertip oximeters outside of situations where portability is the only major concern. However, if this study shows that agreement of the portable fingertip device is within acceptable limits for clinical decision-making, it will improve patient safety through increased, low-cost access to oxygen saturation monitoring. These devices are very compact, efficient, and cheaper than even a modest stethoscope, and thus could potentially become a frequent adjunct to each practitioner's personal equipment.

Literature Review

A literature search of electronic databases (including PubMed and Google Scholar) was performed for published English articles on adult studies which contained, but not limited to, the key terms “pulse oximeter”, “oximetry”, “portable”, “fingertip”, “accuracy”, “agreement”, “adult” revealed a paucity of studies pertaining to the performance of portable fingertip pulse oximeters in adult surgical patients.

Most studies evaluating the accuracy of new pulse oximeters recruit healthy volunteers who are subjected to rebreathing controlled hypoxic gas mixtures under laboratory conditions. An arterial blood sample is drawn and the pulse oximeter’s non-invasive estimation of arterial oxygen saturation is compared to a co-oximeter, which is considered the gold standard. This is performed under ideal laboratory conditions, which includes controlling for subject movement, ambient light, etc.

Various unpublished accuracy studies have been performed on individual manufacturers’ portable fingertip pulse oximeters (29). They are not peer reviewed and usually recruit healthy adult volunteers under laboratory controlled hypoxic conditions.

Presently there is not sufficient published evidence that portable fingertip pulse oximeters are as accurate as standard pulse oximeters in estimating arterial oxygen saturation in adult surgical patients with various co-morbidities in a clinical setting, as opposed to the controlled environment of a laboratory.

The goal of the WHO SSSL initiative is to provide inexpensive, high-quality pulse oximeters to low- and middle-income countries (LMICs) in order to improve surgical safety (30) Dr Dubowitz and Dr Lipnick are founders and directors of the non-profit charitable organisation ‘Global Partners in Anaesthesia and Surgery’ and the ‘Lifebox’ oximetry project operate in parallel to the WHO SSSL initiative to provide “a low-cost, high-quality pulse oximeter for low- and middle-income countries”. The Lifebox pulse oximeter was identified as a suitable item of equipment which fulfilled the WHO’s requirements. It is, however, a handheld device, which is larger and less compact than portable fingertip oximeters, and considerably more expensive

(approximately R3500 vs. <R800 for the portable fingertip pulse oximeter used in this study) (25).

Dubowitz et al. demonstrated that the Lifebox portable pulse oximeter met International Organisation for Standardization (ISO) and FDA 510(k) standards, when testing the device on 57 healthy volunteers under controlled hypoxic conditions (25). Arterial blood gas samples were taken and compared to a multi-wavelength oximeter. The Lifebox oximeter, however, is a handheld device (thus larger than a portable fingertip pulse oximeter) and approximately five times more expensive.

Lipnick et al., further reviewed the accuracy of six low-cost portable fingertip pulse oximeters in 2016 (26). Results showed that only two units met ISO and FDA standards in the SaO₂ range of 70 – 100%. The remaining oximeters demonstrated deteriorating accuracy at lower arterial oxygen saturations. Controlled hypoxic gas mixtures were inspired by the volunteers and arterial blood samples drawn, which were compared to a multi-wavelength oximeter in a similar fashion to the Lifebox study. Limitations of this study included the use of healthy volunteers, being tested under ideal conditions (motionless subjects with good peripheral perfusion). In addition, the majority of the subjects were Asian and Caucasian.

A study involving 55 dental patients in Brazil found no statistically significant difference between a portable fingertip and hospital pulse oximeters (31). The non-invasive SpO₂ of each device was measured by simultaneous application of the fingertip probes at six time intervals during the dental procedures. The American Society of Anaesthesiologists (ASA) grade of the patients was not stated, however, patients with cardiac or respiratory conditions, pregnant women and children were excluded. A shortfall of this study was that the data was analysed using both a Bland-Altman graph and Pearson correlation coefficient. The latter is not an appropriate method for use when comparing agreement between two different items of equipment (32). It did, however, include patients in a dental setting, and not merely healthy volunteers in a laboratory scenario.

An additional study in 2015 attempted to examine the agreement between a portable fingertip pulse oximeter (Maxtec MD300 C2) and SaO₂ measured by a laboratory blood gas analyser in the clinical setting (33). Patients in a pulmonary and renal intermediate care unit were recruited by convenience sampling when a “therapeutically prescribed” arterial blood gas was

required. The SaO₂ was then compared to SpO₂ derived by the test portable fingertip pulse oximeter which was applied within three minutes of the blood gas sample.

The authors noted an unacceptable difference in bias and precision values, especially when SaO₂ ≤93%. There were, however, some significant methodological flaws, including the study being probably underpowered (n=32) to detect a significant difference. The pulse oximeter was also not applied simultaneously while the arterial blood sample was drawn. Indications for 21 of the 32 samples included changes in level of consciousness and/ or shortness of breath, which means that the delay of up to three minutes in obtaining the SpO₂ may have resulted in the investigators measuring a different value to that obtained by the arterial blood gas sample. The exclusion criteria were also not consistent with many previous published studies that highlighted the common causes of errors in arterial saturation measurement by oximeters.

Research Problem

We hypothesize that portable fingertip pulse oximeters (specifically, for this study, the Contec CMS50D Fingertip Pulse Oximeter model which is widely available and in clinical use), provides acceptable agreement (within 3%), with operating theatre and bedside oximeters in clinical use, and thus can be used for clinical decision-making at single moments in time.

The null hypothesis is that agreement is not acceptable (greater than 3% limits of agreement).

We will perform a pragmatic, in-service assessment in the perioperative clinical context in the operating theatres, recovery rooms and intensive care units (ICUs) to ascertain the limits of agreement using the Bland-Altman analysis method.

Aims & Objectives

Primary Aim:

The primary aim of the study is to determine if a portable fingertip pulse oximeter is sufficiently agreement within 3% (± 1.96 SD) for bedside clinical decision-making in comparison to our conventional bedside pulse oximeters in the operating theatre, recovery room and ICU setting.

Secondary Aims:

The secondary aims of the study are to:

- Ascertain whether the pulse rates obtained from the devices are in agreement
- Determine if relative darkness of skin pigment adversely affects the limits of agreement of the device.

Objectives of the Study:

In order to achieve the aims of the study the following objectives will be sought: To simultaneously measure and record the peripheral arterial oxygenation values obtained using a portable fingertip pulse oximeter and conventional bedside pulse oximeter. The heart rate and skin tone of the subjects will also be recorded.

The data will be analysed using the Bland-Altman method. The goal of this study is to test whether these results can be obtained in the perioperative setting using adult surgical patients with various comorbidities.

Methodology

Study Design:

This is a prospective, quantitative equipment comparison study which aims to document the simultaneous, non-invasive measurement of peripheral arterial oxygen saturation and heart rate obtained with portable fingertip and conventional bedside pulse oximeters, in the perioperative setting, involving adult surgical patients.

Setting & Subjects:

The study will take place at Groote Schuur Hospital, which is a tertiary-level institution in Cape Town, South Africa over a continuous four-week period. Measurements will be obtained from patients in the operating rooms, recovery room and ICU on at least a daily basis. A sample size of at least 100 data sets is considered adequate to perform a Bland-Altman analysis (34). For this study, we will attempt to obtain 200 measurements during the study period.

Recruitment:

Participants will be recruited by convenience sampling. All patients compliant with the inclusion criteria will be included in the study. No specific patient information will be recorded, thus ensuring complete patient anonymity.

Inclusion Criteria:

All adult surgical patients ≥ 18 years of age who present for elective or emergency surgery from all surgical fields are considered eligible for this study, providing no exclusion criteria are met. Data will be collected throughout the perioperative period, i.e. in anaesthesia pre-assessment areas, induction rooms, operating theatres, recovery rooms, PAHCU and ICU.

Exclusion Criteria:

Patients who have conditions known to cause inaccuracies in pulse oximeter readings will be excluded from the study, which includes (14,15,17,18,20,21,24,35):

- Patients with contact precautions due to high risk of transmission of infectious disease (e.g. drug-resistant infections in ICU)
- Significant hypotension (systolic blood pressure <80mmHg) or hypo-perfusion/ vasoconstriction of the fingers to be measured
- Motion artefacts due to excessive patient movements
- Known presence of variant haemoglobin species (e.g. carboxy-haemoglobin, methaemoglobin, structural haemoglobinopathies)
- Intra-operative dye use (e.g. methylene blue, indigo carmine, indo-cyanine green)
- Nail polish and black henna
- Tape or bandages over the fingers, which may interfere with the optical path
- Inadequate pulse oximetry tracing

Data Collection & Measurements:

Data is to be collected by the authors.

Quantitative data will be recorded on a data collection form evaluating:

- SpO₂ and heart rate
- Skin colour as estimated by the Fitzpatrick scale
- Qualitative strength of wave form signal (good, poor, absent)

The Fitzpatrick scale was selected rather than other methods (e.g. von Luschan scale or reflectance spectrophotometry) for reasons of simplicity, repeatability and cost containment.

Measurement method:

- Simultaneous application of portable fingertip (Contec CMS50D) and conventional bedside pulse oximeter (Nihon-Kohden LifeScope BSM 3562) probes on non-adjacent fingers of the same hand, preferably on non-blood pressure cuff arm
- Confirm waveform on both oximeters
- Time averaging for each oximeter - reading taken at 30 seconds post-application
- No interruption to current pulse oximeter if present
- One data-pair noted per subject
- Skin tone documented

The Contec CMS50D Fingertip Pulse Oximeter was selected as the test device for this study because of its relatively low cost, ease of availability in South Africa and it was one of two devices identified in the Lipnick et al study that met ISO and FDA standards in healthy test subjects. The Nihon-Kohden LifeScope bedside monitor is an industry-standard device in current use in the theatre and ICU environments.

Data Management:

Data capture forms will be collected and collated. The information will be captured in excel for further statistical analysis. No patient details will be recorded at any time. Data will be entered into a spreadsheet with archiving in password-protected cloud storage. Physical backup copy on USB flash drive will be locked in a secure area in the Department of Anaesthesia.

Data Analysis:

Method of comparison

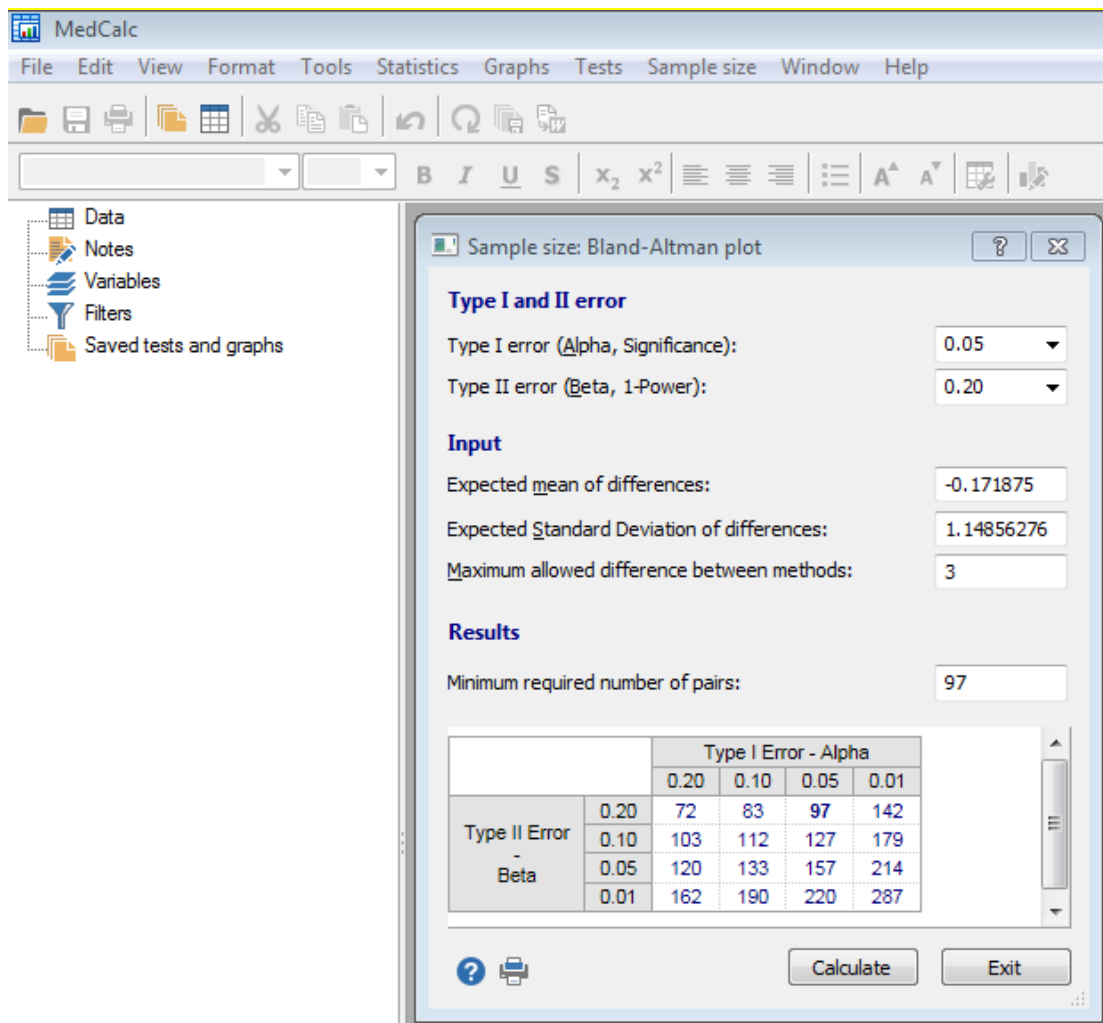
Bland and Altman have established bias and precision estimates as the standard reported statistic when comparing agreement between a new or less-established measurement technique with an established one (32,36–39). Their 1986 Lancet paper ranked number 29 in the list of top 100 most-cited papers (2014), with currently more than 37 000 citations.

The Bland-Altman plot (or mean difference plot), is a graphical comparison of two different quantitative measurement techniques, which measure the same variable. The difference between the two measurement methods ($A - B$) is plotted against the averages of the methods ($(A+B)/2$). The average (referred to as the bias) and standard deviation (SD) of the differences is calculated. Precision is defined as 1 SD above and below the bias and represents random error in the data (38).

Bland and Altman recommend using 95% limits of agreement (bias plus or minus 1.96 SD). The two measurement techniques can be considered interchangeable when the limits of agreement are small and not of clinical importance, which must be defined a priori. It is important to note that the width of the confidence interval represents precision (repeatability). For this study, we have determined that an SpO₂ difference of less than 3% is not of clinical importance, which is in keeping with the relevant ISO standard (ISO 80601-2-61:2017) and FDA testing protocol (40). The FDA guidance specifically recommends using the Bland-Altman method with an accepted minimum of 200 sample pairs. It should be noted that while the emphasis of this testing process is on device accuracy in comparison to co-oximetry (rather than our pragmatic model of clinical decision-making), they also specify an acceptable limit of 3% difference.

The issue of estimating a sample size for the Bland-Altman method has been raised for some time in the literature. While calculating a sample size is not required for the method as described above, there is some utility in being able to do so to plan studies. Liu et al. in 2016 propose a new mathematical method using the theory of statistical inference and Monte-Carlo simulation to address this problem (41). In response to the ongoing question of sample size

in the initial ethics review of this study's protocol, we have thus used Liu's method to confirm that our proposed number of samples will be adequate. An expected bias (mean of differences) and standard deviation of differences was calculated from pilot data, and Liu's calculation performed using the MedCalc software (www.medcalc.org) for a maximum 3% difference, using a Type I error of 0.05 and Type II error of 0.20. The calculated minimum number of pairs for this level of agreement would be 97, confirming Bland & Altman's suggested minimum value. MedCalc provides an output for different levels of Type I and II error, and we note from the output that our suggested sample of 200 pairs would meet/exceed the requirements for a significance of $p=0.01$ and power of 90%. (Interestingly, 300 samples, if achievable, could drop this to 0.01 and 99% power). The output is included below.



On this basis, we have established that we will use a sample size of 200 pairs of measurements.

The data analysis will be performed by calculation with Microsoft Excel and confirmed with SPSS software.

Ethical & Legal Considerations

To ensure complete anonymity, no personal patient information or details will be recorded on the data collection form. Only the following data will be recorded:

- Saturation (SpO₂)
- Heart rate
- Setting (induction/theatre/ICU etc)
- Skin tone (Fitzpatrick scale)
- Waveform quality (good, poor or absent)

No further data on with regard to patient demographics, ASA grade, comorbidities etc. will be recorded.

Recruitment will not affect clinical care. The two pulse oximeters used in the study will be applied simultaneously to any patient monitoring equipment, which may be applied to the patient. Thereby, ensuring no disruption in, for example, continuous monitoring that may be present in the recovery room.

Possible risks:

Pulse oximetry is essentially harmless to patients. The only possible theoretical risk is cross-contamination. The fingertip probes will be disinfected between measurements using an alcohol wipe. Any bodily fluids will be avoided. Patients with open wounds on their hands, or who have contract precautions due to risk of infectious disease transmission, will be excluded from the study.

Privacy and confidentiality:

No patient identifiable information will be recorded and data will be captured in a sequential manner (e.g. number 1 – 200).

Consent:

Signed informed consent will be waived for the following reasons:

- Brief, non-invasive application of a standard monitoring device
- Pulse oximetry forms part of the routine observations performed on all surgical patients (blood pressure, pulse rate, oxygen saturation, respiratory rate and temperature measurement) on admission, intra-operatively and post-operatively until full recovery from anaesthesia
- Pulse oximeter already attached to the patient for monitoring purposes (e.g. in recovery room) will not be disturbed (as far as possible)
- No risk of physical harm to patients
- No personal or protected information will be gathered, results will be anonymous
- No additional information gathered that is not already being gathered/recorded
- Theoretical risk of cross-infection – probe to be cleaned with alcohol-based disinfectant between uses (as per standard hygiene and infection control principles)
- During data collection, should any patient be found to have unrecognised hypoxia, standard treatment will immediately be commenced and the treating doctor notified

Reimbursement for participation:

There will be no reimbursement offered.

Resources & Cost

Standard/bedside pulse oximeters will be used where they are in place in the operating theatres, recovery room and ICUs. For additional measurements, a mobile unit will be loaned from the Department of Anaesthesia, Groote Schuur Hospital at no additional cost. The author will use his own portable fingertip pulse oximeter which has already been purchased. Data analysis will be performed by the study Supervisor.

Reporting of Results

Results of the audit will be written up as part of the MMed dissertation, and submitted for grading. These results, once compiled will be made available.

Conflicts of Interest

None to declare.

Study Significance

The significance of this study into the performance of portable fingertip pulse oximeters in adult surgical patients will result in the availability of cheaper devices, deemed as vital anaesthetic equipment by the WHO and various anaesthetic regulatory bodies, in lower income medical facilities. It will also give anaesthetists and other medical personal the confidence to make clinical decisions based on these highly portable devices, thereby making pulse oximeters more available in resource-limited areas. It will also add further data to existing studies and help assess whether darker skin pigment affects the performance of these devices in the clinical setting, which is highly relevant in an African country like South Africa.

Bibliography

1. Merry AF, Eichhorn JH, Wilson IH. Extending the WHO “Safe Surgery Saves Lives” project through Global Oximetry. *Anaesthesia* [Internet]. 2009 Oct 1 [cited 2017 Jun 21];64(10):1045–8. Available from: <http://doi.wiley.com/10.1111/j.1365-2044.2009.06104.x>
2. Bettings P, Diedericks J, Fourie P, Joubert I, Kluyts H, Lundgren C, et al. South African Society of Anaesthesiologists Practice Guidelines 2012 Revision. *South African J Anaest Analg*. 2013;19(1):S1-42.
3. Mitchell J. Recommendations for standards of monitoring during anaesthesia and recovery. *Anaesthesia* [Internet]. 2001;56(5):488–488. Available from: <http://doi.wiley.com/10.1046/j.1365-2044.2001.02047-7.x>
4. Haynes A, Weiser T, Berry WR, Lipsitz SR, Breiza t AS. A surgical safety checklist to reduce morbidity and mortality in a global population. *N Engl J Med*. 2009;360:491.
5. Walker I, Merry A, Wilson I, McHugh G, O’Sullivan E, Thoms G, et al. Global oximetry: An international anaesthesia quality improvement project. *Anaesthesia*. 2009;64(10):1051–60.
6. World Health Organization. Global Pulse Oximetry Project. First Int Consult Meet. 2008;(October).
7. Merry A, Cooper J, Soyannwo O, Wilson I, Eichhorn J. International Standards for a Safe Practice of Anesthesia 2010. *Can J Anaesth* [Internet]. 2010 Nov [cited 2017 Jun 19];57(11):1027–34. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20857254>
8. Plüddemann A, Thompson M, Heneghan C, Price C. Pulse oximetry in primary care: primary care diagnostic technology update. *Br J Gen Pract* [Internet]. 2011 [cited 2017 Jun 19];61(586):358–9. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3080222/pdf/bjgp61-358.pdf>
9. Crawford Mechem C. Pulse oximetry in adults [Internet]. UpToDate. 2016 [cited 2017 Jun 21]. Available from: [https://www.uptodate.com/contents/pulse-oximetry-in-adults?source=search_result&search=pulse oximeters&selectedTitle=1~150#H411369682](https://www.uptodate.com/contents/pulse-oximetry-in-adults?source=search_result&search=pulse%20oximeters&selectedTitle=1~150#H411369682)
10. McKay W, Noble W. Critical incidents detected by pulse oximetry during anaesthesia. *Can J Anaesth*. 1988;35(3):265–9.
11. Pedersen T, Nicholson A, Hovhannisyan K, Moller AM, Smith AF LS. Pulse oximetry for perioperative monitoring. *Cochrane Database Syst Rev*. 2014;(3):CD002013.

12. World Alliance for Patient Safety. WHO surgical safety checklist and implementation manual [Internet]. WHO. World Health Organization; 2008 [cited 2017 Jun 21]. Available from: http://www.who.int/patientsafety/safesurgery/ss_checklist/en/
13. Hines R, Barash P, Watrous G, O'Connor T. Complications Occurring in the Postanesthesia Care Unit: A Survey. *Anesth Analg* [Internet]. 1992 [cited 2017 Jun 21];74(4):pg:503-509. Available from: http://journals.lww.com/anesthesia-analgia/Abstract/1992/04000/Complications_Occurring_in_the_Postanesthesia_Care.6.aspx
14. Moller JT, Pedersen T, Rasmussen LS, Jensen PF, Pedersen BD, Ravlo O, et al. Randomized evaluation of pulse oximetry in 20,802 patients: I. Design, demography, pulse oximetry failure rate, and overall complication rate. *Anesthesiology* [Internet]. 1993;78(3):436–44. Available from: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=8457044
15. Moller J, Johannessen N, Espersen K, Ravlo O, Pedersen B, Jensen P, Rasmussen N, Rasmussen L, Pedersen T CJ. Randomized Evaluation of Pulse Oximetry in 20,802 Patients; II: Perioperative Events and Postoperative Complications. *Anesthesiology*. 1993;78(3):445–53.
16. King CJ. Extending the WHO “safe surgery saves lives” project through global oximetry. Vol. 65, *Anaesthesia*. 2010. p. 857–8.
17. Sinex J. Pulse oximetry: Principles and limitations. *Am J Emerg Med*. 1999;17(1):59–66.
18. Jubran A. Pulse oximetry. *Crit Care* [Internet]. 2015;19(1):272. Available from: <http://ccforum.com/content/19/1/272>
19. Jubran A. Advances in respiratory monitoring during mechanical ventilation. *Chest*. 1999;116(5):1416–25.
20. Chitilian H, Kaczka D, Vidal Melo M. Miller's Anesthesia [Internet]. Eighth Edi. Miller R, editor. Elsevier Saunders; 2015 [cited 2017 Jun 21]. 1541-1579.e8 p. Available from: <https://www-clinicalkey-com.ezproxy.uct.ac.za/#!/content/book/3-s2.0-B9780702052835000515?scrollTo=%23hl0000989>
21. Jensen LA et al. Meta-analysis of arterial oxygen saturation monitoring by pulse oximetry in adults. *Hear Lung J Acute Crit Care*. 1998;27(6):387–408.
22. Nickerson B, Sarkisian C, Tremper K. Bias and precision of pulse oximeters and arterial oximeters. *Chest*. 1988;93(3):515–7.

23. Ralston A, Webb RK, Runciman WB. Potential errors in pulse oximetry. I. Pulse oximeter evaluation. *Anaesthesia*. 1991;46(3):202–6.
24. Clayton D, Webb R, Ralston A, Duthie D, Runciman W. A comparison of the performance of 20 pulse oximeters under conditions of poor perfusion. *Anaesthesia* [Internet]. 1991;46(1):3–10. Available from: <http://doi.wiley.com/10.1111/j.1365-2044.1991.tb09303.x>
25. Dubowitz G, Breyer K, Lipnick M, Sall J, Feiner J, Ikeda K, et al. Accuracy of the Lifebox pulse oximeter during hypoxia in healthy volunteers. *Anaesthesia*. 2013;68(12):1220–3.
26. Lipnick M, Feiner J, Au P, Bernstein M, Bickler P. The Accuracy of 6 Inexpensive Pulse Oximeters Not Cleared by the Food and Drug Administration: The Possible Global Public Health Implications. *Anesth Analg*. 2016;123(2):338–45.
27. Webb R, Ralston A RW. Potential errors in pulse oximetry. II. Effects of changes in saturation and signal quality. *Anaesthesia* [Internet]. 1991 Mar 1 [cited 2017 Jun 18];46(3):207–12. Available from: <http://doi.wiley.com/10.1111/j.1365-2044.1991.tb09411.x>
28. Taylor M, Whitwam J. The accuracy of pulse oximeters. *Anaesthesia* [Internet]. 2007 Feb 22 [cited 2017 Jun 21];43(3):229–32. Available from: <http://doi.wiley.com/10.1111/j.1365-2044.1988.tb05549.x>
29. Colechin E, Bousfield D, Reay C, Sims A. Market review: Pulse oximeters in primary and prehospital care. 2010;(March). Available from: www.cep.dh.gov.uk/CEPProducts/Catalogue.aspx
30. World Health Organization. WHO guidelines for safe surgery: safe surgery saves lives. WHO [Internet]. 2014 [cited 2017 Jun 21]; Available from: http://who.int/patientsafety/safesurgery/tools_resources/9789241598552/en/
31. Takeshita WM, Iwaki LCV, Pupim D, Filho L. Evaluation of accuracy of portable fingertip pulse oximeter, as compared to that of a hospital oximeter with digital sensor. *Indian J Dent Res* [Internet]. 2013;24(5):542. Available from: <http://www.ijdr.in/text.asp?2013/24/5/542/123362>
32. Bland J, Altman D. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*. 1986;327(8476):307–310.
33. Jones M, Olorvida E, Monger K, Yarborough V, Bennetts H, Harris D, et al. How Well Do Inexpensive, Portable Pulse Oximeter Values Agree with Arterial Oxygenation Saturation in Acutely Ill Patients? *Medsurg Nurs* [Internet]. 2015;24(6):391–6. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26863701>

34. Bland M. How can I decide the sample size for a repeatability study [Internet]. 2010 [cited 2017 Jun 21]. p. 1–3. Available from: <https://www-users.york.ac.uk/~mb55/meas/sizemeth.htm>
35. Bickler P, Feiner J, Severinghaus J. Effects of skin pigmentation on pulse oximeter accuracy at low saturation. *Anesthesiology*. 2005;102(4):715–9.
36. Bland JM, Altman DG. Comparing methods of measurement: why plotting difference against standard method is misleading. *Lancet* [Internet]. 1995;346(8982):1085–7. Available from: <http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&id=7564793&retmode=ref&cmd=prlinks>
37. Bland JM, Altman DG. Measurement in medicine: the analysis of method comparison studies. *Stat*. 1986;32(July 1981):307–17.
38. Hanneman S. Design, analysis and interpretation of method-comparision studies. *AACN Adv Crit Care*. 2010;19(2):223–34.
39. Bland JM, Altman DG. Measuring agreement in method comparison studies. *Stat Methods Med Res* [Internet]. 1999 [cited 2017 Jun 19];8(2):135–60. Available from: <http://journals.sagepub.com.ezproxy.uct.ac.za/doi/pdf/10.1177/096228029900800204>
40. Food and Drug Administration. Pulse Oximeters - Premarket Notification Submissions [510(k)s] Guidance for Industry and Food and Drug Administration Staff. 2015;510:1–19. Available from: <https://www.fda.gov/RegulatoryInformation/Guidances/ucm341718.htm>
41. Lu MJ, Zhong WH, Liu YX, Miao HZ, Li YC, Ji MH. Sample Size for Assessing Agreement between Two Methods of Measurement by Bland-Altman Method. *Int J Biostat*. 2016;12(2).

Appendices

Please find Research Protocol attachments under the heading **Part D – Appendices**.

Part B – Structured Literature Review

A literature search of electronic databases (including PubMed and Google Scholar) was performed for published English articles on adult studies which contained, but not limited to, the key terms “pulse oximeter”, “oximetry”, “portable”, “fingertip”, “accuracy”, “agreement”, “adult” revealed a paucity of studies pertaining to the performance of portable fingertip pulse oximeters in adult surgical patients.

Most studies evaluating the accuracy of new pulse oximeters recruit healthy volunteers who are subjected to rebreathing controlled hypoxic gas mixtures under laboratory conditions. An arterial blood sample is drawn, and the pulse oximeter’s non-invasive estimation of arterial oxygen saturation is compared to a co-oximeter, which is considered the gold standard. This is performed under ideal laboratory conditions, which includes controlling for subject movement, ambient light, etc.

Various unpublished accuracy studies have been performed on individual manufacturers’ portable fingertip pulse oximeters.⁽¹⁾ They are not peer reviewed and usually recruit healthy adult volunteers under laboratory controlled hypoxic conditions.

Presently there is not sufficient published evidence that portable fingertip pulse oximeters are as accurate as standard pulse oximeters in estimating arterial oxygen saturation in adult surgical patients with various co-morbidities in a clinical setting, as opposed to the controlled environment of a laboratory.

The goal of the WHO SSSL initiative is to provide inexpensive, high-quality pulse oximeters to low- and middle-income countries (LMICs) in order to improve surgical safety.⁽²⁾ Dr Dubowitz and Dr Lipnick are founders and directors of the non-profit charitable organisation ‘Global Partners in Anaesthesia and Surgery’ and the ‘Lifebox’ oximetry project operate in parallel to the WHO SSSL initiative to provide “a low-cost, high-quality pulse oximeter for low- and middle-income countries”. The Lifebox pulse oximeter was identified as a suitable item of equipment which fulfilled the WHO’s requirements. It is, however, a handheld device, which is larger and less compact than portable fingertip oximeters, and considerably more expensive (approximately R3500 vs. <R800 for the portable fingertip pulse oximeter used in this study).⁽³⁾

Dubowitz et al. demonstrated that the Lifebox portable pulse oximeter met International Organisation for Standardization (ISO) and FDA 510(k) standards, when testing the device on 57 healthy volunteers under controlled hypoxic conditions.⁽³⁾ Arterial blood gas samples were taken and compared to a multi-wavelength oximeter.

Lipnick et al., further reviewed the accuracy of six low-cost portable fingertip pulse oximeters in 2016.⁽⁴⁾ Results showed that only two units met ISO and FDA standards in the SaO₂ range of 70 – 100%. The remaining oximeters demonstrated deteriorating accuracy at lower arterial oxygen saturations. Controlled hypoxic gas mixtures were inspired by the volunteers and arterial blood samples drawn, which were compared to a multi-wavelength oximeter in a similar fashion to the Lifebox study. Limitations of this study included the use of healthy volunteers, being tested under ideal conditions (motionless subjects with good peripheral perfusion). In addition, the majority of the subjects were Asian and Caucasian.

A study involving 55 dental patients in Brazil found no statistically significant difference between a portable fingertip and hospital pulse oximeters.⁽⁵⁾ The non-invasive SpO₂ of each device was measured by simultaneous application of the fingertip probes at six time intervals during the dental procedures. The American Society of Anaesthesiologists (ASA) grade of the patients was not stated, however, patients with cardiac or respiratory conditions, pregnant women and children were excluded. A shortfall of this study was that the data was analysed using both a Bland-Altman graph and Pearson correlation coefficient. The latter is not an appropriate method for use when comparing agreement between two different items of equipment.⁽⁶⁾ It did, however, include patients in a dental setting, and not merely healthy volunteers in a laboratory scenario.

An additional study in 2015 attempted to examine the agreement between a portable fingertip pulse oximeter (Maxtec MD300 C2) and SaO₂ measured by a laboratory blood gas analyser in the clinical setting.⁽⁷⁾ Patients in a pulmonary and renal intermediate care unit were recruited by convenience sampling when a “therapeutically prescribed” arterial blood gas was required. The SaO₂ was then compared to SpO₂ derived by the test portable fingertip pulse oximeter which was applied within three minutes of the blood gas sample.

The authors noted an unacceptable difference in bias and precision values, especially when $\text{SaO}_2 \leq 93\%$. There were, however, some significant methodological flaws, including the study being probably underpowered ($n=32$) to detect a significant difference. The pulse oximeter was also not applied simultaneously while the arterial blood sample was drawn. Indications for 21 of the 32 samples included changes in level of consciousness and/ or shortness of breath, which means that the delay of up to three minutes in obtaining the SpO_2 may have resulted in the investigators measuring a different value to that obtained by the arterial blood gas sample. The exclusion criteria were also not consistent with many previous published studies that highlighted the common causes of errors in arterial saturation measurement by oximeters.

Due to the paucity of accuracy studies utilizing portable fingertip pulse oximeters in patients in the clinical setting, this study aimed to pragmatically investigate the performance of these devices in an adequate number of adult surgical patients in a hospital/theatre environment comparing them to the current standard bedside pulse oximeters.

Bibliography

1. Colechin E, Bousfield D, Reay C, Sims A. Market review: Pulse oximeters in primary and prehospital care. 2010;(March). Available from: www.cep.dh.gov.uk/CEPProducts/Catalogue.aspx
2. World Health Organization. WHO guidelines for safe surgery: safe surgery saves lives. WHO [Internet]. 2014 [cited 2017 Jun 21]; Available from: http://who.int/patientsafety/safesurgery/tools_resources/9789241598552/en/
3. Dubowitz G, Breyer K, Lipnick M, Sall J, Feiner J, Ikeda K, et al. Accuracy of the Lifebox pulse oximeter during hypoxia in healthy volunteers. *Anaesthesia*. 2013;68(12):1220–3.
4. Lipnick M, Feiner J, Au P, Bernstein M, Bickler P. The Accuracy of 6 Inexpensive Pulse Oximeters Not Cleared by the Food and Drug Administration: The Possible Global Public Health Implications. *Anesth Analg*. 2016;123(2):338–45.
5. Takeshita WM, Iwaki LCV, Pupim D, Filho L. Evaluation of accuracy of portable fingertip pulse oximeter, as compared to that of a hospital oximeter with digital sensor. *Indian J Dent Res* [Internet]. 2013;24(5):542. Available from: <http://www.ijdr.in/text.asp?2013/24/5/542/123362>

6. Bland J, Altman D. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*. 1986;327(8476):307–310.
7. Jones M, Olorvida E, Monger K, Yarborough V, Bennetts H, Harris D, et al. How Well Do Inexpensive, Portable Pulse Oximeter Values Agree with Arterial Oxygenation Saturation in Acutely Ill Patients? *Medsurg Nurs* [Internet]. 2015;24(6):391–6. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26863701>

Part C - Publication-ready Manuscript

The manuscript for the purposes of this dissertation has been formatted for the South African Medical Journal. The 'Author Guidelines' for the journal can be found online at <http://www.samj.org.za/index.php/samj/about/submissions#Research> or reproduced in **Part D - Appendices.**

Perioperative Comparison of the Agreement between a Portable Fingertip Pulse Oximeter vs. a Conventional Bedside Pulse Oximeter in Adult Patients (COMFORT Trial)

Principal Investigator:

Smith, Reuben, FCA(SA), Registrar, Department of Anaesthesia & Perioperative Medicine, University of Cape Town

reubensmith@hotmail.co.za

Supervisor/ Investigator:

Hofmeyr, Ross, FCA(SA), Associate Professor, Department of Anaesthesia & Perioperative Medicine, University of Cape Town

ross.hofmeyr@uct.ac.za

Abstract

Background

Low-cost, portable fingertip pulse oximeters are widely available to health professionals and the public. They are often not tested to ISO standards, or only undergo accuracy studies in healthy volunteers under ideal laboratory conditions. This study aims to pragmatically evaluate the agreement between one such device and a conventional bedside pulse oximeter in a clinical setting, in patients with varied comorbidities and skin pigmentations.

Methods

A single-centre equipment comparison study was conducted. Simultaneous measurements were obtained in 220 patients with both a Contec CMS50D Fingertip Pulse Oximeter and a Nihon Kohden Life Scope MU-631 RK conventional bedside monitor. Peripheral oxygen saturations (SpO₂) and pulse rates were documented, and patients skin tone was recorded using the Fitzpatrick scale. Data was assessed using a Bland-Altman analysis with bias, precision and limits of agreement (LOA) calculated with 95% confidence intervals. *A priori* acceptability for LOA was determined to be 3%, in keeping with international standards.

Results

Mean difference (therefore bias) between the conventional and portable fingertip oximeters for all data was -0,55% (95% CI -0,73 to -0,36%). Upper and lower limits of agreement (95% CI) were 2,16 (1,84 to 2,47) and -3,25 (-3,56 to -2,94) %. Regression analysis demonstrated worsening agreement with decreasing SpO₂. When samples were separated into “normal” (SpO₂ ≥ 93%) and “hypoxaemic” (SpO₂ < 93%) groups, the normal range displayed acceptable agreement between the two oximeters (bias -0,20 with LOA 2,20 to -2,27%), while the hypoxaemic group fell outside the study’s *a priori* limits. Heart rate measurements had mean difference (LOA) of -0,43 (-5,61 to 4,76) beats per minute. The study was not powered to detect difference among the skin tones, but demonstrated no trend for this parameter to alter the SpO₂ measurements.

Conclusions

During normoxia, portable fingertip pulse oximeters are reliable indicators of SpO₂ and pulse rates in patients with various comorbidities in a pragmatic clinical context. However, they display worsening agreement with conventional pulse oximeters during hypoxaemia. Skin tones do not appear to adversely affect measurements.

What questions this study addressed

This pragmatic, prospective study compared the agreement between the measured arterial oxygen saturation levels and pulse rates using a portable fingertip versus a conventional bedside pulse oximeter in adult patients, presenting for elective and emergency surgery, in a clinical setting.

What this study adds to our knowledge

This study found that there is sufficient agreement between the arterial oxygen saturations and pulse rates measured by a portable fingertip and conventional bedside pulse oximeters amongst adult (surgical) patients who are not hypoxaemic in the clinical setting. However, as saturations dropped into the hypoxaemic range (less than 93%), agreement between the devices worsened. Additionally, it found no significant influence by skin tone on the measurements, although the study was not powered to convincingly detect this outcome.

How this study might change clinical practice

Low-cost portable fingertip pulse oximeters marketed for non-medical use are often not tested in humans under clinical conditions. The measurements obtained by these portable and affordable items of equipment have therefore been regarded with skepticism by medical staff. This study demonstrates that one such pulse oximeter is sufficiently as accurate as a far more expensive bedside pulse oximeter when used to exclude hypoxia. Similar studies can be done using other similar equipment to promote access to these vital medical instruments in resource limited areas.

Keywords: perioperative, portable, monitoring, plethysmography, pulse oximetry, oxygen

Additional relevant MeSH terms: Hypoxia, Signs and Symptoms, Respiratory Signs and Symptoms

Abbreviations: SpO₂, oxygen saturation measured by pulse oximetry; SaO₂, arterial oxygen saturation; WHO, World Health Organization

Introduction

The ability to accurately and non-invasively assess a patient's arterial oxygen saturation has become an accepted standard of care in the perioperative period.⁽¹⁾ Pulse oximetry is considered an essential item of equipment for providing safe anaesthesia by various regulatory bodies throughout the world, including the South African Society of Anaesthesiologists^(2,3) and the World Federation of Societies of Anaesthesiologists (WFSA), who adopted the International Standards for a Safe Practice of Anaesthesia since 1992.⁽⁴⁾ Pulse oximeters are included in the World Health Organization's (WHO) Surgical Safety Checklist (SSC),⁽⁵⁾ which is used in health facilities throughout the world prior to the commencement of a surgical procedure. Studies have demonstrated that the WHO SSC has nearly doubled patients' likelihood of receiving proven standards of surgical care, and that there was a substantial reduction in complications and deaths.⁽⁶⁾

Pulse oximetry is non-invasive, safe and currently performed routinely on all surgical patients during admission, intra-operatively and post-operatively, without requiring specific consent. It is more cost-effective, less painful, easier to perform, and more readily available than arterial blood gas analysis. It has largely replaced this method in many clinical situations, unless carbon dioxide or acid-base status is specifically required. Portable fingertip pulse oximeters have the additional benefits of being cost-effective, highly compact, portable, battery operated, and easy to use.

When pulse oximeters are manufactured, they are tested for accuracy against blood gas analysis in healthy volunteers breathing hypoxic gas mixtures under ideal laboratory conditions. There are published standards from the USA Food and Drug Administration (FDA) on how this should be performed, including statistical methods appropriate for device comparison, such as Bland-Altman analysis.⁽⁷⁾

A review of recent literature reveals a paucity of accuracy studies utilizing portable fingertip pulse oximeters in patients in the clinical setting. This study aims to pragmatically investigate the performance of these devices in adult surgical patients in a hospital/theatre environment.

The significance of this study into the performance of portable fingertip pulse oximeters may result in the availability of cheaper devices in medical facilities in low-/middle-income areas. It will also give anaesthetists and other medical personal the confidence to make clinical decisions based on these highly portable devices. It may also add further data to existing studies and help assess whether darker skin pigment affects the performance of these devices in the clinical setting, which is highly relevant in an African country like South Africa.

Methods

Patients

This prospective, quantitative equipment comparison study took place at Groote Schuur Hospital, a tertiary-level institution in Cape Town, South Africa, over a four-week period. Institutional approval was granted by the University of Cape Town's (UCT) Human Research Ethics Committee (HREC 572/2017). Written informed consent was waived on provision that no patient-identifiable data was collected, and that pulse oximetry was already being used for routine monitoring purposes. Verbal consent was obtained from conscious patients. All adult surgical patients ≥ 18 years of age who presented for elective or emergency surgery were considered eligible for the study and recruited by convenience sampling. Exclusion criteria (Table 1) were conditions known to cause inaccuracies in pulse oximetry, or infectious disease with a high risk of transmission. ⁽⁸⁻¹⁴⁾

Table 1. Exclusion criteria

Significantly low blood pressure or cold peripheries

Excessive patient movement

Abnormal Hb variants

Certain dyes used during the operation (e.g. methylene blue)

Nail polish/ black henna

Bandages/ tape etc. on the hand/ finger

Inadequate pulse oximeter trace

Measurements

Data was recorded by the principal author into a Microsoft Excel spreadsheet and archived in password-protected cloud storage. The Contec CMS50D Fingertip Pulse Oximeter was selected as the test device for this study because of its relatively low cost, ease of availability in South Africa, and that it was one of two devices identified that met ISO and FDA standards in healthy test subjects in a prior study.⁽¹⁵⁾ The device was purchased privately by the authors. A Nihon Kohden Life Scope MU-631 RK bedside monitor was provided by the Department of Anaesthesia and Perioperative Medicine, Groote Schuur Hospital to be used for the control measurements. It is a commonly used monitor within the hospital, and was calibrated by the manufacturer.

Sample size was calculated using results obtained from an unpublished pilot study performed using the same methods. The Monte-Carlo simulation method, as outlined by Lu & Zhong, was used utilizing MedCalc Statistical Software version 18.6 (MedCalc, Ostend, Belgium; <http://www.medcalc.org>)^(16,17) A maximum SpO₂ difference of 3%, Type I error 0.05 and type II error 0.01 gave a sample size estimate of 220.

The portable fingertip and conventional bedside pulse oximeter probes were applied simultaneously to the same hand, contralateral to the blood pressure cuff. Once the waveform on both pulse oximeters was confirmed, readings were taken at 30 seconds post-application to allow for the time averaging of each pulse oximeter. Non-patient identifiable data was recorded, limited to: SpO₂, heart rate, skin colour (estimated by the Fitzpatrick scale) and qualitative strength of wave form signal (good or poor). The Fitzpatrick scale was selected rather than other methods (e.g. von Luschan scale or reflectance spectrophotometry) for reasons of simplicity, repeatability and cost containment. There was no interruption to existing patient monitors. The study devices were cleaned with a commercial antiseptic solution between patients.

Statistical Analysis

Bland and Altman have established bias and precision estimates as the standard reported statistic when comparing agreement between a new or less-established measurement technique with an established one.⁽¹⁸⁻²²⁾ When the *a priori* limits of agreement are small (95%

limits of agreement defined as bias plus or minus 1.96 SD), and not of clinical importance, the two measurement techniques can be considered interchangeable. For this study, we have determined that an SpO₂ difference of less than 3% is not of clinical importance, which is in keeping with the ISO and FDA testing protocol. Data analysis was performed by the authors with Medcalc (as above).

Results

We obtained 220 simultaneous pulse oximetry measurements. The clinical setting, waveform quality and skin tone classifications are summarized in Table II. Mean difference (bias) between the conventional and portable fingertip oximeters for all data was -0,55% (95% CI -0,73 to -0,36%). Upper and lower limits of agreement (95% CI) were 2,16 (1,84 to 2,47) and -3,25 (-3,56 to -2,94) %. Regression analysis demonstrated worsening agreement with decreasing SpO₂. When samples were separated into “normal” (SpO₂ ≥ 93%) and “hypoxaemic” (SpO₂ < 93%) groups, the normal range displayed acceptable agreement between the two oximeters (bias -0,20 with LOA 2,20 to -2,27%), while the hypoxaemic group fell outside the study’s *a priori* limits. Heart rate measurements had mean difference (LOA) of -0,43 (-5,61 to 4,76) beats per minute. The study was not powered to detect difference among the skin tones, but demonstrated no trend for this parameter to alter the SpO₂ measurements.

Table 2. Summary of data

SpO₂ range	All	≥ 93%	< 93%
n	220	164	56
Mean difference (bias) (%)	-0.55 (-0,73 to -0,36)	-0.20 (-0.38 to -0.01)	-1.57 (-1.92 to -1.22)
Lower LOA (%)	-3.25 (-3,56 to -2,94)	-2.60 (-2.92 to -2.27)	-4.13 (-4.73 to -3.53)
Upper LOA (%)	2.16 (1,84 to 2,47)	2.20 (1.88 to 2.53)	0.99 (0.37 to 1.59)
Pulse rates			

n	220		
Mean difference (bias) %	-0.43 (-0.78 to -0.08)		
Lower LOA (95% CI) %	-5.61 (-6.22 to -5.01)		
Upper LOA (95% CI) %	4.76 (4.16 to 5.37)		
Skin tone (Fitzpatrick scale)	n (%)		
I (Pale white skin, e.g. British)	12 (5.5%)		
II (White skin, e.g. Scandinavian)	28 (12.7%)		
III (Light brown skin, e.g. Central European)	69 (31.4%)		
IV (Moderate brown/ olive skin, e.g. Asian, Latino)	45 (20.5%)		
V (Dark brown skin, e.g. Native American)	28 (12.7%)		
VI (Very dark/ black skin, e.g. African)	38 (17.3%)		
Location	n (%)		
ICU	60 (27.3%)		
Recovery room	110 (50%)		
Respiratory clinic	31 (14.1%)		
Theatre	19 (8.6%)		

SpO₂, oxygen saturation measured by pulse oximetry; n, number of paired measurements; LOA, limits of agreement; mean difference (bias) and LOA with 95% confidence intervals in parentheses

Fig. 1. Bland-Altman plot for all SpO₂ measurements

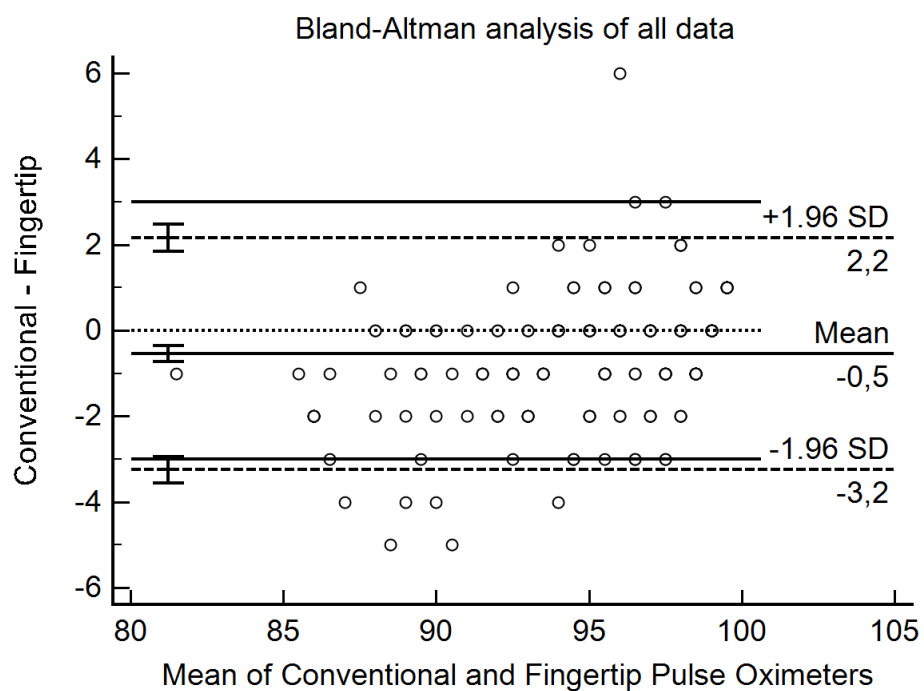


Fig. 2. Bland-Altman plot for SpO₂ measurements $\geq 93\%$

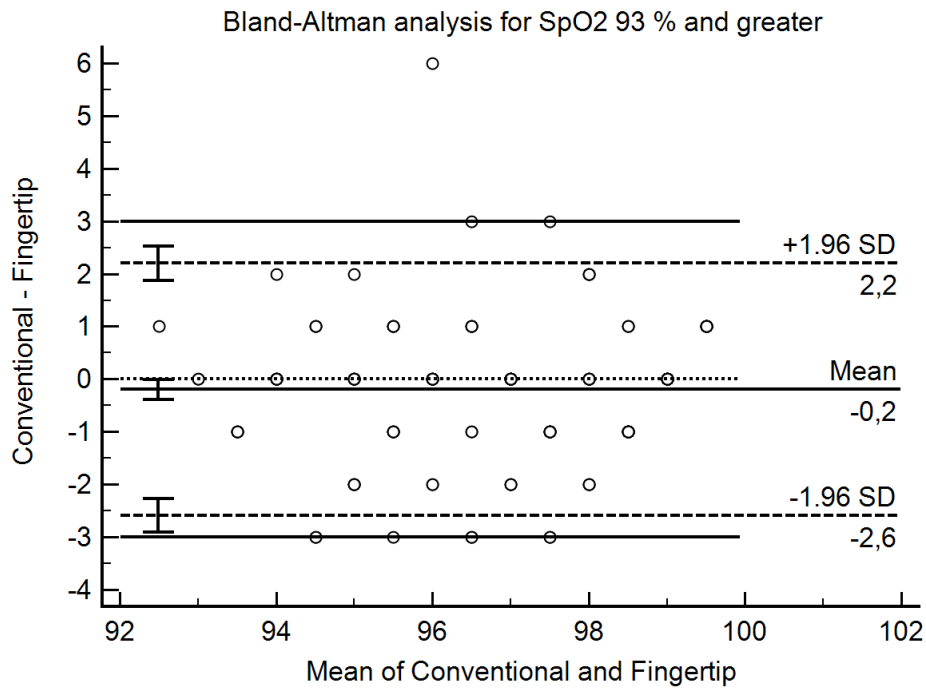


Fig. 3. Bland-Altman plot for SpO2 measurements <93%

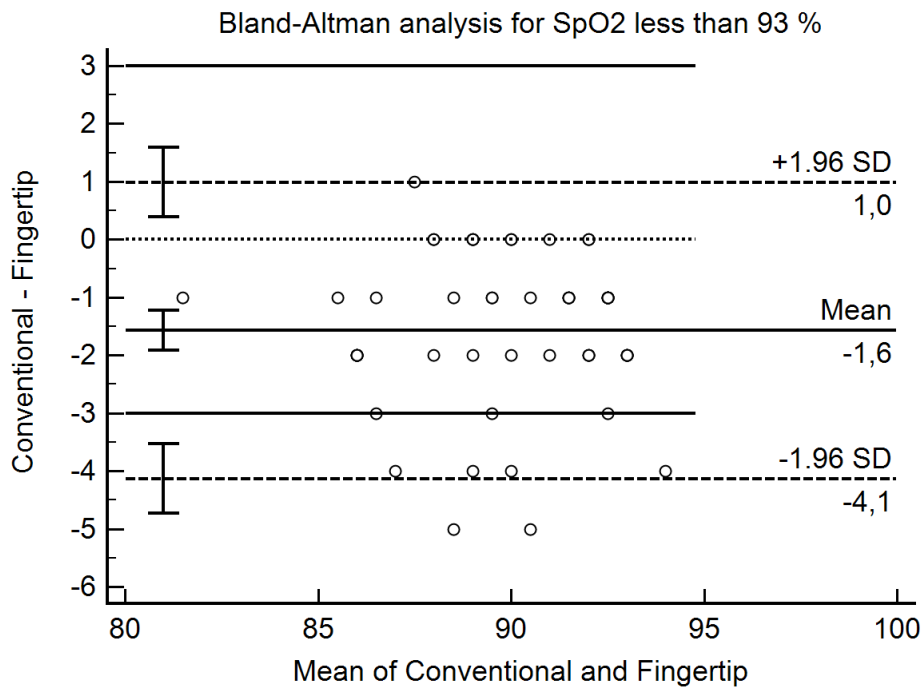


Fig. 4. Bland-Altman plot for pulse rate measurements

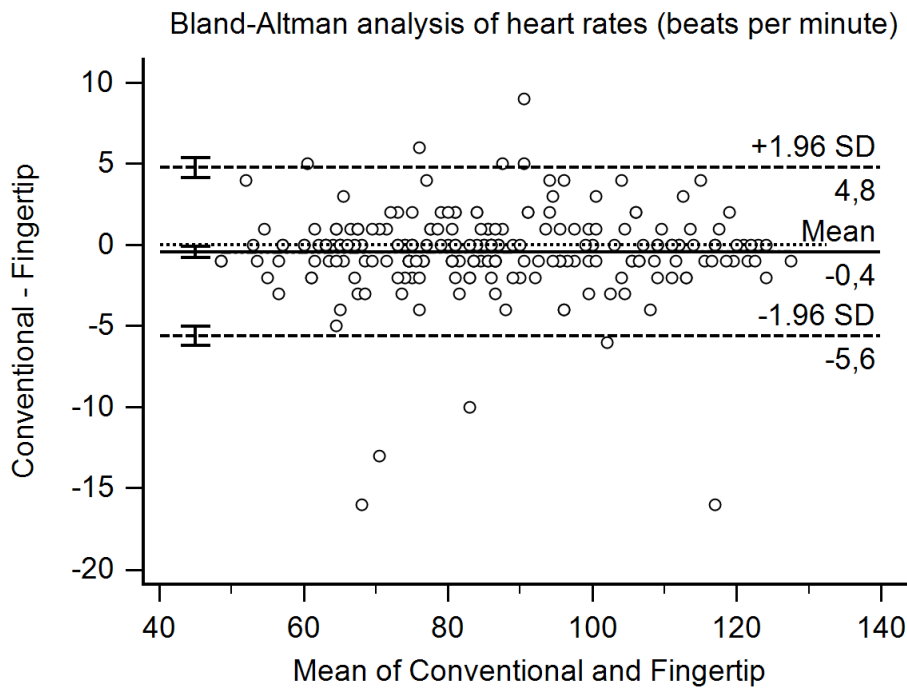
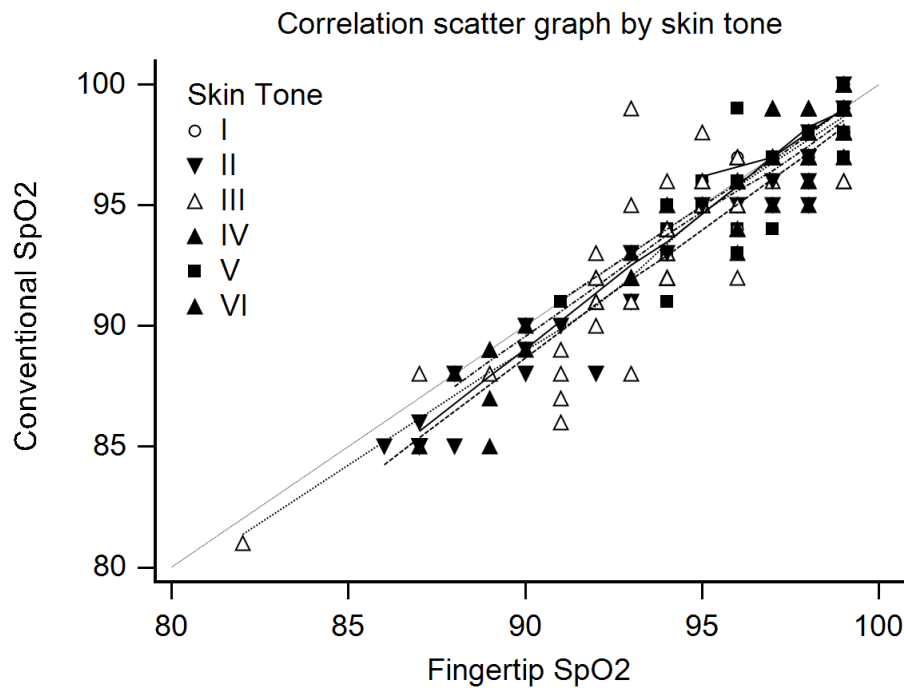


Fig. 5. Oximeter correlation by skin tone classification



Discussion

Pulse oximeters noninvasively measure and display the heart rate and estimated peripheral arterial haemoglobin oxygen saturation (SpO₂) derived from photoplethysmographic measurements at two rapidly alternating different wavelengths of light. (10–12,23) Oxygenated blood (oxyhaemoglobin) and deoxygenated blood (deoxyhaemoglobin) differ in their absorption of red and infrared light. Measurement is accomplished by utilising the Beer-Lambert Law, which states that absorption at a specific wavelength is proportional to the distance through the specific medium traversed by the light rays. A sensor containing a light emitting diode and a light detecting photodiode is typically placed on a cutaneous vascular bed, such as a fingertip or earlobe, which can be transilluminated. Arterial pulsations are identified by plethysmography, allowing corrections for light absorption by non-pulsating venous blood and tissue. The ratio of the absorptions at the red and infrared wavelengths is analysed by a microprocessor and SpO₂ estimated from a stored calibration curve.

Oximeter testing is based on experimental measurements in healthy volunteers who are subjected to rebreathing controlled hypoxic gas mixtures under laboratory conditions, which includes controlling for subject movement, ambient light, etc. Oxygen saturation of haemoglobin is then determined by both the pulse oximeter (SpO₂) and in vitro laboratory multi-wavelength co-oximeter (SaO₂, considered as the gold standard for measurement of arterial oxygen saturation). Each manufacturer's exact calibration curve is proprietary. Pulse oximeters are inaccurate at low blood oxygen saturations because researchers are limited in the degree of hypoxaemia inducible in volunteers. The FDA requires pulse oximeters marketed for medical use to be tested in the SaO₂ range 70 - 100%. The shape of the calibration curves must be extrapolated at oxygen saturations below these levels.

Numerous studies have confirmed the accuracy of conventional pulse oximeters when compared to co-oximeters in the clinically relevant range of arterial oxygen saturation.(13,24–26) Accuracy progressively deteriorates below a SaO₂ of 90%. Presently, there is insufficient published evidence that portable fingertip pulse oximeters are as accurate as standard pulse oximeters in estimating arterial oxygen saturation in a clinical setting, as opposed to the controlled environment of a laboratory. Various unpublished accuracy studies have been performed on individual manufacturers' portable fingertip pulse oximeters.(27) They are not peer reviewed and usually recruit healthy adult volunteers under laboratory controlled hypoxic conditions.

Most portable fingertip pulse oximeters marketed for non-medical use to consumers do not undergo stringent testing as laid out by the FDA and other regulatory bodies.(15) Lipnick et al. found only two of six such commonly used devices met ISO and FDA. Of these, one was the portable fingertip pulse oximeter included in this study. All oximeters demonstrated deteriorating accuracy at lower arterial oxygen saturations. Some of the important limitations the authors identified with the study were the ideal conditions under which the pulse oximeters were tested (motionless hands with good perfusion values in a laboratory utilizing controlled hypoxic gas mixtures) and the use of healthy volunteers. They warned about extrapolating this useful data to the clinical scenario where multiple factors and patient co-morbidities could potentially affect the pulse oximeters' accuracy. The majority of the volunteers had lighter skin tones, and thus was not representative of a population such as South Africa.

A study involving 55 dental patients in Brazil found no statistically significant difference between a portable fingertip and hospital pulse oximeters. (28) The non-invasive SpO₂ of

each device was measured by simultaneous application of the fingertip probes at six time intervals during the dental procedures. A shortfall of this study was that the data was analysed using both a Bland-Altman graph and Pearson correlation coefficient. The latter is not an appropriate method for use when comparing agreement between two different items of equipment. (18) It did, however, include patients in a dental setting, and not merely healthy volunteers in a laboratory scenario.

An additional study in 2015 attempted to examine the agreement between a portable fingertip pulse oximeter (Maxtec MD300 C2) and SaO₂ measured by a laboratory blood gas analyser in the clinical setting. (29) Patients in a pulmonary and renal intermediate care unit were recruited by convenience sampling when a “therapeutically prescribed” arterial blood gas was required. The SaO₂ was then compared to SpO₂ derived by the test portable fingertip pulse oximeter which was applied within three minutes of the blood gas sample.

The authors noted an unacceptable difference in bias and precision values, especially when SaO₂ ≤93%. There were, however, some significant methodological flaws, including the study being underpowered (n=32) to detect a significant difference. The pulse oximeter was also not applied simultaneously while the arterial blood sample was drawn. Indications for 21 of the 32 samples included changes in level of consciousness and/ or shortness of breath, which means that the delay of up to three minutes in obtaining the SpO₂ may have resulted in the investigators measuring a different value to that obtained by the arterial blood gas sample. The exclusion criteria were also not consistent with many previous published studies that highlighted the common causes of errors in arterial saturation measurement by oximeters.

This study added value to the existing literature as it evaluated the performance of portable fingertip pulse oximeters in the clinical setting utilizing patients with varying ASA status and more heterogeneous skin tones. Another merit of the study was that data measurements were obtained across a range of clinical settings (ICU, recovery room, clinic, theatre).

One of the inherent limitations of this pragmatic study was the skewed data obtained when measuring SpO₂ in the clinical setting. The majority of samples (91.4%) were in the SpO₂ range ≥90%. One could argue that this is a more accurate reflection of real life SpO₂ encountered in daily clinical practice. However, the true value of an accurate pulse oximeter

lies in its ability to correctly identify a hypoxemic patient who would require prompt intervention. The study does not add information to the question regarding accuracy at SpO₂ <80%.

Clinicians could infer from this study that portable fingertip pulse oximeter readings ≥93% are reassuring while <93% requires further investigations and prompt treatment, as the patient may be mildly to profoundly hypoxic.

The portable fingertip pulse oximeter only displayed a two-digit reading for SpO₂, therefore omitted the value of 100%. This slightly altered the bias, but as there is no clinically meaningful difference between saturations of 99 and 100%, we elected to include these differences, as it reflected the pragmatic nature of the study.

While the study does include a range of skin tones more representative of South African population demographics than previous studies, each subgroup is underpowered to detect a statistically significant difference. Future studies could be designed with sufficient power to detect a statistically significant difference due to various skin tones. The authors noted no clinically significant difference in pulse rates or SpO₂ values among lighter and darker pigmented patients, and both statistical and graphical analysis of the trends in measurement by skin tone grouping show no difference between the devices. Lack of more patient specific data (e.g. age, sex, ASA status) makes more detailed analysis of the data impossible. The difference in averaging time of the two devices may have adversely affected the data in situations where saturations were changing rapidly, as one might encounter in a setting such as the recovery room.

Conclusion

This pragmatic study demonstrated that a portable fingertip pulse oximeter was accurate (within 3% SpO₂) in perioperative patients with normal oxygenation (oxygen saturation of ≥93%) when compared to a bedside pulse oximeter. Similar to other studies, the accuracy deteriorated with progressive hypoxia. Pragmatically, a measurement of <93% on the portable device is cause for concern, and further investigation and management for hypoxia is necessary. We found that darker skin pigmentation showed no trend to an effect on the portable fingertip pulse oximeter. Pulse rates measured by the portable devices were within clinically acceptable accuracy.

Disclosure statement

The authors have no financial or personal relationship(s) which may have inappropriately influenced the performance of this study.

References

1. Merry AF, Eichhorn JH, Wilson IH. Extending the WHO “Safe Surgery Saves Lives” project through Global Oximetry. *Anaesthesia* [Internet]. 2009 Oct 1 [cited 2017 Jun 21];64(10):1045–8. Available from: <http://doi.wiley.com/10.1111/j.1365-2044.2009.06104.x>
2. Bettings P, Diedericks J, Fourie P, Joubert I, Kluyts H, Lundgren C, et al. South African Society of Anaesthesiologists Practice Guidelines 2012 Revision. *South African J Anaest Analg*. 2013;19(1):S1-42.
3. Mitchell J. Recommendations for standards of monitoring during anaesthesia and recovery. *Anaesthesia* [Internet]. 2001;56(5):488–488. Available from: <http://doi.wiley.com/10.1046/j.1365-2044.2001.02047-7.x>
4. Merry A, Cooper J, Soyannwo O, Wilson I, Eichhorn J. International Standards for a Safe Practice of Anesthesia 2010. *Can J Anaesth* [Internet]. 2010 Nov [cited 2017 Jun 19];57(11):1027–34. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20857254>
5. World Alliance for Patient Safety. WHO surgical safety checklist and implementation manual [Internet]. WHO. World Health Organization; 2008 [cited 2017 Jun 21]. Available from: http://www.who.int/patientsafety/safesurgery/ss_checklist/en/
6. Haynes A, Weiser T, Berry WR, Lipsitz SR, Breiza t AS. A surgical safety checklist to reduce morbidity and mortality in a global population. *N Engl J Med*. 2009;360:491.
7. Food and Drug Administration. Pulse Oximeters - Premarket Notification Submissions [510(k)s] Guidance for Industry and Food and Drug Administration Staff. 2015;510:1–19. Available from: <https://www.fda.gov/RegulatoryInformation/Guidances/ucm341718.htm>
8. Moller JT, Pedersen T, Rasmussen LS, Jensen PF, Pedersen BD, Ravlo O, et al. Randomized evaluation of pulse oximetry in 20,802 patients: I. Design, demography, pulse oximetry failure rate, and overall complication rate. *Anesthesiology* [Internet]. 1993;78(3):436–44. Available from: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=8457044

9. Moller JT, Johannessen NW, Espersen K, Ravlo O, Pedersen BD, Jensen PF, et al. Randomized evaluation of pulse oximetry in 20,802 patients: II. Perioperative events and postoperative complications. *Anesthesiology*. 1993;
10. Sinex J. Pulse oximetry: Principles and limitations. *Am J Emerg Med*. 1999;17(1):59–66.
11. Jubran A. Pulse oximetry. *Crit Care [Internet]*. 2015;19(1):272. Available from: <http://ccforum.com/content/19/1/272>
12. Chitilian H, Kaczka D, Vidal Melo M. Miller's Anesthesia [Internet]. Eighth Edi. Miller R, editor. Elsevier Saunders; 2015 [cited 2017 Jun 21]. 1541-1579.e8 p. Available from: <https://www-clinicalkey-com.ezproxy.uct.ac.za/#!/content/book/3-s2.0-B9780702052835000515?scrollTo=%23hl0000989>
13. Jensen LA et al. Meta-analysis of arterial oxygen saturation monitoring by pulse oximetry in adults. *Hear Lung J Acute Crit Care*. 1998;27(6):387–408.
14. Bickler P, Feiner J, Severinghaus J. Effects of skin pigmentation on pulse oximeter accuracy at low saturation. *Anesthesiology*. 2005;102(4):715–9.
15. Lipnick M, Feiner J, Au P, Bernstein M, Bickler P. The Accuracy of 6 Inexpensive Pulse Oximeters Not Cleared by the Food and Drug Administration: The Possible Global Public Health Implications. *Anesth Analg*. 2016;123(2):338–45.
16. Lu MJ, Zhong WH, Liu YX, Miao HZ, Li YC, Ji MH. Sample Size for Assessing Agreement between Two Methods of Measurement by Bland-Altman Method. *Int J Biostat*. 2016;12(2).
17. Bland M. How can I decide the sample size for a repeatability study [Internet]. 2010 [cited 2017 Jun 21]. p. 1–3. Available from: <https://www-users.york.ac.uk/~mb55/meas/sizemeth.htm>
18. Bland J, Altman D. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*. 1986;327(8476):307–310.
19. Bland JM, Altman DG. Comparing methods of measurement: why plotting difference against standard method is misleading. *Lancet [Internet]*. 1995;346(8982):1085–7. Available from: <http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&id=7564793&retmode=ref&cmd=prlinks>
20. Bland JM, Altman DG. Measurement in medicine: the analysis of method comparison studies. *Stat*. 1986;32(July 1981):307–17.

21. Hanneman S. Design, analysis and interpretation of method-comparision studies. *AACN Adv Crit Care*. 2010;19(2):223–34.
22. Bland JM, Altman DG. Measuring agreement in method comparison studies. *Stat Methods Med Res [Internet]*. 1999 [cited 2017 Jun 19];8(2):135–60. Available from: <http://journals.sagepub.com.ezproxy.uct.ac.za/doi/pdf/10.1177/096228029900800204>
23. Jubran A. Advances in respiratory monitoring during mechanical ventilation. *Chest*. 1999;116(5):1416–25.
24. Webb R, Ralston A RW. Potential errors in pulse oximetry. II. Effects of changes in saturation and signal quality. *Anaesthesia [Internet]*. 1991 Mar 1 [cited 2017 Jun 18];46(3):207–12. Available from: <http://doi.wiley.com/10.1111/j.1365-2044.1991.tb09411.x>
25. Taylor M, Whitwam J. The accuracy of pulse oximeters. *Anaesthesia [Internet]*. 2007 Feb 22 [cited 2017 Jun 21];43(3):229–32. Available from: <http://doi.wiley.com/10.1111/j.1365-2044.1988.tb05549.x>
26. Nickerson B, Sarkisian C, Tremper K. Bias and precision of pulse oximeters and arterial oximeters. *Chest*. 1988;93(3):515–7.
27. Colechin E, Bousfield D, Reay C, Sims A. Market review: Pulse oximeters in primary and prehospital care. 2010;(March). Available from: www.cep.dh.gov.uk/CEPProducts/Catalogue.aspx
28. Takeshita WM, Iwaki LCV, Pupim D, Filho L. Evaluation of accuracy of portable fingertip pulse oximeter, as compared to that of a hospital oximeter with digital sensor. *Indian J Dent Res [Internet]*. 2013;24(5):542. Available from: <http://www.ijdr.in/text.asp?2013/24/5/542/123362>
29. Jones M, Olorvida E, Monger K, Yarborough V, Bennetts H, Harris D, et al. How Well Do Inexpensive, Portable Pulse Oximeter Values Agree with Arterial Oxygenation Saturation in Acutely Ill Patients? *Medsurg Nurs [Internet]*. 2015;24(6):391–6. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/26863701>

Part D - Appendices

Synopsis – Perioperative Comparison of the Agreement between a Portable Fingertip Pulse Oximeter vs. Conventional Bedside Pulse Oximeter in Adult Surgical Patients

Background

Perioperative accurate measurement of a patient's arterial haemoglobin oxygen saturation has become an accepted standard of care amongst anaesthetists around the world.

Oxygen (O₂) is predominantly carried in the blood by haemoglobin (Hb) and a normal O₂ saturation level is above 94%. This can be directly measured by a laboratory co-oximeter (termed SaO₂) but is invasive (requires blood to be drawn from an artery), painful to the patient, results are obtained slowly depending on how far the laboratory is from the patient and its workload and requires expertise by the person drawing the blood and the co-oximeter operator.

Pulse oximeters are items of medical equipment that noninvasively estimate a patient's O₂ saturation (termed SpO₂) and heart rate by passing two different wavelengths of light (infrared and red) through a sensor that can be placed on a fingertip, toe, earlobe etc. The information from the sensor is analyzed by a microprocessor and SpO₂ estimated from a stored, proprietary calibration curve. This method of measurement is safe, painless, more readily available, easier to perform, faster and cheaper than co-oximeter.

Studies have confirmed the accuracy of pulse oximeters compared to co-oximeters, which are considered the 'gold standard' for measuring O₂ saturation.

Various regulatory bodies throughout the world, including the South African Society of Anaesthesiologists, consider pulse oximeters essential in providing a safe anaesthetic. They

are included in the World Health Organization's (WHO) Surgical Safety Checklist (SSC). The SSC has been adopted throughout the world as a vital checklist to be completed before the commencement of every surgical procedure. It ensures that the correct operation is performed on the correct patient on the correct body area and that all relevant personnel, equipment, antibiotic prophylaxis and relevant precautions are in place before the start of an operation. Studies have conclusively shown that the implementation of the WHO SSC has resulted in a doubling of patients' chances of receiving proven standards of surgical care and that there was a substantial reduction in complications and deaths.

There has been much emphasis by the WHO and initiatives, like the Global Pulse Oximetry Project, to develop and identify affordable, robust pulse oximeters that can be supplied to every operating room in the developing world that does not yet have these items.

Pulse oximeter use is not limited to theatres, they are also utilized throughout the hospital: in the recovery room, intensive care unit, emergency department, wards etc. Outside the hospital setting, they can be used by general practitioners, expedition medics, paramedics, patients themselves who require home oxygenation monitoring etc.

Purpose & objectives of the study

Portable fingertip pulse oximeters are highly transportable (they can fit in a pocket, small bag, be worn around the neck), easy to use, operate on batteries and safe. But their main advantages are convenience and cost, they are approximately 10 – 100 times cheaper than the pulse oximeters used in hospitals, depending on the model's functionality.

Few studies have been found that compare the accuracy of portable fingertip pulse oximeters to the convention hospital ones. Of those identified, they invariably recruit healthy volunteers who are tested under controlled conditions in a laboratory.

This study aims to compare the agreement between a portable fingertip pulse oximeter and a conventional bedside pulse oximeter in adult surgical patients with various co-morbidities in the hospital setting. It is important to highlight that this study will be different to conventional pulse oximetry equipment comparison studies in two ways: we aim to recruit real patients with

actual medical conditions vs healthy volunteers. And secondly, the hospital setting vs the ideal, controlled conditions of a laboratory. This lends itself to real world clinical application.

Agreement is a term used to describe whether one item of equipment measures a variable, in this study that is SpO₂, to an acceptable degree compared to an established method of measurement. If there is an acceptable level of agreement then we can confidently use the new device (portable fingertip pulse oximeter) to reliably measure a patient's SpO₂.

A secondary objective is to assess whether the heart rates measured by the two devices are similar.

Study design

This is an equipment comparison study which will evaluate the simultaneous, non-invasive measurement of SpO₂ and heart rates on individual patients using 2 different pulse oximeters.


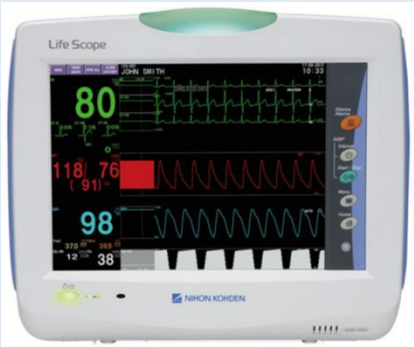
	Contec CMS50D Fingertip Pulse Oximeter	Nihon-Kohden LifeScope BSM 3562
		
Cost	Approx. R500 - R800	Approx. R200 000
Size	5.7 x 3.1 x 3.2 cm	37 x 31 x 17.2 cm
Weight	+/- 50 g (including batteries)	6.2 kg

Table 1. Basic comparison between study pulse oximeters

The portable fingertip pulse oximeter has been privately purchased by the author for the sole purpose of this study and the conventional pulse oximeter will be loaned from Groote Schuur

Hospital. It represents a commonly used model found throughout the hospital and has been calibrated and serviced by the manufacturer.

Adult (>18 years) patients at Groote Schuur hospital presenting for elective and emergency surgery in all disciplines will be included in the study unless they meet any of the exclusion criteria. These are medical or technical conditions known to affect the performance of pulse oximeters.

Exclusion criteria
Significantly low blood pressure or cold peripheries
Excessive patient movement
Abnormal Hb variants
Certain dyes used during the operation (e.g. methylene blue)
Nail polish/ black henna
Bandages/ tape etc. on the hand/ finger
Inadequate pulse oximeter trace

The study author will recruit eligible patients by convenience sampling until 200 measurements have been taken. Each patient's SpO₂ will only be measured once. This is the minimum recommended number of observations for a statistically significant result to be found.

Patient's vital signs (including SpO₂, heart rate, blood pressure) are routinely measured and monitored during the perioperative period (before, during and after an operation) until they are discharged home. The study pulse oximeter probes will be placed onto the patient's fingers simultaneously and will not interfere with any existing monitoring equipment already in place. Any abnormalities in SpO₂ or heart rate will be immediately reported to the treating doctor involved if they are not present and appropriate management instituted. The study will therefore not adversely affect patient care.

After application of the fingertip probes, the author will wait 30 seconds before confirming the quality of a waveform tracing on each probe. This allows sufficient time for each pulse oximeter to calculate the estimated SpO₂. If the waveform tracing is poor/ absent for both oximeters then it will be assumed that a patient/ technical factor precludes the accurate usage of a pulse oximeter on that patient and data will not be recorded. When a satisfactory tracing has been confirmed, the displayed SpO₂ and heart rate will be documented. The patient's skin colour will also be recorded using The Fitzpatrick scale (see Appendices).

Data will be analyzed using a Bland and Altman plot and bias and precision estimates. This method has been internationally established as the standard reported statistic when comparing agreement between a new measurement technique with an established one. Data analysis will be performed by the study Supervisor.

There should be no significant additional cost in performing this study. Except for a commercial alcohol-based disinfectant which will be used to clean the fingertip probes between samples. This will be minimal.

Ethical and legal considerations

Confidentiality

To ensure complete anonymity, no patient identifiable information will be recorded on the data collection form. Measurements will be captured in a sequential numerical manner (e.g. numbers 1 – 200).

Possible risks:

Pulse oximetry is essentially harmless to patients. The only possible theoretical risk is cross-contamination. The fingertip probes will be disinfected between usage using an alcohol wipe. Any bodily fluids will be avoided. Recruitment will not affect clinical care (as outlined under Study design).

Reimbursement for participation

There will be no reimbursement offered.

Informed consent

Written consent will be waived for the following reasons:

- Brief (30 seconds), non-invasive application of a standard monitoring device
- No risk of physical harm to patients
- Pulse oximetry forms part of the routine vital signs performed on all surgical patients (blood pressure, pulse rate, oxygen saturation, respiratory rate and temperature measurement) during admission to hospital, intra-operatively and post-operatively until full recovery from anaesthesia
- Pulse oximeter already attached to the patient for monitoring purposes (e.g. in the recovery room) will not be disturbed
- No patient identifiable information will be gathered, results will be anonymous
- No additional information gathered that is not already being gathered/recorded
- Theoretical risk of cross-infection – probe to be cleaned with alcohol-based disinfectant between uses (as per standard hygiene and infection control principles)
- During data collection, should any patient be found to have unrecognized low SpO₂, standard treatment will immediately be commenced, and the treating doctor notified

A brief explanation about the study will be supplied to conscious patients and information leaflets will be available (see Appendices).

Potential benefits to patients and society

This study into the performance of portable fingertip pulse oximeters in adult surgical patients could result in the availability of cheaper devices, deemed as vital anaesthetic equipment by the WHO and various anaesthetic regulatory bodies, in lower income medical facilities. It will also give anaesthetists and other medical personal the confidence to make clinical decisions based on these highly portable devices, thereby making pulse oximeters more available in

resource limited areas. It will also add further data to existing studies and help assess whether darker skin tone affects the performance of these devices in the clinical setting, which is highly relevant in an African country like South Africa.

Motivation for Expedited Review



Department of Anaesthesia

Faculty of Health Science,
Anzio Road, Observatory
Western Cape, South Africa 7925
Telephone: (021) 406-6143
Fax No. (021) 406-6589
GSH departmental line: (021) 404-5004

Professorial Staff:

JLC Swanevelder, MB ChB, MMed (Anes) (U Stellen), FCA (SA), FRCA (Hon)
Head of Department
Email: justiaan.swanevelder@uct.ac.za
RA Dyer BScHons (U Stellen) MBChB (UCT), FCA (SA), PhD
2nd Chair of Anaesthesia
Email: robert.dyer@uct.ac.za
Administrative Officer: C Wynngaard, Email: cheryl.wynngaard@uct.ac.za

Dear Professor Blockman,

Re: Expedited review of study assessing fingertip pulse oximeters

We hope this letter finds you well.

As discussed telephonically, we wish to request expedited ethics review and waiving of written informed consent for this study, which will assess the agreement between low-cost, lightly portable fingertip pulse oximetry devices with our conventional perioperative bedside machines.

Pulse oximetry is essentially harmless to patients. To ensure complete anonymity, no personal patient information or details will be recorded on the data collection form. Recruitment will not affect clinical care. The two pulse oximeters used in the study will be applied simultaneously to any patient monitoring equipment, which may be applied to the patient. Thereby, ensuring no disruption in, for example, continuous monitoring that may be present in the recovery room.

The only possible theoretical risk is cross-contamination. The fingertip probes will be disinfected between measurements using an alcohol wipe. Any bodily fluids will be avoided. Patients with open wounds on their hands, or who have contract precautions due to risk of infectious disease transmission, will be excluded from the study.

The significance of this study into the performance of portable fingertip pulse oximeters in adult surgical patients will result in the availability of cheaper devices, deemed as vital anaesthetic equipment by the WHO and various anaesthetic regulatory bodies, in lower income medical facilities. It will also give anaesthetists and other medical personal the confidence to make clinical decisions based on these highly portable devices, thereby making pulse oximeters more available in resource-limited areas. It will also add further data to existing studies and help assess whether darker skin pigment affects the performance of these devices in the clinical setting, which is highly relevant in an African country like South Africa.

Thank you for your time and consideration,

Dr Reuben Smith
Senior Registrar
MMed Candidate

Dr Ross Hofmeyr
Consultant Anaesthesiologist
MMed Supervisor

Department of Anaesthesia & Perioperative Medicine

Data Collection Sheet

Data Collection Sheet


Sample Number	SpO2 (%) (PFO)	SpO2 (%) (BPO)	Pulse Rate (beats/min)	Skin Tone	Setting	Signal
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
13						
14						
15						
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Note:

Drop-down lists allow selection of the appropriate skin tone, setting and signal strength, according to the following options:

Skin Tone	Signal	Setting
I	Good	PreOp Assess
II	Poor	Theatre
III	Absent	Recovery room
IV		ICU/PAHCU
V		
VI		


Data Insert for Portable Fingertip Pulse Oximeter



CORATE Pulse Oximeter
User Manual

CONTEC MEDICAL SYSTEMS CO., LTD
Address: No. 112 Shengyuan Road Street, Economic & Technical Development Zone,
Qidongqiang, Huzhou Province, PEOPLE'S REPUBLIC OF CHINA
Tel: 0566-325-811430
Fax: 0566-325-811586

Manufactured and Distributed by
CMS MOBILITY INC



CMS50D

Instructions to User

Dear users, thank you for purchasing the Corate CMS 50D Pulse Oximeter. In case of modifications and software updates, the information contained in this document is subject to change without notice.

The Manual describes, in accordance with the Pulse Oximeter's features and requirements, main structure, functions, specifications, correct methods for transportation, installation, usage, operation, repair, maintenance and storage, etc., as well as the safety procedures to protect both the user and equipment. Refer to the respective chapters for details.

Please read the Manual very carefully before using this equipment. These instructions describe the operating procedures to be followed strictly. Failure to follow these instructions could lead to measurement abnormality, equipment damage and personal injury. The manufacturer is NOT responsible for the safety, reliability and performance issues and any measurement abnormality, personal injury and equipment damage due to user's negligence of the operating instructions. The manufacturer's warranty service does not cover such faults. Due to constant revision, the specific products you received may not be totally in accordance with the description of this User Manual. We sincerely apologize for that.

WARNING:

- User might experience discomfort if the device is used for a prolonged period of time. It is recommended that the sensor should not be applied to the same finger for over 2 hours.
- The device should not be clipped on tender skin.
- The light (infrared is invisible) emitted from the device is harmful to the eyes. The user should not stare at the light.
- User should not use apply enamel or other makeup on the fingertip.
- **Warning: Keep cord and handset away from children as the included handset may present an strangulation or choking hazard to small children. Adult supervision required; never leave children unattended with cord or handset.**
- The user's fingernail should not be too long.
- **This device is not intended to diagnose or treat any medical condition or disease. It is intended for non-medical use to healthy people to monitor their pulse and blood oxygen levels during sports and/or aviation only. People who need SpO2 and pulse rate measurements because of a medical condition should consult the device and should consult with their physician.**

1 Safety

1.1 Instructions for Safe Operations

- Check the main unit and all accessories periodically to make sure that there is no visible damage that may affect your safety and monitoring performance. It is recommended that the device should be inspected once a week at least. When there is obvious damage, stop using the monitor.
- Necessary maintenance must be performed by qualified service engineers ONLY. Users are not permitted to maintain it by themselves.
- The oximeter should not be used together with device not specified in User's Manual. Only accompanied accessories should be used with this device.
- This product is authorized before leaving factory.

1.2 Warnings

- Explosive hazard—DO NOT use the oximeter in environment with inflammable gas.
- Individuals who are allergic to rubber should not use this device.
- The pulse oximeter has no SpO2 alarm and it is not meant for continuous monitoring.
- The disposal of the pulse oximeter, accessories and packing material (including battery, plastic bags, foams and paper boxes) should follow local laws and regulations.
- Please make sure that the device and accessories are in complete accordance with the packing list, or the device might not function normally.

1.3 Attention

- Keep the oximeter away from dust, vibration, corrosive substances, explosive materials, high temperature and moisture.
- If the oximeter gets wet, please stop operating it.
- When the pulse oximeter is moved from a cold environment to a warm indoor hand environment, please do not use it immediately.
- DO NOT operate keys on the panel with sharp materials.
- High temperature or high pressure steam disinfection of the oximeter is not permitted. Refer to User Manual in the relative chapter for instructions of cleaning and disinfection.
- Do not immerse the oximeter in liquid. When it needs cleaning, please wipe its surface with medical alcohol by soft material. Do not spray any liquid on the device directly.
- When cleaning the device with water, the temperature should be lower than 50°C.
- For fingers which are too thin or too cold, it would probably affect the normal measurement of the user's SpO2 and pulse rate. Please clip on a thicker finger such as the thumb, index or middle finger deeply into the probe.
- Do not use the device on infant or newborn child.
- The product is suitable for children above four years old and adults (Weight should be between 15kg to 110kg).
- The device may not work for everyone. If you are unable to achieve stable readings, discontinue use.
- The update period of data is less than 5 seconds but might change based on different individual pulse rate.
- If abnormal conditions appear on the screen during the test process, pull out the finger and return to normal use.
- The normal shelf life of the device is three years.
- The handset attached the product is made from non-allergic material. If you are sensitive to it, stop using it. In addition, the handset could present a choking hazard. Please use extreme caution when using it.
- The instrument does not have a low-voltage alarm function. It only shows the low voltage on the LED screen. Please change the battery when the battery is used up.
- The instrument does not have alarm functions. Do not use the device in situations where alarms are required.
- Batteries must be removed if the device is going to be stored for more than one month, or the batteries may leak.
- A flexible circuit connects the two parts of the device. Do not twist or pull on the connection.

1.4 Indication for Use

The Fingertip Pulse Oximeter is a non-invasive device intended for the spot-check of oxygen saturation of arterial hemoglobin (SpO2) and the pulse rate of adult and children. This device is not intended for continuous monitoring.

2 Overview

SpO2 stands for peripheral capillary oxygen saturation. Oxygen saturation is defined as the ratio of oxyhemoglobin (HHbO) to the total concentration of hemoglobin (i.e. Oxyhemoglobin + reduced hemoglobin) present in the blood. It is an important physiological parameter involved in respiration and circulation. For that purpose, our company developed the Pulse Oximeter which can measure your SpO2 and pulse rate simultaneously. The Pulse Oximeter feature herein is small, portable, non-invasive and easy to use. The user only needs to insert a finger into the chamber to measure his/her SpO2 and Pulse Rate.

2.1 Features

- Operation of the product is simple and convenient.
- The product is small, light (total weight is about 50g including batteries) and easy to use.
- Power consumption of the product is low and the two originally equipped AAA batteries can be operated continuously for 20 hours.
- The product will automatically be powered off when no signal is in the product within 5 seconds.
- Includes 2% hemoglobin to indicate strength of blood flow.
- Rotational OLED display for viewing convenience.

2.2 Major Applications and Scope of Application

The Pulse Oximeter can be used to measure human Hemoglobin Saturation and pulse rate through finger, and indicate the pulse intensity by the bar display. The product is designed to be used by athletes, pilots or anyone who wants to obtain their SpO2 and pulse rate on the go.

Using the product is not suitable for continuous use.

Do not use the device if the user is suffering from infections by carbon monoxide. The device should not be used under such circumstances.

2.4 Environment Requirements

Storage Environment

- Temperature: -40°C~+60°C
- Relative Humidity: ≤95%

Operating Environment

- Temperature: 10°C~40°C
- Relative Humidity: ≤95%
- Atmospheric pressure: 700hPa~1060hPa

3 Technical Specifications

3.1 Principle of Measurement

Oxygenated blood absorbs light at 660nm (red light), whereas deoxygenated blood absorbs light preferentially at 940nm (infra-red). A pulse oximeter works by passing a beam of red and infrared light through a pulsating capillary bed and then measure the amount of red and infrared light emerging from the human nail tip via a sensor. The relative absorption of light by oxyhemoglobin (HHbO) and deoxyhemoglobin is then processed according to the Beer Lambert's law and the result is a qualitative measurement of the user's oxyhemoglobin status (i.e. Oxygen saturation level (SpO2)).

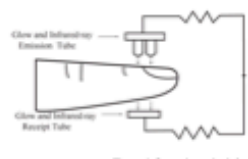


Figure 1 Operating principle

3.2 Caution

1. The finger should be placed properly such that it is exactly in between the infra-red Emission tube and infrared sensor line (the attached illustration of this manual, Figure 1 & 3), or else it may cause inaccurate measurement.
2. The pulse oximeter should not be used on any finger where blood flow might be restricted. For example, a limb with arterial canal or blood pressure cuff or receiving intravenous injection.
3. Make sure the optical path is free from any optical obstructions like rubberized fabric.
4. Excessive ambient light may affect the measuring result. It includes fluorescent lamp, deal relay light, infrared heater, direct sunlight and etc.
5. Structural action of the subject or extreme electromagnetic interference may also affect the accuracy.
6. Iceber cases, use enamel or other makeup on the finger.

3.5 Limitations

1. As the measurement is taken on the basis of the arterial pulse, substantial pulsating blood flow of subject is required. For a subject with weak pulse due to shock, low ambient body temperature, major bleeding, or use of vascular constricting drug, the pulse oximeter might not be able to take a reading. In this case, the measurement will also be more sensitive to interference.
2. For those with a substantial amount of staining (dilation drug such as methylene blue, indigo green and indigo NaCl), or carbon monoxide hemoglobin (COHb), or methemoglobin (Me-Hb) or thalassaemic hemoglobin, and some with vitreous problem, the SpO2 determination by this monitor may be inaccurate.
3. The drugs like dopamine, procaine, pilocarpine, lidocaine and bupivacaine may also affect the accuracy of your SpO2 levels.

4 Technical Specifications

1. Display Format: OLED Display.
2. SpO2 Measuring Range: 0% ~ 100%.
3. Pulse Rate Measuring Range: 30 bpm ~ 250 bpm.
4. Pulse Wave Display: columnation display and the waveform display.
5. Power Requirement: ≥1.5V AAA alkaline battery, adaptable range: 2.6V~3.6V.
6. Power Consumption: Less than 32mA.
7. Resolution: 1% for SpO2 and 1 bpm for Pulse Rate.
8. Measurement Accuracy: ±2% in stage of 70%~100% SpO2, and meaningless when stage being smaller than 70%. ±2 bpm during the pulse rate range of 30~99 bpm and ±2% during the pulse rate range of 100~250 bpm.
9. Measurement Performance in low blood perfusion condition: SpO2 and pulse rate can be shown during low blood perfusion. However, SpO2 error is ±4%, pulse rate error is ±2 bpm or ±2% (whichever larger).
8. Resistance to surrounding light: The deviation between the value measured in the condition of non-made light or indoor natural light and that of darkness is less than ±1%.
9. Equipped with a function switch. The Oximeter will automatically power off if the finger is removed after 5 seconds.
9. Optical Sensor

Red light (wavelength is 660nm, 6.65mW)
Infrared (wavelength is 940nm, 6.75mW)

5 Accessories

- One Hanging rope;
- Two AAA batteries;
- One silicon cover;
- One User Manual.

6 Installation

6.1 View of the Front Panel

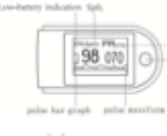


Figure 2 Front view




Figure 3 Batteries installation




Figure 4

6.2 Battery

Step 1. Refer to Figure 3 and insert two AAA size batteries properly in the right direction.

Step 2. Replace the cover.

These take care when you insert the batteries. Improper insertion may damage the device.

6.3 Mounting the Hanging Rope

Step 1. Put the end of the rope through the hole.


Step 2. Put an end of the rope through the first one and then tighten it.

7 Operating Guide

- 1) Insert the two batteries properly to the direction, and then replace the cover.
- 2) Open the clips as shown in Figure 5.

Dr Reuben Smith - MMed Dissertation - COMFORT Trial

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- Figure 5 Put finger in position
- Put your finger into the rubber cushions of the clip (make sure the finger is in the right position) and then clip the finger.
 - Press the switch button once on front panel.
 - Do not move the finger and try to keep the body stationary.
 - Get the information directly from screen display.
 - The button  has three functions. When the device is powered off, pressing the button will power it on; When the device is powered on, pressing the button quickly (<1 sec) will change the direction of the screen (See Figure 6-11), holding the button for longer than a second will change the brightness of the screen.
 - Wait for the wavelength and amplitude of the plethysmograph wave to be stabilized before taking reading.

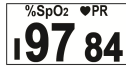


Figure 6 Display mode one



Figure 7 Display mode two

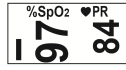


Figure 8 Display mode three



Figure 9 Display mode four

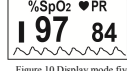


Figure 10 Display mode five

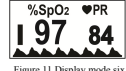


Figure 11 Display mode six

8 Repairing and Maintenance

- Fingernails and the luminescent tube should be on the same side.**
- Do not immerse the device in liquid.**
- It is recommended that the device should be kept in a dry environment. Humidity may reduce the useful life of the device, or even damage it.**

9 Troubleshooting

Trouble	Possible Reason	Solution
The SpO ₂ and Pulse Rate cannot be displayed normally	1. The finger is not properly positioned. 2. The user's SpO ₂ is too low to be detected.	1. Place the finger properly and try again. 2. Try again; Make sure nothing is impeding your blood flow
The SpO ₂ and Pulse Rate values change erratically	1. The finger is not placed deep enough into the device. 2. The finger or the user is moving.	1. Place the finger properly and try again. 2. Keep stationary as much as possible during measurement
The device cannot be turned on	1. The batteries are drained or almost drained. 2. The batteries are not inserted properly. 3. The malfunction of the device.	1. Change batteries. 2. Reinstall batteries. 3. Please contact the local service center.
The display turns off suddenly	1. The device will power off automatically if the finger is withdrawn after 5 seconds. 2. The batteries are almost drained.	1. Press the power button to turn it back on. 2. Change batteries.

10 Key of Symbols

Symbol	Description
	Type BF
	Warning - See User Manual
	Blood oxygen saturation (%)
	Pulse rate (bpm)
	The battery voltage indication is deficient (change the battery in time avoiding the inexact measure)
	1. no finger inserted 2. An indicator of signal inadequacy
	battery positive electrode
	battery cathode
	1. Power switch 2. change direction of the screen 3. Change brightness of the screen
	Serial number
	Alarm inhibit
	WEEE (2002/96/EC)
	International Protection
	This item is compliant with Medical Device Directive 93/42/EEC of June 14, 1993, a directive of the European Economic Community. However, this is not a medical device and is not intended to diagnose or treat any medical condition or disease.

11 Function Specification

Display Information	Display Mode
The Pulse Oxygen Saturation (SpO ₂)	OLED
Pulse Rate (PR)	OLED
Pulse Intensity (bar-graph)	OLED bar-graph display
Pulse wave	OLED
SpO₂ Parameter Specification	
Measuring range	0%-100%, (the resolution is 1%)
Accuracy	70%-100%±2%, Below 70% unspecified
Optical Sensor	Red light (wavelength is 660nm) Infrared (wavelength is 880nm)
Pulse Parameter Specification	
Measuring range	30bpm-250bpm (the resolution is 1 bpm)
Accuracy	±2bpm or ±2% select larger
Pulse Intensity	
Range	Continuous bar-graph display. Increased height indicates stronger pulse.
Battery Requirement	
1.5V (AAA size) alkaline batteries × 2 or rechargeable battery	
Battery Useful Life	
Two batteries can work continuously for 20 hours	
Dimensions and Weight	
Dimensions	57(L) × 31(W) × 32(H) mm
Weight	About 50g (with the batteries)

Appendix


Guidance and manufacturer's declaration-electromagnetic emission for all EQUIPMENT and SYSTEMS

Guidance and manufacturer's declaration -electromagnetic emission		
The CMS50D Pulse Oximeter is intended for use in the electromagnetic environment specified below. The customer of the user of CMS50D Pulse Oximeter should assure that it is used in such an environment.		
Emission test	compliance	Electromagnetic environment-guidance
RF emissions CISPR 11	Group 1	The CMS50D Pulse Oximeter uses RF energy only for their internal function. Therefore, its RF emissions are very low and are not likely to cause any interference in nearby electronic equipment.
RF emissions CISPR 11	Class B	The CMS50D Pulse Oximeter is suitable for use in all establishments, including domestic establishments and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
Harmonic emissions IEC 61000-3-2	Not applicable	
Voltage fluctuations/ flicker emission IEC 61000-3-3	Not applicable	

Guidance and manufacturer's declaration-electromagnetic immunity for all EQUIPMENT and SYSTEMS

Guidance and manufacturer's declaration-electromagnetic immunity			
The CMS50D Pulse Oximeter is intended for use in the electromagnetic environment specified below. The user of CMS50D Pulse Oximeter should assure that it is used in such an environment.			
Immunity test	IEC60601 test level	Compliance level	Electromagnetic environment-guidance
Electrostatic discharge (ESD) IEC 61000-4-2	±6KV contact ±8KV air	±6KV contact ±8KV air	Floors should be wood, concrete or ceramic tile. If floor are covered with synthetic material, the relative humidity should be at least 30%.
Power frequency (50Hz) magnetic field IEC 61000-4-8	3A/m	3A/m	Power frequency magnetic fields should be at levels characteristic of a typical location in a typical commercial or hospital environment

Guidance and manufacturer's declaration-electromagnetic immunity for EQUIPMENT and SYSTEMS that are not LIFE-SUPPORTING

Guidance and manufacturer's declaration-electromagnetic immunity			
The CMS50D Pulse Oximeter is intended for use in the electromagnetic environment specified below. The customer or the user of CMS50D Pulse Oximeter should assure that it is used in such an environment.			
Immunity test	IEC60601 test level	Compliance level	Electromagnetic environment -guidance
Radiated RF ICE 61000-4-3	3V/m 80MHz to 2.5GHz	3V/m	Portable and mobile RF communication equipment should be used no closer to any part of the CMS50D Pulse Oximeter, including cables, than the recommended separation distance calculated from the equation applicable to the frequency of the transmitter. recommended separation distance $d = \left[\frac{3.5}{E_1} \right] \sqrt{P}$ 80MHz to 800MHz $d = \left[\frac{7}{E_1} \right] \sqrt{P}$ 800MHz to 2.5GHz Where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer and d is the recommended separation distance in meters (m). Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey, * should be less than the compliance level in each frequency range. Interference may occur in the vicinity of equipment marked with the following symbol: 
NOTE 1 At 80MHz and 800MHz, the higher frequency range applies. NOTE 2 These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people. * Field strengths from fixed transmitters, such as base stations for radio (cellular/cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which The CMS50D Pulse Oximeter is used exceeds the applicable RF compliance level above, the CMS50D Pulse Oximeter should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as reorienting or relocating the CMS50D Pulse Oximeter. * Over the frequency range 150 KHz to 80 MHz, field strengths should be less than 3V/m.			

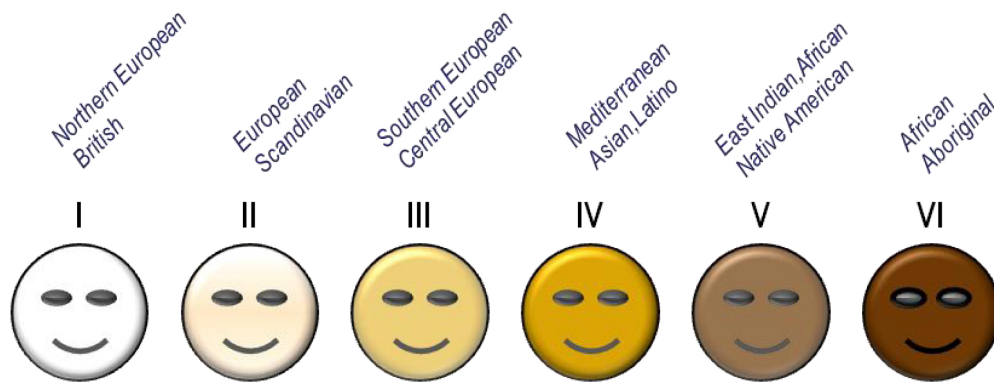
Recommended separation distances between portable and mobile RF communications equipment and the EQUIPMENT or SYSTEM for EQUIPMENT or SYSTEM that not LIFE-SUPPORTING

Recommended separation distances between portable and mobile RF communications equipment and the CMS50D Pulse Oximeter			
The CMS50D Pulse Oximeter is intended for use in the electromagnetic environment in which radiated RF disturbances are controlled. The customer or the user of the CMS50D Pulse Oximeter can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF communications equipment (transmitters) and the CMS50D Pulse Oximeter as recommended below, according to the maximum output power of the communications equipment.			
Rated maximum output power of transmitter (W)	Separation distance according to frequency of transmitter (m)		
	150KHz to 80MHz	80MHz to 800MHz	800MHz to 2.5GHz
	$d = \left[\frac{3.5}{E_1} \right] \sqrt{P}$	$d = \left[\frac{3.5}{E_1} \right] \sqrt{P}$	$d = \left[\frac{7}{E_1} \right] \sqrt{P}$
0.01	0.12	0.12	0.23
0.1	0.37	0.37	0.74
1	1.17	1.17	2.33
10	3.69	3.69	7.38
100	11.67	11.67	23.33
For transmitters rated at a maximum output power not listed above, the recommended separation distance in meters (m) can be estimated using the equation applicable to the frequency of the transmitter, where P is the maximum output power rating of the transmitter in watts (W) according to the transmitter manufacturer. NOTE 1 At 80MHz and 800MHz, the separation distance for the higher frequency range applies. NOTE 2 These guidelines may not apply in all situations. Electromagnetic propagation is affected by absorption and reflection from structures, objects and people.			

The Fitzpatrick Scale - Numerical Classification Schema for Human Skin Colour

The Fitzpatrick Scale

A numerical classification schema for human skin colour



Patient information leaflet – Pulse oximetry

The most important function of our blood is to carry oxygen to the body. We can easily and painlessly measure the amount of oxygen in the blood by using a device called a pulse oximeter, which shines a light through the skin (usually on a finger) and calculates how much light has been absorbed by the blood cells. This causes no harm, and is done continuously in hundreds of thousands of cases around the world every day. In fact, pulse oximetry is considered by groups such as the World Health Organisation to be an essential part of patient safety equipment when doing operations. Most healthy people have oxygen saturations (the percentage of the blood cells that are carrying oxygen) of 94-100%.



Conventional hospital pulse oximeters are connected to and displayed on large expensive monitors, which makes them difficult to transport and use at the bedside, or in resource-limited settings. Today, compact fingertip pulse oximeters have been cheaply produced that can fit into a pocket. This could be very valuable in our African setting. The purpose of this study is to discover if the fingertip devices give the same measurement as the conventional monitors we use everyday in the hospital.

We are asking patients to volunteer to have us record their oxygen saturations with both a fingertip and conventional pulse oximeter while undergoing routine care before, during and after surgery in the hospital. This might be in the preoperative assessment area, induction rooms, operating theatres, recovery, ICU or High Care. The measurements take less than a minute, and do not cause any discomfort or harm. No participants in the study will be given any payment or other compensation, but the information we gain may help many patients – particularly in resource-limited settings – in the future. Your participation is completely anonymous. We will only record information about the oxygen saturation, quality of the signal, and your skin colour (to help assess if this affects the readings). Your name, age, procedure and other medical information will not be recorded. Whether or not you decide to take part will not affect the quality of your care at the hospital.

This study has ethical approval from the University of Cape Town Human Research Ethics Committee (HREC xxx/2017). If you would like more information, you may contact the study doctors (Dr Reuben Smith or Prof Ross Hofmeyr) on 021 404 5003, or the HREC on 021 406 6338.

This leaflet makes use of free patient information provided by the American Thoracic Society in their *ATS Patient Information Series*. The full leaflet and further info is available online at <https://www.thoracic.org/patients/patient-resources/resources/pulse-oximetry.pdf>

Human Research Ethics Committee (HREC) Approval Letter



UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee



Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: sumayah.arietdien@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

18 January 2018

HREC REF: 572/2017

Dr R Hofmeyr
Department of Anaesthesia & Perioperative Medicine
D-23
NGSH

Dear Dr Hofmeyr

PROJECT TITLE: PERIOPERATIVE COMPARISON OF THE AGREEMENT BETWEEN A PORTABLE FINGERTIP PULSE OXIMETER VS. CONVENTIONAL BEDSIDE PULSE OXIMETER IN ADULT PATIENTS (MMED CANDIDATE - DR R SMITH)

Thank you for your response letter dated 11 January 2018, addressing the issues raised by the Human Research Ethics Committee (HREC).

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 January 2019.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

We acknowledge that the student: Dr R Smith will also be involved in this study.

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

HREC 572/2017

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines.

The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

HREC 572/2017

Trial record **1 of 1** for: NCT03496493

Previous Study | [Return to List](#) | Next Study

COMparison of Portable Fingertip Versus Conventional Pulse OximeteRs Trial (COMFORT)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. **▲** [Know the risks and potential benefits](#) of clinical studies and talk to your health care provider before participating. Read our [disclaimer](#) for details.

ClinicalTrials.gov Identifier:
 NCT03496493

[Recruitment Status](#) ⓘ: Recruiting
[First Posted](#) ⓘ: April 12, 2018
[Last Update Posted](#) ⓘ: May 2, 2018

See [Contacts and Locations](#)

Sponsor:

University of Cape Town

Information provided by (Responsible Party):

Ross Hofmeyr, University of Cape Town

[Study Details](#)

[Tabular View](#)

[No Results Posted](#)

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[How to Read a Study Record](#)

Tracking Information	
First Submitted Date	January 20, 2018
First Posted Date	April 12, 2018
Last Update Posted Date	May 2, 2018

Actual Study Start Date	April 15, 2018
Estimated Primary Completion Date	June 11, 2018 (Final data collection date for primary outcome measure)
Current Primary Outcome Measures (submitted: April 5, 2018)	<p>Saturation measurement agreement [Time Frame: 1 minute]</p> <p>Bland-Altman analysis of saturation measurement pairs, with a priori acceptable limits of agreement (1.96 x SD measurement differences) within 3%. This is in accordance with ISO and FDA guidelines for testing of these devices (see relevant standard).</p>
Original Primary Outcome Measures	<i>Same as current</i>
Change History	Complete list of historical versions of study NCT03496493 on ClinicalTrials.gov Archive Site
Current Secondary Outcome Measures (submitted: April 5, 2018)	<ul style="list-style-type: none"> • Average root mean square difference [Time Frame: 1 minute] Average root mean square difference in saturation pairs between the oximeters of less than 3% • Skin tone effect [Time Frame: 1 minute] Subgroup analysis of effect of skin tone (Fitzpatrick scale) on oximeter agreement (provisional on adequate recruitment across groups) • Perfusion (pulse magnitude) effect on oximeter agreement [Time Frame: 1 minute] Subgroup analysis of effect of magnitude of pulse waveform signal (as an indication of finger perfusion on oximeter agreement. This will be graded qualitatively as good, poor, or absent waveform, and is provisional on adequate recruitment across groups.
Original Secondary Outcome Measures	<i>Same as current</i>
Current Other Outcome Measures	<i>Not Provided</i>
Original Other Outcome Measures	<i>Not Provided</i>
Descriptive Information	
Brief Title	COMparison of Portable Fingertip Versus Conventional Pulse OximeteRs Trial
Official Title	Perioperative Comparison of the Agreement Between a Portable Fingertip Pulse Oximeter Versus Conventional Bedside Pulse Oximeter in Adult Patients

<p>Brief Summary</p>	<p>Perioperative non-invasive measurement of a patient's peripheral arterial oxygen saturation has become an accepted standard of care endorsed by anaesthesiologists and their regulatory bodies throughout the world. Pulse oximeters are an integral item on the World Health Organisation's Surgical Safety Checklist which is performed prior to the commencement of every surgical procedure. They are also utilised by other medical professionals and patients in various scenarios. When compared to conventional bedside pulse oximeters, portable fingertip devices have the advantages of cost-effectiveness, high portability, ease of use and battery operation. A review of recent literature reveals a paucity of accuracy studies in adult patients with various comorbidities in the clinical setting. Most data has been obtained under ideal laboratory conditions utilizing healthy adult volunteers. This study aims to pragmatically investigate the performance of a portable fingertip pulse oximeter in adult patients in a hospital setting.</p>
<p>Detailed Description</p>	<p>The purpose of this prospective, quantitative study is to compare the agreement between the measured arterial oxygen saturation levels using a portable fingertip versus a conventional bedside pulse oximeter in adult surgical patients, presenting for elective and emergency surgery to Groote Schuur Hospital over a four-week period. Adult surgical patients, not meeting any exclusion criteria, who present for elective or emergency surgery will be recruited. 200 data pairs (SpO₂, heart rate and skin tone) will be recorded in the perioperative period (operating rooms, recovery room and intensive care unit).</p> <p>Existing monitoring devices will not be disturbed. The agreement between the two devices will be compared using a Bland-Altman plot, Microsoft Excel and SPSS software. A root mean square difference value will also be calculated from these values.</p> <p>No sensitive or personal patient information will be recorded, and pulse oximetry is essential harmless. Potential cross-infection will be avoided by excluding patients with known communicable diseases or open wounds/ bodily fluids in the area to have the oximeter probes applied. The study devices will be disinfected after each use. Recruitment will not affect clinical care.</p> <p>The significance of this study into the performance of portable fingertip pulse oximeters in adult surgical patients will result in the availability of cheaper devices, deemed as vital anaesthetic equipment by the WHO and various anaesthetic regulatory bodies, in lower income medical facilities. It will also give anaesthetists and other medical personal the confidence to make clinical decisions based on these highly portable devices, thereby making pulse oximeters more available in resource limited areas. It will also add further data to existing studies and help assess whether darker skin pigment affects the performance of these devices in the clinical setting, which is highly relevant in</p>

	an African country like South Africa.
Study Type	Observational
Study Design	Observational Model: Cohort Time Perspective: Prospective
Target Follow-Up Duration	<i>Not Provided</i>
Biospecimen	<i>Not Provided</i>
Sampling Method	Non-Probability Sample
Study Population	All adult surgical patients presenting for elective or emergency surgery within an academic teaching hospital. Patients will have measurements made in the perioperative period in areas where conventional monitoring of pulse oximetry occurs, such as anaesthesia preassessment areas, induction rooms, operating theatres, recovery areas, ICU and PAHCU.
Condition	<ul style="list-style-type: none"> • Anesthesia • Hypoxemia
Intervention	<p>Device: All patients</p> <p>Peripheral arterial oxygen saturation recording with both study devices</p> <p>Other Names:</p> <ul style="list-style-type: none"> • Nihon-Kohden Lifescope BSM 3562 patient monitor • Contec CMS50D fingertip pulse oximeter
Study Groups/Cohorts	<p>All patients</p> <p>All patients enrolled in trial will have peripheral oxygen saturation simultaneously recorded with both study devices on non-adjacent (second and fourth) fingers of the same hand.</p> <p>Intervention: Device: All patients</p>
Publications *	<i>Not Provided</i>
<p>* Includes publications given by the data provider as well as publications identified by ClinicalTrials.gov Identifier (NCT Number) in Medline.</p>	
Recruitment Information	
Recruitment Status	Recruiting
Estimated Enrollment	200

(submitted: April 5, 2018)	
Original Estimated Enrollment	<i>Same as current</i>
Estimated Study Completion Date	December 31, 2018
Estimated Primary Completion Date	June 11, 2018 (Final data collection date for primary outcome measure)
Eligibility Criteria	<p>Inclusion Criteria:</p> <ul style="list-style-type: none"> • Adult surgical patients presenting for elective or emergency surgery <p>Exclusion Criteria:</p> <ul style="list-style-type: none"> • Contact precautions due to high risk of transmissible infectious disease • Significant hypotension or hypoperfusion (systolic blood pressure <80 mmHg, or hypothermia) • Motion artefacts due to excessive patient movements • Known presence of variant haemoglobin species (eg. carboxy- or methaemoglobin) • Intraoperative dye use (eg. methylene blue or indocyanine green) • Nail polish or black henna • Tape or bandages over the fingers • Absent/inadequate pulse oximetry tracing on existing monitor
Sex/Gender	Sexes Eligible for Study: All
Ages	18 Years and older (Adult, Older Adult)
Accepts Healthy Volunteers	<i>Not Provided</i>
Contacts	Contact: Ross Hofmeyr, FCA(SA) +27214045003 ross.hofmeyr@uct.ac.za
Listed Location Countries	South Africa
Removed Location Countries	
Administrative Information	
NCT Number	NCT03496493
Other Study ID Numbers	UCT_Anaes_201801

Has Data Monitoring Committee	No
U.S. FDA-regulated Product	Studies a U.S. FDA-regulated Drug Product: No Studies a U.S. FDA-regulated Device Product: Yes Device Product Not Approved or Cleared by U.S. FDA: No Pediatric Postmarket Surveillance of a Device Product: No Product Manufactured in and Exported from the U.S.: No
IPD Sharing Statement	Plan to Share IPD: Yes Plan Description: Raw study data will be uploaded to an open sharing platform (www.researchgate.org or similar) after publication of the study. Supporting Materials: Study Protocol Supporting Materials: Statistical Analysis Plan (SAP) Time Frame: Upon publication of the study, to remain available indefinitely. Access Criteria: Open access after publication URL: http://
Responsible Party	Ross Hofmeyr, University of Cape Town
Study Sponsor	University of Cape Town
Collaborators	<i>Not Provided</i>
Investigators	Principal Investigator: Ross Hofmeyr, FCA(SA) University of Cape Town
PRS Account	University of Cape Town
Verification Date	May 2018

Instructions to Authors: South African Medical Journal

Please note - this information is copied directly from: <http://www.samj.org.za/index.php/samj/about/submissions#Research>

Author Guidelines

Please view the [Author Tutorial](#) for guidance on how to submit on Editorial Manager.

Please take the time to familiarise yourself with the policies and processes below. If you still have any questions, please do not hesitate to ask our editorial staff (tel.: +27 (0)21 532 1281, email: submissions@hmpg.co.za).

SAMJ policies

- Types of articles considered by the SAMJ
- Article Processing Charges
- Authorship
- Conflict of interest
- Research ethics committee approval
- Clinical trials
- Protection of patient's rights to privacy
- Copyright notice
- Privacy statement
- Ethnic classification
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Manuscript preparation

- Preparing an article for anonymous review
- General article format/layout
- Preparation notes by article type
- Illustrations
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From submission to acceptance

- Submission and peer-review
- Production process
- Changing contact details or authorship

Publication

- Online versus print
- Errata and retractions
- Indexing

SAMJ Policies

Type of articles considered by the SAMJ

The SAMJ will no longer limit the articles accepted to those that have 'general medical content', but is intending to capture the spectrum of medical and health sciences, grouped by relevance to the country's burdens of disease. This content will include research in the social sciences and economics that is relevant to the medical issues around our burden of disease. Please see '[A new vision for the SAMJ – and a call for papers](#)' for a full discussion of the new directions for the SAMJ.

We accept the following types of articles:

- [Research](#)
- [Reviews](#)
- [Clinical trials](#)
- [Editorials](#)
- [In Practice](#) (Previously Forum incl. Case Reports)
- [Correspondence](#)
- [Obituaries](#)
- [Book reviews](#)

- [Ad hoc supplements](#) e.g. guidelines, conference/congress abstracts, Festschrifts*

The following articles are by invitation only:

- Guest editorial
- Continuing Medical Education (CME)

*Contact claudian@hmpg.co.za for information on submitting ad hoc/commissioned supplements, including guidelines, conference/congress abstracts, Festschrifts, etc.

Publication Fees

All articles published in the South African Medical Journal are open access and freely available online upon publication. This is made possible by applying a business model to offset the costs of peer review management, copyediting, design and production, by charging a publication fee of R5 250 (ex vat) for each research article published. The charge applies only to Research articles submitted after 1 March 2017. The publication fee is standard and does not vary based on length, colour, figures, or other elements.

When submitting a Research article to the SAMJ, the submitting author must agree to pay the publication fee should the article be accepted for publication. The publication fee is payable when your manuscript is editorially accepted and before production commences for publication. The submitting author will be notified that payment is due and given details on the available methods of payment. Prompt payment is advised; the article will not enter into production until payment is received. Queries can be directed to claudian@hmpg.co.za.

Please refer to the section on 'Sponsored Supplements' regarding the publication of supplements, where a charge is applicable. Queries can be directed to dianes@hmpg.co.za or claudian@hmpg.co.za

Authorship

Named authors must consent to publication. Authorship should be based on: (i) substantial contribution to conceptualisation, design, analysis and interpretation of data; (ii) drafting or critical revision of important scientific content; or (iii) approval of the version to be published. These conditions must all be met (uniform requirements for manuscripts submitted to biomedical journals; refer to www.icmje.org)

If authors' names are added or deleted after submission of an article, or the order of the names is changed, all authors must agree to this in writing.

Please note that co-authors will be requested to verify their contribution upon submission. Non-verification may lead to delays in the processing of submissions.

Author contributions should be listed/described in the manuscript.

Conflicts of interest

Conflicts of interest can derive from any kind of relationship or association that may influence authors' or reviewers' opinions about the subject matter of a paper. The existence of a conflict – whether actual, perceived or potential – does not preclude publication of an article. However, we aim to ensure that, in such cases, readers have all the information they need to enable them to make an informed assessment about a publication's message and conclusions. We require that both authors and reviewers declare all sources of support for their research, any personal or financial relationships (including honoraria, speaking fees, gifts received, etc) with relevant individuals or organisations connected to the topic of the paper, and any association with a product or subject that may constitute a real, perceived or potential conflict of interest. If you are unsure whether a specific relationship constitutes a conflict, please contact the editorial team for advice. If a conflict remains undisclosed and is later brought to the attention of the editorial team, it will be considered a serious issue prompting an investigation with the possibility of retraction.

Research ethics committee approval

Authors must provide evidence of Research Ethics Committee approval of the research where relevant. Ensure the correct, full ethics committee name and reference number is included in the manuscript.

If the study was carried out using data from provincial healthcare facilities, or required active data collection through facility visits or staff interviews, approval should be sought from the relevant provincial authorities. For South African authors, please refer to the guidelines for submission to the [National Health Research Database](#). Research involving human subjects must be conducted according to the principles outlined in the Declaration of Helsinki. Please refer to the National Department of Health's guideline on [structures to](#) ensure that the appropriate requirements for conducting research have been met, and that the HPCSA's [Researchers have](#) been adhered to.

Clinical trials

As per the recommendations published by the International Committee of Medical Journal Editors (ICMJE), clinical trial research is any research that assigns individuals to an intervention, with or without a concurrent comparison/control group to study the cause-and-effect relationship between the intervention and health outcomes. All clinical trials should be registered with the appropriate national clinical trial registry (or any international primary register, if relevant), and the trial registration number should be cited at the end of the abstract. All clinical trial reports must also contain a data sharing statement as per the recommendations of the ICMJE. Statements are to indicate:

- whether individual deidentified participant data will be shared;
- what data in particular will be shared; whether additional, related documents will be available;
- when the data will become available and for how long; by what access criteria data will be shared.

Please see the ICJME announcement for further details and illustrative examples of data sharing statements: [ICMJE Data Sharing Statements for Clinical Trials](#)

Since 1st December 2005, all clinical trials conducted in South Africa have been required to be registered in the South African National Clinical Trials Register. The SAMJ therefore

requires that clinical trials be registered in the relevant public trials registry at or before the time of first patient enrolment as a condition for publication. The trial registry name and registration number must be included in the manuscript.

Please refer to the general guidelines for all papers at the top of this article for additional requirements with respect to ethics approval, funding, author contributions, etc. The format of original research articles should be followed for reporting of clinical trial results.

Protection of rights to privacy

Patient

Information that would enable identification of individual patients should not be published in written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) has given informed written consent for publication and distribution. We further recommend that the published article is disseminated not only to the involved researchers but also to the patients/participants from whom the data was drawn. Refer to [Protection of Research Participants](#). The signed consent form should be submitted with the manuscript to enable verification by the editorial team.

Other individuals

Any individual who is identifiable in an image must provide [written agreement](#) that the image may be used in that context in the SAMJ.

Copyright notice

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Material submitted for publication in the SAMJ is accepted provided it has not been published or submitted for publication elsewhere. Please inform the editorial team if the main findings of your paper have been presented at a conference and published in abstract form, to avoid copyright infringement. The SAMJ does not hold itself responsible for statements made by the authors.

Previously published images

If an image/figure has been previously published, permission to reproduce or alter it must be obtained by the authors from the original publisher and the figure legend must give full credit to the original source. This credit should be accompanied by a letter indicating that permission to reproduce the image has been granted to the author/s. This letter should be uploaded as a supplementary file during submission.

Privacy statement

The SAMJ is committed to protecting the privacy of its website and submission system users. The names, personal particulars and email addresses entered in the website or submission system will not be made available to third parties without the user's permission or due process. By registering to use the website or submission system, users consent to receive communication from the SAMJ or its publisher HMPG on matters relating to the journal or associated publications. Queries with regard to privacy may be directed to publishing@hmpg.co.za.

Ethnic/race classification

Use of racial or ethnicity classifications in research is fraught with problems. If you choose to use a research design that involves classification of participants based on race or ethnicity, or discuss issues with reference to such classifications, please ensure that you include a detailed rationale for doing so, ensure that the categories you describe are carefully defined, and that socioeconomic, cultural and lifestyle variables that may underlie perceived racial disparities are appropriately controlled for. Please also clearly specify whether race or ethnicity is classified as reported by the patient (self-identifying) or as perceived by the investigators. Please note that it is not appropriate to use self-reported or investigator-assigned racial or ethnic categories for genetic studies.

Continuing Professional Development (CPD)

SAMJ is an HPCSA-accredited service provider of CPD materials. Principal authors can earn up to 15 CPD continuing education units (CEUs) for publishing an article; co-authors are eligible to earn up to 5 CEUs; and reviewers of articles can earn 3 CEUs. Each month, SAMJ also publishes a CPD-accredited questionnaire relating to the academic content of the journal. Successful completion of the questionnaire with a pass rate of 70% will earn the reader 3 CEUs. Administration of our CPD programme is managed by Medical Practice Consulting. To complete questionnaires and obtain certificates, please visit [MRP Consulting](#)

Manuscript preparation

Preparing an article for anonymous review

To ensure a fair and unbiased review process, all submissions are to include an anonymised version of the manuscript. The exceptions to this are Correspondence, Book reviews and Obituary submissions.

Submitting a manuscript that needs additional blinding can slow down your review process, so please be sure to follow these simple guidelines as much as possible:

- An anonymous version should not contain any author, affiliation or particular institutional details that will enable identification.
- Please remove title page, acknowledgements, contact details, funding grants to a named person, and any running headers of author names.
- Mask self-citations by referring to your own work in third person.

General article format/layout

Accepted manuscripts that are not in the correct format specified in these guidelines will be returned to the author(s) for correction, which will delay publication.

General:

- Manuscripts must be written in UK English.
- The manuscript must be in Microsoft Word format. Text must be single-spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes).
- Please make your article concise, even if it is below the word limit.
- Qualifications, full affiliation (department, school/faculty, institution, city, country) and contact details of ALL authors must be provided in the manuscript and in the online submission process.
- Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.
- Include sections on Acknowledgements, Conflict of Interest, Author Contributions and Funding sources. If none is applicable, please state 'none'.
- Scientific measurements must be expressed in SI units except: blood pressure (mmHg) and haemoglobin (g/dL).
- Litres is denoted with an uppercase L e.g. 'mL' for millilitres).
- Units should be preceded by a space (except for % and °C), e.g. '40 kg' and '20 cm' but '50%' and '19°C'.
- Please be sure to insert proper symbols e.g. μ not u for micro, α not a for alpha, β not B for beta, etc.
- Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160.
- Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'
- Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.
- If you wish material to be in a box, simply indicate this in the text. You may use the table format –this is the only exception. Please DO NOT use fill, format lines and so on.

SAMJ is a generalist medical journal, therefore for articles covering genetics, it is the responsibility of authors to apply the following:

- Please ensure that all genes are in italics, and proteins/enzymes/hormones are not.

- Ensure that all genes are presented in the correct case e.g. TP53 not Tp53.

****NB:** Copyeditors cannot be expected to pick up and correct errors wrt the above, although they will raise queries where concerned.

- Define all genes, proteins and related shorthand terms at first mention, e.g. '188del11' can be glossed as 'an 11 bp deletion at nucleotide 188.'

- Use the latest approved gene or protein symbol as appropriate:

- Human Gene Mapping Workshop (HGMW): genetic notations and symbols
- HUGO Gene Nomenclature Committee: approved gene symbols and nomenclature
- OMIM: Online Mendelian Inheritance in Man (MIM) nomenclature and instructions
- Bennet et al. Standardized human pedigree nomenclature: Update and assessment of the recommendations of the National Society of Genetic Counselors. *J Genet Counsel* 2008;17:424-433: standard human pedigree nomenclature.

Preparation notes by article type

- Research
- Editorials
- CME
- In Practice and Case reports
- Reviews
- Clinical trials
- Correspondence
- Obituaries
- Book reviews
- Guidelines

Research

Guideline word limit: 4 000 words

Research articles describe the background, methods, results and conclusions of an original research study. The article should contain the following sections: introduction, methods, results, discussion and conclusion, and should include a structured abstract (see below). The introduction should be concise – no more than three paragraphs – on the background to the research question, and must include references to other relevant published studies that clearly

lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important clinical question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. Describe the study methods in as much detail as possible so that others would be able to replicate the study should they need to. Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section, which should consider primary outcomes first before any secondary or tertiary findings or post-hoc analyses. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

Select figures and tables for your paper carefully and sparingly. Use only those figures that provided added value to the paper, over and above what is written in the text.

Do not replicate data in tables and in text .

Structured abstract

- This should be 250-400 words, with the following recommended headings:
 - Background: why the study is being done and how it relates to other published work.
 - Objectives: what the study intends to find out
 - Methods: must include study design, number of participants, description of the intervention, primary and secondary outcomes, any specific analyses that were done on the data.
 - Results: first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.
 - Conclusion: must be supported by the data, include recommendations for further study/actions.
- Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors.
- Do not include any references in the abstracts.

Main article

All articles are to include the following main sections: Introduction/Background, Methods, Results, Discussion, Conclusions.

The following are additional heading or section options that may appear within these:

- Objectives (within Introduction/Background): a clear statement of the main aim of the study and the major hypothesis tested or research question posed
- Design (within Methods): including factors such as prospective, randomisation, blinding, placebo control, case control, crossover, criterion standards for diagnostic tests, etc.
- Setting (within Methods): level of care, e.g. primary, secondary, number of participating centres.
- Participants (instead of patients or subjects; within Methods): numbers entering and completing the study, sex, age and any other biological, behavioural, social or cultural factors (e.g. smoking status, socioeconomic group, educational attainment, co-existing disease indicators, etc) that may have an impact on the study results. Clearly define how participants were enrolled, and describe selection and exclusion criteria.
- Interventions (within Methods): what, how, when and for how long. Typically for randomised controlled trials, crossover trials, and before and after studies.
- Main outcome measures (within Methods): those as planned in the protocol, and those ultimately measured. Explain differences, if any.

Results

- Start with description of the population and sample. Include key characteristics of comparison groups.
- Main results with (for quantitative studies) 95% confidence intervals and, where appropriate, the exact level of statistical significance and the number need to treat/harm. Whenever possible, state absolute rather than relative risks.
- Do not replicate data in tables and in text.
- If presenting mean and standard deviations, specify this clearly. Our house style is to present this as follows:
- E.g.: The mean (SD) birth weight was 2 500 (1 210) g. Do not use the \pm symbol for mean (SD).
- Leave interpretation to the Discussion section. The Results section should just report the findings as per the Methods section.

Discussion

Please ensure that the discussion is concise and follows this overall structure – sub-headings are not needed:

- Statement of principal findings
- Strengths and weaknesses of the study
- Contribution to the body of knowledge
- Strengths and weaknesses in relation to other studies
- The meaning of the study – e.g. what this study means to clinicians and policymakers
- Unanswered questions and recommendations for future research

Conclusions

This may be the only section readers look at, therefore write it carefully. Include primary conclusions and their implications, suggesting areas for further research if appropriate. Do not go beyond the data in the article.

Editorials

Guideline word limit: 1 000 words

These opinion or comment articles are usually commissioned but we are happy to consider and peer review unsolicited editorials. Editorials should be accessible and interesting to readers without specialist knowledge of the subject under discussion and should have an element of topicality (why is a comment on this issue relevant now?) There should be a clear message to the piece, supported by evidence.

Please make clear the type of evidence that supports each key statement, e.g.:

- expert opinion
- personal clinical experience
- observational studies
- trials
- systematic reviews.

CME (by invite only)

CME is intended to provide readers with practical, up-to-date information on medical and related matters. It is aimed at those who are not specialists in the field.

From January 2016, all CME articles will be printed in full in the SAMJ. Please try to adhere strictly to the guidelines on word count as we have a page limit for the print issue of the SAMJ. We reserve the right to place some tables and reference lists online if this is necessary for space.

In practice, this means that each CME topic usually covers two issues of the print issue of the SAMJ.

The guest editor, in consultation with the editor, is responsible for convening a team of authors, deciding on the subjects to be covered and for reviewing the manuscripts submitted. The suggestion is for 4 - 5 articles, although there is some room for flexibility contingent on discussions with the editor.

For queries about these guidelines please feel free to contact the CME editor, Dr Bridget Farham, by email (ugqirha@iafrica.com) or telephone (+27 (0)21 789 2331).

Review process

The guest editor reviews the articles and returns them to the CME editor for review and final approval.

Guest editorials

Guideline word limit: 1 000 words

- Include the guest editor's personal details (qualifications, positions, affiliation, e-mail address, and a short personal profile (50words)).
- If possible, include a photograph of the author(s) at high enough resolution for print. It is preferable to provide two guest editorials, one for each issue, so that the content of the articles in each issue is covered.

Articles

Guideline word limit: 2 000 - 3 000 words

- Each article requires an abstract of ±200 words.
- The editor reserves the right to shorten articles but will send a substantially shortened article back for author approval.

Personal details

Please supply: Your qualifications, position and affiliations and MP number (used for CPD points); Address, telephone number and fax number, and your e-mail address; and a short personal profile (50words)and a few words about your current fields of interest.

In Practice

Guideline word limit: 2 000 - 3 000words

This section includes articles that would previously have been accepted into the Forum section, and case reports.

In practice articles are those that draw attention to specific issues of clinical, economic or political interest regarding medicine and healthcare in southern Africa. They are assigned to a topic:

- Case report
- Clinical practice
- Clinical alert
- Issues in medicine
- Issues in public health
- Healthcare delivery
- Consensus/Position statement
- Medicine and the environment
- Medicine and the law
- Cochrane corner

An In Practice article should follow the following format – sub-headings are not necessary, but may be used for clarity:

- Author affiliations and qualifications: to be the same as for Research. Provide all authors' names and initials, qualifications and full affiliations, and corresponding author.
- Short abstract: does not need to be structured, but should capture the essential features of the article
- Introduction: the reason for the article and the issue being addressed
- Recent research, discussion, local policy around the issue – include your own research where appropriate
- All statements should be referenced and, if opinion only, this should be stated
- Discussion: how this article adds to the discussion around a particular topic
- If a clinical practice or policy point is at issue, this needs to be emphasised, using a box with highlights if appropriate.

Essentially In practice is an opportunity for a more discursive approach to topics of clinical, economic or political importance in southern African health systems. It is not an opportunity to put forward unsubstantiated opinions!

Case reports

The SAMJ has recently started to accept case reports. The cases must come from Africa, preferably southern Africa unless the condition is common to all African countries, and must be either a completely new description of a clinical condition or result (use Google!) or a case that highlights important practice or management issues.

Please use the following format for case reports:

- Title of case: do not include the words 'a case report' in the title
- Summary/abstract: up to 150 words summarising the case presentation and outcome
- Background: why is this case important and why did you write it up?
- Case presentation: presenting features, medical, social, family history as appropriate
- Case management: should be according to best practice, and if not, please explain why
- Investigations, if relevant: save space by simply saying 'normal' if, for example, renal function was completely normal, rather than listing normal results, highlight the abnormal – or indeed the normal if this is clinically significant
- Differential diagnosis, if relevant

- Treatment, if relevant
- Outcome and follow-up
- Discussion – a VERY BRIEF review of similar published cases
- Teaching points: 3 - 5 bullet points
- References: as per the SAMJ house style
- Tables and figures: keep to a minimum. Use clinical images where relevant – we need hi-res versions for print, and identifiable persons must have a consent form
- Patient consent: please include a statement about patient consent to a written case report. This should be uploaded as a supplementary file.

Clinical trials

Guideline word limit: 4000 words

As per the recommendations published by the International Committee of Medical Journal Editors (ICMJE), clinical trial research is any research that assigns individuals to an intervention, with or without a concurrent comparison/control group to study the cause-and-effect relationship between the intervention and health outcomes. All clinical trials should be registered with the appropriate national clinical trial registry (or any international primary register, if relevant), and the trial registration number should be cited at the end of the abstract. Since 1st December 2005, all clinical trials conducted in South Africa have been required to be registered in the [South African National Clinical Trials Register](#). The SAMJ therefore requires that clinical trials be registered in the relevant public trials registry at or before the time of first patient enrollment as a condition for publication. The trial registry name and registration number must be included in the manuscript.

Please refer to the general guidelines for all papers at the top of this article for additional requirements with respect to ethics approval, funding, author contributions, etc. The format of original research articles should be followed for reporting of clinical trial results.

Review articles

Guideline word limit: 4 000 words

These are welcome, but should be either commissioned or discussed with the Editor before submission. A review article should provide a clear, up-to-date account of the topic and be aimed at non-specialist hospital doctors and general practitioners.

Please ensure that your article includes:

- Abstract: unstructured, of about 100-150 words, explaining the review and why it is important
- Methods: Outline the sources and selection methods, including search strategy and keywords used for identifying references from online bibliographic databases. Discuss the quality of evidence.
- When writing: clarify the evidence you used for key statements and the strength of the evidence. Do not present statements or opinions without such evidence, or if you have to, say that there is little or no evidence and that this is opinion. Avoid specialist jargon and abbreviations, and provide advice specific to southern Africa.
- Personal details: Please supply your qualifications, position and affiliations and MP number (used for CPD points); address, telephone number and fax number, and your e-mail address; and a short personal profile (50 words) and a few words about your current fields of interest.

Correspondence (Letters to the Editor)

Guideline word limit: 500 words

Letters to the editor should relate either to a paper or article published by the SAMJ or to a topical issue of particular relevance to the journal's readership

- May include only one illustration or table
- Must include a correspondence address.

Book reviews

Guideline word limit: 400 words

Should be about 400 words and must be accompanied by the publication details of the book. Provide a hi-res image of the cover if possible (with permission from the copyright holder).

Obituaries

Guideline word limit: 400 words

Should be offered within the first year of the practitioner's death, and may be accompanied by a photograph.

Guidelines

Guidelines should always be discussed with the Editor prior to submission.

Because of the intensive review process required to ensure Guidelines are independent, evidence-based and free from commercial bias, they are usually published as a supplement to the SAMJ, the costs of which must be covered by sponsorship, advertising or payment by the guideline authors/association. We will provide a quote based on the expected length of the guideline and whether it is to appear online only, or in print, which must be accepted by the body putting the guidelines together before submitting the work to the SAMJ.

The Editor reserves the right to determine the scheduling of supplements. Understandably, a delay in publication must be anticipated dependent upon editorial workflow.

All guidelines should include a clear, transparent statement about all sources of funding and an explicit, clear statement of conflicts of interest of any of the participants in the guidelines about industry funding for lectures, research, conference participation etc.

All guidelines should be structured according to [Agree II](#).

Please access this website before putting the guidelines together, download the Agree 11 instrument and use this to put the guidelines together.

All submitted guidelines will be sent to the local Agree II appraisal committee for review and must be endorsed by an appropriate body prior to consideration and all conflicts of interest expressed.

A structured abstract not exceeding 400 words (recommended sub-headings: Background, Recommendations, Conclusion) is required. Sections and sub-sections must be numbered consecutively (e.g. 1. Introduction; 1.1 Definitions; 2.etc.) and summarised in a Table of Contents.

Illustrations/photos/scans

- If illustrations submitted have been published elsewhere, the author(s) should provide consent to republication obtained from the copyright holder.
- Figures must be numbered in Arabic numerals and referred to in the text e.g. '(Fig. 1)'.
• Each figure must have a caption/legend: Fig. 1. Description (any abbreviations in full).
- All images must be of high enough resolution/quality for print.
- All illustrations (graphs, diagrams, charts, etc.) must be in PDF or jpeg form.
- Ensure all graph axes are labelled appropriately, with a heading/description and units (as necessary) indicated. Do not include decimal places if not necessary e.g. 0; 1.0; 2.0; 3.0; 4.0 etc.
- Scans/photos showing a specific feature e.g. Intermediate magnification micrograph of a low malignant potential (LMP) mucinous ovarian tumour. (H&E stain). –include an arrow to show the tumour.
- Each image must be attached individually as a 'supplementary file' upon submission (not solely embedded in the accompanying manuscript) and named Fig. 1, Fig. 2, etc.

Tables

- Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged.
- Large tables will generally not be accepted for publication in their entirety. Please consider shortening and using the text to highlight specific important sections, or offer a large table as an addendum to the publication, but available in full on request from the author
- Embed/include each table in the manuscript Word file - do not provide separately as supplementary files.
- Number each table in Arabic numerals (Table 1, Table 2, etc.) and refer to consecutively in the text.
- Tables must be cell-based (i.e. not constructed with text boxes or tabs) and editable.
- Ensure each table has a concise title and column headings, and include units where necessary.
- Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

Do not: Use [Enter] within a row to make 'new rows':

Rather:

Each row of data must have its own proper row:

Do not: use separate columns for n and %:

Rather:

Combine into one column, n (%):

Do not: have overlapping categories, e.g.:

Rather:

Use <> symbols or numbers that don't overlap:

References

NB: Only complete, correctly formatted reference lists in Vancouver style will be accepted. Reference lists must be generated manually and not with the use of reference manager software. Endnotes must not be used.

- Authors must verify references from original sources.
- Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization,^[2] and others.^[3,4-6]
- All references should be listed at the end of the article in numerical order of appearance in the Vancouver style (not alphabetical order).
- Approved abbreviations of journal titles must be used; see the [List of Journals in Index Medicus](#).
- Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al.

- Volume and issue numbers should be given.
- First and last page, in full, should be given e.g.: 1215-1217 not 1215-17.
- Wherever possible, references must be accompanied by a digital object identifier (DOI) link). Authors are encouraged to use the DOI lookup service offered by [CrossRef](#):
 - On the Crossref homepage, paste the article title into the 'Metadata search' box.
 - Look for the correct, matching article in the list of results.
 - Click Actions > Cite
 - Alongside 'url =' copy the URL between { }.
 - Provide as follows, e.g.: <https://doi.org/10.7196/07294.937.98x>

Some examples:

- Journal references: Price NC, Jacobs NN, Roberts DA, et al. Importance of asking about glaucoma. *Stat Med* 1998;289(1):350-355. <http://dx.doi.org/10.1000/hgjr.182>
- Book references: Jeffcoate N. *Principles of Gynaecology*. 4th ed. London: Butterworth, 1975:96-101.
- Chapter/section in a book: Weinstein L, Swartz MN. Pathogenic Properties of Invading Microorganisms. In: Sodeman WA, Sodeman WA, eds. *Pathologic Physiology: Mechanisms of Disease*. Philadelphia: WB Saunders, 1974:457-472.
- Internet references: World Health Organization. *The World Health Report 2002 - Reducing Risks, Promoting Healthy Life*. Geneva: WHO, 2002. <http://www.who.int/whr/2002> (accessed 16 January 2010).
- Legal references
 - Government Gazettes:

National Department of Health, South Africa. National Policy for Health Act, 1990 (Act No. 116 of 1990). Free primary health care services. *Government Gazette No. 17507:1514*. 1996.

In this example, 17507 is the Gazette Number. This is followed by :1514 - this is the notice number in this Gazette.

- Provincial Gazettes:

Gauteng Province, South Africa; Department of Agriculture, Conservation, Environment and Land Affairs. Publication of the Gauteng health care waste management draft regulations. *Gauteng Provincial Gazette No. 373:3003*, 2003.

- Acts:

South Africa. National Health Act No. 61 of 2003.

- Regulations to an Act:

South Africa. National Health Act of 2003. Regulations: Rendering of clinical forensic medicine services. Government Gazette No. 35099, 2012. (Published under Government Notice R176).

- Bills:

South Africa. Traditional Health Practitioners Bill, No. B66B-2003, 2006.

- Green/white papers:

South Africa. Department of Health Green Paper: National Health Insurance in South Africa. 2011.

- Case law:

Rex v Jopp and Another 1949 (4) SA 11 (N)

Rex v Jopp and Another: Name of the parties concerned

1949: Date of decision (or when the case was heard)

(4): Volume number

SA: SA Law Reports

11: Page or section number

(N): In this case Natal - where the case was heard. Similarly, (C) would indicate Cape, (G) Gauteng, and so on.

NOTE: no . after the v

- Other references (e.g. reports) should follow the same format: Author(s). Title. Publisher place: Publisher name, year; pages.
- Cited manuscripts that have been accepted but not yet published can be included as references followed by '(in press)'.
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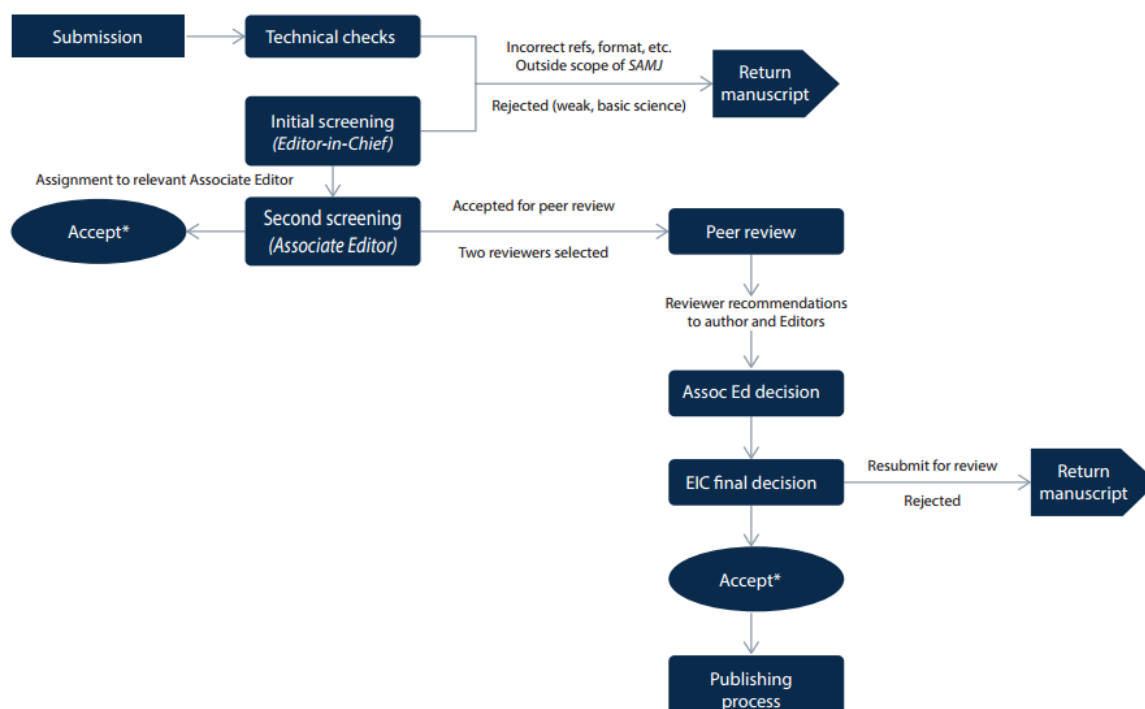
From submission to acceptance

Submission and peer-review

To submit an article:

- Please ensure that you have prepared your manuscript in line with the SAMJ requirements.
- All submissions should be submitted via [Editorial Manager](#)
- The following are required for your submission to be complete:
 - Anonymous manuscript (unless otherwise stated)
 - [Author Agreement form](#)
 - Manuscript
 - Any supplementary files: figures, datasets, patient consent form, permissions for published images, etc.
- Once the submission has been successfully processed on Editorial Manager, it will undergo a technical check by the Editorial Office before it will be assigned to an editor who will handle the review process. If the author guidelines have not been appropriately followed, the manuscript may be sent back to the author for correcting.

Peer-review process



*Manuscripts accepted at this point are limited to Editorials, Correspondence, Obituaries, Book reviews, Abstracts, CME
**Some minor revisions may be requested

Production process

The following process will follow:

1. An accepted manuscript is passed to a Managing Editor to assign to a copyeditor (CE).
2. The CE copyedits in Word, working on house style, format, spelling/grammar/punctuation, sense and consistency, and preparation for typesetting.
3. If the CE has an author queries, he/she will contact the corresponding author and send them the copyedited Word doc, asking them to solve the queries by means of track changes or comment boxes.
4. The authors are typically asked to respond within 1-3 days. Any comments/changes must be clearly indicated e.g. by means of track changes. Do not work in the original manuscript - work in the copyedited file sent to you and make your changes clear.
5. The CE will finalise the article and then it will be typeset.
6. Once typeset, the CE will send a PDF of the file to the authors to complete their final check, while simultaneously sending to the 2nd-eye proofreader.
7. The authors are typically asked to complete their final check and sign-off within 1-2 days. No major additional changes can be accommodated at this point.
8. The CE implements the authors' and proofreader's mark-ups, finalises the file, and prepares it for the upcoming issue.

Changing contact details or authorship

Please notify the Editorial Department of any contact detail changes, including email, to facilitate communication.

Publication

Online v. print

The SAMJ is an online journal. The online version of the journal is the one that has the widest circulation, is indexed by bibliographic databases including PubMed and SciELO, and is accessible in academic libraries. A printed edition, containing material selected by the Editor

is also published each month and distributed to the membership of the South African Medical Association.

Online

- The full text of all accepted articles is published in full online, open access.
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- You may want to make use of the advantages of online publication e.g. specify web links to other sources, images, data or even a short video.

Print

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Errata and retractions

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We will investigate the issue and provide feedback. If appropriate, we will correct the web version immediately, and will publish an erratum in the next issue. The correction will be indexed, as PubMed has a function for linking errata back to the original article. All investigations will be conducted in accordance with guidelines provided by the Committee on Publication Ethics ([COPE](#)).

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- Index Medicus (Medline/PubMed)
- ExcerptaMedica (EMBASE)
- Biological Abstracts (BIOSIS)
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5. Illustrations/figures are high resolution/quality (not compressed) and in an acceptable format (PDF or jpeg). These must be submitted individually as 'supplementary files' (not solely embedded in the manuscript).
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7. Where possible, references are accompanied by a digital object identifier (DOI).
8. An abstract has been included where applicable.
9. The research was approved by a Research Ethics Committee (if applicable)
10. Any conflict of interest (or competing interests) is indicated by the author(s).

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Contact Information

Candidate:

Dr Reuben Nathanael Smith

c/o Department of Anaesthesia & Perioperative Medicine

University of Cape Town

Floor D23

Groote Schuur Hospital

Main Road

Observatory

Cape Town

7935

SOUTH AFRICA

Telephone: +27 21 404 5003

Email: reubensmith@hotmail.co.za

Supervisor:

Associate Professor Ross Hofmeyr

Address as above

Telephone: +27 21 404 5003

Email: ross.hofmeyr@uct.ac.za

Departmental Research Chair:

Professor Bruce Biccard

Address as above

Telephone: +27 21 404 5015

Email: bruce.biccard@uct.ac.za

UCT Human Research Ethics Committee:

Faculty of Health Sciences

Human Research Ethics Committee

Room E53-46

Old Main Building

Groote Schuur Hospital

Observatory

7935

SOUTH AFRICA

Telephone: +27 21 406 6492

Email: shuretta.thomas@uct.ac.za

Website: <http://www.health.uct.ac.za/fhs/research/humanethics/about>