



# Postoperative outcomes associated with surgical care for women in Africa: An international risk-adjusted analysis

Amy Frances Paterson

[amyfrancespaterson@gmail.com](mailto:amyfrancespaterson@gmail.com)

072 248 3360

PTRAMY003

University of Cape Town  
MSc Medicine in Global Surgery dissertation  
Submitted: September 2021, Revised: January 2022

The copyright of this thesis vests in the author. No quotation from it or information derived from it is to be published without full acknowledgement of the source. The thesis is to be used for private study or non-commercial research purposes only.

Published by the University of Cape Town (UCT) in terms of the non-exclusive license granted to UCT by the author.

## Declaration

I, Amy Frances Paterson, 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. This work has not been reported or published prior to registration for the abovementioned degree.

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

Signed by candidate

Amy Paterson (candidate)

Date: 17 August 2021

## Acknowledgements, Format and Contributions

This thesis is submitted in published/publication-ready format. It is submitted as two manuscripts relating to the same topic. The first (Chapter One) is an editorial piece that has been accepted for publication by the South African Journal of Obstetrics and Gynaecology and is intended as an introduction to the topic of non-obstetric surgical outcomes for women. The second manuscript (Chapter Two) is a sub-study/secondary analysis of the non-obstetric, non-gynaecological female data from the African Surgical Outcomes Study and the International Surgical Outcomes Study. This second manuscript is submitted in publication-ready format according to The Lancet Global Health's instructions for authors.

As the candidate, I wrote the first drafts of both the Chapter One editorial/perspective piece and the Chapter Two research paper and then edited the drafts according to input from all co-authors. I am the first author of both papers.

My supervisors, Professor Salome Maswime and Professor Bruce Biccard, assisted with the research project's design and planning as well as critical review and editing of both manuscripts. They are co-authors of both the accepted manuscript (Chapter One) and the prepared manuscript (Chapter Two).

Professor Biccard assisted with accessing the African Surgical Outcomes Study (ASOS) data and doing the data analysis in Statistical Package for the Social Sciences (SPSS).

Anneli Hardy is a statistical consultant for the University of Cape Town's Department of Statistical Sciences and advised on statistical analysis methods, reviewed the statistical outcomes with me and ran the data analyses that required STATA. Anneli Hardy is a co-author of the research paper in Chapter Two.

Professor Rupert Pearse assisted with gaining access to the relevant International Surgical Outcomes Study (ISOS) data and reviewed the research manuscript in Chapter Two. Professor Pearse is a co-author of the Chapter Two manuscript.

Professor Lydia Cairncross and Dr Tracey Adams are co-authors of the perspective piece in Chapter One and offered critical review of the manuscript.

I also wish to acknowledge the local investigators and original authors of both the African Surgical Outcomes Study and International Surgical Outcomes Study which this dissertation is a sub-study of. Their details can be found on [clinicaltrials.gov](http://clinicaltrials.gov) as well on the studies' respective websites [asos.org.za](http://asos.org.za) and [isos.org.uk](http://isos.org.uk).

## Table of Contents

|  |    |
|--|----|
| Declaration .....                                    | 1  |
| Acknowledgements, Format and Contributions .....     | 2  |
| List of Appendices .....                             | 4  |
| List of Tables .....                                 | 4  |
| List of Figures .....                                | 4  |
| Abbreviations.....                                   | 5  |
| Abstract.....  | 6  |
| Chapter One: Introduction (accepted editorial) ..... | 7  |
| Chapter Two: Publication-ready Manuscript .....      | 12 |
| Research in context .....                            | 12 |
| Introduction .....                                   | 13 |
| Methods.....   | 14 |
| Results.....   | 16 |
| Discussion .....                                     | 23 |
| References .....                                     | 25 |
| Appendices/Supplementary Material.....               | 27 |

## List of Appendices

**Appendix 1:** Supplementary tables

**Appendix 2:** African Surgical Outcomes Study (ASOS) Case Record Form

**Appendix 3:** International Surgical Outcomes Study (ISOS) Case Record Form

**Appendix 4:** Patient outcomes definition guide for the African Surgical Outcomes Study

**Appendix 5:** Ethics approval letter from the University of Cape Town's Human Research Ethics Committee

**Appendix 6:** STROBE checklist for cohort studies

**Appendix 7:** Letter of acceptance of editorial from SAJOG

**Appendix 8:** The Lancet Global Health Instructions for Authors

## List of Tables

**Table 1.** Characteristics of cohorts

**Table 2.** Complications

**Table 3.** Risk adjusted analysis of risk factors associated with severe postoperative complications in women undergoing non-obstetric, non-gynaecological surgery

**Supplementary Table 1.** Comparison of African Surgical Outcomes Study (ASOS) and International Surgical Outcomes Surgery (ISOS) methods, setting and participants

**Supplementary Table 2.** Surgical Outcomes for African Surgical Outcomes Study (ASOS) and International Surgical Outcomes Surgery (ISOS) cohort

**Supplementary Table 3.** Two-way ANOVA of age and surgical procedure

**Supplementary Table 4.** Sensitivity analysis with baseline haemoglobin

## List of Figures

**Figure 1.** African Surgical Outcomes Study (ASOS) cohort: recruitment and exclusion strategy

**Figure 2.** International Surgical Outcomes Study (ASOS) cohort: recruitment and exclusion strategy

## Abbreviations

aOR: adjusted odds ratio

ARDS: acute respiratory distress syndrome

ASA: American Society of Anesthesiologists

ASOS: African Surgical Outcomes Study

CI: Confidence interval

COPD: chronic obstructive pulmonary disease

COVID-19: Corona virus disease of 2019

DF: degrees of freedom

GIT: gastrointestinal tract

HICs: high-income countries

HREC: Human Research Ethics Committee

IQR: interquartile range

ISOS: International Surgical Outcomes Study

LMICs: low- and middle-income countries

NR: not reported

SAJOG: South African Journal of Obstetrics and Gynaecology

SPSS: Statistical Package for the Social Sciences

VIFs: variance inflation factors

WHO: World Health Organization

## Abstract

### **Background**

There is an increasing call for a broader approach to women's surgical care in low- and middle-income countries, beyond access to caesarean section. While obstetric outcomes in Africa are well described, outcomes following non-obstetric surgical care for women in Africa are relatively unknown.

### **Methods**

We did a secondary analysis of the African Surgical Outcomes Study (ASOS) focusing on severe postoperative complications (defined as death and severe complications) in females following non-obstetric, non-gynaecological surgical procedures. ASOS was a seven-day, African multi-centre prospective observational cohort study of adult ( $\geq 18$  years) patients undergoing surgery in 25 African countries. These African outcomes were compared to international outcomes from the International Surgical Outcomes Study (ISOS) in a risk-adjusted logistic regression analysis.

### **Findings**

There were 1498 African participants and 18449 international participants who met the inclusion criteria. The African cohort were younger than the international cohort of women (47 (17) years versus 57 (17);  $p < 0.0001$ ) and had a lower preoperative risk profile. Severe complications occurred in 41 (2.8%) of 1471 patients of the African cohort, and 431 (2.3%) of 18449 patients in the ISOS cohort, with in-hospital mortality following severe complications of 20/41 (48.8%) in ASOS and 78/431 (18.1%) in ISOS. The adjusted odds ratio for a woman in Africa developing a severe postoperative complication following elective non-obstetric, non-gynaecological surgery compared to the international incidence was 2.114 (95% CI 1.468 – 3.042,  $p < 0.0001$ ).

### **Interpretation**

Women living in Africa have double the odds of severe postoperative complications following elective non-obstetric, non-gynaecological surgery compared to international incidences.

### **Funding**

None

**Word count: 249**

## Chapter One: Introduction (accepted editorial)

*This introduction is in the format of an editorial/perspective piece accepted for publication by the South African Journal of Obstetrics and Gynaecology (SAJOG) that was written as an introduction to the topic of research in Chapter Two. Official correspondence from the journal regarding acceptance of the manuscript for publication can be found in the appendices (Appendix 7).*

### **Improving Surgical and Medical Outcomes, beyond Maternal Mortality Paterson A, Cairncross L, Adams T, Biccard BM, Maswime S**

Significant progress has been made in reducing the number of women who die from complications of childbirth globally, but the lack of timely and safe essential surgery and medical care continues to impact the ability of women to participate fully in their economies and communities. The emerging discipline of global surgery provides an opportunity to establish an agenda for women's health that is comprehensive, addresses inequity, and recognises the role of women in society.

As health systems attempt to address the estimated 28 million operations that have been cancelled or postponed globally owing to the COVID-19 pandemic<sup>1</sup>, we argue that non-obstetric surgical and adjuvant care and the outcomes of these interventions for women in Africa deserve consideration. This is a focus that is long overdue.

Women in Africa warrant special attention in the realm of global surgery because, firstly, as women, they are affected by both a high burden of sex-specific surgical diseases and gender-specific barriers in accessing care. Secondly, and equally importantly, women in Africa are part of a high-impact population group due to their central roles in family and community well-being, healthcare provision and substantial – albeit under-recognised – contributions to macroeconomic development.<sup>2</sup> The Lancet Commission on Women and Health<sup>2</sup> argues that women's health is not only a goal in itself but also a key strategy for sustainable societal advancement. This is particularly true in many low- and middle-income countries (LMICs) as urbanisation and shifts in family structure require women to take on responsibility as breadwinners while maintaining traditional household and caregiving responsibilities.<sup>3,4</sup>

Through global health initiatives, governments and multinational organisations, a global focus has been placed on obstetric outcomes. This focus has supported the significant work of the maternal health community in highlighting and addressing emergency obstetric surgical care in Africa, which is critical in its own regard and instrumental in bringing about broader change.<sup>5,6</sup> While there remains much work to be done, with the maternal mortality rate after caesarean delivery in Africa 50 times higher than that of high-income countries (HICs),<sup>6</sup> the focus on maternal mortality and introduction of careful auditing processes have held leaders in the health system accountable for these outcomes. This has resulted in improved funding for the necessary interventions as well as more rapid and effective policy change. This focus should be a catalyst for further focus on women's surgical and medical care for conditions such as breast and cervical cancer which continue to affect women, and their capacity to be caregivers and productive society members beyond the 42 days following childbirth.

Each year premature death from gynaecological and breast cancers is a largely preventable tragedy for over one million women and families globally.<sup>7</sup> In HICs, there is significant advocacy and funding for research and treatment of these cancers, but in many African countries and other LMICs, these diseases receive far less attention.<sup>8</sup> The resulting substantial disability and death, often in the prime of a woman's life, and subsequent disruption of family life, loss to the national economy and exacerbation of the poverty cycle, has historically been ignored.<sup>8</sup>

In 2018, the World Health Organisation called for the elimination of cervical cancer globally.<sup>9</sup> Theoretically this is possible, yet we are a far cry away from achieving it. Cervical cancer remains the leading cause of cancer-related death in women in Africa.<sup>10</sup> More than 311 000 deaths from the disease occurred in 2018.<sup>10</sup> More women therefore died from cervical cancer alone than from complications of pregnancy or childbirth (295 000 maternal deaths at the end of 2017).<sup>8,11</sup>

Around 87% of women who die from cervical cancer live in LMICs.<sup>8</sup> Although effective interventions exist to reduce this stark inequity, most women have limited opportunities to access these life-saving interventions.<sup>8</sup> In many resource-poor regions, implementation of human papillomavirus vaccination is limited, as is access to early detection programmes and treatment of premalignant lesions.

While an increase in cervical cancer screening is urgently needed, a matched increase in capacity for treatment is equally required.<sup>8</sup> Early-stage cervical cancer can be surgically managed with a five-year survival rate of more than 80%.<sup>12</sup> Chemoradiation is the standard of care for locally advanced disease, whereas chemotherapy is used in the palliative setting. Surgery, radiotherapy and chemotherapy have been recognised by the World Health Organization (WHO) as cost-effective, high-impact interventions for the treatment of early-stage cervical cancer as well as for more advanced stages of the disease.<sup>9</sup> However, in some LMICs less than 5% of these cervical cancer patients have access to safe, effective and timely cancer surgery.<sup>13</sup> There is a dearth of data regarding access to radio- and chemotherapy in LMICs but it is believed to be similarly limited.<sup>8</sup> Improving access to these life-saving modalities, as well as health intelligence systems, therefore requires significant political action and investment. Given the high mortality rate in LMICs, palliative care also needs to be upscaled and integrated into treatment plans.

Just over half of all breast cancer cases occur in LMICs.<sup>14</sup> Age-standardised mortality rates in parts of Africa are among the highest in the world due to a younger average age at diagnosis, detection at later stages of the disease and difficulties in accessing treatment.<sup>15</sup>

There are stark disparities in breast and cervical cancer survivorship between HICs and LMICs, with the 5-year net survival rate varying by up to 30% between regions.<sup>8</sup> This should be of international concern. Where a woman lives, and her socioeconomic status should not mean the difference between life and death.<sup>8</sup>

Alongside the burden of untreated cancer, the health landscape for women is still worrisome in many other ways.<sup>16</sup> Some 200 million women have no access to modern contraception.<sup>16</sup> An estimated 25 million women have unsafe abortions every year.<sup>16</sup> One in three women experience sexual violence.<sup>16</sup> These issues impact dramatically on the surgical burden of disease and disempowerment of women.

Up to 100 000 women develop obstetric fistulae every year<sup>17</sup> with only 15 000 receiving surgical treatment.<sup>18</sup> This lack of surgery creates cohorts of women who are socially stigmatised to the point of isolation and simultaneously unable to live independently. Likewise, early pregnancy loss and infertility often have long-term emotional and social impacts on women.<sup>19</sup> The maternal health community have emphasised that, while mortality is a major indicator used to monitor health, morbidity also has a significant impact on patients' lives and is often under-recorded and under-recognised.<sup>20</sup> The conceptual framework defined for including 'near miss' morbidities when considering obstetric outcomes needs to be carried over into non-obstetric surgical care.

Despite being neglected, the linkages between access to essential surgical and medical care and gender equity are clear. While surgery was once regarded as an expensive and advanced intervention, the global surgery and maternal health communities have led the charge in proving that surgery is a crucial and cost-effective component of a responsive and resilient health system.<sup>21</sup> As we mitigate the impact of the Covid-19 pandemic on maternal health and surgical care, special attention in the form of accurate auditing, accountability from governments and healthcare leaders, increased investment and effective policy change needs to be given to comprehensive surgical and medical care for women in Africa.

**Word count:** 1169

**Acknowledgement:**

The Global Surgery fellowship programme is funded by the South African Medical Research Council's Midcareer Scientist Grant.

**Contributors:**

The first draft was written by AP.

LC, TA, SM and BMB critically reviewed the paper. Editing was done by all authors.

**Conflicts of interest:**

The authors have no conflicts of interest to declare.

**References:**

1. COVIDSurg collaborative. Elective surgery cancellations due to the COVID-19 pandemic: global predictive modelling to inform surgical recovery plans. *Br J Surg* 2020; 107:1440–49. <https://doi.org/10.1002/bjs.11746>
2. Langer A, Meleis A, Knaul FM, Atun R, Aran M, Arreola-Ornelas H, et al. Women and Health: The key for sustainable development. *Lancet* 2015;386(9999):1165–210. [https://doi.org/10.1016/S0140-6736\(15\)60497-4](https://doi.org/10.1016/S0140-6736(15)60497-4)
3. Horton R, Ceschia A. Making women count. *Lancet* 2015;386(9999):1112–4. [https://doi.org/10.1016/S0140-6736\(15\)60964-3](https://doi.org/10.1016/S0140-6736(15)60964-3)
4. Lundgren R, Burgess S, Chantelois H, Oregede S, Kerner B, Kågesten A. Processing gender: lived experiences of reproducing and transforming gender norms over the life course of young

- people in Northern Uganda. *Cult Health Sex* 2019;21(4):387–403. <https://doi.org/10.1080/13691058.2018.1471160>
5. Alkema L, Chou D, Hogan D, Zhang S, Moller A, Gemmill A, et al. Global, regional, and national levels and trends in maternal mortality between 1990 and 2015, with scenario-based projections to 2030: A systematic analysis by the UN Maternal Mortality Estimation Inter-Agency Group. *Lancet* 2016;387(10017):462–74. [https://doi.org/10.1016/S0140-6736\(15\)00838-7](https://doi.org/10.1016/S0140-6736(15)00838-7)
  6. Bishop D, Dyer R, Maswime S, Rodseth R, Van Dyk D, Kluyts H, et al. Maternal and neonatal outcomes after caesarean delivery in the African Surgical Outcomes Study: a 7-day prospective observational cohort study. *Lancet Glob Health* 2019;7(4):513–22. [https://doi.org/10.1016/S2214-109X\(19\)30036-1](https://doi.org/10.1016/S2214-109X(19)30036-1)
  7. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018;68(6):394–424. <https://doi.org/10.3322/caac.21492>
  8. Ginsburg O, Bray F, Coleman M, Vanderpuye V, Eniu A, Kotha S, et al. The global burden of women’s cancers: a grand challenge in global health. *Lancet* 2017;389(10071):847–60. [https://doi.org/10.1016/S0140-6736\(16\)31392-7](https://doi.org/10.1016/S0140-6736(16)31392-7)
  9. World Health Organization. Draft: Global strategy towards eliminating cervical cancer as a public health problem [pdf]. April 2020. Available from: <https://www.who.int/publications/m/item/draft-global-strategy-towards-eliminating-cervical-cancer-as-a-public-health-problem> [Accessed 7 March 2021]
  10. Arbyn M, Weiderpass E, Bruni L, De Sanjosé S, Saraiya M, Ferlay J, et al. Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. *Lancet Glob Health* 2020;8(2):191–203. [https://doi.org/10.1016/S2214-109X\(19\)30482-6](https://doi.org/10.1016/S2214-109X(19)30482-6)
  11. Trends in maternal mortality: 2000 to 2017: estimates by WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division. Geneva: World Health Organization; 2019. [https://www.unfpa.org/sites/default/files/pub-pdf/Maternal\\_mortality\\_report.pdf](https://www.unfpa.org/sites/default/files/pub-pdf/Maternal_mortality_report.pdf) [Accessed 9 December 2021]
  12. Cancer.Net. Cervical cancer: statistics. January 2021. Available from: <https://www.cancer.net/cancer-types/cervical-cancer/statistics> [Accessed 13 April 2021]
  13. Chinula L, Hicks M, Chiudzu G, Tang J, et al. A tailored approach to building specialized surgical oncology capacity: Early experiences and outcomes in Malawi. *Gynecol Oncol Rep*. 2018;26:60-65
  14. Youlden D, Cramb S, Yip CH, Baade P. Incidence and mortality of female breast cancer in the Asia-Pacific region. *Cancer Biol Med* 2014;11(2):101–15. doi: 10.7497/j.issn.2095-3941.2014.02.005
  15. Azubuike SO, Muirhead C, Hayes L, McNally R. Rising global burden of breast cancer: The case of sub-Saharan Africa (with emphasis on Nigeria) and implications for regional

- development: A review. *World J Surg Onc* 2018;16. <https://doi.org/10.1186/s12957-018-1345-2>
16. Starrs A. A Lancet Commission on sexual and reproductive health and rights: going beyond the Sustainable Development Goals. *Lancet* 2015;386(9999):1111–2. [https://doi.org/10.1016/S0140-6736\(15\)00250-0](https://doi.org/10.1016/S0140-6736(15)00250-0)
  17. Lewis G, De Bernis L, editors. *Obstetric Fistula: Guiding Principles for Clinical Management and Programme Development Documents*. [pdf]. World Health Organization. 2006;81. Available from: <https://apps.who.int/iris/handle/10665/43343> [Accessed 7 March 2021]
  18. Letchworth P, MacLaren E, Duffy S. Obstetric fistula: a paradigm shift is needed in research and prevention. *BJOG* 2018;125;925–8. <https://doi.org/10.1111/1471-0528.15110>
  19. Farren J, Mitchell-Jones N, Verbakel J, Timmerman D, Jalnbrand M, Bourne T. The psychological impact of early pregnancy loss. *Hum Reprod Update* 2018;24(6):731–49. <https://doi.org/10.1093/humupd/dmy025>
  20. Geller S. Defining a conceptual framework for near-miss maternal morbidity. *J Am Med Womens Assoc* 2002;57(3):135–9.
  21. Meara JG, Leather AJM, Hagander L, Alkire BC, Alonso N, Ameh EA, et al. Global Surgery 2030: Evidence and solutions for achieving health, welfare, and economic development. *Lancet* 2015;386:569–624. [https://doi.org/10.1016/S0140-6736\(15\)60160-X](https://doi.org/10.1016/S0140-6736(15)60160-X)

## Chapter Two: Publication-ready Manuscript

*This manuscript has been prepared to submit to The Lancet Global Health for publication. The Instructions for Authors can be found as in Appendix 8.*

### **Postoperative outcomes associated with surgical care for women in Africa: An international risk-adjusted analysis**

**Paterson A, Maswime S, Hardy A, Pearse RM, Biccard BM**

#### Research in context

##### *Evidence before this study*

Improving women's surgical care is a global health priority. While there is a need to increase access to surgical care for women in African countries, it is important that this surgery is safe and excess postoperative complications and deaths are prevented.

A prospective cohort study by the International Surgical Outcomes Study (ISOS) group in 27 low-, middle- and high-income countries showed that poor patient outcomes are common after elective inpatient surgery. This study design was replicated in 25 African countries by the African Surgical Outcomes Study (ASOS) group, which found that despite a low-risk profile and few postoperative complications, patients in Africa had a higher postoperative mortality rate than the global average. A sub-study of ASOS found that women in Africa were more likely to die following caesarean section. The morbidity and mortality for women undergoing non-obstetric surgery in Africa is, however, unknown.

We searched the published literature between 2010 and 2021 using Medline and the Cochrane library in May 2020 and again in August 2021 with the search terms “women” OR “female” AND “surgical” OR “procedural” OR “operative” AND “outcomes” AND “Africa”. 137 Medline articles and 1417 Cochrane reviews were found which reported outcomes for specific procedures and specific regions of Africa, however on abstract screening none of these articles were found to give an overview of non-obstetric surgical outcomes for women in Africa.

Our review of the literature suggests that research specifically into women's surgical outcomes in Africa has predominantly highlighted the high preventable mortality related to caesarean sections. While there is an increasing adoption of a comprehensive approach to women's health and surgical care in the literature, the non-obstetric surgical outcomes for women in Africa remain relatively unknown, with the data available being limited to specific regions and conditions.

##### *Added value of this study*

This study describes the outcomes associated with non-obstetric, non-gynaecological surgery for women in Africa compared to an appropriate international cohort. The risk adjusted outcomes suggest that women living in Africa have double the odds of having a severe postoperative complication or death following non-obstetric, non-gynaecological elective surgery compared to international complication rates. We also found that women in Africa

have a higher rate of failure to rescue (complications resulting in mortality) compared to the overall African cohort, at nearly threefold international comparators.

### *Implications of all the available evidence*

The significantly increased risk adjusted odds of having a severe postoperative complication for women in Africa may highlight health system weaknesses, such as surgical infrastructure and workforce, that need to be addressed in Africa. The higher failure to rescue rate for women in Africa may highlight gender inequality in postoperative treatment in Africa. Due to the central role women play in family and community well-being, healthcare provision and macroeconomic development, this difference in surgical outcomes is likely to have a significant impact on the affected communities. While this study offers a broad overview to motivate for safer holistic surgical care for women in Africa, it also identifies the need for more region-specific and condition-specific research into surgical outcomes for women in Africa.

## Introduction

### *Background/rationale*

Improving women's health is a critical component of the sustainable development goals.<sup>1</sup> This is particularly true in many low- and middle-income countries (LMICs) where urbanisation and shifts in family structure are increasingly requiring women to become breadwinners, while maintaining traditional household and caregiving responsibilities.<sup>2,3</sup> Over the last two decades a large proportion of the global focus on women's health has appropriately been placed on obstetric outcomes.<sup>4,5</sup> Research into women's surgical care has predominantly highlighted the high preventable mortality related to caesarean sections in LMICs.<sup>4,5</sup>

While improving obstetric outcomes remains a key priority in global health, increasingly there is a revealed need for a broader approach to women's surgical care, beyond access to caesarean section.<sup>1,3,6-8</sup> In order to move towards equitable surgical health for women, the current quality of non-obstetric surgical care for women in LMICs needs to be measured.<sup>9</sup> While obstetric outcomes in Africa are frequently described, publicised and scrutinised, the state of non-obstetric surgical care for women in Africa is relatively unspoken of and unknown.

### *Objectives*

This study's objective was to compare the non-obstetric, non-gynaecological surgical outcomes for women in Africa, to international outcomes using a risk-adjusted analysis of severe postoperative complications. We hypothesized that after adjusting for patient profile and for procedure-specific risk factors, women in Africa would have worse surgical outcomes from non-obstetric surgery than an international cohort.

## Methods

### *Study design*

This study is a secondary analysis of the African Surgical Outcomes Study (ASOS).<sup>10</sup> ASOS was a seven-day, African national multi-centre prospective observational cohort study of adult ( $\geq 18$  years) patients undergoing surgery in 25 African countries. This sub-study focuses specifically on the analysis of the female, non-obstetric, non-gynaecological surgical data collected during ASOS. These data are compared to international outcomes from the International Surgical Outcomes Study (ISOS).<sup>11</sup> The ASOS protocol was modelled on the ISOS protocol, and the studies therefore have similar methods, definitions and variables allowing for meaningful comparison (Supplementary Table 1).

### *Setting and participants*

The settings and participants for both ASOS and ISOS have been previously described<sup>10,11</sup> and are summarised in Supplementary Table 1. The inclusion criteria for this sub-study were all female patients admitted in participating hospitals undergoing elective, non-obstetric, non-gynaecological surgery with a planned overnight stay in the hospital. The inclusion criterion of ‘non-obstetric, non-gynaecological’ surgery only was determined by the ISOS case report form which did not distinguish between gynaecological and obstetric surgery separately. ISOS also only included elective cases, and therefore all urgent and emergent surgery was excluded from the ASOS cohort. The African data was removed from the ISOS cohort.

### *Ethics and consent*

The primary ethics approval for data collection for ASOS was from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal, South Africa (BE306/15). Regulatory approval for data collection varied between countries, with some requiring ethics approval and others only data governance approval. All sites approved a waiver of consent, except the University of the Witwatersrand (South Africa), which required informed consent from all patients with deferred consent for patients who could not give consent before surgery. Permission to use the ASOS data was obtained through BMB.

For the ISOS study, regulatory requirements differed between countries, with some requiring research ethics approval and some requiring only data governance approval. In the UK, the study was approved by the Yorkshire & Humber Research Ethics Committee (reference: 13/YH/0371) Permission to use the ISOS data was obtained through RMP.

Ethics approval for this sub-study of the data was obtained from the University of Cape Town’s Human Research Ethics Committee (reference 447/2020).

### *Variables and data sources/measurement*

ASOS adopted the International Surgical Outcomes Study (ISOS) definitions, with minor changes, to provide internationally comparable surgical outcomes data for Africa.<sup>11,12</sup> The definition and grading of complications were according to the European Perioperative Clinical Outcome definitions.<sup>12</sup> The data definition file used for ISOS was adopted for ASOS which ensured consistency in data definitions and interpretation (Supplementary File). The same potential risk factors were collected for in-hospital mortality and postoperative complications. Authorised access to the databases was used for this sub-study’s data

collection, on a password protected laptop. Data is presented as aggregate data. This study is reported according to the STROBE statement.<sup>13</sup>

### *Outcomes*

This sub-study has two primary outcomes. The first primary outcome measure is in-hospital postoperative complications, censored at 30 days following surgery and assessed and graded as mild, moderate, or severe according to consensus definitions, as used in the ASOS and ISOS studies. The second primary outcome is a risk adjusted analysis of in-hospital severe postoperative complications (censored at 30 days) in Africa in comparison to international incidences. Severe in-hospital postoperative complications are defined as a composite outcome of severe complications and in-hospital mortality. The secondary outcome is a description of the pre-operative characteristics of the study participants.

### *Study size*

Since this study is a secondary analysis of two existing cohort studies, the study size was predetermined. Details as to how the sub-study exclusion strategy resulted in the ASOS and ISOS sub-study cohort sizes can be found in Figure 1 and Figure 2.

### *Statistical analysis*

Categorical variables were described as proportions and compared using chi-square tests and Fisher's exact tests as appropriate. Continuous variables were described as mean and standard deviation if normally distributed or median and inter-quartile range if not normally distributed. Comparisons of continuous variables between groups were performed using t-tests or Mann Whitney U tests as appropriate. Univariate analysis was performed to test factors associated with the adverse outcomes of postoperative complications and in-hospital death. We wrote a statistical analysis plan for sub-study before data inspection and analysis.

All preoperative variables that were consistent between ISOS and ASOS were included in this sub-study. Patient risk factors included were age, preoperative haemoglobin, smoker status, American Society of Anesthesiologists (ASA) category, and preoperative chronic comorbid conditions (coronary artery disease, congestive heart failure, diabetes, cirrhosis, metastatic cancer, hypertension, stroke, or chronic obstructive pulmonary disease). Procedure specific factors included were the category of surgery (orthopaedic, breast, upper gastrointestinal, lower gastrointestinal, hepatobiliary, urological (kidney), vascular, head and neck, plastics, cardiac, thoracic lung, neurosurgery, and other), the severity of surgery (minor, intermediate, or major), and whether or not a surgical safety checklist was used.

To assess whether specific surgical disciplines were skewing the mean age for either cohort we did a two-way ANOVA. We did an analysis of the extent of missingness of our data which showed that all variables had 0.5% or less missing values. We therefore chose to perform a complete case analysis in which patients with missing data were excluded from an analysis.

To compare African non-obstetric, non-gynaecological surgical outcomes with international outcomes, given the potential differences in patient profile and disease profile, we used a logistic regression model for the risk adjusted analysis. We controlled for the impact of patient risk factors (age, smoker status, American Society of Anesthesiologists (ASA) category, and preoperative chronic comorbid conditions (coronary artery disease, congestive

heart failure, diabetes, cirrhosis, metastatic cancer, hypertension, stroke, or chronic obstructive pulmonary disease)), surgery-specific characteristics (category of surgery (orthopaedic, breast, upper gastrointestinal, lower gastrointestinal, hepatobiliary, urological (kidney), vascular, head and neck, plastics, cardiac, thoracic lung, neurosurgery, and other), the severity of surgery (minor, intermediate, or major)), and whether or not a surgical safety checklist was used in the analysis. Hosmer–Lemeshow goodness-of-fit statistics were used to test model calibration. We assessed for multi-collinearity between potential categorical risk predictors by identification of a variance inflation factor using linear regression; we excluded risk predictors with a variance inflation factor of more than 3. We also plotted the standardised Pearson residuals to evaluate the residuals for outliers. We report results of the risk adjusted analysis as an adjusted odds ratio (aOR) with 95% confidence interval (CI).  $p < 0.05$  was considered statistically significant.

We planned a sensitivity analysis which included preoperative haemoglobin in the model, as anaemia has been associated with postoperative morbidity and mortality, and the prevalence of anaemia is higher in Africa than the rest of the world.<sup>14,15</sup>

We did statistical analyses using the IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, N.Y., USA)<sup>16</sup>. STATA/IC (v16.1)<sup>17</sup> was used to calculate the variance inflation factors (VIFs) and to do the two-way ANOVA.

#### *Role of the funding source*

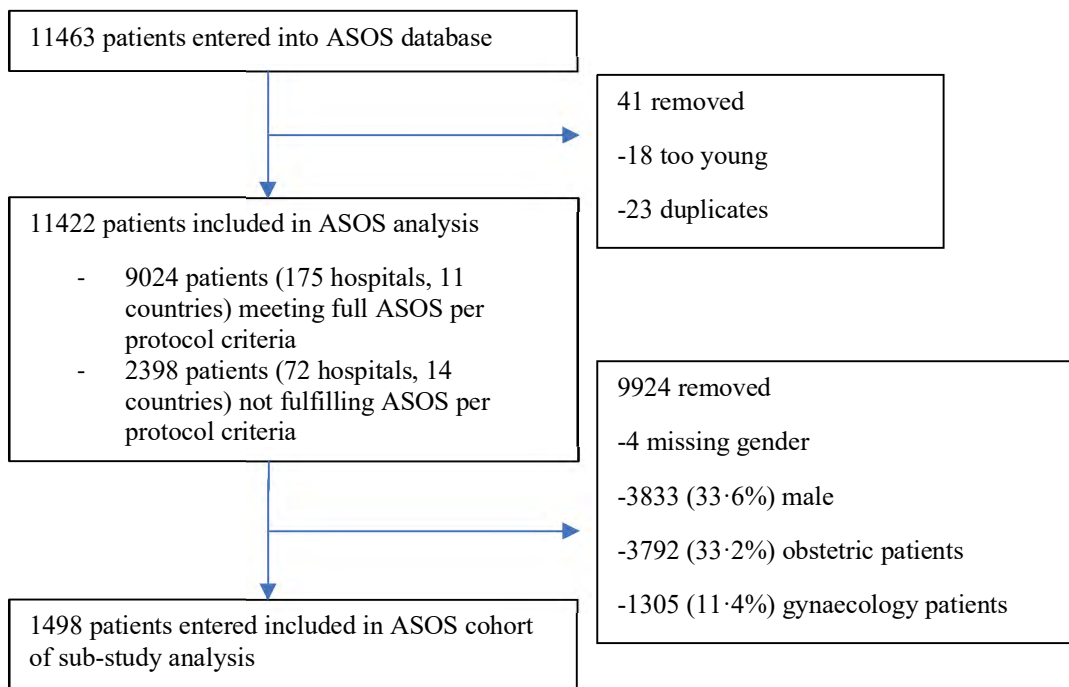
The funders of the original studies had no role in the study design, data collection, data analysis, data interpretation, or writing of the paper.

## Results

### *Participants*

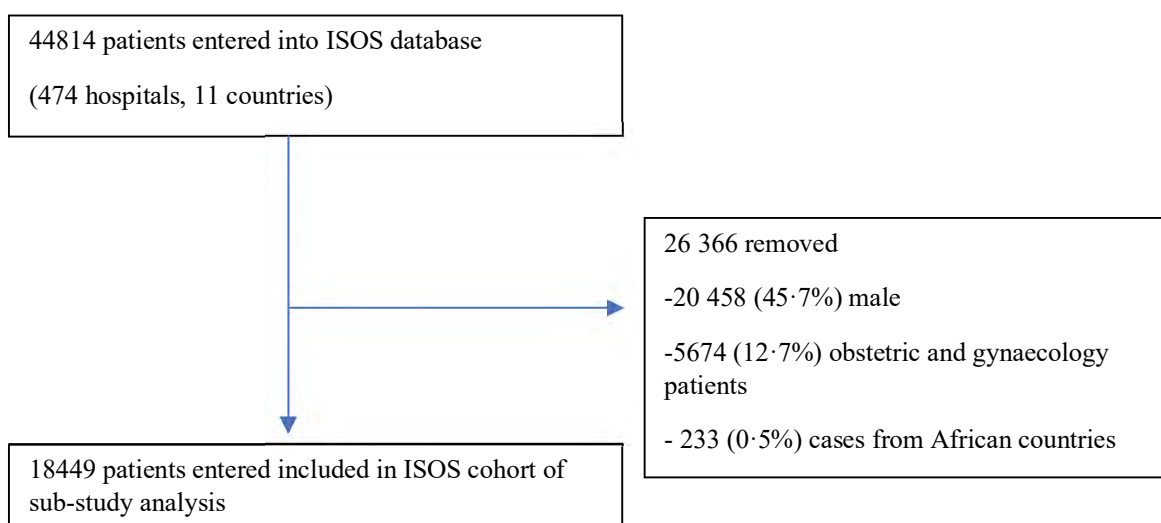
The African Surgical Outcomes Study recruited 11 422 patients (median age 29, IQR 10–70) from 247 hospitals in 25 African countries during the national cohort weeks. These countries included 14 low-income countries (Benin, Burundi, Congo, Democratic Republic of the Congo, Ethiopia, The Gambia, Madagascar, Mali, Niger, Senegal, Tanzania, Togo, Uganda, and Zimbabwe) and 11 middle-income countries (Algeria, Cameroon, Egypt, Ghana, Kenya, Libya, Mauritius, Namibia, Nigeria, South Africa, and Zambia). Further details regarding the exact country and hospital specific data can be found in Supplementary Table 1.

For this sub-study, 9924 patients from the ASOS data base were removed from the cohort: four with missing gender data, 3833 (33.6%) males, 3792 (33.2%) obstetric patients, 1305 (11.4%) gynaecology patients and 990 (10.0%) urgent or emergent cases resulting in an African cohort of 1498 participants.



**Figure 1: African Surgical Outcomes Study (ASOS) cohort: recruitment and exclusion strategy**

For ISOS, data describing 44 814 patients were collected from 474 hospitals in the following countries and regions: Australia, Austria, Belgium, Brazil, Canada, China, Denmark, France, Germany, Greece, Hong Kong, Indonesia, Italy, Malaysia, The Netherlands, New Zealand, Nigeria, Portugal, Romania, Russia, South Africa, Spain, Sweden, Switzerland, Uganda, UK, and USA. After removing 20 458 (45.7%) male patients and 5674 (12.7%) obstetric and gynaecology patients and the 233 (0.5%) African cases, there were 18449 international patients included in the international cohort of the sub-study.



**Figure 2: International Surgical Outcomes Study (ISOS) cohort: recruitment and exclusion strategy**

### Descriptive data: Baseline characteristics

Most patients in the African cohort had a low pre-operative risk profile in comparison to the international cohort of women (Table 1). The African cohort were on average a decade younger than the international cohort (47 (17) vs 57 (17) years;  $p < 0.0001$ ). In the two-way ANOVA this was found to be approximately consistent throughout the different procedure categories, apart from the category of 'other' procedures (57 (18) vs 55 (17) (Supplementary Table 3)). A significant difference in ASA physical status score between the cohorts, with a greater proportion of African participants with a score of one (661 (44.4%) of 1490 participants vs 4246 (23.1%) of 18416 participants), while more international participants had an ASA score of three or four ((166 (11.1%) of 1490 participants vs 4114 (22.3%) of 18416 participants) and (16 (1.1%) of 1490 participants vs 373 (2.0%) of 18416 participants) respectively).

The median haemoglobin was lower in the African cohort (12.3 [IQR: 11.0 – 13.3] vs 12.8 [IQR 11.8 – 13.7],  $p < 0.0001$ ). The international cohort had a significantly higher incidence of all baseline comorbidities measured (coronary artery disease, congestive heart failure, cirrhosis, metastatic cancer, hypertension, stroke or chronic obstructive pulmonary disease) apart from diabetes which was the most prevalent known comorbidity for both cohorts at over 10% of participants (Table 1). The most common non-obstetric, non-gynaecological category of surgery for both cohorts was orthopaedic surgery (Table 1). The World Health Organization (WHO) Safe Surgery Checklist or a similar surgical checklist was used in 16735 (90.7%) of 18442 international cases and 946 (63.6%) of 1487 cases in the African cohort.

**Table 1. Characteristics of cohorts**

| Characteristics            | Overall            | ASOS (n=1498)   | ISOS (n=18449)    | p-value |
|----------------------------|--------------------|-----------------|-------------------|---------|
| Age in years (m, SD)       | 55.87 (16.97)      | 47.28 (17.34)   | 56.56 (16.76)     | <0.0001 |
| Current smoker             | 2159/19851 (10.9)  | 140/1488 (9.4)  | 2019/18363 (11.0) | 0.059   |
| <b>ASA physical status</b> |                    |                 |                   |         |
| 1                          | 4907/19906 (24.7)  | 661/1490 (44.4) | 4246/18416 (23.1) | <0.0001 |
| 2                          | 10330/19906 (51.9) | 647/1490 (43.4) | 9683/18416 (52.6) |         |
| 3                          | 4280/19906 (21.5)  | 166/1490 (11.1) | 4114/18416 (22.3) |         |
| 4                          | 389/19906 (2.0)    | 16/1490 (1.1)   | 373/18416 (2.0)   |         |
| <b>Comorbidities</b>       |                    |                 |                   |         |
| Coronary Artery Disease    | 1493/19907 (7.5)   | 37/1498 (2.5)   | 1456/18409 (7.9)  | <0.0001 |
| Congestive Heart Failure   | 753/19907 (3.8)    | 24/1498 (1.6)   | 729/18409 (4.0)   | <0.0001 |
| Diabetes Mellitus          | 2158/19907 (10.8)  | 152/1498 (10.1) | 2006/18409 (10.9) | 0.37    |
| Cirrhosis                  | 130/19907 (0.7)    | 3/1498 (0.2)    | 127/18409 (0.7)   | 0.024   |

|                            |                    |                 |                    |         |
|----------------------------|--------------------|-----------------|--------------------|---------|
| Metastatic cancer          | 738/19907 (3·7)    | 37/1498 (2·5)   | 701/18409 (3·8)    | 0·0084  |
| Stroke                     | 560/19907 (2·8)    | 15/1498 (1·0)   | 545/18409 (3·0)    | <0·0001 |
| COPD/asthma                | 1761/19907 (8·8)   | 70/1498 (4·7)   | 1691/18409 (9·2)   | <0·0001 |
| Other                      | 8827/19907 (44·3)  | 540/1498 (36·0) | 8287/18409 (45·0)  | <0·0001 |
| <b>Severity</b>            |                    |                 |                    | <0·0001 |
| Minor                      | 3972/19936 (19·9)  | 499/1495 (33·4) | 3473/18441 (18·8)  |         |
| Intermediate               | 8942/19936 (44·9)  | 601/1495 (40·2) | 8341/18441 (45·2)  |         |
| Major                      | 7022/19936 (35·2)  | 395/1495 (26·4) | 6627/18441 (35·9)  |         |
| <b>Checklist use</b>       | 17681/19929 (88·7) | 946/1487 (63·6) | 16735/18442 (90·7) | <0·0001 |
| <b>Category of Surgery</b> |                    |                 |                    | <0·0001 |
| Orthopaedic                | 5191/19940 (36·4)  | 341/1493 (22·8) | 4850/12784 (37·9)  |         |
| Breast                     | 1638/19940 (11·5)  | 167/1493 (11·2) | 1471/12784 (11·5)  |         |
| Upper GIT                  | 73/19940 (0·5)     | 73/1493 (4·9)   | 1012/12784 (5·5)   |         |
| Lower GIT                  | 124/19940 (0·9)    | 124/1493 (8·3)  | 1292/12784 (7·0)   |         |
| Hepatobiliary              | 1473/19940 (10·3)  | 103/1493 (6·9)  | 1370/12784 (10·7)  |         |
| Urology and kidney         | 1348/19940 (9·4)   | 100/1493 (6·7)  | 1248/12784 (9·8)   |         |
| Vascular                   | 598/19940 (4·2)    | 40/1493 (2·7)   | 558/12784 (4·4)    |         |
| Head and neck              | 174/19940 (1·2)    | 174/1493 (11·7) | 3359/12784 (18·2)  |         |
| Plastics/ Cutaneous        | 926/19940 (6·5)    | 124/1493 (8·3)  | 802/12784 (6·3)    |         |
| Thoracic (lung and other)  | 480/19940 (3·4)    | 26/1493 (1·7)   | 454/12784 (3·6)    |         |
| Neurosurgery               | 35/19940 (0·2)     | 35/1493 (2·3)   | NR                 |         |
| Cardiac                    | 602/19940 (4·2)    | 19/1493 (1·3)   | 583/12784 (4·6)    |         |
| Other                      | 1615/19940 (11·3)  | 167/1493 (11·2) | 1448/12784 (11·3)  |         |

Denominators vary with the completeness of the data. ASOS=African Surgical Outcomes Study. ISOS=International Surgical Outcomes Study. m=mean. SD=standard deviation. ASA=American Society of Anesthesiologists. COPD = chronic obstructive pulmonary disease. GIT=gastrointestinal tract. NR=not reported. Data are n/N (valid %). Denominators vary with the completeness of the data. P value is for Pearson Chi-square test of independence.

### *Outcome data: Complications*

Overall, 472 (2·4%) of 19920 patients had severe complications and 98 (0·5%) of 19920 patients had died by 30 days post-surgery. From the international cohort 431 (2·3%) of 18449 patients had severe complications, and 78 (0·4%) had died by 30 days post-surgery. Thus, 78 (18%) of the 431 international participants who developed severe complications died by 30 days. From the African cohort 41 (2·8%) of 1471 patients had severe complications. 20 (48·8%) of the 41 African participants who developed severe complications died within 30 days. Failure to rescue (mortality following complications) was therefore 2·7 times higher in the African cohort.

The most common complication for both cohorts was superficial surgical site infection (55 (3·8%) of 1452 ASOS participants and 532 (2·9%) of 18448 ISOS participants (Table 2)), with no difference between the two cohorts when stratified into 'mild, moderate and severe' ( $\chi^2(3): 5\cdot273, p=0\cdot15$ ). There was, however, a significantly increased frequency of arrhythmia as a complication in the international cohort compared to the African cohort ( $\chi^2(3): 29\cdot334, p<0\cdot0001$ ) but significantly more cardiac arrests in Africa (12 (0·8%) of 1450 patients vs 61 (0·3%) of 18448 patients;  $p=0\cdot0026$ ).

**Table 2. Complications**

| Complications                      | Total            | ASOS          | ISOS             |
|------------------------------------|------------------|---------------|------------------|
| <b>Infectious complications</b>    |                  |               |                  |
| Superficial surgical site          | 587/19900 (2.9)  | 55/1452 (3.8) | 532/18448 (2.9)  |
| Deep surgical site                 | 242/19901 (1.2)  | 17/1453 (1.2) | 225/18448 (1.2)  |
| Body cavity                        | 139/19901 (0.7)  | 6/1453 (0.4)  | 133/18448 (0.7)  |
| Pneumonia                          | 245/19900 (1.2)  | 17/1453 (1.2) | 228/18447 (1.2)  |
| Urinary tract                      | 293/19901 (1.5)  | 6/1453 (0.4)  | 287/18448 (1.6)  |
| Blood stream                       | 162/19901 (0.8)  | 7/1453 (0.5)  | 155/18448 (0.8)  |
| <b>Cardiovascular</b>              |                  |               |                  |
| Myocardial infarction              | 51/19901 (0.3)   | 1/1453 (0.1)  | 50/18448 (0.3)   |
| Arrhythmia                         | 466/19901 (2.3)  | 4/1453 (0.3)  | 462/18448 (2.5)  |
| Pulmonary oedema                   | 125/19901 (0.6)  | 1/1453 (0.1)  | 124/18448 (0.7)  |
| Pulmonary embolism                 | 34/19901 (0.2)   | 3/1453 (0.2)  | 31/18448 (0.2)   |
| Stroke                             | 52/19895 (0.3)   | 4/1447 (0.3)  | 48/18448 (0.3)   |
| Cardiac arrest                     | 73/19898 (0.4)   | 12/1450 (0.8) | 61/18448 (0.3)   |
| <b>Miscellaneous complications</b> |                  |               |                  |
| Gastro-intestinal bleed            | 95/19901 (0.5)   | 4/1453 (0.3)  | 91/18448 (0.5)   |
| Acute kidney injury                | 280/19901 (1.4)  | 12/1453 (0.8) | 268/18448 (1.5)  |
| Postoperative bleed                | 601/19900 (3.0)  | 40/1452 (2.8) | 561/18448 (3.0)  |
| ARDS                               | 49/19901 (0.2)   | 2/1453 (0.1)  | 47/18448 (0.3)   |
| Anastomotic breakdown              | 75/19900 (0.4)   | 6/1453 (0.4)  | 69/18447 (0.4)   |
| Other                              | 1264/19897 (6.4) | 44/1449 (3.0) | 1209/18448 (6.6) |

Data are n/N (valid %). Denominators vary with the completeness of the data. ASOS=African Surgical Outcomes Study. ISOS=International Surgical Outcomes Study. ARDS=Acute respiratory distress syndrome.

*Main results: Risk adjusted analysis*

After adjusting for risk-profile, a woman in Africa has twice the odds (aOR: 2·114, 95% CI: 1·468 – 3·042,  $p < 0\cdot0001$ ) of having a severe postoperative complication following non-obstetric, non-gynaecological surgery compared to the international incidence (Table 3). Hosmer–Lemeshow goodness-of-fit statistics indicated that the models were well calibrated, with a good match between observed and expected outcomes. Residuals showed that the assumptions for regression analyses were met.

**Table 3. Risk adjusted analysis of risk factors associated with severe postoperative complications in women undergoing non-obstetric, non-gynaecological surgery**

|                            | Odds ratio | 95% CI         | Wald    | df | significance |
|----------------------------|------------|----------------|---------|----|--------------|
| <b>age</b>                 | 1·019      | 1·012 – 1·026  | 26·737  | 1  | <0·0001      |
| <b>current smoker</b>      | 1·049      | 0·765 – 1·439  | 0·088   | 1  | 0·77         |
| <b>ASA</b>                 |            |                |         |    |              |
| 1                          | Reference  |                |         |    |              |
| 2                          | 1·510      | 1·005 – 2·270  | 3·933   | 1  | 0·047        |
| 3                          | 3·964      | 2·589 – 6·068  | 40·165  | 1  | <0·0001      |
| 4                          | 9·097      | 5·408 – 15·302 | 69·240  | 1  | <0·0001      |
| <b>Comorbidities</b>       |            |                |         |    |              |
| Coronary artery disease    | 0·809      | 0·614–1·066    | 2·271   | 1  | 0·13         |
| Congestive heart failure   | 1·929      | 1·446 – 2·573  | 19·992  | 1  | <0·0001      |
| Diabetes                   | 1·101      | 0·858 – 1·413  | 0·571   | 1  | 0·45         |
| Cirrhosis                  | 2·137      | 1·073 – 4·258  | 4·664   | 1  | 0·03         |
| Metastatic cancer          | 1·739      | 1·230 – 2·457  | 9·827   | 1  | 0·0017       |
| Stroke                     | 1·154      | 0·781 – 1·705  | 0·518   | 1  | 0·47         |
| COPD                       | 1·015      | 0·763 – 1·351  | 0·010   | 1  | 0·92         |
| <b>Severity of surgery</b> |            |                |         |    |              |
| Mild                       | Reference  |                |         |    |              |
| Moderate                   | 1·392      | 0·983 – 1·971  | 3·480   | 1  | 0·062        |
| Severe                     | 2·476      | 1·760 – 3·485  | 27·056  | 1  | <0·0001      |
| <b>Checklist use</b>       | 1·359      | 1·035 – 1·785  | 4·874   | 1  | 0·027        |
| <b>Surgical Category</b>   |            |                |         |    |              |
| Orthopaedics               | Reference  |                |         |    |              |
| Breast                     | 1·011      | 0·590 – 1·734  | 0·002   | 1  | 0·97         |
| Upper GI                   | 3·059      | 2·102 – 4·451  | 34·131  | 1  | <0·0001      |
| Lower GI                   | 2·752      | 1·935 – 3·914  | 31·706  | 1  | <0·0001      |
| Hepatobiliary              | 1·365      | 0·844 – 2·205  | 1·612   | 1  | 0·20         |
| Urology kidney             | 1·357      | 0·841 – 2·189  | 1·561   | 1  | 0·21         |
| Vascular                   | 2·498      | 1·596 – 3·911  | 16·041  | 1  | <0·0001      |
| Head and neck              | 1·145      | 0·778 – 1·686  | 0·471   | 1  | 0·49         |
| Plastics                   | 2·424      | 1·470 – 4·000  | 12·019  | 1  | 0·0001       |
| Cardiac                    | 3·009      | 2·083 – 4·348  | 34·419  | 1  | <0·0001      |
| Thoracic lung              | 1·580      | 0·896 – 2·784  | 2·503   | 1  | 0·11         |
| Neurosurgery               | 2·708      | 0·590 – 12·440 | 1·640   | 1  | 0·20         |
| Other                      | 1·264      | 0·783 – 2·040  | 0·918   | 1  | 0·34         |
| <b>African setting</b>     | 2·114      | 1·468 – 3·042  | 16·223  | 1  | <0·0001      |
| Constant                   | 0·001      |                | 427·230 | 1  | <0·0001      |

ASA=American Society of Anesthesiologists. COPD = chronic obstructive pulmonary disease. GIT = gastrointestinal tract. CI = confidence interval. DF = degrees of freedom. P value is for Pearson Chi-square test of independence.

### *Sensitivity analysis*

The sensitivity analysis including the preoperative haemoglobin in the logistic regression model, supports the findings of the main analysis (Supplementary Table 4). In this sensitivity analysis model the adjusted odds ratio for severe postoperative complications following non-obstetric, non-gynaecological surgery in Africa was 1·995, 95% CI: 1·359 – 2·930,  $p=0\cdot0004$ .

## Discussion

### *Key results and interpretation*

The main finding of this study is that after adjusting for risk-profile, women living in Africa have double the odds of having a severe postoperative complication or death following non-obstetric, non-gynaecological elective surgery compared to international rates. Failure to rescue (complications resulting in mortality) in surgical patients are reported as twice as high in Africa compared to international cohorts<sup>10</sup>, however women in Africa have a higher rate of failure to rescue at nearly threefold international comparators. The risk adjusted outcomes may therefore highlight the inequity in the health systems between the two cohorts and the higher failure to rescue may highlight gender inequality in postoperative treatment in Africa. Due to the central role women play in family and community well-being, healthcare provision and macroeconomic development, this difference in surgical outcomes is likely to have a significant impact on the affected communities.<sup>1</sup>

Some of our findings are consistent with other studies that compared African and international cohorts, as in the full ASOS cohort.<sup>10</sup> The women in the African cohort were significantly younger with a lower risk profile than the international cohort. This is likely due to most African countries having a relatively young population (average life expectancy for women in Africa is 65 versus a global average of 75 years)<sup>18</sup> and higher rates of trauma resulting in disability-adjusted life years (DALYs) in Africa being at least two times higher than any other region.<sup>19</sup> This study is an example of how this younger, healthier preoperative profile may mask the real differences in care between the two cohorts and result in the appearance of similar outcomes in the unadjusted severe postoperative complication rates.

The finding that half of the participants who developed severe complications in the African cohort had died by 30 days is a particular cause for concern. This significantly higher mortality rate for those who developed severe complications in Africa is in keeping with the conclusion from ASOS that ‘failure-to-rescue’ is a major cause of mortality in African systems.<sup>10</sup> ASOS suggested that this is likely due to scarce workforce resources (with a median of 0·7 perioperative specialists per 100 000 in the population while the inflection point for safe surgical care is approximately 10 – 20 specialists per 100 000 in the population) and poor early warning systems to detect physiological deterioration of patients.<sup>10</sup> The fact that this ‘failure-to-rescue’ was significantly higher in the women-only African cohort than in the overall African cohort suggests gender inequality in peri-operative surgical care in Africa. The high prevalence of diabetes in both cohorts is a reminder that non-communicable diseases of lifestyle, which are mostly prioritised as health issues in HICs currently equally affect LMICs. The finding of a lower median haemoglobin in African cohorts has previously been described.<sup>18</sup> A multicentre prospective observational study in South Africa found that the prevalence of preoperative anaemia in elective non-cardiac, non-

obstetric surgical patients was 28% with approximately 40% being due to iron deficiency anaemia, with iron supplements being under-utilised preoperatively.<sup>21</sup> This reveals an ongoing opportunity to improve preoperative optimisation. The higher prevalence of anaemia in Africa, however, could not account for the worse postoperative outcomes we report in African female surgical patients as demonstrated in the sensitivity analysis.

Human immunodeficiency virus (HIV) status was not recorded in ISOS and therefore it was unfortunately not possible to include this variable in the risk adjusted analysis. In ASOS HIV status was not independently associated with outcomes.<sup>10</sup>

It has previously been shown that a surgical safety checklist is less frequently used in LMICs than high income countries and that this has been associated with an increase in complications.<sup>22,23</sup> Our results support this statement. However, our finding of increased odds of severe postoperative complications for woman in Africa was after adjusting for the use of a checklist and therefore the difference in outcomes cannot be attributed to a lack of the use of the surgical checklist. This emphasises that there are multiple other health system weaknesses, such as surgical infrastructure and workforce, that need to be addressed.

#### *Strengths, limitations and generalisability*

The main strengths of this study are the following: we describe comprehensively the state of non-obstetric, non-gynaecological surgical outcomes for women in Africa compared to an appropriate international cohort. The cohorts are from a wide range of settings with minimal missing data. The study also has limitations. There may be other risk factors that could modify the outcomes demonstrated in this paper, for example risk factors included in Charlson's comorbidity index, that were not captured in the ISOS and ASOS datasets. The timing difference between ISOS and ASOS may have had an impact on the results due to potential improvement or worsening of health system conditions between the data collection periods. While this study offers a broad overview, which we believe is an important starting point in terms of advocacy, it does not give region-specific details and it must be read with an understanding that 'Africa is not a monolith'<sup>24</sup> with vast differences existing between and within the different countries' health systems. There is, therefore, a need for country-specific research on the state of women's comprehensive surgical care. There is also need for a comparison of gynaecological outcomes as well as a comparison of urgent/emergent surgical outcomes, which have previously been found to be an area with even greater discrepancies between African and international outcomes.<sup>25</sup> Finally, more research is needed on the impact of the preventable death of a woman in Africa, and in other LMICs.

In conclusion, this study provides evidence of health systems and gender inequality which are adversely affecting the surgical outcomes of women in Africa.

**Word count:** 3063

**Funding:**  
None

**Acknowledgements:**

The Global Surgery fellowship programme is funded by the South African Medical Research Council's Midcareer Scientist Grant.

**Contributions:**

First draft: A Paterson

Data Analysis: BM Biccard, A Hardy, A Paterson

Critical review and editing: S Maswime, BM Biccard, RM Pearse

**Conflicts of interest:**

The authors have no conflicts of interest to declare.

**Data Sharing Statement:**

Data will be disclosed only upon request and approval of the proposed use of the data by the Steering Committees of both ISOS and ASOS. Data are available to the journal for evaluation of reported analyses. Data will be de-identified for participant, hospital and country, and will be available with a signed data access agreement.

The ASOS and ISOS study protocols as well as further information on the studies are available on [clinicaltrials.gov](http://clinicaltrials.gov) as well on the studies' respective websites [asos.org.za](http://asos.org.za) and [isos.org.uk](http://isos.org.uk).

References

1. Langer A, Meleis A, Knaul FM, et al. Women and health: the key for sustainable development. *Lancet* 2015;386(9999):1165–210. DOI: 10.1016/S0140-6736(15)60497-4.
2. Lundgren R, Burgess S, Chantelois H, Oregede S, Kerner B, Kågesten A. Processing gender: lived experiences of reproducing and transforming gender norms over the life course of young people in Northern Uganda. *Cult Health Sex.* 2019;21(4):387–403. DOI: 10.1080/13691058.2018.1471160.
3. Horton R, Ceschia A. Making women count. *Lancet* 2015;386(9999):1112–4. DOI: 10.1016/S0140-6736(15)60964-3.
4. Pucher P, Macdonnell M, Arulkumaran S. Global lessons on transforming strategy into action to save mothers' lives. *Int J Gynaecol Obstet.* 2013;123(2):167–72. DOI: 10.1016/j.ijgo.2013.05.009.
5. Bishop D, Dyer R, Maswime S, et al. Maternal and neonatal outcomes after caesarean delivery in the African Surgical Outcomes Study: a 7-day prospective observational cohort study. *Lancet Glob Health* 2019;7(4):513–22. DOI: 10.1016/S2214-109X(19)30036-1.
6. Heise L, Greene M, Opper N, et al. Gender inequality and restrictive gender norms: framing the challenges to health. *Lancet* 2019;393(10189):2440–54. DOI: 10.1016/S0140-6736(19)30652-X
7. Ginsburg O, Bray F, Coleman M, et al. The global burden of women's cancers: a grand challenge in global health. *Lancet* 2017;389(10071):847–60. DOI: 10.1016/S0140-6736(16)31392-7.
8. Faught W, Gill R, Ng-Kamstra J. Women's Health and Surgical Care: Moving from maternal health to comprehensive surgical systems. *J Obstet Gynaecol Can.* 2015;37(10):894–6. DOI: 10.1016/s1701-2163(16)30024-x.
9. Scott K, Jha A. Putting Quality on the Global Health Agenda. *N Engl J Med* 2014;371(1):3–5. DOI: 10.1056/NEJMp1402157.

10. Biccard B, Madiba T, Kluyts H, et al. Perioperative patient outcomes in the African Surgical Outcomes Study: a 7-day prospective observational cohort study. *Lancet* 2018;391(10130):1589–98. DOI: 10.1016/S0140-6736(18)30001-1
11. International Surgical Outcomes Study group. Global patient outcomes after elective surgery: prospective cohort study in 27 low-, middle- and high-income countries. *Br J Anaesth.* 2016;117(5):601–9. DOI: 10.1093/bja/aew316
12. Jammer I, Wickboldt N, Sander M, et al. Standards for definitions and use of outcome measures for clinical effectiveness research in perioperative medicine: European Perioperative Clinical Outcome (EPCO) definitions: a statement from the ESA-ESICM joint taskforce on perioperative outcome measures. *Eur J Anaesthesiol.* 2015;32:88–105. DOI: 10.1097/EJA.000000000000118.
13. von Elm E, Altman DG, Egger M, Pocock SJ, Gotsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *PLoS Med* 2007;4: e296. DOI: 10.1371/journal.pmed.0040296
14. Musallam KM, Tamim HM, Richards T, et al. Preoperative anaemia and postoperative outcomes in non-cardiac surgery: a retrospective cohort study. *Lancet* 2011;378:1396-407
15. Kassebaum NJ, Jasrasaria R, Naghavi M, et al. A systematic analysis of global anemia burden from 1990 to 2010. *Blood* 2014;123:615-24
16. IBM Corp. 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp
17. StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC.
18. Statista. Average life expectancy in Africa for those born in 2020, by gender and region. [Internet]. Statista Research Department. [published 2021 January 20; cited 2021 July 5]. Available from: <https://www.statista.com/statistics/274511/life-expectancy-in-africa/>
19. World Health Organization. Global Burden of Disease 2004. Part 4: Burden of disease: DALYs. [pdf]. World Health Organization. [published 2008; cited 2021 July 5]. Available from: [https://www.who.int/healthinfo/global\\_burden\\_disease/GBD\\_report\\_2004update\\_part4.pdf](https://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_part4.pdf)
20. Sincavage J, Robinson B, Msosa VJ, Katete C, Purcell L, Charles A. Preoperative anemia and surgical outcomes following laparotomy in a resource-limited setting. *Am J Surg.* 2020;S0002-9610(20)30810-2. DOI: 10.1016/j.amjsurg.2020.12.032
21. Conradie WS, Biesman-Simons T, Roodt F, et al. A multicentre prospective observational study of the prevalence of preoperative anaemia and iron deficiency in adult elective surgical patients in hospitals in Western Cape Province, South Africa. *S Afr Med J.* 2019;110(1):65-68. DOI: 10.7196/SAMJ.2019.v110i1.14051
22. GlobalSurg Collaborative. Pooled analysis of WHO Surgical Safety Checklist use and mortality after emergency laparotomy. *Br J Surg.* 2019;106(2):e103-112. DOI: 10.1002/bjs.11051.
23. Delisle M, Pradarelli JC, Panda N, Korisanszky L, Sonnay Y, Lipsitz S et al. Variation in global uptake of the Surgical Safety Checklist. *Br J Surg.* 2020; 107(2):e151-60. DOI: 10.1002/bjs.11321.
24. Bookholane H. Opinion: A reminder during COVID-19 — Africa is not a monolith. [Internet]. *Devex.* [published 2020 May 27; cited 2021 June 26]. Available from: <https://www.devex.com/news/opinion-a-reminder-during-covid-19-africa-is-not-a-monolith-97300>
25. GlobalSurg Collaborative. Mortality of emergency abdominal surgery in high-, middle- and low-income countries. *Br J Surg.* 2016;103(8):971-88. DOI: 10.1002/bjs.10151.

**Appendix 1: Supplementary Tables**

**Supplementary Table 1: Comparison of African Surgical Outcomes Study (ASOS) and International Surgical Outcomes Surgery (ISOS) methods, setting and participants**

|  | ISOS   | ASOS   |
|--|--|--|
| <b>Location</b>  | 474 hospitals in the following 27 countries and regions were recruited: Australia, Austria, Belgium, Brazil, Canada, China, Denmark, France, Germany, Greece, Hong Kong, Indonesia, Italy, Malaysia, The Netherlands, New Zealand, Nigeria, Portugal, Romania, Russia, South Africa, Spain, Sweden, Switzerland, Uganda, UK, and USA.  | 247 hospitals were recruited from 25 African countries for participation, namely Benin, Burundi, Congo, Democratic Republic of the Congo, Ethiopia, The Gambia, Madagascar, Mali, Niger, Senegal, Tanzania, Togo, Uganda, Zimbabwe, Algeria, Cameroon, Egypt, Ghana, Kenya, Libya, Mauritius, Namibia, Nigeria, South Africa, and Zambia.  |
| <b>Description of setting</b>                                | Seven countries were classed as middle income and one as low income, with 134 participating hospitals between them. Hospitals had a median of 550 (range 329–850) ward beds and 21 (range 10–38) critical care beds. The median critical care capacity (ratio of critical care beds to total hospital beds) was 4% (IQR 2–6). A total of 310 hospitals (66%) were affiliated with a university. Seventy-seven percent of hospitals provided only government funded health care, 3% only privately funded health care, and 21% were funded by both sources.   | 14 low-income countries and 11 middle-income countries. 173 (80%) of 216 were government-funded hospitals, 28 (12%) were privately funded, and 15 (7%) were jointly funded. 103 (49%) of 212 were university-affiliated hospitals. 45 (21%) of 216 were primary-level hospitals (defined as mainly obstetrics and gynaecology, and general surgery), 68 (31%) were secondary-level (defined as highly differentiated by function with five to ten clinical specialities), and 103 (48%) were tertiary-level (defined as specialised staff or technical support). Each hospital served a median population of 810 000 people (IQR 200 000–2 000 000), with a median of 300 beds (140–545), four operating rooms (2–7), and three critical care beds (0–7) providing invasive ventilation. 0.9% of hospital beds (IQR 0–2.0) were critical care beds. Hospitals were staffed by a median of three specialist surgeons (IQR 1–8), one specialist anaesthetist (0–5), and two specialist obstetricians (0–5), with a median of 0.7 (0.2–1.9) of any specialist per 100 000 population. |
| <b>Recruitment methods</b>                                   | In each country individuals were approached to act as national coordinators using contacts in national and international specialist societies in surgery and anaesthesia. Individual participating hospitals were then identified through a global online recruitment campaign led by the study management group and through the direct approach of the national coordinators. Nominations for participation were then confirmed as appropriate through discussion with national coordinators. The study website provided all study documentation and guidance on study procedures ( <a href="http://www.isos.org.uk/documents">www.isos.org.uk/documents</a> ). | A collaborative network of more than 1000 health-care professionals was established across Africa through personal invitations to colleagues, invitations to surgical and anaesthesia societies, a website and a Twitter feed. BMB made country visits where possible to meet with local study investigators. A website provided investigator support, in the form of a regularly updated page of frequently asked questions, the protocol, case report forms, and an outcomes definitions document in English and French. In each country, as many hospitals as possible were recruited using a convenience sampling strategy.  |
| <b>Recruitment/data collection dates</b>                     | Each country selected a single recruitment week between April and June 2014.   | Each country selected a single recruitment week between February and May, 2016.  |
| <b>Eligibility: patient inclusion and exclusion criteria</b> | All adult patients (aged over 18 years) undergoing elective surgery during the 7-day study period with a planned overnight stay in a hospital were eligible for inclusion. Patients undergoing emergency surgery, planned day surgery or radiological procedures not requiring anaesthesia were excluded.  | All patients (aged over 18 years) undergoing elective and non-elective surgery with a planned overnight hospital stay following surgery during the study week were eligible for inclusion. Patients undergoing planned day surgery or radiological procedures not requiring anaesthesia were excluded.   |
| <b>Eligibility: Country/hospital inclusion criteria</b>      | A minimum of ten centres from any country was required for participation and   | The criteria for inclusion of country data were initially set as: at least ten hospitals   |

|   |  |  |
|---|--|--|
|   | only centres including 10 valid patients were included in the data analysis.   | or at least half the surgical centres if fewer than ten hospitals in the country were required, as well as submission of the total number of eligible patients during recruitment week, and provision of data describing at least 90% of the eligible patients from each site. Unfortunately, 14 of the 25 participating countries could not fulfil these requirements. However, the findings of ASOS were similar between the full cohort, and the representative cohort. On this basis a decision was made to use the full cohort.                 |
| <b>Sources and methods of selection of participants</b> | Centres were asked to include all eligible patients in the study.  | Centres were asked to include all eligible patients in the study.  |
| <b>Ethics approval</b>                                  | Regulatory requirements differed between countries, with some requiring research ethics approval and some requiring only data governance approval. In the UK, the study was approved by the Yorkshire & Humber Research Ethics Committee (reference: 13/YH/0371).  | Regulatory approval varied between countries, with some requiring ethics approval and others only data governance approval. The primary ethics approval was from the Biomedical Research Ethics Committee of the University of KwaZulu Natal, South Africa (BE306/15).   |
| <b>Data collection</b>                                  | Data describing consecutive patients were collected until hospital discharge on paper case record forms. Data were censored at 30 days following surgery for patients who remained in the hospital. Data were anonymised before entry onto a secure Internet-based electronic case record form designed specifically for ISOS, which incorporated automated checks for plausibility, consistency and completeness. | Data describing consecutive patients were collected on paper case-record forms until hospital discharge and censored at 30 days following surgery for patients who remained in hospital. Data were anonymised during the transcription process using Research Electronic Data Capture (REDCap) tools hosted by Safe Surgery South Africa. REDCap is a secure, web-based application designed to support data capture for research studies. Soft limits were set for data entry, prompting investigators when data were entered outside these limits. |
| <b>Sample size</b>                                      | 44 814 patients  | 11 422 patients  |

**Supplementary Table 2. Surgical Outcomes for African Surgical Outcomes Study (ASOS) and International Surgical Outcomes Surgery (ISOS) cohort**

| Complication                                  | Overall         | ASOS          | ISOS            | p-value |
|---|-----------------|---------------|-----------------|---------|
| <b>Infectious complications</b>               |                 |               |                 |         |
| <b>Superficial surgical site infection</b>    |                 |               |                 | 0.15    |
| Mild  | 323/19900 (1.6) | 30/1452 (2.1) | 293/18448 (1.6) |         |
| Moderate                                      | 211/19900 (1.1) | 22/1452 (1.5) | 189/18448 (1.0) |         |
| Severe  | 53/19900 (0.3)  | 3/1452 (0.2)  | 50/18448 (0.3)  |         |
| <b>Deep surgical site infection</b>           |                 |               |                 | 0.43    |
| Mild  | 52/19901 (0.3)  | 6/1453 (0.4)  | 46/18448 (0.2)  |         |
| Moderate                                      | 112/19901 (0.6) | 8/1453 (0.6)  | 104/18448 (0.6) |         |
| Severe  | 78/19901 (0.4)  | 3/1453 (0.2)  | 75/18448 (0.4)  |         |
| <b>Body cavity infection</b>                  |                 |               |                 | 0.73    |
| Mild  | 39/19762 (0.2)  | 1/1453 (0.1)  | 38/18448 (0.2)  |         |
| Moderate                                      | 60/19762 (0.3)  | 3/1453 (0.2)  | 57/18448 (0.3)  |         |
| Severe  | 40/19762 (0.2)  | 2/1453 (0.1)  | 38/18448 (0.2)  |         |
| <b>Post-operative pneumonia</b>               |                 |               |                 | 0.89    |
| Mild  | 91/19900 (0.5)  | 7/1453 (0.5)  | 84/18447 (0.5)  |         |
| Moderate                                      | 108/19900 (0.5) | 8/1453 (0.6)  | 100/18447 (0.5) |         |
| Severe  | 46/19900 (0.2)  | 2/1453 (0.1)  | 44/18447 (0.2)  |         |
| <b>Post-operative urinary tract infection</b> |                 |               |                 | 0.0060  |
| Mild  | 120/19901 (0.6) | 3/1453 (0.2)  | 117/18448 (0.6) |         |
| Moderate                                      | 149/19901 (0.7) | 2/1453 (0.1)  | 147/18448 (0.8) |         |
| Severe  | 24/19901 (0.1)  | 1/1453 (0.1)  | 23/18448 (0.1)  |         |
| <b>Blood stream infection</b>                 |                 |               |                 | 0.57    |
| Mild  | 57/19901 (0.3)  | 2/1453 (0.1)  | 55/18448 (0.3)  |         |
| Moderate                                      | 59/19901 (0.3)  | 2/1453 (0.1)  | 57/18448 (0.3)  |         |
| Severe  | 46/19901 (0.2)  | 3/1453 (0.2)  | 43/18448 (0.2)  |         |
| <b>Cardiovascular complications</b>           |                 |               |                 |         |
| <b>Myocardial infarction</b>                  |                 |               |                 | 0.73    |
| Mild  | 19/19901 (0.1)  | 1/1453 (0.1)  | 18/18448 (0.1)  |         |
| Moderate                                      | 12/19901 (0.1)  | 0/1453 (0.0)  | 12/18448 (0.1)  |         |
| Severe  | 20/19901 (0.1)  | 0/1453 (0.0)  | 20/18448 (0.1)  |         |
| <b>Arrhythmia</b>                             |                 |               |                 | <0.0001 |
| Mild  | 191/19901 (1.0) | 2/1453 (0.1)  | 189/18448 (1.0) |         |
| Moderate                                      | 198/19901 (1.0) | 1/1453 (0.1)  | 197/18448 (1.1) |         |
| Severe  | 77/19901 (0.4)  | 1/1453 (0.1)  | 76/18448 (0.4)  |         |
| <b>Pulmonary oedema</b>                       |                 |               |                 | 0.040   |
| Mild  | 51/19901 (0.3)  | 1/1453 (0.1)  | 50/18448 (0.3)  |         |
| Moderate                                      | 50/19901 (0.3)  | 0/1453 (0.0)  | 50/18448 (0.3)  |         |
| Severe  | 24/19901 (0.1)  | 0/1453 (0.0)  | 24/18448 (0.1)  |         |
| <b>Pulmonary embolism</b>                     |                 |               |                 | 0.38    |
| Mild  | 6/19901 (0.0)   | 0/1453 (0.0)  | 6/18448 (0.0)   |         |
| Moderate                                      | 10/19901 (0.1)  | 0/1453 (0.0)  | 10/18448 (0.1)  |         |
| Severe  | 18/19901 (0.1)  | 3/1453 (0.2)  | 15/18448 (0.1)  |         |
| <b>Post-operative stroke</b>                  |                 |               |                 | 0.71    |
| Mild  | 16/19895 (0.1)  | 2/1447 (0.1)  | 14/18448 (0.1)  |         |
| Moderate                                      | 14/19895 (0.1)  | 1/1447 (0.1)  | 13/18448 (0.1)  |         |
| Severe  | 22/19895 (0.1)  | 1/1447 (0.1)  | 21/18448 (0.1)  |         |
| <b>Post-operative cardiac arrest</b>          |                 |               |                 | 0.0026  |
| Severe  | 73/19898 (0.4)  | 12/1450 (0.8) | 61/18448 (0.3)  |         |
| <b>Miscellaneous complications</b>            |                 |               |                 |         |
| <b>Gastrointestinal bleed</b>                 |                 |               |                 | 0.49    |
| Mild  | 47/19901 (0.2)  | 2/1453 (0.1)  | 45/18448 (0.2)  |         |
| Moderate                                      | 25/19901 (0.1)  | 0/1453 (0.0)  | 25/18448 (0.1)  |         |
| Severe  | 23/19901 (0.1)  | 2/1453 (0.1)  | 21/18448 (0.1)  |         |
| <b>Acute kidney injury</b>                    |                 |               |                 | 0.15    |
| Mild  | 157/19901 (0.8) | 7/1453 (0.5)  | 150/18448 (0.8) |         |
| Moderate                                      | 67/19901 (0.3)  | 1/1453 (0.1)  | 66/18448 (0.4)  |         |
| Severe  | 56/19901 (0.3)  | 4/1453 (0.3)  | 52/18448 (0.3)  |         |
| <b>Post-operative bleed</b>                   |                 |               |                 | <0.0001 |
| Mild  | 479/19900 (2.4) | 7/1452 (0.5)  | 472/18448 (2.6) |         |
| Moderate                                      | 115/19900 (0.6) | 26/1452 (1.8) | 89/18448 (0.5)  |         |
| Severe  | 7/19900 (0.0)   | 7/1452 (0.5)  | 0/18448 (0.0)   |         |
| <b>Post-operative ARDS</b>                    |                 |               |                 | 0.95    |
| Mild  | 16/19901 (0.1)  | 1/1453 (0.1)  | 15/18448 (0.1)  |         |
| Moderate                                      | 13/19901 (0.1)  | 0/1453 (0.0)  | 13/18448 (0.1)  |         |
| Severe  | 20/19901 (0.1)  | 1/1453 (0.1)  | 19/18448 (0.1)  |         |
| <b>Anastomotic leak</b>                       |                 |               |                 | 0.19    |
| Mild  | 15/19900 (0.1)  | 2/1453 (0.1)  | 13/18447(0.1)   |         |

|                            |                 |               |                 |        |
|----------------------------|-----------------|---------------|-----------------|--------|
| <b>Moderate</b>            | 26/19900 (0.1)  | 0/1453 (0.0)  | 26/18447(0.1)   |        |
| <b>Severe</b>              | 34/19900 (0.2)  | 4/1453 (0.3)  | 30/18447(0.2)   |        |
| <b>Other complications</b> |                 |               |                 | 0.0003 |
| <b>Mild</b>                | 618/19897 (3.1) | 24/1449 (1.7) | 594/18448 (3.2) |        |
| <b>Moderate</b>            | 485/19897 (2.4) | 20/1449 (1.4) | 465/18448 (2.5) |        |
| <b>Severe</b>              | 160/19897 (0.8) | 10/1449 (0.7) | 150/18448 (0.8) |        |

Denominators vary with the completeness of the data. ARDS = acute respiratory distress syndrome. Data are n/N (valid %). P value is for Pearson Chi-square test of independence or Fisher exact test.

**Supplementary Table 3: Two-way ANOVA of age and surgical procedure**

|                        | ASOS        | ISOS        | Total       |
|------------------------|-------------|-------------|-------------|
| Orthopaedics           | 49.3 (17.8) | 61.6 (16.6) | 60.7 (16.9) |
| Breast                 | 46.5 (16.3) | 52.5 (15.1) | 51.9 (15.4) |
| Upper gastrointestinal | 46.1 (16.0) | 53.5 (15.3) | 53.0 (15.5) |
| Lower gastrointestinal | 44.4 (17.0) | 58.5 (16.8) | 57.2 (17.3) |
| Hepatobiliary          | 44.6 (14.6) | 54.1 (15.3) | 53.5 (15.5) |
| Urology (kidney)       | 45.9 (16.9) | 57.0 (15.8) | 56.2 (16.1) |
| Vascular               | 49.4 (16.7) | 61.4 (15.5) | 60.6 (15.9) |
| Head and Neck          | 42.1 (16.3) | 51.2 (16.5) | 50.8 (16.6) |
| Plastics               | 43.3 (17.5) | 53.9 (17.8) | 52.5 (18.1) |
| Cardiac                | 53.3 (15.5) | 64.0 (15.4) | 63.7 (15.5) |
| Thoracic lung          | 47.6 (15.9) | 57.1 (15.2) | 56.6 (15.4) |
| Neurosurgery           | 45.4 (15.4) | ..          | 46.4 (15.4) |
| Other                  | 57.0 (17.7) | 55.1 (16.8) | 55.3 (16.9) |
| Total                  | 47.3 (17.3) | 56.6 (16.8) | 55.9 (17.0) |

Data are mean (standard deviation). ASOS = African Surgical Outcomes Study. ISOS = International Surgical Outcomes Study.

**Supplementary Table 4. Sensitivity analysis with baseline haemoglobin**

|                          | Odds ratio | 95% CI         | Wald    | df | significance |
|--------------------------|------------|----------------|---------|----|--------------|
| baseline haemoglobin     | 0.881      | 0.839 – 0.924  | 26.435  | 1  | <0.0001      |
| age                      | 1.018      | 1.011 – 1.026  | 22.969  | 1  | <0.0001      |
| current smoker           | 1.119      | 0.802 – 1.561  | 0.438   | 1  | 0.51         |
| ASA                      |            |                |         |    |              |
| 1                        | Reference  |                |         |    |              |
| 2                        | 1.817      | 1.135 – 2.910  | 6.186   | 1  | 0.013        |
| 3                        | 4.668      | 2.872 – 7.588  | 38.633  | 1  | <0.0001      |
| 4                        | 9.589      | 5.383 – 17.081 | 58.894  | 1  | <0.0001      |
| Comorbidities            |            |                |         |    |              |
| Coronary artery disease  | 0.805      | 0.606-1.070    | 2.232   | 1  | 0.14         |
| Congestive heart failure | 1.803      | 1.339 – 2.429  | 15.062  | 1  | <0.0001      |
| Diabetes                 | 1.046      | 0.807 – 1.355  | 0.115   | 1  | 0.73         |
| Cirrhosis                | 2.050      | 1.023 – 4.105  | 4.102   | 1  | 0.043        |
| Metastatic cancer        | 1.744      | 1.227 – 2.480  | 9.597   | 1  | 0.0019       |
| Stroke                   | 1.133      | 0.756 – 1.699  | 0.367   | 1  | 0.55         |
| COPD                     | 1.104      | 0.823 – 1.482  | 0.436   | 1  | 0.51         |
| Severity of surgery      |            |                |         |    |              |
| Mild                     | Reference  |                |         |    |              |
| Moderate                 | 1.288      | 0.892 – 1.861  | 1.819   | 1  | 0.177        |
| Severe                   | 2.352      | 1.644 – 3.364  | 21.930  | 1  | <0.0001      |
| Checklist use            | 1.349      | 1.014 – 1.793  | 4.228   | 1  | 0.040        |
| Surgical Category        |            |                |         |    |              |
| Orthopaedics             | Reference  |                |         |    |              |
| Breast                   | 0.874      | 0.477 – 1.601  | 0.191   | 1  | 0.66         |
| Upper GI                 | 2.856      | 1.928 – 4.231  | 27.384  | 1  | <0.0001      |
| Lower GI                 | 2.603      | 1.810 – 3.743  | 26.656  | 1  | <0.0001      |
| Hepatobiliary            | 1.285      | 0.778 – 2.124  | 0.957   | 1  | 0.33         |
| Urology kidney           | 1.315      | 0.803 – 2.153  | 1.181   | 1  | 0.28         |
| Vascular                 | 2.401      | 1.514 – 3.808  | 13.868  | 1  | <0.0001      |
| Head and neck            | 1.134      | 0.750 – 1.716  | 0.355   | 1  | 0.55         |
| Plastics                 | 2.315      | 1.352 – 3.961  | 9.371   | 1  | 0.0022       |
| Cardiac                  | 3.067      | 2.103 – 4.474  | 33.856  | 1  | <0.0001      |
| Thoracic lung            | 1.252      | 0.674 – 2.326  | 0.506   | 1  | 0.48         |
| Neurosurgery             | 2.632      | 0.563 – 12.301 | 1.513   | 1  | 0.22         |
| Other                    | 1.359      | 0.822 – 2.246  | 1.427   | 1  | 0.23         |
| African setting          | 1.995      | 1.359 – 2.930  | 12.420  | 1  | <0.0001      |
| Constant                 | 0.005      |                | 128.445 | 1  | <0.0001      |

ASA=American Society of Anesthesiologists. COPD = chronic obstructive pulmonary disease. GIT = gastrointestinal tract. CI = confidence interval. DF = degrees of freedom. P value is for Pearson Chi-square test of independence.

## Appendix 2: African Surgical Outcomes Study (ASOS)

Age  years      Gender  M  F      Current smoker  Y  N

ASA  I  II  III  IV  V      Black ethnicity (eGFR)  Y  N

**Chronic co-morbid disease (tick all that apply):**

- |   |   |  |
|---|---|--|
| <input type="checkbox"/> Coronary artery disease              | <input type="checkbox"/> Congestive heart failure | <input type="checkbox"/> Diabetes mellitus |
| <input type="checkbox"/> Cirrhosis                            | <input type="checkbox"/> Metastatic cancer        | <input type="checkbox"/> Hypertension      |
| <input type="checkbox"/> Stroke or Transient ischaemic attack | <input type="checkbox"/> COPD / Asthma            | <input type="checkbox"/> HIV / AIDS        |
| <input type="checkbox"/> Chronic renal disease                |   |  |

**Most recent blood results (no more than 28 days before surgery):**

Haemoglobin  g/dL      Leucocytes  x10<sup>9</sup>/L      Creatinine  μmol/L

Start of surgery time (24h) & date: h h : m m      d d m m 2016

**Anaesthetic technique (✓)**  General  Spinal  Epidural  Sedation  Local  Other regional

**Surgical procedure category (select *single* most appropriate):**

- |  |  |  |
|--|--|--|
| <input type="checkbox"/> Orthopaedic             | <input type="checkbox"/> Breast                  | <input type="checkbox"/> Obstetrics              |
| <input type="checkbox"/> Gynaecology             | <input type="checkbox"/> Upper gastro-intestinal | <input type="checkbox"/> Lower gastro-intestinal |
| <input type="checkbox"/> Hepato-biliary          | <input type="checkbox"/> Urology & Kidney        | <input type="checkbox"/> Vascular                |
| <input type="checkbox"/> Head and neck           | <input type="checkbox"/> Plastics / Cutaneous    | <input type="checkbox"/> Cardiac                 |
| <input type="checkbox"/> Thoracic (lung & other) | <input type="checkbox"/> Thoracic (gut)          | <input type="checkbox"/> Neurosurgery            |
| <input type="checkbox"/> Cardiac surgery         |  |  |

Urgency of surgery:  Elective  Urgent  Emergency

Severity of surgery:  Minor  Intermediate  Major

Primary indication for surgery:  Infective  Non-communicable disease  Traumatic injury

Surgical checklist used (e.g. WHO checklist)  Y  N

Blood loss during surgery:  ml      Duration of surgery:  minutes

Critical care immediately after surgery  Y  N

**Anaesthetic complications:**  Failed intubation  Aspiration  Cardiac arrest  Severe hypoxia

**Most senior anaesthetist present in operating room:**

Specialist  Physician non specialist  Non physician or nurse anaesthetist  No anaesthetist

**Most senior surgeon present in operating room:**

Specialist  Physician non specialist  Non physician or nurse surgeon

ASOS unique patient ID

✂ -----

Patient name: \_\_\_\_\_      DOB d d m m y y y y

Patient hospital number : \_\_\_\_\_

## Postoperative Follow Up

### Infection

|                           |                               |                                   |                                 |                               |
|---------------------------|-------------------------------|-----------------------------------|---------------------------------|-------------------------------|
| Superficial surgical site | Mild <input type="checkbox"/> | Moderate <input type="checkbox"/> | Severe <input type="checkbox"/> | None <input type="checkbox"/> |
| Deep surgical site        | Mild <input type="checkbox"/> | Moderate <input type="checkbox"/> | Severe <input type="checkbox"/> | None <input type="checkbox"/> |
| Body cavity               | Mild <input type="checkbox"/> | Moderate <input type="checkbox"/> | Severe <input type="checkbox"/> | None <input type="checkbox"/> |
| Pneumonia                 | Mild <input type="checkbox"/> | Moderate <input type="checkbox"/> | Severe <input type="checkbox"/> | None <input type="checkbox"/> |
| Urinary tract             | Mild <input type="checkbox"/> | Moderate <input type="checkbox"/> | Severe <input type="checkbox"/> | None <input type="checkbox"/> |
| Bloodstream               | Mild <input type="checkbox"/> | Moderate <input type="checkbox"/> | Severe <input type="checkbox"/> | None <input type="checkbox"/> |

### Cardiovascular

|                       |                               |                                   |                                 |                               |
|-----------------------|-------------------------------|-----------------------------------|---------------------------------|-------------------------------|
| Myocardial infarction | Mild <input type="checkbox"/> | Moderate <input type="checkbox"/> | Severe <input type="checkbox"/> | None <input type="checkbox"/> |
| Arrhythmia            | Mild <input type="checkbox"/> | Moderate <input type="checkbox"/> | Severe <input type="checkbox"/> | None <input type="checkbox"/> |
| Pulmonary oedema      | Mild <input type="checkbox"/> | Moderate <input type="checkbox"/> | Severe <input type="checkbox"/> | None <input type="checkbox"/> |
| Pulmonary embolism    | Mild <input type="checkbox"/> | Moderate <input type="checkbox"/> | Severe <input type="checkbox"/> | None <input type="checkbox"/> |
| Stroke                | Mild <input type="checkbox"/> | Moderate <input type="checkbox"/> | Severe <input type="checkbox"/> | None <input type="checkbox"/> |
| Cardiac arrest        |                               |                                   | Severe <input type="checkbox"/> | None <input type="checkbox"/> |

### Miscellaneous complications

|                         |                               |                                   |                                 |                               |
|-------------------------|-------------------------------|-----------------------------------|---------------------------------|-------------------------------|
| Gastro-intestinal bleed | Mild <input type="checkbox"/> | Moderate <input type="checkbox"/> | Severe <input type="checkbox"/> | None <input type="checkbox"/> |
| Acute kidney injury     | Mild <input type="checkbox"/> | Moderate <input type="checkbox"/> | Severe <input type="checkbox"/> | None <input type="checkbox"/> |
| Postoperative bleed     |                               | Moderate <input type="checkbox"/> | Severe <input type="checkbox"/> | None <input type="checkbox"/> |
| ARDS                    | Mild <input type="checkbox"/> | Moderate <input type="checkbox"/> | Severe <input type="checkbox"/> | None <input type="checkbox"/> |
| Anastomotic breakdown   | Mild <input type="checkbox"/> | Moderate <input type="checkbox"/> | Severe <input type="checkbox"/> | None <input type="checkbox"/> |
| Other                   | Mild <input type="checkbox"/> | Moderate <input type="checkbox"/> | Severe <input type="checkbox"/> | None <input type="checkbox"/> |

Critical care admission to treat postoperative complications  No  Yes

Days in critical care after surgery 

|   |   |
|---|---|
| d | d |
|---|---|

Days in hospital after surgery 

|   |   |
|---|---|
| d | d |
|---|---|

Status at hospital discharge or 30<sup>th</sup> postoperative in-hospital day  Alive  Dead

ASOS unique patient ID 

|  |  |  |  |  |  |  |  |  |  |
|--|--|--|--|--|--|--|--|--|--|
|  |  |  |  |  |  |  |  |  |  |
|--|--|--|--|--|--|--|--|--|--|

✂ \_\_\_\_\_

Patient name: \_\_\_\_\_ DOB 

|   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|
| d | d | m | m | y | y | y | y |
|---|---|---|---|---|---|---|---|

Patient hospital number : \_\_\_\_\_

## Guidance for use of paper case record form (CRF)

Remove this page before use in data collection

1. This CRF is provided in a format which can be edited. If required, national co-ordinators should edit the blood results units to fit with those used in your country (eg some hospitals measure creatinine in  $\mu\text{mol/L}$  whilst in others  $\text{mg/dL}$  is standard). In some countries there will be differences in the use of units between hospitals so local edits may also be required. The internet based CRF will allow you to choose the units for each hospital.
2. Baseline data will often be readily available to anaesthetists during surgery whilst follow-up data on complications may be most easily collected by surgeons.
3. Investigators should write the patient name and date of birth on the CRF. When you enter the data on the internet based CRF you will receive an ASOS patient ID. Please write this on the paper CRF as well in case we need to contact you to check your data.
4. Please take care to enter the date clearly and correctly. Mistakes are common data describing time and date.
5. We only ask about black ethnicity to calculate estimated glomerular filtration rate.

ASOS unique patient ID

|  |  |  |  |  |  |  |  |  |  |
|--|--|--|--|--|--|--|--|--|--|
|  |  |  |  |  |  |  |  |  |  |
|--|--|--|--|--|--|--|--|--|--|

✂ -----

Patient name: \_\_\_\_\_

DOB

|   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|
| d | d | m | m | y | y | y | y |
|---|---|---|---|---|---|---|---|

Patient hospital number : \_\_\_\_\_

Patient name: .....

Date of birth: dd/mm/yyyy

### Appendix 3: International Surgical Outcomes Study Case Record Form v2.3

For use with Outcomes definitions guide

Age  years      Gender  M  F      Current smoker  Y  N

ASA  I  II  III  IV      Black ethnicity (eGFR)  Y  N

Chronic Disease (*tick all that apply*):

- Coronary Artery Disease
- Heart Failure
- Diabetes Mellitus
- Cirrhosis
- Metastatic cancer
- Stroke
- COPD / Asthma
- Other

Most recent blood results (no more than 28 days before surgery):

Haemoglobin  .  g/L      Leucocytes  .  x10<sup>9</sup>/L

Sodium  mmol/L      Creatinine  .  µmol/L

Anaesthesia induction time & date:

|   |   |   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| : | H | H | m | m | D | D | 0 | M | 2 | 0 | 1 | 4 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|

Anaesthetic technique (*tick all that apply*)

- General
- Spinal
- Epidural
- Sedation / Local

Surgical procedure category (*single best answer*):

- Orthopaedic
- Breast
- Obstetrics & Gynaecology
- Urology & Kidney
- Upper gastro-intestinal
- Lower gastro-intestinal
- Hepato-biliary
- Vascular
- Head and neck
- Plastics / Cutaneous
- Cardiac
- Thoracic (lung & other)
- Thoracic (gut)
- Other

Severity of surgery       Minor       Intermediate       Major

Laparoscopic surgery       Y       N

Cancer surgery       Y       N

Surgical checklist used (eg WHO checklist)       Y       N

Critical care immediately after surgery       Y       N

Data entry staff use only

ISOS patient Identifier:

Patient name: .....

Date of birth: dd/mm/yyyy

**Outcome after surgery**

**Infection**

- Superficial surgical site    Mild     Moderate     Severe     None
- Deep surgical site    Mild     Moderate     Severe     None
- Body cavity    Mild     Moderate     Severe     None
- Pneumonia    Mild     Moderate     Severe     None
- Urinary tract    Mild     Moderate     Severe     None
- Bloodstream    Mild     Moderate     Severe     None

**Cardiovascular**

- Myocardial infarction    Mild     Moderate     Severe     None
- Arrhythmia    Mild     Moderate     Severe     None
- Pulmonary oedema    Mild     Moderate     Severe     None
- Pulmonary embolism    Mild     Moderate     Severe     None
- Stroke    Mild     Moderate     Severe     None
- Cardiac arrest    Severe     None

**Other**

- Gastro-intestinal bleed    Mild     Moderate     Severe     None
- Acute kidney injury    Mild     Moderate     Severe     None
- Post-operative bleed    Moderate     Severe     None
- ARDS    Mild     Moderate     Severe     None
- Anastomotic leak    Mild     Moderate     Severe     None
- Other    Mild     Moderate     Severe     None

**Treatment for post-operative complications:**

- Drug therapy, blood transfusion or parenteral nutrition     Y     N
- Surgical or radiological procedure     Y     N
- Critical care admission     Y     N

Hours in Post-Anaesthetic Care Unit after surgery

|   |   |
|---|---|
| h | h |
|---|---|

Days in critical care after surgery

|   |   |
|---|---|
| d | d |
|---|---|

Days in hospital after surgery

|   |   |
|---|---|
| d | d |
|---|---|

Status at 30 days after surgery

Alive

Dead

Data entry staff use only

ISOS patient Identifier: 

|  |  |  |  |  |
|--|--|--|--|--|
|  |  |  |  |  |
|--|--|--|--|--|

|  |  |  |  |  |
|--|--|--|--|--|
|  |  |  |  |  |
|--|--|--|--|--|

Patient name: .....

Date of birth: dd/mm/yyyy

## Guidance for use of paper case record form (CRF)

Remove this page before use in data collection

1. This CRF is provided in a format which can be edited. If required, national co-ordinators should edit the blood results units to fit with those used in your country (eg most UK hospitals measure creatinine in  $\mu\text{mol/L}$  whilst in the USA mg/dL is standard). In some countries there will be differences in the use of units between hospitals so local edits may also be required. The internet based CRF will allow you to choose the units for each hospital.
2. Baseline data will often be readily available to anaesthetists during surgery whilst follow-up data on complications may be most easily collected by surgeons.
3. Investigators should write the patient name and date of birth on the CRF. When you enter the data on the internet based CRF you will receive an ISOS patient ID. Please write this on the paper CRF as well in case we need to contact you to check your data.
4. Please take care to enter the date clearly and correctly. Mistakes are common data describing time and date.
5. We only ask about black ethnicity to calculate estimated glomerular filtration rate.

---

Data entry staff use only

ISOS patient Identifier: 

|  |  |  |  |  |  |
|--|--|--|--|--|--|
|  |  |  |  |  |  |
|--|--|--|--|--|--|

|  |  |  |  |  |
|--|--|--|--|--|
|  |  |  |  |  |
|--|--|--|--|--|

**Appendix 4:**  
**Patient outcomes definition guide for the African Surgical Outcomes Study (ASOS)**

**Table of Contents**

Definitions of anaesthetic complications ..... 2

    Failed intubation: ..... 2

    Aspiration:..... 2

    Cardiac arrest:..... 2

    Severe hypoxia:..... 2

Definitions and grading of surgical complications ..... 3

    Acute Kidney Injury (AKI)..... 4

    Acute Respiratory Distress Syndrome (ARDS)..... 5

    Anastomotic breakdown ..... 6

    Arrhythmia..... 7

    Cardiac arrest..... 8

    (Cardiogenic) pulmonary oedema..... 9

    Gastro-intestinal bleed ..... 10

    Bloodstream infection ..... 11

    Myocardial infarction ..... 12

    Pneumonia ..... 13

    Postoperative haemorrhage ..... 14

    Pulmonary embolism (PE)..... 15

    Stroke ..... 16

    Surgical site infection (superficial) ..... 17

    Surgical site infection (deep) ..... 18

    Surgical site infection (organ/space) ..... 19

    Urinary tract infection..... 20

Hospital resource use after surgery ..... 21

    Critical care admission to treat postoperative complications:..... 21

    Days in critical care after surgery: ..... 21

    Days in hospital after surgery:..... 21

    Status at hospital discharge or 30<sup>th</sup> postoperative in-hospital day: ..... 21

Reference ..... 22

## Definitions of anaesthetic complications

The following definitions are provided for guidance where the nature of a possible complication following anaesthesia is uncertain.

### Failed intubation:

Failure to place the endotracheal tube after multiple intubation attempts.

### Aspiration:

Regurgitation or vomiting of gastric contents which has passed through the larynx into the trachea or tracheobronchial tree.

### Cardiac arrest:

Cardiac arrest associated with the induction or maintenance of general anaesthesia, regional anaesthesia or airway manipulation.

Cardiac arrest is defined as the cessation of cardiac mechanical activity, as confirmed by the absence of signs of circulation. ECG changes may corroborate the incidence of cardiac arrest.

### Severe hypoxia:

Hypoxia with a peripheral saturation of <90% on pulse oximetry, or clinical impression of hypoxia in the absence of a pulse oximeter.

## Definitions and grading of surgical complications

The following definitions and grading are provided for guidance where the nature and severity of a possible complication following surgery is uncertain. These definitions are based on the 'Standards for definitions and use of outcome measures for clinical effectiveness research in perioperative medicine: European Perioperative Clinical Outcome (EPCO) definitions: a statement from the ESA-ESICM joint taskforce on perioperative outcome measures'.<sup>1</sup>

## Acute Kidney Injury (AKI)

| <b>Acute Kidney Injury (AKI) Stage</b> | <b>Serum creatinine</b>   | <b>Urine output</b>                                    |
|--|---|--|
| Mild                                   | Increase of 1.5-1.9 times baseline value within 7 days or $\geq 0.3$ mg/dL (27 $\mu$ mol/L) within 48 hours   | $\leq 0.5$ ml/kg/h for 6-12 hours                      |
| Moderate                               | Increase of 2.0-2.9 times baseline value within 7 days  | $\leq 0.5$ ml/kg/h for 12 hours                        |
| Severe                                 | Increase of 3.0 times baseline within 7 days or increase in serum creatinine to $\geq 4.0$ mg/dL ( $\geq 354$ $\mu$ mol/L) with an acute rise of $>0.5$ mg/dL ( $>44$ $\mu$ mol/L) or initiation of renal replacement therapy | $\leq 0.3$ ml/kg/h for 24 hours or Anuria for 12 hours |

**Guidance:** Baseline serum creatinine must be measured before surgery but an estimated value can be used if the patient does not have chronic kidney disease.

## Acute Respiratory Distress Syndrome (ARDS)

Respiratory failure, or new or worsening respiratory symptoms, commencing within one week of surgery; and a chest radiograph or computed tomography scan which demonstrates bilateral opacities not fully explained by effusions, lobar/lung collapse, or nodules; and respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g. echocardiography) to exclude hydrostatic oedema if no risk factor is present.

### **Severity grading:**

Mild: PaO<sub>2</sub>:FiO<sub>2</sub> between 200 and 300 mmHg with PEEP or CPAP ≥5 cmH<sub>2</sub>O

Moderate: PaO<sub>2</sub>:FiO<sub>2</sub> between 100 and 200 mmHg with PEEP ≥5 cmH<sub>2</sub>O

Severe: PaO<sub>2</sub>:FiO<sub>2</sub> ≤100 mmHg with PEEP ≥5 cmH<sub>2</sub>O

### **Guidance:**

If altitude is higher than 1000 m, a correction factor should be calculated as follows: (PaO<sub>2</sub>:FiO<sub>2</sub> x [barometric pressure/760 mmHg]). PEEP, positive end-expiratory pressure; CPAP, non-invasive continuous positive airways pressure

### Anastomotic breakdown

Leak of luminal contents from a surgical connection between two hollow viscera. The luminal contents may emerge either through the wound or at the drain site, or they may collect near the anastomosis, causing fever, abscess, septicaemia, metabolic disturbance and/or multiple-organ failure. The escape of luminal contents from the site of the anastomosis into an adjacent localised area, detected by imaging, in the absence of clinical symptoms and signs should be recorded as a sub-clinical leak.

#### **Severity grading:**

Mild: Results in only temporary harm and would not usually require specific clinical treatment.

Moderate: More serious complication but one which does not usually result in permanent harm or functional limitation. Usually requires clinical treatment.

Severe: Results in significant prolongation of hospital stay and/or permanent functional limitation or death. Almost always requires clinical treatment.

## Arrhythmia

Electrocardiograph (ECG) evidence of cardiac rhythm disturbance.

### **Severity grading:**

Mild: Results in only temporary harm and would not usually require specific clinical treatment.

Moderate: More serious complication but one which does not usually result in permanent harm or functional limitation. Usually requires clinical treatment.

Severe: Results in significant prolongation of hospital stay and/or permanent functional limitation or death. Almost always requires clinical treatment.

### Cardiac arrest

The cessation of cardiac mechanical activity, as confirmed by the absence of signs of circulation. ECG changes may corroborate the incidence of cardiac arrest.

**Severity grading:** None

## (Cardiogenic) pulmonary oedema

Evidence of fluid accumulation in the alveoli due to poor cardiac function.

### **Severity grading:**

Mild: Results in only temporary harm and would not usually require specific clinical treatment.

Moderate: More serious complication but one which does not usually result in permanent harm or functional limitation. Usually requires clinical treatment.

Severe: Results in significant prolongation of hospital stay and/or permanent functional limitation or death. Almost always requires clinical treatment.

## Gastro-intestinal bleed

Unambiguous clinical or endoscopic evidence of blood in the gastro-intestinal tract.

Upper gastrointestinal bleeding is that originating from the oesophagus, stomach and duodenum. Lower gastro-intestinal bleeding originates from the small bowel and colon.

### **Severity:**

Mild: Results in only temporary harm and would not usually require specific clinical treatment.

Moderate: More serious complication but one which does not usually result in permanent harm or functional limitation. Usually requires clinical treatment.

Severe: Results in significant prolongation of hospital stay and/or permanent functional limitation or death. Almost always requires clinical treatment.

## Bloodstream infection

An infection which is not related to infection at another site and which meets at least one of the following criteria:

1. Patient has a recognised pathogen cultured from blood cultures which is not related to an infection at another site
2. Patient has at least one of the following signs or symptoms: fever ( $>38^{\circ}\text{C}$ ), chills, or hypotension and at least one of the following:
  - a. common skin contaminant cultured from two or more blood cultures drawn on separate occasions
  - b. common skin contaminant cultured from at least one blood culture from a patient with an intravascular line, and a physician starts antimicrobial therapy
  - c. positive blood antigen test

### **Severity:**

Mild: Results in only temporary harm and would not usually require specific clinical treatment.

Moderate: More serious complication but one which does not usually result in permanent harm or functional limitation. Usually requires clinical treatment.

Severe: Results in significant prolongation of hospital stay and/or permanent functional limitation or death. Almost always requires clinical treatment.

## Myocardial infarction

Increase in serum cardiac biomarker values (preferably cardiac troponin) with at least one value above the 99th percentile upper reference limit and at least one of the following criteria:

1. Symptoms of ischaemia
2. New or presumed new ST-segment or T-wave ECG changes or new left bundle branch block
3. Development of pathological Q-waves on ECG
4. Radiological or echocardiographic evidence of new loss of viable myocardium or new regional wall motion abnormality
5. Identification of an intra-coronary thrombus at angiography or autopsy

### **Severity grading:**

Mild: Results in only temporary harm and would not usually require specific clinical treatment.

Moderate: More serious complication but one which does not usually result in permanent harm or functional limitation. Usually requires clinical treatment.

Severe: Results in significant prolongation of hospital stay and/or permanent functional limitation or death. Almost always requires clinical treatment.

## Pneumonia

Chest radiographs with new or progressive and persistent infiltrates, or consolidation, or cavitation, and at least one of the following:

1. fever ( $>38^{\circ}\text{C}$ ) with no other recognized cause
2. leucopaenia ( $<4,000$  white blood cells/ $\text{mm}^3$ ) or leucocytosis ( $>12,000$  white blood cells/ $\text{mm}^3$ )
3. for adults  $>70$  years old, altered mental status with no other recognised cause;

and at least two of the following:

1. new onset of purulent sputum or change in character of sputum, or increased respiratory secretions, or increased suctioning requirements
2. new onset or worsening cough, or dyspnoea, or tachypnoea
3. rales or bronchial breath sounds
4. worsening gas exchange (hypoxaemia, increased oxygen requirement or increased ventilator demand)

**Guidance:** Two radiographs are required for patients with underlying pulmonary or cardiac disease. The definition may be used to identify ventilator associated pneumonia.

### Severity:

Mild: Results in only temporary harm and would not usually require specific clinical treatment.

Moderate: More serious complication but one which does not usually result in permanent harm or functional limitation. Usually requires clinical treatment.

Severe: Results in significant prolongation of hospital stay and/or permanent functional limitation or death. Almost always requires clinical treatment.

### Postoperative haemorrhage

Blood loss occurring within 72 hours after the end of surgery which would normally result in transfusion of blood. Gastro-intestinal bleeding is defined above.

**Severity:**

Mild: Not applicable

Moderate: More serious complication but one which does not usually result in permanent harm or functional limitation. Usually requires clinical treatment.

Severe: Results in significant prolongation of hospital stay and/or permanent functional limitation or death. Almost always requires clinical treatment.

## Pulmonary embolism (PE)

A new blood clot or thrombus within the pulmonary arterial system.

**Guidance:** Appropriate diagnostic tests include scintigraphy and CT angiography. Plasma D-dimer measurement is not recommended as a diagnostic test in the first three weeks following surgery.

### **Severity:**

**Mild:** Results in only temporary harm and would not usually require specific clinical treatment.

**Moderate:** More serious complication but one which does not usually result in permanent harm or functional limitation. Usually requires clinical treatment.

**Severe:** Results in significant prolongation of hospital stay and/or permanent functional limitation or death. Almost always requires clinical treatment.

## Stroke

Embolic, thrombotic, or haemorrhagic cerebral event with persistent residual motor, sensory, or cognitive dysfunction (e.g. hemiplegia, hemiparesis, aphasia, sensory deficit, impaired memory).

### **Severity:**

Mild: Results in only temporary harm and would not usually require specific clinical treatment.

Moderate: More serious complication but one which does not usually result in permanent harm or functional limitation. Usually requires clinical treatment.

Severe: Results in significant prolongation of hospital stay and/or permanent functional limitation or death. Almost always requires clinical treatment.

### Surgical site infection (superficial)

Infection involving only superficial surgical incision which meets the following criteria:

1. Infection occurs within 30 days after surgery and
2. Involves only skin and subcutaneous tissues of the incision and
3. The patient has at least one of the following:
  - a. purulent drainage from the superficial incision
  - b. organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision and at least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat, or superficial incision is deliberately opened by surgeon and is culture positive or not cultured. A culture-negative finding does not meet this criterion.
  - c. diagnosis of a incisional surgical site infection by a surgeon or attending physician

#### **Severity:**

Mild: Results in only temporary harm and would not usually require specific clinical treatment.

Moderate: More serious complication but one which does not usually result in permanent harm or functional limitation. Usually requires clinical treatment.

Severe: Results in significant prolongation of hospital stay and/or permanent functional limitation or death. Almost always requires clinical treatment.

### Surgical site infection (deep)

An infection which involves both superficial and deep parts of surgical incision and meets the following criteria:

1. Infection occurs within 30 days after surgery if no surgical implant is left in place or one year if an implant is in place and
2. The infection appears to be related to the surgical procedure and involves deep soft tissues of the incision (e.g. fascial and muscle layers) and
3. The patient has at least one of the following:
  - a. purulent drainage from the deep incision but not from the organ/space component of the surgical site
  - b. a deep incision spontaneously dehisces or is deliberately opened by a surgeon and is culture-positive or no cultures were taken whilst the patient has at least one of the following signs or symptoms of infection: fever ( $>38^{\circ}\text{C}$ ) or localized pain or tenderness. A culture-negative finding does not meet this criterion.
  - c. an abscess or other evidence of infection involving the deep incision is found on direct examination, during surgery, or by histopathologic or radiologic examination
  - d. diagnosis of a deep incisional surgical site infection by a surgeon or attending physician

#### **Severity:**

Mild: Results in only temporary harm and would not usually require specific clinical treatment.

Moderate: More serious complication but one which does not usually result in permanent harm or functional limitation. Usually requires clinical treatment.

Severe: Results in significant prolongation of hospital stay and/or permanent functional limitation or death. Almost always requires clinical treatment.

### Surgical site infection (organ/space)

An infection which involves any part of the body excluding the fascia or muscle layers and meets the following criteria:

1. Infection occurs within 30 days after surgery and
2. The infection appears to be related to the surgical procedure and involves any part of the body, excluding the skin incision, fascia, or muscle layers, that is opened or manipulated during the operative procedure and
3. The patient has at least one of the following:
  - a. purulent drainage from a drain that is placed through a stab wound into the organ/space
  - b. organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/ space
  - c. an abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination
  - d. diagnosis of an organ/space surgical site infection by a surgeon or attending physician

#### **Severity:**

Mild: Results in only temporary harm and would not usually require specific clinical treatment.

Moderate: More serious complication but one which does not usually result in permanent harm or functional limitation. Usually requires clinical treatment.

Severe: Results in significant prolongation of hospital stay and/or permanent functional limitation or death. Almost always requires clinical treatment.

## Urinary tract infection

An infection associated with at least one of the following signs or symptoms which should be identified within a 24 hour period; fever ( $>38\text{ }^{\circ}\text{C}$ ), urgency, frequency, dysuria, suprapubic tenderness, costovertebral angle pain or tenderness with no other recognised cause, and a positive urine culture of  $\geq 10^5$  colony forming units/mL with no more than two species of microorganisms.

### **Severity:**

Mild: Results in only temporary harm and would not usually require specific clinical treatment.

Moderate: More serious complication but one which does not usually result in permanent harm or functional limitation. Usually requires clinical treatment.

Severe: Results in significant prolongation of hospital stay and/or permanent functional limitation or death. Almost always requires clinical treatment.

## Hospital resource use after surgery

We will collect some basic data to describe the treatment resources patients received after surgery.

### Critical care admission to treat postoperative complications:

Postoperative complications requiring admission to critical care to treat the postoperative complications or provide critical care support necessitated by the severity of the postoperative complications.

**Days in critical care after surgery:** Total number of days in critical care within the first 30 days after surgery. May include multiple admissions and planned admission to critical care immediately after surgery.

**Days in hospital after surgery:** Total number of days in hospital after surgery.

**Status at hospital discharge or 30<sup>th</sup> postoperative in-hospital day:** The survival status of the patient at hospital discharge, or at the 30 in-hospital day (if the patient had not yet been discharged following surgery). The study is censored at the 30<sup>th</sup> in hospital postoperative day.

## Reference

1. Jammer I, Wickboldt N, Sander M, et al. Standards for definitions and use of outcome measures for clinical effectiveness research in perioperative medicine: European Perioperative Clinical Outcome (EPCO) definitions: a statement from the ESA-ESICM joint taskforce on perioperative outcome measures. *Eur J Anaesthesiol* 2015;**32**(2):88-105.



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



Room G50- Old Main Building  
Groote Schuur Hospital  
Observatory 7925  
Telephone [021] 406 6492  
Email: [hrec-enquiries@uct.ac.za](mailto:hrec-enquiries@uct.ac.za)  
Website: [www.health.uct.ac.za/fhs/research/humanethics/forms](http://www.health.uct.ac.za/fhs/research/humanethics/forms)

08 September 2020

**HREC REF: 447/2020**

**Prof S Maswime**  
Department of Surgery  
J-45, OMB  
Email: [Salome.maswime@uct.ac.za](mailto:Salome.maswime@uct.ac.za)  
Student: [amyfrancespaterson@gmail.com](mailto:amyfrancespaterson@gmail.com)

Dear Prof Maswime

**PROJECT TITLE: AFRICAN SURGICAL OUTCOMES STUDY (ASOS)-MSc-CANDIDATE DR AMY PATERSON-SUB-STUDY LINKIED TO R004/2016**

Thank you for your response letter, addressing the issues raised by the Faculty of Health Sciences Human Research Ethics Committee (HREC).

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

**This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19, dated 17 March 2020.**

**Approval is granted for one year until the 30 September 2021.**

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](http://www.health.uct.ac.za/fhs/research/humanethics/forms))

**The HREC acknowledge that the student: - Dr Amy Paterson 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**

HREC REF: 447/2020(001)

Federal Wide Assurance Number: FWA00001637,  
Institutional Review Board (IRB) number: IRB00001938  
NHREC-registration number: REC-210208-007

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 Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use: 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..

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

|                              | <b>Item No</b> | <b>Recommendation</b>   |
|------------------------------|----------------|---|
| <b>Title and abstract</b>    | 1              | (a) Indicate the study's design with a commonly used term in the title or the abstract<br>(b) Provide in the abstract an informative and balanced summary of what was done and what was found   |
| <b>Introduction</b>          |                |   |
| Background/rationale         | 2              | Explain the scientific background and rationale for the investigation being reported  |
| Objectives                   | 3              | State specific objectives, including any prespecified hypotheses  |
| <b>Methods</b>               |                |   |
| Study design                 | 4              | Present key elements of study design early in the paper   |
| Setting                      | 5              | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection   |
| Participants                 | 6              | (a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>(b) For matched studies, give matching criteria and number of exposed and unexposed   |
| Variables                    | 7              | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable  |
| Data sources/<br>measurement | 8*             | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group  |
| Bias                         | 9              | Describe any efforts to address potential sources of bias   |
| Study size                   | 10             | Explain how the study size was arrived at   |
| Quantitative variables       | 11             | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why  |
| Statistical methods          | 12             | (a) Describe all statistical methods, including those used to control for confounding<br>(b) Describe any methods used to examine subgroups and interactions<br>(c) Explain how missing data were addressed<br>(d) If applicable, explain how loss to follow-up was addressed<br>(e) Describe any sensitivity analyses  |
| <b>Results</b>               |                |   |
| Participants                 | 13*            | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed<br>(b) Give reasons for non-participation at each stage<br>(c) Consider use of a flow diagram   |
| Descriptive data             | 14*            | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders<br>(b) Indicate number of participants with missing data for each variable of interest<br>(c) Summarise follow-up time (eg, average and total amount)  |
| Outcome data                 | 15*            | Report numbers of outcome events or summary measures over time  |
| Main results                 | 16             | (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included<br>(b) Report category boundaries when continuous variables were categorized<br>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |

|                          |    |  |
|--------------------------|----|--|
| Other analyses           | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses   |
| <b>Discussion</b>        |    |  |
| Key results              | 18 | Summarise key results with reference to study objectives   |
| Limitations              | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias                 |
| Interpretation           | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence |
| Generalisability         | 21 | Discuss the generalisability (external validity) of the study results  |
| <b>Other information</b> |    |  |
| Funding                  | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based              |

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.



# THE SOUTH AFRICAN MEDICAL ASSOCIATION

Tel: +27 (0)12 481 2000 | Fax: +27 (0)12 481 2100 | [www.samedical.org](http://www.samedical.org)  
Block F | Castle Walk Office Park | Nossob Street | Erasmuskloof | Ext 3 | Pretoria | 0181  
PO Box 74789 | Lynnwood Ridge | 0040  
Reg No 1927/000136/08 | NPC

25 August 2021

Dear Dr Paterson

This letter serves to confirm that the manuscript titled 'Improving surgical and medical outcomes, beyond maternal mortality' which you have co-authored and submitted to the South African Journal of Obstetrics and Gynaecology, was accepted for publication.

Co-authors include: L Cairncross, T Adams, BM Biccard, S Maswime

The article is scheduled to appear in the following issue: SAJOG Vol 27 (1).

We thank you for considering the South African Journal of Obstetrics and Gynaecology as an avenue for publication of your work.

Yours sincerely  
Claudia Naidu

Managing Editor  
Publishing Department  
South African Medical Association

*The Lancet Global Health* publishes high-quality original research, commentary, and correspondence on the following subjects as they pertain to low- and middle-income countries: reproductive, maternal, neonatal, and child health; adolescent health; infectious diseases, including neglected tropical diseases; non-communicable diseases; mental health; the global health workforce; health systems; public health; and health policy. Wherever possible, figures and good quality photographs (colour or black and white) should be used to supplement and to enhance the text. We also welcome videos. Further details on the different sections of *The Lancet Global Health*, and how to submit to the journal, are provided below. If you require further clarification, the journal's editorial staff will be pleased to help (email [globalhealth@lancet.com](mailto:globalhealth@lancet.com)).

Manuscripts must be solely the work of the author(s) stated, must not have been previously published elsewhere, and must not be under consideration by another journal. *The Lancet* journals are signatories of the [Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals](#), issued by the International Committee of Medical Journal Editors (ICMJE Recommendations), and to the Committee on Publication Ethics (COPE) code of conduct for editors. We follow [COPE's guidelines](#).

[Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals](#)  
<http://www.icmje.org>

## How to submit your paper

### Manuscript submission

Manuscript submission to all *Lancet* journals is free. Payment of article processing fees is made after acceptance (see later). Manuscripts should be submitted online via the *The Lancet Global Health's* online submission and peer review website (known as EM) at [www.editorialmanager.com/langlh](http://www.editorialmanager.com/langlh)

- Simply log on to EM and follow the on-screen instructions for all submissions
- If you have not used EM before, you will need to register first. In EM, the corresponding author is the person who enters the manuscript details and uploads the submission files
- Inclusion of illustrations (eg, photographs, graphs, diagrams) is a prerequisite for many publication types. Submission of original and editable artwork files is encouraged. Digital photography files should have a resolution of at least 300 dpi and be at least 107 mm wide. Before and after images should be taken with the same intensity, direction, and colour of light.
- In almost all cases, if you have a finished manuscript, you should submit it, rather than contacting *The Lancet Global Health* to enquire whether an unseen manuscript is likely to be accepted. Unless you have been asked by the Editor to submit by email, you should use the online system for all types of submission, including Correspondence
- If you have any technical problems or questions, please contact our dedicated customer support:

For the Americas: +1 888 8347287 (09:00 to 17:00 central standard time)

For Asia and Pacific: +81 3 55615032 (09:30 to 17:30 Japan standard time)

For Europe and rest of the world: +44 1865 843577 (08:30 to 17:00 GMT)

For Chinese-speaking customers: +86 10 85208780 (9:00 to 17:30 China standard time)

For Spanish-speaking customers: +34 932 406176 (09:00 to 17:00 GMT)

For French-speaking customers: +33 171 165608 (09:00 to 17:00 GMT)

Email: [globalhealth@lancet.com](mailto:globalhealth@lancet.com)

### Covering letter

- You should upload your covering letter at the "Enter Comments" stage of the online submission process

### First submissions to *The Lancet Global Health* should include:

- 1 Covering letter
- 2 Manuscript including tables and panels
- 3 Figures
- 4 Author statement form (see next section)
- 5 Declaration of interests and source of funding statements (see next section)
- 6 In-press papers—one copy of each with acceptance letters
- 7 Protocols and CONSORT details for randomised controlled trials (see Articles)
- 8 We encourage disclosure of correspondence from other journals and reviewers, if previously submitted, and we might contact relevant editors of such journals
- 9 Research in context panel, for all primary research Articles

- Use the covering letter to explain why your paper should be published in *The Lancet Global Health* rather than elsewhere

## Statements, permissions, and signatures

### Authors and contributors

- Designated authors should meet all four criteria for authorship in the ICMJE Recommendations
- All authors, and all contributors (including medical writers and editors), should specify their individual contributions at the end of the text
- We require that more than one author has verified the underlying data. The contributors statement should state who those authors are.
- We encourage collaboration and coauthorship with colleagues in the locations where the research is conducted
- The *Lancet* Group takes a neutral position with respect to territorial claims in institutional affiliations
- When choosing coauthors, we ask lead authors to be mindful of the benefits of diversity in authorship and to consider inviting coauthors who reflect diversity in every sense, including (but not limited to) background, career-stage, gender, geography, and race
- *The Lancet Global Health* will not publish any paper unless we have the signatures of all authors
- We suggest you use the [author statement form](#) and upload the signed copy with your submission

[COPE Core Practices](https://publicationethics.org/core-practices)  
<https://publicationethics.org/core-practices>

[ICMJE Recommendations](http://www.icmje.org)  
<http://www.icmje.org>

[Author statement form](https://www.thelancet.com/for-authors/forms?section=tlgh-author-sig)  
<https://www.thelancet.com/for-authors/forms?section=tlgh-author-sig>

- Please include written consent of any cited individual(s) noted in acknowledgments or personal communications
- For author groups of more than 30 members, we encourage use of a collaborator or study group for any additional authors. For this collaborator or study group, if they wish to be indexed to the paper, please provide a separate document with a table of first names and surnames of all members of the group (this is to ensure that PubMed and similar databases encode the names correctly).

### Forms and signatures

For Comments and Correspondence, we require you to upload your forms at submission. For original research (Articles), we will request these forms after peer review. The following signed statements are required:

- **Authors' contributions**
- **Conflicts of interest statements** (ICMJE forms)
- Statements of role, if any, of medical writer or editor
- Acknowledgments—written consent of cited individual
- Personal communications—written consent of cited individual
- Use of copyright-protected material—signed permission statements from author and publisher

These statements can be scanned and submitted electronically with your submission. Please note that *The Lancet* journals will accept hand-signed and electronic (typewritten) signatures.

### Declaration of interests

A conflict of interest exists when professional judgement concerning a primary interest (such as patients' welfare or validity of research) may be influenced by a secondary interest (such as financial gain). Financial relationships are easily identifiable, but conflicts can also occur because of personal relationships or rivalries, academic competition, or intellectual beliefs. A conflict can be actual or potential, and full disclosure to the Editor of all relationships is a requisite. Purposeful failure to disclose conflicts is a form of misconduct and might lead to publication of a correction or even to retraction. All submissions to *The Lancet Global Health* must include disclosure of all relationships in which there is a potential or actual conflict of interest, even if it not directly relevant to the submitted work. The Editor may use such information as a basis for editorial decisions and will publish all disclosures that authors declare on their conflict of interests form. It is the corresponding author's responsibility to check that all declarations made by authors on their conflicts of interest form are included at the end of the manuscript. Agreements between authors and study sponsors that interfere with authors' access to all of a study's data, or that interfere with their ability to analyse and interpret the data and to prepare and publish manuscripts independently, may represent conflicts of interest, and should be avoided. Authors may be required to provide the journal with any such agreements in confidence.

- At the end of the text, under a subheading "Declaration of interests", all authors must disclose any financial and personal relationships with other people or organisations, even if it does not directly relate to the submitted work. Examples of financial conflicts include employment, consultancies, stock ownership, honoraria, paid expert testimony, patents or patent applications, and travel grants, all within 3 years of beginning the work submitted. If there are no conflicts of interest, authors should state that none exist
- All authors are required to provide a Conflict of Interest Statement

and should complete a standard form, which is available at <https://www.thelancet.com/for-authors/forms?section=icmje-coi>. The form has been modified by the ICMJE following consultation with authors and editors. Further information is available in a joint ICMJE statement published on July 1, 2010. For more information see *Lancet* 2009; 374: 1395–96.

- For Comments, *The Lancet Global Health* will not publish if an author, within the past 3 years, and with a relevant company or competitor, has any stocks or shares, equity, a contract of employment, or a named position on a company board; or has been asked by any organisation other than *The Lancet Global Health* to write, be named on, or to submit the paper (see *Lancet* 2004; 363: 2–3)

### Role of the funding source

- All sources of funding should be declared as an acknowledgment at the end of the text
- At the end of the Methods section, under a subheading "Role of the funding source", authors must describe the role of the study sponsor(s), if any, in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication
- If there is no Methods section, the role of the funding source should be stated as an acknowledgment. If the funding source had no such involvement, the authors should state this
- All authors should confirm that they had full access to all the data in the study and accept responsibility to submit for publication.

### Role of medical writer or editor

- If a medical writer or editor was involved in the creation of your manuscript, we need a signed statement from the corresponding author to include their name and information about funding of this person
- This information should be added to the Acknowledgments or Contributors section
- We require signed statements from any medical writers or editors declaring that they have given permission to be named as an author, as a contributor, or in the Acknowledgments section

### Patient and other consents

- Appropriate written consents, permissions, and releases must be obtained where you wish to include any case details, personal information, and/or images of patients or other individuals in *The Lancet* journals in order to comply with all applicable laws and regulations concerning privacy and/or security of personal information. Studies on patients or volunteers need approval from an ethics committee and informed consent from participants. These should be documented in your paper.
- Do not use "blackout" bars or similar devices to anonymise patients in clinical images: if you have taken consent appropriately masking is not needed.
- Since the consent form needs to comply with the relevant legal requirements of your particular jurisdiction, we do not provide sample forms; this is your responsibility. Your affiliated institution should be able to provide an appropriate form.
- For the purposes of publishing in *The Lancet* journals, a **consent**, permission, or release should include, without limitation, publication in all formats (including print, electronic, and

ICMJE COI form  
<https://www.thelancet.com/for-authors/forms?section=icmje-coi>  
Joint ICMJE statement  
<https://www.thelancet.com/for-authors/forms?section=icmje-statement>

Patient Consent form  
<http://www.thelancet.com/pb/assets/raw/Lancet/authors/lancet-consent-form.pdf>

websites), in sublicensed and reprinted versions (including translations), and in other works and products.

- To respect your patient's and any other individual's privacy, please do not send signed forms to *The Lancet Global Health*. Please instead complete the patient consent section of the [Author statements](#) while retaining copies of the signed forms in the event they should be needed.
- If consent, permission, or release is made subject to any conditions, *The Lancet Global Health* must be made aware in writing of all such conditions before publication.
- For more information about our policy, please visit <https://www.elsevier.com/about/our-business/policies/patient-consent>.

### Types of article and manuscript requirements

Please ensure that anything you submit to *The Lancet Global Health* follows the guidelines provided for each article type. For instruction on how to format the text of your paper, including tables, figures, panels, and references, please see our [Formatting guidelines](#).

## Red section (Articles)

### Articles

- The Lancet Global Health* prioritises reports of original research that are likely to change clinical practice or thinking
- We invite submission of all clinical trials, whether phase 1, 2, 3, or 4. For phase 1 trials, we consider those of a novel substance for a novel indication, if there is a strong or unexpected beneficial or adverse response, or a novel mechanism of action
- We require the registration of all interventional trials, whether early or late phase, in a primary register that participates in [WHO's International Clinical Trial Registry Platform](#) (see *Lancet* 2007; **369**: 1909–11) or in [ClinicalTrials.gov](#), in accord with [ICMJE recommendations](#). We also encourage full public disclosure of the minimum 21-item trial registration dataset at the time of registration and before recruitment of the first participant (see *Lancet* 2006; **367**: 1631–35). The registry must be independent of for-profit interest
- Reports of trials must conform to [CONSORT 2010 guidelines](#) and should be submitted with their protocols
- All reports of randomised trials should include a section entitled Randomisation and masking, within the Methods section. Please refer to *The Lancet's* [formatting guidelines for randomised trials](#)
- Cluster-randomised trials must be reported according to [CONSORT extended guidelines](#)
- Randomised trials that report harms must be described according to [extended CONSORT guidelines](#)
- Studies of diagnostic accuracy must be reported according to [STARD guidelines](#)
- Observational studies (cohort, case-control, or cross-sectional designs) must be reported according to the [STROBE statement](#), and should be submitted with their protocols
- We encourage the registration of all observational studies on a WHO-compliant registry (see *Lancet* 2010; **375**: 348)
- Genetic association studies must be reported according to [STREGA guidelines](#)
- Systematic reviews and meta-analyses must be reported according to [PRISMA guidelines](#). Please refer to *The Lancet's*

[formatting guidelines for systematic reviews and meta-analyses](#).

- Reports of studies of global health estimates should be reported according to the [GATHER](#) statement (see *Lancet* 2016; **388**: e19–23)
- Clinical trials that report interventions using artificial intelligence must be described according to the [CONSORT-AI Extension guidelines](#) and their protocols must be described according to the [SPIRIT-AI Extension guidelines](#)
- To find reporting guidelines see: <http://www.equator-network.org>

### All Articles should, as relevant:

- Be up to 3500 words (4500 for randomised controlled trials) with 30 references (the word count is for the manuscript text only)
- Include an abstract (semistructured summary), with five paragraphs (Background, Methods, Findings, Interpretation, and Funding), not exceeding 250 words. Our electronic submission system will ask you to copy and paste this section at the "Submit Abstract" stage
- For randomised trials, the abstract should adhere to CONSORT extensions: abstracts (see *Lancet* 2008; **371**: 281–83)
- When reporting Kaplan-Meier survival data, at each timepoint, authors must include numbers at risk, and are encouraged to include the number of censored patients.
- For intervention studies, the abstract should include the primary outcome expressed as the difference between groups with a confidence interval on that difference (absolute differences are more useful than relative ones). Secondary outcomes can be included as long as they are clearly marked as secondary and all such outcomes are reported
- Use the recommended international non-proprietary name (rINN) for drug names. Ensure that the dose, route, and frequency of administration of any drug you mention are correct
- Use gene names approved by the [Human Gene Organisation](#). Novel gene sequences should be deposited in a public database (GenBank, EMBL, or DDBJ), and the accession number provided. Authors of microarray papers should include in their submission the information recommended by the [MIAME guidelines](#). Authors should also submit their experimental details to one of the publicly available databases: [ArrayExpress](#) or [GEO](#)
- Include any necessary additional data as part of your EM submission
- All accepted Articles should include a link to the full study protocol published on the authors' institutional website (see *Lancet* 2009; **373**: 992 and *Lancet* 2010; **375**: 348)
- We encourage researchers to enrol women and ethnic groups into clinical trials of all phases, and to plan to analyse data by sex and by race
- For all study types, we encourage correct use of the terms sex (when reporting biological factors) and gender (when reporting identity, psychosocial, or cultural factors). Where possible, report the sex and/or gender of study participants, and describe the methods used to determine sex and gender. Separate reporting of data by demographic variables, such as age and sex, facilitates pooling of data for subgroups across studies and should be routine, unless inappropriate. Discuss the influence or association of variables, such as sex and/or gender, on your findings, where appropriate, and the limitations of the data.

[CONSORT-AI Extension guidelines](#)

[https://doi.org/10.1016/S2589-7500\(20\)30218-1](https://doi.org/10.1016/S2589-7500(20)30218-1)

[SPRIT-AI Extension guidelines](#)

[https://doi.org/10.1016/S2589-7500\(20\)30219-3](https://doi.org/10.1016/S2589-7500(20)30219-3)

To find reporting guidelines, see <http://www.equator-network.org>

[WHO's International Clinical Trial Registry Platform](#)

<http://www.who.int/ictrp/network/trds/en/index.html>

[Clinical trials](#)

<http://clinicaltrials.gov>

[ICMJE recommendations](#)

<http://icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html>

[CONSORT 2010 guidelines](#)

<http://www.consort-statement.org/consort-2010>

[CONSORT extended guidelines](#)

<http://www.consort-statement.org/extensions/extensions/>

[STARD guidelines](#)

<http://www.equator-network.org/reporting-guidelines/stard/>

[STROBE statement](#)

<http://www.strobe-statement.org/>

[Formatting guidelines for randomised trials](#)

<https://www.thelancet.com/for-authors/forms?section=rct>

[STREGA guidelines](#)

<http://www.equator-network.org/reporting-guidelines/strobe-strega/>

[PRISMA guidelines](#)

<http://www.prisma-statement.org/>

[GATHER statement](#)

[http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(16\)30388-9/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(16)30388-9/fulltext)

[Human Gene Organisation](#)

<http://www.genenames.org/>

[MIAME guidelines](#)

<http://fged.org/projects/miame/>

[Formatting guidelines for meta-analyses](#)

<https://www.thelancet.com/for-authors/forms?section=meta-analysis>

[Array and GEO](#)

<http://www.ebi.ac.uk/microarray-as/ae/>  
<http://www.ncbi.nlm.nih.gov/geo>

### Putting research into context

- All research papers (including systematic reviews/meta-analyses) submitted to any journal in *The Lancet* family must include a panel putting their research into context with previous work in the format outlined below (see *Lancet* 2014; 384: 2176–77, for the original rationale). This panel should not contain references. Editors will use this information at the first assessment stage and peer reviewers will be specifically asked to check the content and accuracy
- The Discussion section should contain a full description and discussion of the context. Authors are also invited to either report their own, up-to-date systematic review or cite a recent systematic review of other trials, putting their trial into context of the review

MENDELEY data  
<https://data.mendeley.com>

#### Research in context

##### Evidence before this study

This section should include a description of all the evidence that the authors considered before undertaking this study. Authors should briefly state: the sources (databases, journal or book reference lists, etc) searched; the criteria used to include or exclude studies (including the exact start and end dates of the search), which should not be limited to English language publications; the search terms used; the quality (risk of bias) of that evidence; and the pooled estimate derived from meta-analysis of the evidence, if appropriate.

##### Added value of this study

Authors should describe here how their findings add value to the existing evidence.

##### Implications of all the available evidence

Authors should state the implications for practice or policy and future research of their study combined with existing evidence.

*Research in context panels should not contain references; key studies mentioned here should be referenced in the main text.*

### Data sharing

From September 21, 2020, all submitted research Articles must contain a data sharing statement, to be included at the end of the manuscript. Data sharing statements must include:

- Whether data collected for the study, including individual participant data and a data dictionary defining each field in the set, will be made available to others (“undecided” is not an acceptable answer);
- What data will be made available (deidentified participant data, participant data with identifiers, data dictionary, or other specified data set);
- Whether additional, related documents will be available (eg, study protocol, statistical analysis plan, informed consent form);
- When these data will be available (beginning and end date, or “with publication”, as applicable);
- Where the data will be made available (including complete URLs or email addresses if relevant);
- By what access criteria data will be shared (including with whom, for what types of analyses, by what mechanism – eg, with or without investigator support, after approval of

a proposal, with a signed data access agreement - or any additional restrictions).

See [table](#) for examples. Clinical trials that begin enrolling participants on or after Jan 1, 2019, must include a data sharing plan in the trial’s registration. If the data sharing plan changes after registration, this should be reflected in the statement submitted and published, and updated in the registry record. [Mendeley Data](#) is a secure online repository for research data, permitting archiving of any file type and assigning a permanent and unique digital object identifier (DOI) so that the files can be easily referenced. If authors wish to share their supporting data, and have not already made alternative arrangements, a Mendeley DOI can be referred to in the data sharing statement.

### Blue section (Comment, Correspondence)

#### Editorial

- Editorials are the voice of *The Lancet Global Health*, and are written in-house by the journal’s editorial-writing team and signed “*The Lancet Global Health*”

#### Comment

- This section contains Commentaries that accompany papers published in *The Lancet Global Health* or on issues of wide-reaching concern in global health. Comments linked to policy decisions are welcomed. Most Comments are commissioned, but unsolicited Comments (no more than 750 words, ten references, and one figure, panel, or small table) are also welcome. Comments may be peer reviewed
- The place to respond to something we have published is in our **Correspondence** section
- See **Conflicts of Interest** guidelines for comments

#### Correspondence

- Letters should be written in response to previous content published in *The Lancet Global Health*
- Letters for publication must reach us within 4 weeks of publication of the original item and should be no longer than 400 words
- Letters of general interest, unlinked to items published in the journal, can be up to 400 words long
- Correspondence letters are not usually peer reviewed, but we might invite replies from the authors of the original publication, or pass on letters to these authors
- Only one table or figure is permitted, and there should be no more than five references and five authors
- All accepted letters are edited. Proofs will be sent out to authors before publication

#### Corrections

- Any substantial error in any article published in *The Lancet Global Health* should be corrected as soon as possible. Blame is not apportioned; the important thing is to set the record straight.
- The *Lancet* journals have a [policy](#) for types of errors that we do and do not correct. We will always correct any error affecting a non-proprietary drug name, dose, or unit, any numerical error in the results, or any factual error in the interpretation of results.

## Green section (Reviews, Viewpoints, Health Policy, Commissions, Series)

### Reviews

Reviews should be either a definitive overview of a major topic connected with global health or an update of knowledge in a somewhat narrower field of current interest. Manuscripts will be assessed in-house and those judged suitable will be peer reviewed before an editorial decision is made. Reviews should be no more than 4500 words, with a maximum of 75 references. References selected for publication should be chosen for their importance, ease of access, and for the “further reading” opportunities they provide; citations to papers published in non-peer-reviewed supplements are discouraged. In addition to references, authors should consider supplying a short list of useful websites where readers can find further information on the subject. A 150 word unstructured summary should be included. Use of up to five illustrations is encouraged to aid the reader. Complete transparency about the choice of material included is important to any Review paper. Therefore, all Reviews should include a brief section entitled “Search strategy and selection criteria” stating the sources (including databases, MeSH and free text search terms and filters, and reference lists from journals or books) of the material covered, and the criteria used to include or exclude studies. Since these papers should be comprehensive, we encourage citation of publications in non-English languages. Systematic reviews should be submitted as Original Research, not Reviews.

### Viewpoint

Viewpoints are opinion pieces that use the best evidence to develop a robust argument on a topic of immediate relevance to global health. They should have a novel and clear point to make, with the aim of provoking transformational thinking at a high level. Length guidelines are up to 2500 words and 30 references.

### Health Policy

Health Policy papers should cover developments in global health related to policy, guideline development, health systems, or economics. A mix of original research, narrative review, and advocacy can be included, as long as these elements are clearly identified. Health Policy papers are shorter than Original Research Articles at around 2500 words and 20 references, with a 150 word unstructured summary. One or two figures or tables can be included.

### Commissions

Topics for *The Lancet Global Health* Commissions are generally selected by our editors, who work with academic partners to identify the most pressing issues in science, medicine, and global health with the aim of producing recommendations to change public policy or improve practice. Projects usually last 2–3 years, and author groups will represent a broad range of international expertise. All *The Lancet Global Health* Commissions are academic publications and are subject to the same rigorous peer review process as all other research papers published in our journals. *The Lancet Global Health* does not provide direct financial support to Commissioners for the research or writing of the reports. Funding is sought directly by authors, with oversight from our editors

### Series

Series are collections of papers (usually between three and five) on a broad topic within the global health field. They are generally commissioned by the editors, but suggestions are welcome by email. We would not consider a large collection of papers on a narrow topic—eg, a single global health programme. This type of collection is better suited to a journal supplement (*The Lancet Global Health* does not publish supplements).

## Formatting guidelines

### Language

- Manuscripts should be submitted in English. Authors writing in Chinese, Portuguese, or Spanish may wish to use the Webshop (<http://webshop.elsevier.com/language-services>) to provide an English translation of their manuscript for submission.

### Title page

- A brief title, author name(s), preferred degree (one only), affiliation(s), and full address(es) of the authors must be included. The name and address of the corresponding author should be separately and clearly indicated with email and telephone details.

### Formatting of text

- Type a single space at the end of each sentence
- Do not use bold face for emphasis within text
- We use a comma before the final “and” or “or” in a list of items
- Type decimal points midline (ie, 23.4, not 23.4). To create a midline decimal on a PC: hold down ALT key and type 0183 on the number pad, or on a Mac: ALT shift 9
- Numbers one to ten are written out in words unless they are used as a unit of measurement, except in figures and tables
- Use single hard-returns to separate paragraphs. Do not use tabs or indents to start a paragraph
- Do not use the automated features of your software, such as hyphenation, endnotes, headers, or footers (especially for references). Please use page numbering
- Guidelines on formatting tables are available in the [artwork guidelines](#)

### References

- Cite references in the text sequentially in the Vancouver numbering style, as a superscripted number after any punctuation mark. For example:
 

“...as reported by Saito and colleagues.<sup>15</sup>”
- Two references are cited separated by a comma, with no space. Three or more consecutive references are given as a range with an en rule. To create an en rule on a PC: hold down CTRL key and minus sign on the number pad, or on a Mac: ALT hyphen
- References in tables, figures, and panels should be in numerical order according to where the item is cited in the text
- Here is an example for a journal reference (note the use of tab, bold, italic, and the en rule or “long” hyphen):
 

“15[tab]Saito N, Ebara S, Ohotsuka K, Kumeta J, Takaoka K. Natural history of scoliosis in spastic cerebral palsy. *Lancet* 1998; **351**: 1687–[en rule]92.”
- Give any subpart to the title of the article
- If there are six authors or fewer, give all six in the form:

### Formatting guidelines for text, tables, and figures

Guidelines on formatting of text, tables, and figures can be found at <https://www.thelancet.com/pb/assets/raw/Lancet/authors/artwork-guidelines.pdf>

surname space initials comma

- If there are seven or more give the first three in the same way, followed by et al
- For a book, give any editors and the publisher, the city of publication, and year of publication
- For a chapter or section of a book, also give the authors and title of the section, and the page numbers
- For online material, please cite the URL, together with the date you accessed the website
- Online journal articles can be cited using the DOI number
- Do not put references in the Summary

### Figures

Our in-house illustrators redraw most figures into *Lancet* style. The quality of the files we receive from authors has a direct effect on the accuracy and time taken to prepare figures that are suitable for publication.

We have different criteria for photographic and illustrative files, the following notes are a summary of our ideal requirements, but a detailed description is in the [artwork guidelines](#)

- For images (photographs or photographic images) that are used as part of illustration or image composite figures we require a file that is no less than 300 dpi when set at its final printed size. Ideal file formats are TIF or JPG
- For trial profiles, study profiles, and CONSORT diagrams, please supply as an editable flow diagram in Word (.doc) or PowerPoint (.ppt) file
- For illustrations (all non-photographic line-work and general drawing) we require editable vector files that contain selectable geometry and fonts (editable text). The editability of files depends on the package they were created in, but as a rule we would prefer to receive any of the following: Adobe Illustrator (.ai) file; Adobe Illustrator or generic .eps files exported from a graphics program; vector-based PDF, PowerPoint, or Word file; or SVG file. If authors are unable to supply files in any these formats, our in-house illustrators can offer guidance on whether it is more economical to export or convert the file into another format, or to redraw from scratch. When files are exported to eps files, we would prefer text to be exported "as text" rather than "as objects", which is especially crucial for files such as forest plots in which there is a lot of text
- If your figures are annotated, please supply two copies of each of these figures as separate files (one annotated copy and one non-annotated and editable copy). Our in-house illustrators will annotate according to journal style using the annotated figures as a guide. For multi-part figures, please supply the individual parts as well as a combined version to be used as a guide for our illustrators to recreate the files
- Images that have been published previously should be accompanied by a statement indicating permission to reproduce the image. If required, further assistance can be obtained from the editorial team. If you have used previously published images, you must obtain permission from the copyright holder of the paper, which might be the authors or the publisher. If all the figures are your own and have not been published before, then this requirement does not apply

### Drug names

For more on neuroscience-based nomenclature see [http://www.thelancet.com/pdfs/journals/lanpsy/PIIS2215-0366\(17\)30098-6.pdf](http://www.thelancet.com/pdfs/journals/lanpsy/PIIS2215-0366(17)30098-6.pdf)

### Guidelines for supplementary material

All material should be submitted as one PDF (with numbered pages) with the paper and will be peer reviewed. Material will be published at the discretion of *The Lancet* journals' editors. For clinical trials, we encourage authors to include a copy of the study protocol. All material should be provided in English.

### Text

- Main heading for the web extra material should be in 12 point Times New Roman font **BOLD**
- Text should be in 10 point Times New Roman font, single spaced
- Headings should be in 10 point **BOLD**

### Tables

- Main table heading should be in 10 point Times New Roman font **BOLD**
- Legends should be in 10 point, single spaced
- Tables should be in 8 point Times New Roman font, single spaced
- Headings within tables should be in 8 point **BOLD**

### Data

- Numbers in text and tables should always be provided if % is shown
- Means should be accompanied by SDs, and medians by IQR
- p values should be given to two significant figures, unless  $p < 0.0001$

### Drug names

- Recommended international non-proprietary name (rINN) is required
- We encourage use of neuroscience-based nomenclature for psychotropic drugs

### References

- Vancouver style—eg,  
Smith A, Jones B, Clements S. Clinical transplantation of tissue-engineered airway. *Lancet* 2008; **372**: 1201–09.  
  
Hourigan P. Ankle injuries. In: Chan D, ed. Sports medicine. London: Elsevier, 2008: 230–47.
- Numbered in order of mention in appendix and numbered separately from references in the full paper

### Figures

- All images must have a minimum resolution of 300 dpi, width 107 mm
- Main figure heading should be in 10 point Times New Roman font **BOLD**
- Legends should be in 10 point, single spaced

### Audio/video material

- The paper to which the audio or video clip relates should be mentioned in the recording
- Audio clip and video files should be accompanied with brief

text explaining the content of the audio, names of interviewers/ interviewees, date of recording, and place of recording if relevant

- Written consent from all parties must be obtained (see also the above section on **Patient and other consents**)

### Audio

- Audio material submitted as an mp3 file, no larger than 50 Mb
- Your paper may be selected for a podcast. If so, the Web Editor will contact you to arrange a pre-recorded interview to discuss your paper. For more information, see [Audio](#)

### Video

- Video material should be submitted in .mp4 format with aspect ratio of 16:9, and be no larger than 50 Mb
- We welcome your videos and invite you to submit any video material (reports, interviews, scans, imaging) for consideration in the online journal. Please ensure that all those featured in the video have given permission for publication (see also the previous section on **Patient and other consents**)
- All video files can be submitted alongside your article in EM

### Disclosure of results before publication

- Presentation of data at a scientific meeting, as a poster, abstract, orally, on a CD, or as an abstract on the web, or on a preprint server does not conflict with submission to the *Lancet* journals. As a member journal of the International Committee for Medical Journal Editors, *The Lancet Global Health* does not regard results that are posted in the same clinical trials registry in which primary registration resides as a previous publication, if the results are presented in the form of a brief structured abstract or table
- The *Lancet* journals operate an embargo system, whereby journalists are given access to papers and press releases ahead of publication, allowing them a protected window to develop their stories. We believe that this window can help encourage balanced and accurate coverage of peer-reviewed scientific and medical research to inform public debate. As such, we ask that authors and their institutions refrain from actively seeking media attention for articles that have been submitted to *The Lancet Global Health* or that are available as a preprint. The important steps of thorough peer review and experienced editorial scrutiny and guidance, together with putting research findings into a wider context and highlighting implications for clinical practice, will make the final published paper in *The Lancet Global Health* very different to the submitted or preprint version. Coverage that results from pre-publication communication can impact media interest at the time of publication and our ability to support responsible journalism
- For more information on Preprints with *The Lancet*, please see [www.thelancet.com/preprints](http://www.thelancet.com/preprints). For additional questions regarding media, please contact [pressrelease@lancet.com](mailto:pressrelease@lancet.com)

### Online publication

- *The Lancet Global Health* publishes papers online as they become ready. You will be informed at least a week in advance of the Online publication date

## How The Lancet Global Health handles your paper

### Acknowledgment

- Receipt of your paper will be acknowledged by an email containing a reference number, which should be used in all future communications

### Checking for plagiarism, duplicate publication, and text recycling

- At our discretion, material that we are interested in publishing will be checked by editors using CrossCheck (see [Lancet 2011; 377: 281–82](#)). We expect that such papers are written in a way that offers new thinking without recycling previously published text.

Audio  
<http://www.thelancet.com/audio>

### Peer review

- *The Lancet Global Health* operates a single-blind peer review process
- Every Article and Meta-analysis published in *The Lancet Global Health* has been peer reviewed. Occasional contributions (eg, Commentaries) are accepted without peer review
- On submission to *The Lancet Global Health*, your report will first be read by one or more of the journal's staff of physicians and scientists. This is an important feature of our selection process and many papers are turned away on the basis of in-house assessment alone. That decision will be communicated quickly
- Research papers are followed by peer review by at least three reviewers. You will receive notification of which editor is handling the peer review of your paper.

### Decision

- Submissions that survive in-house and peer review might be referred back to authors for revision. This is an invitation to present the best possible paper for further scrutiny by the journal; it is not an acceptance
- Authors should give priority to such revisions; the journal will reciprocate by making a final decision quickly
- Two copies of the revised version should be sent back, one of which should be highlighted to show where changes have been made. Detailed responses to reviewers' comments, in a covering letter, are also necessary

### The Lancet journals and other Elsevier journals

- If your paper is rejected by *The Lancet Global Health*, we might judge it suitable to pass to other editors in the *Lancet*-group for consideration or to editors of other relevant journals within Elsevier's portfolio

### Appeals

- Sometimes editors make mistakes. When we do, we like to hear about them. If an author believes that an editor has made an error in declining a paper, we welcome an appeal. In your appeal letter, which should be sent to [globalhealth@lancet.com](mailto:globalhealth@lancet.com), please state why you think the decision is mistaken, and set out your specific responses to any peer reviewers' comments if those seem to have been the main cause of rejection
- At least two editors will decide whether to invite a revised manuscript and whether re-review, or otherwise, is indicated

### Proofs

- *The Lancet* journals employ highly skilled Assistant Editors, and it is likely that your paper will be substantially edited after acceptance to ensure that it is accurate, clear, and understandable to a wide readership
- All figures will be redrawn into *The Lancet Global Health* style by our in-house illustrators
- You will receive a proof from an Assistant Editor. That proof should be corrected and returned within 48 h

### Editorial research

- We are keen to better understand and improve editorial conduct, decision making, and issues related to peer review. Therefore, we occasionally take part in or conduct editorial research. Your submitted paper might be used in such research. If you do not want your paper entered into such a study, please let us know in your covering letter. Your decision to take part or not will have no effect on the editorial decision on your paper

### Open access policy

#### Article processing charges

- No subscription or pay-per-view charges will apply to any content published in *The Lancet Global Health*. In order to cover the costs of reviewing, copy editing, layout, and online hosting and archiving, the journal will charge an article processing fee of \$5000 upon acceptance of submitted full-length papers (no fee will apply to Comment or Correspondence). The fee reflects the anticipated low ratio of acceptance to submission. *The Lancet Global Health* follows the gold open access publishing model. Authors wishing to publish under the green open access model should consider one of *The Lancet's* hybrid journals.
- If all authors are from group A countries of the Health Inter Network Access to Research Initiative (HINARI), they will automatically be presented with a full fee waiver
- If all authors are from a HINARI group B country, or authors are from a mix of group A and B countries, they will automatically be presented with a 50% fee waiver
- We will always make it possible to publish an accepted Article regardless of ability to pay. If an author group is unable to pay the full fee the corresponding author should contact the [Editor in Chief](#) to discuss discount or waiver options
- The editorial decision to accept is taken independently and usually before such a request is made. Payments are processed by a department unconnected to *The Lancet Global Health's* editorial department

### Copyright and reuse

Articles are published under Creative Commons licensing, which enables authors to retain copyright while allowing others to copy, distribute, and make some uses of their work, provided full credit is given to them as originators. Articles with commercial funding only (eg, from a drug or device manufacturer or other for-profit organisation) are required to use a [CC BY-NC-ND](#) licence. Articles with funding from another source (or no funding) can choose either [CC BY-NC-ND](#) or [CC BY](#) (please check with your funder whether a

specific creative commons license is preferred). Authors will be asked to sign an exclusive licence (or non-exclusive licence for government employees) to permit our publisher, Elsevier, to publish the work.

For Creative Commons licensing see <http://creativecommons.org/licenses/>

### Ombudsman

For information about what our ombudsman can and cannot investigate, articles about past ombudsmen, and how to contact the current ombudsman see <https://www.thelancet.com/ombudsman>.

### What happens after publication?

#### Press release

Press releases are issued by *The Lancet* journals' press office for selected content published in our journals. You will be advised in advance if your paper has been selected for press release. *The Lancet* journals' media relations team will contact you with detailed instructions about the embargo for your paper, and will provide a draft press release for your comments ahead of the publication date. If your institute or funder are planning to press release your paper, please let your Assistant Editor know in the first instance, and they will provide you with details on *The Lancet's* press release policy, embargo dates, and how to receive finalised PDFs of your paper to share with journalists.

#### Author interview

Your paper may be selected for a podcast. If so, the Web Editor will contact you to arrange a pre recorded interview to discuss your paper. For more information, see [Audio](#)

#### Data storage

Authors may be required to provide the raw data for research papers when they are under review and up to 10 years after publication in *The Lancet Global Health*

#### Responsible sharing

*The Lancet* supports responsible sharing. We recognise that authors want to share their papers and we encourage this. Find out how you can share your paper [here](#).

For Creative Commons licensing see <http://creativecommons.org/licenses/>

For further details on *The Lancet's* ombudsman see <http://www.thelancet.com/ombudsman>

[Press release](http://www.thelancet.com/press-room)  
<http://www.thelancet.com/press-room>

For HINARI countries see <http://www.who.int/hinari/eligibility/en>

[Responsible sharing](http://www.elsevier.com/sharing-articles)  
[www.elsevier.com/sharing-articles](http://www.elsevier.com/sharing-articles)