A QUALITY IMPROVEMENT PROJECT EVALUATING THE PERI-OPERATIVE IMPLEMENTATION OF A HYPERTENSION MANAGEMENT PROTOCOL BY ANAESTHESIOLOGISTS AT SEVEN GOVERNMENT HOSPITALS IN THE WESTERN CAPE.

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"A MULTI-CENTER, CROSS-SECTIONAL QUALITY IMPROVEMENT PROJECT: THE PERI-OPERATIVE IMPLEMENTATION OF A HYPERTENSION PROTOCOL BY ANESTHESIOLOGISTS"

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DECLARATION

I, Claire-Louise Pfister, 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.
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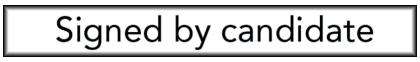

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ABSTRACT

BACKGROUND: Hypertension is a common risk factor for cardiovascular morbidity and mortality, with a high prevalence in patients presenting for elective surgery. In limited resource environments, patients have poor access to primary care physicians, limiting the efficacy of life-style modification for the initial management of hypertension in the community. In these circumstances, the perioperative period presents a unique opportunity for diagnosis and initiation and/or modification of pharmacotherapy of hypertension. Anesthesiologists are ideally placed to lead this aspect of perioperative medicine.

METHODS: In collaboration with expert physicians, we designed and implemented an algorithm for the diagnosis of hypertension and subsequent initiation or modification of anti-hypertensive therapy, or referral to a physician. The study was a multi-center, cross-sectional quality improvement project in seven hospitals in the Western Cape, South Africa. On the day before scheduled elective surgery, adult in-patients had two sets of blood pressure (BP) readings taken, one by nurses and the other by anesthesiologists, using a noninvasive automated blood pressure device. These were averaged on an electronic database, to diagnose hypertension. Patients with normal BP or well-controlled hypertension required no further management. Those with borderline BP received educational pamphlets. Patients with stage 1 or 2 hypertension were managed with medication according to the algorithm, starting 1 day postoperatively, and provided with educational pamphlets. Patients with stage 3 disease were referred to a physician. The primary outcome was adherence by the anesthesiologist to the algorithm, defined as initiation of the prescribed medication. An 80% adherence rate was considered successful implementation. The secondary outcome was the issue of the antihypertensive medication at discharge.

RESULTS: Two hundred and ninety-eight patients were screened for hypertension. One hundred and six patients were eligible for the quality improvement project. Thirty-seven (34.9%) had borderline blood pressure readings, 43 (40.6%) had stage 1-, 22 (20.8%) stage 2-, and 4 (3.8%) stage 3 hypertension respectively. The adherence rate by the anesthesiologist was 84.0% (95% confidence interval (CI) 77.0% to 91.0%) for initiation of anti-hypertensive therapy. It was noted that 55.5% (95% CI 46.2% to 65.1%) received their medication upon discharge.

CONCLUSIONS: Anesthesiologists successfully implemented a quality improvement project for diagnosis and management of hypertension in the perioperative period. This has the potential to reduce the public health burden of hypertension in limited resource environments. Successful ongoing prescription and follow-up requires cooperation within a multi-disciplinary team involving anesthesiologists, surgeons, nurses, pharmacists and physicians.

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The authors acknowledge the cooperation of the Provincial Government of the Western Cape in the performance of this multi-center research study, and the enthusiasm and cooperation of the theatre-, ward- and pharmacy staff from all seven public sector-, government-funded hospitals.

The site co-ordinators (anesthesiologists) at the participating centres, New Somerset-, Paarl-, Victoria-, Mitchell's Plain-, Worcester-, and George Hospital. No other external funding or competing interests are declared by the authors.

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LIST OF ABBREVIATIONS

AOBP: Automated office blood pressure

BP: Blood Pressure

CI: Confidence Interval

ICMJE: International Committee of Medical Journal Editors

SASA: South African Society of Anaesthesiologists

SD: Standard deviation

SPSS: Statistical Package for the Social Sciences

SQUIRE: Standards for Quality Improvement Reporting

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Abstract:

BACKGROUND: Hypertension is a common risk factor for cardiovascular morbidity and mortality, with a high prevalence in patients presenting for elective surgery. In limited resource environments, patients have poor access to primary care physicians, limiting the efficacy of life-style modification for the initial management of hypertension in the community. In these circumstances, the perioperative period presents a unique opportunity for diagnosis and initiation and/or modification of pharmacotherapy of hypertension. Anesthesiologists are ideally placed to lead this aspect of perioperative medicine.

METHODS: In collaboration with expert physicians, we designed and implemented an algorithm for the diagnosis of hypertension and subsequent initiation or modification of anti-hypertensive therapy, or referral to a physician. The study was a multi-center, cross-sectional quality improvement project in seven hospitals in the Western Cape, South Africa. On the day before scheduled elective surgery, adult in-patients had two sets of blood pressure (BP) readings taken, one by nurses and the other by anesthesiologists, using a noninvasive automated blood pressure device. These were averaged on an electronic database, to diagnose hypertension. Patients with normal BP or well-controlled hypertension required no further management. Those with borderline BP received educational pamphlets. Patients with stage 1 or 2 hypertension were managed with medication according to the algorithm, starting 1 day postoperatively, and provided with educational pamphlets. Patients with stage 3 disease were referred to a physician. The primary outcome was adherence by the anesthesiologist to the algorithm, defined as initiation of the prescribed medication. An 80% adherence rate was considered successful implementation. The secondary outcome was the issue of the antihypertensive medication at discharge.

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CONCLUSIONS: Anesthesiologists successfully implemented a quality improvement project for diagnosis and management of hypertension in the perioperative period. This has the potential to reduce the public health burden of hypertension in limited resource environments. Successful ongoing prescription and follow-up requires cooperation within a multi-disciplinary team involving anesthesiologists, surgeons, nurses, pharmacists and physicians.

Glossary of Terms

AOBP: Automated office blood pressure

BP: Blood Pressure

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SPSS: Statistical Package for the Social Sciences

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Key Points Summary

Question: Can anesthesiologists assist in the perioperative diagnosis and management of chronic hypertension?

Findings: Anesthesiologists successfully implemented an algorithm directing antihypertensive therapy in the perioperative period.

Meaning: Anesthesiologists can contribute to the reduction of the public health burden of hypertension in limited resource environments.

Introduction:

Globally, cardiovascular disease is the leading cause of death.[1] Hypertension is a major risk factor, and if uncontrolled, predisposes the individual to myocardial infarction, heart failure, stroke and kidney disease.[2] Hypertension is common, affecting over 1 billion people worldwide, and is the one of the leading causes of mortality from cardiovascular diseases in Africa.[3-5] Failure to diagnose and treat hypertension is regarded as poor medicine, and potentially indefensible.[5,6]

Hypertension is usually identified and treated in the primary health care setting.[6] However, in a resource-limited environment such as South Africa, the diagnosis and management of hypertension is inadequately addressed within the primary health care system. There is limited access to general practitioners and physicians, and life-style changes are difficult to implement and unlikely to be successful.[3] The prevalence of hypertension in the adult population of South Africa is about 30%.[7,8] Urbanization and an ageing population, amongst other developing trends, suggests that the prevalence of hypertension is projected to increase significantly in the future. The medical and socio-economic implications of this increasing burden on cardiovascular disease could be far-reaching.[6]

When patients present for elective surgery, there is an expectation that other markers of their health will be evaluated and treated accordingly. In patients presenting for non-cardiac elective surgery, hypertension is one of the most commonly encountered comorbidities, with an estimated prevalence of 20-25%.[7] In a recent South African study, approximately 50% of elective patients age 18 years and older presenting for non-cardiac elective surgery were identified as having

hypertension.[9,10] Ten percent of these patients were newly diagnosed with hypertension, and 40% were found to have poorly controlled hypertension.[9] This presents a unique opportunity for perioperative clinicians, led by anesthesiologists, to diagnose and treat chronic hypertension perioperatively and potentially alleviate some of the burden of hypertensive disease on an already resource-limited primary health care system.[10]

The primary aim of this study was for anesthesiologists, in collaboration with nurses, physicians and surgeons, to identify patients at the preoperative visit with previously undiagnosed, or poorly controlled chronic hypertension. An algorithm was designed and introduced to diagnose and manage these patients' hypertension. In addition, patients were given letters which included information about hypertension, advice on life-style modification, and the importance of follow-up at the primary health care facility.

Methods:

Study approval was obtained from the University of Cape Town Faculty of Health Sciences Human Research Ethics Committee (HREC 489/2019), and from the Western Cape Department of Health. In addition, institutional approval was granted by all participating centers. Written informed consent was obtained from all subjects participating in the project. The project was registered at ClinicalTrials.gov (NCT03921086, Principal Investigator:Bruce Biccard, Date of registration: 20/02/2019). The Revised Standards for Quality Improvement Reporting (SQUIRE) were followed.[11]

A simple algorithm for the diagnosis of hypertension and initiation or modification of anti-hypertensive therapy, or referral to a physician, was designed and implemented in collaboration with the Department of Medicine of the University of Cape Town. This included expert guidance from the Head of the Hypertension Clinic at Groote Schuur Hospital (Professor Brian Rayner), and was in accordance with the South African Hypertension Practice Guideline of 2014 [12] (Figure 1). Table 1 shows the categories of hypertension. Pre-intervention site initiation, and education of anesthesiologists, nurses and surgeons, was carried out either in person, via email or video and voice conference calls at each of the hospitals. Education took place in the form of formal presentations at academic meetings, and on-the-job presentations to nurses and doctors in surgical wards. Posters (Supplemental material: 1) and electronic copies of the algorithm for diagnosis and management of hypertension, including indications for- and contraindications to the groups of anti-hypertensive medications to be prescribed, were widely distributed to all involved, and

standardized patient educational pamphlets and clinic letters were developed (Supplemental Material: 2-5).

This was a multi-center, prospective, cross-sectional, interventional quality improvement project conducted at seven public sector, government-funded hospitals in the Western Cape, South Africa. This was conducted over a five-day period in each institution, between January and March 2019. Eligible participants were all adult in-patients undergoing elective surgery with BP above the normal range,[12,13] which included newly diagnosed hypertensives and those with poorly controlled hypertension. Exclusion criteria were cardiac-, obstetric-, radiological or ophthalmic procedures under local anaesthesia, and patients with blood pressures within normal ranges, including those with well controlled hypertension.

All consenting patients presenting at the in-hospital preoperative visit the day before their surgery, were screened for hypertension. The BP measurements were conducted using the automated office blood pressure method (AOBP), in accordance with recommendations in the Joint Guidelines from the Association of Anesthesiologists of Great Britain and Ireland, the British Hypertension Society, and the Canadian Hypertension Guideline.[13,14] The measurements were performed the day prior to surgery, to mitigate the effect of anxiety on BP. The automated device used was a Dinamap Carescape Monitor (Woodley Equipment Company Ltd), which has been validated.[15] Blood pressure measurements were taken using the appropriate cuff size, the patient was seated, after 10 minutes' rest. Five readings were done at 1- minute intervals, by both nursing staff and the anesthesiologist (10 readings in total), at separate time periods. The first reading in each set was discarded and the remaining four averaged, to make the diagnosis of hypertension.

The research team designed an electronic form on REDCap,[16] a secure web application for building and managing online surveys and databases, which automatically averaged the 8 readings of the nurses and anesthesiologists.

Information collected at the preoperative visit by the attending anesthesiologist included demographic data (sex, age, weight, height), comorbidities, and current antihypertensive therapy. The anesthesiologist then assessed and managed the patient according to the algorithm on the electronic database (Figure 1). Patients with normal BP or well-controlled hypertension were excluded from further management. Those with borderline BP received educational pamphlets. Patients with stage 1 or 2 hypertension were managed with medication according to the algorithm, and educational pamphlets, and those with stage 3 disease were referred to a physician. Anti-hypertensive medication was commenced on the day after surgery. Adherence to prescription of anti-hypertensive medication at discharge was confirmed using the JAC Medicines Management System,[17] a computer-based dispensing and inventory management system in widespread use in the Western Cape. The primary outcome was the adherence of the anesthesiologist to the hypertension algorithm introduced in the quality improvement project. The secondary outcome was the issue of the antihypertensive medication at discharge.

Calculation of Sample Size:

The sample size for the primary outcome was determined by the adherence to the algorithm as defined by the initiation of the prescribed medication. An adherence rate of 80% was considered as successful implementation of the quality improvement project. Based on a sample size of 100 patients, an accuracy of ± 8% was predicted (80%, 95%CI 72-88%). Allowing for a drop-out of 10 patients, we planned to recruit 110 subjects. Based on a previous study on peri-operative hypertension in the Western Cape, the required study duration was 5 days to achieve the sample size for the primary outcome.[9,10]

Statistical Methods:

Results are presented as number, percentage, mean and standard deviation (SD), as appropriate. Statistical analysis was conducted using the IBM Statistical Package for the Social Sciences (SPSS) version 25 (SPSS Inc., Chicago, IL, USA).

Results:

The study recruitment is shown in Figure 2. Two hundred and ninety-eight patients were screened for hypertension. One hundred and six patients were eligible for the quality improvement project. Of the 106 patients, 45 were male, and 61 female. The mean (SD) systolic- and diastolic BPs were 150 (17) and 85 (11) mmHg respectively, at the preoperative visit. The mean (SD) age was 55 (15) years. The overall mean (SD) body mass index of patients with stage 1, 2, and 3 hypertension was 30.5 (8.0) $kg.m^{-2}$. The prevalence of co-existing cardiovascular comorbidities in patients with hypertension is shown in Table 2.

The prevalence of the stages of hypertension are shown in Table 3.

We found an adherence rate by anesthesiologists of 84.0% (95% CI 77.0% to 91.0%) with correct initiation of therapy according to the algorithm. It was noted that 55.5% (95% CI 46.2% to 65.1%) of patients received medication upon discharge from the hospital.

Discussion:

In this multi-center, cross-sectional quality improvement project, a simple algorithm was designed for the diagnosis of hypertension and initiation or modification of anti-hypertensive therapy. The principal finding was that this quality improvement project could be successfully implemented preoperatively by anesthesiologists as the leaders of a multi-disciplinary team. We found an adherence rate of 84% to the initiation of appropriate therapy by anesthesiologists, in hypertensive patients scheduled for elective surgery, which by the study definition was considered a successful implementation of this quality improvement project.

The secondary outcome finding of a relatively low percentage of patients receiving the introduced antihypertensive medications upon hospital discharge, despite the successful implementation by anesthesiologists may be the result of several factors. These could include discontinuation of medication by the surgical team for various reasons, or inadequate communication between the anesthesiologist initiating the therapy and the surgical team, who then failed to prescribe the medication at discharge. It is possible that in smaller hospitals the adherence rate may be higher, due to better communication within a smaller multidisciplinary team. This suggests that implementation of this quality improvement project would require further communication and support at discharge to ensure antihypertensive medication prescription post discharge.

The strengths of this study suggest that a short-term quality improvement intervention has the potential to improve quality of care in cardiovascular disease, in

low-resource environments similar to those in many areas of South Africa. This is potentially an important public health intervention, when one considers that hypertension is associated with nearly 10% of all deaths in South Africa[7], and that 25% of all elective adult surgical patients would benefit from further management of their hypertension.[9] This can be done by educating health care providers and implementing a guideline which will lead to improved, standardized and sustained quality of care for all surgical patients with hypertension.[1] Our study served to initiate improved preoperative management of hypertension, after recent findings by Van der Spuy and Crowther et al [9,10] suggested that the preoperative period is an opportunity to address this important public health challenge. In the present study, anesthesiologists were able to lead the perioperative group of nurses and physicians in adhering to the algorithm, allowing for early diagnosis and management of hypertension. This work represents a further aspect of the now well accepted role of the anesthesiologist in the field of Perioperative Medicine.[18]

A further strength of the study was that it was designed to mitigate against 'white coat' hypertension and observer bias. The use of automated office BP measurement (AOBP) in this study is considered to be more accurate than conventional BP measurement.[19] It is more predictive of target organ damage and very closely correlates with day-time ambulatory BP, and significantly mitigates the "white coat" effect. In addition, all data was captured electronically, excluding observer bias. The small risk that patients would be incorrectly diagnosed as hypertensive, was minimized by measuring the BP at the preoperative in-hospital visit, the day before surgery, thereby also reducing the risk of the "white coat" effect that might occur on the day of surgery. In addition, the threshold for pharmacological treatment (140/90

mmHg) was higher than many current guidelines.[14] Another strength of the study was early recognition and referral of patients with stage 3 hypertension to a physician.

The study had certain limitations. The introduction of antihypertensive medication may have resulted in minor side-effects, however, national guidelines were followed. This ensured patient safety in a similar manner to the initiation of anti-hypertensive therapy practiced in a primary health care setting. It could be argued that introduction of anti-hypertensive therapy in the surgical period is safer than in a primary care setting, due to the in-hospital status of the patients during therapy initiation and modification.

Well-designed freely available electronic programs or web-based applications such as REDCap could simplify diagnosis of chronic conditions such as hypertension, not only for anesthesiologists, but also for any doctor. In addition, the JAC pharmacy database provides an invaluable management information resource with respect to the follow up of patients and their medications after discharge. All central hospitals in the Western Cape, South Africa, but not all clinics, have access to this resource. These applications could have widespread implications for public health in resource-poor countries, where access to simple web-based applications could guide diagnosis and therapy, and simple databases could allow tracking of patients to ensure patient adherence to therapy. This is of particular importance when physician availability is limited.

Further research is required to assess patient adherence to medication. Primary health care clinic follow-up should also be evaluated, since management of hypertension involves physician diagnosis and treatment, as well as patient adherence to prescribed drugs.

Conclusion:

In conclusion, hypertension is common in patients presenting for non-obstetric, non-cardiac elective surgery. The use of a simple algorithm which outlines the stages of hypertension and the recommended drug management, including drug side effects and contraindications, allows for successful diagnosis and management of hypertension by anesthesiologists at the pre-operative visit. This approach has the ability to reduce some of the burden of hypertension on the primary health care system in a resource limited environment such as South Africa. However, co-operation is required within a multi-disciplinary team involving surgeons, nurses, pharmacists and physicians, in order to ensure that ongoing prescription and follow-up is successful. Future research is required to establish long term compliance rates, and the impact of the application of this algorithm on control of hypertension.

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Acknowledgements:

The project was registered at ClinicalTrials.gov (NCT - NCT03921086). The authors acknowledge the cooperation of the Provincial Government of the Western Cape in the performance of this multi-center research study, and the enthusiasm and cooperation of the theatre-, ward- and pharmacy staff from all seven public sector-, government-funded hospitals. We thank the site co-ordinators (anesthesiologists) at the participating centres, New Somerset-, Paarl-, Victoria-, Mitchell's Plain-, Worcester-, and George Hospital. No other external funding or competing interests are declared by the authors.

Author contributions:

Please note that this submission has 17 authors from a multicenter, prospective, observational study of seven hospitals in the Western Cape (South Africa). All 17 authors listed below meet the following criteria of the International Committee of Medical Journal Editors (ICMJE). We have itemized their contributions according to the ICMJE criteria below:

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In addition, all authors gave their final approval of the version to be published, and agreed to be accountable for all aspects, accuracy and integrity of the work.

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TABLES AND FIGURES

Table 1: Definitions and classification of office blood pressure (BP), adapted from the South African Hypertension Practice Guideline of 2014, and AAGBI guidelines

Stage	Systolic BP* (mmHg)	Diastolic BP (mmHg)
Normal	< 120	< 80
Optimal	120 – 129	80 - 84
High normal	130 – 139	85 - 89
Borderline BP*	135 - 140	85 - 90
Grade 1	140 - 159	90 - 99
Grade 2	160 - 179	100 - 109
Grade 3	≥ 180	≥ 110
Isolated systolic BP	≥ 140	< 90
Isolated diastolic BP	< 140	≥ 90

*BP: blood pressure

Table 2: Co-existing cardiovascular comorbidities in the hypertensive patients

Co-morbidity	Frequency (percent)
Coronary artery disease	11 (10.4%)
Heart failure	2 (1.9%)
Stroke	4 (3.8%)
Diabetes	16 (15.7%)
Chronic kidney disease	6 (5.7%)

Table 3 Distribution of stages of hypertension, classified according to the South African Hypertension Practice Guidelines [4]

Stage hypertension	N	Percentage
Borderline: 135-140/85-90 mmHg	37	34.9
Stage 1: BP: 141-159/91-99 mmHg	43	40.6
Stage 2: BP: 160-179/100-109 mmHg	22	20.8
Stage 3: BP: 180/110 mmHg	4	3.8
Total	106	100

Figure 1 Algorithm for initiating or escalating anti-hypertensive medication

(According to the South African Hypertension Practice guideline)

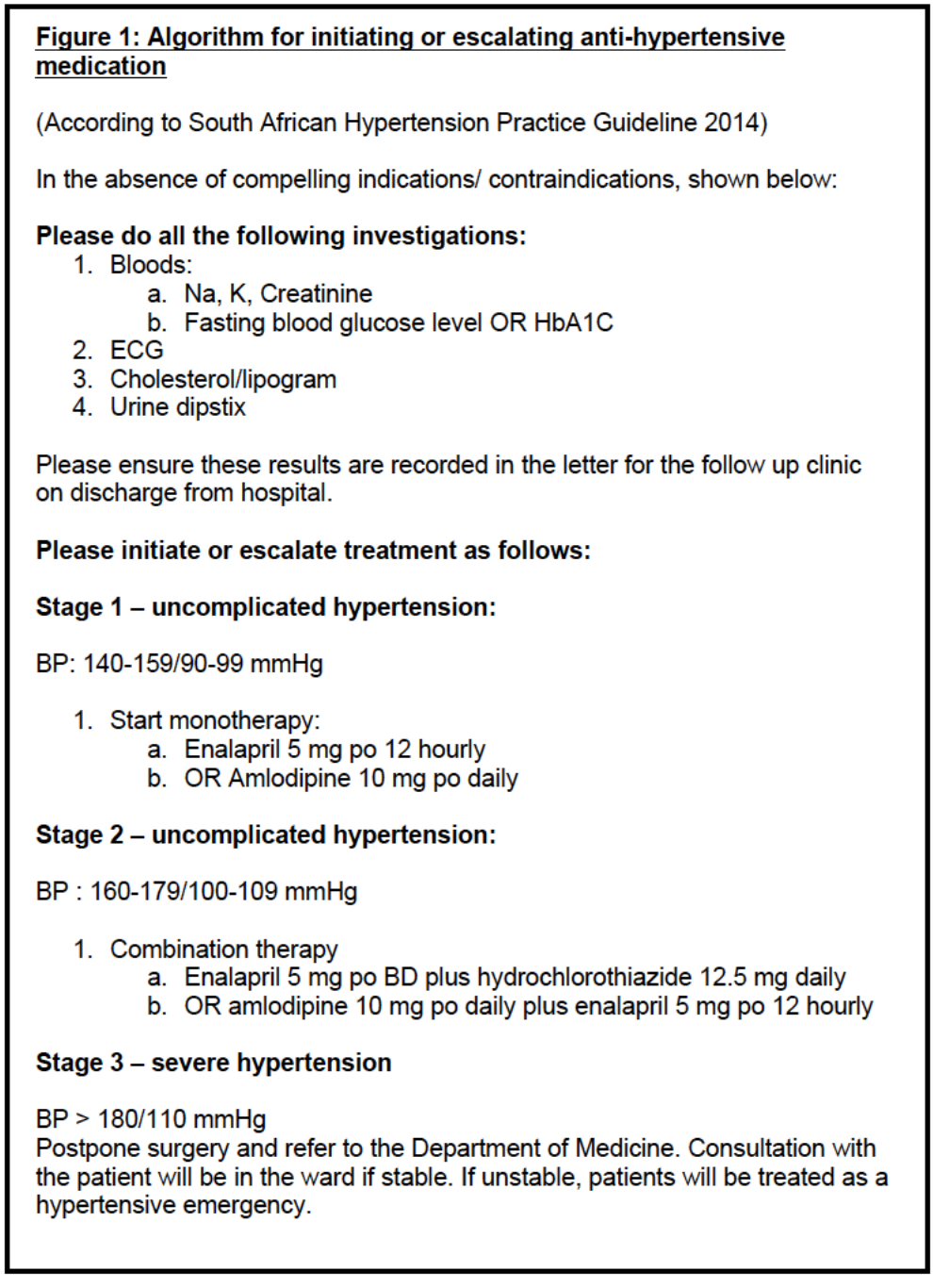


Figure 1: Algorithm for initiating or escalating anti-hypertensive medication

(According to South African Hypertension Practice Guideline 2014)

In the absence of compelling indications/ contraindications, shown below:

Please do all the following investigations:

1. Bloods:
    a. Na, K, Creatinine
    b. Fasting blood glucose level OR HbA1C
2. ECG
3. Cholesterol/lipogram
4. Urine dipstix

Please ensure these results are recorded in the letter for the follow up clinic on discharge from hospital.

Please initiate or escalate treatment as follows:

Stage 1 – uncomplicated hypertension:

BP: 140-159/90-99 mmHg

1. Start monotherapy:
    a. Enalapril 5 mg po 12 hourly
    b. OR Amlodipine 10 mg po daily

Stage 2 – uncomplicated hypertension:

BP : 160-179/100-109 mmHg

1. Combination therapy
    a. Enalapril 5 mg po BD plus hydrochlorothiazide 12.5 mg daily
    b. OR amlodipine 10 mg po daily plus enalapril 5 mg po 12 hourly

Stage 3 – severe hypertension

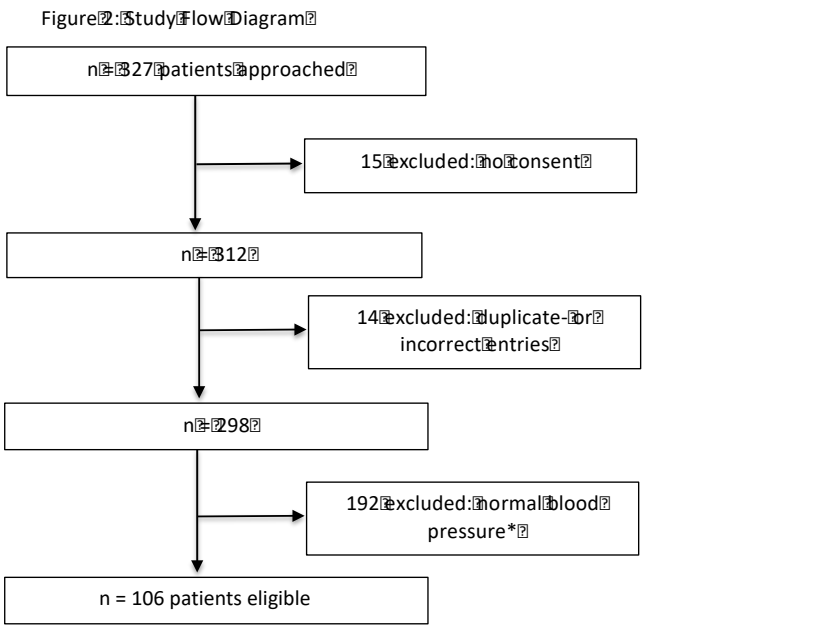
BP > 180/110 mmHg
Postpone surgery and refer to the Department of Medicine. Consultation with the patient will be in the ward if stable. If unstable, patients will be treated as a hypertensive emergency.

Indications for- and contra-indications to the antihypertensive medications to be prescribed*

Class	Conditions favouring use	Compelling contra-indications	Possible contra-indications
Diuretics (Hydrochloro-thiazide)	• Heart failure • Elderly hypertensives • Isolated systolic hypertension • Hypertensives of African origin	• Gout	• Pregnancy • Beta-blockers (especially atenolol)
CCB† (Amlodipine)	• Elderly patients • Isolated systolic hypertension • Angina pectoris • Peripheral vascular disease • Carotid atherosclerosis • Pregnancy		• Tachyarrhythmias • Heart failure (especially with reduced ejection fraction)
ACEI‡ (Enalapril)	• Heart failure • Left ventricular dysfunction • Post-myocardial infarction • Non-diabetic nephropathy • Type 1 diabetic nephropathy • Prevention of diabetic microalbuminuria • Proteinuria	• Pregnancy • Hyperkalaemia • Bilateral renal artery stenosis • Angioneurotic oedema	

*Modified from Seedat et al[11]
†CCB, calcium channel blocker; ‡ACEI, angiotensin-converting enzyme inhibitor

Figure 2 Study flow diagram



*Normal blood pressure indicates patients without hypertension or patients with well-controlled hypertension

APPENDICES

Appendix 1: Data capture instrument

All data was captured electronically using REDCap with an electronic questionnaire on the following link:

https://redcap.ansa.org.za/surveys/index.php?s=7RDDLJ834N

Appendix 2: Consent form

INFORMED CONSENT FORM

Title of Study:
A multicentre, cross-sectional quality improvement project: evaluating the implementation of a hypertension guideline protocol by perioperative clinicians.
Investigators: Dr Claire-Louise Pfister, Dr Margot Flint, Dr Marcin Nejthardt, Dr Francois Roodt, Prof Robert Dyer, Prof Justiaan Swanevelder, Prof Bruce Biccard, Prof Brian Rayner.
Department of Anaesthesia and Perioperative Medicine, University of Cape Town, South Africa

INFORMATION
You are being approached to be a part of a research study on blood pressure. The doctors that are running this study are trying to improve the management of your blood pressure if they identify that it is higher than normal.
If you have no objection, the doctors would appreciate your permission to collect information relating to your blood pressure measured in the ward, any medication you are currently taking to control your blood pressure, and any medication which is started during the study to control your blood pressure. This study will benefit you, as your high blood pressure will be treated timeously. You will be given some more information about your blood pressure and a letter for follow up at your local clinic to continue your medication in the future.
If you agree to be a part of this study, the doctors will collect the following information, which is routinely recorded in hospital:
• Your blood pressure, and factors known to be associated with high blood pressure and blood pressure medication.
When you enter this study, we will perform some standard investigations that are a normal part of managing high blood pressure. These will include:

- Some blood tests to check your kidney function (the organs often damaged by high blood pressure).
- An ECG (to check your heart function).
- A blood sugar test (high blood sugar is commonly associated with high blood pressure).

Any relevant results will be shared with you and managed appropriately according to the South African Hypertension Guideline of 2014.
This information will be stored both on paper and on computer. To protect your privacy, the information will be labelled in a way that you are not identified. If the results of these studies are published, your identity will be kept confidential.
By signing this form, you are allowing the use of this information for the research study.
These research projects have been approved by the Human Research Ethics Committee of the University of Cape Town. If you have any ethical concerns or questions about your rights or welfare as a participant in this research, the Human Research Ethics Committee can be contacted on 021 406 6338.
Please read this form carefully and ask the investigator (study doctor) to explain any words or information that are not clear to you. This will help to ensure that you understand the details of your participation before you give your consent. You will be

given a copy of this consent form to take home with you. The doctors will answer any questions you may have about this consent form and about the study.

What will happen if I sign this form but don't want to be in the study later on?

If you decide at any time that you don't want to be a part of this study, you can let one of the doctors know. Taking part is purely voluntary and by not agreeing to take part will not affect your normal care for surgery.

The UCT's Faculty of Health Sciences Human Research Ethics Committee can be contacted on 021 406 6338 in case you have any ethical concerns or questions about your rights or welfare as a participant on this research study.

CONSENT STATEMENT

I therefore certify the following:

- I have read the above information form and understand that the study involves research.
- I understand that the doctors will make a copy of some of my routinely recorded data from my standard patient care.
- I have had the opportunity to ask questions. All my questions have been answered to my satisfaction.
- I understand that any information that leaves the doctor's office will be de-identified (i.e., identifying information will be removed from the documents).

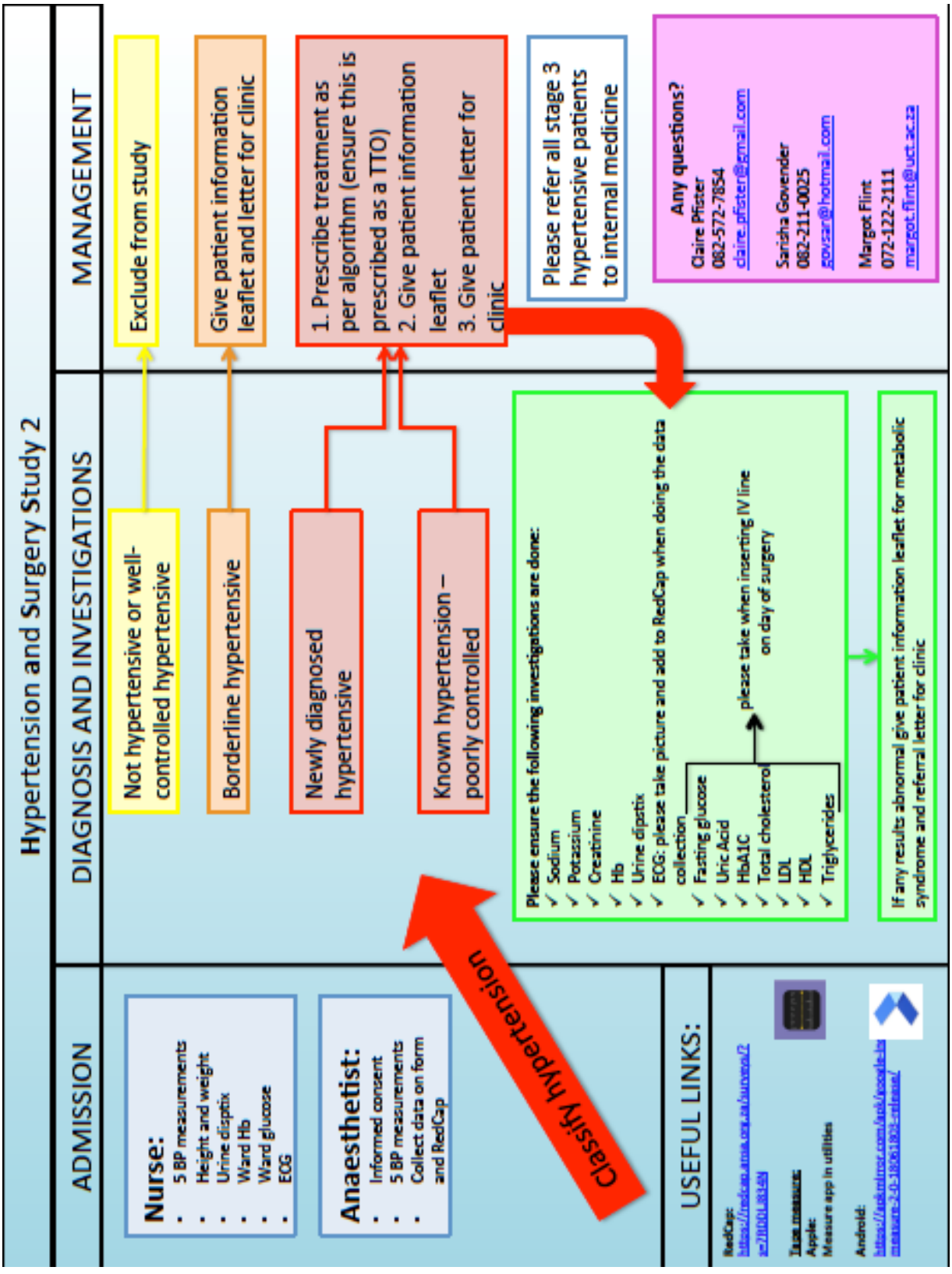
_____YES _____ NO

Name of Participant/Legal Representative (printed) **Signature**

Name of person obtaining consent (printed) **Signature** **Date:**

Appendix 3: Supplemental Material

a. Educational flow diagram for anaesthetists, ward doctors and nursing staff



b. Educational pamphlet for patients diagnosed with hypertension

Dear Patient

During your time in hospital, you were found to have high blood pressure. This is a condition called Hypertension. The doctor has started you on some medication and performed some tests. To answer any questions you may have, please read the points below:

What is blood pressure?

Blood pressure refers to the pressure that blood applies to the inner walls of the arteries. Arteries carry blood from the heart to other organs and parts of the body.

Do I have high blood pressure?

Yes. You were diagnosed as having hypertension by the doctor before you went for your operation. There are not usually any symptoms of high blood pressure.

Is it serious?

Hypertension is a lifelong condition which needs to be treated and managed. If it is not treated properly, the high blood pressure increases the strain on your heart and arteries, eventually causing organ damage. It can increase your risk of having heart failure, a heart attack, stroke and kidney failure.

Is there a cure?

There is no cure for high blood pressure, but it can be managed well with medication that you need to take every day, and by making some changes to your lifestyle. A medicine to lower your blood pressure will be given to you by a doctor or nurse. You need to make sure you take the medicine every day and follow up at your local clinic or hospital regularly, so that you always have a supply of your pills and the doctors and nurses can measure your blood pressure and make sure it is under control.

How can I help myself?

There is a lot you can do yourself to help improve your blood pressure:

- Stop smoking
- Reduce the amount of salt in your diet
- Avoid drinking too much alcohol
- Lose weight if you are overweight or obese

- Eat more fruit and vegetables
- Eat more fibre
- Eat more fish
- Exercise at least 30 minutes per day, most days of the week
- Drink less caffeine (less than 2 cups of coffee per day)

What are the side effects from antihypertensive medication?

Most of these are mild and may go away over time. Some common side effects of high blood pressure medicines include:

- Cough
- Diarrhoea or constipation
- Dizziness or lightheadedness
- Erection problems
- Feeling nervous
- Feeling tired, weak, drowsy, or a lack of energy
- Headache
- Nausea or vomiting
- Skin rash
- Weight loss or gain without trying

Tell your doctor or nurse as soon as possible if you have side effects or if the side effects are causing you problems. Most of the time, making changes to the dose of medicine or when you take it can help reduce side effects.

Never change the dose or stop taking a medicine on your own. Always talk to your doctor or nurse first.

Where to get more information:

- Ask your doctor or nurse
- The following websites are useful:
    - www.uptodate.com/patients
    - www.cdc.gov/dhdsp/index.htm
    - www.americanheart.org

- www.nhlbi.nih.gov

Please take the letter that the doctors gave to you, to your next appointment at a Clinic or Hospital, to ensure that you continue to receive the correct management, and so that your blood pressure will continue to be controlled.

c. Letter for local primary health care facility for patients diagnosed with hypertension

Dear Patient

Please present this letter to your follow up clinic at your first visit:

To Whom It May Concern:

This patient was diagnosed with hypertension as part of a perioperative quality improvement project involving the following hospitals: Groote Schuur-, George-, Mitchells Plain District-, New Somerset-, Paarl-, Victoria-, and Worcester Provincial Hospital.

He/she has commenced taking the following medication:

-
-
-
-
-

Please continue this medication and measure the patient's blood pressure according to your normal protocol at their follow up visits.

These are the results of the latest investigations:

a. Sodium: Potassium: Creatinine:

b. Fasting blood glucose level OR HbA1C:

2. ECG:

3. Cholesterol/lipogram:

4. Urine dipstix:

Thank you for your assistance in continuing the management of this patient's hypertension!

d. Educational pamphlet for patients with blood pressure in the borderline range

Dear Patient

During your time in hospital, you were found to have blood pressure that is higher than normal. Your blood pressure was not high enough to start you on treatment, but it should be checked regularly at your local clinic. To answer any questions you may have, please read the points below:

What is blood pressure?

Blood pressure refers to the pressure that blood applies to the inner walls of the arteries. Arteries carry blood from the heart to other organs and parts of the body.

Is it serious?

Hypertension is a lifelong condition which needs to be treated and managed. If it is not treated properly, the high blood pressure increases the strain on your heart and arteries, eventually causing organ damage. It can increase your risk of having heart failure, a heart attack, stroke and kidney failure. If your blood pressure is not high enough for treatment, it is recommended that you make some changes to your lifestyle and have it checked regularly at your local clinic.

Is there a cure?

There is no cure for high blood pressure, but it can be managed well with medication that you need to take every day, and by making some changes to your lifestyle. You need to make sure you and follow up at your local clinic or hospital regularly, so that the doctors and nurses can measure your blood pressure and make sure it is under control.

How can I help myself?

There is a lot you can do yourself to help improve your blood pressure:

- Stop smoking
- Reduce the amount of salt in your diet
- Avoid drinking too much alcohol
- Lose weight if you are overweight or obese
- Eat more fruit and vegetables
- Eat more fibre

- Eat more fish
- Exercise at least 30 minutes per day, most days of the week
- Drink less caffeine (less than 2 cups of coffee per day)

Where to get more information:

- Ask your doctor or nurse
- The following websites are useful:
    - www.uptodate.com/patients
    - www.cdc.gov/dhdsp/index.htm
    - www.americanheart.org
    - www.nhlbi.nih.gov

Please take the letter that the doctors gave to you, to your next appointment at a Clinic or Hospital, to ensure that you continue to receive the correct management, and so that your blood pressure will continue to be controlled.

e. Letter for local primary health care facility for patients diagnosed with hypertension

Dear Patient

Please present this letter to your follow up clinic at your first visit:

To Whom It May Concern:

This patient was diagnosed with borderline hypertension as part of a perioperative quality improvement project involving the following hospitals: Groote Schuur-, George-, Mitchells Plain District-, New Somerset-, Paarl-, Victoria-, and Worcester Provincial Hospital.

Please will you measure their blood pressure again and ensure it is within the normal range. Should it be normal, please follow up as per your protocol. Should it be raised, please initiate antihypertensive treatment as per your institution's practices.

Thank you for your assistance in continuing the management of this patient's hypertension.

Appendix 4: Ethics Approval

a. Human Research Ethics Committee Approval

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

Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6626
Email: shuretta.thomas@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

13 November 2018

HREC REF: 489/2018

Prof B Biccard
Anaesthesia
NGSH, D23

Dear Prof Biccard

PROJECT TITLE: HYPERTENSION AND SURGERY STUDY - 2 (MMED CANDIDATE - DR C PFISTER)

Thank you for submitting your response to the Faculty of Health Sciences Human Research Ethics Committee dated 29 October 2018.

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

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

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

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.

The HREC acknowledge that the student, Dr Claire Pfister will also be involved in this study.

Yours sincerely

Signature Removed

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938
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

b. Provincial approval:

Western Cape Government
Health

GROOTE SCHUUR HOSPITAL
Enquiries: Dr Bernadette Eick
E-mail :Bernadette.Eick@westerncape.gov.za

Professor B. Biccard & Dr M. Flint
Anaesthetic & Perioperative Medicine

E-mail: bruce.biccard@uct.ac.za / margot.flint@uct.ac.za

Dear Professor Biccard & Dr Flint

RESEARCH PROJECT: 1) Hypertensive and Surgery Study – 2 (MMed Dr Claire-Louise Pfister)
RESEARCH PROJECT: 2) Compliance Report: A Multicentre Study of Newly Diagnosed (HASS 2) Hypertensive Patients to Treatment

Your recent letter to the hospital refers.

You are granted permission to proceed with your research, which is valid until **30 November 2019.**

Please note the following:

a) Your research may not interfere with normal patient care.
b) Hospital staff may not be asked to assist with the research.
c) No additional costs to the hospital should be incurred i.e. Lab, consumables or stationary.
d) **No patient folders may be removed from the premises or be inaccessible.**
e) Please provide the research assistant/field worker with a copy of this letter as verification of approval.
f) Confidentiality must be maintained at all times.
g) Should you at any time require photographs of your subjects, please obtain the necessary indemnity forms from our Public Relations Office (E45 OMB or ext. 2187/2188).
h) Should you require additional research time beyond the stipulated expiry date, please apply for an extension.
i) Please discuss the study with the HOD before commencing.
j) Please introduce yourself to the person in charge of an area before commencing.
k) On completion of your research, please forward any recommendations/findings that can be beneficial to use to take further action that may inform redevelopment of future policy / review guidelines.
l) Kindly submit a copy of the publication or report to this office on completion of the research.

I would like to wish you every success with the project.

Yours sincerely

Signature Removed

DR BERNADETTE EICK
CHIEF OPERATIONAL OFFICER
Date: 14 December 2018

C.C. Mr. L. Naidoo
Dr S. Peters
Dr T. Numanoglu

G46 Management Suite, Old Main Building, Observatory 7925
Tel: +27 21 404 6288 fax: +27 21 404 6125

Private Bag X, Observatory, 7935
www.capegateway.go.v.za

Appendix 5: Instructions to authors

Anesthesia & Analgesia

The Gold Standard in Anesthesiology

Taken from http://edmgr.ovid.com/aa/accounts/ifauth.htm
For ease of reading I have greyed out those sections which were irrelevant to the instruction for this paper.

Anesthesia & Analgesia

The Gold Standard in Anesthesiology

We greatly appreciate your interest in submitting your manuscript to *Anesthesia & Analgesia*. Our goal is to provide authors with a thorough yet timely review of their submissions. All initial decisions should be completed within 6 weeks, except for Review Articles and Special Articles, which may take up to 8 weeks. Authors will be updated as to the status of their manuscript via Editorial Manager.

Notice: The **Instructions for Authors** for *Anesthesia & Analgesia* have been further revised. New submissions should be prepared according to the Instructions that follow. Failure to do so may result in your submission being returned without review.

This now current Version 3.2 of these Instructions for Authors replaces the earlier Version 3.1.

As of July 1, 2019, *Anesthesia & Analgesia* is not receiving or considering new Brief Report manuscript submissions.

Brief Report manuscripts that have been submitted prior to July 1, 2019 will undergo a complete review and final decision by *Anesthesia & Analgesia*. Previously accepted Brief Report manuscripts will still be published by *Anesthesia & Analgesia*.

Authors seeking to submit to *A&A Practice* (formerly *A&A Case Reports*) can find its separate *A&A Practice* Instructions for Authors and submit their papers through the *A&A Practice* Editorial Manager Submission Site.

As of January 1, 2018, all Echo Rounds and Echo Didactics articles are published online only in A&A Practice. Please refer to these separate *A&A Practice* Instructions for Authors for Echo Rounds and Echo Didactics submissions.

A&A Practice remains fully editorially aligned and operationally integrated yet distinct from Anesthesia & Analgesia.

Mission and Scope

Anesthesia & Analgesia exists for the benefit of patients under the care of health care professionals engaged in the disciplines broadly related to anesthesiology, perioperative medicine, critical care medicine, and pain medicine. The Journal furthers the care of these patients by reporting the fundamental advances in the science of these clinical disciplines and by documenting

the clinical, laboratory, and administrative advances that guide therapy. *Anesthesia & Analgesia* seeks a balance between definitive clinical and management investigations and outstanding basic scientific reports. The Journal welcomes original manuscripts containing rigorous design and analysis, even if unusual in their approach.

Authors are encouraged to read this editorial, which describes some of the previous changes to the editorial philosophy of *Anesthesia & Analgesia*: Pittet JF, Vetter TR. Continuing the Terra Firma and Establishing a New EQUATOR for *Anesthesia & Analgesia*. Anesth Analg. 2016;123(1):8-9.

Authors are strongly encouraged to adhere to the fundamentals of English grammar, syntax, punctuation, and composition.

Authors are encouraged to read this excellent synopsis on the fundamentals of writing a research report: Sessler DI, Shafer S. Writing Research Reports. Anesthesia & Analgesia. 2018;126(1):330-337.

If a paper is poorly written and thus difficult to understand, it will likely **not** receive as favorable a review, despite presenting strong science and/or novel information. If indicated, please consider using a Language Editing Service (see below) to address this issue **before** your initial submission.

***Anesthesia & Analgesia* Instructions for Authors**

Anesthesia & Analgesia has specific **Instructions for Authors** for submitting articles, which are found below. We strongly encourage all authors to read these instructions completely and carefully, and to prepare their manuscripts in accordance with these instructions.

Articles that are not submitted in accordance with our instructions may be returned for revision prior to peer-review or rejected outright.

Brevity is crucial for a well-written and effective scholarly article. Particular attention should thus be paid to the listed word count, reference count, and table/figure limits for each article type, both for an initial submission and any subsequent revisions.

The word count, reference count, and table/figure limits will be strictly enforced, resulting in a manuscript being returned to the author(s) for revision prior to any initial or a subsequent peer-review.

Occasionally, authors will be asked by the Journal Editorial Board to resubmit their work as a different article type. If so, this subsequent manuscript will be handled as an entirely new submission, with a corresponding new assigned manuscript number.

Any changes (additions or deletions) of authors will need to be justified and clearly communicated. See below, **Section 8.A. Role of Authors and Contributors**.

Please note that a **Glossary of Terms** is now required for all submissions to A&A Practice (except Letter to the Editor). See below, Section 6.

Questions?

If you have a question specifically for the Editor-in-Chief, Dr. Jean-Francois Pittet, please email him at jpittet@iars.org, or contact the Deputy Editor-in-Chief, Dr. Thomas Vetter at thomas.vetter@austin.utexas.edu

If you have questions about these submission instructions, or the Journal peer review process in general, please contact the **Editorial Office** via editor@anesthesia-analgesia.org

Manuscripts may only be submitted via the Editorial Manager online submission system:

Submit your manuscript to *Anesthesia & Analgesia* here.

Submit your manuscript to *A&A Practice* here.

If you are new to our journal, our **Visual User Guide for Authors** will help you step-by-step to create an author account and to submit your new manuscript via Editorial Manager.

If you are submitting a revised manuscript, our **User Guide for Revisions** will help you step-by-step to submit your revised manuscript via Editorial Manager.

Download a PDF version of the full Instructions for Authors of *Anesthesia & Analgesia*

INSTRUCTIONS FOR AUTHORS

SECTION 1: *ANESTHESIA & ANALGESIA* ARTICLE TYPES (Back to Contents): Each is described in detail below.

Systematic Review Articles

Meta-Analysis

Editorial

The Open Mind

Special Article

Letter to the Editor

Book and Multimedia Reviews

Meeting Report

DESCRIPTIONS OF SPECIFIC ARTICLE TYPES

Anesthesia & Analgesia

Original Clinical, Health Services, or Educational Research Report (Back to Top)

- An Original Clinical, Health Services, or Educational Research Report describes an investigation that focuses on the clinical practice of anesthesiology, perioperative medicine, critical care medicine, or pain medicine.
- Original Clinical, Health Services, or Educational Research Reports span the spectrum of patient-reported outcomes, clinical effectiveness, quality and performance improvement, patient safety, health services delivery, dissemination and implementation science, health policy, healthcare economics, population health, and education.
- An Original Clinical, Health Services, or Education Research Report includes a Title Page and structured Abstract of no more than **400 words**.
- A "Key Points" summary is also provided, which describes the Question, Findings, and Meaning, each composed of **one sentence**.
- These Reports are divided into four sections: Introduction, Methods, Results, and Discussion.
- The Introduction section should be focused and contain no more than **400 words**. The Introduction succinctly describes, in a series of short paragraphs, the significance of the topic, pertinent background, rationale for the study, *a priori* study aims or objectives, and primary study hypothesis, and if appropriate, secondary study hypothesis.
- The Discussion section should also be focused and contain no more than **1,000 words**. The Discussion succinctly interprets the primary findings of the study and how they relate to previous published findings. The limitations of the present study are clearly stated. If applicable, future, related research opportunities are briefly proposed.
- An Original Clinical, Health Services, or Education Research Report ranges in total length from **1,500 to 4,000 words** (not counting the Abstract and references), with no more than **30-40 references** and **4-6 tables and/or figures**. Online supplemental material can be provided when appropriate.
- Study Reporting Requirement (EQUATOR)
- Instructions for Manuscript preparation
- Instructions for Figure preparation
- Instructions for Table preparation

- Instructions for Supplemental Material

Original Laboratory Research Report (Back to Top)

- An **Original Laboratory Research Report** describes an investigation that focuses on an aspect of basic science related to anesthesiology, perioperative medicine, critical care medicine, or pain medicine.
- Original Laboratory Research Reports span the spectrum of cell biology, immunology, neurobiology, biochemistry, pharmacology, microbiology, and genetics.
- An Original Laboratory Research Report includes a Title Page and structured Abstract of no more than **400 words**.
- A "Key Points" summary is also provided, which describes the Question, Findings, and Meaning, each composed of **one sentence**.
- These Reports are divided into four sections: Introduction, Methods, Results, and Discussion.
- The Introduction section should be focused and contain no more than **400 words**. The Introduction succinctly describes, in a series of short paragraphs, the significance of the topic, pertinent background, rationale for the study, *a priori* study aims or objectives, and primary study hypothesis, and if appropriate, secondary study hypothesis.
- The Discussion section should also be focused and contain no more than **1,000 words**. The Discussion succinctly interprets the primary findings of the study and how they relate to previous published findings. The limitations of the present study are clearly stated. If applicable, future, related research opportunities are briefly proposed.
- An Original Laboratory Research Report ranges in total length from **1,500 to 4,000 words** (not counting the Abstract and references), with no more than **30-40 references** and **4-6 tables and/or figures**. Online supplemental material can be provided when appropriate.
- Study Reporting Requirement (EQUATOR)
- Instructions for Manuscript preparation
- Instructions for Figure preparation
- Instructions for Table preparation
- Instructions for Supplemental Material

Narrative and Systematic Review Articles (Back to Top)

- A **Narrative Review Article** or **Systematic Review Article** synthesizes previously published material into an integrated presentation of the current understanding of a topic.
- A Narrative Review can be either **focused** or **comprehensive**, based on its topic and scope.
- A Narrative Review Article should describe aspects of a topic about which scientific and evidence-based consensus exists, as well as aspects that remain controversial and are thus topics for ongoing and future research.
- A duly noted and entitled **Consensus Practice Guideline** is considered a specific type of a **focused Narrative Review**.
- A duly noted and entitled **Statistical Grand Rounds** is another specific type of a **focused Narrative Review** of the conventional or novel application of contemporary quantitative sciences (i.e., statistics, epidemiology, or database management) to issues of concern to anesthesia, critical care or pain researchers. Here the inclusion of programing code and/or illustrative datasets as online supplemental material is encouraged.

- For a Systematic Review, a formal strategy to search and to critically evaluate the medical literature should be applied and well-described. Such explicit methods are used in a Systematic Review to minimize bias in its content and findings.
- All Review Articles include a Title Page and an unstructured Abstract with no more than **400 words**.
- The Introduction section should be focused and contain no more than **400 words**.
- The Discussion section should also be focused and contain no more than **1,000 words**.
- A Review Article ranges in total length from **1,500 to 5,000 words** (not counting the Abstract and references), with up to **150 references** and **4-6 tables and/or figures**. Online supplemental material can be provided when appropriate.
- Exceptions to these word count, reference count, and table/figure limits may be granted at the discretion of the Journal Editorial Board for a **Consensus Practice Guideline** manuscript.
- Study Reporting Requirement (EQUATOR)
- Instructions for Manuscript preparation
- Instructions for Figure preparation
- Instructions for Table preparation
- Instructions for Supplemental Material

Meta-Analysis (Back to Top)

- A **Meta-Analysis** uses analytic techniques to combine the quantitative results from existing individual studies, which are initially identified via a **Systematic Review**, thereby (a) allowing for a more precise estimate of the magnitude of benefit or harm of an intervention and/or (b) increasing the applicability of the results to a broader range of patients.
- A Meta-Analysis should not be written and submitted as a Systematic Review Article but as a separate submission type.
- A Meta-Analysis includes a Title Page and structured Abstract of no more than **400 words**.
- A "Key Points" summary is also provided, which describes the Question, Findings, and Meaning, each composed of **one sentence**
- These manuscripts are divided into four sections: Introduction, Methods, Results, and Discussion.
- The Introduction section should be focused and contain no more than **400 words**.
- The Discussion section should also be focused and contain no more than **1,000 words**.
- A Meta-Analysis ranges in total length from **1,500 to 5,000 words** (not counting the Abstract and references), with no more than **150 references** and **4-6 tables and/or figures**. Online supplemental material can be provided when appropriate.
- Study Reporting Requirement (EQUATOR)
- Instructions for Manuscript preparation
- Instructions for Figure preparation
- Instructions for Table preparation
- Instructions for Supplemental Material

Editorial (Back to Top)

- Editorials are *solicited* by the Editorial Board
- An Editorial either (a) provides an editorial perspective on an article published in the Journal or (b) expresses the general policies or opinions of the Journal Editorial Board. If an Editorial is intended to provide an expert perspective on an article or topic published in the Journal, it is typically solicited from reviewer(s) who provided unusually thoughtful

insight during the peer-review process, and which the Editors believe should be shared with the Journal readership.
- An Editorial includes a Title but not an Abstract.
- An Editorial contains no more than **2000 words** (not counting the references), with no more than **15 references** and occasionally **1 table and/or 1 figure**.
- Instructions for Manuscript preparation
- Instructions for Figure preparation
- Instructions for Table preparation
- Instructions for Supplemental Material

The Open Mind (Back to Top)

- The Open Mind is a unique forum for thoughtful, scholarly, and preferably well-referenced perspectives. The Open Mind is intended to stimulate lively yet civil discussion. It is a forum for (a) challenging myths or dogma and/or (b) proposing new approaches or solutions to an important issue facing the anesthesiology community.
- Descriptive data collection and reporting are not permitted with The Open Mind submission.
- Comparative data collection and analyses are not permitted with The Open Mind submission.
- Submissions to The Open Mind include a Title Page but not an Abstract.
- An Open Mind article ranges in total length from **1,500 to 3,000 words** (not counting the references), with up to **20 references** and **2-3 tables and/or figures**.
- These tables or figures can be reproductions of previously published, illustrative data with the required appropriate attribution and permission.
- Instructions for Manuscript preparation
- Instructions for Figure preparation
- Instructions for Table preparation
- Instructions for Supplemental Material

Special Article (Back to Top)

- A Special Article is intended for when authors occasionally seek to publish a scholarly manuscript that does not fit one of the other above article types.
- A Special Article can also be invited by the Editorial Board to examine a specific novel topic.
- After first communicating directly in writing with and obtaining written pre-approval from the Journal Editor-in-Chief, a manuscript may be submitted as a Special Article. This initial communication to the Journal Editor-in-Chief must include a Title and an Abstract for the proposed Special Article submission.
- When submitted, the cover letter for a Special Article manuscript must state that the corresponding author has first communicated directly with and obtained written approval from the Journal Editor-in-Chief.
- Descriptive data collection and reporting are not permitted with a Special Article submission.
- Comparative data collection and analyses are not permitted with a Special Article submission.
- All Special Articles include a Title Page and an unstructured Abstract with no more than **400 words**.
- A Special Article ranges in total length from **1,000 to 5,000 words** (not counting the Abstract and references), with up to **150 references** and **4-6 tables and/or figures**.

- These tables or figures can be reproductions of previously published, illustrative data with the required appropriate attribution and permission.
- Instructions for Manuscript preparation
- Instructions for Figure preparation
- Instructions for Table preparation
- Instructions for Supplemental Material

Letter to the Editor (Back to Top)

- A Letter to the Editor is intended to offer brief, objective, and constructive comments or criticism concerning a previously published article. A Letter to the Editor is not intended to provide other communication of general interest to the readership. Such correspondence submissions are also not a venue for Case Reports, and authors must attest during the submission process, in their cover letter, that a case description is not included in their correspondence.
- A Letter to the Editor should be brief, with no more than **1000 words**. Six or fewer references, a small table or a pertinent illustration may be provided.
- All Letters to the Editor should be submitted via the *Anesthesia & Analgesia* Online Submission and Review System and not via email or postal service.
- Letters are edited by the Correspondence Editor, sometimes extensively, to sharpen their focus. A Letter to the Editor may be sent for peer review, at the discretion of the Correspondence Editor.
- A Letter to the Editor that is written in response to a published paper must be submitted no later than 3 months after the first of day of the month of the original article's **print publication date**.
- Instructions for Manuscript preparation

Book and Multimedia Reviews (Back to Top)

- A Book and Multimedia Review reports on a current publication about anesthesiology, perioperative medicine, critical care medicine, or pain medicine, or a book on another topic that is directly relevant to the practicing clinician.
- Publishers interested in having their book or multimedia material reviewed by the Journal should first contact our Media Reviews editor at: bookreviews@iars.org.
- A Book Review contains no more than **750 words**. The title page for all book reviews must include the following information regarding the book you reviewed: Title. Author Name(s). Publisher, Year, Number of Pages, Paperback Price (USD), eBook Price (USD), ISBN: Number (Paperback), Number (eBook).
- Additional recommendations on preparing a Book or Multimedia Review can be found at this online link.
- Instructions for Manuscript preparation

Meeting Report (Back to Top)

- A Meeting Report is a scholarly outline of the program and content of a scientific meeting.
- A Meeting Report may be organized temporally (day by day) or thematically (topic by topic).
- Authors interested in submitting meeting reports should first contact our Media Reviews editor at bookreviews@iars.org to confirm that the meeting is of general interest to the readership.
- A Meeting report does not have an Abstract and contains no more than **1500 words**.

- Instructions for Manuscript preparation

SECTION 2: ARTICLE TYPES AT A GLANCE (Back to Contents)

Particular attention should be paid to the listed word count, reference count, and table/figure limits for each article type, both for an initial submission and any subsequent revisions.

These listed limits for word count, reference count, and tables/figures will be strictly enforced, resulting in a manuscript being returned to the author(s) for revision prior to any initial or a subsequent peer-review.

Anesthesia & Analgesia ARTICLE TYPES AT A GLANCE							
Manuscript Type	**Abstract:**	**Figures/Tables Limit**	**Reference Count Limit**	**Word Count Limit**	**Sections**	**Supplemental Material**	**Additional Information**
Clinical, Health Services, or Education Report	Structured 400 word limit & Key Points Summary	4 to 6 tables and/or figures	30-40	1500-4000 (not including abstract and references)	Introduction, Methods, Results, and Discussion	When appropriate	EQUATOR checklist
Laboratory Research Report	Structured 400 word limit & Key Points Summary	4 to 6 tables and/or figures	30-40	1500-4000 (not including abstract and references)	Introduction, Methods, Results, and Discussion	When appropriate	EQUATOR checklist
Narrative Review Articles	Unstructured 400 word limit	4-6 tables and/or figures	150	1,500 to 5,000 words (not including abstract and references)		The inclusion of programing code/illustrative datasets as online supplemental material is encouraged	EQUATOR checklist
Systematic Review Article	Unstructured 400 word limit	4-6 tables and/or figures	150	1,500 to 5,000 words (not including abstract and references)		When appropriate	EQUATOR checklist
Meta-Analysis	Structured 400 word limit & Key Points Summary	4-6 tables and/or figure	150	1,500 to 5,000 words (not including abstract and references)		When appropriate	EQUATOR checklist
Editorial ***Solicited by the***	NA	1 table and/or 1 figure	15	Less than 2000 words (not including references)		When appropriate	EQUATOR checklist

Editorial Board							
The Open Mind	NA	2-3 tables and/or figures	20	1500 to 3000 words (not including references)		When appropriate	EQUATOR checklist
Special Article ***Solicited by the Editorial Board***	Unstructured 400 words	4-6 tables and/or figures	150	1000-5000 (not including abstract and reference)		When appropriate	EQUATOR checklist
Letter to the Editor and Reply - for Anesthesia & Analgesia	NA	Small table or a pertinent illustration may be provided.	6 or less	1000			EQUATOR checklist
Book and Multimedia Review	NA	NA	Reference the publication	750			EQUATOR checklist
Meeting Report	NA	NA		Less than 1500	May be organized temporally (day by day) or thematically (topic by topic).		EQUATOR checklist

SECTION 3: STANDARDIZED STUDY REPORTING REQUIREMENTS (Back to Contents)

A. Enhancing the Quality of and Transparency of Health Research (EQUATOR) Network

The Enhancing the Quality of and Transparency of Health Research (EQUATOR) Network was created to monitor and to propagate the proper use of guidelines to improve the quality of scientific publications by promoting transparent and accurate reporting of human subjects, health services, and animal research.

As advocated by the EQUATOR Network, *Anesthesia & Analgesia* strongly encourages adherence to the applicable statement/guidelines and checklist for all submitted research-related manuscripts (see Table below). Manuscripts adhering to the applicable statement/guidelines and checklist will typically receive a more favorable review by the Journal.

Adhering to the applicable statement/guidelines and checklist promotes consistent study design and manuscript content, which are major advantages for the Journal's authors, reviewers, editors, and readers.

Authors should consult the EQUATOR Network webpage and/or the webpage URL or citation listed in the Table below for the most current version of the specific, applicable **statement or guideline and its checklist**.

- **The applicable study checklist should be completed and uploaded under the EQUATOR Checklist File category at the time of initial manuscript submission via Editorial Manager.**

Acronym	Full Title of Guideline	Webpage URL or Citation
CONSORT	Consolidated Standards of Reporting Trials (See footnote* below)	http://www.consort-statement.org/
TREND	Transparent Reporting of Evaluations with Nonrandomized Designs	http://www.cdc.gov/trendstatement/
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology	http://www.strobe-statement.org/
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses	http://www.prisma-statement.org/
SQUIRE	**Standards for Quality Improvement Reporting Excellence**	http://www.squire-statement.org/
SRQR or COREG	Standards for Reporting Qualitative Research Consolidated Criteria for Reporting Qualitative Research	PMID: 24979285 PMID: 17872937
CHEERS	Consolidated Health Economic Evaluation Reporting Standards	http://www.ispor.org/Health-Economic-Evaluation-Publication-CHEERS-Guidelines.asp
STARD or TRIPOD	Standards for Accurate Reporting of Diagnostic Tests *Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis Or Diagnosis*	http://www.stard-statement.org/ http://www.tripod-statement.org/

STREGA	Strengthening the Reporting of Genetic Associations	http://www.equator-network.org/reporting-guidelines/strobe-strega/
ARRIVE	Animal Research: Reporting of *In Vivo* Experiments	http://www.nc3rs.org.uk/arrive-guidelines

* The main CONSORT Statement is based on the "standard" two-group parallel design. However, there are several different types of randomized trials, some of which have different designs (e.g., cluster, non-inferiority and equivalence, or pragmatic trials), interventions (e.g., herbal medicinal, non-pharmacological, or acupuncture) and data (e.g., harms), for which specific CONSORT Extensions exist.

B. SPECIFIC STUDY TYPE AND ASSOCIATED PUBLISHED GUIDELINE

1. Randomized Controlled Trials. Authors reporting the results of a **randomized controlled trial** must follow the CONSORT statement and provide a completed CONSORT checklist. Authors must also provide a CONSORT flow diagram as Figure 1 of the submitted manuscript.

Please note that there are CONSORT Extensions for several different types of randomized trials, and the most applicable Extension should be followed by authors.

2. Non-Randomized Controlled Trials. Authors reporting the results of a **non-randomized controlled trial** must follow the TREND statement and provide a completed TREND checklist.

3. Observational Studies. Authors reporting the results of a **cohort, case-cohort, nested case-control, case-control, or cross-sectional study (or any other type of observational study of human subjects)**, or a retrospective data collection study must follow the STROBE statement and provide a completed STROBE checklist.

Authors submitting the results of such a quantitative observational study should clearly indicate (a) whether the primary outcome(s) were defined and established *a priori* at initiation of the study design or were created post hoc during data exploration ("data mining") and accompanying statistical analysis and (b) whether subgroup or sensitivity analyses were identified and established *a priori* or *post hoc*. For studies evaluating a treatment effect, indicate whether and how a clinically meaningful effect size was defined, once again either *a priori* or *post hoc*.

For further insights and directions, see Eisenach JC, Kheterpal S, Houle TT. Reporting of Observational Research in ANESTHESIOLOGY: The Importance of the Analysis Plan. Anesthesiology. 2016;124(5):998-1000.

4. Systematic Review or Meta-analysis. Authors reporting a **systematic review** or **meta-analysis of randomized trials or cohort studies** must follow the PRISMA (previously named QUOROM) Statement and provide a completed PRISMA checklist. Authors must also submit a PRISMA flow diagram as Figure 1 of the submitted manuscript.

5. Quality Improvement Research. Authors reporting the results of a **quality improvement study** must follow the SQUIRE 2.0 guidelines and provide a completed SQUIRE 2.0 checklist.

6. Qualitative Research. Authors reporting the results of a **qualitative study** (e.g., in-depth interviews and focus groups) must provide a completed SRQR checklist.

Alternatively, authors reporting the results of a **qualitative study** can provide a completed COREG checklist.

7. Mixed Methods Research. No definitive guidelines have been created for mixed (qualitative/quantitative) research. However, authors reporting the results of a mixed methods research study can reference the Good Reporting of A Mixed Methods Study (GRAMMS) framework.

See the following pertinent references:

Cameron RA, Trudy D, Scott R, Ezaz A, Aswini S. Lessons from the field: Applying the Good Reporting of A Mixed Methods Study (GRAMMS) framework'. Electronic Journal of Business Research Methods. 2013. https://works.bepress.com/roslyn_cameron/131/

O'Cathain A, Murphy E, Nicholl J. The quality of mixed methods studies in health services research. J Health Serv Res Policy. 2008;13(2):92-98.

O'Cathain A, Murphy E, Nicholl J. Three techniques for integrating data in mixed methods studies. BMJ. 2010 Sep 17;341:c4587.

8. Health Economic Evaluation Research. Authors reporting the results of a **health economic evaluation research study** must follow the CHEERS guidelines and provide a completed CHEERS checklist.

9. Diagnostic Accuracy. Authors reporting a **study of the accuracy of a diagnostic test** must follow the STARD statement and provide a completed STARD checklist. Authors must also provide a STARD flow diagram as Figure 1 of the submitted manuscript.

Alternatively, authors reporting studies of the accuracy of diagnostic tests can follow the TRIPOD Statement and provide a completed TRIPOD checklist.

10. Genetic Association Studies. Authors reporting a **genetic association study** must follow the STREGA guidelines and must submit a completed STREGA checklist.

11. Animal Studies. Authors reporting an **animal study** must follow the ARRIVE guidelines and must submit the ARRIVE checklist.

SECTION 4: STANDARDS FOR STATISTICAL METHODS AND STATISTICAL REPORTING (Back to Contents)

All authors who are presenting data and data analyses in their manuscripts submitted to the Journal are now required to attest via Editorial Manager that they have reviewed sections 4A and 4B below and have implemented all of the relevant items.

This should be done preferably before implementing their study data collection but certainly as they undertook their statistical analyses and prepared their manuscript for initial submission and any requested revision(s).

While *Anesthesia & Analgesia* has elected not to implement a required formal statistical checklist to be completed and submitted by authors, adhering to the guidelines below

will avoid delays in the review process and generally improve the likelihood of publication.

A. Statistical Analyses and Methods as Promulgated by the Statistical Analyses and Methods in the Published Literature (SAMPL) Guidelines

As advocated by the EQUATOR Network, *Anesthesia & Analgesia strongly* endorses adherence to the Statistical Analyses and Methods in the Published Literature (SAMPL) Guidelines.

Please see Lang TA, Altman DG. Basic statistical reporting for articles published in biomedical journals: The "Statistical Analyses and Methods in the Published Literature" or "The SAMPL Guidelines." Handbook, European Association of Science Editors. 2013:23-6.

The SAMPL Guidelines can be accessed at http://www.equator-network.org/reporting-guidelines/sampl/.

B. For All Studies That Include Data Analysis and/or Estimation

BASIC STATISTICAL METHODS AND REPORTING THAT SHOULD BE INCLUDED IN ALL QUANTITATIVE MANUSCRIPTS.

The items outlined below are commonly missing or deficient in submitted manuscripts, leading to a lengthier and less favorable statistical review.

Authors are this strongly encouraged to proactively address all of these issues.

At the time of their initial online manuscript submission, the corresponding author will be asked to attest to reviewing and the online supplement that provides details for the following outline.

Click HERE to access this online supplement.

PLEASE NOTE: EACH MANUSCRIPT WILL BE EXPLICITLY EVALUATED ON EACH OF THESE ITEMS DURING ITS STATISTICAL REVIEW.

1. Abstract clearly and accurately states the study objectives/hypotheses and clearly describes data analysis and study findings
2. Study objectives and/or hypotheses clearly stated
3. Study design is appropriate for the stated aims
4. Primary and secondary outcomes clearly identified and defined
5. Statistical methods appropriate and clearly described
6. Baseline comparisons for randomized trial assessed with standardized difference, not P-values
7. Assumptions of the statistical analyses appropriately assessed
8. Type I error/multiple testing adequately addressed
9. Missing data appropriately described and handled
10. Sample size justified
11. Results section follows clearly from the study objectives and statistical methods
12. Treatment effect estimates and their variability are reported
13. Confounding is carefully addressed for observational studies
14. Tables and Figures clear and self-explanatory
15. Limitations of design and statistical methods clearly described
16. Conclusions and Interpretations justified by the design and results

- Causation/association – use words connoting association for observational studies
- Say "Non-significant" instead of "similar/equivalent"
- Make inference on population not sample
- Trend -- Do not say "trend" for non-significant findings

17. P-values appropriately reported
18. "Multivariable" instead of "multivariate" when multiple independent variables

SECTION 5: DIGITAL COPYRIGHT TRANSFER AGREEMENT (Back to Contents)

An Electronic Copyright Transfer and Disclosure Questionnaire is completed by the corresponding author during submission.

Upon submission, the co-authors are emailed a hyperlink to verify their co-authorship and complete the electronic Copyright Transfer and Disclosure Form within Editorial Manager.

Questions About the Copyright Transfer and Disclosure Form?

Please contact our editorial office at editor@anesthesia-analgesia.org

SECTION 6: OPEN ACCESS OPTION FOR PUBLICATION (Back to Contents)

Authors of accepted peer-reviewed articles have the choice to pay a fee to allow perpetual unrestricted online access to their published article to readers globally, immediately upon publication. Please see the **Open Access page** for more details.

SECTION 7: *ANESTHESIA & ANALGESIA* MANUSCRIPT PREPARATION (Back to Contents)

Manuscript Organization

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Manuscript Organization (Back to Top)

ALL articles should be arranged in the following order.

1. Manuscript, as a single file, consisting of Title Page, Abstract (not required for all article types – see Articles At A Glance), Body Text, References. Page numbers should be included, line numbers should not be included.
2. Tables (each Table should be a separate .doc file or placed at the end of the manuscript file)
3. Figure Legends (placed consecutively, in numerical order, all on the same page)
4. Figures (each Figure should be uploaded as a separate file)
5. Appendices (each Appendix should be a separate file)

Title Page (Back to Top)

- Article Title
- First name, middle initial, and last name of each author, with their highest academic degree (M.D., Ph.D., *etc.*), and institutional affiliations.
- Name, mailing address, phone number, and e-mail address of the corresponding author.
- Disclosure of funding received for the work from National Institutes of Health (NIH), Wellcome Trust, Howard Hughes Medical Institute (HHMI), and all other financial support, including departmental or institutional funding. If no funding received, state Financial Disclosures: None
- Please list any conflicts of interest the authors have had within the 36 months of submission. If no conflicts, state Conflicts of interest: None
- Clinical trial number and registry URL, if applicable.

- **List the word count of the Abstract, Introduction, and Discussion. Also list the overall word count for the entire body of text (excluding Abstract and References).**
- Abbreviated Title (running head) that states the essence of the article (< 50 characters). This is not required for all article types (see above).
- List each author's individual contribution to the manuscript. For each author, please list the individual contribution using the following text: "Author Name: This author helped…"

Abstract (Back to Top)

Manuscript Type	Abstract Type	Number of words
Original Clinical Research Report	Structured	400
Original Laboratory Research Report	Structured	400
Narrative Review	Unstructured	400
Systematic Review	Unstructured	400
Meta-Analysis	Structured	400
Editorial	NA	NA
The Open Mind	NA	NA
Special Article	Unstructured	400
Letter to the Editor	NA	NA
Book and Multimedia Review	NA	NA
Meeting Report	NA	NA

- Structured abstracts should use the following sections: Background, Methods, Results and Conclusions.
- Please include the abstract in the main document file after the title page. You will also be prompted to include the abstract text during the submission process in Editorial Manager.

Key Points Summary (Back to Top)

For Original Clinical/Laboratory Research Reports and Meta-Analyses, a "Key Points" summary should be included directly underneath the structured abstract. The key points summary should describe the Question, Findings, and Meaning, each composed of one sentence. Please format the summary as three bullet points:

- Question: [One Sentence Text]
- Findings: [One Sentence Text]
- Meaning: [One Sentence Text]

Glossary of Terms (Back to Top)

A Glossary of Terms must be provided for ALL abbreviations/acronyms appearing in the manuscript, including trial names. Additionally, all abbreviations/acronyms must be spelled out upon first mention in both the Abstract and in the main Body of the paper, followed by the abbreviations/acronyms in parentheses; thereafter, the abbreviation/acronym should be used. Authors do not need to define standard abbreviations for standard units of

measurements (e.g., kg, ml) in the Glossary of Terms. The Glossary of Terms should be included after the Abstract in the main manuscript file (or after the Title Page for articles without an Abstract) and before the Body of text.

Body (Back to Top)

The body of the manuscript should typically be divided into four parts (does not apply to all article types – See Article Types At A Glance):

- Textual material (body text, tables, figure legends etc.) should be submitted as a .doc or .docx word processing file
- 12 point Arial or Times New Roman font
- Introduction (new page). This should rarely exceed one page in length.
    - Should ideally contain only 4 to 5 short paragraphs: (1) significance, (2) background, (2) rationale, and (3) the study's aims or objectives and if applicable, (5) primary study hypothesis, and if appropriate, the secondary study hypothesis.
    - Avoid the temptation and frequent tendency to provide an extensive literature review in the Introduction.
- Methods (new page)
    - A subsection entitled "Statistical Analysis" should appear at the end of the Methods section when appropriateA statement that the study was approved by the appropriate IRB/Research Ethics Committee and written informed patient consent was obtained, or that the requirement for written informed consent was waived. (See section C Protection of Human Subjects).
    - If applicable, authors should include their clinical trial registration number, registry, principle investigator and date of registration. (See section G Registration of Clinical Trials)
    - A statement indicating the author has followed the appropriate EQUATOR guidelines should be included in the Methods section.
        - Example: "This manuscript adheres to the applicable CONSORT guidelines."
    - A subsection entitled "Statistical Analysis" should appear at the end of the Methods section when appropriate
- Results (new page)
- Discussion (new page). Focuses on the findings in the current work

Acknowledgements (Back to Top)

For acknowledgement of individuals or organizations, provide complete name, degrees, academic rank, department, institutional affiliation, city, state, and country. Add description of the contribution to the study.

References (Back to Top)

- *Anesthesia & Analgesia* follows the American Medical Associate (AMA) citation style; Consult the American Medical Association Manual of Style, 10th ed., New York, Oxford University Press, 2007, for style.
- Number references (as superscripts) in the sequence they appear in the text.
- In text, tables, and legends, identify references with superscript Arabic numerals.

- If there are 6 or fewer authors/editors, list all 6; if there are more than 6, list the first 3 followed by "et al."
- Abbreviate names of journals according to the journals abbreviation list maintained by PubMed
- Manuscripts "In Press" – A "manuscript in press" is defined as an article that has been accepted for publication, but has not yet been published by the accepting journal, in print or online and is being cited as basis for the study being described in the submitted manuscript. Please submit an electronic copy (Word, PDF) of any "In Press" manuscript that is cited in the reference list, labeled as "In Press, Reference # ___."
- During revision, please double-check and confirm that your reference list and in-text reference citations are correct and updated to match the revised version of your manuscript. All references must appear in your reference list (even if the reference is not yet published), and a corresponding reference citation must also be cited in your manuscript for every reference listed in the reference list. In-text reference citations must appear in chronological order upon first mention in the manuscript.

Tables (Back to Top)

- *Anesthesia & Analgesia* follows the American Medical Associate (AMA) table format.
- Tables should be uploaded as a separate Word file or presented in the main document word file, just after the references.
- Use a separate page for each table.
- Individual tables should not exceed two typed pages. If a table exceeds two typed pages, start a new table on the subsequent page.
- For any table that exceeds two typed pages and cannot be divided into a new table, the table should be submitted as a supplemental digital content file (see formatting requirements for Supplemental Digital Content files below).
- Double-space all table material.
- Do not submit tables as photographs or pasted images. Tables should be black and white only.
- Number the tables consecutively and cite them consecutively (on first instance) in the text.
- Do not create multi-part tables (e.g., Table 1A, Table 1B). Such tables should instead be cited as "Table 1," "Table 2," etc.
- Each table should have a brief title.
- Each column in a table should have a brief column header name.
- Use footnotes (not table titles or column headings) for explanatory matter and definitions of acronyms or abbreviations. Acronyms and abbreviations must be described with footnotes even if they are defined in the text or in other tables or figures.
- For footnotes within a table, use lower-case italicized letters in sequential alphabetical order.
- If you include a block of data, a table, or a figure from another source, whether published or unpublished, acknowledge the original source.

Appendices (Back to Top)

- Uploaded as a separate file or in the main document file at the end of the body of text.

- Each appendix must be cited within the text, in consecutive order.
- Appendix content counts towards the table and/or figure limits. If the inclusion of an appendix exceeds the table and/or figure limit for the respective article type, submit the appendix as a supplemental digital content file.

Figure Legends (Back to Top)

- Supply a legend for each figure.
- Group figure legends on a single page just after the references
- If a figure has multiple panels (e.g., left, right or A, B, C) please specify each panel in the legend.
- Repeat definitions of any acronyms or abbreviations used in the figure in its legend.

Figures (Back to Top)

- Figures should be uploaded as separate .tiff, .jpeg, .pdf or .pptx files. Figures will have to be uploaded at a resolution of 300 dpi or higher at acceptance.
- Figures with multiple panels should be condensed into a single file for each figure (for example, Figure 1A through 1F should be in one file, Figures 2a through 2F should be in a second file, etc.). Each individual panel should be labeled with a capital letter.
- *Anesthesia & Analgesia* publishes in full color, and encourage authors to use color to increase the clarity of figures.
- Standard colors should be used (black, red, green, blue, cyan, magenta, orange, and gray).
- Avoid colors that are difficult to see on the printed page (e.g., yellow) or are visually distracting (e.g., pink).
- Figure backgrounds and plot areas should be white, not grey.
- Axis lines and ticks should be black and thick enough to clearly frame the image.
- Axis labels should be large enough to be easily readable and printed in black.
- Number figures consecutively. Supply a brief title for each. Cite figures in the text in consecutive, numerical order on first instance.
- If a figure has already been published, acknowledge the original source. You must obtain and submit written permission from the copyright holder to reproduce the material when you submit the manuscript for review. Unpublished figures require permission of the author. Permission is required to reproduce any previously published material except for documents or figures in the public domain. See Permissions
- Define in a footnote all acronyms or abbreviations used in each figure.

Video preparation(Back to Top)

The video clip(s) accompanying A&A submissions should conform to the following:

- Formatted in MPEG, QuickTime (MOV), Windows Media Video (WMV) or MP4.
- Play on *both* Windows and Macintosh platforms. The review process will be delayed if the Editorial Office cannot play your video clip.
- Individual size should not exceed 15 MB. Use video-compression software to reduce video size if necessary.

- Optimal video frame dimensions of 480 x 360 pixels and 640 x 480 pixels. Videos of 320 x 240 pixels have inadequate resolution for teaching.
- Duration of individual video clip should be less than 15-25 seconds.
- Combinations of clips: If you combine several video clips, for example several TEE echocardiographic loops, please provide adequate time for each segment, and leave a suitable gap between the videos. Use appropriate labeling to ensure that the viewer can understand the timing of the pathology and events. Labeling can be added with video editing programs such as Adobe Premiere or iMovie.
- Authors should complete a video checklist form for each video when submitting a revised manuscript. The video checklist form provides the information necessary to upload the video on the journal website's video gallery.

Supplemental Material (Back to Top)

- Authors may submit separate supplemental material to enhance their article's text and to be considered for online-only posting.
- Supplemental material may include the following types of content: text documents, graphs, tables, figures, audio, and video.
- Cite all supplemental digital content consecutively in the text (i.e., each supplemenalt file is numbered starting with 1)
- Citations should include the type of material submitted, should be clearly labeled, and should include a sequential number (Example "Supplemental Figure1", "Supplemental Table 1", "Supplemental Video 1").
- Supplemental Legends should be submitted at the end of the manuscript file and should provide a brief description of the supplemental content. For example: "Supplemental Table 1: Lists all medications used in this study."
- Each supplemental digital content file must be composed to standalone. For example, tables and figures must include titles, legends, and/or footnotes, following journal style, so the viewer can fully understand the supplemental content on its own. Production will not make any edits to the supplemental files; they will be presented as submitted.
- It is recommended to group multiple supplemental figures/tables into one supplemental digital content file when submitting. Each file will be given a permanent hyperlink when the Publisher prepares the supplemental digital content for posting. To avoid excessive hyperlinks in your publication, please group figures/tables.
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Additional Information (Back to Top)

- Units of Measurement

Use metric units. The units for pressures are mmHg or cmH2O. Diagonal slashes are acceptable for simple units, *e.g.*, mg/kg; when more than two items are present, negative exponents should be used, *i.e.*, ml · kg^{-1} · min^{-1} instead of ml/kg/min.

- Glossary of Terms and Abbreviations

  A Glossary of Terms must be provided for ALL abbreviations/acronyms appearing in the manuscript, including trial names. Additionally, all abbreviations/acronyms must be spelled out upon first mention in both the abstract and in the main body of the paper, followed by the abbreviations/acronyms in parentheses; thereafter, the abbreviation/acronym should be used. Authors do not need to define standard abbreviations for standard units of measurements (e.g., kg, ml) in the Glossary of Terms. The Glossary of Terms should be included after the abstract in the main manuscript file (or after the title page for articles without abstracts).

- Drug Names and Equipment

  Use generic names. If a brand name must be used, insert it in parentheses after the generic name. Provide manufacturer's name, city, state, and country. Be careful about the use of trademarked terms (*e.g.*, Thrombelastography™, TEG™, *etc.*).

- Statistical Analysis

  Detailed statistical methodology must be reported. Describe randomization procedures and the specific tests used to examine each part of the results; do not simply list a series of tests. Care should be taken with respect to a) parametric vs. nonparametric data, b) corrections for multiple comparisons, and c) rounding errors (summary statistics should not contain more significant digits than the original data). Median range (or percentiles) is preferred for nonparametric data.

- Patient Identification

  Do not use patients' names, initials, or hospital numbers. An individual (other than an author) must not be recognizable in photographs unless written consent of the subject has been obtained and is provided at the time of submission.

Permissions (Back to Top)

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Language Editing Services (Back to Top)

Articles submitted to the Journal must be written with a solid basis of English language. Awkward or non-intelligible English grammar and syntax can adversely affect the review process and the likelihood of acceptance of a manuscript. **Authors whose native language is not English should thus strongly consider having their manuscript copy-edited by a native English language medical/technical writer prior to initial submission.**

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Section 8: EDITORIAL, ETHICAL AND LEGAL REQUIREMENTS (Back to Contents)

Anesthesia & Analgesia follows the International Committee of Medical Journal Editors (ICMJE) "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals"**.**

All authors submitting a manuscript to *Anesthesia & Analgesia* are required to understand and to adhere to the material below.

A. Role of Authors and Contributors

Anesthesia & Analgesia adheres to the ICMJE recommendations for defining the role of authors and non-author contributors

Anesthesia & Analgesia therefore defines manuscript **Authors** as meeting all of the following 4 criteria:

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND

2. Drafting the work or revising it critically for important intellectual content; AND

3. Final approval of the version to be published; AND

4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Those individuals who do not meet all four criteria for authorship can be referred to as Collaborators as defined by the NLM and MEDLINE/PubMed: https://www.nlm.nih.gov/pubs/techbull/ma08/ma08_collaborators.html. These Collaborators are individually but separately listed as such on the Title Page of the submission. These Collaborators will be listed in a separate section at the end of the paper when it is published by Anesthesia & Analgesia. This section entitled "Collaborators" will be placed immediately after the Body of the text, to be followed by Acknowledgements, then Disclosures, and lastly, References.

If the manuscript has been authored by a subset of members of and/or on behalf of a larger group, that larger group can be listed by its formal name, which is preferably placed after the list of formally named authors.

Each manuscript must have a Corresponding Author. The corresponding author serves as the primary contact during the submission and review process on behalf of all co-authors. Upon submission, the corresponding author is required to attest to the validity and legitimacy of the data and interpretation. The corresponding author is responsible for ensuring that all authors have reviewed the manuscript and have completed the conflict of interest disclosures. If the manuscript is accepted, the corresponding author is responsible for reviewing the proof.

If during the manuscript review process or with a complete resubmission, an initial author is deleted or another author is added, this change must be justified in the revision cover letter. The deleted or added author must be formally notified in writing, with a copy of this co-author correspondence sent to the Journal Editorial Office.

Upon acceptance, the Editorial Office will also require a completed Authorship Change Verification form, finalizing the agreed upon authorship order for the accepted submission from each author listed, as well as, those who were added or removed. Authors may include all electronic signatures on one pdf form to finalize the agreement that the authorship order is correct.

B. Author Conflict of Interest

Anesthesia & Analgesia endorses the ICMJE recommendations for defining the role of authors' conflict of interest.

- *Anesthesia & Analgesia* holds that a conflict of interest exists when professional judgment concerning the primary interest, including patients' welfare or the validity of research, may be influenced by a secondary interest like financial gain. Perceptions of conflict of interest are as important as actual conflicts of interest.

- Authors therefore must define all funding sources supporting their work. This includes departmental, hospital, or institutional funds. The authors must disclose commercial associations that might pose a conflict of interest in connection with the work submitted. Financial relationships such as employment, consultancies, stock ownership or options, honoraria, patents, and paid expert testimony must also be reported.

C. Protection of Human Subjects

Research is a systematic investigation for the creation of generalizable knowledge. Any investigation submitted for publication demonstrates intent to create generalizable knowledge, and thus constitutes research.

The name of the institutional research ethical review and oversight committee varies with country and local custom. In the United States, this committee is called the Institutional Review Board (IRB). Other countries may use other terms (e.g., "Research Ethics Committee") for their research ethical review committee. "Institutional Review Board" is used here generically to refer to the local board that reviews the ethical treatment of human subjects and grants institutional approval for the study.

- Regardless of the country of origin, all clinical investigators undertaking human subjects research must abide by the "Ethical Principles for Medical Research Involving Human Subjects" outlined in the Declaration of Helsinki, and adopted in October 2000 by the World Medical Association.

Clinical studies not meeting the Declaration of Helsinki criteria will not be considered for publication. If published research is subsequently found to be noncompliant, it will be retracted.

- On the basis of the Declaration of Helsinki, *Anesthesia & Analgesia* requires that all manuscripts reporting clinical research state in the first paragraph of the Methods section that:

1. The study was approved by the appropriate Institutional Review Board (IRB), and

2. Written informed consent was obtained from all subjects, a legal surrogate, the parents or legal guardians for minor subjects, or that the requirement for written informed consent was waived by the Institutional Review Board (IRB).

The Editors of *Anesthesia & Analgesia* may question the authors about the details of the IRB review, informed consent forms, or the consent process. On occasion, the Editor-in-Chief may request a copy of the approved IRB application from the author. Lack of appropriate consent or its documentation will be grounds for rejection or subsequent retraction.

- Patients also have a right to privacy regarding their protected health information (PHI). Access to their protected health information (PHI) should not occur without their written authorization of use or disclosure of PHI for the explicit purposes of (a) research or (b) an expanded case series (with an N > 3). Under certain circumstances, the requirement for patient written authorization may be waived by the Institutional Review Board (IRB).

D. Investigational Drugs

The Editorial Board of *Anesthesia & Analgesia* may exercise judgment about the ethics of a clinical trial involving investigational drugs that differs from the view of the investigators' Institutional Review Board. This situation most frequently occurs in studies involving neuraxial or perineural drug administration; drug studies in children; and nonconformity in dose, route, or indication ("off-label" use).

- Studies using drugs injected into the neuraxial (caudal, intrathecal, or epidural) or perineural space must meet at least one of three criteria:

1. The drug is approved for neuraxial or perineural administration by the United States (US) Food and Drug Administration (FDA) or the equivalent regulatory agency for the country in which the study took place.

2. The drug is not approved for neuraxial or perineural use, but it is widely used and accepted for neuraxial (e.g., fentanyl) or perineural administration. The publication of dosing guidelines in multiple textbooks represents a reasonable demonstration that a drug is widely used and accepted for neuraxial or perineural administration.

3. The study is performed under an Investigational New Drug (IND) or Biologics License Application (BLA) application approved by the US FDA or the equivalent agency in the investigator's country.

- *Anesthesia & Analgesia* is committed to expanding knowledge of the clinical pharmacology of drugs in children. However, studying drugs in children when there is no pediatric indication poses ethical concerns. Therefore, studies of drugs in children must meet at least one of three criteria:

1. The drug is approved for pediatric administration by the US FDA or an equivalent regulatory agency.

2. The drug is not approved for use in children but is widely used and accepted for pediatric administration. A reasonable demonstration that the drug is clinically accepted for use in children is when the administration in the study is consistent with the route, dose, and indication reported in multiple textbooks.

3. The study is done under an IND application approved by the US FDA or the equivalent agency in the investigator's country. Investigators in the United States are directed to the FDA website for further information on obtaining an investigator IND.

Anesthesia & Analgesia will not publish a paper describing a retrospective assessment involving pediatric drug administration, if the treatment would be considered inappropriate or unethical in a prospective trial.

- Drugs are commonly used off-label in clinical trials, and the practice is generally acceptable. However, the Editorial Board of *Anesthesia & Analgesia* reserves the right not to review a manuscript describing off-label administration of a drug if the Editorial Board believes the study posed unacceptable risk to subjects. To preclude such a determination, investigators are encouraged to obtain an Investigator IND

from the US FDA or an equivalent agency in their country before initiating studies involving off-label drug administration.

E. Registration of Clinical Trials

All clinical trials involving assignment of patients to treatment groups must be registered prior to the start of the trial and any patient enrollment is undertaken.

The registry, registration number, principal investigator's name, and date of registration must be stated in the first paragraph of the Methods section of the manuscript.

Authors must state in the Methods section of their manuscript that registration of their clinical trial occurred prior to the start of the trial and any patient enrollment undertaken.

A number of registries have been approved by the International Committee of Medical Journal Editors (http://www.icmje.org/about-icmje/faqs/clinical-trials-registration/), including http://www.clinicaltrials.gov (the most commonly used registry in the United States), http://isrctn.org, http://www.umin.ac.jp/ctr/index/htm, http://www.anzctr.org.au, and http://www.trialregister.nl. Submissions that have registered with the European Clinical Trials Database, EudraCT (https://eudract.ema.europa.eu/) meet this requirement.

F. Protection of Animal Subjects

Manuscripts describing investigations performed in vertebrate animals must explicitly state that the study was approved by the authors' Institutional Review Board for animal research (e.g., Institutional Animal Care and Use Committee, IACUC). The Journal expects humane and ethical treatment of all experimental animals, and requires that the study has been conducted in a manner that does not inflict unnecessary pain or discomfort upon the animals, as outlined by the United States Public Health Service Policy on Humane Care and Use of Laboratory Animals and the Guide for the Care and Use of Laboratory Animals (1996), prepared by the National Academy of Sciences' Institute for Laboratory Animal Research. A statement to this effect should appear at the beginning of the Methods section of the manuscript.

G. Plagiarism

Plagiarism is the use of previously published material without attribution. **The Editorial Office screens all submitted manuscripts for plagiarism, using a sophisticated software program, prior to peer review.** This software screening process identifies passages of text that have been previously published and generates a qualitative/quantitative report. This report is reviewed by the Journal Editorial Board and its support staff.

Text copied from previously published work is interpreted using the following taxonomy:

- *Intellectual theft* is misrepresentation by an author that words and ideas previously published by another author represent the plagiarist's own scholarship. It is the most serious form of plagiarism. Intellectual theft identified during screening

results in immediate rejection of the manuscript and a request for an explanation from the author.

- *Intellectual sloth* is the use of the words of another author to avoid the effort of writing new text. It commonly occurs when descriptions of research methodology are taken from prior publications. It is less serious than intellectual theft, because the text is generic and of no particular value. Submissions containing intellectual sloth are typically returned to the authors with a request that the copied text either correctly cite the original author or be rewritten in the authors' own words.
- *Plagiarism for scientific English* occurs when authors uncomfortable using scientific English compose their manuscripts as a patchwork of previously published sentences and paragraphs. Papers constructed in such a manner are rejected outright, primarily because patchwork plagiarism suggests that the authors may not understand the text they have submitted for publication.
- *Technical plagiarism* is the use of verbatim text not identified as taken verbatim, but simply referenced to the original source. The offense is a technical one, and authors are simply asked to correct it prior to peer review.
- "*Self-plagiarism"* occurs when an author uses his or her verbatim words from a previous manuscript in a new submission. Provided the authors are not engaged in duplicate publication, the Journal does not view "self-plagiarism" as misconduct. Authors are permitted to reuse their own words, and are encouraged to do so when describing identical research methods in multiple papers.

H. Duplicate Submission or Duplicate Publication

- *Duplicate submission* is concurrent submission of a nearly identical manuscript to two journals. It is improper for authors to submit a manuscript describing essentially the same research simultaneously to more than one peer-reviewed research journal. Authors should not submit the same manuscript, in the same or different languages, simultaneously to more than one journal. Duplicate submissions identified during peer review will be immediately rejected. Duplicate submissions that are discovered after publication in the Journal will be retracted.
- *Duplicate publication* is prior publication of a manuscript with considerable content overlap, particularly in the research results, by the same author or co-authors. Prior publication may be in the same language or it may be a translation (usually from the author's native language to English). Submitted manuscripts must not have been published elsewhere, in whole or in part, on paper or electronically. This includes personal, departmental, educational, or other Internet sites. This does not apply to abstracts of scientific meetings or to lecture handouts (*e.g.*, IARS Annual Meeting, ASA Annual Meeting). *Anesthesia & Analgesia* requests that authors inform the Journal when results of a submitted manuscript have been previously presented or published in *any* venue. If a manuscript has been published previously, the submission to *Anesthesia & Analgesia* will be rejected unless it has already been published by the Journal, in which case it will be retracted.

I. Scientific Misconduct

When *Anesthesia & Analgesia* has concerns or receives allegations of scientific misconduct, *Anesthesia & Analgesia* reserves the right to proceed according to the procedures described below.

Anesthesia & Analgesia recognize its responsibility to appropriately address concerns allegations of misconduct. Examples of misconduct include: fraud, data fabrication, data falsification, plagiarism, improper designations of authorship, duplicate publication, misappropriation of others' research, failure to disclose conflict(s) of interest, and failure to comply with applicable legislative or regulatory requirements. Misconduct also includes failure to comply with any rules, policies, or procedures implemented by *Anesthesia & Analgesia*.

In general, *Anesthesia & Analgesia* follows the recommendations of the Committee on Publication Ethics (COPE) when working to address allegations of misconduct. When a concern or allegation is raised involved parties generally will be contacted to provide an explanation of the situation. As needed, *Anesthesia & Analgesia* may also contact the institution at which the study was conducted and any other involved journals. *Anesthesia & Analgesia* will attempt to determine whether there was misconduct and the Editor-in-Chief will respond with an appropriate action. Examples of action include:

- Sending a letter of explanation only to the person(s) involved or against whom the allegation is made.
- Sending a letter of reprimand to the same person(s), warning of the consequences of future, similar instances.
- Sending a letter to the relevant head of the educational institution and/or financial sponsor of the person(s) involved, expressing the concerns and information collected.
- Publishing in *Anesthesia & Analgesia* a notice of duplicate publication, "salami" publishing, plagiarism, or other misconduct, if clearly documented. In cases of ghostwritten manuscripts, the notice may include the names of the responsible companies as well as the submitting author(s).
- Providing specific names to the media and/or government organizations, if contacted regarding the misconduct.
- Formally withdrawing or retracting the article from *Anesthesia & Analgesia*, and informing readers and indexing authorities
- Banning an author or authors from publishing any manuscript in Anesthesiology for a specified time period, with notice to the author(s) institution.

Section 9: Common Reasons Why a Submission is Returned Without Review (Back to Contents)

- Incomplete Title Page - e.g., missing conflict of interest statement for each author or incomplete author information
- Abstract is missing in the Word file or not properly structured.
- Missing page numbers
- Entire manuscript is not double-spaced
- Methods section does not specifically state that the required Institutional Review Board (IRB) or Research Ethics Committee approval was obtained; and if applicable, a written informed consent and/or HIPAA Authorization form was completed for each enrolled patient.
- References do not adhere to AMA style (see above).
- The above noted word count, reference count, and table/figure count limits are not followed for a specific article type.

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29 January 2021

Dear Dr Enright

Revison: Manuscript reference number: AA-D-20-00216 "A multi-center, cross-sectional quality improvement project: the perioperative implementation of a hypertension protocol by anesthesiologists"

Thank you for the opportunity to provide a revision of our paper. We have itemised the queries with a written description of our changes. We have submitted a revised manuscript with all changes in red font as requested.

Executive Section Editor Comments to the Author:

Thank you for submitting this very interesting MS to A&A.

Major strengths: An attempt to address and manage a very common problem in medicine, not just in anesthesia
Major weaknesses: Numbers are relatively small. Would need expansion to be sure of real outcomes

The statistical editor and reviewer #2 have made some very significant comments about the study methodology. I would appreciate it if you looked at these very carefully and tried to address their issues. I align a little more with Reviewer #1 in the sense that this is an important illustration of what might be possible for anesthesiologists to achieve in their role as peri-operative physicians.
Poorly controlled or uncontrolled hypertension is a very common problem not just in LMICs but also in HICs. Any system whereby it can be better managed would be a benefit. As demonstrated in this study, anesthesiologists are in a unique position to 'set the ball rolling' as it were in patients presenting for surgery. I do not have a great

deal to add to what the reviewers have said but i will go through the paper as presented.

Response: Thank you.

1. P7 L52/53: Does 'physician' here mean a specialist in Internal Medicine? I suspect it does. This occurs throughout the paper. I think it would be wise to clarify this especially for North American readers who would not be familiar with the use of 'physician' in this context. You could include it in your glossary of terms and or mention it once and then continue with whichever term you choose.

Response 1: Yes, a “physician” is a specialist in Internal Medicine. We have added the term to the glossary and edited it in the text above as such : Perhaps the best term for a US audience is internist

“Patients with stage 3 disease were referred to a physician (Internal Medicine specialist).”

2. P8 L12/14: I assume this means 55.5% of the patients diagnosed with hypertension ie of the 69 patients?

Response 2: We apologise for the confusion. This was 55.5% of the total of 106 patients included, and not only those diagnosed with hypertension.

We included the “management of all patients with borderline blood pressure and higher” in the statistical analysis. Adherence to the algorithm did not only imply initiation or adjustment of appropriate pharmacotherapy, but also all further aspects, please see below.

In other words, as detailed in the algorithm:

If a patient was diagnosed with stage 1 or 2 hypertension, they were appropriately initiated on the correct medication. If there was poor control of existing hypertension, the medication was adjusted. If they were not initiated on medication, or if the medication was incorrect, this was interpreted as non-adherence to the algorithm.

Similarly, if a patient was diagnosed with “borderline hypertension”, they were issued a letter informing them and their local clinic about their condition, and how to proceed. If this step was followed, it was interpreted as adherence to the algorithm. If they were not issued with this letter, or were prescribed medication inappropriately, this was defined as non-adherence to the algorithm.

Thereafter, we examined the medication scripts on the JAC pharmacy database, which detailed which medications were issued to patients at discharge. If the same

medication prescribed initially was issued at discharge, this was interpreted as adherence to the algorithm.

We have clarified this in the text with the following revision; '*The adherence rate by the anesthesiologist for diagnosis and management according to the algorithm was 89/106 (84.0%;95% confidence interval (CI) 77.0% to 91.0%). There was adherence to the full algorithm (initiation or adjustment of antihypertensive therapy, together with the correct prescription at the time of discharge from hospital) in 59/106 (55.5%;95% CI 46.2% to 65.1%).*'3. P11 L31/33: "suggest'

Response 3: Thank you, we have edited as suggested.

4. P14 L28/30: It would be helpful for North American/HIC readers to know that most patients in LMICs are admitted preoperatively. That would not be usual here so you need to clarify this.

Response 4: Thank you. We have edited the text as follows:

"*In the public sector in South Africa, many patients scheduled for elective surgery are admitted the day before their surgery and are examined by an anesthesiologist. This is to allow for travel plans for the patients (who sometimes live far away from hospitals and do not have the means to arrive on the day of their surgery), and time for the necessary preoperative medical work-up to be performed*.

All consenting patients presenting at the in-hospital preoperative visit the day before their surgery, were screened for hypertension."

5. P18 L31/32: There could be a lot of reasons for the patient going home without a Rx for medications. See comments from Reviewer 2. I think this needs further discussion. Perhaps it is an area for future follow-up?

Response 5: We agree. We have added to the discussion as follows:

"*This suggests that implementation of this quality improvement project would require further communication and support to ensure the prescription and dispensation of antihypertensive medication at discharge from hospital. It is difficult to pin-point specific reasons for this lack of adherence. Further research would be required to determine the multifactorial causes for this discrepancy*."

6. L56/57: Why did you decide on this threshold?

Response 6: We decided on this threshold because:

- It is the definition of "Stage 1 Hypertension" as determined by our national guidelines.
- It was an added safety measure, to prevent over-diagnosis of hypertension in a patient who could be normotensive.

7. P19 L15/16: It could also be argued that out of hospital measurements would be more accurate.
It would be very interesting to see follow-up on how many patients actually went to a clinic and continued with their Rx.

Response 7: An initial plan as part of a sub-study was to attempt to follow up on these patients at their local clinics by way of examining adherence to continuation of medication. Unfortunately, it was only discovered later that not all clinics use the JAC database. In fact, many of these smaller outlying clinics do not have computers or access to the internet. These factors make follow-up very difficult. However, we do intend attempting to do a follow up sub-study.

Thank you
Angela

Statistical Editor Comments:

I appreciate the opportunity to review your manuscript. Please find below some important areas in which the manuscript can be clarified or improved from the statistical perspective. A main issue is that there is no concurrent or previous control group to compare to assess whether the program improves outcomes. Therefore, authors need to temper their conclusions and consider the study to be purely descriptive in nature. Second, it seem it would have been better to choose a primary outcome that was relevant to all participants, not just those in a particular category, and thus be able to evaluate how the providers did for all patients.

1. P7L4-21. At end of this paragraph authors should state the study objective.

Response 1: Thank you. We have added the objective to the end of the paragraph as follows:

"*Anesthesiologists are ideally placed to lead this aspect of perioperative medicine. The study objective was for anesthesiologists, as part of a multidisciplinary team, to identify patients at the preoperative visit with previously undiagnosed-, or poorly controlled chronic hypertension, and follow a simple management algorithm*."

2. P7L55. It is not clear why only those with stage 1 or 2 were included in the primary outcome of adherence – not stage 3 or those with borderline BP.

Response 2: Thank you. Please see response 4.

3. P7L57-59. Again, the secondary outcome only includes those in stage 1 or 2, apparently.

Response 3: Thank you. Please see response 4.

4. P15L38-42. Authors say "primary outcome was the adherence of the

anesthesiologist to the
hypertension algorithm", which appears (although not clear) to only include those with stage 1 or 2 (N=67)? If so, this seems to be a weak primary outcome. A stronger outcome would include all patients who qualified to participate in the program (N=106) – for e.g., whether or not they were handled correctly. A better and more detailed explanation for the chosen outcome is needed. As well, it needs to be justified.

Response 4: Apologies, that this needs clarification. We did in fact include all 106 eligible participants. As mentioned in Response 2 to Executive Section Editor Comments to the Author:

We included the "*management of all patients with borderline blood pressure and higher*" in the statistical analysis. Adherence to the algorithm did not only imply initiation or adjustment of appropriate pharmacotherapy, but also all further aspects, please see below.

In other words, as detailed in the algorithm:

If a patient was diagnosed with stage 1 or 2 hypertension, they were appropriately initiated on the correct medication. If there was poor control of existing hypertension, the medication was adjusted. If they were not initiated on medication, or if the medication was incorrect, this was interpreted as non-adherence to the algorithm.

Similarly, if a patient was diagnosed with "borderline hypertension", they were issued a letter informing them and their local clinic about their condition, and how to proceed. If this step was followed, it was interpreted as adherence to the algorithm. If they were not issued with this letter, or were prescribed medication inappropriately, this was defined as non-adherence to the algorithm.

Thereafter, we examined the medication scripts on the JAC pharmacy database, which detailed which medications were issued to patients at discharge. If the same medication prescribed initially was issued at discharge, this was interpreted as adherence to the algorithm.

We have clarified in the text in the Methods section on page 15 as follows:

"*Patients with normal BP or well-controlled hypertension were excluded from further management. The patients eligible for participation in the study were managed according to the algorithm as follows:*
Those with borderline BP received educational pamphlets. Patients with stage 1 or 2 hypertension were managed with medication and educational pamphlets, and those with stage 3 disease were referred to a physician for appropriate management at a specialist level. Following these steps or not, defined adherence or non-adherence to the algorithm."

5. Primary outcome. Did authors consider making follow-up blood pressures the primary outcome?

Response 5: Yes, we did. Our initial objective was however to establish the feasibility of applying a simple algorithm. We recognise the importance of the follow-up blood pressure and, as part of the quality improvement process, further research could be aimed at looking at this aspect, as well as the long-term impact on cardiovascular disease in South Africa. The last sentence in the Discussion alludes to this outcome for future work; '*Further research is required to assess patient adherence to medication. Primary health care clinic follow-up should also be evaluated, since management of hypertension involves physician diagnosis and treatment, as well as patient adherence to prescribed drugs.'*

6. P8L10-15, P17L29-37. Please also give the ratios here. For example, what is the numerator and denominator for the 84%? And for the 56%? Should be in the main results and abstract results.

Response 6: Thank you, this has been corrected.

7. P18L53-59. "improve quality of care". Authors cannot make this conclusion because they did not report results for similar providers who were not part of the intervention – i.e., there is no comparison group. They could compare the studied patients/providers to those having surgery in the same facilities before the study began (using segmented regression), or to patients in other hospitals who had surgery in the same time period as the study patients (cross-sectional study). But with the current design authors can only describe what they found – no claim that the results were due to the intervention.

Response 7: We agree that we are not justified in concluding that quality of care has been improved by this study. We have changed the sentence in the Discussion to reflect that the quality improvement intervention was successfully implemented, and that this could lead to further studies aimed to improve quality of care in this field:

"The strength of this study was that a short-term quality improvement intervention was successfully implemented, which is the first step towards further initiatives for the improvement of quality of care in cardiovascular disease, in low-resource environments similar to those in many areas of South Africa."

8. P20L7-22. As mentioned in the previous comment, a large limitation of the study is that there is no control group without the intervention – that could have been the period before it was introduced, or a concurrent control group from different facilities. The current design therefore does not allow any inference on whether the program was effective.

Response 8: We agree. We have however not drawn any conclusions as to whether the management and control of hypertension will improve; we only draw conclusions on the implementation of an algorithm by anesthesiologists. We have therefore added the following text to the limitations;

"Furthermore, it is not possible to determine whether this intervention significantly improved the quality of in hospital antihypertensive care due to the lack of a control group in this study. The study demonstrated good adherence to the algorithm by anesthesiologists, however, further investigations are needed to determine the potential impact on quality of care."

Reviewer Comments to the Author:

Reviewer #1:

There is an increasing role in perioperative medicine for Anesthesiologists especially in countries with limited health care resources. Presenting for surgery offers a unique opportunity to diagnose co-morbidities, especially hypertension, and to initiate appropriate treatment as part of the routine preoperative evaluation. You have developed an algorithm and demonstrated that it was adhered to in over 80% of patients. In 55% medication, as proposed, was still given to patients at discharge. However, as patients and their general practitioners were informed of the diagnosis and of the treatment initiated it is not unlikely that hypertension treatment would be continued in the longer-term, thus reducing the risk of cardiovascular complications in more than 55.5% of patients. This could be stressed in the discussion. Because of the number of patients is relatively small this is a proof of concept, yet it has profound implications. As the proposed algorithm was developed by a multidisciplinary group it offers an effective approach to a common problem.

Response: Thank you for these comments.

A few minor points:

1. Abstract
Page 7, line 50: patients with stage 3 hypertension were referred to a physician. The algorithm states that surgery was postponed. This should be stressed in the abstract.

Response 1: Thank you. We have amended the abstract as follows:

"*Patients with stage 1 or 2 hypertension were managed with medication according to the algorithm, starting 1 day postoperatively, and provided with educational pamphlets. Patients with stage 3 disease had their surgery postponed and were referred to a physician (Internal Medicine specialist).*"

2. Table 1 Classifies hypertension as grades but in the text always as stages (also in Table 3). As you state that Table 1 was "adapted" from SA Hypertension Practice and AAGBI guidelines, the "adaptation" could include using stages rather than grades for consistency.

Response 2: Thank you. It should be "stages". We have corrected the table accordingly.

3. How many patients had poorly controlled hypertension? These patients clearly benefited from the algorithm and reinforces its value and should be discussed.

Response 3: We have added to the result section as follows:

"The prevalence of co-existing cardiovascular comorbidities in patients with hypertension is shown in Table 2. Of the 106 patients recruited, 60 had poorly controlled hypertension (56.7%)."

We have added the following text to the discussion;

"*This is potentially an important public health intervention, when one considers that hypertension is associated with nearly 10% of all deaths in South Africa, that over 50% of all elective adult South African surgical patients are hypertensive,[9] and this study has shown that 56.7% of known hypertensives are inadequately managed and can benefit from a perioperative hypertension quality improvement project*."

Reviewer #2:

In their single-country, multi-centre prospective, cross-sectional, interventional quality improvement study, Dr. Pfister et al seek to demonstrate how anesthesiologists may be involved in both diagnosing and treating medical disease in the perioperative setting. Specifically, a team of preoperative nurses and an anesthesiologist at each site implemented a hypertension diagnosis protocol used in the preoperative clinic for patients presenting with non-cardiac and non-obstetric surgery. Patients were subsequently managed according to their degree of hypertension, with the institution (or escalation) of blood pressure lowering therapy on postoperative day 1. The primary and secondary outcomes were the adherence of the anesthesiologist to the hypertension algorithm and to the presence of antihypertensive therapy at discharge (for those patients treated with anti-hypertensives).

Dr. Pfister and colleague's QI study is highly relevant globally as anesthesiology rapidly evolves within the sphere of perioperative medicine. The authors cite resource-limitation in South Africa as part of the intervention's rationale. This is not unique to upper middle-income countries like South Africa which broadens the study's relevance: Indeed, today's context shows a physician shortage globally that is only forecast to worsen. For example, this would be as relevant an initiative in rural Canada, a high-income country, as it is in South Africa. Dr. Pfister et al demonstrate several ideas in their paper. First, anesthesiologists can play an expanded role as perioperative physicians. Such a role can function in a manner complimentary to surgeons and primary care providers. Second, the perioperative pathway provides some conventionally untapped opportunities to meaningfully contribute to enhancing the health of the surgical population. That said, the paper has a number of significant weaknesses that make it less effective in illustrating these points and falls short for the purposes of publication in Anesthesia & Analgesia.

Response: Thank you for your comments. We agree with this reviewer that our study could be relevant locally as well as globally, and we agree that the role of anesthesiologists is indeed expanding to that of perioperative physicians. We will attempt to address or clarify each concern mentioned by the reviewer.

1. Introduction

In their introduction, the authors describe the epidemiology of hypertension, both generally and in South Africa. Its characterization seems primarily with respect to it as a stand-alone chronic disease (essential hypertension). The authors fail to characterize the relevance of hypertension in the specific setting of surgery, including hypertension secondary to the surgical or other pathologies (e.g., pheochromocytoma, valvular disease, arterial vascular disease, among others). The specific context of hypertension for the surgical population is entirely relevant to the discussion.

Response 1: Thank you for your comment. Our quality improvement project was, first and foremost, a public health initiative designed to tackle the problem of chronic essential hypertension in a resource-limited country like South Africa. We have added the following text to the introduction:

"Essential hypertension accounts for 95% of all cases of hypertension.[11] The remaining 5% of cases include secondary causes such as renovascular disease, renal failure, pheochromocytoma, aldosteronism, or genetic causes. The primary aim of this study was for anesthesiologists, in collaboration with nurses, physicians and surgeons, to identify patients at the preoperative visit with previously undiagnosed, or poorly controlled essential hypertension."

2. Methods
The methods outlined by Dr Pfister et al discuss the required elements. I note that the patients were all assessed within the "in-hospital preoperative visit". It was not clear to this reviewer whether the patients were admitted the day before surgery or if this took place in an ambulatory clinic setting.

Response 2: Thank you. We omitted to specifically list day case surgery as an exclusion, but did mention that patients were admitted the day before surgery. We have adjusted the text for clarity on page 14:

"*Eligible participants were all adult in-patients admitted on the day prior to surgery, undergoing elective surgery with BP above the normal range,[12,13] which included newly diagnosed hypertensives and those with poorly controlled hypertension. Exclusion criteria were cardiac-, obstetric-, and day case surgery, as well as radiological or ophthalmic procedures under local anaesthesia, and patients with blood pressures within normal ranges, including those with well controlled hypertension.*

In the public sector in South Africa, many patients scheduled for elective surgery are admitted the day before their surgery and are examined by an anesthesiologist. This is to allow for travel plans for the patients (who sometimes live far away from hospitals and do not have the means to arrive on the day of their surgery) and time for the necessary preoperative medical work-up to be performed.

All consenting patients presenting at the in-hospital preoperative visit the day before their surgery, were screened for hypertension."

3. In terms of the diagnosis of hypertension, the authors describe a highly simplified diagnostic scheme. While simple, it is not clear to this author whether such an algorithm is valid. For example, the UK's NICE Guideline (NG136, August 2019) posits that a diagnosis of hypertension should be confirmed using ambulatory blood pressure monitoring ((ABPM) or home blood pressure monitoring (HBPM)). These guidelines also suggest assessing patients for target-organ damage. The Canadian guidelines (2019) put forward a similar approach: an office visit followed by out of office measurement. The 2014 South African guidelines themselves suggest measurement on three occasions for titrating anti-hypertensive therapies. While this reviewer recognizes the variability in guidelines, the authors may have better substantiated the validity of their algorithm beyond simply citing the South African Hypertension Practice Guideline (2014).

Response 3: Thank you for your comments.

In our setting in South Africa, patients are usually diagnosed with hypertension at their primary health care facility. These facilities are sometimes staffed with one or two doctors, but many of them are only staffed with nurses. Our public health system resources do not have the capacity for home ambulatory monitoring or home BP monitoring. Furthermore, follow-up visits on 3 separate occasions would also be difficult for many of our patients. As a result, many patients with hypertension are missed or do not return to their primary health care facility for further readings. The perioperative surgical care pathway was chosen as a point of contact for these patients.

As mentioned on P14, L32-41, we referred to the South African, Canadian and AAGBI hypertension guidelines. Our method was the best possible compromise between simplicity and accuracy, in the perioperative setting. However, as we practice in South Africa, it was necessary for us to follow the South African guidelines.

However, for surgical patients it was not possible to measure the blood pressure on three separate occasions to titrate the antihypertensive medication. To simplify the process of diagnosis and implementation, we made several measurements of blood pressure on the day prior to surgery, as described. We also decided on automated office BP (AOBP) as our preferred method. This was considered acceptable, based on the findings of Myers et al in 2010 (reference 19). AOBP was found to be more accurate than conventional BP measurement. It was more predictive of target organ damage, very closely correlated with day-time ambulatory BP, and significantly mitigated the “white coat” effect.

With respect to target organ damage associated with hypertension, this study also included a substudy of the associated target organ damage. For that substudy, we took baseline blood samples, performed an ECG, and measured urine dipstix. These results were included in the algorithm and were assessed as part of a substudy of this quality improvement initiative, examining overall cardiovascular risk associated with hypertension, which is currently awaiting publication. We did not include the substudy in this submission, as it detracts from the primary objectives of this quality improvement project, and the understanding thereof. A comment on the assessment of target organ damage has been added to the Methods section, page 16:

"*Furthermore, baseline kidney function, fasting blood glucose, lipogram, HbA_1C, urine dipsticks, and an ECG to assess left ventricular hypertrophy were performed to assess for hypertension-mediated organ damage and cardiovascular risk . These were included in the algorithm and were assessed as part of a sub-study of this quality improvement initiative, examining overall cardiovascular risk associated with hypertension, which is the subject of a separate publication*."

4. The methods also failed to describe in adequate detail how follow-up was to be organized. The patient documents [page 38] describe a "follow up clinic". It was unclear whether this was surgical follow-up or follow-up with a primary care physician or provider. In either case, the study would be strengthened by the authors giving consideration to the fact that patients prescribed on new medications require medical follow-up, both for ongoing disease management and also for therapy titration and optimization. If patients did not have a primary care provider, were they provided with one at discharge?

Response 4: Thank you. We would like to clarify as follows:

Patients in South Africa do not have a "primary care physician or provider". As mentioned in response 3, patients attend a local clinic, close to their homes, that is sometimes staffed with one or two doctors. Some facilities are staffed only by nurses. We have added a brief paragraph on page 16 of Methods, describing the procedure followed: *"All patients were given a letter addressed to their local primary health care facility describing the in-hospital management of their hypertension, and encouraged to attend a month after discharge. This was a medical follow up for ongoing disease management and for therapy titration and optimization."*

5. Results
This reviewer found it challenging to understand the relevant characteristics of the study sample. For example, while Table 2 lists selective co-existing cardiovascular comorbidities, it fails to identify, for example, whether peripheral vascular disease or valvular disease was among the comorbidities of hypertensive patients (as two examples). The authors also failed to describe the distribution of the types of surgeries patients presented for (e.g., general, endocrine, oncologic, orthopedic, plastics, vascular, etc.) as well as the length of stays for the study's sample. This is relevant in discussing aspects of the study's primary and secondary outcomes. This reviewer also wondered what happened to patients presenting with Stage 3 hypertension. Were they removed from the study (n=106) or was the sample size adjusted for the discussion of the secondary outcome?

Response 5:

Table 2 lists the current recognised cardiovascular comorbidities in hypertensive patients for increased cardiovascular risk in the perioperative period, according to Lee's Revised Cardiac Risk Index.

Unfortunately, the sample size is too small to discuss the breakdown of surgical disciplines in this study, and this was also not an objective of the present study. We therefore did not collect these surgical disciplines data.

We described the referral of Stage 3 patients to an Internal Medicine specialist, on page 15 in the Methods section. A phrase has been added for completion, so that the sentence now reads: "*Patients with stage 1 or 2 hypertension were managed with medication and educational pamphlets, and those with stage 3 disease had their surgery postponed were referred to a physician for appropriate management at a specialist level*."

6. Discussion
In their discussion, the authors note that the primary outcome demonstrated an 84% adherence by anesthesiologists in initiating the algorithm. This reviewer was curious as to the authors interpretation of that adherence rate (beyond exceeding the 80% acceptability threshold). In interpreting the secondary outcome, adherence to discharging with treatment, this reviewer might suggest there could be more going on than inadequate communication. If a patient were in hospital for a protracted period, it is conceivable that other factors led to a reduction in a patient's blood pressure. It is also possible that other medical and surgical treatments interacted with the patient's diagnosis of hypertension. Could non-adherence to treatment at discharge have been a consequence of over-treatment in hospital? As mentioned, it is possible that hypertension was misdiagnosed at the outset, resulting in no need for subsequent therapy. This reviewer was curious as to which patients (i.e., those with Stage 1, 2, or 3 hypertension) were least likely to be discharged on medication. This study would have been strengthened by further analyzing the data set for interacting variables.

Response 6:

Though an arbitrary proportion, it was felt an 80% adherence to the implementation of the algorithm would be encouraging in a pilot study, which would inform the team concerning improving this proportion to 100%.

We agree that there are many factors influencing postoperative blood pressure, and have responded to a similar query by Dr Enright, as follows: *"This suggests that implementation of this quality improvement project would require further communication and support to ensure the prescription of antihypertensive medication at discharge from hospital. It is difficult to pin-point specific reasons for this lack of adherence. Further research would be required to determine the multifactorial causes for this discrepancy*."

Unfortunately, the sample size was too small to analyse exactly which patients were least likely to be discharged on medication.

7. This reviewer concurs with the authors assertion that an initiative like this has the potential to improve patient care, particularly for those with undiagnosed on under-diagnosed concomitant medical disease. The authors should be recognized for their attempts to implement a simple intervention which certainly demonstrates

anesthesiologists' roles as perioperative physicians. This reviewer is less convinced that misdiagnosis due to 'white coat' hypertension was abated through this study's methods, particularly given the wider view that office and hospital-based blood pressure measurements may benefit from being validated outside of these settings. The 'white coat' effect however would likely have the greatest effect on patients with Stage 1 hypertension.

Response 7: Thank you for raising this concern. We attempted to mitigate the “white coat” effect by performing AOBP and taking two sets of multiple readings by two different practitioners. An additional safety measure was to perform these the day before surgery. We acknowledge that this is not ideal but argued that it would be the best way to handle the challenges of our environment, the best compromise between simplicity and accuracy.

Thank you for giving us the opportunity to revise and resubmit our paper. We hope that these revisions are to your satisfaction. Thank you for your interest in our submission.

Regards

Claire Pfister, on behalf of all the authors.

Appendix 7: Anesthesia and Analgesia acceptance letter

ANESTHESIA & ANALGESIA®

Claire-Louise Pfister, MBBCh
University of Cape Town Department of Anaesthesia and Perioperative Medicine
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Cape Town Western Cape 7925
SOUTH AFRICA

RE: MS#: AA-D-20-00216R1 "A multi-center, cross-sectional quality improvement project: the perioperative implementation of a hypertension protocol by anesthesiologists"

Dear Dr Pfister:

It is a pleasure to accept your manuscript entitled, "A multi-center, cross-sectional quality improvement project: the perioperative implementation of a hypertension protocol by anesthesiologists", in its current form for publication in Anesthesia & Analgesia.

Your manuscript will undergo copyediting after being sent to the publisher.

Thank you for your contribution to the journal!

With all good wishes,

Angela Enright, MB, FRCPC
Executive Section Editor
Anesthesia & Analgesia

Jean-Francois Pittet, MD
Editor-in-Chief
Anesthesia & Analgesia

****

Reviewer Comments to Author (if applicable):

Thank you for a very nice revision addressing all the points raised by the reviewers and the statistical editor.
I have invited Dr Pierre Foex to write an accompanying editorial to your article.
Well done.
Angela

All comments have been adequately addressed -- thank you.

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a. Article Title - A multi-center, cross-sectional quality improvement project: the perioperative implementation of a hypertension protocol by anesthesiologists
b. Manuscript Number - AA-D-20-00216R1

Thank you for your contribution to Anesthesia & Analgesia. I look forward to future submissions from you and your colleagues.

Appendix 8: Corrections/Rebuttal

This is the comment from Examiner 2:

"I only have one minor query. Current fasting guidelines demand no intake of solid foods for 6 hours prior to anaesthesia. Certain of the blood tests drawn at insertion of the intravenous line usually demand a longer solid food fasting period viz the fasting blood glucose and cholesterol / triglyceride tests. This was not mentioned in the patient consent form or in the text. What protocol in terms of fasting was followed for these tests?"

Comment/Rebuttal.

Thank you for your comment.

All patients were nil per mouth from 22:00 the night before, according to routine fasting guidelines, for their operations the following day. This ensured that the blood tests requiring fasting results were accounted for.