The Reuse of Circular External Fixator Components:

An Assessment of Safety and Potential Savings

by

Kudzai Chironga

Master of Medicine (MMed)

(CHRKUD005)

This study is a partial fulfilment of the requirements for the degree
Master of Medicine in Orthopaedic Surgery

University of Cape Town

Supervisor:

A/Professor Maritz Laubscher
Division of Orthopaedic Surgery
Groote Schuur Hospital
Department of Orthopaedic Surgery
maritzl@msn.com

December 2021

Table of Contents

Declaration: Student

I, Kudzai Chironga, hereby declare that the work on which this thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university. I authorise the University to reproduce this work for the purpose of research, either the whole or any portion of the contents, in any manner whatsoever. I further declare the following:

1. I know that plagiarism is a serious form of academic dishonesty.
2. I have read the document about avoiding plagiarism, am familiar with its contents and have avoided all forms of plagiarism mentioned there.
3. Where I have used the words of others, I have indicated this by the use of quotation marks.
4. I have referenced all quotations and properly acknowledged other ideas borrowed from others.
5. I have not and shall not allow others to plagiarise my work.
6. I declare that this is my own work.
7. I am attaching the summary of the Turnitin match overview

Signature: Signed by candidate **Date:** 23/12/2021

Declaration: Supervisor

This study was conducted from April 2019 to November 2020 under the supervision of A/Professor Maritz Laubscher, Department of Orthopaedic Surgery, University of Cape Town.

As the candidates Supervisor, I have approved this dissertation for submission.

Signature: **Date:** 27/12/2021

Abstract

Purpose: Cost saving strategies are important especially in a resource constrained environment. One such strategy well supported in literature is the reuse of temporary monolateral external fixator components, a strategy we utilize at our institution. The aim of the study was to determine the safety and cost saving associated with the reuse of definitive circular external fixator components in a resource constrained environment.

Method: We performed a retrospective review of all adult patients who were treated with either new or reused circular external fixators from a single manufacturer between January and December 2017. Reused circular external fixator components, excluding half pins and wires, were subjected to an in-house reprocessing protocol. Cost savings were calculated as the difference between the price of a completely new frame and the amount invoiced for new components only in a reused frame.

Results: 33 patients were included in the study with an average age of 31.9 years. The mean duration of treatment with a circular external fixator was 5.8 months. No mechanical failure events were recorded during the study period. Our institution saved approximately 52% (R717 503.89) and 63 % (R136 568.19) of expected total cost for hexapod and Ilizarov frames respectively.

Conclusion: The strategy of reusing circular external fixator components is unconventional and this study was conducted to evaluate the safety and potential savings in a resource constrained environment. We demonstrated this practice to be reasonably safe and to result in significant cost savings which might be relevant in low-and-middle income countries (LMICs).

Acknowledgements and contributions

The author acknowledges Melody R. Kozah for assisting with proof reading. The authors did not receive any financial support to complete this research study.

All the authors contributed to the study. Data collection and analysis were performed by Kudzai Chironga as well as writing up the first draft of the manuscript. This was done under the supervision of Maritz Laubscher and Stefan Swanepoel. Roopam Dey assisted with tabulating the data collected into graphical representation. All authors including Michael Held and Simon Matthew Graham commented on subsequent drafts, read through and approved the final manuscript.

This article has been published in the European Journal of Orthopaedic Surgery and Traumatology (EJOST) and is available at:
https://doi.org/10.1007/s00590-021-03169-9

List of tables and figures

Abbreviations

LMICs - low-and-middle income countries

SUDs - single use medical devices

HICs - higher income countries

SIP - Specialized instrument processing unit

TSF - Taylor Spatial frame

EJOST - The European Journal of Orthopaedic Surgery and Traumatology

PART A: MANUSCRIPT IN ARTICLE FORMAT

The Reuse of Circular External Fixator Components: An Assessment of Safety and Potential Savings

Author names and affiliations

Kudzai Chironga[1,*], Stefan Swanepoel[1], Roopam Dey[1], Simon Matthew Graham[1, 2, 3], Michael Held[1], Maritz Laubscher[1]

[1]Orthopaedic Research Unit, University of Cape Town, Cape Town, South Africa
[2]Institute of Population Health Sciences, University of Liverpool, Liverpool UK
[3]Department of Orthopaedic and Trauma Surgery, Liverpool University Teaching Hospital Trust, Liverpool, UK

[*]**Corresponding author:**
Kudzai Chironga
Email address; kchironga@gmail.com

ORCID
Kudzai Chironga: 0000-0003-2941-2562
Roopam Dey: 0000-0002-3616-1995
Simon Matthew Graham: 0000-0002-4091-7548
Michael Held: 0000-0002-0671-0439

Keywords:

Reuse, circular external fixator, reprocessing, low-and-middle income countries (LMICs), safety, cost savings

Abstract

Purpose: Cost saving strategies are important especially in a resource constrained environment. One such strategy well supported in literature is the reuse of temporary monolateral external fixator components, a strategy we utilize at our institution. The aim of the study was to determine the safety and cost saving associated with the reuse of definitive circular external fixator components in a resource constrained environment.

Method: We performed a retrospective review of all adult patients who were treated with either new or reused circular external fixators from a single manufacturer between January and December 2017. Reused circular external fixator components, excluding half pins and wires, were subjected to an in-house reprocessing protocol. Cost savings were calculated as the difference between the price of a completely new frame and the amount invoiced for new components only in a reused frame.

Results: 33 patients were included in the study with an average age of 31.9 years. The mean duration of treatment with a circular external fixator was 5.8 months. No mechanical failure events were recorded during the study period. Our institution saved approximately 52% (R717 503.89) and 63 % (R136 568.19) of expected total cost for hexapod and Ilizarov frames respectively.

Conclusion: The strategy of reusing circular external fixator components is unconventional and this study was conducted to evaluate the safety and potential savings in a resource constrained environment. We demonstrated this practice to be reasonably safe and to result in significant cost savings which might be relevant in low-and-middle income countries (LMICs).

Introduction

The spiralling cost of healthcare in countries across the globe has emphasized the need for cost saving strategies. One such strategy is the reuse of single use medical devices (SUDs) in an effort to contain healthcare costs [1], especially in low-and-middle income countries (LMICs) with inadequate resources [2][3][4].

The reuse of temporary external fixator components has become common practice in many countries [5]. An estimated cost saving of 25% has been reported after reprocessing of temporary external fixator components denoted as SUDs by the manufacturer [6][7][8][9]. Several studies also show that temporary external fixator components are safe for reuse for no more than two episodes before failure rates increase [9][10].

There is however paucity of literature on treatment with reused circular external fixator components. Circular external fixator components are typically more expensive than temporary external fixators, however they provide greater stability permitting their use as definitive treatment for extended periods of time with full weight bearing [11].

The Limb Reconstruction Unit at our institution follows a reuse policy of all circular external fixator components. All wires and half pins are discarded, and the remaining components of the devices are subjected to a basic in-house reprocessing protocol prior to re-application. While this strategy is frequently applied in LMICs, it is unconventional in higher income countries (HICs). The aim of the study was to determine the safety and cost saving associated with the reuse of circular external fixator components in LMICs.

Materials and methods

We conducted a retrospective review of a prospectively collected database and included all adult patients treated with a new or reused circular external fixator from a single manufacturer between January and December 2017. All cases treated with a circular external fixator from our sole supplier Smith and Nephew (Memphis, Tennessee, USA) with follow-up until union were included. Each reused circular external fixator component excluding half pins and wires was subjected to a basic in-house reprocessing protocol, which involves several stages from the time of removal of the frame as outlined in (**Figure 1**).

Figure 1: A basic in-house reprocessing protocol flow chart showing the stages through which circular external fixator components undergo upon removal for reuse.

At the time of removal of the circular external fixator, the components are completely disassembled, and a visual inspection is performed. Any components incorporating rings, struts, bolts, rods, and nuts with macroscopic visible damage are discarded. As outlined in Figure 1, the pre-treatment stage involves cleaning of the reusable components in a sluice room with an enzymatic cleaning detergent. Components are soaked in the solution for 2-10 minutes to remove organic material. The components are rinsed thoroughly in warm water and then air dried, air pressure hose dried or cloth dried. The components are then sent to the specialized instrument processing unit (SIP) where components are reassessed to determine if Stage 1 was adequate. This is then followed by the packaging stage where the components are packaged in a sealing paper. The packaged components then undergo sterilization in the autoclave at 135 degrees Celsius for 35 minutes followed by 8 minutes of drying time. This process

guarantees a sterile shelf life of a month after which reprocessing of the components must be repeated. Prior to use, the operating surgeon visually inspects the components again for any detectable faults, specifically pertaining to moving parts or adjustable components.

Data collected was for all patients treated with a circular external fixator between January to December 2017. The data included patient demographics; the primary indication for application of a circular external fixator and the duration of application of the frame. Safety was measured by evaluating mechanical failure events (*defined as a break in any of the reused components or a failure to adjust any of the adjustable components*). No data was collected on pin site sepsis and activity related pain.

The total cost of a new Ilizarov (Smith and Nephew Ilizarov, Memphis, Tennessee, USA) and hexapod (Smith and Nephew Taylor Spatial frame (TSF), Memphis, Tennessee, USA) frame were R27 254.71 and R55 559.86 respectively. According to the local tender process, a single exit price was charged for a completely new circular external fixator, not influenced by the number of components used. When a reused frame (*defined as a frame assembled with any reused components)* was applied, the supplier only billed for individual new components (*inclusive of wires and half pins*). The cost was determined from the invoice issued by the supplier for only new circular external fixator components used in the frame, based on the 2017 tender document. Cost savings were then calculated as the difference between the single exit price for a completely new frame and the amount invoiced for only new components in a reused frame.

Results

A total of 33 patients had a circular external fixator applied during the period of January to December 2017. 31 patients had a circular external fixator applied, as an index procedure and 2 as a revision procedure for deformity correction and non-union. A hexapod (TSF) frame was applied in 25 patients and an Ilizarov frame in 8 patients, and all the frames were applied on the tibia. 26 male and 7 female patients were included with an average age of 31.9 years (range 13-56). No patients were excluded from the analysis. No patients were lost to follow-up and no mechanical failure events of any of the reused circular external fixator components were recorded during this period.

Complex, open tibia and fibula fractures and deformity correction were the most common indications for application of a circular external fixator, constituting 12 and 8 patients respectively as shown in (**Figure 2**). The mean duration of treatment with a frame in situ was 5.8 months (range 2.3–16) as shown in (**Figure 3**).

Figure 2: A pie chart representing the various indications for a circular external fixator frame application, with a predominance for complex open tibia and fibula fractures

Figure 3: A box plot showing the duration of circular external fixator frame application for various indications, ranging from 3.9±1.4 months to 8.7±5.6 months with an average duration of 5.8±3.1 months

Cost analysis

The total cost for a new hexapod (TSF) frame according to the tender document was R55 559.86. If all 25 patients who had a hexapod (TSF) frame applied, used a completely new frame construct, a total of R1 388 996.50 would have been paid by our institution. Only 8 out of the 25 patients had a new hexapod (TSF) frame applied. The remaining 17 patients had reused hexapod (TSF) frames applied at a total cost of R227 013.73 (average cost per reused hexapod (TSF) frame of R13 353.75). This led to a total cost saving for hexapod (TSF) frames of R717 503.89 (average saving per hexapod (TSF) of R28 700.15) equivalent to 51.7 %. All patients who had Ilizarov frames had reused components applied. R136 568.19 which is equivalent to 62.6 % was saved against a potential total cost of R218 037.68 which would have been paid if only new Ilizarov frames were used as shown in (**Figure 4**).

Figure 4: The graph shows the total cost of 8 completely new Ilizarov frames against the cost of new components only (half pins and wires) in a reused Ilizarov frame, with the cost difference between the two showing savings of ZAR 136 5686.19.

Discussion

The strategy of reusing circular external fixators is unconventional. We demonstrated that the reuse of single use circular external fixation components is reasonably safe and results in significant cost savings to the treating institution. This strategy is relevant in LMICs however it may not be feasible or applicable in HICs, where there is a concern around indemnity of reusing devices intended as SUDs by the manufacturer.

The reprocessing of SUDs in LMICs has gained popularity resulting in savings of as much as 50% of the cost [1]. Such reprocessing strategies have been implemented utilizing third party recertification companies, original equipment manufacturers or

individual institutions in certain cases [5][6][12]. Our institution utilizes a basic in-house reprocessing strategy. Some developed countries utilize regulated reprocessing protocols, adhering to similar regulations of the manufacturer [6][7]. This is however opposed to some developing countries like India and Brazil were it is done in an unregulated manner [1]. This brings about concerns of litigation, which can be avoided if the original equipment manufacturer is used for reprocessing. There is however unclear legal consequences or any literature found on litigation pertaining to the reuse of reprocessed SUDs like external fixators [6][5]. It is also unclear if there is any advantage in using the manufacturer or third party recertification companies for reprocessing over simple reuse of components thereby introducing unnecessary added expenses [5].

Our study on reuse of circular external fixators found no mechanical failure events, rendering them reasonably safe for reuse despite paucity of literature in support of this practice. A previous animal study on reuse of slotted and cannulated bolts, which are considered inferior components of a circular external fixator concluded that these components could be reused at least 3-6 times respectively [13]. It was also suggested that the mechanical strength of modern external fixator components is far in excess of what is necessary to stabilize fractures, and subsequently affirmed that labelling these as SUDs may be inappropriate [5]. Another recent study used combined TSF and Ilizarov frames to reduce TSF costs. The TSF was used to achieve reduction and subsequently removed to allow recycling in a large number of patients. No failure of recertified parts was reported during the course of that study [14]. Considering these findings, it would seem reasonable to reuse circular external fixator components excluding the half pins and wires which are inserted into the patient's bone, expecting no mechanical failure events for at least 2-3 uses. This is similar to previous studies where no mechanical failure events were recorded with reuse of temporary external fixators [5][12].

Matsuura and Lounici studied load and cycle dependent tests using a unilateral external fixator **(***Dynafix – selected for testing because of its multiple type joint mechanisms*), focusing on low-load, high-cycle tests (*partial weight bearing*) and high load, low cycle tests (*full weight bearing*) and the results showed that none of the fixators failed after three simulated uses in the former [10]. However, hairline cracks were noted in

some of the fixators after the second use. The fixators that underwent high load, low cycle tests all failed. Further studies looking at economic impact and safety of reprocessing selected external fixator components have supported the reuse of temporary external fixators at least 2-3 times with good outcomes [12][15]. As such reuse of temporary external fixators for 2-3 cycles has been considered safe in non-weight bearing status. However, our cohort does not have a log of the number of times a component was reused in weight bearing status, a measure which we should consider, as such future research should focus on the number of cycles that components can be reused for safely.

Our institution saved 52 % and 63 % of expected total cost for hexapod and Ilizarov frames respectively in the year 2017. There is however to our knowledge no current literature that shows potential savings with reuse of circular external fixators, unlike temporary external fixators where average savings of between 21.3 % and 25 % have been realized [12][15]. Similar savings of around 50% which are comparable to our study have however been demonstrated in other studies focused on reuse of SUDs other than external fixator components like endoscopic devices, cardiological and nephrology catheters as well as linear suturing machines and harmonic ACE scissors [1][16].

Limitations in our study include use of a single manufacturer for circular external fixator components, a small sample size, no record of the number of times the circular external fixator components were reused, which may have a direct impact on safety concerns. No functional or patient outcome measures like difficulty in mobilisation, limitations in range of motion, chronic leg pain or pin site sepsis associated with completely new or reused frames were included. We also did not have a testing protocol comparable to the manufacturer's standards. Visual inspection of the components was deemed sufficient as such any hairline cracks that might have potentially been identified using standardized reprocessing protocols would have been missed, despite our reports of no mechanical failure events. Despite not integrating the cost of the in-house reprocessing protocol, indisputably significant cost savings can be achieved.

Conclusion

This study has demonstrated that reuse of circular external fixator components is reasonably safe and cost effective, resulting in over 50% and 60% cost savings for hexapod (TSF) and Ilizarov frames respectively. Reuse of circular external fixator components may be safely practiced in LMICs, while there might be concerns around indemnity on their reuse in HICs. Further research should focus on defining the safe number of cycles as well as examining possible functional and patient outcome differences between patients with reused and those with completely new frame components in order to indisputably conclude on safety concerns.

Table and Figures

Figure 1: A basic in-house reprocessing protocol flow chart showing the stages through which circular external fixator components undergo upon removal for reuse.

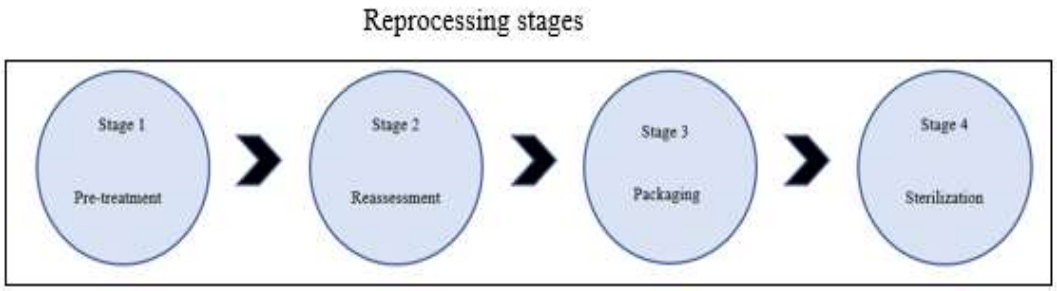


Figure 1: A basic in-house reprocessing protocol flow chart showing the stages through which circular external fixator components undergo upon removal for reuse.

Figure 2: A pie chart representing the various indications for a circular external fixator frame application, with a predominance for complex open tibia and fibula fractures

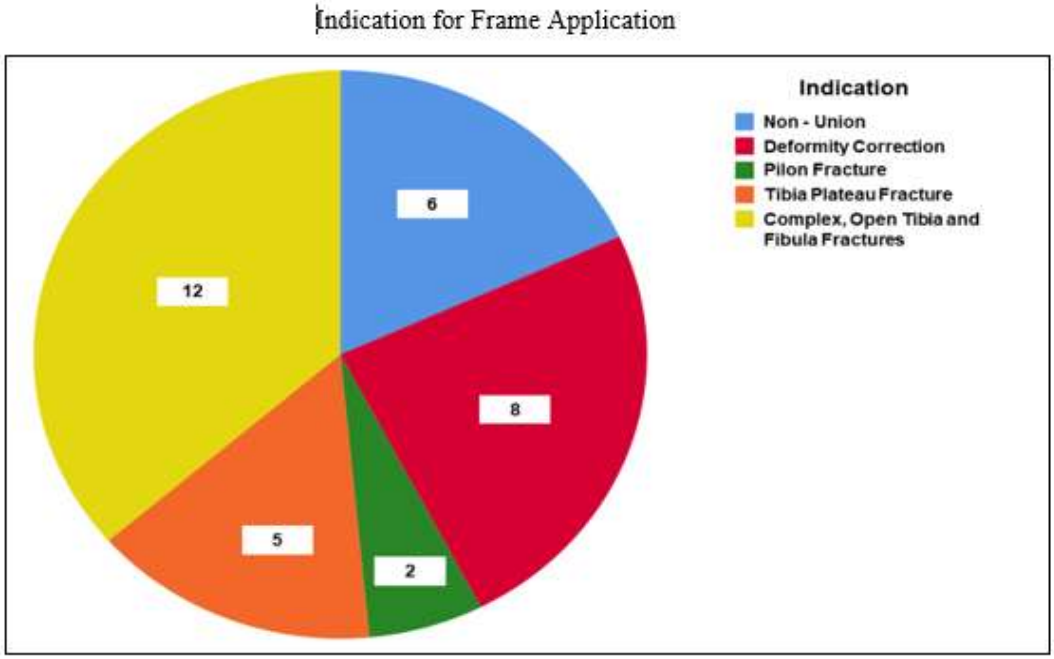


Figure 2: A pie chart representing the various indications for a circular external fixator frame application, with a predominance for complex open tibia and fibula fractures.

Figure 3: A box plot showing the duration of circular external fixator frame application for various indications, ranging from 3.9±1.4 months to 8.7±5.6 months with an average duration of 5.8±3.1 months

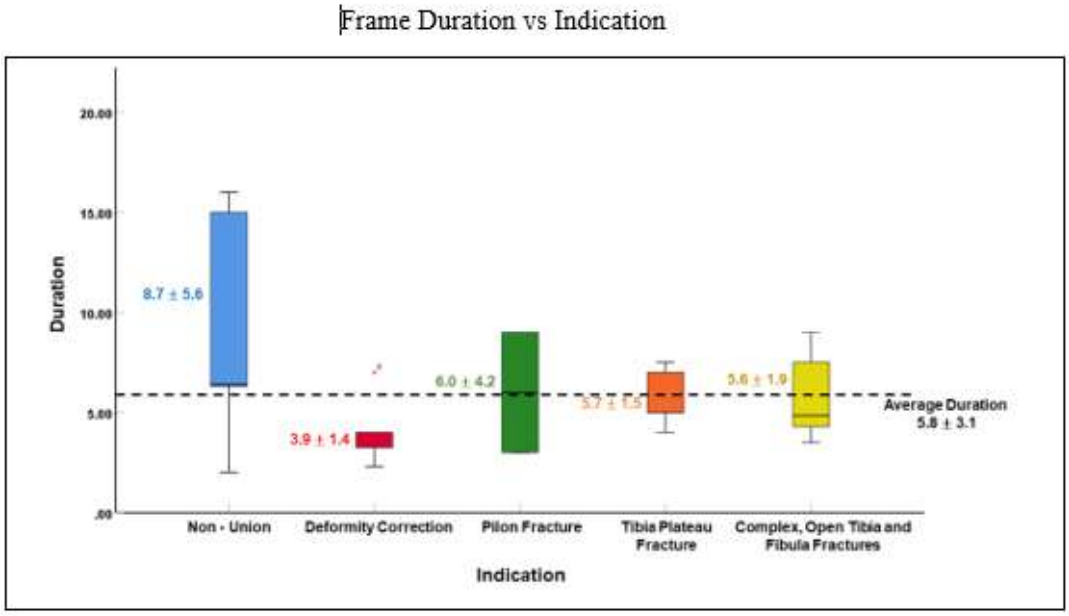


Figure 3: A box plot showing the duration of circular external fixator frame application for various indications, ranging from 3.9±1.4 months to 8.7±5.6 months with an average duration of 5.8±3.1 months.

Figure 4: The graph shows the total cost of 8 completely new Ilizarov frames against the cost of new components only (half pins and wires) in a reused Ilizarov frame, with the cost difference between the two showing savings of ZAR 136 5686.19.

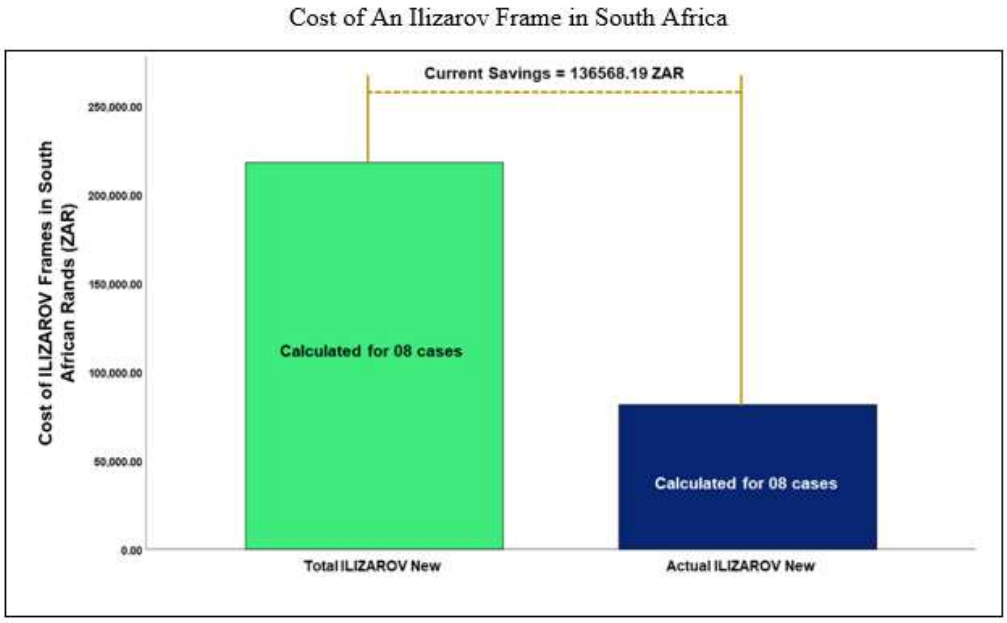


Figure 4: The graph shows (*in green*) the total cost of 8 completely new Ilizarov frames against (*in blue*) the cost of new components only (half pins and wires) in a reused frame, with the cost difference between the two showing savings of ZAR 136 5686.19.

References

1. Hussain M, Balsara KP, Nagral S (2012) Reuse of single-use devices: Looking back, looking forward. Natl Med J India 25:151–155
2. Danesi V, Cristofolini L, Stea S, et al (2011) Re-use of explanted osteosynthesis devices: A reliable and inexpensive reprocessing protocol. Injury 42:1101–1106. https://doi.org/10.1016/j.injury.2011.02.006
3. Mahapatra S, Rengarajan N (2017) Use of recycled external fixators in management of compound injuries. Expert Rev Med Devices 14:83–85. https://doi.org/10.1080/17434440.2017.1265886
4. Pulate A, Olivier LC, Agashe S, et al (2001) Adaption of Ilizarov ring fixator to the economic situation of developing countries. Arch Orthop Trauma Surg 121:79–82. https://doi.org/10.1007/s004020000159
5. Chaus GW, Dukes C, Hak DJ, et al (2014) Analysis of usage and associated cost of external fixators at an urban level 1 trauma centre. Injury 45:1611–1613. https://doi.org/10.1016/j.injury.2014.04.031
6. Thamyongkit S, Bachabi M, Thompson JM, et al (2018) Use of reprocessed external fixators in orthopaedic surgery: A survey of 243 orthopaedic trauma surgeons. Patient Saf Surg 12:1–7. https://doi.org/10.1186/s13037-018-0156-2
7. Sung JK, Levin R, Siegel J, et al (2008) Reuse of external fixation components: A randomized trial. J Orthop Trauma 22:126–130. https://doi.org/10.1097/BOT.0b013e318162e55c
8. Sabesan VJ, Petersen-Fitts GR, Ramthun KW, et al (2018) Strategies to Contain Cost Associated with Orthopaedic Care. JBJS Rev 6:e3. https://doi.org/10.2106/JBJS.RVW.17.00040
9. Hayek KR, Parikh HR, McCreary DL, et al (2019) Cost Variation in

Temporizing External Fixation of Tibial Plateau Fractures. J Orthop Trauma 33:S5–S10. https://doi.org/10.1097/BOT.0000000000001620

10. Matsuura M, Lounici S (2003) Assessment of External Fixator Reusability Using Load- and Cycle-Dependent Tests. 275–281. https://doi.org/10.1097/01.blo.0000037443.23683.7c
11. Watson MA, Mathias KJ, Maffulli N (2000) External ring fixators: An overview. Proc Inst Mech Eng Part H J Eng Med 214:459–470. https://doi.org/10.1243/0954411001535480
12. Horwitz BDS, Schabel KLS, Higgins TF (2007) The Economic Impact of Reprocessing External Fixation Components. 2132–2136. https://doi.org/10.2106/JBJS.F.01409
13. Wosar MA, Marcellin-little DJ, Roe SC (2002) Influence of Bolt Tightening Torque, Wire Size, and Component Reuse on Wire Fixation in Circular External Fixation. 571–576. https://doi.org/10.1053/jvet.2002.34672
14. Khalifa R, Abdelgawad A, Thabet AM (2020) The Versatility of Taylor Spatial Frame in Treating Complex Posttraumatic Deformities of The Lower Extremity. 9:90–96
15. Dirschl DR (2006) Reuse of Selected External Fixator Components is Safe and Should Be Supported. J Orthop Trauma 20:43–46. https://doi.org/10.1097/01.bot.0000189883.21163.40
16. De Sousa Martins B, Melo JQE, Logarinho Monteiro J, et al (2018) Reprocessing of Single-Use Medical Devices: Clinical and Financial Results. Port J Public Heal 36:150–156. https://doi.org/10.1159/000496299

Declarations

Funding

No funding or any form of grants were received in order to conduct this study.

Conflicts of Interest

The authors have no conflicts of interest to declare pertaining to the content of this article.

Availability of data and material

The data supporting the findings of this study is available on REDCap® a secure online database which is not publicly available. Data is however available upon reasonable request from the corresponding author with permission using a University of Cape Town third party account.

Code availability

Not applicable

Authors' contributions

All the authors contributed to the study. Data collection and analysis was performed by Kudzai Chironga as well as writing up the first draft of the manuscript. This was done under the supervision of Maritz Laubscher and Stefan Swanepoel. Roopam Dey assisted with tabulating the data collected into graphical representation. All authors including Michael Held and Simon Matthew Graham commented on subsequent drafts, read through and approved the final manuscript.

PART B: APPENDICES

EJOST Instructions to Authors

Instructions for Authors

Types of papers

The following types of articles will be considered for publication:

- Original articles:

  Original Articles should have no more than 2,500 words with an abstract of 150 words (in some cases, a maximum of 250 words is also acceptable), no more than 5 figures and 3 tables, and a maximum of 25 references.

- Review articles:

  These articles are exhaustive studies, either original papers or review of the literature. They should not exceed 20 typed written pages and the references should be limited to 50.

  The PRISMA guidelines should be followed for reporting of systematic reviews: http://www.prisma-statement.org

- Technical notes:

  They should not normally exceed 1500 words. The articles should be introduced by an abstract with key words.

  For Technical Notes, the abstract should have no subheadings. The abstract should be followed by three to five key words, which should be drawn from the Medical Subject Headings (MeSH) list of Index Medicus.

  The technical notes can be illustrated by not more than 4 figures and 2 tables.

- Letters to Editors:

  These will be published at the discretion of the editor. Letters to the Editor are limited to 500 words and 5 references.

- Case Reports and Up-to Date Review:

  Exceptionally rare and well written case reports may be accepted as long as a thorough review of the literature is undertaken. The authors are encouraged to rethink and rewrite their work, structuring it as a review of the literature for the respective pathology and make the presentation of clinical facts as an

example for this review. In this respect the number of references may be upgraded to 25. A table associated with this report should include the references, the year of publication, the particularity of the observation and remarks for each reading.

Manuscript Submission

Submission of a manuscript implies: that the work described has not been published before; that it is not under consideration for publication anywhere else; that its publication has been approved by all co-authors, if any, as well as by the responsible authorities – tacitly or explicitly – at the institute where the work has been carried out. The publisher will not be held legally responsible should there be any claims for compensation.

Permissions

Authors wishing to include figures, tables, or text passages that have already been published elsewhere are required to obtain permission from the copyright owner(s) for both the print and online format and to include evidence that such permission has been granted when submitting their papers. Any material received without such evidence will be assumed to originate from the authors.

Online Submission

Please follow the hyperlink "Submit manuscript" on the right and upload all of your manuscript files following the instructions given on the screen.

Please ensure you provide all relevant editable source files. Failing to submit these source files might cause unnecessary delays in the review and production process.

References

The reference style as described in the Instructions for Authors is mandatory.

Title Page

Please make sure your title page contains the following information.

Title

The title should be concise and informative.

Author information

- The name(s) of the author(s)
- The affiliation(s) of the author(s), i.e., institution, (department), city, (state), country
- A clear indication and an active e-mail address of the corresponding author

- If available, the 16-digit ORCID of the author(s)

If address information is provided with the affiliation(s) it will also be published.

For authors that are (temporarily) unaffiliated we will only capture their city and country of residence, not their e-mail address unless specifically requested.

Abstract

Please provide a structured abstract of 150 to 250 words which should be divided into the following sections:

- Purpose (stating the main purposes and research question)
- Methods
- Results
- Conclusion

For life science journals only (when applicable)

- Trial registration number and date of registration for prospectively registered trials
- Trial registration number and date of registration followed by “retrospectively registered”, for retrospectively registered trials

Keywords

Please provide 4 to 6 keywords which can be used for indexing purposes.

Statements and Declarations

The following statements should be included under the heading "Statements and Declarations" for inclusion in the published paper. Please note that submissions that do not include relevant declarations will be returned as incomplete.

- **Competing Interests:** Authors are required to disclose financial or non-financial interests that are directly or indirectly related to the work submitted for publication. Please refer to “Competing Interests and Funding” below for more information on how to complete this section.

Please see the relevant sections in the submission guidelines for further information as well as various examples of wording. Please revise/customize the sample statements according to your own needs.

Important Note:

Please don't forget to add a summary statement, that reflects what is recorded in the potential conflict of interest disclosure form(s).

Text Formatting

Manuscripts should be submitted in Word.

- Use a normal, plain font (e.g., 10-point Times Roman) for text.
- Use italics for emphasis.
- Use the automatic page numbering function to number the pages.
- Do not use field functions.
- Use tab stops or other commands for indents, not the space bar.
- Use the table function, not spreadsheets, to make tables.
- Use the equation editor or MathType for equations.
- Save your file in docx format (Word 2007 or higher) or doc format (older Word versions).

Manuscripts with mathematical content can also be submitted in LaTeX. We recommend using Springer Nature's LaTeX template.

Headings

Please use no more than three levels of displayed headings.

Abbreviations

Abbreviations should be defined at first mention and used consistently thereafter.

Footnotes

Footnotes can be used to give additional information, which may include the citation of a reference included in the reference list. They should not consist solely of a reference citation, and they should never include the bibliographic details of a reference. They should also not contain any figures or tables.

Footnotes to the text are numbered consecutively; those to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data). Footnotes to the title or the authors of the article are not given reference symbols.

Always use footnotes instead of endnotes.

Acknowledgments

Acknowledgments of people, grants, funds, etc. should be placed in a separate section on the title page. The names of funding organizations should be written in full.

Please note: Submit your manuscript without line numbers (line numbers will be added automatically later).

References

Citation

Reference citations in the text should be identified by numbers in square brackets. Some examples:

1. Negotiation research spans many disciplines [3].

2. This result was later contradicted by Becker and Seligman [5].

3. This effect has been widely studied [1-3, 7].

Reference list

The list of references should only include works that are cited in the text and that have been published or accepted for publication. Personal communications and unpublished works should only be mentioned in the text.

The entries in the list should be numbered consecutively.

If available, please always include DOIs as full DOI links in your reference list (e.g., “https://doi.org/abc”).

- Journal article

  Gamelin FX, Baquet G, Berthoin S, Thevenet D, Nourry C, Nottin S, Bosquet L (2009) Effect of high intensity intermittent training on heart rate variability in prepubescent children. Eur J Appl Physiol 105:731-738. https://doi.org/10.1007/s00421-008-0955-8

  Ideally, the names of all authors should be provided, but the usage of “et al” in long author lists will also be accepted:

  Smith J, Jones M Jr, Houghton L et al (1999) Future of health insurance. N Engl J Med 965:325–329

- Article by DOI

  Slifka MK, Whitton JL (2000) Clinical implications of dysregulated cytokine production. J Mol Med. https://doi.org/10.1007/s001090000086

- Book

  South J, Blass B (2001) The future of modern genomics. Blackwell, London

- Book chapter

Brown B, Aaron M (2001) The politics of nature. In: Smith J (ed) The rise of modern genomics, 3rd edn. Wiley, New York, pp 230-257

- Online document

Cartwright J (2007) Big stars have weather too. IOP Publishing PhysicsWeb. http://physicsweb.org/articles/news/11/6/16/1. Accessed 26 June 2007

- Dissertation

Trent JW (1975) Experimental acute renal failure. Dissertation, University of California

Always use the standard abbreviation of a journal's name according to the ISSN List of Title Word Abbreviations, see

ISSN.org LTWA

If you are unsure, please use the full journal title.

Authors preparing their manuscript in LaTeX can use the bibliography style file sn-basic.bst which is included in the Springer Nature Article Template.

Tables

- All tables are to be numbered using Arabic numerals.
- Tables should always be cited in text in consecutive numerical order.
- For each table, please supply a table caption (title) explaining the components of the table.
- Identify any previously published material by giving the original source in the form of a reference at the end of the table caption.
- Footnotes to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data) and included beneath the table body.

Artwork

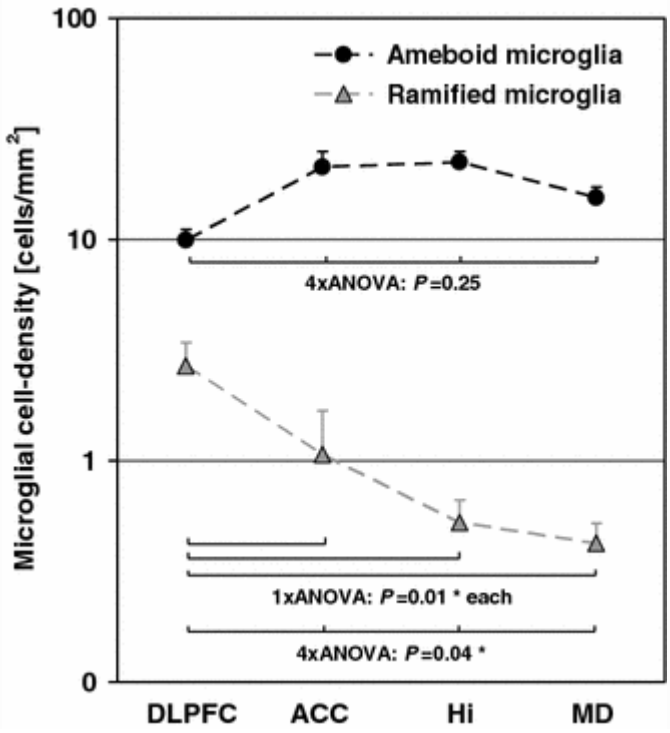
For the best quality final product, it is highly recommended that you submit all of your artwork – photographs, line drawings, etc. – in an electronic format. Your art will then be produced to the highest standards with the greatest accuracy to detail. The published work will directly reflect the quality of the artwork provided.

Electronic Figure Submission

- Supply all figures electronically.
- Indicate what graphics program was used to create the artwork.

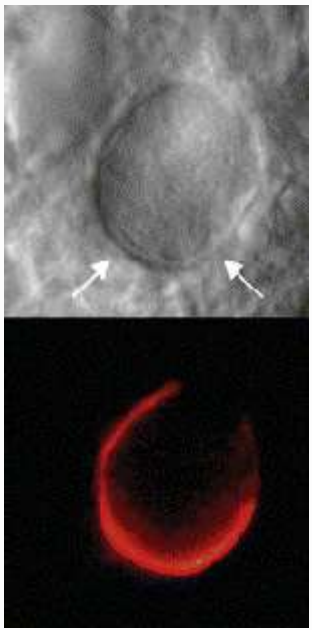
- For vector graphics, the preferred format is EPS; for halftones, please use TIFF format. MS Office files are also acceptable.
- Vector graphics containing fonts must have the fonts embedded in the files.
- Name your figure files with "Fig" and the figure number, e.g., Fig1.eps.

Line Art



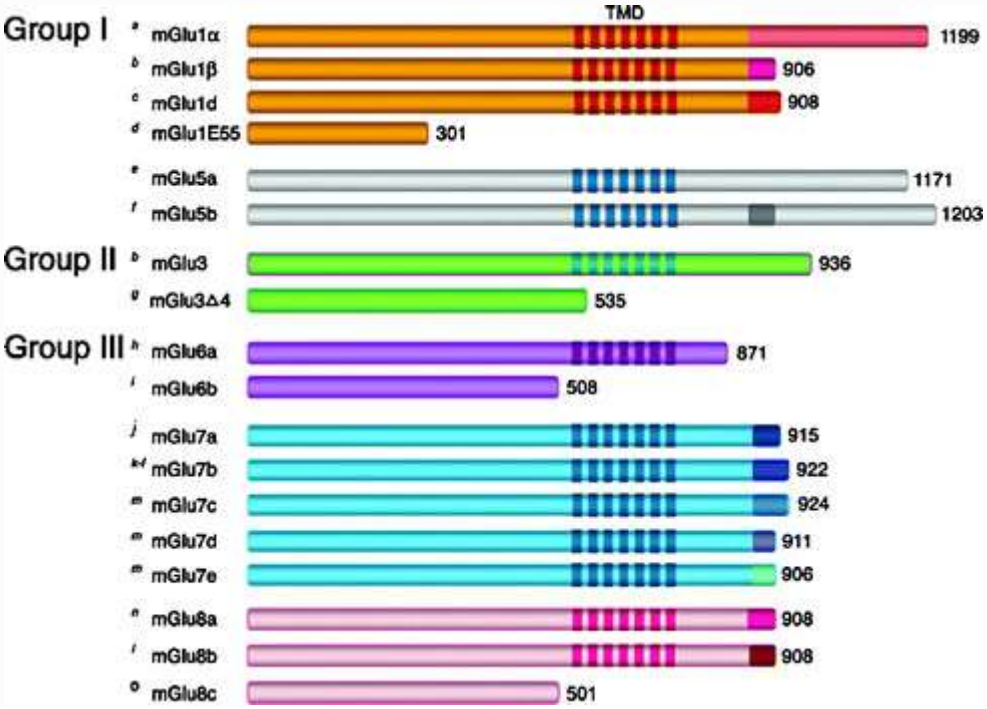
- Definition: Black and white graphic with no shading.
- Do not use faint lines and/or lettering and check that all lines and lettering within the figures are legible at final size.
- All lines should be at least 0.1 mm (0.3 pt) wide.
- Scanned line drawings and line drawings in bitmap format should have a minimum resolution of 1200 dpi.
- Vector graphics containing fonts must have the fonts embedded in the files.

Halftone Art



- Definition: Photographs, drawings, or paintings with fine shading, etc.
- If any magnification is used in the photographs, indicate this by using scale bars within the figures themselves.
- Halftones should have a minimum resolution of 300 dpi.

Combination Art



- Definition: a combination of halftone and line art, e.g., halftones containing line drawing, extensive lettering, color diagrams, etc.
- Combination artwork should have a minimum resolution of 600 dpi.

Color Art

- Color art is free of charge for print and online publication.
- Color illustrations should be submitted as RGB.

Figure Lettering

- To add lettering, it is best to use Helvetica or Arial (sans serif fonts).
- Keep lettering consistently sized throughout your final-sized artwork, usually about 2–3 mm (8–12 pt).
- Variance of type size within an illustration should be minimal, e.g., do not use 8-pt type on an axis and 20-pt type for the axis label.
- Avoid effects such as shading, outline letters, etc.
- Do not include titles or captions within your illustrations.

Figure Numbering

- All figures are to be numbered using Arabic numerals.
- Figures should always be cited in text in consecutive numerical order.
- Figure parts should be denoted by lowercase letters (a, b, c, etc.).
- If an appendix appears in your article and it contains one or more figures, continue the consecutive numbering of the main text. Do not number the appendix figures, "A1, A2, A3, etc." Figures in online appendices [Supplementary Information (SI)] should, however, be numbered separately.

Figure Captions

- Each figure should have a concise caption describing accurately what the figure depicts. Include the captions in the text file of the manuscript, not in the figure file.
- Figure captions begin with the term Fig. in bold type, followed by the figure number, also in bold type.
- No punctuation is to be included after the number, nor is any punctuation to be placed at the end of the caption.
- Identify all elements found in the figure in the figure caption; and use boxes, circles, etc., as coordinate points in graphs.
- Identify previously published material by giving the original source in the form of a reference citation at the end of the figure caption.

Figure Placement and Size

- When preparing your figures, size figures to fit in the column width.
- For large-sized journals the figures should be 84 mm (for double-column text areas), or 174 mm (for single-column text areas) wide and not higher than 234 mm.
- For small-sized journals, the figures should be 119 mm wide and not higher than 195 mm.

Permissions

If you include figures that have already been published elsewhere, you must obtain permission from the copyright owner(s) for both the print and online format. Please be aware that some publishers do not grant electronic rights for free and that Springer will not be able to refund any costs that may have occurred to receive these permissions. In such cases, material from other sources should be used.

Accessibility

In order to give people of all abilities and disabilities access to the content of your figures, please make sure that

- All figures have descriptive captions (blind users could then use a text-to-speech software or a text-to-Braille hardware)
- Patterns are used instead of or in addition to colors for conveying information (color-blind users would then be able to distinguish the visual elements)
- Any figure lettering has a contrast ratio of at least 4.5:1

Supplementary Information (SI)

Springer accepts electronic multimedia files (animations, movies, audio, etc.) and other supplementary files to be published online along with an article or a book chapter. This feature can add dimension to the author's article, as certain information cannot be printed or is more convenient in electronic form.

Before submitting research datasets as Supplementary Information, authors should read the journal's Research data policy. We encourage research data to be archived in data repositories wherever possible.

Submission

- Supply all supplementary material in standard file formats.
- Please include in each file the following information: article title, journal name, author names; affiliation and e-mail address of the corresponding author.
- To accommodate user downloads, please keep in mind that larger-sized files may require very long download times and that some users may experience other problems during downloading.
- High resolution (streamable quality) videos can be submitted up to a maximum of 25GB; low resolution videos should not be larger than 5GB.

Audio, Video, and Animations

- Aspect ratio: 16:9 or 4:3
- Maximum file size: 25 GB for high resolution files; 5 GB for low resolution files
- Minimum video duration: 1 sec

- Supported file formats: avi, wmv, mp4, mov, m2p, mp2, mpg, mpeg, flv, mxf, mts, m4v, 3gp

Text and Presentations

- Submit your material in PDF format; .doc or .ppt files are not suitable for long-term viability.
- A collection of figures may also be combined in a PDF file.

Spreadsheets

- Spreadsheets should be submitted as .csv or .xlsx files (MS Excel).

Specialized Formats

- Specialized format such as .pdb (chemical), .wrl (VRML), .nb (Mathematica notebook), and .tex can also be supplied.

Collecting Multiple Files

- It is possible to collect multiple files in a .zip or .gz file.

Numbering

- If supplying any supplementary material, the text must make specific mention of the material as a citation, similar to that of figures and tables.
- Refer to the supplementary files as “Online Resource”, e.g., "... as shown in the animation (Online Resource 3)", “... additional data are given in Online Resource 4”.
- Name the files consecutively, e.g., “ESM_3.mpg”, “ESM_4.pdf”.

Captions

- For each supplementary material, please supply a concise caption describing the content of the file.

Processing of supplementary files

- Supplementary Information (SI) will be published as received from the author without any conversion, editing, or reformatting.

Accessibility

In order to give people of all abilities and disabilities access to the content of your supplementary files, please make sure that

- The manuscript contains a descriptive caption for each supplementary material

- Video files do not contain anything that flashes more than three times per second (so that users prone to seizures caused by such effects are not put at risk)

Competing Interests

Authors are requested to disclose interests that are directly or indirectly related to the work submitted for publication. Interests within the last 3 years of beginning the work (conducting the research and preparing the work for submission) should be reported. Interests outside the 3-year time frame must be disclosed if they could reasonably be perceived as influencing the submitted work. Disclosure of interests provides a complete and transparent process and helps readers form their own judgments of potential bias. This is not meant to imply that a financial relationship with an organization that sponsored the research or compensation received for consultancy work is inappropriate.

Editorial Board Members and Editors are required to declare any competing interests and may be excluded from the peer review process if a competing interest exists. In addition, they should exclude themselves from handling manuscripts in cases where there is a competing interest. This may include – but is not limited to – having previously published with one or more of the authors, and sharing the same institution as one or more of the authors. Where an Editor or Editorial Board Member is on the author list, they must declare this in the competing interests' section on the submitted manuscript. If they are an author or have any other competing interest regarding a specific manuscript, another Editor or member of the Editorial Board will be assigned to assume responsibility for overseeing peer review. These submissions are subject to the exact same review process as any other manuscript. Editorial Board Members are welcome to submit papers to the journal. These submissions are not given any priority over other manuscripts, and Editorial Board Member status has no bearing on editorial consideration.

Interests that should be considered and disclosed but are not limited to the following:

Funding: Research grants from funding agencies (please give the research funder and the grant number) and/or research support (including salaries, equipment, supplies, reimbursement for attending symposia, and other expenses) by organizations that may gain or lose financially through publication of this manuscript.

Employment: Recent (while engaged in the research project), present or anticipated employment by any organization that may gain or lose financially through publication of this manuscript. This includes multiple affiliations (if applicable).

Financial interests: Stocks or shares in companies (including holdings of spouse and/or children) that may gain or lose financially through publication of this manuscript; consultation fees or other forms of remuneration from organizations that may gain or lose financially; patents or patent applications whose value may be affected by publication of this manuscript.

It is difficult to specify a threshold at which a financial interest becomes significant, any such figure is necessarily arbitrary, so one possible practical guideline is the following: "Any undeclared financial interest that could embarrass the author were it to become publicly known after the work was published."

Non-financial interests: In addition, authors are requested to disclose interests that go beyond financial interests that could impart bias on the work submitted for publication such as professional interests, personal relationships or personal beliefs (amongst others). Examples include, but are not limited to: position on editorial board, advisory board or board of directors or other type of management relationships; writing and/or consulting for educational purposes; expert witness; mentoring relations; and so forth.

Primary research articles require a disclosure statement. Review articles present an expert synthesis of evidence and may be treated as an authoritative work on a subject. Review articles therefore require a disclosure statement. Other article types such as editorials, book reviews, comments (amongst others) may, dependent on their content, require a disclosure statement. If you are unclear whether your article type requires a disclosure statement, please contact the Editor-in-Chief.

Please note that, in addition to the above requirements, funding information (given that funding is a potential competing interest (as mentioned above)) needs to be disclosed upon submission of the manuscript in the peer review system. This information will automatically be added to the Record of CrossMark, however it is **not added** to the manuscript itself. Under 'summary of requirements' (see below) funding information should be included in the '**Declarations**' section.

Summary of requirements

The above should be summarized in a statement and included on **a title page that is separate from the manuscript** with a section entitled "**Declarations**" when submitting a paper. Having all statements in one place allows for a consistent and unified review of the information by the Editor-in-Chief and/or peer reviewers and may speed up the handling of the paper. Declarations include Funding, Competing interests, Ethics approval, Consent, Data, Materials and/or Code availability and Authors' contribution statements. **Please use the title page for providing the statements.**

Once and if the paper is accepted for publication, the production department will put the respective statements in a distinctly identified section clearly visible for readers.

Please see the various examples of wording below and revise/customize the sample statements according to your own needs.

When all authors have the same (or no) competing interests and/or funding it is sufficient to use one blanket statement.

Examples of statements to be used when funding has been received:

- Partial financial support was received from [...]
- The research leading to these results received funding from […] under Grant Agreement No[…].
- This study was funded by […]
- This work was supported by […] (Grant numbers […] and […]

Examples of statements to be used when there is no funding:

- The authors did not receive support from any organization for the submitted work.
- No funding was received to assist with the preparation of this manuscript.
- No funding was received for conducting this study.
- No funds, grants, or other support was received.

Examples of statements to be used when there are interests to declare:

- **Financial interests:** Author A has received research support from Company A. Author B has received a speaker honorarium from Company Wand owns stock in Company X. Author C is consultant to company Y.

  Non-financial interests: Author C is an unpaid member of committee Z.

- **Financial interests:** The authors declare they have no financial interests.

  Non-financial interests: Author A is on the board of directors of Y and receives no compensation as member of the board of directors.

- **Financial interests:** Author A received a speaking fee from Y for Z. Author B receives a salary from association X. X where s/he is the Executive Director.

  Non-financial interests: none.

- **Financial interests:** Author A and B declare they have no financial interests. Author C has received speaker and consultant honoraria from Company M and Company N. Dr. C has received speaker honorarium and research funding from Company M and Company O. Author D has received travel support from Company O.

  Non-financial interests: Author D has served on advisory boards for Company M, Company N and Company O.

Examples of statements to be used when authors have nothing to declare:

- The authors have no relevant financial or non-financial interests to disclose.
- The authors have no competing interests to declare that are relevant to the content of this article.
- All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

- The authors have no financial or proprietary interests in any material discussed in this article.

Authors are responsible for correctness of the statements provided in the manuscript. See also Authorship Principles. The Editor-in-Chief reserves the right to reject submissions that do not meet the guidelines described in this section.

Ethical standards

Manuscripts submitted for publication must contain a declaration that the experiments comply with the current laws of the country in which they were performed. Please include this note in a separate section before the reference list.

Experimental Subjects/Animals

All authors are expected to abide by accepted ethical standards. In investigations that involve human subjects or laboratory animals, authors should provide an explicit statement in Materials and Methods that the experimental protocols were approved by the appropriate institutional review committee and meet the guidelines of their responsible governmental agency. In the case of human subjects, informed consent is essential.

All randomized controlled clinical trials (RCTs) should conform to the CONSORT

criteria. The corresponding author should indicate whether the RCT has been registered or not.

CONSORT Criteria

CONSORT (Consolidated Standards of Reporting Trials)

For Information on the most updated Consort Statement and to download the Consort E-Checklist and the E-flowchart, go to:

CONSORT statement

If relevant, the below reporting guidelines should be followed:

- STARD (for reporting of diagnostic accuracy studies)
- STROBE (for reporting of observational studies in epidemology) http://www.strobe-statement.org
- PRISMA (for reporting of systematic reviews) http://www.prisma-statement.org
- MOOSE (for reporting of meta-analyses of observational studies)

Clinical Trial Registration

All trials must be registered in a public trials registry that is acceptable to the International Committee of Medical Journals Editors (ICMJE):

ICMJE Criteria

Research Data Policy

This journal operates a type 1 research data policy. The journal encourages authors, where possible and applicable, to deposit data that support the findings of their research in a public repository. Authors and editors who do not have a preferred repository should consult Springer Nature's list of repositories and research data policy.

List of Repositories

Research Data Policy

General repositories - for all types of research data - such as figshare and Dryad may also be used.

Datasets that are assigned digital object identifiers (DOIs) by a data repository may be cited in the reference list. Data citations should include the minimum information recommended by DataCite: authors, title, publisher (repository name), identifier.

DataCite

If the journal that you're submitting to uses double-blind peer review and you are providing reviewers with access to your data (for example via a repository link, supplementary information or data on request), it is strongly suggested that the authorship in the data is also blinded. There are data repositories that can assist with this and/or will create a link to mask the authorship of your data.

Authors who need help understanding our data sharing policies, help finding a suitable data repository, or help organising and sharing research data can access our Author Support portal for additional guidance.

Ethical Responsibilities of Authors

This journal is committed to upholding the integrity of the scientific record. As a member of the Committee on Publication Ethics (COPE) the journal will follow the COPE guidelines on how to deal with potential acts of misconduct.

Authors should refrain from misrepresenting research results which could damage the trust in the journal, the professionalism of scientific authorship, and ultimately the entire scientific endeavour. Maintaining integrity of the research and its

presentation is helped by following the rules of good scientific practice, which include*:

- The manuscript should not be submitted to more than one journal for simultaneous consideration.
- The submitted work should be original and should not have been published elsewhere in any form or language (partially or in full), unless the new work concerns an expansion of previous work. (Please provide transparency on the re-use of material to avoid the concerns about text-recycling ('self-plagiarism').
- A single study should not be split up into several parts to increase the quantity of submissions and submitted to various journals or to one journal over time (i.e., 'salami-slicing/publishing').
- Concurrent or secondary publication is sometimes justifiable, provided certain conditions are met. Examples include: translations or a manuscript that is intended for a different group of readers.
- Results should be presented clearly, honestly, and without fabrication, falsification or inappropriate data manipulation (including image based manipulation). Authors should adhere to discipline-specific rules for acquiring, selecting and processing data.
- No data, text, or theories by others are presented as if they were the author's own ('plagiarism'). Proper acknowledgements to other works must be given (this includes material that is closely copied (near verbatim), summarized and/or paraphrased), quotation marks (to indicate words taken from another source) are used for verbatim copying of material, and permissions secured for material that is copyrighted.

Important note: the journal may use software to screen for plagiarism.

- Authors should make sure they have permissions for the use of software, questionnaires/(web) surveys and scales in their studies (if appropriate).
- Research articles and non-research articles (e.g., Opinion, Review, and Commentary articles) must cite appropriate and relevant literature in support of the claims made. Excessive and inappropriate self-citation or coordinated efforts among several authors to collectively self-cite is strongly discouraged.
- Authors should avoid untrue statements about an entity (who can be an individual person or a company) or descriptions of their behavior or actions that could potentially be seen as personal attacks or allegations about that person.
- Research that may be misapplied to pose a threat to public health or national security should be clearly identified in the manuscript (e.g., dual use of research). Examples include creation of harmful consequences of biological agents or toxins, disruption of immunity of vaccines, unusual hazards in the use of chemicals, weaponization of research/technology (amongst others).
- Authors are strongly advised to ensure the author group, the Corresponding Author, and the order of authors are all correct at submission. Adding and/or deleting authors during the revision stages is generally not permitted, but in some cases may be warranted. Reasons for changes in authorship should be explained in detail. Please note that changes to authorship cannot be made after acceptance of a manuscript.

*All of the above are guidelines and authors need to make sure to respect third parties' rights such as copyright and/or moral rights.

Upon request authors should be prepared to send relevant documentation or data in order to verify the validity of the results presented. This could be in the form of raw data, samples, records, etc. Sensitive information in the form of confidential or proprietary data is excluded.

If there is suspicion of misbehavior or alleged fraud the Journal and/or Publisher will carry out an investigation following COPE guidelines. If, after investigation, there are valid concerns, the author(s) concerned will be contacted under their given e-mail address and given an opportunity to address the issue. Depending on the situation, this may result in the Journal's and/or Publisher's implementation of the following measures, including, but not limited to:

- If the manuscript is still under consideration, it may be rejected and returned to the author.
- If the article has already been published online, depending on the nature and severity of the infraction:

  - an erratum/correction may be placed with the article

  - an expression of concern may be placed with the article

  - or in severe cases retraction of the article may occur.

The reason will be given in the published erratum/correction, expression of concern or retraction note. Please note that retraction means that the article is **maintained on the platform**, watermarked "retracted" and the explanation for the retraction is provided in a note linked to the watermarked article.

- The author's institution may be informed
- A notice of suspected transgression of ethical standards in the peer review system may be included as part of the author's and article's bibliographic record.

Fundamental errors

Authors have an obligation to correct mistakes once they discover a significant error or inaccuracy in their published article. The author(s) is/are requested to contact the journal and explain in what sense the error is impacting the article. A decision on how to correct the literature will depend on the nature of the error. This may be a correction or retraction. The retraction note should provide transparency which parts of the article are impacted by the error.

Suggesting / excluding reviewers

Authors are welcome to suggest suitable reviewers and/or request the exclusion of certain individuals when they submit their manuscripts. When suggesting reviewers,

authors should make sure they are totally independent and not connected to the work in any way. It is strongly recommended to suggest a mix of reviewers from different countries and different institutions. When suggesting reviewers, the Corresponding Author must provide an institutional email address for each suggested reviewer, or, if this is not possible to include other means of verifying the identity such as a link to a personal homepage, a link to the publication record or a researcher or author ID in the submission letter. Please note that the Journal may not use the suggestions, but suggestions are appreciated and may help facilitate the peer review process.

Authorship principles

These guidelines describe authorship principles and good authorship practices to which prospective authors should adhere to.

Authorship clarified

The Journal and Publisher assume all authors agreed with the content and that all gave explicit consent to submit and that they obtained consent from the responsible authorities at the institute/organization where the work has been carried out, **before** the work is submitted.

The Publisher does not prescribe the kinds of contributions that warrant authorship. It is recommended that authors adhere to the guidelines for authorship that are applicable in their specific research field. In absence of specific guidelines, it is recommended to adhere to the following guidelines*:

All authors whose names appear on the submission

1) made substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data; or the creation of new software used in the work;

2) drafted the work or revised it critically for important intellectual content;

3) approved the version to be published; and

4) agree 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.

* Based on/adapted from:

ICMJE, Defining the Role of Authors and Contributors,

Transparency in authors' contributions and responsibilities to promote integrity in scientific publication, McNutt at all, PNAS February 27, 2018

Disclosures and declarations

All authors are requested to include information regarding sources of funding, financial or non-financial interests, study-specific approval by the appropriate ethics committee for research involving humans and/or animals, informed consent if the research involved human participants, and a statement on welfare of animals if the research involved animals (as appropriate).

The decision whether such information should be included is not only dependent on the scope of the journal, but also the scope of the article. Work submitted for publication may have implications for public health or general welfare and in those cases, it is the responsibility of all authors to include the appropriate disclosures and declarations.

Data transparency

All authors are requested to make sure that all data and materials as well as software application or custom code support their published claims and comply with field standards. Please note that journals may have individual policies on (sharing) research data in concordance with disciplinary norms and expectations.

Role of the Corresponding Author

One author is assigned as Corresponding Author and acts on behalf of all co-authors and ensures that questions related to the accuracy or integrity of any part of the work are appropriately addressed.

The Corresponding Author is responsible for the following requirements:

- ensuring that all listed authors have approved the manuscript before submission, including the names and order of authors;
- managing all communication between the Journal and all co-authors, before and after publication; *
- providing transparency on re-use of material and mention any unpublished material (for example manuscripts in press) included in the manuscript in a cover letter to the Editor;
- making sure disclosures, declarations and transparency on data statements from all authors are included in the manuscript as appropriate (see above).

* The requirement of managing all communication between the journal and all co-authors during submission and proofing may be delegated to a Contact or Submitting Author. In this case, please make sure the Corresponding Author is clearly indicated in the manuscript.

Author contributions

In absence of specific instructions and in research fields where it is possible to describe discrete efforts, the Publisher recommends authors to include contribution

statements in the work that specifies the contribution of every author in order to promote transparency. These contributions should be listed at the separate title page.

Examples of such statement(s) are shown below:

• Free text:

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [full name], [full name] and [full name]. The first draft of the manuscript was written by [full name] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Example: CRediT taxonomy:

• Conceptualization: [full name], …; Methodology: [full name], …; Formal analysis and investigation: [full name], …; Writing - original draft preparation: [full name, …]; Writing - review and editing: [full name], …; Funding acquisition: [full name], …; Resources: [full name], …; Supervision: [full name],….

For **review articles** where discrete statements are less applicable a statement should be included who had the idea for the article, who performed the literature search and data analysis, and who drafted and/or critically revised the work.

For articles that are based primarily on the **student's dissertation or thesis**, it is recommended that the student is usually listed as principal author:

A Graduate Student's Guide to Determining Authorship Credit and Authorship Order, APA Science Student Council 2006

Affiliation

The primary affiliation for each author should be the institution where the majority of their work was done. If an author has subsequently moved, the current address may additionally be stated. Addresses will not be updated or changed after publication of the article.

Changes to authorship

Authors are strongly advised to ensure the correct author group, the Corresponding Author, and the order of authors at submission. Changes of authorship by adding or deleting authors, and/or changes in Corresponding Author, and/or changes in the sequence of authors are **not** accepted **after acceptance** of a manuscript.

- **Please note that author names will be published exactly as they appear on the accepted submission!**

Please make sure that the names of all authors are present and correctly spelled, and that addresses and affiliations are current.

Adding and/or deleting authors at revision stage are generally not permitted, but in some cases, it may be warranted. Reasons for these changes in authorship should be explained. Approval of the change during revision is at the discretion of the Editor-in-Chief. Please note that journals may have individual policies on adding and/or deleting authors during revision stage.

Author identification

Authors are recommended to use their ORCID ID when submitting an article for consideration or acquire an ORCID ID via the submission process.

Deceased or incapacitated authors

For cases in which a co-author dies or is incapacitated during the writing, submission, or peer-review process, and the co-authors feel it is appropriate to include the author, co-authors should obtain approval from a (legal) representative which could be a direct relative.

Authorship issues or disputes

In the case of an authorship dispute during peer review or after acceptance and publication, the Journal will not be in a position to investigate or adjudicate. Authors will be asked to resolve the dispute themselves. If they are unable the Journal reserves the right to withdraw a manuscript from the editorial process or in case of a published paper raise the issue with the authors' institution(s) and abide by its guidelines.

Confidentiality

Authors should treat all communication with the Journal as confidential which includes correspondence with direct representatives from the Journal such as Editors-in-Chief and/or Handling Editors and reviewers' reports unless explicit consent has been received to share information.

After Acceptance

Upon acceptance, your article will be exported to Production to undergo typesetting. Once typesetting is complete, you will receive a link asking you to confirm your affiliation, choose the publishing model for your article as well as arrange rights and payment of any associated publication cost.

Once you have completed this, your article will be processed and you will receive the proofs.

Article publishing agreement

Depending on the ownership of the journal and its policies, you will either grant the Publisher an exclusive licence to publish the article or will be asked to transfer copyright of the article to the Publisher.

Offprints

Offprints can be ordered by the corresponding author.

Color illustrations

Publication of color illustrations is free of charge.

Proof reading

The purpose of the proof is to check for typesetting or conversion errors and the completeness and accuracy of the text, tables and figures. Substantial changes in content, e.g., new results, corrected values, title and authorship, are not allowed without the approval of the Editor.

After online publication, further changes can only be made in the form of an Erratum, which will be hyperlinked to the article.

Online First

The article will be published online after receipt of the corrected proofs. This is the official first publication citable with the DOI. After release of the printed version, the paper can also be cited by issue and page numbers.

Open Choice

Open Choice allows you to publish open access in more than 1850 Springer Nature journals, making your research more visible and accessible immediately on publication.

Article processing charges (APCs) vary by journal – view the full list

Benefits:

- Increased researcher engagement: Open Choice enables access by anyone with an internet connection, immediately on publication.
- Higher visibility and impact: In Springer hybrid journals, OA articles are accessed 4 times more often on average, and cited 1.7 more times on average*.
- Easy compliance with funder and institutional mandates: Many funders require open access publishing, and some take compliance into account when assessing future grant applications.

It is easy to find funding to support open access – please see our funding and support pages for more information.

*) Within the first three years of publication. Springer Nature hybrid journal OA impact analysis, 2018.

Open Choice

Funding and Support pages

Copyright and license term – CC BY

Open Choice articles do not require transfer of copyright as the copyright remains with the author. In opting for open access, the author(s) agree to publish the article under the Creative Commons Attribution License.

Find more about the license agreement

English Language Editing

For editors and reviewers to accurately assess the work presented in your manuscript you need to ensure the English language is of sufficient quality to be understood. If you need help with writing in English you should consider:

- Getting a fast, free online grammar check.
- Asking a colleague who is proficient in English to review your manuscript for clarity.
- Visiting the English language tutorial which covers the common mistakes when writing in English.
- Using a professional language editing service where editors will improve the English to ensure that your meaning is clear and identify problems that require your review. Two such services are provided by our affiliates Nature Research Editing Service and American Journal Experts. Springer authors are entitled to a 10% discount on their first submission to either of these services, simply follow the links below.

Please note that the use of a language editing service is not a requirement for publication in this journal and does not imply or guarantee that the article will be selected for peer review or accepted.

If your manuscript is accepted it will be checked by our copyeditors for spelling and formal style before publication.

Language

Articles and abstracts must be in English.

Editorial procedure

Double-blind peer review

This journal follows a double-blind reviewing procedure. This means that the author will remain anonymous to the reviewers throughout peer review. It is the responsibility of the author to anonymize the manuscript and any associated materials.

- Author names, affiliations and any other potentially identifying information should be removed from the manuscript text and any accompanying files (such as figures of supplementary material);
- A separate Title Page should be submitted, containing title, author names, affiliations, and the contact information of the corresponding author. Any acknowledgements, disclosures, or funding information should also be included on this page;
- Authors should avoid citing their own work in a way that could reveal their identity.

All submissions undergo initial editorial triage by the Editor-in-Chief. Manuscripts that satisfy the scope and quality standards of the journal are then evaluated by an Associate Editor and peer reviewers according to subject area. A decision is made based on the consensus of at least two expert opinions.

EJOST Reviewers comments

Manuscript Number: EJOS-D-21-00722
Article Title: The Reuse of Circular External Fixator Components: An Assessment of Safety and Potential Savings
European Journal of Orthopaedic Surgery & Traumatology

Dear Dr Chironga,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript.

Your revision is due by 20 Nov 2021.

"Please make sure to submit your editable source files (i. e. Word, TeX)."

To submit a revision, go to https://www.editorialmanager.com/ejos/ and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Best regards,

Cyril Mauffrey
Editor-in-Chief
European Journal of Orthopaedic Surgery & Traumatology

COMMENTS TO THE AUTHOR:

Reviewer's Responses to Questions

Content of manuscript

Purpose

Reviewer #2:
*Clear

Reviewer #3:
*Unclear

Originality

Reviewer #2:
*Acceptable

Reviewer #3:
*Acceptable

Importance of the subject

Reviewer #2:
*Poor

Reviewer #3:
*Poor

Integration of the most recent data

Reviewer #2:
*Some points are overdeveloped when considering aims and scopes of EJOST

Reviewer #3:
*Insufficient

Scientific writing/structure

Reviewer #2:
*Acceptable/to be modified

Reviewer #3:
*Acceptable/to be modified

Content of manuscript : Reviewer’s comments/suggestions

Reviewer #2: Please see below

Reviewer #3: This current study was designed to determine the safety and cost saving associated with the reuse of circular external fixator components in a resource constrained environment.

Materials

Reviewer #2:

*Inappropriate

Reviewer #3:
*Inappropriate

Materials : Reviewer’s comments/suggestions

Reviewer #2: Please see below

Reviewer #3: Authors performed a retrospective review of all adult patients who were treated with a circular external fixator from a single manufacturer between January and December 2017.

Methods

Reviewer #2:
*Need clarification

Reviewer #3:
*Need clarification

Methods : Reviewer’s comments/suggestions

Reviewer #2: Please see below

Reviewer #3: Cost savings were calculated as the difference between the price of a completely new frame and the amount invoiced for new components only in a reused frame, based on their suppliers 2017 tender document.

References

The number of references

Reviewer #2:
*Outstanding literature review/citations

Reviewer #3:
*Insufficient

References : Reviewer’s comments/suggestions

Reviewer #2: Please see below

Reviewer #3: 15 references are included to complete the text. All of them were published from 2000 to 2019.

Iconography and charts

Iconography

Reviewer #2:
*Too large

Reviewer #3:
*Satisfactory/need explanation

Charts

Reviewer #2:
*Adequate

Reviewer #3:
*Adequate

Iconography and charts : Reviewer’s comments/suggestions

Reviewer #2: Please see below

Reviewer #3: 4 figures and legends support the study.

Reviewer #2: Thank you for giving me the opportunity to review this manuscript on the reuse of external fixators. I understand the difficulties that some of our colleagues may face due to lack of resources. However, as the authors successfully point out at their discussion section, similar studies have been already published in the related literature supporting the reuse of the external fixators. What does this small case series (33 patients) add to the existing evidence? Obviously, costs are expected to be significantly decreased, using the same resterilized devices. But, can safety be assessed by such a small number of cases? I am afraid that the results of this study are not strong enough to change current practice or give any new insights on the subject, so I would hesitate to suggest publication.

Reviewer #3: Please provide your comments to the author

—

Response letter and manuscript adjustment

UNIVERSITY OF CAPE TOWN

Division of Orthopaedic Surgery
H49 OMB
Groote Schuur Hospital
Observatory 7925
Cape Town - South Africa
Telephone: (-27-21) 406 6157/ 8
Telefax: (-27-21) 447-2709

05 November 2021

Cyril Mauffrey
Editor-In-Chief
European Journal of Orthopaedic Surgery & Traumatology

Dear Editor-In-Chief and reviewers

Response to reviewers' comments:

Manuscript Number: EJOS-D-21-00722

Article Title: The Reuse of Circular External Fixator Components: An Assessment of Safety and Potential Savings

I hope I find you well.

I would like to sincerely thank you for reviewing and considering our paper. We greatly appreciated your input in terms of comments and suggestions. As advised, we have looked at them and have addressed them accordingly.

The revised manuscript was uploaded as instructed and we hope that it will meet your most favourable response and will be acceptable to you resulting in publication in your journal.

Kind regards

Kudzai Chironga

Reviewers' comments to authors and response by author(s)

Reviewer No	Original comments of the reviewer	Reply by author(s)	Heading /Page No of changes
#3	**Purpose** - unclear	**Purpose -** The purpose was re-phrased illustrating that reuse of temporary monolateral external fixators is well supported in literature contrary to the reuse of circular external fixator components which is the focus of this study.	**Abstract/Page 2**
#2/#3	**Importance of the subject** - poor	There is a paucity of literature concerning the reuse of circular external fixator components as opposed to the reuse of temporary external fixators, which is well supported in literature. The study seeks to highlight the need to support the reuse of definitive circular external fixator components to significantly curb healthcare costs in LMICs with inadequate resources since they are far much more expensive compared to temporary external fixators.	
#2	**Integration of the most recent data** – some points are overdeveloped when considering the aims and scope of EJOST	This study has no well published literature to reference from specifically pertaining to reuse of circular external fixators. As such some points had to be developed having been extrapolated from literature that has already been published on reuse of temporary external fixators.	

		We feel this study is relevant for our setting and can potentially change practice in LMICs, allowing this practice to be done in a more regulated manner. We hope this will be acceptable to you.	
#3	**Integration of the most recent data** - Insufficient	There is a paucity of literature concerning the reuse of circular external fixator components as opposed to the reuse of temporary external fixators, which is well supported in literature. One animal study (Reference [13]) was used in the initial manuscript and another (Reference [14]) has been added in the revised manuscript. These two studies to our knowledge are the only ones we came across that had the most recent data pertaining to reuse of circular external fixator components relevant to this study. No other relevant studies concerning reuse of circular external fixator components could be identified as such integration of the most recent data was limited.	
#2/#3	**Scientific writing/structure** – acceptable/ to be modified	Some modifications have been made within the manuscript as guided by comments from the reviewers.	
#2/#3	**Materials** - Inappropriate	Our study only used circular external fixator components from a single manufacturer because they were our sole supplier of external	

		fixator components, as such this may be a source of bias and may potentially skew the outcomes measures. As a result, we have included it as a limitation to the study. We also found it imperative to outline how the reprocessing protocol is executed at our institution where the study was conducted. We hope this is acceptable to you.	**Limitations/Page 9**
#2/#3	**Methods** – need clarification	The last paragraph relating to cost of the frames under Materials and methods was rephrased for clarity	**Page 5**
#3	**References -** Insufficient	As previously mentioned, there is a paucity of literature on reuse of circular external fixator components contrary to reuse of temporary external fixator components. Only 2 studies, references [13] and [14] were identified that sited the reuse of some components of a circular external fixator. The remainder of the references were centred on reuse of other medical devices denoted as SUDs illustrating safety and cost effectiveness, which are the same outcome measures we focused on in this study. Reference [14] published in 2020 was added and cited in the discussion.	**Discussion/Page 8**

		There is now a total of 16 references.	
#2	**Iconography** – too large	Reduction in size of the images resulted in failure to read the words on the images. May you kindly consider accepting the iconography in the current form.	
#2	**Iconography and charts**: reviewers' comments/Suggestions Thank you for giving me the opportunity to review this manuscript on the reuse of external fixators. I understand the difficulties that some of our colleagues may face due to lack of resources. However, as the authors successfully point out at their discussion section, similar studies have been already published in the related literature supporting the reuse of the external fixators. What does this small case series (33 patients) add to the existing evidence? Obviously, costs are expected to be significantly decreased, using the same resterilized devices. But, can safety be assessed by such a small number of cases? I am afraid that the results of this study are not strong enough to change current practice or give any new insights on the subject, so I would hesitate to suggest publication.	Granted there have been studies published in relation to reuse of external fixators, however these studies mainly focused on reuse of temporary external fixators and only two studies to our knowledge were identified which concentrated on reuse of circular external fixator components in which one was an animal study. A small sample size of 33 patients was a limitation as a result of the low volume of patients who met the criteria for application of a circular external fixator in the time period included in the study. Undoubtably cost savings were achieved however in as much as we did not record any mechanical failure events, further studies with larger sample sizes focused on reuse of circular external fixators may be of benefit to ultimately determine safety and the safe number of circles these components can be subjected to for reuse.	

EJOST acceptance letter

Ref.: Ms. No. EJOS-D-21-00722R1
The Reuse of Circular External Fixator Components: An Assessment of Safety and Potential Savings
European Journal of Orthopaedic Surgery & Traumatology

Dear Dr Chironga,

We would like to confirm acceptance of the above-mentioned manuscript for publication in our journal European Journal of Orthopaedic Surgery & Traumatology.

As the next step, you will receive proofs of your article. Please check them carefully and send them back to the address indicated.

Thank you for submitting your work to this journal.

Sincerely yours,

Cyril Mauffrey
Editor-in-Chief
European Journal of Orthopaedic Surgery & Traumatology

Confirmation of publication

SPRINGER NATURE

SN SharedIt

Dear Author,

We are pleased to inform you that your article "The reuse of circular external fixator components: an assessment of safety and potential savings" has been published online in European Journal of Orthopaedic Surgery & Traumatology. As part of the Springer Nature Content Sharing Initiative, you can publicly share full-text access to a view-only version of your paper by using the following SharedIt link:

https://rdcu.be/cBZ4J

Readers of your article via the shared link will also be able to use Enhanced PDF features such as annotation tools, one-click supplements, citation file exports and article metrics.

We encourage you to forward this link to your co-authors and post it on your social media accounts. You can get started with this easy plan. Sharing your paper is a great way to improve the visibility of your work. There are no restrictions on the number of people you may share this link with, how many times they can view the linked article or where you can post the link online.

More information on Springer Nature's commitment to content sharing and the SharedIt initiative is available here.

Sincerely,
Springer Nature

The Springer Nature SharedIt Initiative is powered by readcube technology.

HREC approval letter

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

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

05 April 2019

HREC REF: 198/2019

Dr M Laubscher
Division of Orthopaedic Surgery
H49 OMB

Dear Dr Laubscher

PROJECT TITLE: THE RE-USE OF CIRCULAR EXTERNAL FIXATOR COMPONENTS: AN ASSESSMENT OF SAFETY AND POTENTIAL SAVINGS (MASTERS CANDIDATE - DR K CHIRONGA)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

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 April 2020.

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

We acknowledge that the student: Dr Kudzai Chironga will also be involved in this study.

Please quote the HREC REF in all your correspondence.

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

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

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

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

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use: Good Clinical Practice (ICH GCP), South African Good Clinical Practice Guidelines (DoH 2006), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines. The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

UNIVERSITY OF CAPE TOWN

HUMAN RESEARCH ETHICS COMMITTEE
22 NOV 2021
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

FHS016: Annual Progress Report / Renewal

HREC office use only (FWA00001637; IRB00001938) This serves as notification of annual approval, including any documentation described below.			
☑ Approved	Annual progress report	Approved until/next renewal date	30.11.22
☐ Not approved	See attached comments		
Signature Chairperson of the HREC/ Designee		Date Signed	24/11/21

Note: Please email this form and supporting documents (if applicable) in a combined pdf-file to hrec-enquiries@uct.ac.za.
Please clarify your plan for research-related activities during COVID-19 lockdown.
Please use the latest form found on our website:
http://www.health.uct.ac.za/fhs/research/humanethics/forms

Comments to PI from the HREC	
	Thank you for your Study Deviation HREC Chair Signature Date: 24/11/21

Principal Investigator to complete the f

1. Protocol information

Date (when submitting this form)	17/11/2021		
HREC REF Number	196/2019	Current Ethics Approval was granted until	30/04/21
Protocol title	The re-use of circular external fixator components: An assessment of safety and potential savings		
Protocol number (if applicable)	2019/034		
Are there any sub-studies linked to this study?	☐ Yes	✓ No	
If yes, could you please provide the HREC Reference number for all sub-studies? **Note:** A separate FHS016 must be submitted for each sub-study			
Principal Investigator	Professor Maritz Laubscher		

(Note: Please complete the Closure form (FHS018) if the study is completed within the approval period)

Department / Office Internal Mail Address	Division of Orthopaedic surgery, H49 OMB, Groote Schuur Hospital, Observatory, 7923, Cape Town, South Africa

1.1 Does this protocol receive US Federal funding?	☐ Yes	✓ No
1.2 If the study receives US Federal Funding, does the annual report require full committee approval? **Note:** Any annual approvals for **Full Committee** review MUST be submitted on the monthly HREC submission dates. (Please send electronic copy for full committee review to hrec-submissions@uct.ac.za)	☐ Yes	✓ No

If yes in 1.2 please complete section 1.3 below for invoicing purposes

1.3 Ethics Renewal Fee

Please (**tick** ✓)appropriate box for billing purposes:

Submission Type	Description	New fee (Vat incl.)	tick ✓
Research funded solely from UCT departmental/ divisional/group budget	Annual evaluation of research progress report for re-certification	**R0.00**	☐
Non-sponsored student research for degree purposes at UCT/Other Universities & Colleges	Annual evaluation of research progress report for re-certification	**R0.00**	✓
Annual re-certification / Progress report (FHS016 Form)	Clinical Trial & International Grant Funded Research - Annual evaluation of research progress report for re-certification for Full Committee Approval	**R7500.00**	☐
Annual re-certification / Progress report (FHS016 Form)	Clinical Trial & International Grant Funded Research - Annual evaluation of research progress report for re-certification for Expedited review	**R3 710.00**	☐
Annual re-certification / Progress report (FHS016 Form)	National grant funded research - Annual evaluation of research progress report for re-certification for Full Committee Approval	**R6000.00**	☐
Annual re-certification / Progress report (FHS016 Form)	National Grant funded research for Annual evaluation of research progress report for re-certification for Expedited review	**R1 500.00**	☐

NB: Protocols funded by UCT (e.g. departmental funding / student research) and by certain grant funding organizations (e.g. MRC, NRF, CANSA,) are exempt from these charges.

Please provide details for invoicing, either complete section 1 or 2:

1. **Invoice billing – Directly to Sponsor**

Sponsor's name	
Billing Address of Sponsor:	
Vat Number:	

Contact person	
Telephone number	
Email Address	

2. Internal Journal Billing:		
Fund Number:		
Cost Centre Number:		
Account Holder Name:		
Division of Account Holder:		

2. List of documentation for approval

N/A

3. Protocol status (tick ✓)

☐	Open Enrolment	
☐	Closed to enrolment (tick ✓)	
✓	Research-related activities are ongoing	
☐	Research-related activities are complete, long-term follow-up only	
☐	Research-related activities are complete, data analysis only	
☐	Main study is complete but sub-study research-related activities are ongoing	
☐	Study is closed → Please submit a Study Closure Form (FHS010)	

4. Enrolment

Number of participants enrolled to date	N/A	
Number of participants enrolled, since last HREC Progress report (continuing review)	N/A	
Additional number of participants still required	N/A	

5. Refusals

Total number of refusals (participants invited to join the study, but refused to take part)	N/A

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

6. Cumulative summary of participants

Total number of participants who provided consent	N/A
Number of participants determined to be ineligible (i.e. after screening)	N/A
Number of participants currently active on the study	N/A
Number of participants completed study (without events leading to withdrawal)	N/A
Number of participants withdrawn at participants' request (i.e. changed their mind)	N/A
Number of participants withdrawn by PI due to toxicity or adverse events	N/A
Number of participants withdrawn by PI for other reasons (e.g. pregnancy, poor compliance)	N/A
Number of participants lost to follow-up. Please comment below on reasons for loss of follow-up.	N/A
Number of participants no longer taking part for reasons not listed above. Please provide reasons below:	N/A

7. Progress of study

Please provide a brief summary of the research to date including the overall progress and the progress since the last annual report as well as any relevant comments/issues you would like to report to the HREC:

The research write was completed and a manuscript was submitted for publication and was accepted in EJOST (European Journal of orthopaedic surgery and Traumatology) on 16/11/2021

8. Protocol violations and exceptions (tick ✓ all that apply)

✓	No prior violations or exceptions have occurred since the original approval
☐	Prior violations or exceptions have been reported since the last review and have already been acknowledged or approved
☐	Unreported minor violations that have occurred since the last review, as well as significant deviations not yet reported, are attached for review

9. Amendments (tick ✓ all that apply)

✓	No Prior amendments have been made since the original approval

☐	Prior amendments have been reported since the last review and have already been approved
☐	New protocol changes/ amendments are requested as part of this continuing review (See note below)

Note: If new protocol changes are being requested in this review, please complete an amendment form (FHS008).
Specific changes in the amended protocol and consent/assent forms must be **bolded**, italicised or tracked and all changes must include a rationale.

10. Adverse events

10.1 Please provide below or attach a narrative summary of serious adverse events and/ or unanticipated problems since the last progress report. Please indicate changes made to the protocol and informed consent document(s) as a result (if not already reported to the HREC). Please comment on whether causality to any study procedure or intervention could be established.
N/A

10.2 Have participants received appropriate treatment/ follow-up/ referral when indicated (e.g., in the case of abnormal or incidental clinical findings, distress or anxiety)?		
☐ Yes	☐ No	✓ Not applicable
If yes, please describe:		

11. Summary of Monitoring and Audit Activities (tick ✓)

11.1 Was this study monitored or audited by an external agency (e.g. SAHPRA, FDA)?		
☐ Yes	☐ No	✓ Not applicable

11.2 Did a Data and Safety Monitoring Board publish a report?		
☐ Yes	☐ No	✓ Not applicable

11.3 If yes, please identify the agency and attach a summary of the findings.					
Agency Name		Report attached	☐ Yes	☐ No	✓ Not applicable
		DSMB report attached	☐ Yes	☐ No	✓ Not applicable

11.4 Has there been any agency, institutional or other inquiry into non-compliance in this study, or any finding of non-compliance concerning a member of the research team?		
☐ Yes	✓ No	
If yes, please explain:		

(Note: Please complete the Closure form (FHS010) if the study is completed within the approval period)

12. Level of risk (tick ✓)

12.1 In light of your experience of this research, please indicate whether the level of risk to participants has:

☐	Increased
☐	Decreased
✓	Shown no change

If there has been a change, please explain:

12.2 Please provide a narrative summary of recent relevant literature that may have a bearing on the level of risk.

N/A

13. Insurance

Please confirm that valid no fault insurance is still in place? (tick ✓)

☐ Yes ✓ No

If yes, please complete the following:

Insurer's name:			
Policy no.		*Coverage Period:	

For UCT sponsored studies please liaise the Insurance office via fhs.ap.onsorahi@uct.ac.za regarding the required documentation and information required obtain a renewed UCT No-fault Insurance Certificate.

14. Statement of conflict of interest

Has there been any change in the conflict-of-interest status of this protocol since the original approval? (tick ✓)

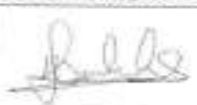
☐ Yes ✓ No

If yes, please explain and if necessary, attach a revised conflict of interest statement (Section #7 in the New Protocol Application Form FHS013):

UNIVERSITY OF CAPE TOWN
FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

15. Signature

My signature certifies that the above is complete and correct.

Signature of PI		Date	18/11/2021

UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

Form FHS006: Protocol Amendment

HREC office use only (FWA00001637; IRB00001938)			
☑ Approved	☑ Type of review: Expedited	☐ Full committee	
This serves as notification that all changes and documentation described below are approved.			
Signature HREC Chairperson / Designee		Date	24/11/21

Note: All **Major** amendments must include a **Cover Letter** and a local **PI Synopsis** justifying the changes for the amendment. Please note that incomplete amendment submissions will not be reviewed.

Please email this form and supporting documents (if applicable) in a combined pdf-file to hrec-enquiries@uct.ac.za with subject line: FHS006 + (HREC Reference number).

The latest forms are found on our website.

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

Please also clarify your plan for research-related activities during COVID-19 lockdown

HUMAN RESEARCH ETHICS COMMITTEE
22 NOV 2021
FACULTY OF HEALTH SCIENCES
UNIVERSITY OF CAPE TOWN

Comments from the HREC to the Principal Investigator:

Note: The approval of this protocol amendment does not grant annual approval. Please complete the FHS016 / FHS017 form for annual approval at least one month before study expiration.

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	18/11/2021
HREC REF Number	198/2019
Protocol Title	The re-use of circular external fixator components: An assessment of safety and potential savings
Protocol Number (if applicable)	2019/034
Principal Investigator	Professor Maritz Laubscher
Department / Office Internal Mail Address	Division of Orthopaedic surgery, H49 OMB, Groote Schuur Hospital, Observatory, 7923, Cape Town, South Africa

1.1 Is this a major or a minor amendment? (see FHS006hb) Major (tick box) Minor (tick box)	☐ Major	✓ Minor

1.2 Does this protocol receive US Federal funding?	☐ Yes	✓ No
1.3 If the amendment is a major amendment and receives US Federal Funding, does the amendment require full committee approval? **Note:** Any protocol amendments for **Full Committee Review** MUST be submitted on the monthly HREC submission dates. (Please email an electronic copy to hrec-enquiries@uct.ac.za)	☐ Yes	✓ No
1.4 Did the initial study require UCT No-Fault Insurance	☐ Yes	✓ No

2. List of Proposed Amendments with Revised Version Numbers and Dates

Please itemise on the page below, all amendments with revised version numbers and dates, which need approval.
This page will be detached, signed and returned to the PI as notification of approval. Please add extra pages if necessary.

1) Kindly requesting for renewal of a lapsed HREC FHS016: Annual Progress Report / Renewal

3. Protocol status (tick ✓)

☐	Open to enrolment
☐	No participants have been enrolled
	Closed to enrolment (tick ✓)
✓	Research-related activities are ongoing
☐	Research-related activities are complete, long-term follow-up only
☐	Research-related activities are complete, data analysis only

4. Proposed changes will affect: (tick ✓ all the categories that apply)

Protocol	
☐	Study objectives, design (including investigator's brochure, clinical activities, study length)
☐	Study instruments, questionnaires, interview schedules
☐	Sample size
☐	Recruitment methods
☐	Eligibility criteria (inclusion and exclusion criteria)

☐	Drug/device (composition, amount, schedule, route of administration, combination with other drugs/devices, safety information)
☐	Data collection/ analysis
☐	Principal Investigator. (Please attach revised conflict of interest and PI declaration statements. Refer sections 7 and 8.4 in the New Protocol Application Form FHS013)
☐	Consent form and information sheet
☐	Recruitment materials (e.g., advertisements)
☐	Administrative (e.g., change in sponsor's name, change in contact information)
✓	Other. Please specify: **Lapsed HREC FHS016: Annual Progress Report / Renewal**

Note: Amendment changes involving study length, sample size, additional sites and eligibility criteria (i.e. inclusion of minors and /or pregnant woman) need to be declared to the insurance office. Please liaise via fhs.allresearch@uct.ac.za regarding the required documentation and information to be submitted to obtain an updated UCT No-fault Insurance Certificate- it should be included herewith

4.1 In your opinion, will there be any **increase** in risk, discomfort or inconvenience to participants?	☐ Yes	✓ No
If yes, please provide a detailed justification/explanation:		

4.2 What follow-up action do you propose for participants who are already enrolled in the study?	
☐	Inform current participants as soon as possible
☐	Re-consent current participants with revised consent/assent forms (append)
✓	No action required
☐	Other. Please describe

5. Detailed description of the change(s)

Please attach, for each amendment, a summary of all changes which clearly indicates:

i. Old wording (e.g., ~~strikethrough~~ text, CHANGED FROM and CHANGED TO)

ii. New wording (e.g., italicized, **bold**, tracked)

iii. Detailed rationale/ justification/ explanation for each change

6. Ethics Review for Amendment Levy – cost including vat

Amendment Review Costs including VAT

Please tick amount to be billed:

Submission Type	Description	New fee (Vat incl.)	tick ✓
Research funded solely from UCT departmental/ divisional/group budget	Major/Minor Amendments	R0,00	☐
Non-sponsored student research for degree purposes at UCT/Other Universities & Colleges	Major/Minor Amendments	R0,00	✓
Protocol amendment - Major (FHS006 Form)	Clinical Trial & International Grant Funded Research - Any changes to the protocol that requires Full Committee review	R8 000,00	☐
Protocol amendment - Major (FHS006 Form)	Clinical Trial & International Grant Funded Research - Any change to the protocol that requires Expedited review that does not require Full Committee Review	R5 000,00	☐
Protocol amendment - Minor (FHS006 Form)	Clinical Trial & International Grant Funded Research - Minor amendments, administrative changes that do not affect study design e.g. changes to informed consent form, changes in study staff, etc.	R2 250,00	☐
Protocol amendment - Major (FHS006 Form)	National grant funded research - Any change to the protocol that requires Full Committee review	R7 000,00	☐
Protocol amendment - Major (FHS006 Form)	National grant funded research - Any change to the protocol that requires Expedited review that does not require Full Committee review	R2 500,00	☐
Protocol amendment - Minor (FHS006 Form)	National grant funded research - Minor amendments, administrative changes that do not affect study design e.g. changes to informed consent form, changes in study staff, etc.	R1 000,00	☐

NB: Protocols funded by UCT (e.g. departmental funding / student research) and by certain grant funding organizations (e.g. MRC, NRF, CANSA,) are exempt from these charges.

Please provide details for invoicing, either complete section 1 or 2

1. Invoice billing – Directly to Sponsor

Sponsor's name:	
Billing Address of Sponsor:	
Vat Number:	
Contact person:	
Telephone number:	
Email Address:	

2. Internal Journal Billing:		
Fund Number:		
Cost Centre Number:		
Account Holder Name:		
Division of Account Holder:		

7. Amendment Submission checklist (tick ✓)

7.1 Please tick that all the documents are attached before submitting to the HREC.
NB: Incomplete submissions will not be processed

✓	Latest FHS006 form completed with all sections completed as per our website
☐	Cover Letter
✓	PI Justification/ Summary for the reasons for the amendment
☐	Protocol - Track changes & Clean Copy (where necessary)
☐	Informed Consent Forms (ICF), if applicable (Any changes made to ICF tracked & clean copy)
✓	Any other additional documentation in support of amendment – **Previously renewed FHS016 form**
☐	Updated no fault insurance certificate (if applicable)

Please email this form and supporting documents (if applicable) in a combined pdf-file to hrec-enquiries@uct.ac.za with subject line: FHS006 + (HREC Reference number). The latest forms are found on our website.

8. Signature

My signature certifies that I will maintain the anonymity and/ or confidentiality of information collected in this research. If at any time I want to share or re-use the information for purposes other than those disclosed in the original approval, I will seek further approval from the HREC.

Signature of PI		Date	18/11/2021

Turnitin: plagiarism receipt, report and declaration

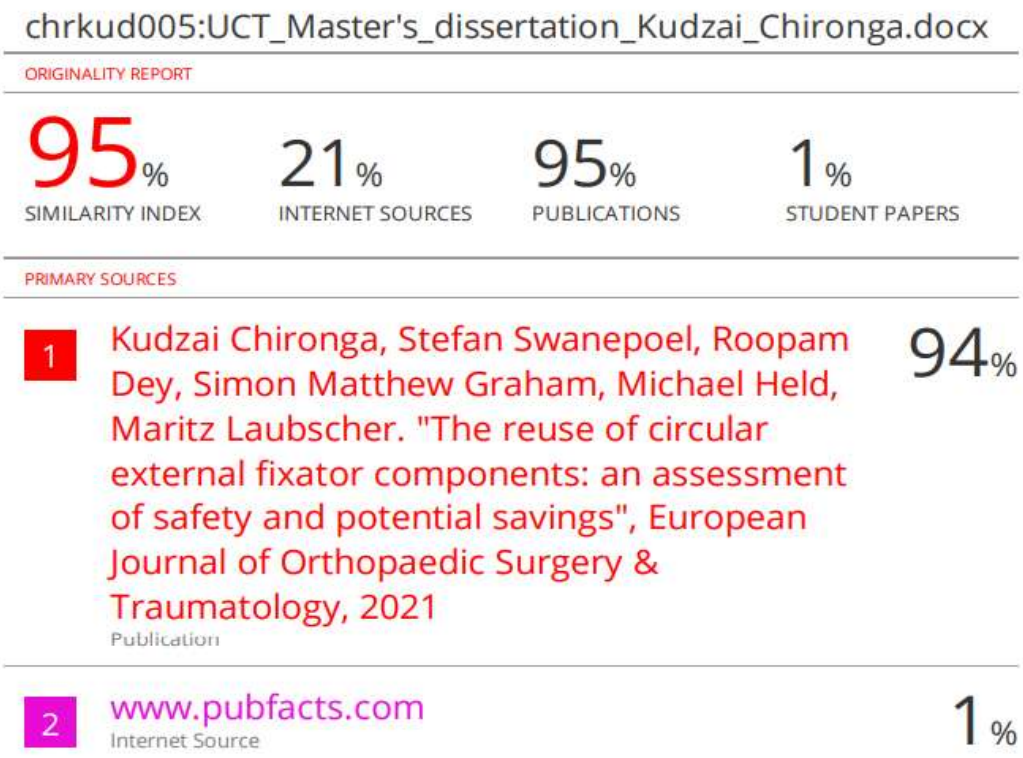
turnitin

Digital Receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

Submission author:	Kudzai Chironga
Assignment title:	For TurnItIn Submission
Submission title:	chrkud005:UCT_Master's_dissertation_Kudzai_Chironga.docx
File name:	82d1-ce7f7430eb8b_UCT_Master_s_dissertation_Kudzai_Chir...
File size:	194.5K
Page count:	12
Word count:	2,789
Character count:	15,833
Submission date:	26-Dec-2021 01:15PM (UTC+0200)
Submission ID:	1735700990

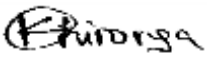


Plagiarism Declaration

"This thesis/dissertation has been submitted to the Turnitin module (or equivalent similarity and originality checking software) and I confirm that my supervisor has seen my report and any concerns revealed by such have been resolved with my supervisor."

Name: Kudzai Chironga

Student number: CHRKUD005

Signature: 

Date: 26/12/2021