THE PROFILE OF PATIENTS ATTENDING THE GROOTE SCHUUR HOSPITAL CHRONIC PAIN MANAGEMENT CLINIC

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ABSTRACT

Title: Profile of patients attending a chronic pain management clinic in Cape Town, South Africa

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Key words: Chronic pain, Profile, Global data, Developing Countries

Introduction

Chronic pain affects 10- 25% of the population worldwide. However, studies of people with chronic pain have primarily been conducted in WEIRD (Western, Educated, Industrialised, Rich and Democratic) countries. There is a paucity of data from developing countries with the existing biased data being used to guide treatment of patients in developing countries. To address this knowledge gap, we have analysed the data of 623 patients attending the Chronic Pain Management Clinic (CPMC), at a tertiary facility in Cape Town, South Africa. The profile of the patients was compared to the global data.

Methods

A cross-sectional study of patients who attended the CPMC was conducted to describe their profile according to age, sociodemographic characteristics, health, gender and use of illicit drugs.

Results

The typical patient attending the CPMC was of middle age, female gender, of low educational level and less advantageous socio-economic status. They were also more likely to be on a disability grant and suffer from anxiety and depression.

Conclusion

The profile of the patients attending the CPMC was found to be similar to those from WEIRD countries. These results suggest that we can apply global data of people with chronic pain to patients attending this clinic.

PUBLICATION-READY MANUSCRIPT

This dissertation has been prepared for the journal South African Family Practice (Appendix A – instructions for authors). The formatting used is Calibri, font size 12, and referencing used is Vancouver Style.

INTRODUCTION

Chronic pain is a debilitating condition affecting billions of people worldwide (1). While chronic pain has been extensively described in high income countries, less data are available for people living in low- to middle-income countries. However, current systematic reviews based on the limited existing data show the prevalence is similar in both developing and developed countries (2). Global prevalence of chronic pain is 10- 25% (3).In South Africa, 1 in 5, or 20% of people suffer from chronic pain (4).

Chronic pain is defined as any pain that is experienced on most days, lasting or recurring for more than three months (5). To clarify the description of chronic pain, Loeser et al., describes chronic pain as a maladaptive process whereby there is a derangement in the restoration homeostasis (6). In this model, acute pain is associated with normal tissue healing processes during the first, inflammatory phase of healing (seven to ten days), the second regenerative phase of healing (six weeks), and possibly even during the third, remodelling phase of healing up to three months. Chronic pain, however, is regarded as a maladaptive process in which homeostasis has not been restored, with pain persisting beyond normal tissue healing times i.e., beyond three months (6). Essentially, chronic pain is pain that is present on most days for more than three months, with the three-month timeline selected because most tissues have healed by three months (7)(6).

While the term chronic pain is widely used, it is perhaps not helpful if used in isolation. There has been a shift towards a mechanism-based classification of pain to assist clinicians with analysing underlying pathology which may be contributing to pain. The focus on mechanism aims to contribute to more efficient, mechanism-based pain management. The three mechanism-based classifications of pain are: nociceptive, neuropathic and nociplastic pain (7).

Neuropathic pain arises from lesion or disease in the sensory nerves which translates into a heightened or altered painful response to stimuli (8). It often co-exists with other disorders, more commonly in metabolic disorders like diabetes mellitus, in inflammatory, and

autoimmune disorders and often in post infectious conditions like herpes. Nociceptive pain is pain which occurs after damage to non-neural tissues, thereby activating sensory neurones known as nociceptors which relay information about potentially noxious stimuli which are interpreted cortically as pain. Nociplastic pain, according to the IASP task force, is defined as "pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain." (9). These mechanistic pain categories are not exclusive. A person suffering from chronic pain can present with compound presentations of any of the three forms of pain described above: nociplastic, neuropathic and nociceptive pain. The intricacy of pain and its complex mechanisms are yet to be elucidated; however, numerous biopsychosocial risk factors have been identified as increasing the risk that someone will develop chronic pain.

Risk factors for chronic pain:

The biopsychosocial factors which have been clearly identified as contributing to risk for developing chronic pain are gender; poverty; adverse childhood events (ACEs); low levels of social support; age; physical activity; and co-morbidities including mental health disorders and non-communicable diseases. A clear and distinct correlation has emerged from numerous studies on gender and chronic pain with the female sex having a preponderance for developing chronic pain (10). Multiple reasons are theorised to contribute to this; traditional gender roles, coping mechanisms, mood disorders, and biological and political factors amongst others.

The social determinants of health have been repeatedly identified as increasing risk for chronic pain. A glaring theme that surfaces from studies of people living with chronic pain is their socioeconomic disparity. Poverty, low levels of education, and a lack of health insurance coverage or access to health care services have been identified as risk factors for chronic pain. Dahlhamer et al., found that the age-corrected occurrence of pain and chronic pain were appreciably lower for adults who obtained at least a bachelor's degree with respect to all other levels of education (11). People suffering from pain are less likely to seek treatment or help for their pain if they are socially disadvantaged, or unable to pay for their treatment. Thus, chronic pain is more apt to develop in those populations.

Finally, a factor which contributes to the development of pain in vulnerable populations such as those living in poverty, is a lack of social support. For example, people living with HIV who feel stigmatised, marginalised and who discern an unfairness regarding their condition are more prone to suffer from chronic pain (12). People living in poverty are also often at risk of having endured adverse childhood events (ACEs) which also increases risk for developing chronic pain.

An ACE is described as a nefarious event before the age of 18 years, which can be sexual or physical trauma, neglect, humiliation, or incarceration (13). Links between ACEs, catastrophising and changes in neuronal pathways are associated with an increased predisposition to developing chronic pain (14). Consequently, experiencing an ACE leads to a 2-to-3-fold increase in the risk of chronic pain later in life.

Age also plays a contributing role in the development of chronic pain. In a comparative study it was found that chronic pain is most likely to occur in people of middle age (15). In a report from the National Centre for Health Statistics in the United States, 29% of adults between 45-64 years reported pain lasting more than a day in the month before the study was conducted (16). Increasing prevalence of pain with age may be associated with the physiological changes of aging but may also be disease related.

Co-morbidities increase the risk that people will develop chronic pain. Other than the well-established role of depression and anxiety as contributors to chronic pain; other comorbidities also have a significant influence. Heart failure, diabetes and sleep disturbances have been shown to be more prevalent in patients suffering from chronic pain (17). This may stem from increased incidence of inflammation, ischaemia due to decreased blood flow and neuropathy. Those patients often have a poor quality of life and may have concurrent depression (18). Other co-morbidities which may contribute to chronic pain are osteoarthritis and rheumatoid arthritis, Herpes, Human Immunodeficiency Virus (HIV) and musculoskeletal conditions.

The psychological effects of chronic pain on the individual may manifest as depression and anxiety, or vice versa worsening the social and economic output of the patient (19).

Depression, and chronic pain have been shown to share similar neuroplasticity and neurohumoral changes. It is estimated that the mean prevalence of pain in patients with depression is 65 % (20).

From the qualitative data gathered, the most prominent themes of depressed patients with chronic pain, were decreased ability to carry out physical activity; interference in carrying out professional duties; sleep and mood disturbances; disruptions in social life; and in relationships (21). People with a low quality of life are more prone to develop chronic pain (22). They often have poor social support, and altered coping mechanisms, low self-esteem, feelings of injustice, and difficulty accessing resources.

Most of the data referenced above stems from studies conducted in western, educated, industrialised, rich and democratic (WEIRD) populations. There is a paucity of studies from less developed countries like South Africa. Prior to extrapolating WEIRD data to our patients, we need more descriptive data to explore whether the consequences and risk factors for chronic pain as described above are consistent. Consequently, a cross-sectional descriptive study of a South African group of people living with chronic pain was conducted to describe the characteristics of the patient population and to explore whether the data from western countries can be applied to the patients in South Africa.

METHODS

A retrospective, cross sectional chart review was conducted to describe the characteristics of patients attending the Chronic Pain Management Clinic (CPMC) at a tertiary hospital, Groote Schuur (GSH) in Cape Town, South Africa. An existing data set of 623 patients who had attending the CPMPC from June 2010 to June 2017 was accessed for this study. The sample size included all patients attending the CPMC during this time frame, of which 42 of the patients were excluded due to incomplete data in their folders, which left 623 (95%) patients to be included in this study. The data were categorised according to sociodemographic profile, health profile, and use of recreational drugs. The data were imported from an Excel spreadsheet for statistical analysis using Statistica (23).

Statistical Analysis:

Distribution of numerical data (age, pain severity scores, pain interference score) was assessed using the Kolmogorov-Smirnov test. Normally distributed data are reported as mean ± SD, data which were not normally distributed are reported as median (interquartile range). The remaining data were nominal (named) and ordinal (ordered) and are reported as frequencies.

RESULTS

Sociodemographic profile:

Age was normally distributed (K-S d=0.04, $p>0.20$). The mean age was 52.79 years (±14.30). The majority of patients were women (428; 68.7%) and were unemployed (315; 50.56%) (Table 1). Most of them qualified to receive full or partial subsidisation for their treatment (546; 87.64%), with 139 (22.31%) receiving a disability grant. In terms of education, most patients had not completed the full 12 years of schooling available in South Africa (328; 52.65%).

Table 1: Sociodemographic profile (n= 623)

CATEGORY	Mean (SD)
AGE	52.79y (±14.30)
GENDER	Number (%)
Female	428 (68.70%)
Male	195 (31.30%)
EMPLOYMENT STATUS	
Employed	158 (25.36%)
Unemployed	315 (50.56%)
Pensioner	150 (24.08%)
INCOME CATEGORY	
H0 (full subsidisation for pensioners and unemployed)	240 (38.52%)
H1 (partial subsidisation, earning <ZAR70 000 per annum)	225 (36.11%)
H2 (partial subsidisation, earning from ZAR70 000 to ZAR250 000 per annum)	50 (8.03%)
H3 (partial subsidisation, earning >ZAR250 000 per annum)	31 (4.98%)
P (no subsidisation with external funding e.g., employer, medical aid)	77 (12.36%)
DISABILITY GRANT	
None	484 (77.69%)
State disability grant	136 (21.83%)
Private disability grant	3 (0.48%)
LEVEL OF EDUCATION	
None	7 (1.12%
Primary school (Grades 1-7)	111 (17.82%)
Secondary school (Grades 8-11)	210 (33.71%)
Completed secondary school (Grade 12)	152 (24.40%)
Tertiary education	49 (7.87%)
Missing data	94 (15.09%)

Health profile:

Patients were referred from a range of primary, secondary, and tertiary clinics with the majority being referred from Orthopaedics (248; 39.81%), at the tertiary level (Table 2).

Table 2: Sources of referrals (n=623)

SOURCE OF REFERRAL	COUNT (n)	PERCENT (%)
Orthopaedics	248	39.80
Primary healthcare	70	11.23
Neurosurgery	53	8.50
Rheumatology	31	4.97
Gynaecology	24	3.85
Internal Medicine	24	3.85
Neurology	21	3.37
General Surgery	19	3.04
Psychiatry	18	2.88
Endocrine	12	1.92
Urology	12	1.92
Occupational Therapy	9	1.44
Vascular Surgery	9	1.44
Physiotherapy	8	1.28
Secondary Level Hospital	7	1.12
Hepatobiliary	7	1.12
Maxillo-facial Surgery	6	0.96
Ophthalmology	4	0.64
Cardiothoracic	4	0.64
ENT	3	0.48
Oncology	3	0.48
GIT	3	0.48
Plastic Surgery	3	0.48
Private Pain Clinic	3	0.48
Dermatology	2	0.32
Geriatric Medicine	2	0.32
Family Physician	2	0.32
Renal Transplant	2	0.32
Breast Surgery	2	0.32
Anaesthesia	2	0.32
Occupational Health	2	0.32
Trauma	2	0.32
Medical	1	0.16
Emergency Unit	1	0.16
Cardiology	1	0.16

Cardiothoracic surgery	1	0.16
Genetics	1	0.16
Rehabilitation Unit	1	0.16

Recreational drug use:

Most of the patients reported not using any recreational drugs. However, several patients reported using tobacco, and/or alcohol and/or cannabis (Table 3).

Table 3: Recreational Drug Use (n=623)

	COUNT (n)	PERCENT (%)
None	357	57.30
Tobacco	188	30.27
Alcohol	35	5.61
Tobacco and Alcohol	31	4.97
Tobacco and Alcohol and Cannabis	5	0.80
Cannabis	3	0.48
Tobacco and Cannabis	3	0.48
Alcohol and Cannabis	1	0.16

Mental health disorders:

Pre-existing mental health disorders were reported by many patients. 43.4 % of patients attending the pain clinic reported some form of mental illness, of which 73 % reported a prior diagnosis of depression (Table 4).

Table 4: Mental Disorders (n=623)

CONDITION	COUNT (n)	PERCENT (%)
Depression	197	31.62
Anxiety	54	8.67
Bipolar mood disorder	4	0.64
Bulimia/Anorexia/Eating disorder	3	0.48
Post-traumatic stress disorder	3	0.48
Borderline personality disorder/Personality disorder	3	0.48

Opioid dependency	2	0.32
OCD and Impulse Control Disorder	2	0.32
Benzodiazepine dependency and bipolar mood disorder	1	0.16
ADHD	1	0.16

Pain:

All the patients reported having pain for more than three months on presenting to the clinic and completed the Brief Pain Inventory. The pain severity and pain interference scores were not normally distributed (K-S d=0.40, p<0.01; K-S d=0.39, p<0.01) and are therefore reported as medians (interquartile range). The patients reported severe pain with a median PSS of 8 (IQR: 6.5-9) and a median PIS of 8 (IQR:6-9).

DISCUSSION

We have described the characteristics of 623 patients presenting to the CPMC of GSH. The typical patient attending this clinic was female, middle-aged, had low income and low educational attainment. Most had disability grants and were referred from the department of orthopaedics.

The majority of patients were female. A female preponderance to develop chronic pain has been well established and reported worldwide (24). In this study, 68,7 % of the patients were women, a figure which corresponds to that reported in studies conducted in WEIRD populations (25). Women are at greater risk of developing chronic pain due to a variety of factors, including hormonal, socio-economic, and cultural. At this clinic, where patients also had low levels of education and income, the biological vulnerability of women may be exacerbated by psychosocial factors. Globally, women are far more likely to report chronic pain than men (26).

Typical of the global population of people living with chronic pain, the median age of our patients was 52.79 years (±14.30) (27). An increasing prevalence of chronic pain with age is often attributed to a musculoskeletal origin, osteoarthritis or to other chronic pain conditions associated with central sensitisation (28). There are also clear associations between chronic pain and enhanced cognitive decline and premature death. Older people (>65 years) suffering from chronic pain are more likely to also suffer from social isolation, dementia, and disability

(29). Cruz-Almeida and Al (2019) showed that chronic pain has been associated with brain atrophy in older patients compared to their pain free peers of the same age group (30).

Regarding the socio-economic status of our patients, 87.64 % were on partial or full subsidy for their treatment costs due to low levels of income. As discussed in the introduction, there is a clear correlation between poverty and chronic pain. In a 2018 German study, prevalence of chronic pain was associated with household income with patients from low-income households more likely to have pain (31).

It is notable that less than a quarter of the patients had completed all 12 years of schooling. From our data, it appears that people suffering from chronic pain have less advantageous lives with the multiple social and economic challenges of poverty. Global studies reflect similar findings with poverty and low levels of education being identified as risk factors for chronic pain. A study from Iran attributed high levels of chronic pain in patients with a basic educational background to a lack of knowledge and giving less attention given to their health with survival issues taking priority (32). A Canadian study showed a similar strong association between low educational attainment and back pain (33). Poverty and low levels of education are common in low middle-income countries like South Africa. Being poor and having less education as risk factors for chronic pain may suggest that the prevalence of chronic pain, and high impact or disabling chronic pain may be higher in these populations. However, a paucity of population-based data on the prevalence of chronic pain in low- and middle-income countries makes testing this hypothesis challenging.

The commonly reported co-occurrence of chronic pain and mental health disorders reported in other populations (34), was clear in our data with 43.3 % of patients attending the clinic reporting a history of mental illness. The majority, 31.67 %, reported having suffered from depression and 8.67 % suffered from anxiety. Data from WHO that worldwide, one in five primary health care patients have pain, and these patients are four times more likely to have a chronic depressive disorder or anxiety (35). This overlap is hypothesised to be due to the considerable overlaps between the mechanisms of chronic pain and depression. The same areas of the brain have been shown to be involved with mood and injury to sensory neuronal pathways. The existence of chronic pain and depression in the same patient indicates a worse

prognosis than those who suffer from either pain or depression alone. The processes of maladaptive neuronal plasticity and central sensitisation have been blamed for this occurrence (36). Hence, our data aligns with global studies.

Most of the patients referred to the CPMC were referred from the Department of Orthopaedics. Injury to the musculoskeletal system, that is bones, ligaments and tendons often leads to nociceptive triggers, like neurotransmitters and inflammatory substances to be released and ultimately cause pain. In addition, central nervous system responses to those triggers may also contribute to sensitisation which may be maintained beyond tissue healing time (37). Moreover, the high prevalence rate of trauma in South Africa may result in a large vulnerable population of people who were previously managed orthopaedically.(38)

This study is limited by misclassification bias, the reliance on the patient's history as being true and accurate, and as a cross-sectional study association rather than causation is established. Presence of confounders is also a limitation of this study.

A more comprehensive understanding of the South African pain demographics can be achieved by studying the patient population from private hospitals and pain clinics from government facilities in the Western Cape and in the other provinces.
Further research in chronic pain pertaining to the South African population is warranted.

CONCLUSION

The analysis of our data pertaining to patients attending the chronic pain clinic of a tertiary centre in South Africa was compared to studies conducted in WEIRD populations. The prominent risk factors for developing chronic pain were recognisable in our patient population: gender, age group, educational level, mental health status, and socioeconomic status. It appears that the population of patients with chronic pain attending the CPMC are similar to those reported on from WEIRD populations. The findings of our study support the application of global data on people with chronic pain being applied to patients attending this South African CPMC with high levels of poverty and trauma.

COMPETING INTERESTS

The authors declare that they have no financial or personal relationship(s) that may have inappropriately influenced them in the writing of this article.

AUTHOR CONTRIBUTIONS

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DATA AVAILABILITY

The data used in this study were extracted from patient records by Dr Joe Van Vreede for the completion of his dissertation (UCT HREC number 505/2018) “Prevalence of depression in patients attending a chronic pain management clinic in South Africa.”

DISCLAIMER

The views presented in this study are solely that of the author(s) involved and do not represent those of the University of Cape Town or Groote Schuur Hospital.

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APPENDIX A – SUBMISSION GUIDELINES

SUBMISSION GUIDELINES

Types of articles published | Formatting requirements | Blinding your manuscript | Submission checklist | Compulsory forms

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Style and format
References
Permission to use copyright material

Ethical considerations structure
Ethical considerations

Acknowledgements structure
Acknowledgements
Competing interests
Author contributions
Funding information
Data availability statement
Disclaimer

Style and format

File format

- Manuscript files can be in the following formats: DOC, DOCX, or RTF. Microsoft Word documents should not be locked or protected.
- LaTeX documents (.tex) should be converted into Microsoft Word (.doc) before submission online.
- Rich Text Format (RTF): Users of other word processing packages should save or convert their files to RTF before uploading. Many free tools are available that will make this process easier.

Length
Manuscripts should adhere to the author guidelines of the journal. There are restrictions on word count, number of figures, or amount of supporting information.

Font
Use a standard font size and any standard font family.

Special characters
Do not use the font named 'Symbol'. To add symbols to the manuscript, use the Insert → Symbol function in your word processor or paste in the appropriate Unicode character. Refer to our AOSIS house style guide on mathematical and Unicode font guidelines.

Headings
Ensure that formatting for headings is consistent in the manuscript. Limit manuscript sections and sub-sections to four heading levels. To avoid confusion during the review and production process, ensure that the different heading levels used in your work are visually distinct from one another. The simplest way to achieve this is to use different font sizes and/or a combination of bold/italics for different heading levels.

Keywords
Identify eight keywords that represent the content of your manuscript and are specific to your field or sub-field. Test your keywords: when you enter your keywords into the various journal and academic databases like Google Scholar, do the results include papers similar to your topic? If not, revise the terms until they do.

Layout and spacing
Manuscript text should have a 1.5 line spacing.

Page and line numbers
Include page numbers and line numbers in the manuscript file. Use continuous line numbers (do not restart the numbering on each page).

Footnotes
Footnotes are not ideal. If your manuscript contains footnotes, move the information into the main text or the reference list, depending on the content.

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Ethical considerations

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Competing interests
Author contributions
Funding information
Data availability statement
Disclaimer

Language
Manuscripts must be written in British English, according to the Oxford English Dictionary (avoid Americanisms [e.g. use 's' and not 'z' spellings], and set your version of Microsoft Word default language to UK English). Refer to the AOSIS house style guide for more information.

Abbreviations
Define abbreviations upon first appearance in the text. Do not use non-standard abbreviations unless they appear at least three times in the text. Keep abbreviations to a minimum.

Illustrations
Illustrations fall into two categories:

- Figures: Photographs, drawings, diagrams, graphs, flowcharts, maps, etc.
- Tables and/or Boxes: Text and/or numbers arranged in orderly columns and rows.

Every time a Figure, Table and/or Box is presented in your manuscript, it should be referred to three times:

- In a legend, which includes a number, a title, and its source. The legend is placed below a Figure and above a Table and/or Box. The source section should consist of the in-text citation, creator or owner and its year of creation, and any other attribution required as stipulated by the permission received (person and place) to reproduce.
- In the body of your written manuscript. You should include an in-text citation and a sentence or two about the image explaining what it illustrates and why it is there.
- As a reference entry within your reference list.

AOSIS house style
The manuscript must adhere to the **AOSIS house style guide**.

References

Referencing style guide
The manuscript must adhere to the **Vancouver referencing style**.

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The following information will assist you in understanding your responsibilities and in requesting permission to reproduce copyrighted material in your work. All permissions granted must be submitted to the journal together with your manuscript, and you must ensure that a clearly written source accompanies the work.

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APPENDIX B – LETTER OF ETHICAL APPROVAL

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

Room 650- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-submissions@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

21 June 2021

HREC REF: 388/2021

Prof R Parker
Division of Anaesthesia & Peri-operative Medicine
D23 NGSH
Email: Romy.parker@uct.ac.za
Student: faadhilakeenoo@gmail.com

Dear Prof Parker

PROJECT TITLE: THE CHARACTERISTICS OF PATIENTS ATTENDING A CHRONIC PAIN MANAGEMENT CLINIC IN SOUTH AFRICA: A RETROSPECTIVE CHART REVIEW-DR FAADHILA KEENOO-SUB-STUDY LINKED TO 505/2018

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.

This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19, dated 17 March 2020 & 06 July 2020.

Approval is granted for one year until the 30 June 2022.

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)

The HREC acknowledge that the student: Dr Faadhila Keenoo will also be involved in this study.

Please quote the HREC REF 388/2021 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.

HREC/REF 388/2021sa

Yours sincerely

pp TBurgess

PROFESSOR M BLOCKMAN
CHAIRPERSON, FACULTY OF HEALTH SCIENCES 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 2020), based on the Association of the British Pharmaceutical Industry Guidelines (ABPI), and Declaration of Helsinki (2013) guidelines. The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

HREC/REF 388/2021sa