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Antibiotic knowledge and prescribing practices of doctors working in tertiary hospitals in Johannesburg

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2020
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ANTIBIOTIC KNOWLEDGE AND PRESCRIBING PRACTICES OF DOCTORS WORKING IN TERTIARY HOSPITALS IN JOHANNESBURG

0603904H

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A research report submitted to the Faculty of Science, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine in the branch of Internal Medicine

20 October 2020

Declaration

I declare that this research report is my own, unaided work.
It is being submitted for the Degree of Master of Medicine at the University of the Witwatersrand, Johannesburg.
This research report is submitted in the publishable format as recognised by the Faculty of Health Sciences.
It has not been submitted before for any degree or examination at any other University.



_____

Signed on the 20th day of October 2020 at Johannesburg

Dedication

I dedicate this research project to previous generations of females in my family who were not afforded the opportunity of tertiary education. I find it a privilege to represent you all. To my family for your support, thank-you.

Abstract

Antimicrobial resistance currently poses an increasing public health risk worldwide. Antimicrobial stewardship has a large role to play in minimising further development of antimicrobial resistance and protecting the future use of antimicrobial agents. Health care workers are an important target for implementation of this stewardship.

This study aimed to evaluate the antimicrobial knowledge and prescribing practices of doctors working in tertiary hospitals in Johannesburg. Information collected included questions on antimicrobial knowledge. prescription choice for specific infections, perceptions regarding antimicrobial resistance and factors influencing antimicrobial prescription.

This was a cross sectional study using a self-administered questionnaire. Doctors of all levels of qualification within the Department of Internal Medicine working in Helen Joseph Hospital (HJH), Chris Hani Baragwanath Academic Hospital (CHBAH) and Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) were invited to participate.

A total of 108 medical doctors participated. Only 56% said they were confident in their prescription practices. Fewer than half (47%) had received education between 1-3 times on this topic within the last year, while 15% said they had not received any education. The majority of participants scored between 33-67% on antimicrobial knowledge questions regarding specific infections. Three quarters of respondents agreed that antimicrobials are over prescribed in South Africa and 94% responded that they are overprescribed worldwide. Almost every participant (98%) indicated that they would like more teaching on this topic.

The doctors who participated in this study prescribe antimicrobial agents on a regular basis, but a large portion are not confident in their knowledge to do so. Theoretical questions identified gaps in knowledge regarding treatment of common infectious diseases across all levels of qualification. While the doctors acknowledged antimicrobial resistance as a local and international problem, they indicated that they would like further teaching on the topic. Antimicrobial stewardship teaching rounds would be an excellent way to implement this.

Acknowledgements

I would like to thank Dr Jeremy Nel and Dr Michelle Venter for their assistance in supervising this research project. Their support and guidance throughout this process has been invaluable.

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Nomenclature

AMR	Antimicrobial resistance
ASPs	Antimicrobial stewardship programs
CHBAH	Chris Hani Baragwanath Academic Hospital
CMJAH	Charlotte Maxeke Johannesburg Academic Hospital
EML	Essential medicines list
HCW	Health care worker
HIV	Human immunodeficiency virus
HJH	Helen Joseph Hospital
ICU	Intensive care unit
IDSA	Infectious Diseases Society of America
MRSA	Methicillin resistant *Staphylococcus aureus*
SAASP	South African Antimicrobial Stewardship Program
TB	Tuberculosis
USA	United States of America
WHO	World Health Organisation

1. CHAPTER 1- PROTOCOL AND EXTENDED LITERATURE REVIEW

1.1 Introduction

The 75th anniversary of the first human administration of penicillin was celebrated in 2016. The development of antimicrobials has greatly influenced the practice of medicine, but has been increasingly threatened by the subsequent emergence of resistance. In the early 1940s, only a few years after penicillin use became wide-spread, the development of penicillin-resistant bacterial strains were already observed. [(1)] In 1945 which was just 4 years after the first administration of penicillin, Alexander Fleming first warned about the overuse of antimicrobials. [(2)] Antimicrobial resistance has subsequently become a major worldwide public health risk which threatens the practice of modern medicine.

1.2 The Impact of Antimicrobial Resistance

The deleterious effects of drug-resistant organisms have been devastating and thus far been documented in both developing and developed nations. Although a worldwide problem, there is far more data for developed nations and very limited data in developing countries, such as South Africa, with regards to antimicrobial consumption. Annually, antimicrobial resistance (AMR) is responsible for approximately 23 000 deaths in the United States of America (USA). [(3)] A meta-analysis reviewing rates of methicillin resistant *Staphylococcus aureus* (MRSA) in intensive care units (ICUs) worldwide showed that the highest rates were found in the USA. [(4)] Indeed, MRSA is reported to result in higher mortality annually in the USA than Parkinson's disease, Human Immunodeficiency Virus (HIV), emphysema and homicide combined. [(4)] Much less data is available for South Africa. A study conducted in 2006 reported that 33% of *Streptococcus* isolates found in adults with community acquired pneumonia were penicillin-resistant. [(5)] Furthermore, 25% of isolates were found to be resistant to erythromycin in the same study.

Apart from increases in morbidity and mortality, AMR also poses an economic burden to the patient and to the healthcare system, as well as decreasing available therapeutic options. [(6)]

1.3 The Development of Antimicrobial Resistance

The development of resistance is thought to arise from a number of factors. Overwhelmingly, the most important of these factors is the misuse of antimicrobials in both the agricultural and medical fields, due to inappropriate prescription and overuse. [(7)]

Factors which determine misuse and overuse of antimicrobials within the healthcare setting include healthcare worker (HCW) knowledge, experience levels, attitudes towards the prescription of antimicrobial agents and their diagnostic skills. In low income countries, other contributing factors include poor infection control practices within hospitals as well as self-medication and not completing the prescribed treatment duration of antimicrobials. [(8)]

In South Africa, where there is a large burden of HIV and tuberculosis (TB), there is a high rate of opportunistic and community-acquired infection. [9] In the state sector in South Africa, antimicrobial prescription is guided by National Guidelines and essential medicines lists (EMLs), however antimicrobial prescription is fairly unregulated in the private sector.

1.4 Assessing Factors Resulting in Increased Antimicrobial Resistance

In 2015, a systematic review was done to evaluate baseline knowledge, beliefs and perceptions of HCWs worldwide regarding AMR. It also assessed how they believed they could reduce the incidence of AMR. Results showed that while most HCWs were aware of AMR, they weren't aware of the prevalence or the main causative mechanisms behind the increasing rates of AMR. [3] Interestingly, a significant portion of HCWs identified AMR as a national and international problem, however they believed it to be one that affected other institutions or practitioners more than themselves. It was also identified by HCWs as a problem affecting mostly hospital institutions rather than primary health care facilities. [3] These findings raise the issue of self-evaluation.

A report was published by the Center for Disease Dynamics, Economics & Policy in 2015 which appealed for worldwide strengthening of antimicrobial stewardship programs (ASPs) in an effort to maintain, preserve and protect current antimicrobial agents. [10] The Infectious Diseases Society of America (IDSA) defines antimicrobial stewardship as, "Coordinated interventions to improve and measure the appropriate prescription of antimicrobial agents by the selection of the optimal drug regimen- including dose, duration and route". [11] The World Health Organisation (WHO) Global Strategy defines the appropriate use of antimicrobials as, "The cost-effective use of antimicrobials which maximises clinical therapeutic effect while minimising both drug-related toxicity and the development of AMR". [12] Key elements in ASPs include accountability and education. However, the most important modifiable factor driving AMR is knowledge of health care practitioners about antimicrobial drug prescription.

A study was conducted along with the implementation of ASPs across 47 hospitals in South Africa, in both urban and rural settings . [13] It involved various interventions that were implemented with the aim of reducing unnecessary antimicrobial prescription. Over a period of 5 years, the intervention was shown to reduce antimicrobial consumption by 18%. While a major limitation of this study was that patient outcomes were not recorded, this result does demonstrate the effectiveness of such programs within our resourced-limited setting.

Guidelines exist to rationally guide the approach towards the treatment of infections. These guidelines are often not well known or adhered to by HCWs. As an example, it is estimated that antimicrobials continue to be inappropriately prescribed in between 30-50% of cases seen in the USA. [1] The South African Antimicrobial Stewardship Program (SAASP) Pocket Guide to Antimicrobial Prescribing is an example of a free antimicrobial prescribing resource that is available locally. [14] These guidelines have been formulated from both local and international guidelines as well as key publications on common infections. The SAASP guidelines are easily accessible online or via the SAASP application on a mobile platform. They recommend a best-practice approach to the management of common infections and also promote standard infection control recommendations.

Even with guidelines to guide the use of antimicrobials, it is still up to the HCWs discretion, knowledge and decision making as to when or how to use antimicrobial agents. International questionnaires have assessed doctors' knowledge of antimicrobials and have found varying results across different countries. In a survey conducted at Johns Hopkins in Baltimore in the USA, the overall score achieved on antimicrobial knowledge was 28% (this represented a combined score of 34% on basic questions and 15% on more advanced questions). [(7)] This questionnaire was given to residents across different sub-specialties and included ten questions on antimicrobial knowledge. Most (72%) participants agreed that antimicrobials were overused in their hospital, with 77% responding that they thought local antimicrobial guidelines were more effective than national guidelines. In 2011, a similar survey was conducted in Lima, Peru. [(15)] In this study, 256 respondents scored well on seven questions assessing antimicrobial knowledge, with the average correct rate being six out of seven questions (86%). These questions addressed frequency of antimicrobial prescription and influencing factors thereof, awareness of the scope of antimicrobial resistance, as well as attitudes toward future interventions to improve prescription practices. A similar questionnaire was done at the University Hospital of Kisangani in Congo. The questionnaire was based on the one from the study conducted in Peru. However, results here were quite different, with the average score being low: 4.9 out of 8 (61%). [(8)] More recently, a survey was done in Namibia through the University of Potchefstroom with 44 participants. This particular questionnaire assessed knowledge and access to treatment guidelines, common practices of antimicrobial prescribing, knowledge of local sensitivity patterns and strategies for preventing antimicrobial resistance. This survey also showed that knowledge of standard treatment guidelines was poor. Sixty nine percent responded that they did not have access to Namibian treatment guidelines. Eighty percent of the respondents were not aware of local sensitivity data. This questionnaire however, had a poor response rate of 10%. [(16)]

The WHO identified undergraduate medical students as a very important group to target in the pursuit to contain the epidemic of AMR. (16) This issue has been highlighted as a potential point for meaningful intervention, as inadequate teaching would subsequently lead to inappropriate prescribing habits.
In 2012, a study was published in the USA assessing the perceptions and knowledge medical students toward antimicrobial stewardship. (17) An electronic survey was used for 316 fourth year students across 3 Universities. It found that most students identified AMR as problematic and acknowledged the importance of rational antimicrobial use. However, on the knowledge questions students scored 51% on average when asked about the management of urinary tract infections, identification of the spectrum of commonly used antimicrobial agents and the mechanisms of AMR. (17)

In May 2017, a questionnaire was posed to medical students across three South African Universities. Students participating in this study were from the University of Witwatersrand, the University of Cape Town and the University of the Free State. The questionnaire aimed to investigate their level of knowledge and undergraduate education of antimicrobials, as well as how well-prepared they felt they were for antimicrobial prescribing. (16) It is important to note that questions within this study were based on the standardised SASSP guidelines. Most students reported using a combination of sources for their knowledge on antimicrobials. This included online resources, other HCWs (consultants and registrars), as well as textbooks. The scores on the theoretical knowledge questions averaged 50% across the 3 institutions.

Perhaps the most significant finding from this study was that only 33% of students felt confident after completing their respective undergraduate programs, to safely and effectively prescribe antimicrobials. Regarding antimicrobial education, 95% responded that they would appreciate more teaching on appropriate prescribing practices. Respondents also felt that they weren't well prepared with regards to knowledge of dosing durations or how to interpret antibiograms. Within the knowledge section, a low overall mean score of 50% was obtained. Considering that in tertiary academic hospitals the bulk of prescribing is done by junior staff, these statistics suggest to us that we potentially need to direct more teaching toward this group during their undergraduate training when it comes to antimicrobials.

In South Africa, to date there has been no similar questionnaire or survey done on practicing clinicians. Given the differing international results across developed as well as developing countries, it is difficult to predict what local results would demonstrate. Should South African doctors report practices which are not in keeping with the accepted best practice, this evidence could be used to motivate for further teaching on this topic at both the undergraduate as well as the postgraduate level. Evaluating perceptions of antimicrobial resistance prevalence, both within respondents' own hospitals as well as nationally, will provide insight into the level of clinician awareness of the problem. Comparing knowledge responses at different levels of qualification would also provide information on where interventions may best be aimed.

2. Aim of the Study

The aim of the study will be to survey the antimicrobial prescribing practices and perceptions of antibiotic resistance and usage amongst doctors within the Internal Medicine Department in three tertiary state hospitals in Johannesburg, South Africa.

3. Study Objectives

- To evaluate the antimicrobial prescription practices of doctors within the medical departments at three tertiary state hospitals in Johannesburg, South Africa.
- To evaluate the primary source of antimicrobial knowledge amongst these doctors.
- To evaluate help-seeking behavior in cases when decisions regarding antimicrobial choice is difficult.
- To assess the perceptions of doctors within the department regarding over-use of antimicrobials and the prevalence of antibiotic resistance in both their hospitals and other hospitals within South Africa.
- To identify whether doctors within Internal Medicine Department would be receptive towards further teaching on antibiotic stewardship principles.
- To evaluate whether the level of seniority within the Department of Internal Medicine (stratified into three groups: interns and medical officers, registrars, and consultants) influences the above factors.

4. Methods

This study will be a cross-sectional observational study. A voluntary self-administered questionnaire will be given to medical doctors of all levels of training within the Department of Internal Medicine at either Helen Joseph Hospital (HJH), Chris Hani Baragwanath Academic Hospital (CHBAH) and Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) during the months of July-September 2019. Medical interns, medical officers, registrars and consultants will be invited to participate.

The questions for this survey are based on a validated international questionnaire initially described in the USA and subsequently used in similar studies in Peru and the Democratic Republic of Congo. [7,8,15] The survey is composed of 18 questions. It is sub-divided into three categories of questions: antimicrobial knowledge and learning, treatment of specific infections, and perceptions regarding antimicrobial resistance and further teaching. These questions will be evaluated by two infectious diseases consultants prior to administering the questionnaire to ensure that questions are posed correctly, and that there is minimal misinterpretation by respondents. These consultants will not participate in the study thereafter.

This survey will be in the form of a paper copy. These will be made available at scheduled Internal Medicine academic meetings at all participating hospitals. This will be done on two occasions at CHBAH and once at both CMJAH and HJH. The questionnaires will be made available in a box at the entrance to the meeting and an announcement will be made for participants to voluntarily complete the survey. Completed questionnaires will then be collected in a box after of the meeting. Participants will be able to complete the questionnaire over 60-90 minutes. Participants will be requested to not use any resources to assist answering the questions, however no additional measures to avoid the use of smart phones or textbooks will be enforced. Anonymity of respondents will be was maintained as no names are documented on the response sheets. Participants will be reminded not to participate should they have already completed a survey previously (to avoid duplication of responses).
The survey will be open to all levels of doctor including interns, medical officers, registrars and consultants. The questionnaire will record the level of qualification of the respondent, in order to analyse and compare results obtained across different groups.

Sample size is calculated with an anticipated 50% response rate. With an estimated total number of potential respondents of 265 doctors within the Internal Medicine Department across all three hospitals (approximately 85 interns, 100 registrars and 80 consultants). Using a 95% confidence level and a 5% error margin, the recommended sample size required was calculated at 158 responses. This was calculated using the following calculation: $x = Z(^{c}/_{100})^{2}r(100\text{-}r)$ $n = {}^{Nx}/_{((N\text{-}1)E^{2}+x)}$ $E = \text{Sqrt}\,[{}^{(N-n)x}/_{n(N\text{-}1)}]$

Of the total 158 responses, at least 60 registrars (38%), 50 interns (32%) and 47 consultants (30%) responses are required to have an adequate representation of each group.

5. Data Analysis

Data will be extracted from the responses and thereafter captured on Microsoft Excel. This data will be imported into Stata 15® for statistical analysis.

Categorical data will be analysed by means of percentages and frequencies, as well as means, medians, standard deviations and/or interquartile ranges. A Chi-squared test will be used to calculate possible associations between certain responses and level of qualification.

6. Ethics

This study will make use of data recorded on voluntary questionnaires from doctors employed in the public sector, within the Department of Internal Medicine at the University of the Witwatersrand, Johannesburg. There was no potential benefit or harm to the participants.

Complete anonymity of the participants will be ensured by not recording any identifiers on the response sheet, and by the placement of the completed questionnaire into a collection box.

Permission to conduct the study will be obtained from the Head of the Department of Internal Medicine. Ethics clearance will be obtained from the Wits Human Research Ethics Committee (Medical). The ethics clearance certificate number M171180.

7. Project Outline

Item	Month											
	Apr 2019	May 2019	June 2019	July 2019	Aug 2019	Sep 2019	Oct 2019	Nov 2019	Dec 2019	Jan 2020	Feb 2020	Mar 2020
Protocol submission and assessment												
Ethics application												
Data collection												
Data analysis												
Research write up												
Research submission												

8. Budget and Funding

This project will be self-funded and no costs will be incurred by the hospital.

Item	Cost
Stationery	R1 000
Total	R1 000

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2. CHAPTER 2 – PROPOSED MANUSCRIPT

2.1 Background

The development of antibiotics has greatly influenced the practice of medicine, but it has been increasingly threatened by the subsequent emergence of resistance. In the early 1940s, only a few years after penicillin use became wide-spread, the development of penicillin-resistant strains were already observed(1), and in 1945 Alexander Fleming first warned about overuse of antibiotics(2). This, however, did not prevent the further development of resistant strains to almost all antibiotics in subsequent years. Antimicrobial resistance has become a major worldwide public health risk.

The deleterious effects of drug-resistant organisms have been devastating and thus far been documented in both developing and developed nations. A meta-analysis reviewing rates of methicillin resistant *Staphyloccocus aureus* (MRSA) in intensive care units (ICUs) worldwide showed that the highest rates were found in the United States of America(3). MRSA is reported to kill more patients in the USA per year than Parkinson's disease, Human Immunodeficiency Virus, emphysema and homicide combined(3). Far less data is available for South Africa, although a study done in 2006 reported that 33% of *Streptococcus* isolates found in adults with community acquired pneumonia were penicillin-resistant(4). Furthermore 25% of isolates were found to be resistant to erythromycin. Considering that *Streptococcus pneumoniae* is the commonest aetiological agent for bacterial infection world-wide, this is very concerning. Apart from this increase in morbidity and mortality, antimicrobial resistance also poses an economic burden to the patient and the healthcare system, as well as decreasing available therapeutic options(5).

The development of resistance has thought to be linked to a number of factors. By far the most important is human antibiotic use. This misuse of antibiotics is attributed to both inappropriate prescription and overuse(6). Factors which determine this include healthcare workers' knowledge or experience levels, their attitudes and their diagnostic skills. In low income countries, other contributing factors include poor infection control practices within hospitals as well as communities, self-medication and not completing the prescribed treatment duration(7).

In 2015 a report was published by the Center for Disease Dynamics, Economics & Policy which appealed for worldwide strengthening of antibiotic stewardship programs in an effort to maintain, preserve and protect our current antimicrobial agents(8). The Infectious Diseases Society of America (IDSA) defines antibiotic stewardship as coordinated interventions to improve and measure the appropriate prescription of antimicrobial agents by the selection of the optimal drug regimen- including dose, duration and route(9). The World Health Organization Global Strategy defines the appropriate use of antimicrobials as the cost-effective use of antimicrobials which maximizes clinical therapeutic effect while minimizing both drug-related toxicity and the development of antimicrobial resistance(10). Some of the key elements in antibiotic stewardship programs include accountability and education. However, by far the most important modifiable factor driving antimicrobial resistance is knowledge of healthcare practitioners about antimicrobial drug prescription.

Guidelines exist to rationally guide the treatment of infections. These guidelines are often not well known or adhered to by healthcare workers. For instance, it is estimated that antibiotics are still being inappropriately prescribed in about 30-50% of cases seen in the USA(1). The South African Antibiotic Stewardship Program (SAASP) Pocket Guide to Antibiotic Prescribing is an excellent example of a resource available locally(11). These guidelines have been formulated from local and international guidelines as well as key publications on common infections. The SAASP guidelines are easily accessible online or via the SAASP application. They recommend a best-practice approach to the management of common infections and also promote standard infection control recommendations.

International questionnaires have assessed doctors' knowledge of antibiotics and have found varying results across different countries. In a survey conducted at Johns Hopkins in Baltimore, USA, the overall score achieved on antimicrobial knowledge was 28% (34% on basic questions and 15% on more advanced questions)(7). This questionnaire was given to residents across different sub-specialties and included ten questions on antimicrobial knowledge. Seventy-two percent of participants agreed that antibiotics were overused in their hospital, with 77% responding that they though local antimicrobial guidelines were more effective than national guidelines. In 2011, a survey was done in Lima, Peru(12). 256 respondents scored well on seven questions testing antimicrobial knowledge with the average being six out of seven questions. These questions addressed frequency of antimicrobial prescription and influencing factors thereof, awareness of the scope of antimicrobial resistance as well as attitudes toward future interventions to improve prescription. Subsequently, a similar questionnaire was done at the University Hospital of Kisangani, Congo. The questionnaire was based on the one from Peru. However, results here were quite different, with the average score being low - 4.9 out of 8(13). More recently, a survey was done in Namibia via the University of Potchefstroom with 44 participants. This particular questionnaire looked at knowledge and possession of treatment guidelines, common practices of antibiotic prescribing, knowledge of local sensitivity patterns and strategies for preventing antibiotic resistance. This survey also showed that knowledge of standard treatment guidelines were poor(14). 69% responded that they did not have possession of Namibian treatment guidelines. 80% of the respondents also weren't aware of local sensitivity data collected. This questionnaire however, had a poor response rate of 10%.

In May 2017, a questionnaire done on medical students across three South African Universities was published. It looked at their knowledge and education of antimicrobials as well as how well prepared they feel they are for antibiotic prescribing(15). Students participating were from University of Witwatersrand, University of Cape Town & University of the Free State. It is important to note that questions were also based on the SASSP guidelines. Regarding education, 95% responded that they would appreciate more teaching an appropriate prescribing. Respondents also felt that they weren't well prepared when it came to knowledge of dosing durations or how to interpret antibiograms. Within the knowledge section, a low overall mean score of 50% was obtained.

In South Africa, there has been no similar questionnaire or survey done on practicing clinicians. Given the differing international results across developed as well as developing countries, it is difficult to predict what

local results would show. Should South African doctors report practices which are not in keeping with the accepted best practice, this evidence could be used to motivate for further teaching on this topic at undergraduate as well as postgraduate level. Evaluating perceptions of antimicrobial resistance prevalence, both within respondents' own hospitals as well as nationally, will provide insight into the level of clinician awareness of the problem. Comparing responses at different levels of qualification would also provide information on where interventions may best be aimed.

2.2 Study Objectives

- To evaluate the antimicrobial prescription practices of doctors within the medical departments at three tertiary state hospitals in Johannesburg, South Africa.
- To evaluate the primary source of antimicrobial knowledge amongst these doctors.
- To evaluate help-seeking behavior in cases when decisions regarding antimicrobial choice is difficult.
- To assess the perceptions of doctors within the department regarding over-use of antimicrobials and the prevalence of antibiotic resistance in both their hospitals and other hospitals within South Africa.
- To identify whether doctors within internal medicine department would be receptive towards further teaching on antibiotic stewardship principles.
- To evaluate whether the level of seniority within the department of internal Medicine (stratified into three groups: interns and medical officers, registrars, and consultants) influences the above factors.

2.3 Methodology

This was a cross sectional study. There were 108 participants which included doctors of all levels of qualification working in the department of medicine at Chris Hani Baragwanath Academic Hospital, Helen joseph Hospital and Charlotte Maxeke Johannesburg Academic Hospital between July and September 2018. Sample size was calculated with an anticipated 50% response rate. With an estimated total number of potential respondents of 265 doctors with the Internal Medicine Department across all three hopsitals. Using a 95% confidence level and a 5% error margin, target sample size required was calculated at 158 responses. This was calculated using the following calculation: $x = Z(^{c}/_{100})^{2}r(100\text{-}r)$ $n = {}^{Nx}/_{((N\text{-}1)E^{2}+x)}$ $E = \text{Sqrt}\left[{}^{(N-n)x}/_{n(N\text{-}1)}\right]$. Unfortunately this number of responses was not obtained during the allocated time period.

Data collection tool included a self-administered questionnaire. This questionnaire was based on a validated questionnaire that had been used in similar international studies.(6,12,13) It comprised of 18 questions and was subdivided into three categories of questions: antimicrobial knowledge and learning, treatment of specific infections, and perceptions regarding antimicrobial resistance and further teaching. All members of the department of medicine at the three hospitals who were present during academic meetings were invited to participate. Anonymity was maintained as no names were put on questionnaires; only the level of qualification was specified. Once complete they were placed in a box at the front of the room for collection.

Ethical approval for the study was obtained from the University of the Witwatersrand's Human Research Ethics Committee

2.4 Results

In total, 108 responses (from a possible 265 doctors) were obtained. Of the responses, 30 (28%) were from the intern/medical officer group, 58 (53%) from medical registrars and 20 (19%) from consultants within the Department of Internal Medicine at the University of the Witwatersrand.

2.4.1 Antimicrobial knowledge and learning

A combination of sources including advice from colleagues on the same level as well as more senior colleagues and guidelines (both local & international) were identified by 68% of respondents as their source of knowledge on antimicrobial prescribing.
The more junior staff members (medical interns, medical officers and medical registrars) were more likely to get information from their colleagues on their same level as well as their seniors than from guidelines with 21% of registrars and 26% of medical officers and interns choosing this answer. 0% of consultants said colleagues were their source of information alone however 78% of them answered that they use a combination of guidelines with information from colleagues.

Overall, 56% of participating doctors said that they were confident in their knowledge of prescription of antimicrobials, 37% were neutral toward their knowledge and 7% were not confident at all. In terms of those doctors who identified themselves as not being confident at all, 17% were from the intern/medical officer group, 5% from the registrar group, 0% were from the consultant group. Of those doctors who self-reported being confident or very confident with antimicrobial prescription, 80% were from the group of the consultants, 55% were from the group of the registrars and 40% were from the group of the interns/medical officers. Almost all respondents across all three groups (85%) said that they were likely to review an antimicrobial prescription decision that they weren't sure of with a senior / infectious diseases specialist.

When surveyed about the amount of antimicrobial teaching they had received in the previous year, almost half of the respondents had received teaching between 1-3 times (47.2%). Of note is that 26% of the intern / medical officer group said they had not received any teaching on this topic in the past year.

2.4.2 Antimicrobial prescription for specific infections

When asked about the frequency that participants prescribed antimicrobials, 44% said that they prescribed antimicrobial agents more than once a day.

In order to assess theoretical knowledge around the prescription of antimicrobial agents, 6 theoretical knowledge questions were posed within the questionnaire. These questions were based on the current South African

Antimicrobial Stewardship Program (SAASP) guidelines, which are freely available to treating clinicians. Results (correct answers out of a possible 6 questions) are represented in Figure 1.

Most of the respondents did not score well on these questions, with only a single respondent (0.9%) correctly answering all 6 questions, and 5% of respondents answering 5 out of 6 questions correctly. The majority of respondents (87%) scored between 2- 4 out of a possible 6 correct answers, and 7% of respondents answered either zero or one question correctly. In particular, the question regarding duration of therapy of metronidazole for *C. difficile* infection was answered very poorly with 67.6% of respondents getting it incorrect.

The question with the least amount of correct answers (the indications to administer antimicrobials in acute diarrhea) was answered incorrectly by 84.2% of participants. For this particular question 84.4% of registrars as well as 83.3% of the intern/ medical officer group answered incorrectly.

The overall correct response rates to the 6 questions posed are represented in table 1

Table 1: Overall correct results from knowledge questions

Question	Percentage of Correct Responses
Which of the following antimicrobials has the best activity against anaerobes?	92.6%
Methicillin resistant - *Staphylococcus aureus* is susceptible to	86.1%
Which of the following drugs would be your best choice for an infection requiring good CSF drug penetration?	38.9%
How long would you usually treat *C. difficile* for when using metronidazole?	32.4%
Which intravenous drug would be your first choice as an alternative to Co-amoxiclav (Augmentin®) in severely penicillin-allergic patients with a community-acquired pneumonia?	26.9%
Which of the following is NOT an indication to prescribe antimicrobials in a patient presenting with acute diarrhoea?	15.8%

2.4.3 Perceptions regarding antimicrobial resistance

An overwhelming majority of doctors surveyed (81%) agreed that antimicrobials are over-prescribed in the hospitals in which they work (81%) as well as in other hospitals (75%) in South Africa.

In terms of Antimicrobial Resistance, 86% agreed that AMR is a significant problem in their hospital and across South Africa, 10% giving a neutral answer, and 4% disagreeing. Almost all respondents (94%) believe that AMR is a significant problem worldwide. There was little variation in the responses to these questions between the three groups of doctors surveyed (figure 2).

2.4.4 Factors influencing antimicrobial prescription

When asked which factor has the greatest influence of their decision to start antimicrobials in a patient on presentation, 42% of participants responded that a high C-reactive protein/ procalcitonin level would influence their decision to start an antimicrobial. This finding was evenly spread across all 3 groups surveyed. Pyrexia and tachycardia would be the predominant factor in 37% of doctors, 19% said specimen culture and 1% said if they were unsure of the diagnosis. No respondent said that a patient requesting antimicrobials would influence their decision. The three respondent subgroups answered similarly to this question.

Almost every doctor surveyed (98%) answered that they would like additional training or education programs on antimicrobial prescribing.

2.5 Discussion

The findings of this survey were similar to the systematic review done across South African medical schools in 2017(15) in many ways. As was described previously, the majority of participants acknowledge that AMR is a significant problem and that antimicrobials are over-prescribed. Theoretical knowledge questions in this survey were answered just as poorly as studies targeting undergraduate medical students, even though our particular survey was aimed at qualified doctors of different levels, whose knowledge and experience should be better. This finding may reflect that teaching regarding antimicrobial prescription, microbiology and pharmacology at undergraduate level in South Africa needs improvement.

The majority of the respondents said that they prescribe antimicrobial agents more than once a day (43% of interns and medical officers and 45% of registrars). This finding indicates the high number of antimicrobial prescriptions that are written daily in the setting of an academic hospital. This again highlights the importance of having good prescribing practices and good infection control knowledge to prevent the unnecessary use of these agents and subsequently to avoid the development of AMR.

It was found that junior staff comprising medical interns and medical officers lack confidence in prescribing antimicrobials and this is most likely due to inadequate teaching during undergraduate training as well as lack of experience. This represents a consistency with surveys done locally and internationally, with lack of confidence being highlighted by participants (9,15,16). This highlights a good oppourtunity for antimicrobial teaching by more senior staff. Medical registrars work closely with junior staff on a daily basis, and almost one quarter of junior doctors listed their senior colleagues as their source for information on antimicrobial prescribing. A significant portion of respondents also said they had neutral feelings towards their confidence. This may encompass other individuals who are unsure of the extent of their knowledge, and represent a further oppourtunity for teaching. Of the junior staff group, a quarter said that they had not received any antimicrobial teaching in the previous year. This finding indicates that there is a significant lack of emphasis on in-service training of individuals not part of a formal academic program. As mentioned above, while medical registrars should implement more teaching into their day to day activities with interns and medical officers, this does not eliminate the need for formal teaching within clinical units on antimicrobial stewardship and infection control. One practical way to
implement this would be to host weekly or monthly antimicrobial stewardship rounds within the Department of Medicine.

The fact that a large proportion of participants indicated that they use a combination of sources from which to gain their antimicrobial knowledge is good, in that they recognise multiple resources and have the ability to cross-reference guidelines, evidence and common practices. Almost all participants surveyed agreed that they would benefit from further training and teaching on the topic. This finding was also echoed in similar surveys done amongst medical students in the USA(7) , which found that students identified a need for more teaching on antimicrobials.

This study was limited by response rates that were poorer than anticipated, despite multiple oppourtunities to complete the survey. This may have been due to time limitations or lack of interest of targeted population. As with any questionnaire that assesses both perception and theoretical knowledge, it may be anticipated that the more diligent, enthusiastic or knowledgeable individuals may have been more likely to complete the survey. These individuals are also more likely to be attending academic meetings and would be the respondents found at those meetings. The departmental academic meetings are usually attended by mostly medical registrars and less so by interns or consultants. This may account for why far fewer responses were obtained by those groups and why the majority of responses were from medical registrars. The data aimed to sample three large academic hospitals within the University of the Witwatersrand cluster, and so our findings may not be generalizable to other hospitals or centres. As with surveys that assess behaviour, social desirability bias may have limited extrapolation of findings, as respondents may be more likely to give the answer which would be viewed as desirable rather than a true answer. In this survey, it may have led to over reporting of good antimicrobial stewardship practices.

Despite the aforementioned shortcomings, the study provides useful data from which important conclusions may be made, adds valuable information to the existing body of knowledge with regard to current perceptions and

practice regarding the prescription of antimicrobial agents, as well as AMR. It serves to highlight the urgent unmet need within medical education surrounding antimicrobial teaching at both an undergraduate, as well as at a postgraduate level.

2.6 Conclusion

This study aimed to evaluate antimicrobial knowledge and prescribing practices of doctors working in tertiary hospitals in Johannesburg. It confirmed that doctors who participated, prescribe antimicrobials on a regular basis and also identified gaps in knowledge regarding antimicrobials and appropriate use thereof across all levels of qualification. This study also found that these doctors agree that antimicrobial resistance is an important problem locally & internationally. They agree that they would benefit from more teaching as a large proportion are not very confident in their prescribing skills. We suggest the implementation of further antimicrobial stewardship programs at these 3 hospitals namely: Charlotte Maxeke Johannesburg Academic Hospital, Chris Hani Baragwanath Academic Hospital & Helen Joseph Hospitals. These programs could include discussion around current guidelines on managing common infections as well as infection control and could be targeted at all levels of qualification. The program should also emphasize the appropriate stewardship of these antimicrobial agents in order to discourage the further development of antimicrobial resistance in our setting.

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CHAPTER THREE – APPENDICES

3.1 Figure 1

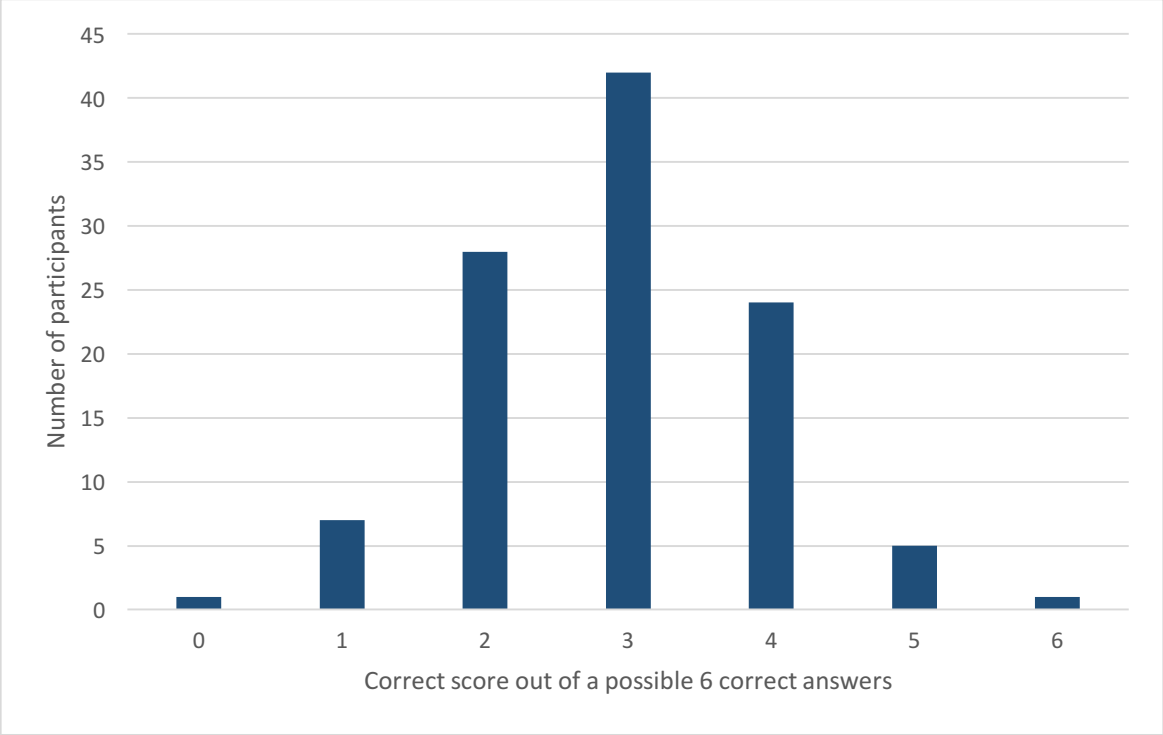


Figure 1: Participant correct score for knowledge questions

3.2 Figure 2

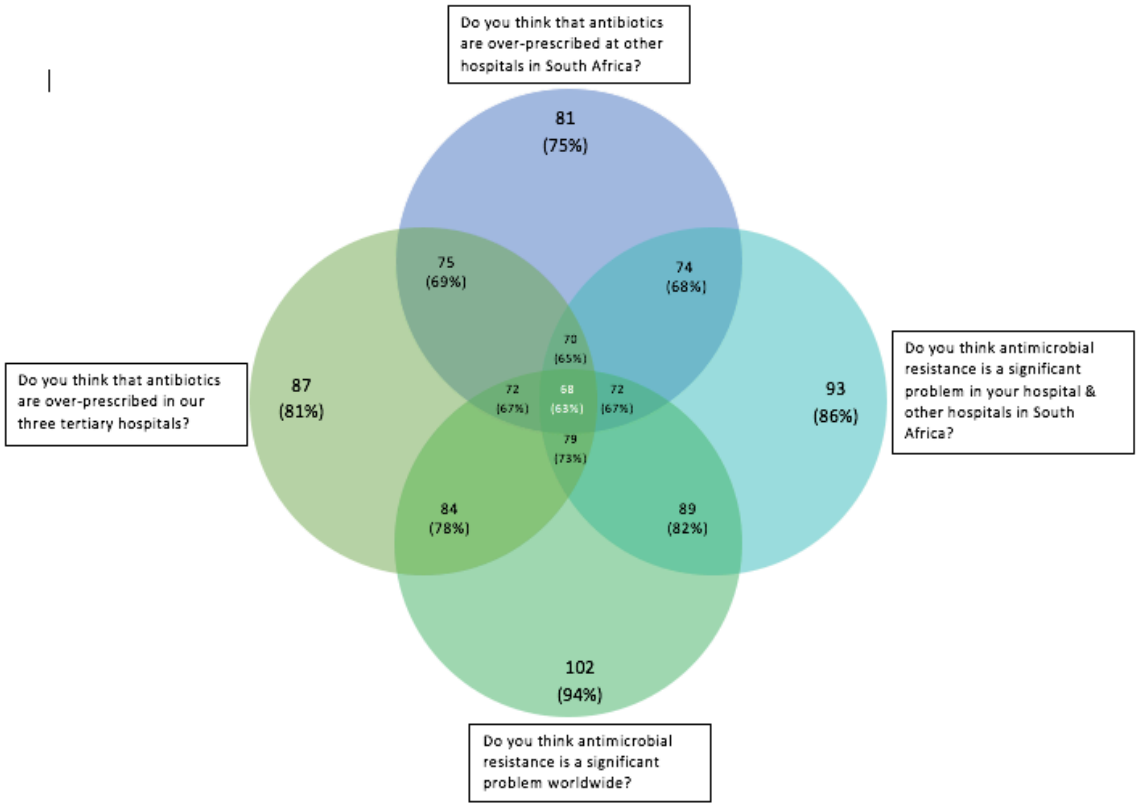


Figure 2: Perceptions of antimicrobial resistance and prescription practices

3.4 Table 1

Question	Percentage of Correct Responses
Which of the following antimicrobials has the best activity against anaerobes?	92.6%
Methicillin resistant - *Staphylococcus aureus* is susceptible to	86.1%
Which of the following drugs would be your best choice for an infection requiring good CSF drug penetration?	38.9%
How long would you usually treat *C. difficile* for when using metronidazole?	32.4%
Which intravenous drug would be your first choice as an alternative to Co-amoxiclav (Augmentin®) in severely penicillin-allergic patients with a community-acquired pneumonia?	26.9%
Which of the following is NOT an indication to prescribe antimicrobials in a patient presenting with acute diarrhoea?	15.8%

Table 1: Overall correct results from knowledge questions

3.5 Study Questionnaire

Level of qualification:

Intern / Medical Officer ☐

Registrar ☐

Consultant ☐

PLEASE SELECT A SINGLE ANSWER FOR EACH OF THE BELOW QUESTIONS

A. Antimicrobial knowledge & learning

Where do you get your knowledge on antimicrobial prescribing from?

1) Advice from colleagues on the same level as you
2) Information from senior colleagues
3) South African guidelines
4) International guidelines
5) All of the above

How confident are you in your knowledge of appropriate prescription of antimicrobials and antimicrobials?

1) Very confident
2) Confident
3) Neutral
4) Low confidence
5) Not confident at all

During the last year, how often have you received teaching on antimicrobials?

1) 0 times
2) 1-3 times
3) 4-6 times
4) 6-9 times
5) >10 times

When unsure of your decision to prescribe antimicrobials how likely are you to review it with a senior colleague / infectious diseases consultant?

1) Very likely
2) Likely
3) Neutral
4) Unlikely
5) Highly Unlikely

B. Antimicrobial prescription choice for specific infections

How many times a day do you prescribe antimicrobials?

1) More than once a day
2) Once a day
3) 1-3 times per week?
4) 4-6 times per week?
5) Less than once a week?

How long would you usually treat *C. difficile* for when using metronidazole?

1) 5 days
2) 7 days
3) 10 days
4) 14 days
5) until diarrhoea resolves

Which of the following is NOT an indication to prescribe antimicrobials in a patient presenting with acute diarrhoea?

1) no resolution after 48 hours
2) associated dehydration
3) associated leucocytes on stool microscopy
4) bloody diarrhoea
5) Fever > 38°C

Which of the following antimicrobials has the best activity against anaerobes?

1) Metronidazole
2) Ceftriaxone
3) Ciprofloxacin
4) Co-trimoxazole
5) Azithromycin

Which of the following drugs would be your best choice for an infection requiring good CSF drug penetration?

1) Clindamycin
2) Co-amoxiclav (Augmentin®)
3) Amikacin
4) Linezolid
5) Daptomycin

Which intravenous drug would be your first choice as an alternative to Co-amoxiclav (Augmentin®) in severely penicillin-allergic patients with a community-acquired pneumonia?

1) moxifloxacin
2) ampicillin
3) vancomycin
4) sulfamethoxazole-trimethoprim
5) azithromycin

Methicillin resistant - *Staphylococcus aureus* is susceptible to:

1) Cefuroxime
2) Ceftriaxone
3) Cefazolin
4) Cloxacillin
5) None of the above

C. Perceptions regarding antimicrobial resistance

Do you think that antimicrobials are over-prescribed at Chris Hani Baragwanath Academic Hospital; Helen Joseph Hospital and Charlotte Maxeke Johannesburg Academic Hospital?

1) Strongly agree
2) Agree
3) Neutral
4) Disagree
5) Strongly disagree

Do you think that antimicrobials are over-prescribed at other hospitals in South Africa?

1) Strongly agree
2) Agree
3) Neutral
4) Disagree
5) Strongly disagree

Do you think antimicrobial resistance is a significant problem in your hospital & other hospitals in South Africa?

1) Strongly agree
2) Agree
3) Neutral
4) Disagree
5) Strongly disagree

Do you think antimicrobial resistance is a significant problem worldwide?

1) Strongly agree
2) Agree
3) Neutral
4) Disagree
5) Strongly disagree

D. Factors influencing antimicrobial prescription

Which factor has the greatest influence on your decision to start antimicrobials in a patient on presentation

1) Pyrexia & tachycardia
2) Patient requesting it
3) Biochemical features of sepsis (high CRP/PCT)
4) Specimen culture
5) Unsure what diagnosis is

Does the need for approval of certain antimicrobials (e.g. consultant authorization, or infectious diseases authorization) incline you to select an alternative antimicrobial?

1) Strongly agree
2) Agree
3) Neutral
4) Disagree
5) Strongly disagree

E. Antimicrobial teaching

Would you like additional training or educational programs on antimicrobial prescribing?

1) Strongly agree
2) Agree
3) Neutral
4) Disagree
5) Strongly disagree

3.6 Approvals

3.6.1 Permission letter from Department of Internal Medicine



Department of Internal Medicine

7 York road, Parktown, 2193, South Africa Telegrams 'Witsmed' Fax: +27 11 643 8777 Tel: +27 11 488 4622

3 November 2017

Prof Peter Cleaton-Jones,
Chairman,
Wits Human Research Ethics Committee (Medical).

Dear Prof Cleaton-Jones,

Re: Request for permission to undertake research within the Department of Internal Medicine.

The purpose of this letter is to grant Dr Stacey Norsworthy permission to conduct research at the Department of Internal Medicine.

The project is entitled: *Survey of antibiotic knowledge and prescribing practices of doctors working at tertiary state hospitals in Johannesburg, South Africa*, and entails her interviewing interns, medical officers, medical registrars and consultants currently working in all three teaching hospitals attached to the Wits teaching circuit on aspects related to antibiotic use.

This approval is subject to all the conditions set by the Wits Human Research Ethics Committee (Medical) and all the necessary approvals from the various authorities.

Sincerely,

A/Prof Colin Nigel Menezes,
MD, MMed (Int Med), Dip HIV Mang (SA), DTM&H, FCP (SA), Cert ID (SA), PhD

Academic Head, Department of Internal Medicine,
School of Clinical Medicine.

Phone: Hospital: +27 11 933 8940; University: +27 11 488 3621
Fax: +27 86 553 3582
Email: colin.menezes@wits.ac.za

3.6.2 Ethics Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R14/49 Drs S Norsworthy and J Nel

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
CLEARANCE CERTIFICATE NO. M171180

NAME: (Principal Investigator)	Drs S Norsworthy and J Nel
DEPARTMENT:	School of Clinical Medicine Department of Medicine Division of Internal Medicine Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	Survey of antibiotic knowledge and prescribing practices of doctors working at tertiary state hospitals in Johannesburg, South Africa
DATE CONSIDERED:	24/11/2017
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr M Venter
APPROVED BY:	Professor CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	16/03/2018

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

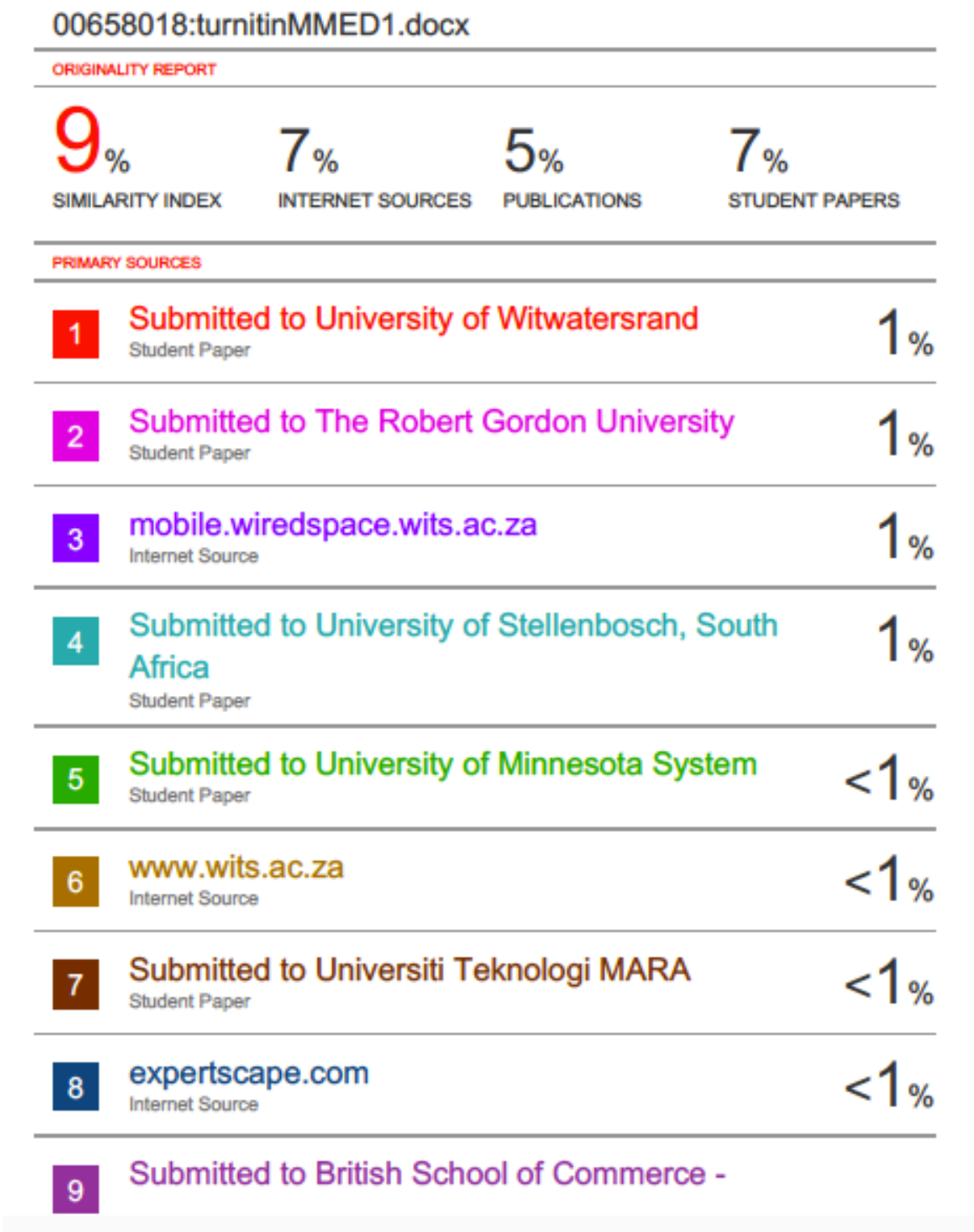
DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on 3rd floor, Phillip V Tobias Building, Parktown, University of the Witwatersrand, Johannesburg.
I/We fully understand the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated from the research protocol as approved, I/we undertake to resubmit to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. in this case, the study was initially reviewed in **November** and will therefore be due in the month of **November** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature — Date: 7/12/2017

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

3.7 Turn-it-in Report



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