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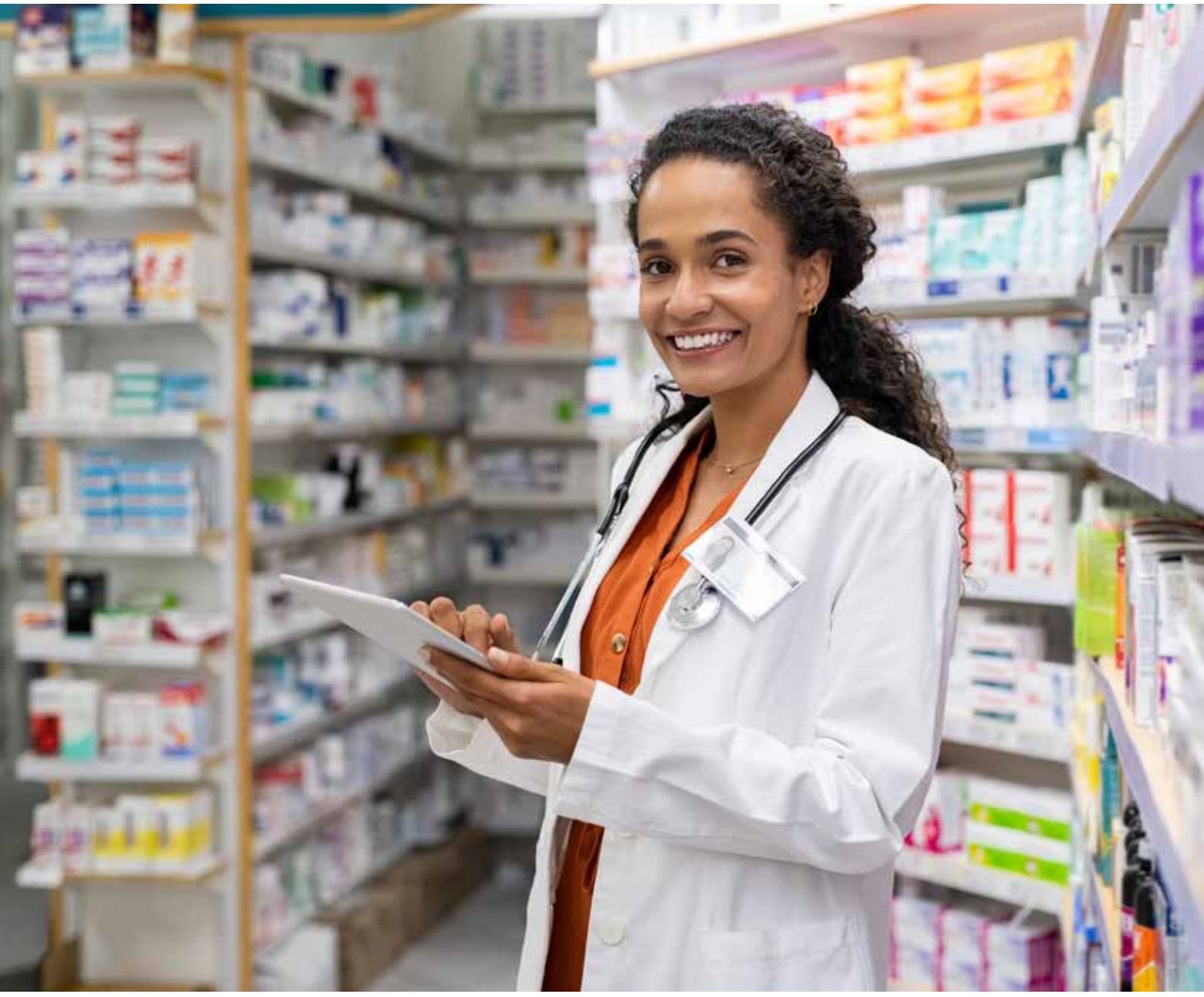

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SAPJ Author Guidelines

Thank you for choosing SAPJ in which to publish your paper.

Aims, scope and review policy

SAPJ is aimed at the continuing professional development of the South African pharmacist in a variety of practice settings, including clinical pharmaceutical care practitioners in a community or hospital pharmacy environment, and pharmacists in academic and industrial practice.

The journal accepts specific clinical reviews on self-medication topics (symptomatic therapy) and information on prescription medication (therapy in clinical context), and provides pharmacists with essential information for referring customers for early medical attention should it be required. SAPJ further recognises that the role of the pharmacist continually evolves to meet the needs of the population. An example of this is the provision of accessible, basic primary health care services in community pharmacies.

Papers dealing with medicines safety issues, including the safe and appropriate prescription, administration and use of medication as well as pharmacovigilance, are strongly advocated in SAPJ. SAPJ further supports pharmacists in transforming the pharmacy into an accessible, basic primary health care facility for preventing and treating primary health care conditions through diagnosis, screening and treatment.

The journal is currently indexed by Google Scholar via www.sapj.co.za and enjoys wide international exposure. An 'electronic long, paper short' policy will be followed for original papers where abstracts of original papers are featured in the printed copy with the full version available online.

Online submission

All articles must now be submitted online at www.sapj.co.za

The electronic submission process will prompt you to check off the following declarations:

1. This manuscript has currently only been submitted to SAPJ and has not been published previously.
2. This work is original and all third party contributions (images, ideas and results) have been duly attributed to the originator(s).
3. Permission to publish licensed material (tables, figures, graphs) has been obtained and the letter of approval and proof of payment for royalties have been submitted as supplementary files.
4. The submitting/corresponding author is duly authorised to herewith assign copyright to Medical and Pharmaceutical Publications (Pty) Ltd
5. All co-authors have made significant contributions to the manuscript to qualify as co-authors.
6. Ethics committee approval has been obtained for original studies and is clearly stated in the methodology.
7. A conflict of interest statement has been included where appropriate.
8. A title page has been uploaded as a separate supplementary file and the submission adheres to the instructions to authors in terms of all technical aspects of the manuscript.

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Article sections and length

The following contributions are accepted (word counts include abstracts, tables and references):

Original research:	3 200–4 000 words
Evidence- based pharmacy practice:	3 200–4 000 words
Reviews:	2 400–3 200 words
Case studies:	1 800 words
Scientific letters:	1 200–1 800 words
Letters to the editor:	400–800 words

For a full version of the SAPJ author guidelines, please visit www.sapj.co.za

Evolving Horizons: The South African Pharmaceutical Journal in 2024

Natalie Schellack

As we embark on a new year in the South African pharmacy landscape, the South African Pharmaceutical Journal (SAPJ) is poised to spearhead the discourse on the profession's evolution and transformation. In this editorial, I reflect on the forthcoming year, which promises to be an eventful one.

Enhancing the SAPJ's content and impact

In 2024, the SAPJ will introduce a series of new features to enrich the content and expand its reach. Firstly, we will be publishing articles that explore the impact of unprofessional behaviour on patient safety, as exemplified by two cautionary tales. Secondly, we will delve into the identity of the pharmacist, a topic that is crucial for the profession's self-reflection and growth. Thirdly, we will feature articles on young and upcoming pharmacists, highlighting their contributions and perspectives.

Diversifying the editorial board

To enhance the journal's exposure and diversity, we will be appointing an editorial board in 2024. This board will be comprised of professionals from various sectors of the pharmacy field, ensuring a multifaceted perspective that includes diversity in the content we publish.

Continuous Professional Development (CPD)

To further enrich the learning experience for our readers, every review paper will now include three questions for CPD. These questions will be designed to stimulate critical thinking and encourage the application of knowledge to real-world scenarios.

South Africa hosts the World Congress of Pharmacy and Pharmaceutical Sciences

In a historic first for sub-Saharan Africa, the 82nd International Pharmaceutical Federation's (FIP) World Congress on Pharmacy and Pharmaceutical Sciences will be hosted in Cape Town, South Africa, from 1–4 September 2024 at the Cape Town International Convention Centre (CTICC). The Pharmaceutical Society of South Africa (PSSA), the largest voluntary professional association for pharmacists and pharmacy support personnel in the country, is the congress partner for the 82nd International Pharmaceutical Federation's (FIP) World Congress on Pharmacy and Pharmaceutical Sciences. The theme for this event is *"Innovating for the future of healthcare."*

Farewell to a pioneer

We will be missing Mr Ivan Kotze, who is retiring in March 2024. Mr Kotze has been the Executive Director of the Pharmaceutical Society of South Africa (PSSA) since 1994 and has represented the PSSA at the International Pharmaceutical Federation (FIP) for the last 30 years. He has served as a Trustee of the PPS Holdings Trust and has been involved in various capacities within the pharmacy profession for many years.

His dedication to the profession and his unwavering commitment to the advancement of pharmacy in South Africa have left an indelible mark on the field. Mr Kotze's leadership has been instrumental in shaping the PSSA's role as a key stakeholder in the pharmacy profession, and his retirement will be a significant loss for the organisation and the broader community. We are grateful for his contributions to the profession of pharmacy and wish him a fulfilling and well-deserved retirement.

Looking ahead with optimism

As we embark on this new year, I am filled with optimism and excitement for the future of pharmacy in South Africa. I look forward to a year of collaboration, innovation, and growth, and I invite you to join me on this journey. Together, we can shape the future of pharmacy and contribute to the betterment of healthcare in South Africa and beyond.

President's Message

Tshifhiwa Rabali
PSSA President

As we step into 2024, our profession is undergoing daily changes, encompassing both positive and negative aspects. The year 2023 witnessed significant progress achieved by the PSSA, particularly in the continued growth of our membership. This was facilitated by the ongoing initiative to rejuvenate and support the smaller branches, a program that is set to persist until the leadership is fully satisfied. Furthermore, the revival of inactive branches is also a key focus. Members are strongly encouraged to actively voice their concerns within their respective branches and to demand accountability from their leaders, especially in terms of upholding and implementing the constitution in all facets of their work.

There has also been a lot of comments that were submitted to different stakeholders like the National Department of Health (NDoH), South African Pharmacy Council (SAPC), and others. This engagement is set to continue throughout the year, aiming to enhance the Society's visibility and encourage more colleagues to join. Additionally, all existing Society programs, along with new initiatives, will persist, ensuring a comprehensive and sustained approach to the Society's objectives.

This year, 2024, we also pride ourselves by being the first country on the African continent to be hosting the International Federation of Pharmacists Congress (FIP). We urge all of you colleagues to be part of this once in a lifetime experience of having our colleagues from all over the world gathering on our doorstep.

One of the SAPC's Notice board was about the experience that might be needed when a pharmacist is recruited as a Responsible Pharmacist. This has been a thorny issue in many circles as there has been a trend of hiring and allowing pharmacists who have just completed their community service year to be Responsible Pharmacists with no experience at all and that puts our fellow colleagues in a precarious situation as mistakes might happen and jeopardise their young career but because of monetary remuneration, the person takes the position.

The Pharmaceutical Society of South Africa's stand is clear on this issue as we don't want our colleagues to be in the wrong because of someone who is going to benefit by employing them as a Responsible Pharmacist. Experience will always be a good thing to have before taking that huge responsibility. The proposal from SAPC is that the pharmacist should have at least 3 years of practising as a pharmacist, which we are ready to engage with them on, but not on the proposal of having a short course, as that will be more burdening to our colleagues with council fees that are already not affordable and the course is not justified.

The National Health Insurance (NHI) Bill has emerged as a prominent issue in 2023 following its passage by the NCOP in parliament. The bill is currently awaiting the President's signature to become law. The PSSA has established communication with a senior NHI official, and there have been email exchanges between the PSSA and the official. The Society aims to arrange a meeting with the official during the year or extend an invitation to the next National Executive Committee (NEC) meeting, facilitating direct engagement with colleagues. The PSSA is committed to monitoring the developments related to this issue.

Furthermore, it is essential to acknowledge the significant contributions of the YPG. The Society encourages the YPG to sustain their commendable work, emphasizing their pivotal role as the future of the profession. The PSSA advocates for the YPG's active presence across all branches to foster collective growth within the Society. Additionally, the ongoing success of the mentorship program underscores the importance of its continuation, as it serves as a platform for the transfer of knowledge from seasoned pharmacists to their younger counterparts.

The coming NEC meeting in February 2024, will be the last with Ivan Kotzé as the Executive Director of PSSA after being with us for so many years. It is befitting for me to say the following to him on behalf of the PSSA: I would like to wish you well during your retirement and be blessed in whatever you want to do in future. Your presence at the Society has been like a pillar holding a structure for all the years. We've seen and heard all the good things that you did for the Society and for that, we thank you very much Sir.

Breaking New Ground: South Africa Hosts the 82nd FIP World Congress on Pharmacy and Pharmaceutical Sciences

In 2024, it will be the first time in FIP's 112 years of existence that the World Congress will be hosted in sub-Saharan Africa. The bid process to bring this World Congress to Africa commenced in 2017 when the PSSA submitted its first bid to FIP. After being unsuccessful initially and delays resulting from the COVID-19 pandemic, the time has finally arrived to welcome the global pharmacy profession to the southern tip of Africa in 2024. The Pharmaceutical Society of South Africa (PSSA) is the congress partner for the 82nd International Pharmaceutical Federation's (FIP) World Congress on Pharmacy and Pharmaceutical Sciences. The Congress will take place in Cape Town, South Africa, from 1-4 September 2024 at the Cape Town International Convention Centre (CTICC). The theme is "Innovating for the future of healthcare".

Attending the annual FIP World Congress is indeed a once-in-a-lifetime experience. Due to the financial commitment of travelling abroad, not many South Africans have been able to utilise the opportunity of attending this global event. Bringing the FIP World Congress to South Africa is the most accessible opportunity for South African pharmacists and pharmacist's assistants to learn from and network with global experts.

Registration to attend the Congress

Registration for the Congress opens in January 2024. Participants will either register as ordinary participants (pharmacists and qualified pharmacist's assistants graduating before September 2016; and non-pharmacists) or as recent graduates (current BPharm students; current learner pharmacist's assistants; and recent graduates who graduated/qualified after September 2016).

The registration fees are tiered over three tiers. The early bird registration will end on 31 May 2024, followed by the second registration deadline on 15 August 2024, leaving the last registrations close to the Congress.

The Congress registration fee for participants will include the following:

- Attendance of the "Pharmacy in South Africa" session on Sunday, 1 September 2024.
- Attendance of the First Timers' Reception on Sunday, 1 September 2024, for delegates attending an FIP Congress for the first time.
- Attendance of the Opening Ceremony on Sunday, 1 September 2024.
- Attendance of the Welcome Reception on Sunday evening, 1 September 2024, in the exhibition hall.
- Admission to all academic sessions from Monday, 2 September to Wednesday, 4 September 2024.
- Access to the exhibition and the poster sessions from Monday, 2 September to Wednesday, 4 September 2024.
- Coffee, tea, and lunch breaks from Monday, 2 September to Wednesday, 4 September 2024 (excluding Sunday, 1 September 2024).
- Name tag and lanyard.
- Congress bag (only if pre-ordered).
- Access to all submitted abstracts online.
- Final pocket programme (only if pre-ordered).
- Access to the congress application, including the list of participants (name and country).
- Access to a website where you can download the presentation slides of the speakers who gave permission (from 5 September 2024).

A typical day at the Congress will commence formally at 09h00, with a 90-minute plenary session to set the theme for the day. These plenary sessions will showcase keynote speakers from around the world and experts in their respective fields of pharmacy. Before this plenary, breakfast symposiums on relevant topics, as well as sessions hosting a variety of FIP Member Organisations who showcase pharmacy, sciences, and education in their countries, commence at 07h30.

After a tea and coffee break of 30 minutes in the exhibition hall, parallel sessions commence at 11h00 and run till 12h30. These parallel sessions are universal and link with the congress theme, sub-themes, and day's theme. These sessions were proposed and developed by the FIP structures, which include the sections, special interest groups, technical advisory groups, FIP Education

Programme outline

	SUNDAY 1 SEPTEMBER 2024	**MON**DAY 2 SEPTEMBER 2024	**TUES**DAY 3 SEPTEMBER 2024	**WED**NESDAY 4 SEPTEMBER 2024
Early morning	-	Industry breakfast symposia	Industry breakfast symposia	Industry breakfast symposia
Morning	Workshops & Pharmacy in South Africa	Plenary session & Parallel sessions	Plenary session & Parallel sessions	Plenary session & Parallel sessions
Lunch	Industry lunch symposia	Industry lunch symposia	Industry lunch symposia	Industry lunch symposia
Afternoon	Opening Ceremony	Plenary session & Parallel sessions	Plenary session & Parallel sessions	Plenary session
Evening	Welcome Reception	Section & SIG dinners	ECPG evening	Closing dinner

Figure 1: indicates a simplistic outline of the Congress programme.

and the Early Career Pharmaceutical Group (ECPG) (previously known as FIP's Young Pharmacists' Group).

During the 2-hour lunch break from 12h30 to 14h30, participants can visit the exhibition hall where various poster presenters will showcase their research applicable to different sectors or special interest groups related to pharmacy. There will also be lunchtime symposiums on relevant clinical or scientific topics.

In the afternoon, there will again be parallel sessions running for 90 minutes, followed by a tea and coffee break at 16h00 before the academic programme concludes with a 60-minute plenary session, which will conclude the discussion and theme of the day with keynote speakers.

Closer to the Congress, pre- or post-congress workshops or symposiums may be advertised. These may be a half or full-day event, and a clear indication of what participants can expect will be included in the communication. These events are mostly not included in the Congress registration fee, and interested participants will have to pay for them in addition to the Congress registration fee.

Social events during the Congress

Apart from working hard during the day when attending sessions, interacting with poster presenters, networking, and building relationships, there are also several social events to consider joining in the evenings.

Attendance at the Welcome Reception in the exhibition hall on Sunday, 1 September 2024, is included as part of the registration process. Light finger food and drinks will be served as we celebrate the start of Pharmacy Month 2024.

On the evening of Monday, 2 September, all FIP Sections will host a dinner where like-minded colleagues can network and engage with peers with the same interests. There are currently eight FIP Sections:

- Academic pharmacy
- Clinical biology
- Community pharmacy
- Health and medicines information
- Hospital pharmacy
- Industrial pharmacy
- Military and emergency pharmacy
- Social and administrative pharmacy

All scientists are invited to the Board of Pharmaceutical Sciences dinner. To attend any of these dinners, participants must book a ticket during registration. These dinners are formal sit-down events with a three-course meal or similar. The venues for all dinners will be near or in the V&A Waterfront.

For the Comrades and parkrun enthusiasts, there will be a 5 km fun run on Tuesday, 3 September 2024, at 07h00 in the Waterfront vicinity. Participation is through a donation to the FIP Foundation for Research and Education and can also be booked during registration.

The youngsters will have an Early Career Social night, organised by the FIP ECPG and the International Pharmaceutical Student Federation (IPSF). Eligible participants can book tickets to attend the evening during the registration process. Light finger food and drinks will be served, and the event will occur at the V&A Waterfront. All other delegates to make their own arrangements with local colleagues they haven't seen in a while or newly founded friendships with international colleagues.

The final social event will be the Congress Closing Dinner on Wednesday, 4 September 2024. This formal sit-down event will be the last opportunity to enjoy this once in a lifetime event with local and international colleagues. The dinner will take place at the V&A Waterfront and transport between the CTICC and venue will be available. Tickets to the closing dinner can be booked during the registration process.

Keep in mind that space is limited for all social events, and that once tickets are sold out, no additional seats can be added. Participants interested in joining social events should not wait until last minute to book tickets.

General registration information

Payment of registration fee: all fees must be paid by credit card (Visa, Eurocard/Mastercard or PayPal) during the registration process. Instructions for payment will be available on the payment page of the registration website. For security reasons, FIP does not manually charge credit cards from their office. Your registration will only be finalised once the full registration amount has been paid and received.

After completing your registration, you will receive an automatically generated email/invoice acknowledging your registration submission and confirming your payment. If you do not receive this, please check your spam filter before emailing congress@fip.org. ***Note: the PSSA is not managing the Congress registrations.***

In the last week of August 2024, you will receive a final information email, including a link to view all submitted abstracts. Please view the terms and conditions for cancellation of registration on the congress website here: https://capetown2024.fip.org/registration/registration-guidelines/

To avoid unnecessary printing, all participants will be emailed their certificate of congress attendance as a PDF within 10 days of the close of the Congress. Accompanying persons do not receive a certificate of attendance.

The Congress registration fee does not include accommodation or transportation to and from Cape Town. Each participant should book their preferred accommodation and method of travel themselves based on their needs.

Enquiries

For more information or clarity regarding the 2024 FIP World Congress, contact Mariet at mariet@pssa.org.za or at 0124709560.

All registration queries should be directed to FIP at congress@fip.org.

Visit the official Congress website for more information: https://capetown2024.fip.org/

The PSSA/Alpha Pharm distance learning programme 2024

The PSSA/Alpha Pharm distance learning programme continues to offer pharmacists useful, practical, up-to-date information that enables them to provide optimal pharmaceutical care to their patients.

Module 1, 2024 – Gastro-oesophageal reflux disease (GORD) – an update for the pharmacist

Occasional reflux is normal and can occur in healthy infants, children, and adults, most often after eating a meal. These episodes are brief and do not cause bothersome symptoms or complications. In contrast, people with gastro-oesophageal reflux disease (GORD) experience bothersome symptoms or damage to the oesophagus because of the acid reflux.

Gastro-oesophageal reflux disease (GORD) is one of the most common gastrointestinal conditions, affecting 10 to 20% of adults in Western societies. It also occurs frequently in infants.

Much has changed but much has remained the same in the management of GORD. For example, although proton pump inhibitors (PPIs) remain the medical treatment of choice for GORD, some publications have raised questions about adverse events, raising questions about the long-term use and over-prescribing of PPIs.

This module provides evidence-based recommendations and practical guidance for the pharmacist on the management of GORD, including both lifestyle and treatment approaches.

For more information about this programme, contact Gill or Glynis at Insight Medicine Information on 011 706 6939 or email: cpdalphapharm@insightmed.co.za.

The PSSA/Alpha Pharm clinical education programme 2024 for pharmacy staff

The PSSA/Alpha Pharm pharmacy staff clinical education programme continues to offer front-shop assistants or pharmacist's assistants up-to-date information that enables them to provide optimal pharmaceutical care to their patients. All pharmacy staff need to be familiar with the use of unscheduled medicines and should be reminded of when it is necessary to refer the patient to the pharmacist.

Module 1, 2024 – Heartburn

Heartburn is a burning feeling in the middle of the chest behind the breastbone. It is caused by stomach acid travelling up towards the throat (i.e. acid reflux).

Occasional reflux is normal and can occur in healthy infants, children, and adults, most often after a meal. Many people experience heartburn from time to time, caused or worsened by certain foods or drinks, smoking, pregnancy, stress, and anxiety. Recurrent heartburn, however, is one of the main symptoms of gastro-oesophageal reflux disease (GORD).

Several simple lifestyle and dietary changes can help reduce or prevent heartburn. Patients presenting in the pharmacy with mild and intermittent symptoms of heartburn may be managed with over-the-counter (OTC) medicines such as antacids or alginate-antacid combinations. Patients presenting with more frequent symptoms (two or more episodes a week) and patients not responding to antacids may be managed with a short course of other OTC acid-reducing medicines.

Heartburn is common and usually responds well to these interventions. However, it is important for the front shop staff in the pharmacy to recognise patients with persistent or recurring heartburn, or unusual or more severe symptoms who require referral to the doctor.

This module discusses heartburn and the management of heartburn in the community pharmacy setting with lifestyle and dietary changes and OTC medicines.

If you would like to participate in the PSSA/Alpha Pharm pharmacy staff clinical education programme, please contact Gill or Glynis for further information on 011 706 6939 or email: cpdalphapharm@insightmed.co.za.

2023 in Reflection – Celebrating milestones, navigating challenges, and empowering Young Pharmacists for a dynamic future

1. PSSA YPG appoints its first ever Subcommittee!

The PSSA YPG, through the leadership of the Steering Committee, appointed its first ever Subcommittee in October 2023. These members are actively involved in the expansion of the PSSA. The subcommittee functions as a mechanism to increase the reach, interest and active participation in matters of the profession by young pharmacists nationwide.

A. Chair Subcommittee – This subcommittee consists of sector and provincial liaisons. The members of this subcommittee play a vital role of representing, building beneficial relationships, and collaboration with sectors and provincial branches of the PSSA.

B. Project Subcommittee – The PSSA YPG's projects are planned and implemented by this subcommittee. These projects cater to the development and growth of pharmacist interns, community service pharmacists and post-community service pharmacists.

C. Public Relations Subcommittee – This subcommittee is mainly responsible for coordinating the communication from the YPG to the members through the PSSA YPG's social media platforms, the SAPJ and newsletters.

For more information on the young pharmacists that are on the subcommittees check our social media pages.

2. Pharmacy Students' Corner: Preparing for Internship Webinar

The PSSA YPG historically hosted successful webinars that addressed young pharmacists and assisted them in their journey and this year was no different. The YPG hosted an internship readiness webinar on 14 November 2023. The guest speakers included PSSA's Dr Mariet Eksteen, Nathan van Wyk, a 2023 CSP, Thandeka Njapha, the SAAHIP KZN Coastal Chairperson and KZNDoH Depot manager and Luyanda Khumalo, the PSSA YPG Project Coordinator. Over 75 pharmacy students attended and were provided with crucial information regarding their internship year, challenges they may encounter, CPDs, the PSSA's support and much more!

Navigating the future – 2024, a year of growth and innovation for Young Pharmacists

The PSSA YPG is looking forward to the New Year with excitement. We will be launching more stimulating projects for South African young pharmacists to engage with, whilst striving to elevate those that are currently running.

1. Mentorship Programme

The PSSA YPG Mentorship Programme aims to grow the next generation of young leaders in the pharmacy profession. It allows the Society to have its members guide the professional and personal development of young pharmacists. The 2024 cycle will focus on developing competent young pharmacists that can contribute to the growth and advancement of the profession.

2. International Pharmaceutical Federation (FIP) Cape Town 2024

The 82nd FIP World Congress of Pharmacy and Pharmaceutical Sciences will be hosted at the Cape Town International Convention Centre (CTICC), from 1 to 4 September under the theme "Innovating for the future of healthcare". The PSSA YPG encourages young

pharmacists to start planning early to attend this congress. Young pharmacists can look forward to remarkable presentations, social events, and networking opportunities with some of the world's best pharmacists. Refer to Newsletter #10 (2023) for more details on the PSSA YPG's attendance package.

3. PSSA YPG Celebrates its 10 Year Anniversary

The PSSA YPG will be celebrating its 10-year anniversary in 2024 and we will be reflecting on some of the major accomplishments over the past decade. There are many more exciting projects and updates that are coming up and we encourage all members to follow our social media pages for more details.

Feel free to reach out to us at
Email: ypg@pssa.org.za
Facebook: Young Pharmacists' Group of PSSA
Instagram: @pssaypg
Young pharmacists – connected, engaged, empowered and inspired!

Impact of pharmacist-led interventions in improving adherence to glaucoma medications in the geriatric population

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Abstract

Objectives: Geriatric patients can be non-adherent to ophthalmic glaucoma medications because of complex eye drops instillation techniques and forgetfulness, so pharmacists can play their part in improving the clinical outcomes of patients by acting as care providers. The purpose of the current study was to implement various pharmacist-led interventions to improve adherence to glaucoma medications and to evaluate the outcomes of interventions in the geriatric population.

Methods: The Morisky Green Levine (MGL) adherence scale was used for analysis because it measures the extent of non-adherence and analyses the reasons for it. The interview-based sessions were conducted with control and interventional groups followed by educational interventions, including techniques for eye drop instillation, graphical images, precautionary measures, and individual patient counselling for the interventional group. Patients were asked to complete the adherence scale after the conclusion of every follow-up session for a duration of 6 months.

Results: After 6 months of pharmacist-led interventions, a significant shift was found in the interventional group from low to high adherence according to MGL scale evaluation. Moreover, the number of patients in the interventional group whose intraocular pressure was in the safe range significantly increased and follow-up sessions significantly improved the patient's knowledge about glaucoma.

Conclusion: The results of this pharmacist-led educational interventional study showed it was effective in improving adherence to glaucoma medications in the geriatric patients, who showed better adherence scores and improved intraocular pressure.

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Introduction

Glaucoma is the second leading cause of blindness worldwide and is associated with optic nerve damage. The condition is asymptomatic in the earlier stages, consequently leading to irreversible vision loss.[1] Increased intraocular pressure (IOP) is the marker of disease progression in primary open angle glaucoma (POAG) and angle closure glaucoma.[2] In normal tension glaucoma, the IOP lies in the physiological range of 12–22 mmHg, but the disease still prevails.[3] Ageing is among several risk factors for aggravation of glaucoma in geriatric patients because of comorbidities, forgetfulness, poor medication-taking behaviour, and non-adherence.[4]

Ophthalmic drops for the conventional treatment of glaucoma include a combination therapy of β blockers, prostaglandin analogues, cholinergic agonists, and α agonists.[5] Geriatric patients have been found to be non-adherent to ophthalmic glaucoma medications because of a complex eye drops instillation technique and forgetfulness.[6] Patients should be verbally and practically guided about the instillation method of eye drops.[7] Patients often find it difficult to direct the ophthalmic dispensing bottle into their eyes properly, which leads to under-dosing.[8] Different studies have been conducted to highlight this issue. For instance, a study was designed to evaluate the effects of physician-led educational interventions on patients with glaucoma who were potentially non-adherent. The results depicted a non-significant difference in patient medication adherence, suggesting that team collaboration could show improved outcomes.[9] Another group-based educational intervention study was conducted in patients with glaucoma by using questionnaires, relevant videos, and brochures. The outcomes were favourable, including self-reported adherence, beliefs about medication, knowledge of glaucoma, and maintenance of adherence.[10] Older populations are found to be more compliant towards medication regimes after receiving standard education, a medication schedule, and verbal communication.[11] Interactive education sessions for patients with glaucoma have been found to be beneficial for medication compliance.[12] There are several factors affecting glaucoma treatment adherence, including lack of communication between patient and care provider.[13] Moreover, another study concluded that the IOP in patients with glaucoma could be managed by improving the patient–provider communication approach and

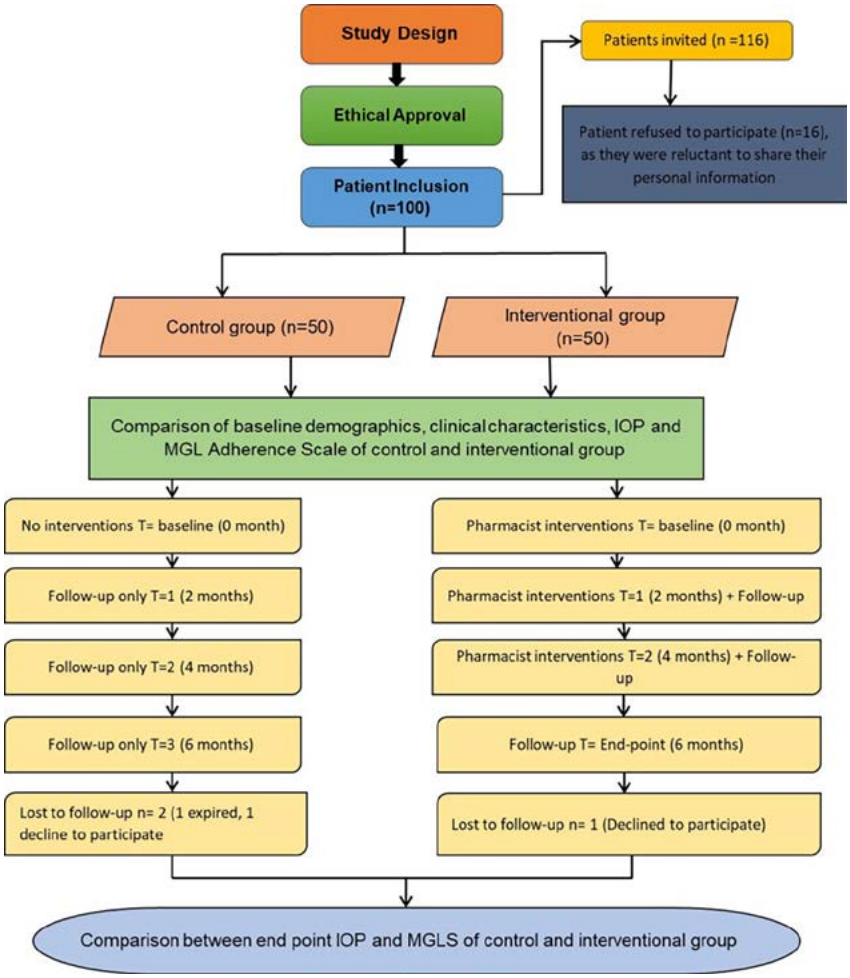

Figure 1: A comprehensive study design showing recruitment and comparison of control and interventional groups. MGLS, Morisky Green Levine adherence scale.

patient input.[14] This evidence suggests that pharmacists can play the part of care provider by using therapeutic management, thus improving the clinical outcomes of patients.[15]

The objective of this cross-sectional prospective study was to implement various pharmacist-led interventions on geriatric patients with glaucoma and to evaluate the outcomes of these interventions. Some previous studies suggest that pharmacists should play the part of care provider to patients with glaucoma, helping them to maintain their IOP within the safe range.[9] The effects of previous studies on medication adherence did not seem to last for a long time. This could be due to lack of sufficient follow-up sessions with patients, which suggests that repeated interactions and more follow-up are required to achieve prolonged benefits. Therefore, this study focuses on three consecutive counselling sessions with geriatric patients with glaucoma every 2 months for a duration of 6 months.

In this study, we used the Morisky Green Levine (MGL) adherence scale. This scale was chosen as it not only measures the extent of non-adherence but also analyses the reasons for it. The interview-based sessions were conducted with control and interventional groups at baseline to collect relevant demographic and medical data. Later, educational interventions were given to the interventional group, including guidance on the technique for eye drops instillation, providing glaucoma-related brochures, graphical images, precautionary measures, lifestyle modification advice, and individual patient counselling. Patients were asked to complete the adherence scale after the conclusion of every follow-up session for a period of 6 months, and the data were statistically evaluated through application of SPSS software.

Materials and methods

Study design

A cross-sectional interventional study was conducted at the Department of Ophthalmology, Services Institute of Medical Sciences (SIMS), a public sector hospital in Lahore, Pakistan. The study was approved by the Institutional Review Board of SIMS under reference number IRB/2019/532/SIMS. Informed written consent was obtained from all the participants in the control and interventional groups in their native language, and the study objective was thoroughly explained. Before the start of the study, participants were informed of the study's objective and health benefits. All the participants agreed to use the collected data for scientific research purposes only. A comprehensive study design is shown in the Figure 1.

Patient recruitment

Geriatric patients with glaucoma who were aged 60 and older and had been prescribed one or more glaucoma medications were recruited while attending the Ophthalmology Department of SIMS as outpatients from 25 April to 20 May 2019. Patients who were completely blind due to glaucoma were excluded as they would affect the study outcomes. Quantitative measurement on the adherence scale and follow-ups were continued from May 2019 to October 2019 in three follow-up sessions. A tonometry test was performed for this purpose. This test is a diagnostic tool to measure the pressure inside your eye (IOP). This measurement helps doctors to determine whether or not there is a risk of glaucoma. The test was performed by two trained technicians in the presence of a supervisor who had completed a Bachelor of Science in Optometry. The average number of tests performed per day by a single technician was 10. The study was conducted in a public sector hospital in Lahore, Pakistan, which is usually operational during the day between 08:00 and 14:00. Therefore, tonometry was performed during laboratory hours from 09:00 to 13:00. The technicians who performed the test were masked to randomisation because they were kept blinded about the

study being conducted. They tested the study participants in the same way they tested other patients. One hundred patients were recruited for the study; fifty were randomly assigned to the control group and 50 to the interventional group using a block randomisation technique.

Interventions

Study subjects attended the Ophthalmology Department of SIMS for routine monthly visits and free medication. Patients' baseline demographics, clinical characteristics, medical and medication history were collected from their hospital medical files. Patients in the control group (n = 50) were observed by the researcher while they followed their usual care. Patients in the interventional group were provided with pharmacist-led interventions in addition to routine medical care at baseline (T = 0), and after the second (T = 1), fourth (T = 2), and sixth (T = 3) month. Interventions included a dose calendar as a reminder of patients' routine drug regimen and brochures about glaucoma in their native language, including precautionary measures, instructions, and lifestyle modifications. The standard interventions of the Glaucoma Research Foundation are provided in online supplemental data. Patients were also shown the technique for instillation of eye drops as recommended by the Glaucoma Research Foundation, San Francisco, CA.

Study outcomes

The primary study outcome was adherence to medications, evaluated after permission by using the MGL adherence scale, which consisted of four questions.

Among the different adherence scales, the most widespread is the MGL adherence scale. This scale was originally designed as a four-item scale with yes or no responses; however, since 2008 an eight-item version is also available. Irrespective of the scale type, the results are usually interpreted in the same way (the lowest the score, the most likely patients are adherent to treatment). Typically, patients are considered adherent when their score is at least 1–2 points for the MGL adherence scale. Due to excellent reliability, the MGL adherence scales are the most accepted adherence measures and are recommended as screening tools in clinical trials.

Each question is worth one point and the total score depicts the level of individual patient medication adherence; a score of 0 = high, 1–2 = medium, and scores 3–4 = low adherence.[16] Secondary outcomes include improvement in IOP of the study population. The IOP observed at baseline (T = 0 month) from tonometry results was compared with the IOP at the second, fourth, and sixth months. A self-designed, validated questionnaire was used as the study instrument in which patient demographics (age, socioeconomic status, and gender), clinical characteristics (comorbidities, medical and medication history), and glaucoma-related questions (disease history, eye surgery, and eye injury) were recorded. The eye drop instillation technique was also shown to patients through a video in a combined session where the researcher depicted the instillation technique using ophthalmic drops. Patient knowledge about glaucoma was also assessed at baseline and at the endpoint through close-ended questions, including whether they had any knowledge about (1) adherence to medication, (2) the consequences of non-adherence, (3) IOP range, (4) eye drop instillation technique, and (5) whether they had been through previous counselling sessions about glaucoma. These data were collected directly from patients and their medical files. Adherence scores and IOP recorded at baseline were compared with those recorded at each follow-up after two consecutive months until a period of 6 months. The questionnaire was validated through Cronbach's α with a value of 0.61 and translated into the native language through a double-blinding method with the help of language experts.

The research was conducted under the supervision of the intervention pharmacist who had been working as a hospital pharmacist in a private sector hospital in Lahore, Pakistan for the past 3 years. A training programme under the consultant ophthalmologist of the Department of Ophthalmology, SIMS was conducted and all studies were performed in the same hospital. This was a 2-week training programme in which all the basics of the Goldmann applanation tonometry test, eye drop instillation technique, and guidelines to counsel patients with glaucoma were covered. Furthermore, the researcher maintained intermittent contact with study participants in the interventional group for 2 months by using a social media application 'WhatsApp' group that included all the participants. In this group, the researcher consistently sent reminder texts and voice messages about medication adherence and its importance.

Statistical analysis

IBM SPSS Statistics 25 was used for statistical analysis. Demographics and clinical characteristics recorded at baseline were analysed through descriptive statistics. The proportions were compared using c^2 or Fisher's exact test, where appropriate. Mean adherence scores and IOP values of the control and interventional groups were compared before and after the interventions through paired t tests. For comparison of control and interventional groups classified in different IOP ranges, the Student t test was used at each interval. A comparison of the proportion of patients in the control and interventional groups with low, medium, and high adherence on the MGL adherence scale was performed by using the c^2 test. A p-value ≤ 0.05 was considered statistically significant.

Results

The results show that patients in the control and interventional groups had similar baseline demographics, including mean age, gender, literacy, employment, financial status, and comorbid conditions (p > 0.05 for all), as expressed in online supplemental Table I.

Glaucoma-related characteristics including symptoms, duration of disease, and IOP at baseline were similar in the control and interventional groups (p > 0.05), except for glaucoma medication, where patients in the interventional group were more likely to

Table I: Number of patients in control and interventional groups responding yes or no to MGL adherence scale from baseline to endpoint

Questions	Follow-ups	Control group (*n* = 50)		Interventional group (*n* = 50)		Total (*n*= 100)		*p*-value
		No	Yes	No	Yes	No	Yes	
		n (%)	*n* (%)	*n* (%)	*n* (%)	*n*	*n*	
Do you ever forget to instil your eye drops?	T=0	18 (36)	32 (64)	23 (46)	27 (54)	41	59	0.309
	T=1	19 (38)	31 (62)	27 (54)	23 (46)	46	54	0.07
	T=2	19 (38)	31 (62)	38 (76)	12 (24)	57	43	0.001*
	T=3	19 (38)	29 (58)	42 (84)	7 (14)	61	36	0.000*
Are you careless at times about instilling your eye drops?	T=0	18 (36)	32 (64)	20 (40)	30 (60)	38	62	0.68
	T=1	17 (34)	33 (66)	47 (94)	3 (6)	64	36	0.03
	T=2	17 (34)	33 (66)	48 (96)	2 (4)	65	35	0.010*
	T=3	15 (30)	33 (66)	47 (94)	2 (4)	62	35	0.000*
When you feel better, do you sometimes stop instilling your eye drops?	T=0	22 (44)	28 (56)	23 (46)	27 (54)	50	50	0.687
	T=1	29 (58)	21 (42)	41 (82)	9 (18)	70	30	0.009
	T=2	29 (58)	21 (42)	47 (94)	3 (6)	76	24	0.010*
	T=3	29 (58)	19 (38)	49 (98)	0	80	20	0.000*
Sometimes, when you feel worse, do you stop instilling your eye drops?	T=0	22 (44)	28 (56)	35 (70)	15 (30)	57	43	0.009
	T=1	23 (46)	27 (54)	38 (76)	12 (24)	61	39	0.035
	T=2	23 (46)	27 (54)	40 (80)	10 (20)	63	37	0.010*
	T=3	23 (46)	25 (50)	45 (90)	4 (8)	68	29	0.000*

*T=0, 1, 2, and 3 shows baseline, two months, four months, and six months, respectively. These questions are modified from Morisky Green Levine (MGL) adherence scale.

Table II: Comparison of patients in control and interventional groups with low, medium and high adherence on MGL adherence scale

	Group	Score 3–4 (low), *n* (%)	Score 1–2 (medium), n *n* (%)	Score 0 (high), *n* (%)	**p*- value
Baseline	Control	34 (68)	14 (28)	2 (4)	0.274
	Interventional	38 (76)	11 (22)	1 (2)	
Endpoint	Control	30 (60)	16 (32)	2 (4)	0.039*
	Interventional	6 (12)	19 (38)	19 (38)	

*Significant P value<0.05. Comparison of patients in control and interventional groups with low, medium and high adherence calculated using c2 test.

Table III: Improvement in mean MGL adherence score and IOP from baseline to endpoint (within group analysis)

Group	Baseline		Endpoint		Improvement		*t* value		**p*- value	
	MGL score	IOP (mmHg)	MGL score	IOP (mmHg)	MGL score	IOP (mmHg)*	MGL score	IOP	MGL score	IOP
Control group	3.3±1.5	21.5±8.8	3.09±1.2	20.0±8.4	0.22±0.2	1.4±0.4	2.89	4.23	0.358	0.061
Interventional group	3.28±1.3	21.8±9.3	1.18±0.91	16.1±9.4	2.1±0.4	5.7±0.07	5.61	7.95	0.017*	0.001

*Paired t test significant values<0.05 and data given as mean±SD, where p values between control and interventional groups are calculated using a paired sample t test and improvement in IOP is calculated in mmHg. IOP, intraocular pressure; MGL, Morisky Green Levine.

be on monotherapy compared with the control group according to statistical analysis ($p < 0.05$), as shown in online supplemental Table II.

Adherence to therapy

The MGL adherence scale was used to measure the adherence of both groups at baseline (T = 0), two follow-ups (T = 1, T = 2), and endpoint (T = 3). Each of the four questions consists of two possible answers: yes scores 1 while no scores 0. The lower the score on this scale, the more likely the patient is adherent to medication; 0, 1–2, and 3–4 scores depict high, medium, and low adherence, respectively.[16] The questions also indicate the reason for the patient's non-adherence, such as forgetfulness, carelessness, and missing dose intentionally after feeling better or worse. The number of patients with a 0 score for each question increased from T = 0 (baseline) to T = 3 (endpoint), as reflected in Table I.

The overall shift of interventional group's patients moving from low to high adherence in MGL Adherence Scale is shown in Table II, where both groups show no significant difference at baseline ($p = 0.274$) while after 6 months of pharmacist-led interventions, a significant difference between control and interventional groups can be seen at the endpoint ($p = 0.039$ which is < 0.05).

The mean MGL scores of control and interventional groups were analysed at baseline and compared with those at the endpoint

Table IV: Intraocular pressure status between treatment groups from baseline to endpoint

IOP (mmHg)	Control group	Interventional group	*p- value
Baseline			0.187
<15	3 (6)	6 (12)	
15–20	13 (26)	9 (18)	
21–22	23 (46)	25 (50)	
>22	11 (22)	10 (20)	
T=1			0.097
<15	4 (8)	7 (14)	
15–20	15 (15)	13 (26)	
21–22	22 (44)	23 (46)	
>22	9 (18)	7 (14)	
T=2			0.030*
<15	6 (12)	14 (28)	
15–20	16 (32)	21 (42)	
21–22	18 (36)	11 (22)	
>22	9 (18)	2 (4)	
Endpoint			0.018*
<15	7 (14)	15 (30)	
15–20	14 (28)	29 (58)	
21–22	20 (40)	2 (4)	
>22	7 (14)	2 (4)	

*P values calculated between control and interventional groups using independent t test with significant t test values<0.05. IOP, intraocular pressure.

using a paired t test. A significant relationship was found between the scores of patients in the interventional group before and after the educational interventions by pharmacists, as displayed in Table III.

Intraocular pressure

With the evident improvement in adherence scores of patients in the interventional group, improvement in IOP was also a marker of improved patient adherence to IOP-lowering medications. The IOP range was categorised into four classes: < 15, 15–20, 21–22, and > 22 mmHg. Patients were allocated into these classes according to their baseline IOP and followed up to the endpoint. By the end of the study, the number of patients in the interventional group who were classified in the safer IOP ranges (< 15 and 15–20 mmHg; $p < 0.05$) significantly increased, as shown in Table IV. The mean IOP between the control and interventional groups also showed significant improvement.

Patient glaucoma knowledge

The interventions consisted of one-on-one verbal counselling sessions with the individual patients at each follow-up session. The combined session also made patients in the interventional group aware of their normal and pathological IOP, the importance of sticking to their medication regime, and the ultimate consequences of non-adherence, such as irreversible blindness. These sessions significantly ($p < 0.05$) improved the patients' knowledge about glaucoma, including the importance of medication adherence, the consequences of non-adherence, and the standard four-step eye drop instillation technique, in comparison to the control group at endpoints, as expressed in Table V.

Although patients in the control and interventional groups had some prior knowledge about their IOP and they had also had brief counselling from their prescriber, the values show statistical significance for both groups even before interventions (at baseline). Furthermore, the differences in basic education levels of the patients in both groups could also have influenced the significant values of 'Patient glaucoma knowledge'; 40% of patients were graduates while the remaining 60% were undergraduates. Such differences could make the former patients more vigilant about their disease compared with the latter group.

Discussion

This study evaluated the impact of pharmacist-led interventions on glaucoma medication adherence in the geriatric population for 6 months. The primary objective of this study was to implement various pharmacist-led interventions and to evaluate their effect in geriatric patients with glaucoma. We found that the provision of individual verbal counselling, relevant material written in the

Table V: Comparison of glaucoma knowledge between control and interventional groups at baseline and follow-up

Questions	Follow-up	Control groupn (%)		Interventional group *n* (%)		*p-value
		Yes	No	Yes	No	
Importance of medicationadherence	Baseline	22 (-44)	28 (-56)	26 (-52)	24 (-42)	0.241
	Endpoint	24 (-48)	24 (-48)	46 (-92)	3 (-6)	0.030*
Consequencesof non-adherence	Baseline	26 (-52)	24 (-48)	28 (-56)	22 (-44)	0.283
	Endpoint	24 (-48)	24 (-48)	46 (-92)	3 (-6)	0.029*
Intraocular pressureknowledge	Baseline	32 (-64)	18 (-36)	35 (-70)	15 (-30)	0.010*
	Endpoint	35 (-70)	13 (-26)	49 (-98)	0	0.024*
Standard eye dropsinstillation technique	Baseline	18 (-36)	32 (-64)	22 (-44)	28 (-56)	0.198
	Endpoint	20 (-40)	28 (-56)	49 (-98)	0	0.010*
Prior counseling-sessionabout glaucoma	Baseline	36 (-72)	14 (-28)	37 (-74)	13 (-26)	0.045*
	Endpoint	42 (-84)	6 (-12)	49 (-98)	0	0.001*

*P-values between control and the interventional groups were compared using paired t-test for each question and paired t-test significant values < 0.05.

native language, a dose calendar to overcome forgetfulness, demonstration of eye drop instillation technique, and one-on-one pharmacist–patient interaction significantly improved adherence and IOP in geriatric patients with glaucoma.

Previously, such studies were conducted on larger cohorts with physician-centric interventions where no significant improvement in adherence was observed, and the researcher suggested that team collaboration with pharmacists might have a greater effect on medication adherence.[9] There are several other publications that used different approaches, for instance, telephone reminders and customised letters to improve appointment adherence in patients with glaucoma.[17] Similar research with the same study population (n = 100) found that patient education-based programmes are significant (p = 0.001) in improving patient knowledge about glaucoma.[12] Our study also provides significant results in this context, suggesting that it is possible to achieve better treatment outcomes with the inclusion of patient education programmes in conventional treatment methods. According to WHO's 2018 report on workforce alliance in Pakistan, the density of physicians is one per 10 000 patients, which has an immense burden on physicians[18]; the inclusion of pharmacists in patient counselling and education could be beneficial in improving patient compliance.

Our research includes several strategies to improve adherence, although we are not certain which aspect of our interventions proved out to be more effective. In future, further research should consider individual components of interventional programmes. A demonstration of the eye drop instillation technique to educate patients about safe and proper administration of ophthalmic drops, therapeutic hygiene, minimization of medication wastage, and accurate dosing was an effective intervention aid. In their study, Colome and colleagues concluded that eye drop administration in the geriatric population is a difficult activity and it can affect the expected treatment outcomes.[7] In overburdened public sector hospitals, the need for instructions about eye drop instillation can be overlooked. So, other healthcare workers such as pharmacists and nurses can assist in the management of ophthalmic diseases such as glaucoma and cataract.

Improvement in adherence produced lower IOP in the interventional group as patients became more conscious about their disease condition and medication adherence. Exceptions to improving IOP could include a few patients who had undergone changes in their medication regime or older patients who had been facing difficulties in administering their drops due to joint diseases such as arthritis. Only 72% of patients with newly prescribed medications refilled their prescription in a 12-month study to evaluate primary medication non-adherence.[19] Medication administration related problems due to comorbidities might be overcome by involving a family member in the care-giving process.[20] The results also suggest the need for the development of sustained release drugs and long-term effective treatment alternatives.

For geriatric patients, forgetfulness remains a constraining factor, even after three counselling and education sessions. Laster and colleagues recommend the use of alarms or similar electronic devices to act as reminders for older patients who are using pilocarpine ophthalmic drops.[21] We are living in the era of the internet and cell phones and the use of such devices to our best interests could do wonders in such healthcare management programmes. The availability of free medication in public sector hospitals in developing countries is also a huge constraint towards non-adherence as many patients in the lower-middle class cannot afford to buy their medications. In our study, the patients did not face any such problems, which might also contribute to improved adherence. More studies should be conducted on this particular aspect to evaluate the effect of medication non-availability on adherence in the lower-middle class population entitled to public sector hospitals.

Limitations

Our study has some limitations to be considered. Randomisation was not based on patients who were potentially non-adherent. Both groups had few patients who were already compliant with their medication regime, which could have influenced the results being significant. Also, few patients in the control group improved their adherence scores (4% of patients moved from low to medium adherence scores) and had better IOP (8% patients improved their IOP to ≤ 15 mmHg) at the endpoint compared with baseline. These results are influenced by physician interaction with patients, which could also have affected the results of the interventional group. Moreover, there was a difference in the level of education of the patients. Those having graduate degrees were in a better position to understand and comply with the educational interventions compared with patients with lower education levels. Our study was based on a small cohort (n = 100), which makes it convenient for the pharmacist to interact with patients individually. For larger cohorts, the results might differ. Additionally, this study did not analyse the effects of multiple dosage regimens on adherence. Patients with comorbidities might have to administer medications for each of their chronic conditions, which could affect overall patient compliance. Glaucoma is often treated by monotherapy with β blockers or prostaglandin analogues. If monotherapy is not effective in reducing IOP then second-line agents such as α agonists or topical carbonic anhydrase inhibitors can be added to one of the first-line treatment options.[5] Such prescribing might also affect non-adherence in patients undergoing combination therapy, which has not been considered by our study. Moreover, glaucoma medication may reflect glaucoma severity and all questions cannot be answered by one study because of differences between groups.

Conclusion

The pharmacist-led educational interventions in a public sector hospital were effective in improving adherence to glaucoma medications in the geriatric population. The results were complemented by improvements in IOP and adherence scores of

these patients. It is evident from the study that pharmacists can play a vital part in improving medication adherence of patients with glaucoma by providing dose calendars, periodic medication adherence reminders, brochures about disease management, counselling and educational sessions on glaucoma, and demonstrating the correct eye drop instillation technique.

What this paper

What is already known on this subject

- Geriatric patients are non-adherent to glaucoma medications because of complex eye drop instillation techniques.
- Physician-led educational interventions for patients with glaucoma who are non-adherent to medications showed some improved outcomes.

What this study adds

- The present study implemented various pharmacist-led interventions to improve adherence to glaucoma medications.
- The number of patients who were in the range of safe intraocular pressure significantly increased.
- The results showed that geriatric patients with glaucoma had improved adherence to medications.

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Competing interests

None declared.

Patient consent for publication Informed consent was obtained from all individual participants included in the study.

Ethics approval

The study was approved by Institutional Review Board of SIMS under reference No IRB/2019/532/SIMS.

Provenance and peer review

Not commissioned; externally peer reviewed.

Data availability statement

Data are available on reasonable request to corresponding author.

Supplemental material

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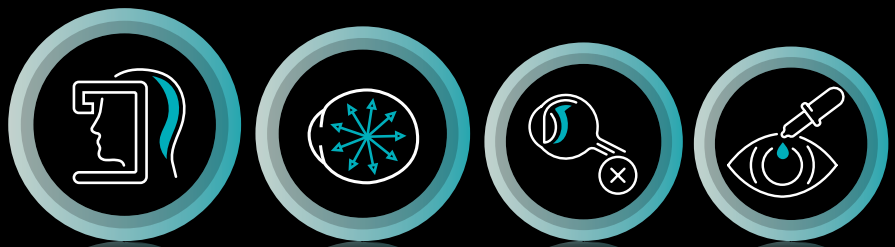

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References: 1. Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. *JAMA.* 2014; **311**(18):1901-1911. **2.** South African Glaucoma Society. Glaucoma algorithm and guidelines for glaucoma, 2016. Available at https://www.sags.co.za/doctors-information. Accessed 12 December 2019. S4 TRAVATAN® Eye Drops, solution (0,004 %), 40 µg of travoprost per ml in a sterile ophthalmic solution, 36/15.4/0333, Novartis SA (Pty) Ltd. S3 SIMBRINZA® 10 mg/ml + 2 mg/ml eye drops, suspension. Reg. No.: 50/15.4/0358. Each ml contains 10 mg of brinzolamide and 2 mg of brimonidine tartrate. S4 DUOTRAV® eye drops, 1 ml of solution contains 40 µg travoprost and 6,83 mg timolol maleate equivalent to 5 mg timolol, A40/15.4/0511, Novartis SA (Pty) Ltd. S3 AZOPTIC® Eye Drops (Suspension), 10 mg brinzolamide per ml, 34/15.4/0382, Novartis SA (Pty) Ltd. S4 AZARGA® eye drops, suspension, 1 ml of suspension contains 10 mg brinzolamide and 5 mg timolol (as timolol maleate), 44 /15.4/0046, Novartis SA (Pty) Ltd. **Note:** Before prescribing, consult full prescribing information.

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NOVARTIS

2023 ART Clinical Guidelines

for the Management of HIV in Adults, Pregnancy and Breastfeeding, Adolescents, Children, Infants and Neonates

June 2023 Version 4

Republic of South Africa National Department of Health

S Afr Pharm J 2024;91(1):20-30

Foreword

South Africa is committed to attaining the UNAIDS 95-95-95 targets to control the HIV epidemic by providing quality healthcare services using highly effective antiretroviral treatment (ART). The principal goal of ART is to attain and maintain viral suppression, which will prevent new HIV infections, increase life expectancy, decrease morbidity and mortality as well as improve the quality of lives of all South Africans, thus contributing to realising the vision of A LONG AND HEALTHY LIFE FOR ALL.

The "Test and Treat All" approach has allowed people living with HIV (PLHIV) to access ART timeously.

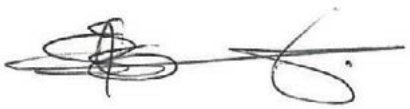
South Africa is committed to using available technology and evidence to continue the fight against HIV. The 2019 guidelines have been revised to include more optimised treatment regimens for all clients, including pregnant and breastfeeding women and children. The National Health Council (NHC) has adopted the new World Health Organization (WHO) recommended first, second and third-line regimens that include Dolutegravir (DTG) as the preferred antiretroviral drug.

I am introducing the 2023 ART guideline, which introduces simplified ART provision and harmonised methods of management of children, adolescents and adults, as well as pregnant women living with HIV/AIDS, TB and other common opportunistic infections. The guidelines also provide guidance on the use of Dolutegravir (DTG) dispersible tablets for children from 3 kg and 4 weeks old.

These guidelines have been revised with the Differentiated Models of Care SOPs to ensure simultaneous consideration and alignment of clinical, adherence and service delivery updates. The Differentiated Models of Care SOPs form part of this guidance to enable optimal use of decentralised and integrated service delivery to promote a patient-centred approach. Effective implementation of these guidelines will increase access to ART services, advance South Africa's ability to control the epidemic and help to achieve the 2030 SDG goals.

I urge all clinicians at PHC clinics, community health centres and hospitals across the board to use these guidelines diligently to offer quality, comprehensive services to the public.

I would like to sincerely thank all the internal and external stakeholders who actively contributed to developing these guidelines.



Dr SSS Buthelezi
Director-General: Health
Date: 24-04-2023

Managing the Client on ART

Monitoring on ART

! Remember to check adherence at every clinical follow-up visit, in a non-judgemental way. Ask open ended questions e.g. "Is there anything that makes it difficult for you to take your treatment?" See also the 'Adherence' section of the ***"ABCDE assessment of an Elevated Viral Load" on page 22***

Providing quality care at the follow-up visit is essential to promote adherence, achieve and sustain viral suppression, minimise side-effects and toxicities, and promote quality of life. A client on ART should be monitored to:

1 Determine clinical response to ART

2 Determine the virological and immunological response to ART

3 Detect and manage any side-effects and toxicities

The following components should be included in the **clinical assessment:**

Weight (adults)
An assessment of trends in weight in adults

Growth and neurodevelopment (children)
An assessment of trends in weight, height, head circumference, and neurodevelopment

! Remember to increase the ART dosage as weight increases!

Screen for TB (see below *) **and other OIs:**
to diagnose and provide treatment; to adjust ART regimen if required; to provide a package of care for AHD if required; to determine if TB preventive therapy is required

WHO clinical staging
to determine response to ART, and CPT eligibility

Screen for pregnancy and ask if planning to conceive as outlined in the table for ***"Baseline Clinical Evaluation" on page 5***

Viral load should be measured to timeously detect problems with adherence or treatment failure

! Remember, any elevated VL > 50 c/mL is a medical emergency!

Assess and manage according to the algorithm ***"VL Monitoring for Clients on TLD" on page 21***

The CD4 count monitors susceptibility to opportunistic infections, identifies clients with advanced HIV disease and informs eligibility for OI prophylaxis.

Monitor routinely after 10 months/DCs on ART (aligned with VL).

Thereafter, stop CD4 monitoring unless:

- CD4 still ≤ 200 cells/mm^3: repeat every 6 months until CD4 > 200
- VL ≥ 1000 c/mL: repeat CD4 every 6 months until VL < 1000 c/mL
- A clinical indication arises, such as a new WHO Stage 3 or 4 condition in a previously well client

Repeat CD4 for clients returning > 90 days after missing a scheduled appointment (see ***"re-engagement algorithm" on page 12***)

Side-effects and ART toxicities can affect adherence and endanger the client's health:

Drug side-effects
Ask about side-effects at each visit (e.g. sleep or gastrointestinal disturbances)

TDF-induced nephrotoxicity
If on TDF, do creatinine and eGFR* at months 3 and 10 (aligned with VL monitoring schedule)
Thereafter, repeat every 12 months
See also ***"Assessing Renal Function" on page 8***

Dyslipidaemia
If on a PI-based regimen, do total cholesterol and triglycerides (TGs) at month 3
If above acceptable range, do fasting cholesterol and TGs and if still above acceptable range, obtain expert advice

Anaemia and neutropaenia
If on AZT, do a full blood count and differential white cell count at months 1 and 3
Thereafter, repeat if clinically indicated

* Screening for TB at follow-up Visits

At every routine follow-up visit:	At every 12-monthly clinical review on ART (aligned with 12-monthly VL)	For symptomatic PLHIV admitted to hospital [in addition to the MTB/Rif Ultra (Xpert)]	For symptomatic PLHIV seen in an outpatient setting [in addition to the MTB/Rif Ultra (Xpert)]
• Do a TB symptom screen. If symptomatic, do a MTB/Rif Ultra (Xpert)	• Routine MTB/Rif Ultra (Xpert) (regardless of TB symptoms)	• Do a U-LAM test	• Do a U-LAM test if: - CD4 count <200 within the last 6 months, or - advanced HIV disease, or - current serious illness.

For more information on the package of care for AHD and the management of specific OIs, please refer to the ***Consolidated ART guideline***

! When monitoring on ART, also integrate monitoring for other chronic conditions (HPT, DM, and mental health) and routinely offer reliable contraception and cervical cancer screening to female clients.

2023 ART Clinical Guidelines (Part II)

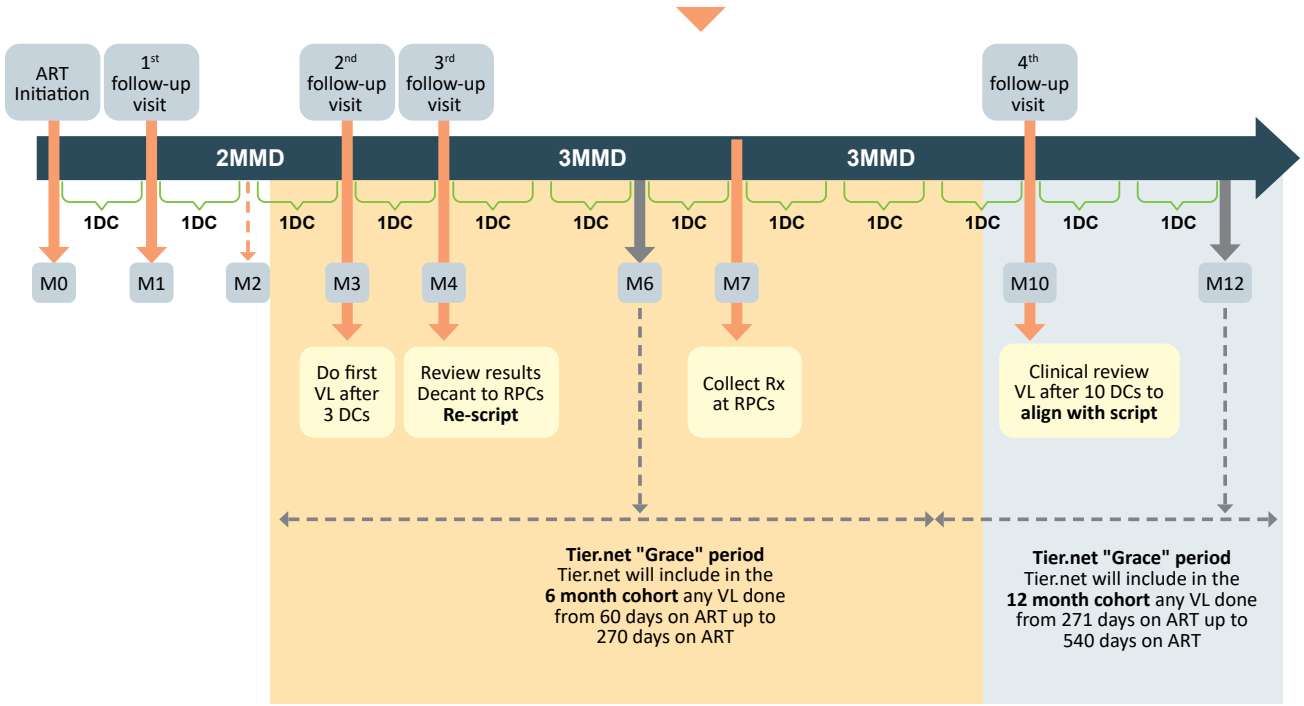
June 2023 Version 4

Republic of South Africa National Department of Health

Routine HIV VL Monitoring Schedule on ART

A dispensing cycle is defined as the number of days for which a client would have treatment if a single standard "monthly" quantity of tablets was dispensed. The term 'dispensing cycle (DC)' is preferred to the previously used term 'month' due to the potential discrepancy that may arise between the days of treatment dispensed (if 28 day pack sizes are used) and the days in a month (on average, 30 days). However, the term dispensing cycle can be applied to single pack sizes of 28 tablets (1DC) or larger pack sizes of 90 tablets (3 DCs).

Routine VL monitoring	Intervention	Comments
First VL after ART initiation	Do 1st VL after **3 dispensing cycles**	• Allows for earlier detection of factors influencing viral suppression • Allows for earlier decanting for suppressed clients to minimise visits and promote continued engagement in care • This VL will form part of the **6 month VL completion cohort** in Tier.net
Second routine VL after ART initiation (in clients who remain virally suppressed)	This VL can be done from **10 dispensing cycles** but should be aligned with the clients scripting cycle	• This VL will form part of the **12 month VL completion cohort** in Tier.net
Third routine VL after ART initiation (in clients who remain virally suppressed)	This VL can be done **from 22 dispensing cycles**, but should be aligned with the clients scripting cycle	• This VL will form part of the 24 month **VL completion cohort** in Tier.net
Fourth and all subsequent VLs	VLs will be taken at intervals of 12 dispensing cycles for all clients who remain virally suppressed	
The timing of dispensing cycles, follow-up visits, and VL monitoring is illustrated in the diagram below		



- For the 1st VL taken after 3 dispensing cycles, clients should be requested to return to the facility one DC later to review results and so that the client can be assessed for RPCs eligibility.
- For all subsequent VL monitoring (and other routine monitoring investigation) in clinically well clients: Clients should be rescripted at the same visit that their VL is taken. Clients should not be required to come back to the facility the following month for VL result review prior to rescript. Rather, recall to the facility only those clients with an elevated VL or other abnormal result.
- Facilities should ensure that results management processes are in place to ensure that results are reviewed by a clinician, that abnormal results are identified, and the client is appropriately actioned. The NHLS Results for Action (RfA) reports are a useful tool to facilitate the review of results.

! Breastfeeding women should have their VL monitored every 6 months starting from the time of delivery

VL Monitoring Algorithm for Clients on TLD

(also applicable to ALD and other DTG-containing regimens)

Routine VL monitoring for virally suppressed clients as outlined in the algorithm
"Routine HIV VL Monitoring on ART" on page 20
VL monitoring should happen every 6 DCs in a breastfeeding woman

VL < 50 c/mL

VL unsuppressed (VL ≥ 50 c/ml)
(This includes previous VL level of 50–999 and VL > 1 000 c/ml)

Do a thorough assessment of the cause of an elevated VL. Consider the possibility of:
A. **A**dherence problems (see *"Enhanced Adherence Support" on page 22*)
B. **B**ugs (Intercurrent infections)
C. In-**C**orrect ART dosage (see Annexure 5 *"Drug Dosing Chart" on page 34*)
D. **D**rug Interactions (see *"Drug Interactions with DTG and Rifampicin-containing TB Treatment" on page 13*)
E. R**E**sistance (if > 2 years on treatment)

Implement interventions to re-suppress the VL, including **Enhanced Adherence Support** if indicated
(See Annexure 3 Enhanced Adherence Counselling)
Recommend **condom use and contraception** as appropriate

Repeat VL after 3 months

Repeat **VL unsuppressed**[1] **(VL > 50 c/ml)**

Re-assess and resolve adherence issues![2]
(See *"ABCDE assessment of an Elevated Viral Load" on page 22*
and Annexure 3 *"Enhanced Adherence Support" on page 22*)

On TLD for **at least 2 years**

On TLD **less than** 2 years[3]

If **Adherence > 80%**[4], and **Two** or more consecutive **VLs ≥ 1 000 c/mL** taken two or more years after starting TLD regimen or at least one VL ≥ 1 000 c/mL and either CD4 < 200 cells/mm^3 or an opportunistic infection

If adherence still suboptimal[4], or persistent low-level viraemia (2 or more consecutive VLs between 50 and 999 c/mL)

Go to the algorithm for
"Management of Confirmed Virological Failure on TLD" on page 23

Repeat VL at next scheduled routine VL
(i.e., in 6 months' time) Intensify efforts to **resolve adherence issues** [2]

1. Due to their high genetic barrier, resistance to a first-line DTG-containing (TLD1) regimen is extremely rare. If other reasons for an unsuppressed VL have been addressed or excluded, e.g., drug interactions, and the client remains unsuppressed at their repeat VL, suboptimal adherence remains the most probable cause for non-suppression. The highest probability of improving adherence would be to remain on a once-daily, well-tolerated, fixed-dose combination regimen (TLD) while identifying and addressing the underlying root causes of non-adherence. 99,9% of these clients will re-suppress on TLD if adherent!
2. Repeat ABCDE assessment as outlined on *"ABCDE assessment of an Elevated Viral Load" on page 22*. Remember to ask about treatment side-effects, the potential cost of transport or loss of income related to clinic visits, non-disclosure, gender-based violence (GBV), and current or prior drug interactions. Current or previous drug interactions with rifampicin, carbamazepine, phenytoin, phenobarbital, or the polyvalent cations may have resulted in the development of resistance.
3. Drug interactions may also warrant an expert discussion and authorisation of a resistance test earlier than 2 years on the regimen. If necessary, discuss with an expert
4. Objective measures of good adherence include at least one of:
   a. Pharmacy refills > 80% in the last 6–12 months (if this is known)
   b. Attendance of > 80% of scheduled clinic visits in the last 6–12 months (if this is known)
   c. Detection of current antiretroviral drug/s in the client's blood or urine, if available

Note: Self-reported adherence is not considered a measure of good adherence!

ART, Antiretroviral therapy; DTG, Dolutegravir; LLV, Low-level viraemia; SOP, Standard operating procedure; TL, Third-line; TLD, fixed-dose combination of tenofovir, lamivudine, DTG; VL, Viral load.

Assessing an Elevated Viral Load

A thorough assessment is essential for any client with a viral load measuring ≥ 50 c/ml			
Adherence	A	Is adherence to medication poor? Ask about factors that may influence adherence e.g. Direct cost of clinic visits to patient, e.g. transport, loss of income, cost of paying another person to take on social responsibilities • Taking time away from existing work, finding work and/or social care responsibilities • Needing to travel for extended periods of time • Medication side-effects • Unpalatable medications • Depression or other mental health conditions • Alcohol or substance abuse • Poor social support and/or GBV • Non-disclosure Pregnant women may experience nausea/vomitting, heartburn, and constipation. Assess the need for symptomatic treatment with an anti-emetic, anti-diarrhea agent, or fiber supplement. Adherence difficulties in young children are often linked to poor tolerability of unpalatable formulations, particularly LPV/r solution. It is important to ask the caregiver about how the child tolerates the medication e.g., does the child refuse to swallow the medicine or spit, or vomit the medicine out?	**Tips** Ask open ended questions e.g. "What makes it difficult for you to collect or take your treatment?", and "How many doses have you missed this week?" Statements like "we all miss a dose now and then" can encourage a client to be more open. Create a safe and non-judgemental space for your client to discuss challenges.
Bugs	B	Check for symptoms and signs of infection. Do a TB and STI screen.	Remember that immune compromised, malnourished, and pregnant clients may not exhibit overt symptoms of TB. If in doubt, do a TB GXP.
Correct Dose	C	Is the client on the correct dose for their weight? This is especially applicable to growing children, or clients with deteriorating renal function or previous renal impairment	
Drug Interactions	D	Are there any potential drug interactions? Consider: • Other prescribed treatment e.g. rifampicin, anti-epilepsy drugs and pregnancy supplements (iron, calcium) • Over the counter treatment e.g., antacids, multivitamins • Other supplements and herbal/traditional medications e.g. St John's wort	See also ***"Drug Interactions with DTG and Rifampicin-containing TB Treatment" on page 13*** If in any doubt, call the **HIV Hotline 0800 212 506** or one of the ***"Helplines" on page 23***
REsistance	E	Consider HIV drug resistance if other causes of virological failure have been excluded and the client is adherent to their medication by an objective measure.	Refer to the algorithm ***"Management of Confirmed Virological Failure on TLD" on page 23***

Clinician considerations for providing Enhanced Adherence Counselling (EAC)

Barrier to adherence	Intervention	EAC indicated?
Difficulty getting to facility to collect treatment	Reduce unnecessary visits through enrolling client in a RPCs model or providing multi-month dispensing (MMD)	No need for EAC
Drug side effects or unpalatability impacting adherence?	Change to more palatable regimen	No need for EAC
Challenges with taking/remembering to take treatment	Provide EAC	

Enhanced Adherence Support

Enhanced Adherence Counselling (EAC) is aimed at non-stable clients presenting with adherence issues or poor treatment response and/or signs of treatment failure. Enhance Adherence Counselling focuses on:

- Providing education on the outcome of their latest clinical assessment and VL results
- Understanding what the client already knows or doesn't know regarding their treatment and the importance of VL suppression
- Doing a mental health screen
- Correcting any misconceptions and allowing flexibility around the most common barriers to adherence (such as alcohol/drug consumption, forgetting doses due to a rigid schedule, etc.).
- Assessing and understanding the barriers that affect the client's adherence
- Developing adherence strategies to overcome these

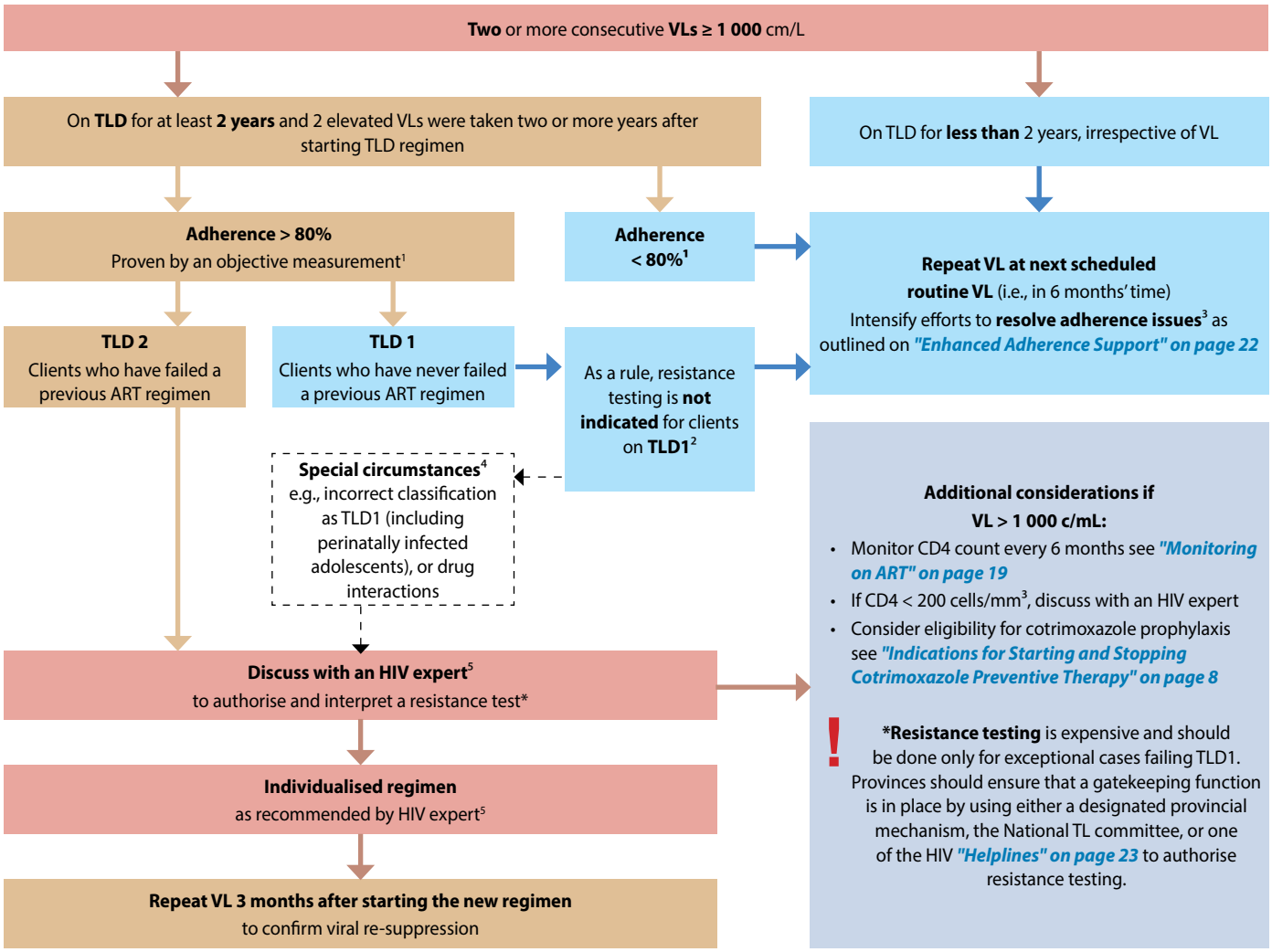
To support the above processes, the following useful tools extracted from the Differentiated Care Models Standard Operating Procedures 2023 included in the annexures:

- SOP 2 Enhanced Adherence Counselling (Annexure 3)
- Mental Health Screen (Annexure 4)
- Child and adolescent disclosure counselling for children living with HIV (Annexure 7)

'better late than never': clients should be counselled they can take their ARVs up to several hours late if they miss their chosen time

Management of Confirmed Virological Failure on TLD

(also applicable to ALD and other DTG-containing regimens)



1. Objective measures of good adherence include at least one of:
   - Pharmacy refills > 80% in the last 6-12 months (if this is known)
   - Attendance of > 80% of scheduled clinic visits in the last 6-12 months (if this is known)
   - Detection of current antiretroviral drug/s in the client's blood or urine, if available
   - Note: Self-reported adherence is not considered a measure of good adherence!
2. Due to their high genetic barrier, resistance to a first-line DTG-containing regimen (TLD1) is extremely rare. If other reasons for an unsuppressed VL have been addressed or excluded, e.g., drug interactions and the client remains unsuppressed at their repeat VL, suboptimal adherence remains the most probable cause for non-suppression. The highest probability of improving adherence would be to remain on a once-daily, well-tolerated, fixed-dose combination regimen (TLD) while identifying and addressing the underlying root causes of non-adherence. 99,9% of these clients will re-suppress on TLD if adherent!
3. Repeat the ABCDE assessment as outlined on *"ABCDE assessment of an Elevated Viral Load" on page 22*. Remember to ask about treatment side-effects, the potential cost of transport or loss of income related to clinic visits, mental health conditions, non-disclosure, poor social support, or substance abuse. If necessary, discuss with an expert or refer to other multidisciplinary team members, if available.
4. Special circumstances that may warrant a resistance test for clients on TLD1 include:
   - Incorrect classification as TLD1 (clients who declare themselves as never having had ART before, but who have actually been exposed to ART and may have failed a regimen in the past)
   - Perinatally infected adolescents: Unless a clearly documented drug history is available, perinatally infected adolescents should be classified as TLD2 due to the high likelihood of ART exposure and virological failure in the past
   - Current or previous drug interactions with rifampicin, carbamazepine, phenytoin, phenobarbital, or the polyvalent cations may have resulted in the development of resistance. Drug interactions may also warrant an expert discussion and authorisation of a resistance test earlier than 2 years on the regimen.

   In these types of exceptional circumstances, TLD1 clients with persistent virological failure despite confirmed good adherence may be discussed with an expert to authorise a resistance test on a case-by-case basis.
5. For advice from an HIV expert, approach an HIV Hotline, an infectious disease specialist, or the Third Line ART committee

If in doubt about any aspect of viral load management or switching to second-line, contact one of the following resources:

National HIV & TB Health Care Worker Hotline: **0800 212 506**

Right to Care Paediatric, Adolescent and Adult HIV Helpline: **082 352 6642**

KZN Paediatric Hotline: **0800 006 603**

ART, Antiretroviral therapy; DTG, Dolutegravir; LLV, Low-level viraemia; TL, Third-line; TLD, fixed-dose combination of tenofovir, lamivudine, DTG; VL, Viral load.

Visit Schedule for Integrated Care for the Mother-baby Pair Living with HIV

Age group	Age of child	Routine visits as per RTHB	Dispensing cycle (DC)	ART Follow-up for baby	ART Follow-up for mother	Immunisations	Feeding advice	Growth monitoring	Development	Head circumference	Vit A	Deworming	Oral Health	TB Screen	Mother's Family planning (FP)
Neonate (birth PCR positive)	1–3 week	3–6 days postnatal visit for mother and baby	1	Follow up 1 week ART initiation, then 1–2 weekly thereafter **Clinical review and renew script Switch to ABC/3TC/DTG if eligible.** Give TCA date in 2 weeks to align with 6-week well-baby visit	2 months ART provided at discharge from labour ward which will last mother until 6 week PN visit		x	x							x**
2–6 months (monthly follow-up)	4 weeks	6 weeks	2*	Clinical review Repeat script for 1DC for baby*	Postnatal clinical review and adherence check-in. Provide breastfeeding support. Provide treatment for 2 DCs (2MMD) for mother	x	x	x						x	
	6 weeks*	10 weeks	3	Clinical review Repeat script for 1DC for baby	If mother received either DMPA (Depo Provera®) or NET-EN (Nur Isterate®) after delivery, give repeat injection at this visit***	x	x	x						x	x
	10 weeks	14 weeks	4	Clinical review **and VL** Repeat script for 1DC for baby	Adherence check-in for mother Provide breastfeeding support. Provide treatment for 3 DCs (3MMD) for mother	x	x	x	x	x				x	
	14 weeks	18 weeks	5	Clinical review and **VL results review** Repeat script for 1DC for baby			x	x	x					x	
	18 weeks	22 weeks	6	Clinical review Repeat script for 1DC for baby			x	x						x	
	22 weeks	26 weeks	7	Clinical review Renew script and provide treatment for 3DCs at a time (3MMD) If any concerns, follow up at shorter intervals	Clinical review and '6-month' VL. Provide breastfeeding support. Script for and provide treatment for 3DCs at a time (3MMD). Alternatively, if VL suppressed, offer RPCs options, if this suits the PCGs needs.	x	x	x	x		x			x	x

HIV can be diagnosed at any age, and the date of ART initiation and timing of VL monitoring will depend on the date of diagnosis. The example below is for an infant with a positive birth PCR and illustrates an ART visit schedule that aligns with the well-baby visit schedule in the RTHB. However, the principles applied here also apply to children with a positive 10-week HIV PCR or a positive 6-month HIV PCR (and HIV tests done at any other time)

The principles are as follows:

1. Wherever possible, try to align the child's ART follow-up visits with the routine well-baby visit schedule in the RTHB
2. Wherever possible, try to align the mother's ART, VL monitoring, and family planning visits with that of the child's visit schedule so the mother-baby pair need only attend the facility once for both consultations on the same day
3. Wherever possible, allow the mother and baby to receive ART at the same facility

* At week 4, switch to DTG if eligible and dispense treatment for the full dispensing cycle (28 days). Review and repeat script at 6 weeks (rather than 8 weeks) to align with the RTHB visit schedule. The additional 2 weeks treatment that the mother-baby pair will have in reserve will allow for alignment with the 6-month RTHB appointment which usually happens around week 26 (compared to 6 DCs of treatment which will only provide enough treatment for 24 weeks)

** Confirm the mother's FP method choice. Inform her that the DMPA injection or the combined oral contraceptive pill (COCP) can be repeated 3-monthly, and will align well with the ART and well- baby visit schedules. Using the NET-EN 2-monthly injection will require additional visits by the mother, as a 2-monthly repeat injection will not always align with the visit schedule outlined above.

*** As per WHO recommendations[1], the repeat injection of DMPA and NET-EN can be given up to 2 weeks early. The repeat DMPA injection can be given up to 4 weeks late without requiring additional contraceptive protection. The repeat NET-EN injection can be given up to 2 weeks late without requiring additional contraceptive protection.

[1]WHO. Selected practice recommendations for contraceptive use. World Health Organization Department of Reproductive Health and Research; 2016.

Age group	Age of child	Routine visits as per RTHB	Dispensing cycle (DC)	ART Follow-up for baby	ART Follow-up for mother	Immunisations	Feeding advice	Growth monitoring	Development	Head circumference	Vit A	Deworming	Oral Health	TB Screen	Mother's Family planing (FP)
6–12 months **3 monthly follow-up**	**30 weeks**	**7 months**	8		Recall to the facility only if the VL is ≥ 50 c/mL		x	x						x	
	34 weeks	**8 months**	9				x	x						x	
	38 weeks	**9 months**	10	Clinical review Renew script and provide treatment for 3DCs at a time (3MMD) If any concerns, follow up at shorter intervals	Provide treatment for 3DCs at a time (3MMD) unless in RPCs Provide breastfeeding support.	x	x	x	x					x	x
	42 weeks	**10 months**	11				x	x						x	
	46 weeks	**11 months**	12*				x	x						x	
	52 weeks*	**12 months (of 30 days)**	13	Clinical review and VL Renew script and provide treatment for 3DCs at a time (3MMD) If any concerns, follow up at shorter intervals	Clinical review and VL Provide breastfeeding support Renew script and provide treatment for 3DCs at a time (3MMD) or offer RPCs options/rescript for RPCs	x	x	x	x	x	x	x	x	x	x
13–24 months **3 monthly follow-up**	**56 weeks**		14	Recall to the facility only if the VL is ≥ 50 c/mL											
	60 weeks		15												
	64 weeks	**15 months**	16	Clinical review Renew script and provide 3DCs of treatment at a time (3MMD) If any concerns, follow up at shorter intervals	Provide treatment for 3DCs at a time (3MMD) Provide breastfeeding support.		x	x	x		x	x		x	x
	68 weeks		17												
	72 weeks		18												
	76 weeks	**18 months**	19	Clinical review Renew script and provide 3DCs of treatment at a time (3MMD) If any concerns, follow up at shorter intervals	6-monthly VL if breastfeeding. Renew script and provide treatment for 3DCs at a time (3MMD) or offer RPCs options/rescript for RPCs. Try to align ART for mother and baby with the well-baby visit schedule	x	x	x	x		x	x		x	x
	80 weeks		20												
	84 weeks		21												
	88 weeks	**21 months**	22	Clinical review Renew script and provide 3DCs of treatment at a time (3MMD) If any concerns, follow up at shorter intervals	Provide treatment for 3DCs at a time (3MMD) Provide breastfeeding support.		x	x						x	x
	92 weeks		23												
	96 weeks		24												
2 until < 5 years **3 monthly follow-up**	**24–59 months**	**At 24 months and 6-monthly thereafter**		**Follow-up visits at 3DC intervals** Renew script and provide treatment for 3DCs at a time (3MMD) Repeat VL at 12 DC intervals If any concerns, follow up at shorter intervals	6-monthly VL if breastfeeding. Renew script and provide treatment for 3DCs at a time (3MMD) or offer RPCs options/rescript for RPCs **Try to align with child's yearly well-baby visit schedule**		Up to 2 years	6-monthly	At 3 years		6-monthly	6-monthly	yearly	3-monthly	3-monthly

Visit Schedule for Integrated Care for Clients already on ART when diagnosed with Drug-sensitive TB

GENERAL PRINCIPLES

- Clinicians should provide integrated TB management at clinical consultation visits. Failure to combine care leads to increased visit schedules and significantly increases the risk of disengagement and loss-to-follow-up (LTF).
- This schedule is for a standard DS-TB treatment (Rx) regimen consisting of 2 months of intensive phase Rx (IP) and 4 months of continuation phase (CP) Rx after a negative smear at the end of the IP.
- This schedule applies to a client already on ART when diagnosed with drug-sensitive TB. A client diagnosed with HIV and TB can also benefit from 2-months supply of ART and TB continuation phase to support adherence and retention.

Integrated visit schedule for a client on ART who develops DS-TB (not in RPCs)		**Months (M) on TB Treatment (Rx)**						
		Intensive Phase (IP) (months 1-2)				**Continuation Phase (CP) (months 3-6)**		
		TB M0	**TB M1 (4 completed weeks)**	**7 wks**	**TB M2 (8 completed weeks)**	**TB M4 (16 completed weeks)**	**23 wks**	**TB M6 (24 completed weeks)**
Integrated TB/ ART clinical consult	TB screening as part of routine care	TB diagnosis and TB Rx initiation	Clinician-managed care at facility		Assess smear conversion and transition to CP of TB Rx, if smear result is negative	Clinician-managed care at facility		Confirm TB Rx completion Assess for RPCs enrolment
Investigations	TB GeneXpert and any other investigations as clinically indicated	Review result		Smear	Review result		Smear	Review end-of-Rx result
ART/TB script	Script ART for 1 month	Combined script for 1 month of IP TB Rx and ART	Combined script for 1 month of IP TB Rx and ART		Combined script for 2 months** of CP TB Rx and ART	Combined script for 2 months** CP of TB Rx and ART"		If eligible for RPCs: RPCs ART script for 6 months
ART-TB drug supply dispensed by facility	Dispense ART for 1 month	Dispense 1 month of IP TB Rx and DTG boosted ART	Dispense 1 month of IP TB Rx and DTG boosted ART		Dispense 2 months of CP TB Rx and 2 months DTG boosted ART	Dispense 2 months of CP TB Rx and 2 months DTG boosted ART		Dispense 3 months of ART
Ask client to return:	If client has TB symptoms or is unwell, ask client to return in 5-7 days for review *	After 4 weeks for clinical review	After 3 weeks for sputum smear	After 1 week for smear results	After 8 weeks for clinical review	After 7 weeks for end of Rx smear	After 1 week for smear results	If eligible and enrolled in RPCs: return for next ART supply at RPCs pick-up point after 3 months

OVERVIEW OF PRINCIPLES FOR TB MANAGEMENT IN PLHIV WHO ARE RECEIVING ART THROUGH AN RPCS MODEL

- If an RPCs client screens positive for TB symptoms at their RPCs clinical review visit but is not acutely unwell, the clinician will rescript for RPCs.
- **If acutely unwell, return to clinician-managed care and do not script for RPCs again. Follow approach in table above.**
- Results (TB investigations and VL) should be reviewed in 5-7 days, or sooner if possible*
- If the patient is diagnosed with TB and/or their VL is ≥ 50c/mL, the patient will return to regular clinician-managed care and should be re-assessed for RPCs enrolment when TB Rx is completed and/or their VL is < 50 c/mL again).
- If the patient **is not diagnosed** with TB (and their VL was suppressed), the patient will continue in RPCs.

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TDF/FTC
Tenofovir disoproxil fumarate (TDF) & emtricitabine (FTC)

PROTEASE INHIBITORS (with booster drug)

ATV/r
Atazanavir (ATV) & ritonavir (r)

DRV/r
Darunavir (DRV) & ritonavir (r)

LPV/r
Lopinavir (LPV) & ritonavir (r)

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SINGLE-TABLET REGIMENS

ALD
Abacavir (ABC), Lamivudine (3TC) & Dolutegravir (DTG)

TLD
Tenofovir disoproxil fumarate (TDF), Lamivudine (3TC) & Dolutegravir (DTG)

TAF-LD
Tenofovir alafenamide (TAF), Lamivudine (3TC) & Dolutegravir (DTG)

TAF-ED
Tenofovir alafenamide (TAF), Emtricitabine (FTC) & Dolutegravir (DTG)

TEE
Tenofovir disoproxil fumarate (TDF), Emtricitabine (FTC) & Efavirenz (EFV)

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ARV, antiretroviral; FDC, fixed-dose combination; HIV, human immunodeficiency virus.

Reference: 1. Van Galen KA, Nellen JF, Nieuwkerk PT. The effect on treatment adherence of administering drugs as fixed-dose combinations versus as separate pills: systematic review and meta-analysis. *AIDS Research and Treatment* 2014. http://dx.doi.org/10.1155/2014/967073.

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Integrated visit schedule for a client in RPCs who develops DS-TB		Months (M) on TB Treatment (Rx)						
		Intensive Phase (IP) (months 1-2)				Continuation Phase (CP) (months 3-6)		
		TB M0 (Rx initiation)	TB M1 (4 completed weeks)	7 wks	TB M2 (8 completed weeks)	TB M4 (16 completed weeks)	23 wks	TB M6 (24 completed weeks)
Integrated TB/ ART clinical consult	RPCs clinical visit with clinician consultation	TB diagnosis and TB Rx initiation De-register from RPCs and continue care at a facility	Clinician-managed care at facility		Assess smear conversion and transition to CP of TB Rx, if smear result is negative	Clinician-managed care at facility		Confirm TB Rx completion Assess for RPCs. If eligible for RPCs: Re-enrol in RPCs
Investigations	VL, eGFR, TB symptom screen and routine TB GeneXpert Any other investigations as clinically indicated	Review result		Smear	Review result		Smear	Review end-of-Rx result
ART/TB script	Repeat 6 month ART script for RPCs (unless acutely unwell)	Script 1 month of IP TB Rx and additional DTG****	Script 1 month of IP TB Rx and additional DTG****		Combined script for 2 months** of CP TB Rx and ART	Combined script for 2 months** of CP TB Rx and ART		If eligible for RPCs: RPCs ART script for 6 months
ART-TB drug supply dispensed by facility	Dispense first 3 months of ART supply from facility***	Dispense 1 month of IP TB Rx	Dispense 1 month of IP TB Rx		Dispense 2 months of CP TB Rx and 2 months of DTG boosted ART	Dispense 2 months of CP TB Rx and 2 months of DTG boosted ART		Dispense 3 months of ART
Ask client to return:	If the client has TB symptoms ask the client to return in 5-7 days for review*	After 4 weeks for clinical review	After 3 weeks for sputum smear	After 1 week for smear results	After 8 weeks for clinical review	After 7 weeks for end of Rx smear	After 1 week for smear results	If eligible and enrolled in RPCs: return for next ART supply at RPCs pick-up point after 3 months

* If the facility does not have a reliable results management and/or recall system in place, it will require the patient to return to the facility within 5-7 days for a combined review of their TB and VL results. If the facility has an effective result management and recall system in place, it may recall only those clients with a positive TB diagnosis and/or a VL ≥ 50 c/mL.

** For TB with longer continuation phases, a 3-month supply can be considered (see DMOC SOP 4) to align TB/ART Rx supply length between investigations and clinical consultations.

*** Clients in RPCs who screen positive for TB but are not acutely unwell can remain in their RPCs until their TB diagnosis is confirmed. After a positive TB screen, the client will continue to be scripted for RPCs with the facility providing the first 3 months ART supply and the RPCs providing the second three month ART supply. Where a facility has an ART stock shortage concern, the script can be adjusted to the facility providing the first 2 months ART supply and the RPCs providing the second 4 months ART supply (4MMD). If the client is subsequently diagnosed with TB, the client will be returned to facility-based care. As they have already received a 3-month supply of ART, they will have ART on hand to cover their intensive phase, and will only require boosted DTG to be scripted. Thereafter ART to be dispensed again at TB M2 (i.e. after 2 completed months of TB treatment). However, where the patient only received a 2-month ART supply because of facility stock shortages, the ART supply on hand will not be sufficient for the full intensive phase of TB treatment, as the ART would have been dispensed a number of days before TB treatment was initiated. ART will need to be topped up at TB M1 to ensure sufficient supply to TB M2. The table accounts for when ART will need to be supplied again with TB treatment based on the patient having received a 3 month ART supply.

**** DTG boosting is required when the client is on rifampicin containing TB treatment. In adults and adolescents, the dosing frequency of DTG should be increased to 50 mg 12-hourly. If on TLD FDC, then add DTG 50 mg 12 hours after TLD dose. For DTG-boosting in children, see "Drug Dosing Chart" on page 34. DTG boosting should continue until 2 weeks after TB treatment has been completed.

Annexures available online at: https://ojs.sabinet.co.za/index.php/sapj/article/view/273/148

An overview of thyroid disorders and their management

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Abstract

Disorders of the thyroid gland are frequently encountered in the clinical practice setting and typically fall into one of two categories, namely hypothyroidism (i.e. deficient levels of circulating thyroid hormone), or hyperthyroidism (or thyrotoxicosis) that involves abnormally high levels of thyroid hormone in the blood stream. This article provides a high-level overview of thyroid function, the two major pathophysiological abnormalities of the thyroid gland, as well as treatment modalities aimed at managing patients with thyroid pathology. In addition, a brief description of two major autoimmune conditions of the thyroid gland, namely Graves' disease and Hashimoto's thyroiditis, is also provided.

Keywords: thyroid gland, thyroxine, triiodothyronine, iodide, hypothyroidism, hyperthyroidism, goitre, thyroid storm, Hashimoto's thyroiditis, Graves' disease, exophthalmos, cretinism, myxoedema

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Introduction

Disorders of the thyroid gland are frequently encountered in the clinical practice setting and typically fall into one of two categories, namely hypothyroidism (i.e. deficient levels of circulating thyroid hormone), or hyperthyroidism (or thyrotoxicosis) that involves abnormally high levels of thyroid hormone in the bloodstream. The two thyroid hormones, T_3 and T_4, play a vital role in a wide variety of body functions, with particular reference to normal growth, neurological and sexual development, as well as basal metabolism.

Overview of thyroid pathophysiology

The thyroid gland forms part of the peripheral endocrine system (i.e. those endocrine glands that are situated *outside* of the central nervous system). It is characteristically shaped like a bowtie (or butterfly), with the central isthmus joining together its two lateral lobes. It is situated in the midline, anterior to the larynx and trachea, and at the level of the C5 to T1 vertebrae. The highly vascular thyroid gland secretes two blood-borne thyroid hormones that regulate the rate of the body's basal metabolism (including energy levels and body temperature), as well as calcitonin that opposes the net effect of parathyroid hormone (PTH) on plasma calcium levels, in the regulation of calcium metabolism. The thyroid hormones also play a vital role in normal growth and development, and can augment the functions and effects of the sympathetic nervous system.[1-5]

The two thyroid hormones, which are secreted by the follicular cells, are triiodothyronine (T_3) and thyroxine (tetraiodothyronine or T_4), which are both synthesised from tyrosine and iodine. Tyrosine is a non-essential amino acid that is synthesised in the body, and the iodine is derived from the diet (i.e. via food and water intake, but could also be supplemented with medication). In the body, the negatively charged iodide ions (I^-) are actively transported from the bloodstream, via the follicular cells, into the colloid of the thyroid gland against a steep concentration (electrochemical) gradient by the sodium-iodide-symporter.[1-5]

About 90% of the secreted T_4 is converted to T_3 in peripheral target tissues outside of the thyroid gland. This process of activation mainly takes place in the liver and kidneys. T_3 is significantly more potent than T_4. Thyroid hormone secretion is regulated via the hypothalamic-pituitary-thyroid gland axis. Thyroid-stimulating hormone (TSH) from the anterior pituitary gland regulates the secretion of T_3 and T_4 into the bloodstream. In turn, TSH-secretion is regulated by thyrotropin-releasing hormone (TRH) from the hypothalamus. Both T_3 and T_4 are capable of exerting negative, or inhibitory, feedback upon the release of TRH and TSH. Refer to Figure 1.[1-5]

Figure 2 illustrates the peripheral metabolic pathways of thyroxine (T_4).

Abnormal secretion of the thyroid hormones

There are two main categories of abnormal thyroid gland functioning, namely hypothyroidism (i.e. insufficient thyroid hormone secretion) and hyperthyroidism (i.e. an excessive secretion of the thyroid hormones).

Hypothyroidism

Hypothyroidism refers to low plasma levels of the thyroid hormones due to their inadequate production or secretion by the thyroid gland. Inadequate levels of circulating thyroid hormone during foetal development and early infancy will result in a condition known as cretinism, which is characterised by dwarfism

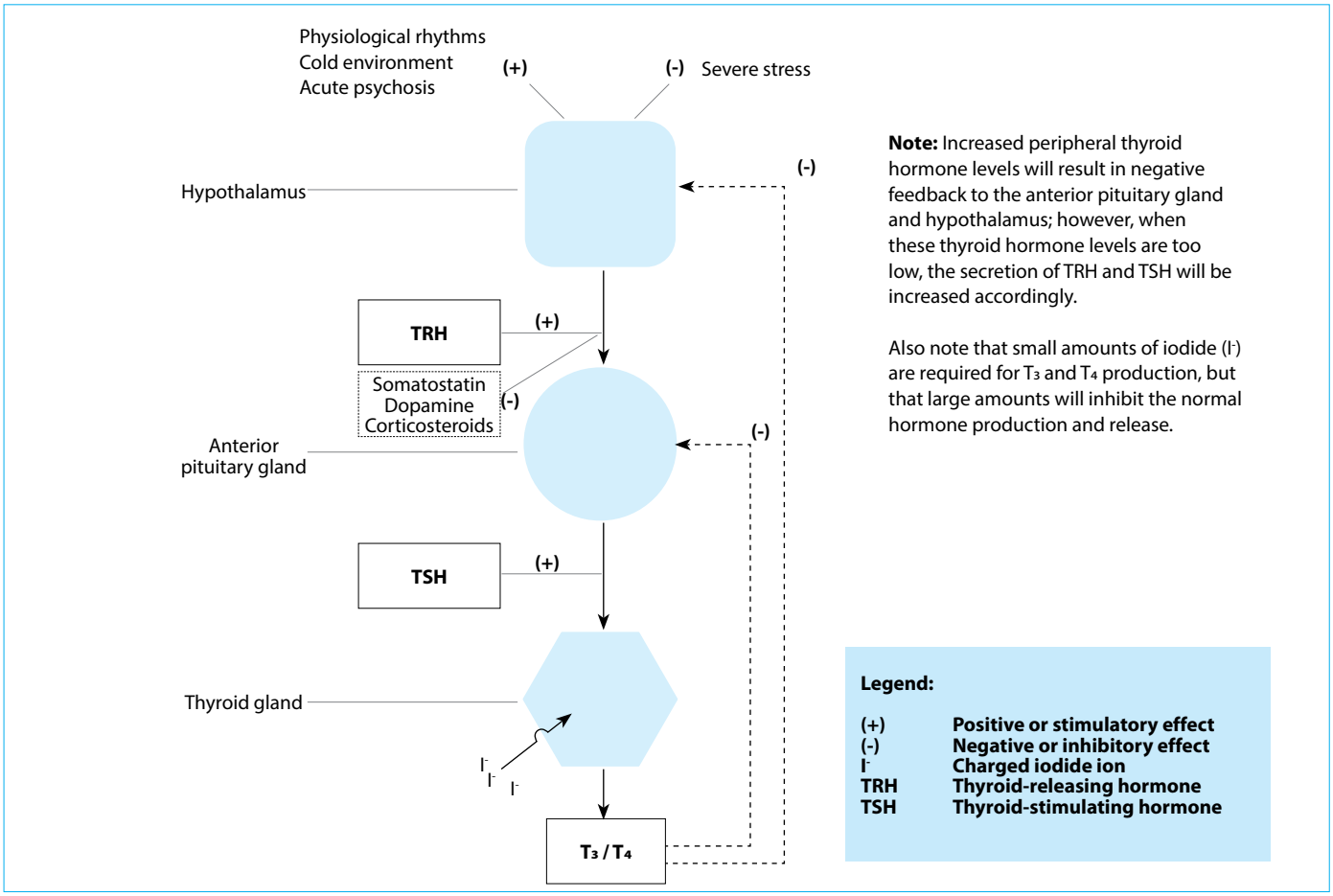

Figure 1: Simplified diagram of the hypothalamic-pituitary-thyroid gland axis[3]

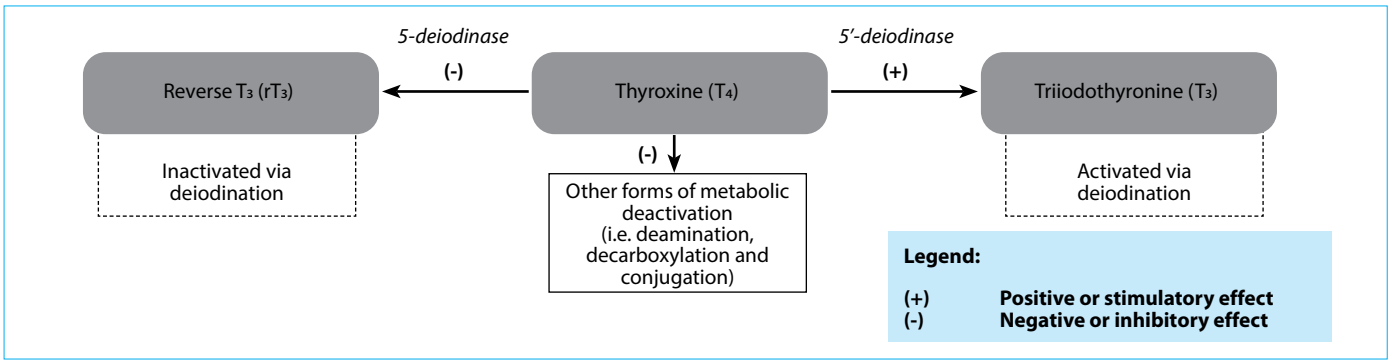

Figure 2: The peripheral metabolism of thyroxine[3]

and irreversible mental retardation. Three underlying mechanisms may result in the hyposecretion of thyroid hormone:[1,3-5]

- Inadequate dietary intake of iodine, which is probably the most common cause of hypothyroidism worldwide
- A secondary insufficiency due to deficient levels of TRH and/or TSH (a few drugs are, amongst other causes, capable of inducing an iatrogenic hypothyroidism.[3] These include the iodides and amiodarone, lithium, the thionamides, ethionamide and aminoglutethimide.)
- As a result of primary gland failure of the thyroid itself (or following its surgical removal via thyroidectomy).

Sufficiently severe cases of hypothyroidism produce and are subsequently referred to as myxoedema. Patients with hypothyroidism experience a generalised slowing-down of all their body functions. Goitre, which refers to enlargement of the thyroid gland, may or may not be present in these patients. A wide variety of clinical signs and symptoms may accompany the condition, both physically and mentally (see Figure 3). In children, there may be a marked hindrance of normal growth and development, including mental retardation.[3,4]

In addition, in the case of Hashimoto's disease (also referred to as Hashimoto's thyroiditis, and considered to be a very common cause of hypothyroidism in adults), patients develop hypo-

functioning of the thyroid gland in the presence of antithyroid auto-antibodies. This condition is characterised by lymphocytic infiltration of the gland itself, and a gradual loss of both thyroid tissue and function.[6] The two major thyroid antigens in patients with Hashimoto's disease are thyroglobulin (Tg) and thyroid peroxidase (TPO), with highly-specific IgG-antibodies against these targets that are present in the serum. However, it is believed that these antibodies are of a somewhat lesser importance in the pathogenesis of the disease, with T-cell mediated cytotoxic effects and activated apoptotic pathways playing a more significant role in the destruction of the thyroid gland.[6]

Hyperthyroidism

The condition is also referred to as thyrotoxicosis, and is the result of excessive, or hypersecretion of thyroid hormone. Hyperthyroidism is most commonly caused by an autoimmune condition known as Graves' disease. The other two causative mechanisms of hyperthyroidism are:

- Thyroid tumours that secrete excessive amounts of thyroid hormone
- A secondary excess due to abnormally high levels of TRH or TSH.[1,5]

In some cases, a subacute thyroiditis (or inflammatory thyroid disease) may also occur.[4]

Common signs and symptoms are highlighted in Figure 3.

Graves' disease is also referred to as toxic goitre. In this autoimmune disorder, antibodies against thyroidal antigens are produced by activated B-lymphocytes. In particular, these antibodies are of the TSH-R Ab [stim] type, meaning that they stimulate the TSH-receptors on the cells of the thyroid gland. In addition, orbital fibrocytes may be stimulated in the same way, ultimately resulting in wide-ranging remodelling of the tissues surrounding the eye. This produces the characteristic protrusion of the eyeballs, referred to as exophthalmos. It follows that the stimulation of thyroidal TSH-receptors will result in an overproduction of thyroid hormones.[3,4]

Laboratory diagnosis of thyroid disorders

Thyroid function tests may be performed, which will typically include the levels of TSH and free T_4, as well as T_3, in the blood -stream. In hypothyroidism, the levels of T_3 and T_4 will be low, with a compensatory increase in the level of TSH. The reverse is found in thyrotoxicosis, where the TSH-level will be decreased, and the free levels of the thyroid hormones conversely increased.[1,5]

The best indicators of adequate thyroid hormone replace therapy, are the TSH and T4- serum levels.[7]

Pharmacology of thyroid and antithyroid drugs

Drug therapy used in the management of thyroid conditions have been utilised for more than a century. Antithyroid drugs (ATDs) are used in the management of hyperthyroidism, whilst drugs used to restore normal thyroid hormone concentrations in body tissue, are used in the management of hypothyroidism (i.e. thyroid hormone replacement therapy). The latter is aimed at providing symptomatic relief, and in newborn infants to prevent neurological deficits (i.e. cretinism), as well as to reverse the biochemical abnormalities associated with hypothyroidism.[3,4,8]

Non-pharmacological management

Non-pharmacological measures can also be used in the management of hypo- and hyperthyroidism. Hyperthyroidism may either be managed by conservative treatment (i.e. ATDs) or by reduction or ablation of the thyroid tissue (e.g. radioactive iodine, thyroidectomy).[12] In the management of hyperthyroidism, the surgical removal of the hyper-secreting thyroid gland is an option in patients with clinical symptoms, which include:[9]

- Large thyroid (> 80 g)
- Severe ophthalmopathy
- Decreased response to ATDs

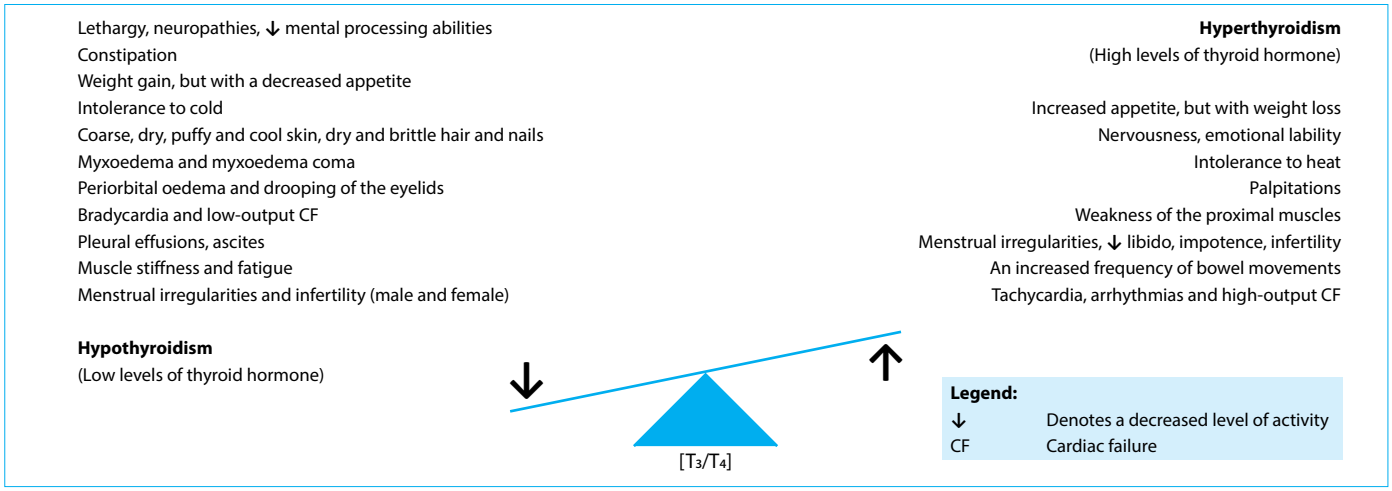

Figure 3: Common signs and symptoms or hypothyroidism *versus* hyperthyroidism[3,4]

Symptomatic hypothyroidism

- TSH-level > 10 mU/litre
- Treatment with levothyroxine (T_4), probably for life
- Liothyronine (T_3) may be used when a rapid response is required (it is more potent and has a higher bio-availability, but a shorter t½ when compared to T_4)

Sub-clinical hypothyroidism

- TSH-level between 5 and 10 mU/litre; free serum thyroxine-level within its reference range
- Routine medicine management is controversial
- Levels should be confirmed after 3 to 6 months and management re-assessed

Symptomatic hypothyroidism with normal TSH-levels

- Assess for possible alternative diagnoses
- Treat accordingly
- Test-dosages of levothyroxine may be initiated to assist in making the diagnosis

Figure 4: Overview of the management of hypothyroidism[3,4,7,10,13,14]

Following a thyroidectomy, hyperthyroidism may be persistent post-surgery in 0.6 % to 17.9 % of patients suffering from Graves' disease, and especially in children. However, the complications of surgery most frequently include hypothyroidism, and less commonly hypoparathyroidism and vocal cord abnormalities.[8,9]

The management of hypothyroidism will depend on the levels of TSH and the presenting symptoms of the patient. Refer to Figure 4 for an overview of the management of hypothyroidism.[10]

Hyperthyroidism

Methimazole, carbimazole, and propylthiouracil (PTU) are relatively simple molecules known as thionamides, and contain a sulfhydryl group and a thiourea moiety within a heterocyclic structure; these drugs are also the mainstay of antithyroid-drug therapy.[8,11,12]Collectively they are referred to as the antithyroid drugs (ATDs). Their main mechanism of action is through the blockade of thyroid hormone synthesis by inhibition of thyroid peroxidase. This enzyme catalyses iodide oxidation, iodination of tyrosine residues onto thyroglobulin, and coupling of the iodotyrosines (monoiodotyrosine, MIT, and diiodotyrosine, DIT) to form the thyronines, tetraiodothyronine or thyroxine (T_4), and triiodothyronine (T_3). An additional effect of PTU is to inhibit monodeiodination of thyroxine to triiodothyronine.[8,11,12] They also have immunosuppressive actions, which are useful in the management and treatment of Graves' disease.

Antithyroid drugs are used in two ways:[8]

- As the primary treatment for hyperthyroidism
- Used in preoperative preparation before radiotherapy or surgery.

The following conditions may be managed with ATDs: Graves' disease, toxic adenoma, and toxic multinodular goitre. In the case of toxic adenoma and toxic multinodular goitre, ATDs are used as a tool to prepare the patient for more definitive treatment. ATDs are used as the primary treatment option in pregnant patients, as well as in children and adolescents.[11,12] It is recommended for the administration of methimazole, specifically during pregnancy, to avoid liver failure associated with propylthiouracil.[14]

When prescribed for Graves' hyperthyroidism, these drugs are used to induce a remission, which is defined as having normal thyroid hormone levels for one year after drug treatment has been stopped.[11,12]

In the management of hyperthyroidism, and when patients are fully compliant with the medicines prescribed, the ATDs may be highly effective. The choice of drug to be used is based on a decision made between the prescriber and the patient. However, methimazole has the advantage of a once-daily dosing regimen and serum thyroxine and triiodothyronine levels decrease more rapidly in patients treated with this drug. The risk of agranulocytosis is also lower with methimazole, and when used in moderate dosages may improve compliance and makes this drug preferable to propylthiouracil.[8,11]

Once a patient has been started on treatment of ATDs, follow-up testing of thyroid function should be undertaken every four to six weeks, until the thyroid function is stable or until the patient is diagnosed as being euthyroid (i.e. having normal thyroid function). Clinically most patients improve considerably after four to twelve weeks; drug dosing can be reduced to maintain normal thyroid function. Administering the incorrect dosage, or not monitoring the dosage, can produce hypothyroidism or even goitre. Treatment with ATDs will normally last for 12 to 18 months.[8]

The term, thyroid storm, refers to a rare, potentially life-threatening, overexaggerated expression of hyperthyroidism, during which the patient may develop the following clinical manifestations:

- Severe agitation and a state of mental confusion
- Hyperthermia
- Overt tachycardia, which may be accompanied by acute cardiac failure
- Loss of consciousness.

Drugs that are typically used in the management of such an episode, include carbimazole, Lugol's solution, propranolol and a suitable glucocorticosteroid. In addition, the patient should be admitted to an intensive care unit and general supportive measures will need to be instituted.[7]

Side-effects experienced with ATDs

ATDs are associated with side-effects that may range from being minor, to being potentially life-threatening or even lethal. Methimazole has dose-related side-effects, whereas

propylthiouracil side-effects seem to be less associated with the actual dosage. The milder side-effects are usually self-limiting and are observed in less than 5% of cases; these side-effects seem to be noticed during the initial phases of treatment when the daily dosage administered is higher than usual.[11,12]

When more severe side-effects are experienced with one agent, another thionamide can serve as a substitute; however, cross-sensitivity has been described in as much as 50% of patient cases.[8,11,12] Side-effects should be evaluated and if serious the drug should be discontinued. Side-effects of the ATDs are listed in Table I and have been provided in the form of a checklist, which may be utilised by the pharmacist in the practice setting.[11,12]

β-*adrenergic blockers*

β-adrenergic blockers are used in symptomatic management of hyperthyroidism due to Graves' disease or toxic nodules awaiting surgery. They are used to reduce the sympathomimetic symptoms induced by hyperthyroidism, such as palpitations, anxiety and tremors, and should be discontinued once the patient becomes euthyroid. All β-blockers may be used in the management of hyperthyroidism; atenolol and nadolol may improve compliance as they only necessitate a once-daily dosing routine. Propranolol may be used in the acute management of thyroid storm. β-blockers should still be used with caution in patients with asthma and heart failure as co-morbid conditions.[7,11]

Radioactive iodine (RAI)

Recurrent hyperthyroidism and Graves' disease may be treated with radioactive iodine. RAI is used as the β- particles emitted causes destruction of thyroid tissue with the end-goal of achieving a patient with either euthyroid or hypothyroid levels. Sodium iodide 131 (^{131}I) is the RAI of choice in the treatment of Graves' disease and toxic autonomous nodules. RAI is a colourless and tasteless liquid. Dosing regimens and the contact-time following the administration of RAI is not well established; however, low dosages may be more convenient for the patient.[11,12]

Iodides

Iodine is a temporary solution that inhibits the release of thyroid hormones for only a few days or weeks (one to two weeks), and for this reason its usefulness is limited to the preparation of patients with Graves' disease for surgery, as well as to treat patients suffering from a thyrotoxic crisis (thyroid storm). The recommended daily adult iodide intake is 150 mcg, up to 250 mcg for children and 200 mcg during pregnancy and lactation. However, chronic use of iodides in pregnancy should be avoided and fetal goitres might result.[3] The inhibitory effect is achieved via the blocking of hormone release, by interfering with hormone biosynthesis through competing with intrathyroidal iodide use. This decreases the size and vascularity of the thyroid gland. Preparations are

Table I: Side-effects of the antithyroid drugs[3,4,11,12,14]

Body system	Side-effect	Frequency (and drug involved)	Experienced by the patient (✓ or ×)
Blood	Mild leukopenia	Relatively frequent	
	Agranulocytosis	Uncommon	
	Aplastic Anaemia	Very rare	
	Thrombocytopenia	Very rare	
	Pancytopenia	Very rare	
Skin	Skin rash	Very common	
	Urticaria	Very common	
	Itching	Very common	
	Generalised rash	Very rare	
	Alopecia	Very rare	
Hepatic (liver)	Hepatocellular necrosis	Rare (PTU)	
	Cholestasis	Very rare (MMI)	
Collagen	Arthralgia	Common	
	SLE-like syndrome	Very rare (PTU>MMI)	
	Vasculitits	Very rare (PTU)	
Embryopathy	Choanal atresia, oesophageal atresia, cardiac defects, aplasia cutis	Very rare (MMI)	
	Situs inversus ± dextrocardia, unilateral kidney a/dysgenesis, cardiac outflow tract defect	Very rare (PTU, uncertain)	
Miscellaneous	Loss of taste	Rare (MMI)	
	Hypothrombinaemia	Rare (PTU)	
	Insulin auto-antibodies	Very rare	

[MMI = methimazole; PTU = propylthiouracil; SLE = Systemic Lupus Erythematosus]

available as either a saturated potassium iodide solution (SSKI) or as a Lugol's solution.[11,12]

Hypothyroidism

When hypothyroidism is left untreated it can result in cardiac failure, psychosis, and coma.[13] Thyroxine-replacement therapy is highly effective and has been used in its rudimentary form since 1891.[13] Correcting myxedema in elderly patients with underlying coronary artery disease should be done with caution as the low levels of thyroid hormone could be providing protection to the heart against, e.g., myocardial infarction. Since the development of the fetal brain depends on maternal thyroxine, a 25-30% increase in thyroxine dose may be necessary in pregnant, hypothyroid patients.[3] The major indications for thyroid-replacement therapy remains:[14]

- Hypothyroidism
- Cretinism
- TSH suppression therapy in patients suffering from thyroid cancer.

Sherwood noted that replacement thyroid hormone pills are used to treat hypothyroidism, except when it is caused by an iodine deficiency, in that case, dietary iodine is prescribed. Levothyroxine (T_4; L-thyroxine) is a synthetic thyroid hormone and remains the drug of choice for thyroid-replacement therapy as it is chemically stable, not expensive, and with uniform potency.[15] Dosages of levothyroxine (LT_4) can be related to bodyweight (dosed at 1.8 µg per kg in adults, 0.5 µg per kg in older adults) and is dosed at higher levels in infants (10-15 mcg/kg/day) and young children.[10,14] When therapy is initiated it should be at the lower end of the calculated dose; i.e. for a 70 kg adult, 125 µg per day.[10] To initiate therapy at 25-50 µg per day and titrating upwards is unnecessary and prolongs the desired response to treatment.[10,15] Dosages should be titrated using serum thyrotropin concentrations and should be undertaken four to six weeks after a new thyroxine dosage has been prescribed. Thereafter, this should be done annually, or whenever a patient presents with persistent symptoms of either hypo- or hyperthyroidism.[1,10,14]

The target level of treatment is determined by the following:[10]

- The patient expressing a sense of well-being, with signs and symptoms decreasing in frequency and severity
- TSH-levels at the lower end of the reference range (0.4 to 2.5 mU/litre).

It is important to avoid a fully-suppressed TSH (< 0.1 mU/litre); each patient should be assessed using TSH-levels and symptoms, and dosed individually.[10] Patient counselling when initiating the therapy should include the advice as listed in Table II.

Side-effects experienced with levothyroxine therapy

Side-effects experienced to thyroid-replacement therapy are related to excessive thyroid hormone action and may include the following:[5,10,12]

- Symptomatic thyrotoxicosis
- Subclinical thyrotoxicosis (with an increase in bone loss)
- Atrial tachyarrhythmias
- Heart failure
- Angina pectoris
- Myocardial infarction.

Patients who were previously diagnosed with underlying ischaemic heart disease may exacerbate myocardial ischemia once euthyroidism has been established: [10,12] Synthetic products very rarely produce allergic or idiosyncratic reactions, as were previously experienced with the natural or animal-derived products.[5]

Hyperthyroidism may lead to a decrease in bone density due to hyper-remodelling of the cortical and trabecular bone, which could result in an increased likelihood of bone fractures.[5] Acute sympathomimetic symptoms and hair loss have also been experienced after thyroxine treatment has been initiated.[13]

Conclusion

The thyroid gland plays a vital role in the maintenance of a normal basal metabolism in the human body. Abnormalities in thyroid

Table II: Patient advice when initiating levothyroxine therapy[10]

Patient advice	Experienced by the patient (✓ or ×)
It may take a week or more for you to start feeling better. Levothyroxine has a half-life of seven days.	
If you miss one dose, the effect might not be noticeable (due to the long half-life), take as soon as you remember.	
Other symptoms (e.g. muscle stiffness/weakness and mental effects may take several months to resolve once the chemical imbalance has been corrected).	
Levothyroxine should be taken on an empty stomach, as it will maximise absorption.	
Treatment will be life-long, and dose adjustments will only be made according to hormone (thyroid) levels. Hormone levels should be taken once a year.	
The following drugs should be avoided or taken with caution when taking levothyroxine therapy: Drugs that will **prevent absorption** of levothyroxine (e.g. calcium salts, ferrous sulphate, aluminium hydroxide, cholestyramine). Drugs that **increase the clearance** of levothyroxine, in other words drugs that will cause a decrease in levothyroxine levels (e.g. phenytoin, carbamazepine, phenobarbitone and rifampicin).	

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Reference: 1. Euthyrox® Tablets approved package insert. February 2020.

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For full prescribing information please refer to the package insert approved by the Medicines Regulatory Authority. MERCK (Pty) Ltd. Reg. No.1970/004059/07. 1 Friesland Drive, Longmeadow Business Estate South, Modderfontein, 1645. Tel. (011) 372-5000. Report adverse events to drug.safety.southeastafrica@merckgroup.com or + 27 11 372 5304 (Fax line). ZA-EUT-00075 March 2023.

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hormone levels could, therefore, have far-reaching effects on various body systems, organs and tissues. Such abnormalities typically fall into one of two categories, namely hypo- or hyperthyroidism, and require effective treatment to either replace the deficient levels of thyroxine in the bloodstream, or to antagonise the excessive levels of circulating thyroid hormone. Patients who are using such therapies in the long-term will require additional monitoring and support by the multidisciplinary team, including the pharmacist.

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Self-medication among medical students: a systematic review and meta-analysis of prevalence, causes, common drugs, and sources of information

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Abstract

Self-medication is one of the most important public health challenges, especially for medical students. Despite the extensive studies conducted in this field, no comprehensive study has been undertaken regarding the various aspects of self-medication. Therefore, this study was conducted to determine the prevalence, causes, types of drugs used, and sources of information on self-medication among medical students. In the present systematic review and meta-analysis, four international databases (Web of Science, Scopus, PubMed, and Excerpta Medica Database) were searched from January 1, 2000, to December 30, 2019. The keywords used were: "Prevalence", "Self Medication", "Medical Students", "Causes", "Resources". To evaluate the quality of the included studies, the tool previously described by Hoy et al. was used. Of the 1 071, searched studies, 76 studies conducted on 29 726 students from 25 countries were selected for the final stage. The prevalence of self-medication in the past year (2019) was found to be 77.6% (95% confidence interval: 74.0–81.2; $I^2 = 99.0\%$). Healthcare workers (39.1%) were found to be the most important source of information on self-medication. In most studies, abdominal problems ($n = 30$) were the most common causes of self-medication. Based on the high prevalence of self-medication among medical students, training courses should be conducted to increase student awareness. Moreover, implementation of strict laws at national level can help to reduce the practice of self-medication.

Keywords: self-medication, prevalence, medical students, meta-analysis

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Introduction

Self-medication is currently one of the most prevalent public health problems worldwide.[1] According to statistical data from the World Health Organization (WHO), more than 50% of medications worldwide are not prescribed correctly or are used by individuals without a doctor's prescription.[2] Different political, cultural, and economic aspects increase the prevalence of self-medication.[3] Although self-medication relieves illness and reduces symptoms, in some cases, such as in antibiotic use, it may be associated with various side-effects, increased drug resistance, long-term hospitalisation, and unsuccessful treatment, along with increased cost to educate the patient and the healthcare workers (HCWs).[4] Furthermore, the use of antidepressants that are associated with several side-effects, such as weight gain and diabetes, has increased by more than 100% in recent years.[5] The prevalence of self-medication in different populations depends on various factors, including age, sex, and degree of self-care and education.[6,7] The prevalence of self-medication is higher in medical science students than in other groups owing to easier access and communication with medical and pharmaceutical centres.[8] Despite individual studies conducted to assess students in medical sciences, no comprehensive study has been performed in this field. Therefore, determining the prevalence of self-medication among medical science students is critical, as they will shape the future of the healthcare industry. Determining the prevalence of self-medication can also help health policy makers plan better strategies to control self-medication. Hence, this study aimed to investigate the prevalence of self-medication among medical students.

Methods

Eligibility criteria and registration

This systematic review and meta-analysis study was performed according to Cochrane's guideline and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[9] The study protocol was registered with PROSPERO (CRD42020165531).

The inclusion criteria were as follows: 1) type of study: cross-sectional studies performed retrospectively and prospectively; 2) studies published in English; and 3) studies performed on medical students. The exclusion criteria were as follows: reviews, letters to the editor, and qualitative studies published before 2000 in non-English languages and performed on children or the elderly. In addition, articles lacking the required quality based on the Hoy tool or full text were excluded. This study aimed to investigate the prevalence of self-medication, the type of medications used, the causes of self-medication, and sources of information on self-medication. In the present study, self-medication was defined as "the use of medicinal products by the consumer to treat self-recognised disorders or symptoms, or the intermittent or continued use of medication prescribed by a physician for chronic or recurring diseases or symptoms," based on the WHO guidelines.[10]

Search strategy

International databases (Web of Science, Scopus, PubMed, and Excerpta Medica Database) were searched from January 1, 2000 to December 30, 2019. The search strategy was developed with the help of a librarian with experience in working on systematic reviews. The search strategy used for PubMed was adopted to search other databases. The PROSPERO database was used to search for the most recent review articles. The keywords were based on MeSH (Medical Subject Headings) and searches of related articles. The keywords used were: "Prevalence", "Self Medication", "Medical Students", "Causes", "Resources".

Selection of studies and data extraction

After searching the databases, the articles were entered into the Endnote software. Next, the articles were screened and duplicate items were excluded. Then, the articles were reviewed based on their titles and abstracts, and irrelevant items were removed. The full text of the articles was then evaluated based on the inclusion criteria and selected for the final stage. Finally, information was extracted. The screening and data extraction stages were separately performed by two researchers (XX and YQ). The consensus method was used when the researchers disagreed on specific studies. Extracted data items included author, year

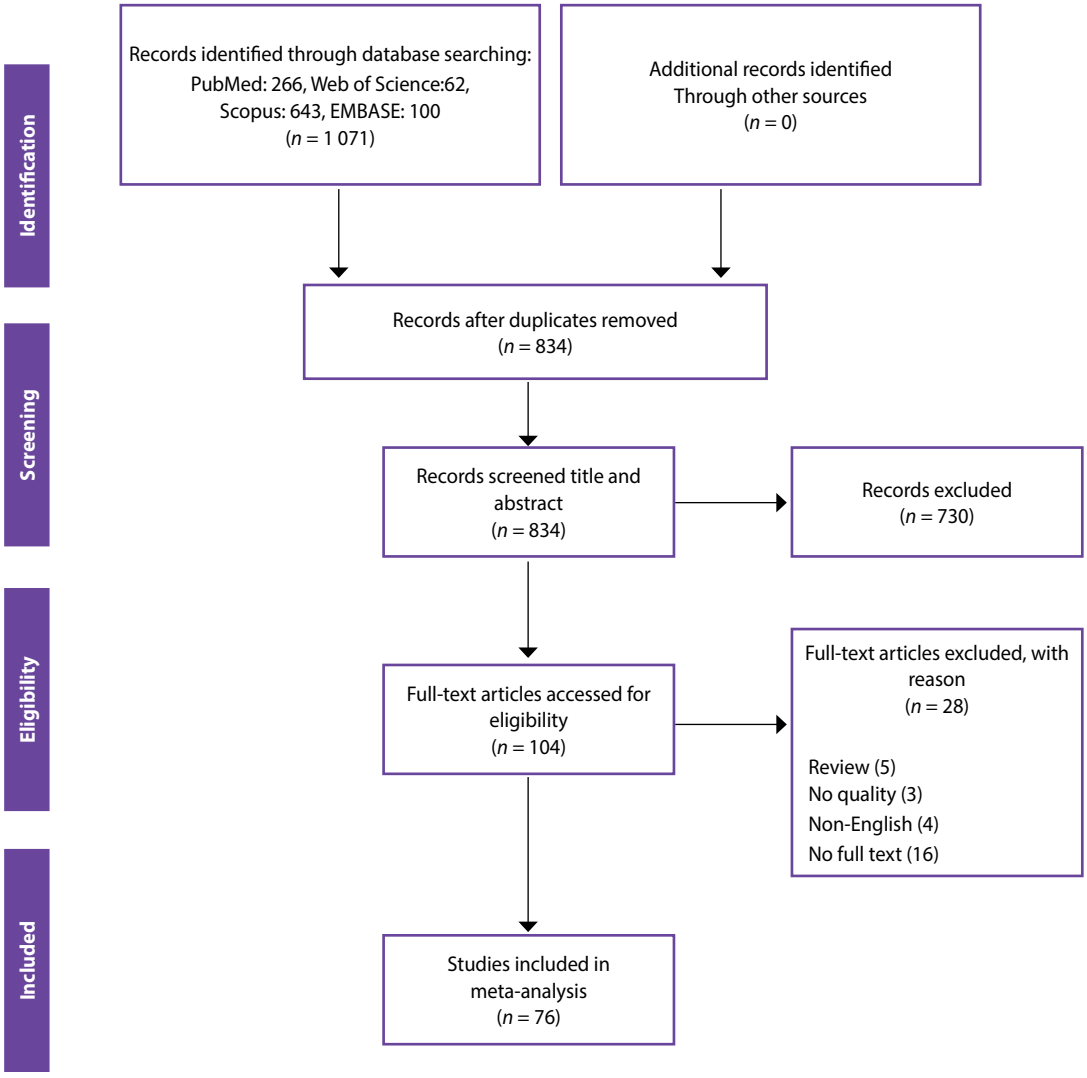

Figure 1: PRISMA Flow Diagram

of publication, country, region based on WHO category, Service Delivery Indicators (SDI) status based on World Bank category, sampling method, demographic characteristics (number of participants, age, sex [male/female]), risk of bias, prevalence of self-medication, source of information, type of drugs, indications for self-medication, and causes of self-medication.

Quality assessment

The Hoy et al.-proposed tool was used to evaluate the quality of the entered studies.[11] This 10-item tool examines studies in terms of bias risk, including internal validity (items 1–4 assess target population, sampling frame, sampling method, and non-response minimal bias) and external validity (items 1–4 assess target population, sampling frame, sampling method, and non-response minimal bias). The quality of the studies entered by the two researchers was evaluated separately, and disagreements were resolved by consulting a third person.

Data analysis

All eligible studies were included after the systematic review. The data were combined using forest plots. The overall prevalence of self-medication, types of drug use, and sources of information were evaluated using a random effects model. Heterogeneity of the preliminary studies was evaluated using the I^2 test. Subgroup analysis was performed to determine the heterogeneity based on the study location and instruments. The meta-analysis was performed using STATA 14 (StataCorp, Texas, United States of America).

Results

Study selection

A total of 1 071 articles were retrieved from the initial searches of the four databases. Of the 834 non-duplicated studies, 730 were excluded due to unrelated titles and abstracts. Of the remaining 104 studies, 76 met the eligibility criteria; among the 28 excluded studies, five were review studies, four were published in non-English languages, three were not of good quality, and 16 did not have full text available (Figure 1).

Study characteristics

A total of 76 studies were conducted with 29 726 students from 25 countries. The age range of the participants was 18–31 years old. Most studies were conducted at the Eastern Mediterranean Region (n = 36) and India (n = 19). In terms of economic status, most studies were performed in countries with low-middle SDI (n = 35). The sampling method used in most of the studies (n = 42) was convenience sampling. Most studies (n = 67) had a low bias risk (Table I).

Prevalence of self-medication

The prevalence of self-medication was assessed in 76 studies conducted across 25 countries. Prevalence was reported according to five time intervals. The time interval lasted one year for 60 studies (78.9%) and the last six months for 10 studies. Furthermore, the last six months, last one month, and last two months were the time intervals for two, three, and one study, respectively.

Prevalence of self-medication in the last year time interval

Of all studies that assessed the prevalence in the last one-year time interval, 44 studies assessed the prevalence of no specific drug, and 11, 4, and 1 assessed self-medication with only antibiotic, analgesic, and sedative or anti-stress drugs, respectively.

The prevalence of self-medication at least once in the last one-year time interval in 44 studies was between 44.8 and 100%, and according to the meta-analysis results, the pooled prevalence of no specific drug self-medication in 16 442 medical science students was 77.6% (95% confidence interval [CI]: 74.0–81.2; I^2 = 99.0%). The pooled prevalence of antibiotic and analgesic drug self-medication was 47.4 and 69.9%, respectively (Figure 2).

Of the 44 studies (no specific drug), 27 studies assessed the prevalence of self-medication based on the type of drug and reported the prevalence of at least one type of drug, such as antibiotics. Of the 44 studies (no specific drug), 24 reported the prevalence of antibiotic self-medication and 11 specifically assessed the antibiotic self-medication. The prevalence of antibiotic self-medication at least once in the last one-year time interval in 35 studies was between 3.0 and 81.1%, and based on the results of the random effect method, the pooled prevalence in 15 361 medical science students was 34.8% (95% CI: 28.1–41.6; I^2 = 99.1%) (Table II).

Of the 44 studies (no specific drug), 19 studies reported the prevalence of an analgesic or antispasmodic drug self-medication, and four studies specifically assessed the analgesic self-medication. The prevalence of analgesic or antispasmodic self-medication at least once in the last one-year time interval in 23 studies was between 7.1 and 86.8%, and based on the results of the random effects method, the pooled prevalence in 9 561 medical science students was 47.1% (95% CI: 36.4–57.9; I^2 = 99.4%). The meta-analysis results for the type of drug showed that the pooled prevalence for analgesics/antispasmodic (47.1%), antipyretics (46%), and non-steroidal anti-inflammatory drugs (NSAIDs 43.5%) were higher than that for other types of drugs (Table II).

Subgroup analysis based on sex showed that the prevalence of self-medication in females was higher than that in males in most studies. Therefore, the overall pooled prevalence of no specific drug self-medication at least once in the last one year time interval in 3 283 male and 6 594 female medical students was 73.9% (95% CI: 66.9–80.9; I^2 = 98.7%) and 77.6% (95% CI: 74.3–81; I^2 = 98.8%), respectively. In addition, the pooled prevalence of analgesic drugs in males and females was 67.3 and 75.6%, respectively (Table III).

Subgroup analysis based on SDI status showed that the pooled prevalence of at least one non-specific drug self-medication in the last year was highest in the high SDI group (82.4%; 95% CI: 75.1–89.7) and lowest in the the low SDI group (72.6%; 95% CI: 55.7–89.4); however, these differences were not significant (Figure 3).

Table I: Summary of included studies

Author (Year)	Country	Region (WHO)	SDI status	Sampling method	Demographic characteristics 1. Participants 2. Age 3. Gender (M/F)	Risk of bias	Prevalence of SM
Abay SM (2010)[18]	Ethiopia	African	Low SDI	Stratified Random	1. 213 2. 17–24 3. 174/39	low	38.4
Abdi A (2018)[19]	Iran	EMRO	High-middle SDI	Stratified Random	1. 250 2. 18–25 3. 69/181	low	89.6
Ahmadi SM (2016)[20]	Iran	EMRO	High-middle SDI	Stratified Random	1. 364 2. 21.63 3. 122/242	low	33.7
Akbar I (2017)[21]	Pakistan	EMRO	Low-middle SDI	Simple Random	1. 175 2. 21 3. 78/194	low	45.7
Al Essa M (2019)[22]	Saudi Arabia	EMRO	High SDI	Census	1. 272 2. NR 3. 78/194	low	73.1
Alam N (2015)[23]	Bangladesh	South-East Asia	Low-middle SDI	Census	1. 500 2. NR 3. 200/3	low	100
Albasheer O B (2016)[24]	Saudi Arabia	EMRO	High SDI	Simple Random	1. 300 2. NR 3. 150/15	low	83.7
Albusalih FA (2017)[25]	Saudi Arabia	EMRO	High SDI	Purposive sampling	1. 450 2. NR 3. 249/201	low	55.1
Al-Hussaini M (2014)[26]	Kuwait	EMRO	High SDI	Simple Random	1. 813 2. NR 3. 213/606	low	97.8
Ali AS (2016)[27]	Pakistan	EMRO	Low-middle SDI	Simple Random	1. 150 2. 23.5 3. 71/79	low	52.7
Alkhatatbeh MJ (2016)[28]	Jordan	EMRO	High-middle SDI	Census	1. 1 317 2. NR 3. 364/953	Moderate	78.5
Al-Rashidi A (2018)[29]	Saudi Arabia	EMRO	High SDI	Census	1. 237 2. NR 3. 0/237	Moderate	73.8
Al-Shagawi MA (2017) [30]	Saudi Arabia	EMRO	High SDI	Convenience	1. 213 2. NR 3. 0/213	low	30
Alshahrani SM (2019)[31]	Saudi Arabia	EMRO	High SDI	Convenience	1. 528 2. NR 3. 237/291	Moderate	98.7
Alshogran OY (2018)[32]	Jordan	EMRO	High-middle SDI	Convenience	1. 504 2. NR 3. 223/281	low	97.2
Alsous M (2018)[33]	Jordan	EMRO	High-middle SDI	Convenience	1. 256 2. 21.56 3. 25/231	low	86.7
Badiger S (2012)[34]	India	South-East Asia	Low-middle SDI	Convenience	1. 200 2. NR 3. 79/121	low	92
Banerjee I (2016)[35]	Nepal	South-East Asia	Low SDI	Convenience	1. 488 2. NR 3. NR	low	81.35

Author (Year)	Country	Region (WHO)	SDI status	Sampling method	Demographic characteristics 1. Participants 2. Age 3. Gender (M/F)	Risk of bias	Prevalence of SM
Barkus A (2016)[36]	Lithuania	Europe	High SDI	Convenience	1. 180 2. NR 3. NR	low	39.4
Benameur T (2019)[37]	Saudi Arabia	EMRO	High SDI	Convenience	1. 150 2. 20.96 3. NR	low	42.6
Betancourt J (2013)[38]	Puerto Rico	American	High SDI	Convenience	1. 275 2. NR 3. 89/186	low	76
Brlić KČ (2014)[39]	Croatia	Europe	High SDI	Convenience	1. 389 2. NR 3. 92/297	Moderate	74.6
Donkor ES (2012)[40]	Ghana	African	Low-middle SDI	Convenience	1. 100 2. NR 3. NR	low	42
Dutta S (2016)[41]	India	South-East Asia	Low-middle SDI	Convenience	1. 292 2. 21.5 3. 172/12	Moderate	71
El Ezz NF (2011)[42]	Egypt	EMRO	Low-middle SDI	Simple Random	1. 300 2. 19.1 3. 99/201	Moderate	55.2
Fatima A (2017)[43]	India	South-East Asia	Low-middle SDI	Convenience	1. 210 2. 22.3 3. NR	low	62.98
Gama AS M. (2017)[44]	Brazil	American	Upper-middle SDI	Convenience	1. 88 2. NR 3. 34/54	low	76
Gyawali S (2015)[45]	Nepal	South-East Asia	Low SDI	Census	1. 276 2. NR 3. 118/158	low	81.9
Harakeh S (2015)[46]	Saudi Arabia	EMRO	High SDI	Simple Random	1. 1042 2. NR 3. 493/549	low	49
Haroun MF (2017)[47]	Syria	EMRO	Low SDI	Simple Random	1. 436 2. NR 3. 207/229	low	54.3
Helal RM (2017)[48]	Egypt	EMRO	Low-middle SDI	Stratified cluster sampling	1. 503 2. 20 3. 92/411	low	62.9
Hu Y (2018) [49]	China	Western Pacific	High-middle SDI	Cluster sampling	1. 1 819 2. 22 3. 661/1 158	low	15.6
Ibrahim NK (2015)[50]	Saudi Arabia	EMRO	High SDI	Stratified Random Sampling	1. 504 2. 22.9 3. 242/262	low	75.2
Iqbal A (2018)[51]	Pakistan	EMRO	Low-middle SDI	Purposive sampling	1. 300 2. 20.76 3. 240/60	low	85.7
Jabeen N (2015)[52]	India	South-East Asia	Low-middle SDI	Convenience	1. 100 2. NR 3. 52/48	low	88
Jairoun A (2019)[53]	UAE	EMRO	High SDI	Simple Random	1. 600 2. NR 3. 486/14	Moderate	45
James H (2006)[54]	Bahrain	EMRO	High SDI	Convenience	1. 134 2. 18.01 3. 43/91	low	44.8

Author (Year)	Country	Region (WHO)	SDI status	Sampling method	Demographic characteristics 1. Participants 2. Age 3. Gender (M/F)	Risk of bias	Prevalence of SM
Jamshed SQ (2016)[55]	Malaysia	Western Pacific	High-middle SDI	Convenience	1. 461 2. 19.55 3. NR	low	57.2
Jayanthi B (2014)[56]	India	South-East Asia	Low-middle SDI	Convenience	1. 162 2. NR 3. NR	low	52.4
Johnson D (2016)[57]	India	South-East Asia	Low-middle SDI	Convenience	1. 736 2. NR 3. 220/516	low	92.39
Kanwal ZG (2018)[58]	Pakistan	EMRO	Low-middle SDI	Simple Random	1. 300 2. NR 3. 92/208	low	N
Karamata VV (2017)[59]	India	South-East Asia	Low-middle SDI	Convenience	1. 518 2. NR 3. 228/29	low	59.2
Kasulkar AA (2015)[60]	India	South-East Asia	Low-middle SDI	Simple Random	1. 488 2. 19.89 3. 230/258	low	71.7
Kitikannakorn N (2007)[61]	Thailand	South-East Asia	High SDI	Convenience	1. 266 2. NR 3. NR	low	92
Klemenc-Ketis Z (2010)[62]	Slovenia	Europe	High SDI	Convenience	1. 650 2. 22.4 3. 524/126	low	92.8
Kumar A (2016)[63]	India	South-East Asia	Low-middle SDI	Convenience	1. 308 2. 21.4 3. NR	low	49.7
Kumar N (2013)[64]	India	South-East Asia	Low-middle SDI	Convenience	1. 440 2. 20.3 3. 190/25	low	78.6
Kumar R (2016)[65]	India	South-East Asia	Low-middle SDI	Simple Random	1. 327 2. 20.8 3. NR	low	74.6
Kumari K (2018)[65]	India	South-East Asia	Low-middle SDI	Census	1. 269 2. NR 3. NR	low	83.2
Latifi A (2017)[66]	Iran	EMRO	High-middle SDI	Cluster sampling	1. 1 269 2. 21.13 3. 503/766	low	80.7
Lukovic JA (2014)[67]	Serbia	Europe	Upper-middle SDI	Convenience	1. 1 293 2. NR 3. 499/794	Moderate	79.9
Martinez JE (2014)[68]	Brazil	American	Upper-middle SDI	Convenience	1. 247 2. 22.35 3. 110/137	low	63.8
Mosaddek ASM (2014) [69]	Bangladesh	South-East Asia	Low-middle SDI	Census	1. 421 2. NR 3. 167/245	low	77.55
Mosaddek AS Md (2017)[70]	Bangladesh	South-East Asia	Low-middle SDI	Census	1. 52 2. NR 3. 21/31	low	47.06
Mumtaz Y (2011)[71]	Pakistan	EMRO	Low-middle SDI	Convenience	1. 104 2. NR 3. NR	low	80.4
Naqvi AA (2016)[72]	Pakistan	EMRO	Low-middle SDI	Convenience	1. 235 2. NR 3. 37/198	low	67.2
Niroomand N (2019)[73]	Iran	EMRO	High-middle SDI	Stratified Random	1. 396 2. NR 3. NR	low	72

Author (Year)	Country	Region (WHO)	SDI status	Sampling method	Demographic characteristics 1. Participants 2. Age 3. Gender (M/F)	Risk of bias	Prevalence of SM
Pan H (2012) [74]	China	Western Pacific	High-middle SDI	Convenience	1. 634 2. NR 3. NR	Moderate	59.2
Parihar A (2018)[75]	India	South-East Asia	Low-middle SDI	Convenience	1. 200 2. NR 3. NR	low	86.5
Patil SB (2014)[76]	India	South-East Asia	Low-middle SDI	Convenience	1. 440 2. 20.4 3. 268/172	low	88.18
Pirzadeh A (2014)[77]	Iran	EMRO	High-middle SDI	Stratified Random	1. 197 2. NR 3. 65/132	low	84.98
Rajesh B (2017)[78]	India	South-East Asia	Low-middle SDI	Convenience	1. 267 2. NR 3. NR	low	66.8
Sajith M (2017)[79]	India	South-East Asia	Low-middle SDI	Convenience	1. 318 2. NR 3. 152/166	low	87.5
Sarahroodi S (2010)[80]	Iran	EMRO	High-middle SDI	Simple Random	1. 99 2. NR 3. 49/50	low	81
Sarahroodi S (2012)[81]	Iran	EMRO	High-middle SDI	Simple Random	1. 564 2. NR 3. 256/308	low	76.6
Sarraf DP (2017)[82]	Nepal	South-East Asia	Low SDI	Convenience	1. 520 2. NR 3. NR	low	48.3
Sawalha A F.(2008)[83]	Palestine	EMRO	Low-Middle SDI	Census	1. 468 2. 19.9 3. NR	low	96.6
Shafiq F (2018)[84]	Pakistan	EMRO	Low-middle SDI	Convenience	1. 73 2. NR 3. 41/32	Moderate	100
Sharif SI (2012)[85]	UAE	EMRO	High SDI	Convenience	1. 169 2. 19.5 3. 153/16	low	86
Sharma A (2015)[86]	India	South-East Asia	Low-middle SDI	Convenience	1. 314 2. 19.03 3. 131/183	low	84.4
Shkreli R (2019)[87]	Albania	Europe	Upper-middle SDI	Convenience	1. 229 2. NR 3. 103/126	low	79.1
Somashekara SC (2019)[88]	India	South-East Asia	Low-middle SDI	Convenience	1. 185 2. NR 3. 95/9	low	81.6
Syed N (2104)[89]	Pakistan	EMRO	Low-middle SDI	Convenience	1. 200 2. NR 3. NR	low	81
Tameez-ud-din A (2019) [90]	Pakistan	EMRO	Low-middle SDI	Convenience	1. 244 2. 21.2 3. NR	low	50.4
Virmani S (2017)[91]	India	South-East Asia	Low-middle SDI	Simple Random	1. 456 2. NR 3. 205/251	low	58
Zhu X (2016) [92]	China	Western Pacific	High-middle SDI	Convenience	1. 279 2. NR 3. NR	low	60.6

NR: none reported

Table II: The result of meta-analysis and pooled prevalence of self-medication in medical students by time interval and type of drug

	Last one year				Last six months				Last one to three months			
	n Sample size	Range of prevalence	Pooled prevalence (95% CI)	.	*n* Sample size	Range of prevalence	Pooled prevalence (95% CI)	.	*n* Sample size	Range of prevalence	Pooled prevalence (95% CI)	.
Antibiotics	35, 15361	3.0–81.1	34.8 (28.1, 41.6)	-	8, 4008	4.3–53.6	29.7 (16.8, 42.6)		4, 1124	8.9–42.3	15.2 (6.2, 24.1)	
NSAIDs	3, 592	34.5–37.1	43.5 (27.2, 59.8)		2, 820	38.1–74.3	53.2 (50.0, 56.4)		1, 213	-	9.4 (6.2, 14.1)	
Antacids/Antiulcer	13, 7007	4.9–39.3	18.7 (13.7, 23.7)	-	5, 3261	6.3–44.1	17.7 (9.2, 26.1)		2, 663	4.7–36.4	13.9 (11.5, 16.3)	
Acetaminophen/ Antitussives	15, 7444	2.9–53.6	26.1 (18.0, 34.3)	-	6, 3204	1.0–84.6	49.0 (8.9, 89.0)		3, 1027	17.8–21.3	19.3 (16.9, 21.7)	
Analgesics/ Antispasmodic	23, 9561	7.1–86.8	47.1 (36.4, 57.9)	-	6, 3188	48.4–81.4	58.8 (48.2, 69.4)		3, 1378	16.8–76.6	44.3 (7.6, 81.0)	
Vitamins	18, 7993	1.3–51.8	22.1 (14.6, 29.6)	-	7, 3708	0.6–67.0	30.9 (12.7, 49.0)		2, 814	11.0–16.7	13.6 (11.3, 16.0)	
Herbal medicine	7, 4516	3.1–39.3	20.5 (12.4, 28.6)	-	5, 2544	2.7–25.9	13.9 (7.6, 20.1)		1, 364	-	6.9 (4.7, 9.9)	
Gastrointestinal drugs	14, 7180	0.4–45.9	16.0 (11.0, 21.1)		6, 2984	0.6–22.8	11.9 (5.3, 18.5)		2, 814	9.3–47.3	20.6 (18.1, 23.1)	
Anti-allergic	18, 7998	4.1–40.9	18.3 (13.7, 22.8)	-	8, 4008	4.7–48.0	20.9 (11.6, 30.2)		1, 364	-	7.1 (4.9, 10.3)	
Psychoactive	-	-	-	-	2, 525	14.0–32.0	20.8 (17.4, 24.2)		1, 364	-	6.6 (4.5, 9.6)	
Tranquilisers/ Sedatives	11, 3861	1.0–58.7	10.9 (6.2, 15.7)	-	5, 2511	0.8–58.4	24.7 (4.6, 44.7)		-	-	-	-
Antipyretics	14, 5978	3.8–92.0	46.0 (30.7, 61.3)	-	6, 3188	2.1–51.8	19.9 (6.6, 33.1)		1, 364	-	2.7 (1.5, 5.0)	
Skin	7, 3803	2.6–43.2	25.1 (14.2, 35.9)	-	2, 778	10.0–12.0	11.8 (9.5, 14.1)		1, 364	-	5.2 (3.4, 8.0)	
Ophthalmic	2, 1778	15.7–34.3	18.9 (17.1, 20.7)	-	2, 778	5.6–26.7	13.3 (11.0, 15.5)		-	-	-	-
Opioids	1, 247	-	4.5 (2.5, 7.8)	-	-	-	-	-	1, 364	-	1.9 (0.9, 3.9)	
Nasal preparations	3, 1790	3.1–10.0	6.4 (0.8, 11.9)	-	-	-	-	-	-	-	-	-
Ear preparations	6, 3243	2.9–13.9	7.6 (4.5, 10.6)		-	-	-	-	-	-	-	-

Of all countries, 18 reported a prevalence of at least one non-specific drug self-medication in the previous year. Of these, 11 countries had only one study, in which the self-medication prevalence was highest in Kuwait (97.8%) and lowest in Bahrain (44.8%). In addition, among the seven countries with two or more studies, the pooled prevalence was highest in Jordan (87.4%) and lowest in Egypt (66%) (Table IV).

Prevalence of self-medication in the last six months time interval

The prevalence of self-medication in the last six months time interval was assessed in 10 studies, of which nine studies assessed the prevalence of no specific drug and one study assessed self-medication of only sedative or anti-stress drug. The prevalence of no specific drug self-medication in the last six months time interval in nine studies was between 48.3% and 99%, and the pooled prevalence was 81.9% (95% CI: 74–89.9; $I^2 = 99\%$) (Figure 4). Among the various types of pharmaceutical groups, the pooled prevalence of analgesics/ antispasmodics (58.8%) and NSAIDs (53.2%) was higher than that of the other types of drugs (Table II).

Prevalence of self-medication in the last one to three months time interval

The prevalence of self-medication in the last one to three months time interval was assessed in six studies, of which four studies assessed the prevalence of no specific drug and the pooled prevalence was 43.2% (95% CI: 32.7–53.8; $I^2 = 92.8\%$) (Figure 4). Among the various types of pharmaceutical groups, the pooled prevalence of analgesics/ antispasmodics (58.8%) and NSAIDs (53.2%) was higher than that of the other types of drugs (Table II).

Sources of information on self-medication

Among the important sources of information on student self-medication, the pooled prevalence of advice from HCWs (39.1%), followed by reading materials and books (32.6%), was higher than that from other sources. The internet was assessed as a source of information in 15 studies, demonstrating a pooled prevalence of 21.6% (95% CI: 15.1, 28.1; $I^2 = 97.8\%$) (Figure 4). The most important sources of information on self-medication

Table III: The result of meta-analysis and pooled prevalence of self-medication in medical students by sex and assessed type of drug in last year

First author, year Drug type	Male		Female	
	Sample size	ES (Estimation statistics)* (95% CI)	Sample size	ES* (95% CI)
Not a specific drug				
Alam N 2015[23]	200	100 (98.1, 100)	300	100 (98.7, 100)
Albasheer OB 2016[24]	150	81.3 (74.3, 86.8)	150	86(79.5, 90.7)
Alkhatatbeh MJ 2016[28]	364	76.4 (71.7, 80.4)	953	79.3 (76.6, 81.8)
Al-Rashidi A 2018[29]	0	-	237	73.8 (67.9, 79)
Alshogran OY 2018[32]	223	33.6 (27.8, 40.1)	281	61.6 (55.8, 67.1)
Badiger S 2012[34]	79	93.7 (86, 97.3)	121	90.9 (84.5, 94.8)
El Ezz NF 2011[42]	99	100 (96.3, 100)	201	100 (98.1, 100)
Fatima A 2017[43]	0	-	210	62.4 (55.7, 68.7)
Gama ASM 2017[44]	50	68 (54.2, 79.2)	66	81.8 (70.9, 89.3)
Gyawali S 2015[45]	118	78 (69.7, 84.5)	158	84.8 (78.4, 89.6)
James H 2006[54]	43	44.2 (30.4, 58.9)	91	45.1 (35.2, 55.3)
Jamshed SQ 2016[55]	0	-	461	57 (52.5, 61.5)
Jayanthi B 2014[56]	0	-	162	52.5 (44.8, 60)
Johnson D 2016[57]	220	81.4 (75.7, 86)	516	97.1 (95.3, 98.2)
Karamata VV 2017[59]	228	47.8 (41.4, 54.3)	290	68.3 (62.7, 73.4)
Kasulkar AA 2015[60]	230	71.7 (65.6, 77.2)	258	71.7 (65.9, 76.9)
Kitikannakorn N 2007[61]	0	-	266	100 (98.6, 100)
Kumar N. 2013[64]	190	75.3 (68.7, 80.9)	250	81.2 (75.9, 85.6)
Kumar R 2016[65]	290	69.7 (64.1, 74.7)	373	74.0 (69.3, 78.2)
Kumari K 2018[93]	133	84.2 (77.1, 89.4)	136	82.4 (75.1, 87.8)
Lukovic JA 2014[67]	499	74.3 (70.3, 78)	794	83.4 (80.6, 85.8)
Mosaddek ASM 2017[70]	21	47.6 (28.3, 67.6)	31	45.2 (29.2, 62.2)
Naqvi AA 2016[72]	37	67.6 (51.5, 80.4)	198	67.2 (60.4, 73.3)
Parihar A 2018[75]	109	91.7 (85.0, 95.6)	91	80.2 (70.9, 87.1)
Overall Random pooled ES	**3 283**	**73.9 (66.9–80.9)**	**6 594**	**77.6 (74.3–81)**
Analgesics drug				
Al Essa M 2019[22]	78	100 (95.3, 100)	194	100 (98.1, 100)
Brlić KČ 2014[39]	92	54.3 (44.2, 64.1)	297	80.8 (75.9, 84.9)
Kumar, A., 2016[63]	176	47.2 (39.9, 54.5)	155	45.2 (37.5, 53)
Overall Random pooled ES	**346**	**67.3 (27.3–100)**	**646**	**75.6 (50–100)**
Antibiotic drug				
Ali AS 2016[27]	71	69.0 (57.5, 78.6)	79	38(28.1, 49)
Hu Y 2018[49]	661	14.8 (12.3, 17.7)	1 158	16.1 (14.1, 18.4)
Overall Random pooled ES	**732**	**18.1 (15.4–20.7)**	**1 237**	**17.0 (14.9–19.1)**

among students of medical sciences were HCWs (39.1%), followed by books and other resources (32.6%).

Reasons for self-medication

The reasons for self-medication were documented in 33 studies. The most common causes of self-medication included abdominal problems (n = 30), pain (n = 29), cough, and the common cold (n = 27) (Table V).

Meta-regression analyses

Meta-regression analyses were conducted for the prevalence of at least one and no specific drug self-medication in the last year time intervals (44 studies). The results of univariate meta-regression analyses showed that the publication year of the study variable did not significantly contribute to the heterogeneity of self-medication prevalence (Coef. = 0.45, p-value = 0.889). Moreover, the sex of the participants (female-to-male ratio) variable was also not significant (Coef. = –0.26, p-value = 0.976).

Discussion

Despite several efforts to increase awareness, self-medication is one of the main problems faced by people, especially medical science students. In some cases, self-medication results in drug resistance, unwanted side-effects, and mortality. To the best of our

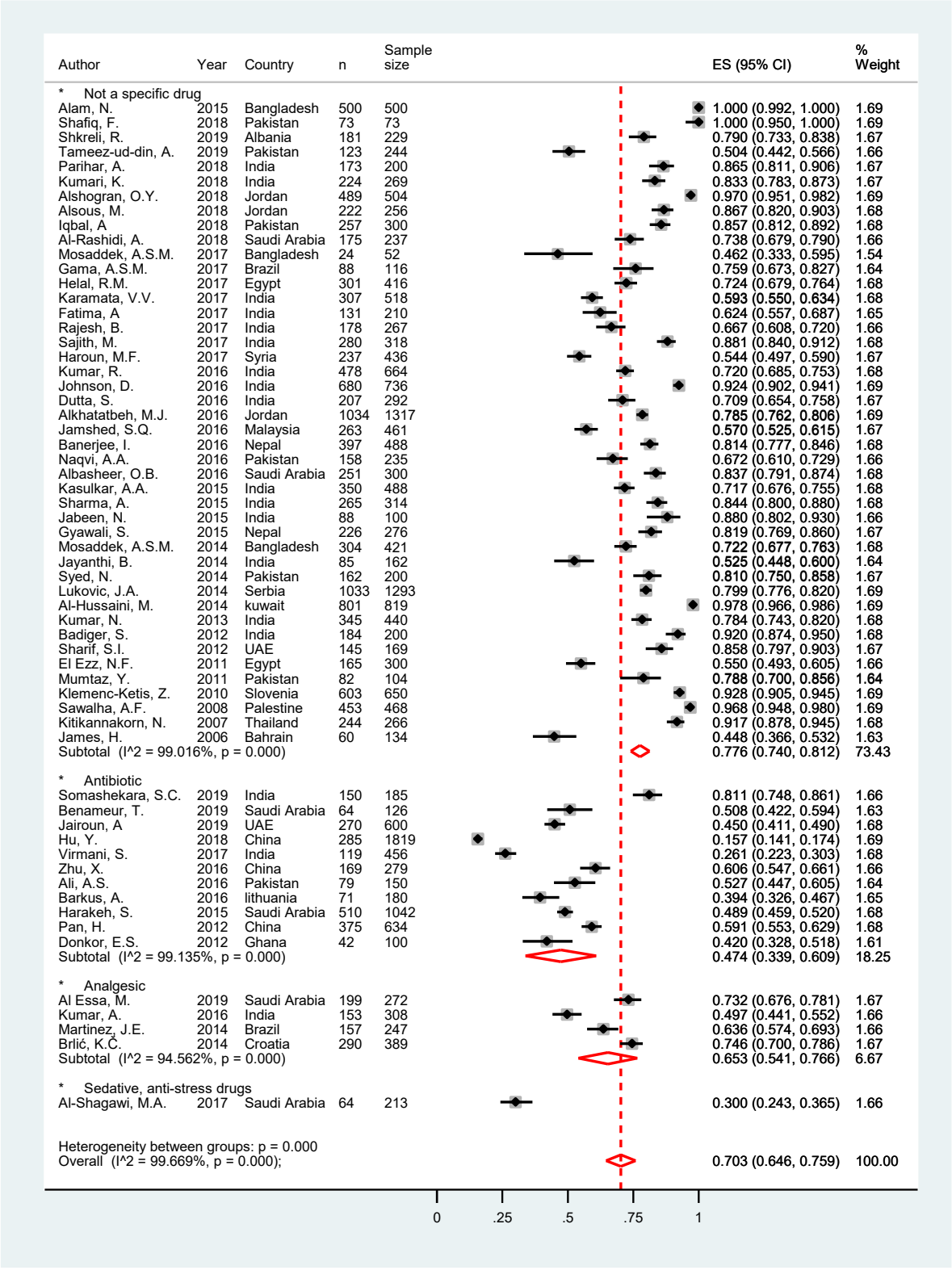

Figure 2: The forest plot of self-medication by type of drug assessed included a study in medical students' last year

knowledge, this is the first systematic review and meta-analysis on the prevalence of self-medication in medical science students. The present analysis included 76 studies involving 29 726 participants, conducted between 2000 and 2019. In most studies, the prevalence of self-medication was calculated over the past year. The findings of this study demonstrated a self-medication prevalence of > 77.6% among medical science students.

In the case of medical science students, the high prevalence of self-medication may be attributed to the easy access to medications and information regarding different types of medications. Furthermore, the prevalence of self-medication demonstrated a large variation, between 28% and 81% in different countries, which can be attributed to methodological differences, including sample size, study method, study duration, information collection

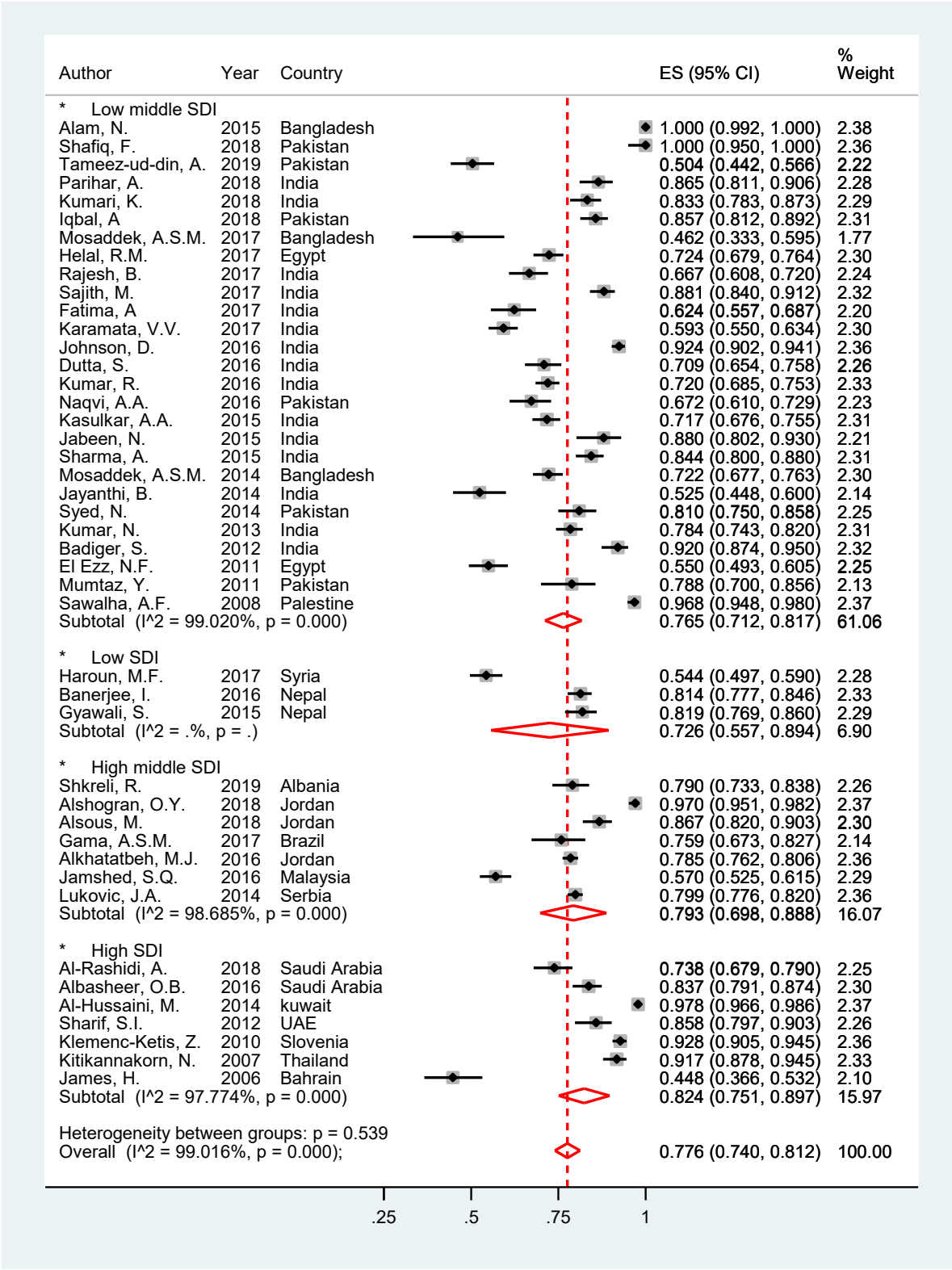

Figure 3: The forest plot of at least one non-specific drug self-medication in medical student in the last year by Socio-Demographic Index (SDI)

method, the country conducting the study, and the location of the study. Additionally, the high prevalence of self-medication among medical science students can be due to the lack of strict regulations for medications prescribed by physicians as well as the distribution and sale of medications in pharmacies. Notably, no similar study has investigated these aspects. However, in a study conducted in the general Indian population, the prevalence of self-medication was 53.57%, which was lower than that observed in the present study.[12] This can be attributed to differences in the sample size investigated, number of studies selected, location of the studies, and the communities assessed in the studies. Furthermore, the prevalence of antibiotic and analgesic use was

Table IV: The result of meta-analysis and pooled prevalence of not specific drug self-medication in medical students last year by country

Country	*n*, Sum of sample size	Range of prevalence	Pooled prevalence (95% CI)	Ref.
Kuwait	1, 819	-	97.8 (96.5 to 98.6)	
Palestine	1, 468	-	96.8 (94.8 to 98)	
Slovenia	1, 650	-	92.8 (90.5 to 94.5)	
Thailand	1, 266	-	91.7 (87.8 to 94.5)	
Jordan	3, 2077	78.5 to 97.0	87.4 (74.3 to 100)	
Nepal	2, 764	81.4 to 81.9	81.5 (78.8 to 84.3)	
Saudi Arabia	2, 537	73.8 to 83.7	80.1 (76.8, 83.5)	
Serbia	1, 1293	-	79.9 (77.6 to 82)	
Albania	1, 229	-	79 (73.3 to 83.8)	
Pakistan	6, 1156	50.4 to 100	77.3 (62.4, 92.2)	
India	15, 5178	52.5 to 92.4	76.7 (70.7, 82.8)	
Brazil	1, 116	-	75.9 (67.3, 82.7)	
Bangladesh	3, 973	46.2 to 100	73.6 (48.5 to 98.8)	
Egypt	2, 716	55.0 to 72.4	66 (62.5 to 69.4)	
UAE	1, 169	-	59.8 (56.7 to 63)	
Malaysia	1, 461	-	57(52.5, 61.5)	
Syria	1, 436	-	54.4 (49.7 to 59)	
Bahrain	1, 134	-	44.8 (36.6 to 53.2)	

Table V: Common causes of self-medication among medical students

Type of drug / Studies	Fever	Pain	Abdominal problems	Headache	Cough Common cold	Skin and hair	Neurological diseases	Musculoskeletal disorders	Psychological problems	Allergy	Menstruation	Infection	Others
Abay SM (2010)[18]	✔	✔	✔	✔	✔	✔							✔
Abdi A (2018)[19]	✔			✔	✔	✔	✔	✔					
Ahmadi SM (2016)[20]	✔			✔	✔	✔			✔	✔			
Al Essa M (2019)[22]	✔	✔	✔	✔				✔		✔			
Albasheer OB (2016)[24]		✔	✔	✔	✔	✔			✔				
Albusalih FA (2017)[25]	✔	✔	✔	✔	✔	✔					✔		✔
Al-Hussaini M (2014)[26]	✔	✔	✔	✔	✔	✔					✔	✔	
Ali AS (2016)[27]	✔	✔	✔		✔							✔	✔
Alkhatatbeh MJ (2016)[28]	✔	✔	✔	✔	✔	✔				✔			✔
Alshahrani SM (2019)[31]	✔	✔	✔	✔	✔	✔			✔			✔	✔
Alshogran OY (2018)[32]	✔	✔	✔	✔	✔	✔					✔	✔	✔
Alsous M (2018)[33]	✔	✔	✔	✔	✔	✔			✔	✔			
Badiger S (2012)[34]	✔		✔	✔	✔				✔				✔
Banerjee I (2016)[35]	✔		✔	✔	✔								
Barkus A (2016)[36]						✔						✔	
Benameur T (2019)[37]	✔		✔		✔	✔						✔	
Fatima A (2017)[43]		✔	✔										
Harakeh S (2015)[46]	✔				✔								

Haroun MF (2017)[47]	✔		✔	✔	✔					✔		✔	
Helal RM (2017)[48]		✔	✔				✔						
Hu Y (2018)[49]	✔	✔	✔	✔	✔								
Jayanthi B (2014)[56]		✔	✔			✔			✔				
Kanwal ZG (2018)[58]	✔		✔	✔	✔					✔			
Kasulkar AA (2015)[60]	✔		✔	✔	✔	✔							
Kumar N (2013)[64]	✔	✔	✔	✔	✔	✔	✔						
Mosaddek ASM (2014)[69]	✔		✔	✔	✔					✔			
Mosaddek AS Md (2017)[70]	✔	✔	✔	✔	✔								
Mumtaz Y (2011)[71]	✔	✔	✔	✔	✔					✔			
Parihar A (2018)[75]	✔		✔	✔	✔						✔		
Patil SB (2014)[76]	✔	✔	✔	✔	✔								
Sajith M (2017)[79]	✔	✔	✔		✔							✔	✔
Shafiq F (2018)[84]	✔		✔	✔						✔			
Sharma A (2015)[86]	✔	✔	✔	✔	✔	✔		✔	✔	✔	✔	✔	✔

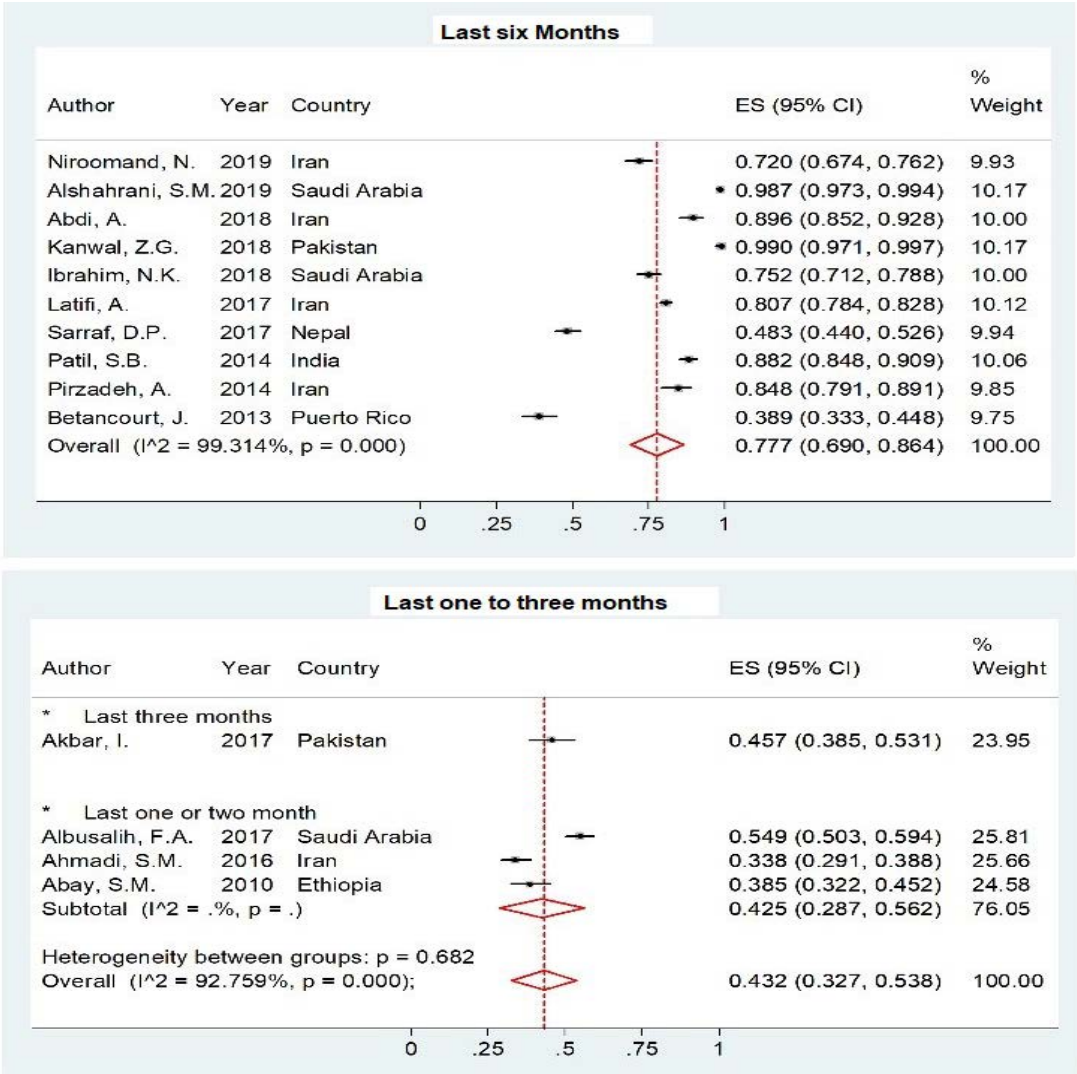

Figure 4: Forest plot of self-medication with no specific drug at least once in the last six months and last one to three months time intervals in medical science students

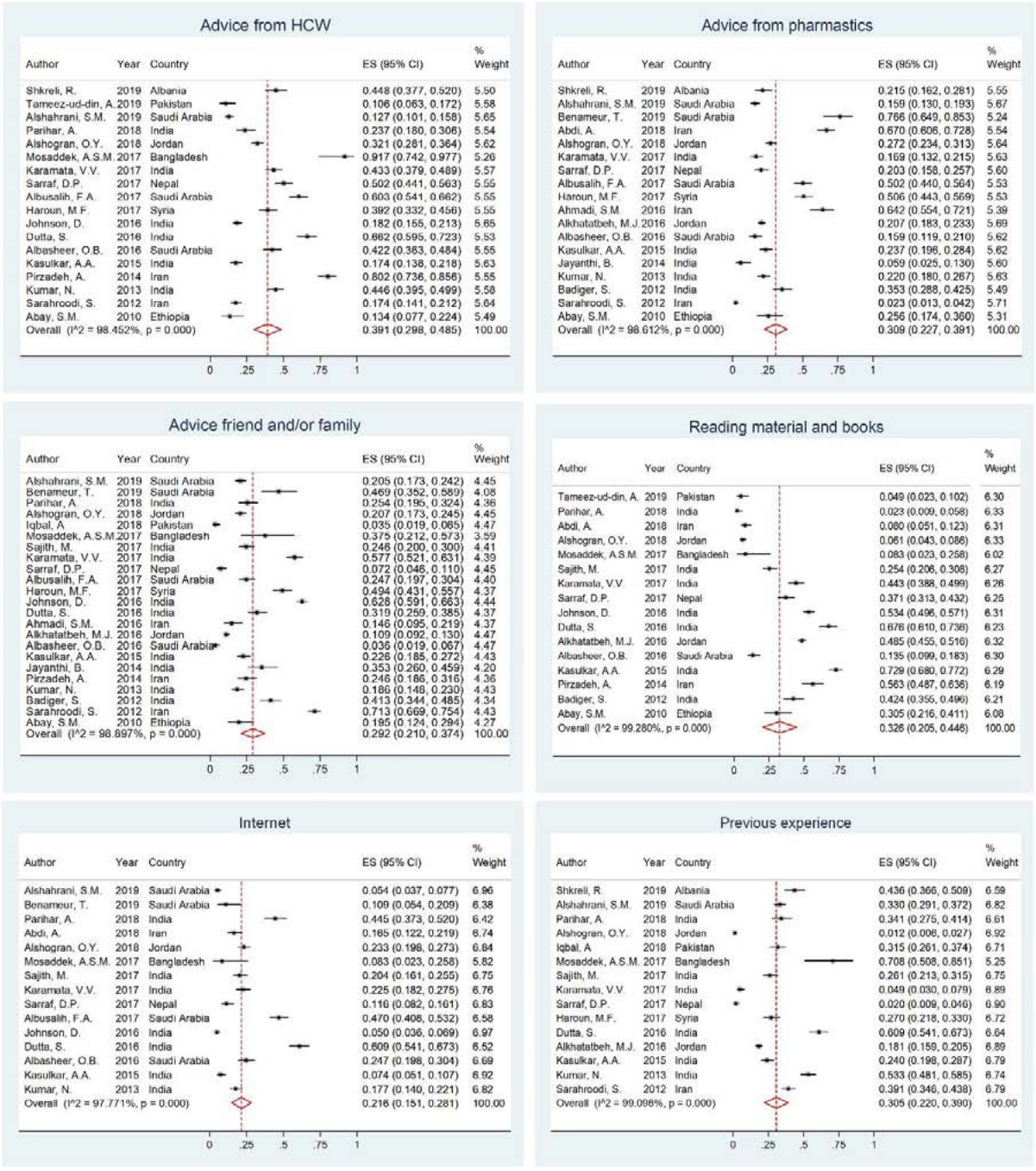

Figure 5: The forest plot of sources of information for self-medication in the medical student had at least one self-medication in the last month to last one year

47.4% and 69.9%, respectively. However, in a previous study, the prevalence of antibiotic use in the general population was reported to be between 18% and 82%.[13]

In a study performed by Ocan et al. on the general population including housewives, the reported prevalence of antibiotic self-medication was 38.8%, which was lower than that in the present study. This difference can be attributed to the type of population studied in the two studies, number of studies included, and the sample size.[14] In studies investigating the general population in Euro-Mediterranean countries, India, and Ethiopia, the prevalence of self-medication was reportedly 40.9%, 53.57%, and 44%, respectively, all of which were lower than those found in the present study.[12,13,15] In the present study, the higher prevalence rates can be due to differences in the target population, number of studies selected, and the greater familiarity of medical science students with medications.

Moreover, the results demonstrated that the most common types of medications used were analgesics (47.1%) and antipyretics (46%). In a study conducted among adolescents by Gualano et al., the most common type of medication used was analgesics.[16] In the present study, the prevalence of self-medication among female students was higher than that observed among male

students (75.6%). In contrast to a previous study that assessed the general population, the prevalence of self-medication in men was higher than that in women.[13] Furthermore, the results demonstrated that the prevalence of self-medication among medical science students was higher in countries with a high SDI status (82.4%). However, the exact cause of the high prevalence of self-medication in countries with higher economic levels remains unclear. In contrast to the current study, the prevalence of self-medication in less developed countries has been reported to be higher in studies assessing the general population owing to the lack of rules and regulations regarding the use of prescription medications.[15]

Among medical science students, the most common sources of information on self-medication were HCWs (39.1%), books and resources (32.6%), and pharmacists. In a study conducted by Alhomoud et al. on the general population, pharmacists were the most common source of information.[13] In India, a study conducted by Rashid et al. revealed that pharmacists, similar to HCWs, were the most important sources of information on self-medication.[12] Therefore, the healthcare sector plays a crucial role in providing training regarding the accurate use of medications, preventing the overuse of medications, and reducing the sale of medications without appropriate prescription. In the present study, students received the necessary information from various sources, including family, friends, and the internet. This illustrates the importance of providing comprehensive and holistic training to the general population through the internet and social networks to ensure the correct use of medications. The most common causes of self-medication include abdominal problems (n = 30), pain (n = 29), cough, and the common cold (n = 27). Systematic reviews have reported that the most common cause of self-medication is the common cold.[13,15,16] However, in a study conducted by Rashid et al., the most common cause of self-medication was headache relief.[12] The exact reason for this difference remains unclear, but can be attributed to variations in the types of communities investigated. Among different populations, presence of different models of self-medication can be attributed to varying and poor levels of knowledge regarding the drug-associated side-effects. Increase in public awareness about the proper use of medications and establishment of strict rules for medication supply, especially among medical science students, can positively impact and reduce the practice of self-medication.[16,17] Furthermore, awareness among medical science students can be increased via brochures, posters, public speeches, and seminars.

Limitations

The most important limitations of the present study are as follows: the studies selected were descriptive; therefore, the specific limitations of these studies should be considered when interpreting the results. Additionally, the selected studies measured the prevalence of self-medication at different time points, making it difficult to determine the overall prevalence. To overcome this limitation, the prevalence of self-medication was reported based on a specific time period. Only studies conducted in English were included in this meta-analysis; hence, non-English studies should also be investigated in the future. The sample sizes of the included studies were small, which needs to be increased in future studies. In most studies, convenience sampling was used based on the researcher's judgment, which could have impacted the study results. Furthermore, homogeneity was higher among studies that used the random effects model to perform the meta-analysis. As a limitation due to gap for publication there may be some new studies which have not been included.

Strengths

To the best of my knowledge, this is the first systematic review to assess the prevalence of self-medication in medical science students. In this study, all possible aspects of self-medication, including prevalence, causes of use, information sources, and types of medications used, were examined. Furthermore, only studies published in high quality scientific journals were included, and the prevalence of self-medication was investigated based on the economic levels of the countries and WHO-defined regions.

Conclusion

This study revealed a high prevalence of self-medication among medical students. The results showed that HCWs were the most important sources of information on self-medication; hence, providing them with accurate information is crucial. To reduce the prevalence of self-medication, our findings can be used as a basis for decision-making by policymakers in the healthcare sector in clinical settings. The results of the present study can help policymakers to better understand the more vulnerable participants, the most important causes of self-medication and common drugs used so as to better manage and limit their use.

Providing and implementing educational interventions to increase the awareness of students regarding the early and late effects of self-medication can help to reduce the prevalence of self-medication among medical science students. In future studies, it is recommended that a standard tool be used to evaluate the prevalence of self-medication. Further qualitative studies in this field can improve our understanding of the sociocultural causes of self-medication.

Conflict of interest

The authors declare no conflict of interest.

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Full list of references available on request

Ketamine infusions for the treatment of mental health conditions

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Abstract

Globally, mental health conditions impose a large burden of disease. Although mental disorders react positively to current pharmacotherapy, ketamine, an anaesthetic, has displayed favourable results in the treatment of depression, anxiety, pain and other mood disorders. Treatment with ketamine could provide an effective, non-invasive treatment option. The background, mechanism of action, uses and benefits of ketamine in the treatment of mood ailments are discussed.

Keywords: ketamine, mental health, infusions

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Introduction

Mental health conditions are ubiquitous and expensive. Effectual treatments have been available for many years; however, the remission is low and relapse is high. A stable remission of symptoms is not achieved in one-third of subjects receiving conventional antidepressant treatment, and it takes a long time before a therapeutic effect is achieved (about two weeks).[1] A single dose of ketamine has been shown to have fast-acting mood-enhancing and anxiolytic effects.[2,3] In the 1960s ketamine was presented as a safe anaesthetic in humans.[4] Ketamine has been seen as a hopeful therapeutic option for treatment-resistant mood ailments.[4] Intravenous (IV) doses of ketamine showed easing of symptoms of major depression in the space of three days.[5] A single dose of ketamine results in a quick reduction in depressive and suicidal ideation 40 minutes post-infusion.[6] In comparison, traditional antidepressants used to treat depression usually take up to four weeks to work. Recent research has indicated that intravenous ketamine may be able to lessen depressive symptoms within a 24-hour period.[2] Ketamine has been shown to quickly reduce suicidal thoughts, with effects that typically last for a week or longer.[7] This review highlights the background, mechanism of action and benefits of ketamine in mood disorders.

Background

Ketamine was discovered by Calvin Stevens in 1962. It was found to have anaesthetic effects, and analgesic effects.[7] It was approved as an anaesthetic by the Food and Drug Administration (FDA) in 1970. Even though the routine use of ketamine is limited, it is often the anaesthetic of choice in developing countries, in situations in which respiratory systems cannot be easily monitored, or where dosing is difficult (e.g. out of hospital emergencies, disaster situations, paediatrics and veterinary medicine).[7]

Mechanism of action

Ketamine is water and lipid soluble and is a racemic mixture of its two enantiomers, (S)-ketamine and (R)-ketamine. It is an antagonist of the ionotropic glutamate N-methyl-D-aspartate (NMDA) receptor.[4] The G protein-coupled NMDA receptors require binding of glutamate and glycine a membrane depolarisation sufficient to expel magnesium (Mg^{2+}) blocking the channel pore, before allowing the influx of calcium (Ca^{2+}) and the propagation of excitatory neurotransmission.[4,7] It is proposed that through disinhibition, low doses of ketamine affect postsynaptic α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors which result in brain derived neurotrophic factor (BDNF) activation that leads to increased synthesis of proteins required for the growth of new synapses.[7] This development of new synapses is thought to be related to antidepressant effects.[7]

Benefits

Ketamine causes analgesia and sedation at doses below a threshold. However, the characteristic dissociative state appears abruptly once the critical dosage threshold is reached, which is approximately 1 to 1.5 mg/kg when given intravenously (IV) or 3 to 4 mg/kg when given intramuscularly (IM).[2,7] Recently, IV ketamine has shown the possibility in reducing symptoms of depression in the space of 2–24 hours.[2] Ketamine has been found to decrease suicidal ideation rapidly with effects usually lasting up to a week.[7] Ketamine has been shown to be effective in reducing drinking in patients with alcohol use disorder (AUD).[7] Several studies have explored the effect of ketamine on anxiety disorders. Reductions in social anxiety disorder and generalised anxiety disorder have been noted in animal models.[8] A decrease in obsessive compulsive disorder (OCD) has been seen but further studies are necessitated.[9] Benefits reported for post-traumatic stress disorder (PTSD) is limited.[9]

Drug interactions

The effectiveness of ketamine may be impacted by the following drugs:[10]

- Benzodiazepines: Ketamine's antidepressant effects may be less effective when taken with high doses of benzodiazapines. Doctors may lower the dosage of any benzodiazepines, like Ativan® and Xanor®, before starting treatment.
- Lamotrigine: This anticonvulsant drug is useful in the treatment of bipolar disorder and epilepsy. The medication treats bipolar disorder by reducing or postponing manic, depressive, or rapid cycling episodes.
- Memantin: Memantin is a type of NMDA blocker. It has an effect on NMDA receptors, which affects how effective ketamine is.
- Any medication that modifies NMDA receptors.

Conclusion

The worldwide burden of mental health conditions is significantly high. There is a need for novel pharmacotherapies that are efficient and rapid. Future studies should focus on optimising administration to better translate the use of ketamine into clinical settings.

Conflict of interest

The author has no conflict of interest.

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Decolonising South Africa's pharmacy curriculum – traditional medicine vs rational medicine: crossing the Rubicon

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Abstract

Traditional medicine has been used in South Africa for centuries, mostly without documentation and formal recognition. The introduction of rational medicines into the South African healthcare system was underpinned by organisation, documentation and largely regulation which made for easy use and capabilities. Recently, the South African educational ministry with the Council for Higher Education emphasised the importance of decolonising the higher education curricula, which, in part, means the incorporation of the traditional healthcare system into rational medicine education that culminates in patient care and recovery. Essentially, this mandate finds fruition in bringing together traditional and rational medicine education that ensures sustainable and meaningful education in the service of the people of South Africa.

Keywords: pharmacy curriculum, traditional medicine, rational medicine

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Case in point

A rurally based minor patient living in one of the Eastern Cape villages in South Africa was bitten by a snake. No one could tell the identity of the snake let alone the patient himself. The minor patient's parents took him to a traditional healer who administered traditional medicine. When the patient's condition deteriorated, the parents took their child to the state hospital's emergency room. With little knowledge of the characteristics of the snake and absolutely no knowledge of the traditional medicine that had been administered, medical doctors and pharmacists were playing a game of Russian roulette in a desperate attempt to reverse the situation which appeared to be worsening before their eyes.

As the situation deteriorated, the patient developed epilepsy and spent weeks in the intensive care unit (ICU), and he is now undergoing rehabilitation.

(Shared by a healthcare provider: Courtesy of Frere Hospital Eastern Cape remaining anonymous.)

Introduction

In the case under discussion, alternative arguments may be offered but this is not the thrust of this paper. More often than not, South Africans residing in rural areas seek medical help from traditional healers, otherwise known as traditional health practitioners (THPs). Normally, treatment is administered, and medicines are given to the patient. Little or no knowledge of the ingredients, picking, compounding, mixing or other processes in the pharmaceutical chain is known except by the administrator. This gives rise to confusion when a patient suffers adverse events, or a misdiagnosis occurs. Training in traditional healing is either ancestral or undertaken at special facilities. These curricula and the practical training involved usually remain undocumented. It is these unknowns that rational medicine grapples with, in that the rational healthcare service providers are unable to effectively continue with rational medicine therapy, thus impacting patient care and recovery.

This paper aims to cross the Rubicon between rational and traditional medicine that has as its ultimate goal: patient care and patient recovery. The method utilised in this paper examines the legal challenges a healthcare provider may encounter firstly, and secondly, with which the Government may be confronted should it fail to protect the right of access to health care.[1] In so doing, the paper brushes over the governmental mandate to decolonise the curriculum by including traditional medicine therapy into the ambit of mainstream learning, so-called. The entire paper relies on the occurrence of harm that ensued in a rural village in the Eastern Cape. The minor patient received both traditional and rational medicine therapies. Both therapies must be congruent with a particular meeting point that culminates in patient care and recovery, which is the thrust of this paper.

Thus, the paper makes recommendations and concludes with its findings.

Traditional medicine vs. rational medicine: a quick overview[2]

Traditional medicine and rational medicine represent two distinct paradigms in the realm of health care and healing. These paradigms diverge significantly in terms of their historical foundations, approaches to treatment, validation processes, and philosophical underpinnings. The following academic comparison elucidates the key disparities between these two approaches:

Traditional medicine

1. *Historical and Cultural Heritage*: Traditional medicine has evolved organically within diverse cultural and historical contexts. It is deeply entrenched in the traditions, beliefs, and indigenous knowledge systems of specific communities. Practices within this paradigm are often handed down through generations.
2. *Natural-Based Therapies*: Traditional medicine predominantly relies on natural remedies, encompassing herbal preparations, botanical extracts, minerals, and animal-derived substances. These remedies are administered in accordance with age-old practices and may incorporate rituals and ceremonies.
3. *Holistic Philosophy*: A distinctive characteristic of traditional medicine is its holistic outlook, wherein health and well-being are perceived as interconnected facets of an individual's life. This approach acknowledges not only physical ailments but also considers psychological, spiritual, and social dimensions.
4. *Empirical Observations*: The effectiveness of traditional remedies is typically rooted in empirical observations and anecdotal evidence, rather than rigorous scientific scrutiny. Consequently, the safety and efficacy of many traditional therapies remain unverified by contemporary biomedical standards.

Rational medicine

1. *Evidence-Based Praxis*: Rational medicine, in stark contrast, is characterised by its unwavering commitment to evidence-based practice. It extensively employs empirical research, clinical trials, and systematic reviews to establish the safety and effectiveness of medical interventions.
2. *Pharmacological and Technological Interventions*: Central to rational medicine is the use of pharmaceutical drugs, surgical procedures, and cutting-edge medical technologies that have undergone exhaustive scientific evaluation. These interventions are subject to rigorous quality control measures.
3. *Specialisation and Expertise*: Modern medicine is marked by a high degree of specialisation among healthcare professionals. Physicians, surgeons, and other specialists receive specialised training and possess in-depth knowledge within their respective fields, facilitating precise diagnosis and treatment.
4. *Patient-Centred Care*: Rational medicine places a strong emphasis on patient-centred care. It engages patients in shared decision-making, considering their individual preferences, values, and needs while upholding the principles of informed consent.
5. *Regulatory Oversight*: Rational medicine is subject to stringent regulatory oversight in most jurisdictions, ensuring that medical treatments and interventions meet established safety and efficacy standards. Regulatory bodies monitor and approve pharmaceuticals, medical devices, and procedures.

Traditional medicine and rational medicine diverge fundamentally in their historical origins, treatment modalities, validation methodologies, and philosophical perspectives. While traditional medicine is rooted in cultural and historical contexts and relies on empiricism, rational medicine adopts a rigorous evidence-based approach, prioritising biomedical research and regulatory oversight. The coexistence of these paradigms within healthcare systems underscores their respective strengths and addresses diverse healthcare needs, promoting a holistic approach to patient care.

The mandate

The South African government mandated all schools and higher education institutions (HEIs) to decolonise schooling and tertiary curricula mindful of the pervasive realities South Africans encounter daily.[3,4] Pharmacy, medicine, and, consequently, medical treatment are included in this mandate. Full well cognizant of the challenges that ensue at HEIs, it is critical to appreciate Government's tall order when unpacking the actual meaning of decolonising the curriculum for meaningful learning and execution of knowledge. Specifically, in the pharmacy impact sphere, traditional medicine has been utilised for centuries and thus must be recognised as part of the patient treatment regimen. Traditional medicine is made by traditional healers. Therefore, this means that the traditional healers must be recognised and trained in traditional medicine and the making thereof.

Pertinent and valid questions arise as to the traditional healers training.

Traditional medicines

The World Health Organisation (WHO) observes that it is difficult to assign one definition to the broad range of characteristics and elements of traditional medicine, but that a working definition is essential. It thus concludes that traditional medicines:

> "[Include] diverse health practices, approaches, knowledge and beliefs incorporating plant, animal and/or mineral-based medicines, spiritual therapies, manual techniques and exercises applied singularly or in combination to maintain well-being, as well as to treat, diagnose or prevent illness".[5]

One of the definitions given for "African Traditional Medicine" by the WHO Centre for Health Development is:

> "The sum total of all knowledge and practices, whether explicable or not, used in diagnosis, prevention and elimination of physical, mental, or societal imbalance, and relying exclusively on practical experience and observation handed down from generation to generation, whether verbally or in writing".[6]

In South Africa, most people associate traditional medicine with the herbs, remedies (or muti) and advice imparted by *sangomas* or *izinyangas* – traditional healers from African indigenous groups – and with strong spiritual components. Traditional healers are generally divided into two categories – those who serve the role of diviner-diagnostician (or diviner-mediums) and those who are healers (or herbalists).[7,8]

The South African Governmental mandate's antipathy

It is not that the health sciences fraternity, namely pharmacy, medicine and nursing are averse to welcoming the late guest into the health sciences ecosystem. It is rather the absence of knowledge of the workings of traditional healing. The intrinsic and important work of traditional healers can simply not be overstated. Indeed, they play a pivotal role in many communities in South Africa.[9]

Though concern has been raised about the vocation, the medium of study, the curricula, registration of qualifications, and the body appositely qualified to assess the "fit and proper" requirements of all professionals, traditional healing and traditional medicine continue to be used. Presently, an exclusive regulatory body for the oversight of the traditional medicine curriculum does not exist. Without detracting from South Africa's historical past, the present is confounding and must be appropriately addressed. Without the proper mechanisms in place, understanding by the rational health sciences is at a loss. The effort of the Governmental mandate will be in vain.[10]

In our case under discussion, the parents took their minor child for treatment to their local traditional healer, who identified the injury as a snake bite. The minor patient was unable to describe the creature of misery. Thus, the parents relied on the local traditional healer's knowledge of venomous snakes in the region. The traditional healer did not inform the parents of this harmful characteristic. Nor did the traditional healer inform the parents of a rational medicinal antidote or the fact that the emitted venom was a neurotoxin.

The traditional healer did not engage in aftercare patient consultation but rather advised the parents to continue with the traditional medicine. The ingredients utilised in compounding the traditional medicine were unknown to the minor patient's parents. Accordingly, the parents were not adequately equipped to care for their minor child.

When the parents administered the traditional medicine to their minor child, they acted on the traditional healer's advice. They did not know whether the traditional medicine or the absence of the administration of the anti-venom caused their minor son's deterioration in health.

All this pertinent information was not available to the parents when they arrived at Frere Hospital. The healthcare team had to commence with a game of Russian roulette in attempting to symptomatically determine what had caused the minor patient's near-fatal injury. To this end, as they worked in collaboration with the pharmacists, and specialist consultants, *inter alia*, the healthcare team was able to safely conclude that the creature bit with neurotoxins into the patient's bloodstream giving rise to the resultant complications. Amongst others, three salient points come to the fore: knowledge, patient care, and ingredients that are known and applicable in rational medicine administration. These important features were absent in the traditional medicine administration. Whereas rational medicine demands disclosure of ingredients in preps, traditional medicine holds these ingredients out to be a secret or some kind of intellectual property. The question arises as to where and how essential ingredients should be patented and/or disclosed. Failure to know essential basic ingredients may well result in contraindications or no treatment in delaying the harmful impact, as demonstrated by our case.

Where such ingredients are disclosed, the regulatory body which should register them, will depend on the classification. It could be the Medicines Control Act, or the South African Health Products Regulatory Authority (SAHPRA). Knowledge of patient care is another salient point that is mostly present when administering rational medicine but was absent and is mostly absent when administering traditional medicine. Knowledge *per se* has already been alluded to earlier on. Questions that inadvertently arise relate to institutional learning, curricula development, and curricula content. It is well known that traditional healers undertake their studies under tutelage that is heritage-based. What assessment tools are in place to benchmark and assess knowledge assimilation? What training and/or qualifications do the educators have?

These questions have severe repercussions for the healthcare sector and do, unfortunately, lead to potential legal challenges.

Red herrings: legal challenges

Chain of causation: factual and legal causation in determining professional negligence

In law, two kinds of causation must be satisfied to succeed in a claim of professional negligence, namely factual causation and legal causation.[11]

Factual causation refers to the actual chain of events that lead to an aggrieved party suffering damages of a personal or pecuniary kind. Factual causation refers to every action or conduct that leads to the event. In our case, it will apply as follows:[12]

The parents took the minor to a traditional healer, considering him to be an expert in healing. The traditional healer, in law, is deemed to have the requisite health knowledge to diagnose the ailment and administer treatment for same.[13*] If the treatment administered bears a positive effect in that it aids the minor

* The Alma Ata Declaration (1978) made by the International Conference on Primary Health Care was a significant milestone for traditional healthcare as it was one of the first to recognise the role of traditional medicine and its practitioners in primary healthcare. The term 'traditional medicine' should not be confused with "complementary medicine" (CAM). See also Traditional Medicine Strategy 2002-2005, World Health Organization WHO/EDM/TRM/2002 (1):7. The WHO draws a distinction between "traditional medicines" and "complementary and alternative medicines". The latter terms relate to practices such as acupuncture, homeopathy and chiropractic systems – thus a "broad set of health care practices that are not part of a country's own tradition, or not integrated into its dominant health care systems". For a study of the use of the role of complementary and alternative medicines in HIV/AIDS, see Crouch R, Elliot T, Lemmens, T and L. Charland Complementary/Alternative health care and HIV/AIDS; Legal, ethical & policy issues in regulation Canadian HIV/AIDS Legal Network; 2001

patient in recovery, then the attribution of blame will be removed from the traditional healer.

Now, it must be borne in mind that every new act in the chain of events is considered when deliberating before a court of law. So, this means that every new act (*actio interveniens*) that creates a new series of events from the initial event will be taken into consideration.[14] In our case, if the diagnosis and treatment attended by the traditional healer caused further deterioration in the minor patient's condition, then the attribution of blame proportionally will be to the traditional healer. Hypothesising that the traditional healer did not diagnose effectively in that he did not know that the creature emitted a neurotoxin which, in fact, negatively impacted the patient's recovery, then most assuredly the extent of the deterioration from the time of injury until the traditional healer's intervention will be assessed by courts of law or similarly situated bodies. In keeping with these instructive legal principles, we can see how the traditional healer may be held legally accountable.

Legal causation limits the liability of the perpetrator by limiting the sequential acts in factual causation.[15] South African courts have applied the reasonable man test to limit liability such that the conduct of the wrongdoer is measured against the reasonable man's conduct, with the latter being the benchmark.[16]

Unlike other matters, a traditional healer, as the name implies, is a person entrusted with the diagnosis and treatment of ailments.[17] Traditional healers fall within the ambit of a "healthcare provider", with the caveat of non-registration with a legally recognised statutory or regulatory body. In the absence of registration with a recognised body, the wrongful acts may be held to account in a court of law.[18] The applicable legal causation test would then be that of a reasonable person, once again. The legal test will not change.

With the traditional healer's incorrect intervention, the staff administering rational medicine will be exempt from liability because the initial injury was further exacerbated. Moreover, the notion of professional negligence for the staff at the hospital will only commence at the time that the minor patient was received for diagnosis and treatment meaning that the minor patient's claim on negligence will only commence as at receipt of the patient.

Fit and proper

Thus, all healthcare professionals must receive adequate training to effectively carry out their duties. The acquisition of adequate training is closely intertwined with knowledge acquisition.

Accreditation

Ordinarily, knowledge acquisition is regulated and assessed by a regulatory body that holds the necessary skills and expertise to determine the course content and its subsequent practical application.

Mentoring and training

Usually, knowledge acquisition is coupled with mentoring and/or training. If mentoring and/or training are considered independently as is the case with traditional healers, then such must be justified and explained to the regulatory body concerned.

Registration of medicines/products (liability)

When anyone in the healthcare sector administers medicines, whether it be rational or traditional medicine, such medicine's essential ingredients must be known. Usually, the medicines are registered in the interests of effective patient care. When the ingredients are known, then subsequent treatment is facilitated with a better rate of success. When the ingredients are unknown as is the case with traditional medicines, patient care may often be detrimentally compromised.

Registration of the ingredients involves a rigorous process of disclosure through application to bodies such as SAPHRA, for example. When medicines are not registered, then the degree of professional negligence is significantly reduced as the patient acts at his own peril.

Recommendations on integrated or complementary education: The Chinese and Indian Traditional medicine paradigms

There are several best international practices in Traditional Medicine compatible with Traditional Healers in South Africa, notwithstanding South Africa's recognition of THPs.** Thus, the existing legislation should be extended to institutional curriculum development. Presented here are models of countries that have included traditional medicine within their academic environment:

Traditional Chinese medicine

The Chinese healthcare system includes traditional medicine as part of its curriculum. A Diploma in Traditional Chinese Medicine blends modern and conventional practices of traditional Chinese medicine, where students learn how to diagnose and prescribe treatment.[19] Basic theories and practices, such as acupuncture, form the core of the curriculum. Once a student completes their traditional Chinese medicine programme, they are qualified to work in Chinese medical hospitals and clinics, Chinese pharmaceutical industries, and educational institutions teaching the practice, *inter alia*.

Students who receive training to become traditional Chinese medicine practitioners typically work as either acupuncturists or, as stated, practitioners. Some choose to open their own practice,

** In South Africa, THPs are regulated in terms of the THP Act of 2007 (which replaced the THP Act of 2004). South African THP legislation is similar to the Namibian THP Bill of 2014, which describes a THP as a person "registered as a THP registered by the registrar.' In Zimbabwe, the Traditional Medical Practitioners Act of 1981 indirectly provides a definition by defining the 'practice of traditional medical practitioners', and like the other two countries, sets up a body (council) to register THPs. While Zimbabwe, South Africa and Namibia do not specifically define THPs, the Tanzanian Traditional and Alternatives Medicines Act of 2002 gives a precise definition of THPs.

while some work on many levels within the industry. A diploma in the discipline allows individuals to pursue several options within the sphere of traditional Chinese medicine, carrying on practices that have been passed down and improved throughout a seemingly endless number of generations.

Traditional Indian medicine

India is widely considered to be the best country for Ayurveda, as it is the birthplace of this ancient healing system. Ayurveda has been practised in India for thousands of years and is deeply ingrained in the country's culture and traditions.[20] A Bachelor of Ayurvedic Medicine and Surgery, or BAMS, is a course that requires five years and six months to complete and teaches the students everything there is to know about Ayurveda and its application in the curing of various diseases.

One must complete a Bachelor of Ayurveda Medicine and Surgery (BAMS) and be registered in the State Council of Indian Medicine/ Central Council of Indian Medicine in order to become an Ayurvedic Practitioner. In India, a student may proceed to earn a master's degree in the form of MD (Ayurveda) and MS (Ayurveda), a PhD, and clinical doctorate degrees in traditional and complementary medicine at the university level.

In European countries, such as Italy, the UK, and Germany, medical doctors may study Ayurvedic medicine within the framework of postgraduate medical education recognised by medical councils and universities.

Populous countries such as China and India have managed to successfully integrate the study, regulation, and training of traditional medicine with centuries of development. Therefore, South Africa is sure to garner from best practices. Institutional and curriculum development, modes of delivery, assessment and internal regulation by Traditional Healers forming cohorts with expertise must engage in discussions with the relevant healthcare regulatory bodies. These bodies must necessarily include the following, *inter alia*:

- The South African Pharmacy Council which is delegated with pharmacy curricula development; or amend the existing qualifications to be accompanied by relevant training post qualifications;
- The South African Health Products Regulatory Authority to patent or register essential ingredients utilised in traditional medicine preps;
- The Minister of Higher Education and Training who will advise on the core components of curricula development.

Conclusion

The salient challenges discussed under the legal implications demonstrate the need for regulation of traditional healers' training, and informed curricula development. This is not going to be an easy task by any means but it must be done given the percentage of the South African population who seek traditional medicine treatment from a traditional healer. Various mechanisms may be employed to ensure patient care. However, the starting point must be one of the curricula developments, their content, mode of delivery and subsequent practical implementation. This must necessarily be accompanied by proper and effective disclosures in the interests of patient care. Regulation and regulatory oversight are key.

The task is not insurmountable, and it requires an amalgamation of differing disciplines to bring meaningful consultation for sustainable health care.

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The renaissance of psychedelic-assisted psychotherapy

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Abstract

Globally, the revival of psychedelic substances for the treatment of mental health conditions has evolved. Conditions such as depression, anxiety, addiction and post-traumatic stress disorder (PTSD) have been investigated. During the 1950s to 1970s psychedelics were regarded as drugs of abuse. Recent clinical trials have shown the efficacy of these substances. The probable harms of psychedelics are from cases where illicit substances were used in non-medical settings. The different types of psychedelics in the treatment of mental health conditions are discussed.

Keywords: psychedelics, psychotherapy, mental health

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Introduction

The word "psychedelic" is made up of two words: "psyche" (soul) and "deloun" (to reveal).[1] Psychedelics have been used in indigenous cultures for many years and have now entered the mainstream arena.[1] The potential of psychedelics to treat mental health conditions is on the rise.[2] They are still illegal in some countries and underground use has been noted.[2] Those who can afford it may travel to countries where some psychedelics are legal (e.g. Jamaica).[3] In 1943 lysergic acid diethylamide (LSD) was discovered by the scientist Albert Hofman and during the 1950s and 1960s research on psychedelics increased.[3] Tens of thousands of patients are thought to have received "psychedelic psychotherapy" over the course of roughly 15 years, thanks to early reports on the distinct potency and remarkable subjective effects of LSD in the early 1950s.[3] This led to the widespread use of psychedelics, and particularly LSD, in research and clinical practice by psychologists and psychiatrists.[3] The ability of psychedelic research to influence and possibly advance psychology and psychiatry thought and practice was increasingly restricted starting in the mid-1960s; however, as popular and countercultural movements embraced the drugs more and more, their societal impact multiplied.[3] The medical community received its first warning about the risks associated with LSD in 1962 from Sidney Cohen. When LSD first arrived in the US in 1949, it was thought to be a psychotomimetic that could induce a model of psychosis.[4] However, intellectuals in Southern California redefined LSD as a psychedelic that could lead to mystical enlightenment in the middle of the 1950s.[4] Even though LSD was only approved for experimental use and was still under investigation, by the late 1950s, psychologists and psychiatrists were using it to treat alcoholism, neuroses, and to boost creativity.[5,6] In 1962, Cohen issued a warning about the dangers of LSD spreading due to his concerns about its popularisation, non-medical use, black market sales, and patients who were harmed by the drug.[4,5] Cohen's 1960 study on the effects of LSD had concluded that the drug was safe if administered in a supervised medical setting. Medical, not social, concerns led to the subsequent government crackdown and regulation of LSD, which came before the drug movement of the 1960s.[4,5] In 1970, the USA classified psychedelics as Schedule I of the Controlled Substances Act, considering them to have no medical value.[3] This ban spread globally which quickly halted psychedelic research.

After years of inactivity, a new cohort of psychedelic science is resurging.[3] Hopeful early work at Johns Hopkins University and Imperial College, London was seen.[4] Positive preliminary reports have now been published on the safety and tolerability of psilocybin for the treatment of obsessive compulsive disorder, alcohol and tobacco addiction as well as major depressive disorder.[3] Both psilocybin and LSD have shown efficacy for the treatment of psychological distress associated with end-of-life situations.[3] The fact that many of these trials report on small sample sizes and are best classified by conventional standards as "safety and tolerability" studies is an important caveat.[3] Psychedelics are a special class of drugs that frequently result in deep psychological and mystical experiences along with vivid hallucinations.[4] The Default Mode Network (DMN) is a collection of linked brain regions that exhibit enhanced temporal coherence while at rest.[5] Numerous studies evaluating the DMN's function in self-referencing, mind-wandering, and autobiographical memories have focused on it.[5] Many neuropsychiatric disorders, including depression, anxiety, obsessive-compulsive disorder, attention deficit hyperactivity disorder, schizophrenia, and PTSD have been linked to altered connectivity in the DMN.[4,5,6] This review aims to cover the different types of psychedelics and their benefits for the treatment of mental health conditions.

Background

Hallucinogens extracted from plants have been used in religious ceremonies for many years.[3] In 1938 Albert Hofmann synthesised

LSD and in 1943 he came into contact with it and described "fantastic pictures, shapes and a kaleidoscope of colours".[7] In 1947, the company Sandoz began to market LSD under the trade name Delysid as a psychotherapy medication and for experimental study for psychoses.[6] In 1960, Harvard psychologist Timothy Leary began experiments under the Harvard Psilocybin Project to determine whether psilocybin was an effective substance in psychotherapy.[7] In the 1964 book, *The Psychedelic Experience*, psychologists Timothy Leary, Ralph Metzner and Richard Alpert stated that a psychedelic drug is like "a chemical key" that "opens the mind, frees the nervous system of its ordinary patterns and structures".[6,7] Since LSD was being used extensively in medically unsupervised settings, the last of Sandoz's patents for its production expired in 1963, leading to an increase in illicit production of the drug.[7] Governments in the US and Europe expressed alarm in 1965 over the use of LSD and psilocybin by the general public.[7] The Drug Abuse Control Amendments were passed by the US Congress, making it illegal to manufacture or sell LSD without a license and compelling researchers who had not received Food and Drug Administration (FDA) exemptions for experimental new drugs to give up their LSD supplies.[7] Experiments with psychedelics decreased and were stopped by the Controlled Substances Act of the Comprehensive Drug Abuse Prevention and Control Act of 1970.[7]

The idea that psychedelic-induced "mystical" or "spiritual" experiences are correlated with participant responses is central to psychedelic-assisted therapy.[7] Based on the 30-item Mystical Experience Questionnaire (MEQ-30) scores of participants, the researchers in studies observed correlations between symptom reduction and the participants' assessments of their psychedelic experiences as personally meaningful.[7] A validated instrument for measuring mystical experiences, the MEQ-30 evaluates seven distinct domains: internal and external unity; noetic quality which is the feeling of perception or revelation experienced during the experience; sacredness; positive mood; transcendence of time/space; and ineffability which is the difficulty of explaining the experience to others.[7] The instrument's validity and reliability have been confirmed by confirmatory factor analyses, and its external and convergent validity have been shown by latent variable scores that positively predict psychedelic-related changes in behaviour, attitudes, and well-being.[7]

Types of psychedelics

Psychedelics can be separated into four classes based on their pharmacological profiles and chemical structures:[7,8]

- classic psychedelics (serotonin 2A [5-HT_{2A}] receptor agonists)
- empathogens or entactogens (mixed serotonin and dopamine reuptake inhibitors and releasers)
- dissociative anaesthetic agents (*N*-methyl-D-aspartate [NMDA] antagonists)
- atypical hallucinogens, which affect multiple neurotransmitter systems.

Forms of administration:[6,8]

- LSD is available in tablet or capsule form, as well as tiny squares of blotting paper or gelatine that have been soaked in the drug before being ingested.
- Psilocybin (magic mushrooms) is eaten raw or cooked, or boiled into a drink. Psilocybin is also used in dried capsule form.
- Dried and ground peyote buttons are found as capsules, while mescaline from the peyote cactus is found as a white powder. Although it can be chewed or smoked, it is typically swallowed.
- Plant-based ayahuasca is a type of hallucinogenic tea. Used historically in some regions of South America.
- Dimethyltryptamine (DMT) is the psychoactive component of ayahuasca and can be found in many different plants. Typically, it is a white synthetic powder.
- Although 0.5 mg/kg of ketamine is the most often used dosage, some patients may respond to as little as 0.1 mg/kg, and others may need as much as 0.75 mg/kg. Traditionally, the ketamine dosage is spread out over 40 minutes.

The type of psychedelic, the dosage, the user's tolerance, whether or not they have taken other drugs, and the user's functioning and mental state will all affect the effects that they experience.

Generally speaking, psychedelics can have the following common effects:[6,8]

- visual, auditory, tactile, and taste hallucinations
- a loss of clarity in perception, such as the ability to "feel" sounds or "hear" colours
- feeling cut off from the physical form
- time, direction, and distance distortions
- relaxation
- elevated heart rate
- dilated eyes
- nausea as well as appetite loss.

Psychedelics do not always produce the same effects.[6] Even if the user has a great "trip" their first time, it doesn't mean they will always be pleasant.[6,8] Everyone is susceptible to experiencing a "bad trip." Fearful hallucinations, acute panic, paranoia, and nausea are some of the symptoms.[6,8] It is also feasible to experience both positive and negative things during the same trip.[8]

The classic psychedelics are separated into phenethylamines and tryptamines. The tryptamines comprise the synthetic LSD as well as the plant-derived indoleamines psilocybin and DMT.[7] The effects of the classical psychedelics vary slightly from one another, but generally speaking, they cause strong emotions, enhanced cognitive flexibility, and changes in perception (such as hallucinations, illusions, distortions, or amplifications in various sensory modalities).[8] Classical psychedelics can cause mystical experiences, ego dissolution, and a sense of interconnectedness among all beings in certain patients who take high enough doses.[8] Additionally, they have the power to cause severe anxiety

and dysphoria.[8] Psilocybin is one of the traditional psychedelics that is thought to be relatively safe and well-tolerated in terms of safety.[8] Serious side-effects were not observed in any of the larger clinical trials examining the use of psilocybin in major depressive disorder.[8] Thirty-three percent of patients had self-limited headaches, and only one patient had a brief increase in blood pressure.[8] No significant cardiac or neurological events occurred.[8] Other dangers include experiencing nausea or vomiting soon after taking psilocybin.[8] Despite the fact that professionals view a personal or first-degree family history of psychosis as a disqualifier for psilocybin-assisted psychotherapy, research participants in clinical trials have not experienced psychotic episodes thus far.[8]

The phenethylamines include methylenedioxymethamphetamine (MDMA) and mescaline.[7,8] The tryptamines share their core structure with the neurotransmitter serotonin (5-HT) and modulate multiple targets, including 5-HT receptors, monoamine transporters, and trace-amine-associated receptors.[8] The entactogen/empathogen MDMA (a phenethylamine) is pharmacologically related to mescaline, amphetamine, and methamphetamine and acts as a serotonin agonist and releases both dopamine and norepinephrine.[8] MDMA is known for fostering interpersonal connectedness, attachment, trust, and empathy.[8,9] MDMA can also result in feelings of euphoria and a sense of purpose.[8,9] In general, MDMA's effects on perception are less dramatic than those of traditional psychedelics, but they can still be noticeable.[8,9] Additionally, it modifies the way users perceive emotions, causing them to react more strongly to positive emotions and to perceive anger in others more slowly.[8,9] There are numerous physiological effects of MDMA such as negative effects on the heart which can result from stimulant-induced tachycardia and hypertension.[8,9] Heat-related injuries can result from hyperthermia, whereas seizures can be brought on by hyponatraemia.[8] There is also a chance of hepatotoxicity and neurotoxicity.[8,9] Thankfully, there hasn't been any evidence of severe toxicity or drug-seeking behaviour in research participants following MDMA administration.[8,9] Even though MDMA is usually regarded as safe in comparison to other recreational drugs, serious side-effects are possible.[8] The dissociative anaesthetic ketamine, which has psychedelic properties, is an NMDA receptor antagonist that has shown antidepressant efficacy across multiple clinical trials and efficacy in decreasing suicidal ideation.[8] While not a classic psychedelic, ketamine can cause dose-dependent dissociation, alterations in the perception of sight and sound, derealisation, "mystical-type" effects, paranoia, and transient confusion.[8] Table I depicts the different types of psychedelics and Figure 1 illustrates the chemical structures.

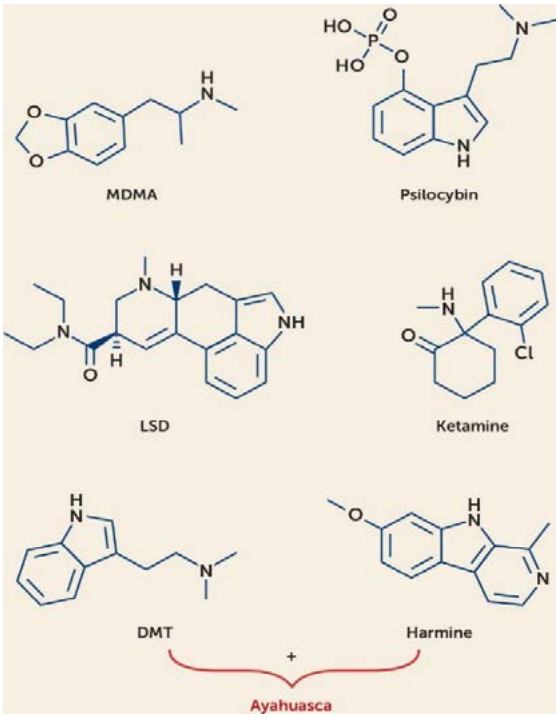

Figure 1: Chemical structures of psychedelics[7]

Microdosing has become more popular recently.[10,11] It is the practice of ingesting sub-hallucinogenic amounts of a psychedelic

Table I: The different types of psychedelics[1,7,9,10,11]

Substance	Derivation	Mechanism of action	Therapeutic uses
LSD	Ergot fungus (*Claviceps purpurea*); morning glory (*Turbina corymbosa*); Hawaiian baby woodrose (*Argyreia nervosa*) — sources of ergine or lysergic acid amide	5-HT_{2A} (serotonin) agonist of pyramidal neurons	Addiction (alcohol), anxiety and associated with mental illness
Psilocybin	Psilocybe and other genera of mushrooms (various species)	5-HT_{2A} (serotonin) agonist of pyramidal neurons	
Ayahuasca brew (admixtures contain DMT)	Chacruna leaf (*Psychotria viridis*); chagropanga vine (*Diplopterys cabrerana*); ayahuasca vine (*Banisteriopsis caapi*); assorted other admixture plants	5-HT_{2A} (serotonin) agonist of pyramidal neurons	Addiction (alcohol, cocaine, tobacco), depression and anxiety
Mescaline	Peyote cactus (*Lophophora williamsii*); San Pedro cactus (*Echinopsis pachanoi*)	5-HT_{2A} (serotonin) agonist of pyramidal neurons	Addiction (alcohol)
MDMA	Sassafras tree (*Sassafras albidum*) — source of safrole, precursor chemical	Serotonin, dopamine and noradrenaline agonist	PTSD
Ibogaine	Derived from Root bark of West African shrub *Tabernantheiboga*	Blocks the uptake of dopamine and serotonin	Stimulant and opiate addiction
Ketamine	Cyclohexane derivative classified as a dissociative anaesthetic	NMDA receptor antagonist	Pain, depression and anxiety

DMT = dimethyltryptamine, LSD = lysergic acid diethylamide, MDMA = methylenedioxymethamphetamine, PTSD = post-traumatic stress disorder

substance.[11] Experts typically define microdosing as taking 5–10% of a full dose of a psychedelic (usually psilocybin or LSD) in order to obtain the drug's purported benefits for mental health without experiencing the hallucinogenic high.

Difficult experiences might be less common with microdosing because it does not require the same level of experience as full-dose research.[11] However, even at the extremely low doses used in microdosing, one may expect less frequent, less intense versions of full-dose challenges to occur (e.g. restlessness, mild anxiety, mild headaches).[11] Microdosing may be studied as a possible adjunct, substitute, or improvement over full-dose interventions for drug use disorders or smoking cessation.[11]

Many reasons are given for microdosing; among the main ones mentioned by survey participants are lowering anxiety and depression, increasing wellbeing, and improving cognitive function.[12] Given how important it is to address mental health issues and improve psychological health and cognition, it is possible that a sizable percentage of microdosers are trying to treat mental illness symptoms or stave off cognitive decline.[12] In fact, microdosers report lower levels of stress, mood enhancements and as well as a reduction in symptoms of PTSD, obsessive-compulsive disorder, depression, and anxiety.[12] Additionally, studies have shown that people may believe microdosing to be more successful than traditional therapies for mental health issues.[12]

In addition to highlighting the importance of therapeutic and wellness reasons for microdosing psychedelic drugs, this analysis of a sizable international sample of adults also found that microdosers had lower levels of anxiety and depression than controls.[12] Additionally, a wide range of microdosing techniques with notable variances in dosage, frequency, and usage of mixtures of psychedelic and non-psychedelic drugs (also known as stacking) were discovered.[12] To learn more about how these specific practices – and microdosing in general – affect the aspects of mood, cognition, and wellbeing that microdosing is meant to improve, further research is necessary.

Conclusion

Psychedelics have revealed great potential in treating mental-health conditions, but their use is restricted by legal hindrances. The debate over psychedelic access and use is progressing, sometimes going beyond the parameters of their therapeutic application and the findings of clinical studies. Best practices, clinical guidelines, and protocols for the medically supervised administration of psychedelics have not yet been developed, despite the fact that research on the supervised clinical use of psychedelic substances has advanced over the past 20 years. The risk is that the market will open up to unsupervised self-medication and recreational use before supervised therapeutic use is established because the perception of psychedelics as effective treatments for mental health disorders – a view that is strongly supported by an increasing number of advocacy groups and commercial interests– will spread more quickly than scientific evidence. This might even jeopardise the advancement of psychotherapy using psychedelics. There is also a chance that not everyone will be able to receive the supervised medical treatment and psychotherapy as this will probably need significant resources such as infrastructure and qualified personnel. This could lead to the emergence of a dangerous black market for these therapies with all the dangers that come with mishandling and abusing an unlicensed profession. Retreats that cater to psychedelic tourism and other commercial interests are outpacing clinical evidence of psychedelics' therapeutic benefits. This is evident in some US jurisdictions where policy developments are occurring. The aforementioned factors have the potential to foster the growth and establishment of markets that lack regulation or oversight regarding the quality of substances and "therapies". This, in turn, may make it easier for people to use psychedelic substances for recreational, non-medical, and unsupervised purposes.

Continued research on the usefulness of psychedelics for the treatment of psychiatric disorders is necessary. The future of psychedelic psychotherapies involves alliances between patients, psychiatrists and other healthcare workers. Risk-benefit assessments for individuals will be required.

Conflict of interest

The author has no conflict of interest.

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Presidential Report 2024

Nhlanhla G Mafarafara

President, SAAHIP

Introduction

Nhlanhla G Mafarafara

Eight months into the term of Office, I am pleased to present this report covering the activities of the hospital sector since March 2023 to date. Our efforts continue with an endeavour to contribute towards a more collaborative hospital pharmacy practice. In this report I shed highlights of my delegated travel to the FIP World Congress in September 2023, some of the status updates on our focus areas, leadership changes in the branches, our collaborative efforts to build the sector and the future.

The period from March 2023 to May 2023 was a moment of finding what we are potentially capable of. The following period, May to August was what I call introspection moment for the leadership of SAAHIP following the functional, systematic, and strategic commitments that were made by branch chairpersons during the closing of the focus area reports at the AGM held March 2023. The commitment could be summed up in the following "we are committed to deliver the ideals of the Association." Achieving these results or manifestation of the commitments requires more effort on both the leaders and the members. Our emphasis is in the questions we have been asking ourselves since February 2023 stemming from a pursuit to redefine and recraft our value proposition as an Association and create an impact.

Let me invite you into what we had to ask ourselves as we launched into 2023/24 term of office in attempt to raise the standard of our value proposition. Our value proposition is and will always evolve. It evolves based on a fixed value change model that is used by big corporates, banks, countries, etc. and it asks 6 questions aimed at answering one question: How can we serve our customers better in a way that increases our value proposition and gives us competitive edge? We asked (and I hope you will do the same and write back to us with more contribution):

- What do we exist for?
- How do we currently deliver our service to our members?
- What do we need to stop doing?
- What do we need to do less of?
- What do we need to do more (increase the standard)?
- What do we need to introduce?

In all these, we are in a renewed effort to engage all key players, identify hindrances (both internally and externally), analyse the cost of serving our members and measure the outcomes. It's a long stretch, and we are on track.

Let me update the sector on the year behind us.

National Executive Committee

SAAHIP term officially started on 11 March 2023. During the recent AGM, the following people were elected into office:

- President: Nhlanhla G Mafarafara
- Vice President: Obey Madzingo
- National Secretary: Carrie de Beer
- Honorary treasurer: Danielle Tshabalala

Following the elections, branches also had some changes, thus the table below shows the branch leadership.

Table I: SAAHIP National Executive Committee (current)

Nhlanhla G Mafarafara – National President	Jackson Mahlaba (Northern Gauteng)
Obey Madzingo – Vice President	Salome Makofane (Limpopo)
Carrie De beer – National Secretary	Ignatius Muller (North-West)
Danielle Tshabalala – Honorary Treasurer	Seshnee Moodley (Eastern Cape)
Shawn Zeelie – Past President	Rahul Golbahram (Northern Cape/ Free State)
Rashmi Gosai (Southern Gauteng)	Thanushya Pillaye (co-opted)
Brent Sin Hidge (Western Cape)	Lourens van der Merwe (co-opted)
Vusi Dlamini (KwaZulu-Natal Inland)	Lorraine Osman (co-opted)
Nomfundo Zwane (Mpumalanga)	Refiloe Mogale (co-opted)
Thandeka Njapha (KwaZulu-Natal Coastal)	Joggie Hattingh (co-opted)

We thank Paul Voigt (WC), Dameeka Kika (NC/FS), Yvette Joubert (NW) and Sylvesta Mogale for their leadership and contribution in SAAHIP. Our work is supported by Anri Hornsveld at the PSSA office and her contribution is invaluable to this sector.

Membership

The Association currently has membership of 3368 members, which shows a growth of 373 new members from the last report given

Table II: SAAHIP membership report

Branch	Members		Branch	Members	
	2023	2024		2023	2024
Northern Cape/Free State	149	169	Southern Gauteng	440	458
Western Cape	577	585	Northern Gauteng	254	282
Mpumalanga	149	160	KZN-Coastal	422	529
Limpopo	183	266	KZN-Inland	336	323
Eastern Cape	324	415	Northwest	158	178
Non-resident	3	3			
TOTAL				2995	3368

in the 2023 Presidential report. The biggest membership growth (numerically) is in the KZN Coastal Branch. The membership growth could be attributed to the visibility of the Association through various activities across the branches.

Follow-up matters from 2023 General Council

During the 66th Annual General Meeting, general council members raised a concern relating to poor access to TB medicines in the private sector hospitals. To find out the depth of the matter and to seek a solution, we engaged our members in the private sector and found out that some of the drugs are hard to get, including Rifafour® which is accessed through Section 21. TB being the leading cause of death among people living with HIV, it is critical to improve access and availability of medicines to the public. On 14 April, SAAHIP wrote a letter to the Director General with proposed interventions. The letter has since been acknowledged by the DG's office, however there was no feedback.

FIP

I had the privilege of representing South Africa as SAAHIP President during the recent FIP World congress in Brisbane. To this effect, a separate report is written for SAAHIP. However, the following are key highlights:

- Pharmacists should take a lead in designing systems for digital health where pharmacy is concerned.
- There is a need to strengthen pharmaceutical intervention in non-communicable diseases within the aging population. This is an open opportunity for pharmacists.
- Collaboration is critical for achieving SDGs, and pharmacists play a big role in collaborative healthcare.
- The world is moving from disease centred care to patient centred care.
- South Africa and Africa to do an internal assessment on the application of the Basel Statements. FIP member organisations to also look at aligning some of their activities with the Basel Statements.

Comments on Board Notices

SAAHIP has made and submitted comments on the following board notices:

- Board Notice 481: Proposed competency standards for Industrial pharmacists, clinical pharmacists and radiopharmacists
- Board Notice 513: Proposed competency standards for a pharmacist who provides public health pharmacy and management services in South Africa

Correspondences and engagements

Engagement with Heads of Pharmaceutical Services

We had a meeting with National Department of Health (Heads of Pharmaceutical Services and Heads of Pharmaceutical Depots) on 23 November 2023 in which we presented on Harmonization of Pharmaceutical Services. During the meeting, the following was presented:

- Details about who SAAHIP is and what we have been doing
- Basel Statements assessment and utilisation in South Africa
- Existing opportunities for collaboration between SAAHIP and Pharmaceutical Services within NDoH and Provinces, including strengthening district health services through district pharmacists
- Full utilisation of hospital pharmacists (in leadership, management, antimicrobial stewardship, patient safety initiatives and primary healthcare)
- Sustainable future of pharmacy in South Africa

FIP engagements

A newsletter was issued on 21 July 2023 by the PSSA following a request to participate in it. The results of the contributions will be published by FIP in due course.

The Africa Region of FIP Hospital Section has been working towards positioning Hospital Pharmacy in Africa. A meeting was also held with the executive leadership of FIP HPS to discuss the current developments in Africa. The team also plans on extending the FIP Basel Statement global project to more African Countries in 2025 .

Other countries have BPharm while others have PharmD as entry level qualification (see table III)

Further to this, we have been looking at comparing the practice of hospital pharmacy in different African countries in an effort of harmonisation of pharmaceutical services. Hospital pharmacy practice in Africa is unevenly advanced with countries like South

Table III: Pharmacy in African Countries							
RSA	Kenya	Tanzania	Cameroon	Morocco	Ghana	Zambia	Uganda
BPharm	BPharm	BPharm	PharmD	PharmD	PharmD	BPharm	BPharm
4 Years	5 Years	4 Years	7 Years	6 Years	6 Years	5 Years	4 Years
Clinical Pharmacy recognition							
Not yet legislated	Recognised	Not yet recognised	Recognised	Recognised	Recognised	Recognised	Recognised

Africa and Kenya being well established, some (Tanzania) with newly established national hospital pharmacy section and others (Cameroon and Morocco) still advocating for establishment of hospital pharmacy section. Training of pharmacists still varies from 4 to 7-year undergraduate qualification.

European Association of Hospital Pharmacists

We received correspondence from EAHP requesting partnership with SAAHIP to work with them on a digital medicines management project for developing countries. The project includes a nationwide assessment of technologies used for medicines management working with different stakeholders such as National Department of Health, Private Hospital Groups, Nursing Council and SAAHIP. There will be a round table discussion to map out the full methodology, deeds determination and implementation process on 14 March 2024 at the Sandton Convention Centre. Results will be shared with the sector as the process unfolds.

National Projects (Focus Areas)

The updated and adopted focus areas for 2023 were discussed in the Exco reports (February and May 2023). Very limited work has been done on the focus areas. Currently solid plans for implementation of focus areas exist for Media, Marketing and Branding, Compliance with Standards (in partnership with Limpopo Department of Health), Leadership and governance (in partnership with Mpumalanga Department of health) as well as the Conference focus area. The Western Cape branch is working with other stakeholders including SAACP in the NHI's model for Contracting Unit for Primary Health Care services.

Credit is given to the Media, Marketing and Branding Team for taking our May resolution and giving it a twist. In May, it was resolved that a spotlight should be shone on SAAHIP leaders. So far, the initiative of SAAHIP #35under35 was a great success. The feedback from young pharmacists who were profiled was very positive. The campaign on women's month profiled women in hospital pharmacy.

Furthermore, in August, SAAHIP put a spotlight on 42 women who are doing exceptional work in leadership, research and mentoring other women in their spaces.

These two campaigns created a buzz on social media. Its impact on membership growth is not assessed but has indeed proven to create a different kind of engagement.

With this, a 360 degree may be warranted as part of revising the full strategic output of the focus area.

National Health Insurance (NHI)

The implementation of National Health Insurance in South Africa is receiving new attention. SAAHIP formed a task team during the August meeting to look at the initiative and its application in hospital practice within NHI.

Social Responsibility

SAAHIP has so far paid a total of R72 905 towards Operation Smiles which paid for 13 smiles. We appreciate the efforts of our branches and members in raising these funds and enabling the social responsibility of SAAHIP to thrive. In October 19 to 22, SAAHIP participated in an Operation Smile Drive in the Eastern Cape. SAAHIP was represented by Robyn Wates (separate report written by WC branch is available).

SAAHIP's social responsibility keeps on touching other areas of society such as NC/FC initiatives in supporting children in paediatric wards during Mandela day. The team also donated toys and clothes to the children as well as running Soup Days to feed the needy and collecting and donating sanatory towels.

SAAHIP branches continue to support high school learners as showcased during Pharmacy Month.

Conclusion

There is still more work to be done. SAAHIP is a voluntary organisation. The leadership roles that members take are also voluntary, thus we appreciate the sacrifice on behalf of the profession. Be that as it may, once one takes up the role, it should be taken very seriously as each leader becomes a pen that's ready to write. Both action and inaction are a permanent ink that is writing a story of significance or non-thereof.

The year 2024 will be the year where we look back over a seven-year implementation of the Focus Areas as reference for our great plans as we plan on what needs to be done and achieved over the next five to six years (hospital pharmacy in South Africa 2030). A mammoth task awaits all of us.

South Africa's Hospital Pharmacy Sector needs to shine some light during the upcoming International Pharmaceutical Federation congress to be hosted from 1-4 September 2024 in Cape town. We hope to see many hospital pharmacists there.

SAAHIP – Women's Month Campaign

S.A. Association of Hospital and Institutional Pharmacists

S.A. Vereniging van Hospitaal en Inrigtings Aptekers

A sectoral division of the Pharmaceutical Society of South Africa

On the 9th of August 1956, women across South Africa decided that they had had spent enough time being complacent about the atrocious apartheid regime, pass laws and the overall dire situation that the country was in and rallied together and marched to the Union buildings in Pretoria. Women from all walks of life, some clad in traditional wear, some with children on their backs, came together and spoke in one voice. This was a display of courage and resilience and showed that women are definitely a force to be reckoned with. These events played a pivotal role in our country's democracy and should never be forgotten. The event is remembered and celebrated annually by the country as our National Women's Day during the month of August.

The pharmaceutical profession is fortunate to be blessed with female leaders of a similar caliber, displaying the same strength and resilience, daily. The South African association of hospital and institutional pharmacists (SAAHIP) decided that it is necessary showcase and celebrate these incredible women during the month of August. The request for nominees was disseminated via the SAAHIP Branch chairs, the SAAHIP membership, marketing and branding stream and all SAAHIP social media platforms. The response was overwhelming, having received 42 (breakdown shown in Table I), very worthy nominees from across the country. The nominees were then asked to supply us with information where we could document their qualifications, current positions, their own journey in the pharmaceutical profession and how they have empowered others, in particular females in the profession. 42 social media flyers were created and uploaded onto the National SAAHIP social media platforms.

The pharmaceutical profession can safely say that we have some of the most educated, talented and accomplished group of females. SAAHIP was able to display these attributes via the creation of the social media flyers. The nominees showcased have made incredible sacrifices for their teams, mentored immeasurable amounts of students, assistants and pharmacist interns, and overall have put their passion for the profession first whilst still trying to balance work and family life and have made valuable contributions that will ensure young, emerging pharmacists follow suit. There was also a definite trend amongst the nominees of continuous learning, self-development and overall empowerment of others. We can therefore conclude that the pharmaceutical profession has female pharmacists who are a force to be reckoned with. They are quickly taking on more leadership and management roles in our profession, making significant leaps and bounds. They have become trailblazers in all sectors of pharmacy and SAAHIP celebrates these incredible women!

Dr. Seshnee Moodley

SAAHIP Membership, Marketing and Branding Lead

SAAHIP EC Chairperson

Table I: Nominees per Branch

Branch	No. of Submissions	Names
Northern Gauteng	6	1. Dr. Pumzile Skosana 2. Leonaye Erwee 3. Dalene Kuisis 4. Beverley Summers 5. Sofia Fourie 6. Prof Hanlie Meyer
Southern Gauteng	2	1. Jacquie Fox 2. Rofhiwa Midana Mulibana SHONI
Mpumalanga	5	1. Jeanet Steyn 2. Margaret Moloto 3. Mamolefe Selokela 4. Phindile Hlope 5. Phindile Mnyanga-Ndlovu
North West	2	1. Elna Davies 2. Yvette Joubert
Free State/Northern Cape	2	1. Geziena Kruger-Swanepoel 2. Bonolo Teki
Eastern Cape	5	1. Dianne Paton 2. Nolitha Olayi Gubula 3. Salmone Petrus 4. Xoliswa Mjikijela 5. Alice Lategan
Western Cape	2	1. Kaajal Chetty 2. Nadine Carol Butler
KZN Coastal	2	1. Nerina Banwari 2. Nirupa Misra
KZN Inland	1	1. Renesha Bikraj
Limpopo	6	1. Cynthia Moleboge Ramahuma 2. Salome Makofana 3. Pelepele Lerato Maketa 4. Amelia Mashaba 5. Mavis Shivambu 6. Razeeya Khan
Presco	9	1. Dr. Seshnee Moodley 2. Anri Hornsveld 3. Thandeka Njapha 4. Thanushya Naidoo 5. Refiloe Mogale 6. Danielle Tshabala 7. Lorraine Osman 8. Natalie Shellack 9. Mariet Eksteen
Total	42	

Legal requirements governing electronic prescriptions

Gary Black
(Dip.Pharm) FPS

Introduction

The digitalisation of patient records, transmission and sharing of patient information, orders and prescriptions is a reality with significant advantages for pharmacy practice, if correctly applied. We consider here some of the concerns of pharmacists with regards to the electronic generation, transmission and signing of prescriptions, in particular.

What does the law say?

The preparation (writing), signing and transmission of prescriptions and orders for medicine electronically is permissible provided that appropriate technology is used in compliance with the *Electronic Communications and Transactions Act no. 25 of 2002*. (ECT Act) The purpose of the ECT Act, is to legalise and regularise electronic communications and prevent abuse of communication systems.

This has been accommodated in the **Regulations to the Medicines and Related Substances Act 101 of 1965**: **General Regulations** as follows:

33. (1) Every prescription for a medicine shall be-
(a) written in legible print;
(b) hand or typewritten; or
(c) prepared with an electronic agent as defined by and in compliance with the Electronic Communications and Transactions Act, 2002 (Act No. 25 of 2002)

(2) A prescription shall be signed -
(a) person; or
(b) in the case of a prescription prepared in accordance with sub regulation (1) (c), with an advanced electronic signature as per section 13 of the Electronic Communications and Transactions Act, 2002 (Act No. 25 of 2002), by an authorised prescriber.

34. (1) Every order for a medicine or scheduled substance shall be-
(a) written in legible print;
(b) hand or typewritten; or
(c) prepared with an electronic agent as defined by and in compliance with the Electronic Communications and Transactions Act, 2002 (Act No. 25 of 2002).

(2) An order for a medicine or scheduled substance shall be signed-
(a) in person; or
(b) in the case of an order prepared in accordance with sub regulation (1) (c), with an advanced electronic signature as per the Electronic Communications and Transactions Act, (Act No. 25 of 2002), by the pharmacist, pharmacist's assistant practising in accordance with the scope of practice prescribed in terms of the Pharmacy Act or authorised prescriber placing the order.

There are therefore **2 important criteria** to be met for an electronic prescription to be valid in accordance with Regulations stated above:

i. The preparation and transmission of the electronic prescription must be generated on a system (***electronic agent***) whereby
   - the integrity of the information is maintained and the information remains complete and unaltered
   - the prescription can be displayed, reproduced (printed or stored) in its original form (see 14.1 and 14.2 of the ECT Act)

ii. The prescription must be signed using an ***advanced electronic signature (AES)***

Advanced Electronic Signatures

An "***advanced electronic signature"*** is defined in the ECT Act as:

> *"advanced electronic signature" means an electronic signature which results from a process which has been accredited by the Authority as provided for in section 37;"*

The "Authority" provided for in this definition has been established by the Department Telecommunications and Postal Services and is known as the South African Accreditation Authority. Providers of authentication products and services which have been accredited by the Accreditation Authority include *Law Trusted Third Party Services (Pty) Limited ("LAWtrust"), the South African Post Office Limited ("SAPO Trust Centre")* and *Trust Factory (Pty)Ltd.*

Accredited service providers supply authenticated products and services which include registered advanced electronic signatures (AES) which are stored securely.

Such authenticated advanced electronic signatures must meet the following criteria:

They,

- are uniquely linked to the user;
- are capable of identifying that user;
- are created using a means that can be maintained under the sole control of that user;
- will be linked to the data or data messages to which they relate in such a manner that any subsequent change of the data or data messages is detectable;
- are based on face-to-face identification of the user.

Practical application in prescribing

- The prescriber would subscribe to an authenticated electronic system provided by an accredited service provider in compliance with the ECT Act.
- This includes the registration and use of his AES to be attached to the electronic prescription which can be sent via a secure transmission to the pharmacy of the patient's choice.
- In reading the prescription the pharmacy would have a similar system in place with an access code which is used to open, read, print and store the script securely.
- In each case a unique PIN is provided to access the prescription. This PIN may be given to the patient who could then visit their pharmacy of choice and give the PIN to the pharmacist to access the prescription.
- The patient may use the PIN to see and read his prescription but would only be able to print a copy encrypted with a message stating that this is a "read only" prescription, not for dispensing.

NOTE:

All prescriptions (including S5 and S6 scripts) correctly prepared, written and transmitted using authenticated systems and bearing an AES as described above, are legal, irrespective of the schedule status of the medicine involved.

On 13 June 2023, the PSSA hosted a webinar titled, ***Understanding digital scripting (including electronic prescribing and advanced electronic signatures*) presented by EM Guidance which not only explains their own system comprehensively, but also covers many of the legal and practical requirements of digital prescribing.** The webinar presentation and handouts, including a Q&A document are available on the Society website.

Whilst the Society cannot endorse any particular product, it does recognise the information provided by EM Guidance as a valuable, useful resource, compliant with the legal requirements of the Medicines Act, Pharmacy Act and the Electronic Communications Act.

What about other forms of electronically prepared prescriptions and signatures?

The ECT Act defines an ***"electronic signature"*** as:

"electronic signature" *means data attached to, incorporated in, or logically associated with other data and which is intended by the user to serve as a signature;*

This definition includes any information that is intended to be used as a signature, regardless of the security of the signature or the data with which the signature is associated. This would typically be a signature on a paper document which is scanned onto the computer or signed directly onto a computer/device using something like an electronic pen or a scanned copy of a signature. Prescriptions are sometimes prepared this way and then faxed or sent electronically via SMS, Whatsapp or scanned and e-mailed to the patient or pharmacy.

Such systems and signatures do not comply with the requirements of the Medicines Act Regulations.

Considering the fact that S5 and S6 medicines are often abused and prescriptions forged, pharmacists were reminded of their legal and ethical obligations in a previous newsletter as follows:

Pharmacists are reminded of the requirement of sub-regulation 33(4), which states that "The pharmacist who dispenses a prescription shall verify the authenticity of all prescriptions so dispensed."

The PSSA suggests some of the following measures when receiving a faxed or emailed prescription to prevent abuse and misuse of medicines including Schedule 5 and Schedule 6:

- *Only accept an emailed or faxed prescription from the prescriber's rooms directly and not from the patient.*
- *Ensure that the prescription is legible and that the copy received will last and not fade with time.*
- *Ensure that the prescriber is an authorised prescriber and registered with the relevant authority.*
- *Ensure that the prescription is valid and legal, as you would when receiving an original hardcopy prescription.*
- *When there is any doubt, rather contact the prescriber before dispensing the prescription.*
- *Ensure that all activities are documented.*

The above actions are particularly applicable when dealing with patients and/or doctors who are not known to the pharmacy. If in doubt, and to act in the interests of the patient, a 48-hour emergency supply of medicine could be supplied until the original prescription was obtained.

What about use of an Advanced Electronic signature by a pharmacist?

There is an increasing use of digitalisation of prescriptions, records and communication in pharmacy practice. If digital signatures are to be used by pharmacists where signatures are legally required in practice, only an AES may be used.

Consider the requirements in sections 13(1), (2) and (3) of the ECT Act, more specifically the following:

"Signature" 13.(1) Where the signature of a person is required by law and such law does not specify the type of signature, that requirement in

relation to a data message is met only if an advanced electronic signature is used."

IMPORTANT NOTE: If a digital signature is to be used to authenticate any document or authorise any professional decision/action, only an AES will be legally acceptable.

Firstly: *Pharmacists may be required to sign a prescription as the prescriber/initiator of treatment*:

As can be seen above, the requirements of using an electronic signature for a prescription (Reg. 33(2)(b)) or order of medicine (Reg. 34(2)(b)) specify that only an Advanced Electronic Signature (AES) may be used.

If pharmacists wish to sign electronically for PIT, EPC or PCDT prescriptions and orders for medicine (e.g. S6 medicine orders) only an AES may be used.

Secondly: *Pharmacists' signatures are legally required in various other instances in practice:*

There are many other instances where a pharmacist's signature is required by law or which may need to be scrutinised for authenticity including the following:

a) *Signing of all prescriptions* or copies thereof to verify the authenticity of the dispensed prescription and thereby accepting accountability and liability for the correctness of the dispensing of the medicine and confirming that the medicine was supplied. (see Medicines Act section *22A. Control of medicines and Scheduled substances(6)(q)* and *Regulation 33(4)* and *GPP 2.7.1.2(f) Signing the prescription.*

b) *Endorsement of prescriptions:* For example, consider GPP 2.7.3 *Safety in dispensing procedures* and 2.7.3.1 *Interpretation of prescription*. The prescription must be endorsed according to any action taken e.g. telephonic confirmation.

c) *Signing confirmation of test results and referral documents:* e.g. see GPP 2.13.5 *Minimum standards for the performance of HIV tests* and 2.13.5.7 *Documentation and record keeping*. All referral documents must be signed by the pharmacist or other health care professional, as a confirmation that the test had been done by a professional person.

d) *Signing of Scheduled medicine registers*

e) *Signing off on work done* by PAs e.g. prepacking

Some practical advantages of digital prescriptions

Legibility

Poor handwriting by authorised prescribers leads to misinterpretation by pharmacists and subsequent dispensing errors. Electronically prepared prescriptions will mitigate or eliminate such errors.

Prescriber clearly identified

There are many doctor's group practices which use one format of a script pad on which all the doctor's names appear. It is then sometimes difficult to identify the relevant doctor from the signature. This problem does not arise with correctly prepared digital prescriptions because the AES is uniquely linked to a particular doctor and easily identifiable.

Easy to supply/access the original script

Often, when prescriptions are provided verbally or are supposed to be faxed or e-mailed, they never reach the pharmacy, which has a legal obligation to retain and store the original script. Once the prescriber has generated the prescription on the electronic system it is easily accessible to the pharmacy to be downloaded, printed and stored. The electronic prescription is also retained on the system for the legally required time period.

Endorsement of repeats

Repeats of the prescription are recorded on the electronic record and can be viewed by any pharmacy which the patient visits. i.e. if a patient is travelling, they could get their repeat from a different pharmacy provided the access PIN is available. There is no need for the patient to retain an original, with the possibility of losing it.

More secure, no fraudulent alterations

The use of paper is insecure and can easily lead to fraudulent alterations. This failing is addressed by the use of electronic prescriptions which are generated, signed, and transmitted in accordance with the requirements of the ECT Act.

Furthermore, the practice of "pharmacy hopping" by patients who abuse their prescribed medicine, might be discouraged as the electronic prescription and the recording of each repeat is visible to the pharmacist who is then in a position to question early and/or too frequent refills of the script.

Conclusion

If correctly implemented, the digitalisation of prescriptions, orders, records and communications, hold many advantages for pharmacy practice. Pharmacists should embrace the new technologies available as a solution to many problems currently experienced in the paper-based system but must be aware of the legal requirements and ethical obligayions in doing so.

Disclaimer: This document is a guideline and does not necessarily reflect official policy of the Pharmaceutical Society of SA. Anyone wishing to implement proposals made in this document, must do so in accordance with the requirements of the Pharmacy Act, Medicines & Related Substances Act and all other relevant legislation, and, if necessary, should seek legal advice to ensure compliance.

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News

Semaglutide's slimming properties shifts the scales towards scarcity and shams

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Abstract

Semaglutide, a glucagon-like peptide-1 receptor agonist (GLP-1 RA), has gained attention for its complementary benefits of effective glycaemic control and body weight reduction. However, a concerning trend has emerged as semaglutide, particularly Ozempic®, intended for the treatment of type 2 diabetes, is prescribed off-label for its weight loss properties, leading to a worldwide stock shortage and complicating the treatment of diabetes patients stabilised on this medicine. The surge in demand, fuelled by social media coverage and celebrity endorsements, has prompted the production of counterfeit 'Ozempic' products, some containing insulin, posing serious health risks. Health regulatory authorities globally are actively monitoring and warning against counterfeit products, emphasising the importance of using authentic medicines obtained through legal medicine supply chains, prescribed by healthcare professionals. SAHPRA has urged the public to use only registered Ozempic® products, highlighting the health risks associated with unregistered and falsified medicines, and to report any suspicious products.

Keywords: GLP-1 RA; glucagon-like peptide-1 receptor agonist; Ozempic®; semaglutide; type 2 diabetes mellitus

Introduction

In South Africa, the challenge of diabetes and obesity poses significant health concerns and high costs to the healthcare system.[1] Semaglutide was introduced as an effective treatment for type 2 diabetes, offering the dual solution of glycaemic control and weight loss.[2] In South Africa, semaglutide is marketed under the trade name Ozempic®.[3] Due to the observed efficacy of Ozempic® in promoting weight loss, it is being prescribed off-label for this property, although it is indicated only for the treatment of type 2 diabetes. This unintended usage has led to a shortage, exacerbating the difficulties faced by those in need of diabetes treatment.[4] Semaglutide is a glucagon-like peptide-1 receptor agonist (GLP-1 RA), that exerts its action by selectively binding to and activating the GLP-1 receptor. The GLP-1 receptor is the target for endogenous GLP-1, a physiological hormone that has various actions on glucose, mediated by GLP-1 receptors. Semaglutide lowers blood glucose levels by stimulating insulin secretion and reducing glucagon secretion in a glucose-dependent manner. Therefore, in the presence of elevated blood glucose, insulin secretion is increased while glucagon secretion is suppressed. Additionally, the mechanism of blood glucose reduction includes a slight delay in gastric emptying during the early postprandial phase. Semaglutide is also indicated for patients with type 2 diabetes in combination with established cardiovascular disease to reduce the risk of major adverse cardiovascular events.[3]

Products and indications

Semaglutide (Ozempic®) is not the only GLP-1 RA registered in South Africa. Exenatide (Byetta® and Bydureon BCise®) and dulaglutide (Trulicity®) are also indicated in the treatment of type 2 diabetes mellitus as add-on therapy together with other glucose-lowering medicines, diet and exercise, if adequate glycaemic control is not achieved. Byetta® is injected subcutaneously twice daily while Bydureon BCise® and Trulicity® are injected once weekly, like Ozempic®. Exenatide and dulaglutide does not cause significant weight loss. Victoza® (liraglutide) is injected daily and is registered for the treatment of type 2 diabetes. Saxenda®, also containing the active pharmaceutical ingredient liraglutide and injected once daily, is the only GLP-1 receptor agonist registered in South Africa specifically for weight loss. For weight loss, the dose administered is significantly higher than the dose used to treat diabetes, in the case of semaglutide and liraglutide.[4]

Efficacy and safety

The efficacy of semaglutide in the treatment of type 2 diabetes mellitus has been established and the added benefit of weight loss has been proven.[2] Hu et al. recently reviewed the efficacy and tolerability of subcutaneous semaglutide compared to placebo or other antidiabetic agents. In this review, 17 clinical trials enrolling a total of 14 940 type 2 diabetes patients were included. It was shown that semaglutide significantly reduced blood glucose, body weight and systolic blood pressure, thereby exerting an indirect cardiovascular protective effect. Semaglutide showed beneficial effects on glycosylated haemoglobin A1C (HbA1C) control. The most common treatment-related side effects were mild to moderate gastrointestinal disturbances, similar to those experienced when using other GLP-1 RAs. These effects were dose-dependent and included mainly nausea, diarrhoea and vomiting. The

Active pharmaceutical ingredient	Trade name	Registered Indications
Semaglutide	Ozempic®	Treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise: • as monotherapy when metformin is considered inappropriate due to intolerance or contraindications. • as combination therapy with oral anti-diabetic medici=nes (metformin, thiazoledinediones, sulphonylurea), basal insulin with or without metformin and pre-mix insulin. • to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction or nonfatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.[3]
Dulaglutide	Trulicity®	• An adjunct to diet and exercise to improve glycaemic control in adults and paediatric patients 10 years of age and older with type 2 diabetes mellitus. • To reduce the risk of major adverse cardiovascular events in adults with type 2 diabetes mellitus who have established cardiovascular disease or multiple cardiovascular risk factors.[5]
Exenatide	Byetta®	• Add-on therapy for adult patients with type 2 diabetes mellitus inadequately controlled by lifestyle modification and other oral antidiabetic therapy. • Add-on therapy to basal insulin with or without other oral antidiabetic therapy in adults who have not achieved adequate glycaemic control with oral antidiabetic agents.[6]
	Bydureon BCise®	Adults 18 years and older with type 2 diabetes mellitus to improve glycaemic control in combination with other glucose-lowering medicinal products including basal insulin, when the therapy in use, together with diet and exercise, does not provide adequate glycaemic control.[7]
Liraglutide	Victoza®	An adjunct to diet and exercise to achieve glycaemic control in patients with type 2 diabetes mellitus. Indicated for once-daily administration as: • monotherapy • combination therapy with one or more oral antidiabetic medicines (metformin, sulphonylureas, sodium-glucose cotransporter 2 inhibitor (SGLT2i) or a thiazolidinedione) when previous therapy does not provide adequate glycaemic control. • combination therapy with insulin in patients not achieving adequate glycaemic control with Victoza® and metformin.[8]
	Saxenda®	An adjunct to a reduced-calorie diet and increased physical activity for medically supervised chronic weight management programme in adult patients with an initial Body Mass Index (BMI) of: • ≥ 30 kg/m² (obese), or • ≥ 27 kg/m² to < 30 kg/m² (overweight) in the presence of at least one weight related comorbidity such as dysglycaemia (pre-diabetes and type 2 diabetes mellitus), hypertension, dyslipidaemia, or obstructive sleep apnoea. Adolescents: Saxenda® can be used as an adjunct to a healthy nutrition and physical activity counselling for weight management in adolescent patients from the age of 12 years and above with: • body weight above 60 kg and • obesity (BMI corresponding to ≥30 kg/m² for adults by international cut-off points)*.[9]

gastrointestinal effects of this class of medicines may be explained by its binding to GLP-1 receptors in the gastrointestinal tract which slows gastric emptying. In addition, the activation of central GLP-1 receptors may exacerbate anorexia and satiety, resulting in gastrointestinal discomfort. This review noted no statistically significant differences in the incidence of increased risk of acute pancreatitis and diabetic retinopathy when comparing semaglutide to other antidiabetic agents.[2] The use of Ozempic® (semaglutide) carries a risk of thyroid C-Cell tumours and it is contraindicated in patients with a personal or family history of medullary thyroid carcinoma (MTC) and in patients with multiple endocrine neoplasia syndrome type 2 (MEN 2). Instances of medullary thyroid carcinoma (MTC) have been documented in individuals undergoing treatment with liraglutide during the post-marketing period. However, the information is insufficient to confirm or rule out a causal connection between the use of GLP-1 receptor agonists and MTC in humans. Consequently, patients should be counselled regarding recognising the symptoms of thyroid tumours; for example, persistent hoarseness, dysphagia, dyspnoea or a mass in the neck.[3]

Scarcity and scams

Ozempic® was approved by the Food and Drug Administration (FDA) in the USA for the treatment of adults with type 2 diabetes in December 2017. In January 2020, it was approved for cardiovascular risk reduction in adults with type 2 diabetes with known heart disease. More recently, in March 2022, the FDA approved a higher dose Ozempic® (2 mg) providing increased glycaemic control in adults with type 2 diabetes.[10] Ozempic® was approved in the treatment of type 2 diabetes in the United Kingdom in 2019[11] and in South Africa in July 2020.[3] Due to the soar in demand for Ozempic®, stocks have dwindled globally. This shortage is fuelled by wide social media coverage such as the use of Ozempic® by celebrities.[12] Despite unabated production, 24 hours per day, 7 days per week, Novo Nordisk expects shortages to last until at least mid-2024.[11] Reuters highlighted some of the shortage issues in the UK on 18 November, describing a real-life scenario where an affluent executive battling weight gain had a nine-month supply of Ozempic® in stock while a type 2 diabetic retiree who is relying on National Health Insurance (NHI) is uncertain when she will get her next dose. Despite a directive by the British government to prescribe semaglutide only to treat diabetes and not for weight loss, regulatory

bodies do not have the power to prohibit physicians from prescribing medicines that they believe can help their patient, even in times of shortages.[11] This is also the situation in the USA and South Africa.

The Medicines and Healthcare products Regulatory Agency (MHRA) released a drug safety update on 23 November 2023 that potentially harmful, falsified Ozempic® and Saxenda® products have been seized in the UK. No falsified Ozempic® pens were seized before January 2023, while up to October 2023, 369 potentially falsified pens were seized. They emphasised that patients should be reminded that medicines purchased outside of the legal supply chain, may not contain the ingredients stated on the label. Relabelled Ozempic® and Saxenda® pens which contained insulin was seized in the UK. Some patients had to be hospitalised and showed serious side effects like hypoglycaemic shock. Healthcare professionals and the public were advised to remain vigilant for symptoms indicating hypoclycaemia such as dizziness, sweating and blurred vision and to quarantine and retain suspect products for testing.[13]

NBC News reported on 28 December 2023 that the FDA seized thousands of counterfeit units of Ozempic® and was working with Novo Nordisk to determine the content. The European Medicines Agency (EMA) reported that counterfeit Ozempic® products were identified at wholesalers in the UK and European Union. These fake Ozempic® pens were labelled in German. German authorities stated in November that counterfeit Ozempic® products seized contained insulin. The Austrian Federal Office for Safety in Healthcare reported that several people were hospitalised after using fake products resulting in hypoglycaemia and seizures.[14] The Partnership for Safe Medicines, which tracks counterfeit injectable diabetes and weight loss GLP-1 agonists globally, noted that counterfeit products have been discovered in Australia, Austria, Azerbaijan, Belgium, Egypt, Germany, Iraq, Ireland, Jordan, Lebanon, Nigeria, Russia, South Africa, Turkey, United Kingdom and Uzbekistan. The website also contains tips on how to recognise authentic and counterfeit Ozempic® pens and images of black market semaglutide purchased online.[15]

The South African Health Products Regulatory Authority (SAHPRA) urged the public in a media release on 11 December 2023 to ensure that they only use registered Ozempic® products as they have been made aware of falsified 'Ozempic' being sold on the market and online. They are also aware of advertisements regarding unauthorised Ozempic® and/or semaglutide-containing products spread *via* social media platforms and radio stations. SAHPRA reiterated that Ozempic® is not registered for weight loss in South Africa. A healthcare practitioner may prescribe this product for off-label use as the practitioner would monitor the patient's treatment. Novo Nordisk South Africa, Holder of the Certificate of Registration (HCR), has acknowledged a nationwide shortage of Ozempic® stock, leading to restricted access to treatment for individuals with diabetes. This situation may have opened the door for the influx of falsified or counterfeit products into the market, falsely claiming to be Ozempic® and potentially being used off-label for weight loss. Consumers should exercise caution when encountering online offers for products purporting to be Ozempic® or semaglutide. It is crucial to note that there are currently no generic equivalents of this medicine in South Africa. Therefore, any product not produced by Novo Nordisk and claiming to contain semaglutide is likely to be fraudulent or counterfeit. In South Africa, only one product in two presentations, Ozempic® 0.25 mg and 0.5 mg/dose and Ozempic® 1 mg/dose pens, is registered.[16] On 13 December 2023, SAPHRA released their position on compounded semaglutide products. Semaglutide can be compounded as it is included in a medicine that has been registered by SAHPRA. However, only active ingredients that are included in a product registered by SAHPRA may be used and it must be in accordance with the conditions and requirements contained in the Medicines and Related Substances Act (101 of 1965). It is illegal to compound a medicine using a form of semaglutide that is not in a registered product, e.g. salt forms such as semaglutide acetate and semaglutide sodium, as it has not been reviewed for quality, safety and efficacy.[17] SAHPRA emphasised that these unregistered, substandard and falsified medicines are a serious health risk to the public and encouraged consumers to report any suspected products that are falsely claiming to work like Ozempic®. SAHPRA's 24-hour hotline number is 0800 204 307 or alternatively the web reporting facility: https://bit.ly/3nrku5t can be used.[16,17]

Future outlook

Semaglutide under the tradename Wegovy® is already registered as a weight loss medicine overseas and it may be registered in the future in South Africa as well. This contains higher doses of semaglutide focused on weight loss.[4] Another molecule, tirzepatide, exhibits dual action as a glucose-dependent insulinotropic peptide (GIP) and GLP-1 receptor agonist. Tirzepatide was shown to be dose-dependently more effective compared to GLP-1 RAs, placebo and basal insulin on glycaemic efficacy and body weight reduction. However, it was also associated with an increased incidence of gastrointestinal effects such as nausea. Increased incidences of vomiting and diarrhoea was noted especially with higher dose tirzepatide (15 mg) which caused a higher trial discontinuation rate. All doses were considered safe with regards to serious adverse events and mortality.[18] Tirzepatide, produced by Eli Lilly, is not yet available in South Africa but is registered for weight loss overseas (Mounjaro®, Zepbound®).[19] There is only one orally administered GLP-1 RA currently available; semaglutide tablets 7/14 mg (Rybelsus®), registered only for the treatment of type 2 diabetes, is administered once daily. It is not registered in South Africa, but it is registered for the treatment of type 2 diabetes overseas.[4]

Concluding remarks

The widespread use and promotion of Ozempic® as a popular weight loss medicine and its wide footprint on social media for this purpose has resulted in a shortage of the authentic product. Consequently, unscrupulous individuals have taken advantage of this demand by producing counterfeit medicines which poses a potential danger to consumers. Health regulatory authorities globally are on the lookout for counterfeit products and have warned patients to use only authentic products prescribed by their doctor.

For the time being it is important for health professionals and the public to be aware of the challenges facing this type of diabetes/weight loss medicine. Ozempic® is intended for and registered in South Africa for the treatment of type 2 diabetes. Ozempic® is manufactured

by Novo Nordisk and any other product claiming to be 'Ozempic' or that is called Izempic which is not manufactured by Novo Nordisk is likely to be falsified. It would seem from using the Google search engine that it is currently possible to buy Ozempic®/semaglutide containing products online. It is crucial to avoid taking any medicine that was not prescribed for you, especially when it is acquired from unconventional sources such as social media platforms, online vendors or beauty spas. Doctors make treatment decisions to prescribe medications only after taking a patient's medical history into consideration as those with a genetic predisposition to thyroid cancer for example may be at high risk. The use of every medicine is associated with benefits as well as potential risks, stressing the importance of treatment initialisation under the care of a qualified healthcare professional.

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The National Pharmacy Museum has a new home

Lynette Terblanche

PSSA Southern Gauteng Branch member

The 52 Glenhove Road building was home to an extensive collection of books (some dating back to as early as 1886), fondly known as the Pharmacy Library, as well as the National Pharmacy Museum, with numerous displays showcasing the rich heritage of our noble profession. The sale of 52 Glenhove Road necessitated the relocation of the Library and the Museum.

It was very important that suitable premises be found that continue to display the history of Pharmacy, and the PSSA Southern Gauteng (SG) Branch is deeply indebted to Aspen Pharmacare for providing alternative premises for the museum.

The relocation process was no mean feat; all exhibits were marked according to their respective display cabinets, wrapped, and boxed, and transported to a holding area on the Pharmacare campus, from where the items were moved to the current display area, once the additional display cabinets were installed and other renovations to the designated area were complete.

It soon became clear that space was limited and that not all the exhibits could be displayed in the new premises; some exhibits, such as the dispensary shelving donated to the Museum in commemoration of Cecil Abrahamson, were non-negotiable and have been accommodated.

The accompanying photographs illustrate the different displays in the new premises; displays in cabinets have been created according to specific themes within the pharmacy profession. All items have been indexed and an inventory list of all displays is available.

Fortunately, several duplicate and excess items could be donated to the Pharmacy Department at Wits University, including an extensive collection of dry plant and animal material, traditional medicines, as well as glass laboratory equipment.

In addition, the Branch would like to acknowledge A-Thermal who agreed to destroy the bottled substances and medicines at no cost to the Society. We salute you for this service to pharmacy!

The National Pharmacy Museum and Library has, for several years, been administered and financed by The Southern Gauteng Branch of the Pharmaceutical Society. To cement the concept of a National

Entrance area

Ampoule filling equipment

Legend to exhibits in entrance area

The dispensary

Pharmacy Museum, much of the administration has been transferred to the National Office, for which we are very grateful. The Museum is now a fully-fledged Section 21 Company (not-for-profit company) with a bank account into which donations can be made and claimed back from SARS. More details will be made available later.

We hope to appoint a curator soon who will offer guided tours of the museum.

Unfortunately, the Library could not be housed on the same premises as the Museum; the Library found a home at 6 Fort Street, Illovo Extension, on the premises of the PSSA Southern Gauteng offices.

All duplicate books have been removed and books have been arranged on specially built shelving according to subject matter in a separate facility on the property. In due course, we hope to have a list of all available books published on the PSSA website.

Should any member be interested in acquiring such specific publication, this will be available at a nominal cost (donation to the museum.)

How to visit the museum?

1. Make your way to Health Care Park in Woodlands Drive, Woodmead during office hours.
2. At the entrance to the Park, inform the security guard that you are visiting the museum.
3. You will be directed to Building 1 where the museum is situated.

Tools of the trade

Laboratory, manufacturing filling exhibition

Pharmaceutical Practitioner

South African Association of Community Pharmacists

My opinion

Johannes Ravele

SAACP President

"In life, change is inevitable. In business, change is vital" – Warren G. Bennies.

Johannes Ravele

In the same breath, change can be scary, and can be a moment of crisis. Certainly, sudden change creates uncertainty, causes anxiety, which is typified by a feeling of worry, nervousness, or unease, particularly about an imminent event or something with an uncertain outcome, and fear of the unknown, but gradual change prepares us for a certain future. As humans, we can adapt and strategise new ways of doing things. We have the time to assess, objectively, facts at hand and come up with the best possible solution that will yield the results that we desire.

It is the same with community pharmacy. We are facing change in many aspects and we need to be able to identify such, come up with possible best solutions and see which ones to implement.

The big question is: are we ready to change?

Community pharmacy is going through transformation and if we remain static, we shall not realise the positive changes that are unfolding in front of us.

Do we have space for clinical pharmacists in community pharmacy?

Let us first see what they can do:

The practice of clinical pharmacy embraces the philosophy of pharmaceutical care, which is the care from a practitioner for a patient in the field of drug-related needs in order to assure optimal pharmacotherapy. Pharmaceutical care, as contextualized in clinical pharmacy, is the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life. It is a patient-centred approach that involves pharmacists providing patient care that optimises medication therapy and promotes health and disease prevention.

Key aspects of pharmaceutical care in clinical pharmacy include:

- **Patient-centred**: Pharmaceutical care is focused on the interests of the patient and aims to improve their quality of life
- **Responsibility**: Pharmacists take responsibility for a patient's drug therapy needs and are held accountable for this commitment
- **Continuous monitoring**: Pharmaceutical care involves systematically and continuously monitoring the clinical and psychosocial effects of drug therapy on a patient
- **Optimisation of pharmacotherapy**: The goal is to ensure optimal pharmacotherapy for the patient, which includes safe, convenient, and effective drug use

Clinical pharmacists, play a crucial role in providing pharmaceutical care to patients. This specialised pharmacy service is essential for improving health outcomes and optimising medication therapy.

Can a clinical pharmacist diagnose and treat?

In South Africa, pharmacists who have completed the Primary Care Drug Therapy (PCDT) training can diagnose and treat minor ailments and prescribe Schedule 1 and 2 medications as part of Pharmacist Initiated Therapy (PIT). The PCDT training equips pharmacists with the necessary skills for comprehensive patient management at the primary care level, including the management of chronic conditions such as hypertension and diabetes. The South African Pharmacy Council has published the scope of practice and competency standards for PCDT pharmacists.

The primary health care conditions that PCDT pharmacists may treat are classified according to the chapters of the South African Primary Health Care Standard Treatment Guidelines (STGs).

Having clinical pharmacists in community practices (including general practitioner (GPs) and community centres and pharmacies) means that GPs can focus their skills where they are most needed, for example in diagnosing and treating patients with more complex conditions. Unfortunately, currently the ethical rules of conduct for practitioners registered under the Health Professions Act, 1974 places a restriction on medical doctors collaborating with other health care professionals not registered under the Health Professionals Act. Proposed changes to the ethical rules were published for comment to address this. The amended ethical rules have not yet been published for implementation.

I believe that in a group practice setup, they have a role to play, especially taking into cognizance NHI and what it is expected to achieve.

In community pharmacy, it may be a tall order as not all practitioners write the ICD10 codes for ease of reference. Secondly, we have no access to patients' files to see the notes that the practitioner has scribbled. Thirdly, they are not easy to get hold of. We take a long time trying to contact them and on rare occasions, we succeed. Lastly, we have limitations as we are not directly related to patient care as they are out-patients.

It would be interesting to hear your opinion on clinical pharmacists in community pharmacy practice. The role of community pharmacists in providing clinical services is evolving globally, with a changing focus on the provision of clinical services within the healthcare system. The range of clinical services offered by community pharmacists varies widely from one setting to another, and the social and environmental context of community pharmacy can impact the implementation of these services.

The impact of community pharmacists in South Africa is significant, as they play a pivotal role in providing health education and services to the population. Community pharmacies in South Africa can provide routine HIV testing and treatment services, as well as emergency care for minor ailments. There are approximately 3 580 registered community pharmacies in South Africa, with 1 110 (31%) being corporate chain pharmacies located in cities and the remainder being individually owned, many of which are in less populated poorer settings.

In a study by Vera H. Buss et al, on the impact of clinical services provided by community pharmacies on the Australian healthcare system: a review of the literature, community pharmacies are well located to deliver healthcare services due to convenience and accessibility. The range of services offered by community pharmacies is comprehensive. Despite this, the clinical interventions provided in pharmacies appeared not to be coordinated and this led to the proposal that more efforts should be put into linking the individual services and better integrating them with the patient care provided by the general practitioners and other health professionals. It is unfortunate that the South African system is in the same boat, where our services are not interlinked and integrated and this creates a mammoth task in providing an optimal service to patients.

In Canada, clinical pharmacists collaborate directly with patients and physicians to determine the ideal treatment plan for each patient. They are medication experts in your care team whereas physicians are experts in the anatomy and physiology. Pharmacists are drug experts, whereas clinical pharmacists take this knowledge and apply it to clinical scenarios. They perform functions beyond fundamental dispensing and order-processing activities. This typically involves optimisation of medication selection, dosing, and monitoring.

Depending on the province or territory, the pharmacist may accomplish this by performing an expanded scope of activities such as adaptation of prescriptions, prescribing for minor ailments, ordering, or interpreting laboratory tests and administering drugs, including injections for immunisation or other purposes. In South Africa, some of these activities are covered by PCDT pharmacists and those pharmacists that trained for immunisation and injection technique and family planning. When the PIMART case is over, we hope to see more scope being covered by community pharmacists.

In the United Kingdom, clinical pharmacists can work directly with patients as part of the GP team, for expert advice on medication, to ensure that the chronic medication that the patient is taking is optimal for the condition. It is interesting to note that the clinical pharmacist can change the prescribed medication or change the quantity that the patient is taking if such medication has adverse effect on the patient.

They can also do health checks like taking blood pressure or making appointments for patients to have other tests, like blood tests. It is contentious that they may be able to prescribe medicines in the same way as the doctor.

In recent years, South Africa has experienced notable changes in pharmacy practice regulations and legislation, particularly concerning the acceptance of electronic prescriptions and the introduction of telemedicine services within community pharmacies. Electronic prescriptions are now permissible, provided they comply with Regulation 33 of the General Regulations to the Medicine Act, which mandates the creation of a permanent prescription record. Additionally, telemedicine services allow patients to consult a general practitioner via a monitor within the pharmacy, with the pharmacist subsequently dispensing the prescribed medications to the patient for a minimal fee.

Looking ahead, further technological advancements in community pharmacy practice are anticipated. These may include the establishment of a central database for codeine-containing products by the South African Health Products Regulatory Authority (SAHPRA). Embracing such changes is crucial, as they have the potential to positively impact the communities served by pharmacies, contributing to the reduction of medicine abuse and the enhancement of professional activities. The future of community pharmacy practice in South Africa is also influenced by the proposed new qualification for pharmacists, specifically the development of a postgraduate diploma in Pharmacy for Authorized Pharmacist Prescribers. This qualification is expected to enable community pharmacies to offer expanded services, marking a significant shift in the role of pharmacists within the healthcare system. However, challenges such as open ownership and the need for collaborative efforts to address outstanding issues remain pertinent. Despite these challenges, the evolving landscape of community pharmacy practice in South Africa presents an opportunity for stakeholders to shape the profession's future direction. Therefore, it is essential for the pharmacy community to engage in discussions about the future of community pharmacy and work together to ensure that the profession is prepared to embrace and effectively leverage upcoming technological and regulatory changes.

In conclusion, the evolving regulatory and technological landscape of community pharmacy practice in South Africa presents both opportunities and challenges. Embracing these changes and actively engaging in discussions about the future of the profession are vital steps in ensuring that community pharmacies are well-prepared to meet the evolving healthcare needs of the population.

"The strength of the team is each individual member. The strength of each member is the team" – Phil Jackson.

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Celebrating Pharmacy Month: a handful of colour jam

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When was the last time you had some fun?

The last week of September 2023 was filled with colourful hands, celebrations, fun and education to unite to promote patient healthcare.

The clinical pharmacy team at the School of Pharmacy (SOP) at the University of the Western Cape (UWC) collaborated with the postgraduate committee and the UWCAPS team to present a colour jam event on campus. The team also worked with the pharmacy at New Somerset hospital to host a similar event there. The purpose of the colour jam event was to raise awareness about antimicrobial resistance, and how we as healthcare professionals and communities can combat resistance to promote patient health. Furthermore, the event provided an opportunity to raise awareness about the critical role of pharmacists within the healthcare system.

The clinical pharmacy team and collaborators invited students, staff and patients to their painting station at the front area of the SOP building and the coffee shop area at the hospital. The team member asked the individual to choose a colour to paint their hand with. While the team member painted the individual's hand, they used the opportunity to educate the individual about the meaning of the colour they chose, how it relates to antimicrobial resistance, the role of pharmacy and their role as patient or provider in preserving antibiotics.

Several themes were discussed on the day, aimed to increase awareness and knowledge about the role of the pharmacist and the public's role in the following:

- Antimicrobial stewardship (definition and concept of antimicrobial resistance, the difference between viral, fungal and bacterial infections, responsible antibiotic prescribing, rational antimicrobial use, and the meaning of resistant, intermediate or susceptible infections),
- Infection prevention and control (hand hygiene and handwashing technique, contact precautions, prevention of infection through vaccinations),
- Adverse drug reaction reporting (why report, when to report and how to report, and the difference between side-effects and adverse reactions).

We decided to use colours to represent different types of microbes to make it more fun to remember. These were our colour key:

- Green = sensitive bacteria
- Orange = intermediate resistant bacteria
- Red = resistant bacteria
- Purple = virus
- Yellow = fungi

Each individual was asked to imprint their hand on the white cloth with paint to make their pledge to unite in the promotion of patient healthcare and rational antimicrobial use. Some hand prints were very creative creating new types of organisms. After they made their painted pledge, they could wash their hands with soap and water at the second station. Sanitiser was also available, and patients could see that the "microbes" came off better with the soap and water.

Individuals were also encouraged to take a photo using the selfie-frame, which was handmade by the clinical pharmacy team. The colourful hand prints are now portrayed in the hospital and the SOP building to showcase our pledges.

Everyone LOVED the station! It was a hot topic on the day and some staff were even late for their meetings because they first wanted to get their hands painted. The students appreciated the staff visiting the station on campus. At the hospital, it was a hit! Some of the moms visited from the paediatric ward and came to learn about antimicrobial stewardship and infection prevention. Patients were encouraged to go paint their hand after receiving their repeat prescription at the pharmacy. The staff were also very engaged, and when the stand closed after a while some doctors that missed the initial commotion came to paint their hands in the pharmacy. The selfie frame was the favourite – everyone wanted a photo or more with the beautiful frame.

The colour jam was a great fun initiative to educate the public on various important topics and how we can take ownership and unite to promote healthcare together. We decided to include the hospital staff as well as a way of "pledging" to use antimicrobials rationally, and this also set the stage for collaboration and relationship building.

It was a team effort between patients and personnel, emphasising that healthcare is both the patient and the healthcare worker's responsibility. It is only by working together that we can achieve a patient's individual health goals, as well as the bigger public health goals.

Learning should be fun, and what is more fun than painting!

Watch a snippet of the day at New Somerset Hospital here: https://drive.google.com/file/d/1yCIc9SRO8PPhJAMsRa6sEOOScE52S9fd/view?usp=sharing

Pharmacy Month

Nicole Barnes

At Netcare Blaauwberg Hospital Pharmacy, we decided to do what we can to promote healthy living in both our patients and staffs' lives. We put up a table in the front of the pharmacy filled with fresh apples and pears to give to patients and staff along with a healthy living quote or tip.

On the first day myself, Brent Sin Hidge and our two interns, Lara Naude and Yamkela Boya, took turns during our lunch breaks and free time to hand out the fruit to patients and staff.

On the second day we endeavoured to provide free blood pressure and glucose testing but unfortunately didn't have the staff capacity and will look into doing this better in 2024. So we continued handing out fruit, promoting healthy living and spreading the theme of Pharmacy Month: Pharmacists united in providing healthcare for all patients.

The third day saw us handing out capsule shaped sugar cookies (made by our intern, Lara), sponsored note books with pens and nursing watches to staff and patients who could answer us one simple question: What does a pharmacist do other than dispensing?

Throughout the week we held a competition with the nursing staff to show us #HowILiveHealthy by uploading a photo of their healthy lunch, a healthy recipe or tip or some exercise they completed in the last week. All these photos were uploaded onto a disposable camera app and we chose the best 6 to win some prizes! We handed out the prizes on the last day of our Pharmacy Month activities.

We realised you can plan ahead but there will always be hiccups along the way. We are hoping that next year we will get the opportunity to show nursing that we too can provide primary healthcare in the form of vital checks and OTC medication advice. These events and competition really brought the nursing team closer to the pharmacy team and showed us their support by interacting with our stall, showing interest in the Pharmacy Month theme and entering our competition.

We hope to obtain more sponsored items next year to spoil the pharmacy and our staff that work as hard as the heart of the hospital.

I am extremely passionate about our profession and look forward to promoting the good work we do in the future not only during Pharmacy Month.

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