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References: 1. Ferrous Forte® Somal professional information, August 2022. **2.** Ferrous Forte Tablets professional information, September 2021. **3.** Kim HJ, Bae SH, Kim HJ, *et al*. Cytotoxicity, Intestinal Transport, and Bioavailability of Dispersible Iron and Zinc Supplements. *Front Microbiol*. 2017;8:749. doi:10.3389/fmicb.2017.00749. **4.** Data on file, iNova Pharmaceuticals. 2022. **5.** Sucrosomial iron patent document.

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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.

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Editorial

Advancing HIV management in South Africa: challenges and opportunities in achieving the 95-95-95 goals

Natalie Schellack
Editor: SA Pharmaceutical Journal

South Africa has made significant strides in HIV management, yet challenges persist in achieving the UNAIDS 95-95-95 goals. The country's HIV response is guided by the National Strategic Plan for HIV, TB and STIs 2023–2028, which aligns with global targets.[1] Despite progress, South Africa faces complex obstacles in fully realising these ambitious objectives.

Recent data from the Sixth South African National HIV Prevalence, Incidence, and Behaviour Survey (SABSSM VI) indicates that HIV prevalence in South Africa has decreased from 14.0% in 2017 to 12.7% in 2022, translating to approximately 7.8 million people living with HIV in 2022.[2] This reduction is attributed to various factors, including fewer new infections, more children born HIV-negative, and improved life expectancy for people living with HIV.

The South African government has implemented several policy changes to enhance HIV management. A notable initiative is the Pharmacy Initiated Management of Antiretroviral Therapy (PIMART) program, approved by the South African Pharmacy Council in 2020.[3] PIMART aims to expand access to HIV services by allowing trained pharmacists to prescribe antiretrovirals. However, the implementation of PIMART is currently on hold due to legal challenges and ongoing multi-council consultations.

Progress towards the 95-95-95 goals has been mixed. SABSSM VI revealed that among people aged 15 years and older living with HIV in South Africa in 2022, 90% were aware of their status, 91% of those aware were on antiretroviral treatment (ART), and 94% of those on ART were virally suppressed.[2] While these figures show improvement from 2017, they fall short of the 95-95-95 targets.

Several factors contribute to the challenges in reaching these goals. Treatment disengagement is a significant issue, with an estimated one million people living with HIV who have previously taken ART not currently on treatment.[4] This highlights the need for improved retention strategies and support systems for individuals on ART.

Another concern is late initiation of treatment. In 2023, over 46 000 adults started taking ART only after their CD4 counts had dropped below 200 cells per cubic millimetre of blood, indicating a compromised immune system.[5] This suggests that despite widespread HIV testing, a subset of the population is not accessing treatment in a timely manner.

Gender disparities also pose challenges. Women, particularly adolescent girls and young women aged 15–24, remain disproportionately affected by HIV.[6] Biological factors, societal norms, and behavioural patterns contribute to their increased vulnerability.

Declining condom use is another worrying trend. Overall condom usage in South Africa decreased from 38.5% in 2017 to 31.8% in 2022.[2] This decline in preventive measures could potentially lead to an increase in new infections if not addressed.

The South African government has recognised these challenges and is implementing various strategies to overcome them. These include targeted interventions for key populations, expansion of community-based HIV services, and integration of HIV care into primary healthcare systems.[4] The government is also exploring innovative approaches such as long-acting injectable antiretroviral therapy, which has shown promise in improving treatment adherence.

In conclusion, while South Africa has made substantial progress in HIV management, achieving the 95-95-95 goals requires addressing multiple complex factors. Continued efforts in policy implementation, community engagement, and innovative treatment approaches are essential to overcome the remaining obstacles and ultimately end the HIV epidemic in South Africa.

As we reflect on the progress in HIV care, we must also acknowledge the contributions of those who have dedicated their lives to the pharmacy profession. It is with great sadness that we note the passing of David Sieff, a pillar of the South African pharmacy community.[7] David's unwavering commitment to the profession, particularly his work as editor of the Golden Mortar publication, has left an indelible mark on pharmacy practice in South Africa.[8]

David Sieff's career spanned all sectors of pharmacy, from community practice to hospital and hospice care. His numerous awards, including Honorary Life Memberships and the prestigious Julius Israelsohn award, testify to his distinguished career and significant contributions to the field.[7] David's passion for learning, commitment to patients,

and tireless efforts in pharmacy education serve as an inspiration to all in the profession.

As we continue to strive towards ending the HIV epidemic, we can draw inspiration from dedicated professionals like David Sieff. Their commitment to patient care and professional excellence sets a high standard for all pharmacists to aspire to in our ongoing fight against HIV/AIDS.

As we approach the festive season, we extend warm wishes to all our readers. May the New Year bring renewed hope, improved health outcomes, and continued progress in our collective efforts against HIV/AIDS.

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The plight of unemployed pharmacists and pharmacist's assistants

Tshifhiwa Rabali
PSSA President

Every year, it is becoming increasingly clear that securing employment for pharmacists and pharmacist's assistants will become more challenging. As more pharmacists are being trained, job opportunities will dwindle, largely due to factors such as government budget cuts and the ongoing economic downturn in our country. As the PSSA, we must facilitate a national dialogue on this critical issue. This conversation will allow us to better understand and analyse the challenges at hand, while generating innovative solutions to ensure that our colleagues can continue practicing their profession and receive fair compensation.

Currently, the PSSA is actively addressing the issue of pharmacist's assistants in the Eastern Cape who have not been integrated into the public health sector. We sought to be advised on the avenues explored to create sustainable employment for pharmacists' assistants. We also advocated for the recognition of the importance of the pharmacists' assistants' role in the healthcare system as this would assist in alleviating the strain on other healthcare providers and improve the efficiency and quality of patient care. We are hopeful for a progressive outcome.

For pharmacists who are currently unemployed, starting their own practices could be a promising opportunity to not only create self-employment, but it could also generate employment opportunities for other pharmacists and pharmacist's assistants who are out of work. However, one of the main challenges in starting independent pharmacies is securing the necessary funding. This issue could be addressed through the proposed national dialogue, where potential solutions, such as improving access to funding or creating loan facilities tailored to support pharmacists can be explored.

There is so much that we are doing as pharmacists on a daily basis, and we all know the impact that we are making amongst the different communities in our country. There is need for ongoing emphasis on ensuring that pharmacists fully exercise their professional roles and document all interventions made during practice. We need to adopt an approach of documenting our activities as this will not only enhance transparency but also provide important evidence when engaging with funders on fee negotiations. It is therefore necessary that we commit to these efforts to advance our profession. I salute you all and urge you to continue serving the communities and the country at large.

Lastly, I would like to wish you all a good and imperative safe festive season with your families and friends and to those who will be travelling, I wish you safe travels until we meet again in the new year.

I thank you all.

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 5, 2024 – Vaccine-preventable childhood illnesses

Now more than ever, ensuring that children are up to date with their routine immunisations is crucially important. This module brings you up-to-speed with the latest changes in the Expanded Programme on Immunisation in South Africa (EPI-SA). It covers how vaccines work and addresses common misconceptions. The pharmacist is ideally positioned to play a key role in promoting vaccine confidence and increasing vaccination uptake in order to help prevent and ultimately eliminate potentially dangerous infectious illnesses.

Despite the many successes of the EPI, we now see a large backslide in childhood vaccinations. In June 2024, UNICEF announced that approximately 200 000 children in South Africa are so-called "zero-dose" children, meaning that they are not fully vaccinated against any childhood illnesses at all.

This module discusses common vaccine-preventable childhood illnesses and provides an update on the revised EPI schedule and vaccines available in the private (and public) sector. It also addresses the challenges of vaccine hesitancy and emphasises the role pharmacists play as a trusted source of information in addressing vaccine hesitancy to improve immunisation coverage.

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 pharmacists' 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 5, 2024 – Nappy rash

Nappy rash is a type of dermatitis (i.e. swelling or irritation of the skin) and refers to the rash that develops on skin that is covered by a diaper (nappy). It is one of the most common skin conditions seen in infants and children, affecting more than 50% of infants at some point.

Nappy rash is most commonly caused by irritation of the skin as a result of increased moisture, prolonged contact with urine or faeces and other irritants like detergents, but there are other causes as well, such as infection or an allergy. Sometimes, illness or the early introduction of solids can also precipitate a nappy rash.

Fortunately, most cases of nappy rash are short-lived and resolve with home treatment. This module discusses the most common causes and treatment of nappy rash, as well as ways to help prevent nappy rash.

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.

Early Career Pharmacists Making a Global Impact

As a member organisation of the FIP Early Career Pharmaceutical Group (ECPG), the PSSA YPG is proud to report on the inspiring global actions of young pharmacists highlighted in the 2024 FIP ECPG Annual Report. This year, the ECPG has continued to demonstrate its commitment to advancing the professional growth of early-career pharmacists, fostering innovation, leadership, and collaboration across 101 countries. The ECPG saw a 25% increase in membership this year, underscoring the importance of its mission in shaping the future of pharmacy through the engagement of young professionals, educators, and scientists worldwide.

Leadership Development and Professional Growth

A standout achievement in 2024 was the Early Career Leadership Development (ECLD) Scholarship programme, which empowered six early-career pharmacists to attend the FIP World Congress and participate in the Leadership Development Workshop (LDW). Supported by the FIP Foundation, this initiative covered travel, accommodation, and congress registration, ensuring the scholars could fully engage in leadership training and networking opportunities. These young leaders, hailing from diverse regions, including Africa, the Americas, and Southeast Asia, had the skills and mentorship necessary to drive change in their respective countries, creating a ripple effect in pharmacy practice globally.

The Ton Hoek Scholarship: Celebrating Excellence in Leadership

One of the most prestigious recognitions within the ECPG is the Ton Hoek Scholarship, named in honour of the late General Secretary of FIP, Mr Ton Hoek. Each year, this scholarship is awarded to one of the ECLD Scholars who has demonstrated exceptional leadership in advancing pharmacy practice, education, or pharmaceutical sciences. The 2024 recipient, Mr Praveen Devanandan from India, stood out for his remarkable contributions to the profession through his leadership project.

The scholarship provides financial support for the scholar to attend the FIP Congress for a second consecutive year, where they mentor new LDW participants and present the outcomes of their project. This prestigious award not only recognises the recipient's accomplishments but also positions them as potential global leaders in pharmacy. By engaging with international mentors and peers, the Ton Hoek Scholar builds a lasting network and gains deeper insights into the global challenges and opportunities shaping the future of healthcare.

Mentorship and Volunteering: Building Global Pharmacy Leaders

The Mentorship Programme, another key initiative of the ECPG, continues to be a cornerstone of professional development. In 2024, the programme was enhanced through collaboration with FIP Women in Science and Education (FIPWiSE) and launched during the FIP Congress in Cape Town. This year, 21 mentors and 19 mentees participated in the programme, creating valuable

mentorship bonds that will influence the next generation of global pharmacy leaders.

In addition to mentorship, the ECPG also saw success with its Remote Volunteering Program, which offers early-career pharmacists the chance to contribute to critical projects from anywhere in the world. One notable initiative was the Pharmacy Technician and Support Workforce Surveillance Project, where participants worked remotely to contribute to research and data collection. This programme illustrates how geographical barriers are broken down, allowing young pharmacists to engage in meaningful professional growth and collaboration, regardless of location.

As PSSA YPG continues to contribute to the global landscape of early-career pharmacy, the achievements of the FIP ECPG inspire and motivate young pharmacists in South Africa to engage, lead, and collaborate globally. Let's continue to build on these global successes and drive positive change in our profession.

Imagine travelling to Denmark, meeting inspiring pharmacists from around the world, and making memories that will shape your career. Whether you're into leadership, volunteering, or just building your network, this is your chance.

So, what are you waiting for? Join PSSA YPG, get involved in our events, and let's make the 2025 Congress the biggest one yet! For more info and to stay updated, follow us on social media or check out our newsletters. Let's do this!

PSSA Southern Gauteng Symposium 2024: Advancing Pharmacy Practice

The PSSA Southern Gauteng Annual September Symposium held on 28 September 2024 at Wits Medical School, showcased the continued dedication of South African pharmacists to advancing the profession. Under the theme "Empowering Pharmacists through Advancement of the Pharmacy Profession," the symposium featured diverse presentations highlighting pharmacists' critical role in healthcare.

Keynote addresses from PSSA President Mr Tshifhiwa Rabali and Executive Director Ms Refiloe Mogale emphasised the pivotal role of the PSSA in driving professional development and advocacy for pharmacists across all sectors. Throughout the event, pharmacists from community, hospital, and industry sectors shared their unique insights and contributions to advancing patient care.

During the Community Pharmacy session, Mr Frans Landman spoke passionately about his work as a PCDT pharmacist, detailing how primary healthcare can be delivered effectively to populations unable to afford medical aid. Similarly, Mr Bandela Mgoqi showcased his innovative web platform that reduces patient wait times at Kalafong Hospital, illustrating how technology can streamline healthcare services and enhance patient experiences.

The Hospital Pharmacy session, chaired by Ms Rashmi Gosai, focused on the role of clinical pharmacists and the potential of pharmacogenomics in delivering personalised treatment. The session also highlighted the critical role of pharmacists in improving patient health outcomes through collaborations with healthcare stakeholders, as presented by Ms Shoni Mulibana of Right2Care.

The final Industry session, chaired by YPG's Provincial Liaison, Esther Shuping, showcased the diverse career paths available in pharmacy. From cannabis cultivation to vaccine development, speakers such as Ms Melani Botes and Ms Phyllis Njiru provided a glimpse into the cutting-edge work being done by pharmacists in South Africa.

The symposium was a resounding success. It celebrated pharmacists' contributions and reaffirmed the importance of continued professional development in advancing patient care. Congratulations to the organisers and all involved for delivering such an impactful event.

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!

Evaluation of the labelling adherence of the food-associated effects of selected pharmacotherapy

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Abstract

Background: Pharmacotherapy and dietary interventions often work together to enhance patient treatment and outcomes. Yet, food-associated effects, including food-drug interactions, remain a significant challenge, especially for oral pharmacotherapy. These interactions can undermine the safety and efficacy of medications and negatively impact patients' nutritional status. Despite medicinal package inserts being the primary source of such information, studies from other countries highlight inconsistencies and inadequacies in the labelling of food-drug interactions. In South Africa, this critical issue remains largely unexplored, leaving potential risks unaddressed. The study aimed to evaluate the adherence of professional and patient information leaflets to labelling regulations concerning food-associated effects, providing some insight on a crucial yet often overlooked aspect of patient safety.

Methods: The South African Health Products Regulatory Authority (SAHPRA) labelling guidelines were used to evaluate the adherence to labelling of food-associated effects in the professional and patient information leaflets of warfarin, statins, fluoroquinolone and tetracycline antibiotics.

Results: The leaflets showed partial adherence to SAHPRA labelling guidelines. Food-drug interaction information was either lacking or inadequately described, particularly in relation to the mechanism of interaction, clinical outcomes, or recommendations. Although the information was mostly presented under appropriate headings, it was not always available under recommended sections and rarely cross-referenced.

Conclusions: The labelling of food-associated effects in the evaluated professional and patient information leaflets was partially adherent to SAHPRA labelling guidelines, which may hinder effective guidance for healthcare professionals and patients. Although a small sample, non-adherence is evident and suggests bolstering is needed to mitigate potentially clinically significant interactions.

Keywords: food-associated effects, food-drug interactions, labelling adherence, medicinal package inserts, patient information leaflets, professional information, South African Health Products Regulatory Authority

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Introduction

Food often constitutes an essential part of patients' therapeutic plans and healthy lifestyles.[1] Pharmacotherapy and dietary interventions often have complementary effects in healthcare practice.[2] However, food-associated effects, including food-drug interactions (FDIs), remain a challenge in patient treatment, especially for oral pharmacotherapy.[3] These effects include indirect and direct interactions between food and medications. For instance, food may indirectly alter medications' pharmacokinetic properties, for example, altering orally-administered medications' absorption by changing the gastrointestinal environment following a meal.[3] Conversely, food can directly interact with medications, where specific nutrients alter the medications' pharmacokinetics and/or pharmacodynamics, or medications can affect the patients' nutrient availability or nutritional status.[1,4]

Several studies highlight the clinical significance and implications of FDIs or food-associated effects.[1,4-6] Some food-associated effects may be beneficial to patients.[1,5] For instance, food can aid medications' absorption in the gastrointestinal tract.[5] However, some food-associated effects can be detrimental and result in therapeutic failure, or unexpected and exacerbated adverse effects of medications.[4,6] For example, calcium-rich foods can chemically complex with tetracycline or fluoroquinolone antibiotics, decreasing their gastrointestinal absorption, bioavailability and therapeutic outcomes.[7,8] Grapefruit juice inhibits atorvastatin[9] and simvastatin's CYP3A4-mediated metabolism, thus increasing their plasma levels and adverse effects, such as the risk of rhabdomyolysis.[10,11]

It is important that healthcare professionals (HCPs) have adequate information and work together in interdisciplinary teams to prevent or manage detrimental food-associated effects.[12-14] It is imperative that patients are provided with accurate and adequate information of food-associated effects to consider during therapy.[15] However, studies show that HCPs' and patients' knowledge of FDIs is inadequate.[12-16] Poor education and the unreliability of medicinal package inserts were identified as possible contributing factors, which may contribute to poor practices.[14,15] These include some HCPs not counselling patients on FDIs, and patients taking their medications with coffee or fruit juices which may predispose them to FDIs.[14,15]

In South Africa, a pivotal source of medication information are medicinal package inserts which contain professional information (PI) for HCPs, and patient information leaflets (PILs) for patients.[17,18] The PI is equivalent to the Summary of Product Characteristics (SmPC), a European document that informs HCPs how to administer medications safely and effectively.[17] The general regulations made in terms of the Medicines and Related Substances Act, 1965 (Act 101 of 1965), require a PI (Regulation 11) and PIL (Regulation 12) to accompany each medicine.[17,18] As such the South African Health Products Regulatory Authority (SAHPRA) requires pharmaceutical companies to include PIs and PILs in their applications when registering new medications (Regulation 16[3][g]).[17,18] According to SAHPRA labelling guidelines, PIs and PILs should contain adequate and comprehensive information of clinically significant FDIs and food-associated effects.[17,18] Therefore, if PIs and PILs meet their objectives, they aid HCPs in approaching healthcare from an informed perspective.[19]

Although other countries have reported labelling inconsistencies, such information in South Africa is lacking.[19-21] South African research thus far has focused on patients' and HCPs' knowledge, attitudes, and practices of FDIs in only one province.[13,15] Therefore, this study evaluated the labelling adherence of food-associated effects of selected pharmacotherapy in accordance with SAHPRA labelling guidelines.

Methods

The study obtained ethics approval from the Faculty of Health Sciences Research Ethics Committee (reference number: 248/2023). Four medications with clinically significant FDIs (warfarin, statins, tetracycline, and fluoroquinolone antibiotics) were selected, and their PIs and PILs sourced from SAHPRA's PI and PIL Repository.[22] To determine how general food-associated effects and FDIs information should be labelled in the PIs and PILs, two labelling guidelines were obtained from SAHPRA: Guideline for Professional Information for Human Medicines (Categories A and D) and the Guideline for Patient Information Leaflet for Human Medicines (Categories A and D).[17,18]

The guidelines were used to determine i) the sections that should contain food-associated effects information including clinically significant FDIs, and ii) the type of information that should be provided for clinically significant FDIs, and how it should be described. A focused search was conducted for each medicine via PubMed to create exemplars for comparison. To determine

Table I: The South African Health Products Regulatory Authority labelling guidelines for professional information and patient information leaflets reproduced verbatim from the guideline documents.

South African Health Products Regulatory Authority Guideline for Professional Information for Human Medicines (Categories A and D) SAHPGL-CEM-02_v5 2022[17]	
Sections that should contain food effects and food-drug interactions information	**Information that should be in the sections and how it should be presented**
Section 4.2: Posology and method of administration	The intake of the medicine in relation to fluid and food intake should be mentioned, with a cross-reference to Section 4.5 in case of specific interaction e.g. with alcohol, grapefruit, or milk.
Section 4.4: Warnings and precautions	In specific cases where the food-drug interactions are of major clinical importance, precautionary measures should be described in this section and cross-referenced to Section 4.5.
Section 4.5: Interaction with other medicines and other forms of interaction	Section 4.5 should be presented in the simplest way and a tabulated format may be used where there are numerous interactions. Information should include: • Relevant interactions with food or alcohol with a cross-reference from other sections; • Pharmacodynamic effects with a possibility of clinically significant potentiation or harmful additive effects; • Recommendations for clinically relevant interactions: ◦ Should state where concomitant use is not recommended (cross-reference to Section 4.4). ◦ Precautions including dose adjustment and specific situations where required (cross reference to Section 4.2 or 4.4). • Any clinical manifestations and effects on plasma levels and area under the curve of parent compounds or active metabolites and/or laboratory parameters; • Mechanism of interaction should be described if known; • Additional information on special populations should be given: ◦ If the impact of interaction is more severe in the elderly population, this should be stated. ◦ Food-drug interactions leading to a recommendation on co-administration with food should be specified whether they are relevant for paediatric use (especially newborns and infants whose diet is different, e.g. 100% milk).
South African Health Products Regulatory Authority Guideline for Patient Information Leaflet for Human Medicines (Categories A and D) SAHPGL-CEM-03_v7 2022[18]	
Section 2 under *with<food><and><drink><alcohol>*	• Should mention what the patient needs to know about food, drinks, and alcohol when taking the medicine. • Interactions not related to medicines should be mentioned here if reference is made in Section 4.5 of the professional information. • This section should not be used to tell patients whether their medicine should be taken before, during, or after meals as this should be addressed in section 3, but a cross-reference to Section 3 can be made.
Section 3 under *How to <take><use> the medicine*	Should state whether the medicine should be taken before or after meals.

adherence for labelling and description, the information found in PIs and PILs was compared to the exemplars following the SAHPRA guidelines.

Results and discussion

South African Health Products Regulatory Authority labelling guidelines

Table I provides an overview of the information necessitated for the PI and PILs. Food-associated effects information should be presented in three sections of the PI. Section 4.5 "Interaction with other medicines and other forms of interaction" should fully describe clinically significant FDIs.[17] This includes the mechanism of interaction, pharmacodynamic effects, clinical manifestations, effects on plasma levels and area under the curve (AUC), recommendations or precautions, and additional information on special populations.[17] For FDIs with major clinical relevance, precautionary measures should be described in Section 4.4 "Warnings and Precautions" with a cross-reference to Section 4.5.[17] Section 4.2 "Posology and Method of Administration" should address the intake of the medication in relation to food and fluid intake, where a reference should be made in Section 4.5 in cases of specific FDIs.[17] For the PIL, food-associated effects information should be presented in two sections of the PIL. Section 2 "With food, drink, and alcohol" should mention specific FDIs, provided that reference is made in Section 4.5 of the PI.[18] Furthermore, Section 3 should state whether the medication should be taken before or after meals.[18]

Labelling adherence of food-associated effects in SAHPRA-approved PIs and PILs

The presence of food-associated effects information in PIs and PILs

Eighteen medicinal products from the selected pharmacotherapy (four warfarin, seven statins, one tetracycline, and six fluoroquinolone medications) were sourced. All medications had PIs available, however, only 13 had PILs. For food-associated effects that result from indirect interactions between food and medications, the timing and administration of medications in relation to meal intake becomes important. The evaluated medications can be administered before or after meals. The majority (n = 9) of the PILs acknowledged that administration can occur before or after meals in Section 3. The selected medications can directly interact with certain foods/drinks.[7-10,23,24] As such, further analysis of the PIs and PILs focused on the specific FDIs of the selected pharmacotherapy.

While there are reports of other foods/drinks that can interact with the selected medications, this study only assessed the labelling adherence of the most common and clinically significant interactions between warfarin and vitamin K-containing foods, tetracyclines/fluoroquinolones and dairy products, and statins and grapefruit juice.[25,26] Although food-associated effects may result in clinically significant changes, studies report a lack of information not always mentioned in medicinal package inserts.[19-21,27-28] The study was in agreement with these reports as a few PIs (n = 6) and PILs (n = 3) completely lacked FDI information, highlighting a lack of adherence to SAHPRA guidelines in labelling clinically significant FDIs.[17,18]

The lack of labelling adherence is concerning, particularly for the medicinal samples used in this study. Warfarin, statins, tetracycline, and fluoroquinolone antibiotics are among the most studied and documented clinically significant FDIs.[26] Not labelling or insufficiently describing these medications' FDIs can hinder proper patient counselling, compromising safety and efficacy.[19]

The presentation of FDIs information under recommended sections and headings in PIs and PILs, as well as cross-referencing for PIs

While the presence of FDI information in PIs and PILs is important, so is the presentation under appropriate sections and headings.[17,18] Cross-referencing across the various sections avoids repetition of information, enabling HCPs or patients to easily navigate through the PIs and PILs.[17,18] The headings the FDIs were presented under were considered appropriate if they were specific (e.g. "*with<food><and><drink><alcohol>*"), bolded, and clear for the reader as stated by SAHPRA labelling guidelines.[17,18] The PIs (n = 18) and PILs (n = 12) provided the FDI information under appropriate headings, with one exception where a warfarin PIL did not mention the FDI information under the SAHPRA recommended heading "with<food><and><drink><alcohol>" in Section 2. The FDI was mentioned amidst other physiological aspects that can decrease the effect of warfarin, which could lead to it being overlooked. Furthermore, the FDI information in the PIs and PILs was not always presented in the recommended sections and rarely cross-referenced (Table II).

The presentation of FDIs in the recommended sections varied among the PIs and PILs. The majority (n = 11) of the PILs had the information present in Section 2. Although most of the PIs (n = 12) had FDIs information present in Section 4.5, only a minority (n = 4) contained FDIs information in Section 4.2 and Section 4.4. Only four PIs cross-referenced the information, however, inconsistently.

Inadequately describing FDIs hampers the effectivity of leaflets as a source of information.[19] Thus, PIs and PILs should adequately, comprehensively, and appropriately describe the information for HCPs and patients to enable proper patient counselling to prevent and treat FDIs.[19,20] According to the SAHPRA guidelines, a full description of a FDI entails the foods or drinks that interact with the medication, mechanism of interaction, clinical outcome, and recommendations to prevent the interaction.[17] However, as summarised below and detailed in Tables III and IV, a lack of adherence to SAHPRA labelling guidelines and inadequate description of FDIs information in the PIs and PILs were evident.

The description of FDIs information in warfarin, tetracyclines, fluoroquinolones, and statins PIs and PILs sourced from the SAHPRA website

Warfarin medicinal products

Foods such as green leafy vegetables, lettuce, broccoli, and spinach contain large amounts of vitamin K, which antagonises warfarin's

Table II: Presentation of food-drug interactions information in recommended sections, appropriate headings, and cross-referencing across the different sections of professional information and patient information leaflets. Green (sections contain the information, under appropriate headings, cross-referencing is applied for professional information), yellow (sections lack either one or more of the adherence measures), red (complete lack of adherence measures), grey (patient information leaflet not available).

Samples	Section 2 of PIL	Section 3 of PIL	Section 4.2 of PI	Section 4.4 of PI	Section 4.5 of PI
Warfarin					
Warfarin 1	• Information present • Inappropriate heading	• Information not present	• Information not present	• Information present • Appropriate heading • Cross-referencing applied	• Information present • Appropriate heading • Cross-referencing not applied
Warfarin 2	• PIL not available	• PIL not available	• Information not present	• Information not present	• Information not present
Warfarin 3	• Information present • Appropriate heading	• Information present • Appropriate heading	• Information not present	• Information present • Appropriate heading • Cross-referencing applied	• Information present • Appropriate heading • Cross-referencing not applied
Warfarin 4	• Information present • Appropriate heading	• Information present • Appropriate heading	• Information not present	• Information present • Appropriate heading • Cross-referencing applied	• Information present • Appropriate heading • Cross-referencing not applied
Statins					
Simvastatin 1	• Information present • Appropriate heading	• Information not present	• Information present • Appropriate heading • Cross-refencing not applied	• Information present • Appropriate heading • Cross-refencing not applied	• Information present • Appropriate heading • Cross-refencing not applied
Simvastatin 2	• Information present • Appropriate heading	• Information present • Appropriate heading	• Information not present	• Information not present	• Information present • Appropriate heading • Cross-refencing not applied
Simvastatin 3	• Information present • Appropriate heading	• Information present • Appropriate heading	• Information not present	• Information not present	• Information present • Appropriate heading • Cross-refencing not applied
Simvastatin 4	• PIL not available	• PIL not available	• Information not present	• Information not present	• Information not present
Simvastatin 5	• Information not present	• Information present • Appropriate heading	• Information not present	• Information not present	• Information not present
Atorvastatin 6	• Information present • Appropriate heading	• Information present • Appropriate heading	• Information not present	• Information not present	• Information present • Appropriate heading • Cross-referencing applied
Atorvastatin 7	• Information present • Appropriate heading	• Information present • Appropriate heading	• Information not present	• Information not present	• Information present • Appropriate heading • Cross-referencing not applied
Fluoroquinolones					
Ciprofloxacin 1	• PIL not available	• PIL not available	• Information not present	• Information not present	• Information not present
Ciprofloxacin 2	• PIL not available	• PIL not available	• Information present • Appropriate heading • No cross-referencing	• Information not present	• Information present • Appropriate heading • Cross-referencing not applied
Ciprofloxacin 3	• Information present • Appropriate heading	• Information present • Appropriate heading	• Information present • Appropriate heading • Cross-referencing applied	• Information not present	• Information present • Appropriate heading • Cross-referencing not applied
Ciprofloxacin 4	• PIL not available	• PIL not available	• Information not present	• Information not present	• Information present • Appropriate heading • Cross-referencing not applied
Levofloxacin 5	• Information not present	• Information present • Appropriate heading	• Information not present	• Information not present	• Information not present
Levofloxacin 6	• Information present • Appropriate heading	• Information not present	• Information not present	• Information not present	• Information not present
Tetracycline					
Tetracycline 1	• Information present • Appropriate heading	• Information not present	• Information present • Appropriate heading • Cross-referencing not applied	• Information not present	• Information present • Appropriate heading • Cross-referencing not applied

Table III: Document analysis of professional information for food-drug interactions information taken verbatim from the leaflets, where the exemplar provides the necessary information to which all other samples were benchmarked. Adherence measures for description: foods or drinks that interact with the medication, mechanism of interaction, clinical outcome, and recommendations/precautions. Green (adherence measure fully described), yellow (adherence measure partially described), red (complete lack of information).

Warfarin sample	Foods/Drinks	Mechanism of interaction	Clinical outcomes	Recommendations or precautions
Exemplar	**Vitamin K-containing foods (such as green leafy vegetables, lettuce, broccoli, and spinach)[23]**	**Vitamin K antagonises warfarin's vitamin K reductase inhibitory activity by facilitating clotting factor synthesis and activation[23]**	**The blood-thinning effect of warfarin is antagonised, leading to unstable coagulation[23] i.e. lowered prothrombin time (PT)[29]**	**Although completely avoiding these foods is not necessary, a consistent diet of vitamin K should be maintained while vitamin K dosage is closely monitored to avoid countering warfarin's anticoagulatory effect[29]**
Warfarin 1	Liver, broccoli, brussels sprouts, and green leafy vegetables contain large amounts of vitamin K	Mechanism not provided or explained	Anticoagulation control can be affected by sudden changes in diet	Patients should seek medical advice before making major diet changes
Warfarin 2	Information not provided	Information not provided	Information not provided	Information not provided
Warfarin 3	Liver, broccoli, brussels sprouts, and green leafy vegetables contain large amounts of vitamin K	Mechanism not provided or explained	Foods interacting with warfarin can affect prothrombin time, and anticoagulation control can be affected by sudden changes in diet	Patients should seek medical advice before making major diet changes
Warfarin 4	Liver, broccoli, brussels sprouts, and green leafy vegetables contain large amounts of vitamin K	Mechanism not provided or explained	Anticoagulation control can be affected by sudden changes in diet	Patients should seek medical advice before making major diet changes
Statin sample	**Foods/Drinks**	**Mechanism of interaction**	**Clinical outcomes**	**Recommendations or precautions**
Exemplar	**Grapefruit juice[9,10]**	**Grapefruit juice irreversibly inhibits CYP3A4-mediated pre-systemic metabolism of atorvastatin[9] and simvastatin[10]**	**Reduced metabolism increases the AUC and Cmax of atorvastatin[9] and simvastatin,[10] which increases the risk of statin-induced rhabdomyolysis[11]**	**Concomitant administration of large quantities of grapefruit juice (1 L daily) and these statins should be avoided or the dose of these statins should be reduced[9,10] to avoid rhabdomyolysis**
Simvastatin 1	Grapefruit juice	Grapefruit juice inhibits CYP3A4	Concomitant intake of large quantities of grapefruit juice (over 1 L daily) and 240 mL (in the morning) with the statin (in the evening) led to a 7-fold and 1.9-fold increase exposure to simvastatin, respectively, in previous studies	Patients should avoid the concomitant use of grapefruit juice and the statin
Simvastatin 2	Grapefruit juice	Grapefruit juice inhibits CYP3A4	Inhibition of CYP3A4 may result in high plasma levels of the statin (this is supported by findings from studies)	Patients should avoid the concomitant use of grapefruit juice and the statin
Simvastatin 3	Grapefruit juice	Grapefruit juice inhibits CYP3A4	Inhibition of CYP3A4 may result in high plasma levels of the statin increasing the risk of myopathy	Grapefruit juice is contraindicated, and patients should avoid the concomitant use of the statin and large quantities of grapefruit juice (more than 1L daily)
Simvastatin 4	Information not provided	Information not provided	Information not provided	Information not provided
Simvastatin 5	Information not provided	Information not provided	Information not provided	Information not provided
Atorvastatin 6	Grapefruit juice	Grapefruit juice inhibits CYP3A4	Inhibition of CYP3A4 can increase the plasma concentration of the statin	Grapefruit juice is contraindicated, and patients should avoid the combination of the statin and grapefruit juice
Atorvastatin 7	Grapefruit juice	Grapefruit juice inhibits CYP3A4	Inhibition of CYP3A4 can increase the plasma concentration of the statin	Patients should avoid the combination of the statin and grapefruit juice
Fluoroquinolone and tetracycline sample	**Foods/Drinks**	**Mechanism of FDI**	**Clinical effect on absorption and bioavailability**	**Recommendations or precautions**
Exemplar	**Calcium-rich foods such as dairy products or mineral-fortified drinks alone, (milk,[7,8] yoghurt,[8] calcium-fortified orange juice) [24]**	**Chemical complexation of fluoroquinolones or tetracyclines and calcium reduces their gastrointestinal absorption[7,8]**	**The chemical complexation with calcium reduces the absorption and bioavailability of fluoroquinolones[8] and tetracyclines[7]**	**Patients need to avoid calcium-rich foods for at least two hours before or after taking fluoroquinolones or tetracyclines[25]**
Ciprofloxacin 1	Information not provided	Information not provided	Information not provided	Information not provided
Ciprofloxacin 2	Calcium rich foods such as dairy products or mineral fortified drinks (milk, yoghurt, calcium fortified orange juice)	Mechanism of FDI not mentioned or explained	The interaction may reduce the absorption of the fluoroquinolone but dietary calcium as part of a meal does not significantly affect absorption	Patients should avoid concurrent use of these foods/drinks and the fluoroquinolone

Table III: *Continued*

Ciprofloxacin 3	Calcium rich foods such as dairy products or mineral fortified drinks (milk, yoghurt, calcium fortified orange juice)	Mechanism not mentioned or explained	The interaction may reduce the absorption of the fluoroquinolone but calcium as part of a meal does not significantly affect absorption	Patients should avoid concurrent use of these foods/drinks and the fluoroquinolone
Ciprofloxacin 4	Calcium rich foods such as dairy products or mineral fortified drinks (milk, yoghurt, calcium fortified orange juice)	Mechanism not mentioned or explained	The interaction reduces the absorption of the fluoroquinolone but calcium as part of a meal does not significantly affect absorption	Patients should avoid concurrent use of these foods/drinks and the fluoroquinolone
Levofloxacin 5	Information not provided	Information not provided	Information not provided	Information not provided
Levofloxacin 6	Information not provided	Information not provided	Information not provided	Information not provided
Tetracycline 1	Milk	Mechanism not mentioned or explained	Clinical effect not mentioned	Patients should avoid the concomitant use of the tetracycline and milk. Milk should not be taken within two hours before or after taking the tetracycline

vitamin K reductase inhibitory activity by facilitating clotting factor synthesis and activation.[23] As such, warfarin's anticoagulant properties are pharmacodynamically antagonised, leading to unstable coagulation,[23] as seen by the lowered prothrombin time.[28] Completely avoiding these foods is not necessary, but to ensure therapeutic efficacy, patients should maintain a consistent diet of vitamin K while HCPs closely monitor its dosage.[28]

Of the four warfarin samples, all had PIs, while only one lacked a PIL. The FDI's information was found in three out of four PIs, and in all three PILs. While interacting foods and the lack of anticoagulant control were mentioned in all, none of them described the mechanism of interaction. Inconsistent description of how prothrombin time, bleeding time or coagulation were altered by dietary changes was observed.

All three PIs and PILs advised that patients should seek medical advice before making major diet changes. However, the recommendation lacked the specific and detailed precautions that HCPs should advise patients to take. Therefore, the recommendation might be ineffective in situations where the HCPs are not fully informed about this interaction. Couris et al. reported inadequate knowledge of warfarin-vitamin K interactions among HCPs.[16] If PILs advise patients to consult HCPs, while their PIs lack the full description and recommendations pertaining to this FDI, that could lead to improper patient counselling, subsequently, resulting in warfarin therapeutic failure or adverse medical repercussions such as haemorrhagic complications.[16,26]

Fluoroquinolone and tetracycline antibiotics medicinal products

Calcium-rich foods such as dairy products or mineral-fortified drinks alone (milk, yoghurt, calcium-fortified orange juice) can interact with fluoroquinolones and tetracyclines as the chemical complexation of these medications and calcium reduces their gastrointestinal absorption and bioavailability.[7,8,24] Therefore, patients need to avoid calcium-rich foods for at least two hours before or after taking fluoroquinolones and tetracyclines.[25]

The reduced absorption and bioavailability of fluoroquinolones can lead to reduced therapeutic efficacy or even antibiotic resistance, predisposing patients to treatment failure.[4] However, out of all the medicinal samples, FDI's labelling adherence was poorer for fluoroquinolones. Of seven PIs assessed (six fluoroquinolones and one tetracycline), only three fluoroquinolone PIs and the tetracycline PI contained FDI information. Four PILs were available on the SAHPRA website (three fluoroquinolones and one tetracycline), and only one fluoroquinolone and the tetracycline PIL contained FDI information. All the fluoroquinolone samples listed the interacting foods and drinks. Concerningly, the tetracycline sample only mentioned milk, which may lead to the misconception that patients can take the medication with other dairy or calcium-containing products not mentioned.

Similar to the warfarin samples, the mechanism of interaction was lacking in all PIs and PILs. The fluoroquinolones' PIs mentioned that the interaction may reduce absorption, while this information was lacking in the tetracycline PI. While some PIs and PILs recommended that patients should avoid concurrent use of these foods or drinks with the medications, only a minority (one PI and two PILs) mentioned specific timing recommendations, such as taking the medications two hours before or after consuming the foods/drinks.

Statin medicinal products

Grapefruit juice irreversibly inhibits the CYP3A4-mediated-presystemic metabolism of statins (simvastatin and atorvastatin), increasing their AUC, maximum plasma concentration (Cmax), and the risk of rhabdomyolysis.[9-11] Therefore, the concomitant administration of large quantities of grapefruit juice (1 L) alongside these statins should be avoided, or the dose of the statins should be reduced to avoid rhabdomyolysis.[9,10]

Of the seven statin samples, all had PIs, while only one lacked a PIL. The FDIs information was found in five PIs and PILs and grapefruit juice was mentioned in all. CYP3A4 inhibition or induction is one of the most commonly documented pharmacokinetic interactions and a major consideration in the safe and effective use of statins.[20] However, similar to Saito et al., the mechanism of interaction was

Table IV: Document analysis of patient information leaflets for food-drug interactions information taken verbatim from the leaflets, where the exemplar provides the necessary information to which all other samples were benchmarked. Adherence measures for description: foods or drinks that interact with the medication, clinical outcome, and recommendations/precautions. Green (adherence measure fully described), yellow (adherence measure partially described), red (complete lack of information).

Warfarin sample	**Foods/Drinks**	**FDI clinical effects**	**Recommendations and precautions**
Exemplar	**Vitamin K-containing foods (such as green leafy vegetables, lettuce, broccoli, and spinach)[23]**	**The blood-thinning effect of warfarin is antagonised leading to unstable coagulation,[23] i.e. lowered prothrombin (INR) time[29]**	**Although completely avoiding these foods is not necessary, a consistent diet of vitamin K should be maintained while vitamin K dosage is closely monitored to avoid countering warfarin's anticoagulatory effect[29]**
Warfarin 1	Liver, broccoli, brussels sprouts, and green leafy vegetables contain large amounts of vitamin K	Vitamin K-containing foods decrease the effect of warfarin	Patients should not make any major changes to their diets while taking the warfarin
Warfarin 2	PIL not available	PIL not available	PIL not available
Warfarin 3	Liver, broccoli, brussels sprouts, and green leafy vegetables contain large amounts of vitamin K	Sudden changes to diet can affect the patient's bleeding time	Patients should seek medical advice before undertaking any major changes in their diet
Warfarin 4	Liver, broccoli, brussels sprouts, and green leafy vegetables contain large amounts of vitamin K	Sudden changes to diet can affect the patient's bleeding time	Patients should seek medical advice before undertaking any major changes in their diet
Statin sample	**Foods/Drinks**	**FDI clinical effects**	**Recommendations or precautions**
Exemplar	**Grapefruit juice[9,10]**	**Reduced metabolism increases the AUC and Cmax of atorvastatin[9] and simvastatin,[10] which increases the risk of rhabdomyolysis[11]**	**Concomitant administration of large quantities of grapefruit juice (1 L daily) and these statins should be avoided, or the dose of these statins should be reduced[9,10] to avoid rhabdomyolysis**
Simvastatin 1	Grapefruit juice	Grapefruit juice contains one or more components that alter how the body uses the statin	Consuming grapefruit should be avoided
Simvastatin 2	Grapefruit juice	There is an interaction with CYP3A4 inhibitors and there may be a similar interaction with grapefruit juice	Recommendations or precautions not given
Simvastatin 3	Grapefruit juice	Grapefruit juice can prevent the body from breaking down the statin, increasing the risk of the muscle side effects of unexplained muscle pain, tenderness, or weakness	Patients should avoid large quantities of grapefruit juice (more than 1L daily)
Simvastatin 4	PIL not available	PIL not available	PIL not available
Simvastatin 5	Information not provided	Information not provided	Information not provided
Atorvastatin 6	Grapefruit juice	Grapefruit juice and the statin could lead to an undesirable interaction	The combination of grapefruit juice and the statin should be avoided
Atorvastatin 7	Grapefruit juice	Grapefruit juice can interact with the satin	Patients should not take the statin if they drink excessive amounts of grapefruit juice regularly
Fluoroquinolone and tetracycline sample	**Foods/Drinks**	**FDI clinical effects**	**Recommendations or precautions**
Exemplar	**Calcium-rich foods such as dairy products or mineral fortified drinks alone (milk,[8] yoghurt,[8] calcium fortified orange juice[24])**	**The chemical complexation with calcium reduces the absorption and bioavailability of fluoroquinolones[8] and tetracyclines[7]**	**Patients need to avoid calcium-rich foods for at least two hours before or after taking fluoroquinolones or tetracyclines[25]**
Ciprofloxacin 1	PIL not available	PIL not available	PIL not available
Ciprofloxacin 2	PIL not available	PIL not available	PIL not available
Ciprofloxacin 3	Dairy products (milk and yoghurt) and calcium-fortified juices	Large amounts of dairy products particularly milk or yoghurt may slow down the uptake of the fluoroquinolone	Patients should not take the fluoroquinolone with dairy products or calcium- fortified juices and recommend that the fluoroquinolone should be taken 1 to 2 hours before or at least 4 hours after these foods
Ciprofloxacin 4	PIL not available	PIL not available	PIL not available
Levofloxacin 5	Information not provided	Information not provided	Information not provided
Levofloxacin 6	Information not provided	Information not provided	Information not provided
Tetracycline 1	Milk	The absorption of the tetracycline is not affected by moderate amounts of milk	Recommendations or precautions to prevent the FDI are not given

described by only one PI and PIL.[20] Moreover, both in this analysis and that of Saito et al., no information on AUC changes were noted, with a rare mention on the effect on Cmax and increased risk of rhabdomyolysis.[20]

In addition to the inadequate description of the FDI, a lack of or inadequate description of recommendations was observed in some of the PIs and PILs. The PIs and PILs advised against the concomitant use of the statins and grapefruit juice, with one exception where excessive grapefruit juice drinkers were advised not to use the statin. However, only one PI and PIL mentioned the quantity of grapefruit juice to be avoided, making this recommendation ineffective in situations where HCPs and patients lack the same information.

Overall, the PIs and PILs did not meet SAHPRA labelling requirements, both in quantity and quality, potentially due to various factors. One possible factor is the source references used for PIs during the registration process. SAHPRA labelling guidelines state that peer-reviewed journals, the most recently approved innovator SmPC/PI from a recognised regulatory authority, or the most recent SAHPRA-approved innovator PI can be used as source references.[17] The PubMed-focused search for the FDIs of warfarin, statins, fluoroquinolones, and tetracycline showed that these interactions are fully described in the literature.[17] However, the evaluated PIs and PILs had inadequate information and often displayed similar word-for-word inconsistencies. For example, all warfarin PIs did not mention how HCPs should prevent the interaction and only advised patients to seek medical advice, whereas PIs should include detailed guidance for HCPs. These inconsistencies suggest that pharmaceutical manufacturers may rely heavily on other approved PIs or SmPCs. San Miguel et al. also reported SmPCs to be a suboptimum source of FDIs information.[19] Therefore, using recently approved PIs or SmPCs as the only source of labelling FDIs may result in a cycle of unresolved inconsistencies. Pharmaceutical companies are advised to not only source FDI's information from already approved PIs or SmPCs, but to also confirm with peer-reviewed journals.

In addition to source references for labelling FDIs, the approval dates of the PIs and PILs, and the overall approval process by regulatory authorities are notable factors to consider. Labelling guidelines for PIs and PILs have been in place since the early 2000s under the Medicines Control Council (MCC), with the transition to SAHPRA in 2019 introducing the first set of SAHPRA-specific guidelines. Of the evaluated PIs (n = 18) and PILs (n = 13), eight PIs and four PILs were approved under MCC, while the remaining ten PIs and nine PILs were approved under SAHPRA. Notably, the year of approval might have influenced the absence of FDI's information. The majority of the leaflets that lacked FDI information (five PIs and two PILs) were approved before 2019, while a minority (one PI and one PIL) were approved after. However, discrepancies in the description of FDIs persisted in the majority of the PIs (n = 11) and PILs (n = 9), regardless of their approval dates. These findings highlight a need for SAHPRA to ensure compliance to labelling guidelines and to ensure that PIs and PILs are consistently updated to address any FDI information discrepancies, thereby meeting current standards. Addressing these gaps is crucial, as ineffective labelling of FDI information can impact the safety and efficacy of medications.

The study findings align with those of San Miguel et al, suggesting that the inadequate labelling of FDI information in medicinal package inserts may reflect a broader issue where regulatory and pharmaceutical practices overlook the importance of FDIs.[26] Acknowledging the lengthy process of medicine registration, including the proposal of PIs and PILs by pharmaceutical companies and their assessment and approval by regulatory authorities, there is potential for improvement in addressing these gaps.[17,18]

Limitations of the study

The small sample size used for the selected PIs and PILs was a limitation and thus the study findings may not be generalisable to all existing PIs and PILs. However, along with literature findings, the analysis of the PIs and PILs highlighted non-adherence and inconsistencies in the labelling of food-associated effects especially FDIs, which may impact healthcare practice.

Conclusion

The study highlights that although the impact food has on medications' efficacy is acknowledged, it is often understated in the PIs and PILs. Studies show that food-associated effects information, especially that of FDIs, is not always present in medicinal package inserts. Furthermore, if it is present, the FDIs information is often inadequately described. The conducted study also showed a lack of and inadequate description of FDIs in PIs and PILs of warfarin, statins, tetracycline, and fluoroquinolone antibiotics. Moreover, PIs and PILs did not always describe FDI information in the recommended sections and cross-referencing was rarely applied. Thus, the PIs and PILs of the selected pharmacotherapy were partially adherent to the SAHPRA labelling guidelines. The absence of FDI information in medicinal package inserts makes them an impracticable source of such information for HCPs, which may impact optimal patient counselling. Therefore, it is recommended that pharmaceutical companies and regulatory authorities work together to improve adherence to SAHPRA labelling guidelines. Due to the long regulatory procedures that surround the update of PIs and PILs information, it is recommended that future studies investigate other educative methods. Access to adequate FDIs or any food-associated effects information will allow HCPs and patients to prevent clinically significant FDIs or any food-associated effects, resulting in the safe and effective use of medications and food.

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Conflict of interest

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Exploring treatment awareness and adherence among type 2 diabetes patients in Lahore, Pakistan

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Aim: In this study, patients with type 2 diabetes in Lahore, Pakistan had their medication knowledge and adherence assessed. Knowledge of diabetes and demographic information were also assessed.

Methods: A face-to-face interview provided a structured questionnaire with four sections as part of a cross-sectional study.

Results: Four hundred and two (402) patients in total, participated in the survey/questionnaire. Most participants (259, 64.4%) were between 40–60 years old. Results indicated that study participants were taking an average of 1.91 ± 1.00 drugs overall, and 1.72 ± 0.58 medications specifically for diabetes. Most individuals (171, 42.5%) were on oral antidiabetic drugs only. A strong correlation was found between diabetes awareness, education level, and the total number of drugs taken. On the other hand, the mean score (2.20 ± 1.17) for pharmaceutical knowledge on the questionnaire was less than the desired level of knowledge. Gender, family history, and the total number of medications used have all been strongly correlated with medication knowledge. Current findings didn't show any connection between medication knowledge, adherence, and diabetes understanding.

Conclusions: Regarding Lahore, Pakistan's type 2 diabetes patients, this study sheds light on their understanding of the condition and the drugs they take. While the factors show no significant differences, the rate of non-adherence remains concerning. It will take further research to fully comprehend the reasons behind these patients' non-adherence.

Keywords: T2D, IDF, IGT, diabetes prevalence, Pakistan, medication adherence, medication knowledge, glycaemic control, HbA1c

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Introduction

Insulin resistance in tissues, coupled with inadequate insulin production, leads to elevated blood glucose levels in people with type 2 diabetes mellitus (T2DM), a common metabolic disease.[1] According to the World Health Organization's (WHO) Global Report on Diabetes, the number of diabetics has tripled since 1980 to 422 million and is expected to increase to 693 million by 2045.[2,3] Inadequate management of diabetes may lead to several complications including renal disease (nephropathy), neuropathy, retinopathy, lower-extremity amputation and cardiovascular disease (including myocardial infarction and stroke), leading to a significantly increased risk of morbidity and mortality amongst diabetics. Although there is no known treatment for type 2 diabetes, lifestyle changes, medicine, and insulin therapy can help control blood glucose levels and avert related health problems. This distinguishes T2DM from type 1 diabetes mellitus (T1DM) and gestational diabetes by a progressive reduction in β-cell insulin production in conjunction with insulin resistance, unlike T1DM and gestational diabetes.[2] High-calorie meals, sedentary lifestyles, obesity rates, and an aging population are some of the factors that are contributing to the rising prevalence of type 2 diabetes.[4,5] The emergence of type 2 diabetes (T2DM) is influenced by a combination of environmental and genetic factors, including childhood growth patterns, gut flora, age, obesity, physical inactivity, and lifestyle choices.[1,2,6,7]

Millions of people worldwide suffer from T2DM, making it an alarmingly common condition. In the upcoming years it is anticipated that the disease burden will increase significantly.[2] A multifunctional strategy involving medicine, lifestyle changes, and blood glucose monitoring is necessary for the effective management of type 2 diabetes. A balanced diet and regular exercise are two examples of lifestyle changes that are essential for treating type 2 diabetes and lowering the risk of complications.[8] Furthermore, addressing modifiable risk factors can aid in lowering the incidence and progression of type 2 diabetes, including obesity, physical inactivity, and poor dietary habits. To manage type 2 diabetes and avoid complications, early diagnosis and intervention are crucial. Screening for obesity, sedentary lifestyle, and family history are among the risk factors for type 2 diabetes that can help with early diagnosis and timely treatment initiation. The oral glucose tolerance test (OGTT) and fasting plasma glucose (FPG) are easily accessible tests for the detection and diagnosis of diabetes. Two high readings of FPG > 7.0 mmol/L (126 mg/dL) or OGTT plasma glucose ≥ 11.1 mmol/L (200 mg/dL) after two hours are required, according to WHO and ADA criteria. Levels of glycated haemoglobin (HbA1c) are another tool for monitoring. The International Expert Committee (IEC) suggested eliminating "pre-diabetes" and replacing it with HbA1c ≥ 6.5% in the diagnostic criteria.[8] Prioritising specificity above the normality range of HbA1c in the diagnosis of diabetes allows for a balance between potential misdiagnosis and clinical impact. Maintaining a body mass index (BMI) of 25 kg/m^2, eating a high-fibre, low-saturated-fat diet with a low glycaemic index, exercising frequently, giving up smoking, and consuming modest amounts of alcohol are all part of managing type 2 diabetes. Personalised lifestyle advice that takes into account each person's modification in lifestyle is essential since it can avert the majority of type 2 diabetes cases.[8]

Non-insulin antidiabetics include, amongst others, the following: metformin (biguanide), gliclazide (sulfonylurea), pioglitazone (thiazolidinedione), sitagliptin (DPP-4 inhibitor), liraglutide (GLP1-agonist) and empagliflozin (SGLT2-inhibitor). Distinct processes are employed by each class to regulate their blood glucose levels.[8-10] Even though combination therapy can cause problems such as side effects, toxicity, and decreased compliance, it is frequently required for effective management. Better efficacy and safety profiles for the management of type 2 diabetes may come from the development of new drugs with multiple targets or from the co-formulation of current ones.[7,8]

It has been shown that having a solid understanding of medications positively correlates with improving treatment adherence, quality of life, and pharmacotherapy outcomes. For this reason, it is essential to treat diseases and reduce the incidence of adverse medication responses.[11] Appropriate patient education is one of the requirements for a patient's participation in decreasing medication errors. Despite this, more research is needed to evaluate hospital patients' awareness of their medications.[12] Polypharmacy affects a lot of outpatients, which raises the risk of additional health problems like drug interactions and potential toxicity.[13]

The information that patients need to know to use their drugs correctly is referred to as their knowledge of their medications. This also includes the therapeutic goal, dosage, timing of administration, safety considerations, storage methods, as well as potential interactions and side effects.[14] Inadequate patient medication knowledge can lead to unpleasant drug reactions, the development of new health problems, medication abuse, and a decline in the effectiveness of prescribed drugs.[15] Because adverse medication reactions are so common, they are regarded as a major public health concern. To investigate the previously highlighted concerns in more detail, the goals of this study were to assess T2DM patients' medication understanding and adherence. The association between drug awareness and adherence was another goal of this investigation.

Methods

Study design and settings

Using a cross-sectional study design, the project was carried out from October 10, 2023 to December 1, 2023. In-person questions using a researcher-administered questionnaire were used to collect data. Individuals who met the requirements for inclusion were interviewed. Jinnah Hospital in Lahore served as the site of the data collection. For this research, 404 participants were interviewed. However, inadequate details led to the discarding of data from two subjects. Thus, this study comprised the data from 402 participants.

Sample size

Those patients who fulfilled the inclusion criteria were asked to participate in this investigation. The patients were those collecting their prescriptions from the outpatient pharmacy and those going to their appointments at the diabetic clinic while waiting for their appointments with the doctor at the diabetic care centres. The sample size was determined using Daniel, 1999.[16]

Ethical approval

The medical superintendent of each institute approved the study to be carried out. Before any data was collected, a variety of approaches were used to increase the validity of the findings and decrease misrepresentation and misunderstanding.

Personal information was never requested from patients, including residential addresses, national codes, first and second names, or any other information that could compromise their privacy. The study's research aims, response confidentiality, and the patients' opportunity to withdraw from the trial without consequence or impact on their care were all explained to the patients.

Inclusion and exclusion criteria

To make it possible for patients with type 2 diabetes to become familiar with the challenges and opportunities related to managing their diabetes on their own, the following requirements had to be adhered to: 1. the patient had to be a Pakistani national aged < 40 or older; 2. they had to be willing to participate in an interview in Urdu within the hospital premises; and 3. they had to have had a T2DM diagnosis for at least half a year. Patients with type 1 diabetes mellitus and those using anti-diabetic medications for purposes other than diabetes, patients with cognitive impairments like dementia, or were pregnant, and had other types of diabetes were excluded from consideration.

Statistical analysis

IBM SPSS 20 version was used to analyse the gathered data. Descriptive statistics were used to describe the clinical and demographic characteristics. The responses to categorical variables were shown using frequency counts and percentages. The relationship between the demographic factors and medication knowledge as well as the relationship between medication knowledge and medication adherence were examined using a Pearson correlation test. A significant threshold of $p < 0.05$ was established.

Questionnaire and score measurement

An expert in language translation translated the English questionnaire into Urdu, and then the questionnaire was translated back into English for precision and clarity. The survey was divided into four parts. Questions analysing the sociodemographic characteristics and clinical status of patients were included in the first segment. By employing the Diabetes Knowledge Questionnaire (DKQ) created by Garcia et al., the second portion evaluated the patients' knowledge of diabetes.[17] There were 24 situations in the tool, and there were three possible answers: "yes," "no," and "I don't know." One point was given for a correct response, while zero points were given for an erroneous response ("I don't

know" is regarded as incorrect). The total points granted to each patient were averaged to determine their overall score, with 0 and 24 serving as the minimum and maximum scores, respectively. A higher score denoted a greater understanding of diabetes. The questionnaire developed by McPherson et al. and Okuyan et al. was adopted in the study by G Mekonnen and D Gelayee, and was used in the third section to gauge the patient's understanding of their anti-diabetic drugs.[17,18] There were seven verified yes/no questions in this area. The number of right answers determined the overall drug knowledge score; one point was awarded for each right answer, and zero for any erroneous or omitted responses. Each participant received an extra point for accurately answering question 2 in the section by stating the precise mechanism of their drug. Thus, an 8 was the maximum score for this segment, and a 0 was the lowest. A score of ≥ 5 indicated a high level of expertise. Using a technique developed by specialists for a study conducted by Arifulla M et al., the fourth component assessed a patient's adherence to their pharmaceutical regimen.[19] Questions about adherence and related issues were included in this section. A yes-or-no question was used to report medication adherence.

Results

Demographic data

Table I presents the demographic features of all 402 participants who contributed data to the study. At that time, the individuals' average total number of drugs taken was 1.91 ± 1.00 (95% CI: 0.81, 1.01). The average amount of anti-diabetic drugs used by the subjects was 2.19 ± 0.790 (95% CI: 0.11, 0.27). For their antidiabetic regimen, the majority of patients (171, 41.5%) were exclusively using oral anti-diabetic drugs.

Diabetes knowledge questionnaire

Table II lists the scores that each participant received for their answers. The majority of participants answered questions 1, 2, 3, 4, 7, 10, 11, 12, 13, 14, 21 and 21 incorrectly. Regarding question 1, 104 (25.9%) participants believed that overeating sugar and sweet food could cause diabetes. Similarly (180, 44.8%) did not know that diabetes is usually caused by the body failing to produce enough insulin. Many participants (53, 13.2%) believed that the kidneys' inability to filter sugar out of the urine was the cause of diabetes; 152 (37.8%) participants did not know that the kidneys are the main organs for insulin production. Nearly equal numbers of participants (139, 34.6%) thought that diabetes could be cured provided they followed their medication regimen and led a healthy lifestyle. A small number of candidates (91, 22.6%) thought that with frequent physical activity, the need for insulin and other diabetic drugs would increase.

A notable percentage (155, 38.6%) did not know the two subtypes of insulin. Many participants (89, 22.1%) did not know that overindulgence in meals could set off an insulin reaction that leads to dangerously low blood sugar levels. About 135 (33.6%) candidates believed that for the management of diabetes, medication is more important than diet and exercise. Remarkably

Table I: Sociodemographic details of participants (*n* = 402)

Details	*n* (%)
Age (year)	
< 40	60 (14.9)
40–60	259 (64.4)
> 60	83 (20.6)
Gender	
Male	174 (43.3)
Female	228 (56.7)
Education level	
No formal education	131 (32.6)
Primary school	93 (23.1)
Secondary school	69 (17.2)
Higher education	109 (27.1)
Occupation	
Retired	31 (7.7)
Unemployed	155 (38.6)
Private sector	52 (12.9)
Government sector	75 (18.7)
Self-employed	72 (17.9)
Student	17 (4.2)
Family history	
Yes	296 (73.6)
No	93 (23.1)
Not sure	13 (3.2)
Duration since diagnosed with T2DM	
6–11 months	48 (11.9)
1–4 years	131 (32.6)
5–9 years	110 (27.4)
> 10 years	113 (28.1)
Participants' anti-diabetic therapy	
Insulin only	94 (23.4)
Insulin combined with oral medication	137 (34.1)
Oral medication only	171 (42.5)

75 (18.7%) participants were unaware that diabetes is associated with poor circulation. Most respondents (85, 21.1%) incorrectly associated sweating and shaking with signs of hypoglycaemia, while 123 (30.6%) were unsure or uninformed that frequent urination and thirst were indicators of hyperglycaemia. The average score on the DKQ is 11.10, with a standard deviation of 2.952. The DKQ has a maximum score of 24, with 0 being the minimum. A higher DKQ score is indicative of a better understanding of the disease. Figure 1 reveals a middle skew in the distribution, indicating that a larger proportion of participants scored below the mean. This suggests a notable number of participants with an average level of knowledge regarding diabetes.

Medication knowledge

Most of the subjects could not identify the anti-diabetic drugs they were taking (291, 72.4%). A somewhat moderate proportion

Table II: Number of participants with correct answers to the questions in the diabetes knowledge questionnaire

Questions	*n* (%)
1. Diabetes is a result of excessive sugar and sweet food consumption.	104 (25.2)
2. Ineffective insulin in the body is typically the root cause of diabetes.	180 (44.8)
3. The inability of the kidneys to filter sugar from the urine is the root cause of diabetes.	53 (13.2)
4. Kidneys make insulin.	152 (37.8)
5. Blood sugar levels typically rise in diabetes if left untreated.	315 (78.4)
6. There is a greater probability that my children will develop diabetes if I do.	299 (74.4)
7. Curing diabetes is possible.	139 (34.6)
8. A blood sugar level of 11.7 mmol/L at fasting is excessive (11.7 mmol/L is equal to 210.6 mg/dL.)	240 (59.7)
9. Testing my urine is the best way to determine whether I have diabetes.	84 (20.9)
10. The demand for insulin or other diabetic medications will rise with regular activity.	91 (22.6)
11. Insulin-dependent type 1 and non-insulin-dependent type 2 diabetes are the two primary subtypes	155 (38.6)
12. Too much food can trigger an insulin response, which results in severe hypoglycaemia.	89 (22.1)
13. Medication is more crucial for managing diabetes than food and exercise.	135 (33.6)
14. Poor circulation is frequently a symptom of diabetes.	75 (18.7)
15. Diabetics have a slower rate of wound healing.	354 (88.1)
16. Diabetics should exercise special caution when trimming their toenails.	357 (89.0)
17. A cut should be cleaned with iodine and alcohol if you have diabetes.	334 (83.1)
18. The foods I eat and how I prepare them are crucial.	282 (70.1)
19. My kidneys may suffer from diabetes.	346 (86.1)
20. Diabetics may lack sensation in their hands, fingers, and feet.	350 (87.1)
21. High blood sugar levels might cause trembling and perspiration.	85 (21.1)
22. Low blood sugar is indicated by frequent urination and extreme thirst.	123 (30.6)
23. Diabetics can wear tight elastic hoses or stockings without harm.	254 (63.2)
24. Special foods are a large part of a diabetic diet.	369 (91.8)

of the subjects (254, 63.2%) were unaware of the purpose of their anti-diabetic drugs. Most individuals demonstrated correct administration of anti-diabetic drugs (369, 91.8%), including dosage, frequency, and mode of administration. Nearly every participant knew when to take their anti-diabetic drugs (301, 74.9%). However, the research revealed that the subjects were unaware of any potentially negative effects from the anti-diabetic drugs they were taking (305, 75.9%).

Unfortunately, more than 50% of the individuals were unaware of what to do if they had any adverse consequences (308, 76.6%). Although the question "Do you know what to do if you miss a dose of your medication(s)?" was not part of the scoring system for medication knowledge, it was found that 295 people (73.4%) were unaware of what to do in such a situation. On the medication knowledge questionnaire, a maximum score of seven and a minimum score of zero were possible. This questionnaire had a mean score of 2.20 (SD = 1.169) and Figure 2 displays the distribution of pharmaceutical knowledge.

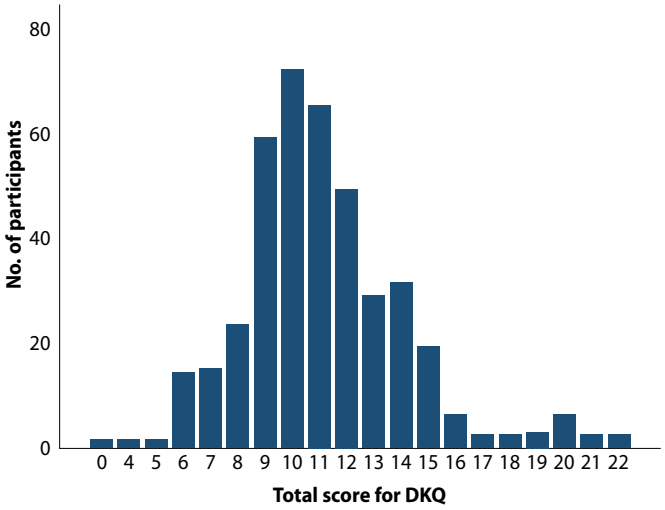

Figure 1: Distribution of participants and overall diabetes knowledge questionnaire scores

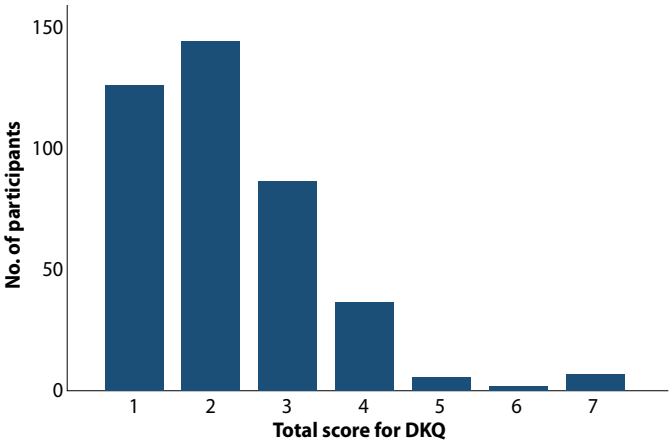

Figure 2: Distribution of participants and overall medication knowledge questionnaire scores

Medication adherence

Few participants (107, 26.0%) admitted to having skipped their anti-diabetic medication dosages for various reasons. Lack of knowledge was cited by non-adherent individuals (57, 14.2%). A small number of them (9, 2.2%) said that their non-adherence was due to side effects. In addition, several gave reasons other than those stated in the questionnaire, such as having no medication on hand at home, not taking medication or cutting back on dosage when feeling better, having a hectic schedule, not wanting to rely on medication, and bitter taste. The majority of individuals (372, 92.5%) did not routinely check their blood glucose levels. Some suggested that the single-use needles' high cost was the cause of this. Several participants (207, 51.5%) stated that they understood the significance of taking their anti-diabetic drugs. Some of the

participants said that their doctor did not offer them information about diabetes; instead, they received it from their nutritionist and/or nurses. But over half said their doctor had not provided them with information about their anti-diabetic drugs (197, 49%).

This is because the doctor did not provide them with any additional information on their drugs, instead informing them that the pharmacists and/or dispensers would advise them regarding their medications. The majority of participants (239, 59.5%) did not participate in choosing their course of treatment. For individuals who participated in the decision-making process, the primary focus was on starting insulin therapy. It was up to the participants to decide whether or not they were willing to begin taking insulin. Regarding their medical issues and/or prescription drugs, nearly all participants (357, 88.8%) said they felt at ease asking their doctors questions. This study set out to assess the associations between medication adherence, medicine knowledge, diabetes knowledge, and demographic characteristics. Table III displays the measurement and tabulation of their correlation.

Table III: The significant relationship between the variables

	p-value and CI	Correlation coefficient
Diabetes knowledge with:		
Education level	< 0.05 (95% CI: 0.021, 0.305)	0.163
Family history	> 0.05 (95% CI: -0.24, 0.584)	0.190
Total medications taken	< 0.05 (95% CI: -0.382, -0.046)	-0.214
Medication knowledge with:		
Gender	< 0.05 (95% CI: 0.080, 0.388)	0.234
Family history	< 0.05 (95% CI: -0.391, -0.014)	-0.211
Total medications taken	< 0.05 (95% CI: -0.207, 0.010)	-0.109

Discussion

The study aimed to determine the Lahore, Pakistan T2DM patients' medication knowledge and adherence to their anti-diabetic regimens. With a prevalence of 6.9%, diabetes mellitus ranks as the 10th most common cause of death in Lahore, Pakistan. Given the prevalence of diabetes in Lahore, Pakistan, ensuring patients' adherence to anti-diabetic medication is one of the steps performed to reduce their exposure to unintended complications of diabetes.[20] For the diabetes knowledge questionnaire, a majority of the participants thought that excessive sugar intake could result in diabetes (262, 63.6%). Albeit the fact that consuming sweets can raise the blood glucose level, diabetes is a metabolic disorder in which severe hyperglycaemia is one of its markers.[21] This question's ambiguity can be the cause of the misunderstanding. A higher chance of developing type 2 diabetes has been linked to changes in lifestyle. As a result, participants may have misinterpreted the idea that consuming sweets in excess causes diabetes.[22]

Additionally, participants indicated that they believed the kidneys had a significant involvement in the development of diabetes. This misperception may arise from the fact that renal disease is a frequent yet serious complication among type 2 diabetics.[23] Participants could not tell whether urine testing was the most effective method of diagnosing diabetes (84, 20.9%). This might be because some participants said they could not tell how high their blood sugar was by looking at their urine when they went to the bathroom; as foamy urine is a sign of elevated blood sugar.[24] Several participants (30.6% and 21.1%, respectively) felt confused by the indications of hypoglycaemia and hyperglycaemia. Patients with diabetes should be aware of the symptoms of hypo- and hyperglycaemia since this will help them make safe and informed decisions, such as taking their medication or eating more sweets.[25]

Using the Starr County Diabetes Knowledge Questionnaire in Urdu, a cross-sectional study was carried out in one of the health centres in Pakistan. As per the study, there was no significant correlation ($p < 0.05$) between the participants' diabetes awareness and their gender, education level, family history of diabetes, and anti-diabetic therapy.[26] The majority of participants (47.7%) showed moderate levels of diabetes knowledge, according to a self-administered questionnaire-based study conducted in Malaysia by Abbasi et al. in 2018. Utilising the Translated Michigan Diabetes Knowledge Test (MDKT), the participants' diabetes knowledge was assessed. Age, education level, occupation, and the kind of anti-diabetic medication were among the variables in this study that were substantially correlated with diabetes knowledge.[27,28] Table III illustrates no substantial correlation between diabetes awareness and factors such as education level, family history, and total number of drugs taken. The participants' scores on the diabetes knowledge questionnaire showed a significance with educational attainment ($p = 0.001$, $r = 0.163$). However, according to research conducted by Bukhsh et al. (2019) and Abbasi et al. (2018), the participants' scores on the diabetes knowledge questionnaire increased with increasing educational attainment.[26,27] One study revealed that the patients' understanding of diabetes was inadequate. Therefore, it is advised that healthcare professionals focus more on diabetes education, particularly regarding nutritional principles.[29,30] There is no noteworthy relationship between diabetes knowledge history and family history of the disease ($p = 0.053$, $r = 0.190$). For European American and African American people from high-risk coronary artery disease (CAD) families, the relevance of family history to the incidence of type 2 diabetes varies. African Americans have a considerably more saturated positive family history structure than European Americans, which makes it harder to identify at-risk individuals unless numerous family members are impacted.

In contrast, European Americans have a dose-dependent risk connection. Simply because of this conclusion, significant public health initiatives aimed at preventing diabetes in African Americans should be launched. More investigation into the genetic, biochemical, and environmental factors causing racial variations as well as a deeper comprehension of the connection between incident T2DM and family history in different racial and ethnic groups should result in improved preventive measures.[31] Additionally, there was a significant relationship ($p = 0.031$,

r = -0.214) between the participants' diabetes knowledge level and the number of medications they were taking. A score of at least five indicated a good degree of medication knowledge. The average score for medication knowledge was 2.20 ± 1.17, indicating that most participants' understanding of their anti-diabetic drugs was below average. Out of all participants, only twelve (2.99%) had a score of ≥ 5. The majority of participants (291, 70.6%) were unable to list all of their anti-diabetic drugs, and 305 participants (74.0%) were unaware that their anti-diabetic drugs could have negative effects. It is not unexpected that the majority of participants were unable to list all of their anti-diabetic medications together with their side effects, since polypharmacy is prevalent among them, with a mean of 1.91 ± 1.00 for all prescriptions used.

However, as hypoglycaemia is a common occurrence for people on anti-diabetic drugs, patients must recognise this common side effect so that they can take the necessary action to address it. Good communication between the physician and patient is essential to address the risk of hypoglycaemia resulting from potential therapeutic misunderstanding and to minimise hypoglycaemia episodes.[32] A few of the subjects were unaware of the proper technique for administering their anti-diabetic drugs. Before the modifications, it was noted that most individuals who provided incorrect answers continued to take their medications. Inadequate dosing might lead to harmful pharmacological responses and pharmaceutical abuse.[33] Participants' scores on drug awareness were significantly impacted by factors such as gender, family history of diabetes, and total number of medications used.

Compared to males, women were found to know more about their prescriptions (the mean score was 1 and 2 respectively). A family history of diabetes improved a participant's performance on the pharmaceutical understanding questionnaire compared to those who knew nothing about the illness (p = 0.031, r = -0.211). Medication knowledge and adherence significantly correlated, according to the current study. This may have been the result of several circumstances. Some individuals whose medication knowledge was not up to par demonstrated adherence to their prescribed regimen (347, 83.7%) because their prescription schedule was organised using a pill box or with assistance from family members (334, 81.1%). Furthermore, it's possible that the participants' medication adherence was influenced by the fact that they didn't have to worry about paying for their prescriptions (347, 84.2%).

Another significant social component brought up by the respondents was the interaction between the patient and the physician, wherein a positive relationship was described as a facilitator and vice versa. A patient's confidence and capacity to manage a chronic condition like diabetes were enhanced by effective communication between the patient and the doctor, which enhanced medication adherence.[34] Consequently, healthcare providers who were assisting them in developing rapport and using their abilities to provide patient-centred care must have the proper training. Furthermore, patient medication adherence to diabetes has been enhanced by pharmacist-led interventions, which may be viewed as an addition to the University Diabetes Centre's present support services.[35] It is possible for non-adherence to diabetic treatment to be unintentional (forgetting) or intentional (decision-making).[36] The gap between medication adherence (MMAS-8) and diabetic control (HbA1c) among some interviewees, where some low adherents had good diabetic control, may be explained by intentional non-adherence.

The study conducted by Sweileh et al. (2014) revealed that a client's attitude towards medication adherence is contingent upon their perceptions regarding the significance of taking prescribed medications for the treatment of their health condition and the associated repercussions.[37] The hypothesis was that patients with diabetes who believed that taking their anti-diabetic drugs was important and who had a positive attitude toward medicine would be more likely to take them as directed. However, patients with diabetes who felt that their diabetes treatment was bad for them and who thought their regimen was bad were more likely not to take their prescriptions as prescribed.[37] Consequently, one may conclude that medical belief and adherence are related. The Morisky Medication Adherence Scale (MMAS-8) was used in an Iranian study to measure medication adherence in patients with type 2 diabetes. The results showed that most participants (59.12%) had moderate adherence, while 27.2% had low adherence to their prescribed regimen. One of the study's important variables for medication adherence was age.[38] The results of this investigation showed no significant relationship between drug knowledge, adherence to a prescribed regimen, and diabetes understanding. The same theory was supported by a 2018 study which found no evidence of a significant relationship between medication adherence and diabetes knowledge.[39] Nonetheless, research has been done to support the idea that there is a strong correlation between medication adherence and diabetes knowledge. Accordingly, one study from 2020 found that among patients with type 2 diabetes, there was a small but favourable connection (p < 0.01) between medication adherence and diabetes awareness.[40] A 2011 study also found that a lower incidence of medication adherence was linked to inadequate diabetes awareness.[41]

Moreover, it has been observed in two research projects that medicine awareness significantly predicts medication adherence (p < 0.001).[18,42] While the rate is higher in underdeveloped nations, the reported mean rate of non-adherence in industrialised nations is only 50%. The study's non-adherence rate of 14.2% does not support the premise, given that Lahore, Pakistan is a developing nation.[43] It is necessary to take action to increase these patients' adherence to further improve their health. Setting a reminder for patients to take their medications was one of the incentives, particularly since in the current study, the inability to check glucose regularly was the primary cause of non-adherence. Personalised patient education, such as educating patients about the unique dangers if they stop taking their medication, is another intervention that has been shown to increase adherence.[44] It has been demonstrated that comprehensive and individualised

pharmacist interventions, like streamlining treatment regimens, are beneficial in helping patients remember to take their prescriptions.[45] Health professionals, especially pharmacists (who are the least used group in Pakistan), should therefore be involved in the dissemination of disease-related education and counselling to increase patients' functional health literacy about self-monitoring and care practices for chronic diseases in hospitals as well as community settings.[46]

We interviewed every member of the sample, ensuring that the data-gathering process remained consistent. Additionally, because just one researcher assisted with the interview, participants were able to get clarification on any questions they had.

Similar to previous research, this study has certain intrinsic limitations. Because the medication adherence questionnaire in this study involves self-reporting, there is a chance that recollection bias and a lack of transparency will alter the true rate of medication adherence.

Conclusion

This study looked at the medication adherence and knowledge of T2DM patients in Lahore, Pakistan. It was found that most of the patients did not know enough about the medications they were taking to control their diabetes. Furthermore, it was shown that nearly 14% of the patients did not take their T2DM medication as prescribed. It was found that knowledge of diabetes was highly correlated with education level and total number of drugs consumed. Gender, family history, and the total number of medications used were all strongly correlated with medication knowledge. Nevertheless, no apparent connection was found between medication knowledge, adherence to treatment, and diabetes knowledge. The degree of medication awareness and the non-adherence rate were markedly low, even in the absence of any link. Strategies including the usage of mobile phone applications for reminders and individualised patient education have been put into place to lessen these problems. However, to optimise their effectiveness and efficiency, these techniques need to be reviewed and improved. Future research on other pertinent factors, including diet, blood glucose level, and body mass index, may provide more light on the relationship between adherence to medicine and medication knowledge. Better diabetes preventive and management strategies still require the planning of both individualised and group education programmes. Prioritising behavioural therapy and counselling is important for subjects with little experience.

Conflict of interest

The authors declare no conflict of interest.

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Ethical approval

Prior to commencement of the study ethical approval was obtained from the following ethical review board: Riphah Institute of Pharmaceutical Sciences Human & Animal Ethics Committee (007184)

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Full list of references available on request

Mental health update – update on depression with a focus on vortioxetine

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Depression, identified by the World Health Organization (WHO) in the International Classification of Diseases (ICD-11) as a complicated and multifaceted condition, affects around 280 million people globally. In sub-Saharan Africa, mental health disorders, including depression, account for nearly 10% of the total disease burden, with depressive disorders being the most frequently diagnosed. Symptoms of depression can range from feelings of worthlessness and difficulty concentrating to sleep disruptions and suicidal ideation. Among the different types of depression, major depressive disorder is the most prevalent. Extensive research has explored potential mechanisms contributing to depression, including genetic, neurochemical, and hormonal influences, such as those involving the hypothalamic-pituitary-adrenal axis. While both pharmacological and non-pharmacological treatments can effectively manage depression, antidepressants are typically the first choice. Vortioxetine, an antidepressant with multimodal activity, stands out due to its unique mechanism of action, combining serotonin transporter inhibition with direct modulation of 5-HT receptors. When left untreated, depression can result in serious physical, emotional and behavioural health concerns. This review seeks to summarise current theories on the origins of depression and treatment strategies, with a focus on the therapeutic potential of vortioxetine.

Keywords: depression, vortioxetine, antidepressant therapy, modulating 5-HT, serotonin transporter inhibitor.

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Introduction

Depression, or major depressive disorder (MDD), remains one of the leading psychiatric conditions worldwide, affecting approximately 280 million people globally according to the World Health Organization (WHO) in 2022.[1-3] Depression is a rising burden across sub-Saharan Africa and South Africa due to various socioeconomic, cultural, and healthcare-related challenges[4] and recent research showed a rising incidence, especially among at-risk groups like adolescents and those with chronic illnesses. This challenge is further exacerbated by the region's inadequate access to mental healthcare services.[5] MDD is characterised by persistent sadness, diminished interest in activities, and multiple physical and cognitive symptoms that may significantly impair day-to-day functioning.[6-8] Despite advances in treatment options, depression remains underdiagnosed and undertreated, particularly in sub-Saharan Africa, where the stigma associated with mental illness persists.[9-11]

Recent years have seen the introduction of newer antidepressants, with vortioxetine emerging as a prominent treatment option. Vortioxetine, a novel multimodal antidepressant, combines serotonergic receptor modulation with serotonin reuptake inhibition.[12] This review aims to discuss the current understanding of MDD and the role of vortioxetine in its treatment, with a focus on the South African context.

Depression: an overview

MDD is a complex, multifactorial disease influenced by genetic, environmental, and psychosocial factors.[13] The aetiology of depression is still not fully understood, but several theories, including the monoamine hypothesis, stress-related neurochemical changes, and inflammatory processes, offer insights into its pathogenesis.[13] In South Africa, the prevalence of depressive disorders has increased significantly, with approximately 9.8% of the population experiencing some form of depression in 2023. Factors such as socioeconomic disparities, unemployment, and the lingering effects of the COVID-19 pandemic have exacerbated the mental health crisis in the region.[14-15]

Pathogenesis of depression

Neurobiological theories[16-18]

The monoamine hypothesis remains one of the leading explanations for the pathophysiology of depression. It suggests that a deficiency in key neurotransmitters such as serotonin, noradrenaline, and dopamine is central to the upregulation of monoamine neuronal receptors and the onset of depressive symptoms. Additionally, dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis has been implicated in MDD, particularly in individuals exposed to chronic stress. Recent studies have also highlighted the role of inflammation in depression, with elevated levels of pro-inflammatory cytokines observed in individuals with MDD.

Genetic and environmental factors

Literature suggests that approximately 40% of the risk for developing depression is linked to genetic factors, while the remaining 60% is influenced by personal environmental conditions.[19] The risk for developing MDD can predominantly be attributed to the following genetic factors, with specific polymorphisms in the serotonin transporter gene (SLC6A4) linked to increased vulnerability to depression.[19-21] Environmental

Table I: Pharmacological treatment modalities (Adapted from Maldonado-García, et al.)[1]

Category	Mechanism of action	Examples
Selective serotonin reuptake inhibitors (SSRIs)	Increase serotonin levels in the brain by blocking its reuptake, enhancing serotonin activity in the synaptic cleft.	Citalopram, escitalopram, paroxetine, sertraline, fluoxetine, fluvoxamine
Serotonin-noradrenaline reuptake inhibitors (SNRIs)	Prevent the reabsorption of serotonin and noradrenaline in the synapses, boosting receptor stimulation.	Venlafaxine, desvenlafaxine, duloxetine, milnacipran, levomilnacipran
Atypical antidepressants	This group acts through various mechanisms, including: - Bupropion inhibits dopamine and noradrenaline reuptake. - Mirtazapine blocks alpha-2 adrenergic receptors and enhances noradrenaline release and antagonises postsynaptic 5HT2 and 5HT3 receptors. - Agomelatine activates melatonin receptors, particularly MT1 and MT2, and promotes the release of dopamine and norepinephrine.	Bupropion, mirtazapine, agomelatine
Serotonin modulators	Act on different serotonin pathways: - Trazodone and Nefazodone act on serotonin receptors, reducing serotonin reuptake and blocking additional receptors. - Vortioxetine modulates various serotonin receptors and the serotonin transporter.	Nefazodone, trazodone, vilazodone, vortioxetine
Tricyclic antidepressants (TCAs)	Reduce noradrenaline and serotonin reuptake at the presynaptic terminals.	Amitriptyline, clomipramine, doxepin, imipramine, trimipramine, desipramine, nortriptyline, protriptyline, maprotiline, amoxapine
Monoamine oxidase inhibitors (MAOIs)	Block monoamine oxidase enzymes, which break down serotonin, noradrenaline and dopamine.	Moclobemide, tranylcypromine, isocarboxazid, phenelzine

stressors, including early childhood trauma and chronic illnesses, further increase the likelihood of developing MDD.[21]

Vortioxetine: a multimodal antidepressant: mechanism of action[22–25]

Vortioxetine, first approved by the Food and Drug Administration (FDA) in 2013, represents a significant advance in the treatment of depression due to its unique mechanism of action. Unlike traditional selective serotonin reuptake inhibitors (SSRIs), vortioxetine exhibits a distinctive pharmacological profile and multimodal mechanism of action both reuptake inhibition and receptor activity modulation at various serotonergic receptors.

Notably, vortioxetine is the only antidepressant that directly modulates 5-HT activity, acting as a full agonist at 5-HT1A, a partial agonist at 5-HT1B, and an antagonist at 5-HT1D, 5-HT3, and 5-HT7 receptors. Refer to Figure 1 for a description of the mechanism of action of vortioxetine.

The potency ranking of vortioxetine is as follows: 5-HT3 > SERT > 5-HT1B > 5-HT1A = 5-HT7. Vortioxetine has a strong affinity for the serotonin transporter (SERT), and its inhibition increases serotonin levels in the synaptic cleft.

At therapeutic doses, vortioxetine inhibits minimal SERT activity (50%), which may elucidate its lower incidence of sexual side effects compared to other SERT inhibitors, such as SSRIs and SNRIs, which typically exhibit near-complete SERT inhibition at similar doses.

Vortioxetine's multimodal mechanism allows it to enhance neurotransmission in both serotonergic and non-serotonergic pathways, potentially improving cognitive function in addition to alleviating depressive symptoms.[12] This makes vortioxetine particularly suitable for patients who experience cognitive impairments as part of their depressive symptomatology.[26]

Thus, vortioxetine's multimodal activity allows it to exert effects beyond traditional serotonin reuptake inhibition. By modulating various serotonin receptors, it has the potential to not only treat mood-related symptoms of depression but also address cognitive dysfunction and anxiety. Its unique receptor profile allows it to manage a broad spectrum of depressive symptoms while possibly reducing typical side effects like sexual dysfunction and sedation, often seen with other antidepressants.

Clinical efficacy and safety

First approved by the FDA in 2013, vortioxetine has been available for over a decade in more than 83 countries globally. Vortioxetine

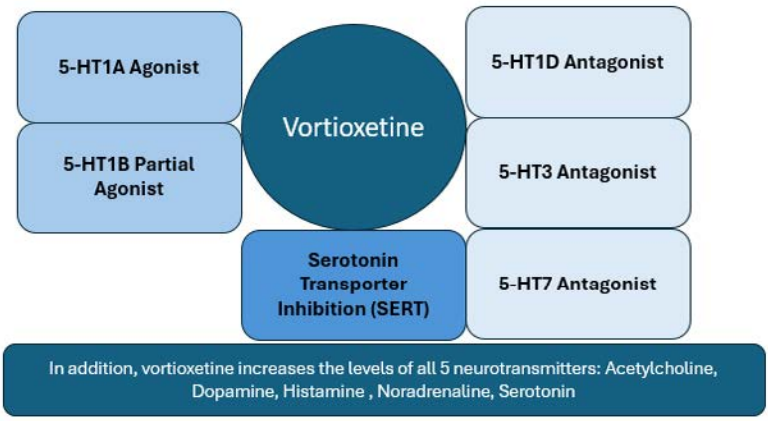

Figure 1: Multimodal mechanism of action of vortioxetine

is supported by evidence from clinical trials involving over 7 000 patients. Several meta-analyses have demonstrated its efficacy in reducing depressive symptoms in MDD.[26]

In a Cochrane review, Koesters et al. (2017) analysed data from 15 studies involving 7 746 participants, including seven trials comparing vortioxetine with a placebo and eight comparing it to SNRIs.[27] Vortioxetine showed higher effectiveness than placebo in terms of response rates (Mantel-Haenszel risk ratio [RR]: 1.35, 95% confidence interval [CI]: 1.22–1.49; 14 studies with 6 220 participants), remission rates (RR: 1.32, 95% CI: 1.15–1.53; 14 studies, 6 220 participants), and reduction in depressive symptoms (mean difference [MD]: -2.94, 95% CI: -4.07 to -1.80; 14 studies, 5 566 participants) as measured by the Montgomery-Asberg Depression Rating Scale (MADRS). Rates of treatment discontinuation showed no significant difference between vortioxetine and placebo (RR: 1.05, 95% CI: 0.93–1.19; 14 studies, 6 220 participants). Additionally, some evidence from eight studies indicated minimal clinically meaningful differences in response or remission rates when comparing vortioxetine to SNRIs.

According to Koesters et al. (2017), there was no significant difference between trials comparing vortioxetine to duloxetine or venlafaxine ($p = 0.09$), but total dropout rates were significantly lower for vortioxetine compared to venlafaxine (RR 0.70, 95% CI 0.52 to 0.93; $p = 0.02$; 2 studies, 767 participants).[27] There was no statistically significant difference between vortioxetine and duloxetine for total dropouts (RR 0.96, 95% CI 0.76–1.21; $p = 0.74$; 6 studies, 2 392 participants).[26]

According to De Diego-Adeliño et al. (2021), switching to vortioxetine as a treatment yielded notable improvements in effectiveness, daily functioning, and quality of life when compared to agomelatine.[28] Comparative analyses further indicated that vortioxetine may achieve higher remission rates and experience fewer discontinuations due to adverse effects than other antidepressants, including bupropion, citalopram, sertraline, or venlafaxine.

Findings from this extensive real-world study by Mattingly et al. (2022), which included 737 patients treated with vortioxetine for 24 weeks, highlight its effectiveness and tolerability in managing MDD within a large, diverse patient group representative of everyday clinical practice.[29] Patients with MDD who received vortioxetine showed clinically meaningful improvements in overall functioning, depressive and cognitive symptoms, performance, and health-related quality of life over the six-month treatment period. In this study, the authors reported that the most substantial benefits were observed when vortioxetine was used as a first-line therapy.

Vortioxetine's safety profile is favourable, showing a lower incidence of common antidepressant-related adverse effects, such as sexual dysfunction compared to traditional SSRIs.[30]

A recent study by Huang et al. (2022) reported improved cognitive performance in patients with MDD.[26] Thus, vortioxetine's favourable tolerability partnered with a lower risk of withdrawal symptoms make vortioxetine a viable long-term treatment option, particularly for patients requiring cognitive support alongside mood stabilisation.[28]

Vortioxetine in the South African context

In South Africa, access to mental healthcare is limited, particularly in rural and underserved areas.[31] Vortioxetine, while available, is often not the first-line treatment due to its higher cost compared to generic SSRIs. However, for patients who do not respond adequately to SSRIs or experience intolerable side effects, vortioxetine offers a valuable alternative.

The **South African Society of Psychiatrists** (**SASOP) guidelines** recommend the use of both pharmacotherapy and psychotherapy for MDD, with first-line treatment typically involving SSRIs.[32] Vortioxetine is increasingly used in patients who do not respond well to SSRIs or SNRIs and may be considered for individuals with cognitive symptoms of MDD.

The **South African Depression and Anxiety Group (SADAG)** plays an advocacy role in ensuring broader access to newer antidepressants and proper treatment across both urban and rural healthcare settings.[33]

Key Information for pharmacists from the approved South African Package Insert[12]

Scheduling: Schedule 5.

Pharmacological class: Vortioxetine is classified as a serotonin modulator and stimulator (SMS) antidepressant.

Indications: Vortioxetine is indicated for the treatment of major depressive disorder and to reduce the risk of relapse.

Formulation: Vortioxetine is available in 5 mg, 10 mg, 15 mg, and 20 mg film-coated tablets, each containing vortioxetine hydrobromide.

Dosing: The typical initial dosage of vortioxetine is 10 mg once daily, which can be taken with or without food. Based on how the patient responds and tolerates the medication, the dosage can be increased to 20 mg. The dose can also be adjusted according to the patient's needs, with a maximum of 20 mg per day or reduced to as low as 5 mg daily if necessary. For older adults or patients prone to side effects, it is advised to start at 5 mg daily. There is limited information available on the use of doses higher than 10 mg per day in elderly individuals. After symptom relief, continuing treatment for at least six months is recommended to maintain the antidepressant effect. No dosage modification is required for patients with renal or hepatic impairments.

Elimination: Vortioxetine has a relatively long half-life of 66 hours, allowing for once daily dosing.

Drug interactions

Pharmacists should be aware of the following important interactions when dispensing vortioxetine:

CYP450 enzyme interactions: Vortioxetine is primarily broken down by the CYP2D6 enzyme. Care must be taken when administering it alongside potent inducers of CYP3A4, such as rifampicin, carbamazepine, or phenytoin, as these can diminish vortioxetine's effectiveness. Conversely, strong CYP2D6 inhibitors, such as bupropion, quinidine, fluoxetine, and paroxetine, can elevate vortioxetine levels in the bloodstream, potentially requiring a reduction in the vortioxetine dose.

Serotonin syndrome: Concurrent use of vortioxetine with other serotonergic medications — such as triptans, SSRIs, SNRIs, opioids, or St. John's Wort — heightens the risk of developing serotonin syndrome, a severe and potentially fatal condition. Vigilant monitoring is essential when vortioxetine is combined with any serotonergic agent.

Monoamine oxidase inhibitors (MAOIs): Vortioxetine is contraindicated with MAOIs due to the risk of serotonin syndrome. A gap of at least 14 days is required between discontinuing an MAOI and starting vortioxetine. Similarly, vortioxetine must be stopped for at least 14 days before beginning an MAOI. The antibiotic, linezolid, a weak MAOI, should also be avoided in patients taking vortioxetine, and if combined, close monitoring for serotonin syndrome is necessary.

Medications that lower the seizure threshold: Antidepressants with serotonergic properties, including vortioxetine, can reduce the seizure threshold. Caution is advised when vortioxetine is used together with medications that can also lower the seizure threshold, such as tricyclic antidepressants, SSRIs, SNRIs, antipsychotics (phenothiazines, thioxanthones, butyrophenones), mefloquine, bupropion, or tramadol.

These considerations are crucial to ensure the safe dispensing of vortioxetine and the prevention of adverse interactions.

Use in pregnancy and lactation

Safety and efficacy in pregnant women have not been established, therefore the package insert recommends against the use of vortioxetine during pregnancy due to potential neonatal risks and complications.

Women are advised not to breastfeed while on vortioxetine due to the lack of safety data and potential excretion in breast milk.

Special populations

The focus on patient populations, such as the elderly and those with renal or hepatic impairment, is crucial for pharmacists to consider.

The safety and efficacy of vortioxetine in children and adolescents aged less than 18 years have not been established.

Elderly: Exposure to vortioxetine is up to 27% higher in elderly patients, necessitating caution, due to the increased risk of side-effects in this population group.

Renal and hepatic impairment: No dose adjustment is needed in patients with renal or hepatic impairment.

Contraindications

Vortioxetine is contraindicated in individuals with known hypersensitivity to vortioxetine.

Special warnings and precautions for use

Haemorrhage: Vortioxetine may lead to irregular bleeding manifestations, including ecchymosis, purpura, and other bleeding events, such as those affecting the gastrointestinal or gynaecological systems. Patients should be monitored carefully if they are on anticoagulants or medications that impact platelet function (e.g. atypical antipsychotics, phenothiazines, many tricyclic antidepressants, nonsteroidal anti-inflammatory drugs [NSAIDs], or aspirin) and if they have known bleeding tendencies or disorders.

Hyponatremia: Hyponatremia, likely resulting from inappropriate antidiuretic hormone secretion (SIADH), has been observed with antidepressants that act on serotonin (SSRIs/SNRIs). Caution is advised in patients who are at higher risk, including the elderly, those with liver cirrhosis, or those on other medications known to induce hyponatremia. If symptomatic hyponatremia occurs, discontinuing vortioxetine should be considered, and suitable medical treatment should be provided.

Side effects

Vortioxetine is generally well-tolerated, with a side effect profile comparable to other antidepressants.

The most frequent adverse effect is nausea, occurring in approximately 20% of patients, particularly within the first two weeks of treatment, which tends to be transient. Other common adverse effects include vomiting, constipation, dizziness, and headache.

Unlike many SSRIs and SNRIs, vortioxetine has a lower incidence of sexual dysfunction. This factor might contribute to better adherence and treatment outcomes.

There is an emphasis on the increased risk of suicidal thoughts, especially in individuals under the age of 25.

There is a possible risk of developing hyponatremia (low sodium levels), particularly in elderly patients, those with liver cirrhosis, or individuals taking other medications, such as diuretics, which can also contribute to hyponatremia.

Reporting any suspected adverse reactions after a medicine has been authorised is crucial as it enables ongoing assessment of the medication's benefit/risk profile. Healthcare professionals are encouraged to report any suspected adverse events to the South

African Health Products Regulatory Authority (SAHPRA) using the '6.04 Adverse Drug Reactions Form', which is available online in the publications section of SAHPRA's website at https://www.sahpra.org.za/Publications/Index/8.

The most recent 2024 vortioxetine approved South African package insert provides further details, which complement the previously extracted information, ensuring that pharmacists have a comprehensive understanding of vortioxetine's usage, safety, and necessary precautions.

Conclusion

Depression remains a major public health challenge in South Africa, with significant social and economic repercussions. Vortioxetine offers a promising treatment option for individuals with MDD, particularly those with cognitive impairments or who do not respond well to first-line SSRIs. Continued research and clinical trials will be essential in further understanding the full therapeutic potential of vortioxetine and ensuring its accessibility to all South Africans in need of effective mental health treatment.

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Conflict of interest

The author declarer that there are no conflicts of interest.

Ethical approval

Ethical approval was not required.

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Semaglutide (Ozempic®): a comprehensive review of its pharmacology, efficacy, and safety profile in type 2 diabetes mellitus and weight management

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Semaglutide, sold under the trade name Ozempic®, is a modified human glucagon-like peptide-1 receptor agonist (GLP-1 RA) indicated for the treatment of type 2 diabetes mellitus (T2DM). Glucagon-like peptide-1 receptor-agonists have shown improved renal and cardiovascular outcomes in patients with chronic kidney disease and established atherosclerotic cardiovascular disease (ASCVD). They work by binding to GLP-1 receptors which are found in different locations in the body. In the brain, they decrease appetite, increase the gastric emptying time in the gastrointestinal tract and promote weight loss. Due to the increased use of semaglutide, there has been a significant increase in reporting of adverse effects (AEs), such as pancreatitis, thyroid tumours, and hypersensitivity. Prescribing semaglutide for weight loss is seen as an off-label use since it is not registered in South Africa for weight management.

Keywords: semaglutide, glucagon-like peptide-1 receptor agonist (GLP-1 RA), type 2 diabetes mellitus, weight-loss

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Introduction

Sub-Saharan Africa has recorded a notable rise in obesity due to lifestyle changes and urbanisation.[1] In South Africa, 68% of women and 31% of men are overweight or obese.[1] The association of weight gain with increased risk of developing life-threatening conditions such as type 2 diabetes mellitus (T2DM), hypertension, heart failure, and non-alcoholic liver disease has imposed a great economic and health burden.[2] This necessitates the need to develop effective, yet non-invasive pharmacotherapeutic options to assist with weight loss.[2] The management of obesity primarily consists of four forms of therapy: lifestyle modification (i.e. diet and exercise), cognitive behavioural therapy, pharmacotherapy, and bariatric surgery.[3] However, socioeconomic factors play a role in the most preferred weight loss options, for example, the majority of those who undergo bariatric surgery have private insurance (e.g. non-government-funded insurance) and a higher median income.[4] When patients with obesity find difficulty in achieving sufficient benefit from lifestyle intervention, pharmacotherapy serves as a good adjunct therapy.[5]

The US Food and Drug Administration (FDA) has approved five agents for weight loss, namely orlistat, phentermine/topiramate, naltrexone/bupropion, semaglutide, and liraglutide respectively, with semaglutide suggested to have superior efficacy.[6] Semaglutide, sold under the trade name Ozempic®, is a modified human glucagon-like peptide-1 (GLP-1 RA) analogue, indicated for the treatment of T2DM.[7] Following the FDA approval of the first GLP-1 RA, exenatide in 2005, six additional subcutaneously administered GLP-1 RAs (semaglutide, dulaglutide, albiglutide, and extended-release exenatide, liraglutide, lixisenatide, and tirzepatide) were introduced on the market.[8] Semaglutide has demonstrated greater efficacy when administered as a weekly dose of 0.5 mg or 1 mg as compared to a combination of oral antidiabetics, insulin glargine, sitagliptin, dulaglutide and semaglutide.[9]

Apart from the management of T2DM through significantly reducing haemoglobin A1c (HbA1c), GLP-1 RAs have proven to improve renal and cardiovascular outcomes, especially in patients with chronic kidney disease and established atherosclerotic cardiovascular disease (ASCVD) and to promote weight loss.[8] In countries such as Canada, the UK, and the USA, once-weekly subcutaneous semaglutide 2.4 mg has been approved for chronic weight management in overweight adults (with weight-related comorbidities) or obesity.[10] However, its use in other regions is still restricted due to issues such as limited effectiveness, apprehensions regarding safety, and high costs.[11] There has been a rise in the use of semaglutide for off-label use in weight loss, with both subcutaneous and oral formulations currently available.[12] Trials of high-dose injectable semaglutide in patients without diabetes have demonstrated confidence in the safety of oral semaglutide in patients without diabetes. However, the impact of high-dose semaglutide may be limited by cost and scant insurance coverage for "weight loss" medications.[13] While the question of safety is underway, given the beneficial metabolic and cardiovascular actions of semaglutide, and the low risk for severe adverse events, semaglutide has an overall favourable risk/benefit profile for patients with T2DM, with less to no record of negative implications in those without T2DM.[12]

A case-control analysis done by Bezin et al.[14] on patients treated with GLP-1 RAs specifically exenatide, liraglutide, and dulaglutide for one to three years found that patients had a significantly higher risk for thyroid cancer and medullary thyroid cancer. At the time when Bezin et al.[14] did the analysis, data on semaglutide was

Table I: Contraindications, warnings and precautions and interactions

Contraindications	Warnings and precautions	Interactions
• Personal or family history of medullary thyroid carcinoma or in patients with multiple endocrine neoplasia syndrome type 2. • Known hypersensitivity to Ozempic® or any of the product components. • Gastroparesis. • Inflammatory bowel disease.	• Pancreatitis has been reported in clinical trials. Discontinue promptly if pancreatitis is suspected. Do not restart if pancreatitis is confirmed. • Diabetic retinopathy complications have been reported in a clinical trial. Patients with a history of diabetic retinopathy should be monitored. • Never share an Ozempic® pen between patients, even if the needle is changed. • Hypoglycaemia, when Ozempic® is used with an insulin secretagogue or insulin, consider lowering the dose of the secretagogue or insulin to reduce the risk of hypoglycaemia. • Can result in acute kidney injury. Monitor renal function in patients with renal impairment reporting severe adverse gastrointestinal reactions. • If signs of hypersensitivity occur, stop using Ozempic® immediately and promptly consult a healthcare professional for guidance. • There have been no clinical trials confirming definitive evidence of semaglutide reducing risks associated with macrovascular outcomes.	• Oral medications interact with Ozempic®, causing delays in gastric emptying. May impact absorption of concomitantly administered oral medications.

missing.[15] Unlike other GLP-1 RAs, there has been no link found between the use of semaglutide and the development of cancer in patients according to the findings of systematic review and meta-analysis. The semaglutide group had no higher risk of developing pancreatic cancer, thyroid cancer, or any other neoplasm than the placebo or active group in the studies that were reviewed.[15] Another systematic review narrowed in on the incident risk for thyroid cancer with semaglutide use and reported a less than 1% chance.[16] These findings correlate with the results found in another study that also demonstrated the advantage that semaglutide has over other GLP-1 Ras.[15]

Class and Mode of Action

Semaglutide belongs to a class of antidiabetic treatments known as GLP-1 RAs, which have similar pharmacokinetic properties as endogenous glucagon-like peptide 1 (GLP-1).[17] In the body, GLP-1, an incretin hormone, is produced from the proglucagon gene and this peptide closely resembles glucagon in structure but has glucose-dependent lowering activity.[18,19] Glucagon is one of the hormones that regulate glucose in the blood by signalling for the breakdown of stored glycogen to release glucose.[19]

GLP-1 RAs work by binding to GLP-1 receptors, which are found in different locations in the body, namely in the islet cells of the pancreas, cells of the kidney, lungs, heart, brain and gastrointestinal tract (GIT)[17] (Refer to Figure 1). In beta cells of the pancreas, the GLP-1 RAs cause an enhanced release of insulin, which is dependent on the glucose in the serum, by activation of the adenylyl cyclase enzyme. This action results in glucose uptake by the cells leading to a decrease in the serum glucose level.[20] Additionally, the GLP-1 RAs will travel to the brain where it decreases appetite and increases the gastric emptying time in the GIT.[20,21]

Due to the overall decreased appetite, semaglutide causes a decrease in body weight and body fat mass, resulting from the lowered energy intake. Additionally, semaglutide causes a change in food preference to foods with less fats.[21]

Indications

Semaglutide initially was developed solely for the management of T2DM but has gradually shifted in terms of its indication. Semaglutide is marketed for its efficacy in the management of obesity, especially in obese adults and adolescents who couldn't achieve significant weight loss without surgical intervention.[23]

Semaglutide is not registered in South Africa for weight management. Registered South African indications include:[21]

Inadequate management of T2DM (in addition to diet and exercise). Lowering the risk of major adverse cardiovascular events in patients with T2DM and existing cardiovascular disease, such as

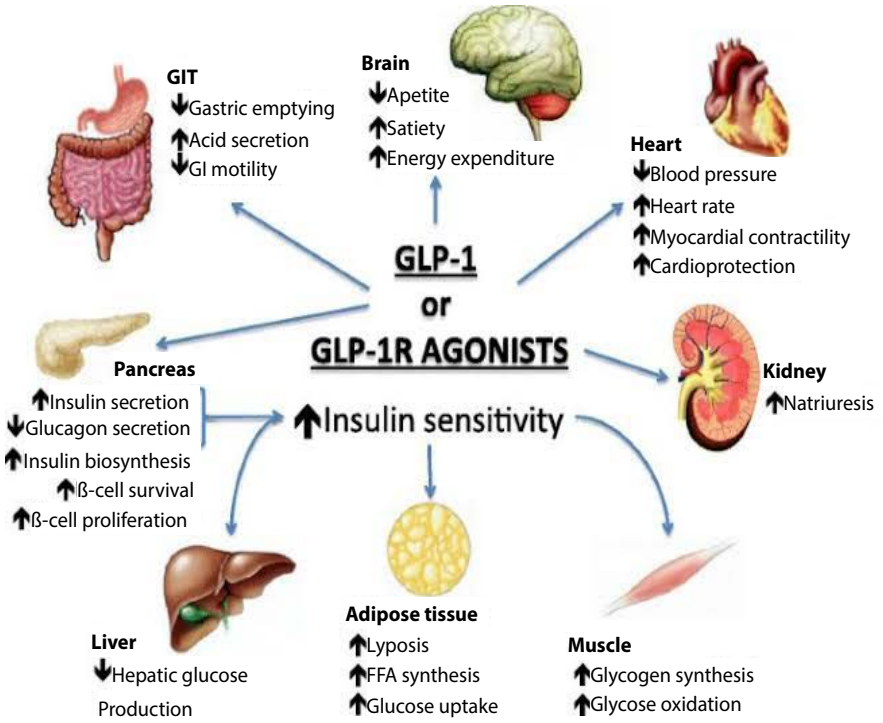

Figure 1: Effects of GLP1/GLP1-RAs on the different organs in the body.[22]

Table II: Common side effects

Frequent	Less frequent
• Nausea • Diarrhoea • Stomach or abdominal pain • Vomiting • Constipation • Rebound weight gain after discontinuation of semaglutide	• Ozempic face (most commonly in the middle-aged and older patients) • Gastroparesis (stomach paralysis) • Nasopharyngitis

non-fatal myocardial infarction, non-fatal stroke, or cardiovascular death.

In terms of possible future indications for semaglutide, it is currently undergoing clinical trials to determine its viability as a possible treatment for a range of health issues such as kidney and heart failure, addiction, Alzheimer's disease, Parkinson's disease and metabolic-related steatohepatitis in obese and non-obese patients.[23]

Contraindications, precautions and drug interactions

The Table I summarises the complications, warnings and precautions, and interactions of semaglutide:[24]

Side effects and adverse drug reactions

Common side effects of semaglutide may resolve after a few days or weeks.[25,26] The side effects of semaglutide can be classified as common side effects, serious side effects, and adverse drug reactions (ADR) as shown in Tables II and III.[27]

The most common side effects of semaglutide are listed in Table II.

Management of side effects

Nausea, vomiting and diarrhoea

Consuming bland, low-fat foods such as dry toast, crackers, rice, soups, gelatin, and ice-cold drinks is recommended to reduce the risk of nausea, vomiting and diarrhoea.[25,27,28] It is also advisable to avoid deep-fried, greasy, oily, or sweet foods, eat slowly, refrain from lying down immediately after eating, and opt for fresh air outdoors rather than staying indoors after meals.[27,28]

Thyroid cancer (boxed warning)

Currently, the risk of developing thyroid cancer is low. However, symptoms such as a lump or swelling in the neck, hoarseness, shortness of breath, or difficulty swallowing, require seeking medical attention immediately, as these may indicate thyroid cancer.[27,16]

Abdominal pain and gallbladder disease

When patients are prescribed semaglutide, it is important to monitor symptoms, such as persistent gastro-intestinal pain, radiating from the abdomen to the back, accompanied by vomiting, that may require immediate medical attention.[29] Furthermore, patients should be monitored for fever, jaundice or clay-coloured stools, as it may indicate gallbladder impairment and will need prompt attention.[27]

Table III: Serious side effects and adverse drug reactions ADRs

Serious side effects	ADRs
• Hypoglycaemia (low blood sugar) • Acute kidney injury/kidney failure • Vision changes	• Pancreatitis (inflammation of the pancreas) • Acute gallbladder disease • Possible thyroid C-cell tumours, including cancer • Hypersensitivity (serious allergic reaction) • Bleeding, blistering, and burning (rare) • Ileus (temporary inhibition of the gastrointestinal contraction)

Visual changes

During treatment with semaglutide, monitor patients for vision changes. It is recommended to provide a comprehensive dilated eye exam at least once a year.[25]

Hypoglycaemia

Semaglutide, in combination with other hypoglycaemic medicine, such as sulfonylureas (glibenclamide) or insulin, should be used with caution, as it may increase the risk of developing hypoglycaemia.[25] Some signs and symptoms of hypoglycaemia include excessive hunger, shakiness, confusion, light-headedness, blurred vision, fast heartbeat, and mood changes.[27] Regular blood glucose monitoring may mitigate the risk of developing hypoglycaemia.[26]

Kidney impairment

Excessive fluid loss caused by diarrhoea, nausea, and vomiting may lead to dehydration, which can worsen kidney damage or pre-existing kidney impairment.[27] Patients must be counselled to drink plenty of fluids to reduce the risk of dehydration.[28]

Hypersensitivity

Patients may develop symptoms of a severe hypersensitivity or allergic reaction, such as rash, itchiness, swollen facial features (lips, tongue or throat), difficulty in breathing or swallowing, fainting or feeling lightheaded, with elevated rapid heartrate.[27,28] Even after discontinuation of semaglutide, side effects may persist, especially when used at the maximum dose of 2 milligrams.[26]

Ongoing research is being conducted to determine the potential long-term side effects of semaglutide for type 2 diabetes and off-label weight loss.[28] The focus is mainly on how the drug could impact the thyroid and gastrointestinal tract.[28] As of January 2024, the FDA reported gastrointestinal disorders, particularly nausea, as the most reported side effect of semaglutide.[26] The FDA continuously reviews the drug's reported side effects while it is on the market. Therefore, it is highly recommended that everyone who is undergoing drug treatment pays close attention and reports any side effects that do not subside over a few weeks.[28]

Use or abuse of semaglutide

A USA study observed a total of 31 542 adverse effects and of these reported, 26.1% (n = 8 249) were from semaglutide use during the period from January 2018 to December 2022. Additionally, semaglutide had the most drug use, abuse and withdrawal-related AEs reported when compared with the other GLP-1 RAs (dulaglutide, liraglutide, exenatide, lixisenatide, tirzepatide, and albiglutide). The increased rate of off-label use of semaglutide, which is not seen with the other GLP-1 RA's, raised concerns about increased misuse or abuse of the drug.[30]

In the South African context, we are one of the countries in sub-Saharan Africa burdened with overweight and obese patients.[31] Owing to that, shortages have been reported of semaglutide for diabetic patients, which may indicate high off-label use driven by a similar weight-loss popularity trend seen in countries like the USA and Britain.[32] The scale of the unmet demands for semaglutide prompted a media release from the South African Health Products Regulatory Authority (SAHPRA) on the 11th of October 2023 warning customers against counterfeit, unregistered drugs available in the market.[32] There is still a need for further studies to be conducted to quantify the use or misuse of semaglutide in South Africa.

Conclusion

Despite its indications for T2DM, semaglutide is used worldwide as a weight-loss drug. If used independently, semaglutide lowers blood sugar levels without raising the risk of hypoglycaemia and slows gastric emptying, which prolongs the sensation of fullness after eating, and functions as an appetite suppressant by focusing on the brain regions that are responsible for hunger and cravings. Writing a semaglutide prescription for weight loss is seen as an off-label use.[33]

In the case of any complaints or experienced side-effects, you are encouraged to report the side effects experienced to the following number: +27 83 379 2104.

Before reporting a side effect, contact your local doctor or another medical health expert if you or the person you are reporting on behalf of is experiencing serious side effects.

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The use of lenvatinib and pembrolizumab after platinum-based chemotherapy in advanced endometrial cancer

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Endometrial cancer is a common cancer in women. While there are several treatment options, there is a need for newer, more effective therapies. One such option is combining lenvatinib, a targeted therapy, with pembrolizumab, an immunotherapy. This combination has shown promising results in treating advanced endometrial cancer, especially after patients have undergone chemotherapy with platinum-based drugs. However, more research is needed to fully understand its benefits and risks. This case report presents a patient with recurrent disease treated with lenvatinib and pembrolizumab, highlighting its potential efficacy.

Keywords: lenvatinib, pembrolizumab, platinum-based chemotherapy, advanced endometrial cancer

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Case report

A 52-year-old female patient presented with a three month history of recurrent vaginal bleeding and persistent pelvic pain after her initial diagnosis of advanced endometrial cancer.

She had previously undergone surgery (total abdominal hysterectomy) followed by chemotherapy with doxorubicin. Although her symptoms initially improved after chemotherapy, they returned and worsened in recent months. The patient reported significant vaginal bleeding and persistent pelvic pain.

The patient had completed four cycles of chemotherapy without any serious side-effects. She had no allergies, no family history of cancer, and did not smoke or drink alcohol. On examination, she appeared fatigued but was otherwise stable. Her blood pressure, heart rate, and other vital signs were within normal limits. During a pelvic exam, a friable (easily bleeding) lesion was found in the vaginal cuff, but no masses were felt. Her full blood count revealed a mild anaemia with haemoglobin of 10.8 g/dL, white blood cell count of 7,2 x 10^9/L, and a platelet count of 220 x10^9/L. Her collective metabolic panel were within normal limits.

A pelvic ultrasound was inconclusive due to the patient's post-hysterectomy status, and no definitive abnormalities were noted. The chest X-ray demonstrated no evidence of metastatic disease. However, a CT scan confirmed the presence of a recurrent mass in the pelvic area involving the vaginal cuff.

Based on the clinical presentation, physical examination findings, and imaging studies, the patient was diagnosed with recurrent advanced endometrial cancer and was referred to a gynaecologic oncologist.

Treatment options depend on several factors, including the extent of disease, previous treatment response, performance status, and overall health. Potential treatment modalities including surgical resection, radiation therapy, and systemic therapies such as targeted agents, immunotherapy, or participation in clinical trials were discussed.

Discussion

This case supports the growing body of evidence that lenvatinib and pembrolizumab can be effective for patients with recurrent endometrial cancer following platinum-based chemotherapy.

Recent studies, highlighted in Table I, including the KEYNOTE-775 trial, have shown that this combination therapy significantly improves both progression-free survival (how long the cancer doesn't worsen) and overall survival compared to other treatments.[1]

These studies suggest that lenvatinib, which blocks certain proteins involved in cancer growth, works well with pembrolizumab, an immunotherapy that helps the immune system fight cancer cells.

In a study by Yonmorei et al. (2022), the study findings were consistent with global data from the KEYNOTE-775 study, showing the effectiveness of lenvatinib and pembrolizumab in Japanese patients with advanced endometrial cancer. The safety profile of the combination therapy was manageable, and no new safety concerns were identified among the Japanese population.[1]

Another trial by Makker et al. (2022) also demonstrated improved progression-free survival and overall survival with lenvatinib and pembrolizumab, compared to placebo plus pembrolizumab. The study found that the combination resulted in a median progression-free survival of 16.7 months and overall survival of 33.2 months. The treatment was well-tolerated, with fatigue, diarrhoea, and hypertension being the most common side-effects.[2]

Lastly, a study by Ott et al. (2017) did not fully evaluate the long-term safety of pembrolizumab and differences in overall survival due to the study's shorter duration.[3]

However, the use of lenvatinib plus pembrolizumab has certain limitations. Many patients experience side-effects, leading to dose reductions or treatment discontinuation. In addition, some

Table I: Summary of key studies on lenvatinib and pembrolizumab in advanced endometrial cancer

Author, Year, Country	Study type	Key results	Study weaknesses
Yonemori et al. (2022), Japan[1]	RCT	- Lenvatinib plus pembrolizumab extended progression-free survival (PFS) in patients with proficient mismatch repair (pMMR) tumours. - Improved overall survival (OS) compared to Treatment of Physician's Choice (TPC). - Well-tolerated with manageable side-effects.	- No significant differences in overall survival. - Conducted in a single country. - Short follow-up for assessing long-term safety.
Makker et al. (2022), USA[2]	RCT	- Lenvatinib plus pembrolizumab significantly prolonged both PFS and OS compared to chemotherapy. - Median PFS: 16.7 months, Median OS: 33.2 months. - Manageable safety profile with fatigue, diarrhoea, and hypertension being common side- effects.	- No placebo arm, making it difficult to attribute results solely to the combination therapy. - Select population; generalisability may be limited. - No assessment of patient-reported outcomes.
Arora et al. (2020), USA[4]	RCT	- Pembrolizumab as monotherapy showed long-lasting efficacy against tumours. - Only four patients experienced grade 3 adverse events. No grade 4 or immune-mediated adverse events.	- Study not powered to detect differences in overall survival. - Single-country study; may not be generalisable. - Short follow-up for long-term safety assessment.
Ott et al. (2017), USA[3]	RCT	**- Objective Response Rate (ORR) of 26.3%. - Median PFS of 8.3 months. - Common adverse events included fatigue, pruritus, and pyrexia.**	**- No placebo arm. - Select population, limited generalisability. - No assessment of patient-reported outcomes.**

RCT = Randomised Controlled Trial

studies lacked patient-reported outcome (PROs) measures, making it unclear how the combination therapy affected the quality of life of patients. Future research should include PROs to better evaluate how these therapies affect patients beyond just survival outcomes.

Conclusion

In summary, the combination of lenvatinib and pembrolizumab has shown significant potential for treating recurrent advanced endometrial cancer, especially in patients who have already undergone platinum-based chemotherapy. The evidence indicates improvements in progression-free and overall survival, with manageable side-effects. This makes the combination a promising option for patients like the one presented in this case report, making her a suitable candidate for this treatment approach.

While lenvatinib plus pembrolizumab offers a promising treatment option, ongoing research and individual patient assessment remain essential to optimise treatment outcomes and minimise side-effects to ensure that the treatment is as effective and tolerable as possible.

Considering the clinical presentation, results of the physical examination, and findings from imaging studies, our patient is diagnosed with recurrent advanced endometrial cancer involving the vaginal cuff. This recurrence has occurred despite prior treatment with doxorubicin-based chemotherapy, which aligns with the inclusion criteria of the aforementioned studies. The use of lenvatinib plus pembrolizumab has shown improved progression-free survival compared to the physician's choice of treatment, as well as improved overall survival. Additionally, the combination therapy has demonstrated a manageable safety profile with adverse events that can be effectively addressed. Given these factors, it is evident that our patient is a suitable candidate for lenvatinib in conjunction with pembrolizumab.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Pharmaceutical waste disposal

Practice Recommendations for Community Pharmacy in South Africa

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Introduction

This recommendation document is designed for community pharmacies to ensure the management of pharmaceutical waste disposal is performed correctly, in accordance with guidelines issued by the South African Pharmacy Council (SAPC), the regulations of Good Pharmacy Practice (GPP), and according to municipal by-laws[1]. Before writing this document, I found that useful practice guidelines on pharmaceutical waste disposal were not readily available, and current Standard Operating Procedures (SOP) insufficient for my requirements. As I am based in Cape Town, I have developed practice settings commonly used in the Western Cape.

Scope

The destruction of medicines and scheduled substances is governed by the Medicines and Related Substances Act, 1965 (Act 101 of 1965) and other applicable legislation[1]. According to the South African Pharmacy Council (SAPC), and Good Pharmacy Practice (GPP) guidelines, all community pharmacies should have and implement a standard operating procedure (SOP) for pharmaceutical waste destruction where applicable. Community pharmacists may refer to this practice recommendation for clarity. Pharmacies should register with a Pharmaceutical Waste Management service provider, or adhere to suitable waste destruction protocols, ensuring compliance with municipal laws. Additionally, pharmacies must maintain proper record-keeping for the storage, transportation, and destruction of pharmaceutical and medical waste[2].

Good Pharmacy Practice Manual and Associated SAPC rules

GPP guidelines on the minimum standards (Chapter 2.32)

It is the responsibility of a pharmacist to ensure that the disposal and destruction of medicines and scheduled substances in a community pharmacy is done in accordance with the guidelines set out in the Good Pharmacy Practice (GPP). These guidelines can be found in chapter 2.32 of the GPP on the minimum standards regarding the destruction and disposal of medicines and scheduled substances. Although not all components of destruction and disposal may be relevant, it does state that "Some of the elements in this standard are not statutory requirements but are good practice which pharmacists would be expected to follow whenever practicable." *(GPP 2.32.3)*

Some of these applications are:

1. A medicine and scheduled substance may be destroyed by a contractor who specialises in waste disposal regarding the disposal of chemical or medicinal waste *(GPP 2.32.5.1)*.
2. The GPP guidelines further suggest that pharmaceutical waste should be separated into six types and labelled accordingly: solid dosage form (tablets and capsules); creams, ointments, and powders; ampoules and liquids in glass; aerosols; radioactive drugs, and cytostatic and cytotoxic medication and scheduled substances *(GPP 2. 32.6)*.
3. In all situations, a pharmacist must use his pharmaceutical knowledge and skill, together with any necessary expert advice from a Local Authority/Provincial Department of Health, to segregate and dispose of materials, and bio-medical waste safely and in accordance with regulations *(GPP 1.2.11.3e)*[2].

Other legislation – responsible persons

Note that the GPP rule 2.32.3.1 mandates that "All destruction must take place in accordance with local municipal regulations regarding the disposal of chemical or medicinal waste. The person responsible for the destruction may be asked to prove that the method used complies with these regulations."

Additionally, GPP rule 2.32.4.1 states that "If a contractor is not used, medicines containing Schedule 1, 2, 3, and 4 substances may only be destroyed in the presence of a pharmacist or an authorized person in charge of a place where medicines and scheduled substances are kept. The pharmacist or authorized person must certify the destruction."

Process Flow - Pharmaceutical Waste Management

The following recommendations could serve as a guide for pharmacists, as practiced by a community pharmacy in the Western Cape. Municipal by-laws may vary in other provinces, and waste disposal SOP steps might differ across pharmacies. Below is a recommended step-by-step process flow summary, followed by details on each step.

Healthcare Risk Waste Management Service Providers

This section outlines how Healthcare Risk Waste Management (HCRW) service providers operate, what to expect, and some practice guidelines for you as the pharmacist on what your

1	Register with a waste management service provider and order containers	Some examples of providers: • Compass Medical Waste® • Averda SA®
2	• Register with your local Dept of Environmental Health • Register with iPWIS (WC)	• City of Cape Town or your local municipality
3	Pharmacy to collect waste for destruction in at least 4 separate types of containers	• S0 to S4 • S5 to S6 • Sharps & infectious materials (if applicable)
4	Waste Management service provider collects waste-filled containers and sends them to an incinerator	• Receive a waste destruction manifest per container
5	Pharmacy to record the type and weight of waste generated on the IPWIS website, or similar, & file all documents	• Registration document with the waste provider • Registration document as a waste generator with municipality • Signed waste destruction manifest for each container collected

Figure 1: Summary of process flow for pharmaceutical waste management in a community pharmacy

responsibilities and duties will be when working with HCRW management service providers.

1. Choose your healthcare Risk Waste (HCRW) management service provider, also known as the Pharmaceutical Waste Management service provider. This pharmacy uses Compass Medical Waste®. Other service providers include Averda SA® and several others.
2. This is the company that will supply the empty disposal containers, collect the filled ones, transport them to their depot for sorting (Medical Waste Transporter). It will then dispose of the waste (Medical Waste Disposer), either internally or at an approved incinerator site, or both.
3. Register with the HCRW provider for the type of waste you intend to generate. This would be: "Pharmaceutical Waste" and/or "Medical Waste" (sharps and infectious material waste).
4. Pharmaceutical waste includes capsules, tablets, liquids, suppositories, pessaries, and topical applications.
5. You will need at least two green containers for pharmaceutical waste. One for schedules 0-4 and another for schedules 5 and 6, as these need to be separated.
6. Medical waste includes needles, vials, dressings, and infectious and pathological materials. For medical waste, you will need a sharps container and a fibre board box for pathological material.
7. You may choose not to register for medical waste if you will not be generating sharps and pathological waste.
8. Once registered, you will receive a registration certificate. You may be required to produce this certificate during an inspection.
9. For the Western Cape, waste is disposed of by incineration at Vissershok on the West Coast.
10. When your pharmaceutical waste containers are full, email your HCRW management service provider to collect your filled container. Request an empty one at the same time. You may also order empty containers ahead of time.
11. You will receive an invoice from your HCRW management service provider to pay for the container only. The cost for collection of a filled container is noted as zero on the invoice, as this is included as part of the purchase order of an empty container.
12. Start filling your containers up to two-thirds full. Your HCRW management service provider will send you an SOP on the further management of pharmaceutical waste.
13. Incinerator operators recommend that pharmaceutical cardboard packaging is disposed of alongside pharmaceuticals in single-use green pharmaceutical waste containers, to allow for optimal combustion conditions inside the incinerator.
14. A separate green container is required for schedule 5 and 6 pharmaceuticals.
15. For pharmaceutical waste, it is recommended that you use a 10L or 20L for schedules 0-4, and a 5L or 10L for schedules 5 and 6. You may use bigger sizes depending on the waste generated. A 10L container can hold 6-9kg of waste.
16. Once your container is filled as per the protocol document from the HCRW management service provider, send an email to the provider to collect the container.
17. Do not forget to order an empty container at the same time.
18. The HCRW management service provider driver will collect the filled container and weigh it immediately with their scales.
19. You will receive a waste manifest document with a unique number and bar code for that specific container.
20. Take note of the weight (for example 6.5kg). You will need this later for declaration on the online iPWIS submission form to the City of Cape Town. Your own local municipality may have a different process to follow to declare waste.
21. You may be required to present this waste manifest whenever the Department of Health inspects you[3].

Costs associated with the collection of pharmaceutical waste

The following are the costs for collecting of pharmaceutical waste for this pharmacy, as of July 2024, inclusive of VAT. Please note, there is no other cost to be paid upon collection.

- The cost per single green container with lid, for pharmaceutical waste is: R82.90 (5L), R161.32 (10L) and R341.64 (20L).

- The cost for a 50L Medical Waste fibre board box with lid and red liner is R190.25.
- The cost for an 8L yellow rectangular sharps container is R93.86.

Refer to the iPWIS site or your local municipality for a more comprehensive list of service providers in your area.

Disposal of Schedule 5 and 6 Pharmaceutical Waste

This pharmacy uses Compass Medical Waste®.

1. In addition to the above, when it comes to the destruction of schedule 5 and 6 medicines, you are required to submit a request on a specific form to SAHPRA. The completed form is available from SAHPRA. The completed form must be forwarded to SAHPRA at the address or email found below.
2. It is recommended that you contact SAHPRA or your waste management company for the schedule 5 and 6 destruction forms.
3. Compass Medical Waste® has a similar form for the recording of schedule 5 and 6 medicines for destruction. This form may also be used.
4. Copy your HCRW management service provider on the same email to SAHPRA. The waste management service will then send you their approval documentation for the collection of schedules 5 and 6 medicines with their driver. This will be done by the HCRW management service provider once permission has been obtained from SAHPRA. It is the responsibility of the pharmacist to ensure that a representative witnesses and signs the Pharmaceutical Waste Manifest.
5. Any schedule 5 and 6 medicines to be destroyed must be recorded and in the case of schedule 6 medicines, the quantities of medicines to be destroyed must be indicated in the relevant register and signed by the witnesses required in the procedure[1].
6. At the time of this publication, there were no additional costs payable to SAHPRA or the Department of Health for the destruction of scheduled 5 and 6 medicines[4].

Disposal of Sharps and Infectious Material (Medical Waste)

Medical waste includes needles, vials, dressings, and infectious and pathological materials. Besides the steps mentioned above, you must also ensure the following for the proper disposal of sharps and infectious materials:

1. You must be registered as a generator of sharps and infectious/hazardous waste with your HCRW management service provider.
2. You also need to be registered with the Department of Environmental Health in your municipality as an infectious/hazardous waste generator.
3. Ensure that you have ordered the correct containers, i.e., the rectangular yellow 8L sharps container and the 50L Medical Waste fibre board box with lid and red liner.
4. This process is only applicable if you intend to generate medical waste[3].

City of Cape Town Department of Environmental Health (for Registrations & Inspections)

Once registered with a HCRW management service provider, the next step will be to register with your local municipality's Department of Environmental Health as a waste generator.

Below is a recommended guideline of the process to follow for the recording of waste disposal with your local municipality.

1. In the Western Cape, you will need to register with the Environmental Affairs and Development Planning department. Other provinces will have a similar department.
2. Choose the type of waste you intend to generate:
   a. Retail trade in pharmaceutical, medical, cosmetic, and toilet articles.
   b. Healthcare Risk waste (for sharps and infectious and pathological materials).
3. Once registered you will receive your certificate of registration as a medical waste generator.
4. This has your unique pharmacy WIR number (waste information registration) and iPWIS number (Integrated Pollutant and Waste Information System) number.
5. iPWIS is an IT system developed by the Department of Environmental Affairs and Development Planning for the Western Cape Government.
6. Create a username and password on the iPWIS website and register your details.
7. Complete and submit your monthly waste generation report on the Western Cape Government's iPWIS website.
8. You will then receive a waste activity management report for each report you submit.
9. File your waste activity management report. The health inspector may request it when you have an inspection.
10. If your container is not full and has not been collected yet by your waste management company, and you are due to submit your monthly report, then you will need to submit a zero-kilogram quantity monthly on the website, until then.

Steps 3 to 10 are based on the protocol for the Western Cape's Department of Environmental Health. Although other provinces have similar requirements, there will be variations across municipalities.

Department of Health Inspections - local municipality

The City of Cape Town's Department of Environmental Health does bi-annual inspections. These inspections are done by the Environmental Health Officers and will include your Pharmaceutical Waste Management reports, and iPWIS reports. Officers are dispatched from your closest district or sub-district office. Upon inspection, the health officer will draft a report on site and present you with a copy of the report[6].

Essential Checklist for Community Pharmacies

To be considered compliant with the relevant regulations, this pharmacy has put the following essential checklist in place:

- Register with a waste management service provider and your local department of environmental health.
- Adjust your SOPs to reflect your waste disposal activity and procedures, listing all service providers.
- Incorporate your registration certificates issued by your waste management service provider and municipal health authority into your SOPs.
- File all documents in a single file. This should include certificates, invoices, schedule 5 and 6 destruction forms, and inspection reports.
- Ensure you have all the necessary documents on file for any inspections by the SAPC, Department of Health, and Department of Labour.
- Ensure you have access to your iPWIS website and e-mail notifications from iPWIS.
- Familiarize yourself with Chapter 2.32 of the GPP.

Conclusion

Pharmacists in community pharmacies must ensure that the disposal and destruction of medicines are undertaken safely and that the requirements of regulation 27 of the Medicines and Related Substances Act, 101 of 1965, and other municipal regulations are followed. The disposal and destruction processes must have due regard for the environment and reduce harm to public health. It is also important for pharmacists to ensure that any medicine purchase policies and patient-use, are such that it limits the need for destruction, primarily due to none-use and expiration[5]. As pharmacists, we also find ourselves involved in the entire medicines-use chain, including manufacturing and distribution. It is vital that all the role players, including manufacturers, contribute to the safe disposal of unused and expired medicines in a manner that assists all members of the supply chain. This will contribute significantly to the reduction in the discharge of waste into the environment and reduce harm.

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Required Contact Details

Compass Medical Waste®

email compass@compass.za.net and orderswc@compass.za.net

telephone number 031 2679700 or https://www.compasswasteservices.co.za/

Averda SA®

email westerncape@averda.co.za and orderswc@compass.za.net

telephone number 010 1415722 or https://www.averda.com/rsa

SAHPRA Contact Details (July 2024)

Ms Rirhandzu Doris Hlungwani, National Department of Health (NDOH)

South African Health Products Regulatory Authority (SAHPRA)

CSIR Campus SAHPRA Reception

Building 38, 10 Meiring Naude Drive, Brummeria, PRETORIA, 0002

iPWIS contact Details

email ipwis@westerncape.gov.za and https://ipwis.westerncape.gov.za/ipwis3/

Waste Containers – Starter Kit Recommendations

The following are examples of recommended containers and sizes, as a starter kit for community pharmacies. Other sizes are available, depending on the amount of waste you intend to generate.

Figure 1: 20L green plastic pharmaceutical waste container with lid. Ideal for schedule 0 - 4

Figure 2: 5L green plastic pharmaceutical waste container with lid marked for schedule 5 and 6.

Figure 3: 8L yellow plastic sharps disposal container with a red lid

Figure 4: 50L fibre board box with lid and red plastic liner for medical/pathological waste

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4. SAHPRA https://www.sahpra.org.za/wp-content/uploads/2021/11/Medicines-Act-General-Regulations-2017.pdf
5. FIP statement of policy Environmentally Sustainable pharmacy practice: Green Pharmacy https://www.fip.org/file/1535
6. IPWIS user guide https://ipwis.westerncape.gov.za/ipwis3/resources/doc/IpwisUserGuideSeptember2014.pdf

Figure 1

Figure 2

Figure 3

Figure 4

Health Systems Strengthening in the context of Universal Health Coverage

Nhlanhla G Mafarafara

President, SAAHIP

A health system, or healthcare system, is an organisation of people, institutions, and resources that delivers healthcare services to meet the health needs of target populations. Health system strengthening is defined as any combination of initiatives and strategies that leads to better health through improvements in one or more of the health system's functions, measured by increased access, coverage, quality, or efficiency. It is critical to sustaining improvements in health outcomes by reducing morbidities and mortalities. The South African (SA) Lancet National Commission defines a high-quality health system in the South African context as one that "achieves equitable health outcomes and long and healthy life for all."[1]

A well-functioning health system responds in a balanced way to a population's needs and expectations by doing the following (See Figure 1)[1-5] Improving the health status of individuals, families, and communities. South Africa is driving this with a vision of achieving long and healthy lives for all. Life expectancy in South Africa increased from 56.9 in the year 2000 to 65.1 in 2024.[3] Maternal mortality ratio reduced from 249 in 2010 to 86 deaths per 10 000 live births.[4]

- Defending the population against what threatens its health. According to the pharmacist and Minister of Health of Spain, José Manuel Minõnes, "pharmacists support public health programs in many ways, including administration of vaccines, preventing non-communicable disease, reducing antimicrobial resistance and addressing unhealthy behavior and environmental issues, e.g. air pollution."
- Protecting people against the financial consequences of ill health or accessing healthcare. The concept of Universal Health Coverage (UHC) or National Health Insurance (NHI) and Central Chronic Medicines Dispensing and Distribution are also built around improving equity and access to healthcare without regard to economic status.
- Providing equitable access to people-centered care. In this case, the government and health establishments ensure an ongoing and long-term commitment to building relationships with healthcare system users, providers, and the system itself through collaborative decision-making.
- Making it possible for people to participate in decisions that affect their health and the health system. This collaboration rests on the ability of the health system to empower patients' self-care for health and well-being. Self-care is the ability of individuals, families, and communities to promote health, prevent diseases, maintain health, and cope with illness and disability with or without the support of a health worker.[5]
- Building effective collaboration with various institutions and sectors as strategic partners to address social determinants of health.
- Adaptation to changes in health needs by collecting, analysing and using information to support ongoing evidence-based decision-making and implementation for systems quality improvement. Quality is the degree to which health services for individuals and populations increase the likelihood of desired health outcomes, which are consistent with current professional knowledge.[6]

Nhlanhla G Mafarafara

Responsiveness of the health system

Annually, health establishments conduct operational studies that allow patients to participate in on going patient satisfaction and waiting times surveys for the planning and improvement of healthcare. The surveys provide meaningful insights of identifying systems gaps and developing effecting action plans for quality improvements.[7] They also serve a means that healthcare managers use for incorporating patient-centred care.[8] The Office of Health Standards Compliance (OHSC) also conducts studies to ascertain that facilities meet the best standards to deliver healthcare. These studies provide internal system reflection of staff attitude, availability of systems for quality care, availability and accessibility of medicines, quality of care, including food, cleanliness, and clean water, system's ability to empower patients for self-care, and ability to prevent unwanted outcomes in the process of seeking healthcare.

Figure 1 summarises and highlights the different aspects that interface with the delivery of healthcare services in the form of a conceptual framework for high-quality healthcare in South Africa. At the core is a people-centric approach to healthcare instead of a provider-centred one. There is also an appreciation of the actual components that make up the health challenges in the South African context. A well-functioning healthcare system's pillars or building blocks are the main inputs that rest on good leadership and governance (see Table II). Without competent, committed, and vision-driven leadership, a country is unable to produce the actual outputs and achieve the necessary population impact, including achieving all the intrinsic goals, progressively (see Table I).

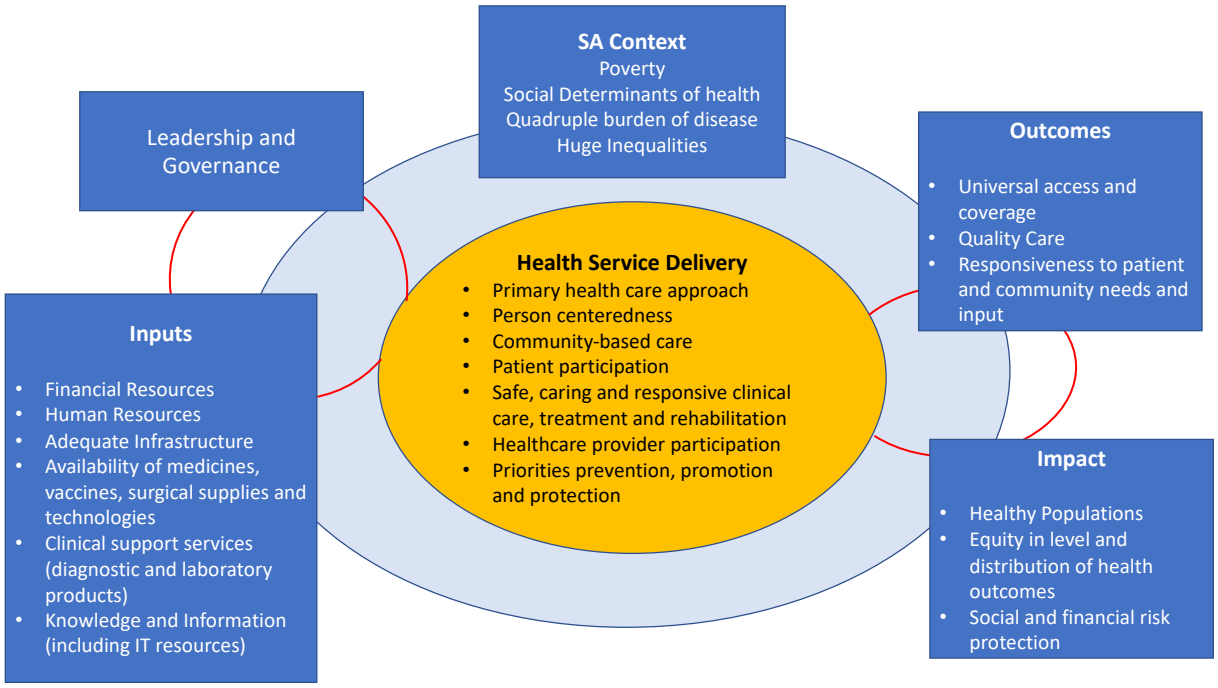

Figure 1: Conceptual framework for high quality in South African healthcare

There also has to be a balance drawn to achieve the health system's intrinsic goals from a micro level (institutionally) and macro level (nationally). It is drawn by balancing quality and equity with efficiency. Murray and Frenk summarise the intrinsic goals of health systems in Table I below.[9,10]

The World Health Organization (WHO) identified the following four components as acceptable definitions of a functional health system in the context of UHC:[11]

- A strong, efficient, well-run health system that meets priority health needs through people-centred integrated care (including services for HIV, tuberculosis, malaria, non-communicable diseases, and maternal and child health). It strongly emphasises health promotion, disease prevention, capacity to treat diseases, and rehabilitation of patients.
- Affordable care for all.
- Access to essential medicines and technologies to diagnose and treat medical conditions.
- Availability of well-trained, motivated health workforce to provide exceptional healthcare services that meet the needs of the people using the best available evidence.

The above are derived from the core pillars of a well-functioning health system (Table II).

What does it take

Achieving this big dream of UHC is a mammoth task. In my previous forum insert titled "Where to from here?[12] "I reflected on conversations and calls to action from the FIP 2024 congress held in Cape Town and invited everyone to see the whole picture and collaborate in generating solutions for South Africa, together. I do not, however, want to turn a blind eye to the fact that progress requires acceptance that change has to happen. Leaders are inundated with the responsibility of managing change without causing casualties along the way as well as solving problems that occur on the way. The best leaders are those who will be able to inspire the confidence of the nation in a changing environment or during turbulence by learning about the future with their teams. Pharmacists today have to carry the key that unlocks the value of pharmacy today for current and future practice.

Here are some proposals to consider.

Lead and learn into the future using exploration, discovery, and action within the pharmacy.[13]

Explore

- Explore current realities with an honest eye and mind, e.g. in AMS, pharmacovigilance, inpatient services, procurement, etc.
- Identify problems/opportunities in each of the areas of your current

Table I: Health Systems intrinsic goals

	Description	Level	Distribution	
Health	Improve and maintain the health of the population	√	√	Efficiency
Responsiveness	Ability to respond to the legitimate expectations of users about non-heath enhancing aspects of care.	√	√	
Fairness in financing and financial risk protection	Protecting households from suffering financial harm or having a large portion of their income used in obtaining healthcare		√	
		Quality	Equity	

Table II: Pillars of a well-functioning health system

Service Delivery	Health system financing	Health workforce	Availability of medicines, vaccines and technologies	Health information systems
- Delivery of effective, safe, quality health interventions to those that need them, when and where needed, with minimum waste of resources - Distribution of health facilities, inpatient beds per 10000 population - Number of OPD visits per 10000 population per year	- Health expenditure - Government expenditure on health - Ratio of household out of pocket expenditure for health	- Sufficient staff, distributed, competent and responsive - Number of HCW per 10000 population - Distribution of HCW by specialisation/ occupation. - Number of health graduates	- Equitable access to essential **medical products, vaccines and technologies** of assured quality, safety, efficacy and cost-effectiveness, and their scientifically sound and cost-effective use - Efficient procurement and supply systems - Equitable access Quality assured products Cost-effective	- System is one that ensures the production, analysis, dissemination and use of reliable and timely information on health determinants, health system performance and health status - Generation of reliable information - Analysis of information - Use of timely and reliable information
Leadership and governance The system should have strategic policy frameworks and are combined with effective oversight and attention to system-design and high level of accountability.				

or prospective function.

- Solicit feedback (patients, staff, other members, and other service recipients)
- Reveal hidden issues (pharmacy systems bottlenecks)
- Gather data (no thumb sucking). Collect, analyse, interpret, and convert data into action.
- Root Cause Analysis for all shortcomings.
- Rethink all issues and action steps. Determine what must be done to address them.

Discover

- As you deepen your understanding through data collection, you will begin to see with new eyes, understand your environment in a different way, and ultimately, develop better solutions for the systems.
- Identify possible solutions in each functional or service area.
- Develop a plan with action steps and focused M&E. Decide what needs to be done, when, by whom, with what resources, and how it will be monitored.
- Anticipate problems and mitigate them beforehand. Identify potential hindrances and develop a strategy against them.

Act

- Test the solutions. Once they work, scale them up. Share the winning solutions as a tool for best practice benchmarking
- Implement the scalable plan
- Monitor and evaluate the results

Conclusion

Wherever you see progress in healthcare, there is a leader who envisioned a better system, developed a model, and actioned it. Health systems are built by humans; they can also be destroyed by humans.

The entire healthcare system is built on the needs of the population. The extent of the responsiveness requires intentional introspection by both the users and providers. Healthcare leaders already have a tool to use to monitor, measure, and report on the performance of health by taking a look into the building blocks, measured against both political and administrative will, to deliver what it is meant to deliver. Managers across all levels of care also need to have clarity on their role and how it impacts the system's deliverables. The convergence point is clear:

- Adequate financing and allocation of human resources as a primary tool for equitable healthcare;
- Strengthening service delivery by improving access and systems of care;
- Continuous quality improvement as a tool for ongoing performance monitoring and reporting on service delivery outcomes and impact.

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Pharmacy Month

Frere Hospital Pharmacy Month

Pharmacy Month is a worldwide celebration of the pharmacy profession and the services we offer to patients. Nationally, the month of September is included in our Health calendar, and the promotion of Pharmacy Month is encouraged to create awareness. The theme for 2024 was "Let's Talk About Vaccines", which is centralised on the promotion of health education, provision of access to primary healthcare and vaccines and empowering patients in regards to vaccinations.

Staff Morale

Pharmacy Month aims to recognise pharmacy personnel and bring about awareness of the profession to others. It is important to raise staff morale in the workplace to have a healthy environment to practice in. The planning team decided to host events that will foster a supportive and appreciative work environment, increase job satisfaction, improve staff morale, and ultimately contribute to a more effective and engaged team of professionals at Frere Pharmacy. Creating an environment where staff is valued and motivated is essential for maintaining high standards of patient care and professional excellence. The goal was to enhance staff motivation, by recognising the efforts of the pharmacy staff and celebrating it. The team planned four different activities aimed at staff morale for the month, but due to time constraints, were limited to achieving two. All pharmacy personnel were included, i.e. pharmacists, pharmacist interns, post basic pharmacist's assistants and learners.

Intervention catcher of the week

An intervention catcher game was planned for the various pharmacy departments, i.e. Inpatient, Outpatient, ARV unit, and Oncology. It was decided that a small award be given to the winning department/team that collects the most interventions. The aim of the game was to identify, document, intervene and report medication errors across the hospital, by use of the existing medication error reporting tool. The interventions were then analysed by the clinical pharmacy team and captured. The "game" was well received by the different departments. The oncology pharmacy team emerged victorious, identifying and documenting a total of 15 medication errors for the period analysed. This achievement not only highlights the critical role that pharmacists play in patient safety but also encourages a culture of continuous improvement within pharmacy practice at Frere Hospital. The pharmacy department was fortunate enough to secure a prize for the winning department.

Handover of the gifts by the pharmacist interns to Oncology Pharmacy, the winners of the intervention catcher competition

Heritage Day Event

The team hosted a bring and share event, to promote camaraderie and provide an opportunity for informal socialising and networking. An invite was extended to the entire pharmacy department, allowing staff to showcase their diverse cultural backgrounds. All were encouraged to wear traditional outfits and share their cultural dishes. The event was a resounding success with staff members proudly displaying their heritage. A potluck-style meal, featuring dishes from various cultures facilitated sharing and appreciation of each other's culinary traditions, took place. The event fostered social interaction among staff members, strengthening relationships and teamwork within the department. The Heritage Day celebration not only provided an enjoyable and enriching experience but also reinforced

Heritage month celebrations

Heritage month celebrations

the importance of cultural diversity in the workplace. It served as a reminder of the unique perspectives and backgrounds that each staff member brings to the pharmacy team.

Community Disease Screening

Pharmacists play an important role when it comes to screening for various diseases, such as Tuberculosis (TB). Screening provides healthcare workers such as pharmacists the opportunity to contribute to early detection leading to optimal therapeutic outcomes. South Africa ranks eighth amongst the top 30 high-TB burden countries, accounting for three per cent of all TB cases worldwide. South Africa is one of 10 countries that face a triple burden of drug- susceptible (DS-TB) and drug-resistant (DR-TB), as well as HIV/TB coinfection. TB is the leading cause of death in the country and the high rate of HIV coinfection continues to accelerate the impact of the epidemic.

Pefferville community TB screening and soup kitchen

The team contacted a local charity organisation, to assist in their weekly soup kitchen and to perform TB screenings on the persons that were present. The interns made use of a validated TB screening tool and conducted 15 TB screenings. Those persons identified with potential TB symptoms were promptly referred for further evaluation and treatment to the nearest identified healthcare facility with a referral note. The interns shared important pharmaceutical advice, educating community members on TB prevention, symptoms, and the importance of seeking medical care. Their presence at the soup kitchen allowed them to engage directly with individuals in need, fostering a supportive environment while addressing health concerns. This initiative not only facilitated essential health screenings but also strengthened the interns' connection with the community, highlighting the critical role of pharmacists in promoting public health and wellness.

Inspiring Future Healthcare Professionals

High school students often find the process of selecting a course in school and institution for further studies overwhelming and daunting. Pharmacy is a profession that is rarely highlighted in schools as a viable career path. The limited information available tends to focus solely on community pharmacy, neglecting other career opportunities within the field. Pharmacy is sometimes viewed as a second choice for those who did not gain admission to medical school or as a stepping stone to pursue a medical degree.

A presentation was developed for the students to highlight the diverse and rewarding profession of pharmacy, covering the following key areas: Role of a Pharmacist, Career Opportunities, Educational

School visits conducted by pharmacist interns

Requirements, and Importance of Pharmacists in Healthcare. The team also compiled a fun, educational video, "A Day in the life of a Hospital Pharmacist" to show the learners. The pharmacist interns visited two public schools, to engage with students about the pharmacy profession and promote awareness of vaccinations. During the visits, discussions centred on the importance of vaccinations, addressing common misconceptions, and encouraging students to understand the benefits of immunisation for individual and community health.

The interactions with the students fostered a lively dialogue, allowing students to ask questions and gain insight. Learners were advised to contact the pharmacy department or the pharmacy training and development co-ordinator if they needed more information, assistance or guidance. Informal feedback from the teachers on-site at both learning institutions, was that the initiative undertaken by the Frere Hospital Pharmacy interns was very rewarding for the learners and it provided some much needed guidance in terms of their career and subject choices.

Social Media Awareness

With the rise of social media as a means for health communication, there is an increased amount of reach to a larger audience, particularly younger persons. The main objective of this social media campaign was to educate and encourage the public about the necessity of vaccinations through the development of interesting educational content, with the intention of ultimately enhancing vaccine uptake and promoting awareness of vaccination.

The team decided to merge social media trends with evidence-based literature to engage the audience on pharmacy-related topics. They researched the various vaccines that are available and developed an evidence-based summary on them, highlighting facts, myths and key points for the general public. Two videos were created and after gaining approval via the internal departmental processes, the videos were posted on social media platforms.

Video 1 "Debunking the Myths around the Flu Vaccine" aimed to clarify common misconceptions about the flu vaccine and provided information to encourage vaccination. Video 2 "It's September and it's Pharmacy Month!", was an introductory video which kicked off Pharmacy Month, highlighting the significance of Pharmacy Month and promoting various activities and initiatives planned for the month. The social media campaign for Pharmacy Month yielded impressive results from the metrics that were analysed. The videos addressed the different aspects of vaccination: debunking vaccine biases, promoting the benefits of vaccination, and encouraging community involvement in vaccination initiatives. Viewers also requested for more content.

We encourage all pharmacy teams to perform similar activities at some point, not just in Pharmacy Month. These activities are rewarding on a personal level, but the most important part was that the Frere Hospital Pharmacy team could contribute positively to the patient's overall well-being and health.

Thank you

The Frere Pharmacy Intern Team 2024 (Camille Harmse, Unathi Makubalo, Okuhle Mpaka, Zuziphe Sobuwa, Nishitaben Vyas, Achuma Yawa and Siphumeze Jikija) and Pharmacy Training and Development Co-ordinator (Dr Seshnee Moodley)

Tribute to David Sieff

23 September 1936 – 30 October 2024

This tribute relates to the very sad loss of my colleague and friend David Sieff.

David always had a great passion for the pharmacy profession giving his time and life unselfishly to his profession which set an expressive example to his colleagues.

He qualified at the Witwatersrand Technikon in 1967, attaining the Diploma in Pharmacy. He worked in all sectors of the pharmacy profession – as a detail representative, community pharmacist, hospital pharmacist and a hospice pharmacist. He was the owner of Libra Pharmacy in Berea, Johannesburg from 1974 to 1990.

He was very involved with the Golden Mortar since 1974 and was appointed as Editor in 1985. He ensured that the profession was always well-informed with pharmacy news and education.

He was a regular attendee at Annual General Meetings of the PSSA and SAACP and rarely missed AGMs, conferences, committee meetings and continuing education sessions.

He regularly scrutinised the minutes of the meetings he attended for correctness.

Photography was one of his hobbies. In the early days David became famous for taking photos with his camera at conferences and of presenters at pharmacy gatherings and was often challenged with the remark "have you got a film in your camera David?"

David's many awards and recognitions within the pharmacy profession bear testament that his was a distinguished career of considerable importance:

- Honorary Life Membership of the National Association of Community Pharmacists
- Honorary Life Membership Southern Gauteng Branch of the Pharmaceutical Society
- Honorary Life Membership of the Southern Gauteng Branch of the South African Association of Community Pharmacists
- Jack Bloom Award
- Fellow of the Pharmaceutical Society of South Africa

I was honoured when in 2023, I moved a Motion to award David with the prestigious Julius Israelsohn Award for dedicated, unstinting and exemplary service to the Pharmacy profession, in particular the South African Association of Community Pharmacists (SAACP).

David Sieff and Bernard Lapidus were instrumental in nominating and seconding me as Chairman of the SAACP Branch Committee – by this action David initiated my involvement with the SAACP and PSSA which initiated my own involvement within organised pharmacy.

In addition to his passion for his work and the various Committees he served on, Dave was a devoted and caring family man. He is survived by his wife Rita, two daughters, Michelle and Robyn, sons-in-law and grandchildren, who he adored. Heartfelt condolences are extended to his family.

Even to the very end when his health was failing, and he was growing weak in mind and body his focus was on the profession and the Golden Mortar.

I salute you my friend in your passing, the time we spent and shared together and what you have contributed to your profession.

May you rest in peace my friend – you will be sadly missed by all.

Gary M Köhn

We are deeply saddened to share the passing of our loyal Branch supporter and the person who tirelessly kept us all informed through his work on the Golden Mortar publication, David Sieff. Our sincerest condolences go out to his family as we all feel the weight of this profound loss.

David was one of our most special colleagues, a true character, and, as we often said, a real mensch. He was much loved by the PSSA

Southern Gauteng Branch, to which he contributed so much and was regarded by many as a father figure. David's dedication to the Golden Mortar was unwavering, and he remained a tireless, committed editor for many years. We could always rely on him as a solid, trusted, and fair sounding board on all things pharmaceutical.

David's selfless contributions were recognised with the prestigious and seldom-awarded Julius Israelson Award for his exceptional service to Community Pharmacy, and he was honoured as a senior Fellow of the Pharmaceutical Society in recognition of his distinguished involvement in the profession. His professional contributions extended to hospital pharmacy, and he was actively involved in our society's affairs until very recently.

Known for his profound respect toward others, his passion for learning, and his commitment to his profession and patients alike, David also had a sharp sense of humour and an enthusiasm for Branch activities that will be sorely missed.

On behalf of the PSSA Southern Gauteng Branch, we extend our heartfelt condolences to his beloved wife, Rita, and to his family during this difficult time.

Val Beaumont

Chairman: PSSA Business Committee

A tribute to David Sieff

David was a dedicated pharmacist who never missed a single branch committee meeting. A true gentleman, he always ensured that we adhered to the constitution of the Society.

David was always ready to lend a hand, especially when it came to correcting the minutes. On the first day of my chairmanship of the SAACP SG branch, he told me he was always available to help whenever needed.

Who can forget David's presence during our virtual meetings? He was always the one to propose the adoption of minutes, having reviewed them thoroughly beforehand. His preparation and dedication to every branch meeting were unmatched.

At the PSSA conference, those who attended will surely remember David with his camera, capturing moments as he always did.

He was a gentle giant, a dedicated pharmacist whose passion for his profession never wavered.

May his soul rest in eternal peace.

Tshif Rabali

President of the Pharmaceutical Society of South Africa

In loving memory of David Sieff ("Uncle Dave")

It is with deep sadness that the South African Association of Hospital and Institutional Pharmacists (SAAHIP) announce the passing of David Sieff, fondly known to many as "Uncle Dave".

Uncle Dave was a remarkable pharmacist whose unwavering dedication to his profession and patients left an indelible mark on all who had the privilege of getting to know him. His commitment to excellence and his passion for healthcare set him apart as a true pioneer and inspiration in our field.

Beyond his professional achievements, Uncle Dave was a man of immense kindness, generosity, and compassion. His warm presence and tireless willingness to guide, support, and uplift those around him made him a cherished colleague and friend. He brought joy, wisdom, and comfort to countless lives, leaving a legacy of healing and hope that will continue to inspire us all.

Uncle Dave's contributions extended far beyond his work. He was a beacon of positivity, always ready to share a kind word, a helping hand, or a moment of laughter. His enduring impact on our profession and the countless individuals he touched is a testament to the extraordinary person he was.

As we mourn the loss of an exceptional colleague and dear friend, we extend our heartfelt condolences to his family and loved ones. May they find solace in the memories of his remarkable life and the knowledge that he was deeply respected and loved by all who knew him.

Uncle Dave's legacy will forever remain a part of SAAHIP and the broader healthcare community. Rest in peace, Uncle Dave—you will be profoundly missed but never forgotten.

Rashmi Gosai

Chairperson of Southern Gauteng

South African Association of Hospital and Institutional Pharmacists

sapj

CPD questionnaire • November/December

Evaluation of the labelling adherence of the food-associated effects of selected pharmacotherapy

1. What is the clinical consequence of taking statins with large quantities of grapefruit juice?

a Lowered plasma levels of the statin
b Increased risk of rhabdomyolysis
c Reduced cholesterol-lowering effects
d Increased gastrointestinal absorption

2. What is the primary purpose of cross-referencing food-drug interactions in professional information?

a To simplify drug administration instructions
b To reduce the length of the PI
c To prevent repetition and improve navigation
d To provide warnings on overdose

3. How should healthcare professionals handle FDIs with warfarin and vitamin K-rich foods?

a Avoid all vitamin K-rich foods entirely
b Stop warfarin if consuming vitamin K-rich foods
c Double the warfarin dose when eating vitamin K-rich foods
d Monitor and maintain a consistent diet of vitamin K

4. Which section of the patient information leaflets is responsible for advising patients whether to take medication before or after meals?

a Section 2
b Section 3
c Section 4.5
d Section 4.2

5. Which section of the professional information should provide information on the timing of medication administration in relation to food?

a Section 4.2: Posology and method of administration
b Section 4.4: Warnings and precautions
c Section 4.5: Interaction with other medicines
d Section 3: Side effects

Mental health update – update on depression with a focus on vortioxetine

6. Vortioxetine distinguishes itself from traditional selective serotonin reuptake inhibitors (SSRIs) by:

a Acting primarily as a selective norepinephrine reuptake inhibitor (SNRI)
b Exclusively inhibiting serotonin reuptake with no receptor modulation
c Combining serotonin transporter inhibition with specific 5-HT receptor modulation, including both agonistic and antagonistic actions
d Primarily enhancing dopamine release through melatonin receptor activation

7. What is the typical starting dose for vortioxetine when prescribed for depression?

a 5 mg twice daily
b 10 mg once daily
c 20 mg once daily
d 15 mg once daily

8. Which of the following is a primary adverse effect of vortioxetine, especially within the first two weeks of treatment?

a Constipation
b Nausea
c Weight gain
d Insomnia

9. Regarding the elimination and drug interactions of vortioxetine, which statement is accurate?

a Vortioxetine has a short half-life requiring twice-daily dosing in most patients
b Vortioxetine is metabolised primarily by CYP3A4, making it sensitive to enzyme inducers like rifampicin
c Since vortioxetine is metabolised primarily by CYP2D6, caution is necessary when used with potent CYP2D6 inhibitors, as these may increase vortioxetine levels
d It is recommended to avoid combining vortioxetine with any antihypertensive drugs due to risk of increased blood pressure

Semaglutide (Ozempic®): a comprehensive review of its pharmacology, efficacy, and safety profile in type 2 diabetes mellitus and weight management

10. Semaglutide is a _____ and indicated for?

a Sulfonylurea, hypertension
b Glucagon-like peptide- agonist, diabetes mellitus type 2
c SGLT2 sodium glucose co-transport 2, diabetes mellitus type 1
d Selective serotonin re-uptake inhibitor, chronic kidney failure

11. Semaglutide has several side effects (common, serious and adverse effects) and these include:

a Depression, apathy, confusion
b Semaglutide face, hypoglycaemia, pancreatitis
c Insomnia, muscle ache, joint pain
d Hypothermia, oedema, cough

12. In which of the following instances is semaglutide not preferable?

a Obesity
b Patients with hypertension
c Patient with history of endocrine neoplasm syndrome
d Patient taking metformin

13. The nausea, vomiting and diarrhoea induced by semaglutide can be correctly managed by doing the following at home:

a Immediately lying down after taking the drug
b Consuming foods like rice and soup
c Taking the medicine with more deep-fried foods
d Skipping doses to help decrease the nausea, vomiting and diarrhoea

The answers for these CPD questions will be in the upcoming issue of the SAPJ.
This activity can contribute towards your CPD compliance.

CPD answers • September/October

1. b	2. d	3. a	4. b	5. a	6. b	7. d
8. c	9. b	10. c	11. c	12. d		

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