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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.

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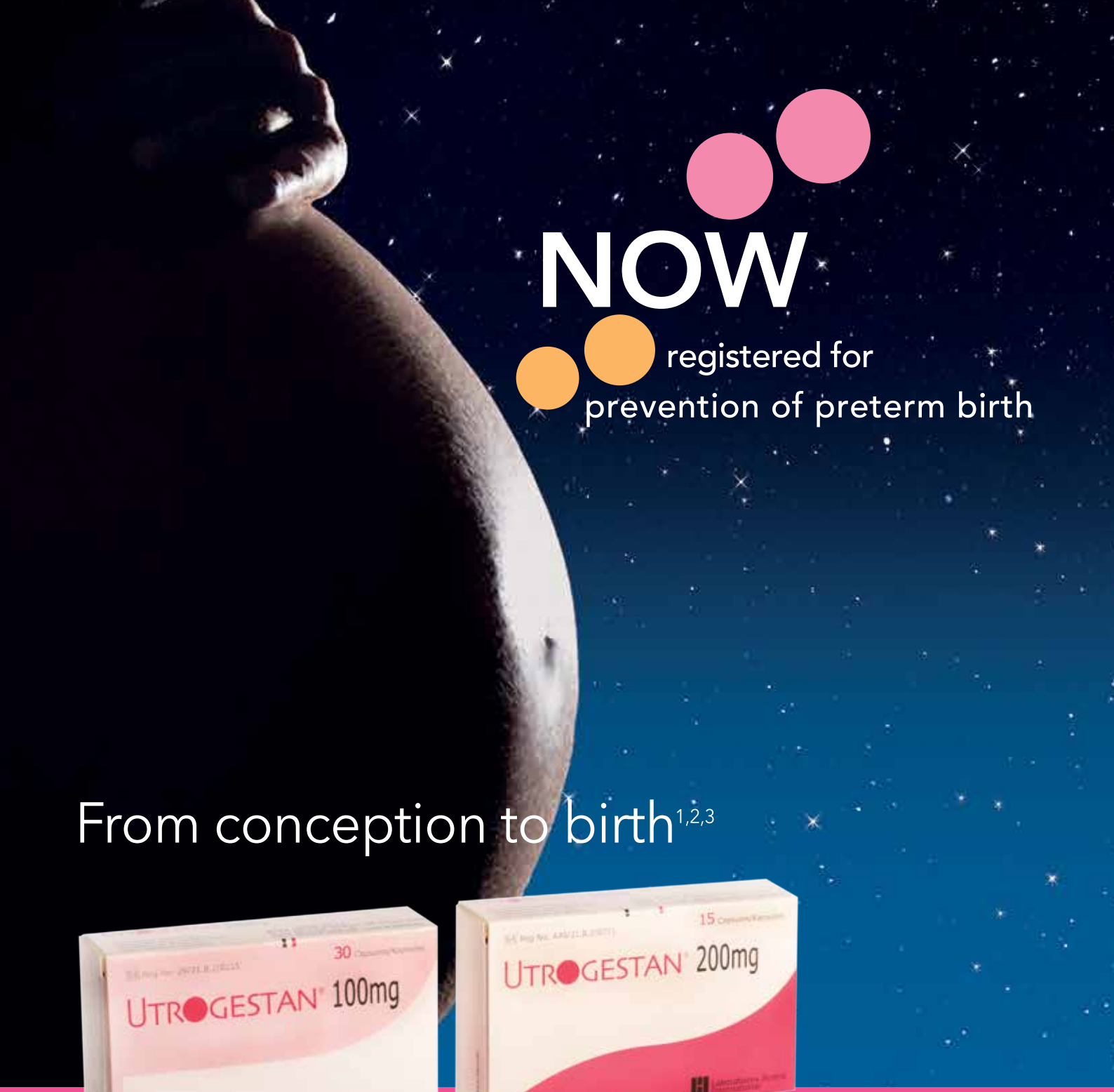

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Editorial

As we publish this special conference issue of the South African Pharmaceutical Journal, coinciding with the South African Association of Hospital and Institutional Pharmacists' (SAAHIP) 37th Annual Conference, it is difficult to not reflect on the transformative landscape of pharmacy in South Africa. This conference theme, *"Future Ready 5.0"*, challenges pharmacists to adapt to technological advancements while maintaining the human touch in pharmaceutical care. Pharmaceutical care is by definition a *patient-centred practice*, where pharmacists assume *responsibility* for a *patient's medication-related needs*, ensuring that drug therapy is appropriately *indicated, effective, safe*, and *convenient* and at the lowest cost to them and their community. This definition has many moving parts, some moving faster than others.

Pharmacists are increasingly called upon to harmonise technological advancements with human-centred care, ensuring optimal healthcare delivery within this rapidly evolving landscape. The integration of digital tools such as Pharmacy Management Systems (PMS) and Clinical Decision Support Systems (CDSS) is crucial for improving medication safety and patient outcomes. Tele-pharmacy services further extend the reach of pharmaceutical care, particularly in underserved communities, by enabling remote consultations, adherence monitoring, and chronic disease management. The expansion of tele-pharmacy aligns with the broader vision of enhancing healthcare accessibility, as outlined in the National Digital Health Strategy for South Africa (2019–2024), which emphasises the role of digital technologies in improving healthcare quality and access.

However, these advancements outpace regulatory frameworks that cannot keep up with innovation. Often it is those in rural settings and that are underserved that need these innovations most, for example, Section 22A(6)(i) of the Medicines and Related Substances Act 101 of 1965 requires a new prescription every 30 days for Schedule 6 medications like methylphenidate. This requirement can lead to treatment interruptions, particularly for patients in remote areas or those with limited mobility.[1] In the realm of electronic prescribing, platforms like EMGuidance Script® and others have emerged as solutions, utilising advanced electronic signatures (AES) to ensure the authenticity and security of prescriptions. These platforms enable the electronic transmission of prescriptions, including those for Schedule 6 medications, provided they meet the legislative requirements outlined in Regulation 33 of the Medicines and Related Substances Act. This technology not only streamlines the prescribing process but also enhances patient safety by reducing errors and improving access to medication.

Pharmacists are constantly challenged to navigate technological advancements, still practising with the regulatory frameworks while addressing broader systemic issues. Pharmacists are, in my opinion, still the unsung heroes of the healthcare team.

Despite their qualifications and readiness to contribute to an overburdened healthcare system, many newly graduated pharmacists remain without permanent roles. Strategic interventions are needed to absorb this skilled workforce into meaningful positions, including incentivising rural placements and fostering entrepreneurship through mentorship programmes (more mentioned in the PSSA Young Pharmacists' Group, 2025). Please support this initiative and young pharmacists in general, excellent mentorship programmes available.

South African pharmacists have to remain vigilant with the recent uncertainty surrounding PEPFAR funding which threatens South Africa's HIV response, potentially leading to over 600 000 HIV-related deaths and 500 000 new infections in the next decade.[2] PEPFAR has been instrumental in supporting the country's HIV programmes, constituting around 18% of the response. Pharmacists play a pivotal role in mitigating this crisis by leveraging programmes such as Pharmacy Initiated Management of Antiretroviral Therapy (PIMART), which empowers trained pharmacists to prescribe antiretrovirals. The matter is still pending verdict from the Constitutional court.[3] By expanding access to HIV prevention and treatment services, pharmacists can enhance medication adherence and improve patient outcomes.[3] Currently, pharmacists (within the Multidisciplinary Team) are already playing a pivotal role in promoting medication adherence through counselling and support, which is crucial for maintaining effective HIV treatment regimens.[4]

I would like to take a moment to acknowledge the invaluable contributions of Dr. Mariet Eksteen, whose dedication to the PSSA has been a beacon of excellence. I have worked with Mariet for many years and in different scenarios and settings. I can say the common denominator for me is her tireless efforts in serving the profession of pharmacy, and, by extension, the public of South Africa. Thank you for your hard work Mariet, you have left an indelible mark on the profession. As you embark on your new chapter, we wish you happiness and success, knowing that you will continue to inspire future generations of pharmacists.

Natalie Schellack
Editor: SA Pharmaceutical Journal

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President's Message

Farewell message to Dr Mariet Eksteen

Tshifhiwa Rabali
PSSA President

I was the Vice-President of the South African Association of Community Pharmacists (SAACP) when discussions began about having a staff member from PSSA National Office represent PSSA at sector meetings. The decision as to who would represent the PSSA was decided by the National Office. Ultimately, Mariet was appointed to represent PSSA National Office during our SAACP NEC meetings. This decision helped forge a stronger, more united relationship between PSSA and SAACP, which continues to this day.

Mariet never missed any of our meetings and she always actively participated during the meeting, bringing valuable information from the PSSA. Her dedication and hard work have been unwavering, and she has excelled in her role with passion and commitment. The significant contribution she made as part of the collective has played a vital role in the growth of the Society, and her efforts have not gone unnoticed.

During the preparations for the International Pharmaceutical Federation (FIP) Congress, it was clear that there was a strong bond between Mariet and the FIP representatives in Cape Town. However, at that time, I did not know that they would eventually recruit Mariet after her significant role in organising the highly successful 82nd FIP Congress.

As Mariet embarks on a new chapter in her career, representing us as pharmacists in this country and as citizens of South Africa, may she be blessed with happiness and success at every step. On behalf of the National Executive Committee of the Pharmaceutical Society of South Africa, all members of the Pharmaceutical Society of South Africa, and all pharmacists in general, I wish you a wonderful and successful journey, Mariet. Go well and know that the PSSA will always miss you.

I thank you.

Saying farewell to Mariet Eksteen

I just wanted to take a moment to express my sincere gratitude for all the hard work, dedication, and contributions you've made to professional development at PSSA. Your passion and commitment have truly made a difference, and you will be greatly missed! Wishing you all the best in your new role at FIP—I'm sure you'll continue to make a meaningful impact. Congratulations, and best of luck on this exciting new chapter!

Lailaa Cajee, PSSA Southern Gauteng Branch

I have known Dr Mariet for a few years now, as a colleague. What a privilege! A dedicated colleague to her work, very discreet with her words and opinion, and sticks to what she believes in. In my interactions with her, I found her to be ethical and with high moral standards. She would not take shortcuts just to meet the needs of the other person. Highly disciplined and organised. At the sector level, she was helpful, informative and resourceful. The sector will surely miss her guidance, contributions and debates. We will surely miss you. We wish you every success in your new role at FIP. May you take with you all the energy that you invested at the SAACP. May this be the beginning of open opportunities for our country. May the South African flag be lifted higher and higher. Go out there and make us proud. We will always value your contributions towards our sector and me on a personal level. It is a fact that you are not lost to the sector as you took your role seriously. In Taki Kyriacos' words, it is farewell but not goodbye.

On behalf of the SAACP and its NEC – Johannes Ravele

Dear Mariet

The YPG has stood on your shoulders since inception in 2024. Not only has it been your baby, but it has also progressed from an infant to a toddler, an adolescent and now a young adult. We hope that this young adult has given you a sense of parental satisfaction. "Thank you" can never capture the gratitude that we feel you deserve from us. However, those are our two words of appreciation for the sacrifices you have made to ensure that we thrive as an interest group of the PSSA. We wish you all the very best with your next endeavour. May it shower you with blessings, good health and ultimately, joy everlasting. In your own words, "If you love your job, you never have to work a day in your life!" May your next chapter provide a satisfying adventure that never feels like work.

With love, PSSA YPG

Dear Mariet

Although our paths crossed for a relatively short time you have left an indelible impression on me personally. Your dedication, your attention to detail and your ability to succinctly summarise situations made your voice one to be heard. We are thrilled for your progress in this industry, and we are so grateful for the huge contribution you have made to us here in South Africa. It is with a heavy heart we bid you farewell. Hope you have an exciting journey with FIP in our wonderful profession. We will definitely follow you on your many social platforms as well. All the very best to you Mariet. Lots of love Regards

Dipti Desai (Mount Edgecombe Pharmacy)

You've been such a valuable part of our team. Your contributions will certainly be missed. I have no doubt that you'll continue to do amazing things in this new chapter of your career. I hope that you find success, growth, and happiness in everything you do.

Take care

Dr KK Naidoo – PSSA Director: KZN Coastal

Through her enthusiasm for the profession, sharp intellect and experience both as an academic and involvement with FIP from a young age, Mariet brought a new dynamic to the work of the Society. During her tenure as a professional officer of the Society we saw great strides made in many areas, particularly in the development of webinars, the establishment of the YPG, mentoring and coaching. Her term on the SAPC helped forge a good relationship between the Society and the SAPC, providing better insight into the work of the Council and helping to resolve a number of problems. Mariet's work ethic, professionalism and determination will be sorely missed but will surely stand her in good stead as she embarks on her new venture with FIP. We wish her well and trust, that as a Fellow of the PSSA, she will continue to share her knowledge, experience, and advice for the benefit of her colleagues.

Regards

Gary Black

Dr Mariet Eksteen **–** It is with great pride and joy that we bid you farewell as you embark on this international journey at FIP. While there will always be that bit of sadness not having your involvement in the daily life of Pharmacy South Africa, we

celebrate your success knowing that one of our own has made it onto this massive international stage. I had the distinct pleasure of working with you on several projects and subcommittees, locally, nationally and internationally and watched you grow into each of these roles and ***perform at an exceptionally high standard***. The highlights for me will be our time at FIP Conferences over the many years, FIP Cape Town 2024, the Codeine Care Initiative and the very important Independent Pharmacy Emergency Fund (IPEF) in 2021. I am confident that you will take with you this ***experience, dedication, loyalty, and leadership qualities*** that you have shown in your role as a student leader all the way to leading the profession on many critical issues over the years. Your commitment in ***bringing the profession together*** on the most difficult issues ***without fear for self*** is certainly one of your standout qualities that we will miss. FIP can certainly look forward to having ***an exceptional staffer and a leader of note.*** Wishing you every success in your new career. Enjoy the journey, the international travel and your newfound international family. Know that ***we will be watching and applauding your success*** and that you will always have a home in Pharmacy South Africa.

Kind regards

Dr Sham Moodley

Dear Mariet, on behalf of the PSSA CWP Branch, I would like to thank you for your determination, vision, and passion. You have been a link to our members, assisting where you can, and to the best of your ability. May you continue to grow as you reach your dreams. You are an inspiration to so many, a true reflection that one can attain great heights. Thank you for your service to our pharmacists and support personnel. We are proud of you and your achievements. Go forth and shine!

Kaajal Chetty - Director: PSSA CWP Branch

Our dearest Mariet, it is with a heavy heart that we collectively say goodbye to you as you head off on your new venture. Your contribution to the Pharmaceutical Society of South Africa has been an indelible one, where you have been a wealth of pharmaceutical knowledge and advice to us all. As the sector that represents the Hospital and Institutional Pharmacists, we humbly thank you for all the effort, advice and mentorship you have provided. Your passion for our profession knows no limits and for this we are deeply grateful. You have had a positive influence on many young pharmacists whilst inspiring us all with your diligent work ethic and dedication to pharmacy. We wish you infinite blessings and prosperity in your future career.

Farewell dear colleague!

Nhlanhla Mafarafara on behalf of SAAHIP NEC

Dear Mariet. As you embark on this new chapter, we want to take a moment to express our deepest gratitude for your dedication, passion, and unwavering commitment. Your contributions have left an indelible mark, and your impact on those around you will be felt for years to come. We remember with much appreciation your assistance with, and contribution to the relief efforts for the pharmacies that were impacted by the unfortunate riots in KwaZulu-Natal. Your selfless and tireless efforts ensured that most of the pharmacies were restored to serve their communities. Your warmth, wisdom, and professionalism have made a lasting difference, and while we are sad to see you go, we are also excited for the opportunities that await you. May this next journey bring you success, joy, and fulfilment. Thank you for everything, Mariet. You will be truly missed but never forgotten! Wishing you all the best in your future endeavours. We are extremely proud of one of our own making a difference to the profession on a global stage. Our loss is FIPs gain. Allow me to end off with a quote from the famous Persian poet, Rumi. He says: "Do not be satisfied with the stories that come before you. Unfold your own myth." Congratulations once again on this achievement and new adventure.

Mehboob Ali Cassim on behalf of the ICPA Board of Directors

Stewardship in crisis: the role of young pharmacists in South Africa's evolving healthcare landscape

Imagine a narrative more significant than any of us—a story written not in accolades or titles but in lives improved and communities uplifted. Every life saved, and every pain eased by medicine is a fragment of a larger story that hinges partly, but significantly, on pharmacists' hands in a multidisciplinary healthcare team. Yet today, that story is under threat. Young pharmacists who are trained to heal, are finding themselves without roles to fulfil. The unemployment crisis facing newly qualified pharmacists in South Africa is more than just a concern; it is an exigent situation that requires urgent attention and action.

Unfortunately, this issue is not unique to young pharmacists. Numerous youth in South Africa find themselves without jobs. StatsSA released a report in 2024, stating that "the percentage of young people ***actively looking*** for work but ***unable to find it*** climbed from 36,8% in 2014 to 45,5% in 2024." This is an 8,7% increase in a space of 10-years, a chronic disease that has been slowly forming over years.

Each year, South African universities produce a significant number of pharmacy graduates. However, it appears that strategic plans that were meant to be designed long ago, did not create the platform to absorb young pharmacists who would provide much needed relief to an overburdened healthcare system. Hence many young pharmacists find themselves qualified, skilled, and ready to serve the population but unable to. The severity of the issue has sparked protests and sit-ins by unemployed pharmacists in provinces such as KwaZulu-Natal and Gauteng. These protests, often led by young pharmacists who are passionate about their profession, demand urgent intervention and employment opportunities.

The PSSA Young Pharmacists' Group distributed a survey titled: Unemployed Young Pharmacists Survey, between 12 and 21 February via a newsletter publication. This survey aimed to collect data on post-community service pharmacists and their experiences with permanent job acquisition. This survey had a total of 216 participants, 185 of them being PSSA members, 10 who have never been members of the PSSA, and 21 previous members who had either resigned voluntarily or were removed due to non-payment of membership fees.

Young pharmacists had the opportunity to list as many barriers to employment as experienced and/or observed. These are listed in Table I.

One can find oneself asking the following questions from the barriers listed:

1. Is the profession truly saturated? If so, are we monitoring the intake of pharmacy students annually and ensuring that there is a strategic plan in place to permanently absorb them into the healthcare space post their community service year?
2. Many job vacancies (including junior positions) state that they need candidates with at least 2–3 years' experience post-community service. Which begs the question: is time spent completing internship and community service disregarded as experience?

Table I: Barriers to finding employment according to young pharmacists

Driver's license, personal transport	Employers' (mis)trust of unstable newly dispensed pharmacists
Differences in dispensing systems	Nepotism, corruption, RP favouritism and bias (pre-filled posts)
Experience in a sector as criteria to submission of application	Post purchasing
Large number of applications, low funding, few vacancies	Internal transfers
Post-freezing	Previous interns/CSP's preference
Bursary holder preference	Saturated market
Applicant Tracking System (ATS) vs CVs	CV structure, interview skills, Z83 form
Relocation costs	"Late" completion of CSP
BEE	Language
Non-negotiable salaries	Pharmacist to Pharmacist's assistant ratio
Over-qualification	Costly additional qualification requirements

3. How can policy-makers monitor the Pharmacist to Pharmacist's assistant ratio ensuring that these ratios are not exploited and young pharmacists are provided increased opportunities for employment?
4. Is post-freezing a reality? How can different stakeholders work together to secure enough funding to absorb young pharmacists?
5. Are we encouraging entrepreneurship among young pharmacists, with sufficient mentorship and funding opportunities?

Experience was the major reason listed in the survey and one can say that whilst it (experience) is the value of a company, it may be a terrifying reality to a young pharmacist.

While urban areas are oversaturated with pharmacists, rural and underserved regions struggle with a critical shortage of healthcare professionals. The importance of rural placements cannot be overstated. From the survey, only 26 respondents were unwilling to move to rural areas due to family responsibilities, safety concerns, and lack of sanitation, easily accessible transport and convenience stores. Other reasons included lack of religious facilities and diet options, distance from major institutions where one can complete post-graduate studies, lack of a support system and mental health challenges. Addressing these disparities requires urgent policy-driven solutions that offer incentives, career development opportunities, and sustainable support for pharmacists in rural areas. The uneven distribution of pharmacists negatively impacts healthcare accessibility, particularly for rural communities where patients already face difficulties obtaining medical care.

Compounding the unemployment crisis are other key factors such as the 2003 regulation allowing non-pharmacists to own pharmacies, initially introduced to expand pharmaceutical services nationwide but has instead concentrated resources in urban centres, where corporate interests thrive, leaving rural communities underserved whilst young pharmacists struggle for employment. It is time to support organisations such as the PSSA's South African Association for Community Pharmacists (SAACP) in their journey of rigorous policy analysis, be informed and vocal about key factors affecting the profession such as this.

From a professional organisation perspective, young pharmacists are encouraged to actively participate in sector and branch activities by attending meetings, contributing to conversations including board notices, attending CPD events and developing a professional network that can mentor and facilitate the development of soft skills, provide sound and experienced advice on practical issues and concerns and ensure wide exposure to opportunities available.

The true identity of a pharmacist is stewardship, not merely dispensing medicine but advocating for patients, ensuring access, and advancing public health. Young pharmacists are encouraged to intelligently advocate and strategise for meaningful change. Their absence due to unemployment affects their personal lives and hampers the healthcare system, as it loses out on their unique contributions to patient care and public health.

Let us not allow unemployment to define us. Instead, let us redefine the profession, ensuring that pharmacists, wherever they are, are recognised, empowered, and able to serve.

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!

Clearing the air: methods and challenges of smoking and vaping cessation

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Abstract

South Africa has a particularly high prevalence of smoking compared to the rest of the world. In spite of the fact that smoking rates in South Africa have been declining since the implementation of tobacco control measures in 1993, there are still an estimated eight million smokers in the country. Smoking has been associated with detrimental health risks and related complications for decades, and such health issues are further compounded by the high incidence of tuberculosis and human immunodeficiency virus/acquired immune deficiency syndrome in the population. Vaping has been offered as an alternative for smoking. This article aims to provide an overview of the importance of smoking cessation, and the nonpharmacological and pharmacological measures aimed at ensuring quitting.

The vaping trend is fueled by the assumption that these products are safer and less harmful than traditional tobacco smoking. The rapid growth of the vaping industry has prompted debates on whether vaping functions as a smoking cessation aid or a gateway for new smokers. The evidence regarding vaping's efficacy in aiding smoking cessation is inconsistent, but there is compelling data suggesting a correlation between vaping and an increase in the number of smokers, particularly among the youth. Notwithstanding the well-established research on the greater harm of tobacco, early studies have already indicated the adverse effects of vaping. Despite the lack of comprehensive health studies, the expanding popularity of electronic cigarettes or electronic nicotine delivery systems such as vapes, especially among the younger demographic, has soared.

Keywords: smoking, smoking cessation, nicotine, nicotine replacement therapy

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Introduction

In line with the requirements of the World Health Organization (WHO) Framework Convention on Tobacco Control, the South African government implemented comprehensive tobacco control measures in 1993, with further amendments in 2007.[1] Although smoking rates have declined by 32% since 1993, there are still an estimated eight million (16.4%) smokers in South Africa.[2] South Africa has a particularly high prevalence of smoking compared to the rest of the world.[3] The effects of smoking are exacerbated by infectious risk factors of chronic obstructive pulmonary disease (COPD), like tuberculosis and human immunodeficiency virus (HIV), of which South Africa has one of the highest burdens globally.[3] The mortality rate for current smokers in South Africa is nearly double that of non- or ex-smokers.[4] Up to a third of all male deaths in South Africa, in adults aged 35 years and older, have recently been attributed to tobacco use. The cost of smoking-related disease to the South African economy is estimated to be R1.2 billion annually.[3]

The popularity of electronic cigarettes (EC) is on the rise among smokers globally.[5] Users commonly cited reasons such as aiding in smoking cessation, alleviating withdrawal symptoms from traditional cigarettes, saving money, and seeking a "smoking" experience with reduced health risks as their motivations for purchasing and using these devices.[6] Tobacco use kills more than eight million people each year, making it one of the biggest public health threats the world has ever faced. Globally, 1.25 billion people use tobacco, with 80% of them living in low- and middle-income countries (LMICs). These countries bear the heaviest burden of tobacco-related illness and deaths.

Vaping was described as a looming crisis threatening the health of children in South Africa. This warning was issued years ago by Prof. Anthony Westwood, a paediatrician at the Red Cross Children's Hospital in Cape Town, concerning the rising prevalence of vaping and e-cigarette use among the nation's youth. Dr. Sharon Nyatsanza, Deputy Director of the National Council Against Smoking, highlighted the significant concern regarding the underage use of e-cigarettes and the high prevalence of vaping among South African youth.

"E-cigarettes pose undeniable health risks; accumulating evidence links their use to serious health conditions such as cancers, respiratory and cardiovascular diseases, chest pains, mouth ulcers, asthma, and an elevated risk of strokes," stated Nyatsanza.

She further noted that young individuals who use e-cigarettes are more likely to transition to regular cigarette smoking and other drug use. With 70% of South African smokers starting before the age of 18, Nyatsanza emphasised that the tobacco industry targets this demographic. She stressed the importance of implementing

public health strategies to prevent early initiation, particularly in Africa, where a significant youth population is emerging.

"Regulation is imperative to safeguard the health of children and the broader population," Nyatsanza concluded.

In a time when vaping is often linked to stylish designs and a plethora of flavours, the harsh reality is often overlooked. Within the vapours, a blend of harmful chemicals lurks, endangering the respiratory health of those who choose to partake.[7] From arsenic, a component found in rat poison, to acrolein from weedkiller, and xylene commonly used in paint strippers – these are just a few of the perilous substances ingested by users every time they take a puff.[8,9]

Aside from the escalating apprehension regarding the potential health hazards associated with vaping, the desire to quit vaping has also been associated with encountering adverse physical effects (such as dry mouth and cough), the increasing expenses related to vaping, and the necessity to overcome dependence on vaping products.[10,11]

A recent study from the University of Cape Town Lung Institute uncovers a worrying trend: a substantial number of South African students are vaping, with nearly 7 000 reported cases.[12] Rates vary across grades, with 26.5% of Grade 12 students admitting to vaping, slightly decreasing in lower grades to 17.4% in Grade 11, 13% in Grade 10, and 10.8% in Grade 9. These results indicate a rising youth interest in vaping, emphasising concerns about its health effects and the importance of parental awareness. Asanda Gcoyi, CEO of the Vapour Products Association of South Africa (VPASA), attributes the growing popularity of vaping among adolescents to factors such as peer pressure, curiosity for new experiences, social stress, and the availability of vaping products from unregulated sellers and online platforms. A study conducted in 2022 by Prof. Richard van Zyl-Smit from the University of Cape Town involving over 5 500 high school students revealed alarming statistics: three out of ten students use their electronic smoking devices within an hour of waking up, nearly a quarter cannot go through a school day without vaping, and more than one in four matriculants are engaged in vaping.[13]

Nicotine dependence

Tobacco products contain nicotine, which is the drug that produces dependence in smokers.[14] Nicotine affects the dopaminergic system in the brain, causing a sense of well-being, and also increases the number of nicotinic receptors.[15,16] Nicotine may be as addictive as heroin, cocaine or alcohol, and yet is viewed as the most socially accepted form of chemical dependence.[14] Nicotine withdrawal symptoms, including headaches, coughing, cravings and increased appetite can be a major barrier to smoking cessation.[15] Sudden mood changes, irritability and restlessness may also cause resistance from the support system members or close relatives of the patient trying to quit.[15] Smoking is an addictive habit, with a strong association with emotions and thoughts, but is also intimately linked to the smoker's daily activities and rituals, like driving or having meals.[14,15] For this reason, it is important to deal with the actual nicotine dependence of a patient, but also to introduce cognitive behavioural therapy to deal with the emotional attachment to smoking.[15]

Vaping products function by heating the e-liquid or e-oil found in cartridges to create an aerosol or vapour, which users then inhale into their lungs. This e-liquid or e-oil may include nicotine, tetrahydrocannabinol (THC), and/or cannabinoid (CBD), as well as various flavourings and additives.[11] The popularity of these devices can be attributed to the abundant flavours these are sold in, ranging from fruity to sweets or even taste like tobacco. The key distinction between smoking conventional cigarettes and vaping lies in the form of inhalation—smoke versus vapour. Smoking involves the ignition of tobacco, delivering nicotine and tar to the lungs through inhaled smoke. Vaping, on the other hand, employs a battery-operated heater, commonly referred to as coils, to heat e-liquid or "e-juice", producing a vapour that is then inhaled. While both methods deliver nicotine to the lungs, they can lead to addiction and result in severe health issues.[17,18] Most common effects start in the lungs where only a few minutes of vaping can cause changes in how the lung functions and exacerbate inflammation.[19] Respiratory symptoms like coughing, sore throat, and dry mouth have also been documented to surge immediately following vaping.[19] Although much remains unknown about the connection between vaping and the onset of chronic respiratory illness, a recent study tracking a significant cohort of individuals (21 000) over several years unveiled that individuals who engaged in vaping were 30% more prone to developing asthma and 60% more prone to developing chronic obstructive pulmonary disease compared to those who never used e-cigarettes.[19] Linkage between e-cigarette usage and heart disease has demonstrated an ability to elevate blood pressure, heart rate, and arterial stiffness.[20] Although there isn't enough research to definitively state that vaping causes heart disease, the risk factors associated with it are heightened by e-cigarette use. Consequently, there's a strong likelihood that vaping negatively impacts heart health. A limited number of studies have indicated that individuals who use e-cigarettes face a greater likelihood of experiencing heart attack, stroke, and angina.[21] While most vapers haven't engaged in vaping for a duration sufficient to ascertain its potential to induce cancer, laboratory research has revealed that the vapours emitted by e-cigarettes have the capability to harm human DNA, thereby presenting a potential pathway to cancer development.

Tobacco use in human immunodeficiency virus and tuberculosis

Tobacco use has multiple effects on the immune system, as it affects the circulating immune cells, mucosal surface defences and other immune cell functions, which results in it being a leading cause of respiratory infections.[4] It was found in a recent study that HIV-positive patients who used tobacco products had a significantly increased mortality rate compared to those who had never smoked, doubling the mortality of smokers with HIV.[22]

It is estimated that around 12% of the population in South Africa is living with HIV, with over 1 700 acquired immune deficiency syndrome-related deaths each day.[23]

Smoking cessation has been shown to reduce the risk of bacterial pneumonia and *Pneumocystis* pneumonia in HIV-positive patients by approximately 27%.[24] HIV-positive patients who smoke have a 20 times greater risk of developing tuberculosis than non-smokers who are infected with HIV.[24]

EVALI incidences and how to recognise it

In 2019, e-cigarette or vaping product use-associated lung injury (EVALI) was officially recognised as a severe pulmonary illness linked to the use of e-cigarettes or vaping products. EVALI was linked to vitamin E acetate (VEA).[25] The majority of individuals diagnosed with EVALI had used THC-containing e-cigarettes, with a significant number of them containing VEA.[26] EVALI is diagnosed based on a combination of clinical features and patient history, with no specific diagnostic test available. The most widely used definition, according to CDC guidance, aims to identify probable and confirmed cases during outbreaks. Confirmed cases are determined by the onset of pulmonary infiltrates on chest X-ray or computed tomography within 90 days of e-cigarette use, with no alternative cause found after medical assessment.[27] EVALI symptoms develop gradually. Lab findings may include elevated white blood cell count and erythrocyte sedimentation rate, though they're often nonspecific.[28] Typically, symptoms appear as respiratory issues with common symptoms like breathlessness, cough, chest pain, and/or bleeding. Additionally, patients may experience gastrointestinal symptoms (nausea, vomiting, and/or diarrhoea) and/or constitutional symptoms (fever, chills, fatigue, and/or weight loss).[27,29] It's important to highlight that e-cigarette use has been linked to up to seven times the likelihood of COVID-19 diagnosis compared to non-users along with an increased risk of COVID-related symptoms.[30,31] Treatment for EVALI often begins with antibiotics, as EVALI-induced respiratory failure can resemble bacterial or viral pneumonia.[32] Supportive oxygen therapy is reportedly administered[33] and most patients receive corticosteroid treatment although those managed without steroids still exhibit rapid clinical improvement.[27,34]

Nonpharmacological interventions

Nonpharmacological approaches to quitting smoking mostly involve motivational interviews and counselling, but other measures include cognitive behavioural therapy, hypnotherapy and acupuncture or electrostimulation.[3,16] Counselling can be performed in several ways, including telephone or on-line counselling, and group or one-on-one patient counselling.[14,16] This method has shown success when at least three or more sessions were attended, or when the counselling was supported by the use of medication to treat nicotine withdrawal.[3,16]

Cognitive behavioural therapy assists the patient with changing habits associated with smoking, and helps to motivate patients to quit.[16] Hypnotherapy has been proposed as a way of lessening the desire to smoke and/or improving the will to stop. However, there has been no convincing efficacy data arising from clinical trials to indicate that there is an advantage to be gained from hypnosis for smoking cessation.[3,16]

Acupuncture and electrostimulation are promoted to aid in smoking cessation by reducing withdrawal symptoms.[3,16] Benefit with respect to the number of people who successfully quit smoking has not been demonstrated in review studies that have compared these therapies to placebo.[3,16]

While established guidelines for effectively managing the cessation of cigarettes exists,[35] there is a notable absence of evidence-based recommendations to support electronic cigarette (EC) users looking to quit vaping. It remains uncertain whether guidelines designed for smoking cessation can be applied to vaping products. Notably, there is a lack of studies evaluating the effectiveness of medications approved by the US Food and Drug Administration (FDA) for smoking cessation in aiding vaping cessation. The efficacy and safety of varenicline for vaping cessation have not undergone examination, emphasising the need for comprehensive research to inform the decisions of health authorities and healthcare providers.

The new article published by the WHO Article 14 on the 8th of July 2024 as guidelines as basic infrastructure needed to promote tobacco cessation and provide effective tobacco dependence treatment said the following in regards to vaping cessation: *"This guideline provides recommendations for supporting adults (individuals aged 18 years and older) to quit the use of any types of tobacco products, including: cigarettes, waterpipe (hookah, shisha) tobacco, various smokeless tobacco products, cigars, cigarillos, roll-your-own tobacco, pipe tobacco, bidis, kreteks and heated tobacco products. E-cigarettes are beyond the scope of this guideline because the potential benefits and harms of using these products are complex and are addressed in a separate body of literature. These products may be addressed in the future as evidence accumulates."* This again calls to attention the importance of more studies to be done.

Children are recognised as being susceptible to nicotine addiction, as highlighted by Murthy and the WHO.[36,37] Due to the potent addictive nature of nicotine products, a considerable percentage of early experiments with these products tend to escalate into habitual, addictive use. The probability of developing addiction is partly influenced by age, with adolescents under 15 years who engage in smoking having an estimated 50% chance of developing nicotine addiction. The risk of addiction further increases with prolonged and repeated smoking.[21] Notably, the majority of tobacco addictions take root before the age of 21 years.[12,38]

The role of the pharmacist

In a study done in 2021 in South Africa, with over 18 208 smokers, researchers determined that of those planning to use any cessation aid were interested in getting help from a pharmacist was 44.6%.[39] This highlights the importance for pharmacists to not

only know pharmacotherapy but also nonpharmacological advice to assist and advise patients.

Identifying the patient

When patients present to primary care facilities and need to have their vital signs assessed, they can be asked whether or not they smoke.[3] Encouragement and assistance provided by members of the multidisciplinary healthcare team increases the likelihood of abstinence.[3] According to the WHO[15] toolkit for brief tobacco interventions, the primary healthcare provider can use the "5 As" (Figure 1) to help to identify patients who are ready to quit. The process can also be used to determine which patients are not prepared to stop smoking, or who think that it is not important to do so.[15] The "5 Rs" model (Figure 2) can be used for the latter patients using a motivational counselling intervention to prepare them to change their minds about smoking cessation.[15]

The 5 As model can assist in identifying patients who are ready to quit and assist them with advice about tobacco use:[15]

- *Ask:* By asking about their use of tobacco, all smokers visiting the healthcare facility will be systematically identified.[15] Enquiries should be made in a friendly, non-accusing way, and tobacco use indicated on the medical notes.[15]

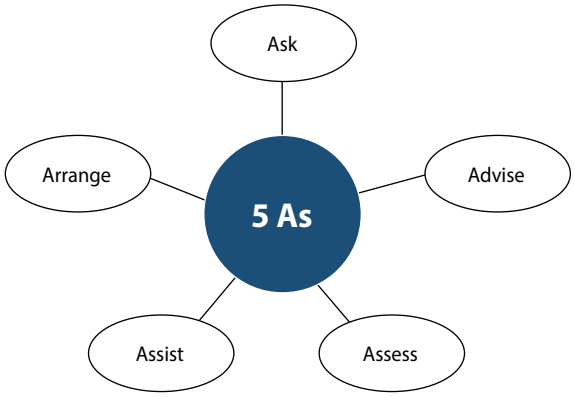

Figure 1: The 5 As intervention process, to be used in patients who are ready to cease smoking[15]

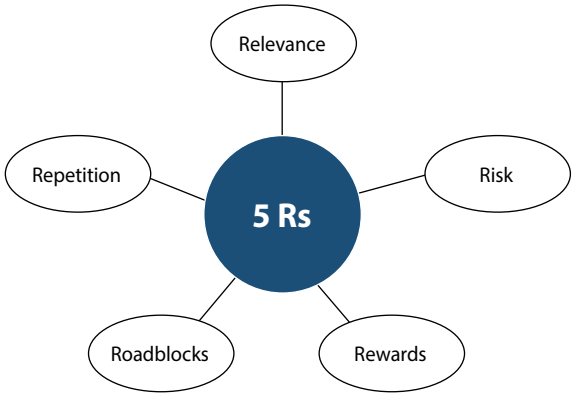

Figure 2: The 5 Rs motivation intervention process, to be used in patients who are not ready to quit smoking[15]

- *Advise:* The advice given should be tailored to the specific patient, must be clear and strong, and aimed at persuading the patient to quit.[15]
- *Assess:* An assessment is undertaken to determine the willingness of the patient to make an attempt to quit.[15]
- *Assist:* This refers to the actions of the healthcare worker with regard to supporting the patient and helping him or her to develop a specific plan to quit, as well as providing support and recommendations on the use of medication.[15]
- *Arrange:* Arranging or planning a follow-up visit or contact with the patient, either in person or by telephone, is important.[15]

The 5 Rs model can be used as a motivational intervention tool to assist patients who are not ready to quit:[15]

- *Relevance:* It is important demonstrate to the patient how quitting would be personally relevant to him or her.[15]
- *Risks:* Highlighting the risks associated with smoking encourages the patient to understand the potentially negative consequences of tobacco use which are relevant to him or her.[15] These risks may include cardiovascular threats, like myocardial infarction (MI) and strokes, and other illnesses such as lung cancer and COPD. Risks also include the threat to wealth or the ensuing financial burden.[15]
- *Rewards:* The patient must be made aware of the potential benefits of stopping tobacco use, for example having improved health and sense of smell and taste, saving money and a general improvement in their well-being.[15]
- *Roadblocks:* It is important to identify barriers that prevent patients from quitting tobacco products, and to provide advice on treatment options that will address these, i.e. withdrawal symptoms, weight gain, depression and the negative presence of other tobacco users.[15]
- *Repetition:* Repetition is indicated if the patient is still not prepared to stop smoking. If this is the case, at a later stage, he or she should be re-assessed for his or her readiness to quit and the intervention repeated.[15]

Identifying patients who are ready to quit smoking and motivational measures to assist patients to quit smoking are every healthcare provider's responsibility.[40] Motivational interviewing is an evidence-based approach to assisting patients to change their tobacco habits.[40] However, counselling and medication have both been shown to be effective in treating tobacco dependence, but using medication together with counselling has been shown to be more effective than either one alone.[14] Table I outlines key patient advice for initiating non-pharmacological smoking and vaping cessation management.

Pharmacological interventions

There is substantial evidence supporting the effectiveness of pharmacological support for smoking cessation with multiple evidence-based guidelines available to inform its use.[47-49] However, when searching for vaping cessation guidelines, few

Table I: Patient advice when initiating non-pharmacological smoking/vaping cessation management[41-46]

Patient advice	Pharmacist has foundational knowledge? (✓ or ×)
Assess willingness to make a cessation attempt – Is the patient willing to make a cessation attempt at this time? **Advise to quit** in a strong, urgent manner. The intervention should **focus** on the **advantages of smoking cessation for health** rather than on the risks of smoking.	☐
Gradually reducing smoking without medication often leads to **persistent cravings and prolonged withdrawal symptoms**. Smokers tend to compensate by increasing their puffing frequency or intensity. Therefore, it's advised to **quit smoking altogether.**	☐
Advise patients to **seek counselling** for regular follow-ups, whether with a physician or psychologist. If the patient, due to financial strain or work hours can't, it is important to instruct the patient in selecting cognitive and behavioural coping strategies for managing nicotine cravings. **Cognitive coping skills** may involve reminding the patient of their motivations for quitting, reassuring them that the urge will diminish, and repeating affirmations such as "smoking is not an option". **Behavioural coping techniques** may include removing oneself from the triggering situation, engaging in distracting activities, practising deep breathing exercises, and seeking support from others.	☐
Advise patients to **develop support-seeking skills**, such as asking for help from family, friends, and coworkers, and creating a smoke-free home. They should also encourage prompt support-seeking by assisting patients in identifying supportive individuals and informing them about community resources like hotlines. **South African Quit line: 011 720 3145 and Whatsapp number: 072 766 7812**	☐
Use the **STAR-method** for initiating cessation. 1) **Choose a date** to begin the journey toward quitting. 2) **Share the decision** to quit smoking with family, friends, and coworkers, seeking their understanding and support. 3) **Prepare for potential obstacles** during the initial weeks of quitting, including managing nicotine withdrawal symptoms (e.g. mood disturbance, insomnia, irritability, difficulty concentrating, increased appetite and weight gain). 4) **Remove tobacco products** from surroundings and avoid smoking in commonly visited areas like home, work, and the car before quitting.	☐

were identified. Some guidance and recommendations that were developed to support smoking cessation generally state that recommendations are inclusive of electronic nicotine delivery systems (ENDS) and other vaping products and despite the lack of evidence, it may be reasonable to manage vaping cessation in a way similar to smoking cessation.[50-51] The available literature and data highlight a gap in knowledge concerning the effectiveness of pharmacotherapy and other interventions for supporting vaping cessation.[51]

Pharmacological therapy should be instituted in conjunction with cognitive behavioural and supportive therapy. Table II lists the therapeutic options that are currently, or soon to be, available.

Nicotine replacement therapy

Nicotine has a relatively short half-life and is not well absorbed.[3,54,55] For this reason, some of the preparations should be taken 1–2 hourly (sublingual tablets) and the patches replaced daily.[3,54,55] When used in conjunction with professional counselling and supportive therapy, the likelihood of reducing the addiction more than doubles.[3,54,55] When used on its own, the chances of cessation of smoking resulting are the same as that of placebo.[3,54,55] Side-effects of these agents include nausea and gastrointestinal cramps, coughing, insomnia and muscle pain. Nicotine may cause coronary spasms in patients with cardiac conditions such as MI, an acute stroke, cardiac arrhythmias and angina, i.e. the stable, unstable or Prinzmetal's variants. Patches might cause local irritation to the skin.[3,54,55] The use of nicotine replacement therapy has been shown to be more effective when combined with a dopamine reuptake inhibitor, such as bupropion.[3,54,55]

Antidepressants

Bupropion hydrochloride which is initially taken as 150 mg daily for three days, then increased to 150 mg twice daily, may be used with nicotine replacement therapy, or on its own. Bupropion lowers the seizure threshold, and patients at risk of seizures should use an alternative option. It should also not be administered to patients with a current or previous diagnosis of an eating, or bipolar mood, disorder.[3,54]

Nortriptyline is an active metabolite of amitriptyline, and although not currently registered in South Africa, it is used elsewhere in patients who have failed nicotine replacement therapy, and bupropion and varenicline.[3,54]

Nicotine receptor partial agonists

Varenicline is available in South Africa, and should be used in combination with cognitive behavioural therapy.[3,56] Reports of an increase in suicide or suicidal behaviour have been noted in patients taking this drug.[3,56] Therefore, when patients are initiated on this agent, they should be monitored for any behavioural or neuropsychiatric changes.[57] Cytisine and dianicline are currently being used, but are not yet available in South Africa.[3,56] These agents act as partial agonists of the central, high-affinity, α4β2-containing, nicotinic acetylcholine receptors (nAChRs).[58] This should relieve withdrawal symptoms and cravings in individuals when they attempt to stop smoking by activating the α4β2 nAChRs and competing for the nicotine at its binding site.[58]

Table II: Pharmacological treatment options for smoking cessation[52-57]

Pharmacological therapy	Mechanism of action	Availability	Prescribing points and additional information
Nicotine replacement therapy (NRT)			
Nicotine transdermal patches	Nicotine binds stereo-selectively to nicotinic-cholinergic receptors (nAChR) at the autonomic ganglia in the adrenal medulla, at neuromuscular junctions, and in the brain. Stimulating effect: exerted mainly in the cortex via locus ceruleus and a reward effect is exerted in the limbic system. At low doses the stimulate effects predominate while at high doses the reward effects predominate.	OTC	Available in 3 strengths (35–52.5 mg) Applied daily for up to 24 hours Therapy starts with 52.5 mg for heavy smokers (> 20 cigarettes/day) and 35 mg for lighter smokers (< 20 cigarettes/day) Max duration of treatment: 3 months Reduce dosage every 3–4 weeks Dosage cannot be adjusted by cutting the plaster
Nicotine Gum	See above	OTC	2–4 mg chewed slowly when the urge to smoke arises Chew for 30 minutes to release the majority of nicotine; stop chewing as soon as the gum flavour is noticeable; once the taste or tingling diminishes, resume slow chewing of the gum; stop chewing again when the taste becomes stronger Maximum: 15 pieces per day Max treatment duration: 3 months Gradually reduce gum use until down to 1–2 pieces per day before stopping
Nicotine inhaler	See above	OTC	0.66–1 mg per spray, whenever there is an urge to smoke 4 strengths available Therapy starts with 1 mg if smoking > 20 cigarettes/day or 0.66 mg if smoking < 20 cigarettes/day Maximum: 60 sprays/day (1 mg) or 90 sprays/day (0.66 mg) Reduce dosage every 3–4 weeks Complete smoking cessation (all forms) required during treatment
Antidepressants			
Bupropion	Selective inhibitor of the neuronal re-uptake of catecholamines (noradrenaline and dopamine) with minimal effect on the re-uptake of indolamines (serotonin) and does not inhibit monoamine oxidase. The mechanism by which bupropion enhances the ability of the patient to abstain from smoking is unknown.	Prescription	Oral (SR tablet): Initial: 150 mg daily; increase to 150 mg twice daily on day 7 Max single dose: 150 mg Max 300 mg/day Start while still smoking; set a "target stop date" within first 2 weeks, ideally within 2nd week Treatment for 7–9 weeks; discontinue if no improvement by week 7 Avoid bedtime dosing to reduce insomnia Food-drug interaction: be cautious when taking bupropion hydrochloride with a high-fat meal, as it may increase exposure to the medication
Nicotine receptor partial agonists			
Varenicline	Binds with high affinity and selectivity at alpha-4 beta-2 neuronal nicotinic acetylcholine receptors (nAChR), where it acts as a partial agonist. It has both agonist activity, with lower intrinsic efficacy than nicotine, and antagonist activities in the presence of nicotine. Nicotine competes for the same human α4β2 nAChR binding site for which varenicline has higher affinity. Therefore, varenicline can effectively block nicotine's ability to fully activate α4β2 receptors and the mesolimbic dopamine system, the neuronal mechanism underlying reinforcement and reward experienced upon smoking.	Prescription	Oral: day 1–3: 0.5 mg daily; days 4–7: 0.5 mg twice daily; day 8 onwards: 1 mg twice daily Treatment duration: 12 weeks; extendable by another 12 weeks if successful Patients should set a quit date 1–2 weeks before starting Consider dose reduction to 0.5 mg twice daily if adverse effects occur After smoking cessation therapy, the risk of relapse is higher immediately post-treatment. For high-risk patients, dose tapering may be considered Motivated patients who didn't quit or relapsed during varenicline therapy may find another attempt with varenicline beneficial
Nicotine vaccine			
Nicotine vaccine	Induces antibodies that bind to nicotine, preventing it from binding to central receptors	Not yet available	–

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2. Tønnesen P, et al. Efficacy of a nicotine mouth spray in smoking cessation. Feb 16-19th, 2011.

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Conclusion

The desire to quit smoking is paramount to the successful execution of a smoking cessation programme. Potential patients need to be identified during routine primary care practices. Those who want to quit can be initiated on the 5 As model, while those that are not yet ready to do so can be assisted through the 5 Rs model. Successful smoking cessation requires a combination of behavioural therapy, social support and the appropriate use of relevant pharmacotherapeutic interventions. Research on vaping is still scant, even though these devices have been on the market for quite some time, with usage surging from as early as 2003. Preliminary studies are beginning to emerge, indicating that vaping, like smoking, may have serious health repercussions. The urgency on closing the knowledge gap on vaping cessation is definite and more research and studies to determine long-term use effects should be a priority. Research and quality checks on the ingredients inside e-juices and vapes also need to be investigated. Currently with no tailor specific treatment for vaping, pharmacological and non-pharmacological treatment is the same as cigarette cessation. Amidst the worsening vaping lung injury crisis, new smoking alternatives continue to emerge. One such alternative is a salt-based formulation. Vaping, akin to a modern siren, entices many youths and cigarette smokers trying to quit and find themselves unable to shake the addiction.

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Management of erectile dysfunction

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Abstract

Erectile dysfunction (ED), or impotence, significantly affects men from the age of 18 years but primarily those over 40 years of age. It is defined as the persistent inability to maintain penile erection sufficient for satisfactory sexual intercourse. EDis a multi-faceted condition that may involve any one (or more) of several different organic causes. Conversely, it may also be psychogenic in nature. This article provides an overview of the current classification, risk factors, impact of COVID-19 diagnosis and management of ED.

Keywords: erectile dysfunction, diabetes-induced erectile dysfunction, impotence

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Introduction

Erectile dysfunction (ED) (or impotence) affects men from 18 years old, and it is defined as the inability to obtain or maintain a penile erection that is sufficient enough for sexual intercourse.[1] This may be accompanied by a lack of desire for sexual intercourse, or ejaculatory problems.[2] While it affects 1–10% of men under 40, the incidence rises to 29% in those aged 40–49, 20–40% in men aged 60–69, and 50–100% in men over 70 years of age.[3] It is strongly associated with cardiovascular disease (CVD), diabetes mellitus, hyperlipidaemia, and hyperhomocysteinaemia, among other metabolic and vascular disorders.[4–6] Age is a significant risk factor, with the likelihood of ED increasing as men get older. ED significantly affects quality of life, relationships, and overall well-being.[7]

Aetiology and pathophysiology of erectile dysfunction

Upon evaluating ED, various factors need to be assessed before a suitable treatment can be decided on (refer to Figure 1).

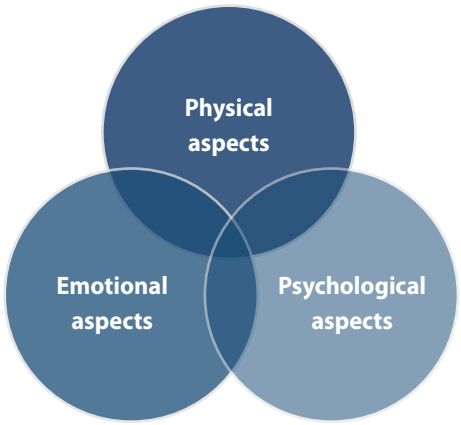

Figure 1: Possible aetiologies of erectile dysfunction[8]

Physical and organic causes

It is essential to address physical or organic causes that may lie at the root of the problem. Major physical and organic causes are summarised in Table I. Neurogenic factors include neurological disorders and neuropathies. The endocrinological disorders have a major impact on hormonal control in males suffering from ED. Androgens are important for sexual desire and maintaining normal sleep-wake erections. However, the latter are not involved in visually induced erections. ED is only reversible or curable in a small number of men, and patients with ED secondary to specific endocrinopathies (e.g. hypogonadism or hyperprolactinaemia) may be curable.[9,10] Certain conditions affect penile arterial supply, which will be classified as vasculogenic ED. These conditions include cigarette smoking, atherosclerosis, hypertension and pelvic irradiation.[11] The microvascular effects of diabetes mellitus can also cause penile arterial insufficiency.[12] Therefore, the pathophysiology associated with diabetes-induced erectile dysfunction (DIED) is multifactorial.[13]

Erectile dysfunction and other health conditions

ED is not just a sexual health issue, it is now recognised as an early marker of several chronic diseases, including CVD, diabetes, metabolic syndrome, and mental health disorders.[6] People living with chronic non-communicable diseases (NCDs) such as diabetes mellitus and CVDs are at significantly increased risk for sexual dysfunction. The estimated prevalence of ED in patients with diabetes in Africa was noted to be as high as 71.45%.[16] Interestingly, ED has been identified as an independent marker for CVD In response to emerging evidence on the risk factors for sexual dysfunction, local guidelines have been adapted to include routine screening of people living with diabetes for sexual dysfunction. Other associated risk factors for sexual dysfunction include

Table I: Physical and organic factors involved in erectile dysfunction[14,15]

Neurogenic erectile dysfunction	Endocrinological erectile dysfunction	Vasculogenic erectile dysfunction	Drug-induced erectile dysfunction	Systemic diseases and general ill health	Cavernous factors (local penile factors)
Central nervous system (cerebral/spinal cord), e.g. following cerebral insult or spinal cord injury, and multiple sclerosis	Diabetes mellitus, hypogonadism and hyperprolactinaemia, hypo- or hyperthyroidism	Arterial: macro- or microangiopathy (e.g. atherosclerosis and trauma)	Refer to Table II	Excessive body weight, especially abdominal obesity (with a waist circumference of > 102 cm in men)	Cavernous fibrosis after priapism or due to other conditions, e.g. Peyronie's disease and/or penile fracture
Peripheral, afferent nervous system (sensory neuropathy, e.g. diabetes mellitus)		Venous: failure of the corporal veno-occlusive mechanism		Smoking, dyslipidaemia, metabolic syndrome, etc.	
Peripheral, efferent nervous system (autonomic neuropathy, or following radical pelvic surgery)		Sinusoidal: fibrosis, failure to relax		Chronic diseases: liver, respiratory and kidney disease	

increased age, depression, mental health conditions, chronic pain, obesity, substance abuse, HIV and certain medications.[16,17]

Erectile dysfunction and diabetes

Several studies have shown that type 2 diabetes (T2D) is associated with lower levels of both total and free testosterone, with an estimated 25–50% prevalence of hypogonadism among affected individuals.[18] The diabetic population exhibits a higher prevalence of metabolic syndrome and obesity, both of which are significantly associated to hypogonadism and ED.[19] As a result, this population experiences health-related declines in quality of life and faces a two to three times higher risk of CVD, independent of age, smoking status, and low-density lipoprotein (LDL) levels. In contrast, individuals with type 1 diabetes (TID) typically maintain normal testosterone levels and rarely develop hypogonadism. It is estimated that ED affects up to 75% of all men with diabetes, it is age correlated and occurs at a younger age in men with diabetes.[12,13]

Erectile dysfunction and cardiovascular diseases

ED is an early manifestation of CVD. In addition to the sexual distress, ED has been identified as a potential early indicator of CVD, which remains the leading cause of mortality globally.[20] This is attributed to the fact that both ED and CVD are vascular disorders sharing common risk factors and underlying pathophysiological mechanisms, including endothelial dysfunction, chronic inflammation, and reduced plasma testosterone levels.[5] Because penile artery size is smaller compared with coronary arteries, the endothelial dysfunction results in a more pronounced reduction in blood flow to erectile tissues than to the coronary circulation.[21] From a clinical standpoint, because ED may precede CVD, it can be used as an early marker to identify men at higher risk of CVD events.[20]

Psychological and emotional components

Several factors can contribute to an increased risk of ED, including lifestyle choices, genetic predisposition, neurological and psychiatric disorders, medication use, and CVDs.[21] However, psychological factors have also been found to play a crucial role in the onset and severity of ED. Stressful life events can be the cause of sexual dysfunction; these may include daily worries about money, work or other significant occurrences.[22] This may be due to the activating and inhibiting mechanisms of the sympathetic and parasympathetic nervous systems. During stressful times, the sympathetic nervous system will release adrenalin, which may counteract the effects of the parasympathetic system on sexual arousal and, therefore, instead of becoming sexually aroused, the penis may be flaccid or not sufficiently erect.[23] Not only will sexual dysfunction have an effect on the individual but also on the couple. Partners of men suffering from sexual dysfunction also

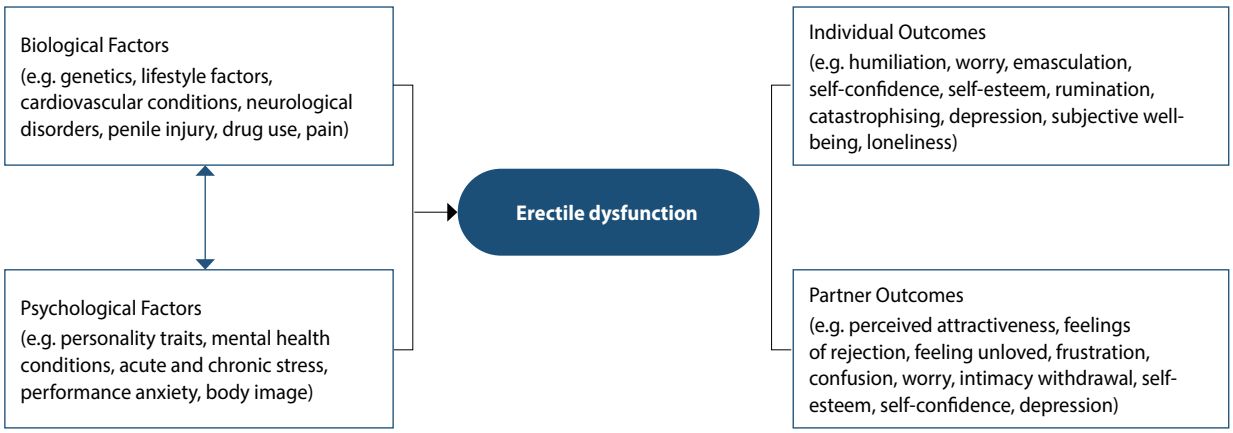

Figure 2: A general model illustration of key psychological contributors and outcomes of erectile dysfunction[24]

suffer in terms of their quality of life. ED may lead to friction in a relationship and when the ED is cured, the quality of life may markedly be increased for both partners. A general model of psychological processes in the experience of ED is illustrated in Figure 2.

An important causative factor for the pharmacist to consider is drug-induced ED. Table II provides a checklist for the pharmacist to review prescriptions when working with patients presenting with ED. The drug classes most commonly associated with drug-induced ED include psychotropic drugs (i.e. the tricyclic antidepressants, selective serotonin-reuptake inhibitors, phenothiazines and butyrophenones) and antihypertensive agents (i.e. the thiazide diuretics and β-blockers) amongst others (refer to Table II).[25,26] The β-blockers have distinct variations within the class, with metoprolol and carvedilol being associated with higher rates of ED, atenolol and bisoprolol with intermediate rates, and nebivolol with the lowest rate of ED.[27] Patients treated with a β-blocker also seem to have a lower number of sexual encounters per month when compared to placebo.[27]

Systemic diseases and general ill health involved in ED include a sedentary lifestyle (i.e. the absence of any physical activity for at least 30 minutes twice a week), smoking, hypertension, metabolic syndrome, other heart diseases (e.g. angina, heart failure, etc.), and dyslipidaemia amongst other conditions.[28]

Ageing has, however, been identified as the primary risk factor for ED. As life expectancy increases, morbidity and disability increase as well. In the ageing male testosterone, dehydroepiandrosterone (DHEA) may decrease together with increased levels of follicle-stimulating hormone (FSH) and luteinising hormone (LH). Even if the testosterone levels are normal the availability to tissues (i.e. the free testosterone levels) may be decreased.[29] In older males, the main areas of sexual dysfunction that are subsequently affected are a lack of sexual desire (or libido) and erectile problems.

Table II: Drugs and other substances involved in erectile dysfunction – a checklist for the pharmacist

Drug involved	Check ✓
Psychotropic drugs	
Tricyclic antidepressants, e.g. amitriptyline, imipramine, clomipramine, dosulepin, lofepramine and trimipramine	☐
Selective serotonin-reuptake inhibitors, e.g. citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine and sertraline	☐
Phenothiazines, e.g. chlorpromazine, trifluoperazine, fluphenazine and prochlorperazine	☐
Butyrophenones, e.g. haloperidol and droperidol	☐
Antihypertensives	
Thiazide diuretics, e.g. hydrochlorothiazide	☐
β-blockers, e.g. metoprolol, carvedilol, etc.	☐
Antiarrhythmics	
Digoxin	☐
Amiodarone	☐
Disopyramide	☐
Antiandrogens	
Gonadotropin-releasing hormone agonists (leuprolide, goserelin and zoladex)	☐
Oncochemotherapy (cyclophosphamide and busulfan)	☐
Flutamide, bicalutamide, cyproterone	☐
Ketoconazole	☐
Spironolactone	☐
Cimetidine	☐
Recreational substances	
Marijuana	☐
Opiates	☐
Cocaine	☐
Nicotine	☐
Alcohol	☐

Diagnosis

The diagnosis of ED (also refer to Figure 3) is based on a thorough assessment, which begins with a basic work-up to identify both modifiable and non-modifiable risk factors associated with the patient's sexual dysfunction.[30,31]

The assessment also involves questioning on the extent of the ED, which may include a question like: *Do you have erection problems (hard enough) during sex?* These questions may provide a positive diagnosis (for more sample questions refer to the International Index of Erectile Function).[32]

Upon confirmation of ED as a diagnosis, the ED can be characterised as either being a primary condition, or existing as a result of another sexual disorder; whether it has always been present or does it vary according to the situation. Assessing if the patient still has spontaneous nocturnal and/or morning erections, and/or in reaction to specific situations (i.e. whether there are good quality spontaneous erections) will rule out physiological causes and indicate that the primary cause of the ED could be psychological in origin.[31]

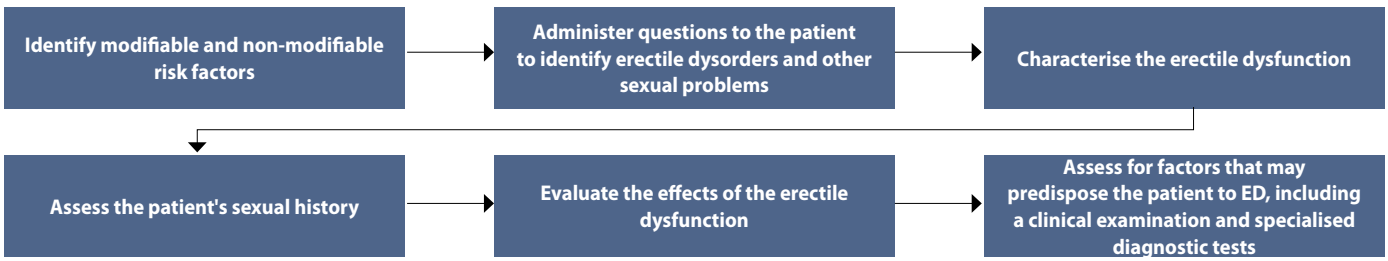

Figure 3: Diagnostic investigations into erectile dysfunction[30,31]

The sexual history should also be assessed, taking into consideration the patient's age, sexual orientation, marital status and previous sexual experiences. The diagnosis should be confirmed with a physical examination to assess the genitourinary anatomy as well as the endocrine, vascular and neurological systems. The physical assessment might also include a more comprehensive cardiovascular examination to measure the heart rate, blood pressure and abdominal circumference.[30]

Laboratory assessment is recommended but not always necessary and may include the following diagnostic tests, based on the patient's medical history as well as the physician's assessment:[30]

- Fasting glucose
- Lipid profile
- Hormone levels, e.g. testosterone, thyroid function, prolactin and luteinising hormone.

Some patients might need further specialised diagnostic tests such as nocturnal penile tumescence and rigidity (NPTR) studies, intracavernous injection test (using a vasoactive agent). This may provide some information on the vascular status of the male and a dynamic duplex ultrasound penile blood flow evaluation.[30] Other tests might include a dynamic infusion cavernosometry/cavernosography for assessment of venous leakage and an internal pudendal arteriography, with this being the most invasive diagnostic test for vasculogenic ED.[30,31] Most of the patients presenting with ED may only need a basic diagnostic work-up, and only in selected cases will more invasive diagnostic procedures be called for.

Management of erectile dysfunction

The effective interplay between four vital factors determines whether a man can achieve and maintain a satisfactory erection for sexual intercourse (see Figure 4). Anatomically the penis is made up of three tube-like structures, namely the ventral *corpus spongiosum* (which surrounds the male urethra and culminates in the glans or tip of the penis), and two dorsal corpora cavernosa. For an erection to occur, the corpora need to become engorged with blood; this necessitates sufficient arterial blood supply to the erectile tissue with a simultaneous occlusion of venous drainage from the corpora.

In terms of nervous system function, the central nervous system (CNS) integrates external sexual stimuli in the medial preoptic area

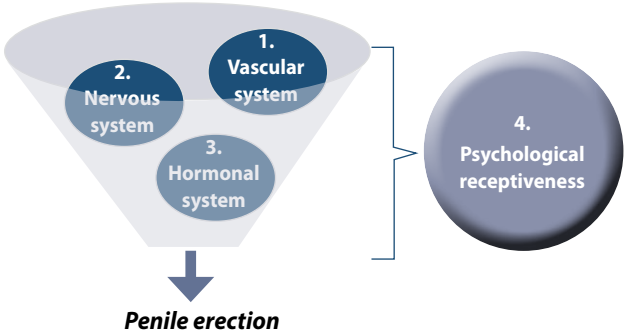

Figure 4: Vital factors that determine normal erectile functioning[32]

of the hypothalamus, where dopamine acts as a proerectogenic neurotransmitter, and is opposed by alpha-2 adrenergic stimulation that results in penile flaccidity.[32]

The autonomic nervous system also plays a vital role in normal erectile functioning, with the parasympathetic nervous system being responsible for achieving the erection via the actions of acetylcholine and the second messengers, cyclic guanosine monophosphate (cGMP) and cyclic adenosine monophosphate (cAMP).[33] Conversely, the erect penis will return to a flaccid state through the actions of noradrenaline (i.e. sympathetic nervous system stimulation) via alpha-2 receptor stimulation, which results in both vascular smooth muscle contraction with a resultant decrease in arterial blood flow in to the corpora and contraction of the sinusoidal (erectile) tissue of the corpora. Some erections may also be the result of a sacral nerve reflex arc, such as the normal nocturnal erections that occur during the sleep cycle. Note that nitric oxide (NO), released from non-adrenergic, non-cholinergic (or NANC) nerves and endothelial cells, also plays a vital role in facilitating a normal penile erection.[32]

Normal testosterone levels are positively linked to normal sexual drive and desire (i.e. libido). ED may therefore develop as a secondary consequence of hypogonadism, which causes decreased testosterone levels. Organic ED results from abnormalities in the vascular, hormonal or nervous system. On the other hand, a lack of psychological receptiveness to sexual stimulation will be classified as psychogenic ED. On average only one in five men with ED suffers from the latter form, with the vast majority of patients having organic causes.[32]

The main aim of ED treatment is to restore and maintain an adequate penile erection for sexual intercourse.[34] As previously mentioned, normal penile erection is a neurovascular phenomenon controlled by psychological factors and coordinated by the endocrine, vascular, and nervous systems.[35] The management of ED involves lifestyle modification such as losing weight, reducing alcohol intake, and avoiding smoking to reduce the impact of comorbid vascular risk factors, and treatment of organic or psychosexual dysfunction with either pharmacotherapy alone or in combination with psychosexual therapy.[36,37] However, pharmacotherapy is perceived as more effective and cost-efficient than the psychosexual therapy.[22] Thus, this review will mainly focus on pharmacotherapy. The pharmacotherapy of ED is classified into two categories i.e. those acting at the local level, and those acting at the central level.[34]

Those acting at the local level mainly aim to either facilitate the relaxation or to reduce the contraction of cavernous smooth muscles.[34] However, those acting at the central level mainly aim to either increase the activities of neurotransmitters/neuropeptides that facilitate penile erection, or to reduce the activity of those that inhibit sexual response.[34] The current pharmacotherapy of ED mainly includes oral phosphodiesterase 5 inhibitor (PDE5I), intracavernosal injection, hormonal replacement therapy, vacuum erection device, penile prosthesis, low-intensity extracorporeal

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shock wave (Li-ESW), and stem cell injection therapy.[36]

Phosphodiesterase 5 inhibitors

PDE5Is are regarded as the first-line treatment of ED. Currently, there are seven PDE5Is, i.e. avanafil, lodenafil, mirodenafil, sildenafil, tadalafil, udenafil, and vardenafil with different dosages and formulations.[38] There are three PDE5Is currently available on the South African market, namely sildenafil, vardenafil and tadalafil. Note, however, that these drugs cannot bring about an erection, but rather require the presence of sexual stimulation. The choice of PDE5I is dependent upon the patient's needs and experience with the agent in question. They differ in terms of their onset and duration of action, as well as their adverse event profile, and therapy may be tailored to either meet an on-demand need, or alternatively, to be used daily (i.e. as a chronic treatment option, which could even result in a curative outcome in the presence of endothelial dysfunction).[39,40]

The most frequently-reported side effects are headache and facial flushing. These drugs act by inhibiting the phosphodiesterase isoenzyme (PDE5) that is responsible for the inactivation of cGMP in the cavernous smooth muscle of the penis.[41] It is well established that during sexual arousal, NO is released from the nerve terminals and endothelial cells in the corpus cavernosum.[42] The NO is known to convert guanylate cyclase to convert guanosine triphosphate (GTP) into cGMP, which induces the smooth muscle relaxation and increased blood flow to the penis. However, within the smooth muscle cells of the corpus cavernosum, there is an enzyme known as phosphodiesterase 5 that cleaves and degrades cGMP into 5'-GMP. The degradation of cGMP will result in the termination of signal transduction essential for the stimulation and maintenance of erection.[43,44] Thus, compounds that potentiate NO-cGMP cell signalling system via the inhibition of PDE5 activity have been developed. By inhibiting PDE5, the PDE5Is restore and maintain the erectile response to sexual stimuli by selectively preventing the degradation of cGMP in the corpus cavernosum.[43] When considering a suitable treatment approach, a distinction will be made between organic and psychogenic ED, since the latter requires psychosexual therapy, whereas the organic causes are varied, but would need targeted therapeutic approaches that may combine both non-pharmacological and pharmacological treatment options. The non-pharmacological options include surgery in selected cases (a penile revascularisation procedure could, for example, benefit a younger patient who suffers from a trauma-related vascular injury to the penile arterial blood supply), or the use of a VED, also referred to as a vacuum constrictive device (VCD). Lifestyle modification may also be of benefit to patients who have risk factors that include cigarette smoking, the consumption of alcohol, obesity and a sedentary lifestyle. The oral PDE5Is constitute the current first-line pharmacotherapeutic agents, followed by intracavernosal injections and transurethral therapy as the second-line options.

Intracavernosal injection

The option of directly injecting a vasodilator into the corpus cavernosum is considered to be a second-line treatment for ED.[45] Alprostadil, or prostaglandin E_1, is the only agent with a registered indication for ED in this setting. Patients and their partners, if preferred or required, need to be trained on the proper technique of injecting such agents into the penile shaft.[45] These injections facilitate penile erection, even in the absence of sexual arousal, and may also prove to be of obvious benefit to men with spinal cord injuries or those who had to undergo radical prostatectomies. The two most commonly-encountered adverse effects associated with intracavernosal injections are priapism and penile fibrosis. Both of these adverse effects may be avoided through the use of proper patient counselling and by closely monitoring the patient's progress and response to treatment.[46]

Hormonal replacement therapy

Testosterone-replacement therapy should only be used in cases where deficient levels of the hormone have been confirmed.[40]

Vacuum erection device

The non-pharmacological options include surgery in selected cases (a penile revascularisation procedure could, for example, benefit a younger patient who suffers from a trauma-related vascular injury to the penile arterial blood supply), or the use of a VED also referred to a VCD.[47]

Penile prosthesis

Surgical implantation of penile prosthetic devices may also be an option, especially in men for whom pharmacotherapy has failed. Penile prostheses are regarded as third-line treatment options for ED. These prostheses may be either semi-rigid or inflatable.[48]

Low-intensity extracorporeal shock wave

Although the oral therapy with PDE5Is has been used as the first-line treatment for erectile dysfunction, some patients respond poorly to these medications. As a result, alternative non-surgical treatments, such as low-intensity extracorporeal shockwave therapy (Li-ESWT), have been explored.[49] Li-ESWT is non-invasive and uses acoustic waves, which can pass through tissue and be focused to target specific areas or organs to induce the desired effects. The major potential advantage of this therapy is the possibility to restore natural erectile function improving sexual life of affected individuals.[49,50]

Stem cell injection therapy

Stem cell therapy (SCT) is being explored as a potentially alternative approach for patients with ED who are unresponsive to PDE5Is.[51] It involves the use of stem cells to regenerate damaged or diseased tissues in the penis, with the goal of restoring erectile function. SCT is believed to work through several different pathways, including neovascularisation, anti-inflammatory effects, tissue regeneration, and neuroprotection.[51,52] The current evidence supporting the use of SCT for ED is primarily based on preclinical studies and small, uncontrolled clinical trials (Level 3–4 evidence).[51,52] There is also

considerable variability in the types of stem cells used, delivery methods, and outcome measures, which makes it difficult to draw definitive conclusions. While SCT has demonstrated some benefits in improving erectile function in some studies, further studies are needed to provide valuable insights into the optimal use of SCT and its potential as a therapeutic option for ED.[51,52] The combination of different regenerative treatments, like SCT with low-intensity shockwave therapy or platelet-rich plasma (PRP), may offer more effective solutions for ED.[51] For instance, a study has shown that combining low-intensity shockwave therapy with PRP injections not only improved erectile function but also prolonged the time to ejaculation. These combination approaches are promising and deserve further research.[54]

Psychological interventions and the importance of counselling

Psychological interventions can enhance treatment adherence, integrate the treatment into sexual relationship, and address psychological factors such as anxiety, negative thought patterns, emotional distress, low self-confidence, intimacy issues, and communication difficulties between partners.[22] Through cognitive-behavioural techniques, individuals learn to address performance anxiety, challenge negative beliefs, and enhance communication skills within a relational context.[22] This approach not only improves sexual function but also fosters resilience against future episodes of ED by promoting healthier coping mechanisms and reducing psychological distress. Psychoeducation and counselling, medication interventions and behavioural strategies are common treatment approaches. There are specific assessment and treatment guidelines for ED in men.

The impact of COVID-19 on erectile dysfunction

In 2020, the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spread worldwide at an unprecedented pace.[55] Although research on the link between COVID-19 and ED is still insufficient, there has been increasing evidence of this association over the past two years.[55] A study identified the presence of SARS-CoV-2 in the vascular endothelial cells of the penis, which are essential for erectile function, in post-COVID-19.[55] Additionally, there was reduction in nitric oxide synthase (NOS) expression which was noted in the corpus cavernosum, which is likely a consequence of endothelial dysfunction.[56] Another factor that influenced overall sexual health, and consequently ED may be the fear of COVID-19 infection, particularly concerns about virus transmission during sexual activity.[58] Some studies suggested that stress, anxiety, and depression were the primary psychological factors which were investigated during COVID-19, and they may have contributed to the development of sexual dysfunction.[55,57,59]

Conclusion

ED is a multi-faceted condition that may involve any one (or more) of several different organic causes. These may belong to the vascular, hormonal or nervous system, or a combination of more than one of them. Conversely, psychogenic ED is the result of psychological factors that reduce an individual's sexual responsiveness and desire. Pharmacotherapy may prove to be highly effective in the management of organic ED, with the oral PDE5Is being the current first-line treatment options of choice. The pharmacist could play a significant role in health promotion within the ED setting, through counselling, the identification of modifiable risk factors including drug-induced ED and drug interactions as well as through health education on the proper use of the various treatment options.

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Overview and management of colds and flu

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Abstract

In South Africa deaths related to colds and flu are at least three times higher when compared to the USA. The burden of HIV and tuberculosis in our country heightens the risk of severe flu-related illness. The common cold and flu are caused by very different viruses that share very similar symptoms. The common cold is a self-limiting upper respiratory tract viral infection and it is caused by the rhinovirus, coronavirus or the adenovirus. It usually resolves within 7–10 days. Flu is caused by the influenza virus and usually presents with headaches, myalgia, fever and body aches. There is no place for antibiotic usage in colds and flu management, and there is no clinical evidence which suggests that using antibiotics alters the course of the disease or prevents secondary infection. Treatment is mainly symptomatic and includes many over-the counter-medicines, specific antiviral agents and herbal treatment.

Keywords: colds, flu, rhinovirus, coronavirus, adenovirus, influenza, upper respiratory tract infections, herbal medicine, antivirals, over-the-counter medicine

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Introduction

The common cold is a self-limiting upper respiratory tract infection which is caused by the rhinovirus, coronavirus or the adenovirus.[1] Symptoms like sneezing, nasal congestion, coughing, sore throat and a low-grade fever are often experienced during the late autumn and winter season, from about early-May to August in South Africa.[2] A person may be contagious after being infected with the virus.[3] The viruses in question are airborne and spread quickly via hand-to-hand contact, or via the inhalation of airborne droplets from sneezing and coughing (also refer to Figure 1 below).[1]

After the virus enters the nasal cavity it damages the ciliated cells resulting in the release of inflammatory mediators and causing inflammation of the nasal tissue lining.[1] The increase in permeability of the capillary cell walls results in oedema. Oedema is responsible for symptoms like sneezing and nasal congestion.[1,3] A postnasal drip may develop, which leads to a sore throat and coughing, which in turn is responsible for the spread of the virus.[1]

Common colds are self-limiting and resolve within seven to ten days without the use of antibiotics. However, some people may end up developing a secondary bacterial infection.[2]

The common cold is often confused with influenza (flu). However, flu is a viral illness caused by a different virus, the influenza virus. It has a high mortality and hospitalisation rate.[4] Influenza can occur all year round but is seen more often from May through winter. Due to the constant evolution of the influenza strains there is a higher fatality rate associated with the virus than with the viruses causing the common cold.[1] This epidemiological pattern reflects the changing nature of the antigenic properties of flu viruses and their subsequent spread, which depends upon multiple factors, including transmissibility of the virus and the susceptibility of the population.[1]

The influenza virus is transmitted via air droplets when a person comes into close contact with an infected person or via self-infection when a person comes into direct contact with an infected person or object.[5]

A rapid onset of fever, headaches, myalgia, body aches and pains, sore throat and rhinitis (runny nose) are associated with flu. These

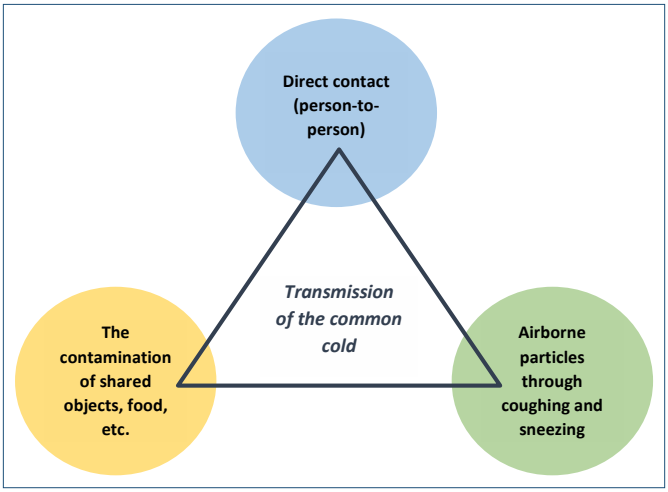

Figure 1. Transmission of viruses that cause colds[2]

Table I. Types of influenza strains and their differences[1]

Virus strain	Influenza A	Influenza B
Who can become infected	Animals and humans	Humans
Severity of infection	Causes pandemics, like swine flu and bird flu	Less severe than influenza A

symptoms generally last for four to five days and then disappear, however a person may experience coughing and malaise for more than 14 days.[1,2] Influenza-like illness (ILI) is an acute respiratory infection that presents with a fever greater than 38˚C, with coughing or pharyngitis. The diagnosis of ILI is rarely based on the patient's clinical picture. Laboratory diagnosis usually includes[6]:

- Virus isolation in cell culture
- A polymerase chain reaction (PCR) test
- Antigen detection

Management of colds and flu

Pharmacotherapy is directed at alleviating associated symptoms. Antibiotics are often prescribed erroneously, and in the absence of a secondary bacterial infection. Antibiotics should only be administered when a bacterial infection has been identified, and should not be used as a preventative measure. The following measures can be used to either prevent or treat the symptoms of a cold and flu (each of these recommendations will be discussed separately)[1,5]:

- A flu vaccine is recommended by, amongst others, the Centers for Disease Control and Prevention (CDC) in the United States of America, as a preventative measure against the acquisition of the influenza virus.
- Selected over-the-counter (OTC) products contain a combination of active ingredients which help with symptomatic relief.
- Drinking plenty of fluids, especially water: Water has been shown to be the best fluid with which to hydrate and lubricate the mucous membranes.
- Vitamins and minerals, e.g. vitamin C and zinc sulphate.
- Antiviral drugs, e.g. neuraminidase inhibitors (zanamivir and oseltamivir), as well as N-methyl D-aspartate receptor antagonists (amantadine and rimantadine).
- Others, such as orally-inhaled anticholinergics, inhaled corticosteroids, herbal solutions and nonsteroidal anti-inflammatory drugs (NSAIDs).

Vitamins and minerals

The prophylactic use of vitamin C has been shown to reduce the risk of developing a cold or flu in certain populations, e.g. athletes, with a reduction of approximately 6% in the disease duration. However, the evidence that supports the use of vitamin C in high dosages to reduce the severity of a cold or flu is lacking and inconclusive.

Zinc may inhibit viral growth, and could possibly reduce the duration of cold symptoms. However, not enough high-quality trials support the routine and high-dosage use of zinc in preventing colds or flu. Some reports have been lodged with the US Food and Drug Administration (FDA) that nasal preparations containing zinc may cause loss of smell. Zinc may also reduce the absorption of certain antibiotics. Food containing calcium and phosphorus can impair the absorption of zinc.[7]

Importance of hydration

Fluid (especially water) helps to lubricate the mucous membranes (and decreases sputum viscosity) of patients suffering from a cold or influenza. However, some literature contradicts this by suggesting that the provision of extra fluid to patients with acute respiratory conditions may cause hyponatraemia and fluid overload, because of the actions of antidiuretic hormone. This hormone is released in adults and children with lower respiratory tract infections and causes water reabsorption from the renal collecting duct. The combination of the increased production of the antidiuretic hormone and extra fluid may lead to fluid overload. Research has not clearly illustrated this in upper respiratory infections yet and water hydration still remains of importance in the treatment of colds and flu.[1,8,9]

Other strategies used to treat colds and flu

Anticholinergic agents, such as inhaled ipratropium bromide, may be used to treat a cough caused by a cold. Nasal preparations have shown some efficacy in reducing rhinorrhoea and sneezing. Inhaled corticosteroids can be used to reduce the swelling and inflammation of the nasal mucosa, but have not been shown to provide any benefit in patients diagnosed with a cold.[1]

Conflicting evidence has emerged about the use of nasal irrigation. Nasal irrigation constitutes a mechanical intervention. It is not classified as a decongestant and does not improve ciliary function. Studies have shown that nasal preparations that contain a certain preservative, namely benzalkonium chloride, may worsen symptoms and infections. Nasal washes that contain a lot of fluid and minimal salt can be used to remove mucus from the nose, removing bacterial products, and improving sinonasal function. Nasal irrigation can be used prior to the administration of topical therapies to ensure true sinus distribution.[1,10]

There are several different OTC medications that can be used to alleviate pain and fever associated with colds and flu. The typical active ingredients are aspirin, paracetamol and caffeine. Aspirin, however, is contraindicated in children who have a viral infection as they are at risk of developing Reye's syndrome.[1,2]

Herbal products and supplements include substances like echinacea, Chinese herbal cold and allergy products, elderberry extracts, *Andrographis paniculata*, *Pelargonium sidoides* and *Acanthopanax senticosus*.[1,11] Refer to Table II for more information.

Flu, or the influenza vaccine

The influenza vaccine is developed each year to protect you against the most common strains of flu. Flu vaccines provoke an immune response to the antigen found on the surfaces of the viruses. Antigenic drift can occur in the viruses, causing resistance to the vaccine.[12] It is for this reason that recommendations are based on the World Health Organization's (WHO) accredited regional laboratories, and changes are made to the composition, in terms of strains of influenza every year.[13,14] This antigenic drift is the reason why the vaccine that is released in September every

Table II. Herbal products and supplements[1,11]

Herbal product	Evidence supporting the use of the medicine	Adverse effects
Echinacea	No evidence supports the use of this product in the treatment of colds and flu.	People who are allergic to Echinacea develop erythema nodosum, which features tender, red nodules under the skin.
Chinese herbal cold and allergy products	No evidence supports the use of this product in colds and flu.	These products also pose the risk of renal damage and cancer as they contain aristolochic acid.
Elderberry extracts	Some evidence supports the use of these extracts in shortening the duration of flu symptoms. *However this has yet to be confirmed by bigger studies.*	These extracts are unsafe when the leaves, stems, unripe fruit or uncooked fruit is consumed.
Pelargonium sidoides (commonly known as African geranium) and *Acanthopanax senticosus*	Literature has confirmed a reduction in the duration of 10 different flu symptoms.	There are isolated reports of liver toxicity; however, no causative relationship has been linked to the herb itself.

Table III. List of individuals who would require the flu vaccine as a matter of priority[1]

Individuals that require the vaccine as a matter of priority	✓
Pregnant women, and women who are planning to fall pregnant during winter	
Patients younger than 18 years of age on chronic aspirin therapy	
HIV-infected patients (CD4 cell count > 100 cells/uL)	
Patients who suffer from any other disease which leaves them immune-compromised	
People who suffer from an underlying medical condition, e.g. diabetes mellitus, COPD, heart disease	
People older than 65 years of age, or infants between 6–49 months of age	
People staying in old age homes, frail care facilities and rehabilitation centres	
Healthcare workers who have direct contact with patients on a daily basis	
Patients who are on glucocorticosteroid therapy for long periods of time	

year in the northern hemisphere is not always exactly the same as that released in February in the southern hemisphere.

Antibodies usually develop within two weeks of the vaccine being administered. A peak in immunity occurs four to six weeks after vaccination, which then gradually wanes again. It therefore does not convey lasting immunity against the influenza virus. Immunisation reduces the likelihood of flu developing in healthy adults by approximately 70–90%.[14] If a family member or house mate has already developed flu, vaccination of other members of the household, within 36–48 hours, will still provide effective protection against the virus.[14]

Some individuals require the flu vaccine as a matter of priority; these involve pregnant women, immune-compromised individuals and others (refer to Table III).

In the southern hemisphere, it is recommended that the vaccine be given in April; however, it can be given throughout the winter season. Figure 2 depicts the adverse effects that are associated with the flu vaccine.[1]

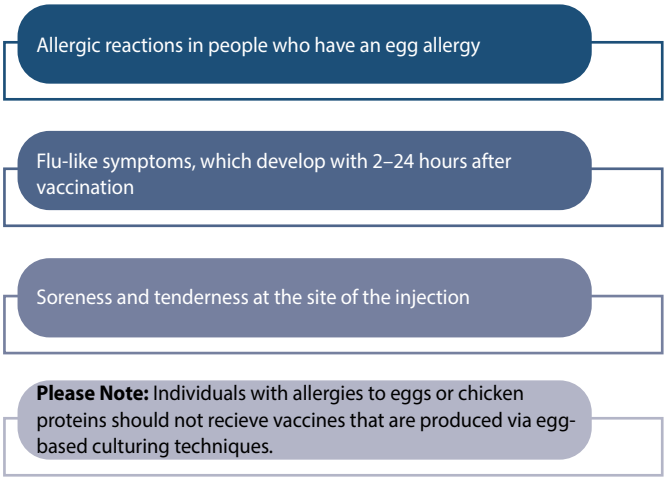

Figure 2. Adverse effects of flu vaccines[12-14]

Combination products used for colds and flu

Treatment is mainly symptomatic and includes many OTC medicines, antivirals and herbal treatment.

Antitussive agents (cough suppressants)

Antitussive agents should only be given for a non-productive, dry, irritating cough (refer to Table IV). Care should be taken when giving antitussive agents as the coughing mechanism serves as a protective function of the body. Coughing clears the throat and the lower respiratory tract of foreign particles and mucus. Coughing that occurs as a result of bronchoconstriction and bronchospasm (coughing in asthma and COPD patients) should be treated with bronchodilators. Coughing that is caused by a lower respiratory tract infection should be managed with appropriate antimicrobial agents.

Antihistamines

Antihistamines play a role in relieving coughs and are often included in cold medications to aid sleep. While they offer limited benefits when used alone for cold and flu symptoms, combining them with decongestants and cough suppressants

Table IV. Over-the-counter medicine for the treatment of colds and flu[1,13]

Preparation	Active ingredient	Indication
Topical decongestants		
Iliadin®	Oxymetazoline HCl (0.100 mg/ml)	Short-term symptomatic relief of nasal congestion
DriNasal® Paediatric	Oxymetazoline HCl (0.25 mg/ml)	Short-term symptomatic relief of nasal congestion
Oxymist®	Oxymetazoline HCl (0.2/0.5 mg/ml)	Short-term symptomatic relief of nasal congestion
Nazene® Adult Nasal Metered Spray	Oxymetazoline HCl (0.5 mg/ml)	Short-term symptomatic relief of nasal congestion
Otrivin®	Xylometazoline HCl (1 mg/ml)	Short-term symptomatic relief of nasal congestion
Sinutab® Nasal Spray	Xylometazoline HCl (1 mg/ml)	Short-term symptomatic relief of nasal congestion
Vibrocil-S®	Phenylephrine and dimethindene (250 mg/100 g)	Short-term symptomatic relief of nasal congestion
Topical corticosteroids		
Beclate Aquanase®	Beclomethasone dipropionate (50 µg/spray)	Maintenance therapy for allergic rhinitis
Beconase®	Beclomethasone dipropionate (50 µg/spray)	Maintenance therapy for allergic rhinitis
Clenil® Aq Nasal Spray	Beclomethasone dipropionate (50 µg/spray)	Maintenance therapy for allergic rhinitis
Flixonase®	Fluticasone propionate (50 µg/spray)	Maintenance therapy for allergic rhinitis
Flomist®	Fluticasone propionate (50 µg/spray)	Maintenance therapy for allergic rhinitis
Flonase®	Fluticasone propionate (50 µg/spray)	Maintenance therapy for allergic rhinitis
Nexomist®	Mometasone furoate (50 µg)	Maintenance therapy for allergic rhinitis
Nasonex®	Mometasone furoate (50 µg)	Maintenance therapy for allergic rhinitis
Rinelon®	Mometasone furoate (50 µg)	Maintenance therapy for allergic rhinitis
Topical antihistamines/anti-allergic agents		
Rhinolast®	Azelastine HCl (0.14 mg/spray)	Short-term intermittent allergic rhinitis
Sinumax Allergy Nasal Spray®	Levocabastine (0.5 mg/ml)	Short-term intermittent allergic rhinits
Systemic nasal decongestants with antihistamines		
Actifed®	Pseudoephedrine HCl (30 mg) Triprolidine HCl (1.25 mg)	Systemic decongestion of nasal mucosa and sinuses associated with colds and flu
Betafed Be-Tabs®	Pseudoephedrine HCl (30 mg) Triprolidine HCl (1.25 mg)	Systemic decongestion of nasal mucosa and sinuses associated with colds and flu
Demazin Syrup®	Phenylephrine HCl (2.5 mg/5 ml) Chlorpheniramine mal (1.25 mg/5 ml)	Systemic decongestion of nasal mucosa and sinuses associated with colds and flu
Demazin ND®	Pseudoephedrine sulphate (120 mg) Loratadine (5 mg)	Systemic decongestion of nasal mucosa and sinuses associated with colds and flu
Systemic decongestant and/or analgesic and/or antihistamine combinations		
Benylin® 4 flu Liquid	Pseudoephedrine HCl (45 mg) Ibuprofen (200 mg)	Symptomatic relief of colds and flu
Benylin® 4 flu Tabs	Diphenhydramine HCl (12,5 mg) Paracet (500 mg) Pseudoephedrine HCl (22.5 mg)	Symptomatic relief of colds and flu
Benylin® Original	Diphenhydramine HCl (12.5 mg), Ammonium Chloride (125 mg)	Symptomatic relief of colds and flu
Benylin® Paediatric	Diphenhydramine (15 mg)	Symptomatic relief of colds and flu
Benylin® Daytime Flu Tablets	Ibuprofen (200 mg), Pseudoephedrine HCl (30 mg)	Symptomatic relief of colds and flu
Benylin® Codeine	Codeine, diphenhydramine HCl (12.5 mg), ammonium chloride (125 mg)	Symptomatic relief of colds and flu
Nurofen® Cold and Flu	Ibuprofen (200 mg) Pseudoephedrine HCl (30 mg)	Symptomatic relief of colds and flu
Sinuclear®	Paracetamol (325 mg) Phenylpropanolamine HCl (18 mg)	Symptomatic relief of colds and flu
Sinugesic®	Paracetamol (500 mg) Pseudoephedrine HCl (30 mg)	Symptomatic relief of colds and flu
Sudafed® Sinus Pain	Paracetamol (500 mg) Pseudoephedrine HCl (60 mg)	Symptomatic relief of colds and flu
Cough preparations		
Mucolytics		
Pholtex Mucus 200®	N-Acetylcysteine	To reduce viscosity of secretions
Solmucol®		
Mucatak®		
Amuco 200®		
ACC 200®		

Preparation	Active ingredient	Indication
Betaphlem®	Carbocisteine	To reduce viscosity of secretions
Bronchette®		
Lessmusec®		
Mucospect®		
Bisolvon®	Bromhexine HCl	To reduce viscosity of secretions
Expectorants		
Benylin Wet Cough Mucus Relief®	Guaifenesin	Cough alleviation
Cough suppressants		
Benylin® Codeine	Codeine, diphenhydramine HCl (12.5 mg), ammonium chloride (125 mg)	Symptomatic relief of a non-productive cough
Benylin® Dry Cough	Dextromethorphan hydrobromide	
Dilinct® Dry Cough		

enhances their effectiveness. In 2006, the FDA cautioned against using promethazine in children under two due to risks of fatal respiratory depression.[15] First-generation antihistamines like chlorpheniramine, brompheniramine, and promethazine help alleviate cold symptoms such as rhinitis and sneezing through their anticholinergic properties.

Histamine is a key mediator in allergic rhinitis and chronic urticaria, making H(1)-receptor antagonists crucial in treating these conditions. However, other mediators are also involved in the inflammatory process, suggesting that drugs targeting a broader range of inflammation could provide better relief. The Allergic Rhinitis and its Impact on Asthma (ARIA) initiative emphasises the importance of identifying ideal antihistamine properties.[5]

Rupatadine is notable for its dual action as a histamine H(1)- and PAF-receptor inhibitor. It has proven effective and well-tolerated in treating allergic rhinitis and chronic idiopathic urticaria. Rupatadine offers quick relief and can be administered once daily due to its prolonged activity. Clinical trials have shown it to be comparable to loratadine, cetirizine, desloratadine, and ebastine in reducing symptoms of seasonal, perennial, or persistent allergic rhinitis. Notably, rupatadine did not exhibit adverse cardiovascular effects or impair cognitive and psychomotor functions in extensive testing. It also improved patient well-being based on quality of life assessments. Overall, rupatadine is a valuable treatment option for allergic rhinitis and chronic urticaria, offering a comprehensive anti-inflammatory profile by targeting multiple inflammatory pathways. [16]

Expectorants and mucolytic agents

Expectorants and mucolytic drugs are used to alter the viscosity of mucous and bronchial secretions, thereby making it easier to cough up sputum.[1,16] There are two ways of achieving this through pharmacological action:

- By using expectorants to increase the volume of bronchial secretions and reduce the viscosity of these secretions. Guaifenesin, sodium citrate and ammonium chloride are examples of expectorants. For obvious reasons, the use of cough mixtures containing an expectorant, as well as an antitussive agent, or combined with an antihistamine, should rather be avoided.
- By using mucolytic agents which act by altering the structure of mucus, thus resulting in a low mucus viscosity. Examples are: carbocisteine, bromhexine and N-acetylcysteine. Dornase alfa (recombinant human DNase) is used in patients with cystic fibrosis.

Non-pharmacological methods, like maintaining a good fluid hydration status and inhaling steam, can also reduce the viscosity of mucous secretions.

Oral decongestants

Oral sympathomimetic, systemic decongestants, like pseudoephedrine phenylpropanolamine and phenylephrine are now mainly available in combination in South Africa.[5] Oral decongestants should only be used for a short period of time and as symptomatic relief for acute coryza, as part of colds and influenza. Topical agents are preferred as they have reduced systemic side effects.[1] Clear warnings should be given to patients about the use of oral decongestants with alcohol or certain drugs such as sedatives.[13,17]

Nasal decongestants

Nasal congestion, a result of vasodilation and oedema of the nasal mucosa, can be alleviated using alpha-1 adrenergic agonists topically (nasal sprays), or orally. These topical decongestants are actually vasoconstrictors and, compared to a placebo, have shown a reduction in airway resistance.[1,5,13,17]

Antiviral agents

Table V. Important differences between zanamivir and oseltamivir[1,18]

Zanamivir	Oseltamivir
Administered through an inhaler.	Available as a suspension and a capsule. It has minor side effects like nausea and vomiting.
May provide a challenge to older patients and patients with a lung disorder.	Dosage adjustments in patients with renal impairment.

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Reference: 1. Eccles R, et al. Rationale for Treatment of Common Cold and Flu with Multi-Ingredient Combination. Open Journal of Respiratory Diseases. 2014 May 23; 4:73-82. S2 Benylin® Four Flu Liquid. Each 20 ml liquid contains: Diphenhydramine Hydrochloride 25 mg; Paracetamol 1 000 mg; Pseudoephedrine Hydrochloride 45 mg. Reg. No. 33/5.8/0345. S2 Benylin® Four Flu Tablets. Each tablet contains: Diphenhydramine Hydrochloride 12,5 mg; Paracetamol 500 mg; Pseudoephedrine Hydrochloride 22,5 mg. Reg. No. 33/5.8/0509. For full prescribing information, refer to the Professional Information approved by the medicines regulatory authority. Consumer Care Contact Centre: www.kenvuecontact.eu. ZA-BYL-2025-137203.

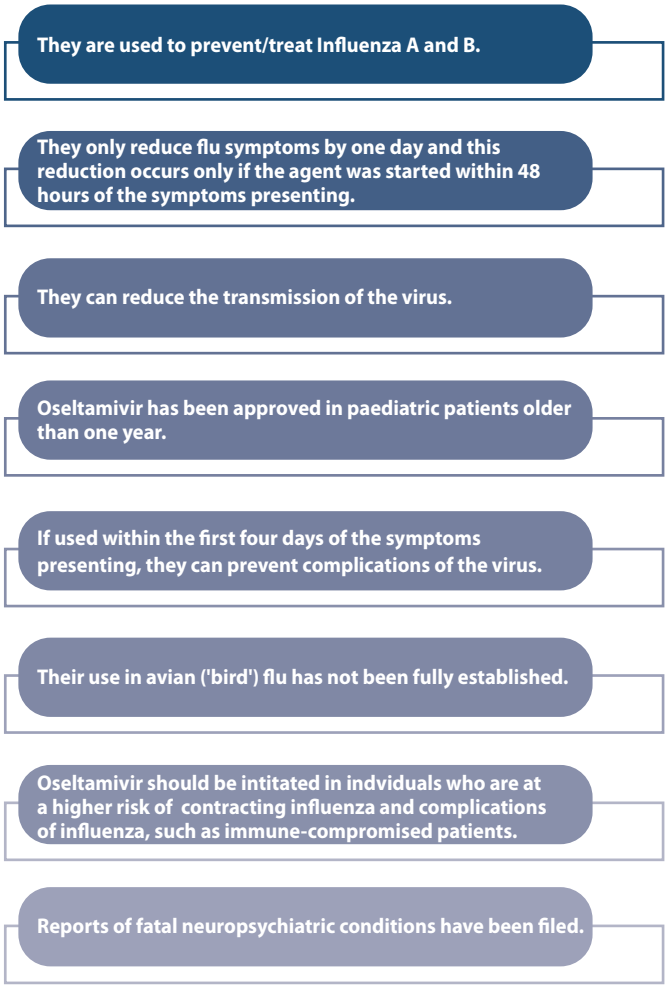

Figure 3. Important information regarding the use of oseltamivir and zanamivir[1,18]

Neuraminidase inhibitors

Two classes of antiviral therapy are available in South Africa: neuraminidase inhibitors and N-Methyl D-aspartate receptor antagonists. They play a major role in the treatment and prevention of both seasonal and avian influenza.[1,18] Zanamivir and oseltamivir are currently available. These drugs are registered for the prophylaxis of the influenza A and B virus, and should be used within the first 24 hours of the onset of the symptoms. These agents act by inhibiting the enzyme involved in viral replication, neuraminidase. Important information regarding the use of these agents is listed in Figure 3.[1,18] Table V denotes the important differences between oseltamivir and zanamivir.

N-methyl D-aspartate receptor antagonists

Amantadine is an antiviral drug that is commonly associated with the treatment of Parkinson's disease. It is, however, also used in the prevention and treatment of influenza A. Amantadine acts by increasing the amount of dopamine from the nigrostriatal pathway and inhibits the reuptake of dopamine by the neurons. Amantadine is currently not recommended for treatment or use as an antiviral agent as there is widespread resistance to the drug.[1,13,18]

If the drug is being used for minor sensitive influenza strains the following should be noted:

- Initiation of amantadine should occur within two days after contracting influenza A as it may reduce the duration of the disease.
- It cannot be used against influenza B.
- There is no literature which supports the drug preventing complications of influenza A.

At the end of World War II, influenza reappeared and prompted the WHO to coordinate a global network of research and surveillance from 1949. Subsequent pandemics, e.g. the so-called Asian flu in 1957, Hong Kong flu in 1968, and the 1976 swine flu scare in the USA, illustrated the role of natural reservoirs, e.g. pigs and wildfowl, as being instrumental in the introduction of new strains of influenza. Immunocompromising conditions such as HIV/AIDS and cancer highlighted the influenza pandemic; however, avian influenza and severe acute respiratory syndrome in the 1990s established new behavioural norms with influenza outbreaks: travel restrictions, mass slaughters of infected livestock, with intensive media interest, and worldwide anxiety. In the early 21st century, influenza remains a substantial cause of mortality.[19]

Conclusion

The global rise in antimicrobial resistance is a call for absolute restraint in the use of antimicrobials, which includes both patients and healthcare professionals. Antibiotics should never be used to treat the common cold or flu, unless there is a secondary bacterial infection. There is insufficient evidence in the literature to support the use of OTC products for the prevention of these viral infections; however, vitamin C and zinc can be used as prophylaxis. Receiving the influenza vaccine may reduce the risk of acquiring seasonal influenza. Treatment is symptomatic; however, the use of many of the OTC medicines is not supported by literature. Certain herbal remedies such as *P. sidoides* extract, *A. paniculata* and elderberry may be effective, although one should always read the safety profile of these remedies before use. Codeine and antihistamines may be used in combination therapies to treat coughs and other cold symptoms. Paracetamol and other NSAIDs may be used to manage pain and fever in adults. Antivirals, such as the neuraminidase inhibitors, can be used in the prevention and treatment of both influenza A and B.

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Air travel and the risk of venous thromboembolism

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Abstract

Passenger air travel is a convenient and frequently used mode of transportation across the globe. However, certain health risks are associated with commercial flights, many of which are inherent to this distinctive method of transportation. It has been shown that air travel innately carries an increased risk of the development of venous thromboembolism (VTE), and although small, this risk is significantly higher than in the general, healthy, non-flying population. Individual air travellers are strongly encouraged to consult a suitable healthcare professional for an individual risk assessment and guidance on suitable or required prophylactic measures prior to undertaking either frequent or long-distance travel via aeroplane.

Keywords: air travel, long-haul flight, DVT, pulmonary embolism, venous thromboembolism, VTE

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Introduction

Millions of passengers traverse the skies annually by making use of the benefits and convenience of domestic and international air travel. However, certain health risks are associated with commercial flights, many of which are inherent to this distinctive mode of transportation. These include medical issues such as hypobaric hypoxia, cosmic radiation exposure and jet lag.[1,2]

This article will focus on the life-altering and potentially life-threatening[1,2] risk of suffering an acute episode of venous thromboembolism (VTE), with particular regard to passenger air travel.

General considerations

It has been shown that a definite association exists between long-haul flights, especially when they are more than eight hours in duration, and VTE. Interestingly enough, the risk for business class travellers is similar to that of travellers in the economy class cabin. However, it is greater for passengers who occupy the non-aisle seats. This is because 75% of air travel-associated episodes of VTE have been linked to immobility during long-distance flights.[3-5]

The risk of VTE is increased with long-haul flights, especially those over eight hours, and is higher for passengers with pre-existing risk factors such as obesity, recent surgery, or genetic predispositions[3-5]

Conversely, the overall risk of developing air travel-related VTE remains very low, but it has still been shown to be significantly higher than that associated with the healthy, non-flying population. It can be said that an average long-haul flight of 12 hours in duration, with 400 passengers on board, will result in a 0.2% incidence rate of symptomatic VTE[3-5] (Figure 1).

Definition of venous thromboembolism

VTE refers to the combination of deep vein thrombosis (DVT) and pulmonary embolism (PE). The underlying pathophysiological process seems to involve venous stasis, with resultant coagulation and thrombus formation. Should a venous thrombus, or a portion of it, become dislodged from a vessel wall in the lower extremity, for example, the resultant embolus will travel through the venous blood circulation to reach the inferior vena cava, the right atrium and right ventricle, the pulmonary artery, and will ultimately become lodged in one of the smaller arteries of the lung, resulting in PE.[2,3]

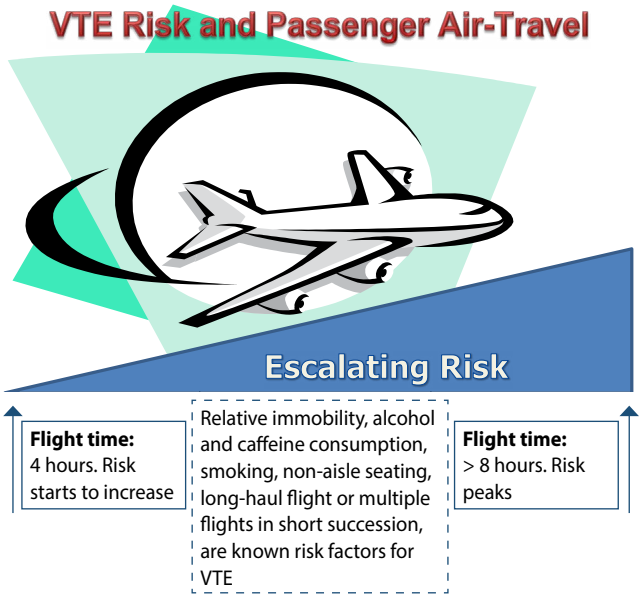

Figure 1: The risk of thromboembolism associated with passenger air travel[1-5]

VTE: venous thromboembolism

As the name implies, the deep veins of the lower extremities constitute the most common sites of DVT. There is a significant risk of acute PE secondary to such venous thrombi, i.e. approximately 50% in the case of DVT in the proximal lower extremity, and roughly 25% in the case of the distal lower extremities.[2-5] Severe PE may prove to be fatal. However, a DVT could develop in the upper extremity as well.

Risk factors for venous thromboembolism, including those that relate to air travel

Generally, the risk factors that are associated with VTE may be classified as either inherited (genetic) or acquired (environmental). The majority of VTE-associated events are linked to a combination of the two. It should also be noted that these risk factors have an additive effect on an individual's propensity for developing VTE.

Various genetic factors may predispose a person to a state of so-called hypercoagulability, and include the following:[3]

- Clotting factor V Leiden mutation, a prothrombin gene mutation (G20210A), or elevated levels of clotting factor VIII (the latter could also be an acquired condition)
- An inherited deficiency of protein C or S, or of antithrombin, a naturally-occurring "anticoagulant"
- Hyperhomocysteinemia

Of the list of acquired risk factors, the following are especially important in the community (i.e. including regular air travellers) setting:[2,3,4,5]

Age and gender-related risk factors

Age and gender-related risk factors include:

- Advancing age, from 40 years onwards
- Women's health-related risks, which include the use of oral contraceptives and hormone-replacement therapy, as well as hypercoagulability of pregnancy and the puerperium
- The male gender
- Frailty and immobility

Associated risk factors with medical illness

Associated risk factors with medical illness include:

- "Lifestyle diseases", such as hypertension, diabetes mellitus and dyslipidemia
- Strokes with paralysis or paresis, acute medical illness (including chronic obstructive pulmonary disease, congestive cardiac failure and pneumonia), antiphospholipid syndrome, nephrotic syndrome and inflammatory bowel disease
- Patients with cardiac pacemakers
- Ambulatory patients with indwelling central venous catheters
- Active cancer and certain cancer chemotherapeutic agents
- Varicose veins and prior episodes of VTE
- Conditions that result in venous insufficiency

Surgical risk factors

Surgical risk factors include:

- Recent trauma resulting in compression of the veins or immobilisation, including plaster cast immobilisation
- Major surgery, especially the larger orthopaedic procedures, such as hip and knee replacement surgery, and the surgical repair of hip fractures

Lifestyle-related risk factors

Lifestyle-related risk factors include:

- Smoking
- Obesity, especially when the body mass index exceeds 30 kg/m^2
- Conditions or circumstances that may result in prolonged immobility and venous stasis, such as long-distance travel, especially air travel, or being bedridden for more than three consecutive days

Additional risk factors for air travellers

Two major risk factors to consider are flight duration and the person's height. Long-haul flights carry a greater risk owing to increased periods of immobility, especially single long-haul flights that last 8-10 hours or more. However, multiple long-haul flights of at least four hours in duration, or frequent flights of any duration which occur in short succession of one another, also carry an increased risk for VTE. In terms of body height, persons who are at an increased risk are those who are shorter than 1.65 m, or taller than 1.85 m in height.[2]

Furthermore, risk factors such as prolonged immobility, which is especially associated with long-haul flights, and with passengers in the non-aisle seats in particular, together with dehydration (with a resultant increase in blood viscosity) and hypobaric hypoxia (due to the pressurised passenger cabin), all increase the risk of VTE associated with air travel in patients who already have one or more of the underlying risk factors for VTE prior to their flight.[1]

Venous thromboembolism prophylaxis for air travellers

VTE that is associated with passenger air travel is an emerging public health concern, but there still seems to be a lack of sufficient evidence in terms of both definite causality and effective prophylactic measures. Yet, a few basic principles, based on current knowledge in this field, may be proposed for the prevention of VTE during air travel, as illustrated in Figure 2.[1,2]

Current recommendations for prevention measures include frequent ambulation, calf muscle exercises, sitting in aisle seats when possible, and the use of compression stockings for those at high risk[4,5]

Anticoagulant prophylaxis

A specific subset of passengers who find themselves at a significantly higher risk of developing acute, air travel-related VTE will require pharmacological intervention in the form of

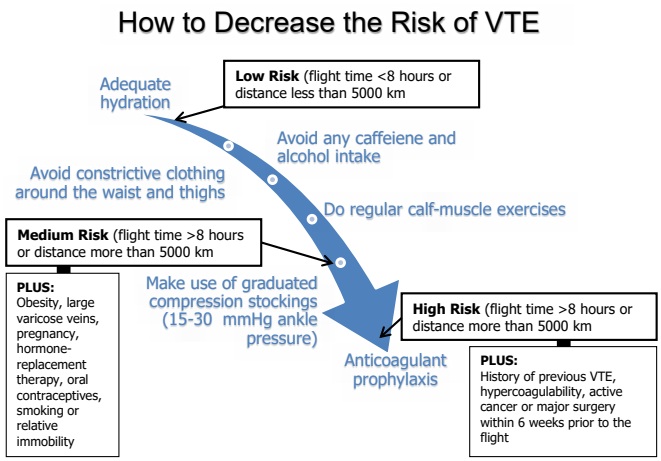

Figure 2: Measures to decrease the risk of air travel-related thromboembolism. Note that these measures are additive, relative to the degree of risk, and should be based on an individual risk assessment[1]

VTE: venous thromboembolism

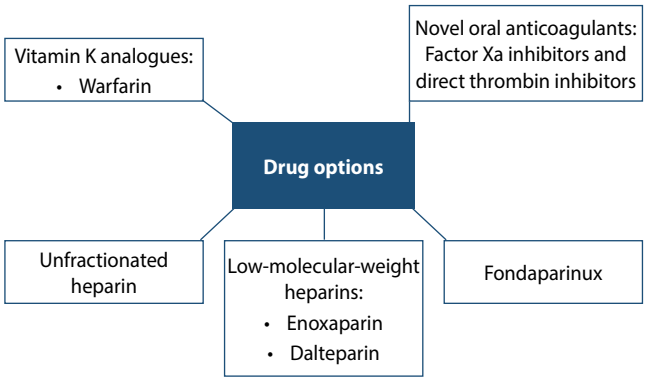

Figure 3: Possible venous thromboembolism prophylaxis drug options

anticoagulant prophylaxis. Figure 3 illustrates the various options that are currently available.

The drugs that are used to prevent VTE and emboli of cardiac origin, as seen in patients with atrial fibrillation for example, are heparin (unfractionated or standard heparin and the newer forms of heparin with low molecular weight, such as enoxaparin and dalteparin), factor Xa inhibitors, and warfarin, a vitamin K antagonist. Apixaban, a direct factor Xa inhibitor, has been extensively studied for its efficacy and safety in preventing VTE. In the context of air travel, while specific studies on apixaban are limited, its pharmacological profile suggests potential benefits. Apixaban has been shown to be effective in reducing the risk of VTE in various clinical settings, such as in patients with atrial fibrillation or those undergoing major orthopaedic surgery. Its oral administration and predictable pharmacokinetics make it a convenient option for travellers. However, its use specifically for air travel-related VTE prevention requires further investigation to establish clear guidelines.[6,7,8] Warfarin inhibits the hepatic synthesis of clotting factors that depend on vitamin K, namely factor II (prothrombin), VII, IX and X (as well as protein C and S). This drug is renowned for its long list of potential drug interactions and variations in individual responses to this drug may be substantial.

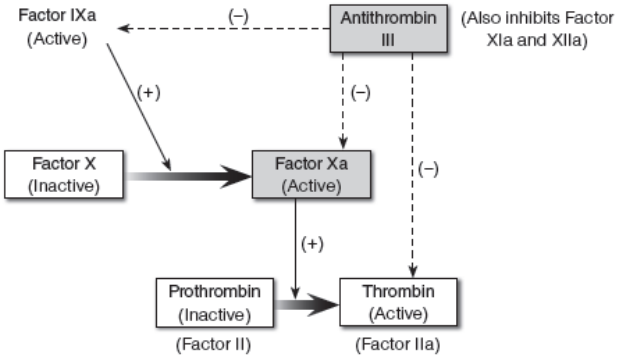

Figure 4: The relationship between factor Xa, thrombin and antithrombin III[5]

Careful monitoring and good compliance are essential for the success of anticoagulant therapy with warfarin.[3,5]

Low-molecular-weight heparins (LMWHs) are fractions of standard heparin and are becoming increasingly more popular than the unfractionated form. Heparin enhances the action of antithrombin III. The two clotting factors that are the most sensitive to the anticoagulant effects of unfractionated heparin (UFH) are factor IIa (thrombin) and Xa, while LMWHs favour factor Xa. Fondaparinux is a synthetic agent that specifically inhibits factor Xa, i.e. the activated form of clotting factor X. The heparins and fondaparinux are indirect thrombin-inhibitors (Figure 4).[3,5]

Patients who receive anticoagulants should be monitored for signs of spontaneous bleeding, including microscopic and macroscopic haematuria, bleeding gums and nosebleeds.

Current recommendations mainly focus on the LMWHs, and the factor Xa inhibitor, fondaparinux.

Low-molecular-weight heparins

LMWHs are obtained from UFH through chemical depolymerisation. The preparation of LMWHs occur through different methods of depolymerisation. To some degree, these varying methods of preparation result in differences in their pharmacokinetic properties and anticoagulant profiles, such that these drugs are not clinically interchangeable.[9] Enoxaparin and dalteparin are the LMWHs of choice for the prophylaxis of VTE during air travel.[2]

Mechanism of action

LMWHs mainly act on coagulation factor Xa, and also, but to a lesser extent, on thrombin (factor IIa). Positioned at the junction of the intrinsic and extrinsic coagulation pathways, factor Xa transforms prothrombin into thrombin. Enoxaparin exerts its effect on this crucial coagulation factor (Xa), which inhibits the successive step in the cascade, the generation of thrombin. Enoxaparin also acts on thrombin, which is essential for the formation of fibrin, a necessary component of blood clots. The added thrombin activity of enoxaparin restricts the intensification of the coagulation cascade by thrombin.[10-14]

Recommended dosage

The recommended dosage is as follows:

- *Enoxaparin sodium:* 40 mg subcutaneously as a single injection just before departure
- *Dalteparin:* 5 000 IU subcutaneously prior to departure[2]

Drug interactions

On every occasion possible, agents which may increase the risk of haemorrhage should be discontinued prior to initiation of LMWH therapy. These agents include medication such as other anticoagulants and platelet inhibitors (including acetylsalicylic acid, salicylates, nonsterioidal anti-inflammatory drugs, dipyridamole or clopidogrel). If co-administration is necessary, close clinical and laboratory monitoring will need to be conducted.[11] Furthermore, it should be noted that aspirin alone is of limited value in this setting. Therefore, it is not recommended for the prevention of air travel-related VTE.[1]

Factor Xa inhibitors

Fondaparinux is an indirect factor Xa inhibitor.[12,16]

Mechanism of action

Fondaparinux is classified as a synthetic analogue of the antithrombin-binding pentasaccharide. This pentasaccharide is also present in UFH or in the LMWHs. Fondaparinux has a molecular weight, which is approximately three times lower than that of LMWHs.[12]

Fondaparinux sodium's antithrombotic activity is the end result of antithrombin III-mediated selective inhibition of factor Xa. The selective binding of fondaparinux to antithrombin III, enhances (approximately 300 times) the natural neutralisation of factor Xa by antithrombin III. Neutralisation of factor Xa disrupts the blood coagulation cascade which inhibits thrombin formation and thrombus development.[13]

Fondaparinux sodium lacks the ability to inactivate thrombin (activated factor II), and has no known effect on platelet function. At recommended dosages, fondaparinux sodium does not prolong prothrombin time and has a very weak effect on activated partial thromboplastin time.[12]

Recommended dosage

It is recommended that a single dosage of 2.5 mg is administered subcutaneously prior to departure.[2]

Drug interactions

Discontinuation of agents that may enhance the risk of haemorrhage prior to initiation of therapy with fondaparinux is recommended unless essential. If co-administration is a must, patients should be monitored closely for haemorrhage.[13]

Adverse effects

The most common adverse effects associated with the use of fondaparinux are bleeding complications and mild local irritation, following subcutaneous injection.[13]

Other potential options

Other potential options include rivaroxaban, dabigatran, apixaban, and other newer oral anticoagulants that are still in clinical development. Their use in the setting of VTE prevention with regard to air travel still needs to be elucidated:

- *Rivaroxaban:* Rivaroxaban is a highly selective, direct factor Xa inhibitor.[17] It is an orally-bioavailable factor Xa inhibitor that selectively blocks the active site of factor Xa, and does not require the presence of a co-factor, such as antithrombin III, for its activity. The activation of factor X to factor Xa through the intrinsic and extrinsic pathways plays an essential role in the cascade of blood coagulation.[14]
- *Dabigatran:* Dabigatran is an oral, reversible, direct thrombin inhibitor.[18] Dabigatran and its active metabolites are competitive, direct thrombin inhibitors. Since thrombin assists with the conversion of fibrinogen into fibrin during the coagulation cascade, its inhibition prevents the development of thrombi. Both free and clot-bound thrombin and thrombin-induced platelet aggregation are inhibited.[15]

Conclusion

It has been shown that air travel inherently carries an increased risk of the development of VTE, and although small, this risk is significantly higher than that in the general, healthy, non-flying population. Individual air travellers are strongly encouraged to consult a suitable healthcare professional prior to undertaking either frequent or long-distance travel via aeroplane for an individual risk assessment and guidance on suitable or required prophylactic measures.

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Investigating the role of knowledge management in the pharmaceutical sector: a systematic review

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Abstract

Background: The pharmaceutical sector, in its routine operations, heavily relies on numerous collaborators who exchange knowledge to maintain high-quality pharmaceutical care. This study examined the extent to which Knowledge Management (KM) impacts organisational performance, identifying the enablers and challenges to effective KM in the pharmaceutical industry. Lack of robust KM strategies is a threat to patient safety as it is linked to drug development delays, supply chain disruptions, medication errors and poor treatment outcomes.

Methods: A systematic literature review following PRISMA was conducted on Google Scholar to examine the role of KM initiatives in pharmaceutical organisations. A total of 21 peer-reviewed papers published in the English language from the year 2013 to date, focusing on KM within the pharmaceutical sector, were included in this study. The articles were selected, screened and examined following the inclusion and exclusion criteria.

Results: A positive relationship exists between Knowledge Management (KM)/Knowledge Sharing (KS) and Organisational Performance (OP), with significant R^2 values ranging from 0.255 to 0.281. The study revealed that knowledge sharing specifically emerged as a significant predictor of organisational performance ($p < 0.05$) and organisational agility ($\beta = 0.348$). These findings suggest that effective KM strategies contribute to business performance optimisation, reinforcing the strategic importance of KM in organisational success.

Conclusion: The pharmaceutical industry can benefit from establishing cross-functional knowledge maps, implementing formal tacit knowledge transfer, developing clear SOPs for knowledge capture and transfer, and ensuring mobile accessibility of knowledge resources. Implementing these KM strategies contributes to higher productivity, quality products and services, market expansion, and increased revenues.

Keywords: knowledge management, pharmaceutical organisations, knowledge sharing, barriers, enablers, organisational learning

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Introduction

The pharmaceutical industry works tirelessly to create medications and treatments that can save lives, leading the way in innovation. In 2023 alone, the pharmaceutical industry spent US$300 billion on Research and Development (R & D).[1] Nonetheless, this industry has many obstacles to overcome, such as protracted research and development cycles, strict regulatory requirements and the ongoing need for innovation in a market that is becoming more and more competitive. Pharmaceutical companies are finding that KM is an essential tool for driving innovation, streamlining operations and preserving a competitive edge in this complex landscape. With new medicines continuously entering the market, new developments in the regulatory field and an expanding focus on customised treatments, there is an increased demand for well-informed and flexible pharmaceutical personnel.[2,3] Through standardisation of best practices across facilities, there is improved tracking and sharing of adverse events, quicker access to drug safety information and alerts, and improved prevention of medication errors through shared learnings.[4,5,6]

Knowledgeable staff is crucial for any organisation, notwithstanding its type, anatomy, processes and services.[7] This knowledge entails a wide array of information that combines experience, rational thought, observation, education, skills and competencies.[8,9] Managing this organisational knowledge involves a set of activities and initiatives employed by an organisation to generate, gather, disseminate and effectively utilise the knowledge.[10] Hu et al.[11] describe KM as an array of competencies and skills an organisation uses to obtain useful information and efficiently share it within the organisation to enhance its activities. In other words, KM is the methodical harmonisation of an organisation's workforce, infrastructure, workflow and structure to get value by exploiting and executing creative concepts.[9]

In the pharmaceutical sector, KM extends beyond just saving and retrieving information. It involves the strategic generation, dissemination, and utilisation of knowledge throughout the entire industry, spanning from drug formulation to patient treatment. Novel treatment solutions require effective knowledge-sharing and collaborative efforts to address health issues.[10]

Thus, the significance of KM in making decisions to enhance pharmaceutical care requires implementing effective approaches to handling knowledge and ultimately facilitating accurate clinical decisions.[2,3] Efficient knowledge management systems position

organisations to tackle these issues with skill and proficiency, promoting the development of life-preserving medicines.[6] For instance, Moderna's swift creation of its COVID-19 vaccine underscores the power of effective KM systems as the vaccine quickly reduced transmission and offered protection against severe disease and its long-term health consequences.[11] In a similar manner, the efficient use of information and resources to improve customer experience and operational efficiency by the Dischem pharmacy chain in South Africa can be attributed to KM.[12]

Problem statement

This study seeks to understand the role of KM practices, the extent to which KM contributes to organisational effectiveness as well as determining the enablers and challenges to effective KM in the pharmaceutical sector. The pharmaceutical sector is knowledge-driven due to R&D initiatives demanded by modern treatment requirements and the need for continuous innovation.[13] Even though the crucial function of KM in promoting innovation and regulatory compliance is well-founded, many pharmaceutical organisations face challenges in implementing KM initiatives.[5,11,14]

The inability to execute strong KM strategies can come at a great cost to the pharmacy profession, often with ramifications. Poor KM is associated with patient safety concerns, medication errors, and poor treatment outcomes.[15] Moreover, a lack of elaborate KM initiatives impedes the ability of pharmaceutical personnel to be involved in evidence-based practices, leading to the adoption of obsolete or inappropriate interventions.[3] This can eventually compromise the quality of pharmaceutical care pharmacists provide and have negative health consequences.[15] Pharmaceutical firms will also face drug development delays, problems with regulatory compliance, supply chain interruptions and a slow market response.

Although KM is growing in popularity as an essential component in enhancing pharmaceutical care and streamlining operations, there is a lack of understanding of the best practices in different pharmaceutical environments. The resultant knowledge gap is a hindrance to the pharmaceutical firms' development of appropriate KM strategies that tackle specific difficulties and barriers in modern pharmaceutical practices and enhance their overall competitive position. By addressing this knowledge gap, this systematic review offers some actionable insights and strategies that could help pharmaceutical companies enhance their capacity for innovation, operational effectiveness and KM.

Theoretical framework

Two types of knowledge have been presented in the literature, specifically tacit knowledge and explicit knowledge. Kothari et al.[16] explain that tacit knowledge is gained through experience and is hard to convey, while explicit knowledge is documented, frequently defined by its formality and easier to express. However, these two types of knowledge do not exist in isolation but are rather intertwined through relationships and exchanges between people.[17]

Attard et al.[17] explain the concept of 'Ba', a common stage or area for knowledge generation and exchange, whether mental or physical. The authors further state that 'Ba' entails the exchange of tacit knowledge (emotional feelings, encounters, mental images) and creates teams amenable to exchanging cultures, traditions, procedures and moral principles. In this way, there is an absorption of explicit knowledge by individual members, expanding their tacit knowledge base as formalised knowledge is related to personal encounters, which are then disseminated and employed in practice to solve organisational problems.[18]

Among the several theories, concepts and approaches to KM, the Socialisation, Externalisation, Combination, and Internalisation (SECI) model is broadly regarded as an important and most widely used theoretical framework to guide KM research.[19] The SECI model regards knowledge generation as an evolving process with constant interaction between tacit and explicit knowledge resulting in socialisation (tacit to tacit), externalisation (tacit to explicit), combination (explicit to explicit) and conversion of explicit to tacit through internalisation.[18,19] The SECI model is enabled by the 'Ba' platforms through the provision of the right atmosphere for knowledge provision processes.[20] In real life, 'Ba' is implemented by interactions such as brainstorming meetings, mentorship activities and online knowledge sharing.[17]

However, the SECI model is riddled with flaws and limitations. Bandera et al.[20] point out that the validity of the model was only shown for the manufacturing firms in Japan and its application may not be generalisable to other organisations. Farnese et al.[17] criticise the model for lacking a solid foundation based on evidence on how it could be applied in practice. Furthermore, Adesina and Ocholla[18] posit that the model fails to take into account the context of use, disregards the learning theory, and is linear and simplistic, making it difficult to codify other knowledge forms.

Bearing in mind that no model is perfect, the SECI model is still very useful in understanding the strategic use of knowledge in organisations as some studies[17,18,19,20] have applied it in KM research. Since it has been used for the majority of KM conceptualisation or descriptive purposes in case studies, the SECI model is considered a theoretical landmark.[18] In addition to fostering innovation and offering a framework for knowledge management procedures, the SECI model assists organisations in understanding how knowledge is produced and disseminated within teams.[17,19]

Literature review

Knowledge sharing

Since merely generating and storing knowledge is not enough, people within organisations must share it for it to be useful. The dissemination of knowledge occurs through social interaction where effective techniques are supported and repetition is avoided.[21] Indeed, the cost of this repetition is greatly reduced by knowledge-sharing systems that empower workers and teams to map out solutions efficiently.[22] Knowledge-sharing

describes various actions and methods (e.g. training sessions and workshops, mentoring programmes, storytelling and anecdotal sharing, discussion forums, online communities and lessons learned databases) people employ to disseminate knowledge into goals, competencies, concepts, information, strategies, creativity and insights that fellow workers can understand.[23] After sharing knowledge, the receiver must then process it in a context that will culminate in the creation of new knowledge.[24]

Although Lilleoere and Hansen[21] qualitatively explored KS methods in pharmaceutical R&D, their findings cannot be generalised to other comparable units or areas of pharmaceutical practice. Similarly, although Qureshi and Evans[22] examined obstacles to knowledge-sharing within and outside the pharmaceutical environment, their data emanated from a single case, limiting the application of the empirical findings. The pharmaceutical sector will therefore benefit from a multiple-case study that examines KS techniques and obstacles within and across organisations.

Benefits of knowledge management

The field of pharmacy is intricate and utilises vast amounts of knowledge, which is anchored on experience.[25] According to Xu and Wei,[23] KM activities have been associated with efficiency, business growth, positive corporate culture, high revenues and reduced costs. The work by two studies[11,15] indicates that KM can predict internal processes in community pharmacies and that rapid growth in competition among businesses is catalysed by knowledge used to enhance productivity. However, even though Mukuria et al.[15] demonstrated a statistically significant relationship between KM and retail pharmacy performance, they did not examine the long-term effects of KM.

Since these intellectual resources can be viewed as a secret weapon used by organisations to attain competitive advantage, KM aims to amass knowledge that creates unique skills that lead to superiority.[4,8] Ajie and Opeke[26] explain that when workers exchange knowledge among themselves and teams, the organisation can leverage its intellectual assets. However, their research indicates that KM impacts financial more than non-financial performance, possibly due to the control on medicine prices.

Effective use of KM by pharmacists is crucial to enhance the quality of pharmaceutical care as technological advancement or context influences professional practice.[25] For instance, tacit knowledge can come in handy in an ethical dilemma where a pharmacist is required to issue a prescription medicine for emergency use, to a person without a prescription.[27] While the findings that KM capacity firms pharmaceutical organisations' competitive edge[11] are important, the role of strong collaboration, coordination and communication between departments ought to be investigated.

Knowledge management strategies

Kothari et al.[16] presented multiple KM strategies that encompass simple techniques (e.g. educational seminars and training), communities of practice, and workflow-based frameworks. Mapping skills and resources is another strategy to enhance KM in an organisation.[14] This mapping approach functions on the premise that the organisation's leadership or external forces may mobilise latent capacity.[16] Mapping knowledge involves gathering information on the knowledge held by each individual which enables the organisation to identify its key knowledge assets and coordinate knowledge-related activities.[28] This coordination may culminate in organisational training, which may be online or otherwise, including debriefings by retiring or resigning experts.[16]

Technology is an essential element of a healthy KM strategy and is now key to pharmaceutical care. Technology is deemed an important solution to enhance pharmaceutical care, the management of patients, the identification of novel interventions and the carrying out of research.[6] While the anatomy of technological systems may differ from one organisation to another, the system facilitates codification, organisation, distribution and maintenance of the organisation's intellectual assets.[16] The strategy of codifying and personalising knowledge effectively aligns with the therapeutic tenets and goals by promoting knowledge exchange and use among healthcare workers.[29]

However, to successfully implement a technology-driven approach, a thorough understanding of the organisational KM activities is needed.[25] Technological innovation is an integral part of KM because technology facilitates the seamless transfer of information which is achieved through the implementation of a system that offers a technical basis.[6] For instance, Shahmoradi et al.[6] revealed that the use of Electronic Health Records (EHR) and Clinical Decision Support Systems (CDSS) streamlines the flow of information between healthcare professionals while enhancing decision-making. As such, these tools are resourceful in constructing interactive techniques that support healthcare professionals in creating knowledge, significantly enhancing patient safety[25] and efficiency, buttressing the benefits outlined by Chiekezie et al.[4]

Technology also enables the creation of discussion platforms using social media such as WhatsApp. Forums formed inside organisations that use smartphone messaging encourage swift conversations permitting members to refer to given knowledge sources and authenticate arguments with their colleagues.[28] The work of Bruce et al.[30] empirically demonstrated that the use of social media in healthcare notably enhances patient-doctor interactions, conveyance of information, patient education and crisis management. However, the use of technology can be marred by high setup costs, poor internet connection, system breakdowns, lack of support and data protection issues.

Another strategy utilises Communities of Practice (CoP), which are groups of people who share a common concern. These communities operate on three pillars: the domain of skills and knowledge exhibited by participants; relational links and psychological attachment among participants; and the collective structures, concepts and resources that participants utilise in their work.[16]

Boundary spanning among CoP enables another benchmarking strategy, where lessons can be drawn from other organisations by exchanging knowledge on the most workable practices.[28] This establishes a favourable working culture, and an increase in profits and growth highlighted by Xu and Wei.[23] However, Kothari et al.[16] caution that virtual CoP may be inappropriate to satisfy every organisation's KM requirements, indicating that all-encompassing KM strategies are neither attainable nor desired.

Barriers to effective KM

Literature is replete with barriers and enablers of knowledge management categorised into organisational, technological, and individual-related. In the pharmaceutical sector, Qureshi and Evans[22] highlight the failure to distinguish tacit from explicit knowledge, the inaccessibility of knowledge, physical and social borders among workers and the lack of valuable knowledge as some of the organisational obstacles to KM. For instance, various research teams or departments can operate independently, hesitant to exchange information because of communication gaps or rivalry. Poor leadership backing, lack of KM champions, lack of resources to implement changes, inadequate infrastructure, and workplace incivility promoted by abusive leadership[16,31] are clear obstacles to KM, including lack of time[12] and lack of executive support.[16]

Workers' poor absorptive capacity, strained relationships between colleagues, inadequate social skills, and the perception that intellectual capital is lost through knowledge exchange were highlighted as barriers to KM.[14,22] Lilleoere and Hansen[21] emphasise that personal beliefs can interfere with knowledge-sharing, for instance, pharmacy workers who are accustomed to their current methods may be reluctant to adopt new knowledge management practices. Lack of motivation and information overload, poor technological competence and inadequate qualifications to occupy certain positions all negatively impact healthcare knowledge-sharing.[16] However, Lilleoere and Hansen[21] indicate that motivation is loosely related to knowledge transfer, implying that knowledge dissemination is not enough for effective knowledge-sharing.

Healthcare technology can be a hindrance to KM due to restricted accessibility to contemporary technology, unfriendly user interface and interoperability problems.[6] Pharmaceutical organisations may face obstacles to KM in inconsistent, malfunctioning or incompatible software and the difficulty of procuring the programme to act as the knowledge base.[22] For example, outdated or incompatible inventory management systems may hinder effective data sharing and analysis across pharmaceutical organisation departments. However, Qureshi and Evans[22] note that these hindrances to KM neither emanate from nor were they empirically tested in the pharmaceutical sector. It is important to carry out case studies in pharmaceutical organisations with effective or failed KM practices to obtain an empirical understanding of the barriers and effective methods to mitigate them.

Methodology

This review conformed to Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) requirements.[32]

Search strategy

A thorough literature search was carried out on Google Scholar to find relevant publications on knowledge management in the pharmaceutical sector. The following keywords were used in the search criteria: "pharmacy", "knowledge management", "pharmacist", "pharmaceutical care", "knowledge-sharing", and "evidence-based practice". Previous studies[33,34] have carried out systematic reviews from a single database, the Web of Science. Logical operators like the "AND" and the "OR" were used to improve the search queries. The broad scope of this research and the availability of a wide range of pertinent sources are ensured by Google Scholar's well-known extensive indexing of academic journals, conference proceedings, theses, and institutional repositories. The review was restricted to works published between 2000 and 2024 to capture the evolution of KM in the pharmaceutical sector since the turn of the millennium. According to Kothari et al.,[16] although KM in other sectors such as business and public policy practised KM from the early 1990s, it only started to gain traction in the healthcare field around 2000.

Inclusion and exclusion criteria

The inclusion criteria accommodated full-text studies that (a) are open access; (b) are peer-reviewed or conference papers; (c) focus on KM in the pharmaceutical sector; (d) are published in English; (e) are published from 2000. Editorials, opinions, unpublished and other non-research articles were excluded.

Data extraction and screening were carried out by two separate researchers. To agree, the two researchers first discussed any differences. A third researcher independently examined the contentious issues and rendered the final decision in situations where discussion failed to produce consensus. The data extracted include the author(s), year, study design, population, KM strategies, barriers and facilitators and main findings.

Data analysis

Thematic analysis was used to locate repeating themes and trends within the extracted data. The synthesis was based on: (1) KM execution in the pharmaceutical field; (2) the barriers to KM in the pharmaceutical field; (3) the facilitators of effective KM strategies; (4) the KM strategies, solutions, or best practices for KM; and (5) impact of KM on pharmaceutical organisations. Initially, the researchers familiarised themselves with the data by meticulously reviewing the incorporated studies to acquire an in-depth comprehension of their material. Crucial themes, results or propositions were identified and manually labelled with codes. These preliminary codes were methodically grouped into possible themes, with the aid of visual mind mapping to investigate code relationships. An iterative review of the theme development process was conducted against the coded extracts

and the complete dataset to guarantee internal consistency and the formation of coherent patterns. Regular researcher meetings helped to refine the themes and provide precise definitions for each one. To make sure themes appropriately reflected the content, a third researcher independently reviewed the papers as part of the validation process. This study followed Synthesis Without Meta-analysis (SWiM) as the focus is on understanding concepts, experiences, or perceptions rather than quantifying effect sizes. The inter-rater reliability was assessed through Cohen's kappa by feeding the data into the PSPP software.

Quality assessment

A checklist proposed by Kitchenham and Charters[35] and adopted by Almansoori et al.[36] was used to assess the quality of the studies. The checklist contains nine questions which can be answered by a Yes (1 point), No (0 point), or a 0.5 point if the answer is between yes and no. A total score of between 0 and 9 indicates the extent to which a study answers the research questions. Any score below 4.5 (50%) indicates shortcomings in a study. The nine questions that form the basis for the assessment are as follows:

a. Is the research aim specified clearly?

b. Did the study achieve its aim?

c. Are the variables considered by the study clearly indicated?

d. Is the context/discipline of the study clearly defined?

e. Are the methods of collecting data sufficiently detailed?

f. Is the study describing the measure's reliability and/or validity?

g. Are the statistical techniques used to analyse the data sufficiently described?

h. Do the findings add to the literature?

i. Does the study add to your knowledge or understanding?

A sample of ten randomly chosen articles from our initial search was used for the pilot test. The modified checklist was independently used by two researchers to assess the comprehensiveness, clarity, and applicability of the pharmaceutical KM literature.

Results

Search results

The search process outlined in the PRISMA diagram in Figure 1 yielded 21 articles reviewed in this study. Even though the target was from 2000, the first paper meeting the criteria emerged in 2013.

Study characteristics

The publishing period of the articles ranged from 2013 to 2024. Most of the studies were quantitative (85.7%) with only three qualitative studies (14.3%) and no mixed methods studies. Most of the studies targeted industrial pharmacy with only two studies conducted in community pharmacies and one in a hospital pharmacy. The study characteristics are shown in Table I.

Table I: Study characteristics

Author/year	Study design	Sample size	Percentage
Ajie & Opeke[26]	Quantitative	362	10.37%
Altaher[24]	Quantitative	224	6.42%
Chiekezie et al.[4]	Quantitative	40	1.15%
Christopher et al.[38]	Quantitative	289	8.28%
Dongo[37]	Quantitative	26	0.74%
Hu et al.[11]	Quantitative	308	8.83%
Filieri et al.[46]	Qualitative	18	0.52%
Haque & Islam[39]	Quantitative	160	4.58%
Hung et al.[47]	Quantitative	98	2.81%
Lilleoere & Hansen[21]	Qualitative	19	0.54%
Mukuria et al.[15]	Quantitative	116	3.32%
Priyavarsha & Sudha[3]	Quantitative	340	9.74%
Qureshi et al.[22]	Qualitative	7	0.20%
Rafique et al.[7]	Quantitative	120	3.44%
Riaz & Hassan[40]	Quantitative	203	5.82%
Saini[41]	Quantitative	50	1.43%
Salih et al.[8]	Quantitative	104	2.98%
Shwiemeh & Yildiran[45]	Quantitative	206	5.90%
Sontoso et al.[31]	Quantitative	311	8.91%
Yuen et al.[9]	Quantitative	379	10.86%
Zubair et al.[48]	Quantitative	110	3.15%
		3490	**100.00%**

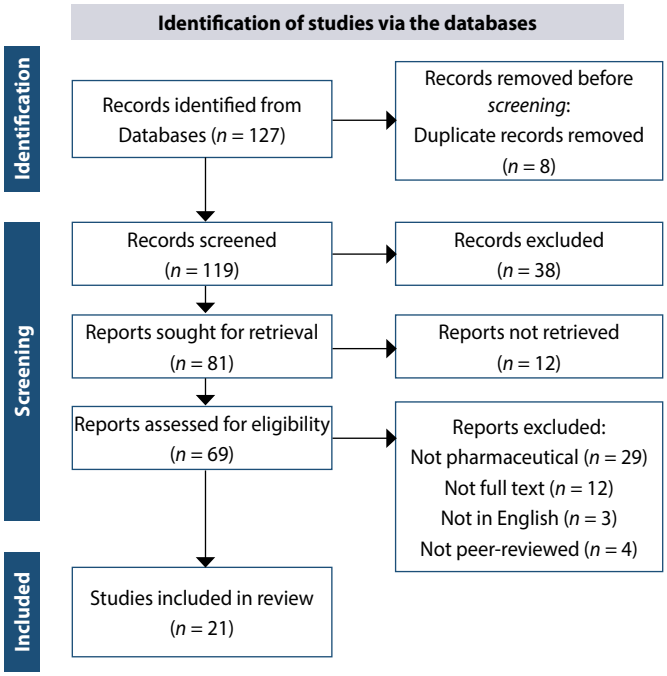

Figure 1: PRISMA flow diagram representing the search process

Distribution of the studies

The studies were conducted in various countries, including Hong Kong, India, Jordan and Nigeria among others. Nigeria, India, Pakistan and Jordan constituted the greatest number of studies,

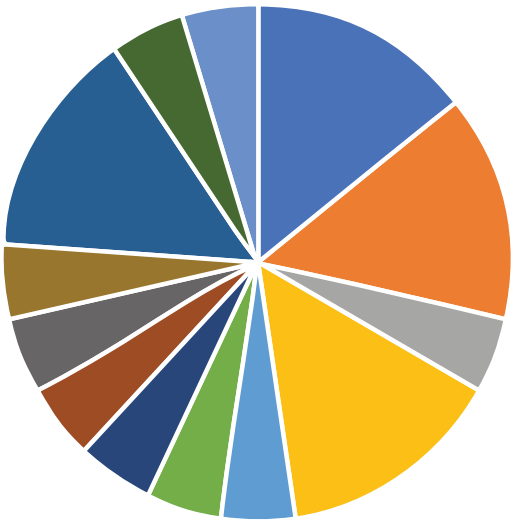

Figure 2: Proportion of the studies by country

with three each, accounting for about 57% of the total. Each of the remaining nine nations – Indonesia, Denmark, Bangladesh, Taiwan, Hong Kong, Australia, and Namibia – contributes one study to the review.

Outcomes measured

The outcomes of interest found across the studies include competitive advantage, organisational performance, innovation, knowledge sharing, and absorptive capacity. Organisational performance was measured in eight studies and innovation was measured in seven studies. Competitive advantage was an outcome of interest in five studies while knowledge-sharing was measured as an outcome in five papers. Only one paper was interested in absorptive capacity as an outcome.

Knowledge sharing and organisational performance

Based on the extracted data, Table II summarises the key findings related to the impact of knowledge sharing on organisational performance. Knowledge sharing is a priority for organisations and significantly impacts the various elements of organisational growth. Organisational performance is at the core of the thematic map.

Table II: A summary of the effect of knowledge management on organisational performance

Study	Sample size	Statistical tool	Statistical result	Implication
Ajie & Opeke[26]	362	Simple linear regression	$R^2 = 0.281$, $p < 0.05$	KS positively influences OP.
Christopher et al.[38]	289	t-test	$= 6.211$, $p = 0.000$	KS and retention positively influence OP.
Haque & Islam[39]	160	Structural equation modelling	Chi Sq = 2.143 RMSEA = 0.085	IT infrastructure and performance measure improves business performance.
Mukuria et al.[15]	116	ANOVA	$R^2 = 0.281$, t = 7.333, $p < 0.05$	Strong =+ve relationship between KM and OP
Priyavarsha & Sudha[3]	340	Structural equation modelling	$R^2 = 0.278$, $p = 0.000$	KM has a +ve effect on OP
Riaz & Hassan[40]	203	Pearson correlation	Correl. = 0.172, level 0.01	Weak +ve correlation between KM process intention and OP
Saini[41]	50	Simple linear regression	$R^2 = 0.255$	KM explains a 25.5% variance in OP.
Salih et al.[8]	104	Multiple linear regression	t = 3.470, β = 0.348, level 0.05	The impact of KS on organisational Agility is +ve

KS = Knowledge Sharing, OP = Organisational Performance, KM = Knowledge Management

Table III: KM barriers and facilitators

Author	KM barriers	KM facilitators
Lilleoere & Hansen[21]	'Knowledge as power', no physical proximity to colleagues, 'not invented here', 'to know what to know', no or weak social relations.	Meetings, physical proximity to colleagues, relocation of professionals and social relations.
Qureshi and Evans[22]	High cost of KS, technology limitations, knowledge hiding, lack of socialisation, lack of trust, non-educational mind-set, organisational politics, poor leadership, and time pressure.	
Dongo[37]	Lack of time, staff resistance, unwillingness to learn, poor communication, staff shortage, lack of reference books, lack of staff rotation, poor understanding of KM, inadequate technology infrastructure, lack of knowledge repository.	Technology, organisational culture, training, active staff participation, WhatsApp.

Barriers and facilitators of KM

Only 3 studies dealt with either barriers or facilitators of KM or both. The barriers and facilitators extracted from the studies are presented in Table III.[21,22,37]

Quality of the studies

All the studies were assessed for quality and relevance. The scores ranged from 5 (55.6%) to 8.5 (94.4%). None of the papers were excluded for review on account of a score of less than 50%.

Inter-rater reliability

Based on Cohen's Kappa analysis for inter-rater reliability across six themes in the systematic review, the kappa values for the themes are Knowledge-Sharing = 0.59, Organisational Performance = 0.81, Competitive Advantage = 0.77, Absorptive Capacity = 0.77, Innovation = 0.63 and Barriers and Facilitators = 0.83.

Discussion

This paper examined the role of knowledge management as a strategy for capturing and sharing knowledge in the pharmaceutical sector.

The geographical distribution of the studies points to a worldwide interest in the subject, with developing nations in Asia and Africa receiving a little more attention than others. Despite the relatively low total number of studies per country, the diversity of countries represented suggests that KM in the pharmaceutical sector is an area of interest for international research. It is interesting to note that this research does not include data from some significant pharmaceutical markets, such as the United States, the United Kingdom or Germany. Different approaches to recording and disseminating KM practices may be the cause of this discrepancy. It is also possible that these practices are either proprietary information, part of larger organisational procedures or documented in non-academic formats like industry white papers and internal reports.

Eight studies examined the impact of KM on organisational performance.[3,4,15,24,38,39,40,41] Ajie and Opeke,[26] with the largest sample size of 362, examined the effect of knowledge-sharing on both financial and non-financial elements of organisational performance. Linear regression findings reported that knowledge sharing explains over 28% of the variance in organisational performance ($R^2 = 0.281$, $p < 0.05$). Businesses, like pharmacies, can increase employee performance by helping them learn about customers' preferences and then tailor their services to meet those needs.

Christopher et al.[38] also found a statistically significant association between knowledge sharing and organisational performance ($t = 6.211$, $p = 0.000$). However, Riaz and Hassan found only a weak positive correlation between KM process intention and organisational performance. This is in sharp contrast with the other seven papers. In a systematic review involving 16 articles, Kosklin et al.[42] indicate that KM can improve organisational financial performance, which enables healthcare organisations to absorb financial stress.

Even though their systematic review is more thorough, contextual variations, performance measurement variations, employee intentions, mediating variable considerations and sample characteristics can account for the contradictory findings. For instance, the relationship between KM and organisational performance can be drastically changed by the presence of mediating variables, such as organisational creativity.

An organisation that advocates for knowledge sharing with trust and candour values its workers as a key resource of knowledge and encourages collaboration.[16] Lilleoere and Hansen[21] suggest that efficient KM could shorten product development cycles and highlight the value of knowledge sharing in accelerating the knowledge creation process within pharmaceutical R&D. Ajie and Opeke[26] concluded that socialisation and externalisation were the more prominent practices of knowledge sharing, in line with the SECI model, emphasising the importance of tacit knowledge in organisations. Tacit knowledge in pharmaceutical organisations includes insights like manufacturing process troubleshooting expertise, comprehension of drug development challenges and the conversion of explicit guidelines into intuitive practice wisdom, all of which improve patient care and safety.[43] Kucharska and Erickson[44] support this and conclude that tacit knowledge positively influences both innovation and organisational performance.

Five studies confirm evidence of the positive influence of KM on competitive advantage.[4,8,11,21,45] Chiekezie et al.[4] established a significant positive correlation between staff training and customer satisfaction (Correlation = 0.848, at the 0.01 level (2-tailed).

Hu et al.[10] demonstrated that three KM elements: innovative capacity ($r = 0.403$); transformative capacity ($r = 0.408$); and absorptive capacity ($r = 0.460$), mediated by supply chain agility, positively influence competitiveness. In this systematic review, seven studies established similar findings, further affirming the role of KM practices in organisational innovation.[3,9,21,38,40,46,47] The interplay between knowledge-sharing and the intellectual capital of both individuals and the organisation promotes innovation and innovative attitudes,[23] leading to competitive advantage. To implement innovation and therefore competitive advantage, pharmaceutical firms must allocate resources towards the education and training of their staff and invest in research and development.[8]

This review also identified several barriers to KM which can be categorised into organisational, technological, cultural, personal and knowledge-related as shown in Table III. It is important to establish a culture of trust in which workers freely engage in knowledge-sharing while promoting socialisation, collaboration, and continuous learning.[48] Identifying barriers presents opportunities that pharmaceutical organisations must leverage for maximum benefit.[49] Managers and pharmacists in pharmaceutical

organisations must recognise these hurdles and co-opt trusted methods based on pharmaceutical systems' management.[50] These methods may include inculcating a culture of learning in teams, creating centralised databases, organised mentorship strategies, standardising knowledge capturing, incentivising knowledge exchange and strict regulatory compliance. Through the use of case studies, Krudys et al.[10] highlight how the regulatory system's KM can improve drug development and regulatory decision-making through the use of standardised data templates, queryable databases and collaborative frameworks.

Using a cross-functional structure allows harnessing knowledge from any part of the organisation, notwithstanding its location.[16] Conducting an assessment of the present workflows, identifying gaps and failures, applying the right tools and stakeholder involvement can add value and unlock more KM opportunities in the pharmaceutical sector. The results of this systematic review are supported by the high agreement on most themes, which also point to areas that could benefit from additional definition or coding process refinement. However, knowledge sharing's lower agreement indicates that to increase consistency, this theme might use a more precise definition or more rater training.

Conclusion

The function of Knowledge Management in pharmaceutical organisations is undeniably crucial for improving the quality of patient care, safety, and streamlining the workflow. The study established evidence that KM practices are associated with pharmaceutical organisations' absorptive capacity, innovation, competitive advantage and organisational performance. Absorptive capacity drives knowledge assimilation, application and absorption which ensures expedited drug development, optimisation of workflows and strengthens regulatory compliance

This review also identified several hindrances to KM which can be classified into organisational, technological, cultural, personal and knowledge-linked. Pharmaceutical organisations must identify these barriers in their particular settings to streamline KM operations and unlock its benefits.

Limitations

The study is limited to selecting research papers from a single database, which potentially results in selection bias. The study also did not conduct a meta-analysis which negatively impacts the generalisability of the findings.

Recommendations

The pharmaceutical industry can benefit from establishing cross-functional knowledge maps, establishing clear KM governance structures and roles, implementing mentoring programmes to transfer tacit knowledge, developing clear SOPs for knowledge capture and transfer, implementing semantic search capabilities across repositories, ensuring mobile accessibility of knowledge resources and establishing Communities of Practice (CoPs) across departments to foster a culture of knowledge sharing. It is worthwhile to conduct more research using a mixed methods approach or longitudinal studies in different pharmaceutical settings such as hospitals and retail pharmacies to capture the impact of KM and its long-term effects on various organisational aspects. There is a critical need for future research to specifically examine KM practices in countries like Germany, the USA and the UK, as the paucity of published studies from these top pharmaceutical markets restricts our comprehension of potentially novel KM practices and effective implementation strategies that could benefit the global pharmaceutical sector.

Conflict of interest

We have no conflicts of interest to disclose.

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Ethics

This study did not disclose any patient information. Issues relating to informed consent and ethical approval were not applicable.

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Vaccines in the fight against antimicrobial resistance – perspectives from South Africa

The Global Antibiotic Resistance Partnership – South Africa (GARP-SA) Group collaborators (the GARP-SA collaborators)

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Abstract

Antimicrobial resistance (AMR), in which microbes adapt to and resist current therapies, is a well-recognised global problem that threatens to reverse gains made by modern medicine in the last decades. AMR is a complex issue; however, at its core, it is driven by the overuse and inappropriate use of antimicrobials. Socioeconomic factors have been identified as significant contributors to the emergence and exacerbation of AMR, especially in populations facing inadequate access to healthcare, poor sanitation services and high morbidity and mortality rates. Weak healthcare systems and water, sanitation and hygiene have been highlighted as fundamental risk factors for AMR emergence and transmission. Behavioural factors, such as purchasing antibiotics without a prescription from a registered healthcare professional, not completing the prescribed course or overly prolonged courses of antibiotics, using antibiotics to treat viral infections, lack of access to quality antibiotics, and the proliferation of substandard or falsified (SF) drugs, have also been identified as significant contributors to AMR. Low- and middle-income countries have a higher incidence of antibiotics being dispensed without a prescription than higher-income countries.

Keywords: antimicrobial resistance, healthcare, sanitation, hygiene, prescription

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Preventing infections precludes the need for antimicrobials and reduces the selection pressure for the development and escalation of antimicrobial resistance (AMR). In this context, vaccines, alongside hygiene and access to clean water, can play a major role in fighting AMR.[1-5] By preventing infections, vaccines limit the emergence and transmission of susceptible and drug-resistant strains, lowering the risk of secondary infections and reducing the need for antimicrobial use (AMU) (Figure 1).[6] However, despite a growing body of evidence on the impact of vaccines in decreasing the emergence of AMR, the link is inadequately leveraged, with little to no integration between AMR and vaccination strategies. The Global Antibiotic Resistance Partnership – South Africa (GARP-SA) group met in Cape Town on 11 October 2023 to review the available evidence on the impact of vaccines on AMR in South Africa (SA) and discuss barriers, enablers and solutions in integrating vaccination as a pivotal strategy in efforts to combat AMR.

Evidence on the impact of vaccines on AMR in South Africa

Recent modelling studies have highlighted the potential impact of vaccines on AMR in SA. The following examples illustrate how existing vaccines and vaccines in development can reduce not only morbidity and mortality of the target disease but also antibiotic use, thereby slowing the emergence of AMR and reducing its burden on public health, the health system and the economy.

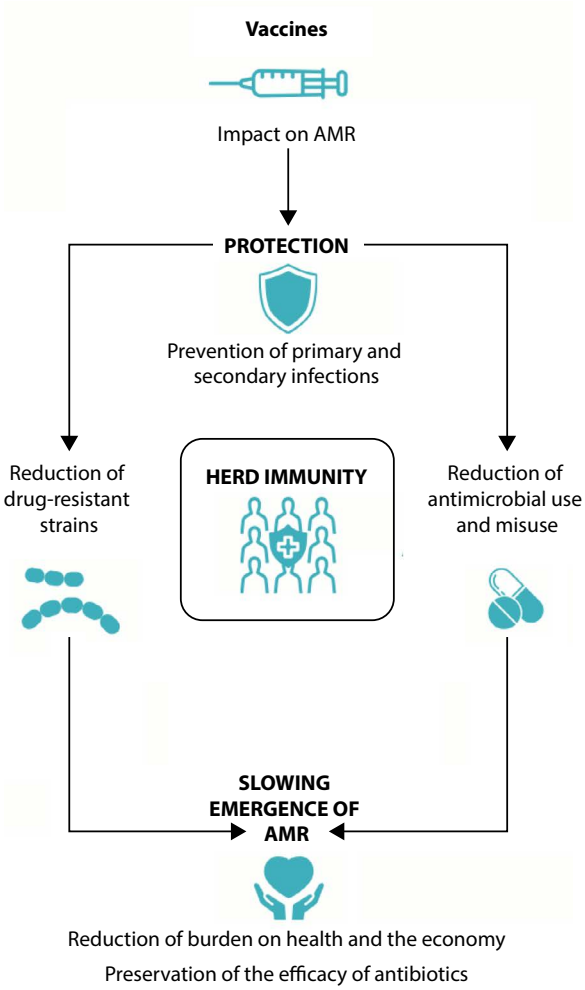

Figure 1: The role of vaccines in addressing antimicrobial resistance (AMR).[6]

Tuberculosis

A hypothetical post-exposure tuberculosis (TB) vaccine for adolescents and adults was projected to avert 10 000 cases of rifam- picin-resistant TB (RR-TB), or 8.3% (95% confidence interval (CI) 7.5–9.2) of all TB cases over 15 years in SA,[7] and to prevent 2 900 RR-TB deaths, or 6.7% (95% CI 5.5–7.8) of all TB deaths. These findings suggest an important role of a post-exposure vaccine in preventing drug-resistant TB for the similar M72/AS01 E vaccine in phase 3 clinical trials.[8]

Pneumococcal disease

A study modelling the impact of the pneumococcal conjugate vaccine (PCV), which has a coverage rate in children in SA of ~83%, estimated that it prevents 6.9 (95% CI 1.1–16) annual cases of antibiotic-treated *Streptococcus pneumoniae*-attributable acute respiratory illness (ARI) per 100 children aged 24–59 months.[9] The same study estimated the incidence of ARI, given PCV protection, as either invasive pneumococcal disease or acute otitis media, at 8.6 (95% CI 1.4–20.5) and 12.4 (95% CI 2–29.5) cases per 100 children aged 24–59 months, respectively, each year. These results indicate that the vaccine has been very effective at preventing antibiotic-treated ARI incidence in the country.

Klebsiella pneumoniae

A mathematical modelling study showed the potential impact of a hypothetical maternal *Klebsiella pneumoniae* vaccine. In SA, assuming a 70% vaccine efficacy and coverage equivalent to the maternal tetanus vaccine, the hypothetical vaccine could avert an estimated 1 717 neonatal sepsis cases and 344 neonatal sepsis deaths annually, accounting for ~4% of all such deaths.[10]

Rotavirus

In addition to vaccines that target bacterial infections, those for viral pathogens can also mitigate AMR by reducing disease incidence, including secondary infections that may be inappropriately treated with antibiotics. For example, evidence shows that the live-attenuated rotavirus vaccine, which was introduced into the national childhood immunisation programme in 2009,[11] could directly prevent an estimated 5.4 (95% CI 0.9–11.1) cases of antibiotic-treated, rotavirus- attributable diarrhoea per 100 children < 2 years of age annually, assuming a coverage rate of 80%.[9] The incidence of this illness (given the vaccine protection) in SA was estimated at 8.1 (95% CI 1.1–17) cases per 100 children,[9] suggesting that the vaccine has been highly effective at preventing inappropriate antibiotic use.

Respiratory syncytial virus

A randomised placebo-controlled trial with > 2 400 SA participants estimated that the maternal respiratory syncytial virus vaccine reduced the incidence of antibiotic prescriptions in the first 3 months of life from 43.1 to 37.3 per 100 children, representing a vaccine efficacy against antimicrobial prescribing of 13.4% (95% CI 1.7–26.3).[12]

Influenza virus

Another study suggested that vaccinating just 30% of the population aged > 65 years against seasonal influenza could avert > 11 000 inappropriate antibiotic prescriptions each year in SA (assuming a vaccine effectiveness of 50%).[13]

Barriers

Despite being a critical tool in AMR mitigation, vaccination as a strategy is unrecognised in this context. Similarly, AMR is not included as a metric in vaccine evaluation strategies. Several factors undermine the relationship between AMR and vaccines, such as inadequate health literacy, inequities in access to healthcare, infrastructure and data gaps, and overall lack of co-ordination between health programmes (Figure 2). Quantitative estimations of how vaccines can mitigate AMR have traditionally been hampered by the lack of electronic patient-level data and local data on the health and economic burden associated with AMR. Mathematical modelling has been able to overcome some of these challenges, and country- specific evidence on the impact of vaccines on AMR has recently been accumulating. These data must now be used to raise awareness and inform immunisation and AMR policies in ways that can impact policy at the national level.

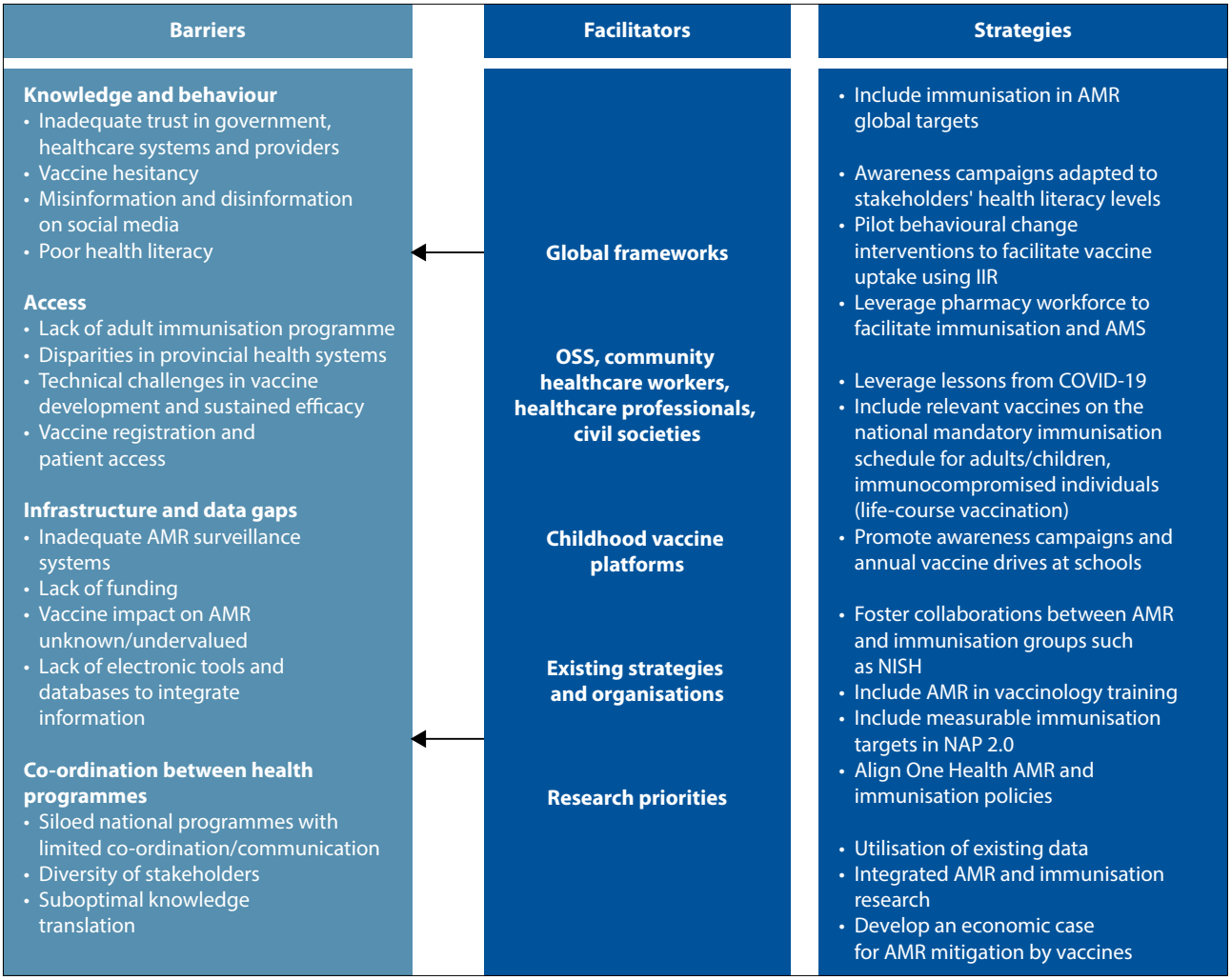

Figure 2: Identified barriers, facilitators and strategies. (AMR = antimicrobial resistance; OSS = Operation Sukuma Sakhe; IIR = intervention and implementation research; AMS = antimicrobial stewardship; NISH = National Immunization Technical Advisory Group Support Hub; NAP 2.0 = National Action Plan version 2.0.)

Another barrier to integrating AMR and immunisation strategies is the lack of co-ordination between different programmes. Although immunisation is mentioned as a tool within infection prevention control in the national AMR strategy in SA, no specific objectives or indicators exist for how it can contribute to reducing AMR.[14] This has been largely due to an inadequate understanding of the AMR burden and the relationship between AMR and vaccines. However, an opportunity has arisen to fill this gap and introduce measurable targets for AMR mitigation through vaccines. In addition to the lack of evidence on the impact of specific vaccines against pathogens relevant to public health, the structural cause for the inadequate integration of these programmes lies in the lack of co-ordination and communication between them, further complicated by the diversity of stakeholders involved.[15]

At the other end of the spectrum, these additional benefits of vaccine uptake must be communicated to the public. However, vaccine hesitancy, often attributable to misinformation and disinformation on social media and other communication platforms, represents an ongoing challenge. An official life-course vaccination strategy has been suggested as an effective way to increase immunisation and decrease AMR. However, despite SA's well-supported and structured childhood vaccination programme, adult vaccinations are not similarly provided within a routine immunisation programme. The lack of an official adult immunisation schedule and accessible adult immunisation programme may also contribute to AMR. Influenza vaccinations have been shown to reduce AMR by preventing infections and reducing AMU by up to 64% among adults, likely reducing the selection pressure that drives AMR.[16] The pneumococcal vaccine has been shown to directly reduce the need for antibiotics and decrease the carriage, transmission and prevalence of drug-resistant invasive pneumococcal disease by up to 30%.[17] However, vaccination alone is not enough to overcome habitual antimicrobial prescribing practices, and this emphasises the need for concurrent, judicious antibiotic-use interventions as part of antimicrobial stewardship (AMS) practices.[17]

Policy-related barriers to implementing a life-course vaccination strategy include high programme costs and difficulty determining and verifying eligibility and prioritisation when supplies are low. Considerable challenges also exist with complacency and

compliance, as adults are less likely to accept vaccinations even when they are available.

Facilitators

Increasing the collaboration between AMR and immunisation initiatives requires a concerted effort among diverse stakeholders, including scientists, clinicians, policy-makers, industry leaders and communities, to enact practical and meaningful change to the working structure. Fortunately, this work can build from a growing body of knowledge on the health and economic case for increased collaboration. Although much of this knowledge is confined to academic journals, such published evidence can influence policy if adapted to the country's health system context and resources. Additionally, SA benefits from a strong and well-funded childhood immunisation programme, which can be leveraged, in addition to the Operation Sukuma Sakhe infrastructure that aims to integrate the services of government in order to ensure that it enriches the lives of SA citizens, for a 'whole of government approach' that encourages ongoing government-community interaction to support meaningful change at the community level.

A comprehensive strategy to increase collaboration between AMR and immunisation initiatives requires recognising mutually beneficial interests, thoroughly understanding barriers and facilitators, and considering all stakeholders, including the pharmaceutical industry and medical insurance companies. The proposed National Health Insurance, which is SA's strategy to reach universal health coverage, could strengthen primary healthcare, including vaccination programmes, improve AMR surveillance and improve adherence to antibiotic regimens.

Investments in vaccines that will reduce the infectious disease burden and address AMR do not solely depend on understanding their value and cost-effectiveness. For many countries, the costs associated with the introduction of and sustainable access to vaccines are prohibitive. SA is a middle-income country (MIC) and, therefore, not eligible for support from GAVI, the Vaccine Alliance. Recent reports from GAVI and partners have acknowledged the challenges MICs face with new vaccine introductions and coverage, prompting GAVI to assess how these countries could be supported. Recently, SA transitioned from PCV 13 (the vaccine that protects against 13 serotypes) to PCV 10 (the vaccine that protects against 10 serotypes) within the childhood immunisation programme. This shift allowed the inclusion of new vaccines into the childhood immunisation schedule. These additions included the introduction of a rubella-containing vaccine and additional booster doses of acellular pertussis vaccines administered to adolescents and during pregnancy. With GAVI's support for MICs, SA could consider introducing PCV 15 or PCV 20, once these vaccines are registered, without incurring additional costs. Additionally, a compelling economic case must be made to the government that sustainable access to affordable vaccines and AMR mitigation will decrease healthcare costs over the long term by reducing resource use and the length of hospital stays. Therefore, including immunisation in the next iteration of SA's National Action Plan on AMR would be beneficial and should highlight clear outcome indicators, such as increased vaccination rates based on specific targets and decreased incidence rates for vaccine-preventable diseases. The power of an effective communication team should not be underestimated. The success of many health-related policies, including vaccinations (childhood, life-course, epidemic-related, etc.), is often in the hands of the public will. The COVID-19 pandemic is an ideal example of this. The speed at which misinformation spread through social media, television and radio far outstripped how fast healthcare professionals could counteract it, resulting in an increase in vaccine hesitancy and a growing antivaccination mindset. Messages to the public must include all literacy levels by using layman's terms, breaking down complex concepts and using visual aids where possible. A top-down approach to improving public health literacy and awareness is to engage pharmacists to promote both immunisation and antimicrobial prescription stewardship. Including health-related topics, such as immunisation and AMR, in high school and tertiary education would also benefit public awareness.

The challenge of presenting the results of mathematical modelling to improve immunisation programmes and reduce AMR could be bypassed by involving policy-makers early in the process, thereby facilitating a better understanding and improved applicability of models to actionable policy. Surveillance used to collect data in these models could benefit from transitioning to web application-based methods for tracking AMR and immunisation.

Conclusion

Faced with evidence on the burden of AMR and mitigating power of vaccines within an AMS programme, it is critical for AMR and immunisation initiatives to harness the full potential of their collaboration. Data must be used to inform policies at the national level and support integrated research projects that can quantify vaccine impact on infectious diseases and AMR. The AMR mitigation potential of vaccines is an important metric that must be considered in their investment case. It will not only form the foundations of a One Health approach, but also provide a platform for more complex stewardship interventions.

Data availability

N/a.

Declaration

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Author contributions

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Conflicts of interest

None.

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The future of pharmacy in South Africa: embracing the digital revolution

Brent Sin Hidge, Rashmi Gosai, Nhlanhla G Mafarafara

South Africa's healthcare landscape is complex, marked by disparities in access, a high burden of disease, changing healthcare policies, and a growing and shifting demand for quality care. Against this backdrop is the proposed National Health Insurance (NHI), the rise of the Fifth Industrial Revolution (5IR), and the increasing role of artificial intelligence (AI) in healthcare and how pharmacy needs to play its part.

The pharmacy profession plays a crucial role, serving as an essential link between patients and healthcare services. It must embrace the transformative potential of digital technologies and IT infrastructure. This article examines the current state of pharmacy in South Africa, highlighting existing digital tools and outlining a vision for a technologically advanced future that enhances pharmacy practice and improves patient outcomes. To meet the current demand, substantial investment and recognition are necessary, especially for the introduction and rollout of technologies that will enhance efficiency.

Current State: A Mixed Bag of Progress and Gaps

Existing technologies include Pharmacy Management Systems (PMS) for dispensing, inventory management, and patient record keeping. The world is swiftly moving toward building infrastructure, knowledge, and practice systems driven by AI robotics and technologies that assist with online ordering, prescription refills, and patient convenience.

Here are four things that describe the current trends:

- AI-driven solutions, including automated dispensing, predictive stock management, and clinical decision support tools, are revolutionising medication management, improving efficiency, and reducing errors. However, the integration of clinical decision support systems, AI, and other advanced technologies into pharmacy practice is still in its infancy.
- Advanced technologies in patient care, including the integration of tele-pharmacy, wearable health devices, and personalised medicine, are expanding the pharmacist's role in chronic disease management, precision medicine, and remote patient care. In South Africa and many low- to middle-income countries, pharmacies still rely on manual processes, which takes time to handle, limiting efficiency and hindering data-driven decision-making. Another challenge is that the interoperability between different PMS systems is often lacking, making it difficult to share crucial patient information between healthcare providers and may impact patient safety.
- Access to digital tools and reliable internet connectivity remains a significant challenge, particularly in rural and underserved communities.
- Expansion of the role of pharmacists. Pharmacists worldwide are transitioning into clinical specialists in areas such as oncology, antimicrobial stewardship, and pharmacogenomics, ensuring optimal medication use and improving patient outcomes.

The vision for the future of pharmacy

Looking into the future, let us look into the pharmacy's role and considerations in NHI, strengthening hospital pharmacy, and digital transformation.

Pharmacy's role in NHI

Hospital pharmacists face unique challenges, including medicine shortages, underfunding, and heavy workloads. Addressing these issues requires:

- Increased investment in pharmaceutical supply chain optimisation to prevent stockouts.
- Strengthened digital health integration, including electronic prescribing and AI-driven inventory management.
- Expansion of clinical pharmacy services in public hospitals to reduce patient complications and hospital readmissions.

Strengthening Hospital Pharmacy

Pharmacists should present data-driven business cases showing how pharmacy innovations:

- Reduce medication errors, lowering legal and financial risks.
- Optimise medicine stock, minimising waste and improving cost-efficiency.
- Improve hospital accreditation and regulatory compliance, ensuring smooth operations.
- Decision makers should look at increasing funding for the provision of pharmaceutical care in terms of technologies, human resources, and infrastructure development.
- Secure funding for the implementation of new pharmacy reforms and procurement of new technologies.
- Pharmacists should take charge of developing and implementing data-driven business cases that positively impact both financial

(contingent liabilities and related financial risks) and clinical value through innovation.

Digital transformation: Imagine a digitally empowered pharmacy landscape

In the foreword of the National Digital Health Strategy for South Africa (2019-2024), Minister of Health, Dr Aaron Motsoaledi wrote "South Africa has fully embraced the potential of digital health technologies to improve the quality and coverage of healthcare, increase access to services and skills, and promote positive changes in health behaviours to prevent the onset of acute and chronic diseases. This, combined with emerging technological advances, sets the scene for digital health to have a larger contribution to our health and well-being more than ever before." This vision remains partially realised; it was loaded with five strategic principles of a person-centred focus, expanded access, innovation for sustainable impact, digital health workforce for economic development, and a whole-of-government approach. To fully realise the potential of pharmacy in South Africa, we need a comprehensive and ambitious vision for its digital future underpinned by patient-centred care and system efficiency and capacity building. Here, we present a 10-point digital pharmacy concept to realise this vision:

1. Universal Access to PMS and Interoperability

Every pharmacy, regardless of size or location, should have access to a good, reliable, and user-friendly PMS. These systems must be interoperable, allowing for the seamless exchange of patient information between pharmacies, hospitals, clinics, and other healthcare providers.

2. Integration of Clinical Decision Support Systems (CDSS)

PMS systems should be integrated with CDSS to provide pharmacists with real-time alerts and recommendations regarding drug interactions, contraindications, and appropriate dosages. It will also help identify patients at high risk for specific conditions, such as diabetes or cardiovascular disease, and prompt them to provide targeted and personalised interventions. CDSS can significantly enhance the accuracy and safety of medication dispensing and improve patient outcomes.

3. Expansion of Tele-pharmacy Services

Tele-pharmacy, the delivery of pharmaceutical care through telecommunications technologies, has immense potential to improve access to medication and pharmaceutical services, particularly in remote and underserved areas. Through video consultations, pharmacists can provide medication counselling, monitor adherence, manage chronic conditions remotely, and specialise in medication therapy management.

4. Leveraging AI and Machine Learning

AI and machine learning can revolutionise pharmacy practice in several ways. AI-powered systems can analyse vast amounts of patient data to identify patterns and predict individual responses to medications. This can enable personalised medication therapy and improve treatment outcomes. AI can also be used to automate repetitive tasks, such as prescription verification and dispensing, freeing up pharmacists' time to focus on direct patient care. Furthermore, AI-powered chatbots can give patients 24/7 access to information about their medications and answer common medicine-related questions.

5. Development of a National Drug Database

A comprehensive national drug database linked to health information exchange (HIE) technologies is essential for ensuring medication safety and preventing drug abuse. Pharmacists can use this database to verify prescriptions, identify potential drug interactions, and track medication use patterns. The database can also be used to monitor drug shortages and identify counterfeit medications.

6. Enhanced Cybersecurity Measures

As pharmacy systems become increasingly digital, robust cybersecurity measures are essential to protect patient data and prevent cyberattacks. Pharmacies must implement strong passwords, encryption, and other security protocols to safeguard sensitive information. Regular security audits and staff training are also crucial to ensure ongoing protection against evolving cyber threats.

7. Investing in Digital Literacy and Training

The successful implementation of digital technologies in pharmacy requires a skilled workforce. Pharmacy personnel need to be trained on how to use new systems and technologies effectively. Digital literacy training should be incorporated into pharmacy education curricula either as a module with generic learning outcomes or as an elective micro-certification module, postgraduate programs, and continuing professional development programs. Furthermore, ongoing support and training should be provided to pharmacy staff to ensure they can keep up with the latest advancements in digital health.

8. Addressing the Digital Divide

Bridging the digital divide is critical to ensuring that all South Africans can benefit from the digital transformation of pharmacy. Government and private sector partnerships are needed to expand access to affordable internet connectivity, particularly in rural and underserved communities. Furthermore, initiatives should be implemented to provide digital literacy training to patients, empowering them to engage with digital health solutions.

9. Regulatory Framework and Data Governance

A clear and supportive regulatory framework is essential to guide the implementation of digital technologies in pharmacy. Regulations should address issues such as data privacy, ethical use, security, and interoperability.

10. Collaboration and Innovation

The digital transformation of pharmacy requires collaboration between various stakeholders, including pharmacists, healthcare providers, technology developers, policymakers, and patients. Open communication and collaboration are essential to identify challenges, develop solutions, and ensure that digital technologies are implemented in a way that meets the needs of all stakeholders.

Conclusion

Fostering a culture of innovation within the pharmacy profession is crucial to driving the development and adoption of new digital health solutions. The future of pharmacy is not just about dispensing medicine—it is about leadership, innovation, and transforming healthcare. Whether in the public or private sector, pharmacists must take the lead in driving innovation, securing investment, and positioning pharmacy as a key component of healthcare delivery. By investing in robust IT infrastructure, promoting interoperability, integrating advanced technologies, and addressing the digital divide, we can create a digitally empowered pharmacy landscape that enhances patient care and service delivery efficiency. This transformation requires a concerted effort from all stakeholders, guided by a clear vision and a commitment to innovation.

Call to Action

We should create a focused expert Technology Advisory Group to exchange views on current activities, problem areas, best practices, and more in technology.

News

The 69th SAPSF Conference: uniting future pharmacists in Gqeberha

Tiko Khosa

Former Media and Communications Officer, SAPSF

The 69th South African Pharmaceutical Students' Federation (SAPSF) Conference, hosted by the Port Elizabeth Pharmacy Students Association (PEPSA), was a significant milestone in the Pharmacy student community. Taking place from 31 January to 02 February at the scenic Willows Resort and Conference Centre in Gqeberha, Eastern Cape. It was the first coastal SAPSF conference since 2015. The event was steered by Conference Convenor, Gamuchirai Nyereyegona, along with a dedicated reception committee, ensuring a well-organised and impactful experience for all attendees. The conference revolved around the theme: **"Shaping the Future of Students through Innovation, Collaboration, and Pharmaceutical Advancements."**

Kicking off the main conference

On Saturday, 01 February, the main conference commenced with an inspiring opening address by Ms Celeste Naude from the Nelson Mandela University Pharmacy Department. Drawing from the venue's name, The Willows, she symbolised the willow tree as a representation of pharmacy students—emphasising resilience and having a strong academic foundation. She further urged attendees to leverage the conference as a networking platform.

Following her, Dr Stavros Nicolaou, a Group Senior Executive for Aspen Pharma Group and a recipient of the prestigious Industrial Pharmacy Section Medal at the 2024 FIP Congress, delivered an insightful virtual address. He spoke about his role during the COVID-19 pandemic as a member of the President's advisory committee, symbolising that pharmacists have a seat at the table. He called on students to embrace their roles as future leaders in the pharmaceutical industry and to make a meaningful impact in patient care and community service.

Ms Mandisa Ngcakani, the Alternate Director of the Independent Community Pharmacy Association (ICPA), addressed the ethical dilemmas faced by those owning independent pharmacies, focusing on finding a balance between passion and profit. She reminded students, "We cannot get to profits without caring for our patients."

Ms Alice Lategan, Chairperson of the PSSA Cape Midlands Branch, shared her journey in pharmacy and encouraged students to find their voice and be actively involved in the profession.

A session led by Lt Colonel Precious Ncayiyana, explored the role of pharmacists in the military, shedding light on this unique and impactful career path. This was followed by the keynote address from Ms Refiloe Mogale, Executive Director of the PSSA, who introduced the PSSA sectors and their advocacy roles for pharmacists. She also discussed emerging pharmaceutical specialties, particularly in response to unemployment challenges, and encouraged students to take on leadership roles and not merely be spectators.

Networking and celebration

After an enlightening day of discussions, students enjoyed a private beach fun day, fostering inter-branch connections and camaraderie. In the evening, the Gala Dinner brought together delegates and distinguished guests. One of the key highlights was the launch of the latest SAPSF publication titled "The Final Chapter of the 2023/24 PresCo", presented by the SAPSF Media and Communications Officer, Mr Tiko Khosa and Editor, Ms Stacey Kundiona.

The Presidential Committee honoured guests, including esteemed speakers and Ms Ntombizodwa Luwaca, Chairperson of the PSSA Young Pharmacists' Group, with special tokens of appreciation. The evening concluded with a motivating speech from Ms Refiloe Mogale, who emphasised the importance of professional networks, mentorship, and remaining connected to the broader pharmacy community.

Final day: reflection and transition

The last day of the conference began with a scenic hike around Nelson Mandela University (NMU), allowing students to explore landmark points and reflect on their journey. The final session of the conference featured branch reports and a Clinical Skills Competition, led by Ms Vuyiseka Ntsalu from NMU's Pharmacy department.

Following the competition, the 2023/24 SAPSF Presidential Committee, led by Mr Tshepiso Masiganuga, was officially dissolved, paving the way for the election of a new leadership team that will carry SAPSF into its next chapter.

Conclusion

The 69th SAPSF Conference was a resounding success, reinforcing the importance of collaboration, leadership, and professional growth within the student community. With a rich lineup of speakers, engaging discussions, and meaningful networking opportunities, this conference set a strong foundation for the future of pharmacy students in South Africa. As SAPSF continues to foster a culture of innovation and excellence, the impact of this gathering will undoubtedly resonate in the years to come.

Cum Laude

Academy of Pharmaceutical Sciences

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Call for Registration and Abstracts for the 2025 conference of the Academy of Pharmaceutical Sciences (APSSA)

It is with great excitement that we announce the call for registration and abstract submissions. You are invited to come and enjoy spring in Cape Town. This year's conference will be a season of new growth and rejuvenation bringing together academic leaders, researchers, pharmacy students, and healthcare professionals to explore ground breaking innovations and research in the pharmaceutical and healthcare industry. The APSSA conference promotes and encourages participation by our younger members through the Young Scientist Competition. We also acknowledge excellence in research, teaching and learning through our Publication Awards and Teacher of the Year Award.

The APSSA is a society with a focus on promoting research in the pharmaceutical sciences. As a sector of PSSA (Pharmaceutical Society of South Africa), the Academy has members from across South Africa and abroad. The 2025 conference is hosted by the School of Pharmacy, University of the Western Cape.

EARLY REGISTRATION FEE:
21 February 2025 - 15 June 2025

STANDARD REGISTRATION FEE:
16 June 2025 - 18 August 2025
No onsite registration

SUBMISSION OF ABSTRACTS:
Opens 21 February 2025 and closes 30 May 2025

LINK TO REGISTER:
https://forms.office.com/r/idZe5MXCaS

Detailed information regarding the registration fees, abstract requirements and competitions are available on the conference registration web page. (https://pssa-academy.org.za/)

FOR ANY FURTHER ENQUIRIES, CONTACT:

nitsa@pssa.org.za
(Registration, abstract, competitions and invoices)

mviljoen@uwc.ac.za
(conference convener)

ACCOMMODATION:

Accommodation in Cape Town is very popular. Prices will vary and availability will be limited. If you would like to stay at the conference venue please book early and directly via their website:

https://www.lagoonbeachhotel.co.za/ **OR**

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School of PHARMACY
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sapj

CPD questionnaire • March/April

Management of erectile dysfunction

1. Which of the following is considered a first-line pharmacotherapeutic agent for erectile dysfunction (ED)?

a Intracavernosal injection of Alprostadil
b Penile prosthesis implantation
c Oral phosphodiesterase 5 inhibitors (PDE5Is)
d Testosterone-replacement therapy, regardless of hormone levels

2. Several health conditions are associated with an increased risk of erectile dysfunction. Which of the following is highlighted as sharing common risk factors and underlying pathophysiological mechanisms with ED?

a Osteoporosis
b Cardiovascular disease (CVD)
c Chronic obstructive pulmonary disease (COPD)
d Glaucoma

3. What is the primary mechanism of action of PDE5 inhibitors in the treatment of ED?

a Increasing testosterone production
b Relaxing the smooth muscle in the prostate gland
c Preventing the degradation of cyclic guanosine monophosphate (cGMP) in the corpus cavernosum
d Stimulating the release of nitric oxide from nerve terminals

4. What potential impact of COVID-19 infection on erectile function has been identified?

a Increased libido due to reduced social interaction
b Elevated testosterone levels promoting heightened sexual drive
c Presence of SARS-CoV-2 in the vascular endothelial cells of the penis
d Decreased risk of endothelial dysfunction

Investigating the role of knowledge management in the pharmaceutical sector: a systematic review

5. Which of the following is NOT the consequences of inadequate knowledge management strategies highlighted in the problem statement?

a Poor regulatory compliance
b Patient safety concerns
c High turnover of pharmacists in hospitals
d Medication errors
e Supply chain disruptions

6. What best describes the concept of "Ba'?

a It is a type of tacit knowledge
b It is a type of explicit knowledge
c It exists in mental form only
d It is the same as the SECI model
e It is a shared platform for knowledge creation and sharing

7. The facilitators and barriers of knowledge management can be classified into:

a Individual, hospital-based, technological
b Individual, technological, organisational
c Hospital-based, individual, organisational
d Hospital-based, community-based, individual
e Hospital-based, community-based, technological

8. The outcomes of interest in this study include the following EXCEPT:

a Knowledge retention
b Absorptive capacity
c Knowledge sharing
d Innovation
e Competitive advantage

Clearing the air: methods and challenges of smoking and vaping cessation

9. According to the text, which of the following is a reason commonly cited by users for purchasing and using electronic cigarettes?

a Increasing social acceptance compared to traditional smoking
b Alleviating withdrawal symptoms from traditional cigarettes
c Being a less addictive alternative to traditional smoking
d Having a wider availability than traditional cigarettes

10. What is the primary drug in tobacco products that produces dependence in smokers, according to the text?

a Tar
b Carbon monoxide
c Nicotine
d Dopamine

11. What was the severe pulmonary illness officially recognised in 2019 as being linked to the use of e-cigarettes or vaping products?

a COPD
b Asthma
c EVALI
d Tuberculosis

12. According to the text, what is a key distinction between smoking conventional cigarettes and vaping?

a Both deliver the same amount of nicotine
b Both involve the ignition of a substance
c The form of inhalation—smoke versus vapour
d Both have been studied extensively for long-term health effects

13.	**What effect can even a few minutes of vaping have on the lungs, according to the text?**
a	It can immediately improve lung function
b	It has no immediate impact on lung health
c	It can cause changes in how the lung functions and exacerbate inflammation
d	It significantly reduces the risk of respiratory symptoms
14.	**In 2019, EVALI was officially linked to the use of e-cigarettes or vaping products and was associated with which substance?**
a	Nicotine
b	Tetrahydrocannabinol (THC)
c	Cannabidiol (CBD)
d	Vitamin E acetate (VEA)

Overview and management of colds and flu

15.	**What is the primary cause of the common cold?**
a	Influenza virus
b	Rhinovirus, coronavirus, or adenovirus
c	Bacterial infections
d	Fungal infections
16.	**Which of the following interventions is most effective in preventing the common cold?**
a	Vitamin C supplements
b	Zinc supplements
c	Handwashing and physical interventions
d	Echinacea supplements
17.	**What is the recommended treatment for influenza to reduce the duration of symptoms?**
a	Antibiotics
b	Over-the-counter pain relievers
c	Neuraminidase inhibitors (e.g. oseltamivir)
d	Corticosteroids
18.	**Which group of individuals requires priority vaccination against influenza?**
a	Healthy adults aged 18-40
b	Pregnant women, immunocompromised individuals, and those with chronic conditions
c	Children under two years without chronic conditions
d	Individuals with mild allergies
19.	**What is the primary reason antibiotics should not be used to treat colds and flu?**
a	They are ineffective against viral infections
b	They can cause allergic reactions
c	They are too expensive
d	They are only available by prescription

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 • January/February 2025

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

13. c 14. a 15. b 16. a

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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. **6.** Data on file, iNova Pharmaceuticals 2024.

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