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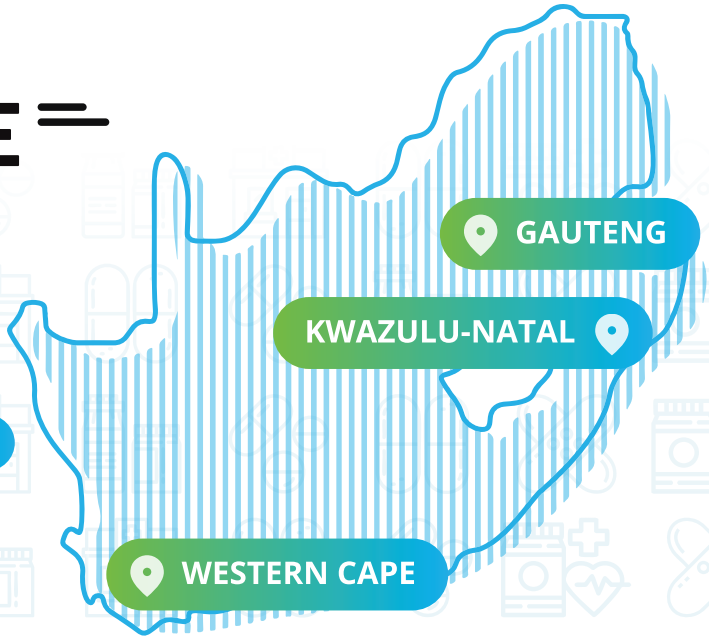

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SAPJ is aimed at the continuing professional development of the South African pharmacist in a variety of practice settings, including clinical pharmaceutical care practitioners in a community or hospital pharmacy environment, and pharmacists in academic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

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

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

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

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Reference: 1. Lokkegaard E et al. Eur Heart J 2008;29:2660-8. 2. Renoux C et al. BMJ 2012;340:c2519. 3. de Lauzon-Guillain, Fournier A, et al. Diabetologia 2009;52:2092-100. 4. L'Hermite M et al. Maturitas 60;2008:185-201. 5. Mueck A.O. CLIMACTERIC 2012:15(Suppl 1):11–7. 6. P. Stute et al. Climacteric 2018, 21:2, 111-122.

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Editorial

Pharmacy's Cassandra Moment

In Greek mythology, Cassandra was blessed with the gift of prophecy but cursed never to be believed. It is an apt metaphor for pharmacy in 2026. For years, pharmacists have warned about the dangers of unchecked antimicrobial resistance, fragile medicine supply chains, underinvestment in training, and the slow erosion of our workforce. We have spoken in meetings, at ward rounds, in boardrooms, on social media, and in the pages of this journal.

In this issue, those warnings take concrete form, the pharmacist internship crisis described by the Pharmaceutical Society of South Africa (PSSA) as a public health concern; the SAAHIP Presidential Report's vision for a "Future Ready" hospital pharmacy; and the President's reflection on innovation from the "tiekie boks" to artificial intelligence. Together, they remind us that pharmacy is not short of insight or evidence. We are short of ears willing and systems able to listen.

Like Cassandra standing on the walls of Troy, many in our profession are left watching predictable problems unfold, preventable stockouts, inappropriate antibiotic use, graduates without posts, and patients who lose trust in a health system that feels indifferent to their suffering. These are not abstract risks. They are now part of daily practice.

Prophecy one: the cracking internship pipeline

The first prophecy concerns our own people. South Africa continues to operate below international benchmarks for pharmacist to population ratios, and every pharmacist in the system matters. Against this backdrop, the shortage of pharmacist internship posts in 2026 is far more than an administrative inconvenience. As the PSSA argues in this issue, it is a systemic risk to medicine access, pharmaceutical governance, and patient care.

An internship is not an optional enrichment year; it is the legally required bridge between qualification and practice. Without it, a Bachelor of Pharmacy degree remains academic. When internship posts are delayed, reduced, or not advertised, that bridge collapses. In KwaZulu-Natal, an initial decision not to advertise posts was reconsidered after *engagement,* but still left more than a hundred graduates without placement. In other provinces, uncertainty and late decisions have held graduates in limbo, unable to serve patients or proceed to community service.

Cassandra warned that the wooden horse at the gates of Troy was not a gift but a threat. When pharmacists warn that chronic understaffing and interruptions in the internship pipeline will hollow out our profession, we are saying the same today's disrupted internship is tomorrow's workforce gap. The PSSA's new Pharmacy Human Resources for Health (HRH) Project is one response a move from reactive crisis management to proactive workforce planning that aligns graduate output, funded posts and service needs.

Prophecy two: AMR, clinical pharmacy and hospital practice

Nowhere is the Cassandra metaphor more apt than in antimicrobial resistance. Pharmacists, together with infectious diseases clinicians and microbiologists, have been warning that our antibiotic use is unsustainable. We have called for robust antimicrobial stewardship (AMS) in every hospital, responsible prescribing in primary care, and consistent patient education in every community pharmacy. We know what is coming if we fail, common infections becoming difficult to treat, routine surgery becoming high risk, and vulnerable patients dying from organisms no longer responsive to available therapy.

The SAAHIP Presidential Report in this issue illustrates both the scale of the challenge and the profession's determination to respond. Under the banner of being *"Future Ready 5.0",* SAAHIP has aligned its work to four pillars shared vision, collaboration, commitment and innovation and to national projects on HR for health, quality and safety, access to essential medicines, clinical pharmacy and AMS, and the ethical use of digital health and AI. Branches have hosted CPDs, outreach campaigns and projects that speak directly to these themes: vaccination drives, guideline based updates on chronic conditions, AMS focused events, and intern orientation workshops preparing pharmacists for clinical roles.

Yet in many facilities, pharmacists who are willing and able to lead AMS and clinical pharmacy services still find that posts are unfunded, time is squeezed, and their role in multidisciplinary teams is underutilised. Cassandra saw the fall of Troy and was dismissed as hysterical. When pharmacists insist that antibiotics are a shared, finite resource not a commodity to be dispensed on demand we are often treated the same way. The work that SAAHIP reports in this issue shows that we are not resigned to that fate; we are building structures that can turn early warnings into sustained change.

Prophecy three: innovation and AI tool or trap?

The third prophecy concerns innovation itself. In the President's message in this issue, we are taken on a journey from the "tiekie boks" and handwritten labels, through early dispensing software, to robotic dispensing and AIenabled systems. Dispensing technology, integrated records and realtime stock systems have already improved safety, efficiency and accountability, particularly during periods of strain such as the COVID-19 pandemic.

Artificial intelligence is the latest chapter in this story. AI tools promise support for medication therapy management, interaction checking, pharmacovigilance, shortage prediction and more personalised care.

Used wisely, they could free pharmacists from repetitive tasks and create more time for direct patient engagement. Used poorly, they could distance us from patients, entrench inequities, or be used to justify further cuts in posts on the basis that "the system" can take over.

Here, too, pharmacists are offering early warnings. We caution that AI is neither a panacea nor a threat in itself; it is a tool that must be shaped by professional judgment, ethics and context. Algorithms trained on incomplete or biased data can amplify harm. Any digital system implemented without meaningful pharmacist involvement risks undermining the very safety it claims to support. SAAHIP's emphasis on "embracing innovation" within a framework of patient centred care, multidisciplinary collaboration and quality improvement echoes this message: innovation must strengthen, not weaken, the human connection at the heart of pharmacy.

From cursed prophet to indispensable partner

If pharmacy is to escape Cassandra's fate, two things must change: how we speak and how others respond.

First, we must continue to speak, but in ways that health systems cannot easily ignore. That means translating concerns about internships, AMR and digitalisation into costed, data driven proposals with clear outcomes. The PSSA HRH Project, with its focus on workforce modelling, distribution, specialist roles and integration into multidisciplinary teams, is one example. SAAHIP's national projects similarly turn frontline frustrations into organised programmes on quality, access and AMS.

Second, policymakers and health leaders must begin to treat pharmacists not as peripheral technicians but as indispensable partners in designing the future. When workforce plans are drafted, when budgets are allocated, when AMR strategies are revised, when AI tools are procured, pharmacists should be at the table from the start. Our warnings about internship bottlenecks, medicine supply, antibiotic misuse and the risks and opportunities of AI are not professional complaints; they are early warning signals from those closest to the system.

Cassandra's tragedy is that she was condemned to be right and ignored. Pharmacy does not have to accept the same ending. In every province that protects and expands funded internship and community service posts, in every hospital that supports clinical pharmacy and AMS, in every institution that implements AI with pharmacists leading its design and governance, we begin to rewrite the story.

The contributions in this issue, from the analysis of the internship crisis to the SAAHIP report on a profession striving to be "Future Ready", to the reflection on innovation show a profession that sees clearly and is acting collectively. The question is whether the broader health system will listen in time.

Natalie Schellack
Editor: SA Pharmaceutical Journal

President's Message

Innovation in Pharmacy: From the "Tiekie Boks" to Artificial Intelligence

When I first arrived at university, innovation looked very different from what it does today. I did not have a mobile phone in my pocket. Communication with home required planning. If you wanted to phone your parents, you had to find a telephone booth, dig through your pockets for coins, and hope the line did not cut out halfway through the conversation. Many South Africans of my generation will remember the familiar sound and feel of the "*tiekie boks*", a small but essential piece of technology that connected us to the people who mattered most.

A few years later, the first cellphones started to appear. They were bulky, expensive, and had batteries that never seemed to last long enough. Messaging, as we know it today, did not exist. We entered the era of Mxit and BlackBerry Messenger. Communication became faster and cheaper, but it was still far from seamless. Many of us developed our own systems to save airtime. One missed call meant, "Can I visit?" Two missed calls meant, "Yes." It was innovation shaped by necessity, context, and limited resources.

We have come a long way since then. Today, many of us sit in meetings on Zoom while simultaneously responding to WhatsApp messages and reviewing documents. This is all done from a single device that fits into the palm of our hand. What once required multiple tools, locations, and a great deal of patience can now be done instantly.

Innovation in pharmacy is not new, but its pace has accelerated significantly. Consider dispensing, which is one of the most fundamental activities in our profession. There was a time when medicine labels were typed or handwritten (like during my community service year), carefully checked, and reprinted if even the smallest error occurred. Records were paper-based, filing cabinets were full, and retrieving information often depended on memory as much as documentation.

Today, many pharmacies use integrated dispensing software that links patient records, medication histories, and stock management systems. Labels are printed automatically, warnings are standardised, and clinical checks are embedded into workflows. Robotic dispensing machines, once viewed as futuristic luxuries, are now operational realities in several hospital and community pharmacy settings. These systems improve efficiency, reduce dispensing errors, and allow pharmacists and pharmacy personnel to spend more time on direct patient care.

Innovation has also reshaped how we manage supply chains, cold-chain monitoring, and regulatory compliance. Barcoding, electronic stock control, and real-time reporting have strengthened accountability and improved medicine availability. During public health emergencies, such as the COVID-19 pandemic, these innovations proved critical in supporting continuity of care and rapid response.

Looking ahead, artificial intelligence (AI) is increasingly part of conversations about the future of pharmacy. AI has the potential to support medication therapy management, identify drug–drug interactions more effectively, assist with pharmacovigilance, and analyse large datasets to inform clinical decision-making. Predictive analytics could help anticipate medicine shortages, while intelligent systems may support adherence monitoring and more personalised care.

However, while technology is impressive, it is important to be clear about its role. AI is a tool, not a replacement for professional judgment. Pharmacy remains a people-centred profession. On the frontline, whether in a busy community pharmacy, a hospital ward, or a primary healthcare clinic, patients do not engage with algorithms. They engage with pharmacists and pharmacy personnel.

Innovation must therefore be embraced in a way that strengthens, rather than weakens, the human connection that defines our profession. Technology should free up time for meaningful patient interaction, not distance us from it. It should support safer practice, better outcomes, and improved access, particularly in a country like South Africa, where health system challenges are complex.

This brings us to an important question: how do we, as a profession, actively embrace innovation rather than simply react to it? Innovation does not only happen in boardrooms or technology companies. Often, it emerges from practice when pharmacists who see inefficiencies, identify unmet needs, and develop practical solutions within real-world constraints.

As the Pharmaceutical Society of South Africa, we believe innovation must be purposeful, ethical, and inclusive. It should enhance professional practice, strengthen the health system, and ultimately improve patient care.

As I reflect on how far we have come, from the "*tiekie boks*" to smartphones, from handwritten labels to robotic dispensing, from paper files to AI-enabled systems, I am reminded that innovation is not something to fear. It is something to shape.

On that note, I must conclude this reflection and send a WhatsApp message to Nitsa at the National Office to arrange flights for my next meeting. Some things, after all, have changed forever.

Renier Coetzee
PSSA President

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PSSA Perspectives

Pharmaceutical Society of South Africa

The pharmacist internship crisis is a public health concern

South Africa continues to operate well below international benchmarks for pharmacist-to-population ratios, with significantly fewer pharmacists per 100 000 people than comparable middle-income countries.[1] In a health system already facing medicine shortages, rising antimicrobial resistance, and increasing service pressures, every pharmacist in the system matters. Against this backdrop, the growing shortage of pharmacist internship posts for 2026 is more than an administrative challenge. It signals a systemic risk to medicine supply, pharmaceutical governance, and patient care. The Pharmaceutical Society of South Africa (PSSA) therefore raises this matter not merely as a professional concern but as a public health priority.

An internship is a legally required step before a pharmacy graduate may register as a practising pharmacist, a mandated bridge between qualification and professional practice. Without it, a Bachelor of Pharmacy degree remains academic. Graduates cannot practise, serve patients, or proceed to community service. The pharmacist workforce pipeline, from student to intern, from intern to community service pharmacist, and ultimately to independent practitioner, must function as an uninterrupted continuum. When one segment fails, the consequences echo through the entire system. Interrupting internships today creates workforce gaps tomorrow.

In several provinces, particularly KwaZulu-Natal and Mpumalanga, pharmacist internship posts were delayed, reduced, or not advertised initially due to funding constraints. While some provinces have largely completed appointments, uncertainty in others has left a significant number of qualified graduates in limbo. In KwaZulu-Natal, an initial decision not to advertise pharmacist internship posts was reconsidered following engagement; however, the number of posts was significantly reduced, leaving over 100 graduates without placements. Private-sector opportunities, which have historically served as a safety net for training capacity, appear more constrained this year, further narrowing options for affected graduates.

Pharmacy has long demonstrated flexibility by allowing internships in the private sector, including industry. While this flexibility has supported training continuity and health system resilience, it is increasingly being interpreted as a substitute for creating funded public-sector pharmacist posts. This trend is deeply concerning. When funded posts are not created and responsibility is implicitly shifted away from coordinated state workforce planning towards market absorption, professional trust is eroded and the pharmacist training pipeline is destabilised, leaving graduates in a precarious position and weakening long-term public-sector pharmaceutical capacity.

Moreover, there is no standardised national allocation system for pharmacy internships. Processes vary by province, leading to uneven outcomes and communication gaps. The Internship and Community Service Programme (ICSP) platform, which facilitates the allocation of internship and community service posts for health professionals within the framework of the Health Professions Act, should be utilised to support the allocation of pharmacists' interns and recognise their training under the Pharmacy Act. Although pharmacy requires the completion of a statutory internship prior to community service, integrating pharmacy internship allocation into the ICSP platform could enhance transparency, equity, and coherence in human resources planning for health.

While this is going on, the PSSA engaged extensively with stakeholders, including the South African Pharmacy Council (SAPC), the National Department of Health (NDoH), Provincial Departments of Health, universities, private hospital groups, industry stakeholders, and professional networks. These engagements included formal submissions, direct negotiations, and urgent advocacy to reconsider decisions and expand posts where possible. While the efforts and outcome were not sufficient to absorb all graduates, they demonstrated that dialogue does produce movement. Workforce funding decisions are complex and compete with multiple urgent health priorities.

This episode underscores a broader and more persistent challenge, the lack of coordinated, evidence-based, long-term pharmacy workforce modelling. Moreover, there is no standardised national allocation system for pharmacy internships. Processes vary by province, leading to uneven outcomes and communication gaps. The Internship and Community Service Programme (ICSP) platform, already used for medical graduates, could be extended to pharmacy to enhance transparency, equity, and planning coherence. Standardisation would not eliminate funding constraints, but it would significantly improve coordination and predictability.

The PSSA, in response, has advanced a national Pharmacy Human Resources for Health (HRH) Project. The initiative aligns with the National HRH Strategy 2030 and seeks to ensure the optimal development, deployment, and recognition of the pharmaceutical

workforce and to align graduate output, funded posts, service delivery needs, and future reforms. Its strategic focus includes:

- Workforce planning and provincial distribution
- Evaluation and optimisation of community service
- Recognition of specialist pharmacist roles
- Integration of pharmacists in multidisciplinary care teams
- Formal inclusion of mid-level pharmacy personnel
- Evidence-based advocacy and interprofessional visibility

The HRH Project is a modelled workforce plan that will address pharmacist unemployment and underutilisation and calls for structured collaboration with government, academia, regulators, and private-sector employers. It will also enable all these partners to anticipate capacity gaps, secure appropriate funding allocations, and prevent recurring disruptions in the professional continuum. The objective is to move from reactive crisis management to proactive system design.

This moment calls for unified, responsible engagement with pharmacists being prioritised in health workforce planning and budgeting processes. It must not fracture the profession but incite it to action. Ensuring the availability of funded internship and community service posts is foundational to medicine access and patient safety. The cost of underinvestment today will be borne by the health system tomorrow. Training capacity is a shared responsibility, and where feasible, expanding accredited internship sites, pharmacists' willingness to train interns, investing in tutor development, and participating in coordinated workforce planning are investments in system stability. Collaboration on data-sharing, workforce dashboards, and curriculum alignment is essential to prevent recurring mismatches between graduate production and absorption capacity.

South Africa cannot afford instability in its pharmacist training continuum. Protecting internship posts is not merely about professional progression. It is about safeguarding the safety of medicines, promoting rational medicine use, and delivering patient-centred care across the country. The 2026 internship crisis should be a turning point, moving from fragmented planning to coordinated strategy, from reactive allocation to proactive modelling, and from perceived silence to structured solidarity. The PSSA will continue to stand with our interns, not only in words, but in sustained, evidence-based action.

Reference

1. https://www.fip.org/file/6343

PSSA/INSIGHT CPD programme

Module 1: Hypertension – an update

The first PSSA/INSIGHT Continuing Education (CE) module for 2026 on Hypertension is now available online. If you have not yet enrolled in this year's CE Programme, then now is the time to do so.

Hypertension is the most prevalent cardiovascular disorder in the world, yet most patients with hypertension do not have their blood pressure under control.

This module on hypertension is important as it outlines the current approach to the diagnosis and management of hypertension in the context of various diverging regional and international hypertension management guidelines.

The module will guide you through accurate blood pressure measurement for screening and monitoring, highlight the risk factors for primary hypertension, and reinforce hypertension staging, treatment targets and overall management.

As one of the most accessible healthcare professionals, pharmacists play a critical role in the prevention, early detection and ongoing management of hypertension. Strengthening your knowledge in this area will enable you to make a meaningful contribution to improved blood pressure control and reduced cardiovascular risk within the communities you serve.

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This module explores high blood pressure, including its causes, risk factors and management. It is aligned with the pharmacist's

hypertension module, enabling all pharmacy team members to engage confidently and professionally with patients and customers, and to contribute meaningfully to reducing the burden of high blood pressure within their communities.

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More than a year of training: The hidden anxiety of Pharmacy Internship

Thinavhuyo Musekene

Pharmacy internship is often described as a year of consolidation, a time to translate theory into practice, build confidence, and prepare for independent professional responsibility. It is presented as a bridge between student-hood and professional identity. While this is true, there is another, less-discussed dimension of internship: the quiet anxiety about what comes next.

For many interns, the year is not only about mastering dispensing accuracy, clinical decision-making or workflow management. It is also about confronting a pressing and often overwhelming question: *Where do I fit within this profession?*

The South African pharmacy sector is diverse and dynamic. Opportunities exist in hospital practice, community pharmacy, industry, academia, regulatory affairs, research, and public health. Yet access to these sectors is not always straightforward. Exposure during undergraduate training can be limited. Internship positions are typically concentrated in hospital or community settings, and positions in alternative sectors may be scarce, competitive or geographically restricted. As a result, many young pharmacists find themselves navigating a narrow pathway while knowing that the profession itself is far broader.

This structural bottleneck creates uncertainty. Interns may aspire to academia but find few entry points. Others may be drawn to industry or regulatory roles but lack networks, mentorship or clear guidance on transitioning. The difficulty is not necessarily a lack of ambition, but a lack of exposure and access. The pathway from internship to specialised or non-traditional sectors can feel opaque.

Beyond career logistics, this uncertainty carries a psychological weight. An internship is a high-responsibility year. Interns are expected to perform competently, adapt quickly, and contribute meaningfully to service delivery. At the same time, they are managing personal transitions, relocation, financial pressures, and the shift into full professional accountability. Layered onto this is the anxiety of employability and long-term career direction.

Conversations about early-career pharmacy often focus on competence and compliance. We speak about CPDs, examinations, and performance metrics. Less frequently do we acknowledge the internal pressures many interns carry: the comparison with peers who appear to have clear career trajectories, the fear of stagnation or the uncertainty of securing posts after community service. This is not a reflection of weakness; it is a natural response to a competitive and evolving professional landscape.

Recognising this hidden anxiety is not about criticising the system, but about strengthening it. Early-career pharmacists would benefit from structured career guidance embedded within internship and community service programmes. Greater exposure to alternative sectors during undergraduate training could broaden awareness of possibilities. Formalised mentorship platforms linking interns with pharmacists in academia, industry, research, and policy could demystify pathways that currently seem inaccessible.

At the same time, it is important to remind ourselves and our incoming colleagues that uncertainty does not equate to failure. Career paths in pharmacy are rarely linear. Many established professionals did not begin in the sector where they ultimately flourished. Exploration, redirection, and growth are part of professional development.

To the new interns: Welcome! You are joining a field that is resilient, adaptable, and deeply impactful. It is normal not to have every step mapped out. It is acceptable to question, to explore, and to evolve. Your internship is more than a checklist year; it is the beginning of professional self-discovery.

If we, as a profession, acknowledge both the opportunities and the anxieties of this transition period, we can create a more supportive and sustainable pathway for the pharmacists who will shape our future.

Why young pharmacists need each other: The power of the YPG

Thinavhuyo Musekene

The transition from internship to independent practice is one of the most formative phases in a pharmacist's career. It is a period marked by increased responsibility, growing clinical autonomy, and important professional decisions. Yet it can also be isolating. Many young pharmacists move from structured academic environments into workplaces where expectations are high, and support systems vary. In this space, connection becomes essential.

The Young Pharmacists Group (YPG) exists to bridge this gap.

Young pharmacists represent the future direction of the profession. They bring fresh perspectives on technology, public health, patient-centred care, and innovation. However, without platforms for engagement and mentorship, these voices can remain unheard. The YPG provides a structured forum where early-career pharmacists can connect, collaborate, and contribute meaningfully to professional discourse.

One of the most valuable aspects of the YPG is its emphasis on mentorship. The early years of practice are filled with questions that extend beyond clinical guidelines: How do I transition into academia? What steps are required to enter the industry? How do I balance postgraduate studies with full-time work? How can I develop leadership skills? These are questions best answered not only through policy documents but through lived experience shared by seasoned professionals.

A well-structured mentorship programme offers more than career advice. It provides reassurance, professional modelling, and access to networks that might otherwise be difficult to enter. Mentorship reduces the sense of professional isolation and normalises uncertainty. It allows young pharmacists to see that career progression is not a single ladder but a landscape of possibilities.

Beyond mentorship, the YPG creates opportunities for leadership development and advocacy. Engaging in professional committees, contributing to policy discussions, and participating in national initiatives fosters confidence and a sense of ownership in the profession. When young pharmacists are actively involved, they are not merely recipients of change; they become architects of it.

The YPG also strengthens professional solidarity. Pharmacy practice can vary significantly between sectors and regions. Through networking events, discussions, and collaborative projects, young pharmacists gain insight into diverse practice environments. This cross-pollination of ideas promotes innovation and a broader understanding of the profession's role within the healthcare system.

Importantly, involvement in the YPG signals a commitment to growth. It reflects a willingness to move beyond the minimum requirements of practice and engage in shaping the profession's trajectory. For early-career pharmacists navigating uncertainty about their place within pharmacy, such involvement can be grounding and empowering.

As we consider the challenges facing interns and community service pharmacists from limited sector exposure to career anxiety, organisations like the YPG become even more significant. They provide structure where there may be ambiguity and community where there may be isolation.

Young pharmacists do not need to navigate the early years alone. By participating in the YPG, seeking mentorship, and contributing actively, they invest not only in their own development but in the sustainability of the profession itself.

The strength of pharmacy lies not only in scientific knowledge or regulatory frameworks, but in its people, particularly those willing to support one another. The YPG embodies this principle. It reminds us that while the journey into professional maturity may be complex, it does not have to be solitary.

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

The influenza vaccine: essential insights for pharmacists in South Africa

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Abstract

Influenza remains a significant cause of seasonal illness and complications in South Africa, particularly among high-risk populations. This article reviews the influenza vaccination pathway from global strain selection to patient counselling, with a focus on the 2026 southern hemisphere vaccine composition. Key topics include identification of priority groups, optimal timing of vaccination, expected effectiveness, and the safety profile of inactivated influenza vaccines.

Practical guidance on vaccine administration and strategies for addressing common misconceptions are also discussed. Strengthening understanding of these elements supports informed clinical recommendations and may improve vaccine uptake, ultimately reducing the burden of influenza.

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The influenza vaccine: from strain selection to patient protection in South Africa

Influenza remains a significant and recurring public health challenge in South Africa, with seasonal peaks typically occurring between May and September. While often perceived as a mild, self-limiting illness, influenza can lead to severe complications, hospitalisation, and death, particularly in a population with a high burden of comorbidities such as HIV, tuberculosis, diabetes, and cardiovascular disease.[1]

Improving vaccination uptake requires more than simply making vaccines available. It depends on a clear understanding of how influenza vaccines are developed, who is most at risk, when vaccination should occur, and how to communicate effectively with patients. A strong grasp of the full pathway, from global strain selection to individual patient counselling, enables more confident recommendations and ultimately contributes to better public health outcomes.[2]

From global surveillance to local protection: understanding the 2026 vaccine

Influenza viruses are constantly evolving. Small genetic changes, known as antigenic drift, allow the virus to evade immunity from previous infection or vaccination.[3] This is why influenza vaccines must be updated annually.

The World Health Organization (WHO), through the Global Influenza Surveillance and Response System (GISRS), monitors circulating influenza strains across more than 140 laboratories worldwide. Data from these centres, including South Africa's National Institute for Communicable Diseases (NICD), is analysed to predict which strains are most likely to dominate in the upcoming influenza season.[3]

For the 2026 southern hemisphere influenza season, the recommended vaccine is trivalent, containing:

- A/Missouri/11/2025 (H1N1)pdm09-like virus
- A/Singapore/GP20238/2024 (H3N2)-like virus
- B/Austria/1359417/2021 (B/Victoria lineage)-like virus

The exclusion of the B/Yamagata lineage reflects its absence from global circulation since 2020.[3]

Once strain selection is finalised (typically in February for the southern hemisphere), vaccine manufacturers begin production, a process that must be completed in time for distribution before the winter season.

In South Africa, vaccine composition aligns with WHO recommendations, ensuring relevance to local epidemiology and circulating strains.

Understanding this process reinforces a key message: annual vaccination is essential because both the virus and immunity change over time.[1,4]

Who should be prioritised for vaccination?

Although influenza vaccination is recommended for everyone aged 6 months and older, certain groups are at significantly higher risk of severe disease, complications, and hospitalisation should they become ill with influenza.

High-risk groups include:

- Pregnant women, at any stage of pregnancy and postpartum
- People living with HIV, due to impaired immune responses
- Individuals with chronic medical conditions, including:
  - Diabetes mellitus
  - Chronic lung disease (asthma, COPD)

- Cardiovascular disease
- Tuberculosis
- Chronic kidney disease
- Obesity

- Older adults (≥ 65 years)
- Children under 5 years, especially those younger than 2 years
- Healthcare workers, due to occupational exposure[1,4-6]

South African surveillance data show that influenza-associated hospitalisation is highest among young children and individuals with HIV or TB, reinforcing the need for targeted vaccination strategies.[1]

It is also important to recognise less commonly highlighted risk groups, such as individuals with neurological conditions or severe obesity (BMI ≥ 40), who may also experience worse outcomes.[7]

Identifying these individuals often occurs during routine interactions, reviewing medication histories, identifying chronic therapies, or recognising pregnancy. These encounters provide important opportunities to recommend vaccination.

Vaccination also contributes to herd immunity, reducing transmission within communities and protecting vulnerable individuals.[5]

Timing and seasonality: when should vaccination occur?

The timing of influenza vaccination is critical to ensure optimal protection during peak transmission.

In South Africa:

- Vaccines are typically available from mid-March.
- Influenza activity usually peaks between May and September.[1]

Vaccination should ideally occur before the onset of peak transmission, allowing time for immunity to develop.

Key counselling points:

- Protective antibodies develop approximately two weeks after vaccination.[4]
- Early vaccination provides optimal protection and will last for the entire flu season and no additional vaccine doses are recommended.[8]
- Vaccination remains beneficial even later in the season.[8]

Annual vaccination is required because:

- Influenza viruses mutate continuously.[5]
- Vaccine-induced immunity declines over time.[4]

Even when strains remain similar, waning immunity reduces protection without revaccination.

Vaccine effectiveness: setting realistic expectations

The influenza vaccine does not provide 100% protection, and its effectiveness varies by season, circulating virus strains, age, health status, and how well the vaccine viruses match those circulating. However, it consistently reduces the risk of severe flu illness, medical visits, hospitalisations, complications, and death, making it a valuable public health intervention even if imperfect.[4]

Vaccine effectiveness (VE) is usually calculated in observational studies (e.g., test-negative design) as the percentage reduction in laboratory-confirmed influenza risk among vaccinated people compared to unvaccinated ones, often among those seeking outpatient care or hospitalised.[9]

Evidence shows:

- 40–60% effectiveness in preventing illness in healthy adults[4]
- Approximately 50% reduction in hospitalisation and severe outcomes[3]

In older adults and immunocompromised individuals, effectiveness may be lower due to weaker immune responses. However, vaccination still significantly reduces the risk of severe illness and complications.[4]

A key counselling point is that influenza vaccination reduces severity, even if infection occurs. This distinction is essential in addressing patient expectations and improving confidence in vaccination. A good analogy is that the flu vaccine is like a seatbelt or helmet, not an impenetrable shield. It gives a substantial risk reduction but does not take the risk away completely.[10]

It is important to recognise that timely vaccination is only one component of comprehensive influenza prevention. Reinforcing standard infection prevention and control measures, such as appropriate hand hygiene, minimising close contact with symptomatic individuals, and advising patients to remain at home when unwell, plays a critical role in reducing transmission and protecting both individual patients and the broader community.[11]

Vaccine characteristics and safety

Influenza vaccines used in South Africa are inactivated vaccines, meaning they contain killed virus particles and cannot cause influenza.[5,11]

For the correct dosing information consult the package insert for the product that is available as dosing can change from year to year and is also dependent on the product being used.

Generally, the following doses are recommended:

- Adults and children ≥ 9 years: 1 dose (0.5 mL IM)
- Children 6 months–8 years (first vaccination): 2 doses, ≥ 4 weeks apart; thereafter a single dose per season[8]

Depending on the product, half doses (0.25ml IM) may be prescribed for children 6 months up to 3 years of age. It is important to consult the relevant package insert.

Safety profile

The influenza vaccine has an excellent safety profile, supported by decades of use in hundreds of millions of people worldwide and continuous monitoring.[5]

Most side effects are mild and short-lived (1–2 days) and include soreness/redness at the injection site (common), low-grade fever, malaise, headache, or muscle aches. Serious events like anaphylaxis are rare and occur in a very small number of cases.[4]

The vaccine is considered safe for pregnant people, children ≥ 6 months, older adults, and those with chronic conditions.[8,11]

Contraindications and precautions

Contraindications

- Severe allergic reaction to a previous influenza vaccine or its components.[4] Egg protein allergy is not a contraindication to influenza vaccine.[11]

Precautions

- Moderate or severe acute illness with or without fever (defer until resolved).[8,11]
- History of Guillain-Barré syndrome within 6 weeks of previous flu vaccination.[8]

From recommendation to administration: practical considerations

Effective vaccination requires attention to both clinical and operational detail.

Screening

Assess:

- Eligibility and age
- Pregnancy status
- Comorbid conditions
- Previous vaccination history
- Contraindications

Administration

- Dose: 0.5 mL intramuscular injection for adults and confirm dose for children in package insert
- Site: deltoid (adults), anterolateral thigh (young children)

Storage

- Maintain cold chain (2–8 °C).
- Avoid freezing.

Post-vaccination

- Observe for immediate reactions.
- Counsel on expected side effects.
- Document appropriately and report any adverse events to the manufacturer of the vaccine.

Effective patient counselling: building confidence and uptake

Clear and confident communication is essential to improving vaccine uptake.

Address common misconceptions

- "The vaccine gives me flu."
  → It is an inactivated vaccine so it cannot cause disease. The side effects after the vaccine are a normal sign of the body's immune system responding to the vaccine.[4,12]
- "I got vaccinated and still got sick."
  → Influenza vaccination reduces severity and complications, even if infection occurs.[4,12]

Use every opportunity

Routine interactions, such as chronic medication collection or seasonal consultations, provide valuable opportunities to recommend vaccination.

A strong, clear recommendation remains one of the most effective drivers of vaccine uptake.[13]

Conclusion

Influenza vaccination is a critical and cost-effective intervention for reducing the burden of seasonal influenza in South Africa. From global strain surveillance and vaccine formulation to local administration and patient counselling, each step in the process contributes to protecting individuals and communities.

A thorough understanding of this continuum enables healthcare professionals to move beyond passive provision towards active advocacy. By identifying high-risk individuals, ensuring timely vaccination, and communicating effectively, meaningful improvements in vaccination coverage can be achieved.

Ultimately, influenza vaccination is not only about preventing infection—it is about reducing severity, preventing complications, and saving lives. Strengthening vaccination efforts each season plays a vital role in building more resilient healthcare systems and healthier communities.

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Otitis externa: What clinicians need to hear: pathophysiology, management and treatment

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Abstract

Otitis externa is a common inflammatory condition affecting the external auditory canal (EAC), characterised by symptoms such as otalgia (ear pain), pruritus (itching), erythema (redness), and otorrhoea (discharge), with a higher incidence in warm and humid environments. The condition may be classified as acute, chronic, or necrotising, with diagnosis primarily based on clinical evaluation and otoscopic examination. The pathophysiology involves disruption of the protective barrier of the ear canal, subsequent microbial colonisation, and host immune responses. Management strategies include both non-pharmacological measures, such as ear canal care (e.g. dry mopping) and moisture avoidance, as well as pharmacological interventions, including topical antimicrobial and anti-inflammatory agents. Systemic therapy is reserved for severe or complicated infections. Key challenges in the management of otitis externa include antimicrobial resistance, appropriate antimicrobial selection, patient adherence, and limited access to specialist care in resource-limited settings. Further research is required to optimise therapeutic strategies, strengthen antimicrobial stewardship, and improve clinical outcomes.

Keywords: otitis externa, swimmers' ear, pain, pharmacological, non-pharmacological

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Introduction

Otitis externa, commonly known as "swimmer's ear", is characterised by inflammation of the external auditory canal (EAC) and remains a common reason for otologic consultation worldwide.[1,2] It is particularly prevalent among swimmers and individuals exposed to frequent moisture or trauma to the ear canal.[1,3] Moisture retention within the ear canal creates an ideal environment conducive to microbial growth, increasing the risk of infection.[4,5] The condition may arise from infective or non-infective causes; however, it is commonly associated with bacterial or fungal pathogens.[1,6,7]

Epidemiology

Otitis externa is a common condition that affects individuals across all age groups; however, it occurs more frequently in children and young adults.[1,8] It is estimated that approximately 10% of individuals will develop the condition at some point in their lives, the majority of cases, approximately 95%, being acute.[1,5,6,9] The incidence varies geographically and seasonally, often increasing in warm and humid climates where water exposure is common.[1,6]

Aetiology

Bacterial infections, primarily caused by the microorganisms, *Pseudomonas aeruginosa* and *Staphylococcus aureus*, which thrive in the moist, warm environment of the canal are responsible for the majority of acute otitis externa cases, whilst in fungal otitis externa, microorganisms such as *Aspergillus* and *Candida* are frequently implicated, particularly in chronic or recurrent cases.[1,6,7,10,11] Routine laboratory tests and microbiological cultures are not required in uncomplicated cases of otitis externa; however, are recommended in recurrent, or treatment-resistant cases.[1,12]

Risk factors for otitis externa

Several factors increase susceptibility to infection of the EAC by disrupting the ear canal's natural protective barrier and facilitating microbial colonisation. Excessive moisture, commonly resulting from swimming, sweating, or prolonged water exposure, is a key risk factor, particularly in warm and humid environments, where moisture retention promotes microbial growth.[1,3,13] Trauma or mechanical irritation from cotton swabs, earphones, or hearing aids can damage the epithelium of the ear canal and compromise the cerumen barrier.[1,14] Dermatological conditions such as eczema or psoriasis further impair skin integrity, while narrow or stenotic external ear canals may trap moisture and debris, creating a favourable environment for infection.[1,9,15] Additional predisposing factors include obstruction within the ear canal, systemic stress, and immunocompromised states, including diabetes mellitus, and patients undergoing chemotherapy or radiotherapy, all of which weaken local and systemic defence mechanisms and increase vulnerability to infection.[1,8,16,17]

Anatomy and physiology of the external auditory canal

The external ear comprises the auricle (pinna) and the EAC (Figure 1).[18] The auricle is responsible for collecting sound waves and directing them into the EAC, which is a slightly curved, tubular structure.[18,19] The EAC extends from the concha of the auricle to the tympanic membrane (eardrum).[18,20] Its walls are made up of cartilage in the outer third and bone in the medial two-thirds, and are lined by skin containing hair follicles, sebaceous glands,

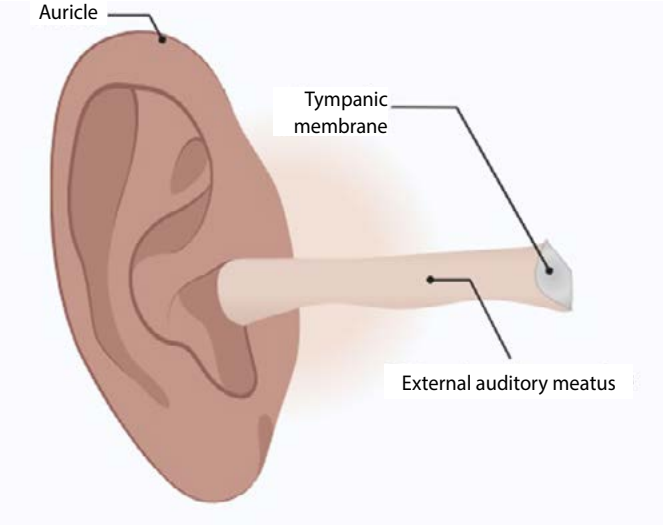

Figure 1: Anatomy of the external auditory canal (Template adapted in https://BioRender.com)

and ceruminous glands.[1,18] The main function of the external ear is to capture sound waves and direct them efficiently toward the tympanic membrane, aiding in hearing.[21] Furthermore, the EAC protects the middle and inner ear from foreign bodies and helps maintain an ideal acoustic environment.[18]

Several mechanisms protect the EAC from injury and infection. Cerumen (earwax), produced by the ceruminous and sebaceous glands, plays an important role in the EAC by trapping dust, debris, and microorganisms, thereby preventing their progression deeper into the ear canal.[22] Cerumen also possesses antimicrobial properties and helps maintain adequate hydration of the canal skin.[23] The presence of hair within the cartilaginous portion of the canal provides a further physical barrier against foreign material.[24] The slightly curved anatomy of the ear canal limits the direct entry of objects, while the epithelial lining undergoes a gradual outward migration, which facilitates the removal of desquamated cells and accumulated debris.[18] Together with reflexive protective mechanisms involving the ear canal and tympanic membrane, these features contribute to the ear's effective mechanical and biological defence system.

Disruption of the external auditory canal barrier

The EAC is protected by keratinised stratified squamous epithelium and cerumen produced from the ceruminous and sebaceous glands.[25] Once the ear's mechanical and biological defence mechanisms have been disrupted or the epithelial lining of the EAC is damaged, otitis externa may develop.[1] The acidic, lipid-rich cerumen, which contains lysozymes, assists in inhibiting fungal and bacterial growth.[4,26] Due to the hydrophobicity of cerumen, water is prevented from entering the canal and penetrating the skin.[4] Consistent cleaning of the ear canal removes the protective cerumen increasing water exposure.[4,27,28] Excessive moisture then leads to maceration, increasing the pH of the canal.[4] Cerumen buildup obstructs the canal leading to the retention of water and debris thereby promoting infection.[4,29] The EAC self-cleans through epithelial migration from the tympanic membrane to the EAC, carrying debris.[29,30-33] Dermatoses, such as eczema, seborrhoeic dermatitis, psoriasis, atopic dermatitis, and allergic dermatitis, as well as acquired or congenital immunodeficiency and diabetes mellitus may increase the risk of developing otitis externa.[4,30,34] Furthermore, the pH may be altered by the use of alkaline eardrops and soapy deposits.[27,28,35,36] Changes in the acidic environment, the lack of cerumen, a buildup of cerumen and trauma to the EAC can lead to a fungal or bacterial infection, resulting in immune and inflammatory responses.[5] Microtrauma from trying to self-clean the ears (cotton swabs, finger nails or other such objects that can scratch the canal) and wearing hearing aids can lead to abrasions within the EAC, permitting microbes into the wounded skin.[28,30,37]

Inflammatory and immune responses

Inflammatory and immune responses are initiated once the acidic environment within the ear has been lost and the protective barrier has been compromised.[1] When cerumen is removed from the ear, the acidic environment and protective barrier are lost.[1] Cerumen provides protection from infection and provides a barrier against foreign bodies by providing microbial protection

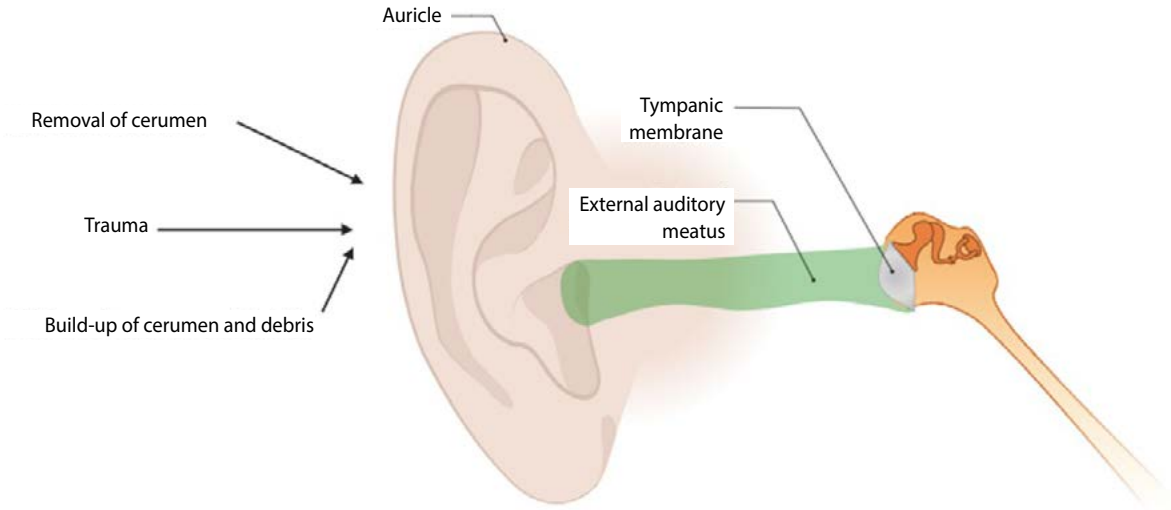

Figure 2: An overview of the pathogenesis of otitis externa. The removal of cerumen, trauma, and buildup of cerumen and debris all contribute to the growth of bacteria, resulting in otitis externa (Template adapted in https://BioRender.com).

to the epithelial lining of the EAC.[23,38] If the epithelial lining is damaged, local inflammation, the colonisation of pathogens and a decrease in the microbiota diversity may result.[39] The inflammatory response is initiated with pain, swelling, redness and warmth.[40] Sensory nociceptors distribute across the skin and upon injury secrete neuropeptides to induce a local inflammatory response including protein extravasation and vasodilation.[40,41] Keratinocytes, a cell type in the epidermis, form a passive physical barrier to pathogens and initiates primary inflammation once danger has been detected.[42] Additionally, keratinocytes respond to inflammatory mediators that are released by immune cells to maintain or amplify inflammation of the skin.[42]

Mechanism of pain and tissue damage

Pain and tissue damage in otitis externa can be attributed to inflammatory immune responses and otalgia.[1] Otalgia is a multifaceted condition involving cranial nerves V, VII, IX, and X and cervical plexus branches C2 and C3.[43] The tympanic membrane and ear canal receive sensory input from these nerves.[43] Cranial nerves IX and X, specifically contribute to otalgia through the larynx, oropharynx and distant organs.[43] Disease progression usually increases erythema and oedema and pain is further exacerbated due to pressure on the tragus and movement of the auricle.[29] Pain intensifies with an increase in severity of infection.[29] If there is obstruction of the canal lumen and adenopathy, auricular cellulitis or parotitis can occur.[4,29,44] Tissue damage may result in severe cases such as malignant otitis externa especially in immunocompromised and diabetic patients.[16] Tissue damage occurs by coagulative necrosis resulting from microangiopathy of the small blood vessels.[45]

Signs and symptoms of otitis externa

A clinical diagnosis of otitis externa requires a complete history and physical examination of the auricle, surrounding skin, and lymph nodes, as well as pneumatic otoscopy.[1,10] The clinical presentation may vary depending on the stage and severity of the condition, with symptoms often including otalgia (ear pain) (often disproportionate to the physical examination findings), pruritus (itching), erythema (redness), and otorrhoea (discharge), which may sometimes lead to hearing impairment and significantly affect the patient's quality of life.[1,29] Systemic symptoms occasionally include a fever accompanied by general malaise.[1] The condition is often classified according to severity into i) mild, characterised by pruritus, slight discomfort, and oedema of the ear canal, ii) moderate, with additional swelling, where the ear canal is partially occluded or blocked, and iii) severe, characterised by complete occlusion or blockage of the ear canal as a result of oedema accompanied by intense pain, swollen or enlarged lymph nodes, and a fever.[1]

Classification of otitis externa

Otitis externa is classified into various categories (Table I) based on the duration of symptoms, extent of inflammation, underlying aetiology (bacterial, fungal, or dermatological), and spread of infection. This classification system assists healthcare professionals in diagnosing the condition, distinguishing between its different clinical forms, and guiding appropriate management and treatment strategies.

Table I: Classification and description of otitis externa

Classification	Description
Acute diffuse otitis externa[1,8,46]	• Most common form of otitis externa • Acute and short-lived, typically lasting days to weeks • Usually bacterial in origin • Involves diffuse inflammation of the entire external ear canal • Frequently associated with swimming and prolonged moisture exposure • Commonly referred to as "swimmer's ear"
Acute localised otitis externa (furunculosis)[8,13,47]	• Localised infection of a hair follicle (furunculosis) • Typically bacterial in origin • Presents as a boil within the external ear canal • Causes severe, localised ear pain • Pain is often exacerbated by movement of the pinna or jaw
Chronic otitis externa[1,8,13]	• Similar in presentation to acute diffuse otitis externa • Persists for more than 3 months despite treatment • Itching is often seen as the predominant symptom
Malignant (necrotising) otitis externa[8,13,48]	• Severe, progressive infection originating in the EAC • Extends into adjacent soft tissues and bone (skull base osteomyelitis) • Occurs predominantly in immunocompromised adults, particularly those with diabetes mellitus • Associated with significant morbidity and requires urgent, aggressive management
Eczematous otitis externa[8,13,49]	• Associated with underlying dermatological or allergic conditions • Itching and inflammation are common symptoms
Otomycosis[8,13,50]	• Fungal infection of the EAC • Most commonly caused by *Aspergillus* or *Candida* species • Characterised by itching, discomfort, and debris within the ear canal

Complications of otitis externa

The most frequent complications of otitis externa include malignant otitis externa and periauricular cellulitis.[13] Additional complications include myringitis, perichondritis, facial cellulitis, and osteomyelitis of the temporal bone.[1,13]

Diagnostic criteria

Otitis externa is diagnosed based on the symptoms of inflammation present in the EAC.[8] Symptoms usually develop within 48 hours and last up to three weeks; and symptoms of ear canal inflammation include itching, ear pain and a sense of

fullness, which may be with or without hearing loss or jaw pain; and signs of ear canal inflammation include tenderness of the tragus or pinna with movement or erythema or oedema of the ear canal, with or without tympanic membrane erythema, otorrhoea, local lymphadenitis or cellulitis of the pinna.[8,10,27] Evaluation includes a history of presenting and associated symptoms, absence of cerumen, local trauma, water exposure, diabetes, local radiotherapy, ear surgeries and inflammatory skin disorders.[10] Physical examinations include an otoscopy of the ear canal, examination of the auricle and surrounding lymph nodes, skin examination and verification of an intact tympanic membrane via pneumatic otoscopy to differentiate between otitis externa from otitis media as well as determining if the tympanic membrane has been perforated as this affects treatment options.[8,10] If the tympanic membrane is not visible, hearing screening tests or audiological examinations can be performed while tone threshold audiogram and tuning-fork examinations are performed to test for conductive hearing loss.[6] Secretions may be swabbed for cultures and undergo pathogen resistance testing.[6] Patient presentation can range from itching with mild discomfort and minimal oedema to complete obstruction of the EAC usually involving the pinna and adjacent skin and severe pain.[10] A mild fever may occur, but temperatures greater than 38.3 °C (101 °F) suggest the spread of infection beyond the EAC.[10] Pain correlates to the severity of disease.[10,51]

Management and treatment of otitis externa

Effective management of otitis externa requires a multifaceted approach that combines both non-pharmacological and pharmacological interventions. A thorough understanding of the aetiology, risk factors, and pathophysiology of this condition is essential for accurate diagnosis, effective treatment, and prevention of complications. The main goals of treatment for otitis externa include treating the infection, pain management, returning the skin of the ear canal to its normal state and promoting cerumen production.[5,6] The use of aural toilet, topical antibiotics and steroids support treatment goals.[5] Topical treatment aims to reduce the chronic inflammation associated with otitis externa.[6]

Non-pharmacological interventions

Otitis externa may result from a build-up of debris in the ear canal, and removal of this debris may relieve symptoms. The EAC becomes more susceptible to trauma as a result of the inflammation and as a result curettes and cerumen spoons should not be used.[4] Suctioning under direct visualisation is the best form of cleansing.[4] The aural toilet is recommended when dry mopping or gentle suctioning is performed under microscopic or otoscopic visualisation.[10] This removes any debris or material obstructing the ear canal.[10] A lavage should be used only when the tympanic membrane is known to be intact, and should be avoided on patients with diabetes.[10] An operating or open otoscope paired with a 5 or 7 Fr Frazier malleable suction tip at low suction works best.[4] Cotton swabs with the cotton fluffed out can be used to clean the EAC.[4] The EAC can swell and the use of a cotton wick can be used for drainage and assist topical applications.[4] Tympanic membranes that are red and visible should be assessed via a tympanometry or pneumatoscope, to assist with determining if associated otitis externa is present.[4]

Pharmacological management

Initial therapy for diffuse, uncomplicated acute otitis externa should be with topical preparations due to their efficacy and safety when compared to placebo.[6,46] Treatment is appropriate in patients without middle ear disease, abscess formation, osteitis or recurring infection.[28] Topical treatments are administered between 7–10 days.[8]

Topical antibiotics

Topical antibiotics such as eardrops treat *Pseudomonas aeruginosa* and *Staphylococcus aureus*, the most common pathogens associated with otitis externa.[6] They are considered to be first-line therapy as they are effective and inexpensive.[10] It is important to consider resistance and culture results, though routine cultures are usually reserved for refractory or complicated cases.[6] As the drugs are administered topically, high local concentrations of drugs can be achieved without the side-effects associated with systemic treatment.[6] Quinolones (ciprofloxacin) are highly effective and do not cause local irritation; however, prolonged treatment can lead to resistance.[6] Preparations of fluoroquinolones require twice-daily dosing and some may be used with a non-intact tympanic membrane.[29] Ofloxacin and ciprofloxacin/dexamethasone can be used if the tympanic membrane is not intact as it has been approved for use in the middle ear.[10] Aminoglycosides (neomycin and gentamycin), while effective, can be ototoxic and should only be administered if the eardrum is intact.[6,29] Neomycin is sensitising in 5–18% of patients and can lead to contact dermatitis.[29, 52-56] The ototoxicity associated with this group has been linked to open middle-ear spaces or prolonged use.[29] Polymyxins (polymyxin B) can also be used.[6] These drugs result in lower recurrence and rapid symptomatic relief of otitis externa compared with placebo.[6,27] Topical antibiotics should not be used for longer than necessary, and ototoxic drugs should not be administered if there is perforation of the eardrum.[6]

Topical corticosteroids and combination therapy

Corticosteroids are administered to lessen oedema and may have minor antimicrobial and antifungal effects, but their main role is anti-inflammatory.[6,57] High-potency corticosteroids are more effective against swelling, inflammation and pain than low-potency corticosteroids.[6,58] Corticosteroid-containing preparations provide rapid symptomatic relief.[10] Corticosteroid use alone lacks strong evidence of effectiveness, but is beneficial when combined with antibacterial agents.[9] Combinations of topical antibiotics and topical corticosteroids reduce swelling, secretions and erythema better than topical antibiotics alone.[6]

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* AOE: Acute Otitis Externa ** AOMT: Acute Otitis Media with Tympanotomy Tubes. References: 1. Cilodex® Approved Professional Information, 13 April 2022. 2. Daniel SJ, *et al.* Guidelines for the treatment of tympanostomy tube otorrhoea. *J Otolaryngol* 2005;34(S2):S60-S63. For full prescribing information, refer to the Professional Information approved by the South African Health Products Regulatory Authority. S4 **CILODEX®** Ear Drops, suspension. 1 ml of suspension contains 3 mg ciprofloxacin (as hydrochloride) and 1 mg dexamethasone preserved with benzalkonium chloride 0,01% (m/v). A39/16.2/0544. Novartis SA (Pty) Ltd. Magwa Crescent West, Waterfall City, Jukskei View, 2090. Tel. (011) 347 6600. Co. Reg. No. 1946/020671/07. **Novartis Adverse Drug Reaction Reporting:** Email: patientsafety.sacg@novartis.com. Web: www.novartis.com/report. Tel: 0861 929-929. **Marketed and Distributed by Adcock Ingram Limited.** Co. Reg. No. 1949/034385/06. Private Bag X69, Bryanston, 2021, South Africa. Customer Care: 0860 ADCOCK/232625. www.adcock.com FA-11267429. Exp.: 09/2026.

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Antifungal agents

Otitis externa caused by fungal infections is usually mild and a 2% acetic acid or a 90–95% alcohol solution can be used.[29] Established infections require topical treatment such as 1% clotrimazole or tolnaftate.[4,29,59,60] Fungal otitis externa can be treated by soaking strips in an antifungal drug such as miconazole, nystatin, clotrimazole or ciclopirox, and placing them in the ear canal.[6] Systemic therapy may be considered if topical therapy is unsafe due to perforation, but not solely based on resistance testing in routine fungal otitis externa, since fungal cultures are not routinely done.[6]

Analgesic and adjunctive therapies

Pain management is one of the main goals in the management of otitis externa. Ear pain usually results from inflammation involving the sensitive periosteum of the bony ear canal.[6] The use of analgesics is recommended to give patients rest, comfort and to allow them to resume their daily activities.[28] Mild to moderate pain can be treated with nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen or acetaminophen/paracetamol.[6,28] Topical local anaesthetics can be used if the tympanic membrane is intact or if a myringotomy tube has been inserted.[6] However, topical local anaesthesia can mask progression of infection and should be reviewed after 48 hours so that the effect of treatment can be evaluated.[6,28] Opioids may be given when symptoms become severe.[10]

Systemic therapy

Topical therapy should be supported by systemic antibiotics if the infection has spread beyond the EAC into the pinna, into deeper tissues causing necrotising otitis externa, when otitis media is present or if the patient has diabetes, human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome (AIDS).[4,28] It is important to note that oral antibiotics are associated with significant adverse effects including diarrhoea, altered nasopharyngeal flora, vomiting, allergic reactions and rashes.[28,35,61,62] Systemic antibiotic therapy also increases the risk of pathogen resistance and disease recurrence.[10]

Management of malignant otitis externa

Malignant otitis externa is an aggressive infection, and management of this condition has been challenging due to the need for long-term therapy and consistent monitoring.[63,64] Additionally, there is a lack of a standardised care protocol.[63] Management includes assessment of clinical signs and symptoms, evaluation of laboratory assays for inflammatory markers, and radiological imaging.[63] Treatment is based on oral antibiotics and pathogen-specific parenteral antibiotics administered for 4–6 weeks, guided by sensitivity and resistance testing.[6,65] If sensitivity and resistance testing does not yield definitive results, empirical antibiotic therapy targeting *Pseudomonas aeruginosa* should be initiated, depending on the severity of the disease.[6] Adjunctive, topical antimicrobial therapy using antimicrobial medicated strips placed in the ear canal can be administered.[6] Surgical removal of bone sequestra and necrotic tissue may be required and strict glycaemic control should be maintained.[6] Hyperbaric oxygen therapy may improve cure rates; however; regular radiological and clinical follow-ups are necessary to monitor treatment response and detect recurrence.[6,60] In cases where malignant otitis externa is diagnosed at an advanced stage, intravenous antibiotic therapy is required.[63]

Conclusion

Otitis externa is a common, potentially complex inflammatory condition of the external ear. Although the majority of cases are acute, the condition encompasses a wide clinical spectrum, ranging from mild, self-limiting disease to severe, life-threatening forms. Management is focused on topical therapy, supported by non-pharmacological interventions such as aural toilet, moisture avoidance, and patient education. Topical antimicrobials, often in combination with corticosteroids, are highly effective for uncomplicated disease, whereas systemic therapy is reserved for severe, complicated, or refractory cases. Further research is required to refine therapeutic approaches, address emerging resistance patterns, and develop standardised protocols for the management of this condition.

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Synbiotic support during and after antibiotics: Why probiotics plus prebiotics – and delivery – matter

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Abstract

The gut microbiome is integral to gastrointestinal and systemic health. Antibiotic therapy is a major driver of gut dysbiosis, characterised by loss of microbial diversity, depletion of beneficial bacteria and expansion of opportunistic and antimicrobial-resistant pathogens. Probiotics reduce antibiotic-associated diarrhoea and support microbiome recovery, while prebiotics selectively support beneficial bacterial growth. When combined as a synbiotic, probiotics and prebiotics provide complementary and synergistic support for gut recovery during and after antibiotic therapy. This article discusses the rationale for synbiotic use, strain-specific probiotic evidence, immune effects, and the importance of targeted delivery for clinical efficacy.

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Introduction

The human gastrointestinal tract harbours a complex microbial ecosystem containing approximately 40 trillion bacterial cells across more than 1 000 species.[1-3] This microbiome contributes to digestion, immune regulation, epithelial integrity and metabolic homeostasis.[2,4]

Disruption of this ecosystem is associated with gastrointestinal disorders such as inflammatory bowel disease and irritable bowel syndrome, as well as systemic conditions including obesity, type 2 diabetes, atopy and neurodegenerative disease.[2,4,5]

Antibiotic exposure can disrupt the microbial balance of the gut microbiome, reducing microbial diversity, facilitating pathogen overgrowth and the emergence of antibiotic-resistant microbes.[4,6] Supporting microbiome recovery during and after antibiotic therapy through synbiotic supplementation (combining probiotics with prebiotics) may help to restore the microbial balance disrupted by antibiotics.[6,7]

Insights into dysbiosis

A stable gut microbiome is sustained by dominant gut phyla such as Firmicutes and Bacteroidetes, which play a critical role in immune modulation, short-chain fatty acid (SCFA) production and maintenance of the intestinal barrier.[7] Many gut microbial species have the potential to cause disease.[8] For example, species from the Enterobacteriaceae family, such as *Escherichia coli* are opportunistic pathogens with the potential to cause severe infections.[8]

Dysbiosis is characterised by loss of beneficial microbes, reduced microbial diversity and overgrowth of potential pathogens.[7] Dysbiosis may be the result of multifactorial disturbances of gut homeostasis, including antibiotic exposure.[7]

Broad-spectrum agents including aminopenicillins (± clavulanate), cephalosporins, clindamycin and fluoroquinolones often drive dysbiosis.[4,6,7] This disruption in the gut microbiome favours overgrowth of opportunistic species, increases the risk of antibiotic-associated diarrhoea (AAD) and *Clostridioides difficile* infection and is associated with longer-term metabolic and inflammatory sequelae.[3,6,7]

Recovery of the gut microbiome is influenced by antibiotic spectrum, dose and duration of treatment and may take weeks to months in some cases.[4,6,7] During this recovery phase, synbiotic interventions may support restoration of the gut microbiome balance disrupted by antibiotic therapy.[6,7]

Probiotics, prebiotics and synbiotics: the concepts

Probiotics

Probiotics are live microorganisms that, when administered in adequate amounts, confer a health benefit on the host.[3] Their effects include pathogen interaction, enhancement of epithelial barrier function, immune modulation and production of beneficial metabolites such as SCFAs.[3,7]

Prebiotics

Prebiotics are selectively fermented, non-digestible substrates that stimulate the growth or activity of beneficial gut bacteria, leading to improved host health.[3] Common examples include fructooligosaccharides (FOS), inulin and galactooligosaccharides (GOS).[3]

Synbiotics

Synbiotics comprise live microorganisms and substrates, i.e., probiotics and prebiotics to provide complementary or synergistic effects to the probiotic organism.[3,9] The principal purpose of a

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synbiotic combination is the improvement of the survival of probiotic microorganisms in the gastrointestinal tract.[9]

The role of probiotics in the management of gut dysbiosis

Clinical evidence supports probiotic use alongside antibiotics to reduce gastrointestinal side-effects such as diarrhoea.[6]

- Witsell et al. demonstrated that *Lactobacillus acidophilus* administered with amoxicillin/clavulanate significantly reduced gastrointestinal complaints and yeast superinfections compared with antibiotic therapy alone.[10]
- Forssten et al. showed that *L. acidophilus* administered as a multistrain formulation during antibiotic treatment can persist in the gut and contribute to microbiome recovery following antibiotic treatment cessation.[11]
- Meta-analyses confirm that probiotics, including *L. acidophilus*, *L. rhamnosus*, *L. casei*, *Bifidobacterium* spp. and *Saccharomyces boulardii*, reduce the risk of antibiotic-associated diarrhoea across age groups, with higher doses associated with greater efficacy.[3,6]

Immune modulatory mechanisms of probiotic bacteria

Probiotics mediate the modulation of both innate and adaptive immune responses in the intestine by stimulating:[12]

- Production of various cytokines and chemokines from dendritic cells, lymphocytes, macrophages, mast cells, granulocytes, and intestinal epithelial cells
- Immunoglobulin A (IgA)-producing cells and consequent IgA secretion

Probiotics can therefore improve the host immune system and induce important beneficial effects, allowing prevention and/or management of immune/inflammatory-related diseases, including diarrhoea.[12]

Probiotic survival: why delivery matters

Probiotic efficacy depends on strain selection, dose, viability and delivery.[13] Probiotic organisms are sensitive to heat, oxygen, moisture and gastric acidity, with poor storage or formulation leading to substantial colony-forming units (CFU) losses before intestinal delivery.[13,14]

Encapsulation technologies aim to protect probiotics during storage and gastrointestinal transit.[14] DUOCAP™ capsule-in-capsule technology enables staged release, with the outer capsule dissolving in the stomach and the inner, acid-resistant capsule releasing the probiotic in the intestine.[15,16]

A word on Probitec

Probitec® is a synbiotic formulation delivering 15 billion CFUs of *Lactobacillus acidophilus* La-14 per capsule, combined with fructooligosaccharides (FOS) as a prebiotic substrate to support the resident beneficial microbes in the gut.[3,16]

Formulated using DUOCAP™ technology, Probitec® protects probiotic viability, ensures targeted intestinal release and supports microbial recovery during and after antibiotic therapy.[16,17] The product maintains labelled CFU potency over its shelf life and can be taken with or without food, including alongside antibiotics.[16]

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The grey zone of thyroid function: Clinical significance and management controversies in subclinical hypothyroidism

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Abstract

Subclinical hypothyroidism (SCH) is defined by elevated serum thyroid-stimulating hormone (TSH) levels with normal thyroxine (T4) concentrations, representing a diagnostic grey zone in thyroid function. Its prevalence ranges from 4–10% among adults, particularly affecting women, yet it often eludes detection due to the subtlety of symptoms. This spectrum is notably heterogeneous: the majority of SCH cases (~3–8% of adults) exhibit mild disease with TSH levels between 4.5 and 10 mIU/L, whereas a smaller fraction (~0.5–1%) presents with severe SCH, characterised by TSH levels ≥ 10 mIU/L — a differentiation that entails significantly divergent prognostic and therapeutic consequences. This review investigates the complexities of SCH, including its potential associations with cardiovascular risk, neurocognitive changes, and progression to overt hypothyroidism (OH). The efficacy of levothyroxine therapy remains contentious, with conflicting studies regarding its role in symptom relief and cardiovascular event reduction. Additionally, the variability in clinical progression complicates the distinction between benign biochemical variations and clinically significant thyroid disorders. By highlighting special clinical scenarios and management controversies, we present approaches to inform clinical decision-making and promote individualised patient care.

Keywords: subclinical hypothyroidism, thyroid-stimulating hormone, levothyroxine, management controversies, age-specific considerations

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Introduction

The thyroid gland produces two main hormones, tetraiodothyronine (thyroxine, T4) and triiodothyronine (T3), that act on virtually all body tissue, affecting functions from metabolism, thermoregulation, and mental activity to bone maintenance. The pituitary gland secretes the thyroid-stimulating hormone (TSH), which regulates thyroid hormone production.[1] When circulating thyroid hormone levels fall, TSH rises to stimulate the thyroid gland. This compensatory mechanism forms the basis for diagnosing thyroid dysfunction. Hypothyroidism, characterised by elevated TSH and reduced circulating T4, has a well-established clinical profile and management pathway.[1-3] In Europe and the United States, hypothyroidism affects roughly 0.2–5.3% and 0.3–3.7% of adults, respectively, while long-term UK data show a higher annual incidence in women than men.[4] Other countries report similarly diverse patterns, and evidence shows a higher incidence of hypothyroidism with increasing age.[4]

However, beyond overt disease lies a less clearly defined group of individuals who fall within the biochemical and clinical "grey zone" of thyroid dysfunction. This condition is known as subclinical hypothyroidism (SCH), and it is characterised by elevated serum TSH levels with normal circulating T4 concentrations. Because individuals with SCH typically experience minimal or no symptoms of thyroid dysfunction, the condition is identified primarily through laboratory findings rather than clinical presentation. Its prevalence varies widely by age (about 4–10% of adults) but is generally reported to be higher in women.[5] Importantly, SCH is not a uniform condition: the majority of affected persons (~3–8%) exhibit mild SCH, characterised by TSH levels between 4.5 and 10 mIU/L, whereas a smaller fraction (~0.5–1%) presents with severe SCH, indicated by TSH levels ≥ 10 mIU/L. This distinction is clinically significant, as the risk of progression, cardiovascular consequences, and the therapeutic evidence vary considerably across these two groupings. A subset of patients (2–5%) with SCH progress to overt hypothyroidism (OH).[3,5] In some cases, however, studies have shown that TSH levels normalise in over 50% of participants within 32 months of follow-up.[5] The clinical relevance of SCH remains a subject of discussion. Some observational studies have linked SCH to adverse cardiovascular outcomes, dyslipidaemia, neurocognitive changes, infertility, and progression to OH, particularly in those with higher TSH levels or thyroid autoimmunity.[3,5] Conversely, several studies failed to demonstrate consistent symptomatic or cardiovascular benefit from levothyroxine (LT4) therapy, especially in older adults and those with mildly elevated TSH. These conflicting data have fuelled controversy regarding screening strategies, treatment thresholds, and long-term management.[5]

Despite decades of research, substantial gaps persist in the understanding and management of SCH. One major challenge lies in distinguishing a benign biochemical finding from an early stage of clinically meaningful thyroid disease. The progression of SCH is variable, with some evidence suggesting that individuals revert spontaneously to euthyroidism, and a proportion progress to OH.[3,5] There are inconsistencies in treatment recommendations, as conflicting evidence exists regarding the benefits of treating SCH. Clinical decision-making remains particularly challenging as clinicians must balance potential benefits, such as symptom

improvement, cardiovascular risk reduction, or prevention of progression, against risks including overtreatment, atrial fibrillation, and bone loss. This review offers a comprehensive and clinically focused analysis of SCH, examining the complexities associated with inconsistent data, biochemical abnormalities, symptom burden, and therapeutic uncertainty. While previous reviews have often addressed individual aspects of SCH in isolation, such as cardiovascular risk, treatment efficacy, or specific populations, the present review synthesises multisystem manifestations, age-specific considerations, special clinical scenarios, and emerging frameworks in personalised medicine within a unified narrative. This integrated approach aims to address the central clinical challenge of SCH: translating ambiguous biochemical findings into actionable, individualised management strategies. This area remains insufficiently explored in the current literature.

Defining the subclinical spectrum

Biochemical definition evolution

SCH is linked to various health issues, notably atherosclerosis, where it may lead to adverse lipid profiles, increased oxidative stress, and insulin resistance. This connection underscores the need to assess thyroid function in individuals at higher cardiometabolic risk. Still, it is crucial to use population-specific reference ranges to interpret thyroid function tests, as numerous factors can influence hormone levels. Iodine nutritional status is particularly significant, with low free thyroxine (FT4) levels often observed in iodine-deficient areas.[6] The TSH, which is inversely related to FT4, is the most sensitive marker for thyroid dysfunction; however, TSH values can vary due to diverse factors unrelated to age or ethnicity, such as lifestyle and geographic conditions.[6] This variation creates challenges in clinical decision-making, exacerbated by potential misapplication of LT4 therapy and inconsistent guideline recommendations on TSH screening. While some authorities suggest routine screening for the general population, others argue that the evidence is insufficient for universal screening, and there is disagreement about initiating LT4 therapy.[7]

Additionally, determining accurate reference ranges is complicated by interlaboratory variability in assay methods.[6] The reference range for TSH in adults is generally accepted as 0.35–4.5 mIU/L, with higher values indicating hypothyroidism;[8] however, pregnant women require trimester-specific ranges due to hormonal changes.[9] The consequences of untreated hypothyroidism include cardiovascular disease and other serious health implications, underscoring the importance of reliable TSH measurement for accurate diagnosis and treatment.[6]

A further complexity in thyroid function assessment is that TSH reference ranges are based on population-level data that do not account for individual thyroid hormone set points. Research indicates that everyone maintains a genetically influenced TSH set point that may vary significantly from population averages, influenced by factors including age, sex, body composition, seasonality, and genetic variations in thyroid hormone transport and metabolism.[10] Thus, a TSH level within the standard "normal" range could represent a significant deviation from an individual's optimal physiological level. At the same time, a mildly elevated TSH might be normal for certain patients.[10] This concept of individuality in set points has important clinical implications for SCH, as it explains why two patients with the same TSH levels may experience different symptom burdens. Consequently, relying solely on population-derived TSH cut-offs is inadequate for treatment decisions, underscoring the need to incorporate individual clinical context alongside biochemical results to prevent both undertreatment and overtreatment.

The TSH controversy

Modern assays can accurately measure TSH levels as low as 0.01 mIU/L, which benefits critically ill patients; however, there is ongoing debate regarding the clinically significant threshold for elevated TSH levels. Concentrations of TSH > 4.5 mIU/L and TSH ≥ 10 mIU/L are linked to increased mortality in conditions such as pulmonary arterial hypertension and postoperative complications in surgeries, namely, acute type A aortic dissection, respectively.[11] Notably, both low-normal (0.39–1.30 mIU/L) and high-normal (2.09–4.60 mIU/L) TSH values in euthyroid individuals have been associated with heightened risks of all-cause and cardiovascular mortality, especially in adults with diabetes.[11] In pregnancy, recommended upper reference limits are lower and trimester-specific: 2.5 mIU/L in the first trimester, 3.0 mIU/L in the second trimester, and 3.5 mIU/L in the third trimester. However, newer guidelines suggest an upper limit of ~4.0 mIU/L in early pregnancy.[9] These adjustments reflect physiological changes unique to gestation.

Multisystem clinical manifestations

The clinical consequences of SCH extend beyond its potential progression to OH. Its effects are multifactorial and interrelated, influencing the cardiovascular, endocrine, metabolic, neurological, and reproductive systems as outlined in Figure 1. These multisystem manifestations are discussed in detail below.

Cardiovascular system

Jankauskas et al.[12] reported a significant link between cardiovascular diseases and SCH, attributing these conditions to inadequate thyroid function. Decreased thyroid activity leads to reduced myocardial contractility at rest and during exercise, partly due to reduced expression of beta-adrenergic receptors, which are vital to heart function. Thyroid hormones enhance cardiac contractility by upregulating alpha myosin heavy chains (a-MHC) and sarcoplasmic reticulum calcium adenosine triphosphatase (SERCA2).[13] Furthermore, thyroid hormones facilitate vasodilation, promoting blood flow and reducing shear stress. Both OH and SCH contribute to arterial stiffness and atherosclerosis, primarily by diminishing nitric oxide (NO) production, a key vasodilator with anti-inflammatory properties.[13] The cardiovascular impact of subclinical hypothyroidism, though moderate, may potentially exacerbate aging-related cardiac changes and increase heart

failure risk. Population studies indicate a correlation between high TSH levels and heart failure occurrences, even when thyroid function appears normal.[14]

Metabolic and endocrine effects

SCH negatively impacts insulin and carbohydrate metabolism and is associated with increased Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) in non-diabetic patients.[15] The condition is linked to obesity, as thyroid hormones regulate fat metabolism, and lower T4 and higher TSH levels contribute to fat accumulation.[16] Reduced thyroid function lowers thermogenesis and energy expenditure, thereby increasing the risk of insulin resistance. Mechanisms may include elevated free fatty acids and disrupted leptin response. TSH correlates positively with insulin resistance and hyperglycaemia and contributes to hepatic glucose production.[16,17] Hypothyroidism also decreases bone turnover but there is insufficient evidence linking it to osteoporosis or skeletal growth issues in children.[17] Additionally, it affects adrenal gland development and the stress response, with high TSH levels associated with increased cortisol levels due to reduced hepatic clearance.[17]

Neuropsychiatric impact

Thyroid hormones significantly influence neuropsychiatric health by modulating adrenergic and serotonergic systems, contributing to conditions such as depression and anxiety.[18] Hypothyroidism is linked to resistant depression and cognitive decline, including memory deficit and lethargy.[18,19] Conversely, while hyperthyroidism is more commonly associated with psychosis, it can exhibit psychotic features as well. Hashimoto's disease, involving autoantibody production against thyroid hormones, is considered a neuropsychiatric disorder, with inflammation affecting the cerebrospinal fluid.[18] Evidence suggests a relationship between thyroid dysfunction and Alzheimer's disease, with hypothyroidism reducing brain-derived neurotrophic factor (BDNF) levels and impairing memory development due to alterations in glutamatergic and cholinergic systems.[19] Additionally, reduced cerebral blood flow in mild hypothyroidism may lead to cognitive impairments and increase the risk of dementia, particularly in the elderly, although findings are inconsistent.[17-19]

Reproductive and developmental

Thyroid function is essential for reproductive health, as it influences hormone balance and reproductive processes, particularly hypothyroidism, which is linked to various reproductive disorders, including irregular menstrual cycles and infertility.[9] Moreover, research indicates that hypothyroidism may lead to delayed ovulation and is prevalent among women facing fertility challenges. Thyroid hormones collaborate with follicle-stimulating hormones for follicle development and are vital for ovulation and corpus luteum formation.[9] High prolactin levels, resulting from untreated hypothyroidism or, in some cases, undiagnosed conditions, can contribute to fertility issues.[20] Elevated TSH can cause premature ovarian insufficiency and

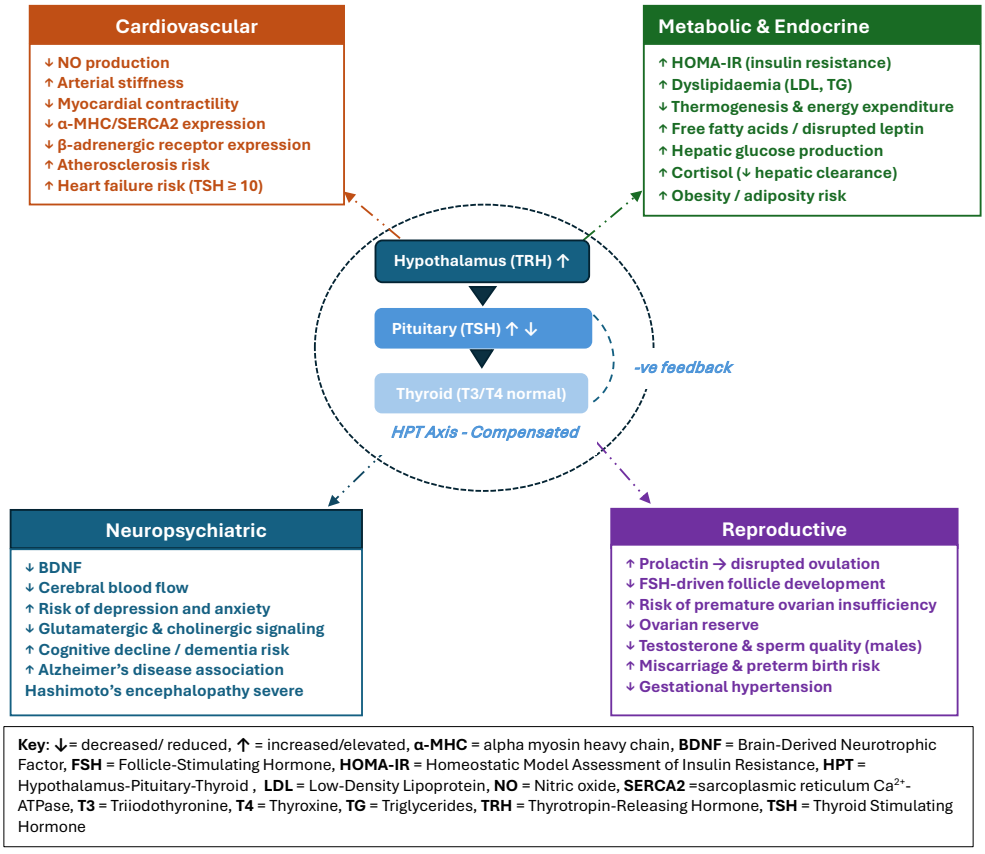

Figure 1: Pathophysiological Mechanisms Linking Subclinical Hypothyroidism (SCH) to Multisystem Effects[9, 12-21]

ovulatory dysfunction.[20,21] Lower ovarian reserve in women with OH or SCH hypothyroidism has been reported.[9,21]

Treatment

Current treatment guidelines

The management of SCH remains contentious within endocrinology, influenced by varying guidelines from prominent international organisations. The American Thyroid Association (ATA) 2014 guidelines suggest considering LT4 therapy for patients with TSH levels over 10 mIU/L due to associated increased risks of heart failure, cardiovascular mortality, and progression to OH. For TSH levels between 4.5 and 10 mIU/L, a personalised strategy is recommended, particularly for younger patients or those with symptoms, goitre, or positive anti-thyroid peroxidase (TPO) antibodies.[22] The European Thyroid Association (ETA) 2013 consensus indicates treatment for individuals under 70 years with persistently elevated TSH above 10 mIU/L, while routine treatment for levels between 4–10 mIU/L is discouraged unless specific risk factors are present.[23] The 2012 guidelines from the American Association of Clinical Endocrinologists (AACE) present a more permissive approach, suggesting the upper limit of normal TSH could be as high as 3.0 mIU/L in certain contexts.[24] Additionally, the 2019 ETA guidelines introduced age-adjusted TSH thresholds, recommending treatment only when TSH levels surpass age-specific reference ranges, particularly noting that elevated TSH in older adults may be physiological rather than indicative of pathology.[25]

Evidence from clinical trials

Randomized controlled trials

Numerous pivotal trials support the treatment of SCH, however these studies often yield contradictory findings. The TRUST trial, published in 2017, is the largest randomised controlled trial (RCT) to date, involving 737 adults aged 65 and older with persistent SCH (TSH 4.6-19.9 mIU/L). It concluded that LT4 therapy did not significantly improve hypothyroid symptoms after one year compared to placebo, as assessed by the Thyroid-Related Quality of Life questionnaire and the Tiredness score.[26] A systematic review by the Institute for Clinical Systems Improvement (ICSI) found limited evidence supporting cardiovascular health benefits of treatment.[27] However, smaller studies have produced mixed results; for instance, an observational study by Razvi et al.[28] reported a reduction in all-cause and cardiovascular mortality among younger patients (< 70 years) treated with levothyroxine, although it did not involve a RCT. Taken together, these findings suggest that a one-size-fits-all approach to the treatment of SCH, without recognising that biochemical correction does not always translate into clinical benefit, particularly in the elderly, may lead to overtreatment. However, the findings in younger patients are based solely on observational studies and do not include robust RCTs. As a result, it is impossible to conclude that treatment reliably improves clinical outcomes.

Meta-analyses findings

Feller et al.[29] conducted a meta-analysis of 21 RCTs involving 2192 participants, finding no significant improvements in quality of life, depressive symptoms, body mass index, or blood pressure with LT4 therapy. Subgroup analyses did not reveal benefits for patients with elevated TSH levels (> 10 mIU/L) or younger individuals. A Cochrane review by Villar et al.[30] on cardiovascular endpoints reported improvements in endothelial function and lipid profiles but did not show a decrease in clinical cardiovascular events. Additionally, a meta-analysis by Rugge et al.[31] published in the Annals of Internal Medicine, concluded that the evidence was insufficient to support routine treatment. These findings raise questions about the efficacy of SCH treatment as there is a disconnect between improved TSH levels and actual clinical outcomes. This suggests that the treatment approach needs to be tailored to improve symptoms rather than solely focusing on biochemical normalisation.

Cardiovascular outcome trials

The association between SCH and cardiovascular disease has been well studied,[13] notably by the Thyroid Studies Collaboration in 2010, which analysed data from 55287 patients. This investigation found a correlation between SCH and increased events and mortality from coronary heart disease (CHD), particularly in patients with TSH levels exceeding 10 mIU/L, as corroborated by Rodondi et al.[32] who reported hazard ratios of 1.89 for mortality in this group. However, intervention trials, such as the TRUST trial sub-study by Stott et al.,[26] have not shown cardiovascular benefits from therapy, suggesting that treatment does not reduce adverse cardiovascular outcomes despite observed associations with risk. This creates a challenge in treatment, as it is still unclear whether cardiovascular disease in SCH patients is a modifiable risk factor that can be improved with LT4 therapy or merely a marker of underlying risk. Therefore, a more multifaceted treatment approach that does not focus solely on biochemical normalisation with LT4 will be required to ensure that therapy leads to meaningful clinical outcomes.

Treatment decision framework

Risk stratification approaches

Current clinical practice in managing thyroid disorders emphasises individualised, risk-based decision-making due to conflicting evidence. ATA/ETA establishes a consensus approach for treatment stratification based on several criteria: TSH levels, with strong treatment considerations for levels above 10 mIU/L, and individualised approaches for levels between 4.5 to 10 mIU/L; age, generally favouring more liberal treatment for patients aged 65 to 70; hypothyroidism symptoms such as fatigue, cold intolerance, and constipation; the presence of thyroid peroxidase antibodies (TPOAb), which increases disease progression risk; cardiovascular risk factors including dyslipidaemia, hypertension, and atherosclerosis; and pregnancy status.[22,24] Additionally, Biondi and Cooper[33] proposed a widely accepted risk assessment model incorporating these factors (see Figure 2 for a comprehensive

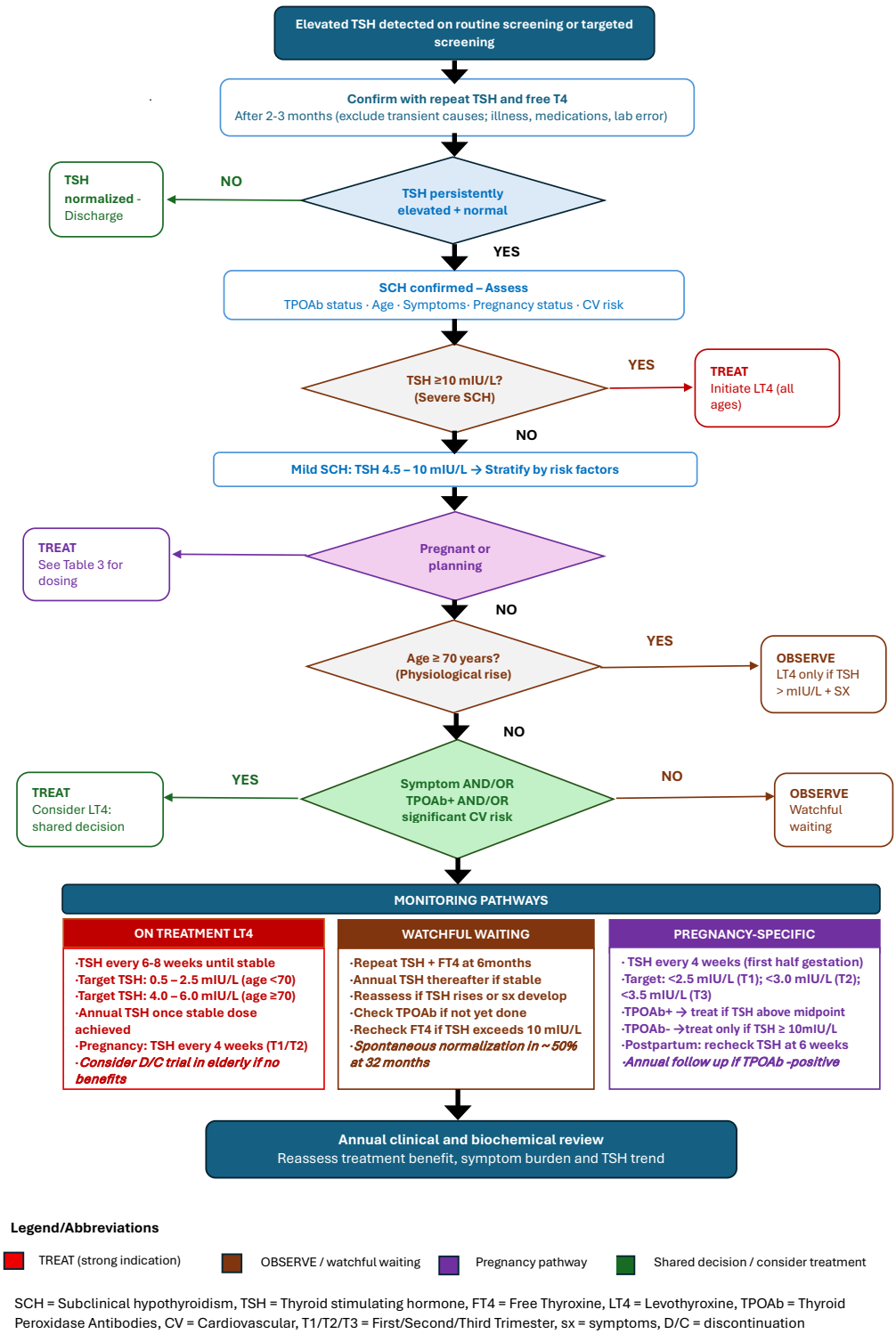

Figure 2: Clinical decision algorithm for the management of subclinical hypothyroidism (SCH), based on ATA 2014, ETA 2013/2019, and AACE 2012 Guideline Recommendations[22-25]

decision-making algorithm). The American College of Physicians recommended against routine treatment for individuals with TSH levels below 10 mIU/L and normal free T4 levels, emphasising the need for shared decision-making under certain conditions.[25]

Symptom assessment tools

Evaluating objective symptoms in thyroid-related conditions is challenging. The Thyroid-Related Quality of Life Patient-Reported Outcome (ThyPRO) questionnaire, validated by Watt et al.,[34] is a key tool for assessing thyroid-specific complaints. The TRUST trial indicates that many symptoms linked to SCH are non-specific and frequent in euthyroid patients, highlighting a complex relationship between thyroid biomarkers and patient-reported symptoms. The Zulewski Clinical Score has been used but lacks adequate sensitivity and specificity for subclinical cases,[35] and research by Canaris et al.[36] suggests poor correlation between symptoms and TSH levels in the subclinical range.

Monitoring strategies

Initial monitoring of patients starting treatment should involve TSH reassessment every 6 to 8 weeks until stabilisation, with a target TSH range of 0.5 to 2.5 mIU/L for younger adults and 4 to 6 mIU/L for those aged 70 or older. Long-term follow-up requires annual monitoring once dosage is stable, and treatment discontinuation trials should be considered for elderly patients without clear benefits. Special monitoring during pregnancy is advised, with TSH checks every 4 weeks in the first half of gestation.[22,37] The specific pathways for both treatment and watchful waiting are detailed in Figure 2.

Treatment is recommended for patients with persistently high TSH (> 10 mIU/L), those who are pregnant or planning pregnancy (target TSH < 2.5 mIU/L), individuals with goitre, rising TSH levels with TPO antibody positivity, significant hypothyroid symptoms, and young patients with TSH > 7–10 mIU/L (under 30–40 years).[9,17] Conversely, observation is preferred for elderly patients with lower TSH levels (< 10 mIU/L), asymptomatic individuals with TSH 4.5–7.0 mIU/L, and those with limited life expectancy or significant comorbidities,[17,38] as elevated TSH may normalise on its own, reducing the need for unnecessary long-term therapy.

Special clinical scenarios

Paediatric population

The incidence of SCH in children is low, primarily idiopathic and mild. It can be associated with conditions like Hashimoto's thyroiditis (HT), goitre, and Down syndrome.[39] Individuals with HT and elevated TSH levels (> 10 mIU/L) require closer monitoring and may need LT4 treatment, unlike asymptomatic children with mild, idiopathic SCH and negative TPO antibodies. Long-term untreated SCH can lead to cardiovascular issues, metabolic disturbances, and cognitive impairments, while growth and bone development typically remain unaffected.[17,39]

Elderly population

SCH is common among older adults and often presents unnoticed as thyroid function declines.[17] While this condition has been linked to cognitive decline and increased fracture risk, several studies do not consistently support these associations.[17,19,38] Higher TSH levels are associated with increased heart failure risk.[38] However, the management of elevated TSH in older adults, especially regarding treatment with LT4, is contentious due to potential risks, including cardiovascular issues and fractures.[17] Evidence suggests that LT4 therapy is most beneficial for those with TSH levels above 7.0 mIU/L, as lower levels do not show significant improvements in symptoms or health outcomes.[38]

Pregnancy and preconception

SCH during pregnancy and preconception poses clinical challenges due to the importance of thyroid hormones for foetal neurodevelopment and maternal health.[2,17] During pregnancy, TSH levels initially decrease due to human chorionic gonadotropin (hCG), then subsequently rise; diagnosis thresholds for SCH are trimester dependent.[9,17] SCH in pregnant women can lead to complications such as gestational hypertension and cognitive impairments in infants, warranting treatment with LT4 for women of childbearing age, especially those planning conception.[17] Monitoring thyroid peroxidase antibody (TPOAb) status is essential, as 50% of TPOAb-positive pregnant women are at higher risk and require LT4 to keep TSH levels below the midpoint range for their trimester.[17] TPOAb-negative women

Table I: Key dosing, TSH targets, and monitoring recommendations in pregnancy and postpartum

Clinical scenario	LT4 Dose (µg/kg/day)	TSH target (mIU/L)	Monitoring frequency	Rationale/Key consideration
Pre-existing hypothyroidism (on LT4 pre-conception)	Increase dose by 25–50% on confirmed pregnancy	< 2.5 (T1); < 3.0 (T2); < 3.5 (T3)	Every 4 weeks in the first half of pregnancy, every 4–6 weeks thereafter	hCG-driven rise in T4 demand increases LT4 requirement from the first trimester; undertreated OH risks foetal neurodevelopmental harm[2,17]
SCH, mild (TSH ≤ 4.2 mIU/L), TPOAb-positive	1.20	Below trimester midpoint: < 2.5 (T1); < 3.0 (T2/T3)	Every 4 weeks until 20 weeks; then every 4–6 weeks	TPOAb-positive women have ~50% higher risk of progression; treatment reduces miscarriage and preterm birth risk[17]
SCH, mild (TSH ≤ 4.2 mIU/L), TPOAb-negative	Observe: LT4 is not routinely recommended	≤ 4.0 (any trimester)	Every 4–6 weeks, recheck if symptoms develop	Evidence for benefit is limited in TPOAb-negative women with mild SCH; watchful monitoring is preferred[2, 37]
SCH, moderate–severe (TSH 4.2–10 mIU/L), any TPOAb status	1.42	< 2.5 (T1); < 3.0 (T2); < 3.5 (T3)	Every 4 weeks until 20 weeks; every 4–6 weeks thereafter	Gestational hypertension, cognitive impairment in offspring, and miscarriage risk are significantly elevated at this TSH range[9,17]
Overt hypothyroidism (TSH ≥10 mIU/L or suppressed FT4)	2.33	< 2.5 (T1); < 3.0 (T2); < 3.5 (T3)	Every 4 weeks until stable, then every 4–6 weeks	Untreated OH carries the highest risk of foetal harm; treatment is mandatory and urgent[2,3]
Postpartum SCH (TSH < 5 mIU/L), TPOAb-positive	Stop therapy; recheck TSH at 6 weeks postpartum	0.5–4.0 (non-pregnant range)	TSH at 6 weeks; if abnormal, repeat at 3 and 6 months; annual TSH thereafter	TPOAb-positive women face an elevated risk of postpartum thyroiditis and long-term hypothyroidism; annual follow-up is warranted[17]
Postpartum SCH, TPOAb-negative	Stop therapy; no routine LT4 required	0.5–4.0 (non-pregnant range)	Recheck TSH for 6 weeks; if normal, no further thyroid-specific follow-up required	Low risk of persistent hypothyroidism postpartum in the absence of autoimmune thyroid disease[17]

typically are initiated on treatment only if TSH exceeds 10 mIU/L. A 2019 meta-analysis by Biondi et al. [37] linked SCH to a higher risk of hypertensive disorders but found limited support for the benefits of LT4 treatment. This raises debates about universal versus targeted screening, with current guidelines favouring high-risk women, potentially missing many cases, especially in iodine-deficient populations with high autoimmune burden.[2] Most SCH cases during pregnancy are temporary, but women with positive TPO antibodies and elevated TSH levels may need persistent monitoring. If treatment is necessary, LT4 dosage is tailored to individual needs, with a focus on normalising thyroid levels preconception to mitigate adverse pregnancy outcomes, as summarised in Table I.[3]

Comorbid conditions

SCH's clinical implications are notably affected by comorbid conditions. SCH is linked to dyslipidaemia, endothelial dysfunction, and raised coronary event risks, particularly when TSH levels exceed 10 mIU/L.[17] In patients with cardiovascular issues, treatment must balance metabolic gains against risks. While LT4 may improve cardiovascular markers, conclusive outcome data are lacking, leading to uncertainty about screening and treatment thresholds.[17] In chronic kidney disease (CKD), SCH is common and may result from altered thyroid hormone metabolism, serving as an independent predictor of CKD progression.[17] Some guidelines suggest thyroid hormone replacement or treatment may slow eGFR decline and improve renal function.[40] Additionally, in polycystic ovary syndrome, SCH is significant due to its association with insulin resistance and other endocrine dysfunctions, suggesting treatment should be considered in select cases. However, prevalence estimates and treatment benefits vary. Further research is essential to determine the specific impact of SCH on metabolic outcomes in these populations.[41]

Drug-induced cases

Several medications, notably amiodarone, lithium, and tyrosine kinase inhibitors (TKIs), can induce SCH, approximately 20% of patients on amiodarone experience thyroid-related side effects, necessitating long-term thyroid function monitoring.[42] Lithium-induced hypothyroidism occurs more frequently in women and during the initial two years of medication. In numerous instances, an underlying factor of autoimmune thyroiditis is present. TKIs like sunitinib and sorafenib lead to hypothyroidism through destructive thyroiditis and reduced iodine uptake.[42] Management of drug-induced SCH requires an individualised approach, including regular TSH monitoring before initiating LT4. Decisions about discontinuing the causative medication can be complicated, and if the medication must be continued, LT4 is typically used to maintain thyroid function while preserving therapeutic benefits.[42]

Emerging perspectives and future directions

Personalised medicine approaches

Personalised medicine approaches aim to tailor treatments to individual symptoms and biology, moving away from generalised therapies. In hypothyroidism, while LT4 is commonly effective,

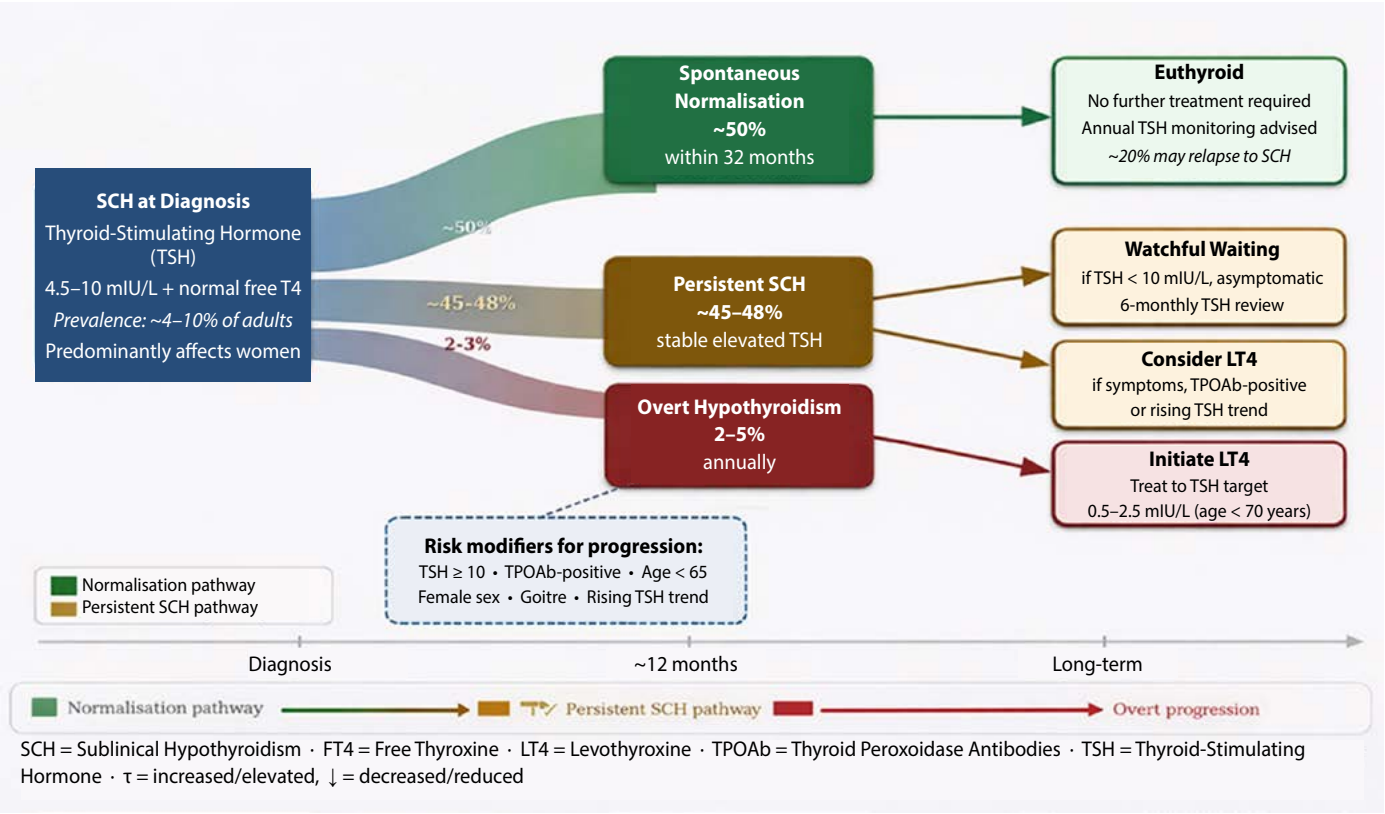

Figure 3: Natural history of subclinical clinical hypothyroidism – progress probabilities: SCH at diagnosis → over time → outcomes of (a) spontaneous normalisation (~50%), (b) persistent SCH, (c) progression to OH (2–5%)[3,5]

many patients remain symptomatic despite normal TSH levels.[43] Genetic variations, particularly in the DIO2 gene, dictate thyroid hormone metabolism, causing some individuals to respond better to combination T3 and T4 therapy.[44] Additionally, each person has a unique TSH set point, influenced by factors such as aging and seasonality, which complicates the ideal treatment approach.[10] TSH may not always reflect true thyroid hormone status, prompting exploration of serum T4 and FT3 levels as better biomarkers.[45] New research highlights the potential of metabolic biomarkers in diagnosing and managing hypothyroidism, with findings suggesting distinct metabolic profiles in hypothyroid individuals. Advances such as the Magnetic Chemiluminescent Immunoassay (MCLIA) kit for detecting thyroid autoantibodies offer promising auxiliary indicators for thyroid function assessment.[45]

Novel therapeutic options

Combination T4/T3 therapy is considered for patients still experiencing symptoms, such as fatigue and cognitive issues despite achieving normal TSH levels from LT4 monotherapy.[43] A systematic review by Nassar et al.[46] reported that individuals on combination therapy had lower serum FT4 and total T4 but higher total T3 levels, while TSH remained similar. Alternative formulations and targeted interventions, including tailored LT4 dosing based on individual profiles, are recommended. Notably, combination therapy may benefit individuals with specific gene polymorphisms and those with persistent symptoms, while special considerations for dosing are necessary in geriatrics and pregnant women.[44]

Research gaps

To improve long-term outcomes for patients undergoing LT3 and/or LT4 therapy, regular clinical and biochemical monitoring is crucial, as shown in Figure 3. An 18-month surveillance period is recommended, as 40% of patients may experience suboptimal dosing, leading to persistent symptoms or increased risks, such as atrial fibrillation.[47] Technological interventions for hypothyroidism diagnosis include AI-assisted ultrasound, the ACR Thyroid Imaging Reporting and Data System (TI-RADS), and digital health tools, which can improve patient stratification.[48] Currently, no validated serum biomarkers reflect tissue-specific thyroid hormone levels; however, potential markers include lipid derivatives and CD5L, which are linked to tissue hypothyroidism.[49] Lastly, while LT4 treatments are relatively low-cost, associated annual expenses can be significant, ranging from $460 to $2555 per patient, with higher costs observed in non-euthyroid patients.[50]

Limitations

The existing evidence base has certain limitations that must be acknowledged. Initially, several relationships outlined in this review, such as those connecting subclinical hypothyroidism (SCH) to cardiovascular risk, metabolic disturbances, and neurocognitive decline, are primarily based on observational studies, which are prone to confounding factors and are unable to demonstrate causality.[3,5,32] The Thyroid Studies Collaboration, conducted by Rodondi et al.,[32] provides the most comprehensive epidemiological data; however, both studies are constrained by their non-interventional design.[32] Secondly, notable heterogeneity is observed across the reviewed studies regarding the laboratory techniques employed to quantify TSH, with interlaboratory variability in assay platforms influencing the comparability of TSH thresholds and reference ranges across different populations.[6] This limits the generalisability of the findings and hinders direct comparisons across guideline recommendations from different organisations. Lastly, results from long-term randomised controlled trials are still limited. The aforementioned TRUST trial monitored patients for only 1 year, leaving the effects of LT4 on significant clinical endpoints, such as cardiovascular events, fractures, and cognitive outcomes, across 5 or more years essentially unexamined.[26] The meta-analyses compiled in this review[29-31] may be influenced by publication bias, as studies yielding null or negative outcomes for LT4 might be underrepresented in the available literature, thereby distorting pooled effect estimates. These limitations collectively highlight the necessity for sufficiently powered, long-term RCTs employing standardised TSH tests and patient-reported outcome measures to address the ongoing uncertainty in the therapy of SCH.

Conclusions

SCH presents a complex challenge within the realm of thyroid function and management. While it affects a significant proportion of the population, particularly women and older adults, the variability in its clinical manifestations and progression necessitates a nuanced approach to diagnosis and treatment. The association of SCH with various health risks, including cardiovascular complications and metabolic disorders, highlights the importance of careful evaluation and monitoring of thyroid function in at-risk individuals. However, the conflicting evidence surrounding the benefits of treatment raises critical questions about the appropriateness of intervention in this population. As the scientific community continues to explore the intricate relationship between thyroid hormones and overall health, there remains an urgent need for more robust research to clarify the long-term effects of SCH and to develop tailored management strategies. Ultimately, a balanced approach that considers individual patient profiles, symptomatology, and the potential risks and benefits of treatment is essential. By integrating emerging perspectives, such as personalised risk assessments and advanced biomarkers, clinicians can enhance their decision-making process, leading to improved outcomes for patients with SCH. Through ongoing dialogue and research, we can bridge the existing knowledge gaps and refine our understanding of this enigmatic condition. Until more definitive evidence emerges, a TSH threshold of ≥ 10 mIU/L remains the clearest indication for LT4 therapy, while shared decision-making is essential for the 4.5–10 mIU/L range.

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Advancing wound care: Antiseptic strategies – povidone-iodine

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Abstract

Microbial contamination remains a major challenge in wound healing and is frequently associated with delayed tissue repair, chronic infection and additional tissue damage. Effective management of microbial burden is, therefore, a central objective in wound care. In this context, topical antiseptics play an important role in limiting microbial proliferation and supporting the healing process.

This review examines the pharmacological properties of commonly used antiseptics in wound management. Particular attention is given to their mechanism of action, antimicrobial spectrum of activity and potential for resistance development. The antiseptics discussed include iodine-based products, biguanides such as chlorhexidine, octenidine, oxidising agents, silver-containing formulations and honey as a natural therapeutic agent.

Unlike antibiotics, which typically act on specific molecular targets, antiseptics exert their broad-spectrum antimicrobial activity through multiple mechanisms. These include disruption of microbial cell membranes, protein denaturation and oxidative damage. Because several cellular targets are affected simultaneously, the likelihood of rapid resistance development is generally reduced.

The selection of an appropriate antiseptic should not rely solely on antimicrobial potency. Factors such as cytotoxicity, tissue compatibility and overall safety must also be considered. Careful selection of antiseptic agents, guided by current evidence, is therefore essential to optimise wound-healing outcomes, while supporting responsible stewardship in pharmacy practice.

Keywords: antiseptics, iodine, chlorhexidine, wound healing, antimicrobial resistance

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Introduction

Topical antibiotics have been considered the treatment of choice for skin infections and infected wounds for many years. However, with the emergence of antimicrobial resistance, the topical use of antiseptics has experienced a renaissance in recent years.[1,2] Concerns about the apparent cytotoxicity of traditional antiseptics led clinicians to be reluctant to use them in wound management.[3]

The normal wound-healing process involves a tightly regulated sequence of inflammation, proliferation and remodelling, mediated by fibroblasts, keratinocytes, endothelial cells and macrophages.[2] However, when a wound fails to progress through the phases of wound healing, chronic wounds may occur. Therefore, a wound infection is defined as the "invasion of a wound by proliferating microorganism to a level that invokes a local and/or systemic response in the host", according to the International Wound Infection Institute.[4]

Comparative analysis: antiseptics, disinfectants and antibiotics

Clear differentiation between antiseptics, disinfectants and antibiotics is essential for appropriate therapeutic selection. The term *antiseptic* is derived from the Greek word *anti* (against) and *sepsis* (rot); literally meaning "against rot".[5] Historically associated with infection prevention, antiseptics are now defined pharmacologically as chemical agents used on skin and mucous membranes to inhibit or destroy microorganisms. Importantly, antiseptics generally exhibit broad-spectrum activity, enabling them to target multiple types of microorganisms simultaneously.[5]

Disinfectants eliminate microorganisms in their active state and inhibit microbial reproduction but are intended for use on inanimate surfaces due to potential tissue toxicity. While topical antibiotics are commonly formulated as creams and ointments, they do not facilitate autolytic debridement or help regulate the moisture management within the wound bed.[5] Another important distinction concerns antimicrobial resistance. Resistance to antibiotics may arise from a single mutation, whereas resistance to topical antiseptics often requires multiple mutations.[6] Antiseptics are typically broad-spectrum and may demonstrate antibacterial, antifungal, and antiviral activity. This broader mechanism of action and lower propensity to develop single-step resistance underscore the relevance of antiseptics in contemporary wound care practice.[5] Early and appropriate application is therefore considered an important component of infection prevention strategies in wound care.[7,8]

Classification and pharmacological action

Several antiseptic classes are commonly employed in wound care practice. Antiseptics exert their effects through pharmacological, metabolic and/or immunological mechanisms. Antiseptics are generally classified as halogenated compounds, alcohol-based agents, biguanides, and quaternary ammoniums. Each class differs in modes of action, antimicrobial spectrum, cytotoxicity profile, tissue compatibility, and suitability for acute versus chronic wounds, as summarised in Table I.

Table I: Antiseptics classification, examples and application[4-10]

Classification	Mode of action	Examples	Application
Halogenated oxidising compounds			
Chlorous agents	Superoxide radicals damage enzymes in the cells and promote apoptosis cell death	Sodium hypochlorite (NaOCl) Hypochlorous acid (HOCl) Dakin's solution (0.05%)	• Act as surface surfactant (0.0125–0.05%) • Antiseptic for skin and mucosal wounds (0.005–0.01%) • Surgical site antiseptic (0.01–0.05%) • Irrigate traumatic, acute or chronic wounds without drainage, e.g., peritoneal cavity • Requires accurate pH monitoring, temperature control, and proper storage (pH above 11 at 20 °C) • No absorption in intact cell layer • Allergic reaction and dermatitis may be observed • Fair biofilm activity • Excellent tissue compatibility • Effectiveness depends on protein load and wound exudate
Iodine-based agents	Releases free iodine from a neutral polymer base, causing oxidation and iodination of fatty acids, amino acids and nucleic acids leading to cell membrane destabilisation	Povidone-iodine (PVP-I)	• Intraoperative rinse reduces incidence of infection (4% PVP-I) • Dilutions of 0.1–1% work faster than a 10% solution due to an increase of free iodine in the solution • 1% solution is sporicidal against spores of *Bacillus subtilis* in 28–93 minutes for a 99% kill • Broad spectrum of antimicrobial activity • Inhibit biofilm development by *Staphylococcus epidermidis (S. epidermidis)*, *Staphylococcus aureus (S. aureus)*, *Klebsiella pneumoniae (K. pneumoniae)*, *Pseudomonas aeruginosa (P. aeruginosa)* and *Candida albicans* (*C. albicans*) • Quick onset of action within 15 seconds–1 minute • Suitable for sharp, cut and lacerated superficial skin and mucous membrane wounds • Not recommended for chronic wounds due to its cytotoxicity • Not teratogenic, neurotoxic or mutagenic • PVP-I is not recommended in newborns, young children, pregnancy or lactation • Contraindicated in thyroid disease and iodine radiotherapy • PVP-I less irritating to the skin than ordinary iodine solution • Risk for allergic reaction in iodine-sensitive individuals (low prevalence of 0.4%) • Fair tissue compatibility • Do not use long term
Alcohol-based compounds	Denaturation of microbial protein component	Ethanol (alcohol) Isopropyl alcohol (isopropanol)	• Optimum concentration: 60–95 % in water: bactericidal, virucidal, mycobactericidal • 70% concentration: skin disinfectant; instrument disinfectant • 70%: preoperative skin disinfectant • Effective combination with chlorhexidine and iodine • Isopropyl alcohol: greater bactericidal than ethanol but twice as toxic
Biguanides	Negatively charged phosphate phospholipid groups bind to the bacterial cell wall, disrupting membrane function and microbial cell death	Polyhexamethylenebiguanide (PHMB)	• Colourless, odourless, non-corrosive, water- and alcohol soluble • Bactericidal within 15–30 minutes • Low absorption to epidermis • Commercially prepared in combination with betaine or Ringer's solution • Concentrations of 0.02%, 0.04% and 0.1%. are sufficient • Impregnated dressings completely eliminate *S. epidermis* strains within 24 hours • Effective against Gram-positive, Gram-negative bacteria and *C. albicans* • Large margin of safety. • Good–excellent tissue compatibility • Excellent tissue compatibility
		Chlorhexidine	• Safe dilutions 0.05–2% solution or gels • Wound irrigation and cleaning • Use as preoperative skin antisepsis and not for wound treatment • Prophylaxis against superficial surgical site infection (SSI), bloodstream infection • Fair biofilm activity • Poor tissue penetration • Undiluted solutions are cytotoxic and delay wound healing • Not to be used on chronic wounds

Table I: *Continued*

Classification	Mode of action	Examples	Application
Quaternary ammoniums	Cationic, surface-active compound allowing OCT to bind to negatively charged surfaces enveloping microbial cell membranes, causing structural disruption	Octenidine (OCT)	• Handwashing gels (0.05–1%) • 0.05–1% concentration microbicidal in 1 minute against bacteria and fungi (*S. aureus*, *C. albicans*) • Acute, traumatic and infected wounds at 0.1% concentration in combination with phenoxyethanol • Oral cavity disinfectant • OCT gels are suitable for burn wounds; superior to PVP-I and silver-containing products • Not absorbed through the skin • Safe to use in babies, pregnant and breastfeeding women • OCT-coated tracheostomy tubes reduce infection in ventilated patients • Coat surgical sutures • Good biofilm activity • Excellent tissue compatibility • Suitable for chronic wounds
Nanocrystalline silver	Impairs cell membrane permeability by modifying bacterial membrane proteins, reacts with sulphur and phosphorus in membrane DNA, leading to H^+ leakage and cell death (apoptosis)		• Used as gel and impregnated dressings • Medical devices coating • Nanoparticle size and shape determine biochemical, physical and antimicrobial properties • Smaller than 10 nm and triangular shape is best • Poor biofilm activity • Fair tissue compatibility • Bactericidal activity against Gram-negative and Gram-positive bacteria, fungi and viruses • Resistant organisms: *E. coli*, *P. aeruginosa*, *K. pneumoniae*
Honey	Immunomodulatory activity Polyphenols in honey accelerate hydroxyl radical formation (H_2O_2) and oxidative strand breakage of DNA		• Pure honey, gel or dressings • Fair biofilm activity • Excellent tissue compatibility • Appropriate for most wounds • Used in conjunction with other antimicrobial agents • Effective against several Gram-positive and Gram-negative skin pathogens (*E. coli*, *S. aureus*)

Therapeutic index

According to Geng et al., higher therapeutic indices (TIs) indicate better safety and effectiveness.[6] The therapeutic indices for the topical antiseptics were predominantly low, typically ranging from 0.5–3.0. Hypochlorous acid produced the highest therapeutic index (TI) for *P. aeruginosa* (8.81), *S. aureus* (6.31) and *E. coli* (5.49). The highest TI value for methicillin-resistant *S. aureus* (12.1) was observed with polyhexamethylene biguanide. The TI of a topical antiseptic was calculated as the ratio of the mean cytotoxic concentration (CT50) in a mammalian cell line to the mean bactericidal concentration (MBC) of a bacterial species. A low value indicates low effectiveness, while higher values indicate high effusiveness ratios.[6]

Ideal antiseptic product

Antiseptics should be safe for general use, free of causing allergic reactions or pain, and not toxic, carcinogenic, or mutagenic. Furthermore, they must not impede the wound healing process. The ideal properties are summarised in Table II.

Table II: Properties of an ideal antiseptic product[4]

Properties of an ideal antiseptic product
It is not toxic, carcinogenic or mutagenic
Non-traumatic
Does not cause an allergic reaction
Does not cause pain
Can handle excess wound exudate
It is fast-acting in acute wounds
Does not cause resistance or cross-resistance
Ability to penetrate biofilm
Suitable chemical and physiological properties that do not colour the skin, an acceptable smell and a suitable consistency
Cost-effective
Easy and safe to use
Tolerability equal to physiological saline

Comparative clinical efficacy: povidone-iodine

Recent clinical evidence underscores the therapeutic value of povidone-iodine (PVP-I) across various wound care and surgical settings. A systematic review by Barringah-Benissan et al. found that iodine-based treatments were associated with significantly better wound-healing outcomes than saline irrigation, with a

relative risk (RR) of 1.85 (95% CI, 1.27–2.69).[7] The clinical utility of PVP-I is largely due to its broad antimicrobial spectrum. According to a narrative review by Alves et al., the extensive antimicrobial spectrum of PVP-I is more beneficial than the restricted antimicrobial activity exhibited by polyhexanide (PHMB) and silver-containing products.[2]

Furthermore, the role of PVP-I in surgical prophylaxis remains robust. In a large-scale randomised controlled trial involving 3360 patients, PVP-I in alcohol was found to be noninferior to chlorhexidine gluconate in alcohol for preventing surgical site infections (SSIs) following cardiac or abdominal surgery.[11]

Conclusion

In summary, the management of the wound microenvironment remains a complex clinical challenge, necessitating a transition from passive cleaning toward proactive, evidence-based antisepsis. While the introduction of newer agents such as polyhexanide and silver-based products has expanded the clinical toolkit, established halogenated compounds, especially PVP-I, continue to demonstrate robust efficacy and a broad antimicrobial spectrum, remaining noninferior to more modern alternatives in many settings. The selection of a topical antiseptic must be guided by the TI, balancing potent bactericidal activity with preservation of mammalian cell viability. As the clinical threat of single-step antibiotic resistance continues to grow, the multi-target mechanisms of broad-spectrum antiseptics offer a sustainable and effective strategy for mitigating microbial burden, preventing early biofilm formation and facilitating the physiological progression of wound healing.

Conflict of interest

The author declares no conflict of interest.

Ethical approval

Ethical approval was not required.

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Prebiotics, probiotics and synbiotics in human health, clinical applications – an update

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Abstract

Probiotics have become well-known and widely used, especially as supplements or add-on therapy, in the prevention and management of antibiotic-associated diarrhoea. However, their mechanisms, strain-specific effects and appropriate clinical use remain poorly understood by both pharmacists and patients. Furthermore, recent reports of an *Alkalihalobacillus clausii* outbreak emphasised the importance of appropriate clinical use of probiotics, particularly in severely immunocompromised patients. This article provides an overview of prebiotics, probiotics and synbiotics, including their mechanisms of action, clinical applications and available products on the local market.

Keywords: prebiotics, probiotics, synbiotics, *Lactobacillaceae* or lactic acid bacteria, gut–brain axis or microbiota

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Introduction

Scientific interest in probiotics dates back to the early 20th century when lactic acid bacteria (*Streptococcus thermophiles* and *Lactobacillus delbruekii* subspecies of *bulgaricus*) in fermented milk products were linked to improved gastrointestinal health.

During a dysentery outbreak among soldiers in World War I, Nissle isolated a non-pathogenic *Escherichia coli* strain from an unaffected individual and later developed it as a therapeutic probiotic *(E. coli)*.[1] The family *Enterobacteriaceae* (Gram-negative rods) were found to be associated with plant material, as well as soil and water.[1] This might be due to the difficult circumstances and lack of hygiene.[1] Soldiers were severely affected by Shigellosis, however, the German Professor Alfred Nissle noticed that one of the soldiers was not affected during this severe outbreak.[1] Through careful research, he isolated a non-pathogenic strain of *E. coli* from the faeces of that soldier. All indications suggested that this non-pathogenic strain had prevented the soldier from acquiring Shigellosis.[1] This was subsequently interpreted to be a so-called probiotic. The strain isolated by Nissle in 1917 is an example of a non-lactic acid bacteria probiotic.[1]

The growth of favourable organisms can be stimulated by microbial factors, and in 1965 Lilly and Stilwell introduced the term "probiotics".[1,2] The beneficial effect from probiotics on the host was emphasised by Roy Fuller in 1989.[1,2] Relevant and commonly used terminology is described in Table I.

What are probiotics?

Probiotics are currently defined as 'live' micro-organisms which, when administered in adequate amounts, confer a health benefit on the host.[4] The host may benefit from probiotics when living micro-organisms are administered in an adequate amount to restore microflora symbiosis in the gastrointestinal (GI) tract.

Most clinically used probiotics belong to genera historically classified as *Lactobacillus, Bifidobacterium, Enterococcus, Lactococcus and Streptococcus*.[5] These Gram-positive bacteria and strains are also found in hair, skin, the mouth, respiratory tract, intestinal tract and other parts of the human body. Favourable strains, such as *Lactobacilllus acidophilus, Lacticaseibacillus rhamnosus, Lactobacillus bulgaricus, Lacticaseibacillus casei, Lactiplantibacillus plantarum*, *Ligilactobacillus salivarius*, *Lactobacillus sporogenes*, and *Bifidobacterium bifidus*, *Bifidobacterium bifidum*, *Bifidobacterium infantis* and *Bifidobacterium longum*, are commonly used in a probiotic formula.[6]

Probiotics that are most frequently encountered contain the predominant and subdominant organisms of the GI microbiota

Table I: General probiotic-related terms and definitions[1,3]

Lactic acid bacteria (LAB)	Gram-positive bacteria which are fermentative, non-pathogenic and non-toxigenic. They produce lactic acid from carbohydrates, which makes them valuable for food fermentation.[1] These species include: *Lactobacillus*, *Lactococcus*, and *Streptococcus thermophiles*[1]
Fermentation	Micro-organisms produce lactic acid, ethanol, and other metabolic end-products to convert food into other products[1]
Species	A group of related bacteria which are highly similar by phenotype but differ in specific characteristics[3]
Bacteriocins	A protein that is produced by some bacteria that constrains or kills closely related species[3]
Mucin	Glycoproteins that contain a high molecular weight and found in the secretion of mucous membranes[3]

and added to different types of food. The yeast species, *Saccharomyces boulardii*, has also been shown to have a beneficial effect on health status. Food industry personnel are interested in these organisms, because of the beneficial effects that they have on health, as well as the history of the safe use of fermented milk products.[7]

Safety is of paramount importance, therefore, probiotics should adhere to specific standards, including their tolerance of gastric acid and bile in the GI tract, ability to adhere to the GI mucosa, their competitive exclusion of pathogens, production of lactic acid and shorter generation time.[8] Additionally, probiotics need to be non-invasive and non-carcinogenic to form normal balanced flora.[8]

The survival of probiotics through the GI tract can be influenced by the acidity of the stomach, the concentration and length of exposure to the acid and bile salt, and the level of bile salt hydrolase activity. Therefore, it is important that probiotics can survive gastric and bile acid when administered so that they can reach the GI tract. They must also be able to colonise the host epithelium and demonstrate a beneficiary effect.[7] It has been shown that non-spore-forming lactobacilli-type probiotics are inactive in the low gastric pH and the bile. Probiotics can be found in food and dietary supplements, such as tablets, capsules and powder. It has been stated that the bacteria may have already been present or added during the preparation of probiotic food. These probiotics should be stored in acceptable conditions to ensure that they have long-term activity and feasibility for use in the general population.[6]

Mechanism of action of probiotics

Probiotics exert multiple, strain-specific effects that include enhancement of epithelial barrier integrity, competitive exclusion of pathogens, production of antimicrobial compounds and metabolites, and modulation of host immune and neuroendocrine signalling pathways.[7] Furthermore, probiotics can produce neurotransmitters in the gut through the gut-brain axis. Specific probiotic stains can modulate the serotonin, gamma-aminobutyric acid (GABA), and dopamine levels, affecting mood, behaviour, gut motility, and stress-related pathways.[9] Within the established brain-gut axis, strains can influence neuromodulator production, vagal signalling and stress-response pathways, although human evidence remains heterogeneous and appears to be condition- and strain-specific.[5,10]

While largely established during the prenatal period and early childhood, these interactions can be modified throughout life by factors such as diet, medication use, and stress.[10] Emerging human evidence suggests that dysregulation of this axis may play a role in brain-gut disorders.[10]

Probiotic bacteria can stimulate the host defence mechanisms by enhancing the immune system, which acts on both humeral and cellular responses. Probiotics can also ease digestion by stabilising the microflora, as well as preventing hypersensitivity-reactions to food antigens.[11] In stimulating the synthesis of immunoglobulins and cytokines, the effects of general probiotics are also associated with modulation of the immune response. *Lactobacillus* spp. shows macrophage activation, as well as an increase of phagocytosis, as confirmed by various clinical studies. Organisms such as bacteria, fungi and viruses are responsible for activation of the inflammatory cascade. Probiotics reduce the inflammatory reaction and simultaneously enhance the immune response. The duration of acute infections, like diarrhoea in children, traveller's diarrhoea and diarrhoea caused by *Clostridium difficile* infection, is effectively reduced by numerous probiotic strains, including *Limosilactobacillus reuteri, L rhamnosus* and *L casei*.[2] Meta-analyses indicate that specific probiotics, particularly *L rhamnosus,* GG and *S. boulardii* CNCM I-745, can reduce the incidence of antibiotic-associated diarrhoea by approximately 40–50% in adults and children, although effect sizes vary by strain, dose and population.[12]

Multiple factors are prominent regarding the beneficial effects of probiotics, although the mechanisms are not yet fully understood. Mechanism of action is achieved as:[13]

Table II: An overview of human intestinal microbiota[2,3,15,16]

Oral cavity (saliva)	*Bacteroides*, *Bifidobacterium*, *Corynebacterium*, *Fusobacterium*, *Lactobacillus*, *Neisseria*, *Staphylococcus*, *Streptococcus*, *Veillonella*[3,15]
Stomach (pH 1-2) Duodenum (pH 6-7)[3]	Only a small number of micro-organisms, because of the low pH[15] < 10^3 bacterial cells per gram of stomach contents[2] Mainly *Enterococcus*, *Helicobacter*, *Lactobacillus*, *Streptococcus*[1,15] Acidic, pancreatic secretions as well as bile secretions cause an unfavourable environment for microbes[1] Stomach: *Bacteroidetes*, *Bifidobacterium*, *Enterobacteriaceae*, *Lactobacillus*, *Streptococcus*, yeasts[3] Duodenum: *Bacteroides*, *Bifidobacterium*, *Enterobacteriaceae*, *Lactobacillus*, *Streptococcus*, *Veillonella*, yeasts[3]
Jejunum and ileum (pH 6-7)[3]	There is a progressive increase in the number and diversity of the bacteria[1] Ileum: *Bacteroides*, *Bifidobacterium*, *Clostridium*, *Enterobacteriaceae*, *Lactobacillus*, *Streptococcus*, yeasts[3]
Colon (pH 5-7)[3]	The large intestine contains a high population of anaerobes[1] The colon contains the majority of gastrointestinal microbes[15] Colon: *Bacteriodetes* such as *Bacteriodaceae*, *Prevotellaceae* and *Rikenellaceae,*[16] *Bifidobacterium*, *Clostridium*, *Coprococcus*, *Enterobacteriaceae*, *Eubacterium*, *Lactobacillus*, *Peptostreptococcus*, *Ruminococcus*, *Streptococcus*[15]
Faeces[3]	Faeces: *Bacteroides, Bifidobacterium, Clostridium, Coprococcus, Enterobacteriaceae, Eubacterium, Lactobacillus, Peptostreptococcus, Ruminococcus, Streptococcus, Veillonella*, yeasts[3]

- The gastrointestinal epithelial barrier function is enhanced
- Pathogen adhesion is inhibited, owing to concomitant probiotic adhesion to the intestinal mucosa
- Pathogenic micro-organisms are excluded through competition with the probiotics
- Anti-microorganism substances are produced
- The immune system is modulated

Immune modulation is achieved through the interaction of the probiotics and the host cells.[14] The target is predominantly gastrointestinal epithelial- and gastrointestinal-associated immune cells in this process.[14] An overview of naturally occurring human intestinal microbiota is provided in Table II.

The non-immune mechanisms and the mucosal immune mechanisms show a positive reaction when stimulated by probiotics, affecting the intestinal ecosystem. This is achieved through antagonism and competition with potential pathogens. Probiotics are mostly recognised for the decrease in the incidence of diarrhoea, as well as the severity of the disorder. Excellent results have been obtained in certain animal models in decreasing colon cancer, probably due to the suppressing activity of certain bacterial enzymes which may have raised the levels of the procarcinogens. Unfortunately, this has not yet been achieved in human models. Probiotics have numerous benefits, which can be classified as either beneficial or non-immunological.[1] Probiotics have the following immunological benefits:[1]

- Increased antigen presentation of B lymphocytes and increased secretory immunoglobulin A production is activated by the local macrophages, and affect the system both locally and systemically
- The cytokine profiles are modulated
- Hypo-responsiveness to food antigens is established

Non-immunological benefits include:[1]

- Food digestion is improved, and increased competition with pathogens for the nutrients is achieved
- The local pH is adjusted to create an unfavourable local environment for pathogens
- Pathogens are inhibited by the production of bacteriocins
- Superoxide radicals are removed
- The epithelial mucin production is stimulated
- The intestinal barrier function is enhanced
- There is competition for adhesion with the pathogens
- The pathogen-derived toxins are modified

Excellent results have been reported in various human studies and animal models regarding the clinical potential of probiotics against many diseases. Probiotics have been reported to:[11]

- Suppress diarrhoea
- Alleviate postoperative complications and lactose intolerance
- Exhibit anti-colorectal cancer and antimicrobial activity
- Reduce irritable bowel symptoms
- Prevent inflammatory bowel disease

To summarise, it can be stated that probiotics are confirmed to be safe and should adhere to certain conditions. For example, probiotics should:[4]

- Not lose their properties during storage
- Normally be present in the human intestines
- Survive in the gastrointestinal tract and colonise the intestinal cells
- Have beneficial effects on human health
- Display antagonism against pathogenic micro-organisms
- Not demonstrate any noticeable side-effects

The potential health benefits of probiotics tend to be strain-specific and generalisations of probiotic benefits do not attribute to different strains within one species.[4] Consequently, caution should be exercised when consuming or prescribing probiotics. This is illustrated by a recent outbreak reported by the National Institute for Communicable Diseases (NICD), which was linked to the use of the Enterogermina probiotic in private hospitals in South Africa.[17] The product contained *Alkalihalobacillus clausii*, and whole-genome sequencing identified Enterogermina as the likely source of *A. clausii bacteraemia*. Although *A. clausii* is generally considered a non-pathogenic bacillus, these findings highlight the need for caution when administering probiotics, specifically to severely immunocompromised patients.

The use of probiotics and prebiotics

Evidence has been demonstrated in some studies, suggesting that probiotics have various clinical applications (see Table III).[2]

Prebiotics

The term 'prebiotic' was first introduced in 1995 and was recently redefined as a beneficial substrate that is selectively used by host micro-organisms.[16] They enhance the growth and activity of specific intestinal strains, and can therefore effect a favourable change in the balance of the intestinal microflora.[2] Prebiotics are mainly dietary fibre, particularly soluble fibre, and are also known as 'colonic food', consisting of specific carbohydrates.[2] Established prebiotics such as inulin, fructo-oligosaccharides and galacto-oligosaccharides are selectively fermented by components of the gut microbiota, leading to increased production of short-chain fatty acids that can modulate luminal pH, epithelial barrier integrity, immune responses and host energy metabolism.[19] The mechanism of action of prebiotics constitutes their effects on the intestinal bacteria through their ability to enhance the amount of beneficial anaerobic bacteria, and to decrease the pathogenic micro-organism population in number.[1,2]

Table III: The clinical applications of probiotics[2]

Probiotic/prebiotic	Recommended dose
Acute diarrhoea in adults	
Enterococcus faecium	10^8 cfu, three times daily
Lacticaseibacillus paracasei or *Lacticaseibacillus rhamnosus*	10^9 cfu twice daily
Saccharomyces boulardii, a strain of *Saccharomyces cerevisiae*	10^9 cfu per capsule of 250 mg, 2–6 capsules per day
Acute infectious diarrhoea	
Lacticaseibacillus rhamnosus	10^{10}-10^{11} cfu, twice daily
Saccharomyces boulardii, a strain of *Saccharomyces cerevisiae*	200 mg, three times daily
Antibiotic associated diarrhoea	
Saccharomyces boulardii, a strain of *Saccharomyces cerevisiae*	250 mg, twice daily
Lacticaseibacillus rhamnosus	10^{10} cfu, once or twice daily, or even 2×10^{10} cfu, twice daily
Enterococcus faecium	10^8 cfu, twice daily
Lacticaseibacillus casei in fermented milk	10^{10} cfu, twice daily
Bacillus clausii (Enterogermina strains)	2×10^9 spores, three times daily
Lactobacillus acidophilus + *Lacticaseibacillus casei*	5×10^{10} cfu, once or twice daily
Clostridium difficile diarrhoea in adults	
Lacticaseibacillus casei in fermented milk	10^{10} cfu, twice daily
Lactobacillus acidophilus + *Bifidobacterium bifidum* (Cultech strains)	2×10^{10} cfu each strain, once daily
Oligofructose	4 g, three times per day
Lacticaseibacillus rhamnosus + *Lactobacillus* acidophilus	10^9 cfu each, once daily
Heliobacter pylori eradication	
Lacticaseibacillus casei in fermented milk	10^{10}-10^{12} cfu daily, for 14 days
Lacticaseibacillus rhamnosus GG	6×10^9 cfu, twice daily
Bacillus clausii (Enterogermina strains)	2×10^9 spores, three times daily
Saccharomyces boulardii, a strain of *Saccharomyces cerevisiae*	500 mg to 1 g or $2\text{-}4 \times 10^9$ cfu per day
Kefir	250 mL twice daily
Limosilactobacillus reuteri	10^8 cfu/day
Nosocomial diarrhoea	
Lacticaseibacillus rhamnosus	10^{10}- 10^{11} cfu, twice daily
Bifidobacterium lactis + *Streptococcus thermophiles*	$10^8 + 10^7$ cfu/g of formula
Prevention of respiratory tract infections in athletes	
Lacticaseibacillus casei (Shirota strain in fermented milk)	10^{10} cfu, once daily
Remission in ulcerative colitis	
Escherichia coli	5×10^{10} viable bac, twice daily
Symptoms of irritable bowel syndrome	
Bifidobacterium infantis	10^8 cfu, once daily
Bifidobacterium animalis in fermented milk	10^{10} cfu, twice daily
Lactobacillus acidophilus	10^{10} cfu per day
Treatment of constipation	
Lactulose	20–40 g/day
Oligofructose	> 20 g/day
Treatment of hepatic encephalopathy	
Lactulose	45–90 g/day
Treatment of mildly active ulcerative colitis or pouchitis	
Mixture of eight strains (one *Streptococcus thermophilus*, four *Lactobacillus*, three *Bifidobacterium*)	2×10^{11} cfu, twice daily

Taxonomic nomenclature follows the 2020 reclassification of the genus *Lactobacillus*[18]

Prebiotics are present in numerous edible plants, such as asparagus, bananas, chicory, garlic, leeks, oats, onions, soybeans and wheat. Raw vegetable matter is also a key component of a high percentage of commercial prebiotics. Production is achieved via an enzymatic method, through the trans-glycosylation of monosaccharides or disaccharides, or the hydrolysis of complex polysaccharides.[2]

Synbiotics

A synbiotic is a nutritional supplement containing both probiotics and prebiotics.[20] Synbiotics can be defined as "a mixture comprising live micro-organisms and substrate(s) selectively utilised by host micro-organisms that confers a health benefit on the host", with complementary and synergistic subtypes distinguished based on how the substrate and micro-organisms interact.[20]

This mixture of probiotics and prebiotics works together to ensure that bacterial microflora in the GI tract remain healthy. Synbiotic products include fermented milk products, such as yoghurt and kefir. This may be regarded as functional food, because it restores the normal bacterial microflora and supplies the necessary food for the normal microflora to proliferate. *Bifidobacteria* and fructo-oligosaccharides, *Lactobacillus* GG, inulin, as well as *Bifidobacteria* and *Lactobacilli* with fructo-oligosaccharides or inulin, are the best combinations of available synbiotics.[20]

An overview of commercially available probiotic, prebiotic and synbiotic products is provided in Table IV.

Conclusion

Probiotics are live non-pathogenic micro-organisms, which have a beneficial effect on the health of the host. They are present in the GI tract without causing any side-effects. Probiotics can be used for several conditions, e.g. antibiotic-induced diarrhoea, irritable bowel syndrome and inflammatory bowel disease. Prebiotics are known to be a non-digestible food ingredient. They exert a favourable change in the balance of intestinal microflora by enhancing the growth and activity of some intestinal strains. Synbiotics, a combination of probiotics and prebiotics, are a nutritional supplement.

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Full list of references available on request

Table IV: Examples of commercially available probiotic, prebiotic and synbiotic products in South Africa[21]

Probiotics*	Organism	Detected using DGGE
BioPro Reuteri® straws	*Limosilactobacillus reuteri*	*Limosilactobacillus reuteri*
BioPro Reuteri® tablets	*Limosilactobacillus reuteri*	*Limosilactobacillus reuteri*
Combiforte® capsules	*Lactobacillus acidophilus* *Bifidobacterium bifidus* *Bifidobacterium longum*	*Lactobacillus acidophilus* *Bifidobacterium infantis*
Infantiforte® capsules	*Bifidobacterium infantis*	*Bifidobacterium infantis*
QuantroFlora®	*Bifidobacterium, Lactobacillus acidophilus, Lactobacillus bulgaricus, and Streptococcus thermophilus*	
PREBIOTICS		
Asparagus, bananas, chicory, garlic, leeks, oats, onions, soybeans and wheat[1]		
SYNBIOTICS		
Yogurt and kefir[3]		

Other products include: ProbiFlora®, Probitec®, Reuterina®, Viral Guard®, Duphalac®
*DGGE = denaturing gradient gel electrophoresis

Knowledge, attitudes, and perceptions of healthcare workers on adverse drug reaction reporting in a government hospital in Botswana

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Abstract

Background: Adverse Drug Reactions (ADRs) are a significant concern in health care, affecting patient safety and healthcare costs. Active surveillance through spontaneous reporting (SR) by healthcare professionals (HCPs) is essential for identifying and managing ADRs. This study aimed to assess the knowledge, attitudes, and perceptions of HCPs at a government hospital in Botswana regarding ADR reporting.

Method: A cross-sectional study was conducted using stratified random sampling. Knowledge was operationalised as prior use of an ADR reporting form, chosen as a practical indicator of familiarity with reporting procedures. Attitudes and perceptions were measured using Likert-scale items, with internal consistency assessed using Cronbach's α. Data analysis included descriptive statistics and Pearson Chi-square test.

Results: Of the 260 distributed questionnaires, 133 were completed (51% response rate). Response rates varied across strata, with pharmacy staff accounting for a smaller proportion of respondents. While 26.3% of participants reported prior training, 39.8% had used an ADR reporting form. A significant association was observed between encountering an ADR and reporting it ($\chi^2 = 42.62$, df = 1, $p < 0.0001$). ADR reporting was rated as highly important (M = 4.67, SD = 0.63), and perceptions reflected moderate agreement with positive views of reporting (M = 3.07, SD = 1.17). Workload (21.8%) and poor communication (5.3%) were cited as barriers, and 22.8% supported regular workshops to improve reporting.

Conclusion: The study revealed a lack of knowledge on ADR reporting among HCPs, leading to underreporting. Despite positive attitudes, factors like workload and communication challenges hinder reporting. Continuous training and workshops are recommended to improve HCPs' reporting skills and promote pharmacovigilance. Integrating digital tools could simplify ADR reporting, reduce barriers, and improve communication among HCPs and regulators.

Keywords: adverse drug reaction, healthcare professional, medication, spontaneous reporting

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A comparative study on efficacy, safety and cost effectiveness analysis between vortioxetine and escitalopram in major depressive disorder

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Abstract

Major depressive disorder (MDD) is a prevalent and debilitating mental health condition. This study aimed to compare the clinical efficacy, safety, and cost-effectiveness of vortioxetine and escitalopram in the treatment of MDD among outpatients at NRI General Hospital, Guntur, Andhra Pradesh. A non-randomised interventional trial was conducted over eight months involving 180 patients diagnosed with MDD based on Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria. Participants were equally divided into two groups, one receiving vortioxetine and the other escitalopram monotherapy. Clinical outcomes were assessed using the Hamilton Depression Rating Scale (HAM-D), and safety was evaluated using the World Health Organization (WHO) causality assessment scale. A pharmacoeconomic analysis was conducted using the incremental cost-effectiveness ratio (ICER). Both groups showed significant improvement in HAM-D scores ($p < 0.0001$), with no statistically significant difference in efficacy between the two treatments, although escitalopram demonstrated slightly greater symptom reduction (mean score reduction: 14.37 vs. 12.7). Vortioxetine, however, was associated with fewer and less severe adverse drug reactions. Cost-effectiveness analysis revealed escitalopram to be more economical than vortioxetine (average cost of ₹2129.44 vs. ₹3448.20 per patient), with a negative ICER indicating it as the more cost-effective option. These findings suggest that escitalopram is the more cost-effective antidepressant for MDD treatment in this study setting, while vortioxetine's favourable safety profile may offer advantages for patients prioritising tolerability, highlighting the importance of individualised treatment selection based on both clinical and economic considerations.

Keywords: major depressive disorder, escitalopram, vortioxetine, clinical efficacy, incremental cost-effectiveness ratio

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Strengthening antivenom access in South Africa: Regulatory priorities and policy actions

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Abstract

The critical antivenom shortage in South Africa is a consequence of fragmented regulations, constrained manufacturing capacity and weak stakeholder coordination. The snakebite envenoming (SBE) burden is preventable if access and equity are prioritised. Priority barriers were identified using the nominal group technique (NGT) through two expert consultations with members of the South African National Snakebite Advisory Group (NSAG). Experts emphasised urgent reforms to regulation, improved surveillance, supply chain governance and clinical guidance. Recommended actions include listing SBE as a notifiable medical condition, streamlining Section 21 import authorisation processes, strengthening national stockholding strategies, and restructuring South African Vaccine Producers (SAVP) through a public-private partnership. Through strong stakeholder engagement and leveraging technical expertise, the chronic antivenom shortage could be reversible. Without immediate regulatory and strategic reform, preventable deaths and disability from snakebite will continue.

Keywords: snake antivenom, access, South African Vaccine Producers, SAHPRA, regulations, stakeholders

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sapj

CPD questionnaire • Vol 2 • 2026

Prebiotics, probiotics and synbiotics in human health, clinical applications an update

1. Which one of the following best describes a probiotic?

a Non-digestible food ingredients that selectively stimulate the growth of beneficial gut bacteria

b Live microorganisms which, when administered in adequate amounts, confer a health benefit on the host

c A mixture of live microorganisms and substrates selectively utilised by host microorganisms

d Any lactic acid–producing bacteria used in food fermentation, regardless of health benefit

2. Which statement regarding synbiotics is most accurate?

a Synbiotics refer to combinations of different probiotic strains only

b Synbiotics are prebiotics that enhance absorption of vitamins in the colon

c Synbiotics are mixtures containing both probiotics and prebiotic substrates that are selectively utilised by host microorganisms and confer a health benefit

d Synbiotics are combinations of antibiotics and probiotics used to prevent resistance

3. Which of the following is a recognised clinical benefit supported by evidence for specific probiotic strains?

a Complete eradication of *Clostridioides difficile* infection in all treated patients

b Reduction in the incidence of antibiotic-associated diarrhoea by certain strains such as *Lacticaseibacillus rhamnosus GG* and *Saccharomyces boulardii*

c Universal prevention of colon cancer in humans

d Replacement of standard therapy in inflammatory bowel disease

Otitis externa: What clinicians need to hear: pathophysiology, management and treatment

4. Which microorganism is most commonly responsible for bacterial otitis externa?

a *Aspergillus* species

b *Candida* species

c *Pseudomonas aeruginosa*

d *Escherichia coli*

e *Klebsiella pneumoniae*

5. Which topical antibiotic is safe to use in acute bacterial otitis externa even if the tympanic membrane is not intact?

a Neomycin

b Gentamicin

c Ciprofloxacin

d Polymyxin B

e Amoxicillin

6. Which of the following topical preparations is most appropriate for reducing inflammation and swelling in bacterial otitis externa?

a Gentamicin

b Neomycin with polymyxin B-hydrocortisone

c Polymyxin B alone

d Acetic acid 10% solution

e Clotrimazole

7. Which of the following is recommended for pain relief in patients with mild to moderate pain from acute otitis externa?

a Morphine

b Ibuprofen

c Ciprofloxacin

d Neomycin-hydrocortisone

e Clotrimazole

Advancing wound care: antiseptic strategies – povidone-iodine

8. Povidone-iodine mechanism of action: Choose the correct option.

a Free iodine causes oxidation of fatty acids, leading to membrane destabilisation.

b Denaturise the microbial protein component.

c Free iodine binds to negatively charged phosphate in the bacterial cell wall, resulting in cell death.

d Impairs membrane permeability.

9. Choose the correct answer regarding chlorhexidine

a Has good antibiofilm activity.

b Undiluted chlorhexidine delays wound healing.

c Impregnated dressings eliminate *Streptococcus epidermidis*.

d Effective in coating of surgical instruments.

10. Comparative clinical efficacy. Choose the best answer

a Povidone-iodine is inferior to chlorhexidine gluconate in preventing surgical site infections.

b Saline irrigation has a significantly better wound-healing outcome than povidone-iodine.

c Povidone-iodine has broader antimicrobial activity than polyhexanide.

d Hypochlorous acid produced the highest Therapeutic Index (TI) value for methicillin-resistant *Staphylococcus aureus*.

11. The correct sequence for wound healing is:

a Proliferation, inflammation, remodelling

b Inflammation, proliferation, remodelling

c Inflammation, remodelling, proliferation

d Proliferation, remodelling, inflammation

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 • Volume 1 • 2026

1. c 2. b 3. b 4. d 5. b 6. c 7. b 8. b 9. a 10. d 11. c 12. c 13. d 14. b 15. b 16. c

Presidential Report to General Council

Dr Seshnee Moodley

President, SAAHIP

Introduction

It is my absolute pleasure and privilege to report to you on the activities of the South African Association of Hospital and Institutional Pharmacists (SAAHIP), the National Executive Committee (NEC) and your elected President for the term April 2025 to March 2026. The foundational principles that have guided us during this term have been the 4 pillars of SAAHIP:

1. **Shared Vision**: Pharmacists need to view the profession as one and apply our efforts synergistically.
2. **Collaboration and Partnership**: Pharmacists must be an integral part of the multidisciplinary team (MDT) and work efficiently with other healthcare workers (HCWs).
3. **Commitmen**t: Pharmacists must commit to excellence, renewal, innovation, continuous learning and sharing of best practices.
4. **Embracing Innovation**: Pharmacists must be open-minded and move with the world as it is moving forward. Adapt and innovate to ensure maximum pharmaceutical performance delivery.

In casting the vision for the term ahead, it was important to ensure that the work the previous leaders set in place continued, recognising the value of the focus areas, the 4 pillars and finding novel ways in which we could ensure delivery as SAAHIP. The vision for 2025/2026 for the hospital pharmacist was simple: to deliver effective patient centric care and medicine related information, whilst being a valued member of the multidisciplinary team by ensuring our role as medicine expert is most prominent. As SAAHIP we needed to support our hospital pharmacists to deliver this patient centric care by equipping them to become effective members of multidisciplinary teams (MDTs) by providing quality projects/webinars/events that facilitate knowledge sharing and continuous professional development (CPD). The branches worked on collaborating on projects and National drives, to both enhance our visibility, but to also contribute towards our professional growth.

National Executive Committee (NEC)

The NEC met virtually 3 times in the term, during which re-alignment to our core values and future output on projects were discussed. One further online meeting was held in May 2025, to discuss the 2025 conference. The latest NEC members are shown in Table I. In April 2025, the NEC welcomed the support of PSSA liaison, Mr Famola Ngobeni, together with additional co-opted members Ms Thanushya Pillay, Mr Joggie Hattingh and Prof. Natalie Schellack who joined the team, bringing with them, their own skills and expertise. During the term, we also welcomed the addition of the YPG/SAAHIP Liaison, Ms Aisha Adam, who currently also serves as the secretary of the SAAHIP membership, marketing and branding (MMB) focus area group. Two new branch chairs (KZN-Inland and Southern Gauteng) joined the NEC platform towards the end of 2025. To the outgoing branch chairpersons, Ms Rashmi Gosai and Mr Vusi Dlamini, I thank you for your tireless commitment to SAAHIP. Mr Dlamini also graciously fulfilled both the role of the KZN-Inland chairperson and National Vice-President during this term, which contributed immensely to the branch stability in KZN-Inland.

Membership

The membership of SAAHIP continues to grow. SAAHIP has been intentional in enhancing our visibility and offering our members the support that they need. The branches have been very active in this regard and have held membership drives, social activities, engaging CPDs and other events. The membership growth is highlighted in Table II. All branches have shown constant growth. The Limpopo branch must be commended for doubling their membership numbers from 2023 to-date, whilst SAAHIP has shown an overall growth of 15% over the period AGM 2023 to-date.

Branch Activities

All 10 Branches have been very committed; ensuring members' needs are prioritised. Branches have hosted a combined total of 39 CPDs and more than 60 activities/events during the term. All branches have actively been involved with the national social media campaigns and Pharmacy Month Project, over and above their activities. Shown in Table III, is a summary of some of these SAAHIP branch activities, CPD

Table I: National Executive Committee			
Presidential Committee Members			
President	Dr Seshnee Moodley		
Vice President	Mr Vusi C Dlamini		
National Secretary	Ms Caroline De Beer		
Honorary Treasurer	Ms Nomfundo Zwane		
Past President	Mr Nhlanhla G Mafarafara	**Office Support**	Mr Famola Ngobeni
Branch Chairpersons			
Eastern Cape	Ms Robyn Wates	**Northern Cape/Free State**	Ms Geziena Swanepoel
KZN Costal	Ms Samkelisiwe Matibela	**Northern Gauteng**	Mr Kesentseng Mahlaba
KZN-Inland	Ms Renesha Bikraj	**Northwest**	Mr Ignatius Muller
Limpopo	Ms Salome Makofane	**Southern Gauteng**	Ms Rofhiwa (Shoni) Mulibana
Mpumalanga	Mr Handsome Mashego	**Western Cape**	Mr Brent Sin Hidge
Co-Opted Members			
Ms Thanushya Pillay Mr Joggie Hattingh Prof. Natalie Schellack Ms Aisha Adam – YPG Rep			

events and highlights. Besides all the branch level activities, there are numerous National projects that SAAHIP is working on, shown in Table IV. These projects were embarked on after a close review of existing focus areas took place, and some additional areas were added or highlighted. This is part of the strategy to enhance quality output at SAAHIP, moving away from just quantity.

Conferences

1. *SAAHIP Conference*

The conference and 68th Annual General Meeting (AGM) took place from 10-12 April 2025. The theme was **FUTURE READY 5.0: *Empowering Hospital pharmacists for tomorrow's healthcare revolution*** and aimed at looking into what the future of South African Hospital Pharmacy practice looks like. Five key thematic issues were noted during the conference, with the hope that SAAHIP will be able to draft future policy statements to influence practice, education and policy in South Africa. The statements are:

NEC members at the National SAAHIP Conference 2025

Table II: SAAHIP Membership Report							
Branch	**AGM 2023**	**AGM 2024**	**Sep-24**	**Jan-25**	**May-25**	**Oct-25**	**Feb-26**
Northern Gauteng	254	282	294	320	343	344	344
Southern Gauteng	440	458	474	501	521	501	513
Mpumalanga	149	160	165	169	186	182	188
Northwest	158	178	181	175	186	183	185
Free State/Northern Cape	149	169	179	187	194	189	188
Eastern Cape	324	415	428	379	405	381	380
Western Cape	577	585	598	612	631	617	624
KZN-Coastal	422	529	534	523	547	560	565
KZN-Inland	336	323	331	304	347	323	324
Limpopo	183	266	291	308	359	336	369
Non-resident	3	3	3	2	2	2	2
Total	**3141**	**3368**	**3478**	**3480**	**3721**	**3618**	**3682**

Table III: Branch Activities

BRANCH	Branch Activities	CPD/Webinars	Branch Highlights
Northern Gauteng	• Influenza catch-up campaign – Vaccinated over 350 people • HPV Advocacy Campaign – Tshwane University of Technology • HPV Advocacy Campaign – Sefako Makgatho Health Sciences University • BPharm 1 meeting with SAAHIP at Tshwane University of Technology • Visited 5 high schools during the Pharmacy Month campaign	• Hybrid workshop and CPD event regarding neuropsychiatric conditions and their pharmacological management • Meet and greet: Intern's guide	Branch has taken over the conference organising portfolio from the previous Branch and are busy with the SAPHEX and SAPC conference planning. There is also work that is being done on the National SAAHIP Conference for 2027
Southern Gauteng	• Collaborated with colleagues from Gauteng DOH for a Mandela Day collection drive. • Collaborated with DanZfit, a Zumba initiative, collection drive for the Khatijakul Kubra Frail Care Centre during women's month. • Pharmacy Month Parkrun: In collaboration with PSSA • The PSSA Southern Gauteng Branch annually hosts a Pharmacy Symposium in celebration of Pharmacy Month. This year's theme was "Think Health. Think Pharmacy: One Profession, Many Roles.", with a specific session for SAAHIP in the programme	• "Medication Management in Geriatric Patients – Focus on Polypharmacy and Deprescribing" • "Managing Mental Health: Empowering Pharmacists as Frontline Advocates" • "Evidence-based changes in pharmacotherapy of common childhood conditions". • Pharmacy Month Symposium – "Think Health. Think Pharmacy: One Profession, Many Roles" • Diabetes Management – Comprehensive Drug Therapy and Lifestyle Management	Responsible for policy and legislation focus area and are developing a strategy to monitor, review and feedback on this topic. Have assisted with the re-launch of the National website
Mpumalanga	• Pharmacist interns and CSP orientation workshop hosted by MPDOH Pharmaceutical Services • The branch delegates attended an Operation Smile campaign held at Rob Ferreira Hospital	• Pharmacist intern CPD workshop focusing on Domain 5 featuring Mr E Hoosen, a CPD assessor from SAPC • CPD on asthma and COPD management • CPD on Health Standards Compliance by OHSC	Strengthening the relationship with the MPDOH Pharmaceutical services and aims to form part of the DOH/HR Task team
North-West	• Visited 3 old age homes during Pharmacy Month to promote the pharmacy profession and the pharmacist's role. • Had 2 talks on rehabilitation safety regarding medication misuse and triggers for addiction. • Visited one primary school and one kindergarten school to speak to the parents about children's health and the pharmacy profession. • YPG outreach to pharmacy students at NWU.	• CPD – Presenter: A Algra. Title: Let me think • WTF2: A Fungal approach (antifungal stewardship) and • Increase the Rhythms: A inotrope approach, virtual CPD	Working together with EC team to provide up-to-date clinical guidelines on the National website
Free State / Northern Cape	• Organised a meet and greet for members in two areas of the vast Northern Cape • NCDOH Health Matters Instagram Live: Pharmacy Month chat and extensive Pharmacy Month activities	• Hosted a virtual webinar on Leadership and Governance in Hospital Pharmacy with Guest Speaker: Dr Mothibi Godfrey Keele	The meet-and-greet events in Kimberley and Springbok were a success, bringing together pharmacists, pharmacist's assistants, their families, and the wider community to celebrate the profession
Eastern Cape	• Livingstone Hospital Care Project • Hosted online Intern Calculations Workshop • Aerobics class fundraiser for Operation Smile in Gqeberha • Pharmacy Month activities	• "Nutrition in the Critically Ill Patient" • "Changes in the Haemophilia Landscape"	Looks after the membership, marketing and branding focus area Social media followers have increased, and national membership has steadily been increasing
Western Cape	• SASFOS Conference presentation on "Non-Surgical Pain Management Options for the Temporomandibular Joint: A Pharmacist's Perspective," by the WC Chairperson • Operation smile Padel fundraiser event	• Sip and learn CPD on parenteral nutrition • Pharmacogenomics (PGx) Winter School (Two-day collaboration with UWC/UP) • AGM Academic Address: "What's in a name – managing risks through appropriate naming" by Prof. Sarel Malan	Launched a "Social Media Reinvention" campaign (Aug–Oct 2025) that increased Instagram reach to 597 unique accounts and garnered over 3 000 views, significantly improving engagement with younger pharmacists Launched the Southern Cape initiative to engage members in George and Knysna, including a planned leadership visit Organised a "Knit-a-thon" wellness event to address pharmacist burnout and mental well-being

KZN-Coastal	• Pharmacist intern orientation workshops collaboration with NdoH and KZN Inland branch • A World Kidney Day quiz was hosted: "Are your kidney's, okay?" • TB Awareness school outreach • Pharmacist intern visit to the National Bioproducts Institute • Extensive Pharmacy Month activities • Yoga session for Operation Smile	• Haemophilia masterclass – Roche CPD • "Expanding role of Pharmacists in Asthma Management" • "Vaccination of high-risk individuals" Pfizer CPD • Virtual CPD on "Corporate wellness and healthcare professionals"	The Quality audit tools (Office of Health Standards Compliance), and Ideal Hospital Realisation and Maintenance have proved that most patients are not counselled on the possible side effects of medicines. The Branch has developed a project in line with their focus area to address the gap in counselling techniques within the pharmacy environment
KZN-Inland	• SAAHIP bylaws quiz • Pharmacy Month activities • Bruntville CHC outreach activities • Social hike at Giba Gorge Park • Pilates morning event	• Virtual webinar "Mastering the Z83 Form and KZN E-Recruitment Portal"	VP presented at ICPA conference Nov 2025 – "Pharmacy United – A collaboration between public and private sector to improve health outcomes' Close ties maintained with PSSA KZN Inland Branch, Rhodes Alumni Chapter, and other partners
Limpopo	• Supported the welcoming function for the University of Limpopo Association for Pharmacy students • Hybrid Pharmacist Interns Pre-registration exam workshop at Pietersburg Hospital • Community outreach initiative at Grace Bible Church Mokopane • Extensive Pharmacy Month activities • The branch held a hospital visit drive during the month of Jan 2026, welcoming new interns and pharmacists in various districts of Limpopo	• Antimicrobial Stewardship Symposium with multi-disciplinary guests from private, public and higher education • Cancer Awareness and Organ donor awareness at Polokwane Hospital and Rethabile clinic in collaboration with Limpopo YPG • Cancer awareness month webinar	Targeting young pharmacists, interns and community service pharmacists through multiple engagements to offer guidance, mentorship and support as they navigate their early years in the hospital pharmacy profession

Table IV: National Projects

Projects	Branch Lead
Quality and Safety of Health Services Project and webinars	KZN-Coastal
Ensuring access to essential medicines webinars	KZN-Inland
MMB survey, website revamp, visibility	Eastern Cape
Governance and Leadership project – Intern webinars	Mpumalanga/Northern Cape/Free State
Conferences (SAPHEX 2026, SAPC 2026 and SAAHIP 2027)	Northern Gauteng, PRESCO
HR for health Project with PSSA	PRESCO
Basel Statement Legacy Project	Past President
AI, digital technology and digitalization TAG project	Western Cape
Clinical Pharmacy Services	Northwest
Pharmacy Month Project	Eastern Cape

Table V: Social media analytics

	Jan 2025	June 2025	October 2025
Facebook account followers	1 116	1 146	1 153
Facebook views (90-day period)	1 019	12 685	24 743
Instagram followers	140	213	270
Instagram views (90-day period)	2 245	13 226	446

- Clinical pharmacy practice
- Public health, leadership and governance
- Medicines usage and supply chain management
- Innovations, technology and artificial intelligence in pharmacy
- Human resources

2. *PSSA Conference 2025*

The National PSSA, "*Evolve*" conference was held in August 2025. The SAAHIP sector was well represented by its members and at least 7 NEC members were in attendance. The conference was thought provoking, provided a platform to share our experiences and was a great opportunity for networking. SAAHIP was able to show our continued commitment to collaboration with our sectors.

3. *Future Conferences*

SAAHIP is set to host our National conference in 2027, after choosing to defer the 2026 conference. The year ahead is still very busy with two exciting National Pharmaceutical conferences on the horizon i.e. South African Pharmaceutical Exhibition (SAPHEX) and South African Pharmacy Council (SAPC), that SAAHIP is an integral part of.

Social Responsibility

The Operation Smile pledge for 2025/2026 amounted to R45 640 which was an increase from R44 000 that was donated in the previous term. This amount covers 9 smiles and will be handed over to Operation Smile. This voluntary contribution and effort that SAAHIP makes towards the Operation Smile initiative is admirable. It is indeed special to be contributing to these life-changing surgeries as SAAHIP. Two of our Southern Gauteng branch Exco members attended on

SAAHIP members at various Operation Smile drives

behalf of the NEC during one of the Op Smile drives and the report back was that this was an incredibly humbling and once in a lifetime experience. Following that the Mpumalanga branch Exco were also afforded an opportunity to attend another drive in their province and the experience was just as rewarding.

Visibility and Advocacy

1. *Social media campaigns*

The SAAHIP National Social media platforms continue to show an increase in followers, which bears testament to the fact that members value these platforms, and the information shared. The objective of this focus area has been to increase or enhance our visibility and attract membership and this has been achieved. This focus area is managed by the vibrant MMB focus area team, headed by the Eastern Cape Chairperson, Ms Robyn Wates, and has constantly produced engaging campaigns and content aligned to the National Health Calendar and hospital pharmacy related topics. The social media accounts have been very active, with more engagement on our National Instagram page. The Instagram account has almost doubled in followers since the beginning of the year 2025, and we had the biggest growth during Pharmacy Month, 2025. Social media account analytics are shown in Table V.

2. *Pharmacy Month Campaign*

SAAHIP embarked on a massive National Pharmacy Month (PM) Campaign during September 2025 under the national theme "Think Health, Think Pharmacy – One Profession, Many Roles". The project was aimed at unifying the 10 branches whilst celebrating the pharmacist and promoting the profession to the public. We were able to showcase the vital role of hospital and institutional pharmacists, inspire and educate learners about pharmacy as a profession, and engage communities through outreach, education, and digital storytelling. A national project plan was developed by the MMB team, led by the Project leader, Ms Aisha Adam, and supervised by MMB Chairperson, Ms Robyn Wates, and included the following:

1. **Pharma 360**: A national school outreach programme
2. **One Hospital, Many Pharmacists/Know Your Pharmacist**:

Table VI: Summary of AGM takeaways

Key Takeaways	Discussion
Attendance	AGM attendance was not ideal despite marketing and invitations going out timeously to Branch members – An investigation into this trend will take place via the SAAHIP MMB Member survey planned for 2026.
Absence of young pharmacists	Same members attend AGM yearly and the non-participation of the young pharmacists was striking. Once again, we endeavour to find out the reason for this via the survey.
AGM process	Differed amongst the branches. Despite being guided by our constitution, it was apparent that some branches differed. This has prompted refresher trainings on the constitution at both Branch and National executive levels.
Branch AGM reports	There were discrepancies noted in these reports i.e. the way they were delivered or presented to the Branch members. This prompted re-circulation of the Branch AGM SOP and manual to all at the National exec level.
SAAHIP visibility	There were concerns raised that SAAHIP is visible for only membership drives. At a National level we are working on quality hospital pharmacy projects and a National online webinar to provide to the membership. The vision is to get the members, but to ensure that the members are satisfied.
SAAHIP History, Legacy and the origin of the Focus Areas	The initial origin of the SAAHIP Focus areas was highlighted in one of the branch AGMs; these were previously known as portfolio reports. This showed the evolution of our SAAHIP activities and highlighted the importance of the work that we are producing.
Relationships with key stakeholders	We need to continue building on these relationships.
Executive member positions	Leadership roles are sometimes taken at Branch level, with minimal background, guidance or mentorship. At a National level we have embarked on revisiting training on our SAAHIP constitution and policies and guidelines have all been re-circulated. We will also be embarking on a training session on leadership, commitment and good governance.

A social media campaign to highlight the multiple roles of pharmacists in hospital

Across the country, the various SAAHIP branches embraced the project plan and delivered with absolute passion. SAAHIP reached more than 39 outreach sites, which included schools, hospitals and community settings, with a rough estimate of 6 000 persons that were impacted directly by our teams. Our members were able to collaborate and work together in unison and move forward with common purpose. The learners that were identified were from disadvantaged sites and were exposed to Pharmacy as a profession and the important role we play as custodians of medicine.

SAAHIP was also tasked with creating social media blurbs for the National DOH and we had our past president, Mr Nhlanhla Mafarafara, represent our sector on a Pharmacy Month interview series on the SABC show, Expresso. The social media aspect of the campaign increased our visibility and highlighted the objectives of the Association, highlighting the theme of Pharmacy Month. Pharmacy Month engagements on our social media accounts were the highest ever recorded. The 2025 Pharmacy Month campaign was an absolute success, where the SAAHIP team was able to celebrate the hospital pharmacist and ourselves, highlighting the vital role that we play in healthcare whilst engaging with communities. The campaign was impactful and solidified our place in healthcare.

3. *SAAHIP Website*

SAAHIP's website was unfortunately outdated and was not serving the purpose of being the "face of the Association". We embarked on a website revival project under the lead of the MMB Chairperson, Ms Robyn Wates and Project team leader Mr Bandela Mgoqi. A website proposal and protocol was devised to ensure continuity and sustainability, and a project team was identified from volunteers on the NEC. The revamped website was launched successfully on World Pharmacists Day on 25 September. We are excited to embark on this new chapter and to see how the presence of an updated website can improve membership and marketing for the Association. From preliminary reports that have been delivered, the website is already generating much attention amongst the members.

4. *Stakeholder engagement*

Various engagements have taken place with the SAPC to discuss their 4th National conference and SAAHIP's contribution to this. SAAHIP also attends the SAPC Stakeholders meeting and contributes to this platform. SAAHIP has also been invited to some universities to speak to their students. In some cases, the branch chairs have represented the President and sector in these activities. This has prompted us to internally look at the memorandum of understanding that exist with some branches and universities and duplicate this across our branches, to improve our uniformity and engagements with these institutions.

5. *Presidential Tour*

The Presidential AGM tour 2025 was a success with many fruitful engagements, new learnings and points of consideration that arose, to enhance both current and future SAAHIP activities. Summary of these AGM crucial points are presented in Table VI. The tour included KZN-Coastal (in-person), Mpumalanga, North-West, Southern Gauteng, KZN-Inland and Eastern Cape (all virtual). I was not able to attend all the branch AGMs, but for the branches that I did, I thank you for the hospitality, warmth and member engagement that you afforded me.

Conclusion

As I reflect on the past term as President, I am amazed at the amount of work that has gone in the engagements that have taken place, the collaborations that have occurred, the numerous CPDs and events that were hosted and the future projects on the horizon. Success and achievements take time. I recognise the leaders that came before me, and I remain deeply appreciative of their contributions to the profession. It is important not to re-invent the wheel, but to re-adjust, recalibrate and optimise it. This presidency has taught me that consistent and incremental movements ahead, are still movements toward a lasting legacy. I am incredibly honoured to have led this great Association of hospital pharmacists and contributed towards the SAAHIP legacy. I thank my NEC and members of the branch executives for the amazing work that was done and for trusting in the vision. Their passion and dedication to the profession does not go unnoticed. It is indeed a labour of love that we all are partaking in, and we will continue to work together to keep that SAAHIP wheel of progress turning.

SAAHIP front and foremost – a force that shapes the future of Hospital Pharmacy!

Cum Laude

Academy of Pharmaceutical Sciences

Deprescribing proton pump inhibitors: Addressing prolonged and unnecessary use in paediatric hospitalised children

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Mieke is the joint winner of the Young Scientist Award in Pharmacy Practice and Clinical Pharmacy awarded at the APSSA Conference in 2025

Background: Proton pump inhibitors (PPIs) are approved for shorth-term (≤ 12 weeks) use in children older than one month. Long-term PPI therapy has been associated with increased risk of gastrointestinal and respiratory infections, fractures and micronutrient deficiencies. This study will be the first to describe paediatric PPI use in hospitalised paediatric patients in South Africa in relation to Hospital Level Paediatric Standard Treatment Guidelines (STG)-recommendations of PPI therapy.

Methods: A retrospective cross-sectional study was conducted across two tertiary public hospitals in South Africa (01 February 2023–31 January 2024). Data from medical records of paediatric hospitalised patients (< 18 years) who received a PPI prescription within the study period were evaluated. Data analysed included demographic data, in-hospital and discharge PPI prescription particulars. Descriptive statistics were used to present the analysed data.

Results: Among 400 patients, only 28% of prescriptions aligned with STG-recommended indications, while 48% of prescriptions were prescribed for non-recommended indications. The median duration of PPI therapy was 31 days and only 7% of prescriptions complied with STG-recommended durations. Long-term use (> 12 weeks) occurred in 17.5% of patients. Deprescribing strategies of PPI prescriptions was employed in 23.8% of cases, predominantly intravenous (IV)-to-oral de-escalation.

Conclusion: The findings highlight STG prescribing deviations and infrequent attempts of PPI deprescribing. Structured PPI prescription review processes, clear STG recommendations and proactive deprescribing strategies are required to promote rational PPI use.

https://doi.org/10.36303/SAPJ.4477

Background

Proton pump inhibitors (PPIs) are approved for short-term (≤ 12 weeks) use in children older than one month.[19-22] Indications include gastro-oesophageal reflux disease (GORD), eosinophilic oesophageal oesophagitis (EOE), eradication of *H. pylori* infection or peptic-ulcer disease (PUD), bleeding of oesophageal varices, gastrointestinal bleeding, or erosions, nausea and vomiting and stress-ulcer prophylaxis (SUP).[14] However, treatment durations are poorly defined in both local and international guidelines. The duration of PPI use in the treatment of GORD, *H. pylori* and bleeding of oesophageal varices is most explicitly described in the literature, with the longest recommended treatment duration between eight- and 12-weeks.[4,6,9,11,13-15]

Long-term PPI use is associated with increased risk of gastrointestinal and lower respiratory tract infections, bone fractures and allergies.[3] It is recommended that a PPI should be prescribed for validated short-term use (≤ 12 weeks) to ensure safe and rational medicine use.[5,7]

Some studies define long-term PPI use in the paediatric population as use exceeding 12 weeks.[5,18] While the STG currently limit PPI use to a maximum of four to eight weeks of therapy.[14] The package inserts of PPIs evaluated in this study generally associate adverse events with PPI use beyond 12 weeks. Additionally, from package inserts of PPIs evaluated in this study, the risk of bone fractures is increased with use beyond one year and vitamin B12 deficiency with use beyond three years.[19-22]

Methods

A retrospective, cross-sectional analysis was conducted at two tertiary public health facilities in South Africa. This study included hospitalised paediatric patients (aged < 18 years) who received at least one PPI prescription during their admission within the study period (01 February 2023–31 January 2024). Data was collected from physical medical records and included demographic information and PPI prescription details. Descriptive statistics summarised PPI use,

Table I: Indications of PPI prescriptions not according to STG recommendations across age groups

	0 –28 days	> 28 days–12 months	> 12–24 months	> 24 months–12 years	> 12–< 18 years	Total
Indications not according to STG n (%)						
Age group	36 (9)	111 (27.8)	46 (11.5)	169 (42.3)	38 (9.5)	400
SUP: mechanical ventilation	14 (60.9)	22 (37.9)	6 (25)	21 (30.4)	5 (27.8)	68
Feeding intolerance	5 (21.7)	15 (27.3)	7 (30.4)	6 (8.2)	2 (11.1)	35
GI issues (vomiting, GI discomfort, diarrhoea)	3 (13)	12 (21.8)	3 (13)	11 (15.1)	3 (16.7)	32
Chemotherapy, corticosteroid, or anticoagulant use	0	0	4 (17.4)	11 (15.1)	3 (16.7)	18
*Other	0	1 (1.8)	0	11 (15.1)	3 (16.7)	13
*GI anomalies	0	4 (7.3)	1 (4.3)	4 (5.5)	1 (5.6)	10
*Signs of bleeding unrelated to GIB	1 (4.3)	1 (1.8)	2 (8.7)	3 (4.1)	2 (11.1)	9
Cerebral palsy without feeding intolerance or GORD	0	0	0	4 (5.5)	1 (5.6)	5
Ingestion of corrosive substance	0	0	0	1 (1.4)	0	1
Total	23	58	24	69	18	192

Percentages are based on total patients within a column.

*Other: SUP: trauma, SUP: cancer, SUP: surgery, otitis media, gastric pull-up

*GI anomalies: Biliary -, duodenal -, oesophageal atresia, laryngomalacia,

*Signs of bleeding unrelated to GIB: bleeding of gums, haemolytic anaemia, haematuria, epistaxis, INR high, low platelets

Gastrointestinal (GI), stress ulcer prophylaxis (SUP), Gastrointestinal bleed (GIB)

appropriate of prescriptions and frequency of deprescribing strategies. Ethical approval was obtained from University of the Western Cape (UWC) Biomedical Research and Ethics Committee (BMREC) and the National Health Research Database under the Western Cape Government Health Department (WC202401_001).

Results

Among 400 paediatric patients, 200 per facility, omeprazole was the most frequently prescribed PPI (79.3%, *n* = 317). Only 28% of prescriptions corresponded to STG-recommended indications, while 48% (*n* = 192) were for indications not according to STG-recommendations. Indications of PPI prescriptions not according to STG recommendations are seen below (*Table I*). Among these, the most frequently prescribed indication was for SUP related to mechanical ventilation at 35.4% (*n* = 68). Additionally, the most frequent indication for all PPI prescription throughout the patient cohort was SUP for mechanical ventilation (17%, *n* = 68). The remaining 24% (*n* = 96) of patients lacked a documented indication, underscoring one of the challenges of retrospective data collection.

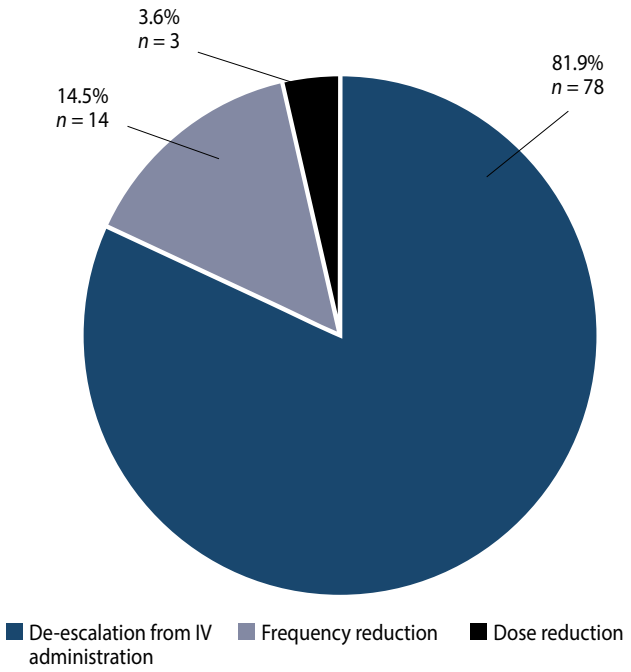

Figure 1: Deprescribing strategies

The median duration of PPI prescriptions use was 31 days (range: 1–251 days). Only 7% (*n* = 28) of prescriptions aligned with STG-recommended duration for the stated indication. Furthermore, 20.8% of patients received a PPI prescription at least a third time during their current hospitalisation. Long-term PPI use (> 12 weeks) was observed in 17.5% (*n* = 70) of patients. The majority (*n* = 228, 57%) of the patients was discharged with a PPI prescription. Omeprazole was the most frequently prescribed PPI (*n* = 194, 85.1%) upon discharge.

PPI prescription deprescribing strategies were employed in 23.8% (*n* = 95) of patients, most commonly de-escalation from IV to oral therapy (81.9%, *n* = 78) *(Figure 1)*.

Notably, 46.3% (*n* = 36) of the patients in whom PPI prescription IV de-escalation was employed were between the ages of 0 days and 12 months. This finding suggests inappropriate initial PPI use according to patients' age. Since pantoprazole is the primary IV PPI available in the public health care setting, however, lacks validation for use in children < 12 months.

Discussion

The findings of this study highlight deviations from STG-recommended PPI prescribing practices in paediatric hospital care. The absence of explicit treatment duration recommendations within the national STG may contribute to unnecessary prolonged PPI therapy. Prescribers

may initiate PPIs for acute conditions, however, fail to discontinue therapy due to the lack of structured medication review processes, clear documentation of initial indication and clear evidence-based recommendations. However, prolonged PPI use (> 12 weeks) may contribute to adverse events such as increased risk of infections,[1,2,7] bone fractures[23] and nutrient malabsorption,[5,12,18] ultimately contributing to polypharmacy. It is imperative for clinicians to navigate the balance between the risk of discontinuing PPI therapy as opposed to the benefit it proposes in reducing the risk of potential adverse events and reducing potential unnecessary medication use.

Three consensus guidelines from India, Canada and the United States offer similar approaches on deprescribing PPI therapy.[8,16-17] Firstly, the importance of systematically re-evaluating the necessity of PPI therapy, especially after the predetermined period of use has passed with symptom improvement (e.g. four weeks of PPI therapy for GORD). Then, deprescribing can be implemented either by abruptly discontinuing PPI therapy or via a tapering regimen, stepping down to alternative acid-suppression therapy (histamine-2-receptor antagonists), intermittent use for a shorth predetermined period, on-demand use or through dose reduction.[8,16-17] There are currently no studies that directly compare different deprescribing strategies and therefore no definitive optimal approach exists.[16] Lastly, all patients without a documented indication or need for PPI therapy should be reviewed and considered for PPI discontinuation.[8,16-17] No PPI deprescribing guidance specific to paediatric patients exists.

Recommendations for practice based on the findings of this study:

1. Evidence-based guidelines should provide explicit recommendations on the duration of PPI therapy for each recommended indication.
2. Evidence-based guidelines should integrate deprescribing protocols of PPI therapy specific to the paediatric population.
3. Pharmacists should play an active role in the review of PPI prescriptions to determine the need for acute use as opposed to continued use, to ensure safe and rational use.

Conclusion

This study highlights discrepancies between PPI prescribing practices and national guideline recommendations in the hospitalised paediatric population. Prolonged and unnecessary therapy remains common, posing avoidable risks to paediatric patients. Clear STG guidance, structured medication review processes and proactive deprescribing strategies are vital to optimise care.

No conflicts of interest and source of funding necessary to declare.

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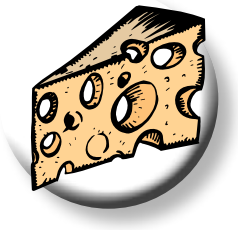

Growing through service: My journey with SAAHIP

The year 2020 was unlike any other. In the wake of lockdowns, the world shifted online, and suddenly opportunities for learning multiplied. I immersed myself in webinars, trainings, and Continuing Professional Development sessions, grateful for the unexpected access to knowledge that the pandemic had unlocked.

While performing routine work one day on my computer at work, a colleague, Ms Akhona Fynn, called and invited me to an online session/meeting. I assumed it was another webinar and gladly accepted, not asking for details. To my surprise, when I logged in, I found myself at the SAAHIP KZN Inland Annual General Meeting. Before I could process what was happening, nominations began, and I was proposed as Executive Secretary by Mr Vusi Dlamini. Shocked and overwhelmed, I called Ms Fynn afterward in a panic, convinced I was unprepared. Her calm reassurance and promise of support gave me the courage to accept the role.

That decision marked the beginning of a transformative journey. Working alongside Mr Vusi Dlamini as Chairperson, Ms Azraa Bassa as Vice Chair, and Ms Akhona Fynn as Immediate Past Chair, I learned the value of teamwork, mentorship, and resilience. We implemented monthly meetings, strengthened branch activities, and built a culture of collaboration.

At the 2023 AGM, I was nominated as Vice Chair. Once again, I doubted myself, but Mr Dlamini's encouragement pushed me forward. He entrusted me with responsibilities that stretched my confidence and skills whether managing committee matters or presenting at national webinars. Each challenge became an opportunity to grow, and I began to take pride in accomplishments that once felt impossible.

By 2025, when Mr Dlamini was nominated as Vice President to the SAAHIP National Committee, I stepped into the role of Branch Chairperson with far less hesitation. The experiences of the past five years had prepared me to lead. I had learned that discomfort is often the birthplace of growth, and that with the support of colleagues, daunting tasks can be managed with success.

Beyond leadership, SAAHIP expanded my professional network across provinces. Through conferences and countless WhatsApp groups, I discovered that pharmacists nationwide share similar challenges and triumphs. These exchanges not only offered solutions but also fostered solidarity. I realised that many colleagues pursue advanced qualifications Master's and Doctoral degrees in Pharmacy, Law, and Business Management which inspired me to embark on my own Master's journey (in my forties).

Being part of SAAHIP awakened talents I had not fully recognised and gave me the platform to nurture them. It showed me that growth often comes from stepping into unfamiliar spaces, supported by a community that believes in you.

A Call to Colleagues

My journey is not unique, it is a testament to what professional associations can do for every pharmacist. By joining and actively participating, you gain more than titles or responsibilities; you gain confidence, mentorship, and a network that stretches across the country. You discover new opportunities, broaden your perspective, and unlock potential you may not even realise you have.

To my colleagues in the KwaZulu-Natal Inland Branch and beyond: you are surrounded by talented, supportive professionals. Reach out, engage, and embrace the opportunities. Joining a professional association is not just about service it is about growth, empowerment, and shaping the future of pharmacy together.

R Bhikraj

Pharma Dynamics launches new neuroscience product, Stresigen, for anxiety management

Pharma Dynamics has expanded its neuroscience portfolio with Stresigen 50 mg, an etifoxine hydrochloride formulation indicated for the psychosomatic manifestations of anxiety. This launch comes at a time where anxiety remains highly prevalent yet often under-recognised and undertreated in primary healthcare settings.

Abdurahmaan Kenny, Product Manager for Branded Generics at Pharma Dynamics, says that in everyday practice, clinicians seek ways to relieve anxiety symptoms while also helping patients maintain daily functioning.

"While existing therapies remain important, there is often a need for additional options to support patients during the early and sometimes challenging phases of treatment. Stresigen fills that gap."

Current treatment guidelines recommend selective serotonin reuptake inhibitors (SSRIs) and serotonin–noradrenaline reuptake inhibitors (SNRIs) as first-line pharmacotherapy, because of their favourable benefit–risk profile.

However, the anxiolytic effect of these antidepressants typically has a latency of two to four weeks, and in some cases up to six weeks, before full therapeutic benefit is realised. During this period, clinicians may prescribe adjunctive anxiolytics to manage symptoms while waiting for antidepressant efficacy to emerge. Benzodiazepines have typically fulfilled that bridging role. However, their association with central nervous system depression - including fatigue, dizziness, slowed reaction time and impaired driving performance, as well as potential tolerance and dependence – continues to be a clinical concern.

As an alternative, etifoxine is a non-benzodiazepine anxiolytic belonging to the benzoxazine class. Rather than acting at the classical benzodiazepine binding site, it works through two complementary biological mechanisms that help regulate the brain's response to stress and anxiety.

First, etifoxine enhances GABAergic neurotransmission by modulating the GABA-A receptor complex at a distinct site from benzodiazepines. Second, it stimulates the production of neurosteroids, which further support GABA-mediated inhibitory pathways. Together, these actions help restore balance in neural circuits involved in anxiety.

Because etifoxine does not bind to the benzodiazepine site, its clinical profile differs from that of classical benzodiazepines. Clinical studies have shown it to be effective in managing anxiety symptoms, including in patients with adjustment disorders, with efficacy comparable to certain benzodiazepines, but with significantly less rebound anxiety after discontinuation and a very low dependence potential.

Importantly, etifoxine has been associated with a low risk of drug dependence or withdrawal symptoms following treatment cessation. Available data further indicate no significant effect on psychomotor performance, vigilance or free recall.

"Anxiety frequently presents with a strong psychosomatic component, including palpitations, gastrointestinal discomfort, tension headaches and disrupted sleep.

"In practice, many patients still need to function at work, drive, study and manage family responsibilities while treatment is being initiated. The aim with Stresigen is to ease anxiety symptoms without compromising alertness or cognitive clarity – particularly during the early stages of therapy when patients are adapting to treatment and stability is essential," explains Kenny.

The recommended dosage for Stresigen is 150 mg to 200 mg per day, taken in two to three divided doses. Treatment typically lasts from a few days to several weeks, with a maximum duration of eight weeks – acting as a short-term or bridging therapy in appropriately selected patients.

Stresigen 50 mg capsules have demonstrated bioequivalence to the originator 50 mg reference formulation and are therefore clinically interchangeable with the branded product. It comes with a cost saving of up to 28% - an important consideration in today's cost-constrained healthcare environment.

Generalised anxiety disorder (GAD) and related conditions are often chronic and relapsing, with both psychological and somatic features contributing to functional impairment.

While antidepressants remain the cornerstone of long-term anxiety management, short-term, well-tolerated anxiolytics continue to play an important role during treatment initiation.

"Stresigen provides clinicians with an additional mechanism within the GABAergic pathway," reinforces Kenny. "It's about expanding the therapeutic toolkit in a way that supports symptom relief while helping patients remain cognitively clear and functionally active."

As anxiety management continues to evolve, the availability of alternative non-benzodiazepine options, such as Stresigen offers greater flexibility in individualising care, enabling clinicians to balance efficacy, tolerability and real-world functioning in everyday practice.

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