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Development and validation of odour identification tests for olfactory assessment in Singapore

Odour identification tests are sensitive to cultural differences, making adaptation to specific populations important. This study develops and validates Scentsor and the Sniffin' Sticks for an accurate olfaction assessment in Singapore (See full article, p. 329).

Illustration by Maria De-Castro

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Utilising a COM-B framework to modify antibiotic prescription behaviours following third molar surgeries

Singapore clinical guideline on parenteral nutrition in adult patients in the acute hospital setting

Fluoride benefits and risks: Lessons from 70 years of water fluoridation in Singapore

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Sniffin' Sticks and Scentsor for integrating the "forgotten sense" into everyday practice

Abhilash Balakrishnan¹ FRCSEd, Neville Wei Yang Teo¹ MMed(ORL), Shuhui Xu¹ MMed(ORL)

The sense of smell has been one of the most neglected of the 5 human senses, perhaps due to its intangible, amorphous, ephemeral and seemingly subjective nature. A survey of the UK public revealed that the sense of smell was valued behind sight, hearing, balance, touch and even taste!¹ Smell testing has also been traditionally sidelined compared to testing of vision, hearing and balance, and is limited mostly to research.

The importance of the sense of smell, however, is highly underestimated. Olfactory dysfunction affects up to 34% of community-dwelling older residents in Singapore, which is higher than the global average of 22.2%.^{2,3} It is associated with various neurodegenerative and health conditions. Cross-sectional studies have shown that olfactory dysfunction is associated with a 2-fold increased risk of cognitive impairment² and a higher hazard ratio of all-cause mortality⁴; and has a strong, graded association with and potential use as a biomarker of frailty.⁵ Longitudinal studies have similarly shown associations between olfactory impairment and development of frailty and cognitive decline.^{6,7} Olfactory dysfunction has also been shown to be an early marker of neurodegenerative diseases, such as Parkinson's disease and Alzheimer's disease.^{8,9}

The COVID-19 pandemic brought olfaction into sharp focus, with sudden smell loss emerging as one of the hallmark symptoms. It sparked off much-needed research and discussions around its repercussions on personal safety, nutrition, quality of life and, increasingly, our understanding of neurocognitive health. The Singapore Smell and Taste Test,¹⁰ consisting of 2 odours and 4 tastes, was developed to rapidly measure smell and taste loss associated with COVID-19. This was an initial attempt to develop a rapid self-administered test with the potential to screen for COVID-19 in communities without easy access to formal COVID-19 testing. This highlighted the need for culturally adapted tools to monitor olfactory function, particularly in diverse, multicultural populations like Singapore where odour familiarity varies widely. Numerous other olfaction-related studies emerged from COVID-19, looking at both short-term

effects and longer-term sequelae of the coronavirus infection.

In this issue of the *Annals*, the authors of the study "Development and validation of odour identification tests for olfactory assessment in Singapore" have set out to address a longstanding gap in the local assessment of olfactory function.¹¹ This study marks a significant advancement by introducing and validating 2 culturally tailored odour identification tests for Singapore: the Singapore-version of Sniffin' Sticks (SS-Sg) and a novel locally developed test named "Scentsor". This work aligns Singapore with other Asian countries—such as Malaysia, Vietnam, Korea and Taiwan¹²⁻¹⁵—that have developed customised smell panels to reflect their population's unique cultural and olfactory landscapes.

The foundational premise of this study—that olfactory identification is inherently culture-bound—is both intuitive and empirically supported. Familiarity with specific odours influences recognition and identification, rendering unmodified foreign-developed tests problematic for non-Western populations. Indeed, this study's Phase 1 survey revealed that over 50% of odour descriptors in the standard Sniffin' Sticks test (SS blue and purple sets) were unfamiliar to most Singaporeans.

This insight is not trivial. Incorrect assumptions about cultural familiarity could result in diagnostic inaccuracies, under-reporting of impairment, or misclassification. By carefully identifying odours recognised by ≥75% of surveyed Singaporeans, the authors created culturally coherent test sets. Notably, familiar odours such as pandan, durian, curry and lemongrass made their way into Scentsor, reflecting local culinary and cultural sensibilities. Furthermore, by creating Scentsor, the authors came up with a completely new set of scents that were not dependent on the Sniffin' Sticks test kits, thereby allowing for less reliance on an odour identification test kit that was developed overseas for a culturally different population. There was further finetuning and replacement of unfamiliar smells in Phase 2. Both tests were further validated in Phase 3 on a robust sample

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¹ Department of Otorhinolaryngology—Head and Neck Surgery, Singapore General Hospital, Singapore

Correspondence: Prof. Abhilash Balakrishnan, Department of Otorhinolaryngology-Head and Neck Surgery, Singapore General Hospital, Outram Rd, Singapore 169608.

Email: abhilash_balakrishnan@yahoo.com.sg

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of 473 healthy individuals aged 21–83 years. This rigorous, multiphase development process lends strong credibility to the tools' validity.

In specialties such as otolaryngology, geriatrics, neurology and primary care, validated olfactory testing can now be feasibly incorporated into routine practice. In otolaryngology, diseases and surgeries that potentially affect the olfactory system, such as chronic rhinosinusitis, will benefit from objective and accurate smell documentation. As biologics like dupilumab and mepolizumab show efficacy in improving smell, validated testing is important for monitoring therapeutic response.

In geriatrics, olfactory testing can be evaluated as a potential low-cost screening tool for various neurodegenerative diseases, like mild cognitive impairment and subclinical Alzheimer's disease. It is predicted that 24% of the Singapore population will be ≥65 by 2030, thereby driving national policies to prioritise healthy ageing. As alluded to by the authors, there are 2 parts to a successful response: recognition of smell and an intact executive function. These customised olfactory tests remove unfamiliarity as a barrier to an accurate response and can help identify at-risk individuals for targeted interventions and mitigate downstream healthcare burdens.

Further possible research efforts can be undertaken to examine how Scentsor and SS-Sg perform in specific disease states such as Parkinson's disease, mild cognitive impairment and depression. Longitudinal studies tracking olfactory function in at-risk populations could uncover early indicators of health decline. Evaluating whether treatment of olfactory dysfunction can prevent or slow the development of neurodegenerative diseases will also be of great public health significance.

The potential of developing a means for individuals to easily access and test their own olfaction at home is also immense, as this can uncover undiagnosed conditions, reduce accident risks (from undetected gas leaks or spoiled food), and identify those at higher risk of isolation or malnutrition due to sensory loss. In addition, integration of odour identification into digital platforms for automated scoring or remote administration will also enhance scalability and accessibility, particularly in community and eldercare settings, and alert healthcare professionals to early olfactory dysfunction in affected individuals.

As Singapore grapples with an ageing population and the long-term complications of COVID-19, olfactory testing may become a staple of routine care, as familiar as hearing tests or blood pressure measurements. SS-Sg and Scentsor offer clinicians, researchers and policymakers a timely and adaptable platform for integrating the "forgotten sense" into everyday practice.

Ethics statement

Not applicable

Declaration

The authors have no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript.

Keywords: odour identification, olfactory assessment, olfactory testing, otorhinolaryngology, Scentsor

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Pulling teeth or pulling together? Time to improve antibiotic prescribing in dentistry

Daphne Yii¹ MSc (Public Health), Yvonne Peijun Zhou¹ MSc (Infectious Diseases),
Shimin Jasmine Chung² FRCP (UK)

Antibiotic use in third molar (3M) surgeries is commonplace despite a growing body of evidence showing that routine prophylactic antibiotics offer little benefit in healthy patients. It also fuels the global public health crisis of antimicrobial resistance (AMR). This practice appears to remain deeply entrenched worldwide and is believed to be significantly caused by behavioural barriers.¹ It is perceived and accepted that antibiotics reduce the likelihood of a post-procedure infection, but clinicians may be blindsided to the associated risks. In 3M surgeries, the number needed to treat (NNT) is 19, which is a relatively high NNT.² This implies that a significant number of healthy patients may potentially experience adverse effects from unnecessary antibiotic exposure.

To address the misuse of antibiotics in 3M surgeries, Yong et al. used a behavioural change model, the COM-B framework, to design interventions and measure their effectiveness.³ In contrast to most antimicrobial stewardship (AMS) initiatives that are led by infectious diseases physicians and infectious diseases pharmacists, this initiative that was led from the ground up by the Division of Oral and Maxillo-facial Surgery (OMS) at the National University Centre for Oral Health Singapore is laudable. First, it reflected the ownership of appropriate antibiotic use by OMS, a surgical specialty. Second, instead of using established core strategies, such as prospective audit and feedback (PAF)/preauthorisation,⁴ the decision by the OMS team to apply behavioural sciences in planning their AMS interventions was strategic and polished. PAF would be too labour-intensive to implement and pre-authorisation of amoxicillin, a commonly used narrow spectrum antibiotic for 3M surgery, would be onerous and unpalatable to prescribers.⁵ They first tried to understand the behavioural factors driving antibiotic prescribing habits. With the capability, opportunity and motivation for behavioural change or COM-B framework, they then systematically addressed the identified issues to improve the capability of the clinicians; created

opportunities for good practice; and motivated the stakeholders by engaging them, addressing their concerns and communicating clear targets of the AMS initiative. With this approach, they significantly reduced antibiotic use for 3M surgeries from 84.45% to 20.89% (way beyond their projected target) without an increase in complication rates, and the results were still sustained for 8 months post-intervention. Their strategy serves as a model to the wider AMS community in dentistry and beyond.⁶

Simply put, Yong et al. worked on the ground and changed practice. The authors invested in identifying facilitators and barriers to behavioural change. Specifically, they were able to (1) identify and address knowledge gaps in AMR and appropriate antibiotic use; (2) empower clinicians through guideline development; (3) allay clinicians' fears of practising differently from group culture, the risk of surgical complications and patient complaints; and (4) develop countermeasures to address prescribers' indifference to AMR.

They also created an ecosystem for a successful antimicrobial stewardship programme (ASP) and embraced the core elements of AMS recommended by the Centers for Disease Control and Prevention. They had the support of their institution's directorate and committed programme leads. They designed strategic interventions using a behavioural change model aimed at both clinicians and patients alike, tracked antibiotic consumption and reported their findings to the relevant stakeholders, and provided evidence-based recommendations to encourage good clinical practice.^{3,7} Furthermore, the authors showcased the importance of involving a multidisciplinary team in driving behavioural change, and we believe it was one of the major factors in the successful implementation of the AMS initiative. Apart from clinicians, they ensured dental assistants, patient service associates and pharmacists were supportive of the initiative as they would be able to counsel patients on appropriate antibiotic use at various

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¹ Department of Pharmacy, Singapore General Hospital, Singapore

² Department of Infectious Diseases, Singapore General Hospital, Singapore

Correspondence: Dr Shimin Jasmine Chung, Department of Infectious Diseases, Singapore General Hospital, 20 College Road, Level 3, Singapore 169856.

Email: jasmine.chung.s.m@singhealth.com.sg

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touchpoints in the patient's journey. Often overlooked in AMS initiatives are the patients, who as recipients of inappropriate antibiotics are key stakeholders, need to be effectively engaged and educated in the areas of AMS and AMR. For example, Yong et al. described instances where patients specifically requested antibiotics post-surgery, inevitably leading to antibiotics being prescribed. From a clinical perspective, there was a clear guidance provided to discontinue antibiotics in 3M surgeries. However, recommendations were nuanced to allow antibiotic use in high-risk patients, such as immunocompromised patients and those at higher risk of infections due to medical comorbidities or surgical complications. Education sessions and resources (e.g. posters) were also provided to empower clinicians to counsel patients against the routine use of antibiotic prophylaxis in 3M surgeries. There was firm commitment to discontinue the AMS interventions should infection rates or patient complaints increase. These, we believe, were important for stakeholder buy-in and centre-wide adoption of practice change.

In addition, the shared decision-making process encouraged ownership of the AMS initiative. Notably, infection rates post-intervention were very low (<1%), which provided very convincing local data that stopping antibiotics post-3M surgery is indeed safe. In a post-intervention focus group discussion, the clinicians expressed both confidence and their commitment to using antibiotics more judiciously. It is clear that there is a niche role for AMS in dentistry. Based on international data, dentists contribute to 10% of total antibiotics prescribed, of which 50–80% of prescriptions are inappropriate.⁸ The focus of the AMS initiative driven by Yong et al. targeted antibiotic use in 3M surgeries, a “high-yield” domain for AMS interventions, but there is still more to be done to promote AMS in dentistry, especially in Singapore.^{1,3,8} In a retrospective study evaluating antibiotic use in primary care in Singapore, it was observed that antibiotics were more likely to be prescribed during a dental consult as compared to other visits, and this is an area worth reviewing.⁹ The development and publication of the first national clinical practice guidelines on antibiotic use in dentistry by the College of Dental Surgeons Singapore in 2024 is a small step forward to drive the AMS agenda in dentistry and would be a useful resource, especially in the primary care setting.¹⁰ In general, ASPs in dentistry are currently not as well-endowed as the more mature ASPs in public acute care hospitals, which are predominantly led by infectious diseases physicians, infectious diseases pharmacists and executives with inputs from the microbiologist and infection preventionists.⁴ Nonetheless, successful AMS initiatives can still be initiated and driven from the ground up by champions within the field, even those who are neither infectious

diseases-trained nor pharmacy-trained. Using behavioural change models to recommend sustainable AMS interventions would be the way forward in healthcare.

Finally, beyond the behavioural sciences involved, the interventions designed by Yong et al. in the study were foremostly clinically sound and user-centric, facilitating adoption and implementation. Their approach was holistic, and they created a microcosm conducive to practice change. This, we believe, was the recipe for their success.

Ethics statement

Not applicable.

Declaration

The authors declare there are no affiliations with or involvement in any organisation or entity with any financial interest in the subject matter or materials discussed in this manuscript.

Keywords: *antimicrobial stewardship, dentistry, infectious diseases, oral and maxillofacial surgery, social science, third molar surgery*

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Development and validation of odour identification tests for olfactory assessment in Singapore

Xinni Xu^{1,2} MMed, Margaret Ru Xiang Zhang^{1,3} MMed, Terese Huiying Low^{1,3} MMed, Yew Kwang Ong¹ MMed

ABSTRACT

Introduction: Odour recognition is influenced by culture. Odour identification tests need to be adapted to a population to accurately assess olfactory function. This study's objectives were to validate the Singapore version of the Sniffin' Sticks (SS-Sg) and a locally-developed odour recognition test (Scentsor) for Singapore.

Method: This prospective study was performed in 3 otolaryngology outpatient clinics in 3 phases (1 May to 15 November 2024). Phase 1 was a survey evaluation of 93 odour descriptors to identify familiar odour descriptors to be used in the tests (n=414); Phase 2 evaluated and finalised SS-Sg and Scentsor to ensure test odours were recognised by $\geq 75\%$ of healthy controls (n=130); and Phase 3 validated both tests on healthy controls (n=473) to obtain normative data, to determine test-retest reliability (n=50), and to assess the ability to distinguish patients with olfactory loss (n=67).

Results: In Phase 1, the unmodified SS blue and purple sets had 15/32 (46.9%) unfamiliar test odours and 25 unfamiliar distractors combined. In Phase 2, after modification, all odours in SS-Sg and Scentsor were correctly identified by $\geq 75\%$ of controls. In Phase 3, normative data (age 21–83 years) was obtained. Both tests had good test-retest reliability (Pearson's correlation coefficient of 0.88 with $P < 0.001$ for SS-Sg; and at 0.90 with $P < 0.001$ for Scentsor). Both tests differentiated among normosmia, hyposmia and anosmia (SS-Sg scores: 12.6 [± 2.4] versus [vs] 9.8 (± 3.2) vs 6.0 (± 2.3) respectively, $P < 0.001$; Scentsor scores: 14.3 [± 1.8] vs 11.3 [± 2.8] vs 5.8 [± 3.4] respectively, $P < 0.001$).

Conclusion: SS-Sg and Scentsor have been validated to assess olfaction in Singapore.

Keywords: odour identification, olfaction, olfactory assessment, otorhinolaryngology, Sniffin' Sticks

CLINICAL IMPACT

What is New

- This study is the first to develop and validate 2 odour identification tests: Sniffin' Sticks (SS-Sg) and Scentsor, for the Singapore population.
- Normative data were obtained for both tests.

Clinical Implications

- Odour identification tests are sensitive to cultural differences. The unmodified SS is not suitable to be used in Singapore due to the high number of unfamiliar odour descriptors.
- SS-Sg or Scentsor should be used in clinical and scientific assessment of quantitative olfactory function in Singapore.

INTRODUCTION

Olfactory dysfunction affects patients under the care of various medical specialties. Its causes include post-viral upper respiratory tract infections, such as that caused by the SARS-CoV-2 virus, post-traumatic

brain injury and neurodegenerative conditions such as Parkinson's disease. The prevalence of olfactory impairment among community-dwelling, older Singapore residents is estimated to be 34.0%,¹ which is higher than the global average of 26.6% reported in a meta-analysis of olfactory dysfunction in the general population.² In addition, olfactory impairment in this group of Singapore residents was shown to be associated with a 2-fold increased risk of cognitive impairment.¹

Accurate assessment and diagnosis of olfactory dysfunction requires olfactory testing with validated olfactory tests, especially as self-rated olfactory function can correlate poorly with psychophysical olfactory test results.^{3,4} Olfactory testing also allows for tracking and documentation of changes in olfactory function over time. Most clinical olfactory tests, especially screening tests, rely on the ability to identify odours among a few multiple-choice options. However, the recognition of an odour relies not only on the ability to detect the odour, but also on

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¹ Department of Otolaryngology—Head & Neck Surgery, National University Hospital, Singapore

² Department of Otolaryngology—Head & Neck Surgery, Alexandra Hospital, Singapore

³ Department of Otolaryngology—Head & Neck Surgery, Ng Teng Fong General Hospital, Singapore

Correspondence: Dr Xinni Xu, Department of Otolaryngology—Head & Neck Surgery, National University Hospital, 5 Lower Kent Ridge Road, Singapore 119074.

Email: xinni_xu@nuhs.edu.sg

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familiarity with the test odour and distractor options. Certain odours may not be familiar to people who are not native to the culture or country where the test had been developed. Therefore, adapting odour identification tests and validating them in the test population to obtain normative data is required in order to interpret results accurately.⁵ This can be done by making modifications to odour descriptors in an internationally accepted psychophysical olfactory test, such as the odour identification component of the Sniffin' Sticks⁶ (SS) test⁷⁻¹¹ (Burghart Messtechnik GmbH, Holm, Germany). Alternatively, novel smell identification tests have also been developed using test odours that are familiar to the specific region.¹²⁻¹⁵

The primary objective of this study was to develop and validate smell identification testing for the Singapore population. Two types of smell identification tests were assessed. The first was the 16-item odour identification component of the SS that was adapted to Singapore residents (SS-Sg). The second was an original odour recognition test comprising 16 Singapore-sourced scents named Scentsor, an amalgam of "scents" and "odour recognition".

METHOD

This prospective study was conducted from 1 May to 15 November 2024. It was carried out in 3 phases (Supplemental Fig. S1), in keeping with that of several studies that developed or modified SS for specific populations.^{7-11,16} All participants were recruited from tertiary outpatient otolaryngology clinics from National University Hospital, Ng Teng Fong General Hospital and Alexandra Hospital. This study was approved by the National Healthcare Group Domain Specific Review Board and participants gave informed consent. All experimental procedures were consistent with the Declaration of Helsinki.

SS consists of odour threshold, discrimination and identification testing. For the purposes of this study, only the identification component of SS is used. The SS identification test consists of 16 felt-tip pens, each impregnated with an odour. To present the odour, the cap of the pen is removed and the pen tip is held about 2 cm in front of the participant's nostrils, alternately for about 3 seconds. The participant identifies the correct odour from 4 multiple-choice options in a forced choice manner. The total number of correct answers corresponds to the test score (minimum 0, maximum 16). There are 2 versions of the SS identification, generally referred to as the blue or purple version, based on the colour coding of the Stick. The blue and purple versions have different test odours. These 2 versions were developed so as to have an alternative set of odours for identification testing, especially when patients may be likely to recall the answers.

Phase 1: Determining odour recognisability

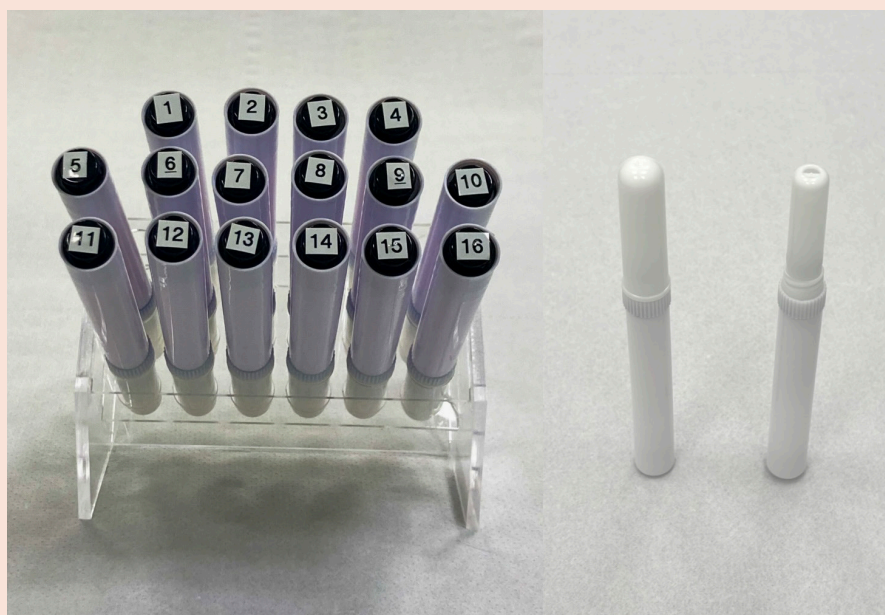
Phase 1 was performed to determine which odours were highly familiar to the Singapore population. A survey was conducted to evaluate a total of 93 odour descriptors. This comprised 69 descriptors used in the SS blue and purple kits as well as 24 new odour descriptors likely to be familiar to Singapore residents. Participants evaluated their familiarity with each odour descriptor using a Likert-type scale ranging from 1 to 5 (i.e. 1=completely unknown odour, 2=unfamiliar, 3=neutral, 4=familiar, 5=highly familiar odour). Scores of 4 and 5 were considered to be familiar to the participant. Odour descriptors identified by $\geq 75\%$ of participants as familiar were defined as recognisable odours. Only recognisable odours were considered candidates for test odours and distractor odour descriptors in the modified olfactory identification tests. The inclusion criteria for survey participants were ≥ 21 years old. The exclusion criterion was cognitive impairment. Surveys with incomplete responses were excluded from analysis.

To form SS-Sg, test odours from the blue and purple sets that were considered to be familiar were selected. Unfamiliar distractor odour descriptors were replaced with familiar descriptors within the same odour family as much as possible (e.g. replacing a non-familiar fruit odour descriptor with a familiar fruit). To form the test odours for Scentsor, 16 odours that were recognisable and locally available were selected as test odours. Only recognisable odour descriptors were used as distractor options. Similar to SS, each test odour from Scentsor had 3 other distractor options. At least 1 of the distractor options belonged to the same odour family as the test odour. To create Scentsor, commercially available unfilled felt-tip pens were filled with liquid odourants dissolved in propylene glycol to a total volume of 4 mL, similar to that of SS.¹⁶ Additionally, the odourised tip was covered such that it would be protected from accidental contact with the subject's nose without affecting odour presentation (Fig. 1). The method of administering and scoring the test was similar to that of SS. Participants were not allowed to go back and change their answers once a new odour had been presented.

Phase 2: Evaluating and finalising the SS-Sg and Scentsor

Phase 2 was performed to test the implemented changes and evaluate if familiar odours were correctly identified in $\geq 75\%$ of participants. Healthy participants were recruited and underwent both SS-Sg and Scentsor at the same sitting. Participants were randomly allocated to undergo either SS-Sg or Scentsor first, using a computer-generated random number table, to reduce bias from smell fatigue. The inclusion criterion was self-rated normal sense of

Fig. 1. Scentsor prototype. A cap is removed before presenting the odour to the subject. The housing over the odourised tip enables delivery of the odour while preventing it from making contact with the subject's nose. If there is any accidental contact, the housing can be cleaned with alcohol wipes without affecting the odour.



smell. This was defined as a score of ≥ 8 on a Visual Analogue Scale-10 (VAS-10) (i.e. 0=not able to smell anything, 5=reduced sense of smell, 10=normal sense of smell). The exclusion criteria were allergic rhinitis, rhinosinusitis, nasal polyposis, sinonasal tumours, previous sinonasal surgery, radiotherapy to the head and neck, smoking, known cognitive impairment, inability to understand or follow instructions for olfactory testing and age < 21 years old. These were determined from history taking. Allergic rhinitis was defined as the presence of ≥ 2 of the following symptoms: rhinorrhoea, nasal obstruction, sneezing and nasal itch,¹⁷ or if the participant had a known positive skin prick test or Immunoglobulin E serum test to environmental allergens. Rhinosinusitis was defined as ≥ 2 symptoms, 1 of which was either nasal obstruction or nasal discharge; and reduction/loss of smell or facial pain/pressure.¹⁸

For each test odour, the percentage of correct answers was obtained. If an odour was correctly identified by $< 75\%$ of participants, the relevant odour descriptors were adjusted. The revised versions of the smell tests were re-evaluated with another group of healthy participants and the percentage of correct answers for each test odour was again obtained.

Phase 3: Validating the SS-Sg and Scentsor

Healthy participants were recruited to generate normative data for both tests. They underwent both tests at the same sitting, the order of which was also

randomly allocated using a computer-generated random number table. The median, mean and 10th percentile scores were obtained and further stratified by age groups and sex. The 10th percentile score was used as the cut-off point between normosmia and hyposmia (i.e. a score below the 10th percentile score was indicative of hyposmia).^{16,19-21} To examine the test-retest reliability of these tests, participants were invited to repeat the tests at 2–8 weeks following the first administration. The time taken to complete each test was measured. The inclusion and exclusion criteria for healthy controls were similar to that of Phase 2.

In addition, patients with olfactory loss were recruited to assess whether both tests could discriminate between normosmia, hyposmia and anosmia. Patients who presented to the otolaryngology outpatient clinics with subjective quantitative olfactory loss were recruited. All patients underwent detailed history taking, nasoendoscopy and both olfactory tests (the order of which was randomised) at the same sitting. The inclusion criteria for patients were subjective olfactory loss secondary to rhinosinusitis, nasal polyposis, traumatic brain injury, post-viral upper respiratory tract infection, iatrogenic and idiopathic causes. The exclusion criteria were < 21 years old, VAS-10 score of ≥ 7 , qualitative olfactory dysfunction (parosmia and/or phantosmia) and cognitive impairment. VAS-10 scores of 0–3 were considered to be subjectively anosmic and scores of 4–6 were

considered to be subjectively hyposmic. SS-Sg and Scentsor scores were compared among subjectively, hyposmic, anosmic and healthy controls.

Statistical analysis

Statistical analysis was performed using Stata version 17 (StataCorp LLC, College Station, TX, US). Statistical significance was set at 0.05. Descriptive statistics for continuous variables were presented as mean (standard deviation [SD]) when normality and homogeneity assumptions were satisfied; otherwise median (interquartile range [IQR]) and *n* (%) were presented for categorical variables. The scores were compared by independent sample *t* tests when normality and homogeneity assumptions were satisfied; otherwise Mann Whitney U or Kruskal Wallis test was used. When the Kruskal Wallis test was used, post-hoc testing was done using Dunn's test with Bonferroni correction. The test-retest reliability of the tests was measured using Pearson's correlation coefficient.

RESULTS

Phase 1: Odour familiarity in the Singapore adult population

There were 414 participants (mean age 40.0 [SD 14.9] years, 159 males [38.4%]) who rated their familiarity with 93 odour descriptors (Table 1). There were 288 (69.6%) Chinese, 58 (14.0%) Malays, 40 (9.7%) Indians and 28 (6.8%) belonging to other races. Within the blue SS set, 27 of 52 (51.9%) unique odour descriptors were recognised by <75% of surveyed participants and considered unfamiliar. This included 6 (36.5%) of 16 test odours in the blue set (cinnamon, liquorice, turpentine, clove, rose, anise). Within the purple SS set, 28 of 49 (57.1%) unique odour descriptors were unfamiliar, including 9 (56.3%) test odours (pear, lilac, grapefruit, raspberry, eucalyptus, peach, mushroom, smoked meat, caramel).

All 10 recognisable odours from the SS blue set (orange, leather, peppermint, banana, lemon, garlic, coffee, apple, pineapple, fish) and 6 of 7 odours from the SS purple set with the highest recognition rates (Coke, grass, ginger, coconut, melon, onion) were selected to form SS-Sg. The original distractor odour descriptors were also modified to include only recognisable descriptors. For example, "blackberry" was replaced with "melon", "mustard" with "ketchup", and "fir" with "lemongrass". Scentsor comprised 9 test odours similar to that of SS-Sg (orange, coffee, lemon, garlic, ginger, banana, pineapple, apple, mint) and 7 original test odours (pepper, curry, smoke,

vinegar, pandan, chocolate, durian) with high recognisability rates.

Phase 2: Evaluation of SS-Sg and Scentsor

Seventy participants (mean age 35.5 [10.8] years, 18 males [25.7%]) evaluated SS-Sg and Scentsor. Thirty-five participants (50%) underwent SS-Sg first. In spite of the modifications, 7 test odours (43.8%) in SS-Sg and 3 test odours (18.8%) in Scentsor had identification rates of <75% (Table 2). The lowest performing odour in SS-Sg (banana; 44.9% recognition rate) was replaced with the lavender test odour, the remaining recognisable odour from the SS purple set. The lowest performing odour in Scentsor (pepper; 58.0% recognition rate) was replaced with a coconut test odour. For the remaining underperforming odours, descriptors were further modified using only familiar descriptors identified in Phase 1.

Sixty participants (mean age 39.1 [6.6] years, 28 males [46.7%]) evaluated the second round of modification. All test odours were correctly identified by >75% of participants. This formed the final version of SS-Sg and Scentsor.

Phase 3: Validation of SS-Sg and Scentsor

Normative data

There were 473 healthy controls (mean age 40.8 [14.5] years, age range 21–83 years, 174 (36.8%) males) who validated and provided normative data for both tests (Table 3). Half of them (*n*=236, 49.9%) performed SS-Sg first. There were 391 (82.7%) Chinese, 31 (6.7%) Malays, 33 (7.0%) Indians and 18 (3.9%) belonging to other races. The overall median score was 13.0 (12.0–14.0) for SS-Sg and 15.0 (14.0–15.0) for Scentsor. The 10th percentile scores of controls in the 21–30 years age group were 11 for SS-Sg and 13 for Scentsor. The mean time taken to complete SS-Sg was 5.3 (3.2) minutes, compared to 4.3 (2.6) minutes for Scentsor (*P*<0.001).

Effect of age

There was a significant negative relationship between age and SS-Sg scores (Spearman's rank correlation=−0.156, *P*=0.001) as well as with Scentsor scores (Spearman's rank correlation=−0.213, *P*<0.001) (Fig. 2). Post-hoc testing indicated that in SS-Sg, healthy controls aged >60 years scored significantly lower scores compared to all other age groups (21–50 years [*P*<0.001], 51–60 years [*P*=0.032]) (Table 3). In addition, controls aged 51–60 years scored significantly lower scores compared to those aged 21–30 years (*P*=0.021) and 31–40 years (*P*=0.025).

Table 1. Recognisability of odour descriptors in an adult Singapore population.

Rank	Odour descriptor	Recognition rate	Rank	Odour descriptor	Recognition rate	Rank	Odour descriptor	Recognition rate	Rank	Odour descriptor	Recognition rate
1	Durian ^a	97.8%	25	Bread	85.3%	49	Peanut	76.3%	73	Grapefruit	54.6%
2	Orange	96.9%	26	Coke	84.5%	50	Dried anchovy ^a	75.9%	74	Spearmint	53.4%
3	Coffee	95.7%	27	Mint	84.5%	51	Chlorine ^a	75.1%	75	Chive	51.5%
4	Lemon	95.4%	28	Cheese	84.1%	52	Bleach ^a	75.0%	76	Plum	50.7%
5	Curry ^a	95.1%	29	Lemongrass ^a	83.6%	53	Nail polish remover ^a	74.9%	77	Eucalyptus	47.8%
6	Smoke	93.7%	30	Peanut butter ^a	82.4%	54	Wood	74.2%	78	Chamomile	47.6%
7	Garbage ^a	93.5%	31	Peppermint	82.4%	55	Honey	73.2%	79	Clove	45.9%
8	Onion	92.3%	32	Ketchup ^a	82.1%	56	Grape	72.7%	80	Anise	45.9%
9	Fish	91.8%	33	Petrol ^a	82.0%	57	Rose	72.7%	81	Walnut	45.2%
10	Wall paint ^a	91.8%	34	Grass	81.9%	58	Cinnamon	72.2%	82	Nutmeg	42.8%
11	Cigarette	91.1%	35	Vanilla	81.4%	59	Peach	71.0%	83	Raspberry	39.9%
12	Garlic	90.3%	36	Cookie	81.2%	60	Menthol	71.0%	84	Currant	40.1%
13	Vinegar ^a	90.1%	37	Sweat ^a	81.2%	61	Pear	70.3%	85	Turpentine	39.1%
14	Ginger	89.6%	38	Jackfruit ^a	79.2%	62	Wine	69.8%	86	Rum	38.4%
15	Pandana	89.4%	39	Melon	79.0%	63	Parsley	69.1%	87	Salami	36.5%
16	Banana	88.7%	40	Honeydew ^a	78.9%	64	Ham	68.6%	88	Blackberry	31.6%
17	Chocolate	88.7%	41	Shoe leather ^a	78.8%	65	Rubber	67.9%	89	Winegum	29.5%
18	Pineapple	87.9%	42	Pomelo ^a	78.6%	66	Caramel	67.2%	90	Liquorice	23.2%
19	Mango ^a	87.8%	43	Strawberry	78.5%	67	Mushroom	65.5%	91	Lilac	19.1%
20	Limea	87.8%	44	Leather	78.3%	68	Smoked meat	64.5%	92	Sauerkraut	15.9%
21	Pepper	87.4%	45	Glue	77.3%	69	Carrot	63.3%	93	Fir	6.8%
22	French fries ^a	86.7%	46	Coconut	77.3%	70	Cherry	58.9%			
23	Apple	86.5%	47	Lavender	76.8%	71	Mustard	58.2%			
24	Toast ^a	85.6%	48	Papaya ^a	76.4%	72	Paprika	55.6%			

^a Odour descriptor not in the original Sniffin' Sticks (blue and purple)

Table 2. Identification rates of test odours in SS-Sg and Scentsor in Phase 2.

SS-Sg			Scentsor	
Number	Odour	Identification rate	Odour	Identification rate
1	Orange	97.1%	Pepper ^c	58.0%
2	Leather ^a	75.9%	Orange	97.1%
3	Peppermint	98.6%	Coffee	97.1%
4	Banana ^b	44.9%	Lemon	96.6%
5	Lemon	94.2%	Curry	72.4%
6	Garlic	69.6%	Smoke	76.8%
7	Coffee	94.2%	Garlic	92.8%
8	Apple	49.3%	Vinegar	88.4%
9	Pineapple	84.1%	Ginger	75.1%
10	Fish	82.3%	Pandan	95.7%
11	Coke	89.9%	Banana	88.4%
12	Grass	58.0%	Chocolate	72.4%
13	Ginger	71.0%	Pineapple	88.4%
14	Coconut	82.6%	Apple	88.6%
15	Melon	78.3%	Mint	88.4%
16	Onion	65.2%	Durian	92.3%

^a Replaced with the descriptor “shoe leather”

^b Replaced with “lavender” test odour in Phase 3

^c Replaced with “coconut” test odour in Phase 3

With Scentsor, healthy controls aged >60 years scored significantly lower scores compared to those aged 21–50 years ($P<0.001$). Healthy controls aged 51–60 years also scored significantly lower scores compared to those aged 21–40 years ($P<0.001$).

Effect of sex

With SS-Sg, there was no significant difference in overall median score between males and females (13 [12–14] for both sexes, $P=0.596$) (Table 3). There was also no significant difference in scores between sexes in all age groups.

With Scentsor, females scored higher than males overall (15 [14–16] versus [vs] 14 [13–15], $P<0.001$). Females scored higher than males in age groups 21–30 years (15 [15–16] vs 14 [14–15], $P<0.001$), 31–40 years (15 [14–16] vs 14 [13–15], $P<0.001$) and 41–50 years (15 [14–16] vs 14 [13–15], $P<0.001$).

Test-retest reliability

Fifty healthy controls (mean age 39.2 [5.2] years, 20 [40.0%] males) repeated both tests after a mean

duration of 2.6 (2.0) weeks. Pearson’s correlation coefficient was 0.88 ($P<0.001$) for SS-Sg and 0.90 ($P<0.001$) for Scentsor.

Patients with subjective olfactory loss

Sixty-seven patients (mean age 50.5 [15.9] years, 34 [50.8%] males) with subjective olfactory loss were recruited. The causes for olfactory loss were chronic rhinosinusitis ($n=40$, 59.7%), post-viral ($n=19$, 28.4%), idiopathic ($n=6$, 9.0%) and post-traumatic brain injury ($n=2$, 3.0%). Forty-two patients had self-rated hyposmia and 25 had self-rated anosmia.

With SS-Sg, there was a significant difference in scores across controls, self-rated hyposmias and self-rated anosmia (χ^2 [2]=85.8, $P<0.001$) (Fig. 3). The mean scores were 12.6 (2.4) for controls, 9.8 (3.2) for self-rated hyposmias and 6.0 (2.3) for self-rated anosmias. Post-hoc comparisons indicated that the mean score of controls was significantly higher than that of self-rated hyposmias ($P<0.001$), which was in turn significantly higher than the scores of self-rated anosmias ($P<0.001$).

Table 3. Healthy controls, SS-Sg and Scentсор scores by age and sex.

Age	21–30 years		31–40 years		41–50 years		51–60 years		>60 years	
n	133		137		82		66		55	
SS-Sg										
Median (IQR)	13 (12-14)		13 (11-14)		13 (12-14)		13 (12-14)		12 (9-13)	
Mean (SD)	13.1 (1.8)		12.8 (2.4)		12.9 (2.1)		12.4 (2.7)		10.7 (3.0)	
10th percentile	11		10		11		9		7	
Sex	Male (n=48)	Female (n=85)	Male (n=47)	Female (n=90)	Male (n=31)	Female (n=51)	Male (n=23)	Female (n=43)	Male (n=25)	Female (n=30)
Mean (SD)	13.3 (1.6)	13.0 (1.9)	12.3 (2.8)	13.0 (2.1)	13.2 (1.9)	12.7 (2.2)	12.2 (2.9)	12.5 (2.7)	9.8 (3.3)	11.4 (2.6)
Median (IQR)	13 (12-15)	13 (12-14)	13 (11-14)	13 (12-14)	14 (13-14)	13 (12-14)	12 (11-14)	13 (12-14)	10 (7-12)	12 (10-13)
10th percentile	11	10	9	10.5	11	10	9	11	5	7
Scentсор										
Median (IQR)	15 (14-16)		15 (14-16)		15 (14-15)		14 (14-15)		14 (12-15)	
Mean (SD)	14.8 (1.3)		14.3 (1.7)		14.4 (1.5)		14.0 (1.8)		13.0 (2.5)	
10th percentile	13		12		13		12		10	
Sex	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Mean (SD)	14.1 (1.0)	15.1 (1.2)	13.3 (1.8)	14.8 (1.4)	13.8 (1.2)	14.8 (1.6)	13.6 (1.9)	14.3 (1.7)	12.3 (2.7)	13.5 (2.3)
Median (IQR)	14 (14-15)	15 (15-16)	14 (13-15)	15 (14-16)	14 (13-15)	15 (14-16)	14 (14-15)	15 (14-15)	12 (12-14)	14 (12-15)
10th percentile	13	14	11	13	12	13	12	13	9	10

IQR: interquartile range; SD: standard deviation

Fig. 2. Scatterplot of SS-Sg and Scentсор scores in male and female subjects over age.

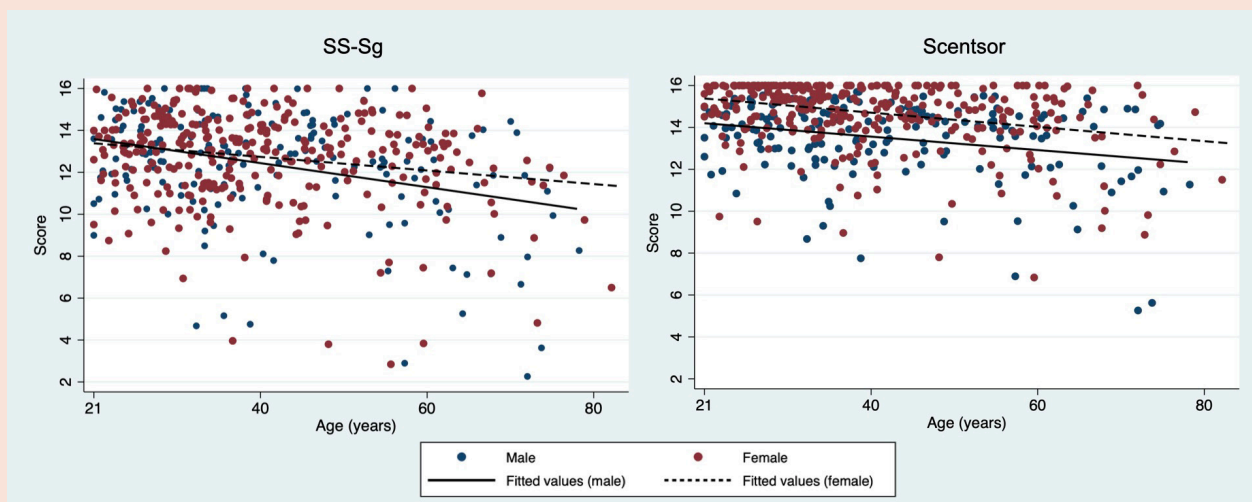
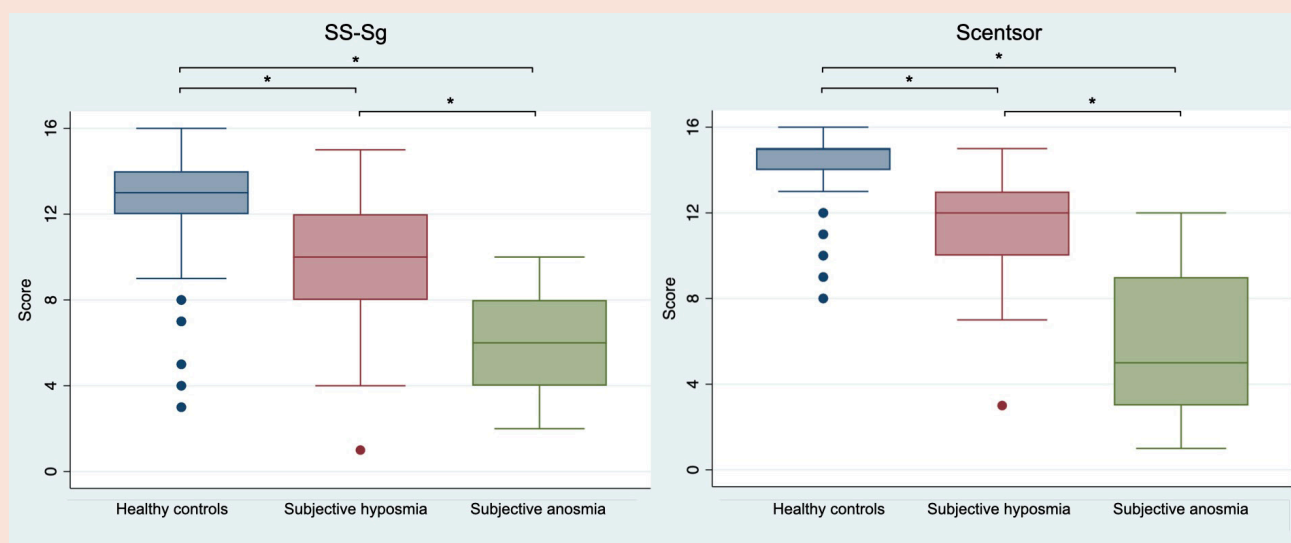


Fig. 3. Boxplot of SS-Sg and Scentsor scores in healthy controls, subjectively hyposmic and subjectively anosmic patients. Asterisk indicates a statistically significant difference.



Similarly, with Scentsor, there was a significant difference in scores across controls, self-rated hyposmias and self-rated anosmias ($\chi^2 [2]=99.9$, $P<0.001$). The median scores were 14.3 (1.8) for controls, 11.3 (2.8) for self-rated hyposmias and 5.8 (3.4) for self-rated anosmias. Post-hoc comparisons indicated that the mean score of controls was significantly higher than that of self-rated hyposmias ($P<0.001$), which was in turn, significantly higher than that of self-rated anosmias ($P<0.001$).

DISCUSSION

Odour identification tests are sensitive to cultural differences. Our study has shown that the unmodified SS was not applicable to the Singapore population, with over half of the odour descriptors in the blue and purple sets unfamiliar to most Singaporeans. This highlights the need for odour identification tests to be adapted and validated in the population of interest before it can be applied.

In this study, SS and Scentsor were adapted and developed respectively for Singapore. Both tests can be used to reliably measure olfactory function in Singapore. They have been validated for the Singapore population and normative data from a large group of healthy controls were obtained. The median scores of 13.0 and 15.0 with SS-Sg and Scentsor, respectively, for normosmic individuals is in keeping with the average scores of 13.7–14.8 in Malaysia,¹¹ China²² and Taiwan,²³ where 16-item odour identification scores have been validated. Both tests have good test-retest reliability. They can distinguish between normosmic, hyposmic and anosmic patients. Both kits are portable, re-usable and arguably cost-

effective. Both tests can be administered in about 5 minutes or less on average, which makes it suitable to be integrated into a busy clinical practice. This will allow accurate assessment and follow-up of olfaction, rather than relying only on self-reported olfactory function. They can also be combined with odour threshold and discrimination tests to form the comprehensive threshold, discrimination and identification olfactory test, which is useful in tracking olfactory dysfunction.

The scores for functional anosmia, defined as quantitatively reduced olfaction to the extent that the sense of smell is not useful in daily life,⁵ is determined by the empiric distribution of scores obtained by anosmic subjects.¹⁹ Obtaining a score of more than 7 by chance is extremely unlikely; a score of 7 and less is therefore considered to be consistent with functional anosmia. The explanation for this is that identification tests are carried out using the forced multiple-choice procedure. Even with anosmia, some chance correct answers are expected. The probability of obtaining a certain number of correct answers by chance can be calculated using the binomial distribution equation. From this, the probability of obtaining more than 7 correct answers is less than 5%.²⁰ A score of 7 or less cannot be distinguished from a purely random result and is therefore interpreted as being consistent with anosmia.²⁰ This was congruous with the findings in our study, in which anosmic patients had mean scores of 6.0 and 5.8 on SS-Sg and Scentsor, respectively.

On the other hand, hyposmia is differentiated from normosmia using the 10th percentile of the distribution of scores in normosmic subjects.^{16,19-21} The

reference group is that of young, healthy adults as they represent the best olfactory performing cohort.^{19,24} In our study, the 10th percentile score of subjects aged 21–30 years was 11 for SS-Sg and 13 for Scentsor. This means that subjects who achieve a score of 8–10 in SS-Sg and a score of 8–12 in Scentsor would be considered hyposmic. Our patients with hyposmia had mean scores of 9.8 and 11.3 on SS-Sg and Scentsor, respectively, which was in keeping with these hyposmia score ranges defined by the normative data. A subject's test score should be defined primarily by this range, even though it can also be interpreted with respect to age group and sex. For example, a 75-year-old male who scores 11 on Scentsor can be considered "normosmic" relative to his age group and sex. However, in terms of his overall ability to smell, he is still considered to be hyposmic. This is similar in principle to the assessment of other human senses. Using hearing assessment as an analogy, if a 75-year-old has an audiogram pure tone average of 35 decibels, his diagnosis is mild hearing loss, even if this level of hearing is reasonably acceptable for his age.

An age-related decline in scores was observed in age groups above 50 years with both SS-Sg and Scentsor, which is consistent with the findings of other studies carried out in other populations.^{8,24–26} This was largely to be expected, as olfactory function generally declines with age.^{27,28} With regard to sex, females scored significantly better than males in Scentsor; however, no significant sex-related differences in scores were observed with the SS-Sg. In general, females typically tend to perform better than males in odour detection and recognition tasks,²⁹ although the difference in absolute test scores is probably small.

Ideally, we would have adapted only 1 SS set, rather than have a combination of blue and purple Sticks. The blue set was the preferred candidate for adaptation as it had fewer unfamiliar test odours than the purple set. However, it was difficult to replace all 6 unfamiliar test odours (cinnamon, liquorice, turpentine, clove, rose, anise) with similar-smelling alternative descriptors that were also familiar to Singaporeans. In the Malaysian version of the SS, "liquorice" was replaced with "fennel seed"¹¹ and in the Taiwanese version of the SS, "clove" was replaced with "wood",²³ both of which are unfamiliar odours in Singapore. This highlights that even among close neighbours in Asia, there is considerable cultural diversity which influences familiarity with odours. Hence, SS-Sg was formed by combining familiar odours from the blue and purple SS. This creates a slight drawback in that Sticks will have to be procured individually to form the SS-Sg. However, having an adapted version of the SS gives an option to assess

olfaction using a set of odours that is standardised internationally.

Scentsor was created as a pragmatic alternative odour identification test using locally-sourced odours. The general feedback from healthy participants was that Scentsor's odours were more recognisable compared to SS-Sg, even when test odours descriptors were the same (e.g. ginger). This might account for the shorter mean test duration with Scentsor, as well as the slightly lower overall SS-Sg scores in spite of adapting all odour descriptors to familiar ones. Familiarity with odours may become more crucial when testing older subjects or screening for neurodegenerative disorders. This is because identifying odours relies on the ability to detect the stimulus as well as to match it to the correct identity, of which the latter requires intact executive function and semantic memory.³⁰ We partially adopted the SS method of odour storage and presentation as it is practical, inexpensive and the odours are minimally exposed to the environment, which prolongs odour longevity and integrity. In addition, for hygiene purposes, we modified the design to protect the odourised tip such that it is not able to touch the participant's nose. In the event that there is accidental contact, the device can be easily disinfected with an alcohol wipe without affecting the odour. As Scentsor is produced locally, it may be a more cost-effective option. For these reasons, Scentsor is our preferred odour identification test.

There are limitations with this study. Healthy controls did not undergo nasoendoscopy to examine the nasal cavity and olfactory cleft. However, we applied stringent inclusion and exclusion criteria to ensure participants were likely to have normal olfactory function. There were more female participants who provided normative data, which could have raised the overall scores, even if the difference in scores between sex may be small. There were fewer participants aged above 50 years old who provided normative data. Future studies may be needed to obtain normative olfactory data in older age groups.

Within Asia, countries that have developed or adapted olfactory identification tests to their own populations include China,²² Malaysia,¹¹ Japan,^{31,32} South Korea,^{33,34} Taiwan,^{14,23} Thailand³⁵ and Vietnam.¹⁵ The authors hope that the validation of SS-Sg and Scentsor will standardise olfactory testing carried out in Singapore. The potential applications for a validated olfactory test are vast. Olfactory impairment is a key symptom of chronic rhinosinusitis. In severe type 2 inflammatory chronic rhinosinusitis with nasal polyps, treatment with biologics requires documentation of anosmia on smell testing,^{18,36} and biologics themselves have the potential to improve anosmia.^{37,38} During the COVID-19 pandemic, olfactory loss was a

prominent symptom,³⁹ and anosmia was reported to have high specificity for the SARS-CoV-2 infection.⁴⁰ Olfactory tests have been used as screening tools for SARS-CoV-2 in the community,⁴¹ emergency department,⁴² among healthcare workers⁴³ and inpatients.⁴⁴ Olfactory loss is an early symptom of neurodegenerative conditions, in particular Parkinson's disease⁴⁵⁻⁴⁷ and Alzheimer's disease.⁴⁸ In older adults, severe olfactory dysfunction is also an early indicator of frailty, a syndrome of accelerated physiologic decline and increased vulnerability to external stressors beyond normal ageing.⁴⁹ These are relevant issues in our ageing society. An odour identification test may be a practical screening tool for early detection of neurodegeneration or frailty in vulnerable individuals.

CONCLUSION

SS-Sg and Scentsor are 2 odour recognition tests that have been validated for the Singapore population. Either of these tests, referenced against the normative data obtained in this study, should be used when assessing olfaction in Singapore.

Supplementary Fig. S1. STROBE flow diagram of participant recruitment.

Acknowledgment

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Ethics statement

This study was approved by the National Healthcare Group Domain Specific Review Board and participants gave informed consent. All experimental procedures were consistent with the Declaration of Helsinki.

Declaration

All the authors have no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript.

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Utilising a COM-B framework to modify antibiotic prescription behaviours following third molar surgeries

Chee Weng Yong¹ BDS, Ruth Choe¹ BDS, Sarah Kho Xian Chua¹ BDS, Jing Li Lum¹ BDS, Wendy Chia-Wei Wang¹ BDS

ABSTRACT

Introduction: Antimicrobial resistance (AMR) poses a critical global health threat, with millions of deaths attributed to it annually. Antibiotic stewardship to combat AMR is the responsibility of all healthcare professionals. Despite evidence suggesting that it is unnecessary, dentists routinely prescribe prophylactic antibiotics following third molar (3M) surgeries.

Method: This mixed-methods study examined the behavioural barriers influencing antibiotic prescribing practices within the Division of Oral and Maxillofacial Surgery at the National University Centre for Oral Health Singapore. This study used the capability, opportunity and motivation for behavioural change or COM-B framework to implement interventions targeting the behavioural barriers.

Results: Pre- and post-intervention data over 6 months showed a significant reduction in antibiotic prescriptions from 84.45% to 20.89%, following the implementation of COM-B strategies ($P < 0.001$). Qualitative feedback from focus group discussions highlighted a positive shift in clinicians' attitudes towards antibiotic reduction, acknowledging the minimal infection risk associated with non-prescribing practices. Notably, complication rates remained stable throughout the study period, indicating no adverse effects from reduced antibiotic usage.

Conclusion: These findings demonstrated that the COM-B model can be successfully applied to modify deeply ingrained prescription habits, and underscored the effectiveness of a structured behavioural change intervention in enhancing compliance with antibiotic stewardship guidelines. The study advocates continuation of initiatives to sustain this positive trend and mitigate AMR in clinical practice.

Keywords: antimicrobial, antibiotic resistance, behavioural change, COM-B framework, third molar surgery

INTRODUCTION

Antimicrobial resistance (AMR) is a critical global public health crisis, associated with 4.7 million deaths worldwide in 2021 alone.¹ Antibiotic stewardship is one of the key interventions in the World Health

CLINICAL IMPACT

What is New

- This study demonstrated the effectiveness of an antibiotic stewardship programme to reduce antibiotic prescription by dental practitioners in Singapore.

Clinical Implications

- The COM-B approach is an effective tool to induce behavioural change in antibiotic prescription.
- Demonstrated reduction in antibiotic prescription can bolster confidence in dental practitioners to reduce unnecessary antibiotic prescription.

Organization's multipronged strategy to combat AMR.² Antibiotic stewardship is a systematic approach aimed to educate and support healthcare professionals in adhering to evidence-based guidelines for antibiotic prescription and administration.

In the field of dentistry, the surgical removal of the third molar (3M) is the most common procedure leading to antibiotic prescription.³ Prophylactic antibiotics are frequently prescribed due to concerns about post-surgical infections given the constant exposure of the surgical site to oral microflora.³ However, systematic reviews demonstrated low infection rates, and the numbers needed to treat ranged from 15 to 19.⁴⁻⁶ Consequently, a growing consensus suggests that prophylactic antibiotics are unnecessary for 3M removals, particularly in healthy adults.⁴⁻⁶

Despite the scientific evidence, many clinicians continue to inappropriately prescribe antibiotics due to various behavioural barriers. These include biases based on past experiences, pressure to prescribe, comfort with existing prescribing practices and a disconnect from the issue of antibiotic resistance.⁷

Behaviour change is needed to improve compliance with antibiotic stewardship. While there are many

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¹ National University Centre for Oral Health Singapore, Singapore

Correspondence: Dr Chee Weng Yong, National University Centre for Oral Health Singapore, 9 Lower Kent Ridge Road, Singapore 119085.

Email: chee_weng_yong@nuhs.edu.sg

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models or strategies available to bring about behavioural change, the COM-B framework is particularly useful for identifying the factors affecting behaviour in a structured manner.^{8,9} Interventions can then be designed based on the factors identified.⁸ The COM-B framework proposes that behavioural change is influenced by 3 factors: capability, opportunity and motivation.⁸ Capability encompasses the knowledge, skills and abilities required to perform the desired behaviour. Opportunity refers to external factors that facilitate behavioural change while motivation refers to the internal processes that drive the individual towards the change. Implementing interventions that target these 3 factors are more likely to result in effective behavioural changes.⁹

Wilding et al. employed COM-B to sequentially identify factors that required correction and determined that an animated film to convey antimicrobial stewardship messages would be the most effective.¹⁰ Participants (n=211) who viewed the test film were statistically significantly less likely to ask their doctor or dentist for antibiotics if they could do without it as compared to participants who viewed the control film (n=206). Similarly, Hayes et al., under the UK AMR National Action Plan, developed the Antibiotic Guardian Youth Badge, a paediatric AMR programme with the aid of the COM-B model. Only 7% of participants (n=147) indicated that they would not adhere to the recommendations of only taking antibiotics when they really need it.¹¹ Like many prior studies on AMR, most studies only investigated how the COM-B model was applied or determined the effectiveness of the model based on qualitative measures.¹⁰⁻¹³

As part of the appropriate care initiative, an antibiotic stewardship programme utilising the COM-B approach was implemented. This study aimed to use the COM-B approach to develop interventions and evaluate the effectiveness of these interventions.

METHOD

Baseline antibiotic practices

The prevailing antibiotic prescription practice within the Division of Oral and Maxillofacial Surgery (OMS) was established through a retrospective review of all patients who underwent surgical removal of their 3M at the National University Centre for Oral Health Singapore from 1 May to 31 July 2024 (pre-intervention period). Ethics review exemption (review not required) was granted by National Healthcare Group Domain Specific Review Board (NHG DSRB Ref 2024-4480). Data were extracted from their electronic health records (Epic; Epic Systems Corporation, Wisconsin, US), including patient demographics (age, sex, medical history and drug allergy), teeth removed, antibiotic prescription

details and postoperative complications. The data were extracted by a clinician who was not involved in the clinical care of the patients and analysed in their anonymised form by the authors. The purpose of the analysis was to determine the baseline antibiotic prescription practice of the clinicians in the absence of any restrictions or guidance on antibiotic prescription for 3M surgeries.

Intervention design

A mixed-methods approach was employed to explore the behavioural factors influencing current antibiotic prescription practice, with an aim to develop a targeted COM-B intervention. These preliminary investigations are summarised in Fig. 1. It consisted of a comprehensive literature review, an electronic survey and focus group discussions with OMS clinicians. The detailed methods and findings are presented in Supplementary Material S1. These preliminary investigations revealed several behavioural barriers including uncertainty about AMR and the benefits of antibiotics, lack of prescription guidance, fear of deviating from the norm, concerns about patient complaints and impact on clinical performance indices (including postoperative infections and unscheduled returns), and indifference towards antibiotic resistance. Based on these findings, interventions were formulated targeting each component of the COM-B model.

Intervention 1: Improving capability

An education session was conducted to enhance clinicians' capability to counsel patients on the evidence against routine antibiotics prescription. A summary of relevant literature was disseminated via email to allow the clinicians to read at their own pace. A set of criteria was also developed to guide clinicians in their prescription decision, including the rationale of the behind the criteria (Table 1).

Intervention 2: Improving opportunity

Interventions under the opportunity category aim to create a supportive environment for behaviour changes across the entire division. Clinicians were assured that the interventions aligned with an institution-wide appropriate care initiative and were supported by the centre's directorate. A commitment was made to discontinue the interventions if a statistically significant increase in infection rates or patient complaints was observed.

Information posters were placed in prominent locations in the operatories and pharmacy to raise awareness of antibiotic stewardship among patients and serve as a reminder to clinicians to modify their antibiotic prescription patterns. Pharmacists and patient service associates were also briefed on appropriate patient counselling techniques.

Fig. 1. COM-B approach to reducing antibiotic prescription.

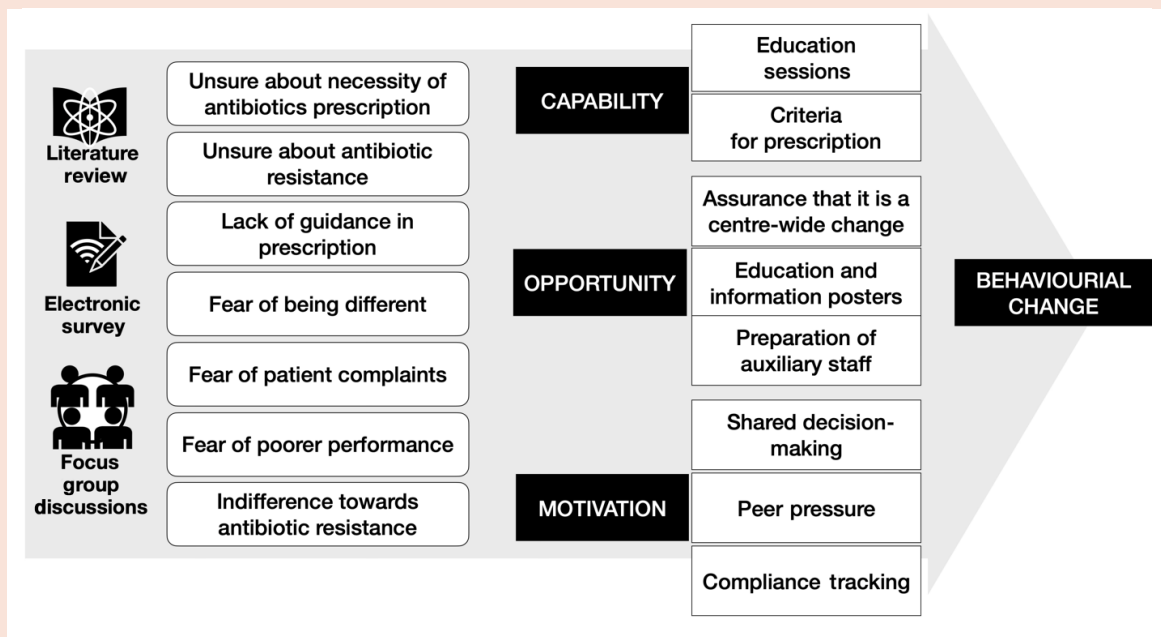


Table 1. Criteria for considering to stop routine antibiotics prescription.

Criteria		Rationale
Patients who are immunocompetent AND		
1	Age ≤ 25 years	Most primary studies either used 25 years of age as the upper limit for inclusion criteria, or as the upper limit for age group classification of "young patients". In these studies, patients aged 25 or younger have low risk of infection after third molar surgeries.
2	Not associated with pathologies such as cyst, tumour or abscess/infection	The cavity that resulted from third molar surgeries are not significantly large and should not predispose patients to infection risks greater than a typical dental extraction.
3	Routine surgical removal whereby surgical time is not extended (not deep, difficult or complex).	Routine surgical removal of third molars is considered a short surgical procedure with low risk of infection.
4	No history of anti-angiogenic agents, anti-resorptive agents or radiotherapy	These therapies have an impact on bone remodelling. It is still debatable whether antibiotics play a role in preventing disease progression.
5	Low-moderate bleeding risk	Even though clinicians may be worried that an infection may arise from a haematoma, local haemostatic measures should be sufficient to prevent the formation of haematoma in these cases.
6	Root tip not left behind	If a root tip was left behind inadvertently, there may be an increased risk of infection, although this has not been definitively reported in the literature. Conversely, if a root tip was not left behind inadvertently, there should not be an increased risk of infection.

Intervention 3: Improving motivations

To enhance motivation, division members were engaged in developing the set of criteria to guide prescription, and their input was sought prior to implementation of the interventions to foster a sense of ownership and involvement. This shared decision-making approach was designed to increase compliance with the proposed changes. By applying

the criteria on the pre-intervention patient data, a 50% reduction in antibiotic prescription following 3M surgery was expected. With agreement from the division, a goal of at least 50% reduction from the pre-intervention prescription rate was set. Clinicians were informed of a common start date and that compliance rates would be shared periodically to encourage positive peer influence.

Post-intervention changes in prescription practices

The post-intervention changes in antibiotic prescription practices were evaluated over 3 months from 1 August to 30 October 2024. Data extracted from the electronic health records were similar to the pre-intervention baseline data extraction. In addition, if antibiotics were prescribed, the reasons for the prescription were recorded.

Post-intervention focus group discussion

A focus group discussion was convened to evaluate clinicians' perception, acceptance and adherence to the changes in antibiotic prescription practices 3 months after the implementation of interventions. All 4 participants of the focus group prescribed antibiotics routinely prior to the intervention. The focus group discussion aimed to explore 4 themes: (1) perception towards the initiative to reduce antibiotic prescription; (2) facilitators to change; (3) barriers to change; and (4) principles in antibiotic prescription. Details of the questions are summarised in Supplementary Material S2.

Data analyses

Statistical analysis was performed using SPSS version 26.0 (IBM Corp, Armonk, NY, US). Fisher's Exact and chi-square tests were done to evaluate the differences in categorical variables between the pre- and post-intervention groups, as well as between patients with and without antibiotics prescribed. Statistical significance was set at $P < 0.05$.

RESULTS

In the 6-month duration of this study, 2057 3M were surgically removed from 1839 patients, with an average age of 24.67 ± 8.11. Patients ≤25 years of age comprised 79.5% of the population. Table 2 summarises the detailed patient demographics. There were no significant differences in these demographics before and after the intervention.

In the 3-month pre-intervention period, antibiotics were prescribed in 84.45% (793/939) of 3M surgeries. After the COM-B interventions were implemented, the proportion of cases in which antibiotics were prescribed was significantly reduced to 20.89% (188/900) of 3M surgeries ($P < 0.001$). Monthly trends over the 3-month post-intervention period revealed a progressive reduction in antibiotic prescription rates, declining from a baseline of >80% to 34.7%, 20.9% and eventually 7% (Fig. 2). For patients ≤25 years of age, the antibiotic prescription rate dropped from 84.80% at baseline to 16.45% post-intervention. Meanwhile, for older adults (>25 years), the antibiotic prescription rate reduced from 82.95% to 36.32%.

There was no statistically significant increase in overall complication rates before and after interven-

tion (3.62% pre-intervention and 4.2% post-intervention, $P = 0.506$). The complications that occurred included persistent pain, bone protrusion and spicules, bleeding, dry socket/alveolar osteitis and surgical site infection. While the surgical site infection rates pre- and post-intervention increased from 0.11% to 0.56%, this increase was not statistically significant ($P = 0.09$). Throughout the study period, no patients who had prophylactic antibiotics developed infection (0/981), whereas 6 out of 856 patients who did not have prophylactic antibiotics developed infection. The number needed to harm (NNH) for antibiotics to prevent surgical site infection was 142.

Of the 6 patients who developed postoperative infection, 4 were healthy males aged between 20 and 22 years, and their postoperative infections achieved full resolution with local irrigation and systemic antibiotics. The remaining 2 patients required incision and drainage in addition to antibiotic therapy; they were an 81-year-old female patient and a 22-year-old male patient who was later diagnosed with type II diabetes mellitus.

No statistically significant differences were found in the dry socket rates in patients with antibiotics (12/981) and without antibiotics (20/856, $P = 0.069$). All cases of dry sockets were managed according to clinical protocol and resolved completely within 1 week of treatment initiation. The NNH for antibiotics to prevent dry socket was 112. Apart from infection and dry socket, the other complications were not conventionally associated with antibiotics.

The reasons for antibiotic prescription were tracked in the post-intervention period. Clinicians were required to indicate a reason for prescribing antibiotics in their treatment notes. The most common reason was that the surgical removal of the 3M was "deep, difficult or complex", followed by "given by previous clinician" and "patient's age" (Table 3). Prescriptions were considered unnecessary if antibiotics had been given because it was "given by previous clinician" or at "patient's request"; these accounted for 42.3%, 8.1% and 0% of the antibiotic prescription over the 3 months after the interventions.

No patients filed complaints regarding either the absence of antimicrobial prescription or occurrence of infection. The most common type of antibiotic prescription was amoxicillin, 500 mg, 3 times a day (TDS) for 5 days. The prescription patterns also included augmentin (amoxicillin-clavulanate) or clindamycin of varying frequency and duration (Supplementary Material S3).

All 4 participants of the focused group prescribed antibiotics routinely prior to the intervention. It consisted of 2 junior (registrars) and 2 senior (associate consultant and consultant) members who

Table 2. Pre- and post-intervention monthly antibiotic prescription patterns and demographic profiles.

	No.	Age, mean (SD)	>25	M	F	#18	#28	#38	#48	Complications
Pre-intervention: First month										
AB (85.15%)	304	24.19 (6.74)	51	247	57	13	16	156	143	7 pain, 3 dry socket, 2 bone protrusion, 1 spicule, 1 bleeding (total 14)
No AB	53	24.75 (9.25)	12	37	16	2	0	28	25	1 infection, 1 pain (total 2)
Subtotal	357	-	63	284	73	15	16	184	168	
Pre-intervention: Second month										
AB (85.82%)	224	24.53 (8.06)	42	166	58	17	14	112	106	3 bone spicules, 3 pain, 4 dry socket, 1 bleeding (total 11)
No AB	37	24.89 (6.49)	10	27	10	1	2	19	17	1 pain (total 1)
Subtotal	261	-	52	193	68	18	16	131	123	
Pre-intervention: Third month										
AB (82.55%)	265	24.01 (6.96)	53	186	79	9	12	130	141	4 dry socket, 1 pain, 2 bone spicules (total 7)
No AB	56	24.98 (8.32)	8	42	14	2	3	29	22	1 dry socket (total 1)
Subtotal	321	-	61	228	93	11	15	159	163	
Post-intervention: First month										
AB (34.7%)	109	26.9 (9.74)	35	76	33	5	4	55	59	1 loose spicule, 2 pain (total 3)
No AB	205	24.35 (7.09)	34	143	62	11	6	98	100	3 infection, 3 dry socket, 1 pain (total 7)
Subtotal	314	-	69	219	95	16	10	153	159	
Post-intervention: Second month										
AB (20.9%)	57	29.49 (12.09)	24	34	23	5	4	31	28	1 pain, 1 dry socket (total 2)
No AB	215	24.67 (8.54)	46	156	59	15	10	107	134	1 dehiscence, 4 pain, 5 dry socket, 1 infection (total 11)
Subtotal	272	-	70	190	82	20	14	138	162	
Post-intervention: Third month										
AB (7%)	22	32.22 (12.60)	14	17	5	1	2	13	9	1 dry socket, 1 bleeding (total 2)
No AB	292	23.63 (8.068)	48	228	64	25	32	156	128	1 pain, 1 bone spicule, 1 infection, 10 dry socket (total 13)
Subtotal	314	-	62	245	69	26	34	169	137	

AB: antibiotics prescribed; SD: standard deviation; F: female; M: male; #18: surgical removal of the upper right third molar; #28: surgical removal of the upper left third molar; #38: surgical removal of the lower left third molar; #48: surgical removal of the lower right third molar; >25: age greater than 25 years

Fig. 2. Relationship of antibiotics prescription and infection rates.

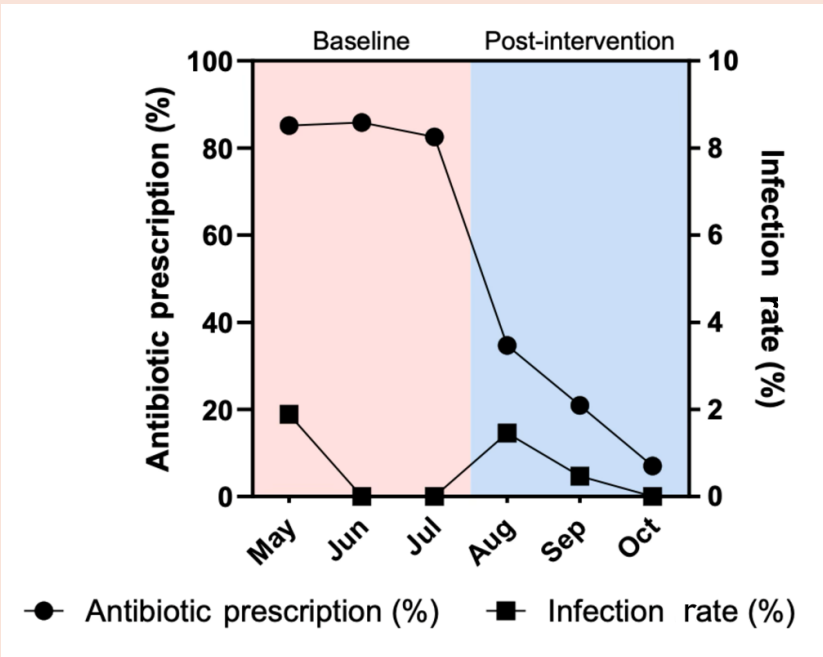


Table 3. Reasons for valid and unnecessary antibiotic prescriptions after third molar surgeries.

	Valid prescriptions								Unnecessary prescriptions		Total
	Age	IS	Haem	Cyst	Infx	DDC	Perio	Root	Prev	Req	
August	15	7	1	1	2	34	1	3	35	12	111
September	10	2	5	3	2	31	1	3	2	3	62
October	8	1	2	1	1	8	0	1	0	0	22
Total	33	10	8	5	5	73	2	7	37	15	195

Age: patient’s age; DDC: deep, difficult or complex; Haem: haematological disorders or haemorrhage; Infx: infection; IS: immunocompromised state; Perio: periodontal disease; Prev: antibiotics given by previous clinician for third molar surgery; Req: patient’s request despite counselling; Root: root left behind

volunteered to participate in the discussion. During the post-intervention focus group discussion, all 4 participants reaffirmed their commitment to prescribing antibiotics only when clinically necessary rather than as routine practice. They identified the following scenarios in which prescribing antibiotics may be warranted:

- Immunocompromised patients
- Cases with increased bleeding risk with potential haematoma formation
- Oro-antral communication
- Root fracture left in situ
- Pre-existing abscess

- Geriatric patients undergoing complex surgery
 - All the participants felt that there were more conditions where antibiotics could have been reduced, such as for middle aged patients and for cases of deeply impacted wisdom teeth. Participants unanimously had a positive perception towards efforts to decrease antibiotic use. They identified several enablers that facilitated reduction in antibiotic prescription:
 - Assurance that the lack of antibiotics will not significantly increase infection risk for healthy patients
 - Success could only be possible because it was a centre-wide change

- Knowing that the rest of the division is also making the change
- Posters were useful when counselling patients
- It becomes easier over time as patients were not prescribed antibiotics for their previous surgery (3M surgery for the other side of the jaw)

DISCUSSION

This study employed a behavioural change approach to reduce unnecessary antibiotic prescription for 3M surgeries. The interventions generated led to a reduction in antibiotic prescriptions from 84.45% to 20.89%, without an increased risk of post-surgical infections. Antibiotics prescribed were mostly deemed to be appropriate, as they were prescribed for patients who did not fit in the recommended criteria to stop routine antibiotics prescription. A multiprong approach was utilised to appreciate the different perspectives towards routine prescription of antibiotics. The investigation revealed that while clinicians were cognisant of AMR resulting from routine antibiotic prescription, they were reluctant to change prescription practice. This would suggest that knowledge alone may not be enough to overcome either the indifference to the problem or the natural passive resistance to change.¹⁴

The COM-B model was found to be a valuable tool in formulating strategies to develop a conducive ecosystem for change.⁹ It allowed for a multidimensional approach where the clinician (who makes the change) feels supported from all tiers (auxiliary staff, peers and superiors). Apart from external impetus, an important motivator is in allowing clinicians to feel that they are part of the decision-making process. Active communication and involvement of the target audience has been shown to be crucial in behavioural change.^{15,16} Through this approach, the antibiotic prescription rates dropped dramatically from 82.55% to 34.71% within a month of the interventions. The reasons for inappropriate antibiotic prescription also correspondingly reduced over the months. The outcome underscores the importance in generating an ecosystem for change, where administrators and leaders avoid a top-down approach, and instead engage their staff when attempting to alter behaviours.

A focus group discussion method was chosen over individual interviews so that active discussion could occur between the participants. The interpersonal and interactive nature of these discussion can elicit information that might not otherwise be gathered from an individual interview. Guest et al. reported that while individual interviews were highly effective at brainstorming for ideas, sensitive and personal disclosures were more likely to occur in focus group discussions.¹⁷ The latter was more suited for our purpose as the discussions were directed at learning

the reasons behind their prescription behaviours. The downside of a focus group discussion includes less in-depth data collected due to the group setting, and a risk of power differences between the participants that could lead to a fear of speaking up. There was a need for positive dynamics between the participants, to mitigate possible fears of repercussions for speaking honestly.

A continued downtrend in antibiotic prescription was observed, with approximately 15% reduction each month during the audit period. The sustained decrease could be attributed to clinicians observing firsthand that infection rates did not increase for their patients, as well as peer pressure from seeing fellow colleagues participating in the change. Applying the list of criteria to the pre-intervention data suggested that we could expect a reduction in antibiotic prescription of 50%, yet the average prescription rates dropped to 20.87%. This substantial reduction was only possible because the clinicians did not strictly adhere to the list of criteria and continued to expand beyond their prior comfort zone. For instance, the proportion of patients older than 25 years who did not receive antibiotics steadily increased over time without a corresponding increase in infection rate among the older patients. This finding highlighted the limitation of using an arbitrary number for age limits. Similarly, participants of the focus group discussion also expressed comfort with withholding prescription of prophylactic antibiotics for patients who did not meet the criteria. This is because they understood that the criteria given was stricter and covered only a subset of patients who did not require antibiotics. However, it was enough to give them the confidence to practice evidence-based medicine to a broader group of patients.

Apart from an overall reduction in antibiotic prescription, unnecessary prescriptions of antibiotics also reduced over the 3 months after the interventions were implemented. Most of the unnecessary prescriptions had been given to prevent confusion to the patients, as many of these patients had been given antibiotics for their previous 3M surgery for the contralateral side prior to the interventions. These were mostly seen during the transition period in the first 2 weeks post-intervention and therefore, rates of antibiotic prescription for this reason reduced significantly by the second and third months (31.5% to 3.2% to 0%). The other common reason for unnecessary antibiotic prescription was “patient’s request”. Although they do not constitute to a significant portion of the antibiotic prescriptions (10.8% to 4.8% to 0%, over 3 months), the reduction of prescription for this reason could reflect either improved counselling skills from the staff over time or that patients were more educated in AMR.

The significant reduction in antibiotic prescription is supported by sound scientific evidence. The results of this study are aligned with previous research, reaffirming the view that stopping routine antibiotics is safe due to the high NNH, particularly given the very low infection rate observed (<1%). While reasons for low infection rate were not explored, potential contributing factors may include sterile practices, a predominantly healthy and young patient population, and clinician expertise.

In this study, we have mapped out 9 interventions. These interventions can also be broadly categorised into social changes, guidelines, education and audits. In a systematic review, Loffler et al. reported that the latter 3 were most often used in promoting antibiotic stewardship in a dental setting, typically in combination. Guidelines are not only useful in setting the standard of practice but also provide a benchmark for comparison. On the other hand, audits, while itself an intervention, can be used to measure the effectiveness of the other interventions. Elouafkaoui et al. compared the prescription patterns of dentists who received individualised audit and feedback (n=1999), and dentists who did not (n=567, control), along with the introduction of national guidelines to both groups.¹⁸ The authors reported that the prescription rates in the intervention group reduced from 8.5 items to 7.5 items per 100 treatment claims.¹⁸ This was compared with the control group, which yielded a decrease from 8.3 items to 7.9 items per 100 treatments.¹⁸ Although the success was not as drastic as that seen in our study, Elouafkaoui et al. demonstrated that these interventions can be successful in a multicentre or a multi-practice setting too.¹⁸

Out of the 9 interventions, 3 are considered to be educational activities. These include education sessions for clinicians on the role of antibiotics in 3M surgeries and the importance of combatting AMR; educational posters for patients; and training of auxiliary staff to counsel patients. Educational interventions are common as they are relatively easy to conduct and can target a large group at once. Teoh et al. employed the use of an online education platform and compared the prescription patterns of dentists 6 weeks before and after the education session.¹⁹ The authors noted a 40.5% reduction in antibiotic prescription and that the percentage of correct prescriptions, according to the Australian therapeutic guidelines, were 74.2%, 93.8% and 100% for amoxicillin, metronidazole and phenoxymethylpenicillin, respectively. This was a significant increase from 2.5%, 0% and 64.7%, respectively.¹⁹ Chate et al. compared the antibiotic prescription patterns of dentists 6 weeks before and after introducing a combination of education sessions,

guidelines and audits to 212 dentists.²⁰ The authors reported a 43.6% reduction in antibiotic prescription. In addition, appropriate prescriptions increased from 29.2% to 48.5%.²⁰

Education should not be limited to clinicians alone. Al-Khatib et al. conducted an online survey of 345 respondents; 33.9% reported to have been pressured by patients to prescribe unnecessary antibiotics at least once per week and 31.9% once per month.²¹ A team-based approach to antibiotic stewardship has been well described in literature. Gross et al. reported how collaborative efforts of dentists, pharmacists and physician leaders led to a 72.9% decrease in antibiotic prescription after their intervention.²² Similarly, Okihata et al. described how a pharmacist-led antibiotic stewardship in a university dental clinic led to a reduction in antibiotic prescriptions.²³ In our study, we have identified the importance of having a united front among all staff involved in a patient's journey, including not only the clinician but dental assistants, patient service associates and pharmacists. This allowed the patients to have multiple opportunities to be counselled on the appropriate prescription of antibiotics.

Our study also implemented systemic interventions, which can influence social factors in antibiotic prescription, such as peer pressure, shared decision-making and giving clinicians reassurance that the intervention is a centre-wide change. The impact of these interventions on antibiotic stewardship in a dental setting is not well reported. Carlsson et al. surveyed 371 medical doctors and the authors reported that the doctor's choice on prescribing antibiotics were strongly correlated with the perceived norms.²⁴ Apart from breaking down perceptions and cultural norms, Krockow et al. also described the potential of crowd-based decision-making in the process of guideline development, which can also improve compliance to these guidelines.²⁵ Shared decision-making not only helped to reduce fear with regard to changing treatment methods, but also bolstered a sense of responsibility towards the guidelines. These interventions may be better able to drive intrinsic motivations towards antibiotic stewardship, and thus, be more sustainable than extrinsic motivations such as audits.

The impact of this study extends beyond the evaluated centre, contributing to the literature relevant to both the dental and Singapore community. Only 3 prior Singapore primary studies on antibiotic use in dentistry were identified. They explored the prophylactic antimicrobial prescribing patterns for infective endocarditis and the efficacy of antibiotics in dental implantology.²⁶⁻²⁸ This study affirms that routine antibiotic prescription following 3M surgery

is unnecessary, and demonstrates that reduction in antibiotic prescriptions will not be detrimental to patient care.

Another important element in AMR is the sustainability of the results. While the interventions had the potential to change the innate motivations of the clinicians towards AMR, there is still a need to maintain regular checks and audits. These will also serve as further external motivation for the clinicians. Following the success of the project, our centre has adopted a target antibiotic prescription rate of <15% for 3M surgeries. This has been maintained for 8 months since the start of the interventions (up to the point of manuscript preparation). In addition, frequent continuing education is required to keep clinicians up to date on evidence-based antibiotic prescription.

This study is not without limitations. First, causal efficacy could not be established due to a lack of randomised patient allocation on antibiotic administration, as the primary intention of the study was a clinical audit and quality improvement, rather than research. Second, the validity of the criteria for patients for whom antibiotics were not necessary could not be assessed; it was noted that not prescribing antibiotics for patients who did not meet the criteria did not appear to increase their infection risk. Third, a longer follow-up period of at least a year would be necessary to determine the true sustainability of the behavioural change. Fourth, this study was limited to only 1 tertiary centre and the external validity to other settings such as primary care practices may be limited, as interventions recommended may not be directly applicable. Last, as the interventions were implemented simultaneously, it was not possible to differentiate the degree of contribution of each intervention to the improvements seen.

CONCLUSION

This study demonstrates that targeted behavioural interventions, rooted in the COM-B framework, can significantly reduce both the overall rate of antibiotic prescriptions and that of unnecessary prescriptions in dental practice, particularly for 3M surgeries. The findings reveal that despite entrenched traditions in antibiotic prescription, clinicians can align their practices with evidence-based guidelines when equipped with the appropriate tools and support. By addressing the behavioural barriers influenced by capability, opportunity and motivation, we cultivated an environment conducive to change, leading to a substantial reduction in antibiotic prescriptions without compromising patient safety. The positive reception of these interventions by clinicians highlights the potential for sustained compliance with antibiotic stewardship initiatives. This study not only underscores the need for systematic approaches to behavioural change in healthcare but also advocates

for a collaborative effort across divisions to enhance the quality of patient care.

Supplementary materials

Supplementary Material S1. Pre-intervention investigations and evaluations.

Supplementary Material S2. Post-intervention focus group discussion guiding questions.

Supplementary Material S3. Type of prescriptions and their cost.

Ethics statement

Ethics review exemption (review not required) was granted by National Healthcare Group Domain Specific Review Board (NHG DSRB Ref 2024-4480).

Declaration

The authors declare they have no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript. This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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Singapore clinical guideline on parenteral nutrition in adult patients in the acute hospital setting

Johnathan Huey Ming Lum¹ MRCP, Hazel Ee Ling Yeong² RD, Pauleon Enjiu Tan³ FRCS, Ennaliza Salazar⁴ MBChB, Tingfeng Lee⁵ BSc (Pharm), Yunn Cheng Ng⁶ MRCP, Janet Ngian Choo Chong⁷ BSc, Pay Wen Yong⁸ BSc, Jeannie Peng Lan Ong⁹ FRCP, Siao Ching Gooi¹⁰ MSc, Kristie Huirong Fan¹¹ MRCP, Weihao Chen¹² MRCP, Mei Yoke Lim¹³ PharmD, Kon Voi Tay¹⁴ FRCS, Doris Hui Lan Ng⁶ PhD (UK)

ABSTRACT

Introduction: The primary objective of this guideline is to establish evidence-based recommendations for the clinical use of parenteral nutrition (PN) in adult patients within the acute hospital setting in Singapore.

Method: An expert workgroup, consisting of healthcare practitioners actively involved in clinical nutrition support across all public health institutions, systematically evaluated existing evidence and addressed clinical questions relating to PN therapy.

Results: This clinical practice guideline developed 30 recommendations for PN therapy, which cover these key aspects related to PN use: indications, patient assessment, titration and formulation of PN bags, access routes and devices, and monitoring and management of PN-related complications.

Conclusion: This guideline provides recommendations to ensure appropriate and safe clinical practice of PN therapy in adult patients within the acute hospital setting.

Keywords: adult, guideline, hospital, nutrition, parenteral

CLINICAL IMPACT

What is New

- This is the clinical practice guideline focused on the practice of parenteral nutrition therapy within Singapore or across the region.

Clinical Implications

- The guideline provides recommendations for consistent, safe, effective and evidence-based practice for parenteral therapy in adult patients within the acute hospital setting.

INTRODUCTION

Parenteral nutrition (PN) is an intravenous nutrition therapy used when oral and/or enteral nutrition (EN) is not possible or is insufficient for complete nutrition. It is an admixture formulation containing essential

nutrients, including dextrose, amino acids, lipid emulsion, electrolytes, vitamins and trace elements, for the maintenance of life. The use of PN is well-established in the acute care setting in Singapore. Most hospitalised patients on PN therapy require it for a short period of time over days or weeks. Although PN can be a beneficial and life-saving therapy, its use is not without risks and it can result in potentially serious complications. Additionally, administration of PN involves significant resource use, including a specialised team of trained healthcare professionals (HCPs) and specialised

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¹ Department of Gastroenterology and Hepatology, Sengkang General Hospital, Singapore

² Department of Nutrition and Dietetics, Khoo Teck Puat Hospital, Singapore

³ Department of Surgery, Khoo Teck Puat Hospital, Singapore

⁴ Department of Gastroenterology and Hepatology, Singapore General Hospital, Singapore

⁵ Division of Pharmacy, Tan Tock Seng Hospital, Singapore

⁶ Department of Gastroenterology and Hepatology, Tan Tock Seng Hospital, Singapore

⁷ Division of Nursing, Singapore General Hospital, Singapore

⁸ Department of Nutrition and Dietetics, Woodlands Health Campus, Singapore

⁹ Department of Gastroenterology and Hepatology, Changi General Hospital, Singapore

¹⁰ Department of Pharmacy, Changi General Hospital, Singapore

¹¹ Department of Gastroenterology and Hepatology, National University Hospital, Singapore

¹² Department of Gastroenterology and Hepatology, Ng Teng Fong General Hospital, Singapore

¹³ Department of Pharmacy, Ng Teng Fong General Hospital, Singapore

¹⁴ Department of Surgery, Woodlands Health Campus, Singapore

Correspondence: Dr Johnathan Huey Ming Lum, Department of Gastroenterology and Hepatology, Sengkang General Hospital, 110 Sengkang E Way, Singapore 544886.

Email: johnathan.lum.h.m@singhealth.com.sg

Dr Doris Hui Lan Ng, Department of Gastroenterology and Hepatology, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng Hospital, Singapore 308433.

Email: doris_hl_ng@ttsh.com.sg

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medical supplies and equipment.¹ The cost of PN can be high due to expenses on of PN bags, blood tests and other associated costs. For example, in an acute care hospital in Singapore, the cost for PN and manpower is approximately SGD1.2 million for 2791 PN days.²

The PN market within the Asia-Pacific region was valued at approximately USD861 million in 2022 and is expected to reach USD1.471 million by 2030.³ Key factors contributing to this growth include the rising incidence of chronic diseases, such as cancer and gastrointestinal disorders. In a study conducted at the largest acute care hospital in Singapore, 182 patients received 194 courses of PN over a year, with a median age of 62 years.⁴ The majority of these patients were surgical patients (82%), followed by medical patients (18%). Common indications included anticipation of non-functioning gut postoperatively, postoperative complications and postoperative ileus. As the prevalence of chronic diseases and complex medical conditions continues to rise, the role of PN in clinical practice in Singapore is likely to expand, making the development of clear and evidence-based clinical practice guidelines essential for optimising patient care.

There is currently no consensus to guide the practice of PN therapy in the local setting or neighbouring regions. Hence, with increasing knowledge from the literature, there is a pressing need to develop a clinical practice guideline to ensure the safe provision of PN. While existing international guidelines, such as those from the American Society for Parenteral and Enteral Nutrition (ASPEN) and the European Society for Clinical Nutrition and Metabolism (ESPEN), provide valuable insights, it may not fully account for regional variations in disease prevalence, healthcare delivery and patient demographics. Developing a local clinical practice guideline for the use of PN in acute care settings in Singapore is crucial for several reasons. First, Singapore's healthcare practices and infrastructure differ from those in other regions. A region-specific guideline ensures that recommendations are practical and applicable within the local context, considering available resources, clinical workflows and resource constraints within the healthcare system. Second, a tailored guideline ensures that clinical practice is standardised and provides consistent care, regardless of healthcare provider. It promotes evidence-based practice, optimises resource use and streamlines training, which can lead to better patient outcomes by ensuring that PN therapy is administered safely and effectively, reducing the risk of complications and improving overall patient care. This current guideline aims to provide evidence-based recommendations to ensure appropriate, safe, efficient and cost-effective clinical

practice of PN therapy in adult patients in the acute care setting within the local context, intended for HCPs (e.g. gastroenterologists, intensivists, dietitians, pharmacists, nurses); policymakers; researchers and educators to ensure comprehensive relevance and applicability across all professionals involved in the administration and regulation of PN therapy. Nevertheless, recommendations provided in this guideline should not substitute the need for HCPs to exercise clinical judgement.

METHOD

The proposal to develop the present guideline was initiated by the Society for Parenteral and Enteral Nutrition (Singapore) (SingSPEN). In May 2021, a workgroup consisting of healthcare experts from the nutrition support services across all 8 public acute care hospitals in Singapore was formed. The group of experts represents different professions, and it included 6 general physicians, 3 pharmacists, 2 surgeons, 2 dietitians and a nurse. The aim was to provide clear and easy-to-follow evidence-based recommendations to practising HCPs who are involved in the prescribing, compounding and administering of PN in the acute care setting.

Clinical questions (CQs) relating to PN therapy were first defined and then divided into 5 domains by the committee members of the workgroup. The 5 domains were indications for PN, assessment of PN patients, titration and formulation of PN, PN access routes and devices, and monitoring and management of PN-related complications. CQs for each domain were allocated to different subgroups based on their expertise. Each subgroup was led by a committee member. A literature search on PubMed/MEDLINE database to identify meta-analyses, systematic reviews and original studies relevant to the assigned CQs was then performed by each group. Examples of the search terms used in each CQ are included in Supplementary Fig. S1. Based on the evidence from the literature, statements of recommendation were proposed, and commentaries detailing the important findings and rationale of the proposed recommendations were documented. The quality of evidence and strength of recommendation were graded using the Grading of Recommendations, Assessment, Development and Evaluation methodology (Supplementary Table S1).

A total of 30 recommendations were formulated to answer all the CQs. Between August 2022 and November 2022, 6 virtual meetings were conducted and the modified Delphi technique was employed to achieve a formal consensus. All members were invited to agree or disagree, to comment and to provide feedback on each recommendation statement. Further revisions were undertaken when deemed necessary.

The strength of the recommendations was based on Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (Association of the Scientific Medical Societies in Germany) guidelines where “strong consensus” is defined as >90% agreement and “consensus” is defined as >75–90% agreement. Detailed commentaries and references supporting each recommendation are provided in

Supplementary Table S2. The completed work on the different domains of the clinical practice of PN therapy was subsequently compiled, edited and finalised before it was circulated to all members in the work-group for review and final agreement of this clinical guideline. The recommendation statements, executive summary, checklist and flowchart are detailed in Tables 1, 2, 3 and Fig. 1, respectively.

Table 1. Summary of clinical questions and recommendation statements.

No.	Clinical questions and recommendation statements	Strength of recommendation	Quality of evidence	Level of agreement
Indications for parenteral nutrition (PN)				
1	What are the indications for PN? • PN is indicated in patients who are unable to meet their nutritional needs orally and/or enterally as a result of suboptimal function of the gastrointestinal tract (GIT) or in whom the GIT is not accessible.	Strong	High	100%
2a	When should PN be initiated? • For patients who are well-nourished on initial assessment, initiating PN can be considered after 5–7 days of not achieving 60% or more of estimated total energy requirement.	Strong	Low	93%
2b	• For patients who are severely malnourished or at high risk of malnutrition, consider initiating PN earlier than 5 days of not achieving 60% or more of estimated total energy requirement.	Strong	Low	93%
3a	What are the contraindications of PN? • Contraindications to PN include patients with critical electrolytes abnormalities, specifically serum potassium <2.5 mmol/L, serum sodium <125 mmol/L, serum phosphate <0.4 mmol/L or serum magnesium <0.5 mmol/L.	Weak	Very low	100%
3b	• Contraindications to PN include patients who have suffered irreversible brain injury or terminal illness where there is a lack of therapeutic goal to prolong life in the inevitable death.	Strong	Moderate	100%
3c	• Contraindications to PN include patients who have no suitable venous access for PN.	Strong	Very low	100%
Assessment of PN patients				
4	Who should assess and manage patients prescribed with PN? • Patients on PN support in hospital should be managed by a nutrition support service consisting of a team of trained physician, nurse, dietitian and pharmacist.	Strong	Low	100%
5a	How often should biochemical parameters be assessed for patients on PN? • All patients should have a baseline biochemical assessment prior to initiation of PN.	Strong	Very low	100%
5b	• After establishing a patient on PN, the frequency of biochemical monitoring should be adjusted according to the patient's clinical progress, nutritional status and stage of PN therapy.	Strong	Very low	100%
6a	What are the nutritional requirements for patients on PN? • Energy expenditure for patients requiring PN should ideally be measured using indirect calorimetry. However, if indirect calorimetry is not available, providing 25–30 kcal/kg/day or using validated predictive equations, taking into account physical activity and stress factor, are acceptable to calculate energy requirement.	Strong	Moderate	100%
6b	• Protein requirements for patients requiring PN should be tailored to individual needs, ranging from 1 to 2 g/kg/day. Higher protein doses may be required for the critically ill, cancer and elderly patients.	Strong	Low	87%

Table 1. Summary of clinical questions and recommendation statements. (Cont'd)

No.	Clinical questions and recommendation statements	Strength of recommendation	Quality of evidence	Level of agreement
7	Which nutritional assessment tool should be used for patients requiring PN? There is currently no nutritional assessment tool developed specifically for patients requiring PN. Validated assessment tools, such as Subjective Global Assessment, are recommended for the diagnosis and determination of the severity of malnutrition.	Strong	Very low	100%
Titration and formulation of PN				
8	How fast should PN be introduced and progress? It is recommended to start at 15–20 kcal/kg/day on day 1 and increasing it progressively to target for non-critically ill patients. Patient's nutritional status and risk of refeeding should be considered when initiating and advancing PN infusion rate.	Weak	Moderate	100%
9	When should PN be discontinued? PN can be reduced and discontinued when the patient is receiving more than 60% of target energy requirement from enteral nutrition and/or oral diet.	Weak	Very low	100%
10	What is the recommended type of lipid emulsion used to compound PN? Fish oil containing injectable lipid emulsion should be used as part of the lipid component of PN.	Strong	High	100%
11a	Should multivitamin and trace elements be added in PN bags? Multivitamins are recommended in patients initiated on PN. In patients at risk of refeeding syndrome, additional intravenous thiamine supplementation for 3–5 days is recommended.	Strong	High	100%
11b	Trace elements are recommended in patients initiated on PN.	Weak	Low	100%
12a	Under what circumstances would additional vitamin or mineral supplementation be required? Additional supplementation of vitamin C is recommended for patients who are critically ill and patients who have had gastrectomy or colorectal resection.	Strong	High	100%
12b	Additional supplementation of zinc (Zn) is recommended for patients with high GIT losses. For every 1L of GIT losses via fistula or stoma, an additional 12–17 mg of Zn should be provided.	Strong	High	100%
13	Are there benefits in adding glutamine in PN bags? Additional supplementation of glutamine is not recommended in patients initiated on PN.	Weak	Low	100%
PN access routes and devices				
14	What types of venous access device should be used for PN? Peripherally inserted central catheter with a dedicated lumen is recommended for PN administration. However, an existing central venous access device (CVAD) in the internal jugular vein can be used for up to 14 days.	Strong	Moderate	100%
15	How should the patency of CVADs be maintained? CVADs should be flushed using normal saline after each use, or weekly if not in use, to maintain catheter patency.	Strong	Moderate	100%
16a	Under what circumstances should peripheral PN (PPN) be considered? PPN can be used as supplemental PN where oral or EN is suboptimal.	Weak	Low	100%
16b	The duration of PPN therapy should not exceed 14 days due to an increased risk of complications related to peripheral intravenous catheters.	Strong	Low	100%

Table 1. Summary of clinical questions and recommendation statements. (Cont'd)

No.	Clinical questions and recommendation statements	Strength of recommendation	Quality of evidence	Level of agreement
17	What osmolarity of PN admixture is safe for peripheral venous use? • Osmolarity of PPN therapy should be maintained at less than 900 mOsm/L to minimise the risk of catheter-related complications.	Strong	Low	93%
Monitoring and management of PN-related complications				
18a	How should patients at risk of refeeding syndrome be managed? • Patients who are at risk of refeeding syndrome are required to have their serum electrolytes monitored daily for the first few days, following which frequency of monitoring can be reduced when serum electrolytes stabilise.	Strong	Moderate	100%
18b	• Serum electrolyte abnormalities should be promptly recognised and corrected.	Strong	High	100%
19	How often should blood glucose be monitored? • Blood glucose levels should be measured every 6 hours at least for the initial 48 hours after initiation of PN therapy.	Weak	Low	100%
20	What is the target blood glucose range? • A target blood glucose ranging 7.8–10 mmol/L is recommended for patients receiving PN.	Strong	Moderate	100%
21	Should insulin be added to PN bags? • Subcutaneous insulin is preferred over the addition of insulin to PN admixtures for glycaemic control. At the discretion of the nutrition support team and guided by local institution practices, short-acting insulin may be added to PN admixture in patients whose clinical conditions and PN requirements are stable.	Weak	Low	100%
22	How often should liver function tests (LFTs) be monitored? • Baseline LFTs should be obtained prior to initiation of PN. LFTs should be monitored on a weekly basis, with a reduction in frequency of monitoring subsequently depending on clinical progress.	Weak	Moderate	100%
23	How should deranged LFTs be managed? • Non-PN-related causes of abnormal LFTs should first be identified and managed accordingly. Overfeeding of PN may also cause abnormal LFTs, hence adjustment of dextrose and/or lipid content of PN admixture may be necessary.	Weak	Moderate	100%
24	How should PN transition from continuous to cyclical infusion? • Cyclic PN can be started when patient is clinically stable and satisfactory glycaemic control is maintained during a fasted state without PN.	Weak	Moderate	100%
25	What is the target serum triglyceride level? • Serum triglyceride should be maintained below 4.6 mmol/L.	Weak	Moderate	100%
26	How should hypertriglyceridaemia be managed? • If serum triglyceride is more than 4.6 mmol/L, dextrose load in PN should be reduced followed by a reduction in injectable lipid emulsion if serum triglyceride level does not improve. PN should be discontinued if serum triglyceride is more than 11.4 mmol/L.	Weak	Moderate	100%
27	How should catheter-related thrombosis (CRT) be managed? • The use of thrombolytic agents and anticoagulation treatment is recommended for CRT, with removal of CVAD if complete resolution from these measures is not achieved.	Strong	Moderate	100%

Table 1. Summary of clinical questions and recommendation statements. (Cont'd)

No.	Clinical questions and recommendation statements	Strength of recommendation	Quality of evidence	Level of agreement
28a	How should catheter-related blood stream infection (CRBSI) be managed? • In the event that CRBSI is suspected, 2 sets of blood cultures should be obtained from both the CVAD and peripheral vein before initiation of antimicrobial therapy.	Strong	Moderate	100%
28b	• In complicated CRBSI, the CVAD should be removed for source control. In uncomplicated CRBSI or in patients with limited vascular access, discussion with an infectious disease specialist is recommended to explore possibility of CVAD salvage.	Strong	Low	100%
29	Should PN be withheld when patient undergoes surgery? • It is not necessary to withhold PN during surgery.	Weak	Low	87%
30	Is tapering of PN and dextrose drip necessary after termination of PN? • Tapering of PN or administration of intravenous dextrose solution after abrupt termination of PN may not be necessary unless the patient is on insulin therapy.	Weak	Low	80%

CLINICAL QUESTIONS AND RECOMMENDATIONS

Indications for parenteral nutrition (PN)

1. What are the indications for PN?

Recommendation 1

PN is indicated in patients who are unable to meet their nutritional needs orally and/or enterally as a result of suboptimal function of the gastrointestinal tract (GIT) or in whom the GIT is not accessible.

Strength of recommendation: Strong

Quality of evidence: High

Level of agreement: 100% (strong consensus)

Commentary: PN provides essential nutrients intravenously and bypasses the GIT. It should only be considered when it is not possible to meet individuals' nutritional needs orally and/or enterally due to suboptimal function of the GIT or when GIT is not accessible. The 5 broad categories of conditions that may require PN are impaired absorption and/or loss of nutrients, mechanical bowel obstruction, clinical need for bowel rest, bowel motility disorders and inability to achieve or maintain enteral access.⁵

Oral and/or EN should be optimised before initiating PN as they are physiologically more advantageous, cost-effective and associated with fewer complications. PN should not be started until all pragmatic approaches to improve tolerance to oral or EN have been attempted.

2. When should PN be initiated?

Recommendation 2a

For patients who are well-nourished on initial assessment, initiating PN can be considered after 5–7 days of not achieving 60% or more of estimated total energy requirement.

Strength of recommendation: Strong

Quality of evidence: Low

Level of agreement: 93% (strong consensus)

Recommendation 2b

For patients who are severely malnourished or at high risk of malnutrition, consider initiating PN earlier than 5 days of not achieving 60% or more of estimated total energy requirement.

Strength of recommendation: Strong

Quality of evidence: Low

Level of agreement: 93% (strong consensus)

Commentary: The optimal time to initiate PN remains debated and unclear. Although some studies^{6–8} found no significant difference in mortality when comparing early PN and late PN, the EPaNIC study⁹ observed that late PN initiation 7 days after admission was associated with lower incidence of infections, earlier recovery from organ failure and shorter hospital stay compared to early PN initiation before 7 days. On the other hand, findings of a recent

retrospective analysis where surgical patients were stratified based on their nutritional risk⁹ revealed that those with high risk of malnutrition who received early supplemental PN within 48 hours after emergency surgery had a better survival when compared to those who did not receive PN earlier.

Hence, taking all the above-mentioned into consideration, we recommend initiating PN after 5–7 days for well-nourished patients who have not been able to achieve 60% or more of estimated total energy requirement and earlier than 5 days for patients who are severely malnourished or at high risk of malnutrition.

3. What are the contraindications of PN?

Recommendation 3a

Contraindications to PN include patients with critical electrolytes abnormalities, specifically serum potassium (K) <2.5 mmol/L, serum sodium (Na) <125 mmol/L, serum phosphate (PO₄) <0.4 mmol/L or serum magnesium (Mg) <0.5 mmol/L.

Strength of recommendation: Weak

Quality of evidence: Very low

Level of agreement: 100% (strong consensus)

Commentary: Metabolic complications can occur during PN administration due to intracellular shifts of glucose, electrolytes and fluid. Refeeding syndrome is a potentially fatal condition that may occur when artificial nutrition is introduced after prolonged starvation or minimal nutrient intake. It is not recommended to start PN for patients who have critical electrolytes abnormalities until it has been adequately corrected.^{10,11} PN should only be initiated

after electrolytes are at an acceptable level after replacement.

Recommendation 3b

Contraindications to PN include patients who have suffered irreversible brain injury or terminal illness where there is a lack of therapeutic goal to prolong life in the inevitable death.

Strength of recommendation: Strong

Quality of evidence: Moderate

Level of agreement: 100% (strong consensus)

Commentary: PN is not encouraged for patients with irreversible brain injury or terminal illness due to its potential complications, cost and futility. Besides, PN therapy may lead to unnecessary prolongation of suffering. PN may, however, be considered in a subgroup of terminally ill cancer patients who have reasonable functional status (Eastern Cooperative Oncology Group <3, Karnofsky Performance Status >50) and with an expected survival of more than 3 months when oral and/or EN is not feasible due to intestinal obstruction or high output fistula.¹²

Recommendation 3c

Contraindications to PN include patients who have no suitable venous access for PN.

Strength of recommendation: Strong

Quality of evidence: Very low

Level of agreement: 100% (strong consensus)

Commentary: The preferred delivery of PN is through central venous access.^{13,14} Delivery of PN through

Table 2. Executive summary.

Subject	Recommendation
Indications of parenteral nutrition (PN)	Patients who are unable to meet their nutritional needs orally and/or enterally as a result of suboptimal function of the gastrointestinal tract (GIT) or in whom where the GIT is not accessible.
Contraindications of PN	- Patients with critical electrolytes abnormalities, such as severe hypokalaemia, hypophosphataemia, hypomagnesaemia or hyponatraemia. - Patients with irreversible brain injury or terminal illness where there is a lack of therapeutic goal to prolong life in the inevitable death. - Patients who have no suitable venous access for PN.
Monitoring of parameters	- Baseline biochemical assessment prior to initiation of PN. - Daily biochemical monitoring and adjusted according to the patient's clinical progress, nutritional status and stage of PN therapy.
Nutritional assessment	Start at 15–20 kcal/kg/day on day 1 and increase it progressively to target providing 25–30 kcal/kg/day or using validated predictive equations, taking into account physical activity and stress factor.

central venous access allows solutions of higher osmolality and volume to be infused as compared to delivery of PN through peripheral venous access. However, if all possible routes for central venous access have been exhausted, PN delivery through the peripheral route may be considered.

Assessment of PN patients

- Who should assess and manage patients prescribed with PN?

Recommendation 4

Patients on PN support in hospital should be managed by a nutrition support service consisting of a team of trained physician, nurse, dietitian and pharmacist.

Strength of recommendation: Strong

Quality of evidence: Low

Level of agreement: 100% (strong consensus)

Commentary: PN is a complex and specialised form of nutrition support. Consulting a multidisciplinary team of HCPs dedicated to PN support has been demonstrated to enhance the quality of care, promote appropriate use of PN, improve clinical outcomes and reduce the incidence of adverse PN-related complications.^{15,16}

- How often should biochemical parameters be assessed for patients on PN?

Recommendation 5a

All patients should have a baseline biochemical assessment prior to initiation of PN.

Strength of recommendation: Strong

Quality of evidence: Very low

Level of agreement: 100% (strong consensus)

Recommendation 5b

After establishing a patient on PN, the frequency of biochemical monitoring should be adjusted according to the patient's clinical progress, nutritional status and stage of PN therapy.

Strength of recommendation: Strong

Quality of evidence: Very low

Level of agreement: 100% (strong consensus)

Commentary: Biochemical monitoring is essential for the detection of potential metabolic complications.¹⁰ Before initiating PN, it is essential to conduct baseline tests assessing renal function (including sodium, potassium, creatinine, urea, bicarbonate and chloride levels), bone metabolism (e.g. calcium, phosphate, magnesium), liver function (including alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, gamma-glutamyl transferase, bilirubin) and lipid profile.

The time interval for biochemical surveillance after PN initiation depends on the patient's clinical progress and nutritional status, as well as the stage of PN therapy that he/she is at.

Biochemical parameters should be reviewed daily for the first few days, and subsequent monitoring can be less frequent depending on patient's clinical status and stability of the biochemical parameters measured.

- What are the nutritional requirements for patients on PN?

Recommendation 6a

Energy expenditure for patients requiring PN should ideally be measured using indirect calorimetry. However, if indirect calorimetry is not available, providing 25–30 kcal/kg/day or using validated predictive equations, taking into account physical activity and stress factor, are acceptable to calculate energy requirement.

Strength of recommendation: Strong

Quality of evidence: Moderate

Level of agreement: 100% (strong consensus)

Commentary: Inappropriate delivery of PN can have detrimental effects on patients' clinical outcomes. Excessive PN has been associated with complications, such as hyperglycaemia, liver dysfunction and weight gain. On the other hand, inadequate PN can lead to macro- and micro-nutrient deficiencies and weight loss. Hence, accurate measurement or calculation of energy requirement is important so that adequate calories can be provided.

Indirect calorimetry is the gold standard for determining resting energy expenditure (REE). In the absence of indirect calorimetry, predictive equations such as Harris-Benedict, Schofield and Mifflin-St Jeor can be used to estimate REE. A practical alternative using standard caloric intake, ranging 25–30

kcal/kg/day with adjustments based on individual clinical conditions, has also been recommended by ESPEN as a reasonable estimate of energy requirement.¹⁷

Recommendation 6b

Protein requirements for patients requiring PN should be tailored to individual needs, ranging from 1 to 2 g/kg/day. Higher protein doses may be required for the critically ill, cancer and elderly patients.

Strength of recommendation: Strong

Quality of evidence: Low

Level of agreement: 87% (consensus)

Commentary: Protein requirements for patients requiring PN vary depending on the clinical condition, nutritional status and metabolic stress. The protein requirement for adults in the acute care setting typically ranges from 1.0 to 2.0 g/kg/day, with higher amounts for patients in severe catabolic states.

In a randomised control trial (RCT)¹⁸ that evaluated the effect of protein intake through PN on muscle strength and clinical outcomes in critically ill patients, those who received higher protein intake (1.2 g/kg/day) showed improved handgrip strength, greater muscle thickness and less fatigue during the first week of intensive care unit (ICU) as compared to those who received less protein intake (0.8 g/kg/day). Similarly, in a large retrospective observational study¹⁹ that assessed the association between protein intake and mortality in non-critically ill older patients receiving PN, higher protein intake (≥ 0.8 g/kg/day) was found to be significantly associated with better survival outcomes. These findings highlight the importance of ensuring adequate protein provision in this vulnerable population to improve clinical outcomes.

In summary, protein requirements should be individualised, with higher protein goals for patients with higher catabolic states such as critical illness, malnutrition or cancer.

7. Which nutritional assessment tool should be used for patients requiring PN?

Recommendation 7

There is currently no nutritional assessment tool developed specifically for patients requiring PN. Validated assessment tools, such as Subjective Global Assessment (SGA), are recommended for

the diagnosis and determination of the severity of malnutrition.

Strength of recommendation: Strong

Quality of evidence: Very low

Level of agreement: 100% (strong consensus)

Commentary: Commonly used nutritional assessment tools, such as SGA, Patient-Generated SGA and Mini Nutritional Assessment, have been validated in both hospital and community settings.^{20,21} However, no specific nutritional assessment tool has been developed or validated among patients requiring PN thus far. Based on current literature, SGA can be used until other validated nutritional assessment tools become available. In addition, the nutrition support team should perform a comprehensive assessment of the patient's baseline anthropometry, biochemistry, clinical signs and symptoms and diet history as part of the nutrition care process for all patients requiring PN.

Titration and formulation of PN

8. How fast should PN be introduced and progress?

Recommendation 8

It is recommended to start at 15–20 kcal/kg/day on day 1 and increasing it progressively to target for non-critically ill patients. Patient's nutritional status and risk of refeeding should be considered when initiating and advancing PN infusion rate.

Strength of recommendation: Weak

Quality of evidence: Moderate

Level of agreement: 100% (strong consensus)

Commentary: Multiple studies^{6,22–26} were included in the analysis of this question. There were vast differences in methodological quality and intervention design among these studies. In the critical care setting, most of these studies^{6,22–24} did not find any significant difference in mortality, length of stay in hospital and in ICU, number of mechanically ventilated days, incidence of organ failure and infection rate when comparing patients in the high-calorie group and patients in the low-calorie group. On the other hand, in the non-ICU setting, little insight could be gained due to the heterogeneity of studies.^{25,26} Therefore, based on our consensus, calorie intake may start with 15–20 kcal/kg/day on day 1 and increase progressively to target by day 3 or day 4 for non-critically ill patients, while

Table 3. Checklist table.

Subject	Recommendation
Parenteral nutrition (PN) initiation	• Indication of initiating PN • Baseline laboratory values • Nutritional assessment
Monitoring	• Baseline tests including renal function tests (sodium, potassium, bicarbonate, urea, creatinine, chloride), bone metabolism (calcium, phosphate), liver function tests (alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, gamma-glutamyl transferase, bilirubin) and lipid profile • Daily biochemical monitoring and adjusted according to the patient's clinical progress, nutritional status and stage of PN therapy • Blood glucose levels every 6 hours for the initial 48 hours of initiating PN therapy • Monitoring of triglyceride levels
Discontinuing	• Achieving 60% of target energy requirement from enteral nutrition and/or oral diet

critically ill patients may necessitate a more cautious approach to calorie progression.

9. When should PN be discontinued?

Recommendation 9

PN can be reduced and discontinued when the patient is receiving more than 60% of target energy requirement from enteral nutrition and/or oral diet.

Strength of recommendation: Weak

Quality of evidence: Very low

Level of agreement: 100% (strong consensus)

Commentary: There is no available data thus far to determine the cut-off point when PN can be discontinued. Clinical judgement is still required, especially for malnourished patients and patients with a complicated hospital course. These patients may require a longer period of PN support and should demonstrate a higher enteral and/or oral intake before PN is discontinued.

The ASPEN and Society of Critical Care Medicine guideline²⁷ suggested that when tolerance to EN is evident, PN should be weaned off when more than 60% of the patient's needs are met orally or enterally.

10. What is the recommended type of lipid emulsion used to compound PN?

Recommendation 10

Fish oil (FO) containing injectable lipid emulsion (ILE) should be used as part of the lipid component of PN.

Strength of recommendation: Strong

Quality of evidence: High

Level of agreement: 100% (strong consensus)

Commentary: ILE should be included in PN formulation to provide a dense source of non-protein energy as well as a source of essential and conditionally essential fatty acids to prevent essential fatty acid deficiency.

Multiple studies²⁸⁻³⁰ were evaluated to determine the most favourable type of ILE to be used in PN therapy. Among the benefits of FO demonstrated in these studies were improvements in biochemical parameters indicating preservation of liver functions,^{28,29} as well as improvement in clinical outcomes such as shorter length of hospital stay²⁹ and reduced rate of nosocomial infections.³⁰

Most of the studies, which were of moderate to high quality of evidence,^{31,32} demonstrated that the use of FO-ILE was associated with reduced mortality, shorter length of hospital stay, fewer mechanical ventilated days and lower infection rate compared to non-FO-ILE. However, there were conflicting data suggesting that there was no mortality advantage with FO-ILE.³³ Taking into consideration the strengths and limitations of the studies included, the authors recommended using FO-ILE as part of the lipid component of PN.

11. Should multivitamin and trace elements be added in PN bags?

Recommendation 11a

Multivitamins are recommended in patients initiated on PN. In patients at risk of refeeding syndrome, additional intravenous thiamine supplementation for 3–5 days is recommended.

Strength of recommendation: Strong

Quality of evidence: High

Level of agreement: 100% (strong consensus)

Commentary: Vitamins are essential micronutrients required for normal cell function, growth and development. The addition of multivitamins to PN formulation for postoperative patients has been found to reduce traumatic stress and improve the metabolic transition from catabolism to anabolism.³⁴ Due to a nationwide shortage of multivitamins in the US in 1997, multiple cases of adverse clinical outcomes related to vitamin deficiency were also reported.^{35,36} Therefore, daily supplementation of multivitamins should be provided to all patients on PN support, especially to those who are malnourished with/without underlying acute illness.

Recommendation 11b

Trace elements are recommended in patients initiated on PN.

Strength of recommendation: Weak

Quality of evidence: Low

Level of agreement: 100% (strong consensus)

Commentary: Most of the available studies³⁴⁻³⁸ suggested that all adult patients on PN support should receive daily supplementation of trace elements. While all adult patients on PN are recommended to receive daily supplementation of trace elements, this should be guided by clinical judgement, particularly in the first month of therapy for patients without pre-existing deficits or critical illness.

12. Under what circumstances would additional vitamin or mineral supplementation be required?

Recommendation 12a

Additional supplementation of vitamin C is recommended for patients who are critically ill and patients who have had gastrectomy or colorectal resection.

Strength of recommendation: Strong

Quality of evidence: High

Level of agreement: 100% (strong consensus)

Commentary: Vitamin C is an antioxidant that protects the body cells from harmful free radicals. Two RCTs^{39,40} had reported that high-dose supplementation of vitamin C was associated with decreased postoperative oxidative stress and improved wound healing among patients who had undergone gastric or colorectal resection. Therefore, special consideration for additional supplementation of intravenous vitamin C of up to 500 mg/day, on top of a standard

dose of multivitamins, should be given to critically ill patients and those who have undergone gastric or colorectal resection.

Recommendation 12b

Additional supplementation of Zinc (Zn) is recommended for patients with high GIT losses. For every 1L of GIT losses via fistula or stoma, an additional 12–17 mg of Zn should be provided.

Strength of recommendation: Strong

Quality of evidence: High

Level of agreement: 100% (strong consensus)

Commentary: In a study of patients with gastrointestinal disease,⁴¹ a Zn replacement equation was derived using a regression analysis. Based on the equation, Zn replacement can be accurately calculated using measured GIT losses. In studies with burns patients,⁴²⁻⁴⁴ it was observed that these patients experienced significant exudative Zn losses, hence higher dosage of Zn should be added to PN.

13. Are there benefits in adding glutamine in PN bags?

Recommendation 13

Additional supplementation of glutamine is not recommended in patients initiated on PN.

Strength of recommendation: Weak

Quality of evidence: Low

Level of agreement: 100% (strong consensus)

Commentary: Several studies had reported that PN with glutamine supplementation was associated with a reduction in infection rates, length of hospital stay and days on mechanical ventilation in critically ill and post-surgical patients.⁴⁵⁻⁴⁸ Subsequent high-quality, large sample multicentre RCT study⁴⁹ showed that glutamine supplementation was associated with increased mortality for critically ill patients with multi-organ failure. Other studies and reviews with moderate to high methodological quality^{47,48} also did not show mortality benefits. Thus, in view of conflicting data and high heterogeneity of studies as well as a lack of recommendations in the international guidelines, the authors do not recommend additional glutamine supplementation in PN.

PN access routes and devices

14. What types of venous access device should be used for PN?

Recommendation 14

Peripherally inserted central catheter (PICC) with a dedicated lumen is recommended for PN administration. However, an existing central venous access device (CVAD) in the internal jugular vein can be used for up to 14 days.

Strength of recommendation: Strong

Quality of evidence: Moderate

Level of agreement: 100% (strong consensus)

Commentary: The choice of venous access for the administration of PN is of paramount importance.⁵⁰ PN should be delivered through a CVAD. PICC is the preferred choice of vascular access for PN therapy as it is cost-effective and is associated with fewer catheter-related complications such as infection, obstruction, dislocation and venous thrombosis.^{50,51}

Femoral catheters, on the other hand, are not recommended for the administration of PN due to their association with increased risk for contamination, infection and venous thrombosis. Hence, PICC is a relatively safe device for the administration of long-term PN as it preserves the integrity of the venous system.⁵²

15. How should the patency of CVADs be maintained?

Recommendation 15

CVADs should be flushed using normal saline after each use, or weekly if not in use, to maintain catheter patency.

Strength of recommendation: Strong

Quality of evidence: Moderate

Level of agreement: 100% (strong consensus)

Commentary: Most CVADs can be safely flushed and locked with normal saline solution when not in use. Although the use of heparin flush to maintain CVAD patency has been recommended in some nursing guidelines, the evidence to support this practice was based on low-quality studies.⁵³ Several systematic reviews^{52,54} have shown that heparin flushes have no significant benefit over normal saline flushes in maintaining catheter patency. Therefore, considering all the above-mentioned reasons, the flushing of CVADs with normal saline solution is recommended.

Current recommendations pertaining to how frequent CVADs should be flushed are conflicting and based on weak evidence.^{55,56} The most appropriate flushing frequency is after each use or weekly if not in use.

16. Under what circumstances should peripheral PN (PPN) be considered?

Recommendation 16a

PPN can be used as supplemental PN where oral or EN is suboptimal.

Strength of recommendation: Weak

Quality of evidence: Low

Level of agreement: 100% (strong consensus)

Recommendation 16b

The duration of PPN therapy should not exceed 14 days due to an increased risk of complications related to peripheral intravenous catheters.

Strength of recommendation: Strong

Quality of evidence: Low

Level of agreement: 100% (strong consensus)

Commentary: In view of the high volume and low nutritional content of PPN, PPN alone is unlikely to be adequate to meet individual's nutritional requirement. Therefore, PPN can be used as a short-term therapy to bridge the nutritional gap during transition periods until CVAD is inserted or as a supplement to oral and/or EN until GIT regains full function.

Peripheral intravenous catheters typically have a short dwell time as the risk of complications increases for every day it is left in place.^{57,58} Thus, the authors do not recommend the use of PPN for more than 14 days.

17. What osmolarity of PN admixture is safe for peripheral venous use?

Recommendation 17

Osmolarity of PPN therapy should be maintained at less than 900 mOsm/L to minimise the risk of catheter-related complications.

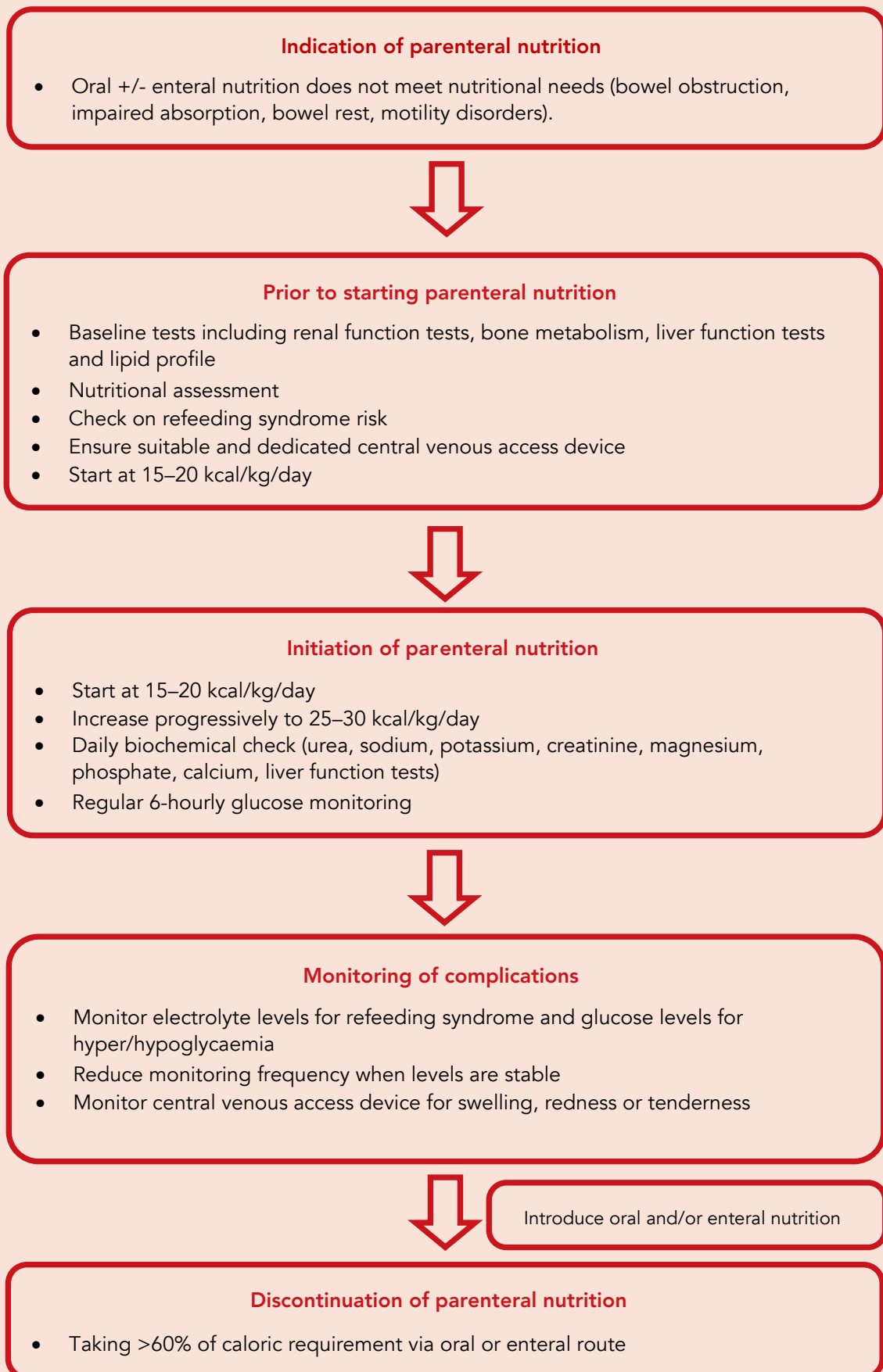
Strength of recommendation: Strong

Quality of evidence: Low

Level of agreement: 93% (strong consensus)

Commentary: PPN is usually reserved for short-term use because the infusion of hypertonic solution into peripheral veins may cause phlebitis and thrombosis. Hence, the osmolarity of the solution should be kept low and this can be achieved by lowering nutrient content and increasing fluid volume of the PPN solution. The osmolarity of less than 900 mOsm/L in PPN has been shown to be well tolerated.^{59,60}

Fig. 1. Flowchart on decision tree on parenteral nutrition in adult patients in the acute hospital setting.



Monitoring and management of PN-related complications

18. How should patients at risk of refeeding syndrome be managed?

Recommendation 18a

Patients who are at risk of refeeding syndrome are required to have their serum electrolytes monitored daily for the first few days, following which frequency of monitoring can be reduced when serum electrolytes stabilise.

Strength of recommendation: Strong

Quality of evidence: Moderate

Level of agreement: 100% (strong consensus)

Recommendation 18b

Serum electrolyte abnormalities should be promptly recognised and corrected.

Strength of recommendation: Strong

Quality of evidence: High

Level of agreement: 100% (strong consensus)

Commentary: Refeeding syndrome is associated with severe and life-threatening complications. However, it is preventable through close monitoring, early detection and timely replacement of serum electrolytes and vitamins. Therefore, serum electrolytes should be monitored daily during the first few days of PN therapy and corrected promptly as refeeding syndrome tends to occur within the first 72 hours after initiation of nutrition therapy.^{61,62} The frequency of monitoring can be reduced subsequently depending on the clinical status, trend of serum electrolyte levels and fluid balance of the patient. Preventive measures through initial controlled hypocaloric feeding have also been found to be associated with reduced risk of refeeding syndrome and improved overall survival.^{24,63}

19. How often should blood glucose be monitored?

Recommendation 19

Blood glucose levels should be measured every 6 hours at least for the initial 48 hours after initiation of PN therapy.

Strength of recommendation: Weak

Quality of evidence: Low

Level of agreement: 100% (strong consensus)

Commentary: Hyperglycaemia and hypoglycaemia are common complications in hospitalised patients receiving PN and are independently associated with adverse clinical outcomes.⁶⁴ Hyperglycaemia is reported to occur in more than half of the patients receiving PN regardless of pre-existing diabetes mellitus.⁶⁴ The increase in blood glucose level results from a combination of factors such as increased stress hormones and insulin resistance due to underlying acute illness, surgery or trauma, as well as delivery of glucose and gluconeogenic substrates through PN.⁶⁶ Hypoglycaemia, on the other hand, tends to result from tight glycaemic control with insulin therapy, abrupt discontinuation of PN, tapering doses of corticosteroids or vasopressors, and improved glycaemic control upon recovery from acute illness or organ failure.⁶⁷

However, guidelines from various international societies^{27,68,69} recommended that blood glucose levels should be monitored every 6 hours for the first 48 hours after PN initiation. Glucose monitoring may be discontinued in non-diabetic patients who are normoglycaemic without insulin therapy after 48 hours of achieving target nutrition infusion.

20. What is the target blood glucose range?

Recommendation 20

A target blood glucose ranging 7.8–10 mmol/L is recommended for patients receiving PN.

Strength of recommendation: Strong

Quality of evidence: Moderate

Level of agreement: 100% (strong consensus)

Commentary: The NICE-SUGAR study⁷⁰ revealed that ICU patients with tight glycaemic control (4.5–6.0 mmol/L) had a higher mortality of 10.1% compared to those on conventional blood glucose control (<10 mmol/L). Subsequent meta-analyses and systemic reviews^{71–74} concurred that there was no evidence that tight glycaemic control with intensive insulin therapy reduced mortality but instead, it increased the risk of hypoglycaemia that was associated with worse outcomes.

Multiple international societies including ASPEN,⁷⁵ American Association of Clinical Endocrinologists,⁷⁶ American Diabetes Association⁷⁶ and Endocrine Society⁶⁷ recommended a target blood glucose ranging 7.8–10.0 mmol/L for adult patients admitted in the acute care setting.

21. Should insulin be added to PN bags?

Recommendation 21

Subcutaneous insulin is preferred over the addition of insulin to PN admixtures for glycaemic control. At the discretion of the nutrition support team and guided by local institution practices, short-acting insulin may be added to PN admixture in patients whose clinical conditions and PN requirements are stable.

Strength of recommendation: Weak

Quality of evidence: Low

Level of agreement: 100% (strong consensus)

Commentary: Insulin therapy is the choice of treatment to correct hyperglycaemia in both diabetic and non-diabetic patients receiving PN.⁷⁷ Insulin can be administered subcutaneously, intravenously or added to PN admixture. The addition of short-acting insulin into PN admixture has the advantage of delivering a steady rate of insulin, which has been reported to provide a smoother glycaemic control without increasing risk of hypoglycaemia.⁷⁸ On the other hand, subcutaneous administration of long-acting insulin is associated with reduced glycaemic variability and facilitates the transition to basal-bolus regimens when PN is reduced or discontinued.⁷⁹

There are concerns pertaining to insulin availability after it is added into PN admixtures with a reported range of 10–95%.⁸⁰ Hence, the addition of insulin to PN admixture is not recommended in patients whose medical conditions and PN requirements are unstable. For these patients, the use of subcutaneous insulin for glycaemic control while receiving PN is recommended.

22. How often should liver function tests (LFTs) be monitored?

Recommendation 22

Baseline LFTs should be obtained prior to initiation of PN. LFTs should be monitored on a weekly basis, with a reduction in frequency of monitoring subsequently depending on clinical progress.

Strength of recommendation: Weak

Quality of evidence: Moderate

Level of agreement: 100% (strong consensus)

Commentary: Derangement of LFTs is common among patients receiving PN. The aetiology is usually multi-factorial and frequently caused by non-PN-related factors, such as pre-existing liver disease,

sepsis, underlying acute illness and drugs. A study reported that 34% of patients had underlying abnormal LFTs prior to starting PN therapy.⁸¹ Hence, it is pertinent to obtain baseline LFTs before PN is initiated and it should be monitored on a weekly basis. Frequency of LFTs monitoring can subsequently be reduced if it is normal.

23. How should deranged LFTs be managed?

Recommendation 23

Non-PN-related causes of abnormal LFTs should first be identified and managed accordingly. Overfeeding of PN may also cause abnormal LFTs, hence adjustment of dextrose and/or lipid content of PN admixture may be necessary.

Strength of recommendation: Weak

Quality of evidence: Moderate

Level of agreement: 100% (strong consensus)

Commentary: PN-related deranged LFTs typically occur after 2 to 4 weeks of PN therapy.^{82,83} The initial management of abnormal LFTs should always include the identification and management of possible non-PN-related causes, such as biliary obstruction, hepatitis and sepsis.⁸⁴ The use of hepatotoxic drugs, especially antibiotics, should be minimised or avoided. Besides, overfeeding patients with PN therapy can also lead to liver dysfunction. Therefore, adjustments to dextrose and lipid content in PN admixture are necessary if liver dysfunction is related to overfeeding.

24. How should PN transition from continuous to cyclical infusion?

Recommendation 24

Cyclic PN can be started when patient is clinically stable and satisfactory glycaemic control is maintained during a fasted state without PN.

Strength of recommendation: Weak

Quality of evidence: Moderate

Level of agreement: 100% (strong consensus)

Commentary: PN is commonly administered through continuous infusion over 24 hours. The duration of PN infusion can gradually be reduced hourly over a period of days or weeks once the patient has achieved target nutritional goals and has remained clinically and biochemically stable.

Cyclic PN has been associated with a lower incidence of PN-related liver disease as it mimics the

physiological function of nutrient metabolism of oral feeding.^{85,86} Additionally, cyclic PN is advantageous for patients who require prolonged PN support as it also allows daytime ambulation and activities when they are not receiving PN.

25. What is the target serum triglyceride level?

Recommendation 25

Serum triglyceride should be maintained below 4.6 mmol/L.

Strength of recommendation: Weak

Quality of evidence: Moderate

Level of agreement: 100% (strong consensus)

Commentary: Hypertriglyceridaemia is a complication associated with the use of PN, with reported incidence ranging from 6% to 38%.^{87,88} As the risk of adverse effects increases when serum level exceeds 4.6 mmol/L, it is recommended that serum triglyceride should be maintained ≤ 4.6 mmol/L during PN therapy.⁸⁹

26. How should hypertriglyceridaemia be managed?

Recommendation 26

If serum triglyceride is more than 4.6 mmol/L, dextrose load in PN should be reduced followed by a reduction in ILE if serum triglyceride level does not improve. PN should be discontinued if serum triglyceride is more than 11.4 mmol/L.

Strength of recommendation: Weak

Quality of evidence: Moderate

Level of agreement: 100% (strong consensus)

Commentary: Dextrose overload is usually the primary cause of hypertriglyceridaemia in patients receiving PN. Therefore, when hypertriglyceridaemia develops, the amount of dextrose in PN should be reduced. Besides PN therapy, other non-PN-related causes should be considered when managing hypertriglyceridaemia. Clinical conditions that predispose patients to hypertriglyceridaemia are sepsis, diabetes, liver failure, renal failure, multiorgan failure, obesity, alcoholism and pancreatitis.⁹⁰⁻⁹² In cases of severe hypertriglyceridaemia where serum triglyceride level exceeds 11.3 mmol/L, PN should be withheld until level normalises.^{90,91}

27. How should catheter-related thrombosis (CRT) be managed?

Recommendation 27

The use of thrombolytic agents and anticoagulation treatment is recommended for CRT, with removal of CVAD if complete resolution from these measures is not achieved.

Strength of recommendation: Strong

Quality of evidence: Moderate

Level of agreement: 100% (strong consensus)

Commentary: CRT is a relatively common complication of CVAD use in PN therapy. Although the removal of blocked CVADs is common practice, some causes of catheter occlusion may be rectified through simple measures. Occluded CVAD caused by build-up of lipid emulsion residue may be cleared by instilling a solution of 70% ethanol into the catheter.⁹³ For occlusion caused by an intraluminal clot or fibrin sheath, thrombolytic agents such as urokinase or alteplase may be used to restore lumen patency.^{94,95} In symptomatic CRT, systemic anticoagulation for at least 3 months is recommended if the existing CVAD remains in situ. The treatment of CRT should include thrombolysis for acute symptomatic cases and anticoagulation therapy for subacute and chronic symptomatic cases. CVAD should be removed if all measures to achieve complete patency fails.

28. How should catheter-related blood (CRBSI) stream infection be managed?

Recommendation 28a

In the event that CRBSI is suspected, 2 sets of blood cultures should be obtained from both the CVAD and peripheral vein before initiation of antimicrobial therapy.

Strength of recommendation: Strong

Quality of evidence: Moderate

Level of agreement: 100% (strong consensus)

Recommendation 28b

In complicated CRBSI, the CVAD should be removed for source control. In uncomplicated CRBSI or in patients with limited vascular access, discussion with an infectious disease specialist is recommended to explore possibility of CVAD salvage.

Strength of recommendation: Strong
 Quality of evidence: Low
 Level of agreement: 100% (strong consensus)

Commentary: Paired blood cultures should be drawn from both the CVAD and a peripheral vein for suspected CRBSI before the initiation of antimicrobial therapy. The initial choice of antimicrobial therapy depends on the severity of the patient's clinical presentation, risk factors for infection and types of potential pathogens suspected.⁹⁶

Complicated CRBSI refers to those that are associated with severe suppurative thrombophlebitis, endocarditis and blood infection that continues despite more than 72 hours of appropriate antimicrobial therapy, or infection due to *Staphylococcus aureus*, *Pseudomonas aeruginosa*, fungi and mycobacteria.⁹⁶ Under such circumstances, CVAD should be removed to prevent undesirable complications such as septic shock and death.⁹⁶⁻⁹⁸

29. Should PN be withheld when patient undergoes surgery?

Recommendation 29

It is not necessary to withhold PN during surgery.

Strength of recommendation: Weak
 Quality of evidence: Low
 Level of agreement: 87% (consensus)

Commentary: Concerns regarding the safety of continuous administration of PN during operative procedures when patients are under metabolic stress of surgery have been raised. Excessive use of fluids intraoperatively can put patients at risk of fluid overload, acid-base imbalance, renal impairment and cardio-respiratory compromise. Currently, there are no studies that have examined the metabolic effects of intraoperative administration of PN and patient outcomes. In view of a lack of evidence to support withholding PN during surgery, the authors recommend that it is not necessary to practice it.

30. Is tapering of PN and dextrose drip necessary after termination of PN?

Recommendation 30

Tapering of PN or administration of intravenous dextrose solution after abrupt termination of PN may not be necessary unless the patient is on insulin therapy.

Strength of recommendation: Weak
 Quality of evidence: Low
 Level of agreement: 80% (consensus)

Commentary: Gradual tapering of PN before cessation is a common practice to prevent rebound hypoglycaemia. However, it has been shown that the body adapts quickly to decreased glucose levels and subsequent need for insulin.^{17,99,100}

Although ESPEN recommended that tapering of PN is not necessary,¹⁷ tapering of PN may be a safety precaution for patients who are susceptible to hypoglycaemia or on insulin therapy. PN infusion rate can be reduced by 50% for 1–2 hours before discontinuation with concurrent close monitoring of blood glucose levels.

CONCLUSION

Despite its life-saving potential as an artificial nutrition support for patients whom nutritional adequacy cannot be met orally and/or enterally, PN carries inherent risks such as infection, metabolic disturbances and catheter-related complications. This clinical practice guideline proposed 30 recommendations for PN support in adult patients within the acute care setting, which cover various aspects of PN, including indications, patient assessment, titration and formulation of PN bags, access routes and devices, and monitoring and management of complications. There are limitations in the current evidence due to the lack of high-quality trials assessing the outcomes of PN therapy in this specific population. While this guideline serves as a guide for HCPs, clinical judgement remains paramount. HCPs should tailor their approach based on individual patient needs, considering factors such as underlying conditions, severity of illness and nutritional status. Regular reassessment and interdisciplinary collaboration are crucial for optimising patient outcomes. Clinical indicators, including refeeding syndrome, hyperglycaemia, hypoglycaemia, catheter-related central line infection and CRT, should be monitored to maintain quality care and measurable outcomes in patients on PN therapy.

Supplementary materials

Fig. S1. Search terms and PRISMA flowchart used for each clinical question (CQ).

Table S1. Grading of Recommendations Assessment, Development and Evaluation.

Table S2. Detailed commentaries and references.

Ethics statement

Not applicable.

Declaration

The authors declare they have no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript. This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors. There was no conflict of interest among the members of the working group.

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Fluoride benefits and risks: Lessons from 70 years of water fluoridation in Singapore

Ruixiang Yee¹ MSc, Huei Jinn Tong² MDentSci, Chai Kiat Chng^{1,3} MDS

ABSTRACT

Fluoride is well-proven to prevent caries. In controlled amounts, its benefits outweigh its risks. A recent systematic review and meta-analysis investigating fluoride exposure and children's intelligence quotient (IQ) scores found limited data and uncertainty in the dose-response association between fluoride exposure and children's IQ at water concentrations <1.5 ppm. Notably, 1.5 ppm is the World Health Organization's threshold for water fluoridation, which is 3 times higher than Singapore's current level of 0.5 ppm. The study's methodology, interpretations and limitations have been questioned. It reignited the debate surrounding fluoride use, particularly in community water fluoridation.

The main adverse effects of excessive fluoride exposure are dental and skeletal fluorosis. Skeletal fluorosis is associated with chronic exposures typically from high fluoride levels in drinking water, often in communities dependent on groundwater. This does not apply to Singapore where its sole water agency regulates and fluoridates the water supply.

Fluoride use in children must be supervised by parents to maximise benefits and minimise risks. This commentary revisits the history of fluoride uses in Singapore, and presents a balanced view and risk-benefit analysis of fluoride use. Physicians and nurses are often the first healthcare professionals that parents consult regarding concerns on their child's health and intelligence. Therefore, interprofessional education can help empower them to educate, identify, and refer persons in need early. Future studies could investigate the benefits and risks of water fluoridation in contemporary Singapore, a developed country with one of the world's highest average IQ and widespread access to fluoride toothpastes.

Keywords: dental caries, fluoride, IQ, oral health, paediatrics, public health, water fluoridation

INTRODUCTION

On 6 January 2025, Taylor et al. published a systematic review and meta-analysis investigating fluoride exposure and children's intelligence quotient (IQ) in the *Journal of the American Medical Association*

Pediatrics (JAMA Pediatrics).¹ They concluded that there were "inverse associations and a dose-response association between fluoride measurements in urine and drinking water and children's IQ" and "limited data and uncertainty in the dose-response association between fluoride exposure and children's IQ when fluoride exposure was estimated by drinking water alone at concentrations less than 1.5 mg/L [ppm]."¹ Within hours, many internet and news sources reported on the controversial article published by the researchers from the Division of Translational Toxicology, National Institute of Environmental Health Sciences, US National Institutes of Health; and ICF International. This reignited the debate on the use of fluoride.

It is critical to evaluate the science behind the systematic review before determining if current practices should be adjusted. Further investigations are required as it may not be possible to determine if the current World Health Organization (WHO)'s threshold of 1.5 ppm is unsafe based on this study alone, given the high heterogeneity in data. Therefore, this commentary is not meant to refute or confirm the study's findings but to contextualise them in a real-world context, particularly that of Singapore where the level of fluoride is lower (0.5 ppm). Furthermore, this commentary examines the different aspects of fluoridation and topical fluoride use, including its effectiveness in preventing dental caries and its risks.

Critical appraisal of systematic review on fluoride exposure and children's IQ

Taylor et al. included a total of 64 cross-sectional studies and 10 prospective cohort studies (Table 1). The majority of the studies were carried out in China and India; none from the US, where the systematic review originates. The main critique is that most studies were carried out in areas where fluoride levels in the water are endemically high (>1.5 ppm). This is 3 times that of the current water fluoride levels in Singapore (0.5 ppm). There was a stark lack of studies from countries with long histories of community fluoridation,

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¹ Dental Service, KK Women's and Children's Hospital, Singapore

² Private Specialist Dental Practice, Singapore

³ Chief Dental Officer's Office, Director-General of Health's Office, Ministry of Health, Singapore

Correspondence: Dr Ruixiang Yee, Dental Service, KK Women's and Children's Hospital, 100 Bukit Timah Rd, Singapore 229899.

Email: yee.ruixiang@singhealth.com.sg

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possibly due to the dearth of published data from these countries. In Asia alone, a high percentage of people in Malaysia (75.5%), Hong Kong (100%), Brunei (95%) and Singapore (100%) receive optimally fluoridated water.²

Table 1. Characteristics of studies included in the systematic review and meta-analysis by Taylor et al. 2025.¹

Countries where the studies were performed (no. of studies)	China (n=45) India (n=12) Iran (n=4) Mexico (n=4) Canada (n=3) Pakistan (n=2) Denmark (n=1) New Zealand (n=1) Spain (n=1) Taiwan (n=1)
Risk of bias of the studies (no. of studies)	High risk of bias (n=52) Low risk of bias (n=22) • Low risk of bias across all 7 risk-of-bias domains (n=13) • Low risk of bias in 6 domains and probably high risk of bias in ≤1 domain (n=9)

The meta-analysis included studies with both higher and lower risk of bias, of which the majority (47 out of 59) were evaluated to be at higher risk of bias. Even for the sub-analysis that included studies with lower risk of bias, there was evidence of substantial heterogeneity in the combined data (high I^2 values). There was also insufficient justification for the selection or omission of studies, and for the calculated individual effect sizes presented in the main analysis. In an editorial published in the same issue,³ Levy highlighted that the studies with lower risk of bias actually showed negligible or negative effect, and the lack of discussion of important recent studies including those from nonendemic fluorosis areas. He also underscored that the meta-analysis had not included more recent primary studies.^{4,5}

In another editorial also published in the same issue, Lanphear et al. argued that the urinary fluoride level is a better biological measure and highlighted Taylor et al.'s findings that urinary fluoride concentrations <1.5 ppm were significantly associated with decreased IQ.⁶ However, the urinary sample collection approaches utilised in all included studies (i.e. spot urinary fluoride or a few 24-hour samples, often not adjusted for dilution) is not a reliably valid measure of long-term fluoride exposure in individuals. There may be variations between days or even within the same day, which can also be affected by the usage of topical fluorides.³

It is concerning that confounding factors were not well controlled. Caution should be exercised when evaluating cross-sectional studies on the associations

between fluoride and intelligence due to the presence of potential confounding factors, such as socioeconomic status, place of residence, maternal intelligence and exposure to other neurotoxic chemicals.⁷ In fact, the measurement of IQ itself with standard IQ tests is fraught with complexities and may not be generalisable across different sociocultural settings, especially in non-Western societies where non-academic skills may be valued more.⁸

These confounders reduce confidence in substantivity and therefore generalisability of the paper. Indeed, based on the data available and methodology, the paper concluded by acknowledging the “uncertainty in the dose-response association between fluoride exposure and children’s IQ when fluoride exposure was estimated by drinking water alone at concentrations less than 1.5 mg/L” (equivalent to the WHO’s current threshold). Furthermore, it is not known how much lower water fluoridation levels should be adjusted to be considered safe for community consumption. The current water fluoridation level in Singapore is 0.5 ppm,⁹ far below the threshold of 1.5 ppm reported in the study by Taylor et al.¹

Benefits of fluoride and community water fluoridation

Fluoride’s benefits are well documented. A 2021 Cochrane review reported high-certainty evidence that toothpastes containing 1000 to 1250 ppm fluoride are more effective than non-fluoride toothpaste in caries prevention, with a positive dose-response effect observed in children and adolescents with decayed, missing and filled surfaces.¹⁰ Consequently, professional dental bodies around the world recommend the use of toothpastes containing at least 1000 ppm fluoride in both children and adults.^{11–16} Other Cochrane reviews have also found a preventive effect of topical fluoride in other forms such as mouthrinses, gels or varnishes.¹⁷

In Singapore, water fluoridation introduced in 1956 effectively reduced dental caries. In a 10-year water fluoridation study, about 300 schoolchildren aged 7 to 9 years selected from 34 schools were examined almost every year between 1957 and 1968. That study reported a 30.8% reduction in primary tooth caries among the children in Singapore where water was fluoridated, while there was no corresponding decline in the control group of the children in Malacca where water was not fluoridated then. The reduction of caries prevalence in permanent teeth was 31.0% and 52.3% in 7- to 9-year-old Malay and Chinese children in Singapore, respectively.¹⁸

In 2018, water fluoridation (≥ 0.7 ppm) in England was associated with a 59% reduction in hospital admissions for dental extractions among young people

aged 0 to 19 years.¹⁹ There is concern that water fluoridation's benefits may be relatively muted with the widespread use of fluoride toothpastes, topical fluoride varnishes and dental sealants from the mid to late 1970s.²⁰ Published data from communities that removed water fluoridation, such as those in Calgary, Canada²¹ and Israel,²² showed an increase in caries, especially in vulnerable populations. Therefore, for vulnerable groups that carry the heaviest disease burden and lowest access to fluoride toothpastes and other forms of prevention, community water fluoridation may remain a passive vehicle to reduce oral health inequalities.²³

Singapore's schoolchildren now have relatively low levels of caries based on WHO standards; this is attributed to factors including Singapore's water fluoridation, School Dental Service (introduced in 1948), improvements in general living conditions, parental education levels and socio-economic conditions over the past decades. Notwithstanding, almost half of Singapore's preschoolers are still affected by early childhood caries. The most common chronic childhood disease may be difficult to overcome, partially due to the plateau effect of water fluoridation, where further increase beyond optimal water fluoride levels would yield diminishing returns in its population caries-prevention benefit.^{24,25} Notably, 16% of preschoolers bear 78% of the burden of disease and 16.5% suffered from rampant caries. These children comprise the smaller but significant percentage of children who often are vulnerable members of lower socioeconomic groups and the indigenous population.²⁴ Therefore, there is a high risk that cessation of water fluoridation in Singapore may further widen oral health inequalities, particularly regarding dental caries in young children from different socioeconomic strata.

Concerns around fluoride toxicity

A side effect of chronic excessive fluoride ingestion is dental fluorosis. Excessive fluoride exposure during enamel formation results in enamel hypomineralisation.²⁶ Depending on the levels of fluoride exposure, the defects can range from faint white speckles to severe brown mottling defects. Various epidemiological dental fluorosis indices have been used across studies, including the Dean's Index (Table 2).²⁷⁻³⁰ A 2024 Cochrane review on dental fluorosis concluded that most studies found mild fluorosis to be a possible side effect of topical fluoride use early in life. However, this conclusion was stated to be at low certainty, due to inconclusive evidence.²⁷

A literature search was conducted on PubMed and MEDLINE, supplemented with Google Scholar, to identify major studies or narratives on water fluoridation and its effects in the Singapore context.^{9,11,18,24,25,31-37} The natural water fluoride content in Singapore was found to be 0.2 ppm. Water fluoridation in Singapore raised it to 0.7 ppm in 1956.¹⁸ The classic 10-year study on water fluoridation by Wong et al. reported the prevalence of dental fluorosis in permanent teeth to be <5% in 7- to 9-year-old children from 1966 to 1968.¹⁸ In 1986, a survey of 1739 Singaporean children aged 9, 12 and 16 years found 42.6% with very mild to mild, 26.3% with moderate and 9.2% with severe dental fluorosis using the Dean's Index.³²

While the authors speculated that the increase in prevalence and severity of dental fluorosis in 1986 was greater than that reported by Wong et al. earlier, they suggested that different methods of clinical examination and indices used may have been a confounding factor. A 1989 survey by the Dental Division of the Ministry of Health, Singapore found that in a cohort of 11- to 13-year-old children where

Table 2. Dean's Index.²⁸⁻³⁰

Score	Criteria
Normal	The enamel represents the usual translucent semi-vitriform type of structure; surface is smooth, glassy, pale, creamy-white translucent.
Questionable	The enamel discloses slight aberrations from the translucency of normal enamel, ranging from a few white flecks or occasional white spots.
Very mild	Small opaque paper-white area scattered irregularly over the tooth covering less than 25% of tooth surface. Premolars/second molars not showing more than 1–2 mm of white opacity at the tip of summit of cusps are also frequently involved in this classification.
Mild	Opaque white area in the enamel of the tooth covering less than 50% of the tooth surface.
Moderate	All enamel tooth surfaces are affected and surfaces subject to attrition show marked wear. Brown stain may be present.
Severe	All enamel surfaces are affected, hypoplastic brown stains are widespread and teeth often present as corroded appearance. The major diagnostic sign of this classification is the discrete or confluent pitting.

83.3% had a history of fluoride toothpaste use before age 6, 61.9% had no/questionable fluorosis, 26.6% had very mild fluorosis and 10.5% had mild fluorosis.^{9,35} Such mild dental fluorosis usually only produces minimal aesthetic challenges with no additional detriment to oral health. The water fluoridation level was subsequently reduced to 0.6 ppm in 1992, and again to 0.5 ppm in 2008.⁹ A follow-up study in 2017 found that only 15.4% (41,651 out of 270,630) of Singaporean students had dental fluorosis (unpublished data from official source: School Dental Services, Health Promotion Board).¹¹

Another chronic side effect is skeletal fluorosis with an increased risk of bony fractures. According to the European Food Safety Authority (EFSA), skeletal fluorosis develops after many years of excessive fluoride intake of 10–20 mg/day.²⁶ Such chronic exposures are typically from residing in areas with high fluoride concentrations in drinking water, usually in communities dependent on ground water.²⁶ This situation does not apply to Singapore where the Public Utilities Board is the nation's sole water agency that fluoridates and regulates water supply.⁹ A typical Singapore resident's approximate daily fluoride intake is estimated to be just 1 mg/day, based on the average recommended water intake of 2 L (equivalent to at least 8 glasses of water—dependent on individual physical needs as well as climate changes³⁸) at 0.5 ppm of fluoride (Table 3). This amount is at least 10 times below the safety threshold of 10–20 mg/day as recommended by the EFSA.²⁶

Other than the aforementioned risks, there is very limited evidence of any other adverse events associated with chronic exposure to fluoride in water at regulated levels.³⁹ Renal or liver injuries are reported to be of concern only at water fluoride levels of 2 ppm or above.⁴⁰ This is irrelevant to the Singapore's context with much lower fluoride levels in water. An FDI World Dental Federation policy also states that there is no evidence of risks to children with renal diseases from water fluoridation and other fluoride sources within the recommended dosages and with precautions of use.⁴¹

Maximising benefit and minimising risks

Over-the-counter (OTC) analgesic/antipyretic paracetamol is efficacious within therapeutic dosages, but overdose can lead to liver toxicity.⁴² Likewise, no other topical agent is likely as cost-effective and well-proven to prevent caries as fluoride. The estimated net cost savings from the US community water fluoridation programme in 2013 were USD 6469 million in 2013, with savings of USD 20 related to caries prevented for every USD 1 spent on water fluoridation.⁴³

Nonetheless, inappropriate use and overdose of fluoride can lead to side effects and toxicity. To mitigate its risks and maximise its benefit, excessive ingestion must be minimised. Parents are responsible for dispensing and supervise its use, teach their children to spit out the toothpaste when they reach an appropriate age, and keep both prescription, and OTC fluoride products (e.g. toothpastes and mouthrinses) out of reach of children to prevent accidental consumption and associated adverse effects. Jointly, regulatory bodies should ensure appropriate labelling of fluoride toothpastes by manufacturers so that informed choices can be made.

The risk of dental fluorosis from over-ingestion affects the aesthetic zone (permanent incisors) predominantly in the first 3 years of life during its calcification/maturation stage, as crown calcification completes by 30 months. Beyond that, the aesthetic risk of dental fluorosis decreases and disappears after 6 years of age, especially after children have learnt to spit.¹² In view of this, a smear (approximately rice grain-sized amount) of toothpaste is recommended for children below 3 years old, and a pea-sized amount is recommended for those aged 3 years and above (Fig. 1).¹¹

For even greater prudence, the Society for Paediatric Dentistry Singapore (SPDS) considered the nation's water fluoridation programme in its recommendations for toothpaste use in children. The SPDS supports the use of toothpaste with at least 1000 ppm fluoride but advises that for children below 2 years of age with low caries risk, parents should discuss with the

Table 3. Estimated consumption of fluoride from public water intake per day in an individual consuming 2 L of water.

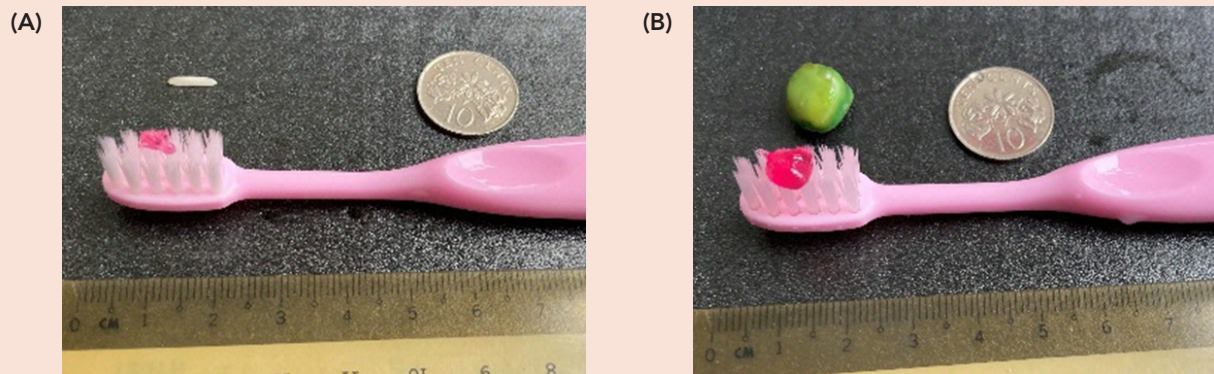
Step-by-step calculation for the total amount of fluoride in 2 L of water when the concentration is 0.5 ppm

Convert concentration from ppm to mg:

- 1 ppm = 1 mg of fluoride per L of water (1 mg/L).
- If the concentration is 0.5 ppm, this means there are 0.5 mg of fluoride per L of water.
- Therefore, in 2 L of water: Total amount of fluoride = 0.5mg/L × 2 L = 1 mg.

Conclusion: The total amount of fluoride in 2 L of water with a concentration of 0.5 ppm fluoride is 1 milligram (mg) of fluoride.

Fig. 1. (A) A smear of toothpaste and (B) a pea-sized amount of toothpaste, placed next to a rice grain and green pea respectively, together with a Singapore 10-cent coin and ruler.



child's dentist when choosing a toothpaste.¹¹ This targeted advice is notable, in contrast to the blanket recommendations in many other countries.¹²⁻¹⁶ This discussion must start at the child's first dental visit, which should occur before age 1 for caries risk assessment and anticipatory guidance, including the appropriate selection and use of toothpaste.¹³

Concluding thoughts: What does this mean for healthcare professionals?

Despite the potential association between high fluoride levels in water and IQ suggested by Taylor et al., the concentrations at which this is a concern are well above levels recommended for water fluoridation (0.7–1.5 ppm). This should not be a concern for Singapore with a water fluoridation level of 0.5 ppm. Singapore ranked third in average IQ in 2019,⁴⁴ and its 70-year history of 100% water fluoridation may provide an invaluable natural experiment for assessing both the efficacy and safety of water fluoridation, especially with a strong central water management system. Nonetheless, future studies could investigate the benefits and risks of water fluoridation in contemporary Singapore, amid the backdrop of improved access to fluoride toothpastes and other preventive measures. These studies should include analysis of vulnerable subpopulations to better understand the impact of community water fluoridation on oral health disparities.

In terms of regulations, it is important that policy-makers re-examine local data periodically, especially in the wake of new controversies, and avoid making abrupt policy shifts without robust, contextual evidence.

Physicians and medical nurses are trusted healthcare professionals whom parents and patients frequently consult and should therefore be well-versed in the science and evidence supporting the use of fluoride. Interprofessional education may empower medical

colleagues who are well-positioned to help identify and refer those in need early, as well as emphasise the importance of the first dental check by age 1 and a healthy mouth as integral components of overall health.

Ethics statement

Not applicable.

Declaration

The authors declare no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript.

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It's virtually a normal delivery! Revolutionising obstetric teaching with emerging technologies

Haojie Cheng¹ PhD, Chang Liu¹ MEng, Eng Tat Khoo¹ PhD, Abhiram Kanneganti² MBBS, Mahesh Choolani^{2,3} PhD, Arundhati Tushar Gosavi^{2,3} MBBS

ABSTRACT

Simulation-based training is a vital tool in obstetrics and gynaecology education, addressing challenges such as limited clinical exposure during short rotation periods and gender-related sensitivities. This need is further underscored by the fact that non-obstetricians and non-midwives often serve as first responders in out-of-hospital and acute care settings where vaginal birth (VB) is imminent. Traditional mannequin-based simulations depend on in-person tutors with demands on time and physical space. In the absence of realistic clinical scenarios, they serve no better than low-fidelity task trainers. Capitalising on recent advancements in affordable virtual reality (VR) head-mounted display (HMD) technology, we developed and iteratively refined a VR-based childbirth training system between 2020 and 2025. Initial user studies demonstrated strong knowledge retention although participants expressed a preference for in-person mannequin-based simulations due to the lack of tactile feedback in VR. To address this limitation, we introduced a mixed reality (MR)-enhanced childbirth training system in 2024. This innovative approach integrates high-precision alignment of virtual elements with physical mannequins and introduces a tactile component to enhance skill acquisition. A pilot study involving 35 Year 4 undergraduate students yielded positive feedback with participants praising the system's heightened realism and opportunities for peer-to-peer interaction. While both VR and MR have distinct advantages and limitations, the affordability and versatility of modern HMD make VR/MR-based training modules highly scalable and adaptable to diverse scenarios, surpassing the single-task limitations of traditional mannequins. This promises to improve training efficiency and expand access to VB training for a broader range of healthcare professionals.

Keywords: medical education, mixed reality, normal vaginal delivery, obstetrics and gynaecology, simulation, virtual reality

INTRODUCTION

Witnessing the start of life in the labour ward is the hallmark of every medical student's obstetrics & gynaecology (O&G) rotation.¹ In recent years, however, there has been a trend away from demonstrating competence in independently conducting routine vaginal births (VBs) towards one of participation or observation due to competing factors, such as limited posting durations, patient aversion to male students² and competition from other healthcare trainees. This reduction in opportunities for medical students to participate in VBs is worrying considering that non-obstetricians/non-midwives are frequently first responders to unexpectedly precipitous VBs occurring out-of-hospital or in acute care settings and that obstetrics comprises a large and continually rising proportion of medicolegal liabilities in developed countries, i.e. 38.2% of all liabilities (about 21 billion GBP)³ in the UK and 54% of malpractice claims in the US.⁴ Given the significant consequences to mother and child arising from improperly carried out VBs, familiarity with the steps involved is important in preventing avoidable complications arising from healthcare provider unfamiliarity. Mannequin-based simulations^{5,6} serve as task trainers but lack interactivity and realism unless incorporated into a hybrid model-driven clinical scenario simulation.⁷ Further, while reusable, these models are often expensive, bulky and require maintenance and spare parts. Teaching sessions also need curricular time, space and skilled tutor involvement with higher manpower needs and preparation if done as part of a complex medical simulation. There is a strong impetus towards creating better and more efficient ways of improving competency in VB through realistic clinical simulations amid a climate of rising medicolegal concerns.

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¹ Immersive Reality Lab, College of Design and Engineering, National University of Singapore, Singapore

² Department of Obstetrics and Gynaecology, National University Centre for Women and Children, National University Health System, Singapore

³ Department of Obstetrics and Gynaecology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

Correspondence: Asst Prof Arundhati Tushar Gosavi, Department of Obstetrics and Gynaecology, National University Centre for Women and Children, National University Health System, Singapore.

Email: arundhati_gosavi@nuhs.edu.sg

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Leveraging self- and distance-learning technologies popularised during the COVID-19 pandemic for procedural training pedagogy, virtual reality (VR)⁸ emerged as a viable solution. However, even high-fidelity VR simulations have limited interactions with physical surroundings and peers due to its fully virtual environment. This limits its role for procedural skills training. Mixed reality (MR) or augmented reality was popularised by Google Glass® (Google X, Mountain View, US) and is an attractive option for merging user virtual and physical environmental interactions in real-time with scalable potential due to the recent release of cost-effective commercial MR-capable headsets.

In 2020, the Department of Obstetrics and Gynaecology, Yong Loo Lin School of Medicine and the Immersive Reality Laboratory, College of Design and Engineering, both of the National University of Singapore, partnered to develop an in-house comprehensive VR childbirth training system using off-the-shelf technology and local programming know-how. In this article, we share our experience with each iteration and the eventual transition to a novel MR version.

Previous VR iterations

Our first iteration of a VR normal childbirth system occurred in 2020, using Unity® (Unity Technologies, San Francisco, US) for virtual content development and the HTC Vive Pro® (HTC, Taoyuan City, Taiwan) and Manus VR® gloves (Manus VR, Eindhoven, Netherlands) for training experience delivery. The Manus gloves replaced conventional gaming controllers or keyboard-mouse set-ups to provide intuitive hand interactions within the virtual environment. A pilot study involving 23 Year 4 students in January 2021 showed it was well-received by participants. The realism of the birthing process and the virtual labour ward environment scored 4.0 and 4.1 out of 5, respectively. Text instruction, audio instruction and virtual hand guides scored 4.1–4.5 for clarity and informativeness. Participants rated its usefulness as 4.0. Nevertheless, it was perceived as less realistic than mannequin simulation with a score of 2.8 and not as intuitive to use with a score of 3.6.

With the release of the standalone Meta Quest 2® headset (Reality Labs, Meta Platforms, Cambridge, US) in the late 2020s, we ported this VR system over and developed the second iteration, ViVaDeX, to teach the second and third stages of VBs (Figs. 1 and 2). ViVaDeX was incorporated into the Year 4 O&G syllabus in academic year 2022–2023. We conducted a cluster-randomised crossover study with 111 participants to compare the effectiveness in knowledge gain and qualitative feedback between VR group against our legacy mannequin (Prompt

Flex®, Limbs & Things, Bristol, UK).⁹ Clinical groups were randomised to either the VR- or mannequin-based simulation and undertook a pre- and post-simulation knowledge quiz before crossing over to the other simulation modality. Both groups had no significant differences in baseline knowledge or familiarity with VR devices and no participant had any prior experience with childbirth. ViVaDeX was associated with a significantly higher change in mean percentage correct scores post-simulation compared to traditional tutor-led mannequin-based teaching (+40.8% versus [vs] +15.1%, $P<0.001$), which is in keeping with a well-established preference for active learning over passive methods and superior learning when audio and animations are incorporated.¹⁰ As all 111 participants eventually experienced both teaching modalities, we conducted a 6-domain feasibility assessment. Interestingly, despite higher objective knowledge gain scores, ViVaDeX had significantly lower median scores in 5 feasibility domains, i.e. knowledge retention (8.05 vs 8.54, $P=0.002$), feedback (12.8 vs 13.2, $P=0.020$), usability (7.80 vs 8.63, $P<0.001$), enjoyment (8.55 vs 8.91, $P=0.003$) and presence (8.09 vs 8.56, $P=0.009$) with no significant difference in the knowledge domain (13.1 vs 13.1, $P=0.981$). This aligns with other studies reporting that instructor-led classes provided insightful learning experiences that e-learning methods often lacked.¹¹ Nevertheless, most participants (42%) preferred a hybrid approach comprising both VR- and mannequin-based simulations with 40% and 5% preferring either only mannequin- or VR-based simulations, respectively.⁹ ViVaDeX was also provided to a batch of 17 midwifery advanced diploma students from Nanyang Polytechnic in May 2024 to assess applicability to other healthcare trainees. Participants reported a generally positive experience, where on a 5-point scale they rated the simulation's mean effectiveness in knowledge acquisition and procedural understanding at 4.26 (standard deviation [SD] 0.86), quality of feedback and flow at 4.12 (SD 0.99), and overall engagement at 4.03 (SD 1.11).

Progression to MR

Encouraged by positive overall receptivity towards ViVaDeX and the successful proof-of-concept that an in-house designed VR programme could teach VB in any empty room without physical instruments, we attempted to address a key limitation and recurring feedback item—the lack of tactile feedback—by using MR technology. For this next iteration, we selected the Meta Quest 3® which was newly released in 2023 and offered higher performance in a compact, cost-effective, MR-capable device.

Despite high-quality graphics and seamless transitions between the MR and VR environments,

Fig. 1. Virtual reality vaginal delivery and complications simulator.



Fig. 2. Virtual labour ward environment.



restrictions in using built-in cameras to feed images in real-time were an obstacle towards fully leveraging on Meta Quest 3®'s hardware capabilities. To address this, we connected the Intel RealSense® camera (Intel Corp, Santa Clara, US), a lightweight external RGB-D

camera, to the headset to provide an alternative source of visual and depth data for MR integration (Fig. 3). This enabled the alignment of virtual objects with physical counterparts using object detection and tracking algorithms which, in this case, was a virtual

labouring mother overlaid on a physical Prompt Flex® mannequin (Fig. 3). Participants could visualise and interact with a virtual delivery trolley, perform an episiotomy, and perform a VB by matching hands with a virtual overlay in passthrough mode. The simulation ended with virtual cord clamping and blood collection.

In 2024, we conducted a pilot study with 35 Year 4 undergraduate students, evaluating their perceptions of this MR simulation with a questionnaire comprising a 5-point Likert-scale and 1 short answer question adapted from Witmer and Singer's Presence Questionnaire and the System Usability Scale.⁹ Despite the MR simulation being a prototype, 82.9% of participants responded Agree or Strongly Agree to the question "How involved were you in the MR environment?" with 65.7% replying as such to "How well could you concentrate on the assigned tasks or required activities rather than on the mechanisms used to perform those tasks or activities?" and 62.9% to "I prefer the MR environment over the VR environment." With respect to interacting with the MR device, only 5.7% of participants indicated Disagree or Strongly Disagree when asked "How well could you move or manipulate objects in the MR environment?" Nevertheless, there is significant room for improvement as only 57.1% indicated Agree or Strongly Agree to "I think I would like to practice using this simulation frequently." Common themes in the qualitative feedback included excitement when switching to the passthrough MR mode and appreciation for tactile feedback and realism provided by overlaying the virtual model on the physical mannequin. While some participants needed more time to adapt, most found the system easy to use. Anecdotally, we noticed more peer-to-peer interaction between participants using MR compared to previous VR sessions. We also intend to evaluate the MR iteration with different healthcare trainees including

midwifery advanced diploma students, family medicine residents and house officers to assess generalisability as a training tool.

Limitations

While our MR pilot was encouraging, several practical barriers remain. Both VR and MR often require onsite technical support during early use, to guide learners and resolve usability issues. Moreover, while MR offers the advantage of integrating a tactile component, it needs physical mannequins that are not required in a fully VR-based simulation. Time and manpower are needed to calibrate the alignment between physical and virtual components. Additionally, the attached external camera increased power consumption and reduced headset battery life to only 2 hours in continuous usage, thus requiring a dedicated power management plan.

Ideally, novel learning tools should be evaluated using the Kirkpatrick model, aiming for level 3 (behavioural change) and level 4 (organisational outcomes). However, as our simulation targeted medical students and was designed to address limited real-life exposure, evaluation was limited to level 1 (satisfaction) and level 2 (knowledge gain). This is a common limitation in medical education studies. We are addressing this in an ongoing trial assessing skill transfer, where students from MR, VR and control groups will be evaluated on their ability to independently perform VB by faculty experts remotely via video-recorded simulation. In due time, these simulations should be evaluated with different groups of healthcare trainees at multinational sites with reduced onsite technical support and interval assessments to understand real-world impact.

Finally, usability issues were noticed in all study groups. These included difficulties in interacting with virtual medical instruments, ergonomic discomfort

Fig. 3. Set-up for mixed reality (MR) simulation.



Note: The set-up comprises Prompt Flex® mannequin with Intel RealSense® camera attached to a Meta Quest 3® headset and user view of an MR simulation with a virtual delivering mother integrated with a real-world table in a classroom.

Table 1. Pros and cons of different simulation modalities in teaching obstetric emergencies.

	Traditional mannequin-based simulation	VR-based simulation	MR-based simulation
Pros	- Well-established tactile component - In-person teaching with an experienced tutor can be more enjoyable - Can be incorporated into a hybrid mannequin-based clinical scenario	Superior immersion within a virtual space	- Less disorientation from surroundings - Tactile component if integrated with a physical model - Involvement of other real-world participants
		MR/VR HMD can be repurposed to any other procedural skills training or simulation	
Cons	- Mannequins are limited by number of costly mannequins purchased - Mannequins are usually a single-task trainer and not realistic	- Can be disorientating - Involvement of other participants would have to be through virtual avatars - Lacks tactile component	Lack of immersion, as surrounding location is real-world site of training
		- High start-up costs due to need to purchase multiple HMDs - Production costs and technical expertise required to create new scenarios	

HMD: head-mounted display; MR: mixed reality; VR: virtual reality

with frequent headset adjustments especially for females with hair buns, minor spatial disorientation when initially entering the virtual space, and lengthened module completion times due to user interface unfamiliarity. Nevertheless, almost all participants progressed with minimal technical help, suggesting issues would likely be circumvented with improved familiarity and more exposure.

DISCUSSION

While mannequins are usually designed for specific tasks, a VR/MR-based system offers modularity and upgradability with minimal requirements for physical space and specialised tutors.^{13,14} The introduction of cost-effective retail head-mounted display (HMD) has enhanced scalability for medical simulation. As demonstrated by our earlier ViVaDeX study,^{9,10} VR/MR-based simulations can serve as an immersive, tutor-independent means of remote learning that is effective in knowledge acquisition through multimodal teaching techniques. Both VR and MR have their strengths and weaknesses (Table 1). VR simulation is superior in immersion, although at the expense of peer-to-peer interaction while MR simulation allows tactile feedback through interaction with real-world items and engagement with other real-world participants. Nevertheless, legacy mannequin-based simulations provide a mature means of hands-on learning that supports “fishbowl”¹⁵ and peer-assisted learning¹⁶ and benefits from direct tutor engagement, which contributes to better learner experiences. A VR/MR approach can serve as a component of a hybrid teaching approach to reduce the strain of limited resources needed for mannequin-based teaching and, with further technology maturation, may be a viable standalone substitute in medical education. There is great potential to integrate this into a suite of

complex and realistic obstetric emergency simulations. We hope this demonstrates the availability of competent local know-how in developing such procedural skills simulations to allow a closer loop for local customisation while maintaining global potential. This will be especially important for high-acuity and low-occurrence scenarios where society has an expectation for competent emergency care delivery.

Ethics statement

Ethical approval was obtained from the National University of Singapore Institutional Review Board (NUS-IRB-2020-606).

Declaration

The authors declare they have no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript. This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

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Perceptions, knowledge and barriers: A survey of healthcare workers on shingles vaccination

Jessica Weizhen Chen¹ FRACP, Chaoyan Dong² PhD, Derrick Chen Wee Aw¹ FRCP

Dear Editor,

In older adults, herpes zoster, also known as shingles, is a common infectious disease. The estimated lifetime risk of shingles in the general population is about 30%;¹ this increases to 50% at age 85 years.² Among the morbidities associated with shingles, postherpetic neuralgia is the most common complication that has a huge negative impact on quality of life.³

In Asia-Pacific countries, the average shingles incidence of 3–10/1000 person-years is rising at around 5% per year.⁴ Shingles is a major public health concern in Singapore given its rapidly ageing population. The recombinant zoster vaccine (Shingrix, GlaxoSmithKline) has been shown in clinical trials to have over 90% effectiveness in preventing shingles and its complications across all age groups above 50 years.⁵ It has higher vaccine efficacy compared to the older live attenuated vaccine (Zostavax, Merck Sharp & Dohme), which is contraindicated in adults with immunosuppression.

The shingles vaccine uptake in adults older than 50 years in the UK is known to be low.⁶ Currently, there is no publicly available data on shingles vaccination uptake rates in Singapore.

Healthcare workers (HCWs) play a vital role in shaping public health practices, hence it is important to understand their perception of the shingles vaccine as it is essential for promoting vaccination.⁷ We present our research findings to better understand vaccination perception among HCWs and explore the nature of their concerns, their knowledge of shingles and their perceived role in responding to the shingles vaccine.

This study employed a cross-sectional design to examine the knowledge of shingles and its vaccination in health care workers in Sengkang General Hospital, a 1000-bed tertiary teaching hospital in the northeast district of Singapore.

The survey questionnaire comprised demographic information and 18 true-false questions on knowledge

of shingles and its vaccination, as well as perception and attitudes on shingles prevention with vaccination. The questionnaire was developed after conducting a literature review of the existing questionnaires on shingles vaccination.

The survey was distributed via hospital email through a survey invite link via forms.sg. Data was collected over a 2-month period from 4 July to 28 August 2024. The data was analysed using SPSS version 28.0 (IBM Corp, Armonk, NY, US).

This survey has been approved by the SingHealth Centralised Institutional Review Board with a waiver of informed consent. Confidentiality and anonymity of the participants were maintained during this survey.

There were a total of 430 respondents including 154 doctors, 252 nurses and 24 pharmacists (response rate 14.3%). The vast majority of respondents were females (307, 71.4%), nurses (252, 58.6%) and attained at least a degree (276, 64.2%).

The knowledge score is the sum of the correct responses for the 13 knowledge questions. The mean knowledge score is 9.24 (standard deviation [SD] of 2.05) for doctors; 6.45 (SD of 2.00) for nurses; and 10.01 (SD of 1.82) for pharmacists. A wide variability was noted in the nurses' scores with a range of 2 to 11. The differences between nurses and doctors, and nurses and pharmacists were significant (1-way analysis of variance $P<0.001$), while that between doctors and pharmacists was not ($P=0.138$).

A positive correlation was demonstrated between education level and knowledge scores. Participants with basic tertiary education (diploma or degree) had a mean score of 7.35, while those with advanced tertiary education (master's and doctorate) had a significantly higher score of 9.41 ($P<0.05$).

However, the study found no correlation between seniority (surrogate marker being the number of years in clinical practice) and knowledge of shingles. As clinicians gain years in their clinical practice,

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¹ Department of General Medicine, Sengkang General Hospital, Singapore

² Education Office, Sengkang General Hospital, Singapore

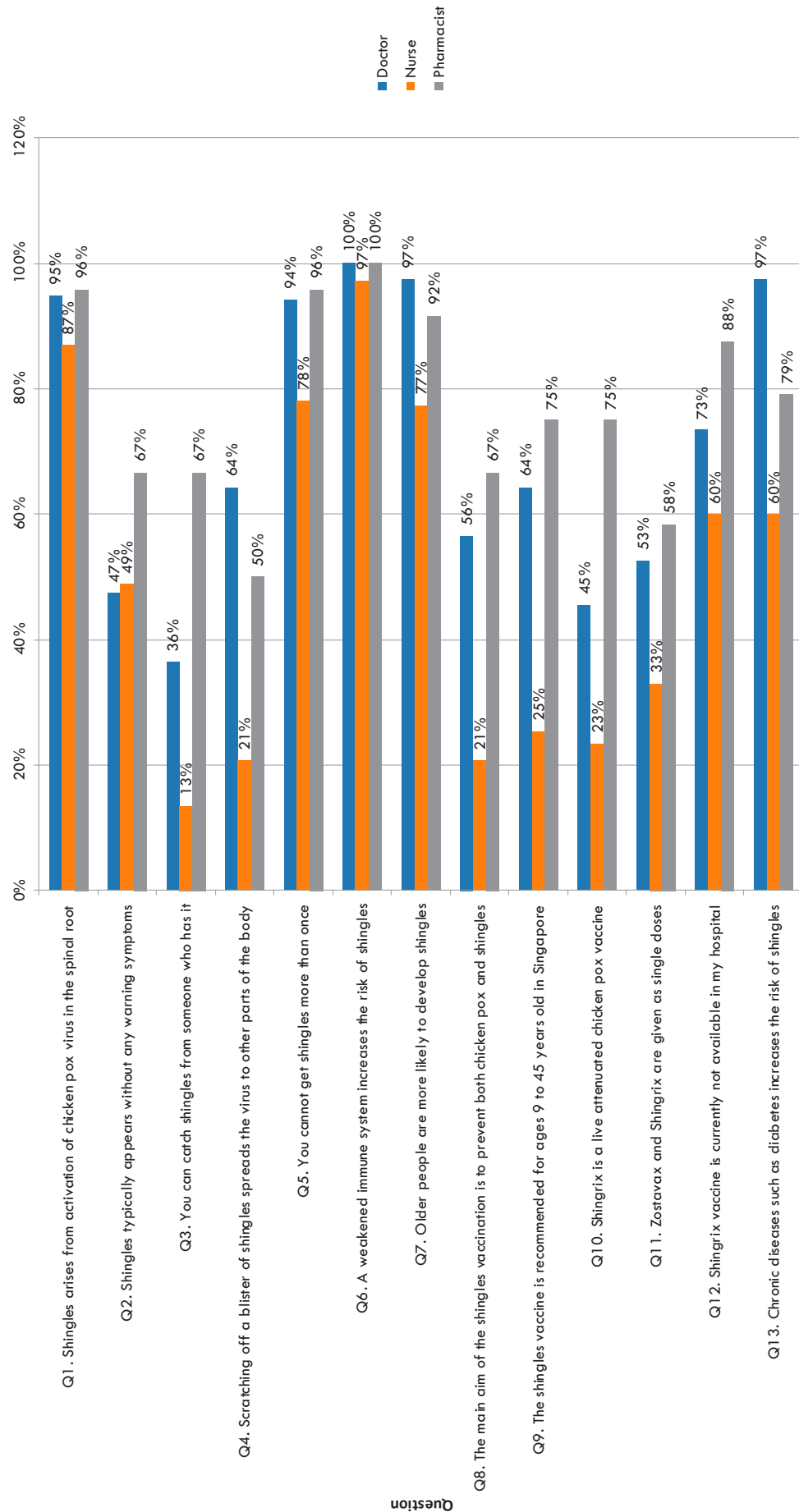
Correspondence: Prof Derrick Chen Wee Aw, Sengkang General Hospital, 110 Sengkang East Way, Singapore 544886.

Email: derrick.aw.c.w@singhealth.com.sg

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Table 1. Participants' knowledge of shingles and its vaccine by speciality.



knowledge from medical training can diminish without reinforcement through practice or ongoing learning.⁸

We explored the perception of shingles vaccination with 5 statements in the survey:

Question 14: “I am not convinced that Shingrix is able to effectively prevent shingles.”

Here, 78.84% of respondents were convinced that Shingrix is effective in preventing shingles. A weak correlation was found with knowledge (coefficient -0.238) indicating that individuals with higher knowledge levels are less likely to express scepticism about the effectiveness of the Shingrix vaccine.

Question 15: “I am confident to provide credible shingles vaccine recommendations to my patients.”

A weak correlation was found with knowledge (coefficient -0.158), suggesting that the more knowledge respondents have about shingles and the vaccine, the slightly less confident they feel when making recommendations. Profession, however, showed a weak positive correlation (coefficient 0.167) with confidence. A slight increase in confidence was observed from doctors (49.35%) to pharmacists (66.67%) to nurses (68.25%). Higher knowledge was paradoxically associated with lower confidence in vaccine recommendations. This may be due to increased awareness of vaccine limitations and ethical dilemmas in balancing patient autonomy with public health advocacy.

Question 16: “My busy work schedule does not allow me to discuss shingles vaccine with patients.”

The affirmative was found in 62.99% of doctors, 55.16% of nurses and 87.50% of pharmacists ($P=0.0051$). Pharmacists being the last point of patient contact through hospital journey with patients have the least bandwidth to discuss vaccination. To address this, strategies such as integrating vaccination prompts into clinic consults, delegating education to trained staff, and leveraging technology such as pre-visit reminders and digital aids can help. Streamlined documentation and institutional support, including protected time or incentives, may further reduce barriers. For pharmacists, brief consultation slots and visual prompts can facilitate vaccine discussions without adding to workload. A team-based approach is essential to overcoming time-related barriers to vaccination counselling.

Question 17: “I find it difficult to communicate with older adults about shingles vaccine.”

The majority of respondents ($n=263$, 61.16%) struggle to discuss the shingles vaccine with older

patients. Communication barriers persist in discussing vaccination with older adults, underscoring the need for structured communication training for HCWs.

Question 18: “In patients who developed or had developed shingles, there is no point to discuss the shingles vaccine with them.”

A small proportion of respondents ($n=71$, 16.51%) felt that discussing the shingles vaccine with patients who developed or had developed shingles was pointless. Knowledge gaps exist regarding post-infection vaccination benefits, highlighting the need for improved public health messaging to ensure patients and HCWs understand that shingles can recur and vaccination reduces future risk.

Our study is the first hospital-based study in Singapore which looked at the healthcare workers' knowledge and perception of shingles and its vaccination.

A key limitation of the questionnaire design is its exclusive use of true-false questions, which can oversimplify complex attitudes and beliefs about vaccination. Question 14 (“I am not convinced that Shingrix is able to effectively prevent shingles”), for instance, is prone to ambiguity. Participants may interpret such questions in nuanced ways that a binary response format cannot capture, leading to potential misrepresentation of their actual views.

Future surveys should cover the cost consideration. Incorporating questions about cost and perceived benefit to patients would be highly relevant especially when exploring barriers to vaccine uptake. Cost is often a pragmatic and psychological barrier, and healthcare providers' perceptions of this can influence how strongly they recommend the vaccine.

As HCWs recommendations remains one of the most important predictors of vaccination among adults as their recommendations directly influence patients' acceptance,⁹ efforts need to be urgently directed at enhancing HCWs' knowledge and addressing misconceptions about the shingles vaccine, thereby empowering them to recommend vaccination and improve uptake among the at-risk adults and particularly the older patients.

Such efforts are particularly vital today since the government has recently announced that Shingrix vaccine was to be incorporated into the National Adult Immunisation Programme from 2026.

Ethics statement

Ethical approval from the SingHealth Centralised Institutional Review Board (2024-3016) with a waiver for informed consent.

Declaration

The authors declare they have no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript.

Keywords: appraisal, attitudes, medical service provider, poll, shingles vaccine

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Making sense of ICD-11 diagnostic criteria of compulsive sexual behavioural disorder

Syidda Amron¹ BSc (Hons), Kandasami Gomathinayagam¹ MRCPsych, Cheng Lee¹ MMED Psych, Song Guo¹ PhD, Hui Shan Tan¹ BPsych

Dear Editor,

Compulsive sexual behaviour disorder (CSBD) is identified by persistent, intense sexual urges that lead to repetitive activities, causing significant distress or impairment over 6 months or more.¹ It is characterised by neglecting important responsibilities, repeated unsuccessful attempts to control the behaviour and continuation despite negative consequences.¹ Crucially, the distress linked to CSBD is not due to moral judgments about sexual behaviour.¹

The inclusion of CSBD in the International Classification of Diseases (ICD-11) in 2018 marks a significant development, offering much-needed clarity for diagnosis and treatment.² This clarity has the potential to enhance clinical practice and advance research within the mental health sector. A clear classification of CSBD can significantly influence funding, public health and clinical guidelines, making standardised classifications like the ICD-11 essential for designing interventions and allocating resources.³ Such clarity facilitates the implementation of standardised treatments, improves the quality and availability of care, supports the effective budgeting of scarce healthcare resources, and reduce the stigma associated with CSBD.⁴

The study team has decided to embark on research aimed at evaluating previous clinical case notes to determine whether earlier clinicians' assessments align with the latest CSBD criteria. This study seeks to break new ground by involving 3 independent reviewers who will collect data from these notes, with inter-rater analysis conducted based on their evaluations. The objective is to address existing challenges in classification and diagnosis, thereby contributing to improved clinical practices, more effective resource allocation and informed policy development, ultimately benefitting individuals affected by CSBD.

The dataset for this review was extracted from a local addiction treatment centre's treatment outcome monitoring database, selecting patients who sought

treatment for sexual-related issues or diagnoses between 2013 and 2018. Three psychiatrist reviewers performed a pilot test on 10 random cases to ensure familiarity with the new ICD-11 CSBD guidelines and to align their expectations and interpretations between the guidelines and the clinical cases. This exercise was intended to help them become familiar with the new ICD-11 CSBD guidelines and to ensure their expectations and interpretations were consistent with both the guidelines and the clinical cases. Their expertise and prior experience in the field played a crucial role in aligning their assessments with the latest diagnostic criteria. Any disagreement was resolved, with support from the research assistants, through formal discussion. All other following case reviews were conducted independently by them.

To measure inter-rater reliability (IRR), percentage agreement and Fleiss' kappa were adopted for analysis because percentage agreement provides a straightforward measure of how well 2 or more observers agree on categorical data, with an acceptable level defined at 70% and above.³ Fleiss' kappa is ideal for calculating IRR involving 3 or more raters, especially when handling categorical data, with interpretation as follows: ≤ 0 (none), 0.01–0.20 (slight), 0.21–0.40 (fair), 0.41–0.60 (moderate), 0.61–0.80 (substantial) and 0.81–1.00 (almost perfect).³

A total of 78 cases (Table 1) were reviewed, with a mean age of 28.29 years (standard deviation [SD]=11.2). The sample consisted of 95% males, majority were of Chinese ethnicity (69.2%), and 56.7% were married. Most cases were from 2018 (26.9%) and 2015 (23.1%). Item 3d (Table 1) revealed to have the highest percentage agreement (86%), while the other items fell below the acceptable threshold. The overall percentage agreement on whether cases satisfied the CSBD criteria was 58%, indicating a lower-than-acceptable agreement level among reviewers. Fleiss' kappa analysis revealed none-to-slight agreement for items 1 ($\kappa=0.137$; $z=2.09$, $P=0.036$) and 3d ($\kappa=0.104$; $z=1.59$, $P=0.0111$). However, items 2, 3a, 3b and 3c showed fair

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¹ National Addiction Management Service, Institute of Mental Health, Singapore

Correspondence: Syidda Amron, National Addictions Management Service, Institute of Mental Health, 10 Buangkok View, Buangkok Green Medical Park, Singapore 539747. Email: syidda_amron@wh.com.sg

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Table 1. Results.

Demographics										
Age details										
Age range		11 to 57								
Mean (±)		28.29 (11.2)								
Sex		n (%)								
Male		74 (95%)								
Female		4 (5%)								
Ethnicity		n (%)								
Chinese		54 (69%)								
Malay		15 (19%)								
Indian		7 (9%)								
Others		2 (3%)								
Marital status		n (%)								
Single		48 (62%)								
Married		28 (36%)								
Separated/widowed/others		2 (2%)								
Year of Admission n (%)										
2013	2014	2015	2016	2017	2018	2019	2020	2021	2023	
2 (2.6%)	3 (3.8%)	18 (23.1%)	10 (12.8%)	4 (5.1%)	21 (26.9%)	10 (12.8%)	2 (2.6%)	7 (9.0%)	1 (1.3%)	

Table 1. Results. (Cont'd)

Percentage agreement and Fleiss' kappa result				Fleiss' kappa		
		Percentage agreement (%)	k	z	P value	
Percentage agreement and Fleiss' kappa for each item						
Item 1.	The pattern of failure to control intense, sexual impulses or urges and resulting repetitive sexual behaviour is manifested over an extended period.	46	0.137	2.09	0.036	
Item 2.	The pattern of repetitive sexual behaviour causes marked distress* or significant impairment in personal, family, social, educational, occupational, or other important areas of functioning. [*Note for rule out] Distress that is entirely related to moral judgments and disapproval about sexual impulses, urges or behaviours is not enough to meet this requirement.	51	0.287	4.38	<0.001	
Item 3a.	Engaging in repetitive sexual activities has become a central focus of the person's life to the point of neglecting health and personal care or other interests, activities and responsibilities.	49	0.236	3.6	<0.001	
Item 3b.	The person has made numerous unsuccessful efforts to control or significantly reduce repetitive sexual behaviour.	68	0.345	5.27	<0.001	
Item 3c.	The person continues to engage in repetitive sexual behaviour despite adverse consequences (e.g. repeated relationship disruption, occupational consequences, negative impact on health).	56	0.261	4.00	<0.001	
Item 3d.	The person continues to engage in repetitive sexual behaviour even when the individual derives little or no satisfaction from it.	86	0.104	1.59	0.111	
Percentage agreement and Fleiss' kappa if cases met with criteria of CSBD						
	CSBD: compulsive sexual behaviour disorder	58	0.304	4.46	<0.001	

agreement, and the overall agreement on whether cases met the CSBD criteria was also fair ($\kappa=0.304$; $z=4.46$, $P<0.001$).

The inclusion of CSBD in the ICD-11 in 2018 introduces unique challenges, particularly when reviewing retrospective cases. In our analysis, we found that only 8% ($n=6$) of the cases reviewed met the CSBD criteria, with only 2 of these cases documented from 2018 onwards. Considering the relatively recent introduction of this diagnosis, we recognise that there is some uncertainty which may lead to confusion due to the subjective interpretation of the diagnostic criteria since their introduction in 2018. Additional factors that may complicate the assessment include: (1) a lack of comprehensive understanding and training regarding the new diagnostic criteria, (2) insufficient corroborative information, and (3) superficial patient information, which could lead to potential under-reporting of CSBD symptoms. This significantly affects the identification and assessment of key disorder criteria across cases. The inconsistency and bias from subjective interpretation and under or overreporting of symptoms may lead to incomplete assessment and inaccurate diagnosis, thereby affecting treatment decision. Additionally, the results identified substantial variability in CSBD diagnoses, with agreement percentages ranging from 46% to 86%. Fleiss' kappa values indicated slight to fair consistency, with values between $\kappa=0.104$ and $\kappa=0.345$. Overall agreement was found to be 58%, with a Fleiss' kappa value of $\kappa=0.304$. The fair to moderate IRR highlights the need for standardised diagnostic procedures to improve consistency in identifying CSBD.

To address inconsistencies in identifying and assessing CSBD, this study recommends regular training for clinicians to standardise clinical diagnoses and ensure proper documentation.⁶ Standardising the practices in care and treatment for CSBD can enhance reliability, resulting in more accurate diagnoses in both clinical and research settings.⁴ One approach is to utilise a manualised method for deriving these criteria, which provides a structured framework that promotes consistency and precision. This method not only streamlines the assessment process but also improves the clarity of diagnoses, benefiting both practitioners and patients. Additionally, given the sensitivity of the condition, establishing positive rapport⁸ and therapeutic trust with patients during their first visit can assist clinicians in formulating concise case notes and appropriately assessing patients.⁷

Our study provides valuable insights into ICD-11's recent inclusion of CSBD, highlighting the need for

clinician training to standardise clinical diagnoses and ensure proper documentation, so as to improve treatment outcomes, ultimately benefitting both clinicians and patients.

Acknowledgments

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We would especially like to thank National Addictions Management Service for providing the resources needed to make this study possible.

Ethics statement

This study was approved by the National Healthcare Group Domain Specific Review Board (2022/00623).

Declaration

No external funding was received for this study. The authors declare they have no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript.

Keywords: *behaviour addiction, clinical competence, compulsive behaviour, compulsive sexual behaviour disorder, consensus, inter-rater testing, standardise reporting*

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Cone beam CT for paranasal sinus and temporal bone: A cost-benefit analysis in Singapore

Kelvin Yong Jie Lim^{*1} MMED (ORL), Jian Li Tan^{*1} FAMS (ORL), Alvin Yong Quan Soon² FRCR (UK), Lay Wai Khin³ PGC, Ming Yann Lim¹ FAMS (ORL), Seng Beng Yeo¹ FAMS (ORL)

Dear Editor,

Cone beam computed tomography (CBCT) has emerged as a valuable imaging tool in otorhinolaryngology or the specialty of ear, nose and throat (ENT), where precise imaging of the sinus and temporal bone pathologies is essential. This paper presents a cost-benefit analysis (CBA) of CBCT in a public healthcare setting, and highlights its monetary and non-monetary benefits—to our knowledge, the first study on these in the Singapore context and in literature. The findings offer insights for policymakers on the feasibility of adopting CBCT as a primary radiological tool in ENT.

This prospective CBA was conducted at Tan Tock Seng Hospital, a tertiary care centre in Singapore, from January 2022 to October 2023. The study included patients aged 18 years and older, who required CBCT or multi-detector computed tomography (MDCT) imaging of the paranasal sinuses or temporal bone. The CBCT machine used was the GiANO HR scanner (NewTom, Italy), while the MDCT machine was the GE CT Revolution Apex 2.2 scanner (GE Healthcare, US). Both machines, purchased 2 years apart, were the closest comparators available and operated under standardised imaging protocols.

Table 1. Comparative cost analysis of CBCT and MDCT.

Metric	CBCT	MDCT	Savings
Average cost per scan, SGD	\$187.50	\$475.13	\$287.63
Annual patient savings (for 518 scans), SGD	\$97,125	\$246,117.34	\$148,992.34
Machine cost per year, SGD	\$33,558.43	\$572,358.43	\$538,800.00
Total annual savings, SGD	-	-	\$688,079.97
Radiation dose, µSv	63	108	42% reduction
Space requirement, m ²	2.59	25	90% reduction
Waiting time for scan, weeks	3	10	7 weeks
Machine type			
Machine cost (after amortisation), SGD	\$22,857.14	\$285,714.29	\$262,857.15
IT testing and integration, SGD	\$7787.00	\$7787.00	0
Renovation cost, SGD	\$1714.29	\$42,857.14	\$41,142.85
Maintenance cost, SGD	\$1200.00	\$236,000.00	\$234,800.00
Manpower cost (1 radiologist and 1 radiographer)	Negates each other		
Cost calculations (hospital's perspective): machine cost per year, SGD	\$33,558.43	\$572,358.43	\$538,800.00

CBCT: cone beam computed tomography; IT: information technology; MDCT: multi-detector computed tomography; SGD: Singapore dollars

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¹ Department of Otorhinolaryngology, Tan Tock Seng Hospital, Singapore
² Department of Diagnostic Radiology, Tan Tock Seng Hospital, Singapore
³ Department of Clinical Research and Innovation Office, Tan Tock Seng Hospital, Singapore
^{*} Joint first authors

Correspondence: Dr Kelvin Yong Jie Lim, Department of Otorhinolaryngology, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, Singapore 308433.
Email: limyjk@gmail.com
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Cost-benefit analysis. Examining patient cost savings, the average cost of a CBCT scan was SGD187.50, compared to SGD475.13 for MDCT, yielding a saving of SGD287.63 per scan. With a switch from MDCT to CBCT for ENT-related scans, patients could save about SGD148,992.34 per year, based on 518 scans annually.

Examining hospital cost savings, the amortised machine cost over 7 years for CBCT was SGD22,857.14, compared to SGD285,714.29 for MDCT. Maintenance costs were markedly lower for CBCT at SGD1200 annually versus SGD236,000 for MDCT. Additional overheads, including information technology (IT) integration and renovations, further highlighted CBCT's economic efficiency. The total annual hospital cost of CBCT was SGD33,558.43, compared to SGD572,358.43 for MDCT, resulting in net hospital savings of SGD538,000. Combined with patient savings, the total annual cost saving was SGD687,792.34.

Examining the benefit-cost ratio (BCR), which is a key metric in economic viability, the BCR for CBCT was 16.06, meaning for every dollar spent, the hospital achieved a return of SGD16.06 in cost savings. This underscores CBCT's financial feasibility for high-volume ENT imaging needs.

Clinical advantages of CBCT. In sinus imaging applications, CBCT is particularly advantageous due to its low radiation dose¹ and high-resolution visualisation of crucial bony landmarks like the uncinate process and skull base. This is critical for chronic rhinosinusitis assessment and surgical planning.²

In intraoperative CBCT in endoscopic sinus surgery (ESS), CBCT has been used intraoperatively for ESS, particularly in the frontal recess. Studies have shown its value in refining surgical strategies and optimising stent placements via a C-arm CBCT.³ At our institution, CBCT images have been integrated into the Stealthstation S8 (Medtronic, Dublin, Ireland) surgical navigation system, enhancing intraoperative precision.⁴ However, our CBCT machine is not a C-arm CBCT and does not offer real-time imaging during surgery.

In temporal bone imaging, CBCT offers superior resolution for fine bony structures in the middle and inner ear compared to MDCT. It also significantly reduces metal artefacts, making it valuable for postoperative imaging of cochlear and middle ear implants. Studies report up to a 60-fold radiation dose reduction compared to MDCT, particularly with a limited field-of-view protocol.

In postoperative imaging of cochlear and middle ear implants, CBCT allows for accurate visualisation

of electrode arrays and their modiolus relationship in cochlear implants. It also reduces metal-related artefacts, improving imaging clarity compared to conventional CT.

In detecting histologically active otosclerosis, CBCT is highly sensitive, with 100% sensitivity in identifying active lesions, particularly hypodense fenestral lesions at the stapes footplate's anterior pole. However, it cannot detect inactive otosclerosis, necessitating careful clinical correlation.

For accessing conductive hearing loss, CBCT provides superior image quality and spatial resolution compared to MDCT while delivering up to 70% lower radiation dose, making it a safer and more efficient imaging option.

Limitations and considerations. Our current CBCT system does not support intravenous contrast, limiting its use for tumour or vascular pathology evaluations. However, most ENT-related imaging does not require contrast, and magnetic resonance imaging (MRI) can address this gap. In our cohort, 37 patients (3.9%) who initially underwent CBCT subsequently required MDCT or MRI due to motion artefacts or complex pathology.

CBCT requires patients to remain still for 20–30 seconds, which may not be suitable for those with cognitive impairments. Image artefacts can also obscure subtle radiological findings, particularly in middle ear scans, due to interference from thick scalp tissue and mastoid bone.

Cost calculations assumed a 1:1 ratio of subsidised to private scans. However, subsidised scans account for approximately 70%, meaning the actual average cost per scan might be slightly lower than calculated. Future studies should refine these estimates by incorporating patient demographics and funding structures.

CBCT systems vary widely in specifications, with over 85 models reported in 2018.⁵ Each system has unique features, meaning findings for one system may not generalise to others. Future research should evaluate multiple CBCT models to provide a broader assessment of cost-effectiveness and clinical utility across different healthcare settings.

Economic viability. The findings strongly support CBCT's economic viability in public healthcare. By replacing MDCT for selected indications, CBCT offers substantial cost savings without compromising diagnostic accuracy. These savings can be reallocated to other critical areas, thus enhancing healthcare delivery.

With lower acquisition and maintenance costs, CBCT requires only 18% of the space needed for an

MDCT machine and operates on standard 220/240-volt outlets, reducing renovation costs. Its affordability makes it an ideal choice for public hospitals operating under budget constraints. CBCT could also be integrated into other specialties, such as orthopaedics and maxillofacial surgery, though further research is needed to address subspecialty-specific requirements.

Practical implications. During the study period, waiting times for MDCT scans averaged 10 weeks, compared to just 3 weeks for CBCT. By diverting ENT-related scans to CBCT, hospitals can alleviate pressure on MDCT machines, thus reducing waiting times and improving patient throughput.

CBCT delivers 42% lower radiation than MDCT, aligning with the “as low as reasonably achievable principle”^{6,7} and reducing long-term radiation risks for patients.⁸

This CBA demonstrates the economic and practical advantages of CBCT in public healthcare. With annual cost savings exceeding SGD687,000 and a BCR of 16.06, CBCT is a highly cost-effective alternative to MDCT for ENT imaging. Beyond monetary benefits, CBCT offers reduced radiation exposure, shorter waiting times and streamlined infrastructure requirements, thus enhancing both patient safety and hospital efficiency.

Policymakers should consider prioritising CBCT for high-volume, non-contrast imaging needs. By adopting cost-effective technologies like CBCT, public healthcare systems can optimise resources, improve patient outcomes and achieve long-term sustainability.

Ethics statement

Not applicable.

Declaration

The authors declare they have no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript.

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81 Kim Keat Road, #11-00 & #12-00 NKF Centre, Singapore 328836

Email: annals@ams.edu.sg | Website: <https://www.annals.edu.sg>