



ANNALS

OFFICIAL JOURNAL OF THE ACADEMY OF MEDICINE, SINGAPORE

VOLUME 55

NUMBER 1

JAN 2026



Sarcopenia: Current evidence, advances in assessment, clinical implementation and future directions

Singapore's first national sarcopenia consortium highlights how research, policy and community engagement can drive population muscle health. (See full article, p. 26)

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ISSN 2972-4066

Annals, Academy of Medicine, Singapore

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Beyond tumour necrosis factor inhibition: Revisiting latent tuberculosis infection testing in rheumatology

Rebecca Grainger^{1,2} PhD

Dear Editor,

Tuberculosis (TB) remains a major public health challenge in Asia and continues to require consideration during clinical decision-making in Singapore. Although the incidence of active TB in Singapore has declined, latent tuberculosis infection (LTBI) remains common, affecting an estimated 5–10% of the population and up to 30% of older adults.¹ For most individuals exposed to *Mycobacterium tuberculosis*, the pathogen persists in a dormant state with immune-mediated containment preventing progression to active disease. However, the lifetime risk of reactivation—estimated at 5–10%—is substantially increased by immune compromise, whether related to ageing, comorbidity, or iatrogenic immunosuppression.¹ This risk has had significant implications for rheumatology practice, where immune-modulating therapies are now central to the management of many immune-inflammatory rheumatic diseases. An increased risk of TB was identified soon after introduction of tumour necrosis factor inhibitors (TNFi), which led to the widespread adoption of LTBI screening prior to TNFi initiation, a practice now firmly embedded in international guidelines and clinical workflows.^{2,3} As the therapeutic landscape has expanded to include multiple non-TNFi biologics, targeted synthetic disease-modifying antirheumatic drugs such as Janus kinase inhibitors, and other immunosuppressive agents, clinicians may have extrapolated this approach beyond TNFi. While such caution is understandable in TB-endemic settings, indiscriminate screening may impose unnecessary costs, delay effective treatment and expose patients to LTBI therapy where benefit may be negligible. The uncertainty surrounding appropriate LTBI screening for non-TNFi therapies is addressed in the consensus statement in this issue, which provides evidence-informed recommendations for contemporary rheumatology practice in Singapore.

The approach taken to address LTBI by the Singapore Chapter of Rheumatology is systematic and clinically pragmatic, providing recommendations

that support informed decision-making in the clinic and at the bedside.⁴ Drawing on a comprehensive systematic literature review addressing the use of interferon-gamma release assay before initiation of number of non-TNFi agents and routine repeated testing for patients on TNFi who have previously tested negative for LTBI, the group applied the GRADE framework to assess the quality of evidence and strength of recommendations. Recommendations were crafted informed through multidisciplinary expert discussion and consensus voting. This methodological approach is well suited to areas where the evidence base is limited, heterogeneous, or indirect.⁵ The inclusion of experienced rheumatologists, together with an infectious disease and respiratory physician with expertise in TB, strengthens the credibility and relevance of the guidance. The consensus conditionally supports LTBI screening with interferon-gamma release assay prior to initiation of tocilizumab, Janus kinase inhibitors and moderate-to-high-dose glucocorticoids, while recommending against routine testing before cyclophosphamide. Importantly, the group also conditionally recommends against routine annual re-testing for LTBI in patients receiving TNFi who have had an initial negative screen, justified by low rates of reactivation in Singapore and a declining background TB incidence. This does not diminish the importance of clinical vigilance: ongoing assessment for TB symptoms and new exposure should remain part of routine care in TB-endemic settings. The restraint demonstrated in these recommendations—recommending careful clinical assessment over indiscriminate testing—represents a key strength of the consensus approach and distinguishes it from more prescriptive approaches.

While firm recommendations are often more satisfying to clinicians, the absence of high-quality evidence in this area necessitates caution. Conditional recommendations are an appropriate response to low-certainty evidence and should not be considered indecisive or lacking authority.⁶ Rather, they explicitly acknowledge uncertainty. In practice, such

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Accepted: 27 January 2026

Published: 29 January 2026

recommendations encourage clinicians to engage patients in informed discussions about the potential benefits and limitations of testing, incorporating individual values, preferences and tolerance for risk. A patient with high concern about TB and low risk tolerance may reasonably favour LTBI testing even when the expected yield is low, particularly if treatment decisions can be made without undue delay. Similarly, clinician judgement remains essential, as factors such as advanced age, frailty, cumulative or combination immunosuppression, and exposure risks may justify screening in selected cases. Conditional recommendations are therefore valuable in discouraging unnecessary testing for the majority, while preserving flexibility for individualised decision-making.

This consensus document has clear practical utility for day-to-day rheumatology care in Singapore. By discouraging LTBI testing where benefit is unlikely, the recommendations can reduce unnecessary delays in initiating effective therapy and avoid treatment of detected LTBI when the actual risk of reactivation with the chosen therapy is low. Given the potential toxicity of LTBI treatment, including hepatotoxicity and drug–drug interactions, this more targeted approach may reduce patient burden, healthcare costs and avoidable harm. It may also help streamline increasingly complex treatment pathways for patients with active inflammatory disease requiring escalation of therapy. Although developed within the Singapore context, the synthesis of evidence and guidance is likely to be relevant to clinicians practising in other settings with similar TB epidemiology. More broadly, the recommendations underscore the importance of clinicians always remaining cognisant of background rates of latent and active TB in their populations. In an increasingly globalised world, this includes consideration of TB risk in migrants originating from countries with higher LTBI prevalence, even when practising in high-income settings with lower overall TB incidence.

While these recommendations reflect the current available evidence, the question of LTBI screening will require periodic re-evaluation as therapeutics and epidemiology evolve. As new classes of immunomodulatory therapies emerge, clinicians will need to consider the implications for TB reactivation, informed by mechanism of action and likely effects on granuloma integrity. Future clinical trials should report TB-related exclusions and baseline LTBI screening clearly and should also be complemented by post-marketing evaluation. Over time, declining TB infections and changing LTBI prevalence—particularly as cohorts with lower lifetime exposure

age—may further alter the balance of benefit and harm associated with routine testing. Population-based pharmacovigilance and epidemiological studies, including international collaborations across TB-endemic and non-endemic regions will become increasingly important. Recommendations on LTBI risk assessment will require updating as evidence evolves. Given that TB remains a major global public health threat and that drug resistance poses an ongoing challenge, clinicians, researchers and policymakers share a responsibility to minimise unnecessary antimicrobial exposure while preventing active disease. Thoughtful, proportionate approaches to LTBI screening represent an important contribution to that goal.

Ethics statement

Not applicable.

Declaration

The author declares 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. The author independently generated the ideas for this editorial and wrote the full manuscript. ChatGPT (GPT-5.2 architecture) was used in January 2026 to generate title ideas and assist with copyediting, aiming to improve readability and minimise grammatical and punctuation errors.

Keywords: *epidemiology, public health, rheumatology, tuberculosis, tumour necrosis factor inhibitors*

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Towards a holistic and improved clinical management of menopause

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As life expectancy increases, women may spend a significant number of years that can amount to almost a third of their life in the post-menopausal life stage.¹ Menopause represents a unique stage in a woman's lifetime, wherein menstrual cycles cease and women experience vasomotor, genitourinary and neurocognitive changes that can impact their quality of life due to the sudden loss of estrogens.² While all women go through menopause, the experience is unique to every individual—often affected by comorbidities, socio-economic factors and cultural beliefs—making its diagnosis and treatment complex.¹ Menopause remains a sensitive topic, often resulting in healthcare providers being unable to manage symptoms and offer efficacious treatment. Therefore, there remains an urgent need to improve the clinical management of menopause globally. There is also a paucity in research on Asian women's health that needs to be addressed, as large population health studies tend to focus on Caucasians only.

In this issue of the *Annals*, Aggarwal et al.³ present a timely and well-curated piece that aims to elucidate the lived experiences of Asian women experiencing menopause, their symptoms and awareness of treatment options, to improve the knowledge resolution of menopause towards optimised clinical management and policy changes. This will form an illuminating piece of work for all healthcare providers dedicated to care for midlife women, especially in the Asian population.

The authors performed a carefully conducted qualitative study, the Menopause and Ageing Research in International Environments – work package 2A (MARIE WP2A) in Singapore and analysed data from 18 women at various stages of perimenopause, menopause and post-menopause using the consolidated criteria for reporting qualitative research criteria. Data from the semi-structured interviews and video conferences were analysed using the Delanerolle and Phiri framework incorporating the interrelated biological, psychological, sociocultural and health system domains. The findings are highly interesting and reveal a diverse range of menopausal symptoms across participants, with significant variations in comorbidities.

Cross-cutting themes across the domains were eloquently described, thus forming a strategic base and framework to integrate the various domains into actionable themes for future management and implementation. For example, within the biological domain, vasomotor/sleep disturbances, musculoskeletal/bone health, genitourinary/sexual health and metabolic/endocrine disturbances of varying severity were reported among the participants. In addition, comorbidity interactions, such as Parkinson's disease or cancer survivorship, were reported to influence menopause symptom severity and affected clinical management for the participants. Mood disturbances and cognitive change were frequently reported by the participants with coping mechanisms ranging from meditation, note-taking to emotional withdrawal within the psychological domain, with the authors sharing that participants who are healthcare professionals also tended to delay seeking menopause care owing to reasons such as time and occupational concerns. Participants also described both extremes of changes in family dynamics. Some participants described reduced intimacy with partners, while others described increased emotional support and accommodation within the sociocultural domain. Varying peer support and workplace cultures also shaped the participants' differing experiences in this domain. Despite this dichotomy, an underlying theme was the stigma and silence of open conversations on menopause, which highlights the strong undertow of traditional and cultural beliefs. Importantly, the authors did report that individual resilience was strengthened by support networks, either from family members or from having workplace flexibility.

Interestingly, the very participation in the study prompted recognition of symptoms and triggered the participants to seek care and symptom management. Thus, within the health system domain, participants commented that access to public and private sectors varied, with private sectors perceived as lacking menopause expertise while public healthcare systems were anticipated to be dismissive. In addition, the prescription of hormone replacement therapy and continuity of care was significantly lacking. These

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Accepted: 27 January 2026

Published: 29 January 2026

findings highlight the potential of the MARIE survey as a structured tool and entry point to menopause care. Ultimately, the authors recognised that the mediating factor that significantly affected symptom burden among the participants was resilience, in the form of healthcare knowledge, supportive networks and coping strategies.

Singapore provides a unique study setting as a high-income nation with a multi-ethnic population and an enhanced healthcare infrastructure for this pertinent study by Aggarwal et al. The real-world data and documented lived experiences of women in the midlife stage revealed a complex network of workplace inequities, healthcare access, sociocultural, psychological and individual factors that have affected their menopause experience. To address these gaps, improvements to clinical management, personalised healthcare, public awareness and policy changes tailored to the different ethnic and religious groups could represent a path towards inclusive and equitable menopause care in Singapore, Asia and beyond.

Ethics statement

Not applicable as there are no study participants.

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: ageing, HRT, menopause, obstetrics and gynaecology, women's health

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Navigating menopause in Singapore: Sociocultural, clinical, and policy implications from a qualitative study (MARIE-Singapore)

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ABSTRACT

Introduction: Menopause is a universal life transition with lived experiences shaped by biological, psychological, sociocultural and systemic factors. In Singapore, where diverse cultural norms intersect with a high-pressure professional environment, little is known about how these influences converge to shape symptom recognition, coping and care.

Methods: This qualitative study formed part of the multi-country MARIE project on menopause and midlife health. Eighteen participants with different menopausal stages were purposively sampled ensuring variation in age, ethnicity, socio-economic status and health status. Semi-structured interviews explored symptom profiles, psychosocial well-being, family and workplace dynamics, and healthcare experiences. Data were analysed

using the Delanerolle and Phiri framework, integrating biological, psychological, sociocultural and health system domains.

Results: Participants described heterogeneous symptom trajectories, with vasomotor, genitourinary and cognitive symptoms as most prominent. Multimorbidity and surgical menopause intensified symptom burden and narrowed treatment options. Anxiety, low mood and brain fog impaired work, particularly without workplace support. Sociocultural silences and misinformation reinforced self-management and delayed care-seeking. Resilience rooted in peer and family support, and culturally familiar coping strategies buffered distress for some. Health system gaps included inconsistent general practitioner's knowledge, reluctance to prescribe hormone therapy and private care costs. Study participation itself triggered symptom

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Accepted: 29 December 2025

Published Online First: 16 January 2026

recognition and help-seeking in some, underscoring menopause invisibility in routine care.

Conclusion: Findings highlight that menopause in Singapore is navigated through intersecting clinical, cultural and structural determinants. Addressing inequities requires embedding women's voices into clinical pathways, training clinicians in culturally competent care, and implementing workplace and public health policies that legitimise menopause as a health and occupational issue.

Keywords: family medicine, induced menopause, medical menopause, menopause, natural menopause, obstetrics and gynaecology, perimenopause, post-menopause, surgical menopause, women's health

CLINICAL IMPACT

What is New

- To our knowledge, this study provides the first qualitative account of Singapore women's menopause experiences, highlighting how cultural silence, lack of information and occupational stress influence the symptom trajectory and engagement with healthcare.
- Systemic gaps identified included variable clinician expertise, reluctance to start hormone therapy and financial costs, which reflect the need for integrated, accessible and evidence-based menopausal care.

Clinical Implications

- The systemic and cultural nuances around menopause are major contributors to delayed recognition and management.
- Standardised clinical training and evidence-based menopause care pathways, sensitised to cultural beliefs and practices, are needed to reduce practice variation and improve quality of care. Integrating these into occupational and public health frameworks will enhance symptom management and improve health equity.

INTRODUCTION

Menopause is a universal life transition in women, marking the end of reproductive capacity through the permanent cessation of menstruation. Globally, the age of natural menopause ranges between 45 and 55 years, with ethnic and geographic variations.^{1,2} While vasomotor symptoms (VMS), sleep disturbance, mood changes and genitourinary problems are widely recognised, their intensity and impact are mediated by intersecting determinants, such as comorbidities, cultural beliefs, occupational settings and health system responsiveness.^{3,4}

Singapore, as a high-income nation with advanced healthcare infrastructure, presents a unique context for exploring these issues.⁵ Its rapidly shifting demographics and multi-ethnic population comprising Chinese, Malay, Indian and Others bring diverse cultural and religious beliefs influencing perceptions of health, ageing and gender roles. Asian perspective of menopause either as a natural process requiring minimal intervention or as a stigmatised marker of ageing and diminished femininity introduces reluctance in discussing symptoms, particularly sexual health, reinforcing silence within families, workplaces and clinical settings.^{6,7}

Clinical pathways for menopause care in Singapore reflect broader global trends of fragmentation and under-recognition. Although specialist services exist, they are not widely utilised, with primary care often serving as the first point of contact. General practitioners (GPs), however, may lack familiarity and confidence in diagnosing and managing menopause. Historical concerns about cancer risk fuel caution and reluctance in prescribing hormonal therapy, despite evolving evidence regarding its safety and effectiveness in appropriate populations.⁸

The intersection of medical comorbidities and menopause introduces an additional layer of complexity.³ Chronic conditions such as hypertension, diabetes, autoimmune disorders and neurological diseases are increasingly prevalent among midlife women in Singapore, in line with global non-communicable disease trends.⁹ Menopause both influences and is influenced by these, altering symptom expression, treatment decisions and care pathways. Surgical or medically induced menopause, particularly in cancer survivors, intensifies the symptom burden, with clinical encounters complicated by treatment contraindications and absence of tailored, integrated care models.¹⁰

Despite these challenges, women's resilience remains a critical mediating factor. Coping strategies rooted in spirituality, exercise, social networks and reframing menopause as a natural life stage buffer distress and foster adaptation.¹¹ However, resilience is unevenly distributed and mediated by socio-economic position, cultural context and access to supportive environments.

Empirical data capturing the lived experiences of Singapore women remain scarce, particularly qualitative accounts that illuminate how symptoms, cultural norms and systemic structures converge. Addressing this gap, the present study employs an equity-oriented qualitative framework to examine the multifaceted experiences of perimenopause, menopause and post-menopause in Singapore. By embedding women's voices into the evidence base, this study aimed to inform clinical practice, workplace strategies and policy interventions that can collectively reduce disparities and improve health outcomes.

METHODS

Study design

This qualitative study formed part of a larger multi-country study of menopause and midlife health called the Menopause and Ageing Research in International Environments – Work Package 2A (MARIE WP2A) with the Singapore arm focusing on lived experiences of individuals undergoing perimenopause, menopause and post-menopause in Singapore. A qualitative design was selected to capture nuanced, in-depth accounts of symptom experiences, healthcare interactions and sociocultural contexts that cannot be adequately represented through quantitative methods.

Sampling and recruitment

Participants were recruited purposively to capture heterogeneity across age, menopausal stage, socio-economic position, ethnicity and healthcare access. Eligibility criteria included: (1) age 18–99 years; (2) self-identifying as experiencing perimenopause, menopause or post-menopause—natural, surgical or medically induced; and (3) Singapore resident for at least 12 months. Exclusion criteria comprised inability to communicate in English or cognitive impairment precluding informed consent. Recruitment was mainly from clinics in a tertiary hospital with some from community networks. Informed consent, outlining the study purpose, voluntary nature and confidentiality assurance was obtained electronically before each interview. In total, 18 participants were interviewed.

Data collection

Semi-structured interviews were conducted between March and May 2025 by trained qualitative researchers with a background in women's health. Interviews took place via secure videoconferencing on Microsoft Teams platform, lasting 45–90 minutes. An interview guide, co-developed with clinical experts and individuals with lived experiences explored biological symptoms, psychological well-being, sociocultural influences and healthcare experiences. The guide allowed flexibility to probe emergent issues in depth. All interviews were audio-recorded and transcribed verbatim by professional transcribers. Identifying details were removed from transcripts and participants were assigned unique identifiers. Quotes used were anonymised. Reflexive field notes documented contextual factors, non-verbal cues and researcher reflections.

Analytical framework

For analysis, the Delanerolle and Phiri framework,¹² a structured model incorporating 4 interrelated domains of biological, psychological, sociocultural and health system enabling systematic exploration of symptom

profiles and care experiences was used alongside Braun and Clarke's 6-step thematic analysis. Analysis proceeded in 4 stages, as described in Table 1.

Coding was conducted inductively within each domain and iteratively refined to capture both unique and recurrent experiences. Two researchers independently coded an initial subset of transcripts and subsequently discussed code application, domain mapping and thematic saturation. Discrepancies were resolved, ensuring reflexivity and analytic consensus.

Reflexivity and positionality

The research team comprised clinicians, public health scientists and patient partners, with diverse professional and personal experiences of menopause. This positionality informed data interpretation while being critically examined throughout the analytic process. Reflexive discussions addressed potential biases, particularly regarding symptom prioritisation, interpretations of healthcare encounters and cultural framing of menopause.

The study received ethical approval from SingHealth Centralised Institutional Review Board (CIRB 2024/2126). All procedures were conducted in accordance with the Declaration of Helsinki and reported following the Consolidated Criteria for Reporting Qualitative Research (COREQ) guidelines. Participants provided informed consent electronically prior to participation. Data were anonymised and securely stored on encrypted servers with restricted access to ensure confidentiality.

RESULTS

Analysis of 18 in-depth interviews (Table 2 with participant characteristics) revealed diverse menopausal trajectories shaped by biological, psychological, socio-cultural and health system factors, with substantial variation in symptom severity and comorbidities. While some participants reported minimal disruption, others experienced multi-domain impact that significantly affected daily functioning, relationships and occupational capacity.

Cross-cutting themes (Table 3), such as comorbidity intersections, delayed symptom recognition, and the moderating effect of resilience and social support, recurred across domains.

Biological domain

Vasomotor and sleep disturbance

VMS ranged from absent or mild (participant identification number [PID]: PID3, PID4, PID17) to severe, sleep-disrupting episodes (PID 1, PID6, PID9, PID10). Night-time hot flushes were particularly problematic, often fragmenting sleep and compounding overall fatigue. In some cases, workplace productivity

Table 1. Four-stage analytical process using the Delanerolle and Phiri¹² framework.

Stage	Description	Key outputs
1. Contextual familiarisation	Immersion in transcripts to understand participants' social, cultural and structural contexts, noting relevant personal histories and intersectional determinants influencing menopausal experiences.	Reflexive notes; preliminary contextual profiles for each participant.
2. Equity-oriented coding	Generation of initial descriptive and interpretive codes reflecting both symptom experiences and equity-linked determinants ^a (e.g. gender norms, healthcare access, socio-economic position, intersecting marginalisations).	Code list with definitions; coding framework incorporating equity dimensions.
3. Framework mapping	Organisation of codes into the 4 domains of the Delanerolle and Phiri framework ^b —biological, ^c psychological, ^d sociocultural, ^e health system ^f —while retaining cross-cutting concepts such as stigma, intersectionality ^g and structural inequality. ^h	Mapped framework with domain-specific subthemes; visual thematic schema. ⁱ
4. Integrative interpretation	Synthesis of patterns within and across domains to elucidate how individual narratives intersect with systemic and structural determinants, generating a coherent analytic storyline.	Thematic narratives; integrated domain-level findings; evidence-informed interpretations.

^a Equity-linked determinants: Socio-economic status, geographic location, cultural beliefs, healthcare access and marginalisation that influence menopausal experiences and outcomes.

^b Delanerolle and Phiri framework: An equity-oriented analytical model that organises findings across 4 domains—biological, psychological, sociocultural and health system—to understand how personal experiences intersect with structural determinants.

^c Biological domain: Includes physiological changes, symptoms, hormonal influences, reproductive history and medical conditions relevant to menopause.

^d Psychological domain: Refers to emotional health, cognitive responses, coping mechanisms, stress and mental well-being.

^e Sociocultural domain: Encompasses social norms, cultural expectations, gender roles, family and community influences, stigma and lived experience.

^f Health system domain: Covers access to healthcare services, service availability, provider communication, referral pathways and barriers within health systems.

^g Intersectionality: The layered interaction of multiple identities (e.g. gender, age, class, marital status) and structural forces that create cumulative disadvantage.

^h Structural inequality: Systemic and institutional barriers that limit equitable access to healthcare, resources and opportunities.

ⁱ Thematic schema: A visual or conceptual map that organises themes and subthemes to illustrate relationships across domains.

and emotional regulation were adversely affected, with participants adopting cooling strategies, evening showers and in rare cases, hormone replacement therapy (HRT), to mitigate symptoms.

"Suddenly I used to wake up with lots of sweat... sometimes for few hours I was not able to sleep." (PID9)

"Turn on the fan and aircon at the same time in order to sleep." (PID1)

Several participants (PID10, PID14) developed or worsened VMS years after their final menstrual period, highlighting variability in onset and the potential for late-emerging needs.

Musculoskeletal (MSK) and bone health

MSK pain and bone density changes were frequent but variably attributed to menopause. In some, MSK pain was the sentinel symptom prompting HRT initiation (PID7), leading to rapid and sustained resolution. Others linked aches to comorbidities such as osteoarthritis (PID16) or previous injuries (PID5), while dualenergy x-ray absorptiometry (DEXA) scan -confirmed osteopenia in PID1 and PID7 underscored the role of oestrogen in bone health.

"Hip pain... very deep-seated... nothing was helping... went away after HRT." (PID7)

"DEXA... still osteopenic... trying to get it up." (PID1)

Weight-bearing exercise and physiotherapy were effective non-pharmacological strategies, though awareness of menopause-bone health links was inconsistent.

Genitourinary and sexual health

Genitourinary syndrome of menopause (GSM) emerged as one of the most consistent burdens across surgical and natural menopause cases. Symptoms included vaginal dryness, dyspareunia, urinary urgency and recurrent infections (PID1, PID6, PID9, PID16). Some experienced marked improvement with topical oestrogen or tibolone (PID10, PID16), while others faced treatment intolerance or contraindication due to cancer history (PID2, PID8).

"It was very uncomfortable even when I just touch that area... painful because it was so dry." (PID1)

"The dryness is like... a magic pill...gone [after tibolone]." (PID16)

Under-recognition of urinary and bladder symptoms as menopause-related delayed appropriate care, particularly among those without prior menopause education.

Metabolic and endocrine interactions

Midlife metabolic shifts were reported, with several participants identifying hypercholesterolaemia (PID1)

Table 2. The participant characteristics of the qualitative data sample.

PID	Age, years	Menopause type	Years since menopause onset	Parity	Key comorbidities	HRT use	Notable symptom profile	Employment status
1	59	Natural	~9	2	Brain tumour, neurological sequelae, osteopenia, hypercholesterolaemia	Yes	Severe GSM, vasomotor, mood disturbance, MSK pain	Consultant/ university educator
2	66	Surgical (hysterectomy + BSO) for uterine cancer	9	4	Cancer history	No	Excessive perspiration, prolapse, late mood symptoms	Part-time sales
3	56	Natural	6	1	No major comorbidities	No	Minimal symptoms, back pain (non-menopause related)	Active employment
4	60	Natural	10	2	Type 2 diabetes	No	Minimal symptoms, occasional joint discomfort	Nurse
5	49	Surgical (subtotal hysterectomy)	NA (ovaries intact)	2	Thyroid cancer	No	Hot flushes, GSM, MSK pain	Not specified
6	56	Natural	2–3	Not specified	No major comorbidities	Yes	Severe vasomotor, GSM, insomnia, mood disturbance	Gynaecologist
7	52	Perimenopause/HRT use	NA	Not specified	Osteopenia	Yes	Severe MSK pain, fatigue	Gynaecologist
8	47	Surgical (hysterectomy + BSO) for ovarian cancer	1	Not specified	Cancer history	No	GSM, hot flushes, sleep disturbance	Not specified
9	53	Natural	3	Not specified	No major comorbidities	No	Nocturnal vasomotor, insomnia, mood change	Former senior bank manager
10	52	Natural	NA	2	SLE	No	Night hot flushes, GSM, skin dryness	Not specified
11	50	Perimenopause	NA	2	ADHD	No	Mood disturbance, sleep disruption, night flushes	Freelance carer
12	57	Natural	5	Not specified	Parkinson's disease	No	Minimal symptoms, mild fatigue	Doctor
13	45	Perimenopause	NA	Not specified	ADHD, hypertension	Yes	Mood/cognitive decline, GSM, fatigue	Not specified
14	61	Natural	7–8	Not specified	Hypertension, diabetes, hypercholesterolaemia	No	Late-onset vasomotor, pruritus, MSK pain	Healthcare worker
15	51	Natural	~5	3	Allergy to topical oestrogen	No	Mild GSM, occasional vasomotor, mood change	Healthcare worker
16	51	Natural	~5	2	Hypertension, hyperlipidaemia pre-diabetes, asthma	Yes	GSM, cognitive change, MSK pain	Administrative worker
17	59	Surgical (hysterectomy) for cancer	6	0	Cancer history	No	Minimal symptoms	Not specified
18	49	Surgical (hysterectomy + BSO) for fibroids	<1	0	No major comorbidities	Yes	GSM, cognitive change, MSK pain	Investment consultant

ADHD: attention deficit/hyperactivity disorder; BSO: bilateral salpingo-oophorectomy; GSM: genitourinary syndrome of menopause; HRT: hormone replacement therapy; MSK: musculoskeletal; NA: not applicable/not available; PID: participant identification number; SLE: systemic lupus erythematosus

Table 3. Thematic table which includes sub-themes, exposures, determinants and practice implications.

Domain	Sub-themes	Exposures	Determinants	Practice implications
Biological	Vasomotor disturbance and sleep disruption	Night sweats, hot flushes, fragmented sleep	Hormonal decline, late-onset vasomotor symptoms, comorbid insomnia	Embed menopause screening into primary care; develop tailored sleep and vasomotor management pathways.
	Musculoskeletal and bone health	Joint pain, osteopenia/osteoporosis, mobility limitations	Oestrogen deficiency, multimorbidity (osteoporosis, arthritis), low awareness of bone health link	Integrate menopause into chronic disease management; routine bone health monitoring.
	Genitourinary and sexual health (GSM)	Vaginal dryness, dyspareunia, urinary urgency	Oestrogen decline, surgical menopause, treatment contraindications (cancer)	Expand access to local oestrogen therapies; train clinicians to proactively address GSM; normalise sexual health in consultations.
	Metabolic and endocrine changes	Hypercholesterolaemia, pre-diabetes	Midlife metabolic transition, multimorbidity	Link menopause care with metabolic disease prevention; lifestyle counselling alongside symptom management.
Psychological	Mood disturbance and anxiety	Irritability, intrusive thoughts, withdrawal	Hormonal fluctuations, work stress, family strain, ADHD/neurodiversity	Integrate mental health support within menopause care; normalise mood symptoms in consultations.
	Cognitive change (brain fog)	Forgetfulness, reduced concentration	Hormonal shifts, occupational stress, ageing stigma	Provide workplace adjustments (flexible deadlines, memory aids); clinician training to distinguish cognitive ageing versus menopause.
	Coping and resilience	Exercise, mindfulness, reframing menopause	Health literacy, supportive networks, socio-economic resources	Build resilience programmes into workplace and community interventions; leverage digital peer support tools.
Socio-cultural	Family and interpersonal dynamics	Reduced intimacy, spousal withdrawal, supportive partners	GSM, stigma around ageing/sexuality, cultural silence	Couple-based counselling; culturally sensitive education for families.
	Peer influence and misinformation	HRT cancer myths, reliance on friends' advice	Lack of public health messaging, cultural conservatism	Launch multilingual, evidence-based campaigns; regulate health misinformation in media.
	Stigma and silence	Reluctance to disclose, avoidance of clinical help	Cultural taboos on ageing/sexuality, gendered expectations	Normalise menopause conversations in schools, workplaces and community groups.
Health system	Access and care pathways	Public/private divide, prohibitive costs	Unequal insurance coverage, socio-economic status	Subsidise menopause care; ensure equitable public access to HRT and counselling.
	Clinical knowledge and attitudes	GP reluctance to prescribe HRT, dismissal of symptoms	Limited training, persistent "hormone phobia"	Introduce menopause modules in medical education; upskill GPs and non-specialists.
	Continuity and integration	Fragmented provision, lack of integrated multimorbidity care	Biomedical silos, absence of structured pathways	Develop 1-stop menopause clinics; embed care in chronic disease management.
	Trigger points for care-seeking	Participation in MARIE survey prompted recognition	Systemic invisibility of menopause in screening	Introduce structured menopause screening tools in primary care and occupational health.

ADHD: attention deficit/hyperactivity disorder; GP: general practitioner; GSM: genitourinary syndrome of menopause; HRT: hormone replacement therapy; MARIE: Menopause and Ageing Research in International Environments

or pre-diabetes (PID16) during routine checks. In cancer survivors (PID5, PID8), endocrine therapy confounded symptom attribution, complicating management. Surgical menopause in oncology patients amplified systemic effects, with rapid oestrogen withdrawal producing intense but sometimes unrecognised symptom clusters.

Cross-cutting biological theme: Comorbidity interaction

Across cases, comorbidities such as autoimmune disease (PID10), Parkinson's disease (PID12), attention deficit/hyperactivity disorder (PID11, PID13) and cancer survivorship (PID2, PID5, PID8, PID17) intersected with menopause to influence symptom profile, care-seeking and management options. These intersections required nuanced clinical assessment but were frequently overlooked.

Psychological domain

Mood disturbance and emotional regulation

Mood changes ranged from mild irritability (PID4, PID15) to severe, prolonged low mood with anxiety and intrusive thoughts (PID1, PID11, PID6). For some, symptoms were cyclical, intensifying during perimenopause (PID13). Interpersonal strain, particularly within families, was common, leading to social and emotional withdrawal as a coping mechanism (PID11).

"Small thing would just trigger me... now it can last for days." (PID11)

"I became anxious... bothersome thoughts... I could not cope as well as before." (PID1)

HRT improved mood stability in those able to access it (PID13, PID18), while others relied on meditation (PID8, PID17) or lifestyle-based strategies.

Cognitive change

Brain fog, forgetfulness and reduced concentration were widely reported (PID1, PID9, PID13, PID16, PID18). These symptoms affected work performance and confidence, prompting compensatory strategies such as note-taking, mental exercises and mindfulness.

"I could quite easily forget within 5 minutes..." (PID18)

"I can be in the middle of sharing something, and I forgot why..." (PID16)

Cognitive impacts were often normalised or attributed to ageing, delaying targeted intervention.

Coping and resilience

Adaptive coping mechanisms included reframing menopause as a natural life stage (PID15), keeping

physically and socially active (PID3, PID15), and spiritual practices (PID4, PID17). Resilience was bolstered by supportive peer or family networks, professional health literacy and workplace flexibility.

Cross-cutting psychological theme: Professional paradox

Healthcare professionals (PID6, PID7, PID12) sometimes delayed their own menopause care despite high knowledge levels, reflecting cultural "hormone phobia," time constraints and occupational role expectations.

Sociocultural domain

Family and interpersonal relationships

Menopause altered family dynamics for many. Spousal withdrawal (PID1) and reduced intimacy linked to GSM (PID9, PID16) affected emotional well-being, while others described understanding and accommodation from partners and children (PID2, PID3).

"Husband... withdrew... kids... told to steer clear of mum." (PID1)

"They just... keep quiet." (PID2)

Peer influence and social narratives

Peers were both sources of misinformation (PID1, PID13) and support (PID4, PID15). Cancer myths about HRT persisted, deterring uptake even in eligible women. Workplace cultures ranged from silence to active engagement through education programmes (PID18).

"Friends... said HRT could be... cancer inducing." (PID1)

Stigma and silence

Participants repeatedly noted the absence of open conversation about menopause (PID13, PID14, PID18). Cultural conservatism and fear of ageing reinforced reluctance to disclose symptoms, especially sexual health concerns.

"People still... don't want to talk about it." (PID13)

"Some people... don't accept the fact they are going through menopause." (PID14)

Cross-cutting sociocultural theme: Community gaps and opportunities

The absence of peer-support groups (PID11) and culturally adapted educational campaigns (PID18) limited collective learning and normalisation. Suggestions included discreet WhatsApp groups, school-based education and leveraging Asian heritage influencers.

Health system domain

Access and pathways

Access varied sharply between public and private sectors. Some had a long-term trusted relationship with their GP (PID9), while others avoided public services anticipating delays or dismissal (PID13). Public specialist services were valued for their comprehensiveness and patient-centred approach (PID18), whereas private care was sometimes seen as commercially driven with less menopause expertise.

"Private... knowledge was very lacking... commercial." (PID18)

"I had to spend a lot of money to go through the private system." (PID13)

Clinical knowledge and attitudes

Participants identified pervasive knowledge gaps among GPs and non-specialists, including normalisation of heavy bleeding (PID1), symptom dismissal (PID2, PID16) and reluctance to prescribe HRT (PID7, PID13). Even in healthcare settings, women reported being questioned about the necessity and duration of HRT.

"Doctors are not trained...they don't know how to prescribe hormone therapy." (PID7)

"The first thing they say is, 'Why are you on it? When are you going to get off it?'" (PID13)

Continuity and integration of care

Positive experiences occurred where continuity existed, such as ongoing GP or specialist relationships (PID9, PID12). Integration of menopause care into chronic disease management was rare but proposed by participants with multimorbidity (PID10, PID16).

Cross-cutting health system theme: Trigger points for care-seeking

Participation in the MARIE survey prompted self-recognition of symptom burden and subsequent help-seeking for several participants (PID6, PID10). This underscores the potential for structured screening tools to act as entry points into care.

Cross-cutting themes narrative: Intersectionality of health status and menopause

Menopause experiences were profoundly shaped by pre-existing health conditions and surgical histories. Autoimmune disorders (PID10), neurological conditions (PID1, PID12, PID13), chronic metabolic disease (PID14, PID16) and cancer survivorship (PID2, PID5, PID8, PID17) altered symptom expression, complicated assessment and limited treatment options. Surgical menopause cases described more abrupt symptom

onset and higher GSM prevalence, though symptom severity varied widely. For many, multimorbidity necessitated integrated care approaches, yet most described fragmented provision (Fig. 1). This intersectional complexity underscores the importance of holistic assessment, where menopause is neither overshadowed by nor isolated from other health conditions.

Resilience as a mediating factor

Personal resilience rooted in health literacy, professional knowledge, coping strategies and supportive social networks significantly moderated symptom burden. Participants with strong partner or workplace support (PID2, PID3, PID15, PID18) reported greater adaptability, even in the face of moderate-to-severe symptoms. Coping mechanisms included structured exercise, mindfulness, reframing menopause as a natural life stage and leveraging peer connections. Workplace-led initiatives (PID16, PID18) and culturally aligned self-care practices (PID8, PID17) provided further buffers. However, resilience was unevenly distributed, with women lacking such resources experiencing greater distress, thus reinforcing existing inequities.

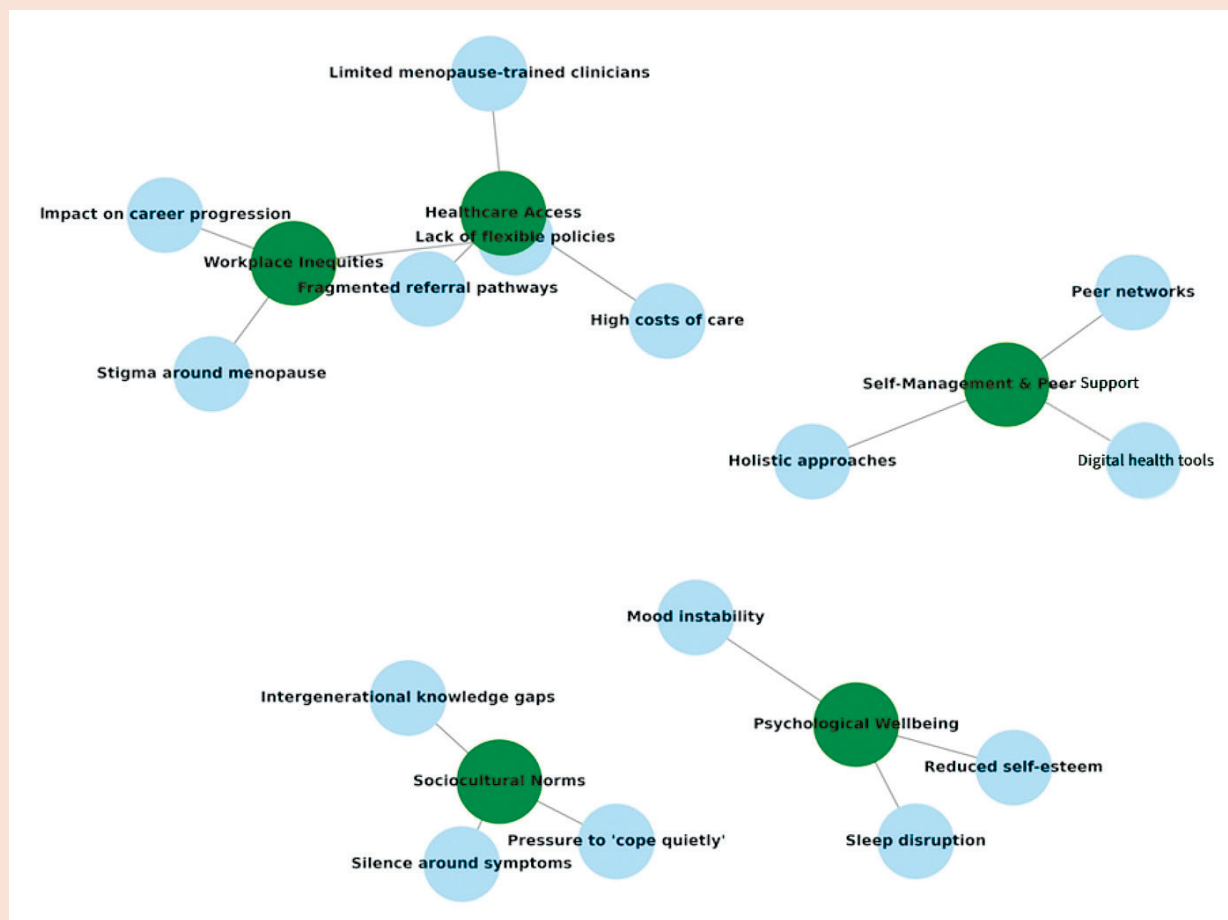
Systemic and cultural silence

Across cases, both institutional and societal silence acted as a structural determinant of delayed recognition and management, fostering reliance on self-navigation and amplifying disparities for those without the means or confidence to advocate for themselves. Cultural conservatism and stigma (PID13, PID14, PID18) limited discussion of sexual health and emotional changes. In healthcare settings, undertrained clinicians often normalised symptoms or dismissed hormonal contributions (PID1, PID2, PID16), leading to missed intervention opportunities. Service invisibility compounded these gaps, with several participants unaware of specialist menopause services (PID10, PID11). This silence extended to workplaces, where only a minority experienced formal menopause policy support.

DISCUSSION

The qualitative analysis of Singapore participants in the MARIE WP2A study revealed a complex interplay between workplace inequities, healthcare access barriers, sociocultural norms, psychological well-being and self-management strategies. Participants described how menopausal symptoms such as vasomotor, cognitive and psychological disturbances intersected with professional responsibilities in high-pressure environments. Stigma and silence, both in professional and social settings, were recurrent threads, influencing not only help-seeking behaviours

Fig. 1. Thematic map presenting key themes and sub-themes identified from the qualitative analysis of Singapore participants in the MARIE WP2A study. Main themes are represented in green, and subthemes in blue, illustrating the relationships between broader domains and specific lived experiences.



but also perceptions of legitimacy regarding symptoms. Thematic connections illustrated a fragmented care landscape in which specialist availability was not well known, costs were prohibitive for some and referral pathways were inconsistent. These dynamics reinforced reliance on informal networks and self-care approaches, particularly digital tools and peer support, which partially mitigated but did not eliminate the cumulative impact on quality of life.

Importantly, several of the barriers described by the Singapore participants—fragmented pathways, uncertainty about specialist access and reliance on informal networks—resonate with challenges documented in lower- and middle-income countries (LMICs), though shaped by different resource contexts. In many LMIC settings, limited formulary availability, unstable supply chains and high out-of-pocket costs restrict access to HRT, while gaps in clinical training and persistent misconceptions further constrain prescribing and help-seeking. These patterns parallel the stigma, silence and informational inequities evi-

dent in the Singapore cohort, suggesting common structural drivers operating at different intensities. Recognising these cross-contextual dynamics is essential for designing equitable, culturally sensitive strategies to strengthen menopausal care across diverse health systems.^{13,14}

Population insights

Singapore's population is characterised by a unique multicultural composition, comprising primarily Chinese, Malay and Indian communities, alongside a smaller proportion of Eurasian and other ethnic groups. This diversity is further shaped by a sizeable expatriate population, adding to the mosaic of languages, cultural norms and health beliefs. Such heterogeneity has profound implications for menopausal care. Health-seeking behaviours, perceptions of menopause, and openness in discussing symptoms are influenced by culturally embedded values—ranging from the Chinese emphasis on balance and traditional medicine, to Malay and Indian norms around modesty

and intergenerational respect. The participant experiences in this study reflected these intersections: some women preferred holistic and herbal approaches rooted in cultural tradition, others prioritised privacy over disclosure even to clinicians, and many highlighted the role of family dynamics in shaping their coping strategies. Tailored interventions that are linguistically accessible, respectful of religious and cultural sensitivities, and inclusive of both biomedical and culturally familiar therapies are essential if care pathways are to be both effective and equitable.

Clinical impact

The lived experiences described by the Singapore participants highlight a need for embedding women's narratives into clinical pathways and co-designing clinical guidelines with patients. Menopause care cannot be effectively delivered if it is narrowly defined through biomedical parameters alone; it must also integrate an understanding of the psychosocial and occupational realities patients face.¹⁵ Lack of alignment of treatment options for menopausal and perimenopausal women among healthcare providers leaves women confused and turning to informal networks for information.¹⁶ Lack of clinician education on appropriate treatment for menopausal symptoms as well as lack of empathy for women's suffering highlight a need for training not only in the pharmacological and non-pharmacological management of symptoms but also in culturally competent communication that addresses stigma and normalises open discussion.¹⁷ Standard consultations should incorporate space for exploring work-related impacts, sleep disturbance and sexual health, while acknowledging patients' own strategies for symptom control.

While the MARIE Singapore sample was predominantly highly educated, this reflects the sociodemographic composition of urban recruitment sites rather than a methodological limitation. Evidence from MARIE studies across multiple countries shows that core menopause experiences—such as symptom misrecognition, delays in care, stigma and unmet needs—are consistent across education levels, with differences largely in intensity rather than type. Health-seeking behaviours observed in this cohort reflect structural factors in Singapore, including access to MediSave/MediShield (mandatory personal medical savings account and national health insurance plan in Singapore), employer benefits and time availability. The persistence of unmet needs among highly educated, health-literate women suggests that women with fewer structural advantages would likely face greater challenges. These observations support the transferability of our thematic findings while highlighting the amplified inequalities experienced by less-resourced populations.

Policy impact

To optimise menopause care in Singapore, policy attention is needed on 3 fronts: workplace regulation, healthcare provision and public health education. Singapore currently ranks first in Asia-Pacific for having a low level of gender inequality with more women participating in the workforce including leadership roles. To complement progress in providing women with equal opportunities in the workplace, financial support for caregivers, and protection against violence and online harms, there is now a need to acknowledge menopause as a legitimate occupational health issue. Introducing workplace accommodations, such as temperature control, flexible hours and protected health disclosures, will support women in workforce going through menopause.^{18,19} This is especially important as Singapore faces a shrinking birth rate and should be encouraging more older workers to continue working.²⁰

On the aspect of healthcare, incorporating menopause management into healthcare subsidies similar to Singapore's Community Health Assist Scheme, and allowing increased insurance coverage will reduce cost and improve access to care.²¹

Public health campaigns, delivered in multiple languages and tailored to different ethnic and religious groups, would help dismantle stigma and equip women with accurate, culturally relevant information. By aligning policy with clinical realities and population needs, Singapore can set a precedent for equitable and inclusive menopause care. We have clarified when statements reflect participant narratives versus established evidence, ensuring that qualitative findings are interpreted without implying causality. These insights contextualised alongside quantitative literature, highlight how lived experiences complement, refine or occasionally challenge existing knowledge on menopause symptoms and health-seeking behaviours. Recommendations are framed as practice- and policy-relevant implications grounded in participants' experiences, rather than as generalised statistical claims, thereby preserving the interpretive validity of the study.

Limitations

The study has several important strengths, and we also acknowledge its limitations. Recruitment primarily via a tertiary hospital may bias the sample toward health-literate individuals, and conducting interviews exclusively in English may exclude some non-English-speaking populations, thereby limiting the transferability of findings. We acknowledge that language and sampling choices may influence this. In Singapore, however, English is the primary language of healthcare delivery, patient information, clinical consultation

and most health system interactions. The decision to conduct interviews in English was therefore taken to ensure conceptual precision and avoid loss of meaning during translation, particularly when describing symptoms and interactions with the healthcare system. Nonetheless, these constraints may reduce representativeness and the applicability of themes across less-resourced or non-English-speaking communities. While qualitative research does not seek statistical generalisability, it aims for analytic transferability. Future research should therefore incorporate community-based recruitment and multilingual data collection to enhance contextual diversity and transferability. To address this issue, the MARIE project, Work Package 2B, incorporates community-level recruitment strategies specifically designed to reach women with lower socio-economic status, limited English proficiency and reduced access to healthcare.

CONCLUSION

This study demonstrates that menopause in Singapore is not solely a biological event, but an experience profoundly shaped by intersecting cultural norms, workplace environments, healthcare pathways and individual resilience. While some women navigated the transition with minimal disruption, others experienced multi-domain burdens that compromised health, relationships and occupational performance. The persistence of stigma and silence within families, communities and health systems was a critical determinant of delayed recognition and inadequate support.

Policy innovation will help normalise menopause in workplaces, reduce financial barriers to treatment and deliver multilingual, culturally sensitive public health education. Embedding resilience-building strategies and ensuring inclusive, equitable care could transform menopause from a silent struggle into a supported life-course transition.

Ethics statement

The study received ethical approval from SingHealth Centralised Institutional Review Board (CIRB 2024/2126). All procedures were conducted in accordance with the Declaration of Helsinki and reported following the COREQ guidelines. Participants provided informed consent electronically prior to participation.

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.

Acknowledgements

MARIE Consortium: Om Kurmi, Donatella Fontana, Aini Hanan binti Azmi, Alyani binti Mohamad Mohsin, Arinze Anthony Onwuegbuna, Artini binti Abidin, Ayyuba Rabi, Chijioke Chimbo, Chinedu Onwuka Ndukwe, Choon-Moy Ho, Chinyere Ukamaka Onubogu, Diana Chin-Lau Suk, Divinefavour Echezona Malachy, Emmanuel Chukwubikem Egwuatu, Eunice Yien-Mei Sim, Farhawa binti Zamri, Fatin Imtithal binti Adnan, Geok-Sim Lim, Halima Bashir Muhammad, Ifeoma Bessie Enweani-Nwokelo, Ikechukwu Innocent Mbachu, Jinn-Yinn Phang, John Yen-Sing Lee, Joseph Ifeanyichukwu Ikechebelu, Juhaida binti Jaafar, Karen Christelle, Kathryn Elliot, Kim-Yen Lee, Kingsley Chidiebere Nwaogu, Lee-Leong Wong, Lydia Ijeoma Eleje, Min-Huang Ngu, Noorhazliza binti Abdul Patah, Nor Fareshah binti Mohd Nasir, Norhazura binti Hamdan, Nnanyelugo Chima Ezeora, Nnaedozie Paul Obiegbu, Nurfauzani binti Ibrahim, Nurul Amalina Jaafar, Odigonma Zinobia Ikpeze, Obinna Kenneth Nnabuchi, Pooja Lama, Puong-Rui Lau, Rakshya Parajuli, Rakesh Swarnakar, Raphael Ugochukwu Chikezie, Rosdina Abd Kahar, Safilah Binti Dahian, Sapana Amatya, Sing-Yew Ting, Siti Nurul Aiman, Sunday Onyemaechi Orij, Susan Chen-Ling Lo, Sylvester Onuegbunam Nweze, Damayanthi Dassanayake, Nimesha Wijayamuni, Prasanna Herath, Thamudi Sundarapperuma, Vaitheswari Rao, Xin-Sheng Wong, Xiu-Sing Wong, Yee-Theng Lau, Heitor Cavalini, Jean Pierre Gafaranga, Emmanuel Habimana, Chigozie Geoffrey Okafor, Assumpta Chiemeka Osunkwo, Gabriel Chidera Edeh, Esther Ogechi John, Kenechukwu Ezekwesili Obi, Oludolamu Oluyemesi Adedayo, Odili Aloysius Okoye, Chukwuemeka Chukwubikem Okoro, Ugoy Sonia Ogbonna, Chinelo Onuegbuna Okoye, Babatunde Rufus Kumuyi, Onyebuchi Lynda Ngozi, Nnenna Josephine Egbonnaji, Oluwasegun Ajala Akanni, Perpetua Kelechi Enyinna, Yusuf Alfa, Theresa Nneoma Otis, Catherine Larko Narh Menka, Kwasi Eba Polley, Isaac Lartey Narh, Bernard B. Borteh, Andy Fairclough, Kingsley Emeka Ekwuazi, Michael Nnaa Otis, Jeremy Van Vlymen, Chidiebere Agbo, Francis Chibuike Anigwe, Kingsley Chukwuebuka Agu, Chiamaka Perpetua Chidozie, Chidimma Judith Anyaeche, Clementine Kanazayire, Jean Damascene Hanyurwimfura, Nwankwo Helen Chinwe, Stella Matutina Isingizwe, Jean Marie Vianney Kabutare, Dorcas Uwimpuhwe, Melanie Maombi, Ange Kantarama, Uchechukwu Kevin Nwanna, Benedict Erhite Amalimeh, Theodimir Sebazungu, Elius Tuyisenge, Yvonne Delphine Nsaba Uwera, Emmanuel Habimana, Nasiru Sani, Amarachi Pearl Nkemdirim, Jean Pierre Gafaranga, Bertin Ngororano, Victor Archibon, Ibe Michael Usman, Baraka Godfrey Mwahi, Filbert Francis Ilaza, Zepherine Pembe, Clement Mwabenga, Mpoki Kaminyoghe, Brenda Mdoligo, Thomas Alone Saida,

Nicodemus E. Mwampashi, Olisaemeka Nnaedozie Okonkwo, Bethel Chinonso Okemeziem, Bethel Nnaemeka Uwakwe, Goodnews Ozioma Igboabuchi and Ifeoma Francisca Ndubuisi.

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Recommendations for screening for latent tuberculosis infection in people with rheumatic diseases: Consensus statement from the Singapore Chapter of Rheumatologists

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ABSTRACT

Introduction: Tuberculosis (TB) remains endemic in Asia, with latent TB infection (LTBI) being prevalent, especially among older adults. People with rheumatic diseases (PRD) who are treated with tumour necrosis factor-alpha inhibitors (TNF-I) are at increased risk of TB reactivation, prompting a strong recommendation for screening and treatment of LTBI prior to initiating TNF-I. However, the need for screening before starting non-TNF-I immunosuppressive agents remains unclear. This consensus statement from Chapter of Rheumatologists, College of Physicians, Academy of Medicine, Singapore, offers recommendations on LTBI screening before initiating non-TNF-I immunosuppressive agents, and the need for repeat LTBI testing in patients on TNF-I who initially tested negative.

Methods:: Systematic literature reviews were performed to evaluate published guidelines and recommendations for LTBI screening before starting non-TNF-I immunosuppressive agents, and the need for repeat testing for LTBI during TNF-I use. Recommendations were formulated based on the evidence and expert opinion according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology.

Results: The consensus comprises 3 overarching principles and 5 recommendations. We conditionally recommend that LTBI screening should be done before starting tocilizumab, Janus kinase inhibitors and moderate-to-high dose glucocorticoids. Conversely, routine screening need not be performed before starting cyclophosphamide. Annual testing for LTBI need not be performed routinely for patients on TNF-I if initial screening is negative.

Conclusion: These recommendations provide guidance for LTBI screening in PRD. All recommendations in this consensus are conditional, reflecting a lack of evidence or low-level evidence. These will be updated as new evidence emerges.

Keywords: immunosuppression, interferon-gamma release assay, latent tuberculosis infection, rheumatology, testing

CLINICAL IMPACT

What is New

- This is the first national consensus to address latent tuberculosis infection (LTBI) screening prior to initiation of non-tumour necrosis factor-alpha inhibitors (TNF-I) in patients with rheumatic diseases.
- It also clarifies the role of repeat LTBI testing in patients on TNF-I who initially tested negative.

Clinical Implications

- These recommendations will help clinicians make informed decisions on when to screen for LTBI, reducing variability in practice and avoiding unnecessary testing, while ensuring patient safety.
- These recommendations support more efficient use of healthcare resources and may inform institutional protocols and national policy in TB-endemic countries like Singapore.

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Acceptance: 17 December 2025

Published Online First: 31 December 2025

INTRODUCTION

Tuberculosis (TB), caused by the *Mycobacterium tuberculosis* complex, is endemic in Asia. Latent TB infection (LTBI) has a prevalence of 12.7% among Singapore residents,¹ with rates of up to 30% in older age groups.² Studies have consistently shown that people with rheumatic diseases (PRD) with LTBI receiving tumour necrosis factor- α inhibitors (TNF-I) have higher risk of developing active TB when compared with healthy controls, although the rates vary across studies.^{3–5} Hence, most international societies and expert groups recommend screening and treating for LTBI prior to starting TNF-I.^{6–8} However, the evidence for screening and treating prior to treatment with non-TNF-I immunosuppressive agents remains unclear. It is also uncertain whether there is a need for routine repeat (e.g. annual) testing in patients on TNF-I if they initially tested negative. In this consensus statement, the Chapter of Rheumatologists, College of Physicians, Academy of Medicine, Singapore (henceforth called “the Chapter”), sought to address questions regarding the need to screen for LTBI prior to treatment with non-TNF-I immunosuppressive agents—specifically, non-TNF-I biologic disease-modifying antirheumatic drugs (bDMARDs), targeted synthetic disease-modifying antirheumatic drugs (tsDMARDs), high-dose glucocorticoids and cyclophosphamide—as well as the need for routine repeat testing for patients on TNF-I who initially tested negative for LTBI.

METHODS

A core working group (CWG, comprising authors Manjari Lahiri, Kar Mun Chong and Yi Wye Lai) was formed to steer the consensus process. Members of the CWG formulated the research questions and performed a systematic literature review to answer them. The CWG developed draft recommendations for rating by an invited task force panel (TFP). A modified Delphi approach was used. The TFP comprised 10 Singapore-based, recognised adult rheumatologists from public and private healthcare institutions in Singapore, 1 infectious diseases specialist and 1 respiratory medicine specialist with a special interest in TB (i.e. authors Stanley Angkodjojo, Peter Pak Moon Cheung, Li-Ching Chew, Caroline Victoria Choong, Warren Fong, Li Yang Hsu, Weng Giap Law, Mona Manghani, Amelia Santosa, Charlotte Su-Lin Tan, Teck Choon Tan and Gim Gee Teng).

A conflict-of-interest declaration was required from all members of the CWG and TFP prior to the consensus process. Li Yang Hsu received honoraria from QIAGEN Singapore Pte Ltd for a speaking engagement. The other members declared no relevant conflicts of interest.

Literature review

Members of the CWG performed a systematic literature review to answer the following research questions (Fig. 1).

Fig. 1. Research questions.

1. Should people with rheumatic diseases (PRD) be tested for latent tuberculosis infection (LTBI) with an interferon-gamma release assay (IGRA) prior to starting the following non-tumour necrosis factor- α inhibitors (TNF-I) immunosuppressive agents?
 - a. Rituximab
 - b. Interleukin-6-receptor inhibitors (specifically tocilizumab)
 - c. Interleukin-17-inhibitors (specifically secukinumab and ixekizumab)
 - d. Interleukin-12/23-inhibitors (specifically ustekinumab), and interleukin 23 inhibitors (specifically guselkumab and risankizumab)
 - e. Abatacept
 - f. Janus kinase inhibitors (JAKi, specifically tofacitinib, baricitinib, upadacitinib and filgotinib)
 - g. Cyclophosphamide
 - h. Moderate- to high-dose glucocorticoids, and if so, what is the threshold dose and duration of glucocorticoids?
2. For PRD on TNF-I who initially tested negative for LTBI, should annual repeat testing be done routinely?

To review the evidence on LTBI screening in PRD, a systematic review of international best practice guidelines and recommendations from rheumatology, infectious disease, gastroenterology and dermatology societies were reviewed. The authors searched PubMed for publications between 2000 and 2024, using a combination of Medical Subject Headings (MeSH) terms and free text (“Latent Tuberculosis”[MeSH] OR “Tuberculosis”[MeSH] OR “Tuberculosis”) AND (“Immunosuppressive Agents”[MeSH] OR “Antirheumatic Agents”[MeSH] OR “Glucocorticoids”[MeSH] OR “Biologic” OR “DMARD”) AND (“Consensus” [MeSH] OR “Consensus Development Conference, NIH” [Publication Type] OR “Consensus Development Conference” [Publication Type] OR “Guidelines as Topic” [MeSH] OR “Practice Guidelines as Topic” [MeSH] OR “Guideline” [Publication Type] OR “Health Planning Guidelines” [MeSH] OR “Standard of Care” [MeSH] OR “Practice Guideline” [Publication Type] OR “Clinical Protocols” [MeSH]). Article types were limited to “Consensus Development Conference”, “Consensus Development Conference, NIH”, “Guideline” and “Practice Guideline”. The filters “English” (language) and “Humans” were also applied. This search yielded 40 citations. The authors screened through the titles and/or abstracts and excluded those that were duplicates or were outdated recommendations from the same body. They also did a manual search of primary licensing and other landmark drug clinical trials and registries.

Creation of draft statements

The CWG compiled findings from the literature review and formulated draft statements for rating by the TFP through an online survey platform. The Appraisal of Guidelines for Research & Evaluation (AGREE) framework⁹ was used in the formulation of the statements (see Supplementary Material Table S1), and Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology¹⁰ was used for assigning level of evidence and strength of recommendations.

Rating of statements by the task force panel

Consensus was developed using a modified Delphi approach. The TFP was provided with a summary of evidence from the reviewed guidelines, trials and registries. For the first round of voting, the TFP was given a link to an online rating form and detailed instructions for rating via electronic mail. Based on the summarised evidence and their clinical expertise, the TFP independently rated each statement on a 5-point Likert scale (1 = strongly disagree, 2 = disagree, 3 = neutral, 4 = agree, 5 = strongly agree). Consensus was achieved if there was at least 70% agreement (agree or strongly agree) or at least 70% disagreement (disagree or strongly disagree). The CWG and TFP then convened in a hybrid (in-person and online) synchronous meeting. One member of the CWG (Manjari Lahiri) moderated the proceedings. Results from the first round of rating were discussed and areas of uncertainties were clarified. Statements that did not reach consensus were reworded if necessary, and a second round of rating was carried out immediately via an online survey during the meeting. Results from the second round of voting were further discussed.

Finalising consensus statements

The final consensus statement was circulated to the TFP after the consensus meeting, and was approved by all members. Following this, the recommendations were reviewed by the College of Physicians, Singapore, Academy of Medicine Singapore, and the Ministry of Health, Singapore. Revisions were made, where appropriate, based on their input, prior to finalisation.

RESULTS

1. We conditionally recommend testing for LTBI with an IGRA in PRD prior to starting interleukin-6-receptor inhibitors e.g. tocilizumab, over not testing.

The level of evidence is low. The European Society of Clinical Microbiology and Infectious Diseases¹¹ and the Canadian Rheumatology Association guidelines¹² specifically recommend testing for LTBI prior to starting

tocilizumab. Most other guidelines^{8,13-16} include generic statements recommending testing for LTBI prior to starting biologics; however, they do not specifically mention tocilizumab. In the AMBITION trial¹⁷ studying the use of tocilizumab in patients with rheumatoid arthritis, patients were screened according to Singapore standards and were excluded if they had active TB or untreated LTBI. In the RADIATE trial,¹⁸ patients with active TB were excluded, but it was not mentioned if LTBI was screened for. In both studies, no opportunistic infections including TB were reported. In the GiACTA trial,¹⁹ it was not mentioned if LTBI testing was done and/or if patients with LTBI were excluded. The British Society for Rheumatology Biologics Register–Rheumatoid Arthritis registry²⁰ did not report any TB cases in the tocilizumab group. Very few cases were reported with tocilizumab use in the Hong Kong Society of Rheumatology Biologics Register.²¹ It was not mentioned if LTBI testing was done and/or if patients with LTBI were excluded.

This statement reached consensus on the first round of voting and was hence not discussed further.

2. We conditionally recommend testing for LTBI with an IGRA in PRD prior to starting JAKi, specifically tofacitinib, baricitinib, upadacitinib and filgotinib, over not testing.

The level of evidence is low. Most guidelines^{11,13,15,22} recommend that the same TB screening algorithm described for biologics should also be followed for patients receiving targeted synthetic disease-modifying antirheumatic drugs.

There is some evidence suggesting that use of JAKi may confer a higher risk for reactivation of LTBI. In clinical trials studying the use of JAKi in rheumatoid arthritis²³⁻²⁵ and psoriatic arthritis,²⁶ patients with active or untreated TB were excluded. In spite of this, a study with pooled data investigating the long-term safety of tofacitinib in the treatment of RA²³ reported 36 patients who developed active TB, 4 of whom had LTBI at screening and were appropriately treated. In another study with pooled data investigating the safety profile of baricitinib,²⁵ 10 patients were reported to have developed active TB. Very few cases of TB have been reported with tofacitinib use in registries.^{21,27,28} It was not mentioned if the patients in these registries had been screened or treated for LTBI prior to the initiation of tofacitinib.

This statement reached consensus on the first round of voting and was hence not discussed further.

3. We conditionally recommend testing for LTBI with an IGRA in PRD prior to starting moderate- to high-dose glucocorticoids (prednisolone equivalent of ≥ 15 mg/day for ≥ 8 weeks), over not testing.

The level of evidence is low. Most guidelines^{13,16,29,30,31} do recommend screening for LTBI for patients who are likely to receive moderate- to high-dose glucocorticoids for a prolonged period of time. There is variation in the dose and duration threshold recommended, but most^{13,30} suggest a threshold daily dose of ≥ 15 mg of prednisolone equivalent for ≥ 4 weeks. These recommendations arose from studies^{32,33} that compared patients on glucocorticoid dose of < 15 mg/day versus ≥ 15 mg/day. These 2 studies provided relevant observational data, but the level of evidence is low as 1 is a cohort study while the other is a case-control study.

Most cohort studies evaluating the incidence of TB and its risk factors showed that use of glucocorticoids was associated with increased risk of developing active TB,³³⁻³⁸ though the doses were not mentioned. It was also not mentioned if LTBI testing was done prior to initiation of glucocorticoids or whether patients with LTBI were excluded.

The TFP agreed that 15 mg/day of prednisolone equivalent is a reasonable dose as it is considered a moderate dose of glucocorticoids. However, in terms of duration, the TFP felt that a threshold duration of 8 weeks would be more pragmatic compared to 4 weeks. As almost all patients who require pulsed intravenous or high-dose oral glucocorticoids are expected to remain on high doses for at least 4 weeks—but may be able to taper the dose beyond 8 weeks—the higher threshold may reduce the burden of over testing. Given that it takes time for latent TB to reactivate, the TFP felt that 8 weeks is a reasonable threshold. Nevertheless, the decision should be individualised, especially if patients have epidemiological or clinical risk factors for latent TB (e.g. history of TB exposure, radiographic findings suggestive or previous or healed TB, residence in or travel from highly TB-endemic regions).

The TFP also acknowledged that in certain time-sensitive situations where patients require urgent treatment, it would not be feasible to delay initiation of glucocorticoids until after commencement of treatment of LTBI. Moreover, IGRA may yield false negative or indeterminate results in patients on high-dose glucocorticoids, and may hence warrant repeat or alternative modality testing subsequently if clinical suspicion remains. Given these limitations, this recommendation aims to serve as a reminder for physicians to minimally perform a risk assessment for patients who may require high-dose glucocorticoids, and monitor closely for reactivation of TB.

Finally, it was also mentioned that while there is insufficient evidence for TB reactivation while on other modes of administration of glucocorticoids, it may be reasonable to consider screening and treatment of

LTBI for PRD prescribed moderate- to high-dose glucocorticoids in all forms.

4. We conditionally recommend against routine testing for LTBI with an IGRA in PRD prior to starting cyclophosphamide.

The level of evidence is low. The European Alliance of Associations for Rheumatology¹³ suggests that a recommendation for cyclophosphamide cannot be made due to the low level of evidence. Most other guidelines^{8,11,12,14-16,22,29,31,39,40} are silent regarding LTBI testing prior to starting cyclophosphamide. Furthermore, most large clinical trials investigating the use of cyclophosphamide in ANCA-associated vasculitis⁴¹ and lupus nephritis^{42,43} did not report an increased risk of TB, though it was not mentioned whether LTBI testing was done or whether patients with LTBI were excluded.

Majority of the TFP disagreed with the statement during the first round of voting. A member of the TFP mentioned that screening for LTBI is also not routinely done in haematology patients on cyclophosphamide.

5. We conditionally recommend against routine repeat testing for LTBI with an IGRA in PRD on TNF-I, if initial testing is negative.

The optimal re-testing strategy for LTBI while on TNF-I therapy in those who initially tested negative remains to be established. While some guidelines are silent on repeat testing, others^{11,12,13,14,39} have suggested repeat testing if there are epidemiological risk factors, such as close contact with active TB cases, countries where TB is endemic, patients with selected underlying medical conditions. Regarding the recommended interval for repeat testing, 2 guidelines^{11,39} suggested annual repeat testing.

A member of the TFP reminded the group that the incidence of reactivated TB in Singapore is only 27 to 28 per 100,000 per year.² The rate of TB has been declining over the past 6 years.⁴⁴ Also, the cost of a single IGRA test in a public-sector hospital is about SGD200. Hence, routine repeat testing in a low-risk group of patients may lead to unnecessary cost with low yield.^{1,2} The TFP felt that instead, need for repeat testing should be individualised, guided by clinical signs and symptoms, known exposure to TB contacts and change in risk factors.

Rituximab

The level of evidence is low. Most guidelines^{8,13-16} include generic statements recommending testing for LTBI prior to starting biologics—but do not specifically mention rituximab. Evidence from small retrospective or observational data suggests that the risk of reactivation of TB with rituximab is low. In published

clinical trials studying the efficacy of rituximab in rheumatoid arthritis,^{45,46} ANCA-associated vasculitis⁴⁷ and lupus nephritis,⁴⁸ it is not mentioned if LTBI testing was done and/or if patients with LTBI were excluded. The REFLEX trial⁴⁶ specifically mentioned that there were no reported cases of TB over 24 weeks of the study. In biologics registries,^{20,21,27,28} very few cases of TB were observed in the rituximab group. Similarly, it was not mentioned if the patients in these registries had been screened or treated for LTBI prior to the initiation of rituximab.

This statement did not reach consensus. The TFP questioned the strength of evidence linking rituximab to an increased risk of TB reactivation. One member commented that the mechanism of action of rituximab primarily targets B cells, and is hence less implicated in TB reactivation compared to therapies affecting T-cell function. It was pointed out that testing for LTBI is also not routinely done in patients with haematological malignancies, where rituximab is commonly used, and no significant safety signals have emerged to date. Others took a more cautious stance, acknowledging that while the evidence is limited, isolated reports of TB reactivation do exist and warrant consideration. It was also pointed out that patients prescribed rituximab are often concurrently receiving other immunosuppressive therapies, including corticosteroids, which could contribute to a cumulative risk of TB reactivation.

Interleukin-17-I, specifically secukinumab and ixekizumab

The level of evidence is low. The Joint American Academy of Dermatology and National Psoriasis Foundation³⁹ and the European Society of Clinical Microbiology and Infectious Diseases guidelines¹¹ recommend screening for LTBI prior to the initiation of interleukin (IL)-17-I. Other guidelines vary in their assessment of risk. In a study pooling data from 21 randomised controlled trials investigating the long-term safety of secukinumab in patients with plaque psoriasis, psoriatic arthritis and ankylosing spondylitis,⁴⁹ it was mentioned that the patients enrolled in these trials were tested for LTBI, and could be included if LTBI treatment was started. No cases of TB reactivation were reported in these trials.

This statement did not reach consensus though the majority (66.7%) of the TFP agreed with testing for LTBI prior to starting IL-17-I on the first round of voting. Members of the TFP commented that the rates of TB may be low due to existing practices of screening and treating LTBI, rather than a truly low risk. They would still opt to treat LTBI in these patients and hence would test for LTBI prior to starting IL-17-I. Moreover, the drug inserts for Cozentyx (secukinumab; Novartis Pharmaceuticals Corp., NJ, USA) and Taltz (ixekizumab; Eli Lilly and Company, IN, USA)

recommend evaluating for TB prior to initiating treatment. It was suggested that from a practical standpoint, since patients considered for IL-17-I often have overlapping indications with TNF-I, LTBI screening would typically be conducted regardless, given the established need for testing prior to initiation of TNF-I. However, others felt that the evidence supporting treating LTBI in these cases is not strong and hence they would not offer screening. One member pointed out that real-world data⁵⁰ in the dermatology field has shown low reactivation rates among patients with LTBI who received IL-17-I. However, it is important to note that the majority of patients in this study received chemoprophylaxis after being screened for LTBI. Data specifically on patients with untreated LTBI who received IL-17-I are limited.

Interleukin-12/23-I, specifically ustekinumab, and Interleukin-23-I, specifically guselkumab and risankizumab

The level of evidence is low. The Joint American Academy of Dermatology and National Psoriasis Foundation³⁹ and the European Society of Clinical Microbiology and Infectious Diseases guidelines¹¹ recommend screening for LTBI prior to the initiation of IL-12/23-I. Other guidelines vary in their assessment of risk. In the PSUMMIT 2 trial⁵¹ investigating the efficacy and safety of ustekinumab in patients with psoriatic arthritis, patients with a history of active TB were excluded. Other patients were tested for LTBI and could be included if LTBI treatment was started. No cases of TB reactivation were reported through week 60. In the DISCOVER-1⁵² and DISCOVER-2 trials⁵³ of guselkumab in patients with psoriatic arthritis, patients with active TB were excluded. Other patients were tested for LTBI and could be included if they were on LTBI treatment. No cases of new-onset TB or reactivation of LTBI occurred through 1 year. Data regarding TB reactivation with IL-12/23-I and IL-23-I use from biologics registries are not yet available.

This statement did not reach consensus. The majority of the TFP concurred that these drugs are less commonly used in Rheumatology. One member remarked that he would test for LTBI in all patients with spondyloarthritis, given the potential need for TNF-I and the associated risk of TB reactivation.

Abatacept

The level of evidence is low. The Canadian Rheumatology Association guidelines¹² specifically recommend testing for LTBI prior to starting abatacept. Most other guidelines^{8,13-16} include generic statements recommending testing for LTBI prior to starting biologics; however, they do not specifically mention abatacept. In biologics registries,^{20,27,28} very few cases of TB were reported with abatacept use. Again, it

was not mentioned if the patients in these registries had been screened or treated for LTBI prior to the initiation of abatacept.

This statement did not reach consensus though the majority (66.7%) of the TFP agreed with testing for LTBI prior to starting abatacept on the second round of voting. The TFP noted that this drug is not commonly used in Singapore.

DISCUSSION

This consensus recommendation provides guidance to healthcare providers regarding screening for LTBI prior to treatment with non-TNF-I immunosuppressive agents (specifically non-TNF-I bDMARDs, tsDMARDs, moderate- to high-dose glucocorticoids and cyclophosphamide), as well as regarding routine

repeat testing for patients on TNF-I who initially tested negative for LTBI. This recommendation is based on an updated literature review, evidence synthesis using the GRADE methodology, and a modified Delphi consensus method. Ten adult rheumatologists, 1 infectious diseases specialist and 1 respiratory medicine specialist with a special interest in TB were convened for this work, which is representative of the healthcare providers for PRD in Singapore. The updated evidence and consensus are intended to help guide decision making for screening and treatment for LTBI prior to starting non-TNF-I immunosuppressive agents, and to remind physicians of nuances to consider for repeat testing for LTBI in patients on TNF-I.

The consensus recommendation achieved strong agreement for screening and treating for LTBI prior

Table 1. Voting results.

No.	Recommendations	Round 1		Round 2	
Reached consensus: Agreement		% agreement	% disagreement	% agreement	% disagreement
1	We recommend that people with rheumatic diseases (PRD) should be tested for latent tuberculosis infection (LTBI) with an interferon-gamma release assay (IGRA) prior to starting interleukin 6 receptor inhibitors, e.g. tocilizumab.	75	8.3	NA	NA
2	We recommend that PRD should be tested for LTBI with an IGRA prior to starting Janus kinase inhibitors (JAKi), specifically tofacitinib, baricitinib, upadacitinib and filgotinib.	83.4	0	NA	NA
3	We recommend that PRD should be tested for LTBI with an IGRA prior to starting moderate- to high-dose glucocorticoids (prednisolone equivalent of ≥15 mg/day for ≥4 weeks). The duration was revised from 4 weeks to 8 weeks before the second round of voting.	66.6	25	75	8.3
Reached consensus: Disagreement		% agreement	% disagreement	% agreement	% disagreement
4	We recommend that PRD should be tested for LTBI with an IGRA prior to starting cyclophosphamide. There was no change in wording for the second round of voting.	25	58.3	8.3	91.7
5	We recommend that testing for LTBI with an IGRA be repeated annually in PRD on tumour necrosis factor-alpha inhibitors (TNF-I), if initial testing is negative. There was no change in wording for the second round of voting.	41.6	41.7	8.3	91.7
Did not reach consensus		% agreement	% disagreement	% agreement	% disagreement
6	Rituximab	33.3	41.6	25	66.7
7	Interleukin-17-inhibitors (IL-17-I), specifically secukinumab and ixekizumab	66.7	16.7	41.7	33.3
8	Interleukin-12/23 inhibitors (IL-12/23-I), specifically ustekinumab, and interleukin 23 inhibitors (IL 23-I), specifically guselkumab and risankizumab	50	33.3	41.7	33.3
9	Abatacept	58.3	25	66.7	16.7

IGRA: interferon gamma release assay; JAKi: Janus kinase inhibitors; LTBI: latent tuberculosis infection; PRD: people with rheumatic diseases; TNF-I: tumour necrosis factor-alpha inhibitors

Table 2. Summary of recommendations.

Recommendations	
1.	We conditionally recommend testing for latent tuberculosis infection (LTBI) with an interferon-gamma release assay (IGRA) in people with rheumatic diseases (PRD) prior to starting interleukin 6 receptor inhibitors, e.g. tocilizumab, over not testing.
2.	We conditionally recommend testing for LTBI with an IGRA in PRD prior to starting Janus kinase inhibitors, specifically tofacitinib, baricitinib, upadacitinib and filgotinib, over not testing.
3.	We conditionally recommend testing for LTBI with an IGRA in PRD prior to starting moderate- to high-dose glucocorticoids (prednisolone equivalent of ≥ 15 mg/day for ≥ 8 weeks) over not testing.
4.	We conditionally recommend against routine testing for LTBI with an IGRA in PRD prior to starting cyclophosphamide.
5.	We conditionally recommend against routine repeat testing for LTBI with an IGRA in PRD on tumour necrosis factor- α inhibitors (TNF-I), if initial testing is negative.

to initiating tocilizumab and JAKi, consistent with recommendations from existing guidelines^{11,12} and real-world evidence of elevated risk of TB reactivation.^{23,25} These recommendations are further supported by the known mechanistic effects of these agents, particularly their disruption of T-cell-mediated immunity, a critical defence against latent TB reactivation.⁵⁴ JAKi block the JAK-STAT signalling pathway, that is critical for cytokine signalling, including interferon-gamma (IFN- γ) which is essential for macrophage activation and control of latent TB. Emerging evidence also suggests additional alteration of regulatory T-cell function, further compromising TB containment.⁵⁵⁻⁵⁷ However, it should be cautioned that delaying initiation of tocilizumab or JAKi while treating LTBI should be balanced against the clinical need for disease control.

Conversely, the majority of the TFP concurred that screening for LTBI need not be done routinely prior to starting cyclophosphamide. For glucocorticoids, the panel endorsed screening for LTBI prior to starting moderate- to high-dose glucocorticoids, defined by the panel as prednisolone equivalent of ≥ 15 mg/day for ≥ 8 weeks. This balances the risk of LTBI reactivation against clinical feasibility in acute settings. The TFP also agreed that repeat testing for LTBI while on TNF-I need not be routinely done in view of Singapore's declining TB rates,⁴⁴ favouring a case-based approach instead, to best optimise resource use. Despite broad consensus on several recommendations, we acknowledge that none achieved unanimous agreement or disagreement. This reflects the paucity of high-level evidence specifically addressing LTBI screening strategies, as much of the current guidance is extra-

polated from observational data and indirect evidence, as well as expert opinion. Prospective studies, ideally randomised controlled trials, or large registry-based cohort studies, that evaluate TB reactivation outcomes under varying screening protocols, are required to strengthen future recommendations. Another limitation is that our recommendations did not consider the cost impact on society or individuals.

In summary, we have synthesised an updated literature review and formulated consensus recommendations on the need for screening for LTBI prior to treatment with non-TNF-I immunosuppressive agents in PRD. This work represents a systematic effort by the Chapter of Rheumatologists, College of Physicians, Academy of Medicine, Singapore. Recommendations for the individual patient need to take into account the patient's clinical condition and risk factors for TB, values, preferences and accessibility to testing for LTBI. These recommendations will undoubtedly evolve as new evidence becomes available.

Supplementary material

Table S1. AGREE reporting checklist.

Acknowledgements

The authors thank the Chapter of Rheumatologists, College of Physicians, Academy of Medicine, Singapore, for providing funding and logistical support for the consensus meeting.

Ethics statement

Not applicable. No ethics approval was required as this manuscript is a consensus statement based solely on literature review and Delphi consensus process, with no involvement of human subjects or patient data.

Declaration

Li Yang Hsu received honoraria from QIAGEN Singapore Pte Ltd for a speaking engagement. The remaining 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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Sarcopenia: Current evidence, advances in assessment, clinical implementation and future directions

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ABSTRACT

Sarcopenia is the progressive loss of muscle strength and mass that is commonly, though not exclusively, associated with increasing age. It has been well established to be associated with increased risk of adverse health outcomes and is a growing public health challenge. Reported prevalence varies widely by setting and diagnostic criteria, complicating surveillance and cross-study comparisons. The recent development of the conceptual definition of sarcopenia by the Global Leadership Initiative in Sarcopenia marks a critical step towards harmonisation. There have been significant advances in our understanding of the pathophysiological basis, biomarkers, assessment, diagnosis and interventions in sarcopenia. Novel biomarkers (including creatinine–cystatin C indices, myokines and composite multi-marker panels) and artificial intelligence-enabled radiomics from computed tomography, magnetic resonance imaging and ultrasound show promise for scalable, opportunistic case-finding, but currently remain research tools requiring large-scale validation and cost-effectiveness assessments. Management remains grounded in resistance exercise and nutrition, although there is ongoing debate on the optimal type of protein as well as the most effective timing of protein intake in relation to exercise and the amount required. Pharmacological and regenerative approaches are under active investigation but have yet to deliver proven, generalisable clinical benefits. Translation into practice hinges on standardised definitions, validated assessment tools and integrated care pathways that embed sarcopenia screening into chronic disease management and public health programmes. Singapore's first national sarcopenia consortium aims to accelerate translation into clinical practice and community care by advancing mechanistic research, validating novel biomarkers and developing scalable interventions to enhance muscle health and promote healthy ageing.

Keywords: biomarkers, population health, sarcopenia

CLINICAL IMPACT

What is New

- Advances in biomarkers and artificial intelligence-driven imaging improve detection but require validation.
- Exercise and protein remain the cornerstone of management; pharmacological and regenerative therapies are emerging.

Clinical Implications

- Sarcopenia is the age-related loss of muscle strength and mass. Integrating sarcopenia screening into chronic disease pathways and community case-finding can enhance care delivery.
- Singapore's first national sarcopenia consortium highlights how research, policy and community engagement can drive population muscle health.

INTRODUCTION

Sarcopenia is the progressive loss of muscle strength and mass,^{1,2} most commonly age-related but also occurring secondary to chronic disease, malnutrition and inactivity. It is significantly associated with physical disability, reduced quality of life, adverse metabolic outcomes and increased mortality.³ The term “sarcopenia” was first coined by Dr Irvin Rosenberg in 1988.⁴ Initially, sarcopenia was defined as the age-related loss of muscle mass. However, the definition has since evolved to include not only reduced muscle mass, but also decreased muscle strength and poor physical performance.⁵ Sarcopenia was recognised

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Accepted: 29 December 2025

Published Online First: 15 January 2026

as an official medical disease in the International Classification of Diseases, Tenth Revision (ICD-10:M62.84) in 2016.⁶ Although prevalence rises steadily with age,⁷ sarcopenia is not solely a disease of ageing. Primary sarcopenia is defined as sarcopenia that results from ageing alone, whereas secondary sarcopenia arises in the context of chronic illness, malnutrition or prolonged inactivity.

Sarcopenia is a significant driver of age-related loss of function.⁸ The total estimated annual cost of hospitalisation for individuals with sarcopenia is USD40.4 billion in the US.⁹ Household-level analyses from China found that sarcopenia increases hospitalisations and the odds of catastrophic health expenditure,¹⁰ although data on the economic impact of sarcopenia in Asian populations are sparse. Beyond its impact on physical disability and frailty, sarcopenia is an important contributor to cardiometabolic diseases.¹¹ Skeletal muscle is increasingly recognised as an endocrine organ,¹² secreting myokines that regulate systemic metabolism, inflammation and vascular health.¹² Loss of muscle mass and strength exacerbates insulin resistance, impairs glucose utilisation¹³ and alters lipid metabolism,¹¹ thereby increasing the risk of type 2 diabetes, obesity, metabolic syndrome, fatty liver and cardiovascular disease.¹¹ Conversely, cardiometabolic disorders accelerate muscle catabolism through mechanisms such as chronic inflammation, mitochondrial dysfunction and hormonal dysregulation, establishing a bidirectional relationship between sarcopenia and metabolic health.¹¹ This interconnection underscores the significance of sarcopenia not only as a geriatric syndrome but also as a systemic condition with implications for morbidity, healthcare costs and population health.

Incorporating sarcopenia screening and management into cardiometabolic disease care pathways¹¹ is essential to improve outcomes and promote healthy longevity. Unlike bone mineral density, muscle mass measurements have not been widely adopted by clinicians,¹⁴ and further work is needed for muscle health to become part of routine care.

A global conceptual definition of sarcopenia

Multiple organisations, including the International Working Group on Sarcopenia,³ the Foundation for the National Institutes of Health,¹⁵ the Asian Working Group for Sarcopenia (AWGS),¹ the Sarcopenia Definition and Outcomes Consortium¹⁶ and the European Working Group on Sarcopenia in Older People (EWGSOP)¹⁷ have proposed criteria and operational definitions of sarcopenia (Table 1). Previously, the definition of sarcopenia generally encompassed 3 key criteria: (1) loss of skeletal muscle mass together with (2) loss of muscle strength and/or (3) reduced

physical performance, with the presence of all 3 criteria being classified as severe sarcopenia. While there are multiple consensus statements and guidelines on sarcopenia, the formation of the Global Leadership Initiative in Sarcopenia (GLIS) has moved us closer towards global consensus.

Formed in 2019, GLIS developed a conceptual definition of sarcopenia, where a key conclusion was that muscle mass, strength and muscle-specific strength were all accepted as “components” of sarcopenia, whereas impaired physical performance was accepted as an “outcome” rather than a “component”.² Significantly, the AWGS 2025 Consensus Update¹ has followed suit and adopted the latest GLIS conceptual definition. The severity staging of sarcopenia has been removed.¹ These developments represent an important step towards unifying the various working group guidelines. GLIS has also developed a standardised glossary of terms commonly used in sarcopenia research,¹⁸ which aims to help advance global research, achieve consensus and facilitate translation into practice.^{2,18}

Prevalence

The prevalence of sarcopenia varies widely, ranging from 9% to 86.5% depending on the context and diagnostic criteria used.¹⁹ A systematic review of 41 studies including 34,955 participants found that the prevalence of sarcopenia was higher in institutionalised (51% in men and 31% in women) and hospitalised (23% in men and 24% in women) older adults compared to community-dwelling older adults (11% in men and 9% in women).²⁰ A recent meta-analysis of 140 studies involving 156,325 older adults across Asia found an overall prevalence of sarcopenia of 16.5% among community-dwelling adults ≥60 years.²¹ In Singapore, prevalence estimates range from 6.1% to 44.3% depending on the setting, assessment methods and diagnostic criteria used.^{22–24} The prevalence of sarcopenia in primary care was 27.4% and 44.3% in specialist outpatient clinics.²² The prevalence in community-dwelling adults ranges from 27% to 32%.^{23,25,26}

Assessment of sarcopenia

Guidelines^{1,17,23} recommend a case-finding approach by utilising screening questionnaires, such as the strength, assistance with walking, rising from a chair, climbing stairs and falls (SARC-F) questionnaire.²⁷ SARC-F is a simple questionnaire (Supplementary Table S1), but it has low-to-moderate sensitivity and high specificity for case detection in community settings.^{27,28} The addition of calf circumference measurement to SARC-F (termed SARC-CalF) has been found to increase the sensitivity in the diagnosis of sarcopenia.^{29,30}

Table 1. Comparative framework: Sarcopenia diagnostic criteria versus GLIS conceptual definition.

Organisation	Muscle strength	Muscle mass (assessment)	Physical performance	Notes/staging
GLIS ² 2024 (conceptual definition)	Reduced muscle strength (core)	Reduced muscle mass (method not yet specified; cut-offs TBD)	Physical performance = outcome, not diagnostic	Core “components” of sarcopenia: muscle mass, muscle strength and muscle-specific strength (muscle strength/muscle size) Physical performance as an “outcome” No severity staging
AWGS ¹ 2025	HGS <28 kg (men), <18 kg (women)	Age-specific cut-offs Age ≥65 years ASM/height ² DXA <7.0 kg/m ² (men), <5.4 kg/m ² (women) BIA <7.0 kg/m ² (men), <5.7 kg/m ² (women) Age 50–64 years ASM/height ² DXA <7.2 kg/m ² (men), <5.5 kg/m ² (women) BIA <7.6 kg/m ² (men), <5.7 kg/m ² (women)	Physical performance = outcome, not diagnostic	Focus shifts from diagnosing a “disease” in older people only → to promoting muscle health across the life course Physical performance as an “outcome” Removed severity staging
SDOC ¹⁶ 2020	HGS <35.5 kg (men), <20 kg (women)	Not required (muscle mass not essential for diagnosis)	Gait speed <0.8 m/s	Sarcopenia defined by ↓ strength and/or ↓ gait speed Mass is supportive but not diagnostic No severity staging
EWGSOP2 ¹⁷ 2019	HGS <27 kg (men), <16 kg (women); 5x chair stand >15s	ASM <20 kg (men), <15 kg (women); ASM/height ² <7.0 kg/m ² (men), <5.5 kg/m ² (women)	Gait speed ≤0.8 m/s; SPPB ≤8; TUG ≥20 s; 400 m walk ≥6 min/non-completion	Probable: ↓ muscle strength Sarcopenia: ↓ muscle strength + ↓ muscle mass Severe: sarcopenia + poor performance
FNIH ¹⁵ 2014	Recommended: HGS <26 kg (men), <16 kg (women) Alternate: HGS _{BMI} <1.0 (men), <0.56 (women)	Recommended: ALM/BMI <0.789 (men), <0.512 (women); ALM <19.75 kg (men), <15.02 kg (women) Alternate: ALM <19.75 kg (men), <15.02 kg (women)	Not included	Suspect: poor physical function Assessment: ↓ strength (HGS) Diagnosis: ↓ strength + ↓ lean body mass (ALM/BMI)
IWGS ³ 2011	Not separately defined	ALM/height ² ≤7.23 kg/m ² (men), ≤5.67 kg/m ² (women)	Gait speed <1.0 m/s	Case finding: specifically consider patients who are bedridden, cannot independently rise from a chair or ↓ gait speed Assessment: perform DXA Diagnosis: ↓ muscle mass + ↓ gait speed

ALM: appendicular lean mass; ASM: appendicular skeletal muscle mass; AWGS: Asian Working Group for Sarcopenia; BIA: bioelectrical impedance analysis; BMI: body mass index; DXA: dual-energy X-ray absorptiometry; EWGSOP2: European Working Group on Sarcopenia in Older People, 2nd consensus; FNIH: Foundation for the National Institutes of Health Sarcopenia Project; GLIS: Global Leadership Initiative on Sarcopenia; HGS: handgrip strength; HGSBMI: handgrip strength adjusted for BMI; IWGS: International Working Group on Sarcopenia; SDOC: Sarcopenia Definition and Outcomes Consortium; SPBB: short physical performance battery; TBD: to be determined; TUG: timed up and go test

Muscle strength, a key feature of sarcopenia, is primarily assessed by handgrip strength (HGS),³¹ with the Jamar or Smedley dynamometers being most recommended.³¹ Most published studies measured both hands or the dominant hand for muscle strength and used the best performance of either 2 or 3 trials. HGS cut-offs are gender-specific, and potential confounders such as hand osteoarthritis and neuromuscular disorders should be considered. The latest AWGS 2025 Consensus Update has recommended a life-course approach towards muscle health, which should expand to include middle-aged adults and cut-offs for those aged 50 years and above.¹

There is currently no consensus over the optimal modalities to assess muscle mass, as different measurement methods have different degrees of predictive value for adverse clinical outcomes^{1,17,23} and new tools emerge.^{32,33} Dual energy X-ray absorptiometry (DXA) is currently the most widely used method to estimate lean mass,³⁴ although lean mass has been found to have limited predictive value for adverse outcomes and functional decline.^{16,34} Multifrequency bioelectrical-impedance analysis (BIA) is recognised as a practical tool for assessing muscle mass. However, its readings can be affected by factors such as hydration status, and it is contraindicated in those with pacemakers or cardiac devices. The Singapore Sarcopenia Clinical Guideline has expressed concern about the lack of robust local validation studies of BIA.²³ It is important to note that cut-off points are population- and device-specific, and BIA devices designed for home use are not recommended due to suboptimal diagnostic accuracy. D3-creatine dilution measures total body muscle mass³⁴ and has been found to be more strongly associated with outcomes such as mobility limitation, injurious falls, physical performance and strength.³⁵ Both methods have unique logistical arrangements, laboratory, personnel and equipment requirements, which limit their widespread use in clinical practice. Computed tomography (CT) and magnetic resonance imaging (MRI) are the gold standard for assessing muscle mass and quality,³² particularly at the L3 level, which correlates well with total body skeletal muscle volume.¹⁷ These imaging techniques provide detailed insights into muscle mass and myosteatosis, which can be quantified using Hounsfield units on CT scans. There is emerging literature on the use of mid-thigh ultrasound in diagnosing sarcopenia.³⁶

Pathophysiology and emerging biomarkers

The pathophysiology of sarcopenia is complex and multifactorial, driven by the dysregulation of protein metabolism, hormonal changes, chronic low-grade inflammation (inflammaging) and neuromuscular factors,¹¹ which in turn are highly influenced by genetic and environmental factors.

Muscle fibre size and quantity begin to progressively decrease from around the fourth to fifth decade, with accelerated loss after the age of 60. By 80 years old, approximately 50% of fibres may be lost compared with young adulthood. The overall decline in fibre number ultimately contributes to muscle atrophy and impaired muscle function, resulting in the development and progression of sarcopenia.³⁷ The maintenance of skeletal muscle mass and function is a dynamic balance between muscle protein synthesis, breakdown and muscle cells in the body. Multiple molecular signalling pathways are involved in maintaining this balance. Insulin-like growth factor 1 (IGF-1) plays a central role in muscle growth, differentiation and regeneration.³⁸ IGF-1 promotes skeletal muscle growth by activating the phosphatidylinositol 3-kinase/protein kinase B/mammalian target of rapamycin (PI3K/Akt/mTOR) pathway.³⁹ With ageing and sarcopenia, IGF-1 levels decline, reducing AKT phosphorylation and mTOR activity. This diminishes protein synthesis and translation efficiency, while activating FoxO transcription factors, which stimulate autophagy and proteasomal degradation, accelerating muscle loss.

Hormonal changes with ageing also contribute to the pathogenesis of sarcopenia. Declines in anabolic and regulatory hormones, including insulin, glucocorticoids, myostatin and testosterone significantly contributes to the pathogenesis of sarcopenia.³⁹ Insulin inhibits skeletal muscle protein breakdown and supports protein synthesis through the regulation of amino acid metabolism. A decline in testosterone levels with ageing is associated with reduced muscle mass and physical performance.⁴⁰ Testosterone promotes protein synthesis, which increases muscle fibre size and has been found to stimulate the mitotic activity of satellite muscle cells. Testosterone also increases IGF-1 expression, which further increases muscle growth.⁴⁰ The transforming growth factor β (TGF- β) signalling pathway negatively regulates skeletal muscle development by inhibiting the expression of specific genes and modulating the proliferation of mesenchymal stem cells (MSCs).⁴¹ Myostatin, which is part of the TGF- β family, regulates the proliferation and differentiation of skeletal muscle fibroblasts. Some studies suggest that suppressing myostatin reduces reactive oxygen species production, enhancing antioxidant defences, which can effectively prevent sarcopenia.³⁹ Myostatin also inhibits AKT phosphorylation, thereby blocking the activation of the IGF-1/PI3K/AKT pathway. In parallel, chronic low-grade inflammation associated with ageing or inflammaging further accelerates muscle loss. This state is characterised by elevated pro-inflammatory cytokines (IL-1 β , IL-6, TNF α) alongside reduced anti-inflammatory mediators, which together promote protein degradation and impair repair mechanisms.⁴² Additional contributors include

excess adiposity, cellular senescence and age-related immune dysfunction, all of which amplify this inflammatory cascade.⁴² Emerging research also suggests a biological link between gut microbiota and skeletal muscle.⁴³ Gut microbiota regulate amino acid biosynthesis, oxidative stress responses, endothelial cell function and IGF-1 synthesis, thereby maintaining the balance between muscle protein synthesis and degradation.⁴⁴

These molecular pathways inform the identification of potential biomarkers of sarcopenia, encompassing both upstream pathophysiology and downstream muscle alterations. Biomarkers can be broadly classified into: (1) non-muscle-specific mechanisms such as inflammatory, hormonal and adipokine markers; (2) musculoskeletal-specific indicators including myokines, follistatin and neuromuscular junction-related proteins; (3) metabolic markers, including those derived from gut microbiota; (4) senescence- and ageing-related markers; (5) genetic and epigenetic factors; and (6) emerging composite or multi-marker indices. A non-exhaustive summary of potential biomarkers of sarcopenia is presented in Table 2.

However, studies investigating the association of biomarkers with sarcopenia, muscle mass, muscle

strength and physical performance have largely reported negative correlations for inflammatory, hormonal, genetic and other biomarker classes.⁴⁵ Only selected biomarkers, such as IGF-1, growth differentiation factor-15 (GDF-15), follistatin, testosterone, circulating CD34-positive cells and microRNA125b-5p, have shown positive correlations.^{13,46} Although the correlations of most biomarkers are statistically significant, the majority exhibit weak or negligible associations, and the search for robust and reliable biomarkers of sarcopenia remains ongoing. There is also interest in examining sex-specific differences in biomarkers, with one study reporting normalised myostatin in men and IGF-1 in women being potential biomarkers for frail individuals with low appendicular lean muscle mass.⁴⁷ At present, no blood or molecular biomarker is recommended for routine clinical diagnosis of sarcopenia; biomarkers remain primarily research tools and do not replace muscle assessment.¹

Management of sarcopenia

The mainstay of the management of sarcopenia is non-pharmacological involving exercise and nutrition.^{23,62,63} Evidence from systematic reviews, meta-analyses and

Table 2. Biomarker categories in sarcopenia.

Category	Examples
Inflammatory biomarkers	CRP, TNF- α , TNF-R1, IL-1 β (chronic low-grade inflammation) IL-6 and IL-10 (when considered as systemic circulating markers) Circulating cell-free mitochondrial DNA (ccf-mtDNA), DAMPs (e.g. HMGB1)
Hormonal and endocrine markers	IGF-1, testosterone, oestradiol, cortisol, DHEA-S Myostatin (GDF-8), follistatin
Adipokines and metabolic regulators	Leptin, adiponectin, visfatin (influence insulin sensitivity, metabolism) 3-methylhistidine (muscle protein breakdown) Uric acid, lactate dehydrogenase (emerging markers)
Musculoskeletal-specific markers	Myokines: myostatin, irisin, GDF-15, BDNF Neuromuscular junction proteins: agrin fragments, neurofilament light chain Extracellular vesicles/exosomes: microRNAs (e.g. miR-133, miR-206)
Senescence and ageing-related markers	p16 ^{INK4a} , p21, p53 (cellular senescence markers) SASP cytokine profile (IL-6, IL-1 β , TNF- α , IL-8 secreted by senescent cells) IL-6/IL-10 ratio as an indicator of inflammaging balance
Gut microbiota-derived markers	Reduced lactobacillus, bifidobacterium; increased enterobacteriaceae, proteobacteria Metabolites: indoxyl sulfate, p-cresyl sulfate, SCFAs
Genetic and epigenetic regulators	Variants in muscle growth genes (e.g. MSTN for myostatin) Circulating microRNAs involved in muscle differentiation/regeneration
Composite/multi-marker indices	Creatinine/cystatin C ratio Combined inflammatory-hormonal panels: IL-6 + IGF-1 + SPARC + MIF

BDNF: brain-derived neurotrophic factor; ccf-mtDNA: circulating cell-free mitochondrial DNA; CRP: C-reactive protein; DAMPs: damage-associated molecular patterns; DHEA-S: dehydroepiandrosterone sulfate; DNA: deoxyribonucleic acid; GDF-15: growth differentiation factor-15; HMGB1: high mobility group box 1; IGF-1: insulin-like growth factor 1; IL: interleukin; MIF: MSTN: myostatin gene (GDF-8); SASP: senescence-associated secretory phenotype; SCFAs: short-chain fatty acids; SPARC: secreted protein acidic and rich in cysteine; TNF- α : tumour necrosis factor- α ; TNF-R1: tumour necrosis factor receptor 1

Note: This list is non-exhaustive.

randomised controlled trials (RCTs) has shown the efficacy of different exercise training modes on muscle mass, muscle strength and physical performance in older people with sarcopenia.^{64,65} A network meta-analysis of 42 RCTs, including 3728 participants with a median follow-up of 12 weeks, found high-to-moderate certainty evidence that resistance exercise, with or without nutritional supplementation, and combined resistance, aerobic and balance training were the most effective strategies for improving quality of life. Exercise with nutritional interventions produced greater improvements in HGS compared with exercise alone.^{64,66} Progressive resistance-based training is advocated as the optimal exercise mode to prevent sarcopenia.^{7,23,62,63,67} A network meta-analysis found that strength improvement involved exercise with higher loads, while improvements in muscle hypertrophy involved multiple sets.⁶⁸ Multicomponent exercises with power and balance/gait training in older adults have also been found to improve the outcomes of older adults with sarcopenia, although the evidence is inconsistent.^{7,62,69} The Singapore Physical Activity Guidelines for older adults specify a target of 150 to 300 minutes of moderate-intensity aerobic physical activity per week and recommend muscle strengthening activities (≥ 2 days/week) as well as multi-component physical activity (≥ 3 days/week) for maintaining muscle strength.⁷⁰

Evidence supporting the effectiveness of nutritional interventions is mixed.^{1,8,71} Protein supplementation has been shown to be effective in improving muscle strength and muscle mass when used as an adjunct to resistance exercise training.^{64,72} Guidelines advocate for increased protein intake in older adults to combat sarcopenia: 1.0–1.2 g/kg body weight (BW)/day for healthy older adults; 1.2–1.5 g/kg BW/day for those with acute or chronic disease; and 2.0 g/kg BW/day for those with frailty, severe illness or malnutrition.^{71,73,74} The evidence for protein supplementation as a stand-alone intervention for sarcopenia is less clear,^{73,75} and ongoing debate surrounds the optimal type of protein such as animal, dairy or plant-based sources, as well as the most effective timing of protein intake in relation to exercise and the amount required.⁷⁵

Specifically in chronic kidney disease (CKD), guidelines taking both geriatric and nephrology concerns into account have been published. Piccoli et al. highlight that adequate energy intake is the first rule to increase protein utilisation whether in high-protein geriatric or low-protein nephrology approaches.⁷⁶ In particular, it is recommended that energy intake should not be allowed to fall below the safety threshold of 20–25 kcal per kg per day, and individual monitoring should support decision making and dietary adjustments. In stage 4 and stage 5 CKD patients who are not on renal replacement therapy, a lower total protein

intake of 0.4–0.8 g per kg per day may be beneficial,⁷⁷ especially in the context of rapidly declining renal function. In CKD patients on renal replacement therapy, the normal dietary protein intake for older adults of 1.2–1.5 g per kg per day is recommended.⁷⁶

Evidence has shown that supplementation with branched-chain amino acids (BCAA), including leucine, increases muscle protein synthesis in different settings. Although the BCAA leucine has been proposed as a promising pharmaconutrient for the prevention and treatment of sarcopenia, results of nutritional intervention studies are not consistent regarding the clinical efficacy of leucine in healthy, active older adults.^{74,78}

Guidelines suggest that vitamin D supplementation (800–1000 IU/day) may be beneficial in older adults with vitamin D insufficiency, which may be useful in patients at risk of sarcopenia.^{23,71} However, evidence for vitamin D supplementation on sarcopenia and muscle health remains equivocal.¹

Advances in the assessment and diagnostic approaches to sarcopenia

In tandem with the discovery of new biomarkers of sarcopenia, indices incorporating creatinine (Cr) and cystatin C (CysC) levels have emerged as potential tools for muscle mass estimation. The Cr-to-CysC ratio (CCR)⁴⁸ and the sarcopenia index, defined as serum Cr multiplied by eGFR (CysC),⁴⁹ show strong correlations with skeletal muscle mass and health outcomes such as mortality⁴⁹ and postoperative complications.⁵⁰ However, as these were observational studies, causal relationships and mechanisms cannot be established. These markers are relevant because Cr is primarily derived from skeletal muscle metabolism, while CysC reflects renal function but is independent of muscle mass.⁵¹ A systematic review of 16 studies involving 5566 participants found that the CCR was the most frequently utilised diagnostic biomarker and had moderate diagnostic accuracy.⁴⁹

To address limitations of current assessment modalities—such as high cost, limited accessibility and sensitivity to physiological confounders—population-specific equations have been derived to estimate appendicular skeletal muscle mass, particularly in resource-limited or retrospective settings.^{52,53} The COCONUT study group developed a calf circumference-based equation, which was validated against DXA using data from the US NHANES 1999–2006 cohort ($n=15,293$ adults)⁵⁴; while Furushima et al. validated an equation based on HGS and anthropometric data against DXA in Japanese men and women.⁵⁵ These equations require further validation across diverse populations and settings before they can be adopted into clinical practice. As described above, there is currently no consensus on the best modalities

to assess muscle mass, as each method has limitations related to logistics, equipment availability, personnel expertise, cost and feasibility in different clinical settings. Therefore, if simpler approaches to estimating muscle mass, such as Cr–CysC-based indices⁵⁶ or anthropometric equations, can reliably predict adverse outcomes, this would represent an important advance and should be emphasised in the context of the ongoing debate between DXA and creatine dilution methods.

Another promising area of innovation is the application of artificial intelligence (AI) and machine learning for radiomics-based evaluation of muscle quantity, quality and fat infiltration (myosteatorsis). Myosteatorsis, which is defined as excessive fat infiltration within skeletal muscle, is commonly used to describe poor muscle quality.⁵⁷ It exhibits a negative correlation with muscle mass and strength and is a growing concern, especially with rising rates of obesity globally.⁵⁸ The identification of visceral fat and myosteatorsis is important, as body mass index alone is not a reliable gauge of obesity and metabolic health.^{11,59} The concomitant presence of sarcopenia and obesity, termed “sarcopenic obesity”, has synergistic effects on adverse outcomes that exceed the additive impact of each condition alone.⁶⁰ Radiomics involves the extraction of large numbers of quantitative features from medical images, enabling a high-dimensional assessment of muscle characteristics that go beyond traditional measures of size or density. By applying AI algorithms to modalities such as CT,^{32,33} MRI⁶¹ and ultrasound,³⁶ muscle volume, architecture, tissue quality and fat infiltration can be characterised with greater precision and reproducibility. AI-enabled approaches to sarcopenia offer the potential for opportunistic, scalable and cost-efficient evaluation.

Pharmacological therapies and innovations on the horizon

To date, no drugs have been approved specifically for the treatment of sarcopenia, and evidence for pharmacological therapies remains limited. There are ongoing trials for several classes of therapeutic agents such as myostatin inhibitors, selective androgen receptor modulators, senolytics and nicotinamide adenine dinucleotide (NAD⁺) precursors, although large-scale, well-powered phase 3 RCTs remain few. Ongoing trials evaluating drugs for sarcopenia and components of sarcopenia identified from ClinicalTrials.gov (as searched on 11 September 2025) are summarised in Supplementary Tables S2–S4. The current literature shows that the myostatin pathway inhibitors lead to increased muscle mass but without proportional functional improvement.⁷⁹ Similarly,

testosterone replacement in older men was found to increase muscle mass, with a transient, non-sustained improvement in muscle strength, but no improvement in physical performance. A dose-dependent increase in testosterone-related adverse events has been reported in older males,⁸⁰ and testosterone is not licensed for use in sarcopenia at present.

Evidence for metformin’s effects on muscle health varies, with the MASTERS trial showing that metformin inhibited muscle mass gains from resistance exercise in older adults.⁸¹ Metformin’s appetite suppression and gastrointestinal side effects adversely affect nutritional intake, especially in older adults.⁸² The recent double-blind RCT MET-PREVENT trial found that metformin did not lead to improvements in muscle mass, grip strength, physical performance or quality of life after a 4-month trial period. Metformin was poorly tolerated by the participants due to adverse effects and led to high discontinuation rates.⁸³

The rise of geroscience, which seeks to reduce the onset and severity of age-related conditions by targeting the underlying biological mechanisms of ageing, broadens the horizon of therapeutics for ageing and sarcopenia.⁸⁴ Gerotherapeutics focuses on pathways such as inflammation, mitochondrial dysfunction, epigenetic regulation, proteostasis and cellular senescence. This approach holds promise for novel approaches to prevent or treat sarcopenia as part of broader healthy ageing strategies. For example, the TAME (Targeting Aging with METformin)⁸⁵ trial aims to assess whether metformin can reduce the burden of age-associated diseases, with sarcopenia as one of its key outcomes.

Advances in regenerative medicine and gene editing technologies such as CRISPR/Cas9,⁸⁶ have created new prospects for muscle restoration. CRISPR/Cas9-mediated knockout of myostatin has been shown to increase muscle mass and strength in animal models.⁸⁷ Stem cell therapy shows promise in muscle regeneration, with MSCs being able to differentiate into myogenic cells and release paracrine factors that support muscle repair.⁸⁸ In addition, other stem cell populations beyond MSCs are also being investigated for their regenerative potential.

Despite these advances, translation to clinical practice remains limited,⁸⁹ hindered by barriers such as high developmental and treatment costs, safety concerns including adverse metabolic and cardiovascular effects, ethical concerns and uncertainties about efficacy in heterogeneous older populations. Standardised definitions and assessment cut-offs, and validation in different populations are necessary before these therapies can be translated clinically and at scale.

Interplay of sarcopenia, frailty and integration with World Health Organization (WHO) Integrated Care for Older People (ICOPE) framework

While recognised as distinct conditions, sarcopenia and frailty share many similarities in aetiology and symptoms.⁹⁰ There is considerable overlap in criteria, clinical outcomes,⁹¹ interventions^{22,26} and underlying pathophysiology.⁹⁰ Frailty is a multidimensional construct reflecting a decline in physiological reserves and function across multiple systems, leading to increased vulnerability to stressors and adverse health outcomes such as falls, disability, hospitalisation and mortality.⁹² Sarcopenia is closely related to physical frailty and may modulate transitions within the frailty status. In recognition of the strong association between sarcopenia, muscle health, frailty and age-related declines in functional capacity, the AWGS 2025 consensus recommends a shift in focus towards muscle health promotion integrated into the WHO ICOPE framework.¹ This integration recognises the synergistic relationship between muscle health promotion, frailty and comprehensive geriatric assessment and their convergence within a population health and health promotion framework. Embedding muscle health within comprehensive geriatric assessments (CGA) and ICOPE frameworks⁹³ supports early detection, targeted intervention and monitoring of frailty and functional decline over time.²⁶

Sarcopenia and chronic diseases

Sarcopenia is highly prevalent among individuals with chronic diseases such as chronic obstructive pulmonary disease,⁹⁴ congestive heart failure,¹¹ chronic liver disease, diabetes mellitus,⁹⁵ chronic kidney disease,⁹⁶ malignancy, stroke and osteoporosis. It is increasingly recognised as both a consequence of, and a risk factor for, the progression of these conditions. Reduced muscle mass and function worsen insulin resistance and cardiometabolic risk.¹¹ Conversely, chronic diseases contribute to the development of sarcopenia—termed “secondary sarcopenia” or disease-related sarcopenia—through mechanisms such as inflammation, hormonal dysregulation, metabolic alterations, malnutrition and reduced physical activity.^{94,96} Muscle loss in secondary sarcopenia is progressive, follows a non-linear trajectory and occurs at a greater magnitude than that observed in primary or age-related sarcopenia.⁹⁷ Management of secondary sarcopenia not only parallels that of primary sarcopenia, with exercise and nutrition as the cornerstones, but also requires targeted treatment of the underlying chronic disease. While universal screening for sarcopenia at the population level is not recommended and the impact on relevant outcomes is not certain, case-finding for sarcopenia in adults ≥ 60 years,

especially in high-risk populations such as those with chronic diseases, is recommended.²³

Accordingly, the integration of sarcopenia assessment and management into multidisciplinary chronic disease care is essential. Routine evaluation of muscle mass and function, alongside interventions such as resistance exercise, nutritional support and emerging pharmacological strategies, should be embedded in disease-specific care pathways. Collaborative models across specialties, involving the multidisciplinary team of dietitians, physiotherapists, health coaches and case managers, are needed to address both the bidirectional impact of sarcopenia on chronic diseases.^{11,24,26}

Sarcopenia in hospitalised patients

Sarcopenia is associated with worse outcomes in hospitalised adults, and hospitalisation can accelerate muscle loss leading to “acute sarcopenia”.⁹⁸ A systematic review of 6 studies found that the incidence of sarcopenia that developed during hospitalisation in older adults was 12–38.7%.⁹⁹ Factors associated with hospitalisation such as systemic inflammation, cytokine storm, bed rest, delirium, acute medical illness, side effects of drugs, surgery, poor oral intake and intensive care unit stays precipitate and accelerate acute muscle loss.¹⁰⁰ Acute sarcopenia can lead to chronic sarcopenia, as recovery from acute muscle wasting is often incomplete, particularly in older adults.^{98,100,101} There is no standardised definition of acute sarcopenia and it is not mentioned in several working group consensus criteria.^{1,16,102} EWGSOP2 recognised acute and chronic sarcopenia as temporal subtypes, using a 6-month duration as the temporal threshold. In general, acute sarcopenia is recognised to be related to acute illness, injury, trauma or surgery. The Australian and New Zealand Society for Sarcopenia and Frailty Research Expert Working Group has published recommendations on screening, diagnosis and management of sarcopenia in hospitalised older adults.¹⁰³ These include the recommendation to assess probable sarcopenia and sarcopenia based on the assessment of muscle strength and muscle mass, the use of calf circumference as a surrogate estimate in the absence of equipment such as DXA and BIA, multidisciplinary interventions and raising awareness and knowledge. However, there remain challenges in applying the recommended assessments to diagnose sarcopenia in acute hospitalised patients. Hospitalised patients may not be able to cooperate with some assessments, such as HGS or physical performance measures.^{100,101} Acute illness can confound the accurate measurement of muscle mass and body composition due to hydration status. More studies are needed to assess the impact of sarcopenia interventions such as physical activity and nutrition in acutely ill patients.

Promoting population muscle health and healthy longevity in Singapore

With a rapidly ageing population, sarcopenia has become a national priority for healthy ageing and population health in Singapore. The launch of the Singapore Clinical Practice Guidelines for Sarcopenia in 2022²³ marked a major milestone, supported by ongoing efforts to raise awareness,¹⁴ expand screening and implement community-based interventions.²⁶ These initiatives adopt a life-course approach to address upstream determinants, aiming to reduce disability, preserve independence and support healthy longevity in older adults.¹⁰⁴

National consortia that link mechanistic research, biomarker validation and implementation science can accelerate translation. By coordinating efforts across the translational pathway, they help ensure that scientific insights are rapidly tested, validated and scaled into clinical and community practice. Singapore has launched one of the world's first national sarcopenia consortia. Entitled MAGNET (Mechanistic Investigation and Clinical Innovation for Sarcopenia Diagnosis and Therapy), the consortium brings together clinicians from various specialties, scientists, allied health professionals and community partners to advance mechanistic research, validate novel

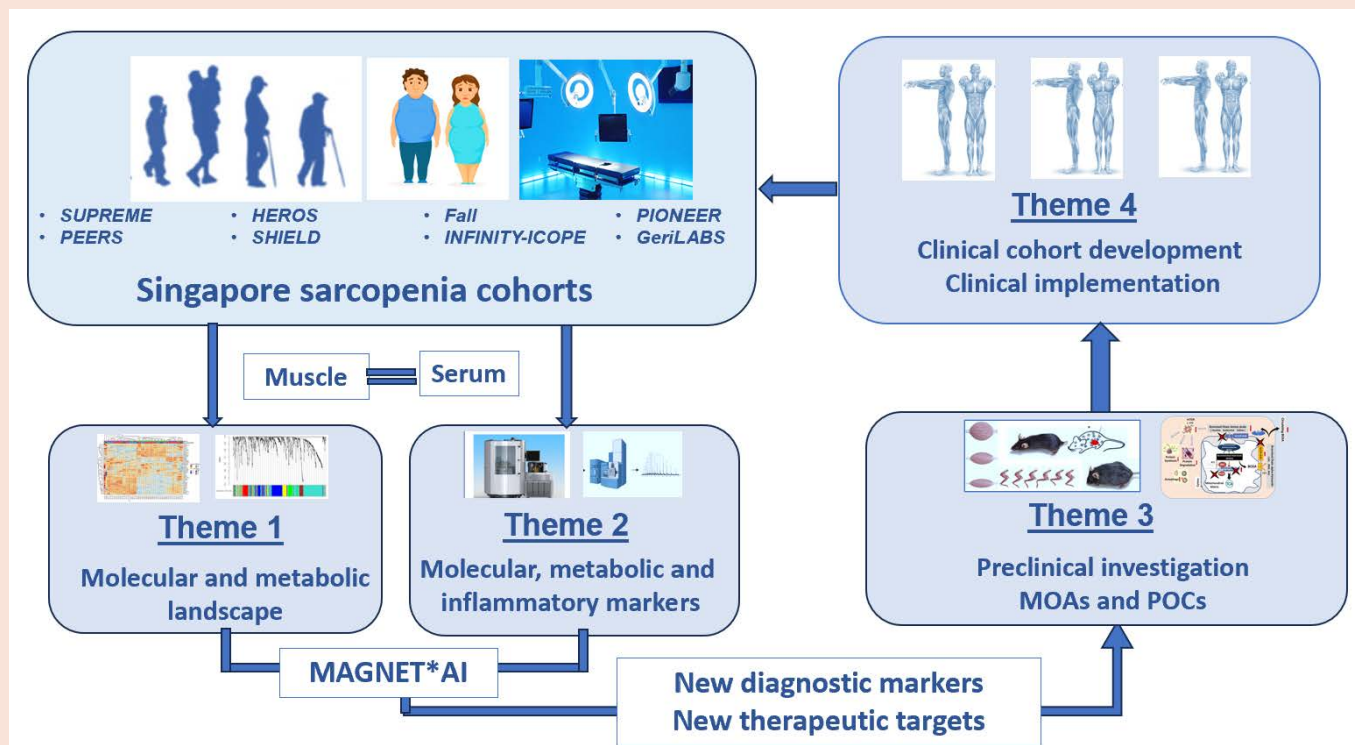
biomarkers and develop scalable interventions for sarcopenia, while accelerating translation into clinical and community settings. MAGNET brings together existing cohorts to form a national sarcopenia database, and further studies are planned that span biomarker discovery, digital health interventions and implementation science approaches to embed muscle health screening and interventions across hospitals and communities (Fig. 1).

The work of MAGNET closely aligns with Singapore's national ageing strategies, including HealthierSG and Age Well SG, which emphasise preventive health, centralised care in the community and precision medicine. Integration with community-based resources—such as active ageing centres, community gyms and exercise programmes for not only older adults but also younger adults who may have sub-clinical sarcopenia—ensures that research findings are rapidly translated into real-world practice. Singapore's first national sarcopenia consortium illustrates how research, policy and community engagement can drive population muscle health.

CONCLUSION

In summary, sarcopenia is a major and growing public health challenge, which significantly affects chronic

Fig. 1. MAGNET (Mechanistic Investigation and Clinical Innovation for Sarcopenia Diagnosis and Therapy): A bench-to-bedside roadmap for sarcopenia.



AI: artificial intelligence; ICOPE: Integrated Care for Older People; MOA: mechanisms of action; POCs: proofs of concept

disease outcomes, functional ability and healthy longevity. Advances in definitions, biomarkers, assessment tools and therapeutics are rapidly reshaping the field, but translation into practice requires standardisation, validation across populations and integration into health systems. Singapore is leveraging these efforts—through national clinical practice guidelines, a national sarcopenia consortium spanning research to clinical translation, and alignment with national strategies such as HealthierSG and Age Well SG—to lay the foundation for a robust ecosystem to manage and promote muscle health. Effective strategies to manage sarcopenia at the individual and population levels have the potential to reduce disability, extend independence and promote healthy ageing.

Supplementary materials

Table S1. SARC-F screening questionnaire.

Table S2. Medications phase 1 clinical trials for sarcopenia identified from ClinicalTrials.gov.

Table S3. Medications phase 2 clinical trials for sarcopenia identified from ClinicalTrials.gov.

Table S4. Medications phases 3 and 4 clinical trials for sarcopenia identified from ClinicalTrials.gov.

Ethics statement

This is a narrative review of published literature and does not require study participants.

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.

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From screening to action: Overcoming challenges in musculoskeletal care

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ABSTRACT

Around the world, millions lose mobility and independence each year due to musculoskeletal disorders. This decline rarely begins suddenly; it often develops silently over years until everyday activities become difficult. By the time symptoms appear, prevention opportunities are often lost. Two urgent challenges must be addressed to change this trajectory. The first is detecting risk early. Advances in movement science, clinical screening and digital health now make early identification possible at scale. Wearable sensors, computer vision and simple functional tests such as gait speed and grip strength provide objective and real-world assessment of mobility and balance. Large population cohorts, biomarker research and artificial intelligence refine risk stratification by identifying early decline and predicting future disability. The second task is in motivating behavioural change once risk is recognised, and this remains the battle yet to be won. Many people hesitate to modify their routines when the benefits may take years to become apparent, as in most musculoskeletal conditions. This makes effective risk communication essential. Messages should be personalised, empathetic and culturally appropriate, helping individuals understand why action matters and how it protects independence and quality of life. Sustained engagement then depends on social support and digital tools that provide feedback and maintain motivation over time. Moving forward, the critical task is to ensure that those identified at risk act on this knowledge, stay engaged long enough for prevention to succeed, and enable musculoskeletal care to move from a reactive care model to true prevention.

Keywords: early diagnosis, health behavior, health communication, musculoskeletal disorders, risk assessment

INTRODUCTION

Musculoskeletal disorders are a leading cause of disability worldwide.¹ Conditions such as physical frailty, osteosarcopenia, mobility decline and falls affect millions of people and are increasingly recognised as major public health concerns.² This recognition is crucial because for most of these conditions, opportunities for prevention are often lost by the time symptoms appear. Functional deterioration is rarely sudden; it is usually preceded by a long period of

subtle decline in strength, balance and mobility that goes unnoticed until it begins to affect daily life. Detecting these problems early, while they are still reversible, offers a critical window to prevent permanent disability and preserve independence.³ In this context, there are 2 major challenges to overcome. The first is to identify risk at the earliest stage, and the second is to bring about behavioural change, ensuring that those identified as high risk take meaningful action to prevent future disability.

The growing burden of musculoskeletal decline

Globally, musculoskeletal disorders contribute substantially to the total years lived with disability, surpassing cardiovascular and respiratory diseases in many regions.¹ Osteoarthritis alone is estimated to affect more than 500 million people,⁴ while sarcopenia and physical frailty together affect up to one-third of adults over the age of 60, depending on the population studied.^{5,6} Falls remain the second leading cause of accidental injury-related deaths across the world, with older adults suffering the greatest number of fatal and disabling falls.⁷ Beyond the immediate suffering of pain, immobility and loss of independence, these disorders lead to a cascade of social and economic consequences. They increase the need for informal caregiving, reduce productivity and create heavy demands on health systems through long-term rehabilitation, surgery and institutional care. As life expectancy continues to rise and populations age, the burden of mobility-limiting conditions is expected to grow further unless preventive strategies are adopted early and systematically.

Traditional healthcare pathways remain primarily symptom-driven. Patients often seek help only after the onset of significant pain, difficulty walking, or a sentinel event such as a fall or fragility fracture. At this stage, much of the functional decline is difficult to reverse, and interventions, even when well designed, are less effective.⁸ This delayed response highlights the need to move away from reactive care that waits for injury or disability to appear and towards a proactive, preventive model that identifies risk before it manifests as disease.

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Accepted: 29 December 2025

Published Online First: 8 January 2026

The first challenge: Detecting risk at an early stage

The first challenge—early risk detection—is becoming more achievable with rapid progress in movement science, clinical screening and digital health.⁹ For many years, clinicians relied on patients' self-reported symptoms, periodic examinations and basic clinical tests, such as handgrip strength or walking speed. While useful, these approaches lack granularity and may overlook the earliest phases of decline, when subtle losses in balance or coordination have begun but remain imperceptible to both patients and clinicians.

Objective measurement of movement

Recent advances in technology have transformed how human movement can be observed and quantified. Wearable sensors—such as accelerometers and gyroscopes, smartphone-based activity monitors and computer vision algorithms—now allow continuous and objective tracking of daily movement.¹⁰ Pressure-sensors can reveal alterations in gait symmetry and foot loading patterns, while inertial measurement units capture stride-to-stride variability and postural sway with high accuracy.¹¹ Computer vision systems using ordinary video cameras can reconstruct joint angles, monitor functional transitions and assess dynamic balance tasks without the need for laboratory-based equipment.¹² These tools have made it possible to observe musculoskeletal function in real-world environments rather than relying only on clinic visits. Clinicians can now monitor how individuals move during routine activities at home or in community settings, detecting small changes that would previously go unnoticed.

Clinical and population-level screening

Alongside sophisticated technologies, well-validated clinical assessments remain valuable. Widely used tests include the Short Physical Performance Battery (SPPB), which combines gait speed, balance and lower-extremity strength assessments, as well as individual measures such as the Timed Up and Go (TUG) test, chair rise time, static and dynamic balance, and handgrip strength. Although simple to perform, these assessments are robust markers of overall musculoskeletal health and show strong associations with morbidity.

In addition, routine radiological investigations, such as computed tomography and magnetic resonance imaging performed for unrelated clinical indications, often contain rich but underused imaging data that can reveal low muscle mass, reduced bone density, vertebral fractures and other markers of osteoporosis or sarcopenia. Opportunistic screening that extracts these measurements using automated or semi-

automated methods has shown promise in identifying high-risk individuals long before symptoms appear.¹³ Translating these incidental findings into musculoskeletal care pathways by flagging at-risk patients for follow-up assessment can significantly extend early detection efforts. As health systems mature towards value-based reimbursement models, using opportunistic imaging markers for risk stratification offers a cost-efficient way to prevent downstream disability and reduce reliance on high-cost interventions.

Moreover, large longitudinal studies, including national ageing cohorts and resources such as the UK Biobank, have generated extensive normative data that enable risk models to account for age, sex, comorbidities and lifestyle factors. Biomarker research is expanding this further by identifying blood-based indicators of inflammation, bone turnover and muscle degradation that may signal early decline long before clinical symptoms appear.

Predictive analytics

When these diverse data streams are collected at scale, powerful statistical and computational methods can identify patterns that are invisible to the human observer. Machine-learning algorithms can map the trajectories of functional decline, cluster individuals into distinct risk profiles and predict the likelihood of falls, fractures or mobility loss over defined time horizons. These predictive models are increasingly capable of recommending tailored interventions, such as targeted exercise, nutritional support or referral for rehabilitation. Several emerging digital platforms integrate gait data, sensor-based metrics and self-reported health information to produce personalised risk scores. This enables clinicians to identify high-risk individuals years before disability develops and to plan early preventive measures. Collectively, these innovations mean that early detection of musculoskeletal decline is now technologically feasible. The challenge is no longer whether we can measure risk, but whether we can convince people to act on it.

The second challenge: Behavioural change

Identifying risk is only half the battle. Helping people to act on that information is far more complex. Awareness of risk does not automatically lead to behaviour change, particularly when the individual feels healthy and perceives no immediate threat. Human behaviour is shaped by a combination of psychological factors, cultural influences, health literacy and social support. Many people struggle to see the value of altering their routines when the benefits may only be apparent years later, a difficulty especially relevant to musculoskeletal health.

Understanding the psychology of prevention

Behavioural science offers useful frameworks to understand why individuals may fail to act despite being informed of risk. The Health Belief Model suggests that people are more likely to engage in preventive action if they perceive themselves as personally susceptible and if they believe the consequences of the condition will be serious.¹⁴ The COM-B model highlights the importance of capability, opportunity and motivation: even when people understand their risk, they may not feel physically able to change, may lack environmental support or may not be sufficiently motivated.¹⁵ In addition, the natural tendency to prioritise immediate comfort over long-term benefit, undermines adherence to prevention strategies.

Communicating risk effectively

Risk communication must therefore be more than the delivery of numerical probabilities or generic warnings.¹⁶ It needs to be personalised, empathetic and framed in terms that resonate with the individual's life priorities.¹⁷ People respond when they understand what is at stake for their independence, social participation and quality of life. For example, explaining that continued muscle weakness could make climbing stairs difficult, reduce the ability to play with grandchildren or threaten the capacity to live alone often makes risk feel real and urgent. Besides, the way of communication should avoid technical jargon, clearly explain why the risk exists, and be adapted to the person's literacy and cultural background.¹⁸ The identity of the person communicating the risk matters as well. Advice given by a trusted clinician, a physiotherapist, a community leader or even a peer who has faced similar risk is often far more persuasive than impersonal campaigns or automated messages.

Maintaining long-term engagement

Even when individuals accept that they are at risk and agree to act, sustaining that behaviour over time remains challenging. Improvements in musculoskeletal health often take time to become noticeable, and people can lose motivation if progress seems slow or invisible. Several strategies can help maintain long-term engagement. Digital platforms can provide regular feedback on progress, such as improvements in walking speed or balance, which reassures individuals that their efforts are working. Group-based exercise programmes and peer-support groups foster accountability and a sense of shared purpose. Breaking long-term prevention into small, achievable milestones allows individuals to celebrate progress early. Gamified applications that reward consistency or encourage friendly competition can make participation more

enjoyable. Tapping on these elements, community-based multicomponent programmes have demonstrated success by combining risk education, motivational coaching and practical adherence supports such as reminders, home safety checks and supervised exercise.¹⁹ These initiatives bridge the gap between early detection and sustained prevention, showing that effective risk communication combined with behavioural nudges can translate knowledge into action.

Integrating prevention into health systems

For meaningful impact, early detection and prevention must become part of routine healthcare rather than isolated research projects. Primary care and community health settings provide a natural entry point. Short functional assessments, simple sensor-based screenings and basic risk questionnaires could be incorporated into regular check-ups. Individuals found to be at elevated risk could then be referred to preventive exercise programmes, physiotherapy-led clinics or tele-rehabilitation platforms. Health systems must also address equity. Digital tools can unintentionally exclude those with limited resources, low digital literacy or reduced access to technology.²⁰ Community-based delivery models, culturally adapted messaging and affordable devices are necessary to ensure that preventive strategies reach those most in need. Policymakers and payers (i.e., insurers, government agencies and employers) should consider incentivising preventive care by covering the cost of early screening and long-term functional health interventions, recognising that the savings from reduced falls, fractures and institutional care are substantial.

Looking ahead: From screening to action

The future of musculoskeletal health will depend not only on our ability to measure decline but also on our success in preventing it. Technological advances have given us sensitive tools to identify risk early. The next frontier is to convert risk awareness into sustained behavioural change at a population level. Achieving this requires integrated ecosystems where clinics, community programmes and digital platforms work together. Behavioural scientists and health communication experts must collaborate with clinicians, engineers and policymakers. Reimbursement models and health system priorities should shift towards maintaining independence and preventing disability, rather than primarily funding treatment after decline has occurred. Most importantly, individuals need to be empowered with clear, personalised and actionable information about their functional health, supported over time to stay engaged and motivated.

If these elements are aligned, the silent decline that now leads so many people into frailty and loss of independence can be intercepted early. Instead of waiting for fractures, falls and severe mobility loss to trigger care, health systems can build proactive pathways that keep people strong, mobile and socially connected throughout life.

Ethics statement

No patient data was used in this article.

Declaration

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. No funding was received in support of this work. ChatGPT (version 5, OpenAI) was used to assist with grammar and syntax; all content was reviewed and approved by the authors, who take full responsibility for the final text.

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HIV self-testing in Singapore is safe, feasible and acceptable: Results from a pilot implementation project

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Dear Editor,

The Joint United Nations Programme on human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) (UNAIDS) has set an ambitious goal to end AIDS by 2030 by achieving the 95-95-95 testing and treatment targets by 2025, where 95% of all people living with HIV should be aware of their HIV status, 95% of all people diagnosed with HIV infection should receive antiretroviral therapy (ART) and 95% of all people receiving ART should have sustained viral suppression.¹ The first of the UNAIDS 95-95-95 targets is particularly important. In Singapore, only 85% of individuals with HIV are aware of their status,² and HIV self-testing (HIVST) has the potential to increase access and close the gap towards achieving the UNAIDS' testing target. From 1 August 2022 to 31 March 2024, the HIVST pilot project was implemented in Singapore to assess real-world acceptability of HIVST and its safe and effective use among at-risk individuals in Singapore, prior to a national roll-out.

The HIVST pilot was implemented at the Action for AIDS (AfA) Anonymous Testing Service (ATS) and the Department of Sexually Transmitted Infection Control (DSC) clinic, using OraQuick HIV Self-Test (OraSure Technologies Inc, Bethlehem, PA, US), the only World Health Organization-prequalified rapid diagnostic test that utilises oral fluid for HIVST and the only Health Sciences Authority-approved kit in Singapore. The pilot was later expanded to include the Mobile Testing Service at AfA from 1 February 2023 and bulk sales of HIVST kits to Project X³ by AfA from 1 October 2023. These 2 expansions were introduced after a year of successful implementation, with no major technical issues or crisis calls reported.

Individuals aged 21 and above (age of majority in Singapore) could purchase up to 3 kits per visit and were asked to complete an anonymous survey. Optional pre-test counselling was offered, and hotline

support was available for technical issues or distress. HIV confirmation testing was complimentary for HIVST users who returned to pilot sites for confirmatory testing.

A total of 3574 HIVST kits were sold to 2107 individuals during the pilot period, with an average of 179 kits sold per month. The buyers were predominantly male (93.8%), aged 21–39 years (65.9%), did not opt for counselling (86.0%) and purchased the kits for self-use (73.7%). More than a quarter of buyers (28.0%) were first-time testers. Of these, only 10.0% opted for pre-test counselling. Half of the users were repeat HIV testers who had never previously used HIVST (50.4%). There were 4 reactive HIVST cases (0.19%) detected, all of whom were linked to care within 1 month. No technical or distress calls were received. Detailed demographic characteristics of individuals who purchased the HIVST kits are shown in Table 1.

In this pilot, HIVST was successfully implemented in Singapore and found to be acceptable, safe and effective, in concurrence with numerous other jurisdictions.^{4,7} The pilot saw a significant proportion of first-time testers (28.0%), comparable to the proportion of first-time testers (33.4%) observed across the 10 anonymous test sites¹ within the same period (unpublished data from the anonymous HIV testing programme). This suggests that HIVST might be reaching those who were not testing for HIV through ATS or other testing modalities, and may prove helpful in Singapore's efforts to achieve the first UNAIDS 95-95-95 target of knowing one's HIV status.

Interestingly, there was no clear correlation observed between counselling uptake and testing experience, as only a small proportion (10.0%) of first-time testers opted for pre-test counselling, suggesting that first-time HIV testers may not require more support than repeat testers. Most users may be comfortable accessing information on their own, regardless of their initial familiarity with HIV or HIV testing. The layered

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Accepted: 21 October 2025

Published Online First: 26 November 2025

Publication: 30 January 2026

Table 1. Demographic characteristics of HIVST users.

	All No. (%)	AfA No. (%)	DSC No. (%)
Unique users	2107	507	1600
No. of HIVST kits sold	3574	870	2704
Sex			
Male	1976 (93.8)	478 (94.3)	1498 (93.6)
Female	124 (5.9)	27 (5.3)	97 (6.1)
Others	5 (0.2)	2 (0.4)	3 (0.2)
Unknown ^a	2 (0.1)	-	2 (0.1)
Age group (years)			
21–29	581 (27.6)	137 (27.0)	444 (27.8)
30–39	807 (38.3)	192 (37.9)	615 (38.4)
40–49	460 (21.8)	134 (26.4)	326 (20.4)
50–59	180 (8.5)	36 (7.1)	144 (9.0)
60 and above	73 (3.5)	8 (1.6)	65 (4.1)
Unknown ^a	6 (0.3)	-	6 (0.4)
Previously declined HIV testing			
Yes	77 (3.7)	15 (3.0)	62 (3.9)
No	2026 (96.2)	492 (97.0)	1534 (95.9)
Unknown ^a	4 (0.2)	-	4 (0.3)
Pre-test counselling			
Yes	296 (14.0)	260 (51.3)	36 (2.3)
No	1811 (86.0)	247 (48.7)	1564 (97.8)
User profile			
First-time tester	591 (28.0)	109 (21.5)	482 (30.1)
Repeat tester who was HIVST naïve	1062 (50.4)	304 (60.0)	758 (47.4)
Repeat tester who was HIVST experienced	451 (21.4)	94 (18.5)	357 (22.3)
Unknown ^a	3 (0.1)	-	3 (0.2)
Use of test kits			
Self-use	1553 (73.7)	353 (69.6)	1200 (75.0)
For partner	113 (5.4)	27 (5.3)	86 (5.4)
For both self and partner	424 (20.1)	122 (24.1)	302 (18.9)
Others ^b	17 (0.8)	5 (1.0)	12 (0.8)

AfA: Action for AIDS; DSC: Department of Sexually Transmitted Infection Control; HIV: human immunodeficiency virus; HIVST: HIV self-testing

^a Some users did not complete or omitted certain questions on the pre-purchase survey.^b For friends or others other than partner.

technical and counselling support provided to all users through the provision of written and video instructions, as well as dedicated, staffed hotline numbers for troubleshooting and/or counselling support, appears to be sufficient given the high levels of education and health literacy in Singapore. However, further study is needed to determine the utility of pre-test counselling, as it remains unclear whether HIVST users declined pre-test counselling because they deemed it unnecessary or considered it intrusive or troublesome.

Several limitations of the pilot were also noted by the authors, such as the age restrictions and purchase limits per user, which may have constrained the reach of HIVST; the sales of HIVST kits were still limited in reach and coverage, owing to the fixed opening hours of both the pilot sites; a second-generation test kit with a longer window period of 3 months after exposure was used in the pilot, which may be less sensitive as compared to blood-based HIVST kits that are usually third- or fourth-generation tests with a shorter window period allowing for diagnosis as early as 2 weeks after exposure.

As it is not uncommon for those under 21 to be sexually active,^{8,9} and since the largest proportion of HIVST users from the pilot are in the younger age group, such limitations may run counter to the intent of HIVST to lower barriers to testing and encourage voluntary testing by all at-risk individuals and their sexual contacts. The available roster of self-test modalities, including finger-prick-based kits and fourth-generation test kits should also be expanded, under prevailing regulatory and safety frameworks in Singapore, to meet the diverse testing needs and preferences of individuals.

With the successful completion of the pilot project, which demonstrated the acceptability, safety and effectiveness of HIVST among at-risk individuals, the authors recommend making HIVST kits available for sale at retail pharmacies nationwide, with the option of online sales by retail pharmacies, analogous to the distribution model for COVID-19 self-test kits. Increased uptake of HIVST could reduce the need for in-person visits to healthcare facilities for HIV testing, which is of particular importance in the context of epidemics or pandemics like COVID-19. Through careful planning and implementation, it has the potential to greatly impact the HIV care continuum in Singapore by offering those at risk of infection the opportunity for early diagnosis and linkage to care.

Ethics statement

This article used anonymous demographic data collected from a pilot sales of HIV self-testing kits in Singapore, commissioned by the Ministry of Health

(MOH), Singapore. The protocol and manuscript were reviewed and approved by senior management at MOH on 13 April 2022 and 1 July 2025, respectively.

Declaration

The HIVST pilot project was funded by MOH, Singapore from FY22 to FY23. 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. All authors have no conflict of interest to declare.

Acknowledgements

The authors would like to thank the other contributing authors unable to be listed: Geraldine Cheng, Lavinia Lin, Daniel Mo, Ng Wen Zhi, Theresa Soon, Jessica Chong, Germaine Chua, Rahman Katama, Shawne Lim, Roslinda and Rayen Tan. The authors would also like to thank MOH for funding this study, and Jessey Markose and Karen Chin for the administrative support throughout the project. Special thanks to all DSC clinic staff, particularly pharmacists Chye Jin Feng and Cheryl Wong Xin Yi, for their efforts and assistance in data collection at the pharmacy point of sales. The authors are also grateful to all AfA staff and volunteers for their efforts and contributions to this pilot project.

Keywords: *HIV, HIV self-testing, HIV testing, pilot implementation, screening*

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Physical activity patterns and associated factors among youths in Singapore: A cross-sectional islandwide community study

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Dear Editor,

Physical activity (PA) plays a critical role in preventing non-communicable diseases and improving mental well-being.¹ PA should commence as a lifelong lifestyle at a young age, but global physical inactivity rates remain high across various age groups.² In Singapore, structured PA is embedded in early schooling through physical education and co-curricular activities (CCAs) but becomes voluntary as youths transit to higher education. With increasing autonomy and academic pressures, PA engagement among older youths may decline. Prior Singapore studies have reported that many adolescents in Singapore fail to meet the World Health Organization's (WHO) recommended 60 minutes of moderate-to-vigorous PA daily.³

While existing research primarily focuses on adults, less is known about the determinants of PA behaviour in youths.^{4,5} This study aimed to assess PA levels among youths in Singapore and identify key behavioural, demographic and contextual factors influencing their PA engagement. The integrated behavioural model (IBM) was used to frame the investigation, focusing on knowledge, attitudes, perceived norms and personal agency.

This study employed a cross-sectional design between August 2023 and November 2024, involving multi-ethnic youths in Singapore. Inclusion criteria were youths aged 15 to 24 years. Youths were excluded if they were serving National Service or have any disabilities preventing engagement in PA. Ethics approval was obtained from the Institutional Review Board in Hwa Chong Institution, Singapore prior to the commencement of the study. Participants were informed about the purpose of the study, and informed of their anonymity and confidentiality prior to starting the survey. Submission of the electronic survey (e-survey) indicated implied consent.

Participants were recruited through social media and street outreach, and they completed an online

e-survey hosted on the Singapore digital forms platform, FormSG. The survey included 53 items across domains such as demographics, mental health, PA-related knowledge and attitudes, social influences, self-efficacy, environmental factors, and the International Physical Activity Questionnaire-Short Form (IPAQ-SF). Mental health and exercise self-efficacy were assessed using the Patient Health Questionnaire-2 (PHQ-2) and Exercise Self-Efficacy Scale, respectively.^{6,7} Metabolic equivalent of task (MET)-minutes per week were derived from IPAQ-SF, and IBM domains were quantified via composite scores.

Descriptive statistics, correlation analysis and multiple linear regression were employed to explore associations. Statistical significance was set at $P \leq 0.05$. All analyses were performed using R version 4.4.2 (R Foundation for Statistical Computing, Vienna, Austria) and SPSS Statistics version 27 (IBM Corp, Armonk, US).

A total of 1188 youths were invited to participate in the study, and 622 responded (52.4%). Consequently, 56 participants were excluded for not meeting eligibility criteria, leaving 566 youths for analysis. More youths were male (51.1%), Chinese (83.6%) and had a normal BMI (54.1%). A large proportion of participants were enrolled in pre-university institutions (39.9%). About 16.4% of youths screened positive for likely depressive disorder using PHQ-2.

The median weekly PA level among participants was 2343 MET-minutes (interquartile range 985–4266 MET-minutes). Based on IPAQ-SF classification, 18.4% of participants were categorised as inactive (<600 MET-minutes), 42.9% as minimally active (600–3000 MET-minutes) and only 38.7% achieved health-enhancing physical activity (HEPA) levels (>3000 MET-minutes). The median daily sitting time was 420 minutes.

Mean IBM construct scores revealed modest to high attitudes and awareness, with a knowledge score of 2.96 out of 6 (standard deviation [SD] 1.33), attitude

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Accepted: 3 October 2025

Published Online First: 6 November 2025

score of 4.14 out of 5 (SD 0.64), perceived norms score of 3.52 out of 5 (SD 0.73) and self-efficacy score of 30.54 out of 40 (SD 5.94).

Linear regression analysis revealed several key determinants of higher PA levels. Participation in sports-related CCAs was positively associated with higher MET-minutes per week ($\beta=1012$, $P=0.027$). Youths with more positive attitudes toward PA ($\beta=649$, $P=0.013$) and those with stronger perceived social

norms ($\beta=467$, $P=0.015$) also exhibited higher PA levels. Conversely, youths who were enrolled in post-secondary institutions had significantly lower PA levels by approximately 1000 MET-minutes per week (all $P<0.05$).

This study also explored the influence of school holidays on youth's PA. Youths who reported engaging in less PA during school breaks recorded significantly lower MET-minutes per week (mean=2371) than those

Table 1. Linear regression for IPAQ-SF MET minutes per week (n=566).

	Overall, no. (%)	Unstandardised β	95% confidence interval	P value
Age, years				
Below 18	372 (65.7)	-	-	-
18 and above	194 (34.3)	-	-	-
Sex				
Female	277 (48.9)	Ref	-	-
Male	289 (51.1)	-148	-666 to 371	0.576
Ethnicity				
Chinese	473 (83.6)	-939	-1973 to 94	0.075
Malay	32 (5.7)	Ref	-	-
Indian	36 (6.4)	-984	-2315 to 348	0.147
Others	25 (4.4)	646	-838 to 2130	0.393
BMI ^a				
Underweight	138 (24.4)	-27	-730 to 676	0.939
Normal	306 (54.1)	457	-136 to 1050	0.131
Overweight/obese	122 (21.6)	Ref	-	-
Housing				
HDB 2 to 3 room flat	31 (5.5)	1338	298 to 2378	0.012
HDB 4 to 5 room flat	236 (41.7)	Ref	-	-
Condominium/executive	222 (39.2)	179	-339 to 698	0.498
Landed property	67 (11.8)	256	-513 to 1024	0.514
Others	10 (1.8)	-558	-2343 to 1226	0.539
Educational institution				
Upper secondary	144 (25.4)	Ref	-	-
ITE/polytechnic	69 (12.2)	-1005	-1907 to 103	0.029
Pre-university	226 (39.9)	-1023	-1685 to -360	0.003
University	107 (18.9)	-1021	-1835 to -208	0.014
Others	20 (3.5)	-69	-1561 to 1424	0.928

Table 1. Linear regression for IPAQ-SF MET minutes per week (n=566). (Cont'd)

	Overall, no. (%)	Unstandardised β	95% confidence interval	P value
Co-curriculum activity				
None	68 (12.0)	Ref	-	-
Clubs and societies	153 (27.0)	-373	-1252 to 506	0.405
Performing arts	121 (21.4)	-306	-1250 to 638	0.525
Sports and games	180 (31.8)	1012	116 to 1908	0.027
Uniformed groups	44 (7.8)	-393	-1593 to 808	0.521
PHQ-2				
Unlikely depressive disorder	473 (83.6)	Ref	-	-
Likely depressive disorder	93 (16.4)	-114	-749 to 520	0.723
Integrated behavioural model construct				
Knowledge score	2.96 (1.33)	67	-112 to 245	0.464
Attitude score	4.14 (0.64)	649	137 to 1161	0.013
Perceived norms score	3.52 (0.73)	467	92 to 843	0.015
Personal agency score	30.54 (5.94)	30	-20 to 80	0.236

BMI: body mass index; HDB: Housing Development Board (public housing in Singapore); IPAQ-SF: International Physical Activity Questionnaire-Short Form; ITE: Institute of Technical Education; MET: metabolic equivalent of task; PHQ-2: Patient Health Questionnaire-2

^a BMI: underweight refers to participants with BMI <18.5 kg/m², normal 18.5–22.9 kg/m² and overweight/obese >23 kg/m².

who maintained (mean=3332) or increased their activity levels (mean=3468) during vacation. Youths with reduced PA outside of school curriculum scored significantly lower across all IBM constructs: knowledge, attitudes, perceived norms and self-efficacy (all $P<0.001$).

Participants reported several barriers that hindered their engagement in PA. The most cited barrier was lack of time (76.5%), followed by lack of self-motivation (56.9%).

The findings underscore the need for multi-level interventions to promote PA among youths in Singapore.⁹ Given that intrinsic attitude and social support were key drivers of PA, public health efforts should focus on strengthening these behavioural drivers.

Peer and family-based strategies may be particularly beneficial in maintaining healthy PA levels.⁸ The results suggest that lack of social support and periods of reduced structure, such as school holidays, leads to significant drops in PA. Fostering supportive peer and family environment, and educating parents about their role in modelling and supporting PA could mitigate this seasonal decline, and reinforce positive

attitudes and habitual engagement in PA. This will support lifelong health, enabling youths to have better quality of life in their later years.

Beyond formal school curriculum, schools should consider implementing flexible, interest-driven sports programmes that accommodate youths' diverse schedules. For effective curriculum and infrastructure planning and implementation, system-based approach and periodical school-based surveys may be necessary to identify periods of highest demand for activities by youths. Schools may consider the deployment of artificial intelligence, automation and innovation to overcome resource and manpower limitations when operationalising these activities to ensure their sustainability and accessibility.

The significant decrease in PA among post-secondary youths highlights the need for system-level support. As youths transit to more autonomous academic settings, academic demands and lack of structured schedules become major barriers to sustained PA engagement. Addressing these barriers through community engagement, peer support and targeted messaging on the cognitive and long-term health benefits of exercise may mitigate the decline.¹⁰

A major strength of this study is the use of validated behavioural tools in a large, multi-ethnic youth study population. However, recruitment may not be representative of the broader youths given its outreach based on ease of access and convenience. Additionally, IPAQ's HEPA threshold exceeds current WHO recommendations and differs across age groups, potentially affecting interpretation. Future studies using objective PA tracking and longitudinal follow-up are warranted.

Given Singapore's national preventive health agenda with the launch of Healthier SG and Grow Well SG, it is imperative to intervene early from young and sustain PA engagement through individuals' life journey. Strategies that reinforce positive attitudes, foster social support and offer enjoyable PA opportunities are crucial to reversing the current trends in youth inactivity.

Ethics statement

Ethics approval was obtained from Institutional Review Board (IRB) in Hwa Chong Institution, Singapore (reference number not available).

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.

Acknowledgments

The authors would like to thank Ma Zhou for his guidance to the students and administrative support to obtain IRB approval. Additionally, the authors would also like to thank Janice Cheng Shu Hui for assisting in data analysis, Samuel Naing Yee Sheng and Tan Rui Qi Rachel from Hwa Chong Institution, as

well as Gordon Kee Yong Jun from NUS Yong Loo Lin School of Medicine for assisting with data collection.

Keywords: *exercise, integrated behavioural model, preventive health, public health, youths*

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No increased incidence of bacterial sexually transmitted infections with PrEP use among men who have sex with men in a clinic cohort

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Dear Editor,

Pre-exposure prophylaxis (PrEP) is a highly effective biomedical intervention to prevent human immunodeficiency virus (HIV) acquisition in at-risk populations, particularly in men who have sex with men (MSM).¹ However, concerns about risk compensation, such as reduced condom use or increased partner numbers, have raised the possibility of rising bacterial sexually transmitted infection (STI) incidence among PrEP users.^{2,3} While some studies report higher STI rates among PrEP users,^{4,5} others suggest that structured PrEP programmes with routine screening may mitigate these risks.⁶ Singapore's Department of STI Control (DSC) Clinic introduced PrEP services in 2018, offering regular reviews, testing and counselling. This study evaluated whether PrEP use was associated with different STI outcomes compared to non-PrEP users within this structured framework.

A retrospective cohort analysis of electronic medical records from the DSC Clinic in Singapore was conducted between January 2018 and December 2023. Eligible participants were MSM aged ≥ 21 years who had at least 1 negative baseline chlamydia or gonorrhoea test and at least 1 subsequent follow-up test. All PrEP users were included. The comparison group comprised MSM not using PrEP. Non-MSM patients were excluded due to small sample size.

For each visit, results across all anatomical (pharyngeal swabs, rectal swabs and urine samples) sites were consolidated, and a visit was considered positive if at least 1 chlamydia or gonorrhoea test was positive. Incident positivity was defined as a positive result following the earliest negative test. To account for differences in testing behaviour, the authors adjusted for the number of tests performed at each visit, the cumulative number of tests a patient had previously undergone, any prior positive results and the interval since the last test. Each variable was categorised for analysis due to data skewness. Analyses focused on chlamydia and gonorrhoea, which were routinely tested. Syphilis serologies were excluded, as interpretation required reference to clinical notes that were not extracted for analysis.

Associations between PrEP use and STI outcomes were evaluated using unadjusted and covariate-adjusted multivariable logistic mixed-effects models. A random effect for patient identifier accounted for repeated visits from the same individual. Fixed effects included for covariate adjustment were demographic factors (age, ethnicity and sexual preference), STI type and the 4 testing-related covariates. Results are reported as odds ratios (ORs) with 95% confidence intervals (CIs). Separate models were fitted for overall bacterial STI, chlamydia alone and gonorrhoea alone. A significance level of 0.05 was selected as the threshold for statistical significance. Statistical analyses were performed using R version 4.5.1 (R Core Team) (R Foundation for Statistical Computing, Vienna, Austria) and RStudio version 2025.05.1+513 (Posit Team) (RStudio Corporation, Massachusetts, US).

This study was approved by the National Healthcare Group Domain Specific Review Board (2023/01000).

A total of 2711 subjects (588 PrEP users, 2364 non-PrEP users) contributed 15,287 non-baseline observations. PrEP users were older (43.0% aged 31–40 versus [vs] 34.3% of non-users), while non-PrEP users were more likely aged 21–30 years (45.3% vs 33.1%). Ethnic distribution was similar. Chinese participants comprised three-quarters of both groups. Nearly all participants reported sex exclusively with men (95.4% of PrEP users vs 91.7% of non-PrEP users), while 8.3% of non-PrEP users and 4.6% of PrEP users reported sex with both men and women.

PrEP users had more frequent follow-ups, contributing a median of 3 visits (interquartile range [IQR] 4) compared with 2 visits (IQR 2) in non-PrEP users, and were more likely to undergo multiple-site testing per visit (65.8% vs 49.4%). They also accumulated more prior testing, with 53.9% having 6–20 previous tests and 21.1% having more than 20, compared with 37.1% and 4.6% of non-PrEP users, respectively. Prior positive results were also more common among PrEP users (24.1% vs 10.0%).

Overall, incident positivity was similar: 10.93% in PrEP users vs 10.71% in non-PrEP users. In the unadjusted mixed-effects model, PrEP use was not significantly

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Accepted: 31 October 2025

Published Online First: 21 November 2025

Table 1. Incident STI outcomes and association with PrEP use.

Outcome	PrEP users, n/N (%)	Non-PrEP users, n/N (%)	OR (95% CI), P value	Adjusted OR (95% CI), ^a P value
Either chlamydia or gonorrhoea	476/4354 (10.9)	1171/10,933 (10.7)	OR 1.05 (0.90–1.23), P=0.53	^a OR 1.07 (0.90–1.27), P=0.45
Chlamydia	237/2162 (11.0)	594/5411 (11.0)	OR 1.02 (0.85–1.23), P=0.81	^a OR 1.03 (0.84–1.27), P=0.76
Gonorrhoea	239/2192 (10.9)	577/5522 (10.4)	OR 1.09 (0.87–1.38), P=0.46	^a OR 1.09 (0.84–1.42), P=0.51

CI: confidence interval; n/N: number of positive incident tests over total number of tests conducted; OR: odds ratio; PrEP: pre-exposure prophylaxis; STI: sexually transmitted infection

^a Adjusted for age, ethnicity, sexual preference, no. of tests per visit, cumulative number of prior tests, prior positive results and interval since last test.

associated with overall STI positivity (OR 1.05, 95% CI 0.90–1.23, $P=0.53$) (Table 1). Sub-analyses by infection type also showed no significant association with PrEP use: chlamydia (OR 1.02, 95% CI 0.85–1.23, $P=0.81$) and gonorrhoea (OR 1.09, 95% CI 0.87–1.38, $P=0.46$). Similar results were seen in the adjusted mixed-effects model, where PrEP use was not significantly associated with overall STI positivity (OR 1.07, 95% CI 0.90–1.27, $P=0.45$), chlamydia positivity (OR 1.03, 95% CI 0.84–1.27, $P=0.76$) and gonorrhoea positivity (OR 1.09, 95% CI 0.84–1.42, $P=0.51$).

This retrospective longitudinal cohort study found no significant association between PrEP use and chlamydia or gonorrhoea incidence among MSM attending a specialist sexual health clinic. Although there were slightly higher odds of positivity among PrEP users, differences were small and not statistically significant.

These findings indicate that structured PrEP services, which include regular STI testing, counselling and prompt treatment, do not contribute to higher STI burden. PrEP users in this study's cohort underwent more frequent and comprehensive testing, which likely enabled earlier detection and treatment. This aligns with other studies showing that increased STI diagnoses among PrEP users largely reflect intensified screening, rather than PrEP itself increasing transmission.^{7,8}

Several limitations should be considered. First, sexual behavioural data such as condom use, number of partners and network factors were not available, limiting the ability to adjust for key risk factors.⁹ Second, tests performed for symptoms and those conducted as routine screening could not be differentiated, as presenting complaints were recorded only in free-text notes and were not extractable for analysis, which may bias comparisons since PrEP users are systematically tested while non-users are more often tested when symptomatic.¹⁰ Third, continuous testing-related variables, such as cumulative test

counts and intervals between tests, were categorised for analysis due to skewed distributions, which may have reduced sensitivity to extreme patterns of very frequent or infrequent testing. Finally, as this study was conducted in a single specialist clinic, findings may not be generalisable to primary care, community-based settings or to other countries where PrEP delivery models may differ.

PrEP use was not associated with significantly different odds of testing positive for chlamydia or gonorrhoea in a structured clinic setting. Comprehensive PrEP services remain essential for HIV prevention and sexual health, without increasing bacterial STI incidences.

Ethics statement

This study was approved by the National Healthcare Group Domain Specific Review Board (2023/01000).

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: *chlamydia, gonorrhoea, HIV, men who have sex with men, pre-exposure prophylaxis, sexually transmitted infections*

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The “silent gap”: Geographic and socioeconomic disparities in Singapore’s cardiometabolic screening

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Dear Editor,

Type 2 diabetes mellitus (T2DM), hypertension and hyperlipidaemia (collectively DHL) are longstanding cardiometabolic risk factors contributing to premature morbidity and mortality globally.^{1–3} Despite clear guidelines on early screening, coverage remains sub-optimal in many healthcare systems, with disproportionate gaps in lower socioeconomic groups.^{4–6} Socioeconomic status (SES) is a multifaceted construct that often influences how much access an individual or community has to essentials such as healthcare, housing, transportation and nutritious food, as well as social resources like political influence, social engagement and autonomy.⁷ In this letter, the authors present key findings from a recent cross-sectional analysis of over 1.1 million residents in western Singapore that highlight missed opportunities for prevention and propose pragmatic implications for clinical practice and health policy.

A cross-sectional study was conducted using anonymous demographic and clinical patient data extracted on 6 May 2024 from the Healthier SG Customer Relationship Management and New Generation Electronic Medical Record. Age, sex, race, housing type and residential postal codes, DHL diagnoses and DHL screening tests were extracted. Postal codes were recoded into the 97 respective subzones grouped into planning areas based on Singapore’s Urban Redevelopment Authority’s Master Plan 2019.⁸ Planning areas are geographical boundaries for urban development. SES was estimated using the Housing Index (HI), a measure of the weighted average number of rooms per unit, where a larger value represents a higher SES.⁹

Among residents with a touchpoint in the regional public health system, DHL screening uptake was 40% for diabetes, 46% for hypertension and only 24%

for hyperlipidaemia, substantially lower than national self-reported rates (79%, 86% and 77%, respectively).¹⁰ Prevalence of hypertension, hyperlipidaemia and T2DM were 13%, 15% and 8%, respectively. Hyperlipidaemia, despite being the most prevalent of the 3 conditions, had the lowest screening uptake.

Screening and prevalence patterns were not uniform across the region. Excluding zones with <100 residents, Bukit Panjang (36.3%), Bukit Batok (36.3%), and Queenstown (35.8%) achieved the highest average DHL screening numbers while Western Water Catchment (18.8%), Sungei Kadut (20.5%) and Jurong East (24.2%) achieved the lowest average DHL screening numbers. Certain residential subzones such as Tengah (19.8%), Bukit Batok (12.9%) and Choa Chu Kang (12.0%) showed high cardiometabolic disease burden, whereas areas like Bukit Timah (5.0%), Sungei Kadut (8.2%) and Queenstown (8.4%) had relatively low prevalence.

Higher socioeconomic status (SES) predicts better screening. The authors’ analysis found that individuals living in higher housing index (HI >5, the proxy for private housing) were less likely to undergo screening within the public system (Table 1). Older age and ethnicity significantly predicted screening and disease prevalence.

The relatively lower screening numbers despite higher prevalence in hyperlipidaemia highlights hyperlipidaemia as the “silent gap” in preventive care, suggesting systemic barriers in preventive lipid screening. While hypertension and diabetes are more readily detected, dyslipidaemia requires a blood test, often fasting, which may discourage participation. The differences in area-specific screening and prevalence numbers underscore the value of granular, subzone-level data in guiding targeted interventions. Interestingly, increasing HI was associated with lower DHL

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Accepted: 2 October 2025

Published Online First: 11 December 2025

Table 1. Housing index-stratified, DHL screening numbers, DHL prevalence numbers and logistic regression results for the association between housing index, age, sex and race.

Screening numbers (%) of residents with:			
	Diabetes	Hypertension	Hyperlipidaemia
HI ≤2	45%	50%	28%
HI >2 to 3	42%	46%	25%
HI >3 to 4	42%	45%	25%
HI >4 to 5	41%	47%	25%
Prevalence numbers (%) of residents with:			
HI ≤2	12%	19%	19%
HI >2 to 3	10%	16%	18%
HI >3 to 4	10%	17%	18%
HI >4 to 5	8%	14%	15%
Odds ratio (95% confidence interval), z-score			
HI ≤2	1.29 (1.23–1.35), 10.09 ^c	1.17 (1.11–1.23), 6.00 ^c	1.32 (1.25–1.40), 9.23 ^c
HI >2 to 3	1.24 (1.20–1.29), 11.94 ^c	1.02 (0.98–1.06), 0.95	1.19 (1.14–1.24), 7.83 ^c
HI >3 to 4	1.27 (1.25–1.30), 23.59 ^c	0.98 (0.96–1.00), -1.79	1.20 (1.17–1.23), 14.36 ^c
HI >4 to 5	1.32 (1.29–1.34), 29.11 ^c	1.06 (1.04–1.08), 5.82 ^c	1.23 (1.21–1.26), 17.92 ^c
Age	1.05 (1.05–1.05), 178.33 ^c	1.02 (1.02–1.02), 50.74 ^c	1.04 (1.03–1.04), 99.41 ^c
Male	1.02 (1.00–1.03), 2.30 ^a	0.87 (0.86–0.88), -20.05 ^c	0.95 (0.94–0.97), -5.63 ^c
Indian	0.95 (0.93–0.98), -3.40 ^b	0.89 (0.87–0.91), -8.87 ^c	1.03 (1.00–1.06), 1.76 ^c
Malay	0.90 (0.88–0.92), -9.53 ^c	0.89 (0.87–0.91), -10.63 ^c	0.86 (0.84–0.88), -10.95 ^c
Others	0.85 (0.82–0.88), -8.33 ^c	1.03 (0.99–1.07), 1.54	0.92 (0.87–0.96), -3.73 ^c

DHL: type 2 diabetes mellitus, hypertension and hyperlipidaemia; HI: housing Index

^a P value<0.05^b P value<0.01^c P value<0.001

Reference group for race is Chinese race.

screening, which contradicts existing understanding that higher SES leads to higher screening numbers due to better health literacy, education levels, job security, income and healthcare access.^{11–14} One speculation could be that residents with a higher SES may prefer to visit private hospitals and clinics for their screening and were hence not captured within the authors' data but captured within the National Population Health Survey data. A previous study has also shown that persistent high utilisers of hospital services are more likely to be of lower SES.¹⁵ This high-lights the need for better inte-gration of private sector data into national surveillance. For lower-SES populations, community-based and after-hours programmes may help overcome barriers.¹⁶ Persistent ethnic differences emphasise the importance of

culturally tailored health promotion where clinicians could adapt communication and leverage community champions to enhance participation.¹⁷ The divergence between EHR-based and self-reported national survey estimates underscores the need for harmonised data sources to better capture the true disease burden.

This analysis benefits from a very large, diverse dataset and granular subzone-level mapping. However, limitations include incomplete capture of private primary care data, cross-sectional design and reliance on housing index as a proxy for SES. Despite these caveats, the findings provide actionable insights for clinical and public health practice.

Despite Singapore's well-developed health system, DHL screening rates in the western region remain

suboptimal, with hyperlipidaemia particularly neglected. Prevalence patterns reveal striking geographic and socioeconomic disparities that call for targeted, area-specific interventions. Clinicians play a pivotal role in closing screening gaps by proactively recommending tests, tailoring interventions to patients' contexts and advocating for better integration of private sector data. Area-specific interventions may be needed to enhance screening uptake and reduce disease burden, regardless of socioeconomic class. These findings can guide resource allocation and SES-specific public health strategies. Achieving equitable prevention of cardiometabolic disease in Singapore requires moving beyond national averages to neighbourhood-level action.

Acknowledgements

The authors would like to express their gratitude to Kylie Heng for her contribution to generating the figures in this article.

Ethics statement

The study was approved as a Review Not Required study by the NUHS Research Office and exempted from ethics board review (NUH-RNR-2024-0031).

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. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Keywords: *cross-sectional analysis, diabetes, hyperlipidaemia, hypertension, public health*

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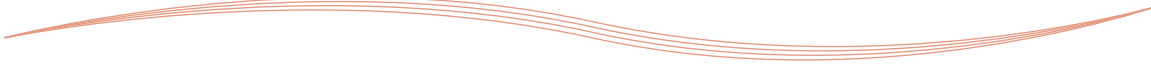
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