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Lifestyle modifications can reduce the risk of type 2 diabetes mellitus (T2DM) and hypertension. A Singapore study examined the association between domain-specific physical activity (e.g. work, transport and leisure) and sedentary behaviour, with T2DM and hypertension.

Individuals with more than 826 metabolic equivalent-minutes of leisure-related physical activity were found to have lower odds of having T2DM and hypertension, compared with those with none. Individuals with more than 8 hours of sedentary time had higher odds of having hypertension compared to those with 0–5 hours of sedentary time. Health promotion strategies can emphasise for moderate levels of leisure-related physical activity, as better than none.

Illustration by Xinyu Li

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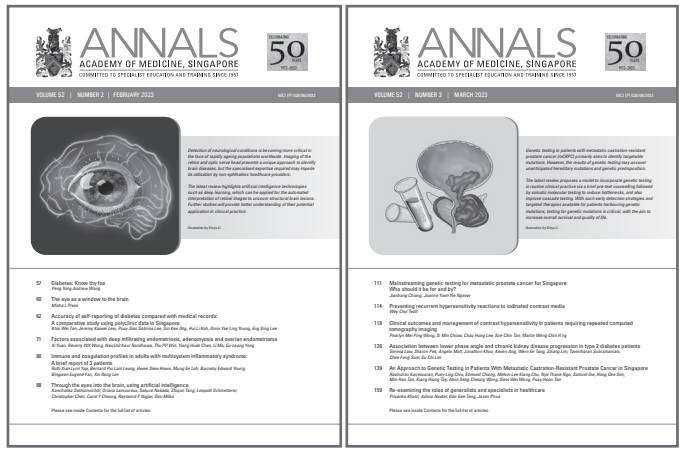

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EDITORIAL

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Promoting physical activity for population health

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The chronic disease burden has risen globally. In Singapore, between 2007 and 2021, the crude prevalence of hyperlipidaemia (8.2–13.9%), hypertension (12.7–15.7%) and diabetes (4.9–6.9%) has increased.[1] Based on the Global Burden of Disease Study (2019), lack of physical activity and other modifiable risk factors contribute 35% of the disability-adjusted life-years burden.[2] Hence, increasing physical activity is a crux in preventing chronic diseases and improving health outcomes.[3,4]

Physical activity has been defined as "any bodily movement produced by skeletal muscles that significantly increases energy expenditure", regardless of intensity or duration.[3,5] Hence, physical activity may occur at any time: during transport between locations (transport-related), as part of work (work-related) or during leisure time (leisure-related). Leisure-related physical activity is a voluntary form of exercise, which usually entails a planned and structured set of repeated movements with or without an explicit direction towards improving physical fitness, such as aerobic capacity, muscle strength, balance, coordination and flexibility.[3,5] The World Health Organization recommends a minimum of 150 minutes of moderate or 75 minutes of vigorous-intensity physical activity per week.[3] Exercise, while often used interchangeably with physical activity, is a subcategory of physical activity. It is characterised as being "planned, structured, and repetitive, in which bodily movements are performed with or without the explicit intent of improving or maintaining of one or more components of physical fitness (i.e. aerobic capacity, muscle strength power and endurance, balance, coordination, and flexibility)."[3]

Benefits of physical activity. Physical activity is instrumental in lowering the risk of premature death and cardiovascular disease while improving mental health, sleep and obesity.[3,4] It has been demonstrated to positively affect drivers of ageing, including chronic mitochondrial dysfunction, inflammatory processes and defective cell autophagy, among others.[3] Physical activity, alongside other lifestyle factors, serves both as a preventive measure in maintaining physiological function and preserving health, as well as a treatment modality, whether in a primary role such as for sarcopaenia or adjunct for managing Parkinson's disease, depression and metabolic diseases.[3]

Benefits of physical activity are particularly significant for older adults, for whom the effects of ageing have accumulated chronically. Ageing results in negative body composition changes: reduced bone density and muscle mass, and increased adipose tissue.[3] Functional capacity and cognitive ability also decline, resulting in decreased ability to perform daily activities independently.[3] These can result in pathological states: general frailty, sarcopaenia, osteoporosis and others. Notably, the increase in adiposity has been linked to metabolic derangements and higher levels of inflammation, predisposing individuals towards diabetes and cardiovascular diseases.[3] Physical activity attenuates the detrimental effects of ageing and thereby delays or improves these disease states.[3] Besides enhancing muscle strength and mobility, such activity optimises body mass and cardiorespiratory fitness, thereby preserving functional ability/independence and ameliorating disease states such as sarcopaenia and osteoporosis. Cognitive function also improves, postulated to be mediated via neurotrophic factors and changes within the cerebral blood flow and brain structures.[3] This also results in improvements among patients suffering from depression, dementia or Parkinson's disease.[3]

In this issue of the *Annals*, Koh et al. provide a cross-sectional observational study looking at the associations between self-reported domain-specific physical activity levels (leisure, work and transport) and point-prevalence of chronic metabolic diseases (diabetes mellitus and hypertension).[6] They found that individuals with higher leisure-related physical activity had lower odds of chronic disease, while those with prolonged sedentary times (>8 hours) had higher odds of chronic disease. However, there appeared to be no such relationship for transport- or work-related physical activity. Of note, the authors also found a dose-response relationship, where increases in leisure physical activity were

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associated with lower odds of diabetes. Although the research is limited by the lack of temporal information, the study's findings are nevertheless in line with existing evidence described before, emphasising the importance of lifestyle modification and physical activity.[3,4]

While increasing overall physical activity has benefits, as evidenced by the lower risks associated with shorter sedentary times, leisure-related physical activity appears to be distinctly superior to transport- or work-related physical activity. Although the exact mechanisms are unclear, it is suggested that the benefits arising from leisure-related physical activity were of sufficient intensity for short periods with ample recovery time, conducted under controlled and self-regulated conditions. This is in contrast to other forms of physical activity where intensity or duration may be insufficient or harmfully excessive, lack appropriate recovery time, or conducted under adverse conditions, such as hot and stressful environments.[3,7]

Challenges to increasing physical activity. It is increasingly recognised that an individual's health is affected by a complex range of social, economic and environmental factors.[8,9] Koh et al. found an association between leisure activity, sedentary time and chronic diseases,[6] highlighting the importance of addressing not just health but also social issues in order to promote healthy behaviours. Subramaniam et al. found multiple factors at the individual, personal, interpersonal, environmental, sociocultural and policy levels that facilitated or obstructed such healthy behaviours in Singapore's context.[9] In particular, the study highlighted the need to address complex interrelated factors that influenced individuals' adoption of behaviours. Within this context, the multifaceted role of the healthcare provider as an educator and supporter is paramount.

Given the complexity of factors driving behaviours, it is therefore insufficient to merely provide the advice of "exercise more". It is necessary to first understand the patient's circumstances and perspectives through a collaborative process of engagement; and subsequently, through various methods, to empower patients in increasing physical activity by evoking motivation and providing continual support. These empowerment measures may include: a collaborative goal-setting process with patient self-monitoring, usage of reward strategies, proactive problem solving (e.g. stimulus control and environmental modification), and tapping social support (such as family, friends and co-workers) and community providers such as the Health Promotion Board (National Steps Challenge) and Sport Singapore (Active SG).[8] Such a collaborative patient-centred approach has been demonstrated to be more effective than a directive approach.[10,11]

Two commonly used approaches are the trans-theoretical model (stages of change) and motivational interviewing. These have demonstrated effectiveness in multiple areas including and beyond that of physical activity.

Increasing physical activity

Transtheoretical model.[10] The transtheoretical model considers behavioural change as a non-linear progression through various stages, influenced by processes undertaken by patients. These include: precontemplation (unaware or not intending to change); contemplation (considering change); preparation (making small changes); action (actively engaged in change); maintenance (continuation of change over a period of time); and relapse (reversion to a previous stage). Each stage describes the patient's state of mind, awareness and their motivational level. The model describes various processes that influence each stage, described as experiential (knowledge, emotions and perceptions regarding physical activity) or behavioural (actions undertaken such as goal setting or environmental modifications). Earlier stages (precontemplation, contemplation) are more strongly influenced by experiential processes, while later stages (preparation, action) are more strongly influenced by behavioural processes. Hence, the actions to be taken by the provider would substantially differ depending on the stage. Application of this model would therefore be a 2-step process: first assessing the patient's stage, before providing the appropriate supportive actions, be it education and awareness raising, or active goal setting and problem solving.

Motivational interviewing.[11] Motivational interviewing is a counselling method focused on behavioural change. It examines the patient's perceptions and circumstances regarding the behaviour (physical activity) and provides support towards the behaviour, while resolving potential obstacles or conflicts. The underlying principles of motivational interviewing are based on it being a non-judgemental and empathic collaboration between healthcare provider and patient, with the intent of respecting patient autonomy and empowering them towards their goals. In practice, this may entail the following: building a relationship (engagement); focusing on high priority areas; evoking the motivation towards change, contextualised within their life priorities ("talking themselves into changing"); and providing aid in concrete action.

In the face of an increasingly ageing population and rising prevalence of chronic diseases, there is a greater emphasis on proactive prevention. Alongside dietary and other lifestyle measures, increasing leisure-related physical activity and reducing sedentary time is one of the key focal points towards improving the health of the individual and of the population. The multifaceted role of the healthcare provider—as educator, motivator and supporter—in empowering patients to increase physical activity is crucial for success.

REFERENCES

1. Health Promotion Board, Singapore. National population health survey 2021, 8 January 2021. https://www.hpb.gov.sg/community/national-population-health-survey/. Accessed 8 February 2023.
2. Ministry of Health, Singapore. Global burden of disease 2019 study findings. https://www.moh.gov.sg/news-highlights/details/global-burden-of-disease-2019-study-findings. Accessed 18 April 2023.
3. Izquierdo M, Merchant RA, Morley JE, et al. International exercise recommendations in older adults (ICFSR): Expert consensus guidelines. J Nutr Health Aging 2021;25:824-53.
4. Ekelund U, Tarp J, Steene-Johannessen J, et al. Dose-response associations between accelerometry measured physical activity and sedentary time and all cause mortality: Systematic review and harmonised meta-analysis. BMJ 2019;366:l4570.
5. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: Definitions and distinctions for health-related research. Public Health Rep 1985;100:126-31.
6. Koh YS, Asharani PV, Devi F, et al. Benefits of leisure-related physical activity and association between sedentary time and risk for hypertension and type 2 diabetes. Ann Acad Med Singap 2023;52:167-9.
7. Holtermann A, Krause N, van der Beek AJ, et al. The physical activity paradox: Six reasons why occupational physical activity (OPA) does not confer the cardiovascular health benefits that leisure time physical activity does. Br J Sports Med 2018;52:149-50.
8. Abraham M, Lim MJ, Tan WS, et al. Global trends towards population health management and key lessons and initiatives in the singapore context. Int J Integr Care 2022;22:19.
9. Subramaniam M, Devi F, AshaRani PV, et al. Barriers and facilitators for adopting a healthy lifestyle in a multi-ethnic population: A qualitative study. PLOS ONE 2022;17:e0277106.
10. Marcus BH, Simkin LR. The transtheoretical model: Applications to exercise behavior. Med Sci Sports Exerc 1994;26:1400-4.
11. Bischof G, Bischof A, Rumpf HJ. Motivational interviewing: An evidence-based approach for use in medical practice. Dtsch Arztebl Int 2021;118:109-15.

EDITORIAL

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Self-esteem and positive body image to overcome female sexual dysfunction

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Human sexuality is arguably one of the main pillars of health, like nutrition and sleep. Improvements in diagnostic and therapeutic biotechnologies have enabled focus on not only deadly diseases, but also on the quality of life and sexual functions of men and women. Digital media also play a considerable role in the social presence and psychological well-being of humans.

The World Health Organization constitution states: "Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity."[1] In this context, sexual function plays a valuable role in human health. In healthy women, the sexual response cycle consists of sexual desire, arousal, orgasm and sexual satisfaction. Any biological, mental or social condition that interferes with this cycle may cause sexual dysfunction and personal distress. Compared with its male counterpart, female sexual dysfunction (FSD) is less studied. The prevalence of FSD, which is estimated to be at 29–40% among women, spans across different age groups.[2,3] Evidence suggests that some medications; culture; and biological (e.g. ageing, hormones, neurological diseases, genitourinary disorders, etc.), cognitive (distraction, negative body image, etc.), behavioral (avoidance), emotional (anxiety, insecurity, etc.), and environmental (obligations, decreased attraction, etc.) states and factors play an aetiological role for FSD.[4,5]

Plenty of studies have been conducted to investigate the interrelation between body mass index (BMI) and FSD, and revealed conflicting results.[6] One study observed that later research have revealed another aspect of the interrelation—that obese women who have eating disorders, lower self-esteem or depressive mood were more likely to suffer from FSD.[6] Therefore, sexuality investigation have focused more on the psychological aspects of body morphology such as self-esteem, subjective body image, appearance anxiety, and depressive mood, rather than actual body size of women in the last decade. A review of studies revealed that distorted body image and appearance anxiety interferes with all domains of sexual function among women.[7] Self-objectification and cognitive distraction during sexual activity are 2 main theories posited to explain the background psychological pathways in the latter context.[8-10] However, the concept of the ''ideal beauty'' propagated all over the world through digital media, alongside genetic and sociocultural factors are on the whole, notable aspects for consideration, in implementing measures to address the interrelation between body image and sexual functioning.

In this issue of the *Annals*, the online survey of young women conducted by Husain et al. investigated the association of BMI, body image and self-esteem with sexual function in young women.[11] Body Image States Scale (BISS), Rosenberg Self-Esteem Scale (RSES), and Female Sexual Function Index (FSFI) were used in the study with the aim to examine this association. A significant correlation was found between the FSFI scores of the 514 respondents with BISS and RSES scores. Lower self-esteem, poorer body image, being married, having 1 child, and perceived mental conditions were found to correlate with FSD. On the opposite end, being overweight (BMI=23.0–27.4 kg/m2) and being of Malay compared with Chinese ethnicity was found to lower odds for FSD. The study concluded that women with a poorer body image and lower self-esteem were more likely to have sexual dysfunction and the abovementioned factors may be better predictors—rather than BMI—to identify the population at risk.

Acknowledging some limitations to the study, such as selection and expression bias, quality of evidence, and lack of advanced body composition measurement methods (e.g. lean body mass, skinfold thickness, etc.), Husain et al.'s study provides added support to how ethnicity and sociocultural environment may shape an individual's psychology in relation to body image and indeed, female sexual function. Notably, the prevalence of FSD in this study was higher than in reports from Western countries.[1,3,7] The study's findings on the comparatively weaker association between BMI and female sexual function index scores are concordant with previous findings indicating the absence of direct

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correlation.[5,6] The findings shine the spotlight on self-esteem and body image as shaped by sociocultural factors; postpartum sexual health in noting the importance of transition, development and support for a new normal routine of sexual function; and the need to improve public knowledge and active observation of body image issues in the clinical setting to trigger conversation about sexual function. The study complements and advances research that have focused solely on the individual's cognitive and emotional disturbances as causes for negative body image and/or sexual dysfunction in women.

Further research is necessary to clarify the exact psychobiological pathways beyond the thoughts, beliefs or perceived shame related to body image, in relation to their possible association between negative body image and female sexual functions. This can enable targeted measures to help individuals overcome sexual dysfunction and improve quality of life.

REFERENCES

1. World Health Organization. Constitution of the World Health Organization. https://www.who.int/about/governance/constitution. Accessed 18 April 2023.
2. Zhang C, Tong J, Zhu L, et al. A population-based epidemiologic study of female sexual dysfunction risk in Mainland China: Prevalence and predictors. J Sex Med 2017;14:1348-56.
3. McCool ME, Zuelke A, Theurich MA, et al. Prevalence of female sexual dysfunction among premenopausal women: A systematic review and meta-analysis of observational studies. Sex Med Rev 2016;4:197-212.
4. Hubin A, De Sutter P, Reynaert C. Etiological factors in female hypoactive sexual desire disorder. Sexologies 2011;20:149-57.
5. Jha S, Thakar R. Female sexual dysfunction. Eur J Obstet Gynecol Reprod Biol 2010;153:117-23.
6. Kadioglu P, YetkinDO, Sanli O, et al. Obesity might not be a risk factor for female sexual dysfunction. BJU Int 2010;106:1357-61.
7. Cihan A, Cihan E. Interrelation Between Appearance Anxiety and Sexual Functions in Women: The Role of Surgical Scars, Morphologic Features, and Accompanying Depression. J Sex Med 2019;16:1769-78.
8. Fredrickson BL, Roberts T-A. Objectification theory: Toward understanding women's lived experiences and mental health risks. Psychol Women Q 1997;21:173-206.
9. Fredrickson BL, Roberts TA, Noll SM, et al. That swimsuit becomes you: Sex differences in self-objectification, restrained eating, and math performance. J Pers Soc Psychol 1998;75:269-84.
10. Dove NL, Wiederman MW. Cognitive distraction and women's sexual functioning. J Sex Marital Ther 2000;26:67-78.
11. Husain FS, Lulla D, Tay TKC, et al. Association between body mass index, body image and self-esteem with sexual function: A survey of young women in Singapore. Ann Acad Med Singap 2023;52:190-8.

ORIGINAL ARTICLE

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Benefits of leisure-related physical activity and association between sedentary time and risk for hypertension and type 2 diabetes

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ABSTRACT

Introduction: Lifestyle modifications can reduce the risk of type 2 diabetes mellitus (T2DM) and hypertension. Our study investigated whether domain-specific physical activity (such as work, transport and leisure) and sedentary behaviour were associated with T2DM and hypertension, and whether these associations were moderated by sex and age.

Method: For this cross-sectional study, data were obtained from a population survey in Singapore (n=2,867) conducted from February 2019 to March 2020. T2DM and hypertension were self-reported. Global physical activity questionnaire was used to assess domain-specific physical activity (in metabolic equivalent of task [MET]-minutes) and sedentary time (in hours). Logistic regression models were generated to examine the abovementioned associations, and adjusted for age, sex, education, ethnicity, personal income, body mass index, diet and hypertension/diabetes. Interaction terms were included individually to investigate whether age and sex moderated the associations.

Results: Individuals with >826 MET-minutes of leisure-related physical activity had lower odds of having T2DM (odds ratio [OR] 0.46, 95% confidence interval [CI] 0.24–0.86) and hypertension (OR 0.59, 95% CI 0.37–0.94) than those with no leisure-related physical activity. Individuals with >8 hours of sedentary time had higher odds of having hypertension (OR 1.69, 95% CI 1.06–2.69) than those with 0–5 hours of sedentary time. Logistic regression models including interaction terms showed that the association between leisure-related physical activity and hypertension was significant for those aged 18–34 (OR 0.15, 95% CI 0.03–0.66) and 50–64 years (OR 0.44, 95% CI 0.21–0.91). The association between sedentary time and hypertension was significant for those aged 18–34 years (OR 15.07, 95% CI 1.69–133.92).

Conclusion: Our results support the widespread promotion of an active lifestyle to lower the prevalence of diabetes and hypertension in Singapore.

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Keywords: Active lifestyle, domain-specific physical activity, global physical activity questionnaire

INTRODUCTION

Diabetes mellitus and hypertension are serious public health issues. Approximately 451 million individuals worldwide aged 18–99 years were living with diabetes in 2017, and this number is expected to increase to 693 million by 2045.[1] More than 90% of all diabetes cases were type 2 diabetes mellitus (T2DM).[2] For hypertension, 1.39 billion adults were estimated to have the condition globally in 2010.[3] These chronic conditions can lead to illnesses with high mortality and morbidity, such as stroke and kidney diseases.[4,5] Although epidemiological studies have established that higher physical activity and lower sedentary time can reduce the risk of diabetes and hypertension,[6-9] significant gaps remain in existing literature.

Firstly, most studies focus on total physical activity or leisure-related physical activity. Emerging literature has suggested that higher physical activity in other domains

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CLINICAL IMPACT

What is New

- Higher leisure-related physical activity was associated with lower odds of diabetes and hypertension.
- Higher sedentary time was associated with higher odds of hypertension.
- The associations between hypertension with leisure-related physical activity and sedentary behaviour vary with age.

Clinical Implications

- Health-promoting organisations can emphasise that low and moderate levels of leisure-related physical activities are better than none.
- Our findings suggest that heightened encouragement to adopt a healthy lifestyle can benefit individuals aged 18–34 and 50–64 years, who are more susceptible to hypertension.

(work and transport) can also lower the risk of diabetes and hypertension, although findings differ across countries and sociodemographic groups.[6-9] A study in the US showed that higher physical activity in all domains (occupation, transport and leisure) lowered the odds of having diabetes.[7] However, a study in Korea found that among men, higher leisure- and transport-related physical activities were associated with lower odds of having diabetes.[6] For women, only higher leisure-related physical activity was associated with lower odds of having diabetes. Work-related physical activity was not associated with diabetes for both sexes.[6]

Secondly, although the effects of leisure-related physical activity and sedentary behaviour on diabetes and hypertension were well-established, the associations between their intensity with diabetes and hypertension vary across sociodemographic groups.[10] A study in Brazil revealed that only men who were sufficiently active in the leisure domain had a lower risk of hypertension (odds ratio [OR] 0.84) than those who were inactive.[10] Conversely, women who were insufficiently active (OR 0.88) and sufficiently active (OR 0.86) in the leisure domain had a lower risk of hypertension than those who were inactive.[10] Another study in Korea found that the association between the length of leisure sedentary time with hypertension and diabetes depends on occupation.[11]

Singapore is a Southeast Asian country with a multiethnic population comprising 75.9% Chinese, 15.0% Malay, 7.5% Indian and 1.6% of other races.[12] The prevalence of diabetes was 9.5% in the period 2019–2020, with a projected increase to 15.9% by 2050.[13,14] Hypertension was estimated to have a prevalence of 35.5% in the period 2019–2020.[14] To counter the rise in these chronic conditions, policymakers in Singapore have been promoting a healthy lifestyle through population-wide campaigns. One initiative is the National Steps Challenge, a campaign that encourages individuals to be physically active by providing wearables to monitor their steps and heart rate, with financial incentives if certain targets are met.[15]

Few studies in Singapore have looked at the widespread promotion of a healthy lifestyle in reducing the risk of T2DM and hypertension.[16] Müller-Riemenschneider et al. have revealed that in Singapore, having a higher level of total leisure-time physical activity was associated with lower diastolic blood pressure.[16] However, having lower diastolic and systolic blood pressure were associated with specific leisure-time physical activities, such as balance exercises (e.g. tai chi and qigong).[16] These associations differed across ethnicities.[16] Limited studies in Singapore have considered the associations between other domain-specific physical activities and sedentary behaviour with hypertension. Furthermore, few studies in Singapore have examined the relationship between domain-specific physical activities and sedentary behaviour with T2DM.[16]

Hence, our study aimed to examine (1) the prevalence of T2DM and hypertension for different levels of domain-specific physical activity (work, transport and leisure) and sedentary time; (2) the association between domain-specific physical activity and sedentary time with T2DM and hypertension; and (3) whether sex and age moderate these associations.

METHOD

The data for this cross-sectional analysis were obtained from a population survey intended to understand the knowledge, attitude and practice of diabetes in Singapore (n=2,895), with a response rate of 66.2%.[17] When stratified by ethnicity, the response rates were as follows: 58.3% for Chinese, 69.3% for Malay, 71.0% for Indian and 66.6% for others. The study was approved by the Institute of Mental Health Institutional Research Committee and the National Healthcare Group Domain-Specific Review Board (reference number: 2018/00430). Written informed consent was obtained from all participants. Parental consent was also obtained

for participants aged 18–20 years. Our analysis utilised data collected from February 2019 to March 2020 (n=2,867). Data collected from 1 April 2020 to 1 September 2020 were excluded (n=28) due to COVID-19 restrictions and social distancing measures, which may have affected physical activity and sedentary time.

The study protocol was described in detail in a previous publication.[17] Briefly, the participants recruited were Singaporeans or permanent residents who lived in Singapore during the study period, aged 18 or above, and fluent in English, Malay, Mandarin or Tamil. Individuals with the following criteria were excluded from the study: age below 18 years, uncontactable due to missing or incomplete address, resided outside Singapore, were institutionalised throughout the study period, or had difficulties completing the survey due to physical, mental or cognitive disability.

One to 2 weeks before the house visit by an interviewer, an invitation letter was sent to the address of potential participants. The letter included information about the survey and a contact number for any enquiries. Data were collected using computer-assisted personal interviews with handheld tablets. If the participant was not at home, a card with the contact details of the interviewer was left behind. A maximum of 10 visits were conducted to reduce the non-response rate. After completing the survey, the participant was given an inconvenience fee.

A disproportionate stratified sampling was performed using the national administrative database to ensure that the sample was representative of the Singapore population.[17] The percentage of participants for each ethnic group (Chinese, Malay and Indian) was set at approximately 30%. The proportion of participants for each age group (18–34, 35–49, 50–65, and >65 years) was fixed at 20%.

Variables: Outcomes and correlates of interest

The outcomes were self-reported T2DM and hypertension. A random sample of participants who reported no diabetes (n=250) was selected to have their fasting glucose and glycosylated haemoglobin (HbA1c) measured via a blood test. The result showed that only a small proportion of the sample (n=19, <10%) had undiagnosed diabetes. The variables of interest were physical activity and sedentary behaviour, which were self-reported using the 16-item global physical activity questionnaire (GPAQ).[18] Moderate and vigorous physical activities were determined in 3 domains: work, transport and leisure. Physical activities are defined as moderate if they lead to a slight rise in breathing or heart rate for at least 10 minutes.[18] Physical activities are considered vigorous if they cause a considerable rise in breathing or heart rate for at least 10 minutes.[18] We calculated the energy expenditure for each domain by multiplying the time variables for each physical activity intensity with metabolic equivalent (MET) values, followed by adding the values for both moderate and vigorous physical activity.[18] Sedentary behaviour was assessed by asking the time spent sitting or reclining during a day.[18] GPAQ was appropriate to assess physical activity and sedentary behaviour because studies in Singapore have shown a moderate correlation between GPAQ and accelerometer-measured physical activity and sedentary behaviour.[19,20]

Control variables

Based on literature,[8,16,21,22] the following control variables were included: age, sex, education, ethnicity, personal income, body mass index (BMI) and Dietary Approaches to Stop Hypertension (DASH) score. The DASH score was calculated based on the responses from the diet screener that was developed and well-validated in Singapore.[23] It assesses food intake by asking participants to rate the frequency of each food/beverage they normally consumed in the previous year using a 10-point scale, ranging from "never/rarely" to "6 or more times per day".

Statistical analysis

Analyses were weighted to adjust for oversampling and post-stratification by ethnicity and age. As a substantial portion of participants had 0 MET-minute for each domain-specific physical activity, we divided each domain-specific physical activity into 3 groups at 0 MET-minute and the mean. This classification method was similarly utilised for another study in Singapore.[16] Sedentary time was divided into tertiles: 0–5 hours, >5–8 hours and >8 hours. The prevalence of diabetes and hypertension stratified by sociodemographic groups, domain-specific physical activities and sedentary behaviour were presented in weighted percentages and unweighted counts.

The associations between domain-specific physical activity and sedentary behaviour with diabetes and hypertension were examined via logistic regression. The models were controlled for age, sex, education, ethnicity, personal income and DASH score. Additional models were run to adjust for BMI and diabetes/hypertension, which were potential mediators.[6,16,24] To determine whether the significant associations identified differ by sex and age group, we individually included

2-way interaction terms in the model. The results were presented in OR and 95% confidence interval (CI). Standard errors were computed using Taylor series linearisation to account for the complex survey sampling design.

All analyses were performed using STATA/MP 17.0 (Stata Corporation, College Station, Texas, US) with a two-sided test at a 5% significance level. All missing data were handled in a listwise manner.

RESULTS

Our study included 2,867 participants. The prevalence of T2DM and hypertension were 8.4% and 20.7%, respectively. Table 1 summarises the prevalence of T2DM and hypertension stratified by sociodemographic groups, domain-specific physical activities, sedentary behaviour and DASH score. The prevalence of T2DM was relatively higher for those aged 65 and above (20.7%), males (9.90%), of Indian ethnicity (14.2%), with primary school qualifications (16.4%), with an income level below SGD2,000 (12.1%) and in the obese BMI range (17.0%). The prevalence of hypertension was relatively higher for those aged 65 and older (52.6%), males (22.4%), those of Chinese ethnicity (21.4%), with primary school education (43.3%), with income less than SGD2,000 (27.5%) and in the obese BMI range (32.2%). The cross-tabulation of age groups and the various domain of physical activity were previously published by Lau et al.[25]

The prevalence of T2DM and hypertension were relatively higher for participants who reported no work-related (T2DM: 9.7%, hypertension: 22.3%) and leisure-related physical activity (T2DM: 13.6%, hypertension: 29.2%). The prevalence of these chronic conditions was similar across different levels of transport-related physical activities and sedentary behaviour. The mean DASH score was similar for participants with T2DM (20.5) and no T2DM (18.9), and participants with hypertension (20.0) and no hypertension (18.8).

Table 2 presents the regression models with T2DM and hypertension as outcomes. Compared to participants with 0 MET-minute of leisure-related physical activity, participants with >826 MET-minutes of leisure-related physical activity had lower odds of having T2DM (OR 0.46, 95% CI 0.24–0.86). The dose-response relationship for leisure-related physical activity was significant (p_{trend}=0.016). For T2DM, no significant interaction effects were observed for sex and age groups.

Compared to participants with 0 MET-minute of leisure-related physical activity, higher leisure-related physical activity was associated with lower odds of having hypertension (OR of >826 MET-minutes 0.59, 95% CI 0.37–0.94) but higher sedentary time was

Table 1. Prevalence of type 2 diabetes mellitus and hypertension by sociodemographic, domain-specific physical activities, sedentary behaviour and DASH score.

	T2DM (n=2867)				Hypertension (n=2849)			
	Yes (n=384)		No (n=2,483)		Yes (n=663)		No (n=2186)	
	n	%	n	%	n	%	n	%
Age group, years								
18–34	4	0.2	810	99.8	19	1.8	793	98.3
35–49	45	3.8	666	96.2	79	11.9	628	88.1
50–64	166	15.5	600	84.5	253	33.2	505	66.8
65 and above	169	20.7	407	79.3	312	52.6	260	47.4
Sex								
Female	188	7.1	1270	93.0	328	19.1	1122	80.9
Male	196	9.9	1213	90.1	335	22.4	1064	77.6
Ethnicity								
Chinese	61	7.3	730	92.7	177	21.4	610	78.6
Malay	143	11.9	818	88.1	241	20.0	713	80.0
Indian	165	14.2	743	85.8	204	16.7	698	83.3
Others	15	4.4	192	95.6	41	15.4	165	84.6

Table 1. Prevalence of type 2 diabetes mellitus and hypertension by sociodemographic, domain-specific physical activities, sedentary behaviour and DASH score. (Cont'd)

	T2DM (n=2867)				Hypertension (n=2849)			
	Yes (n=384)		No (n=2483)		Yes (n=663)		No (n=2186)	
Educational level								
Primary	148	16.4	483	83.6	273	43.3	351	56.7
Secondary	121	11.5	560	88.5	192	24.3	485	75.7
A-level/polytechnic/ vocational school/ITE[a]	71	5.7	789	94.3	112	13.1	744	87.0
Degree and above	44	3.5	651	96.5	86	10.5	606	89.5
Income level (SGD)								
Below 2000	259	12.1	1182	87.9	435	27.5	997	72.5
2000–5999	84	5.7	922	94.3	168	16.3	832	83.7
6000 and above	28	4.9	268	95.1	42	13.9	253	86.1
BMI classification (international)								
Normal range	104	5.2	1149	94.8	219	16.7	1027	83.3
Underweight	3	1.4	147	98.7	12	6.0	137	94.0
Overweight	132	11.8	716	88.2	214	25.4	632	74.6
Obese	85	17.0	330	83.0	130	32.2	279	67.8
Work-related physical activity								
0 MET-minute	203	9.7	1069	90.3	334	22.3	932	77.7
>0–805 MET-minutes	79	6.4	661	93.6	173	21.4	561	78.6
>1805 MET-minutes	102	7.8	753	92.2	156	16.1	693	83.9
Transport-related physical activity								
0 MET-minute	93	8.5	497	91.5	166	22.4	419	77.6
>0–1028 MET-minutes	196	8.4	1277	91.6	343	19.9	1121	80.1
>1038 MET-minutes	95	8.3	709	91.7	154	20.7	646	79.3
Leisure-related physical activity								
0 MET-minute	199	13.6	782	86.4	319	29.2	651	70.9
>0–826 MET-minutes	115	7.5	819	92.5	217	20.5	716	79.5
>826 MET-minutes	70	4.3	882	95.7	127	12.5	819	87.5
Sedentary behaviour								
0–5 hours	157	9.5	1049	90.5	285	22.4	912	77.6
>5–8 hours	117	8.3	792	91.7	195	20.1	708	79.9
>8 hours	109	6.9	642	93.1	182	18.7	566	81.3
Mean DASH score (SD)	20.5 (6.1)		18.9 (4.4)		20.0 (4.8)		18.8 (4.5)	

BMI: body mass index; DASH: Dietary Approaches to Stop Hypertension; ITE: Institute of Technical Education; MET: metabolic equivalent of task; SD: standard deviation
Number of missing data: Income level (n for diabetes = 124, n for hypertension = 122),
BMI classification (n for diabetes = 201, n for hypertension = 199), sedentary behaviour (n for diabetes = 1, n for hypertension = 1).
[a] These are post-secondary educational qualifications.

Table 2. Logistic regression with diabetes and hypertension as the outcome.

	T2DM outcome				Hypertension outcome			
	Model 1[a]		Model 2[b]		Model 1[a]		Model 2[c]	
	OR (95% CI)	Linear p_{trend}	OR (95% CI)	Linear p_{trend}	OR (95% CI)	Linear p_{trend}	OR (95% CI)	Linear p_{trend}
Work-related physical activity		0.554		0.781		0.735		0.867
0 MET-minute (Reference)								
>0–1805 MET-minutes	0.65 (0.39–1.10)		0.64 (0.36–1.14)		1.08 (0.73–1.58)		1.24 (0.82–1.89)	
>1805 MET-minutes	0.86 (0.52–1.42)		0.93 (0.55–1.56)		0.93 (0.60–1.43)		1.04 (0.66–1.64)	
Transport-related physical activity		0.969		0.897		0.454		0.604
0 MET-minute (Reference)								
>0–1028 MET-minutes	0.94 (0.56–1.58)		1.04 (0.57–1.89)		0.67 (0.45–1.01)		0.69 (0.44–1.10)	
>1038 MET-minutes	0.99 (0.56–1.74)		0.96 (0.51–1.80)		0.84 (0.52–1.34)		0.87 (0.52–1.47)	
Leisure-related physical activity		**0.003**		**0.016**		**0.005**		**0.025**
0 MET-minute (Reference)								
>0–826 MET-minutes	0.74 (0.46–1.16)		0.77 (0.47–1.28)		1.03 (0.70–1.53)		1.07 (0.70–1.64)	
>826 MET-minutes	**0.41 (0.23–0.73)**		**0.46 (0.24–0.86)**		**0.54 (0.35–0.83)**		**0.59 (0.37–0.94)**	
Sedentary behaviour		0.500		0.889		**0.014**		**0.026**
0–5 hours (Reference)								
>5–8 hours	1.17 (0.73–1.87)		1.17 (0.69–2.01)		1.27 (0.87–1.85)		1.32 (0.88–1.99)	
>8 hours	1.21 (0.70–2.08)		0.96 (0.53–1.73)		**1.70 (1.11–2.60)**		**1.69 (1.06–2.69)**	

CI: confidence interval; DASH: Dietary Approaches to Stop Hypertension; MET: metabolic equivalent of task; OR: odds ratio; SD: standard deviation; T2DM: type 2 diabetes mellitus

[a] Adjusted for age, sex, ethnicity, education, personal income and DASH score.

[b] Additionally adjusted for body mass index (international) and hypertension.

[c] Additionally adjusted for body mass index (international) and T2DM.

Bold values indicate statistical significance ($P<0.05$).

associated with higher odds of hypertension (OR of >8 hours 1.69, 95% CI 1.06–2.69). The dose-response effects for leisure-related physical activity (p_{trend}=0.025) and sedentary time (p_{trend}=0.026) were significant.

Including interaction terms in the model showed that the associations between hypertension with leisure-related physical activity and sedentary behaviour were moderated by age group (online Supplementary Table S1). Table 3 presents the ORs for these associations by age group. Among participants aged 18–34 and 50–64 years, those who engaged in >826 MET-minutes of leisure-related physical activity had lower odds of having hypertension (OR for 18–34 years 0.15, 95% CI 0.03–0.66; OR for 50–64 years 0.44, 95% CI 0.21–0.91) than those who did not engage in leisure-related physical activity. For participants aged 18–34 years, higher odds of having hypertension were observed for those with >8 hours of sedentary behaviour than those with 0–5 hours of sedentary behaviour (OR 15.07, 95% CI 1.69–133.92).

Table 3. Adjusted odd ratios for leisure-related physical activity-by-age interactions.

	Hypertension OR (95% CI)
Leisure-related physical activity	
>0–826 MET-minutes versus 0 MET-minute	
18–34 years old	0.89 (0.18–4.49)
35–49 years old	0.83 (0.38–1.79)
50–64 years old	1.03 (0.56–1.87)
≥65 years old	1.36 (0.58–3.22)
>826 MET-minutes vs 0 MET-minute	
18–34 years old	**0.15 (0.03– 0.66)**
35–49 years old	0.47 (0.19–1.16)
50–64 years old	**0.44 (0.21–0.91)**
≥65 years old	1.18 (0.55–2.56)
Sedentary behaviour	
>5–8 hours vs 0–5 hours	
18–34 years old	7.46 (0.71–78.8)
35–49 years old	1.74 (0.72–4.26)
50–64 years old	1.08 (0.59–1.97)
≥65 years old	1.41 (0.66–2.99)
>8 hours vs 0–5 hours	
18–34 years old	**15.07 (1.69–133.92)**
35–49 years old	1.72 (0.70–4.20)
50–64 years old	1.75 (0.91–3.38)
≥65 years old	1.30 (0.52–3.25)

CI: confidence interval; DASH: Dietary Approaches to Stop Hypertension; MET: metabolic equivalent of task; OR: odds ratio

Adjusted for age, sex, education, ethnicity, personal income, DASH score, body mass index (international) and diabetes.

Bold values indicate statistical significance (P<0.05).

DISCUSSION

Our study showed that those who did not participate in work-related and leisure-related physical activities had higher prevalence of T2DM and hypertension. Moreover, the odds of having T2DM were lower for participants with higher levels of leisure-related physical activity. Higher levels of leisure-related physical activity were associated with lower odds of hypertension, whereas higher sedentary time was associated with higher odds of hypertension. Furthermore, a high level of leisure-related physical activity (>826 MET-minutes) was associated with lower odds of hypertension for participants aged 18–34 and 50–64 years. A high level of sedentary time (>8 hours) was associated with higher odds of hypertension among those aged 18–34 years.

Our findings on the association between leisure-related physical activity and T2DM is in line with previous studies. A cohort study among Japanese workers revealed that the hazard of T2DM was 0.17 times lower for those with ≥15 MET-hours of leisure-time exercise than those with no leisure-time exercise.[26] Lee et al. also found that in Korea, higher leisure-related physical activity (≥600 MET-minutes/week) lowered the odds of having diabetes for men by 0.15 times and women by 0.27 times.[6] Other studies have demonstrated that exercise can enhance insulin sensitivity for a minimum of 16 hours after exercise and raise glucose absorption stimulated by insulin.[27,28]

Related studies have corroborated our findings on the associations of leisure-related physical activity and sedentary behaviour with hypertension. A meta-analysis of prospective cohort studies revealed that the risk of hypertension was lowered by 0.19 times for high leisure-related physical activity.[29] Another meta-analysis showed that a unit increase in total sedentary behaviour raises the risk of hypertension by 4%.[30] Biological studies have also found that exercise training can reduce the risk of hypertension by producing more nitric oxide, which leads to endothelial vasodilation.[31] Moreover, higher nitric oxide can result in angiogenesis, a process that increases the size and number of blood vessels, and individuals with higher sedentary time produce fewer

vasodilator metabolites due to low metabolic demand.[32] Moreover, their blood vessels in the lower limbs are narrowed due to seated posture.[32] These processes increase peripheral resistance of the blood vessels and lead to a higher risk of hypertension.[32]

Our results showed that the associations between hypertension with leisure-related physical activity and sedentary behaviour vary with age. Although limited epidemiological studies have considered the moderating effect of age on the association between leisure-related physical activity and hypertension, several intervention studies have examined how physical activity can influence endothelium-dependent vasodilation in different age groups. For young adults, a study on a 10-week exercise programme on healthy male military recruits (aged 17–24 years) showed that the programme improved the mean flow-mediated dilation of the intervention group from 2.2% to 3.9%.[33] For older adults, a study showed that a 3-month aerobic exercise programme for males aged 50–76 years enhanced acetylcholine-mediated vasodilation by 30%.[34] However, our findings only showed significant associations between leisure-related physical activity and hypertension among those aged 18–34 and 50–64 years. As we could not explain the lack of association among those aged 35–49 years and those 65 years and above, future studies could explore the reasons for these phenomena.

Although a few studies have examined the moderating effect of age on the association between sedentary behaviour and hypertension, the results were different from our findings. A study that examined the health correlates of hypertension among college students revealed that weekly sitting time was not significantly associated with hypertension.[35] Similarly, another study showed no significant association between sedentary behaviour and blood pressure among university students.[36] This difference could be related to the diverse instruments used to measure sedentary behaviour.

Our study has several implications for health promotion strategies. Firstly, the dose-response association between leisure-related physical activity with T2DM suggests that individuals with higher leisure-related physical activity had a lower prevalence of diabetes (Reference group: 0 MET-minute). Hence, although engaging in >826 MET-minutes of leisure-related physical activity will be more beneficial, health-promoting organisations can still emphasise that small and moderate levels of leisure-related physical activities are better than none. Secondly, participants with higher levels of sedentary time had a high prevalence of hypertension. Hence, reducing the hours of sedentary time, even slightly, may be beneficial in reducing the prevalence of hypertension.

Thirdly, our results showed that the associations between domain-specific physical activity and sedentary time with T2DM and hypertension were significant in certain age groups. As our study was cross-sectional, we could not infer whether physical activity or sedentary time can prevent T2DM or hypertension over time. Nonetheless, our findings suggest that more could be done to encourage a healthy lifestyle for individuals in these age groups. A previous publication by Subramaniam et al.[37] has identified several barriers and facilitators of adopting a healthy lifestyle in Singapore. However, these barriers and facilitators focused on physical activity and nutrition. Future research can explore the reasons for a high sedentary time among individuals aged 50–64 years. Knowing these reasons can help to formulate strategies that disrupt long hours of sedentary time.

Our results are generalisable to the Singapore population since the data are from a nationwide survey. Nevertheless, our study has several limitations. Firstly, the presence of T2DM and hypertension were self-reported. However, <10% of our random sample of participants with no reported diabetes were undiagnosed. Furthermore, studies have shown that self-reported diagnosis is accurate.[38,39] A study by Hansen et al.[38] found a good agreement between self-reported diabetes and practitioner-reported diabetes. Self-reported hypertension also had a moderate agreement with practitioner-reported hypertension.[38] Secondly, we could not account for confounders that were not collected in the study, such as smoking status.[9,16,40] Lastly, we could not infer causality due to the cross-sectional study design. For instance, those with hypertension may be advised to improve their physical activity. Hence, the association between leisure-related physical activity and hypertension may be hard to detect in our study.

CONCLUSION

Our study showed that higher levels of leisure-related physical activity was associated with a lower odds of having T2DM and hypertension. Furthermore, sedentary behaviour was positively associated with hypertension. Future studies could explore the reasons for a high sedentary time among individuals aged 50–64 years. By quantifying these associations, relevant organisations in Singapore can better promote the health benefits of increasing leisure-related physical activity and reducing sedentary time.

Disclosure

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REFERENCES

1. Cho NH, Shaw JE, Karuranga S, et al. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract 2018;138:271-81.
2. Chatterjee S, Khunti K, Davies MJ. Type 2 diabetes. Lancet 2017;389:2239-51.
3. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nat Rev Nephrol 2020;16:223-37.
4. Fisher NDL, Curfman G. Hypertension—A Public Health Challenge of Global Proportions. JAMA 2018;320:1757-9.
5. World Health Organization. Diabetes. https://www.who.int/health-topics/diabetes. Accessed 30 January 2023.
6. Lee EB, Hong S, Min J, et al. Association between domain-specific physical activity and diabetes in Korean adults. Sci Rep 2021;11:13066.
7. Divney AA, Murillo R, Rodriguez F, et al. Diabetes Prevalence by Leisure-, Transportation-, and Occupation-Based Physical Activity Among Racially/Ethnically Diverse U.S. Adults. Diabetes Care 2019;42:1241-7.
8. Ryu M, Lee S, Gym H, et al. Analysis of Association of Occupational Physical Activity, Leisure-Time Physical Activity, and Sedentary Lifestyle with Hypertension according to the Adherence with Aerobic Activity in Women Using Korea National Health and Nutrition Examination Survey 2016-2017 Data. Int J Hypertens 2020;2020:8943492.
9. Millett C, Agrawal S, Sullivan R, et al. Associations between Active Travel to Work and Overweight, Hypertension, and Diabetes in India: A Cross-Sectional Study. PLOS Med 2013; 10:e1001459.
10. Treff C, Benseñor IM, Lotufo PA. Leisure-time and commuting physical activity and high blood pressure: the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). J Hum Hypertens 2017; 31:278-83.
11. Lim MS, Park B, Kong IG, et al. Leisure sedentary time is differentially associated with hypertension, diabetes mellitus, and hyperlipidemia depending on occupation. BMC Public Health 2017;17:278.
12. National Population and Talent Division, Strategy Group, Prime Minister's Office; Singapore Department of Statistics; Ministry of Home Affairs; Immigration & Checkpoints Authority; and Ministry of Manpower. Population in Brief 2020. Published September 2020. https://www.strategygroup.gov.sg/files/media-centre/publications/population-in-brief-2020.pdf. Accessed 30 January 2023.
13. Phan TP, Alkema L, Tai ES, et al. Forecasting the burden of type 2 diabetes in Singapore using a demographic epidemiological model of Singapore. BMJ Open Diabetes Res Care 2014;2:e000012.
14. Epidemiology & Disease Control Division and Policy, Research & Surveillance Group, Ministry of Health, Singapore and Health Promotion Board, Singapore. National Population Heath Survey 2020, November 2021. https://www.moh.gov.sg/docs/librariesprovider5/default-document-library/nphs-2020-survey-report.pdf. Accessed 7 July 2021.
15. HealthHub, Singapore. National Steps Challenge. https://www.healthhub.sg/programmes/37/nsc/community-challenge. Accessed 30 January 2023.
16. Müller-Riemenschneider F, Hong Y, Tan KHX, et al. The association of different types of leisure time physical activities with cardiometabolic outcomes in Singapore—findings from the multi-ethnic cohort study. Int J Environ Res Public Health 2020;17:9030.
17. AshaRani PV, Abdin E, Kumarasan R, et al. Study protocol for a nationwide Knowledge, Attitudes and Practices (KAP) survey on diabetes in Singapore's general population. BMJ Open 2020;10:e037125.
18. Armstrong T, Bull F. Development of the World Health Organization Global Physical Activity Questionnaire (GPAQ). J Public Health 2006;14:66-70.
19. Chu AHY, Ng SHX, Koh D, et al. Reliability and Validity of the Self- and Interviewer-Administered Versions of the Global Physical Activity Questionnaire (GPAQ). PLOS ONE 2015;10:e0136944.
20. Chu AHY, Ng SHX, Koh D, et al. Domain-Specific Adult Sedentary Behaviour Questionnaire (ASBQ) and the GPAQ Single-Item Question: A Reliability and Validity Study in an Asian Population. Int J Environ Res Public Health 2018;15:739.
21. Marques A, Santos T, Martins J, et al. The association between physical activity and chronic diseases in European adults. Eur J Sport Sci 2018;18:140-9.
22. Schulze MB, Hu FB. Dietary patterns and risk of hypertension, type 2 diabetes mellitus, and coronary heart disease. Curr Atheroscler Rep 2002;4:462-7.
23. Whitton C, Ho JCY, Rebello SA, et al. Relative validity and reproducibility of dietary quality scores from a short diet screener in a multi-ethnic Asian population. Public Health Nutr 2018; 21:2735-43.
24. WHO Consultation on Obesity and World Health Organization. Obesity : preventing and managing the global epidemic : report of a WHO consultation. Geneva: World Health Organization; 2000. https://apps.who.int/iris/handle/10665/42330.
25. Lau JH, Nair A, Abdin E, et al. Prevalence and patterns of physical activity, sedentary behaviour, and their association with health-related quality of life within a multi-ethnic Asian population. BMC Public Health 2021;25:1-13.
26. Honda T, Kuwahara K, Nakagawa T, et al. Leisure-time, occupational, and commuting physical activity and risk of type 2 diabetes in Japanese workers: A cohort study. BMC Public Health 2015;15.
27. Borghouts LB, Keizer HA. Exercise and Insulin Sensitivity: A Review. Int J Sports Med 2000;21:1-12.
28. Lim JG, Kang HJ, Stewart KJ. Type 2 Diabetes in Singapore: The Role of Exercise Training for its Prevention and Management. Singapore Med J 2004;45:62-8.
29. Huai P, Xun H, Reilly KH, et al. Physical Activity and Risk of Hypertension. Hypertension 2013;62:1021-6.
30. Guo C, Zhou Q, Zhang D, et al. Association of total sedentary behaviour and television viewing with risk of overweight/obesity, type 2 diabetes and hypertension: A dose–response meta-analysis. Diabetes Obes Metab 2020;22:79-90.
31. Gambardella J, Morelli MB, Wang XJ, et al. Pathophysiological mechanisms underlying the beneficial effects of physical activity in hypertension. J Clin Hypertens (Greenwich) 2020;22:291-5.

32. Dempsey PC, Larsen RN, Dunstan DW, et al. Sitting Less and Moving More. Hypertension 2018;72:1037-46.
33. Clarkson P, Montgomery HE, Mullen MJ, et al. Endothelial Function Exercise Training Enhances Endothelial Function in Young Men. J Am Coll Cardiol 1999;33:1379-85.
34. DeSouza CA, Shapiro LF, Clevenger CM, et al. Regular Aerobic Exercise Prevents and Restores Age-Related Declines in Endothelium-Dependent Vasodilation in Healthy Men. Circulation 2000;102:1351-7.
35. Bairapareddy KC, Kamcheh MMS, Itani RJ, et al. Low physical activity levels are linked to early hypertension risk in college-going young adults. Healthcare (Basel) 2021;9:1258.
36. Tayem YI, Yaseen NA, Khader WT, et al. Prevalence and risk factors of obesity and hypertension among students at a central university in the West Bank. Libyan J Med 2012;7.
37. Subramaniam M, Devi F, AshaRani P, et al. Barriers and facilitators for adopting a healthy lifestyle in a multi-ethnic population: A qualitative study. PLOS ONE 2022;17:e0277106.
38. Hansen H, Schäfer I, Schön G, et al. Agreement between self-reported and general practitioner-reported chronic conditions among multimorbid patients in primary care - results of the MultiCare Cohort Study. BMC Fam Pract 2014;15:39.
39. Haapanen N, Miilunpalo S, Pasanen M, et al. Agreement between Questionnaire Data and Medical Records of Chronic Diseases in Middle-aged and Elderly Finnish Men and Women. Am J Epidemiol 1997;145:762-9.
40. Villegas R, Kearney PM, Perry IJ. The cumulative effect of core lifestyle behaviours on the prevalence of hypertension and dyslipidemia. BMC Public Health 2008;8.

ORIGINAL ARTICLE

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Transitional care strategies at emergency department for elderly patients: A multicentre study in Singapore

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ABSTRACT

Introduction: Transitional care strategies (TCS) initiated for elderly patients prior to emergency department (ED) discharge are important for ensuring effective transition to other care settings. Such strategies have been shown to reduce avoidable acute admissions. This first nationwide study is targeted at public acute hospital EDs in Singapore, and aims to characterise TCS for ED-discharged elderly patients and understand the experiences of healthcare staff in the delivery of TCS.

Method: Seven key informants (KIs), one per ED, completed an online structured questionnaire and semi-structured video conference interview from 8 May to 31 August 2021. The KIs were ED specialists and an ED-trained senior staff nurse who were knowledgeable in geriatric emergency care and had contributed to at least one elder-related TCS. Field notes were compiled, transcribed, anonymised and analysed using thematic analysis.

Results: All 7 EDs have TCS as "usual care" available during office hours, at no extra cost to patients. Common components of TCS include screening, evaluation with comprehensive geriatric assessment, health education and follow-up telecare. TCS implementation was facilitated by organisational support in terms of established protocols and communication platforms, training and collaboration of a multidisciplinary team, and caregiver involvement. Obstacles faced include fragmented communication between personnel, limited resources, and poor buy-in from stakeholders.

Conclusion: Understanding the heterogeneous characteristics of ED-TCS at various hospitals will aid the development of service typology and identify service opportunities. Provider experiences grouped into themes help to inform future strategies for TCS implementation. More research is needed to evaluate patient outcomes and cost-effectiveness of TCS.

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Keywords: Community care services, emergency department, geriatric medicine, transitional care

INTRODUCTION

In Singapore, greater efforts are being directed towards developing an integrated health and social ecosystem under the new Healthier SG strategy announced by the Ministry of Health. This life-course approach aims to promote overall healthier living in collaboration with key community partners (e.g. intermediate and long-term care service providers) by utilising targeted measures of improvement in health outcomes, including the reduction of avoidable readmissions for specific vulnerable populations such as the elderly. This results in growing importance for the development of care strategies at the emergency department (ED) to help reduce avoidable admissions especially for the elderly.

Transitional care strategies (TCS) refer to multi-disciplinary interventions designed to ensure the coordination and continuity of care as patients transfer between health care settings (e.g. between the ED and community health and support services).[1] Many studies have demonstrated that TCS are effective in reducing readmissions and providing better care for the elderly.[2-6]

In recent years, there has been a proliferation of elderly-related TCS initiated in various hospital settings islandwide,[7] including the ED. The services usually

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CLINICAL IMPACT

What is New

- This is the first nationwide study in Singapore on transitional care strategies (TCS) for elderly patients discharged from public acute hospital emergency departments (EDs).
- ED-TCS are heterogeneous. Common characteristics include: screening/assessment at the ED, referral/transition workflows, and patient education.
- Organisational support, multidisciplinary care, caregiver involvement and addressing challenges such as lack of resources are important in ED-TCS implementation.

Clinical Implications

- Better understanding of ED-TCS will aid the development of service typology and identify service opportunities.
- ED-TCS may be broadened to address social determinants of health contributing to reattendance and avoidable admissions.

include an eligibility screening and geriatric assessment, which span domains on functional assessment, multi-morbidity status, psychosocial issues and polypharmacy matters—hence, enabling staff to right-site or prescribe appropriate care.[8-11] Previously, Singapore studies have explored the transition from hospital to home, but to our knowledge, there have been no reviews of TCS at our EDs. This study aims to describe the characteristics of existing TCS for ED-discharged elderly patients from public acute hospitals in Singapore, and understand the experiences of ED healthcare staff in the delivery of TCS.

METHOD

Study design

We used an exploratory mixed-methods study design, comprising a self-developed questionnaire and semi-structured interview for a convenience sample of participants. Seven public hospital EDs were included in this study. Seven key informants (KIs; one per hospital ED) completed an online structured questionnaire and semi-structured video conference interview from 8 May to 31 August 2021. Six were ED physicians, while one was an ED-trained senior staff nurse involved in geriatric emergency care. Ethics approval was sought from the Centralised Institutional Review Board (CIRB Ref: 2021/2273), and the study was deemed to not require further ethical deliberation.

Inclusion criteria

TCS is defined as an intervention or a group of interventions initiated prior to ED discharge for safe and effective transition of ED patients to other care settings.[12] In our study, we focused on TCS that catered to elderly patients aged 65 years and above. Their discharge may be from the (1) main ED; (2) clinical observation unit (such as the short stay unit), extended observation ward, or early diagnostic and observation unit; or (3) ED observation ward. We excluded TCS designed to address: (1) palliative care and terminally ill patients; (2) patients with psychosis, altered behaviour or neuropsychiatric symptoms not due to dementia; and (3) prisoners and persons-in-custody. To be eligible, KIs needed to be: aged 21 years or above; an emergency medicine specialist or emergency-trained geriatric staff nurse of senior rank and above; and contributed to one or more elderly-related TCS within the hospital.

Topic guide development

Expert inputs and a literature review of TCS were used to guide questionnaire development. The questionnaire covers domains such as type of TCS, components of the TCS, patient transition pathway, profile of recipients, key players, setting in which TCS is delivered, and any other information. The questionnaire comprised dichotomous questions (yes/no) and multiple selection questions. In-depth interview (IDI) was chosen as it provided access to depth of information and deeper insights into perspectives and experiences.[13] Findings from the questionnaire and inputs from experts (e.g. ED physicians) were used to develop a semi-structured interview guide, comprising 16 main questions based on 4 main aspects: (1) development of the TCS; (2) overview of TCS components; (3) coordination and interaction among care provider; and (4) feedback, challenges and barriers. Probes were used when deemed appropriate.

Data collection

The questionnaire was completed first to guide the development of the interview. The interview guide was pre-piloted to ensure clarity and appropriateness. Data were collected by 2 medical students who obtained informed consent from all participants. Both students have no prior relationship with the participants and underwent study-specific training involving qualitative

interviewing. After obtaining informed consent, the KIs completed an online questionnaire (Qualtrics, Seattle, WA, US). Semi-structured IDIs were conducted on a separate day. The interviews were recorded and in-depth fieldnotes captured. The interviews ranged from 40–60 minutes. No member checking or follow-up interviews were conducted.

Data analysis

Descriptive statistics were used to summarise the TCS characteristics from the questionnaire. All analyses were performed in Microsoft Excel (Microsoft Corporation, Redmond, WA, US). Inductive thematic analysis based on Braun and Clarke's approach[14] was used to examine the fieldnotes by the first and second authors of this study. The coding and organisation of themes were performed in Microsoft Word (Microsoft Corporation, Redmond, WA, US). Due to its time-bound nature and resource limitations, data or thematic saturation was not reached.

RESULTS

Overview of TCS at public hospital EDs

All EDs had elderly-related TCS available during office hours on weekdays, which were provided to eligible elderly patients as part of "usual care" at no additional cost. Characteristics of the 7 EDs are presented in Table 1, labelled as ED-A, ED-B, ED-C, etc. Components include identification of high-risk elderly patients with validated screening tools, recruitment and referral for on-site interventions, early engagement by various specialties, and patient education. In 6 of the 7 EDs, TCS were targeted at elderly patients or those with functional decline, employing observation medicine units to prepare the patients for their planned care trajectory. In ED-C (Table 1), although the TCS was not specifically designed or limited to the elderly, the patients served were mainly elderly patients.

All TCS adopted a multidisciplinary approach. In all EDs, patient identification and recruitment were done by ED personnel. In addition, 3 EDs had early in-person engagement of Geriatric Medicine physicians. Allied health professionals (AHPs) were also engaged in 6 EDs, reflecting multidisciplinary care. Most EDs (6 out of 7) also had direct ED-to-community-hospital admission pathways. There were telephone helplines for discharged patients requiring ad hoc assistance in 3 EDs. ED-E also utilised telemedicine for discharged patients; this consisted of videocall or telephone consultation performed by their community team of healthcare providers.

Themes in the delivery of TCS

The thematic analysis revealed 4 important themes in terms of the implementation of elderly-related TCS within Singapore's EDs (Fig. 1). Selected quotes from participants are listed below.

Theme 1: Organisational support and established processes for TCS

Sub-theme 1: Established protocols integrated into organisation's mainstream processes

KIs identified established protocols within their organisation as a key facilitator for the delivery of TCS. This was seen in the use of simple screening tools and integration of TCS into the mainstream ED workflow. Comments from the IDIs are presented in quotes.

"*Since it has been integrated into mainstream ED care, no one refuses the service.*" – IDI6

"Patient referred for PT (physiotherapy) assessment but MediSave/MediShield cannot be used; patient has to pay SGD80 in cash, hence a lot may decline in view of other ED charges, e.g. CT (computed tomography) scan." – IDI7

KIs reported that observational medicine units were used for patients undergoing treatment and evaluation. These relatively slower-paced units are more conducive for transitioning to the next phase of care. Admission to such units may also allow patients to utilise the national health savings scheme (MediSave) in Singapore and private health insurance. However, limited subsidies for ancillary TCS services, such as physiotherapy assessment, discouraged some patients from proceeding further with TCS.

Sub-theme 2: Opportunities for education and training

In Singapore, ED nurses involved in TCS implementation are often experienced staff who undergo additional formal training programme and assessment to ensure competence. Some KIs highlighted training opportunities provided by their organisation to improve awareness of TCS, such as inter-organisation knowledge sharing locally and internationally.

"*Nurses have to undergo a standardised training course and pass a competency test to be part of the programme.*" – IDI3

"*[Organisation name omitted] previously came for a visit and the [TCS intervention name omitted] intervention was shared.*" – IDI4

Table 1. Key characteristics of transitional care strategies for emergency department-discharged elderly in 7 acute public hospitals in Singapore.

Emergency department	**A**	**B**	**C**	**D**	**E**	**F**	**G**
Overview of transitional care strategies							
Target age	Elderly	Elderly	Not specific	Elderly	Elderly	Elderly or patients with functional decline	Elderly
Operating hours	Weekdays, office hours	Daily, 7am to 3pm	Ad hoc referral	Sunday evening to Thursday evening	Daily, office hours	Weekdays, office hours	Weekdays, office hours
Components of transitional care strategies							
Screening tool	None	ER^2	None	CFS	CFS	Hospital-developed algorithm	TRST
Assessment tool	CGA	CGA	Clinical judgement	CGA	CGA	CGA	CGA
Patient education	Face-to-face	Face-to-face, individualised written action plan	Phone call, face-to-face	Patient education brochures, face-to-face	Patient education booklet, face-to-face	Face-to-face	Patient education brochures, face-to-face
Utilisation of ED observation unit	Yes	Yes	Not applicable	Yes	Yes	Yes	Yes
Early in-person ED engagement by geriatric physicians	Yes	No	No	Yes	Yes	No	No
Early in-person ED engagement by allied health professionals	Yes PT, MSW, pharmacist	Yes PT, OT, MSW	No	Yes PT, OT, CC	Yes MDT including PT, OT, pharmacist	Yes PT, OT, MSW, ST	Yes PT
Transition to ILTC services	Yes	Yes	No	Yes	Yes	Yes	Yes
Post-discharge helpline availability for patients	No	No	No	Yes	Yes	Yes	No

CC: care coordinator; CFS: clinical frailty scale; CGA: comprehensive geriatric assessment; ED: emergency department; ER^2: emergency room evaluation and recommendation; ILTC: intermediate and long-term care; MDT: multidisciplinary team; MSW: medical social worker; OT: occupational therapist; PT: physiotherapist; ST: speech-language therapy; TRST: triage risk screening tool

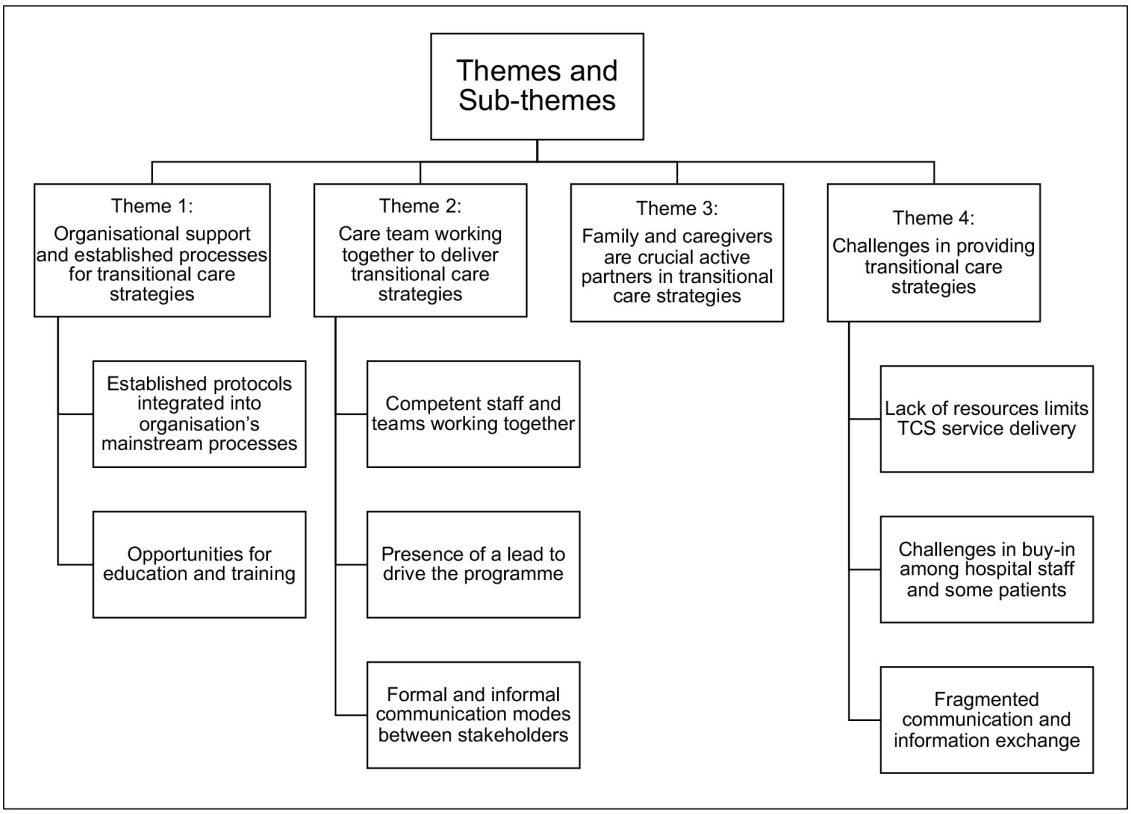

Fig.1 Themes and sub-themes identified.
TCS: transitional care strategies

Theme 2: Care team working together to deliver TCS

Sub-theme 1: Competent staff and teams working together

Most KIs mentioned the specialised expertise of each team as crucial components of TCS. Patients are reviewed by a multidisciplinary team in the ED, including AHPs and geriatric physicians. Some also highlighted that having dedicated teams for care coordination facilitated implementation. Interdisciplinary collaboration between independent and knowledgeable medical professionals enabled the smooth delivery of TCS.

"*The TCS team works closely with the [organisation team name omitted]…. TCS can activate the [organisation name omitted] team for patients suitable for subacute care, complex social issues, and/or require closer follow up... The [organisation name omitted] team will then review the patient and suggest the appropriate disposition and management of the patient*." – IDI1

Most KIs highlighted the Agency for Integrated Care (AIC) as an important case management partner.

Sub-theme 2: Presence of a lead to drive the programme

The presence of a lead, usually a nurse or clinician, was identified as the key to initial set-up of the TCS, and its sustainability in the long run.

"*Lead nurse has been very important to the discussion and implementation of [TCS intervention name omitted]*." – IDI2

Sub-theme 3: Formal and informal communication modes between stakeholders

Multidisciplinary coordination was facilitated by formal and informal modes of communication. KIs reported regular meetings between stakeholders. Digital tools such as electronic clinical documentation systems and emails are used to transmit patient information, while instant messaging applications (e.g. WhatsApp, TigerText [a form of organisational text messaging for medical professionals]) facilitate immediate feedback, especially with community partners. Technology also allowed for data linkages and case clerking between clinical systems during the screening and referral process.

"*WhatsApp chat group facilitates instant feedback sharing, and if needed, can be escalated to the monthly meeting sessions.*" – IDI5

Theme 3: Family and caregivers are crucial active partners in TCS

Involvement of family and caregivers in providing information and decision-making was crucial for patient care. They also play a role in reinforcement of health education transmitted as part of TCS. Patient education in TCS involved different modes of delivery (e.g. verbal and/or visual aids). Education was individualised according to comprehensive geriatric assessment findings, which helped to identify areas with potential knowledge gaps. In some instances, caregivers were engaged, including medically untrained foreign domestic workers who are the main care providers at home. Their involvement was viewed by all KIs as crucial to the success of TCS as the domestic workers help to monitor patient recovery and reinforce medical advice.

"*Elderly care in the ED will almost always involve family members, especially if they have cognitive issues, to reinforce the management (pharmacological, non-pharmacological)*." – IDI6

However, no formal "check-back" was performed to ensure understanding, and the onus lies with patients to raise their queries or dial post-discharge helplines. KIs mentioned that any concerns or caregiver stress raised were also attended to by TCS staff.

Theme 4: Challenges in providing TCS

KIs described challenges and barriers in their efforts to provide TCS, such as fragmented communication loops, lack of interest and limited resources.

Sub-theme 1: Lack of resources limit TCS delivery

Currently, TCS is only available during office hours on weekdays within most organisations. KIs consistently mentioned manpower constraints and limited funding as key barriers to increasing TCS availability. Improving accessibility of these services, such as on weekends, will help more patients and may further prevent admissions.

"*Ideally would like to make the service available beyond office hours, on weekends and 24/7, but limited by manpower… this is my dream*" – IDI7

Sub-theme 2: Challenges in buy-in among hospital staff and some patients

Most KIs mentioned good uptake rates among patients. However, a deviant case was identified where a KI noted that:

"*Some patients—they come to the ED, they just want to get the problem fixed and go home*." – IDI1

Some participants raised challenges getting support from medical staff due to competing priorities such as other clinical duties, and the TCS might be considered as extra work:

"*I think a lot of doctors just want to do their jobs very fast. Because whatever the risks identified, then require the medical doctor to address , then they think that this is actually extra work for them. So, I do have a bit of hard time to convince them for this strategy [TCS]*." – IDI1

"*Of course, nursing manpower is always something that is needed, so trying to convince the nursing officers that this was a need and we needed to take one nurse, or two nurses even, off the daily roster to do this [TCS] screening, that was a challenge and is still a challenge currently.*" – IDI5

Junior doctors on rotational postings who have limited knowledge of TCS form a significant portion of the physician workforce. Thus, local success would depend on ED nurses and permanent doctors to identify suitable candidates. Studies have found that educating medical students on transitional care shows promising results,[15,16] making this an area worth exploring in the future.

"*Senior supervising doctors do not place adequate emphasis on importance of TCS; junior doctors are not aware of or do not make referrals to TCS; junior doctors are not aware or do not make referrals to [name of TCS intervention omitted]*." – IDI5

Sub-theme 3: Fragmented communication and information exchange

Inadequate communication or fragmented information exchange was reported to affect the delivery of TCS. KIs reported the lack of access to integrated health information systems among some TCS partners. Coupled with limitations of formal communication channels, providers are drawn to informal communication methods to ensure timely information exchange.

"*Community providers can call the [TCS intervention name omitted] operator line to inform any issues faced, but rarely is feedback escalated to the ED team*." – IDI3

"*But records from private community services like AIC cannot be seen*." – IDI7

DISCUSSION

To our knowledge, this study is the first mixed-methods study on elderly-related ED-TCS within Singapore. Our findings show that ED-TCS are complex multi-disciplinary interventions[6] delivered by different

providers at varied settings, in a coordinated manner during the full length of stay at the ED. Even though TCS across institutions are heterogeneous, we identified some common characteristics that will help to develop the typology for elderly-related ED-TCS in future: (1) screening and assessment of elderly at the ED; (2) workflows for referral and transition; and (3) patient education.

The use of technology is also seen widely among EDs. Integrated health records systems and communication platforms enable information-sharing within a multidisciplinary care team.[16] Going forward, further development and adoption of a common, integrated and secure communication platform for hospital- and community-based TCS providers is needed.

The wide prevalence of ED-TCS noted from our study indicates a major shift in the focus of our care models from disease-specific care to frailty-centred care in order to meet the multidimensional needs of elderly patients.[17] A Singapore study found that early geriatric specialist intervention in the ED reduced potentially avoidable acute admissions without escalating the risk of reattendance and possibly attenuated frailty progression.[8] Another study found that geriatric assessment in the ED observation unit resulted in objective reduction in both ED reattendance and hospitalisation rates.[10] These highlight the importance of delivering holistic, needs-based geriatric emergency care right from the start of the patient's visit. With well-designed TCS for elderly ED patients fit for discharge, unnecessary hospital admissions may even be avoided.

Established protocols are also crucial in ensuring safe transitional care for elderly patients.[16] Protocolised direct admission of elderly patients at a local ED to the subacute care unit of a partnering community hospital also appeared to reap benefits by removing the need for intervening stays of longer than 24 hours at the acute hospital. This helped to reduce the overall length of stay across both institutions, decrease acute hospital admissions, and cut down the number of patient hand-offs.[9]

Delivery of TCS within the ED often requires flexibility due to time and space constraints. Our study revealed that key roles in TCS for care coordination and liaison was often undertaken by nurses. This has also been reported in other countries.[16] In Singapore, nurses take on flexible roles, often going beyond traditional duties to bridge gaps in patient care.[18] They play an important role in building rapport with patients and care providers. This trust between TCS providers and patients is crucial in overcoming care gaps.[19]

We identified opportunities to incorporate telemedicine into ED-TCS in future. It may be used to enhance interprofessional collaboration remotely or deliver direct services to patients and their caregivers. A Singapore study has found a higher uptake of telehealth services by the elderly during the COVID-19 pandemic,[20] indicating that this is a high-impact, feasible solution worth exploring. Going forward, with a capitation model for healthcare funding, there is the opportunity to sustainably resource EDs to better accomplish TCS through such avenues.

Finally, it is important to note that singular interventions might not be as impactful without an overhauling transformation of the hospital and healthcare system.[21] Aside from TCS and operational processes, EDs in Singapore should look into the "hardware" and infrastructural redesign needed to incorporate geriatric-friendly design principles. With greater attention to population health and community support structures for the elderly to not just "get well", but "live well, age well", the scope of ED-TCS may be broadened to better address other factors, such as social determinants of health among elders and foster closer partnership between EDs and community services.

Limitations

Our study has several limitations. It only looked at elderly-related ED-TCS currently implemented, thus not accounting for those in the planning phase, of which many have been delayed during the COVID-19 pandemic. Also, there was a lack of data saturation as only one KI per ED was recruited, which might impact the findings. However, this study was intended to be exploratory in nature to gather novel insights and experiences from ED staff. Future studies will enrol more participants to garner insights from multiple stakeholders. Furthermore, the findings were reviewed by the head of department of each hospital's ED, to ensure accuracy of what was reported. Lastly, medical student interviewers may have limited insight into clinical care strategies, which may limit exploration on the subject and the depth of the interviews. To mitigate this, interview questions were reviewed by 2 ED specialists (study investigators) to improve information capture.

CONCLUSION

This study sheds light on elderly-related ED-TCS available for elderly patients discharged from 7 public acute hospitals in Singapore. Common components

and characteristics of these TCS were identified. Understanding the heterogeneous characteristics of TCS at various hospitals will aid the development of service typology and identify service opportunities. Factors that facilitated implementation included established workflow protocols, effective usage of communication tools, active involvement of competent personnel, staff training, and caregiver participation. More research is needed to investigate the clinical effectiveness of elderly-related ED-TCS and foster closer partnership with community care providers.

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REFERENCES

1. Coleman EA, Boult C, American Geriatrics Society Health Care Systems Committee. Improving the quality of transitional care for persons with complex care needs. J Am Geriatr Soc 2003;51:556-7.
2. Markle-Reid M, McAiney C, Fisher K, et al. Effectiveness of a nurse-led hospital-to-home transitional care intervention for older adults with multimorbidity and depressive symptoms: A pragmatic randomized controlled trial. PLOS ONE 2021;16:e0254573.
3. Menezes TMO, Oliveira ALB, Santos LB, et al. Hospital transition care for the elderly: an integrative review. Rev Bras Enferm 2019;72(suppl 2):294-301.
4. Allen J, Hutchinson AM, Brown R, et al. Quality care outcomes following transitional care interventions for older people from hospital to home: a systematic review. BMC Health Serv Res 2014;14:346.
5. Kim H, Thyer BA. Does Transitional Care Prevent Older Adults from Rehospitalization? A Review. J Evid Inf Soc Work 2015; 12:261-71.
6. Wee SL, Loke CK, Liang C, et al. Effectiveness of a national transitional care program in reducing acute care use. J Am Geriatr Soc 2014;62:747-53.
7. Ministry of Health, Singapore. Senior minister of state cos speech 2: Better home and community care for our seniors. https://www.moh.gov.sg/news-highlights/details/senior-minister-of-state-cos-speech-2-better-home-and-community-care-for-our-seniors. Accessed 15 April 2023.
8. Chong E, Zhu B, Tan H, et al. Emergency Department Interventions for Frailty (EDIFY): Front-door geriatric care can reduce acute admissions. J Am Med Dir Assoc 2021;22:923-28.e5.
9. Ang SH, Rosario BH, Ngeow KYI, et al. Direct admission from the emergency department to a subacute care ward: An alternative to acute hospitalization. J Am Med Dir Assoc 2020;21:1346-8.
10. Foo CL, Siu VWY, Tan TL, et al. Geriatric assessment and intervention in an emergency department observation unit reduced re-attendance and hospitalisation rates. Australas J Ageing 2012; 31:40-6.
11. Lee KH, Low LL, Allen J, et al. Transitional care for the highest risk patients: Findings of a randomised control study. Int J Integr Care 2015;15:e039.
12. Rennke S, Nguyen OK, Shoeb MH, et al. Hospital-initiated transitional care interventions as a patient safety strategy: A systematic review. Ann Intern Med 2013;158:433-40.
13. Ritchie JLJ, Lewis J, McNaughton Nicholls C, Ormston R (Ed). Qualitative Research Practice: A Guide for Social Science Students and Researchers. London, et al.; Sage Publications; 2003.
14. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol 2006;3:77-101.
15. Buchanan IM, Besdine RW. A systematic review of curricular interventions teaching transitional care to physicians-in-training and physicians. Acad Med 2011;86:628-39.
16. Laugaland K, Aase K, Barach P. Interventions to improve patient safety in transitional care–a review of the evidence. Work 2012; 41(suppl 1):2915-24.
17. Cheah J, Wong LM, Pang HL. Integrate now, create health: Perspectives from Singapore. Int J Integr Care 2010;10:e044.
18. Chen WT, He HG, Chow YL. The evolving roles of nurses providing care at home: A qualitative case study research of a transitional care team. Int J Integr Care 2022;22:3.
19. Baxter R, Shannon R, Murray J, et al. Delivering exceptionally safe transitions of care to older people: a qualitative study of multidisciplinary staff perspectives. BMC Health Serv Res 2020; 20:780.
20. Tan LF, Teng VHW, Seetharaman SK, et al. Facilitating telehealth for older adults during the COVID-19 pandemic and beyond: Strategies from a Singapore geriatric center. Geriatr Gerontol Int 2020;20:993-5.
21. Ang IYH, Tan CS, Nurjono M, et al. Retrospective evaluation of healthcare utilisation and mortality of two post-discharge care programmes in Singapore. BMJ Open 2019;9:e027220.

ORIGINAL ARTICLE

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Association between body mass index, body image and self-esteem with sexual function: A survey of young women in Singapore

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ABSTRACT

Introduction: Obesity is thought to be a negative predictor of sexual function, but the relationship between body mass index (BMI) and sexual function has been inconsistent. Other factors such as body image and self-esteem may mediate this relationship. This study examined the association of BMI, body image and self-esteem with sexual function in young women.

Method: A total of 514 sexually active women aged 21 to 35 years completed an anonymised online questionnaire that used 3 scales to assess body image, self-esteem and female sexual function: Body Image States Scale (BISS), Rosenberg Self-Esteem Scale (RSES) and Female Sexual Function Index (FSFI). Higher scores for BISS, RSES and FSFI indicate more positive body image, higher self-esteem and better sexual function, respectively. Spearman correlation assessed the association among BMI, BISS and RSES scores, and with FSFI scores. Linear and multivariable logistic regression identified risk factors associated with sexual dysfunction (FSFI <26.55).

Results: BISS and RSES scores significantly correlated with FSFI scores (r=0.27 and r=0.32, respectively; both $P<0.001$), indicating that better body image and self-esteem were associated with better sexual function. Risk factors for sexual dysfunction were lower BISS and RSES scores, being married (odds ratio [OR] 1.52; 95% confidence interval [CI] 1.07–2.15), having 1 child (OR 2.45; 95% CI 1.26–4.77) and having a perceived mental condition (OR 3.02; 95% CI 1.44–6.33). Factors in lack of sexual dysfunction include being of Malay ethnicity (OR 0.38; 95% CI 0.21–0.71) and being overweight (OR 0.46; 95% CI 0.27–0.78).

Conclusion: Women with poorer body image and lower self-esteem were more likely to have sexual dysfunction. These perceptions and states did not correlate with being overweight, and were better predictors over BMI to identify the population at-risk.

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Keywords: Female sexual function, obstetrics and gynaecology, sexual health

INTRODUCTION

Satisfaction with sexual activity is a good predictor of global life satisfaction.[1] Problems with sexual function can lead to lower partner satisfaction and affect a woman's mental and physical health.[2] The prevalence of sexual dysfunction in premenopausal women globally was found to be 40.9% (95% confidence interval [CI] 37.1–44.7).[3] In Singapore, it is even higher; a pilot study with 92% of respondents aged below 50 years found that the prevalence of female sexual dysfunction was up to 56.2%,[4] with reported rates of up to 70.9% among older women aged 45 to 69 years.[5] Lower sexual function has also been shown to impact fecundability.[6]

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CLINICAL IMPACT

What is New

- To our knowledge, this is the first study in Singapore assessing the relationship of body mass index, body image and self-esteem in relation to sexual function in young women.

Clinical Implications

- Women with poorer body image and lower self-esteem are more likely to have sexual dysfunction—these perceptions and states do not correlate with being overweight.
- Body image and self-esteem are better predictors than BMI in identifying women at risk of sexual dysfunction.

Contextual factors, psychosexual factors and biological factors contribute to sexual dysfunction. Some of these include marital or relationship difficulties, socioeconomic factors, medical or psychological conditions, medications and previous surgeries.[7] In some studies, total body fat percentage and obesity (measured using body mass index [BMI]) negatively predict sexual functioning.[8] However, body weight and BMI appear to have no significant relationship with sexual function in other studies.[9] This inconsistency in the association may be due to mediating factors such as body image[9] and self-esteem.[10]

Body image refers to how one perceives one's projected physical self, including the feelings towards appearance and beliefs related to appearance.[11] Women have a higher tendency than men to be cognitively distracted by their body appearance during sexual activity, signifying the importance of assessing body image in relation to sexual function.[12] Body image is also closely related to BMI[8]; as BMI increases, body image satisfaction decreases.[13] People with normal BMI may also demonstrate body image dissatisfaction owing to the subjective component of body image and associated appearance anxiety.[13-15] Self-esteem, which is described as the personal emotional evaluation of an individual's worth, has been found to have a mediating role in influencing body image, sexual activity and sexual function.[13] Both body image and self-esteem are heavily influenced by emotion, experiences and exposure to media.[13,16] The recent focus on body image positivity through all forms of media channels[17] may alter the relationship between BMI and body image, and could have implications on self-esteem of young women.

While we have identified the burden of sexual dysfunction on society, how sexual dysfunction is influenced by BMI and its potential mediating factors of body image and self-esteem remains unknown. Data on risk factors and associations are sparse in our population with its unique cultural practices and ethnic diversity. This study focuses on young women of reproductive age as many physiological and hormonal changes can affect sexual function as women age.[5,18] We aimed to assess individual and joint associations between BMI, body image and self-esteem, with sexual function, and identify other risk factors for sexual dysfunction. Information gained from this study will help identify women at risk for sexual dysfunction so that they can undergo proper assessment. It can also serve to direct management strategies for a multi-disciplinary approach in the treatment of sexual dysfunction in these women.

METHOD

Study design and subjects

An anonymised online questionnaire in English was administered from February to August 2021 in Singapore. Sexually active women aged 21 to 35 years who are either Singaporean or permanent residents were included. The lower limit of the age group was 21 years, given the sensitive nature of the questions. The upper limit of 35 years was chosen to focus on young, reproductive-aged women. Understanding sexual function in young women may provide insight into predictive factors affecting fecundability and sexual activity in midlife and beyond.[5] This study was reviewed and approved by the SingHealth Centralised Institutional Review Board (2020/3037). A total of 514 women were recruited.

Recruitment

Recruitment was conducted through a Facebook advertisement as well as through posters put up in a government-based primary care clinic. Paid advertising was chosen to improve recruitment and reach. The questionnaire was hosted on the FormSG website (https://form.gov.sg), a government-based platform that captures classified data. Participation was voluntary and consent was implied for those who completed the questionnaire.

Questionnaire

The questionnaire included basic demographic data, marital status, number of children, smoking and drinking status, gender of sexual partner, number of current sexual partners as well as medical, physical or mental conditions they feel could affect their sexual function. We included 3 scales to assess body image, self-esteem and female sexual dysfunction. The scales used were Body Image States Scale (BISS), the Rosenberg Self-Esteem Scale (RSES) and the Female Sexual Function Index (FSFI). Questionnaires were answered by the participants who used their internet-enabled devices to complete the survey privately.

The BISS is a 6-item scale that assesses body image as a state at a specific point in time. Possible scores range from 6 to 54, in which the lower scores indicate poor body image and higher scores indicate a more positive body image. The BISS is acceptably and internally consistent and applicable to a wide range of contexts as it is easy to administer and assesses both positive and negative experiences as well as the general body image (i.e. not specific to any particular body part).[19,20]

The RSES assesses self-esteem using 10 items administered on a 4-point Likert scale, with possible scores between 0 and 30. Higher scores indicate higher levels of self-esteem. The scale has been validated for use in multiple populations of varying ages.[21] It has high reliability: test-retest correlations are typically in the range of 0.82 to 0.88, and Cronbach α for various samples are in the range of 0.77 to 0.88.[21,22]

The FSFI is a widely used 19-item tool for the assessment of sexual function that incorporates 6 domains: desire, arousal, lubrication, orgasm, satisfaction and pain. It has demonstrated internal consistency, test-retest reliability, and construct and criterion validity.[23,24] It has been translated into various Asian languages such as Malay,[25] Chinese[26] and Urdu,[27] and have been validated afterwards within the various countries. It has also been used in the assessment of sexual dysfunction in both Singapore[5] and Malaysia.[28] An online version of the FSFI has also shown acceptable validity and reliability compared with the paper version.[29]

Sample size

A sample size of 503 achieves 90% power to detect a Spearman correlation in the range of 0.2 to 0.4, at a 5% level of significance. Sample size was calculated using 5,000 Monte Carlo simulations by the Power Analysis and Sample Size software program (PASS 16; NCSS, LLC; Kaysville, Utah, US).

Statistical analyses

The scores of BMI, BISS (representing body image) and RSES (representing self-esteem) with the FSFI scores (representing female sexual dysfunction), including the scores for each domain of the FSFI (desire, arousal, lubrication, orgasm, pain, satisfaction), were computed. Correlations among BMI, BISS and RSES and with FSFI scores were assessed. Higher scores for BISS, RSES and FSFI imply a more positive body image, higher self-esteem and better sexual f unction, respectively. Conversely, lower scores indicate poorer body image, lower self-esteem and poorer sexual function for BISS, RSES and FSFI, respectively.

Continuous variables are expressed as mean ± standard deviation and categorical variables as frequencies and percentages.

Continuous variables were analysed using Spearman correlation. FSFI was categorised as either sexual dysfunction (FSFI <26.55) or normal functioning. Independent samples t-test was used to compare BMI, BISS and RSES scores between the two sexual functioning groups.

Univariable and multivariable logistic regression analyses were used to test the association of different variables with FSFI scores. BMI was categorised as underweight (<18.5kg/m^2), normal (18.5–22.9kg/m^2), overweight (23.0–27.4kg/m^2) and obese (≥27.5 kg/m^2). BISS and RSES scores were divided into tertiles representing low, medium and high values.

For the outcome variable of FSFI, we used a cut-off score of <26.55 to identify sexual dysfunction.[30] This cut-off point was found to have a sensitivity of 88–89% and specificity of 71–73% in detecting sexual dysfunction. It has been used in our local setting and neighbouring populations in diagnosing female sexual dysfunction.[5]

SPSS Statistics software version 26 (IBM Corp, Armonk, US) was used for the preliminary statistical analysis of data and a *P* value of less than 0.05 was considered statistically significant.

RESULTS

A total of 514 completed questionnaires were available for analysis. The mean age of the respondents was 29.6±4.1 years and the mean BMI 23.6±5.5 kg/m^2. Of the respondents, 46.5% (n=239) were classified as having sexual dysfunction (Table 1).

Using Spearman correlation, BMI did not correlate with the FSFI total scores but did with the pain domain. The BISS and RSES scores correlated with the FSFI scores, implying that those with a more positive body

Table 1. Basic demographic and other data obtained from respondents (N=514).

Characteristics	
Age, mean (SD), years	29.6 (4.1)
BMI, mean (SD), kg/m^2	23.6 (5.5)
Ethnicity, no. (%)	
Chinese	348 (68)
Malay	81 (16)
Indian	51 (10)
Other	34 (7)
Marital status: married, no. (%)	255 (50)
No. of children, no. (%)	
0	367 (71)
1	64 (12)
2	54 (11)
>2	25 (4.5)
Other	4 (0.7)
Smokes cigarettes, no. (%)	28 (5)
Drinks alcohol, no. (%)	167 (32)
Gender of sexual partner, no. (%)	
Male	483 (94)
Female	28 (5)
Other	3 (0.6)
Medical condition perceived to affect sexual function, no. (%)	42 (8)
Physical condition perceived to affect sexual function, no. (%)	17 (3)
Mental condition perceived to affect sexual function, no. (%)	45 (9)

BMI: body mass index; SD: standard deviation

image and a higher self-esteem had better sexual function. This finding was consistent across all 6 individual domains of sexual function (Table 2).

BMI negatively correlated with BISS scores, implying that as BMI increases, body image declines. However, BMI did not significantly correlate with self-esteem as measured by RSES (Table 3). BISS scores and RSES scores were positively correlated, implying that as body image improves, self-esteem improves.

An independent samples test was also done to compare the mean scores of BMI, BISS and RSES between the women with sexual dysfunction (FSFI <26.55) and without sexual dysfunction (Table 4). Women with sexual dysfunction had significantly lower mean BISS and RSES scores. There was no significant difference in BMI between both groups of women.

For univariable and multivariable logistic regression analyses, BMI was divided into categories and BISS and RSES scores into tertiles. This was assessed in women with and without sexual dysfunction (Table 5).

In the univariate analysis, women who were underweight (odds ratio [OR] 0.57; 95% CI 0.33–0.98) and overweight (OR 0.57; 95% CI 0.36–0.91) had a reduced risk of sexual dysfunction. Women with lower BISS and RSES scores (scores in the lower and middle tertiles) were at higher risk of sexual dysfunction. Married women (OR 1.52; 95% CI 1.07–2.15), women with 1 child (OR 2.56; 95% CI 1.47–4.45) and women with a mental condition perceived to affect their sexual function (OR 3.08; 95% CI 1.58–6.02) were also at higher risk.

In the multivariable analysis, women who were overweight were less likely to have sexual dysfunction than those with normal BMIs (39.3% vs 53.1%; OR 0.46; 95% CI 0.27–0.78). Women of Malay ethnicity were also less likely to have sexual dysfunction than those of Chinese ethnicity (41.3% vs 49.7%; OR 0.38; 95% CI 0.21–0.71).

One of the risk factors for sexual dysfunction identified was women with 1 child compared with those with none (OR 2.45; 95% CI 1.26–4.77). Women who perceived themselves as having a mental condition that affected their sexual function were also significantly more likely to suffer from sexual dysfunction (OR 3.02; 95% CI 1.44–6.33). In addition, women who scored in the lower tertile of BISS were more likely to have sexual dysfunction than those in the upper tertile (OR 1.84; 95% CI 1.04–3.25). Those with lower RSES scores were more likely to have sexual dysfunction than those who scored in the upper tertile (OR 3.03 [95% CI 1.76–5.22]) and middle tertile (OR 2.01 [95% CI 1.23–3.26]). With increasing BISS and RSES scores, the proportion of women classified as having sexual dysfunction decreased as demonstrated in Fig. 1. However, BMI was related to sexual dysfunction in a way that was inconsistent across the increasing categories.

DISCUSSION

The results from our study gave a glimpse into the modern woman's sexual domains and functioning, and how sexual function is influenced by BMI, body image and self-esteem. Although BMI did not relate linearly to sexual function, after classifying BMI as underweight, normal, overweight or obese, overweight women

Table 2. Spearman correlation of body mass index (BMI), Body Image States Scale (BISS) and Rosenberg Self-Esteem Scale (RSES) scores with Female Sexual Function Index (FSFI) total and individual domain scores.

	Domains of FSFI						FSFI total score
	Desire	**Arousal**	**Lubrication**	**Orgasm**	**Satisfaction**	**Pain**	
BMI							
Correlation coefficient	0.08	-0.02	0.04	0.03	-0.04	0.12	0.04
P value	0.08	0.72	0.43	0.50	0.35	**0.005**	0.36
BISS score							
Correlation coefficient	0.16	0.28	0.16	0.20	0.31	0.11	0.27
P value	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**0.010**	**<0.001**
RSES score							
Correlation coefficient	0.13	0.31	0.22	0.26	0.32	0.16	0.32
P value	**0.004**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**

Statistically significant *P* values ($P<0.05$) in bold.

Table 3. Spearman correlation among body mass index (BMI), Body Image States Scale (BISS) and Rosenberg Self-Esteem Scale (RSES).

	BMI	**BISS Score**
BISS score		
Correlation coefficient	-0.45	-
P value	**<0.001**	-
RSES score		
Correlation coefficient	-0.06	0.51
P value	0.16	**<0.001**

Statistically significant *P* values ($P<0.05$) in bold.

(BMI 23.0–27.4kg/m^2) were less likely to have sexual dysfunction. Obese women (BMI ≥27.5 kg/m^2) were not at higher or lower risk of sexual dysfunction. Supporting these findings is a Malaysian study that found a low prevalence of female sexual dysfunction of 12.3% among overweight and obese women.[28] However, the finding of overweight women being at lower risk of sexual dysfunction is inconsistent with the majority of the current literature, which show either a negative or no relationship.[9,31]

The proposed pathophysiology of how weight affects sexual functioning is threefold: influences from adipose tissue on hormonal changes, effects from pathophysiologic comorbidities such as metabolic disturbances and cardiovascular consequences, and effects of psychological factors such as mood disorders and body image.[32] Overweight and obese women have higher levels of circulating testosterone and lower levels of sex hormone-binding globulin.[33] However, increased testosterone levels do not correlate well with sexual dysfunction in women.[28,31] This would imply that metabolic and cardiovascular effects as well as psychological factors may play a greater role in mediating sexual function in women with higher BMIs.

A possible explanation for our unique finding could be that our young overweight but not obese population may not yet have suffered metabolic consequences. It is also possible that weight gain in early marriage

Table 4. Independent t-test comparing sexual functioning categories.

	Normal (FSFI >26.55)	**Sexual dysfunction (FSFI <26.55)**	**Mean difference (95% CI of difference)**	***P* value**
Mean BMI (kg/m^2)	23.85	23.37	0.47 (-0.48 to 1.43)	0.330
Mean BISS score	5.15	4.49	0.66 (0.41 to 0.91)	**<0.001**
Mean RSES score	18.86	16.05	2.81 (1.92 to 3.71)	**<0.001**

BISS: Body Image States Scale; BMI: body mass index; CI: confidence interval; FSFI: Female Sexual Function Index; RSES: Rosenberg Self-Esteem Scale
Statistically significant *P* values ($P<0.05$) in bold.

Table 5. Univariable and multivariable logistic regression analysis showing the categories that displayed significance between those with female sexual dysfunction and those without.

	Univariable analysis				Multivariable analysis			
	OR	95% CI for OR		*P* value	OR	95% CI for OR		*P* value
		Lower	Upper			Lower	Upper	
Ethnicity								
Chinese (reference)								
Indian	0.71	0.39	1.29	0.257	0.57	0.30	1.10	0.095
Malay	0.71	0.43	1.16	0.173	0.38	0.21	0.71	**0.002**
Other	0.63	0.30	1.29	0.205	0.52	0.23	1.18	0.117
BMI								
Normal (18.5–22.9kg/m^2) (reference)								
Underweight (<18.5kg/m^2)	0.57	0.33	0.98	**0.044**	0.62	0.34	1.12	0.114
Overweight (23.0–27.4kg/m^2)	0.57	0.36	0.91	**0.019**	0.46	0.27	0.78	**0.004**
Obese (≥27.5 kg/m^2)	0.75	0.47	1.18	0.215	0.57	0.32	1.01	0.055
BISS score								
Upper tertile (5.50–8.50) (reference)								
Lower tertile (1.00–4.17)	2.61	1.69	4.03	**<0.001**	1.84	1.04	3.25	**0.037**
Middle tertile (4.33–5.33)	1.72	1.11	2.66	**0.015**	1.44	.88	2.35	0.144
RSES score								
Upper tertile (20–30) (reference)								
Lower tertile (0–15)	3.55	2.27	5.57	**<0.001**	3.03	1.76	5.22	**<0.001**
Middle tertile (16–19)	2.28	1.46	3.56	**<0.001**	2.01	1.23	3.26	**0.005**
Married	1.52	1.07	2.15	**0.019**	1.56	0.98	2.48	0.062
No. of children								
0 (reference)								
1	2.56	1.47	4.45	**<0.001**	2.45	1.26	4.77	**0.008**
2	1.13	0.64	2.00	0.681	1.08	0.52	2.21	0.842
>2	1.21	0.54	2.72	0.649	1.57	0.60	4.11	0.359
Perception of mental condition affecting sexual function	3.08	1.58	6.02	**<0.001**	3.02	1.44	6.33	**0.003**

BISS: Body Image States Scale; BMI: body mass index; CI: confidence interval; OR: odds ratio; RSES: Rosenberg Self-Esteem Scale

Variables that do not appear in the table were not significant in the univariable and multivariable analyses.

Statistically significant *P* values (*P*<0.05) in bold.

may indicate better marital satisfaction,[34] or a BMI in the overweight range may be considered culturally acceptable.[5] Overweight women having a lower risk of sexual dysfunction may also be the effect of multiple media campaigns on body positivity,[14] or of affirmations provided by the partner resulting in improved body image and self-esteem and therefore improved sexual function. These explanations highlight the importance of body image and self-esteem, rather than BMI, in the assessment of sexual function.

In the univariable regression analysis, married women, those with poor body image, those with poor self-esteem and those with a perceived mental condition were more likely to have sexual dysfunction. Women with 1 child

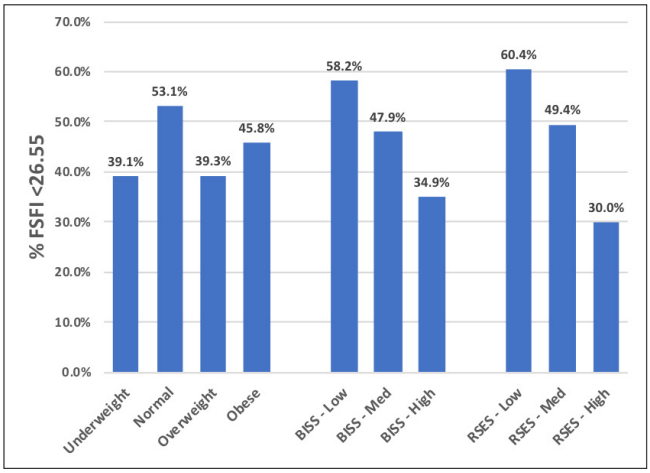

Fig. 1. Proportion of women with sexual dysfunction across the body mass index categories and tertiles of Body Image States Scale (BISS) and Rosenberg Self-Esteem Scale (RSES).
FSFI: Female Sexual Function Index

were 2.4 times more likely than women without children to have sexual dysfunction. Postpartum sexual dysfunction prevalence rates vary from 41% to 83%, with significant worsening in all sexual domains.[35] However, for women with more than 1 child, this association no longer holds. These observations may be accounted for by the smaller numbers of participants with more than 2 children, or due to a new normal routine of sexual function resuming with different expectations postpartum, resulting in fewer women being classified as dysfunctional. Unfortunately, our study did not explore other factors like the age of the child or parents when the child was born, parental roles, and physical or relational circumstances, which could further explain the finding.

Multivariable regression analysis showed that Malay women were less likely to have sexual dysfunction. This observation may be related to cultural or socioeconomic differences that may influence sexual behaviours and practices.[36] According to the National Population Health Survey in 2020, obesity incidence was highest in the Malay population (23.9% vs 7.4% in Chinese).[37] This high incidence may have contributed to obesity not showing any significant association with sexual function.

The women who self-reported a finding of a mental condition were found to be 3 times more likely than those who perceived themselves to have no mental condition to have sexual dysfunction. Mental health has often been found in other studies to be a significant risk factor or predictor of sexual dysfunction in women,[38] which is consistent with our findings. Further studies would be useful to determine the specific aspects of mental health conditions that influence body image and self-esteem, resulting in even higher risks of sexual function.

Findings from this study will be useful for clinicians to identify at-risk patients and the modifiable risk factorsthat are related to sexual problems, and create multidisciplinary treatment plans, if needed, to address sexual dysfunction by tackling the underlying body image and self-esteem problems.

Strengths and limitations

This is the first study in Singapore evaluating the relationship among BMI, body image and self-esteem in the sexual function of young women. An online-based survey was chosen for this research study to take advantage of the internet's ability to optimise reach to individuals who would otherwise be difficult to reach through other channels. The anonymous nature and freedom for respondents to answer in their own time and in a safe space using their own personal devices could help mitigate response bias. We used lower BMI thresholds for risk prediction in Asians,[39,40] as metabolic changes may have an impact on sexual function.

Regarding the limitations, only individuals who understood and read English, and owned and used internet-enabled devices could participate in the study, resulting in selection bias. In view of the sensitive nature of the topic, those with more liberal attitudes towards sex, with more experience with sex, or perhaps suffering from sexual-related problems were likely to participate. Recruitment was conducted through advertising on social media platforms and through posters put up in a primary care clinic, limiting generalisability. Response biases are common in surveys especially when it pertains to sensitive questions, such as weight and sexual function, because of social stigmatisation. This study defined sexual activity to include caressing, foreplay, masturbation and intercourse but did not evaluate for sexual orientation, inclinations and gender identity that could affect sexual practices.

The scales used (BISS, RSES, FSFI) have not been validated in our local population, although they individually have good validity and reliability in various populations globally. We were cognisant that our survey did not assess many other factors that influence sexual function, such as socioeconomic status, educational level, quality of relationship with partner, and sexual issues the partner may be facing. The relationship with the partner can also affect how women view themselves, therefore affecting their body image and self-esteem. Our questionnaires did not evaluate the purpose of

sexual encounters (e.g. procreation, enjoyment, intimacy, obligation) as these encounters can affect sexual experiences and partner relationships.

CONCLUSION

Sexual dysfunction among young women in Singapore can be predicted by issues with body image and self-esteem. Protective factors identified include being of Malay ethnicity and being overweight. Women with poor body image, poor self-esteem, perceived mental health conditions or 1 child are at higher risk of sexual dysfunction—the latter group as possibly requiring time to develop a new normal routine of sexual function, with different expectations postpartum.

As the prevalence of female sexual dysfunction in young women in Singapore is high, we need to invest resources to improve public knowledge on this subject. Actively seeking or incidentally finding issues of body image and self-esteem in young women should trigger conversation about sexual function. Clinicians should be equipped with sufficient knowledge of sexual function, body image and self-esteem to identify women at risk, and subsequently work on improving sexual function by improving body image and self-esteem. Managing sexual dysfunction in young women may help mitigate problems as women transition through menopause. Addressing the problems of sexual function may improve women's sexual relationship with their partners, minimise fertility problems and help them maintain a good quality of life.

REFERENCES

1. Skałacka K, Gerymski R. Sexual activity and life satisfaction in older adults. Psychogeriatrics 2019;19:195-201.
2. Leiblum SR, Koochaki PE, Rodenberg CA, et al. Hypoactive sexual desire disorder in postmenopausal women: US results from the Women's International Study of Health and Sexuality (WISHeS). Menopause 2006;13:46-56.
3. McCool ME, Zuelke A, Theurich MA, et al. Prevalence of female sexual dysfunction among premenopausal women: A systematic review and meta-analysis of observational studies. Sex Med Rev 2016;4:197-212.
4. Safdar F, Eng CLJ, Wai KL, et al. Prevalence of female sexual dysfunction in allied health workers: A cross-sectional pilot study in a tertiary hospital in Singapore. BMC Womens Health 2019; 19:137.
5. Logan S, Thu WPP, Ho K, et al. Sexual inactivity and sexual dysfunction in midlife Singaporean women: A prospective cross-sectional study of prevalence and risk factors. Maturitas 2021;152:1-9.
6. Loy SL, Ku CW, Cheung YB, et al. Fecundability in reproductive aged women at risk of sexual dysfunction and associated risk factors: A prospective preconception cohort study. BMC Pregnancy Childbirth 2021;21:444.
7. Lewis RW, Fugl-Meyer KS, Corona G, et al. Definitions/epidemiology/risk factors for sexual dysfunction. J Sex Med 2010;7:1598-607.
8. Taskin Yilmaz F, Karakoc Kumsar A, Demirel G. The effect of body image on sexual quality of life in obese married women. Health Care Women Int 2019;40:479-92.
9. Faubion SS, Fairbanks F, Kuhle CL, et al. Association between body mass index and female sexual dysfunction: A cross-sectional study from the data registry on experiences of aging, menopause, and sexuality. J Sex Med 2020;17:1971-80.
10. Wu T, Zheng Y. Effect of sexual esteem and sexual communication on the relationship between body image and sexual function in Chinese heterosexual women. J Sex Med 2021;18:474-86.
11. Quinn-Nilas C, Benson L, Milhausen RR, et al. The relationship between body image and domains of sexual functioning among heterosexual, emerging adult women. Sex Med 2016;4:e182-9.
12. Meana M, Nunnink SE. Gender differences in the content of cognitive distraction during sex. J Sex Res 2006;43:59-67.
13. Ahadzadah AS, Rafik-Galea S, Alavi M, et al. Relationship between body mass index, body image and fear of negative evaluation: Moderating role of self-esteem. Health Psychol Open 2018;5:2055102918774251.
14. Radwan H, Hasan HA, Ismat H, et al. Body mass index perception, body image dissatisfaction and their relations with weight-related behaviors among university students. Int J Environ Res Public Health 2019;16:1541.
15. Cihan A, Cihan E. Interrelation between appearance anxiety and sexual functions in women: The role of surgical scars, morphologic features, and accompanying depression. J Sex Med 2019;16:1769-78.
16. Rounsefell Kim, Gibson S, McLean S, et al. Social media, body image and food choices in healthy young adults: A mixed methods systematic review. Nutr Diet 2020;77:19-40.
17. Cohen R, Irwin L, Newton-John T, et al. #bodypositivity: A content analysis of body positive accounts on Instagram. Body image 2019;29:47-57.
18. Heidari M, Ghodusi M, Rezaei P, et al. Sexual function and factors affecting menopause: A systematic review. J Menopausal Med 2019;25:15-27.
19. Cash TF, Fleming EC, Alindogan J, et al. Beyond body image as a trait: The development and validation of the Body Image States Scale. Eat Disord 2002;10:103-13.
20. Thompson JK. The (mis)measurement of body image: Ten strategies to improve assessment for applied and research purposes. Body Image 2004;1:7-14.
21. Robins RW, Hendin HM, Trzesniewski KH. Measuring global self-esteem: Construct validation of a single-item measure and the Rosenberg Self-Esteem Scale. Pers Soc Psychol Bull 2001; 27:151-61.
22. Blascovich J, Tomaka J. Measures of self-esteem. In: Robinson JP, Shaver PR, Wrightsman LS (Ed). Measures of Personality and Social Psychological Attitudes, Volume 1. San Diego: Academic Press; 1991:115-60.
23. Neijenhuijs KI, Hooghiemstra N, Holtmaat K, et al. The Female Sexual Function Index (FSFI)—A systematic review of measurement properties. J Sex Med 2019;16:640-60.
24. Rosen R, Brown C, Heiman J, et al. The Female Sexual Function Index (FSFI): A multidimensional self-report instrument for

the assessment of female sexual function. J Sex Marital Ther 2000;26:191-208.

25. Sidi H, Abdullah N, Puteh SE, et al. The Female Sexual Function Index (FSFI): Validation of the Malay version. J Sex Med 2007;4:1642-54.
26. Sun X, Li C, Jin L, et al. Development and validation of Chinese version of female sexual function index in a Chinese population—A pilot study. J Sex Med 2011;8:1101-11.
27. Rehman KU, Asif Mahmood M, Sheikh SS, et al. The Female Sexual Function Index (FSFI): Translation, validation, and cross-cultural adaptation of an Urdu version "FSFI-U". Sex Med 2015;3:244-50.
28. Abidin A, Draman N, Ismail SB, et al. Female sexual dysfunction among overweight and obese women in Kota Bharu, Malaysia. J Taibah Univ Med Sci 2016;11:159-67.
29. Latorre GF, Bilck PA, Cardoso FL, et al. Confiability and reliability of an online version of the Female Sexual Function Index by test-retest. Rev Bras Ginecol Obstet 2013;35:469-74.
30. Wiegel M, Meston C, Rosen R. The female sexual function index (FSFI): Cross-validation and development of clinical cutoff scores. J Sex Marital Ther 2005;31:1-20.
31. Kadioglu P, Yetkin DO, Sanli O, et al. Obesity might not be a risk factor for female sexual dysfunction. BJU Int 2010;106:1357-61.
32. Rowland DL, McNabney SM, Mann AR. Sexual function, obesity, and weight loss in men and women. Sex Med Rev 2017; 5:323-38.
33. Pasquali R. Obesity and androgens: facts and perspectives. Fertil Steril 2006;85:1319-40.
34. Meltzer AL, Novak SA, McNulty JK, et al. Marital satisfaction predicts weight gain in early marriage. Health Psychol 2013;32:824-7.
35. Gutzeit O, Levy G, Lowenstein L. Postpartum female sexual function: Risk factors for postpartum sexual dysfunction. Sex Med 2020;8:8-13.
36. Wong LP. An exploration of knowledge, attitudes and behaviours of young multiethnic Muslim-majority society in Malaysia in relation to reproductive and premarital sexual practices. BMC Public Health 2012;12:865.
37. Epidemiology & Disease Control Division and Policy, Research & Surveillance Group Ministry of Health and Health Promotion Board, Singapore. National Population Health Survey 2020 (Household Interview and Health Examination). https://www.moh.gov.sg/docs/librariesprovider5/default-document-library/nphs-2020-survey-report.pdf. Accessed 17 April 2023.
38. West SL, Vinikoor LC, Zolnoun D. A systematic review of the literature on female sexual dysfunction prevalence and predictors. Annu Rev Sex Res 2004;15:40-172.
39. Deurenberg-Yap M, Chew SK, Lin VF, et al. Relationships between indices of obesity and its co-morbidities in multi-ethnic Singapore. Int J Obes Relat Metab Disord 2001;25:1554-62.
40. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004;363:157-63.

COMMENTARY

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Artificial intelligence innovation in healthcare: Relevance of reporting guidelines for clinical translation from bench to bedside

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ABSTRACT

Artificial intelligence (AI) and digital innovation are transforming healthcare. Technologies such as machine learning in image analysis, natural language processing in medical chatbots and electronic medical record extraction have the potential to improve screening, diagnostics and prognostication, leading to precision medicine and preventive health. However, it is crucial to ensure that AI research is conducted with scientific rigour to facilitate clinical implementation. Therefore, reporting guidelines have been developed to standardise and streamline the development and validation of AI technologies in health. This commentary proposes a structured approach to utilise these reporting guidelines for the translation of promising AI techniques from research and development into clinical translation, and eventual widespread implementation from bench to bedside.

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Artificial intelligence (AI) and digital innovation have revolutionised many sectors and industries, prominently including healthcare during the coronavirus disease 2019 (COVID-19) pandemic.[1] For example, deep learning, which is a subset of the state-of-the-art machine learning techniques, has shown robust performance in image recognition, speech recognition and natural language processing.[2] In healthcare, machine learning and deep learning are now becoming increasingly adopted as part of segmentation, classification and prediction tasks in image analysis,[3,4] including differentiation between benign and malignant lesions in skin photographs,[5] diabetic retinopathy detection on colour fundus photographs,[6] and detection of COVID-19 or tuberculosis from chest imaging.[7,8] In addition, natural language processing has been heavily adopted in medical chatbots using speech or text,[3] and in the extraction of useful information from electronic medical records.[9] Such AI technologies could be applied in diverse clinical settings, ranging from screening, triaging or remote monitoring at community-based or population-based settings, to performing diagnoses or prognostication in tertiary or quaternary personalised medicine workflows. More recently, the use of deep reinforcement learning techniques has proven to be robust in the prediction of protein folding, potentially unravelling an exciting, untapped avenue for drug discovery research in the proteomics space, albeit in its infancy.[10-12] Prospective validation of AI-based drug intervention that is dynamically tailored to each patient is also being observed.[13]

Other global AI trends and advances, in addition to the above examples, include privacy preserving technologies like federated machine learning, blockchain[14-16], synthetic AI[17] and explainable AI.[18] If used appropriately, AI that is applied in health can bring clinicians a step closer to precision medicine and predictive and preventative health, with the promise of population-wide interventions that could potentially increase early accessibility to appropriate care and greater cost-effectiveness.[19]

To realise the promises of AI in healthcare, it is critical to ensure that AI research is performed and reported with the scientific rigor required for clinical implementation. In this regard, clear reporting guidelines are needed. In parallel with these technological innovations, various AI reporting consensus guidelines have been developed over the past few years, including the Consolidated Standards of Reporting Trials (CONSORT)-AI,[20] Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)-AI,[21] Developmental and Exploratory Clinical Investigations of Decision Support Systems Drive by Artificial Intelligence (DECIDE-AI),[22] Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-AI[23] and Standards for Reporting of Diagnostic Accuracy Study (STARD)-AI.[24] These are helpful in standardizing and streamlining the development and validation of AI technologies in health, but their relevance at different phases of the AI innovation journey is not always clear. This commentary makes the case for the relevance of these reporting guidelines and proposes a structured approach to utilise them for facilitating the translation of promising techniques from research and development into clinical translation and eventual widespread implementation from bench to bedside.

Why the need for reporting guidelines in AI research?

First, a major barrier to widespread clinical implementation is heterogeneity in study methodology and reporting, which impedes the ability of readers (including clinicians) to critically appraise these new AI technologies. Previous systematic reviews and meta-analyses in AI medical imaging suggest that many studies are suboptimally designed and delivered.[25,26] Differences in terminology used as well as differences in AI model statistics further impede the clinicians' ability to reproduce the results, compare different studies and weigh the evidence for clinical use. Second, AI algorithms perform best in the artificial environment in which they are trained and validated, and generalisability of the algorithms may be limited, particularly where there are significant differences in actual clinical workflows across unique settings in which the software platforms or data exchange protocols are different.[26] Efforts to include heterogenous datasets and demonstrate generalisability via external validation sets are making headway. Third, despite promising explainability research looking into the "black box" of certain AI decision-making processes, the lack of clearly defined intended use and users during the creation of AI models can result in excellent AI models failing to find a role in actual clinical practice.[27] Importantly, the mode in which data is acquired versus the quantity of data acquired is a critical consideration that will also impact the actionability and efficacy of the downstream model. For example, in AI-guided clinical decision support, the longitudinal response of a patient exposed to variable dosing (which can provide a comprehensive picture of the patient's potential for favourable treatment response) is assessed, as opposed to assessing a fixed dose and fixed timepoint, which represents only a snapshot of their response. Thus, AI-guided clinical decision support can lead to substantially different treatment options and

outcomes.[28,29] In such an instance, the clinicians themselves play a role in dataset building that can, in turn, align the decision-making processes of the model at the point of care.

To improve clinical translation and acceptance of AI technologies, researchers need to clearly define the intended use, show transparency in their methodology to allow for reproducibility, demonstrate clinical safety, and clearly state the role of the AI technology in current clinical practice. In view of these concerns, several international parties have banded together to develop guidelines to promote transparency and completeness in conducting and in the reporting of AI-related research. The Enhancing the Quality and Transparency of Health Research (EQUATOR) Network is an international initiative that aims to improve the quality of healthcare research by promoting the development and use of robust reporting guidelines. It aims to achieve accurate, complete and transparent reporting of all health research studies to support reproducibility, validity and usefulness.[30]

Overview of existing AI reporting guidelines

Reporting guidelines were developed to specify the minimum information required in published scientific papers and to aid editors, peer reviewers and, most importantly, general readers including clinicians in appraising the quality, value and clinical relevance of these studies. With the recent rise in AI health research, several AI reporting guidelines, some of which serve as an extension of existing medical reporting guidelines, have been proposed to better suit AI studies, which often encompass specific technical details, AI terminology and statistical evaluation that differ from other scientific research. We provide an overview of these guidelines to aid clinicians in appraising AI research and development outcomes for consideration of clinical real-life adoption, aside from their use in the research setting. For the initial research and development phase, STARD-AI[24] and the Transparent Reporting of a Multivariable Prediction Model of Individual Prognosis or Diagnosis (TRIPOD)-AI[31] are useful reporting guidelines to provide a comprehensive framework to develop and test the diagnostic performance of AI algorithms using retrospective data; whereas CONSORT-AI[20] and SPIRIT-AI[21] are mainly for those AI algorithms that have been developed with an established operating threshold and are ready to be tested on a prospective clinical trial dataset. DECIDE-AI was designed to guide early stages of clinical evaluation and analyse the human factors to improve clinical translation of AI studies.[22]

AI diagnostic accuracy testing studies: STARD-AI and QUADAS-AI

STARD-AI is an extension of the STARD guidelines specifically for AI diagnostic test accuracy studies.[24] STARD-AI can be used on a variety of data types, including imaging data, and would be more suitable in the initial research and development stage when retrospective data are used. For diagnostic studies, it is important to specify the intended use environment, set the operating thresholds using preset sensitivity and specificity, and test AI algorithms on independent local and international datasets to illustrate generalisability. Complementary to STARD-AI is QUADAS-AI, which aims to serve as a tool to assess bias and applicability of diagnostic AI systems.[23] STARD-AI and QUADAS-AI are currently under development and, once available, will allow end users to appraise the quality of the AI diagnostic test and allow for comparisons of diagnostic accuracy between studies. A case example will be the use of STARD-AI and QUADAS-AI in a study to evaluate the diagnostic accuracy of a deep learning model for diabetic retinopathy detection on fundus photography.

AI clinical prediction models: TRIPOD-AI and PROBAST-AI

With guidance from the EQUATOR Network, TRIPOD-AI and the Prediction Model Risk of Bias Assessment Tool (PROBAST)-AI are intended as reporting guidelines for studies on AI machine learning-based prediction models and their risk assessment.[31] TRIPOD focuses on improving the transparency of a prediction model irrespective of the methodology,[32] whereas PROBAST puts heavy emphasis on evaluating the risk of bias and applicability of the primary prediction model, especially for a systematic review.[33] Both AI extensions are currently under development and will eventually aid researchers and clinicians to critically appraise machine learning prediction models and provide a standardised tool for the evaluation of study bias among AI studies. For example, TRIPOD-AI or PROBAST-AI will be suitable for a study on a machine learning model that can predict the probability of future cardiac arrest based on clinical and imaging data.

AI clinical trials: SPIRIT-AI and CONSORT-AI

With the support of the EQUATOR Network, SPIRIT and CONSORT are guidelines that are now widely accepted as international standards.[34,35] Further extensions for clinical trials specifically involving AI were published in 2020 and are known as SPIRIT-AI[21] and CONSORT-AI.[20]

SPIRIT-AI and CONSORT-AI were designed by an international multistakeholder group amid mounting recognition that interventions involving AI require rigorous evaluation to prove their impact on health outcomes. Extensions of existing guidelines are required to assist editors, peer reviewers and general readership to understand and critically appraise these AI-related interventions. SPIRIT-AI is a guideline for AI clinical trial protocols, while CONSORT-AI is a guideline for reporting randomised trials using AI (Table 1).

Briefly, SPIRIT-AI included 15 additional items (3 elaborations of existing items in SPIRIT and 12 new AI extensions) and CONSORT-AI included 14 additional items (3 elaborations of existing items in CONSORT and 11 new AI extensions). Proposed AI checklist items were similar in both checklists and included the following: specifying of intended use and users; onsite and offsite requirements for generalisability assessment; inclusion and exclusion criteria at both participant and data input levels; version of AI system utilised; details on data acquisition; selection and pre-processing before analysis; handling of poor quality data; stating of the level of human-AI interaction and level of required expertise; specifying of the AI intervention and intended downstream outputs and their role in clinical pathways and clinical decision-making; detailing of the methods to identify errors and risk mitigation strategies; and the stating of access and license restrictions of the AI intervention. SPIRIT-AI recommended an additional item of describing pre-existing evidence regarding validation of the intended AI intervention (checklist item no. 6 in Table 1). Aside from researchers, clinicians could also use these checklist items during the clinical trial study appraisal processes to aid in evaluating the reproducibility, clinical translation and safety of the proposed AI intervention. A case example in which SPIRIT-AI or CONSORT-AI may be used is a prospective randomised controlled study of polyp detection on diagnostic colonoscopy using a real-time AI-assisted detection system that is compared with standard diagnostic colonoscopy without AI intervention.[36]

General guideline for early clinical evaluation of AI studies: DECIDE-AI

While SPIRIT-AI, CONSORT-AI, STARD-AI, QUADAS-AI, TRIPOD-AI and PROBAST-AI are specific to study design, DECIDE-AI is different and focuses on the early clinical evaluation stage and may be used across a variety of study designs (Table 2).[22] The DECIDE-AI guidelines included 17 AI-specific reporting items and 10 generic reporting items such as description of human factor tools, use cases considered, users involved, patient involvement and any significant change to the clinical workflow or care pathway caused by the AI system. Human factors, such as utility evaluation, safety and the effect of the intervention on the users' physical and cognitive performance, are important considerations in the regulatory process and acceptance of new AI interventions by patients, clinicians, regulatory bodies and potential investors.

In the inception of new AI interventions, developers of AI health technology should take note of available local guidelines that encompass regulatory requirements and legislation, which can assist in subsequent regulatory approval and commercial distribution within the local setting. For example, in Singapore, the Artificial Intelligence in Healthcare Guidelines[37] provide recommendations for both developers (early stage) and implementers of the AI technology (later stage) while taking into account specific legislation such as the Singapore Human Biomedical Research Act, and Personal Data and Protection Act.

Relevance of reporting guidelines at different phases of the AI innovation journey

After understanding the motivation and importance of each of the reporting consensus guidelines, one may then adopt the appropriate reporting guideline at applicable stages of the AI innovation (Fig. 1). First, the initial stage of the AI innovation journey is preclinical or algorithm development. A clinical need or an intended use is first identified and the research idea formulated and refined. Several factors should be taken into account when defining the specific intended use environment: the specific clinical problems, potential benefits, potential risk level, market size, patient demographics or ethnic groups, clinical settings (population-based vs clinic-based), hardware devices, users (patients vs healthcare professionals, general practitioners vs specialists), tasks (segmentation, classification, prediction), imaging specification (e.g. chest x-ray: posterior anterior vs anterior posterior vs lateral; computed tomography or magnetic resonance imaging: with or without contrast, axial vs sagittal vs coronal; retinal imaging: macula-centred vs optic disc-centred), and deployment mode (cloud-based, desktop-based or incorporation into edge devices). The definition of intended use environment is included in all the AI reporting guidelines, given its importance in regulations applicable to software as a medical device (SaMD).

Table 1. Comparison of SPIRIT-AI[21] and CONSORT-AI[20] checklists.

	SPIRIT 2013[21]	**SPIRIT-AI[21]**		**CONSORT 2010[20]**	**CONSORT-AI[20]**
Intended use	**Clinical trial protocol**	**AI-clinical trial protocol**		**Randomised controlled trial**	**AI-randomised controlled trial**
Checklist item no.			**Checklist item no.**		
1	Descriptive title identifying the study design, population, interventions and, if applicable, trial acronym	Indicate that the intervention involves artificial intelligence/ machine learning and specify the type of model Specify the intended use of the AI intervention	1	a) Identification as a randomised trial in the title b) Structured summary of trial design, methods, results, and conclusions	a) Indicate that the intervention involves artificial intelligence/ machine learning and specify the type of model b) State the intended use of the AI intervention within the trial in the title and/or abstract
2	Trial registration: a) Trial identifier and registry name. If not yet registered, name of intended registry. b) All items from the World Health Organization Trial Registration Dataset		23	Registration number and name of trial registry	
3	Protocol date and version identifier			-	
4	Funding: sources and types of financial, material and other support			-	
5	a) Names, affiliations and roles of protocol contributors b) Name and contact information for the trial sponsor c) Role of study sponsor and funders d) Composition, roles and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team and other individuals/groups overseeing the trial			-	
6	a) Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	a) Explain the intended use of the AI intervention in the context of the clinical pathway, including its purpose and its intended users Describe any pre-existing evidence for the AI intervention.	2	a) Scientific background and explanation of rationale	Explain the intended use of the AI intervention in the context of the clinical pathway, including its purpose and its intended users
	b) Explanation for choice of comparators			-	
7	Specific objectives or hypotheses			b) Specific objectives or hypotheses	
8	Description of trial design, including type of trial, allocation ratio and framework		3	a) Description of trial design (such as parallel, factorial) including allocation ratio	
	-			b) Important changes to methods after trial commencement (such as eligibility criteria), with reasons	

Table 1. Comparison of SPIRIT-AI[21] and CONSORT-AI[20] checklists. (Cont'd)

	SPIRIT 2013[21]	SPIRIT-AI[21]		CONSORT 2010[20]	CONSORT-AI[20]
Intended use	**Clinical trial protocol**	**AI-clinical trial protocol**		**Randomised controlled trial**	**AI-randomised controlled trial**
Checklist item no.			**Checklist item no.**		
9	Description of study settings and list of countries where data will be collected Reference to where list of study sites can be obtained	Describe the onsite and offsite requirements needed to integrate the AI intervention into the trial setting	4	b) Settings and locations where the data were collected	Describe how the AI intervention was integrated into the trial setting, including any onsite or offsite requirements
10	Inclusion and exclusion criteria for participants If applicable, eligibility criteria for study centres and individuals who will perform the interventions	State the inclusion and exclusion criteria at the (i) level of participants, AND at the (ii) level of input data		A) Eligibility criteria for participants	State the inclusion and exclusion criteria at the (i) level of participants, AND at the (ii) level of input data.
11	a) Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	(i) State version of AI algorithm used (ii) Specify procedure for acquiring and selecting the input data for the AI intervention (iii) Specify the procedure for assessing and handling poor-quality or unavailable input data (iv) Specify whether there is human–AI interaction in the handling of the input data, and what level of expertise is required for users (v) Specify the output of the AI intervention (vi) Explain the procedure for how the AI intervention's output will contribute to decision-making or other elements of clinical practice	5	The interventions for each group with sufficient details to allow replication, including how and when they were administered.	(i) State version of AI algorithm used (ii) Specify procedure for acquiring and selecting the input data for the AI intervention (iii) Specify the procedure for assessing and handling poor-quality or unavailable input data (iv) Specify whether there is human–AI interaction in the handling of the input data, and what level of expertise is required for users (v) Specify the output of the AI intervention (vi) Explain the procedure for how the AI intervention's output will contribute to decision-making or other elements of clinical practice
	b) Criteria for discontinuing or modifying allocated interventions for a given trial participant			-	
	c) Strategies to improve adherence to intervention protocols and any procedures for monitoring adherence			-	
	d) Relevant concomitant care and intervention			-	

Table 1. Comparison of SPIRIT-AI[21] and CONSORT-AI[20] checklists. (Cont'd)

	SPIRIT 2013[21]	SPIRIT-AI[21]		CONSORT 2010[20]	CONSORT-AI[20]
Intended use	**Clinical trial protocol**	**AI-clinical trial protocol**		**Randomised controlled trial**	**AI-randomised controlled trial**
Checklist item no.			**Checklist item no.**		
12	Primary, secondary and other outcomes, including the specific measurement variable, analysis metric, method of aggregation, and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended		6	a) Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	
13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments and visits for participants. A schematic diagram is highly recommended			b) Any changes to trial outcomes after the trial commenced, with reasons	
14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations		7	a) How sample size was determined	
15	Strategies for achieving adequate participant enrolment to reach target sample size			b) When applicable, explanation of any interim analyses and stopping guidelines	
16	a) Method of generating the allocation sequence and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction should be provided in a separate document that is unavailable to those who enrol participants or assign interventions		8	a) Method used to generate the random allocation sequence b) Type of randomisation; details of any restriction (such as blocking and block size)	
	b) Mechanism of implementing the allocation sequence (e.g. central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned		9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	
	c) Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions		10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	
17	a) Who will be blinded after assignment to interventions and how		11	a) Blinding: If done, who was blinded after assignment to interventions (e.g. participants, care providers, those assessing outcomes) and how	
	b) If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial			b) If relevant, description of the similarity of interventions	
18	a) Plans for assessment and collection of outcome, baseline and other trial data, including any related processes to promote data quality and a description of study instruments along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol			-	
	b) Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols			-	
19	Plans for data entry, coding, security and storage, including any related processes to promote data quality. Reference to where details of data management procedures can be found, if not in the protocol			-	

Table 1. Comparison of SPIRIT-AI[21] and CONSORT-AI[20] checklists. (Cont'd)

	SPIRIT 2013[21]	SPIRIT-AI[21]		CONSORT 2010[20]	CONSORT-AI[20]
Intended use	**Clinical trial protocol**	**AI-clinical trial protocol**		**Randomised controlled trial**	**AI-randomised controlled trial**
Checklist item no.			**Checklist item no.**		
20	a) Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol		12	a) Statistical methods used to compare groups for primary and secondary outcomes	
	b) Methods for any additional analyses			b) Methods for additional analyses, such as subgroup analyses and adjusted analyses	
	c) Definition of analysis population relating to protocol non-adherence (e.g. as randomised analysis) and any statistical methods to handle missing data (e.g. multiple imputation)			-	
	-		13	a) For each group, the numbers of participants who were randomly assigned, received intended treatment and were analysed for the primary outcome	
	-			b) For each group, losses and exclusions after randomisation, together with reasons	
	-		14	a) Dates defining the periods of recruitment and follow-up	
	-			b) Why the trial ended or was stopped	
	-		15	A table showing baseline demographic and clinical characteristics for each group	
	-		16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	
	-		17	a) For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	
	-			b) For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
	-		18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	
21	a) Composition of data monitoring committee; summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a data monitoring committee is not needed			-	
	b) Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial			-	

Table 1. Comparison of SPIRIT-AI[21] and CONSORT-AI[20] checklists. (Cont'd)

	SPIRIT 2013[21]	SPIRIT-AI[21]		CONSORT 2010[20]	CONSORT-AI[20]
Intended use	**Clinical trial protocol**	**AI-clinical trial protocol**		**Randomised controlled trial**	**AI-randomised controlled trial**
Checklist item no.			**Checklist item no.**		
22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	Specify any plans to identify and analyse performance errors. If there are no plans for this, justify why not	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	Describe results of any analysis of performance errors and how errors were identified, where applicable. If no such analysis was planned or done, justify why not
23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor			-	
24	Plans for seeking research ethics committee/ institutional review board approval			-	
25	Plans for communicating important protocol to relevant parties			-	
26	a) Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see item no. 32)			-	
	b) Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable			-	
27	How personal information about potential and enrolled participants will be collected, shared and maintained in order to protect confidentiality before, during and after the trial			-	
28	Financial and other competing interests for principal investigators for the overall trial and each study site			-	
			20	Trial limitations, addressing sources of potential bias, imprecision and, if relevant, multiplicity of analyses	
			21	Generalisability (external validity)	
			22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	
			24	Where the full trial protocol can be accessed, if available	
29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	State whether and how the AI intervention and/or its code can be accessed, including any restrictions to access or reuse	25	Sources of funding and other support (such as supply of drugs), role of funders	State whether and how the AI intervention and/or its code can be accessed, including any restrictions to access or reuse
30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation			-	

Table 1. Comparison of SPIRIT-AI[21] and CONSORT-AI[20] checklists. (Cont'd)

	SPIRIT 2013[21]	SPIRIT-AI[21]	CONSORT 2010[20]	CONSORT-AI[20]
Intended use	**Clinical trial protocol**	**AI-clinical trial protocol**	**Randomised controlled trial**	**AI-randomised controlled trial**
Checklist item no.			**Checklist item no.**	
31	a) Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public and other relevant groups (e.g. via publication, reporting in results databases or other data sharing arrangements), including any publication restrictions		-	
	b) Authorship eligibility guidelines and any intended use of professional writers		-	
	c) Plans, if any, for granting public access to the full protocol, participant-level dataset and statistical code		-	
32	Model consent form and other related documentation given to participants and authorised surrogates		-	
33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable		-	

CONSORT: Consolidated Standards of Reporting Trials; CONSORT-AI: Consolidated Standards of Reporting Trials–Artificial Intelligence; SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials; SPIRIT-AI: Standard Protocol Items: Recommendations for Interventional Trials–Artificial Intelligence

Superscript numbers: Refer to REFERENCES

Second, researchers need to identify the appropriate datasets, which are known as the "dictionaries", to address the defined intended use environment. For data, it is always important to consider the following: data security (de-identification and extraction), labels (ground truth), size, type (structured vs unstructured data, cross sectional vs longitudinal, real-world vs clinical), phenotypes (positive vs control cases from different races), recruitment style with respect to inclusion and exclusion criteria (including the treatment of outliers), imaging devices, data heterogeneity (homogenous vs heterogenous), splitting of the training versus validation versus testing (local vs international), generalisability (representativeness of the target) and quality. In addition, the use of publicly available datasets may allow for reproducibility testing. At the initial research and development phase, the STARD-AI and QUADAS-AI guidelines could be used for reporting diagnostic accuracy and TRIPOD-AI and PROBAST-AI guidelines for the reporting of clinical prediction models using the retrospective or prospective datasets, although most AI researchers could utilise the retrospective datasets collected in the past decades to build the initial AI model.

Third, researchers need to select suitable technical methodologies (i.e. the "brain" that solves tasks) using machine learning or deep learning to analyse test datasets. For technical methodologies, it is important for AI researchers to design a robust AI architecture and operational flow based on the intended use environment. Depending on the data type, AI algorithms could be built as single modal versus multimodal (e.g. early vs late fusion) using machine learning (e.g. random forest, support vector machines, XGBoost) or deep learning (image-based, speech-based or natural language processing-based). For the overall AI architecture, it is critical to design an end-to-end system—from data input to pre-processing steps (contrast enhancement, image adjustment, cropping or centralisation); and inclusion of gradeability algorithm, appropriate machine learning or deep learning techniques, and explainability map using a selected visualisation technique (for image). It is always important to assess the robustness of AI algorithms using a pre-set operating threshold (on the training/validation datasets) to evaluate it on the local or international testing datasets using performance metrics such as the area under the receiver operating characteristic curve, sensitivity, specificity and 95% confidence interval.

Upon completion of AI algorithm and development, researchers should explore the potential technical disclosure of the AI algorithm with the relevant

Table 2. Comparing SPIRIT-AI, CONSORT-AI and DECIDE-AI.

	SPIRIT-AI	CONSORT-AI	DECIDE-AI
Extension of existing guideline	Yes	Yes	No
Stage of intended use	Late clinical trial (phase III) Comparative prospective evaluation	Late clinical trial (phase III) Comparative prospective evaluation	Early clinical trial (phase I and II)
Study design	Clinical trial protocol	Randomised controlled trial	Any
Key focus	Standardisation of reporting	Standardisation of reporting	Assessing clinical utility, safety and human factors

CONSORT-AI: Consolidated Standards of Reporting Trials–Artificial Intelligence; DECIDE-AI: Developmental and Exploratory Clinical Investigations of Decision Support Systems Drive by Artificial Intelligence; SPIRIT-AI: Standard Protocol Items: Recommendations for Interventional Trials–Artificial Intelligence

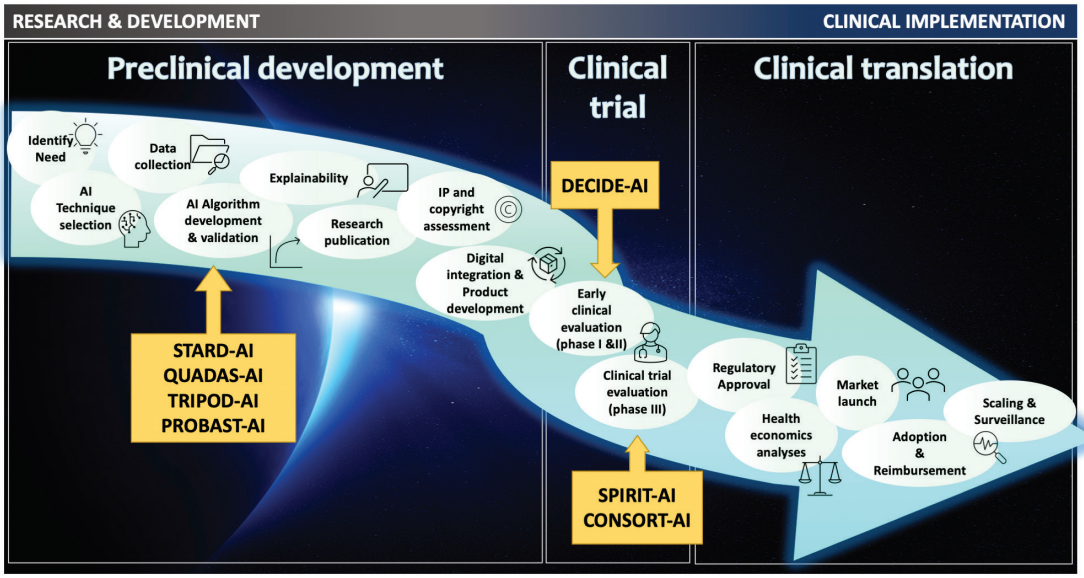

Fig. 1. Stages of the AI innovation.
AI: artificial intelligence; CONSORT-AI: Consolidated Standards of Reporting Trials–Artificial Intelligence; DECIDE-AI: Developmental and Exploratory Clinical Investigations of Decision Support Systems Drive by Artificial Intelligence; IP: intellectual property; PROBAST-AI: Prediction Model Risk of Bias Assessment Tool–Artificial Intelligence; QUADAS-AI: Quality Assessment of Diagnostic Accuracy Studies–Artificial Intelligence; SPIRIT-AI: Standard Protocol Items: Recommendations for Interventional Trials–Artificial Intelligence; STARD-AI: Standards for Reporting of Diagnostic Accuracy Study–Artificial Intelligence; TRIPOD-AI: Transparent Reporting of a Multivariable Prediction Model of Individual Prognosis or Diagnosis–Artificial Intelligence

institutional intellectual property (IP) office should the findings be robust. Given that many AI algorithms are developed using off-the-shelf technical packages, the technology transfer office and IP office often find it challenging to file patents that rely heavily on AI systems for discovery, although these algorithms may be kept as know-hows, trade secrets and intellectual/commercial property. It is always important to address IP-related issues prior to any publication of AI algorithms in the scientific domain to avoid invalidating any potential patent.

Fourth, once the AI technology is deemed to be robust and mature, it will enter the clinical trial stage (Fig. 1). Ideally, a user-friendly and graphical user interface and user experience for the AI algorithms should be deployed at the intended settings when the clinical trials are conducted prospectively. In the early-stage clinical evaluation of AI-based decision support system, the DECIDE-AI guideline could be used to evaluate the performance, safety and human factors of the AI technology, a phase which is equivalent to phase I and II of pharmaceutical trials (Fig. 2), followed by a

larger-scale clinical evaluation using either SPIRIT-AI or CONSORT-AI for clinical trial protocol reporting or randomised controlled trial reporting, respectively. A comparison of the original SPIRIT and CONSORT guidelines with their AI extensions can be found in Table 1. Similar to designing conventional clinical trials, researchers would need to determine the AI-based trial design: randomised controlled versus non-randomised; allocation ratios; inclusion versus exclusion criteria; superiority versus non-inferiority trials; sample size; recruitment sites; and determination of the internationally acceptable gold standards for comparative trials. In addition, in the context of interventional studies, novel trial designs that harness AI-based platforms can potentially identify more responders to treatment.[38,39]

Finally, upon successful completion of clinical trials, the AI technology then moves into the last stage: clinical translation and real-world development (Figs. 1 and 3). Regulatory approval should then be obtained. Regulatory guidelines, such as the International Medical Device Regulators Forum SaMD guidelines used by the US Food and Drug Administration,[40] and local guidelines, such as the Health Sciences Authority regulatory guidelines for SaMD[41] and the Artificial Intelligence in Healthcare Guidelines,[37] may be used.

Beyond regulatory approval, implementation research, health services research and workforce training and education are key aspects to facilitate clinical adoption and implementation (Fig. 3). Health economic analyses including cost-utility analysis, cost-effective analysis, cost-minimisation analysis and cost-benefit analysis may also be performed to assist in acceptance of the AI technology at a policy level.[42] This information can help clinicians, patients and policymakers evaluate the potential applicability and impact of such AI technologies in real-world clinical settings. Timely engagement with key stakeholders including patients, clinicians, healthcare delivery organisation leaders, operational personnel, policymakers, researchers, funders, product manufacturers and relevant medical societies is essential for convergence science, operational changes and actual clinical implementation. Once the AI technology is widely adopted, it is important to evaluate its impact on the population or global health and the society (Fig. 3).

In summary, AI reporting guidelines serve as useful guides for AI developers or users to build and appraise different AI technologies in health at different stages of innovation. To build a robust and clinically useful AI algorithm, it is important to define the intended use; choose or build the right datasets, technical methodology and architecture using the different reporting guidelines; and evaluate the performance using the appropriate statistical analyses. Given the prevailing and evolving SaMD rules, early engagement with applicable

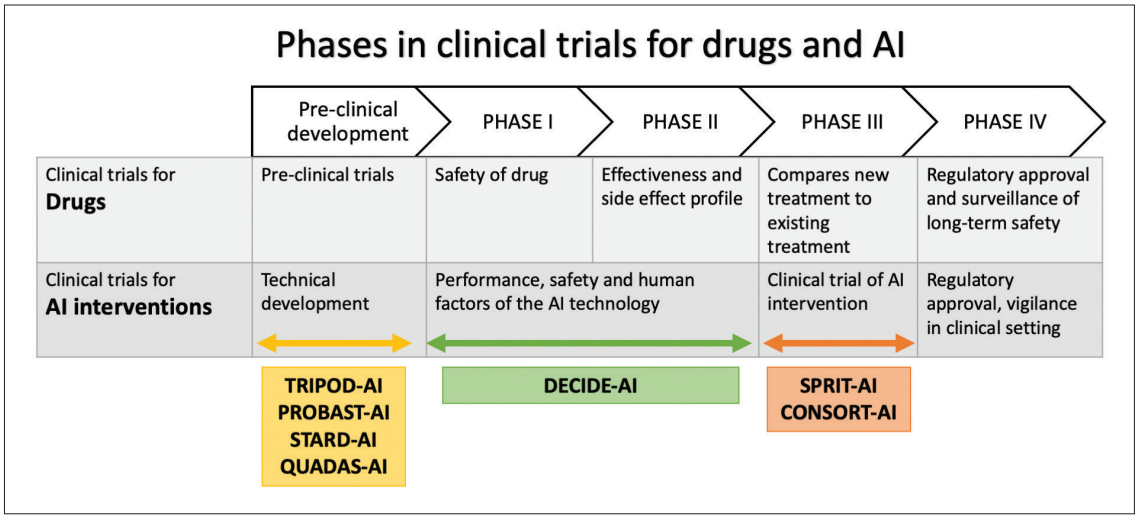

Fig. 2. Phases in clinical trials for drugs and AI.
AI: artificial intelligence; CONSORT-AI: Consolidated Standards of Reporting Trials–Artificial Intelligence; DECIDE-AI: Developmental and Exploratory Clinical Investigations of Decision Support Systems Drive by Artificial Intelligence; PROBAST-AI: Prediction Model Risk of Bias Assessment Tool–Artificial Intelligence; QUADAS-AI: Quality Assessment of Diagnostic Accuracy Studies–Artificial Intelligence; SPIRIT-AI: Standard Protocol Items: Recommendations for Interventional Trials–Artificial Intelligence; STARD-AI: Standards for Reporting of Diagnostic Accuracy Study–Artificial Intelligence; TRIPOD-AI: Transparent Reporting of a Multivariable Prediction Model of Individual Prognosis or Diagnosis–Artificial Intelligence

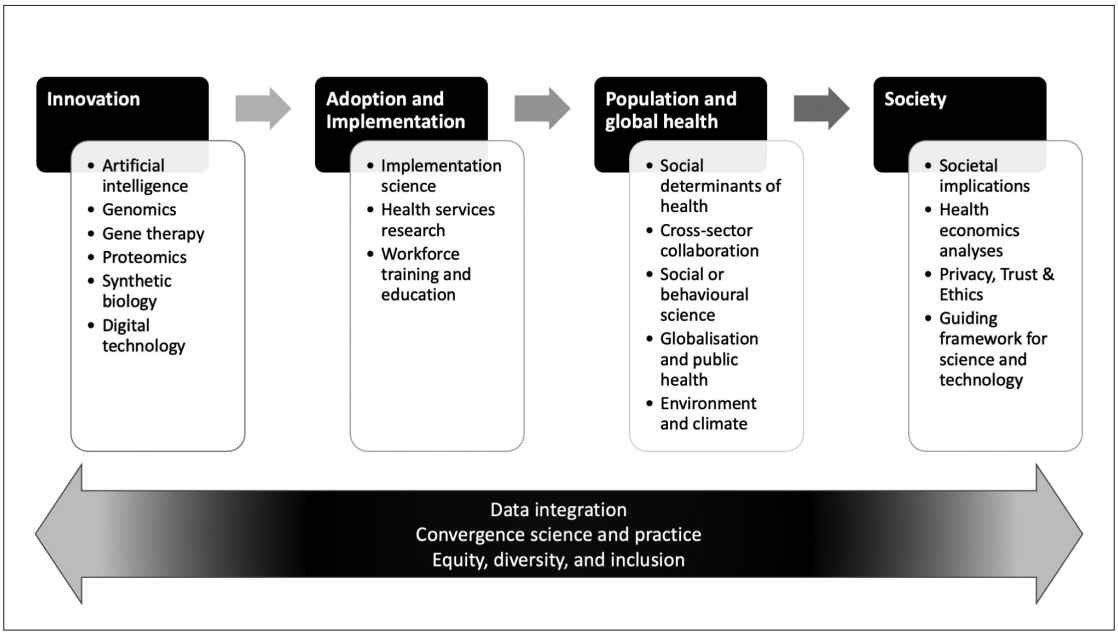

Fig. 3. Key aspects to facilitate clinical adoption, implementation and evaluation of AI innovation.

technology transfer or IP offices and regulatory bodies is key. At the same time, rapid developments in AI research mean that the field must be prepared to adapt and evolve as new techniques emerge. AI has enormous potential to enhance clinical outcomes and experiences for patients. These reporting guidelines are excellent initiatives that involve multiple stakeholders originating from diverse backgrounds (clinicians, allied health professionals, technology developers, bioethicists, patient representatives, industry, regulatory bodies, government and journal editorial boards), and they could play a pivotal role not only in the research settings but also in clinical and governmental policymaking settings to ensure that the continuum of AI innovation from robust and rigorous evaluation to clinical deployment and reimbursement reaches fruition for all AI technologies in medicine.

Disclosure

Dr Daniel SW Ting holds a patent on a deep learning system for detection of retinal diseases, co-founded and holds equity of EyRIS Singapore. Dr Carolyn SP Lam holds a patent on a deep learning system for detection of cardiac disease, co-founded and holds equity in Us2.ai. Dr Dean Ho is scientific co-founder and shareholder of KYAN Therapeutics. He is also a co-inventor of pending patents pertaining to AI-based drug development and personalised medicine.

REFERENCES

1. Ting DSW, Carin L, Dzau V, et al. Digital technology and COVID-19. Nat Med 2020;26:459-61.
2. LeCun Y, Bengio Y, Hinton G. Deep learning. Nature 2015;521:436-44.
3. Esteva A, Robicquet A, Ramsundar B, et al. A guide to deep learning in healthcare. Nat Med 2019;25:24-9.
4. Ting DSW, Liu Y, Burlina P, et al. AI for medical imaging goes deep. Nat Med 2018;24:539-40.
5. Esteva A, Kuprel B, Novoa RA, et al. Dermatologist-level classification of skin cancer with deep neural networks. Nature 2017;542:115-8.
6. Ting DSW, Cheung CYL, Lim G, et al. Development and validation of a deep learning system for diabetic retinopathy and related eye diseases using retinal images from multiethnic populations with diabetes. JAMA 2017;318:2211-23.
7. Lakhani P, Sundaram B. Deep learning at chest radiography: Automated classification of pulmonary tuberculosis by using convolutional neural networks. Radiology 2017;284:574-82.
8. Cleverley J, Piper J, Jones MM. The role of chest radiography in confirming covid-19 pneumonia. BMJ 2020;370:m2426.
9. Rajkomar A, Oren E, Chen K, et al. Scalable and accurate deep learning with electronic health records. NPJ Digit Med 2018;1:18.
10. Jumper J, Evans R, Pritzel A, et al. Highly accurate protein structure prediction with AlphaFold. Nature 2021;596:583-9.
11. Tunyasuvunakool K, Adler J, Wu Z, et al. Highly accurate protein structure prediction for the human proteome. Nature 2021;596:590-6.
12. Senior AW, Evans R, Jumper J, et al. Improved protein structure prediction using potentials from deep learning. Nature 2020; 577:706-10.
13. Gatenby RA, Silva AS, Gillies RJ, et al. Adaptive therapy. Cancer Res 2009;69:4894-903.

14. Ng WY, Tan TE, Movva PVH, et al. Blockchain applications in health care for COVID-19 and beyond: A systematic review. Lancet Digit Health 2021;3:e819-29.
15. Tan TE, Anees A, Chen C, et al. Retinal photograph-based deep learning algorithms for myopia and a blockchain platform to facilitate artificial intelligence medical research: A retrospective multicohort study. Lancet Digit Health 2021;3:e317-29.
16. Ng WY, Tan TE, Xiao Z, et al. Blockchain technology for ophthalmology: Coming of age? Asia Pac J Ophthalmol (Phila) 2021;10:343-7.
17. Chen RJ, Lu MY, Chen TY, et al. Synthetic data in machine learning for medicine and healthcare. Nat Biomed Eng 2021;5:493-7.
18. Tosun AB, Pullara F, Becich MJ, et al. Explainable AI (xAI) for anatomic pathology. Adv Anat Pathol 2020;27:241-50.
19. Xie Y, Nguyen QD, Hamzah H, et al. Artificial intelligence for teleophthalmology-based diabetic retinopathy screening in a national programme: An economic analysis modelling study. Lancet Digit Health 2020;2:e240-9.
20. Liu X, Cruz Rivera S, Moher D, et al; SPIRIT-AI and CONSORT-AI Working Group. Reporting guidelines for clinical trial reports for interventions involving artificial intelligence: The CONSORT-AI extension. Lancet Digit Health 2020;2:e537-48.
21. Rivera SC, Liu X, Chan AW, et al; SPIRIT-AI and CONSORT-AI Working Group. Guidelines for clinical trial protocols for interventions involving artificial intelligence: The SPIRIT-AI extension. BMJ 2020;370:m3210.
22. Vasey B, Nagendran M, Campbell B, et al; DECIDE-AI expert group. Reporting guideline for the early-stage clinical evaluation of decision support systems driven by artificial intelligence: DECIDE-AI. Nat Med 2022;28:924-33.
23. Sounderajah V, Ashrafian H, Rose S, et al. A quality assessment tool for artificial intelligence-centered diagnostic test accuracy studies: QUADAS-AI. Nat Med 2021;27:1663-5.
24. Sounderajah V, Ashrafian H, Golub RM, et al; STARD-AI Steering Committee. Developing a reporting guideline for artificial intelligence-centred diagnostic test accuracy studies: The STARD-AI protocol. BMJ Open 2021;11:e047709.
25. Liu X, Faes L, Kale AU, et al. A comparison of deep learning performance against health-care professionals in detecting diseases from medical imaging: A systematic review and meta-analysis. Lancet Digit Health 2019;1:e271-97.
26. Nagendran M, Chen Y, Lovejoy CA, et al. Artificial intelligence versus clinicians: Systematic review of design, reporting standards, and claims of deep learning studies. BMJ 2020;368:m689.
27. Chesterman S. We, the Robots?: Regulating Artificial Intelligence and the Limits of the Law. Cambridge, UK: Cambridge University Press; 2021.
28. Blasiak A, Truong A, LWJ Tan, et al. PRECISE CURATE.AI: A prospective feasibility trial to dynamically modulate personalized chemotherapy dose with artificial intelligence. J Clin Oncol 2022;40(16 Suppl):1574.
29. Pantuck AJ, Lee DK, Kee T, et al. Artificial intelligence: Modulating BET bromodomain inhibitor ZEN-3694 and enzalutamide combination dosing in a metastatic prostate cancer patient using CURATE.AI, an artificial intelligence platform. Adv Therap 2018;1:1800104.
30. Taylor M, Liu X, Denniston A, et al; SPIRIT-AI and CONSORT-AI Working Group. Raising the bar for randomized trials involving artificial intelligence: The SPIRIT-Artificial Intelligence and CONSORT-Artificial Intelligence guidelines. J Invest Dermatol 2021;141:2109-2111.
31. Collins GS, Dhiman P, Andaur Navarro CL, et al. Protocol for development of a reporting guideline (TRIPOD-AI) and risk of bias tool (PROBAST-AI) for diagnostic and prognostic prediction model studies based on artificial intelligence. BMJ Open 2021;11:e048008.
32. Collins GS, Reitsma JB, Altman DG, et al. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): The TRIPOD statement. BMJ 2015;350:g7594.
33. Moons KGM, Wolff RF, Riley RD, et al. PROBAST: A tool to assess risk of bias and applicability of prediction model studies: Explanation and elaboration. Ann Intern Med 2019;170:W1-33.
34. Chan AW, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Rev Panam Salud Publica 2015;38:506-14.
35. Moher D, Hopewell S, Schulz KF, et al; CONSORT. CONSORT 2010 explanation and elaboration: Updated guidelines for reporting parallel group randomised trials. Int J Surg 2012;10:28-55.
36. Wang P, Berzin TM, Glissen Brown JR, et al. Real-time automatic detection system increases colonoscopic polyp and adenoma detection rates: A prospective randomised controlled study. Gut 2019;68(10):1813-9.
37. Health Sciences Authority. Artificial intelligence in healthcare guidelines (AIHGIe). October 2021. https://www.moh.gov.sg/docs/librariesprovider5/eguides/1-0-artificial-in-healthcare-guidelines-(aihgle)_publishedoct21.pdf. Accessed 19 April 2023.
38. Tan BKJ, Teo CB, Tadeo X, et al. Personalised, Rational, Efficacy-Driven Cancer Drug Dosing via an Artificial Intelligence SystEm (PRECISE): A protocol for the PRECISE CURATE.AI pilot clinical trial. Front Digit Health 2021;3:635524.
39. Blasiak A, Kee TW, Rashid MBM, et al. CURATE.AI-optimized modulation for multiple myeloma: An N-of-1 randomized trial. Cancer Res 2020;80(16 Suppl):CT268.
40. International Medical Device Regulators Forum. Software as a medical device (SaMD): Clinical evaluation. 21 September 2017. https://www.imdrf.org/documents/software-medical-device-samd-clinical-evaluation. Accessed 19 April 2023.
41. Health Sciences Authority. Regulatory guidelines for software medical devices – A life cycle approach. April 2022. https://www.hsa.gov.sg/docs/default-source/hprg-mdb/guidance-documents-for-medical-devices/regulatory-guidelines-for-software-medical-devices---a-life-cycle-approach_r2-(2022-apr)-pub.pdf. Accessed 19 April 2023.
42. Kwee A, Teo ZL, Ting DSW. Digital health in medicine: Important considerations in evaluating health economic analysis. Lancet Reg Health West Pac 2022;23:100476.

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Real-world challenges when facilitating terminal discharge in Singapore

Dear Editor,

During the Ministry of Health workplan seminar held on 2 June 2022, Minister Ong Ye Kung expounded the notion of a good death and outlined the Ministry's vision and strategy for better care (and experience) for all near the end of life.[1] Specifically, he aimed to reduce the number of deaths in hospital among those with life-limiting illness from 61% to 51% in the next 5 years—fulfilling wishes of the majority to die at home. In relation to this, we share early findings of a multiphase research project.

Where any hospitalised patient's death is anticipated and imminent, prompt discharge from hospital to home may be arranged at the family's request.[2,3] This expedited transfer has acquired different labels in the literature: rapid discharge, fast-tracked discharge, or terminal discharge (TD).[3,4,5] In essence, TD is a complex healthcare intervention that involves close partnership between acute care providers and community hospice services.[2,6-9] While perspectives of hospitalists have been documented, the experience of community providers has not been sought.[9,10] Key knowledge gaps include: (1) overall demand and service utilisation[9] and (2) perceptions of service quality, specifically over continuity of care.[10]

We conducted a parallel mixed-methods study to uncover the real-world experience of TD within HCA Hospice, Singapore's largest and oldest home-based palliative care service.[11] Medical records of referrals for TD from January to December 2020 were extracted. First, demographics, number of days in service (service-days), and service utilisation of patients referred for TD were collated and examined. Next, data were compared against a comparator group who were identified as actively dying after admission to home hospice and placed on a "Care-of-the-Dying" Pathway by the home hospice team: Categorical variables (i.e. sex, ethnicity and disease type) were analysed using chi-squared test; the distributions of continuous variables (e.g. age, service-days and mean healthcare utilisation) were compared between groups using independent t-test (for parametric distributions) or Mann-Whitney U test (for non-parametric distributions). Additionally, we surveyed via email 5 clinicians (1 triage nurse, 3 palliative medicine registrars, and 1 principal resident physician) who served as coordinators for TD in HCA. They answered 4 open-ended questions: (1) what defined a TD, (2) variations from norms encountered in practice, (3) critical information they often did not get in referrals and (4) suggestions for improving care. Underpinned by the systemic framework,[12] reflexive thematic analysis of responses was performed by author PHC, a post-doc qualitative methods researcher and Medical Director of the hospice.

Our findings produced 3 key insights. First, TD can be common. HCA received a total of 260 TD referrals (equivalent to 1 TD per workday); 199 (76.5%) were patients not previously known to the hospice; 32 patients did not leave hospital alive, 18 died at home with only telephone support, and 10 remained alive past the data collection period (1 week after 31 December 2020). The remaining 200 patients eventually died under home palliative care. Table 1 displays characteristics and service utilisation of TD and comparator groups. There were significantly more non-cancer patients in the TD group, compared with the non-TD group (P<0.001). The median service-days for deceased TD patients was 4 days; 75.0% died within 7 days of hospital discharge. Finally, within the last week of life, TD patients required significantly more support overall, both via on-site visits and remote telephone support. The differences in service-days and service utilisation between groups were mainly attributable to cancer patients; there was no difference between groups among non-cancer patients.

Second, qualitative findings indicated a need to standardise definitions and eligibility criteria for TD among all stakeholders. TD coordinators voiced concerns that assumptions about TD sometimes differed between themselves and hospital counterparts. This was corroborated by shorter service-days among existing patients assessed to be acutely dying by hospice providers, compared to the TD group (particularly among patients with cancer) as well as the wide variability of service-days among TD patients of up to 121 days. The differential understanding had sometimes frustrated hospice workers, who often prioritised the care of TD patients above other terminally ill patients under their care.

Third, key information was occasionally omitted during transition of care. These include current physical

Table 1. Characteristics of deceased patients who were terminally discharged versus comparator group.

Characteristics	**TD patients (n=200)**	**Non-TD patients (n=434)**	***P* value**
Mean age (SD), years	75.3 (12.7)	74.5 (11.8)	0.438
Disease type, no. (%)			**<0.001**
Cancer	98 (49.0)	372 (85.7)	
Non-cancer	102 (51.0)	62 (14.3)	
Sex, no. (%)			0.557
Male	89 (44.5)	204 (47.0)	
Female	111 (55.5)	230 (53.0)	
Ethnicity, no. (%)			**0.044**
Chinese	150 (75.0)	330 (76.0)	
Malay	25 (12.5)	75 (17.3)	
Indian	13 (6.5)	18 (4.2)	
Others	12 (6.0)	11 (2.5)	
Service-days,[a] days			**0.003**
Median	4	3	
Range	0–121	0–64	
IQR	2.0–7.8	2.0–5.0	
Cancer subgroup			**<0.001**
Non-cancer subgroup			0.358
Service utilisation[b]	**TD patients (n=150)**	**Non-TD patients (n=356)**	
Mean total contacts per service-day, no. (SD)	1.81 (1.29)	1.50 (0.90)	**0.049**
Cancer subgroup			**0.015**
Non-Cancer subgroup			0.389
Mean visits per service-day, no. (SD)	0.72 (0.60)	0.74 (0.45)	**0.045**
Cancer subgroup			0.419
Non-Cancer subgroup			0.647
Mean calls per service-day, no. (SD)	1.10 (0.90)	0.77 (0.70)	**<0.001**
Cancer subgroup			**<0.001**
Non-Cancer subgroup			0.203

IQR; interquartile range; SD: standard deviation

[a] For TD patients, duration of service (service-days) is defined as the number of days from terminal discharge to death. For Non-TD patients, it is defined as the number of days between initiation of "Care-of-the-Dying" Pathway untill death.

[b] Computed for the subset of patients who died within 7 days for both groups (n=150 for TD patients and n=356 for non-TD patients).

Bold values indicate statistical significance ($P<0.05$).

and cognitive status, all medications prepared, whether caregiver training was initiated, patient equipment needs, and special concerns (e.g. family coping levels). Suggestions for better care include invitations for hospital teams to access resource support from palliative care colleagues. TDs are not as prevalent in the acute ward setting; literature further highlights that hospitalists may be unfamiliar with steps involved, particularly if conducted in haste.[2,5] At least 2 survey respondents recounted cases where patients have been discharged home without prior notice to hospice providers, picked up only when a crisis call is made by distressed family caregivers on the out-of-hours hospice helpline.

Patient and organisation-level data on TD from the community provider's perspective have never been reported previously. Our study findings would be of interest to agencies that offer similar rapid care transitions, both locally and outside Singapore. Beyond filling an evidence gap on the community perspective of a complex cross-agency intervention, our study findings also have practice and policy significance. First, a universal understanding (and proper handover) between professional providers potentially fosters seamless transfer of care during a challenging period for a patient. Second, an integrated care model built on these insights and collaboration between hospital and hospice is likely pivotal for good outcomes and patient safety. Third, we believe that quantitative indicators and outcomes reported in our study could be replicated among hospice services: for resource planning, to compare practice, and to consolidate towards population-level data to inform policy.

To conclude, we highlight real-world challenges from our multiphase research project aimed to facilitate terminal discharge in Singapore. Overcoming these challenges will require further longitudinal study with inputs from the triad of stakeholders: family caregivers, hospital providers and hospice workers.

REFERENCES

1. Ministry of Health, Singapore. Speech by Minister for Health, Mr Ong Ye Kung, at the MOH work plan seminar 2022, 2 June 2022. Published 3 June 2022. https://www.moh.gov.sg/news-highlights/details/speech-by-minister-for-health-mr-ong-ye-kung-at-the-moh-work-plan-seminar-2022-2-june-2022. Accessed 24 April 2023.
2. Tan YY, Blackford J. 'Rapid discharge': issues for hospital-based nurses in discharging cancer patients home to die. J Clin Nurs 2015;24:2601-10.
3. Gambles M, Cannell L, Bolger M, et al. Development and implementation of the Rapid Discharge Pathway Version 12 to enable imminently dying patients to die in the place of their choice. Int J Care Pathw 2012;16:14-8.
4. Gerrard R, Campbell J, Minton O, et al. Achieving the preferred place of care for hospitalised patients at the end of life. Palliat Med 2011;25:333-6.
5. Tan YY, Xu ZZ, Pang GS, et al. Facilitating terminal discharge: fulfilling the hospitalised patient's wish for home death in the final hours. Int J Palliat Nurs 2016;22:541-8.
6. Abrashkin KA, Cho HJ, Torgalkar S, et al. Improving transitions of care from hospital to home: what works? Mt Sinai J Med 2012; 79:535-44.
7. Naylor MD, Aiken LH, Kurtzman ET, et a. The importance of transitional care in achieving health reform. Health Aff (Millwood) 2011;30:746-54.
8. Eggen AC, Jalving M, Bosma I, et al. A methodology to systematically analyze the hospital discharge of terminally ill patients. Medicine (Baltimore) 2018;97:e12953.
9. Jones S, Hamilton S, Nicholson A. Rapid discharge from hospital in the last days of life: an evaluation of key issues and the discharge sister role. Int J Palliat Nurs 2015;21:588-95.
10. Smith R, Porock D. Caring for people dying at home: a research study into the needs of community nurses. Int J Palliat Nurs 2009;15:601-8.
11. Shorten A, Smith J. Mixed methods research: expanding the evidence base. Evid Based Nurs 2017;20:74-5.
12. Friedman, BD, Allen KN. Theory & practice in clinical social work. In Brandell JR. Systems Theory. 2nd edition. Thousand Oaks, CA: Sage; 2010.

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Suboptimal adherence to medical therapy in patients undergoing lower limb angioplasty in Singapore

Dear Editor,

Chronic limb-threatening ischaemia (CLTI) is the advanced stage of peripheral arterial disease (PAD) and patients with this condition face a very high risk of major adverse cardiovascular events and mortality. Several guidelines strongly recommend evidence-based medical therapy (EBMT) to reduce cardiovascular risk.[1-3] Specifically, all CLTI patients should be treated with an antiplatelet agent, moderate- to high-intensity statin therapy, anti-hypertensive therapy to control blood pressure, and anti-diabetic therapy to achieve haemoglobin A1c of <7%.[1] Despite these guidelines, adherence to EBMT is highly variable and Asian data are lacking.[4-6] The aim of this study was to understand the usage of EBMT in CLTI patients.

This was a retrospective cohort study of patients with PAD undergoing lower limb angioplasty at the Singapore General Hospital (SGH) between May 2018 and December 2019. This study was reviewed and approved by the SingHealth Institutional Review Board and written informed consent was obtained from all patients. We extracted demographic and clinical data from the SingHealth Electronic Health Intelligence System,[7] supplemented by manual curation to capture missing comorbidities and dispensing records of the drugs of interest in other SingHealth institutions.

We calculated adherence measures for the 4 classes of drugs recommended in the guidelines: statins, antiplatelets, anti-hypertensives and anti-diabetics. The follow-up period included the baseline (1-year period before angioplasty) and observation window (hospital discharge to 1-year post-discharge or death, whichever was earlier). EBMT use at admission was defined as an overlap of treatment episodes with a 90-day allowable gap with the date of admission. As discharge prescriptions are expected to be given on the discharge date, the overlap of the 0-day gap treatment episode with discharge date was used to avoid overestimations of carry-overs from prescriptions given before and during admission. The level of EBMT adherence post-discharge was measured by the proportion of days covered (PDC) over a 1-year period or until death of the patient, whichever was earlier.

Association between EBMT use at discharge and 1-year post-discharge PDC ≥0.80 was analysed using logistic regression. Associations between EBMT use at discharge and clinical outcomes were analysed using competing risks analyses (angioplasty/minor amputation and major amputation) with death as the competing risk or survival analyses (amputation-free survival [AFS] and overall survival) as appropriate. All analyses were conducted using R version 3.5.1.[8] The AdhereR package version 0.8.1 (CRAN, The Comprehensive R Archive Network) was used to calculate adherence measures.[9]

A total of 722 patients with complete data and discharged alive were included in the analysis. The mean age was 70.3 years (standard deviation=11.0) and 61.1% were male. The prevalence of hypertension, hyperlipidaemia and diabetes was 81.4%, 74.9% and 76.3%, respectively.

The levels of use of the 4 drug classes at admission and discharge are shown in Fig. 1. Of those who received antiplatelets at discharge, 307 (46.4%) received monotherapy, with the majority on aspirin (n=231, 75.2%) and clopidogrel (n=75, 24.4%). Only 1 patient received ticagrelor. Of the patients on antiplatelets, 354 (53.6%) were on dual-antiplatelets; the most common combination was aspirin/clopidogrel (n=344, 97.2%), followed by aspirin/ticagrelor (n=7, 2.0%) and aspirin/dipyridamole (n=3, 0.8%).

The numbers of patients who achieved post-discharge PDC≥0.80 for statins, antiplatelets, anti-hypertensives and anti-diabetics were 317 (43.9%), 373 (51.7%), 362 (50.1%) and 288 (39.9%), respectively. The likelihood for achieving PDC≥0.80 was significantly increased with the use of these drugs at discharge: statins (odds ratio [OR] 9.53, 95% confidence interval [CI] 5.88–16.25), antiplatelets (OR 14.07, 95% CI 6.12–40.73), anti-hypertensives (OR 17.78, 95% CI 8.31–46.22), and anti-diabetics (OR 43.66, 95% CI 20.74–112.39).

Patients who received statins and antiplatelets at discharge were more likely to have a subsequent angioplasty or minor amputation within 1-year post-discharge, compared to patients who did not receive these (32.0% versus 22.1%, *P*=0.027 and 30.7% vs 18.0%, *P*=0.014, respectively). Patients who received anti-diabetics at discharge compared to those who did not, were more likely to have a subsequent angioplasty or minor amputation (33.1% vs 21.4%, $P=4.55 \times 10^{-5}$) and major amputation (11.6% vs 7.4%, *P*=0.012), as well as lower AFS (75.2% vs 77.2%, *P*=0.030) and overall survival (83.0% vs 83.3%,

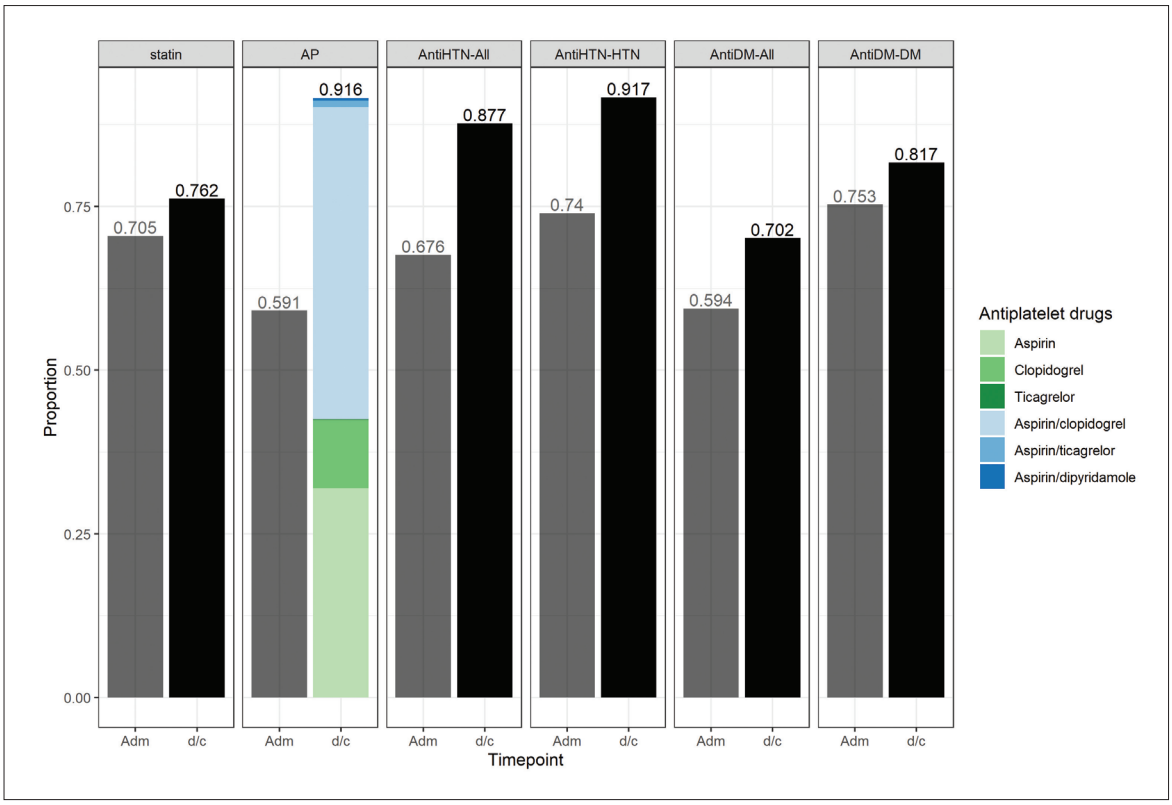

Fig. 1. Evidence-based medical therapy (EBMT) use at admission and discharge. The rates of EBMT use for each drug class at admission and discharge are shown in grey and black bars, respectively. For antiplatelets, the specific drugs are also shown. For anti-hypertensives, results are presented in both the entire cohort (AntiHTN-All) and in patients with hypertension (AntiHTN-HTN). For anti-diabetics, results are presented in both the entire cohort (AntiDM-All) and in patients with diabetes (AntiDM-DM).
Adm: admission; AntiDM: anti-diabetic; AntiHTN: anti-hypertensive; AP: antiplatelet; d/c: discharge; DM: diabetes; HTN: hypertension

P=0.043). Those who received anti-hypertensives at discharge had lower AFS (74.4% vs 85.4%, *P*=0.030) and overall survival (81.8% vs 92.1%, *P*=0.007).

To the best of our knowledge, this is the first detailed drug utilisation study of EBMT in PAD patients in Singapore, adding to the limited body of Asian data in this area.[4,5] Although prescription rates increased at discharge for all 4 drugs classes compared to rates at admission, not all patients received the recommended statin and antiplatelet. Those who were given EBMT at discharge were more likely to be taking them post-discharge. Therefore, the admission for angioplasty is a good opportunity to institute drug utilisation in patients who have not been started on the drugs or were not previously compliant.

SGH joined the Society for Vascular Surgery Vascular Quality Initiative (VQI), an international prospective registry of common vascular procedures since June 2019.[10] Initial results from 265 patients in the first 6 months of VQI data collection indicated higher pre-procedure use of statins and antiplatelets (88.3% and 81.5%, respectively) than our study.[10] Participation in VQI itself might have been an impetus for doctors to prescribe EBMT more religiously. Our results therefore reflect largely the practice before participation in VQI.

A surprising finding in our study was that limb-related outcomes and survival were worse for patients on EBMT at discharge, compared to those who were not; this association could be confounded by certain comorbidities that increased the risk of amputation and death, or procedural complexity.

There are some limitations to this study. Firstly, drugs collected from sources outside the SingHealth cluster would not be captured. However, most patients are likely to follow up within SingHealth since the angioplasty was done in SGH. Secondly, we do not know the reasons patients were not taking the EBMT drugs. Lastly, the adherence measures we report rely on dispensing records. Actual medication adherence could be lower.

In conclusion, we found suboptimal EBMT use in PAD patients undergoing angioplasty in Singapore. We are currently undertaking a qualitative study to

understand the factors behind EBMT adherence in our population to inform future interventions to improve adherence rates.

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REFERENCES

1. Conte MS, Bradbury AW, Kolh P, et al. Global Vascular Guidelines on the Management of Chronic Limb-Threatening Ischemia. Eur J Vasc Endovasc Surg 2019;58:S1-109.E33.
2. Gerhard-Herman MD, Gornik HL, Barrett C, et al. 2016 AHA/ACC Guideline on the Management of Patients With Lower Extremity Peripheral Artery Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2017; 135:e686-725.
3. Abola MTB, Golledge J, Miyata T, et al. Asia-Pacific Consensus Statement on the Management of Peripheral Artery Disease: A Report from the Asian Pacific Society of Atherosclerosis and V ascular Disease Asia-Pacific Peripheral Artery Disease Consensus Statement Project Committee. J Atheroscler Thromb 2020; 27:809-907.
4. Flu HC, Tamsma JT, Lindeman JHN, al. A systematic review of implementation of established recommended secondary prevention measures in patients with PAOD. Eur J Vasc Endovasc Surg 2010;39:70-86.
5. Chan SL, Rajesh R, Tang TY. Evidence-based medical treatment of peripheral arterial disease: A rapid review. Ann Acad Med Singap 2021;50:411-24.
6. Tang TY, Patel A, Soon SXY, et al. Improving medical adherence and antithrombotic management for patients with chronic limb threatening ischaemia in Singapore. Ann Acad Med Singap 2021;50:795-7.
7. Integrated Health Information Systems. Electronic Health Intelligence System. https://www.ihis.com.sg/Project_Showcase/Healthcare_Systems/Pages/eHINTS.aspx. Accessed 30 July 2021.
8. R Core Team. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing. Vienna, Austria; 2014. https://www.R-project.org. Accessed 20 April 2023.
9. Dima AL, Dediu D. Computation of adherence to medication and visualization of medication histories in R with AdhereR: Towards transparent and reproducible use of electronic healthcare data. PLOS ONE 2017;12:e0174426.
10. Soon SXY, Patel A, Chong TT, et al. Distribution of Peripheral Arterial Disease in Patients Undergoing Endovascular Revascularization for Chronic Limb Threatening Ischaemia: Insights from the Vascular Quality Initiative in Singapore. Vasc Specialist Int 2021;37.

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LETTER TO THE EDITOR

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Outcomes of selexipag for treatment of pulmonary arterial hypertension in an Asian population

Dear Editor,

Pulmonary arterial hypertension (PAH) is a progressive condition characterised by increased pulmonary arterial pressure and pulmonary vascular resistance, resulting in right ventricular dysfunction and eventually cardiac failure. In the early days, this was an often a fatal disease with significant morbidity. In recent years, there has been increasing awareness and therapeutic advancements in the field. The introduction of newer and combination therapies, coupled with a risk stratification approach have changed the practice of PAH, with significantly improved patient outcomes.[1] While there are multiple reports on the efficacy and tolerability of PAH treatment from PAH registries in Europe and the US,[2] data for Asians are lacking. Selexipag is an oral selective prostacyclin receptor agonist indicated for PAH treatment. Its efficacy was demonstrated in the GRIPHON trial, a phase 3 randomised controlled trial on 1,156 PAH patients, showing a 40% risk reduction in morbidity and mortality with selexipag.[3] However, data on its real-world safety and efficacy in Asians is limited. As such, we sought to evaluate the clinical characteristics and real-world outcomes of PAH patients initiated on selexipag in Asia.

This was a retrospective study on consecutive PAH patients treated with selexipag in an Asian tertiary cardiac centre up to 2020. Baseline and follow-up data collected include demographics, clinical characteristics and investigation results. Clinical outcomes evaluated include hospitalisation for PAH-related complications and all-cause mortality. Using the COMPERA 2.0 four-strata risk score, patients were risk-stratified into low, intermediate-low, intermediate-high and high mortality risk.[4] This is a validated model used to predict mortality in PAH, comprising 3 variables: World Health Organization functional class (WHO-FC), 6-minute walking distance (6MWD) and N-terminal pro-brain natriuretic peptide (NT-proBNP).[1]

A total of 36 PAH patients were treated with selexipag. The baseline characteristics are presented in Table 1. At baseline, the mean age was 46 years old ± 15.3, and the majority were female (83.3%) and of Chinese ethnicity (52.8%). Most patients were WHO-FC II or III (33.3% and 47.2%, respectively), with a NT-proBNP of 1335rg/mL (557–2918) and 6MWD duration of 327.5 ± 126.4 metres. Prior to initiation of selexipag, a majority of patients were receiving double therapy for PAH (80.6%), with 6 patients (16.7%) receiving monotherapy. At selexipag initiation, using the risk score, 3 patients were at low (8.3%), 11 patients at intermediate-low (30.6%), 12 patients at intermediate-high (33.3%) and 10 patients at high risk (27.8%) of mortality. The duration from PAH diagnosis to selexipag initiation was a median of 47 months (interquartile range [IQR] 49.1). Selexipag was initiated at 200mcg twice-daily dosage in all except one patient (who had started at 200µg once daily). The maximum tolerated dose ranged from 200µg twice daily to 1,400µg twice daily, with the majority tolerating up to 600µg twice daily (58.3%). See Supplementary Fig. S1. Side effects were reported in 23 patients (63.9%), of which headache (27.8%), diarrhoea (30.6%) or musculoskeletal symptoms (27.8%) were predominant. No serious side events were reported.

After a median follow-up of 25.9 ± 23.1 months, selexipag was stopped in 20 patients (55.6%), of which 7 were due to PAH progression requiring intravenous (IV) epoprostenol, and 13 patients due to selexipag-related side effects. The median duration of selexipag therapy in the overall cohort was 8.8 months (IQR 23.1). Of the patients who continued selexipag at last follow-up (n=13), 46.2% showed no change, 15.4% had an improvement, and 38.5% had an increased risk score. In the overall cohort, the majority (75%) had at least one hospitalisation for PAH-related complications and 15 patients (41.7%) demised. Of patients who demised, the majority were of intermediate-high (5 patients, 33%) or high (7 patients, 46.7%) risk status. Comparing connective tissue disorder (CTD)-associated versus non-CTD-associated PAH patients, there were no significant differences in selexipag discontinuation, change in risk scores, or death from any cause (P>0.05). To our knowledge, this is the first paper describing the clinical characteristics and outcomes of Southeast Asian PAH patients treated with selexipag. When compared with Western PAH studies,[3,5] our patient demographics were similar, with predominantly middle-aged female patients of WHO-FC II or III. Majority of patients in our cohort

Table 1. Baseline characteristic of our study cohort.

Baseline characteristics	Overall (N=36)
Age, mean (SD), years	46 (15.3)
Male, no. (%)	6 (16.7)
WHO-FC, no. (%)	
I	2 (6.1)
II	12 (36.4)
III	17 (51.5)
IV	2 (6.1)
NT-proBNP, median (IQR), pg/mL	1335 (2361)
6MWD, mean (SD), m	327.5 (126.4)
Comorbidities, no. (%)	
Ischaemic heart disease	6 (16.7)
Atrial fibrillation	7 (19.4)
Asthma/COPD	4 (11.1)
Obstructive sleep apnoea	8 (22.2)
Chronic kidney disease	5 (13.9)
Connective tissue disorder	15 (41.7)
PAH subtypes, no. (%)	
Idiopathic	18 (50.0)
Congenital heart disease associated	3 (8.3)
Connective tissue disorder associated	15 (41.7)
Baseline transthoracic echocardiogram parameters at time of selexipag initiation	
LVEF, mean (SD), %	63.5 (8.8)
TAPSE, mean (SD), cm	1.7 (0.5)
RA area, mean (SD), cm^2	24.6 (12.1)
Estimated PASP, mean (SD), mmHg	73 (23.6)
Presence of pericardial effusion, no. (%)	8 (22.2)
Baseline haemodynamic data on right heart catheterisation	
Mean pulmonary artery pressure, mean (SD), mmHg	51.4 (9.8)
Mean RA pressure, mean (SD), mmHg	11 (6.0)
Cardiac output, mean (SD), L/min	3.61 (1.2)
PVR, median (IQR), WU	11.6 (8.5)
PAH specific medications, no. (%)	
No medication	1 (2.8)
Monotherapy	6 (16.7)
Double therapy	28 (77.8)
Triple therapy	1 (2.8)
COMPERA 2.0 risk scores, no. (%)	
Low	3 (8.3)
Intermediate-low	11 (30.6)
Intermediate-high	12 (33.3)
High	10 (27.8)
Duration from PAH diagnosis to selexipag initiation, median (IQR), months	47.0 (49.1)
Reported side effects from selexipag, no. (%)	
Headache	10 (27.8)
Diarrhoea	11 (30.6)
Nausea/vomiting	7 (19.4)
Musculoskeletal	10 (27.8)
Duration of selexipag therapy, median (IQR), months	8.8 (23.1)
Follow-up duration, median (IQR), months	25.9 (23.1)

6MWD: 6-minute walking distance; COPD: chronic obstructive pulmonary disease; IQR: interquartile range; LVEF: left ventricular ejection fraction; NT-proBNP: N-terminal pro-brain natriuretic peptide; PAH: pulmonary arterial hypertension; PASP: pulmonary artery systolic pressure; PVR: pulmonary vascular resistance; RA: right atrium; SD: standard deviation; TAPSE: tricuspid annular plane systolic excursion; WHO-FC: World Health Organization functional class

could only tolerate low to medium doses of selexipag (up to 600µg twice daily). This is lower than those described in other studies. In the SPHERE registry on 500 patients in US, the median selexipag dose was 1,200µg twice a day.[6] In the GRIPHON trial, the majority tolerated medium to high doses of selexipag (600µg and above). Nevertheless, the GRIPHON trial reported similar primary outcome rates regardless of selexipag dosing.[3]

When evaluating the safety profile of selexipag, the reported side effects from it in our cohort was lower than other study populations (63.9% versus 72.2% for SPHERE registry[6] and 98.3% for GRIPHON study[3]). Tanabe et al. reported the tolerability of selexipag in 37 Japanese PAH patients over 192 weeks, while all patients reported at least one selexipag-related adverse event; only one patient had a serious event requiring selexipag discontinuation.[7] As such, although side effects are frequently observed with selexipag treatment, the majority are mild.

In our study, less than 10% of the patients had low PAH risk, with more than 60% being intermediate-high or high risk. Seven patients required escalation to IV therapy, and mortality rate was 41.7% after 27 months follow up—this reflects a much higher risk group of PAH patients. In comparison, about half the patients in the GRIPHON trial were of low PAH risk, and patients with multiple comorbidities were excluded.[3] In recent times, with greater focus on risk stratification, there is a shift towards earlier initiation of selexipag. The median duration from PAH diagnosis to selexipag initiation was 47 months but these included patients from early on where risk stratification may not have been routinely performed. Practically, the cost of selexipag therapy and tolerability remain significant barriers in the uptake of selexipag in the Asia. Due to costs, selexipag is often initiated as third-line combination therapy. Of note, selexipag should not be viewed as replacement for IV epoprostenol in high-risk patients who are suitable candidates for IV therapy, and early initiation of IV therapy in this high-risk cohort should be comprehensively considered where available.

Regarding limitations, this was a single centre study with a small sample population and may not reflect the varying practices across Asia. Nevertheless, this study is the first to report data on Southeast Asian PAH patients and may advise further practice in the region.

In conclusion, in this study on an Asian cohort with higher PAH risk, there was a significant subset of patients with disease progression or intolerance to selexipag. Of patients who continued selexipag at last follow-up, about 60% had a stable or improved risk strata. Further work on optimal patient selection and barriers to initiation are warranted.

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REFERENCES

1. Humbert M, Kovacs G, Hoeper MM, et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Heart J 2022;43:3618-731.
2. Awdish R, Cajigas H. Definition, epidemiology and registries of pulmonary hypertension. Heart Fail Rev 2016;21:223-8.
3. Sitbon O, Channick R, Chin KM, et al. Selexipag for the treatment of pulmonary arterial hypertension. N Engl J Med 2015;373: 2522-33.
4. Hoeper MM, Pausch C, Olsson KM, et al. COMPERA 2.0: A refined four-stratum risk assessment model for pulmonary arterial hypertension. Eur Respir J 2022;60:2102311.
5. Farber HW, Miller DP, Poms AD, et al. Five-year outcomes of patients enrolled in the REVEAL registry. Chest 2015;148:1043-54.
6. Kim NH, Hemnes AR, Chakinala MM, et al. Patient and disease characteristics of the first 500 patients with pulmonary arterial hypertension treated with selexipag in real-world settings from SPHERE. J Heart Lung Transplant 2021;40:279-88.
7. Tanabe N, Ikeda S, Tahara N, et al. Efficacy and safety of an orally administered selective prostacyclin receptor agonist, selexipag, in Japanese patients with pulmonary arterial hypertension. Circ J 2017;81:1360-67.

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LETTER TO THE EDITOR

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Sublingual ondansetron for treatment of acute gastroenteritis in children in the children's emergency

Dear Editor,

Acute gastroenteritis (GE) is a leading cause of death globally in children aged below 5 years and the third most common indication for hospital admission in some countries.[1,2] Currently, norovirus is the most common cause of GE in children in developed countries.[3] Rehydration, either orally or intravenously, is the mainstay of treatment to prevent multisystemic complications of dehydration.[4] In recent decades, there has been increased interest in the role of antiemetics (such as ondansetron) in acute GE to reduce the need for intravenous rehydration, hospital admissions, emergency department reattendances, and healthcare expenditure.[5,6]

Ondansetron use in GE has been found to be superior to placebo and other antiemetics in reducing further vomiting, and the need for intravenous hydration and hospitalisation.[7,8] Meta-analyses have shown that ondansetron use for GE in the children's emergency (CE) significantly reduces hospitalisation compared to placebo (relative risk [RR] 0.53, 95% confidence interval [CI] 0.29–0.97 versus OR 2.93, 95% CI 1.69–6.18).[8,9] Given the ease of administration and increasing evidence of its safety and efficacy, paediatric centres have incorporated the use of ondansetron into their practice guidelines.[10,11] However, there is a paucity of evidence regarding factors associated with its success or failure for acute GE in children. Our centre's practice in the CE, National University Hospital, Singapore has been to give a trial of fluids after ondansetron administration, and review the children 30 minutes later to determine ondansetron success or failure. This creates a patient dwell time of 1–2 hours from the point of CE consultation. Thus, identifying factors that can predict success or failure with ondansetron can help clinicians distinguish between patients at high risk of failure with a likely need for monitoring in CE, versus patients who can be discharged early postondansetron.

We report the results of our retrospective cohort study involving paediatric patients (6 months to 18 years of age) who presented with vomiting and received ondansetron at the CE between 1 January and 31 December 2018. This retrospective study was approved by the National Healthcare Group Domain Specific Review Board (Reference number: 2018/01394).

In our practice, patients are given a trial of fluids 30 minutes after ondansetron administration, and then reviewed 30 minutes later to ensure there is no further vomiting before discharge. Inclusion criteria for this study included a clinical diagnosis of acute GE and prescription of sublingual ondansetron in the CE consequently. Patients with alternative diagnoses for their symptoms or who required intravenous therapy were excluded. Patients were identified though pharmacy records. Data extraction from electronic medical records included demographics, vital signs, weight, day of illness, number of vomiting episodes, associated symptoms such as diarrhoea or fever, hydration status, dose of ondansetron given, and outcome post-ondansetron. Outcomes were defined as: (1) early success: successful trial of fluids in CE after sublingual ondansetron; (2) early failure: failed trial of fluids in CE after sublingual ondansetron; (3) total success: successful trial of fluids, not requiring admission and no reattendance within 3 days of initial consult; and (4) total failure: failure of trial of fluids at initial consult, need for admission and any reattendance within 3 days of initial consult. Statistical analysis was performed using SPSS Statistics software version 26.0 (IBM Corp, Armonk, US).

We identified 3,146 patients who fulfilled the inclusion criteria. Of these, we excluded the following: patients with no ongoing vomiting (n=117), and uncertain outcome post-ondansetron (e.g. abscondment or early discharge prior to clinical assessment) (n=50). Data of the remaining 2,979 patients were analysed (Fig. 1).

The mean age of patients diagnosed with GE who received sublingual ondansetron was 4.79 ± 4.03 years and over 50% (1,608/2,979) were males. Average duration of illness upon CE presentation was 1.66 ± 1.19 days (range 1–11 days). Regarding hydration status, 89.8% were a euvolemic, 9% were mildly dehydrated, 1.1% were moderately dehydrated while 0.03% were severely dehydrated (Supplementary Table S1).

Early success was observed in 95.8% (2,854/2,979) of patients. Of these, 2.2% (63/2,854) were admitted nevertheless due to (1) parental request (n=32); (2) patients requiring intravenous rehydration as a result of clinical dehydration (n=13); (3) persistent symptoms such as dizziness, nausea or lethargy (n=8); (4)

investiga-tion of abdominal pain (n=3); and (5) abnormal vital signs and repeated healthcare visits (n=7) (Fig. 1).

A further 7.1% (203/2,854) reattended at CE within 3 days of initial presentation for persistent gastrointestinal symptoms (n=156) and non-gastrointestinal symptoms (n=47); 53.7% (109/203) of these reattendances required admission. Reattendances with persistent gastrointestinal symptoms were more likely to require admission compared with those who reattended for other complaints (60.3% vs 31.9%, P<0.001). Total success rate (i.e. successful trial of fluids after ondansetron dose, not admitted and no reattendance within 3 days for any reason) was 86.9% (2,588/2,979) (Fig. 1).

Early failure was observed in 4.2% (125/2,979) of patients. Over 95% (119/125) of these patients were subsequently admitted; 6 were not admitted due to parental preference. Rate of total failure was 13.1% (391/2,979), comprising early failures, eventual admissions despite initial success with ondansetron, and reattendances despite initial success (Fig. 1).

Clinical features associated with early failure versus early success with ondansetron in paediatric GE included older age (6.5 vs 4.7 years, P=0.008),

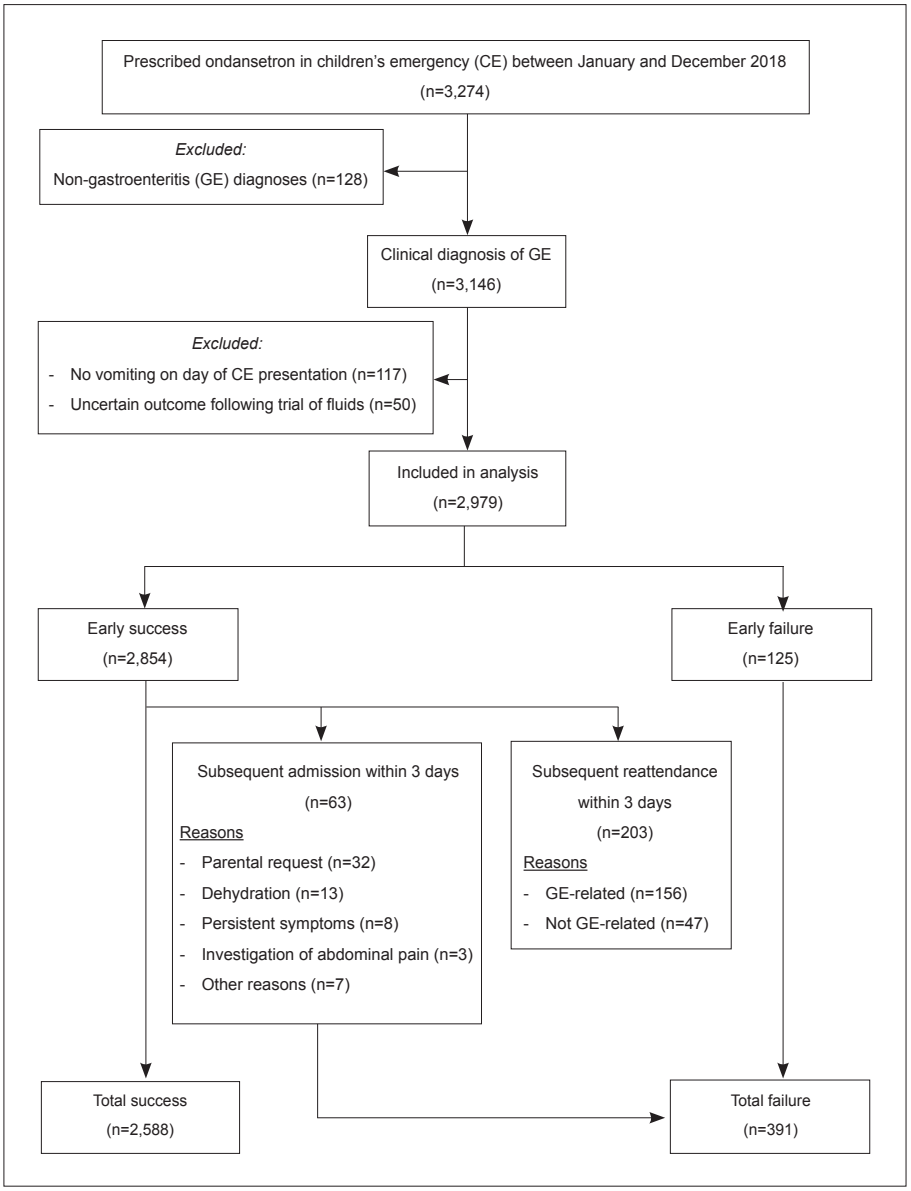

Fig. 1. Study flowchart.
CE: children's emergency; GE: gastroenteritis

higher number (≥6) of vomiting episodes prior to CE presentation (46.4% vs 35.9%, P=0.017) and dehydration (30.4% vs 9.3%, P<0.001) (Supplementary Table S2). Subgroup analysis revealed that children ≥5 years old were more likely to be dehydrated (P<0.001) and present with a higher number of vomiting episodes (P<0.05) compared with children under 5. Dehydration was the only factor significantly associated with total failure versus total success (22.8% vs 8.3%, P<0.001) (Supplementary Table S3).

Our study demonstrated high efficacy with sublingual ondansetron for acute GE in CE. These findings agree with previous studies on the efficacy of ondansetron in viral gastroenteritis and support the continued use of this drug for such clinical indication.[12,13] Closer attention should be paid to older children, children who present with higher number of vomiting episodes, and children with evidence of dehydration, as they are more likely to experience early failure with ondansetron. We included admissions and reattendances both related and unrelated to GE or ondansetron failure under the "total failure" outcome as this accurately reflects real-life clinical setting. Most reattendances were unrelated to gastrointestinal symptoms, and also less likely to truly require admission. Physicians may therefore consider pre-empting parents on the expected course of viral infections and provide anticipatory guidance in order to reduce unnecessary CE visits.

The strength of our study is its large sample size. Limitations include its retrospective nature, missing data, possible non-standardised assessment of patients by physicians, probable recall bias from parental report of symptoms, and possible underestimation of the total failure rate (as patients may have sought medical attention elsewhere after discharge from our CE). Apart from the need for prospective, follow-up studies to confirm our findings, studies on the utility and safety of sublingual ondansetron in primary care settings are warranted.

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REFERENCES

1. World Health Organization. Child mortality (under 5 years), 28 January 2022. https://www.who.int/news-room/fact-sheets/detail/levels-and-trends-in-child-under-5-mortality-in-2020. Accessed 26 March 2022.
2. Lo Vecchio A, Dias JA, Berkley JA, et al. Comparison of Recommendations in Clinical Practice Guidelines for Acute Gastroenteritis in Children. J Pediatr Gastroenterol Nutr 2016; 63:226-35.
3. Payne DC, Vinjé J, Szilagyi PG, et al. Norovirus and medically attended gastroenteritis in U.S. children. N Engl J Med 2013; 368:1121-30.
4. Guarino A, Bruzzese E, Lo Vecchio A. Oral Rehydration Solution—An Essential Therapy for Childhood Gastroenteritis. JAMA Pediatr 2018;172:991.
5. Freedman SB, Steiner MJ, Chan KJ. Oral ondansetron administration in emergency departments to children with gastroenteritis: an economic analysis. PLOS Med 2010;7:e1000350.
6. Hervás D, Armero C, Carrión T, et al. Clinical and economic impact of oral ondansetron for vomiting in a pediatric emergency department. Pediatr Emerg Care 2012;28:1166-8.
7. Danewa AS, Shah D, Batra P, et al. Oral Ondansetron in Management of Dehydrating Diarrhea with Vomiting in Children Aged 3 Months to 5 Years: A Randomized Controlled Trial. J Pediatr 2016;169:105-9.e3.
8. Niño-Serna LF, Acosta-Reyes J, Veroniki AA, et al. Antiemetics in Children With Acute Gastroenteritis: A Meta-analysis. Pediatrics 2020;145:e20193260.
9. Tomasik E, Ziółkowska E, Kołodziej M, et al. Systematic review with meta-analysis: ondansetron for vomiting in children with acute gastroenteritis. Aliment Pharmacol Ther 2016;44:438-46.
10. Children's Health of Orange County. Outpatient Acute Gastroenteritis Guideline, 20 January 2016. https://www.choc.org/wp/wp-content/uploads/careguidelines/OutpatientAcuteGastroenteritisGuidelines.pdf. Accessed 18 March 2022.
11. The Royal Children's Hospital Melbourne. Clinical Practice Guidelines: Gastroenteritis, December 2020. https://www.rch.org.au/clinicalguide/guideline_index/Gastroenteritis. Accessed 18 March 2022.
12. King CK, Glass R, Bresee JS, et al. Managing acute gastroenteritis among children: oral rehydration, maintenance, and nutritional therapy. MMWR Recomm Rep 2003;52(RR-16):1-16.
13. Colletti JE, Brown KM, Sharieff GQ, et al. The management of children with gastroenteritis and dehydration in the emergency department. J Emerg Med 2010;38:686-98.

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