ANNALS

ACADEMY OF MEDICINE, SINGAPORE

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VOLUME 51 | NUMBER 9 | SEPTEMBER 2022

MCI (P) 026/06/2022

Wheeled recreational devices (WRDs) such as bicycles, inline skates, skateboards and scooters can cause significant morbidity and mortality. A recent study examined injuries sustained by children from WRD use and found almost half were soft tissue injuries, followed by fractures. Upper limb, and head and neck regions were the most common sites of injury. Of the patients, 38% had severe injuries with potential morbidity. Children who are heavier and of the school-going age are more prone to developing injuries from the use of wheeled-recreational devices. These children would benefit from protective wrist and elbow guards and helmets.

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Printed by Straits Printers (Pte) Ltd

ISSN 0304-4602

MCI (P) 026/06/2022

Annals, Academy of Medicine, Singapore

Volume 51 | Number 9 | September 2022

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Ann Acad Med Singap 2022;51:523-5
https://doi.org/10.47102/annals-acadmedsg.2022241

Inclusive and safe active mobility

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Physical activity is considered the "best buy" in public health practice to prevent non-communicable diseases. This perspective overshadows the importance of avoiding injuries due to physical activity in vulnerable populations.[1-3] Non-communicable conditions are considered the third most common cause of mortality in people aged 5–19 years.[4] However, injuries are the second most important global cause of mortality in this age group, with road injuries being the most frequent type of injury.[4]

In their study, Chia et al.[5] found that the majority (39%) of non-motorised active mobility device (AMD) injury in Singapore occurs in public spaces (playgrounds, sports facilities and roads). This is in line with previous research in the US[6] and Australia.[3] Not only does AMD injury occurs more frequently in public space, but this location could be associated with higher injury severity. In an earlier study, Rod et al. discussed that injuries from wheeled recreational devices occurring in public spaces were associated with higher injury severity than those occurring in other locations.[3] This highlights the importance of assertive governance for promoting safe active mobility.

A failure to deliver road safety initiatives to prevent AMD injuries might offset some of the projected gains of active mobility.[1,2] However, evidence supports that the health gains of active mobility offset the health burden from traffic incidents due to physical activity.[7] I believe this perspective is accurate, yet the idea that the benefits of active mobility outweigh the health risk associated with traffic incidents is not a solid argument to justify the relatively low attention given to safe active mobility. In addition, there might be unmeasured health outcomes from traffic incidents suggesting the "true" burden of traffic incidents due to active mobility might be underestimated.

One example of a hidden health burden from traffic incidents is pedestrian falls, which have not been traditionally considered a traffic injury despite representing approximately 90% of pedestrian incidents.[8] Moreover, very few studies of pedestrian injury define what a pedestrian is.[2] Authors need to explain what they mean by a pedestrian, as this does not necessarily imply walking. Some jurisdictions like Singapore and the state of Queensland in Australia consider wheeled recreational device users and other wheeled vehicle users a pedestrian.[4] The trauma incidence of such users might not be included in studies quantifying the burden of traffic incidents, given that its primary injury mechanism is a fall. This is evidenced in the findings presented by Chia et al.[5] There are also long-term and psychological health outcomes that could not be quantified as traffic incidents but are indirect consequences of road injuries. For instance, the need for rehabilitation, long-term care, post-traumatic stress syndrome,[4] anxiety and fear of injury, and re-injury. The psychological spectrum from higher perceived risk to anxiety and post-traumatic stress disorder might lead to decreased active mobility participation.[9]

The issues discussed above highlight the importance of examining the epidemiology of AMDs at present, especially considering the scarcity of research conducted in Asian communities. However, there are reasons to believe AMD injury could be a bigger problem in the future:

- More people are living in urban areas.
- There is an increasing worldwide push to move to sustainable and active modes of transport.
- There is a growing variability for commercially available AMDs and motorised wheeled recreational devices.
- There is an increasing number of wearable devices that compete for road users' attention such as smart phones, smart watches and smart glasses.

The interaction of these factors might lead AMDs to have a higher risk of traffic injury in the future. An opposite perspective emerges from the safety in numbers effect, suggesting that the more participants in active mobility there are, the lower the risk of injury to each

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This article was first published online on 9 September 2022 at annals.edu.sg

participant. The current evidence suggests this is the case.[10] However, most of the research conducted on the safety in numbers effect is focused on the occurrence of pedestrian and bicycle crashes/collisions. This implies that the validity of the safety in numbers effect on other mechanisms of road injury, such as falls, needs to be studied. The literature discussing pedestrian falls suggests that falls might be more likely in areas with high volumes of vulnerable road users.[11] In addition, among vulnerable road users, not every user is equal in the level of vulnerability. The interaction of the above factors might also be particularly challenging for children using recreational devices and older adults.[2-4] In the first group, vulnerabilities arise from the lack of cognitive and motor experience to cope with the traffic system. In the case of older adults, this is related to the mental and motor decline associated with biological ageing.

Road safety prevention strategies aimed at the "vulnerable of the vulnerable" also have the potential to give a high return on the invested capital. In the case of children, every injury prevented brings a triple dividend: their health now, their health in the future and the health of the next generation.[1] Moreover, Chia et al.[5] found that the most common type of injuries from AMD are fractures, and the more common anatomical locations of injury are the head and the forearm. These injuries are critical long-term contributors to worse health outcomes in the paediatric population and their transition to adulthood. For instance, forearm fractures have been associated with poor long-term bone mass and strength. Similarly, facial wounds are associated with long-term psychological stress in children due to social stigma.[3] Furthermore, head trauma is the leading cause of mortality and disability in children, and AMD accounts for more than 10% of patients attending emergency departments with head trauma.[3] Moreover, up to 30% of patients with head trauma due to skateboard riding end up with hemiplegia, deafness or facial palsy.[3] The other 70% have an increased risk of intellectual disability, premature mortality, low education and the need for welfare recipiency later in life, even due to mild concussions to the head. In the case of older adults, pedestrian falls are an essential contributor to fall presentations (the most common form of injury in older adults) to the emergency department,[2] and older adults suffer worse health outcomes from a pedestrian fall and vehicle collisions.[1]

The world is experiencing geopolitical and economic challenges that require governments to deliver effective prevention strategies under tight budgets. This highlights the need for cost-effective interventions that could simultaneously impact highly vulnerable populations at multiple levels. Impact-absorbing surfaces could play this multidimensional preventive role in future mobility. They can potentially reduce both the incidence and harm from injuries to various vulnerable road users.[3] Simultaneously tackling the incidence and associated harms would prevent the direct physical health burden of the injuries and the potential long-term mental health consequences, including the development of fear and anxiety of performing physical activity in the public space. This would also foster a more inclusive and safe traffic environment where those more vulnerable to severe trauma are less likely to be inequitably affected by active mobility.

Having presented my current academic perspective on the issue, I would like to provide insights from my personal experience. I have more than 10 years of experience commuting with AMDs and electrical mobility devices in Colombia, Germany and Australia (Fig. 1). I firmly believe that active commuting and car-lite cities are one of the best public health investments a government can make for its citizens. However, the fear of a severe injury is a behavioural barrier for me to engage in these activities more often. It is also one of the most common reasons I receive from my family, friends and colleagues across the above-mentioned countries to not engage in active

Fig. 1. Cross-national active mobility devices and electrical mobility devices used by the author. (A) Mountain bike commuting in Barranquilla, Colombia. (B) Road bike commuting in Brisbane, Australia. (C) City bike commuting in Mainz, Germany. (D) Road bike commuting in Barranquilla, Colombia. (E) Dual motor all-terrain wheel electric longboard commuting in Brisbane, Australia. (F) Polyurethane wheels electric longboard commuting in Brisbane, Australia.

mobility. In this sense, my academic and personal intuition suggests that safe active mobility promotes health through 2 pathways. The first pathway is the direct health gains associated with safe active mobility; the second pathway relates to the perception of security that arises from safe active mobility infrastructure, reducing behavioural barriers to using AMDs. Considering these pathways when designing interventions that promote active mobility could reduce the probability of children and older adults being inequitably affected. Thus, promoting inclusive and safe active mobility requires interdisciplinary risk analysis research that includes both objective (epidemiological) and subjective (psychological) aspects of risk.

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EDITORIAL

Ann Acad Med Singap 2022;51:526-7
https://doi.org/10.47102/annals-acadmedsg.2022314

Different strokes for different folks

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Atrial fibrillation (AF) remains the most common arrhythmia since William Harvey's observation of fibrillating auricles in open chest animal models in 1628. Willem Einthoven first documented ECG tracing of AF in 1906. Fast forward several hundred years since its first observation, AF remains a mystery from its pathogenesis and sustenance to treatment options in the 21st century.

AF is known to confer incremental risk of mortality in population-based studies and poses a substantial morbidity burden in terms of stroke and heart failure.[1] Yet, a one-size approach does not fit all in AF treatment and individualised management with shared decision-making is encouraged in most clinical guidelines.[2] In fact, even the incidence and prevalence of the same arrhythmia differ between populations and communities. These observations further intrigue and complicate how genetics and environments, together with known risk factors and modifiers, intertwine to give rise to, perpetuate and sustain AF. Recent publications have shown racial and sex differences in mortality for AF in different ethnic groups.[3] However, most studies were limited in the West, mainly comparing white versus non-white populations.

Regionally, there are interesting differences observed in the prevalence, clinical correlates and outcomes of AF in heart failure patients across Asia.[4] A previous community-based study in Singapore showed a relatively low AF prevalence rate in the Chinese community over the age of 55 years old.[5] In this issue of the *Annals*, Tan et al. had taken further steps to illustrate the interesting differences in the mortality and incidences in multiethnic Singapore.[6] Albeit the study was retrospective in nature with its limitations and potential unknown confounding variables, the authors ought to be commended on several pertinent observations. Firstly, the study was consistent with the huge prospective observational study, Global Anticoagulant Registry in the Field (GARFIELD-AF)[7] and demonstrated incremental mortality among newly diagnosed AF patients belonging to the 3 main ethnic groups (Chinese, Malays and Indians) in Singapore.

Additionally, increased prevalence of cardiovascular risk factors did not correspond to incremental incidence of AF across the 3 ethnic groups, raising questions of genetic protective effects of variable and questionable significance. The authors also acknowledged that the higher mortality rates observed in their study could be due to the overwhelming majority of newly diagnosed AF reported from hospital admissions compared to community, outpatient settings. Intuitively, this group would be sicker, often with underlying systemic illnesses and multiple comorbidities, thus attributing to the higher risk of mortality. Asymptomatic AF patients in the community, whose first presentation may be a result of associated complications at a later stage, could undermine the true incidence and prevalence. Thus, the conundrum remains on which population groups benefit from cost-effective screening and treatment. Recent published studies attempted to answer this question and more ongoing research will hopefully provide clearer guidance.[8,9]

More than half of the deaths in this study were attributed to non-cardiovascular causes and independent of cardiovascular risk factors. This resurrects the notion of whether AF is a risk factor or risk marker. Given the heterogeneity of ethnicity but living in a shared environment manifesting different mortality outcomes, it may well be that the development of AF indicates the presence and development of underlying comorbidities such as sleep apnoea, obesity, alcohol dependence and lung disease in addition to known cardiovascular risk factors. Timely and appropriate management of such comorbidities, which may create an underlying myocardial substrate for the initiation and sustenance of AF, has been convincingly shown to reduce the burden and improve overall well-being and mortality.

Lastly, the authors advocated an aggressive management of AF and this likely involves early rhythm-control in appropriate patients. The Early treatment of Atrial Fibrillation for Stroke prevention Trial (EAST-AFNET 4) study showed that early rhythm-control for this group of patients was associated

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with a lower risk of adverse cardiovascular outcomes.[10] Locally, increasing awareness of AF with its associated adverse potential sequelae among the population at increased risk is important. Despite the same arrhythmia, but different prevalence, incidence, or hard end points in a heterogeneous ethnic population in Singapore, the same aggressiveness and access to care should be adopted in the approach towards early treatment and management for favourable long-term outcomes in AF.

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EDITORIAL

Ann Acad Med Singap 2022;51:528-30
https://doi.org/10.47102/annals-acadmedsg.2022194

From Astana to Singapore: Primary Health Care is key to the long-term success of Singapore's health system

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The Ministry of Health, Singapore (MOH) has launched a wide-ranging and ambitious initiative for a life-course approach to drive the population's health.[1] This approach aims at ensuring the sustainability of the healthcare system. Crucially, it also embodies core principles of the health systems orientation that have long been advocated by the World Health Organization (WHO) and that is the cornerstone of the health strategy in the United Nations Sustainable Development Goals: Primary Health Care (PHC). PHC is a whole-of-society approach that aims to equitably maximise the health and well-being of all people. It focuses on people's needs and preferences as early as possible along the continuum, from health promotion and disease prevention, to treatment, rehabilitation and palliative care. It brings care as close as feasible to people's everyday environment.[2]

The 1978 Declaration of Alma-Ata was a seminal moment in the history of PHC.[3] Adopted at the International Conference on PHC in the former Kazakh Soviet Socialist Republic that is now Kazakhstan, it birthed a global movement for PHC. Governments, WHO, United Nations Children's Fund (UNICEF) and major global health actors pledged to protect and promote the health of all people in the world and recognised PHC as essential and fundamental to a country's health system, inextricably linked to its socioeconomic development. The declaration provided a framework for the redesign of health systems and called for stakeholders to collaborate on urgent and effective action—both nationally and internationally—to develop, implement and maintain PHC throughout the world.

Fast forward 4 decades since this visionary and ambitious declaration, the uptake of PHC has helped to raise global standards of healthcare and improved health.[4] However, many people in all parts of the world, particularly the poor and vulnerable, continue to have unaddressed health needs, including care for non-communicable and communicable diseases, maternal and child health, mental health, and sexual and reproductive health. Amid the growing needs and emerging health challenges of the 21st century, the vision of Alma-Ata has yet to be realised, largely because of maximising immediate impact through an emphasis on single-disease interventions rather than building comprehensive health systems. Emblematic are the ubiquitous health systems founded on targeted programmes, specialist-led care and intensive use of medical technology. These systems overestimate the benefits of efforts to cure, rather than to prevent disease or to promote health. Other contributory factors include insufficient intersectoral engagement, unregulated commercialisation and suboptimal use of evidence-based policies.

The deep and fundamental consensus remains, however, that the health and well-being of populations are most effectively, equitably and efficiently achieved through a PHC-oriented approach, further substantiated in a corpus of evidence.[2,3] The 2018 Declaration of Astana, signed on the 40th anniversary of the original declaration, reaffirmed solidarity around health as a fundamental human right and PHC as the cornerstone of every sustainable health system to achieve universal health coverage and health-related sustainable development goals.[5] It called for fresh impetus to overcome challenges for PHC that have emerged over the years, including the growing burden of non-communicable diseases (NCDs) and multimorbidity, problems with fragmentation, coordination and continuity of care, shortage and uneven distribution of health workers, disproportionate out-of-pocket spending, rising costs and systemic inefficiencies.[6,7]

Many of these challenges apply to Singapore.[8] The most notable is its rapidly ageing population that faces a rising burden of NCDs, such as cardiovascular and mental health disorders, which contribute to more than 80% of the total disability-adjusted life years of the country. Ageing has increased demands on the entire

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healthcare system, leading to shortfalls in acute hospital beds and intermediate- and long-term care services, plus concerns from the public about the affordability of healthcare. Complicating matters are certain characteristics of the existing PHC system that impede its ability to realise its potential. These include the majority of PHC being provided by single or small-group general practices, many of which have neither the scale nor the resources to manage patients with complex needs. Moreover, the inadequate integration of PHC with other health and social providers impedes the sharing of information that facilitates holistic care.

The 2018 Declaration also clearly articulated for the first time the 3 inter-related and synergistic components of the PHC orientation of health systems: (1) primary care (the first level of care with family medicine at the core of multidisciplinary teams) and public health functions as the central elements of integrated health services; (2) evidence-informed policies and actions across all sectors for comprehensively addressing the broader determinants of health; and (3) empowerment of individuals, families and communities as co-developers of health and social services, self-carers and caregivers. Perhaps more significantly, it clearly distinguished between the 3 fundamentally different concepts that can be conceived as nested within each other in relation to the first component: PHC, Primary Care and Family Medicine. PHC, as a property of health systems in the form of the specific whole-of-society approach based on the 4 components as previously identified; Primary Care, as a specific subsystem as defined by the first level of care, with its core functions of first access, comprehensiveness, continuity, coordination and patient centred care; and Family Medicine, as a medical specialty uniquely characterised by its life course and whole-person (rather than a disease- or health domain-specific) orientation, with particular consideration of patients in the context of their families and communities.

MOH has recognised PHC's importance and taken definitive steps in recent years to transform primary care, enhance its capacity and capabilities, and strengthen public-private partnerships. These include constructing several new polyclinics, expanding coverage of the Community Health Assist Scheme subsidies and enhancing the Primary Care Network programme to provide better support to general practitioners in caring for patients with NCDs. Now it is taking the next step in embracing the wider PHC approach more comprehensively, to address the wider determinants of health along the life course across the whole country. At the core of the recently announced "Healthier SG" population health strategy, focused on promoting overall healthier living, is a nationwide primary care enrolment programme. From the second half of 2023, residents (starting with those 60 years and above) will be invited to enrol with a family physician as their first line of care, supporting their health needs across their life course. This will empower family physicians to build strong doctor-patient relationships and deliver patient-centred care that is focused on prevention and promoting healthy living.

The Declaration of Astana is about attaining health and well-being for all people without distinction, with health systems centred on a strong PHC foundation. The bold move to enlist PHC as the anchor of the national population health strategy is a major step forward in achieving this vision in Singapore. Having a strong and well-equipped Family Medicine that leads high-quality primary care is key.[9,10] While significant strides have been made in recent years to develop more trained Family Physicians, postgraduate training remains non-mandatory for physicians in Primary Care. Moving forward, steps must be taken to increase training uptake and capacity, while maintaining standards and quality. Additionally, the footprint of Family Medicine education in local medical schools must be enhanced in tandem with its increasing importance. This can spur interest and alter preconceived negative perceptions of the field. Furthermore, it will lay a strong foundational understanding of Family Medicine's principles and practice among future healthcare practitioners regardless of eventual vocation, paving the way for a more coordinated and integrated PHC.

A PHC that cost-effectively provides holistic, longitudinal, whole-person care for local communities promises to be the elusive antidote for Singapore's health challenges. Its success in delivering a healthier Singapore will require time and the joint efforts of all stakeholders, including the most important, our patients. We must push ahead together to make a nearly half-century-old vision come to fruition for the sake of our future generations.

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ORIGINAL ARTICLE

Ann Acad Med Singap 2022;51:531-9
https://doi.org/10.47102/annals-acadmedsg.202247

Non-motorised active mobility device use by children in Singapore: Injury patterns and risk factors for severe injury

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ABSTRACT

Introduction: Wheeled recreational devices (WRDs) include tricycles, bicycles, scooters, inline skates, skateboards, longboards and waveboards, and can cause significant morbidity and mortality. This study aimed to describe the epidemiology and nature of injuries sustained by children from WRD use, and risk factors for severe injury.

Method: We described injuries relating to WRD use in children <18 years who presented to the emergency department of an Asian tertiary hospital between 2016 and 2020. Demographic data, site and nature of the injury, and historical trends were analysed. Risk factors for severe injury (defined as fractures or dislocations), Injury Severity Score ≥9, and injuries resulting in hospitalisation, surgery or death were evaluated.

Results: A total of 5,002 patients with 5,507 WRD-related injuries were attended to over the 5-year study period. Median age was 4.7 years. Injuries related to bicycles (54.6%) and scooters (30.3%) were most frequent, followed by skateboards and waveboards (7.4%), inline skates (4.7%), and tricycles (3.0%). Injuries occurred most frequently in public spaces. Soft tissue injuries (49.3%) and fractures (18.7%) were the most common diagnoses. Upper limb (36.4%) and head and neck (29.0%) regions were the most common sites of injury. Among the patients, 1,910 (38%) had severe injuries with potential morbidity. On multivariate analysis, heavier children of the school-going age who use either scooters, skateboards or inline skates are more prone to severe injuries. Involvement in a vehicular collision was a negative predictor.

Conclusion: WRD use in children can result in severe injuries. Wrist and elbow guards, as well as helmets are recommended, along with adequate parental supervision.

Ann Acad Med Singap 2022;51:531-9

Keywords: Bicycle, inline skate, paediatric, scooter, skateboard, trauma, tricycle, wheeled recreational device

INTRODUCTION

The Active Mobility Act was introduced in Singapore in 2017 to promote the safe use of personal mobility devices. Non-motorised active mobility devices (AMDs) are popular among children and include tricycles, bicycles, scooters, inline skates, skateboards, longboards and waveboards. While the use of AMDs contributes towards an active lifestyle and gross motor development, such devices can result in injuries. These injuries are commonly mild and self-resolving,[1-3] but a small proportion can result in significant morbidity and mortality. About 2 to 20% of scooter-related injuries seen in emergency departments (EDs) require hospitalisation,[2,4,5] surgery,[4,6] intensive care unit (ICU) stay or result in death.[2,7,8]

There is an increasing trend of injuries related to AMD use. After the modern scooter was popularised in the US in 2000, there was a more than 25-fold increase in ED-treated injuries, with 19 deaths reported between 1999 and 2001.[8] Injuries vary depending on the type of device used. For example, Keays et al.[9] found a higher proportion of head and neck injuries in longboarders when compared to lower limb extremities in skateboarders, while Aslam et el.[6] highlighted the risk of triplanar ankle fractures from scooter use. Injury prevalence and type

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This article was first published online on 9 September 2022 at annals.edu.sg

CLINICAL IMPACT

What is New

- To our knowledge, this is the first Asian study that describes injuries due to the use of recreational devices among children.
- Heavier children of the school-going age who use either scooters, skateboards or inline skates are more prone to severe injuries.

Clinical Implications

- The use of wrist and elbow guards and helmets should be recommended, along with adequate parental supervision.
- Primary prevention should be targeted at school-going children, users of skateboards, inline skates and scooters, and within public spaces such as playgrounds and sports facilities.

is likely to be affected by trends in AMD popularity and use, such as with the introduction of waveboards and motorised devices.

Despite there being many AMDs on the market, studies thus far have focused on 1 or up to 3 specific device types. Understanding epidemiological trends and injury patterns with different AMDs can highlight particular regions and injuries to look out for, and can aid in primary prevention. While helmet use has been shown to reduce the risk of severe injury[10] and concussive symptoms,[11] not much is known about other risk factors for severe injuries in children. Identifying predictors for severe injuries can aid in risk stratification, and also inform a multipronged public health approach to reduce severe AMD-related injuries in children.

Our study aims to describe the epidemiology of injuries sustained by children from the use of non-motorised AMDs, who presented to the ED of a large Asian tertiary paediatric hospital. We also aimed to evaluate risk factors for severe injury, as defined by fractures or dislocations, Injury Severity Score (ISS) ≥15, injuries requiring hospitalisation, surgery, or resulting in death.

METHOD

Study design

We performed a retrospective chart review of children who presented with injuries to the ED of KK Women's and Children's Hospital (KKH) in Singapore between January 2016 and December 2020.

KKH is one of 2 tertiary paediatric hospitals in Singapore. From 2016 to 2020, it had an annual attendance of 93,991–16,7269, with 16–22% of patients presenting with injuries. Trauma is managed by a multidisciplinary team consisting of emergency physicians, surgeons, anaesthetists and intensivists.

The data were obtained from the hospital's trauma surveillance registry. Data including circumstances of the injury and International Classification of Diseases-coded diagnoses are prospectively entered by the attending emergency physician into a structured data collection form during the patient encounter. If present, more than 1 injury may be coded for each patient. Data from the visit and subsequent outcomes are collated and verified by a trauma coordinator. Injury text descriptions were manually inspected to validate the corresponding mechanism and type of injury, and to ensure inclusion and exclusion criteria were met. The database is accredited by the Association for the Advancement of Automotive Medicine.

This study was given ethics approval by the SingHealth institutional review board (IRB number 2021/2401).

Inclusion and exclusion criteria

The study included patients below 18 years old who presented to the ED with an injury related to the use of a non-motorised AMD. Patients who were passive bystanders hit by AMDs were not included. Devices considered were tricycles, bicycles, scooters, inline skates, skateboards, longboards and waveboards. Electronic devices such as motorised bicycles, electronic scooters and hoverboards were excluded.

Variables and outcome measures

We reviewed demographic data and circumstances of the injury, including the mechanism of injury, place of injury, mode of transport to the ED and type of device involved. A vehicular collision was defined as there being a collision between the device user and a vehicle, with AMD users either colliding with or hit by a vehicle. This included incidents in carparks or with stationary vehicles. Injuries sustained by passive bystanders who were hit by AMDs were not included.

Injury types were classified into 6 broad categories: soft tissue injuries (e.g. lacerations and contusions), fractures, dislocations, crush injuries, specific organ injuries (e.g. neurological, ophthalmological and abdominal) and others/not specified. The site of injury was recorded and further classified into 6 regions: head and neck, upper limb, lower limb, trunk, groin and buttocks, or not specified. The disposition of the patient and subsequent length of stay in hospital were reviewed, along with the need for surgery.

Severe injury was defined as fractures or dislocations, Injury Severity Score (ISS) ≥15, injuries requiring hospitalisation, surgery, or resulting in death.

Statistical analysis

Categorical variables were reported as frequency with percentages, and analysed with chi-square tests. Continuous variables were reported as the median and interquartile range (IQR), and analysed with Wilcoxon rank sum tests. Univariate logistic analysis was performed for severe injury as defined above. Statistically significant variables were entered into a multivariate logistic regression model. Unadjusted and adjusted odds ratios (aOR), together with their 95% confidence intervals (CIs), were presented.

Statistical significance was taken at P value <0.05. Statistical analysis was conducted using R version 4.2.0.

RESULTS

A total of 4,972 patients with non-motorised AMD-related injuries were attended to over the study period, with a total of 5,475 injuries. Two patients were excluded due to age and incomplete data. The median age was 7.8 years (interquartile range [IQR] 4.8–11.6). Injuries related to bicycles (54.6%) and scooters (30.3%) were the most common, with a smaller proportion related to skateboards and waveboards (7.4%), inline skates (4.7%) and tricycles (3.0%) (Table 1). There were no injuries related to longboard use. Tricycle users were younger with a median age of 3.4 years (IQR 2.2–5.3), followed by scooters (6.2, IQR 4.3–8.9), bicycles (8.7, IQR 4.9–12.5), inline skates (10.3, IQR 8.3–12.3) and skateboard users (11.3, IQR 8.9–13.2) (Fig. 1).

The most commonly identified place of injury was public spaces, including playgrounds and sports facilities, followed by homes, roads, and school or childcare facilities (Table 1). Eighty (1.6%) injuries occurred as a result of a vehicular collision, with the remaining due to falls or other incidents.

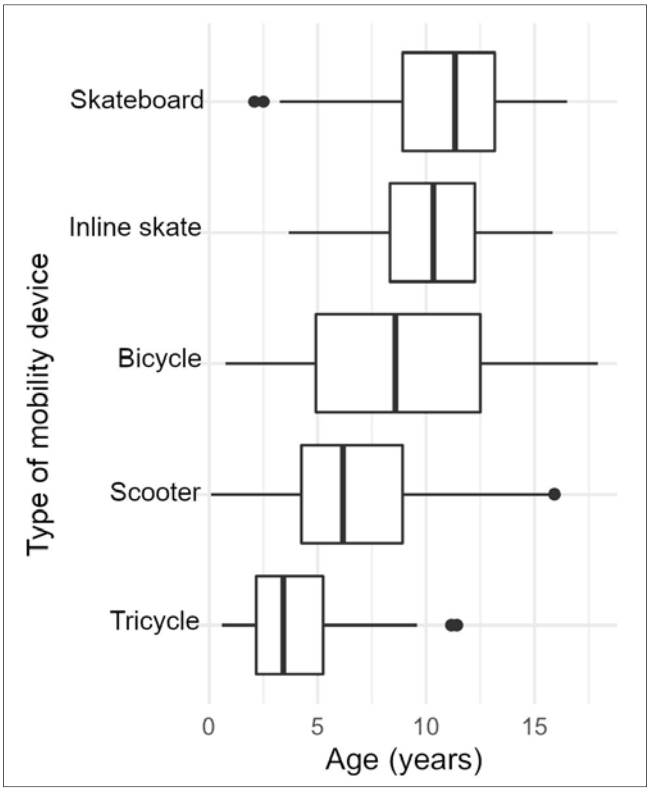

Fig. 1. Age distribution of non-motorised active mobility device-related injuries.

There was a reduction in bicycle- and skateboard-related injuries from 2018–2019, followed by a return to former levels in 2020. The incidence of scooter-related injuries decreased between 2017 and 2020 (Fig. 2).

Of the 5,507 injuries, 2,704 (49.4%) were soft-tissue injuries, 1,995 (36.4%) fractures, dislocations or crush injuries, and 504 (9.2%) organ-involving injuries (including neurological, abdominal, dental and eye injuries) (Table 2). Upper limb injuries were the most common (36.5%), followed by head and neck injuries (29.1%), lower limb (20.4%), trunk (2.8%), and groin or buttock injuries (0.8%) (Fig. 3). The 2 most common specific injuries identified for each device were facial laceration injuries (n=30, 19.8%) followed by head injuries with tricycles (28, 18.4%). These were followed by facial lacerations (327, 20.3%); head injuries with scooters (170, 10.6%); facial lacerations (280, 9.1%); head injuries with bicycles (230, 7.5%); fractures of radius and ulna (71, 18.6%); head injuries with skateboards (28, 7.2%); fractures of radius and ulna (53, 22.6%); and supracondylar humerus fractures with inline skates (20, 8.5%).

Twenty-one (0.42%) patients required admission. The Median length of hospital stay was 2.8 days

Table 1. Demographic data and injury circumstances of patients with wheeled recreational device-related injuries

	Overall	Stratified by severity		*P* value
		Non-severe	Severe	
	n=4972	n=3074	n=1898	
Median age (IQR), years	7.8 (4.8–11.6)	5.5 (4.2–10.8)	9.6 (6.2–12.4)	<0.001
Male sex, no. (%)	3410 (68.6)	2098 (68.2)	1312 (69.1)	0.539
Median weight (IQR), kg	25.9 (17.4–43.0)	22.0 (16.2–37.2)	33.0 (21.4–48.0)	<0.001
Ethnicity, no. (%)				<0.001
Chinese	2299 (46.2)	1451 (47.2)	848 (44.7)	
Malay	1013 (20.4)	598 (19.5)	415 (21.9)	
Indian	948 (19.1)	539 (17.5)	409 (21.5)	
Others	712 (14.3)	486 (15.8)	226 (11.9)	
Year of injury, no. (%)				0.285
2016	1065 (21.4)	651 (21.2)	414 (21.8)	
2017	1113 (22.4)	698 (22.7)	415 (21.9)	
2018	956 (19.2)	578 (18.8)	378 (19.9)	
2019	833 (16.8)	539 (17.5)	294 (15.5)	
2020	1005 (20.2)	608 (19.8)	397 (20.9)	
Mechanism of injury Vehicular collision, no. (%)	80 (1.6)	68 (2.2)	12 (0.6)	<0.001
Place of injury, no. (%)				<0.001
Public places, including playgrounds, sports facilities	1619 (32.6)	878 (28.6)	741 (39.0)	
Home	794 (16.0)	583 (19.0)	211 (11.1)	
Road	330 (6.6)	244 (7.9)	86 (4.5)	
School/childcare centre	110 (2.2)	58 (1.9)	52 (2.7)	
Others	2117 (42.6)	1309 (42.6)	808 (42.6)	
Mode of arrival, no. (%)				0.054
Own transport	4377 (88.7)	2702 (88.3)	1675 (89.2)	
Emergency ambulance	519 (10.5)	338 (11.0)	181 (9.6)	
Others	40 (0.8)	19 (0.6)	21 (1.1)	
Type of device, no. (%)				<0.001
Bicycle	2717 (54.6)	1773 (57.7)	944 (49.7)	
Scooter	1506 (30.3)	962 (31.3)	544 (28.7)	
Skateboard, waveboard	368 (7.4)	161 (5.2)	207 (10.9)	
Inline skate	232 (4.7)	71 (2.3)	161 (8.5)	
Tricycle	149 (3.0)	107 (3.5)	42 (2.2)	

IQR: interquartile range

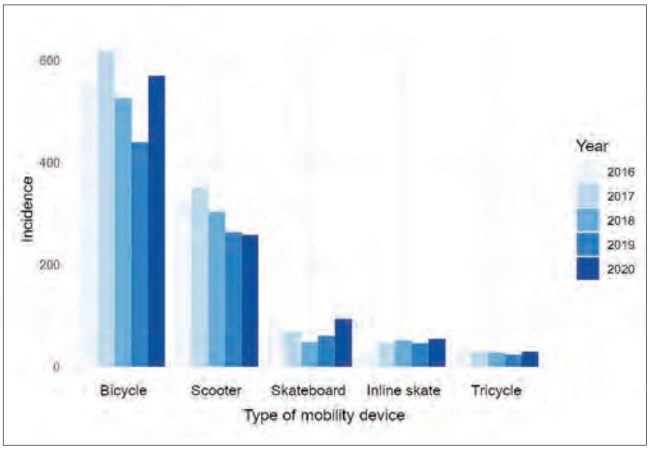

Fig. 2. Incidence of non-motorised active mobility device-related injuries from 2016–2020.

Table 2. Incidence and type of wheeled recreational device-related injuries

Type of injury	Frequency	Percentage
Total	5475	
Soft tissue injury		
Laceration	936	17.1
Contusion	630	11.51
Wound	254	4.64
Sprain, strain	214	3.91
Abrasion	151	2.76
Burn	6	0.11
Other soft tissue injury, not specified	513	9.37
Fracture	1861	33.99
Dislocation	37	0.68
Crush injury	57	1.04
Specific organ injuries		
Neurological injury	429	7.84
Dental injury	37	0.68
Abdominal injury	22	0.4
Eye injury	16	0.29
Not specified	310	5.66
Others	2	0.04

(IQR 1.9–4.8). Six patients (0.12%) required high-dependency care, ranging from 0.6–2.0 days, and 3 (0.06%) patients required intensive care unit (ICU) care, ranging from 0.6–1.6 days. Twenty-eight (0.56%) patients required surgery. There were no mortalities.

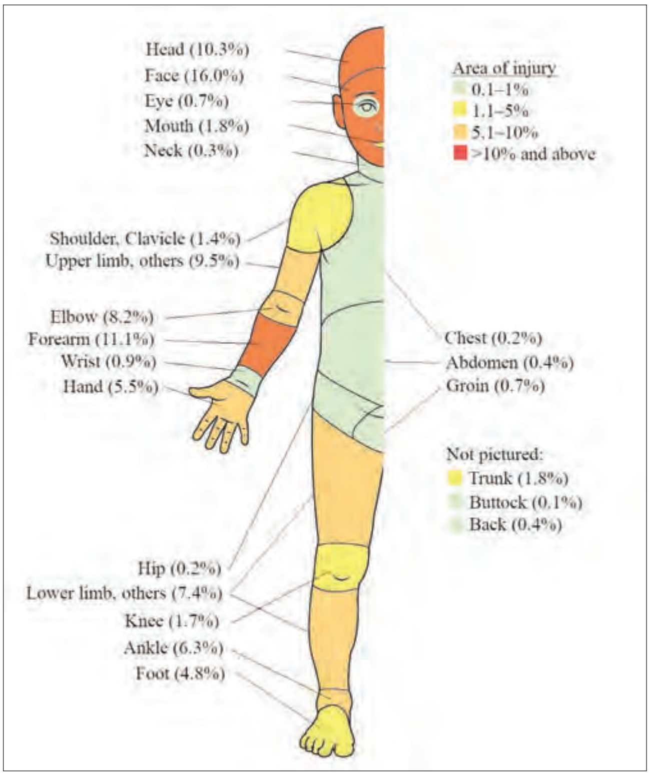

Fig. 3. Site of non-motorised active mobility device-related injuries.

The 3 patients who required ICU care had intraabdominal trauma following a fall from a bicycle, intracranial haemorrhage in a cyclist involved in a vehicular collision, and major head injury from an unwitnessed cycling incident.

Severe injuries were sustained in 1,898 (38.2%) patients. On multivariate analysis (Table 3), patients of school-going age ≥7 years (aOR=1.49, 95% CI 1.25–1.77), heavier weight ≥30kg (aOR 1.83, 95% CI 1.55–2.18), Indian (aOR 1.30, 95% CI 1.10–1.53) or Malay ethnicity (aOR 1.19, 95% CI 1.01–1.39), occurrence in a public (aOR 1.86, 95% CI 1.53–2.26) or unspecified place (aOR 1.41, 95% CI 1.16–1.71), along with scooter (aOR 1.29, 95% CI 1.12–1.49), skateboard (aOR 1.86, 95% CI 1.48–2.35) and inline skate use (aOR 3.37, 95% CI 2.48–4.61) were associated with an increased risk of severe injury. Being involved in a vehicular collision was a negative predictor for severe injury (aOR 0.36, 95% CI 0.18–0.65).

DISCUSSION

In this study, we described the epidemiology of AMD-related injuries in children presenting to the ED of a large tertiary paediatric hospital in Singapore, from injury circumstances to diagnosis at ED, and subsequent disposition and outcome. Soft tissue injuries and fractures

Table 3. Univariate and multivariate analysis for severe injury

	Unadjusted analysis		Adjusted analysis	
	OR (95% CI)	*P* value	Adjusted OR (95% CI)	
School-going age (≥7 years)	2.53 (2.25–2.86)	**<0.001**	1.49 (1.25–1.77)	**<0.001**
Male sex	1.04 (0.92–1.18)	0.518		
Weight ≥30kg	2.54 (2.26–2.86)	**<0.001**	1.83 (1.55–2.18)	**<0.001**
Ethnicity				
Chinese	Ref		Ref	
Malay	1.19 (1.02–1.38)	**0.026**	1.19 (1.01–1.39)	**0.035**
Indian	1.30 (1.11–1.51)	**0.001**	1.30 (1.10–1.53)	**0.002**
Others	0.79 (0.66–0.95)	**0.012**	0.83 (0.69–1.01)	0.058
Mechanism of injury				
Vehicular collision	0.28 (0.14–0.50)	**<0.001**	0.36 (0.18–0.66)	**0.002**
Place of injury				
Home	Ref		Ref	
Public places	2.33 (1.94–2.81)	**<0.001**	1.86 (1.53–2.26)	**<0.001**
Road	0.97 (0.73–1.30)	0.859	0.86 (0.63–1.18)	0.362
School/childcare centres	2.48 (1.65–3.72)	**<0.001**	1.21 (0.77–1.91)	0.403
Others	1.70 (1.43–2.05)	**<0.001**	1.41 (1.16–1.71)	**0.001**
Mode of arrival				
Emergency ambulance	0.86 (0.71–1.04)	0.132		
Type of device				
Bicycle	Ref		Ref	
Scooter	1.06 (0.93–1.21)	0.369	1.29 (1.12–1.49)	**<0.001**
Skateboard, waveboard	2.41 (1.94–3.01)	**<0.001**	1.86 (1.48–2.35)	**<0.001**
Inline skate	4.26 (3.20–5.72)	**<0.001**	3.37 (2.48–4.61)	**<0.001**
Tricycle	0.74 (0.51–1.05)	0.102	1.32 (0.89–1.92)	0.163

CI: confidence interval; OR: odds ratio

were the most common diagnoses, while the head and neck, and upper limb were the most common sites of injury. A significant proportion of patients had severe injuries with potential morbidity. Risk factors for severe injury included increased age and weight, Indian or Malay ethnicity, location of the injury, as well as scooter, skateboard and inline skate use. Conversely, involvement in a vehicular collision was a negative predictor.

The age distribution of patients presenting with non-motorised AMD-related injuries is in keeping with the typical age groups that use each device and previous studies,[2] with tricycle-related injuries more common in younger age groups, and skateboard and inline skate-related injuries more common in older children. Bicycle- and scooter-related injuries spanned a larger age distribution, pointing towards the versatility and popularity of such devices across ages. Outliers of infants and toddlers with bicycle- and skateboard-related injuries included incidents where patients sat on, pulled, or placed fingers into such devices, highlighting the importance of proper storage and securing of AMDs at home and in recreational facilities.

School-going children were at higher risk of severe injuries. Montagna et al. had also noted a higher risk of fractures in children ≥8 years old, although younger children were at higher risk of head and facial injuries.[5]

Older children tend to be larger in size, faster and stronger—features that allow them to go at greater speeds with potential for more serious injury. Teenagers are also more likely to participate in risk-taking behaviour and competitive situations.[12] Education on primary prevention strategies is likely to have higher impact when targeted at school-going age children and their parents. In line with encouraging active play and a shift towards active mobility, schools should play a bigger role in educating parents and children on the risk of such device-related injuries and preventative measures. While traffic safety programmes have been implemented in primary schools since the 1990s,[13] these typically focus on pedestrian safety and could be further expanded.

When compared to bicycles, inline skates, skateboards or waveboards, scooters were independent predictors for severe injury. Previous studies have also found inline skates to have a higher incidence of fractures than skateboards or scooters.[14] These devices tend to be lightweight with low friction wheels, allowing users to obtain high speeds with little effort.

Our findings also highlight particular injury patterns common in each device type, such as head and face injuries with tricycles, scooters and bicycles, and upper limb fractures with skateboards and inline skates. While our data did not specify particular fracture patterns, previous studies have highlighted the risk of distal radial fractures with skateboarding, inline skating and scooting,[15] and in particular Smith-type fractures with volar angulation.[14]

The most common injury type was soft tissue injuries, in keeping with previous studies.[2,5] However, a significant proportion (38%) of patients did have severe injuries. This consists of patients with fractures or dislocations, an ISS score of ≥15, and requiring surgery or admission, hence indicating a requirement for medical intervention and potential morbidity. There was a low admission rate of 0.42%, compared to other studies with admission rates of 2–20% for scooter injuries[2,4,5] and 2.4% with tricycles.[3] There is a risk of significant injuries with potential long-term morbidity and mortality, with several patients suffering intraabdominal or intracranial injury requiring intensive care. Fractures or dislocations can also have both short-term effects such as reduced mobility with limitations in performing day-to-day activities and schooling, and potential long-term effects including a risk of subsequent low bone density.[16] While such fractures are often successfully managed conservatively in the paediatric population, these can have significant sequelae on children and their families.

Involvement in a vehicular collision was found to be a negative predictive factor for severe injuries. Data from the US had previously highlighted deaths with collisions between motor vehicles and skateboard/scooter riders.[17] This may be related to the nature of collisions in our cohort, with the majority being low-velocity incidents occurring in car parks, zebra crossings or traffic lights; or of patients crashing into a stationary vehicle. This can be attributed to higher traffic safety awareness in children and parents in Singapore. Traffic safety programmes have been implemented nationwide in primary schools since the 1990s[13] and continue to be updated. Awareness of potential road-related injuries with boundary setting or close supervision by parents are likely to contribute to a reduction in severe injuries. Parents and children may potentially be more aware of the risk of traffic-related injuries when compared to play at home, in recreational parks, or in schools.

Injuries most commonly involved the upper limb or head and neck regions, and specifically the head, face and forearm (Fig. 2). This suggests key areas of protection with the use of helmets and wrist and elbow guards with such mobility devices. Non-helmet use has been shown to independently increase the risk of concussive symptoms,[11] hospitalisation and major head injury in paediatric AMD incidents,[10] with the main influence on helmet use being parental rules and perceived low levels of danger. The use of wrist guards and elbow pads have been shown to protect against wrist and elbow injuries in adult inline skaters.[18] The American Academy of Pediatrics recommends the use of helmets, knee pads and elbow pads while using scooters, and with the addition of wrist guards while using skateboards.[19] Manufacturers of safety equipment and retailers of AMDs should consider these key areas when designing and promoting safety equipment.

To the best of our knowledge, this is the first Asian study of non-motorised AMD-related injuries in the paediatric population, and the first to analyse a large range of device types. Encompassing a 5-year period at the largest paediatric emergency department in Singapore, it may be representative of national trends related to injuries from AMD use. Data are from a surveillance registry, with injury circumstances detailed at the time of patient encounter in the ED. The larger number of injuries studied also allowed for analysis of risk factors for severe injury.

Over the years, public policy and attitudes have shifted towards promoting active mobility in Singapore.[20] In line with a shift to a car-lite nation and encouraging healthy behaviour, the National Cycling Plan[21] was established as a collaborative governmental effort aimed to make cycling a safe, healthy and convenient transport option for Singaporeans. This included building a comprehensive islandwide cycling network with both intratown and intertown paths, spanning more than 1,300km by 2030. The Active Mobility Act was passed in Singapore in 2017 to regulate the safe use of personal mobility devices,[22] including allowing the use of selective mobility devices such as bicycles, skateboards and electric scooters on public paths subject to a set of rules and codes of conduct. Injuries from AMD use have been increasing in adults,[23] and can be expected to increase in the paediatric population in the future. A proportion of these can be expected to be severe in nature, with considerable public health impact. Apart from regulatory measures to enable safer road-sharing, education on the safe use of such devices from a young age will also be key. This can include the need for age-appropriate use of various devices, adequate supervision, and proper use of protective gear.

Our study should be interpreted in the context of its limitations. Being a single-centre study, our findings may not be applicable in other settings. Our study is not representative of AMD users with minor injuries not requiring care at an ED; Baumgartner et al.[24] noted that of the 29% of paediatric scooter riders who had accidents, 21.3% required medical consultation. There may also be variability in coding by the attending emergency physician, with the diagnoses occasionally coded as non-specific for either injury type or site. No data on the use of safety restraints or protective equipment were collected. There is also a risk of exaggeration of effect with the use of odds ratio instead of relative risk, especially in cross-sectional studies where the outcome is not rare.[25] With severe outcomes identified in 38% of cases in our study, there is a tendency to overbias. The model derived may have been over-optimistic, and requires validation in another population.

Future studies on the impact of preventive measures such as the use of protective gear and safety advice are recommended. While out of the scope of this paper, examining injuries related to electronic-powered devices—including electronic bicycles, scooters, and hoverboards—would also be increasingly important with the rising popularity and potential high-speed injuries with such devices. Public and parental education is key in preventing additional injuries with a focus on appropriate age guidelines for each device, adequate supervision, and proper use of protective gear. This may be targeted at school-going children, users of skateboards, inline skates and scooters, and within public spaces such as playgrounds and sports facilities.

CONCLUSION

The use of non-motorised active mobility devices may result in severe injuries in children. Risk factors for severe injuries included school-going age, increased weight, location of the injury, and scooter, skateboard and inline skate use. The use of wrist and elbow guards, as well as helmets should be recommended, along with adequate parental supervision.

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ORIGINAL ARTICLE

Ann Acad Med Singap 2022;51:540-52
https://doi.org/10.47102/annals-acadmedsg.2022203

Sex and ethnicity modified high 1-year mortality in patients in Singapore with newly diagnosed atrial fibrillation

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ABSTRACT

Introduction: We investigated sex and ethnic differences in the incidence, clinical characteristics and 1-year mortality of patients with newly diagnosed AF in a multi-ethnic population.

Method: This retrospective cohort study of patients diagnosed with AF from 2008 to 2015 was based on medical claims, casemix and subvention data submitted to the Ministry of Health. Patients with AF were matched with controls without AF for age (3-year bands), sex and ethnicity, and categorised as middle-aged (45–64 years) or elderly (≥65 years) among major ethnic groups in Singapore (Chinese, Malay and Indian).

Results: Among 40,602 adults with AF (elderly 74%), Malays had the highest age-standardised incidence rate of AF, followed by Chinese and Indians; and the rate was higher in men. Despite having the worst cardiovascular risk profile, Indians had the lowest prevalence and incidence of AF. The 1-year mortality rate after newly diagnosed AF was 22–26 deaths per 100 people. Newly diagnosed AF was independently associated with increased 1-year all-cause mortality among middle-aged (adjusted odds ratio [AOR] 9.08, 95% confidence interval [CI] 7.36–11.20) and elderly adults (AOR 3.60, 95% CI 3.40–3.80) compared with those without AF. Sex differences in mortality among patients with AF were limited to elderly adults (men: AOR 1.17, 95% CI 1.11–1.24), while Indians were associated with a 30% increased odds of mortality compared with Chinese regardless of age (middle-aged: AOR 1.27, 95% CI 1.09–1.548 elderly: AOR 1.33, 95% CI 1.22–1.45).

Conclusion: Variations in incidence, clinical profile and 1-year mortality of patients with AF in a nationwide cohort were influenced by sex and ethnicity. Newly diagnosed AF portends a worse prognosis and is a marker of high mortality within the first year.

Ann Acad Med Singap 2022;51:540-52

Keywords: Atrial fibrillation, ethnic differences, one-year mortality, sex differences

INTRODUCTION

Atrial fibrillation (AF) is the most common clinically significant arrhythmia and is associated with increased risks of stroke, dementia, heart failure (HF) and death.[1] Globally, 33.5 million people were reported to have AF in 2010,[2] with numbers expected to increase exponentially by 2050.[3-7] While in part due to ageing populations,[8] increasing cardiovascular risk factors and the detection of silent AF further contribute to the growing epidemic.[9]

Apart from modifiable clinical risk factors, non-modifiable factors, including sex and ethnicity, exert varying influences on the prevalence of AF.[10-22] Significant heterogeneities in AF prevalence were observed within Asian populations.[23-25] While not fully understood, these differences may be contributed by the

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CLINICAL IMPACT

What is New

- These nationwide data from Singapore highlight significant sex and ethnic differences in the epidemiology, clinical profile and 1-year mortality rate in newly diagnosed atrial fibrillation (AF).
- This study highlights the significant burden of disease AF carries as our population ages.

Clinical Implications

- The high 1-year mortality after diagnosis calls for AF to be regarded as an important marker of poor prognostic outcomes and premature mortality.
- Early aggressive management of AF and underlying comorbidities should be considered in these high-risk patient groups.

complex interactions between genetic and environmental factors.[26,27] The effects of sex and ethnicity on mortality from AF were, however, more variable, with sex differences not observed[10-13] but ethnic differences among Asians with HF reported.[24]

Despite the high prevalence of hypertension, diabetes and HF in Southeast Asia,[28] there is a paucity of data on AF characteristics and mortality in this region.[29-31] Therefore, we investigated sex and ethnic differences in the incidence, clinical characteristics and 1-year mortality of patients with newly diagnosed AF in a nationwide, multiethnic population in Singapore.

METHOD

This retrospective cohort study on newly diagnosed non-valvular AF from 2008 to 2015 included subjects aged ≥45 years from the 3 major ethnic groups in Singapore (Chinese 74%, Malay 13% and Indian 9%). The sources of diagnosis data comprised anonymised individual patient-level data from medical claims, casemix and subvention data submitted to the Ministry of Health by primary care clinics (public and private) and public hospitals (emergency departments and inpatient units). These cover more than 95% of Singapore's population with minimal selection bias. It was expected that the majority of AF would be identified through available data sources as most Singapore residents would be treated in public healthcare institutions owing to greater accessibility, extensive coverage and higher subsidy. Ethnicity was based on registered ethnicity at birth. Housing type served as a surrogate of socioeconomic status, with private housing (condominiums or private houses) corresponding to higher socioeconomic status and public housing of 1- to 2-room flats or studio apartments corresponding to lower socioeconomic status. Identification of AF and other diseases was based on codes from the International Classification of Diseases (ICD) 9th Revision, Clinical Modification (prior to 2012); and ICD 10th Revision, Australian Modification (from 2012) (Supplementary Table S1 in online Supplementary Materials). The survival status of patients was ascertained from the Singapore Registry of Birth and Death. A matched cohort without AF was obtained by matching each patient with AF to a control without AF who was alive in the index year (year of diagnosis of the matched patient) for age (3-year bands), sex and ethnicity. Population numbers were obtained from the Singapore Department of Statistics' mid-yearly population estimates of Singapore residents for the calculation of AF incidence and prevalence. The study complied with the Declaration of Helsinki and patient consent was waived as only anonymised data were obtained from an administrative database.

Clinical variables

Patients were stratified into 2 age groups: middle-aged (45–64 years) and elderly (≥65 years). An age cut-off of 45 years was chosen as 5% of patients with AF were below 45 years, in order to investigate patients between the 5th and 95th age percentiles. Chronic diseases at baseline were defined as a diagnosis prior to or within 6 months of first diagnosis of AF. The clinical risk factors included hypertension, hyperlipidaemia, renal impairment, end-stage renal failure, ischaemic heart disease (IHD), HF, stroke or transient ischaemic attack, haemorrhagic stroke, systemic embolism, peripheral vascular disease, dementia, depression, hyperthyroidism and cancer. CHA_2DS_2VASc scores were calculated for all patients.[32]

Statistical analyses

Crude AF incidence was estimated by the number of newly diagnosed AF patients among people at risk in the same year (with the number of diagnosed AF cases in the previous year removed from the population number in the current year). Crude AF prevalence was estimated by dividing the number of patients diagnosed with AF before and still alive on 1 January of each year by the population number in the same year. To account for the change in population structure over time, adjusted incidence and prevalence rates were calculated using direct age standardisation and the 2008 resident population as the reference population by 5-year age bands stratified by sex and ethnicity. Crude 1-year mortality was estimated by dividing the number of patients who died in the next calendar year by the number of patients in that year. Baseline characteristics between ethnicities and sexes were compared using the Wilcoxon rank sum test or Kruskal-Wallis test for continuous variables and chi-square test for categorical variables. As specific dates of death were unavailable from the National Death Registry (only the years of death were available to prevent re-identification of patients), logistic regression analyses were performed to compare the odds ratios with 95% confidence intervals (CIs) for mortality within 1 year, between the sex and ethnic groups within the cohort of AF patients, and between patients with and without AF. To determine if 2-way interactions existed between age and sex, age and ethnicity, and sex and ethnicity, these interaction terms were included in logistic regression models. All statistical analyses were performed using STATA/SE version 16 (StataCorp, College Station, US), at 5% level of significance.

RESULTS

From 2008 to 2015, a total of 40,602 adults were newly diagnosed with AF. The middle-aged group made up 10,671 (26%) of the patients with a mean age of 57±5 years, 32% women and 76% Chinese; the rest or 29,931 (74%) were in the elderly group with a mean age of 78±8 years, 52% women and 84% Chinese (online Supplementary Fig. S1). Temporal trends in the prevalence and incidence rates of AF are shown in Fig. 1. In both the middle-aged and elderly groups, a linear increase in the age-sex-ethnicity-adjusted prevalence rates was observed from 2008 to 2015 (middle-aged group: 59.9 to 75.2 per 10,000 people; elderly group: 525.4 to 696.5 per 10,000 people). The age-sex-ethnicity-adjusted incidence rate of AF, however, remained fairly constant between 11 and 14 per 10,000 people in the middle-aged group, while the corresponding rate increased from 101.5 to 107.4 per 10,000 people in the elderly group.

Ethnic and sex differences in incidence of AF

Malays had the highest age-standardised incidence rate (ASIR) of AF, followed by Chinese and Indians, while men had a higher ASIR of AF than women in both age groups (Fig. 1). Malay men had the highest ASIR of AF in both age groups, increasing from 20.8 per 10,000 in 2008 to 23.1 per 10,000 in 2015 in middle-aged adults and 124.5 to 155.9 per 10,000 in elderly adults, while Indian women had the lowest ASIR of AF in both age groups. The ASIR of AF increased from 2008 to 2015 in men of all ethnicities in both age groups, while the ASIR decreased slightly among middle-aged Chinese and Indian women, but increased sharply among Malay elderly women. The temporal trend of AF by sex and ethnicity in both age groups is shown in the online Supplementary Fig. S2.

Ethnic and sex differences in risk profile of AF

Among middle-aged adults, Chinese had the lowest prevalence of hypertension, hyperlipidaemia, diabetes, renal impairment, IHD, HF and peripheral vascular disease compared with Malays and Indians at AF diagnosis ($P<0.05$) (Table 1). Indian men had the highest prevalence of hyperlipidaemia, diabetes, IHD and vascular disease but the lowest prevalence of hyperthyroidism. Among elderly adults, men had a higher prevalence of IHD, HF, haemorrhagic stroke and cancer (online Supplementary Table S2). When stratified by ethnicity, Indians had the highest prevalence of hypertension, hyperlipidaemia, diabetes and IHD in both men and women (Table 2), while Chinese again had the lowest prevalence of hyperlipidaemia, diabetes, renal impairment, IHD and HF but the highest cancer prevalence ($P<0.05$) (online Supplementary Table S3). Compared with patients without AF, those with AF had a higher prevalence of chronic conditions including hypertension, hyperlipidaemia, diabetes, IHD, HF, stroke, renal impairment, cancer, depression, dementia and thyrotoxicosis ($P<0.05$) (online Supplementary Table S4).

Ethnic and sex differences in 1-year mortality

Between 2008 and 2015, the 1-year mortality after AF diagnosis improved but remained high, from 26 to 22 deaths per 100 people (temporal trends stratified by sex, ethnicity and age in Fig. 2). One-year mortality after AF diagnosis was higher in elderly adults but was on the downward trend from 31 to 26 per 100 patients, while remaining fairly constant between 11 and 14 per 100 middle-aged adults (online Supplementary Fig. S3). However, the majority of deaths were non-cardiovascular in both middle-aged and elderly adults (Tables 1 and 2).

Among patients with AF and after adjusting for age, sex, ethnicity, housing type and clinical risk factors, sex differences in 1-year all-cause mortality were limited to elderly adults, with men having a 17% increased odds of mortality compared with women (Table 3). Ethnic differences in 1-year all-cause mortality were observed only between Indians and Chinese, with Indians associated with a 30% increased odds of mortality compared with Chinese in both age groups (Table 3).

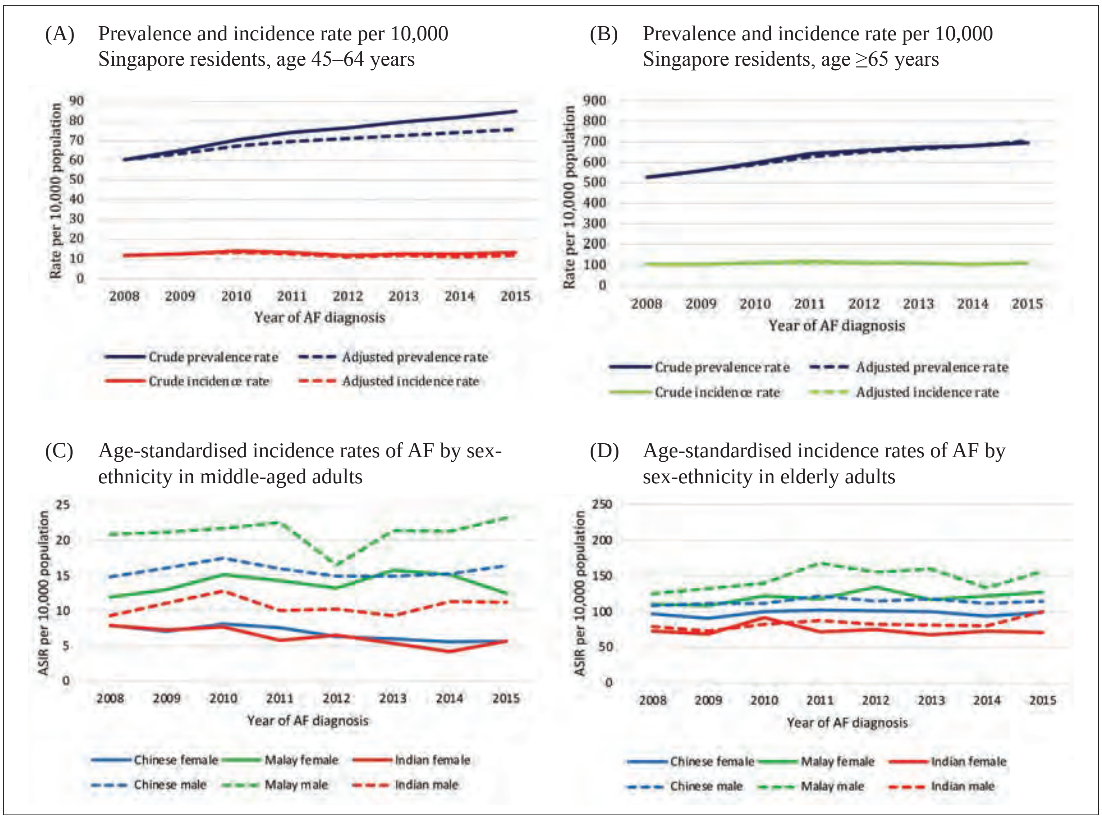

Fig. 1. Crude and age-sex-ethnicity-adjusted (A) prevalence and (B) incidence of atrial fibrillation (AF) in Singapore by age. The prevalence and incidence of AF were almost 10-fold higher in elderly compared with middle-aged adults per 10,000 persons. The age-standardised incidence rate of AF was 10-fold higher in (C) elderly (50–200 per 10,000 persons) compared with (D) middle-aged adults (5–25 per 10,000 persons).

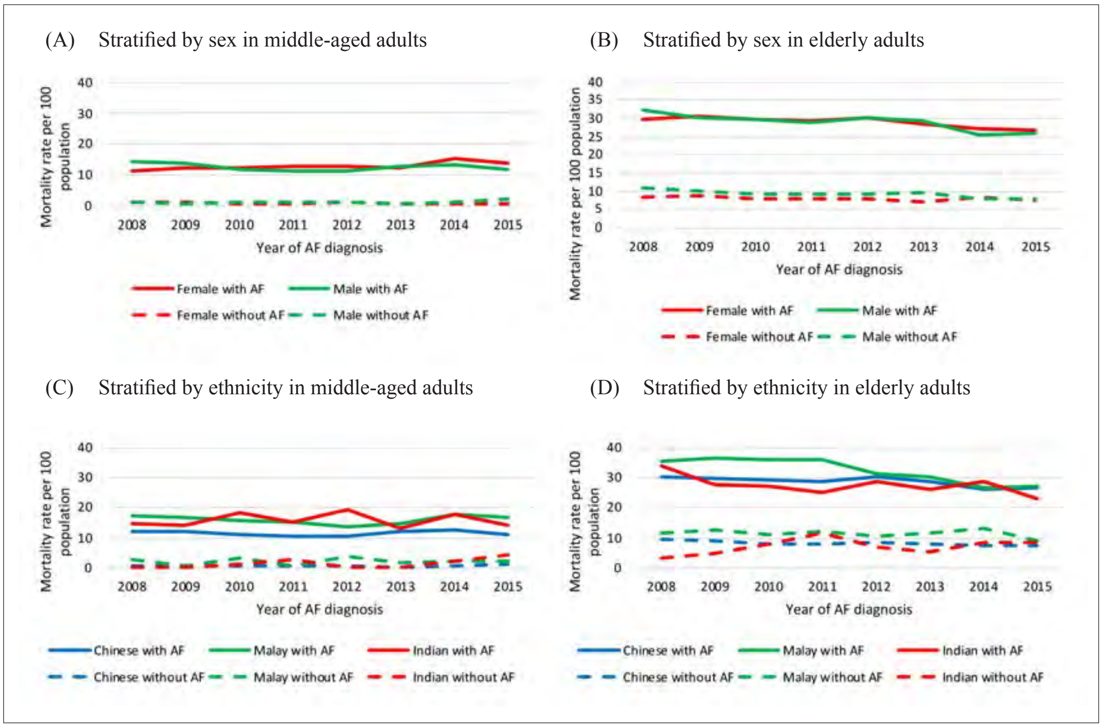

Fig. 2. One-year all-cause mortality rates by age, sex and ethnicity in patients with newly diagnosed atrial fibrillation (AF).

Table 1. Characteristics of patients by sex and ethnicity among middle-aged adults (age 45–64 years)

	Women				Men			
	Chinese (n=2434)	**Malay (n=805)**	**Indian (n=204)**	***P*** [a]	**Chinese (n=5645)**	**Malay (n=1194)**	**Indian (n=389)**	***P*** [a]
Age, years								
Median (IQR)	58 (54–62)	58 (54–61)	59 (53–62)	0.114[b]	58 (54–62)	57 (53–61)	58 (54–61)	<0.001[b]
Mean (SD)	57 (5)	57 (5)	57 (5)		57 (5)	57 (5)	57 (5)	
Housing type, no. (%)								
Public (studio apartments)	182 (7.5)	146 (18.1)	27 (13.2)	<0.001[b,c]	552 (9.8)	162 (13.6)	46 (11.8)	<0.001[b,c,d]
Public (small apartments)	628 (25.8)	210 (26.1)	49 (24.0)		1270 (22.5)	284 (23.8)	106 (27.3)	
Public (medium apartments)	800 (32.9)	270 (33.5)	67 (32.8)		1718 (30.4)	444 (37.2)	110 (28.3)	
Public (large apartments)	537 (22.1)	165 (20.5)	52 (25.5)		1333 (23.6)	278 (23.3)	95 (24.4)	
Private (condominiums)	172 (7.1)	7 (0.9)	6 (2.9)		449 (8.0)	16 (1.3)	21 (5.4)	
Private (houses)	115 (4.7)	7 (0.9)	3 (1.5)		323 (5.7)	10 (0.8)	11 (2.8)	
Place of notification, no. (%)								
Inpatient	1289 (53.0)	567 (70.4)	130 (63.7)	<0.001[b,c,d]	3443 (70.0)	881 (73.8)	290 (74.6)	<0.001[b,c,d]
Public clinic	642 (26.4)	116 (14.4)	38 (18.6)		1111 (19.7)	132 (11.1)	37 (9.5)	
Emergency department	390 (16.0)	117 (14.5)	31 (15.2)		856 (15.2)	162 (13.6)	42 (10.8)	
Private clinic	113 (4.6)	5 (0.6)	5 (2.5)		235 (4.2)	19 (1.6)	20 (5.1)	
CHA_2DS_2VASc score								
Median (IQR)	2 (1–4)	3 (2–5)	3 (2–5)	<0.001[b,c]	2 (1–3)	2 (1–4)	3 (2–4)	<0.001[b,c,d]
Mean (SD)	2.6 (1.5)	3.5 (1.6)	3.4 (1.7)		2.0 (1.6)	2.5 (1.6)	2.7 (1.6)	
0	680 (27.9)	92 (11.4)	29 (14.2)		1091 (19.3)	148 (12.4)	41 (10.5)	
≥2	1754 (72.1)	713 (88.6)	175 (85.8)	<0.001[b,c]	3347 (59.3)	865 (72.5)	301 (77.4)	<0.001[b,c]

Table 1. Characteristics of patients by sex and ethnicity among middle-aged adults (age 45–64 years) (Cont'd)

	Women				Men			
	Chinese (n=2434)	**Malay (n=805)**	**Indian (n=204)**	***P*** [a]	**Chinese (n=5645)**	**Malay (n=1194)**	**Indian (n=389)**	***P*** [a]
Diagnosis prior to or within 6 months after first AF, no. (%)								
Hypertension	1426 (58.6)	623 (77.4)	149 (73.0)	<0.001[b,c]	3682 (65.2)	848 (71.0)	279 (71.7)	<0.001[b,c]
Hyperlipidaemia	1168 (48.0)	571 (70.9)	144 (70.6)	<0.001[b,c]	3188 (56.5)	809 (67.8)	290 (74.6)	<0.001[b,c,d]
Diabetes	657 (27.0)	449 (55.8)	119 (58.3)	<0.001[b,c]	1859 (32.9)	561 (47.0)	214 (55.0)	<0.001[b,c,d]
Renal impairment	345 (14.2)	245 (30.4)	45 (22.1)	<0.001[b,c,d]	819 (14.5)	289 (24.2)	84 (21.6)	<0.001[b,c]
End-stage renal failure	200 (8.2)	125 (15.5)	21 (10.3)	<0.001[b]	368 (6.5)	115 (9.6)	32 (8.2)	0.001[b]
Ischaemic heart disease	579 (23.8)	300 (37.3)	83 (40.7)	<0.001[b,c]	2455 (43.5)	668 (56.0)	265 (68.1)	<0.001[b,c,d]
Chronic heart failure	436 (17.9)	255 (31.7)	60 (29.4)	<0.001[b,c]	1116 (19.8)	402 (33.7)	126 (32.4)	<0.001[b,c]
Stroke/transient ischaemic attack	315 (12.9)	138 (17.1)	28 (13.7)	0.012[b]	893 (15.8)	176 (14.7)	65 (16.7)	0.551
Haemorrhagic stroke	76 (3.1)	30 (3.7)	4 (2.0)	0.447	243 (4.3)	53 (4.4)	20 (5.1)	0.732
Systemic embolism	14 (0.6)	8 (1.0)	4 (2.0)	0.051[c]	39 (0.7)	12 (1.0)	7 (1.8)	0.042^
Vascular disease	69 (2.8)	53 (6.6)	14 (6.9)	<0.001[b,c]	217 (3.8)	67 (5.6)	38 (9.8)	<0.001[b,c,d]
Dementia	2 (0.1)	6 (0.8)	0	0.011[b]	14 (0.3)	2 (0.2)	1 (0.3)	0.904
Depression	62 (2.6)	19 (2.4)	11 (5.4)	0.044[c,d]	100 (1.8)	25 (2.1)	9 (2.3)	0.594
Hyperthyroidism	217 (8.9)	61 (7.6)	9 (4.4)	0.055[c]	190 (3.4)	57 (4.8)	5 (1.3)	0.003[b,c,d]
Cancer	210 (8.6)	51 (6.3)	16 (7.8)	0.116[b]	349 (6.2)	49 (4.1)	19 (4.9)	0.015[b]
All-cause deaths within 1 year from diagnosis of AF, no. (%)	274 (11.3)	132 (16.4)	36 (17.7)	<0.001[b,c]	651 (11.5)	186 (15.6)	58 (14.9)	<0.001[b,c]
Cardiovascular deaths within 1 year from diagnosis of AF, no. (%)	91 (3.7)	51 (6.3)	15 (7.4)	0.001[b,c]	252 (4.5)	103 (8.6)	22 (5.7)	<0.001[b]

AF: atrial fibrillation; IQR: interquartile range; SD: standard deviation

[a] The *P* value indicates whether there is statistically significant difference across the 3 ethnicities while the superscript letters indicate pairwise comparisons

[b] Statistically significant difference between Chinese and Malays, $P<0.05$

[c] Statistically significant difference between Chinese and Indians, $P<0.05$

[d] Statistically significant difference between Malays and Indians, $P<0.05$

Table 2. Characteristics of patients by sex and ethnicity among elderly adults (age ≥65 years)

	Women				Men			
	Chinese (n=13,171)	**Malay (n=1736)**	**Indian (n=664)**	***P*** [a]	**Chinese (n=12,043)**	**Malay (n=1627)**	**Indian (n=690)**	***P*** [a]
Age, years								
Median (IQR)	80 (74–87)	76 (71–82)	77 (72–82)	<0.001[b,c]	76 (70–82)	76 (70–82)	77 (71–83)	0.039[d]
Mean (SD)	81 (8)	77 (7)	77 (7)		77 (8)	76 (7)	77 (8)	
Housing type, no. (%)								
Public (studio apartments)	1384 (10.5)	289 (16.7)	70 (10.5)	<0.001[b,d]	1359 (11.3)	251 (15.4)	116 (16.8)	<0.001[b,c,d]
Public (small apartments)	3518 (26.7)	514 (29.6)	152 (22.9)		3258 (27.1)	523 (32.2)	162 (23.5)	
Public (medium apartments)	3842 (29.2)	535 (30.8)	193 (29.1)		3344 (27.8)	474 (29.1)	171 (24.8)	
Public (large apartments)	2571 (19.5)	356 (20.5)	155 (23.3)		2301 (19.1)	339 (20.8)	130 (18.8)	
Private (condominiums)	786 (6.0)	13 (0.8)	42 (6.3)		740 (6.1)	17 (1.0)	42 (6.1)	
Private (houses)	1070 (8.1)	29 (1.7)	52 (7.8)		1041 (8.6)	23 (1.4)	69 (10.0)	
Place of notification, no. (%)								
Inpatient	9911 (75.3)	1427 (82.2)	508 (76.5)	<0.001[b,d]	9096 (75.5)	1332 (81.9)	545 (79.0)	<0.001[b,c,d]
Public clinic	1606 (12.2)	152 (8.8)	77 (11.6)		1678 (13.9)	176 (10.8)	67 (9.7)	
Emergency department	1214 (9.2)	138 (8.0)	60 (9.0)		924 (7.7)	100 (6.2)	57 (8.3)	
Private clinic	440 (3.3)	19 (1.1)	19 (2.9)		345 (2.9)	19 (1.2)	21 (3.0)	
CHA_2DS_2VASc score								
Median (IQR)	6 (4–7)	6 (4–7)	6 (5–7)	<0.001[c,d]	4 (3–5)	5 (3–6)	5 (4–6)	<0.001[b,c,d]
Mean (SD)	5.6 (1.7)	5.6 (1.7)	5.9 (1.6)		4.2 (1.7)	4.5 (1.7)	4.8 (1.6)	
0	0	0	0		0	0	0	
≥2	13,171 (100.0)	1736 (100.0)	664 (100.0)	Not applicable	11,571 (96.1)	1579 (97.1)	675 (97.8)	0.013[c]

Table 2. Characteristics of patients by sex and ethnicity among elderly adults (age ≥65 years) (Cont'd)

	Women				Men			
	Chinese (n=13,171)	Malay (n=1736)	Indian (n=664)	*P* [a]	Chinese (n=12,043)	Malay (n=1627)	Indian (n=690)	*P* [a]
Diagnosis prior to or within 6 months after first AF, no. (%)								
Hypertension	11,468 (87.1)	1517 (87.4)	607 (91.4)	0.005[c,d]	10,006 (83.1)	1350 (83.0)	615 (89.1)	<0.001[c,d]
Hyperlipidaemia	9050 (68.7)	1268 (73.0)	545 (82.1)	<0.001[b,c,d]	8110 (67.3)	1163 (71.5)	557 (80.7)	<0.001[b,c,d]
Diabetes	5729 (43.5)	972 (56.0)	430 (64.8)	<0.001[b,c,d]	4780 (39.7)	808 (49.7)	428 (62.0)	<0.001[b,c,d]
Renal impairment	3410 (25.9)	622 (35.8)	193 (29.1)	<0.001[b,d]	3329 (27.6)	627 (38.5)	217 (31.5)	<0.001[b,c,d]
End-stage renal failure	804 (6.1)	160 (9.2)	36 (5.4)	<0.001[b,d]	703 (5.8)	121 (7.4)	40 (5.8)	0.038[b]
Diagnosis prior to first AF, no. (%)								
Ischaemic heart disease	5960 (45.3)	878 (50.6)	424 (63.9)	<0.001[b,c,d]	6039 (50.2)	968 (59.5)	485 (70.3)	<0.001[b,c,d]
Chronic heart failure	4138 (31.4)	658 (37.9)	295 (44.4)	<0.001[b,c,d]	3228 (26.8)	625 (38.4)	244 (35.4)	<0.001[b,c]
Stroke/transient ischaemic attack	3981 (30.2)	493 (28.4)	177 (26.7)	0.053[c]	3353 (27.8)	432 (26.6)	187 (27.1)	0.521
Haemorrhagic stroke	680 (5.2)	105 (6.1)	35 (5.3)	0.300	728 (6.1)	102 (6.3)	34 (4.9)	0.439
Systemic embolism	121 (0.9)	23 (1.3)	11 (1.7)	0.059	114 (1.0)	23 (1.4)	6 (0.9)	0.193
Vascular disease	766 (5.8)	130 (7.5)	55 (8.3)	0.001[b,c]	769 (6.4)	101 (6.2)	84 (12.2)	<0.001[c,d]
Dementia	914 (6.9)	100 (5.8)	31 (4.7)	0.018[c]	500 (4.2)	76 (4.7)	43 (6.2)	0.024[c]
Depression	620 (4.7)	59 (3.4)	40 (6.0)	0.011[b,d]	354 (2.9)	35 (2.2)	23 (3.3)	0.153
Hyperthyroidism	435 (3.3)	67 (3.9)	17 (2.6)	0.251	193 (1.6)	25 (1.5)	10 (1.5)	0.938
Cancer	1375 (10.4)	133 (7.7)	45 (6.8)	<0.001[b,c]	1750 (14.5)	122 (7.5)	52 (7.5)	<0.001[b,c]
All-cause deaths within 1 year from diagnosis of AF, no. (%)	3758 (28.5)	556 (32.0)	182 (27.4)	<0.007[b,d]	3419 (28.4)	526 (31.7)	186 (27.0)	0.014[b,d]
Cardiovascular deaths within 1 year from diagnosis of AF, no. (%)	1345 (10.2)	260 (15.0)	72 (10.8)	<0.001[b,d]	1109 (9.2)	233 (14.3)	74 (10.7)	<0.001[b,d]

AF: atrial fibrillation; IQR: interquartile range; SD: standard deviation

[a] The *P* value indicates whether there is statistically significant difference across the 3 ethnicities while the superscript letters indicate pairwise comparisons

[b] Statistically significant difference between Chinese and Malays, $P<0.05$

[c] Statistically significant difference between Chinese and Indians, $P<0.05$

[d] Statistically significant difference between Malays and Indians, $P<0.05$

Table 3. Odds ratio of 1-year all-cause mortality and cardiovascular mortality among patients with atrial fibrillation stratified by age group

	Age 45–64 years		**Age ≥65 years**	
	OR (95% CI)	**AOR (95% CI)[a]**	**OR (95% CI)**	**AOR (95% CI)[a]**
	All-cause mortality			
Sex				
Female	1.00 [reference]	1.00 [reference]	1.00 [reference]	1.00 [reference]
Male	0.96 (0.86–1.08)	1.06 (0.92–1.21)	0.97 (0.93–1.02)	1.17 (1.11–1.24)
Ethnicity				
Chinese	1.00 [reference]	1.00 [reference]	1.00 [reference]	1.00 [reference]
Malay	1.43 (1.15–1.79)	1.15 (0.89–1.48)	0.93 (0.83–1.05)	1.01 (0.89–1.15)
Indian	1.48 (1.30–1.69)	1.27 (1.09–1.48)	1.18 (1.09–1.27)	1.33 (1.22–1.45)
Interaction between age and sex				
Age and male sex	*P*=0.413	*P*=0.437	*P*=0.698	*P*=0.278
Interaction between age and ethnicity				
Age and Malay Age and Indian	*P*=0.199 *P*=0.963	*P*=0.389 *P*=0.759	*P*=0.065 *P*=0.085	*P*=0.415 *P*=0.111
Interaction between sex and ethnicity				
Male sex and Malay Male sex and Indian	*P*=0.310 *P*=0.529	*P*=0.625 *P*=0.482	*P*<0.001 *P*=0.038	*P*<0.001 *P*=0.124
	Cardiovascular mortality			
Sex				
Female	1.00 [reference]	1.00 [reference]	1.00 [reference]	1.00 [reference]
Male	1.17 (0.98–1.40)	1.04 (0.85–1.26)	0.88 (0.82–0.95)	0.99 (0.92–1.07)
Ethnicity				
Chinese	1.00 [reference]	1.00 [reference]	1.00 [reference]	1.00 [reference]
Malay	1.63 (1.18–2.25)	0.95 (0.67–1.35)	1.11 (0.94–1.31)	0.96 (0.81–1.15)
Indian	1.99 (1.66–2.39)	1.36 (1.11–1.67)	1.58 (1.43–1.74)	1.54 (1.38–1.71)
Interaction between age and sex				
Age and male sex	*P*=0.201	*P*=0.139	*P*=0.005	*P*=0.033
Interaction between age and race				
Age and Malay Age and Indian	*P*=0.854 *P*=0.046	*P*=0.922 *P*=0.049	*P*=0.974 *P*=0.095	*P*=0.298 *P*=0.121
Interaction between sex and race				
Male sex and Malay Male sex and Indian	*P*=0.820 *P*=0.244	*P*=0.189 *P*=0.270	*P*=0.118 *P*=0.517	*P*=0.062 *P*=0.694

AOR: adjusted odds ratio; CI: confidence interval; OR: odds ratio
[a] Adjusted for age, sex, ethnicity, housing type, hypertension, diabetes, renal impairment, end-stage renal failure, ischaemic heart disease, chronic heart failure, stroke/transient ischaemic attack, haemorrhagic stroke, systemic embolism, peripheral vascular disease, dementia, depression, hyperthyroidism and cancer

Table 4. Odds ratio of 1-year all-cause mortality in patients with atrial fibrillation compared with those without atrial fibrillation (reference) in subgroups of patients stratified by age group, sex and ethnicity

	Age 45–64 years		Age ≥65 years	
	OR (95% CI)	**AOR (95% CI)[a]**	**OR (95% CI)**	**AOR (95% CI)[a]**
Overall	15.72 (12.95–19.08)	9.08 (7.36–11.20)	5.22 (4.98–5.48)	3.60 (3.40–3.80)
Interaction between age and sex				
Age and male sex	*P*=0.272	*P*=0.281	*P*=0.127	*P*=0.023
Interaction between age and ethnicity				
Age and Malay	*P*=0.778	*P*=0.800	*P*=0.024	*P*=0.342
Age and Indian	*P*=0.813	*P*=0.527	*P*=0.003	*P*=0.012
Interaction between sex and ethnicity				
Male sex and Malay	*P*=0.308	*P*=0.614	*P*<0.001	*P*<0.001
Male sex and Indian	*P*=0.619	*P*=0.550	*P*=0.001	*P*=0.015
Sex				
Female	19.56 (13.49–28.37)	11.29 (7.58–16.79)	5.73 (5.36–6.13)	3.83 (3.54–4.14)
Male	14.31 (11.40–17.97)	8.22 (6.41–10.54)	4.75 (4.44–5.07)	3.37 (3.11–3.64)
Ethnicity				
Chinese	20.09 (15.46–26.11)	12.32 (9.32–16.29)	5.36 (5.09–5.65)	3.75 (3.53–3.99)
Malay	10.10 (7.31–13.95)	5.75 (3.97–8.33)	4.36 (3.83–4.95)	2.83 (2.43–3.28)
Indian	14.11 (7.07–28.17)	5.50 (2.52–12.02)	5.67 (4.48–7.19)	3.26 (2.46–4.33)

AOR: adjusted odds ratio; CI: confidence interval; OR: odds ratio
[a] Adjusted for housing type, hypertension, diabetes, renal impairment, end-stage renal failure, ischaemic heart disease, chronic heart failure, stroke/transient ischaemic attack, haemorrhagic stroke, systemic embolism, peripheral vascular disease, dementia, depression, hyperthyroidism and cancer

With respect to cardiovascular mortality, Indians were noted to have 36% and 54% increased odds of 1-year mortality in the middle-aged and elderly groups, respectively, compared with Chinese in the corresponding groups (Table 3). Age, diabetes, IHD, renal impairment, HF, stroke/transient ischaemic attack, haemorrhagic stroke, systemic embolism, peripheral vascular disease, depression and cancer were associated with all-cause mortality in both age groups, while end-stage renal failure and dementia were also associated with all-cause mortality among elderly adults (online Supplementary Table S5).

The presence of AF in patients conferred a substantially higher risk of mortality compared with matched patients without AF (28% vs 7%, *P*<0.001), with a 9-fold increased odds of mortality among middle-aged adults (adjusted odds ratio [AOR] 9.08, 95% CI 7.36–11.20) and a greater than 3-fold increased odds of mortality among elderly adults (AOR 3.60, 95% CI 3.40–3.80) within a year of diagnosis after adjusting for clinical risk factors (Table 4). Interactions in all-cause mortality were present only among elderly adults and were between age and sex (*P* for age and male = 0.023), age and ethnicity (*P* for age and Indian = 0.012), and sex and ethnicity (*P* for male and Malay <0.001; *P* for male and Indian = 0.015). Among middle-aged adults, AF affected mortality differently in the sex and ethnic categories. AF conferred a greater increase in mortality in women than in men; while Chinese also had a greater increase in mortality compared with Malays and Indians (Table 4). In the elderly population, the increased odds of mortality associated with AF were generally 2- to 3-fold higher across the sexes and ethnicities.

DISCUSSION

In this nationwide multiethnic cohort, we found significant sex and ethnic differences in the incidence, clinical profile and 1-year all-cause mortality among patients with newly diagnosed AF. Despite having the worst cardiovascular risk profile, Indians had the lowest incidence of AF. The development of AF conferred substantially higher risk of mortality within a year of diagnosis compared with no development of AF, with a mortality rate of up to 22–26 per 100 people. Mortality in newly diagnosed AF was influenced by sex and ethnicity, particularly among elderly men and Indians who were more susceptible.

Prevalence and incidence of AF

The prevalence of AF in Asia is approximately 1% but with significant geographical variations.[2,5-7,9] We found an almost 10-fold higher prevalence of AF in elderly adults compared with middle-aged adults, a finding consistent with known age-related effects.[2,8] Within the Asia-Pacific region, the prevalence of AF in Singapore mirrors that of Australia and New Zealand (1.4–4.9%) and is higher than those of other Southeast Asian countries (<2%).[5,29-31] Based on national population data, we report a prevalence of 0.6% among middle-aged adults and 7% in elderly adults, and a steady temporal increase in the prevalence of AF. The higher rates of AF observed in Singapore are not unexpected and are likely due to an ageing population with increased life expectancy, a higher burden of cardiovascular disease and increasing detection of AF.[28] Additionally, Singapore is a high-income country, and the adoption of lifestyles similar to those in affluent Western nations may partly account for AF rates closer to those of Western nations.[5] Despite the steady incidence of AF, mortality rates were on the downward trend from 2010, possibly explained by rapid improvements in the standard of living, healthcare access and increasing emphasis on cardiovascular risk factor prevention and management, as well as the increasing longevity of population in Singapore.

Clinical profile

Regardless of age, women consistently had lower prevalence and incidence of AF. Sex differences in baseline characteristics among elderly adults with AF in Singapore were consistent with previous reports[10-18] and have been attributed to the protective effect of oestrogen on atrial electrophysiological properties, while body mass index had varying effects on atrial mechanical function by sex.[16,33,34] In contrast, disparities in AF risk factors did not correspond to the observed rates of AF among the major ethnic groups in Singapore. Despite the higher prevalence of cardiovascular disease in Indians and Malays compared with Chinese regardless of age or sex, Indians had the lowest rates of AF while Malays had the highest, with higher rates of AF even among Malay women than among Indian men. Low rates of AF among Indians were previously reported within and outside Asia and were attributed to genetic variations. These variations might lead to atrial structural and electrophysiological properties that result in Indians being less susceptible to AF.[24-26] Differences in AF rates between Malays and Chinese are likely a reflection of the higher cardiovascular risk profile among Malays, while differences in local dietary habits and activity levels may also contribute, with the effects of lifestyle modifications on maintenance of sinus rhythm being highlighted previously in a study.[35] The higher prevalence of inpatient diagnoses of AF among Malays may also suggest a worse comorbid status. Despite shared environmental factors within the same country, ethnic differences in AF rates in this population are likely multifactorial, involving clinical risk factors, genetic susceptibility, lifestyle and socioeconomic status.[9,27]

One-year mortality after newly diagnosed AF

The 1-year mortality rate of 22–26 per 100 person-years is far higher than the previously reported rate of 18 per 1,000 patient-years in a meta-analysis,[36] but is similar to that in the Framingham Heart Study, which reported a lower 1-year mortality rate of 11–15% among younger patients aged 55–64 years and a graded increase per decade in those aged above 65 years.[37] The lower mortality previously reported may be due to survival bias, as those studies included patients with known AF who were likely to have survived past the first year of diagnosis compared with our cohort with newly diagnosed AF. Hence, those studies may have included more patients with fewer comorbidities who were generally in better health. For example, patients in our study when compared with those in the Framingham study had higher rates of diabetes (41.9% vs 11.3%), hypertension (80.2% vs 58.4%), myocardial infarction (47.1% vs 28.0%), HF (28.5% vs 21.8%) and stroke (25.2% vs 14.0%).[37] Another reason for the high mortality may be that over two-thirds of our patients were first diagnosed with AF during hospital admissions and not during outpatient clinic encounters; hence, a higher-risk cohort was selected compared to previous studies, with AF possibly picked up at later stages of the disease. The majority of the initial presentations during hospital admissions were likely multifactorial, considering the lack of a systematic community screening programme for AF. Furthermore, most Singapore residents prefer to seek medical care at public hospitals, especially through emergency departments, in order to have easy access to highly subsidised acute care. Hence, AF is often only diagnosed when acutely unwell patients seek emergency care.

Notably, more than half of the deaths in our study were non-cardiovascular in nature, and the predictive effects of AF on mortality were independent of cardiovascular risk factors. AF may be more of a risk marker than a risk factor in this population, occurring in patients at high risk of mortality from other causes. This view is further supported by excess mortality in men within 30 days of AF diagnosis in the Framingham Heart Study, suggesting the role of AF as a marker of terminal illness.[37] Our study extends current evidence by demonstrating ethnic-specific mortality risks among patients with shared environments. Despite having the lowest incidence of AF, Indians had a 30% increased 1-year mortality after diagnosis of AF regardless of age. Although the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) study demonstrated higher adjusted 1-year mortality rates in India compared with Southeast Asia,[38] the higher mortality rate in Indians compared with Chinese in this study was among patients who lived in the same country with less environmental differences. Given the genetic basis that potentially renders Indians less susceptible to AF,[25-27] it is possible that the development of AF among Indians may indicate more advanced stages of systemic disease with an increased likelihood of early mortality. The significantly increased mortality within a year of AF diagnosis, especially among certain patient subgroups, suggests that AF should be considered a marker of poor prognostic outcomes and a harbinger of early mortality. Early aggressive management of AF and underlying comorbidities should be considered in these high-risk patient groups.

Strengths and limitations

The large study population and long study period provide statistically stable estimates and trends. However, we acknowledge the possibility of underestimation or overestimation of the number of AF cases as cases included in this study were based on coded diagnoses submitted by healthcare institutions rather than direct inspection of 12-lead electrocardiograms. Furthermore, ethnic differences in perceptions of healthcare access and thresholds to seeking medical attention might potentially impact the incidence of newly diagnosed AF, although we think it is likely a small effect due to the lack of significant geographical and financial barriers to healthcare in Singapore. Newly diagnosed AF does not imply new-onset AF and may have been detected only late in the course of the disease. However, it is not possible to reliably ascertain the date of AF onset, with current guidelines recommending opportunistic screening for AF only in elderly patients ≥65 years of age.[9] Data collection was made primarily for an administrative database on disease prevalence within Singapore, which precluded in-depth analyses on treatment efficacy and differences in cardiac structure and function. Specific dates of death were unavailable, and only a small proportion of patients would have a lag in death certification and these lags are not expected to affect the time to death significantly. The retrospective nature of this study allowed only inferences to be drawn about the association between AF and death, and may be affected by unknown confounders despite our comprehensive adjustment of clinical covariates in the multivariable models.

CONCLUSION

Among patients from a multiethnic population, variations in incidence, clinical profile and 1-year mortality of patients with AF were influenced by age, sex and ethnicity. Newly diagnosed AF portends a worse prognosis and is a marker of high mortality within the first year.

Acknowledgements

The contributions of all staff at the Singapore Ministry of Health and Department of Statistics for this study are duly acknowledged.

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ORIGINAL ARTICLE

Ann Acad Med Singap 2022;51:553-66
https://doi.org/10.47102/annals-acadmedsg.2022165

Cost analysis of a Patient-Centred Medical Home for community-dwelling older adults with complex needs in Singapore

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ABSTRACT

Introduction: The Patient-Centred Medical Home (PCMH) demonstration in Singapore, launched in November 2016, aimed to deliver integrated and patient-centred care for patients with biopsychosocial needs. Implementation was based on principles of comprehensiveness, coordinated care and shared decision-making.

Method: We conducted a prospective single-arm pre-post study design, which aimed to perform cost analysis of PCMH from the perspectives of patients, healthcare providers and society. We assessed short-to-intermediate-term health-related costs by analysing data on resource use and unit costs of resources.

Results: We analysed 165 participants enrolled in PCMH from November 2017 to April 2020, with mean age of 77 years. Compared to the 3-month period before enrolment, mean total direct and indirect participant costs and total health system costs increased, but these were not statistically significant. There was a significant decrease in mean cost for primary care (government primary care and private general practice) in the first 3-month and second 3-month periods after enrolment, accompanied by a significant decrease in service utilisation and mean costs for PCMH services in the second 3-month period post-enrolment. This suggested a shift in resource costs from primary care to community-based care provided by PCMH, which had added benefits of both clinic-based primary care and home-based care management. Findings were consistent with a lower longer-term cost trajectory for PCMH after the initial onboarding period. Indirect caregiving costs remained stable.

Conclusion: The PCMH care model was associated with reduced costs to the health system and patients for usual primary care, and did not significantly change societal costs.

Ann Acad Med Singap 2022;51:553-66

Keywords: Aged, economic evaluation, health financing, patient-centred care

INTRODUCTION

The Patient-Centred Medical Home (PCMH) is a model of chronic care that replaces episodic primary care, with the delivery of primary care to patients, families and communities. It is guided by the principles of first-contact accessibility, comprehensiveness and whole-person orientation, integration and care coordination, sustained clinician-patient relationships, and quality and safety.[1,2] The PCMH care model shifts from a disease-specific approach to a comprehensive biopsychosocial model that recognises the interplay of physical illnesses, mental disorders, and social and home environmental problems.[3] This biopsychosocial perspective allows for management options that consider tailored preferences and aims for the healthcare of each patient, clinician-patient relationships, patient engagement and quality of life (QoL).[4]

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CLINICAL IMPACT

What is New

- To the best of our knowledge, this is the first cost analysis of a Patient-Centred Medical Home (PCMH) care model in Singapore from the patient, healthcare provider and societal perspectives.

Clinical Implications

- Early evidence suggested that the PCMH care model reduced the out-of-pocket expenses to patients and resource cost to providers for usual primary care, by shifting costs towards community-based primary care delivery.
- The PCMH had added benefits of comprehensive and individualised care for community-dwelling adults.

A few knowledge gaps on the integrated PCMH model still exist. While integrated PCMH models have been shown to improve patient outcomes,[5,6] the impact on overall costs and the relative burden on various stakeholders (patients, healthcare providers and society at large) remain less well-understood. Existing literature has focused on costs to the healthcare system and providers, rather than costs from a patient-centric perspective.[7,8] Studies have also focused on the PCMH model for specific subgroups of patients, including older adults with multimorbidity or diabetic patients only.[9,10] While these studies have merit, their findings may not be generalisable to community-dwelling older adults with a combination of physical, psychological and social care needs. Additionally, it is challenging to draw conclusions on cost outcomes from current studies, due to the mixed findings across different target populations and settings. To illustrate, a pre-post study with controls in the US compared 8 practices that adopted the PCMH model with a group of 24 non-PCMH practices in 2010 to 2011, and reported no significant difference in costs.[11] Other studies showed that the PCMH programme was cost-effective when provided to patients with more chronic conditions or whose conditions were poorly managed at baseline.[9,10] Lastly, there is a dearth of literature on PCMH models in the Asian context. Current findings may not be generalisable to Asia due to differences in health systems and cultural backgrounds.[12]

The integrated PCMH care model in this study is part of a community-wide initiative (Community for Successful Ageing) on an integrated care system of comprehensive programmes and services promoting the well-being and health of older adults in Singapore.[6,13,14] Our integrated PCMH model differs from current advanced primary care models in Singapore that centres on a multidisciplinary team to deliver chronic disease management,[15] or Family Medicine Clinics that provide a "one-stop platform" for individualised chronic condition prevention and management by general practitioners.[16] The integrated PCMH model in this article targets community-dwelling older adults with complex biopsychosocial needs, assessed via social health, psychological and medical evaluations.[6,13,14] Our model follows overarching principles on ageing in place (growing old at home), life-course approach (promoting the earlier implementation of interventions for health), socioecological model of care (health as an outcome of an individual's interaction with family, caregivers and community), and population health management.[6,13,14]

Our study aimed to address gaps in the literature on the evaluation of costs associated with the implementation of an integrated PCMH model for community-dwelling older adults with complex needs. Our study examined costs not only from the health system perspective, but also from the perspectives of patients and the wider society. Findings will also be more generalisable to older populations across Asia.

METHOD

Study design and participants

This study was part of an evaluation of a PCMH demonstration in Singapore that involved concurrent quantitative and qualitative components.[6,14] We applied a prospective single-arm pre-post design that examined 2 time-points of the intervention compared to baseline. First, a true experimental design with randomisation of patients into intervention and control arms was impractical, due to the PCMH being a complex intervention with multiple care components. It would have been challenging to implement, as well as time-consuming and resource-intensive. Second, having a non-randomised parallel control arm was also challenging due to limited resources to involve a control study site that provided usual care, and high refusal rates and low recruitment were expected from patients of the control site. In addition, there were challenges in identifying a suitable control study site that would capture older adults with similar characteristics and health status profiles as the intervention group, but would only deliver usual care. Lastly, the option of utilising historical datasets to act as controls had possible limitations, such as systematic differences between groups due to the time difference in data collection, poor performance of matching techniques as the dataset may not contain suitable controls, and lack of clarity on what constituted usual care for controls.

Study participants with recruited from 1 November 2017 to 30 April 2019. Informed consent was taken from participants or proxies. As mentioned in our previous publications, these were the eligibility criteria included:[6,13]

(1) Patients with high biopsychosocial health risk defined by the 37-item BioPsychoSocial Risk Screener validated in the Singapore setting,[17] pre-existing risk stratification criteria used by referring healthcare institutes, and/or clinical assessment. Functional ability and frailty were not part of the inclusion and exclusion criteria.

(2) Patients aged ≥40 years.[6,13] Cut-off age was chosen to reflect the life-course approach. PCMH services could be provided to patients with complex needs from their fourth decade of life prior to entering old age, for early intervention to prevent further adverse health outcomes.[6,13]

(3) Patients who resided in Whampoa, a geographically defined district in Singapore (total population of 41,000) where the PCMH was located.[6,13]

Intervention

There are advanced primary care models in Singapore, such as the Family Medicine Clinics where family medicine physicians provide individualised care for patients and the Teamlet Care Model where a multidisciplinary team manages non-communicable diseases.[15,16] Our PCMH model differed by targeting community-dwelling older adults with biopsychosocial needs, and has 2 integrated parts: medical care in primary care and psychosocial care in home-based care management.

The intervention was described in detail in our earlier publication.[6] Implementation was based on PCMH values on patient-centredness, comprehensive and coordinated care, accessible services, shared decision-making, and quality and safety.[1] The PCMH was an integrated care intervention comprising physician-led primary care clinics, and home-based care management services led by medical social workers and nurses.[12] Briefly, the intervention involved a multidisciplinary care team (doctors, registered nurses, programme coordinators and care managers), comprehensive needs assessment, and individualised care plans.[6] The initial clinic visit involved comprehensive biopsychosocial assessment and the development of a preliminary individualised care plan with the patient and family members. Subsequent clinic visits reviewed individualised care plans and treated acute conditions.[6] The development of care plans and reviews were discussed at interdisciplinary team meetings. PCMH primary care providers also partnered geriatric specialists from the tertiary acute hospital to provide shared care. Patients determined to have complex biopsychosocial needs at the first or subsequent clinic visits were given home-based care management services.[6] Home-based care management provided extended care in the home setting, and addressed the physical home environment, financial needs, behavioural needs, and support systems by caregivers.[6,13]

Outcome measures

We conducted the cost analysis from the perspectives of patients (out-of-pocket expenditures [OOPE] by patients), healthcare provider (resource cost to the health system) and society:

Patient perspective = **(a)** OOPE on PCMH and non-PCMH health services + **(b)** OOPE of paid care services from domestic helpers or other professional carers + **(c)** work productivity loss by participants due to ill health

Healthcare provider perspective = **(d)** Resource cost of providing PCMH and non-PCMH health services

Societal perspective = **(b)** + **(c)** + **(d)** + work productivity loss and leisure time loss from providing caregiving to participants by family members

Supplementary Table S1 (online Supplementary Material) shows the categories of direct and indirect costs under each perspective.

Cost outcomes included the direct costs of PCMH services, and direct medical and non-medical costs. Healthcare utilisation data in this study was self-reported. Specifically, an adapted Client Service Receipt Inventory (CSRI) survey was administered to participants to collect self-reported data on healthcare utilisation in the past 3-month period from the date of surveys.[18] Surveys were conducted at baseline and repeated at 3 months and 6 months post-enrolment.

Cost to patients (out-of-pocket expenditures by patients)

Table 1 displays how unit prices were derived and unit price of each item.

Table 1. Cost from the patient perspective: Items and unit prices

Items	How this study derived price	Unit price (SGD)
PCMH services		
PCMH clinic services	For each participant, the total PCMH patient payments were extracted from administrative billing information, inclusive of consultation fees, procedure fees and medication fees.	NA
PCMH home-based care management services	Home-based care management services were of no charge to patients.	0
Non-PCMH services		
Government primary care	Based on National Healthcare Group government primary care consultation fee.[a]	13.20 per visit
Private general practice	Based on National Healthcare Group family physician clinic consultation fee.	30.00 per visit
Accident and emergency (A&E)	Based on fees charged by the acute hospital under National Health Group (Tan Tock Seng Hospital, Singapore) that referred patients to the PCMH clinic in this study.	120.00 per visit
Specialist outpatient clinic (SOC)		38.00 for 1st visit, 36.00 for subsequent visits
Outpatient allied health		22.50 per visit
Day surgery		49.00 per session
Inpatient admission	Based on inpatient charges for Singapore citizens per bed day, according to hospital class wards.	35 to 43 for C Class wards
Non-PCMH community care		
Social day care	Out-of-pocket expenses for community care services were based on the total costs given by the Agency for Integrated Care under the Ministry of Health of Singapore, and assumed to be 40% of the total costs based on Graham & Bilger.[19]	17.20 per visit
Day rehabilitation		24.20 per visit
Dementia day care		23.40 per visit
Home medical care		50.00 per visit
Hospice care		50.00 per visit
Escort services		30.40 per visit
Community development council/ Family service centre services		No charge to patients
Hiring domestic helpers for caregiving	We collected self-reported estimated time contributions from informal household-based caregivers (both paid domestic helpers and family caregivers) related to assisting with Activities of Daily Living and Instrumental Activities of Daily Living, supervision of study participants, and/or providing child and elderly care on behalf of study participants. The hourly cost of care provided by domestic helpers at home was based on figures reported by Woo et al.[20]	3.45 per hour
Work productivity loss due to ill health by study participants	Work productivity loss was valued at the median gross monthly income of a full-time employed worker in Singapore, converted to hourly wages based on national average weekly total paid hours worked per employee.	20.22 per hour

PCMH: Patient-Centred Medical Home
[a] The National Healthcare Group is one of the 3 healthcare clusters in Singapore, and the PCMH was under this healthcare cluster.
Superscript numbers: Refer to REFERENCES

Cost to healthcare providers (resource cost to health system)

Table 2 shows the derivation of unit resource costs and unit resource cost for each item, drawing on previous work by Abdin et al.[18] and Graham and Bilger.[19]

Costs to informal caregivers

Table 2 shows the derivation of unit costs for work productivity loss and leisure time loss frm caregiving, based on a local study by Woo et al.[20] and the labour statistics from the 2017 Singapore Yearbook of Manpower Statistics.[21]

Data analysis

To assess the short to intermediate-term health-related cost from different perspectives, we analysed cumulative health-related costs incurred over the quarter (3-month period) immediately before enrolment, from the first quarter post-enrolment (i.e. first 3-month period post-enrolment), and the second quarter post-enrolment from 3 months post-enrolment to 6 months post-enrolment (i.e. second 3-month period post-enrolment). We estimated the change in quarterly costs in the latter 2 periods, with the quarter immediately before enrolment. Costs were converted to 2017's Singapore Dollar amount using the consumer price index for Singapore from the Monetary Authority of Singapore. We reported mean and median costs per-person per-quarter.

Statistical analysis

Sample characteristics of the 165 participants analysed were presented, and data were summarised descriptively as mean and standard deviation. We used multivariable linear regression models with random intercepts and fixed slopes to compare the difference between mean costs per-participant per-quarter, during the first 3-month period post-enrolment and second 3-month period post-enrolment, compared to the 3-month period prior to enrolment. The multivariable regression models had random intercepts to allow for variation by individuals (i.e. between-participant variation), but slopes were fixed as time was not a continuous variable in this study. We recognised that each participant may act as its own control in this single-arm pre-test post-test study design. However, this study still aimed to adjust for observed and unobserved time-invariant differences between participants. The random intercept accounted for such time-invariant between-participant differences by adjusting for a list of covariates. The estimates and statistical significance of estimates would be similar in the unadjusted (not presented) and adjusted models, and we presented results that adjusted for between-participants differences. These methods were consistent with an earlier article that conducted a before-after study without controls to examine the changes in quality of life and patient activation (knowledge, skills, and confidence for self-management) of older adults, and applied multivariable regression modelling to adjust for between-participant differences.[6]

Specifically, this study adjusted for age at enrolment, sex, weighted Charlson Comorbidity Index (CCI) at baseline, having received any formal education (yes/no), housing types in Singapore (1-, 2- and 3-room Housing and Development Board [HDB] apartments; 4-room or larger HDB apartments and Housing and Urban Development Company apartments and executive condominiums) and baseline 13-item Patient Activation Measure (PAM-13) score. Covariates were selected based on plausible relationships with healthcare utilisation. Ethnicity was not included as the sample was predominantly Chinese. Baseline PAM-13 measure was adjusted to account for differences in study participants' underlying knowledge, skills and confidence integral to managing one's own health and healthcare,[22] and was also applied as a covariate in our previous publication.[6]

Statistical significance was determined at $P<0.05$. All analyses were performed on Stata version 14.0 (StataCorp, College Station, US).

RESULTS

Participant characteristics

A total of 238 patients were enrolled into PCMH from 1 November 2017 to 30 April 2019, of which 16 did not fulfil study eligibility criteria. After excluding patients who did not consent to the study (n=34, 14.3%) and were uncontactable (n=3), this study recruited 184 study participants. The final sample analysed was 165 study participants after loss to follow-up at 3 months post-enrolment (n=11, 6.0%) and 6 months post-enrolment (n=8, 4.3%). There were 6 deaths; 1 patient who was retrospectively found to be ineligible; and 12 withdrawals from PCMH due to being housebound, admitted to a long-term care facility, or relocated to be out of the PCMH service boundary. Participant flow diagram has been published previously.[12]

Table 3 displays the sociodemographic characteristics of study participants (n=165). The mean age of study participants was 77 years, with 93.9% aged 60 years and above. The proportion of males was 43.6%, 51.5% were married, a majority of 93.3% were ethnic Chinese, 48.5% had no formal education, and 58.8% stayed in a smaller housing type.

Table 2. Cost from the healthcare provider and societal perspectives: Health services and unit resource costs

Items	Resource cost	Unit cost (SGD)
PCMH services		
Doctor	Unit costs of the PCMH doctor, nurse and care manager services were from the manpower cost per minute for government primary care doctors and other restructured hospital staff from a study in Singapore by Abdin et al.[18]	8.71 per minute
Nurse		1.80 per minute
Care manager	We calculated the unit cost of PCMH clinic visits based on attending professionals and recorded durations of each visit. For home-based care management services, the duration of each home visit was assumed to be 1 hour.	1.80 per minute
Non-PCMH services		
Government primary care	Unit costs were based on the study in Singapore by Abdin et al.[18] The data were presented in manpower of physician cost per minute. To compute per-visit cost estimates, we assigned durations of visit for patients that were representative of our study population from consultations with local experts (A&E visit: 15 minutes; SOC visit: 15 minutes; outpatient allied health visit: 25 minutes; non-PCMH primary care visit: 15 minutes). <u>Sensitivity analysis</u> We conducted sensitivity analyses for resource cost from the healthcare provider perspective, by applying a longer duration of 30 minutes for non-PCMH primary care (government primary care, private general practice), SOC and A&E visits. The main objective of conducting the sensitivity analysis was to present alternative scenarios with higher resource cost estimations from the healthcare provider perspective, to reflect the additional resources needed to provide care to more complex patients. Note: This sensitivity analysis was not applied for price calculations from the patient perspective (Table 1), as these services are likely at a fixed price to patients.	8.71 per minute, 130.65 per visit (sensitivity analysis: 261.30 per visit)
Private general practice		
Accident and emergency (A&E)		18.16 per minute, 272.40 per visit (sensitivity analysis: 544.80 per visit)
Specialist outpatient clinic (SOC)		
Outpatient allied health		1.80 per minute, 45.00 per visit
Day surgery	Estimates for the total resource cost associated with day surgery were based on price estimates provided by Tan Tock Seng Hospital in Singapore, due to the lack of data from the local study by Abdin et al.[18] and other literature.	132.00 per procedure
Inpatient admission	Unit costs were based on the study in Singapore by Abdin et al.[18]	1109.62 per bed per day
Non-PCMH community care		
Social day care	Unit costs of providing community care was based on the study in Singapore by Abdin et al.[18]	35.62 per session
Day rehabilitation		
Dementia day care		
Home medical care		
Hospice care		
Escort services		
Community development council/ Family service centre services		

Table 2. Cost from the healthcare provider and societal perspectives: Health services and unit resource costs (Cont'd)

Items	Resource cost	Unit cost (SGD)
Work productivity loss from caregiving by family members	Based on estimates of time during which family members engaged in caregiving activities and time lost from work to provide caregiving. These were self-reported by study participants, family members and proxies. We used the opportunity cost approach to calculate the value of working time foregone by family members due to their caregiving responsibilities. Based on labour statistics from the 2017 Singapore Yearbook of Manpower Statistics,[21] work productivity loss was valued at the median gross monthly income of a full-time employed worker in Singapore, converted to hourly wages based on national average weekly total paid hours worked per employee (i.e. SGD20.22 per hour).	20.22
Leisure time loss from caregiving by family members	The remaining hours spent on caregiving duties by family members were valued as lost leisure time, and calculated using the replacement cost approach, i.e. to the labour market price of a professional caregiver. Unit cost of caregiving during family member's leisure hours was assumed to be SGD6.31, based on a contemporaneous local study by Woo et al.[20]	6.31

A&E: accident and emergency; PCMH: Patient-Centred Medical Home; SOC: specialist outpatient clinic
Superscript numbers: Refer to REFERENCES

Cost to patients

Table 4 presents the 3-month cumulative cost per-participant per-quarter from a patient perspective. Compared to the 3-month period prior to enrolment, there was a statistically significant decrease in mean cost for non-PCMH primary care (government primary care, private general practice) by SGD9.40 (41.4%) in the first 3-month period post-enrolment and by SGD3.60 (15.9%) in the second 3-month period post-enrolment based on the multivariable regression model.

Compared to the 3-month period prior to enrolment, the mean total cost to study participants was SGD123.10 (13.8%) higher in the first 3-month period post-enrolment and SGD180.20 (20.3%) higher in the second 3-month period post-enrolment, but these were not statistically significant based on the multivariable regression model. There were no statistically significant changes in mean costs from outpatient services (accident & emergency, specialist outpatient clinic, outpatient allied health, day surgery), inpatient admissions, work productivity loss and paid caregiving.

Compared to the first 3 months post-enrolment, there was a statistically significant decrease by SGD12.20 (35.0%) for PCMH services in the second 3 months post-enrolment based on the multivariable regression model.

Cost to healthcare providers (resource cost)

Table 5 presents the 3-month cumulative cost per-participant per-quarter from a healthcare provider perspective. Compared to the 3-month period prior to enrolment, there was a statistically significant decrease in mean cost for non-PCMH primary care (government primary care, private general practice) by SGD50.70 (38.8%) in the first 3-month period post-enrolment and by SGD29.30 (22.4%) in the second 3-month period post-enrolment, which remained significant (but with a larger quantum) in the sensitivity analysis.

Compared to the 3-month period prior to enrolment, mean total cost increased by SGD414.50 (19.0%) at the first 3-month period post-enrolment and by SGD194.70 (8.9%) at the second 3-month period post-enrolment, but these were not significant based on the multivariable regression model. There were no statistically significant changes in mean cost for outpatient services, inpatient admissions, and community care.

Compared to the first 3 months post-enrolment, there was a statistically significant decrease in mean cost by SGD427.30 (51.2%) for PCMH services in the second 3-month period post-enrolment based on the multivariable regression model.

Table 3. Sociodemographic characteristics of study participants

Sociodemographic characteristic	n=165
Age at enrolment, mean (SD), years,	77.0 (9.88)
Age group, no. (%), years,	
40–49	2 (1.21)
50–59	8 (4.85)
60–69	26 (15.76)
70–79	63 (38.18)
80–89	49 (29.70)
≥90	17 (10.30)
Sex, no. (%)	
Male	72 (43.64)
Female	93 (56.36)
Ethnicity, no. (%)	
Chinese	154 (93.33)
Malay	3 (1.82)
Indian	7 (4.24)
Others	1 (0.61)
Marital status, no. (%)	
Single	14 (8.48)
Married	85 (51.52)
Widowed	53 (32.12)
Divorced	13 (7.88)
Education, no. (%)	
No formal education	80 (48.48)
Primary school	51 (30.91)
Secondary school	23 (13.94)
Post-secondary (non-tertiary)	8 (4.85)
Diploma and professional	3 (1.82)
Housing type, no. (%)	
Smaller housing type	
1–2 room HDB apartment	16 (9.70)
3-room HDB apartment	81 (49.09)
Larger housing type	
4-room HDB apartment	47 (28.48)
5-room HDB apartment, HUDC apartment, EC	20 (12.12)
Private condominium/private others	1 (0.61)

Table 3. Sociodemographic characteristics of study participants (Cont'd)

Sociodemographic characteristic	n=165
Employment status, no. (%)	
Employed full-time	14 (8.48)
Employed part-time	13 (7.88)
Unemployed	7 (4.24)
Retired	127 (76.97)
Others	4 (2.42)
Chronic disease status[a]	
Weighted CCI[b]	4.82

CCI: Charlson Comorbidity Index; EC: executive condominium; HDB: Housing and Development Board; HUDC: Housing and Urban Development Company

[a] Chronic disease list: hypertension, high blood cholesterol, arthritis, eyesight problems, back pain, diabetes, hearing problems, incontinence, frequent falls, dementia, heart conditions, stroke, chronic lung disease, osteoporosis, depression, anxiety, neurological diseases, others.

[b] The weighted CCI was used as the summary measure for adjusting for comorbidities in our multivariable linear regression model. The CCI was based on the number of chronic conditions that are each assigned an integer weight from 1 to 6, with a weight of 6 representing the most severe morbidity. The summation of the weighted comorbidity scores resulted in a summary score. In this study, the International Classification of Diseases 10th Revision (ICD-10) codes of study participants were based on a national healthcare administrative database and the PCMH clinic administrative database. Subsequently, we compute the weighted CCIs based on ICD-10 codes.

Cost to society

Table 6 presents the 3-month cumulative cost per study participant per-quarter from a societal perspective. Compared to the 3-month period prior to enrolment, mean total cost increased by SGD559.50 (17.8%) in the first 3-month period post-enrolment and by SGD365.20 (11.6%) in the second 3-month period post-enrolment, with the former being statistically significant and the latter being non-significant based on the multivariable regression models. The mean cost of informal caregiving by family members remained stable.

DISCUSSION

This study evaluated the cost of implementing a PCMH care model with integrated clinic and home-care management services designed for adults with complex needs. Our study contributes to the literature by investigating how implementing a PCMH care model affects cost components for different stakeholders in an Asian context.[12]

Table 4. Cost from the patient perspective: 3-month cumulative cost per study participant

Outcome	$T_{-3months\_enrolment}$		$T_{enrolment\_3months}$		$T_{3months\_6months}$	
	Mean (SD), SGD	Median, SGD	Mean (SD), SGD	Median, SGD	Mean (SD), SGD	Median, SGD
Total cost	889.50 (1941.00)	56.40	1012.60 (1827.00)	87.30	1069.70 (2207.50)	91.10
PCMH services	NA	NA	34.90 (71.70)	6.60	**22.70**[a,c] (49.60)	2.60
Non-PCMH health services						
Non-PCMH primary care: Government primary care and private general practice	22.70 (45.60)	13.20	**13.30**[b] (24.30)	0	**19.10**[a] (59.70)	0
Outpatient services: Accident and emergency (A&E), specialist outpatient clinic (SOC), outpatient allied health, and day surgery	45.90 82.30)	0	42.20 (82.40)	0	46.10 75.70)	0
Inpatient admission	108.60 (476.70)	0	65.40 (299.70)	0	61.80 218.90)	0
Non-PCMH community care: Social day care, day rehabilitation, dementia day care, home medical care, hospice care, escort services, and community development council/ family service centre services	89.60 (310.90)	0	116.80 (409.90)	0	123.30 385.00)	0
Caregiving by domestic helpers	566.90 (1582.20)	0	641.50 (1453.40)	0	682.70 (1456.90)	0
Work productivity loss	55.80 (625.20)	0	98.60 (917.30)	0	114.00 (1192.00)	0

A&E: accident and emergency; PCMH: Patient-Centred Medical Home; SOC: specialist outpatient clinic
$T\text{-}_{3months\_enrolment}$: 3-month period immediately before enrolment
$T_{enrolment\_3months}$: 3-month period from enrolment to 3 months post-enrolment
$T_{3months\_6months}$: 3-month period from 3 months post-enrolment to 6 months post-enrolment
[a] *P* value <0.05; [b] *P* value<0.001
Compared to mean cost at $T_{-3months\_enrolment}$, the change in mean cost using multivariable linear regression modelling that adjusted for age at enrolment, sex, weighted Charlson Comorbidity Index at baseline, having received any formal education (yes/no), housing types in Singapore (1- 2- and 3-room Housing and Development Board [HDB] apartments; 4-room or larger HDB apartments and Housing and Urban Development Company [HUDC] apartments and executive condominiums) and baseline 13-item Patient Activation Measure score.
[c] Reference group was mean cost at $T_{enrolment\_3months}$

Table 5. Cost from the healthcare provider perspective: 3-month cumulative cost per study participant

Outcome	$T_{-3months\_enrolment}$		$T_{enrolment\_3months}$		$T_{3months\_6months}$	
	Mean (SD), SGD	Median, SGD	Mean (SD), SGD	Median, SGD	Mean (SD), SGD	Median, SGD
Total cost	2183.30 (7528.30) SA : 2500.50 7598.10)	272.40 SA544.80	**2597.80**[a] (6486.20) SA:2880.80 (6597.10)	1110.30 1328.70	2378.00 (5831.10) SA: 2677.50 (6026.00)	695.10 SA: 847.00
PCMH services (total)	NA	NA	834.80 (357.50)	801.30	**407.50**[b,c] (308.90)	324.00
Breakdown of manpower costs						
Doctor and nurse	NA	NA	698.70 (314.90)	723.80	330.90 (272.50)	288.30
Care manager	NA	NA	136.20 (251.90)	0	76.60 (155.10)	0
Non-PCMH health services						
Non-PCMH primary care: Government primary care and private general practice	130.70 (211.60) SA: 261.30 (423.10)	130.70 SA: 261.30	**80.00**[b] (130.30) SA: **160.00**[b] (260.64)	0 SA: 0	**101.40**[a] (264.60) SA: **202.70**[a] (529.20)	0 SA: 0
Outpatient services: Accident and emergency (A&E), specialist outpatient clinic (SOC), outpatient allied health, and day surgery	205.40 (328.90) SA: 392. 00 (613.90)	0 SA: 0	212.80 (433.00) SA: 415.90 (851.10)	0 SA: 0	209.50 (339.60) SA: 407.60 (670.20)	0 SA: 0
Inpatient admission	1667.80 (7441.20)	0	1257.60 (6413.70)	0	1419.00 (5550.30)	0
Non-PCMH community care: Social day care, day rehabilitation, dementia day care, home medical care, hospice care, escort services, and community development council/family service centre services	179.40 (611.00)	0	212.60 (677.10)	0	240.70 (645.50)	0

A&E: accident and emergency; PCMH: Patient-Centred Medical Home; SA: sensitivity analysis; SD: standard deviation; SOC: specialist outpatient clinic
Superscript numbers: Refer to REFERENCES
This study assigned durations of visit for patients that were representative of our study population from consultations with local experts—A&E: 15 min; SOC: 15 min; outpatient allied health visit: 25 mins; non-PCMH primary care visit: 15 min. We conducted sensitivity analyses using a longer duration of 30 mins for A&E, SOC and non-PCMH primary care visits (**see Table 3**).
$T\text{-}_{3months\_enrolment}$: 3-month period immediately before enrolment
$T_{enrolment\_3months}$: 3-month period from enrolment to 3 months post-enrolment
$T_{3months\_6months}$: 3-month period from 3 months post-enrolment to 6 months post-enrolment
[a] P value <0.05; [b] P value<0.001
Compared to mean cost at $T_{-3months\_enrolment}$, the change in mean cost using multivariable linear regression modelling that adjusted for age at enrolment, sex, weighted Charlson Comorbidity Index at baseline, having received any formal education (yes/no), housing types in Singapore (1- 2- and 3-room Housing and Development Board [HDB] apartments; 4-room or larger HDB apartments and Housing and Urban Development Company [HUDC] apartments and executive condominiums) and baseline 13-item Patient Activation Measure score.
[c] Reference group was mean cost at $T_{enrolment\_3months}$

Table 6. Cost from the societal perspective: 3-month cumulative cost per study participant

Outcome	$T_{-3months\_enrolment}$		$T_{enrolment\_3months}$		$T_{3months\_6months}$	
	Mean (SD), SGD	Median, SGD	Mean (SD), SGD	Median, SGD	Mean (SD), SGD	Median, SGD
Total cost	3135.20 (8281.20)	392.00	**3694.70**[a] (6882.40)	1250.00	3500.40 (7036.30)	855.90
PCMH services	NA	NA	834.80 (357.50)	801.30	**407.50**[b,c] (308.90)	324.00
Non-PCMH services						
Non-PCMH primary care: Government primary care and private general practice	130.70 (211.60)	130.70	**80.00**[b] (130.30)	0	**101.40**[a] (264.60)	0
Outpatient services: Accident and emergency (A&E), specialist outpatient clinic (SOC), outpatient allied health, and day surgery	205.40 (328.90)	0	212.80 (433.00)	0	209.50 (339.60)	0
Inpatient admission	1667.80 (7441.20)	0	1257.60 (6413.70)	0	1419.00 (5550.30)	0
Non-PCMH community care: Social day care, day rehabilitation, dementia day care, home medical care, hospice care, escort services, and community development council/family service centre services.	179.40 (611.00)	0	212.60 (677.10)	0	240.70 (645.50)	0
Caregiving by domestic helpers	566.90 (1582.20)	0	641.50 (1453.40)	0	682.70 (1456.90)	0
Work productivity loss by study participants	55.80 (625.20)	0	98.60 (917.30)	0	114.00 (1192.00)	0
Caregiving by family members	329.00 (1871.80)	0	356.90 (1299.50)	0	325.60 (1275.10)	0

A&E: accident and emergency; PCMH: Patient-Centred Medical Home; SA: sensitivity analysis; SD: standard deviation; SOC: specialist outpatient clinic
$T_{-3months\_enrolment}$: 3-month period immediately before enrolment
$T_{enrolment\_3months}$: 3-month period from enrolment to 3 months post-enrolment
$T_{3months\_6months}$: 3-month period from 3 months post-enrolment to 6 months post-enrolment
[a] P value <0.05; [b] P value<0.001
Compared to mean cost at $T_{-3months\_enrolment}$, the change in mean cost using multivariable linear regression modelling that adjusted for age at enrolment, sex, weighted Charlson Comorbidity Index at baseline, having received any formal education (yes/no), housing types in Singapore (1- 2- and 3-room Housing and Development Board [HDB] apartments; 4-room or larger HDB apartments and Housing and Urban Development Company [HUDC] apartments and executive condominiums) and baseline 13-item Patient Activation Measure score.
[c] Reference group was mean cost at $T_{enrolment\_3months}$
Reference: Abdin E, Subramaniam M, Achilla E, et al. The Societal Cost of Dementia in Singapore: Results from the WiSE Study. J Alzheimers Dis 2016; 51:439-49.

Although the PCMH has the added benefits of both clinic and home-based care management relative to existing primary care, this study found no evidence that implementing the PCMH model resulted in increased costs from the healthcare system perspective. An initial non-significant increase in mean total per-participant healthcare resource cost was recorded in the first quarter after enrolment, which may be primarily attributed to the higher frequency and longer duration of visits for PCMH providers to conduct initial comprehensive geriatric assessments. It was not unexpected for resource costs to be high during the initial implementation stages of PCMH.[8,9] Importantly, we found that mean total per-participant resource costs subsequently dropped by approximately half in the subsequent quarter, consistent with a fall in resource cost to deliver PCMH services cost per-participant in the second quarter after enrolment.

The estimated mean resource costs associated with non-PCMH primary care consultations (government primary care, private general practice) fell from the first post-enrolment quarter. Given that the estimation only included consultation fees, it was plausible that unmeasured savings were even larger. There were no other significant changes in resource costs associated with other outpatient services (A&E, SOC, outpatient allied health, day surgery), inpatient admissions or community care. This suggested that at the health system level, change was driven primarily by patients' substitution from usual primary care (government primary care/polyclinics, private GP) to community-based primary care by the PCMH. The PCMH model shifted OOPE of patients from non-PCMH primary care towards primary care in the community (i.e. PCMH). Other studies also suggested that implementing PCMH may not increase overall costs to patients and health systems.[8,23]

In the existing literature, findings on costs have been mixed and challenging to interpret due to the different contexts and target populations for PCMH.[8,9,24] Our findings suggest potential for cost savings for patients and their families from longer-term reductions in other formal and informal care. Over our study period, we found no significant changes in the mean cost to patients for other outpatient services and inpatient admissions. At the same time, costs to patients and society associated with formal and informal caregiving remained stable with non-significant changes. From the societal perspective, therefore, the total mean cost per-participant initially rises due to the initial increase in resource use, but it subsequently decreased. We furthermore expect these to reduce with a longer follow-up, as PCMH management further reduces utilisation of services like A&E and hospitalisations.[8,9,24]

Given the evidence of better QoL and patient activation from our previous publication,[6] our findings show that the PCMH model dominates the current standard of care, namely, intervention was both more effective and not more costly. As such, the results are presented in the form of a detailed cost analysis rather than a cost-effectiveness analysis.

A strength of PCMH is its ability to meet the multidimensional needs of patients, such as aspects of comprehensive assessments in the clinic and the home setting, a multidisciplinary care team, individualised care plans, shared decision-making, and empanelment (assignment of patients to primary care providers and care teams, taking into account patient and family preferences). We previously reported improved QoL and patient activation, and this study found no increase in societal cost, and a decrease in cost for usual primary care. We had low loss to follow-up and examined cost analysis holistically from the perspectives of patients, healthcare providers and society. When interpreted together, these findings suggest positive overall system-level outcomes for PCMH.

However, this study had a few limitations. We recognised that the participants recruited were older persons even though persons aged ≥40 years were eligible, which would affect the generalisability of our study. However, most PCMH care models have also focused on older populations.[25] Next, unit prices of PCMH services were based on PCMH administrative data that consisted of fees for consultation, procedures and medications, whereas prices of non-PCMH services included consultation fees. The omitted category of procedures and medications was approximately 30–40% of the total bill. Our results likely understated costs of non-PCMH services to patients. This made PCMH appear relatively expensive by understating cost savings from reducing non-PCMH services. Calculation of resource cost to providers for non-PCMH health services used manpower cost of only doctors due to the lack of data availability, whereas the cost of PCMH included manpower cost of doctors, nurses and care managers. Hence, our findings likely underestimated the resource costs of PCMH services and resource cost-savings from reducing non-PCMH services. Utilisation counts and durations of caregiving were self-reported, but the CSRI survey has been validated and used in Singapore.[18,26] Importantly, we included relevant cost components with unit costs based on the literature. Utility bills, indirect costs (e.g. transportation) and other overhead costs were omitted due to lack of data.

Our study has important implications for practice and policy. Our analysis shows that the PCMH model effectively resulted in an increase in utilisation of community-based primary care services and suggested potential reductions in hospital-based care, consistent with Singapore's national healthcare policy directives to move beyond acute to preventive care, and from hospital to community settings. The model supports multiple mechanisms by which this may occur including more access to higher-quality care. This results in better care outcomes or increased care coordination at the community level, enabling stronger care networks and management of care in the lived environment. These remain to be investigated further. Second, our study recognises that the implementation of a PCMH care model may require a significant amount of initial investment but suggests that offsetting cost savings to the system and patients may be realised in a relatively short period. This makes the PCMH model a potentially more sustainable paradigm for patients with complex care needs. Finally, analysing estimates from different payers' and stakeholders' perspectives shows that the PCMH model is consistently aligned in economic impact and incentives to change. This is especially important in a multipayer health system to support decision-making on benefits and risks, so as to enable a comprehensive practice transformation towards effective team-based PCMH care.[27]

CONCLUSION

Evidence suggested that the PCMH care model shifted the OOPE of patients and resource costs of providers from usual primary care and outpatient services, towards community-based primary care with the added benefits of comprehensive and individualised care for community-dwelling older adults. PCMH reduced costs to the health system and patients for usual primary care and did not increase informal caregiving costs. There may be potential for sustainability and scalability of PCMH.

Ethics approval and consent to participate

This study was registered with ClinicalTrials.gov (Protocol ID: 2017/00352) and was approved by the National Healthcare Group Domain Specific Review Board (NHG DSRB) Singapore (Reference: DSRB 2017/00352). Informed consent was taken from all participants or their proxies. All methods were performed in accordance with the relevant guidelines and regulations.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to strict government confidentially. The corresponding author can be contacted on this matter.

Disclosure

Wong CH is currently affiliated to Tsao Foundation, which was involved in implementing this PCMH demonstration. However, Wong CH was not affiliated to Tsao Foundation at the time of the study conceptualisation and development, analysis and manuscript writing. All other authors had no competing interests.

Funding

This study was funded by the Geriatric Education and Research Institute (GERI) (funding reference: GERI1608).

Acknowledgements

We would like to acknowledge Ms Isabelle Lim Shu Fen and Mr Julian Loke Zhi Liang for their excellent contributions to research administration.

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Ann Acad Med Singap 2022;51:567-74
https://doi.org/10.47102/annals-acadmedsg.2021503

Periodontal disease and systemic health: An update for medical practitioners

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ABSTRACT

Introduction: Chronic periodontal disease is a highly prevalent dental condition affecting tooth-supporting tissues. Scientific evidence is accumulating on links between periodontal disease and various systemic conditions. This narrative review provides a holistic yet succinct overview that would assist medical practitioners to deliver integrated care for better clinical outcomes.

Method: Scientific evidence on associations between periodontal disease and systemic conditions was synthesised and critically appraised. Key findings of latest prospective cohort studies, randomised clinical trials, and meta-analysis were closely assessed and compiled.

Results: A bidirectional relationship has been established, indicating that diabetes and periodontal disease are closely linked and amplify one another, if not successfully controlled. Existing evidence also supports the associations of periodontal disease with cardiovascular diseases and adverse pregnancy outcomes. Successful treatment of periodontal disease and dental prophylaxis has been shown to improve clinical outcomes in these systemic conditions. Other systemic conditions associated with periodontal disease include respiratory diseases, Alzheimer's disease, rheumatoid arthritis and chronic kidney disease. Although the underlying mechanisms remain to be fully elucidated, it is generally accepted that the inflammatory burden of chronic periodontal disease has an important systemic impact.

Conclusion: Oral-systemic links are multifaceted and complex. While evidence linking periodontal disease with a variety of systemic conditions is still emerging, the nature of the relationship is becoming clearer. The updated understanding of these associations warrants the attention of medical experts and policymakers for a concerted effort to develop a patient-centric, integrated model for the treatment of comorbid dental and medical conditions.

Ann Acad Med Singap 2022;51:567-74

Keywords: Cardiovascular diseases, dentistry, diabetes, oral health, periodontal diseases, systemic diseases

INTRODUCTION

Care for the oral cavity lies in the intersection of dentistry and medicine. As the oral cavity serves as an entry to the gastrointestinal tract and the point where the digestion process begins, it is often recognised as an important gateway to dietary and nutritional health. Oral health, however, is also relevant to other aspects of general health. A potential impact of oral infections on systemic health was revealed centuries ago when Hippocrates reportedly cured a patient's rheumatism by pulling out an infected tooth.[1] Nevertheless, the implications of oral health on general health were not fully appreciated until a sizeable body of scientific evidence in the last 3 decades pointed towards a strong oral-systemic link.[2,3]

In particular, periodontal disease, a highly prevalent chronic inflammatory disease of tooth-supporting structures,[4] has been linked to a wide range of common medical conditions.[5,6] Scientific evidence suggests periodontal disease to be associated with type 2 diabetes mellitus (T2DM),[7] cardiovascular disease[8] and adverse pregnancy outcomes,[9] among others. Due to the large volume of data on oral-systemic links accumulated over the last decades, there is a need to closely assess the evidence, interpret the findings in clinical context, and provide medical practitioners with a holistic yet succinct overview. Hence, this narrative review aims to appraise and synthesise evidence on links between periodontal disease and common medical conditions,

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CLINICAL IMPACT

What is New

- Systemic health is closely linked to the state of the oral cavity. Pathologic conditions in the mouth may alter the risk and treatment outcomes of systemic conditions.

Clinical Implications

- Healthcare practitioners are encouraged to proactively engage and educate patients to be more aware of the common signs of periodontal disease and seek necessary dental care in a timely manner.
- As there are common risk factors for periodontal disease and many systemic chronic conditions, medical-dental collaboration for co-management of medical and dental conditions may optimise treatment outcomes, as advocated in some international clinical guidelines.

and provide an update on recent findings reported in literature.

Singapore's population is rapidly ageing, and the burden of periodontal disease and chronic systemic diseases, such as diabetes and cardiometabolic diseases, are expected to significantly increase in the foreseeable future.[10,11] There is a pressing need to address the challenges of prevalent comorbid conditions in order to deliver comprehensive care and improve healthcare outcomes in the Singapore population.

METHOD

Data are compiled from latest prospective cohort studies or randomised controlled trials published from 2000–2021 by searching PubMed, Medline and Google Scholar. Scientific evidence and key findings on associations between periodontal disease and systemic conditions were assessed, synthesised and critically appraised.

RESULTS

Periodontal disease: Pathogenesis and prevalence

Periodontal disease is a chronic inflammatory disease affecting the supporting structures of the teeth. Often referred to as "gum disease", periodontal disease is, however, not confined to the gums. It is characterised by progressive destruction of the whole periodontium, which comprises both soft and hard tissues (i.e. gingiva, cementum, periodontal ligament and alveolar bone).[4]

Fig. 1 highlights the clinical signs of various stages of periodontal disease, ranging from gingivitis to mild, moderate and severe periodontitis. The initial stage of periodontal disease, limited to the soft tissue (gums), is called "gingivitis" and is clinically manifested as red/swollen gums that bleed after toothbrushing. In susceptible individuals, dysregulation of inflammatory and immune pathways leads to chronic inflammation and destruction of periodontal tissues, resulting in an advanced form of the disease known as "periodontitis". Common clinical manifestations of periodontitis include (1) swollen, red gums and periodontal abscesses; (2) disruption of clinical attachment of gums from the tooth surface, resulting in periodontal pockets and receding gums; and (3) tooth migration, tooth mobility and subsequent tooth loss.

Periodontal disease is initiated by uncontrolled inflammatory response to constant colonisation of pathogenic bacteria at the tooth-gum margin.[12] Although bacterial infection is a necessary condition, it is the host's inflammatory response to the microbial challenge that is responsible for the progression of periodontal degradation. Bacterial pathogens trigger the leukocytes of the innate immune system to release pro-inflammatory mediators, such as cytokines, which play an essential role in the progression of periodontal disease. The inflammatory response to periodontal bacteria or their by-products may have systemic effects.[13] This seemingly mild, localised periodontal inflammation could trigger a chronic generalised hyperinflammation condition, disrupt the innate and adaptive immune system, and may cause or aggravate other systemic health issues.

Periodontal disease is very common, with severe periodontitis ranked as the world's 6th most prevalent health condition.[14] Around 1.1 billion cases of severe periodontal disease were reported in 2019, equivalent to approximately 15% of the global population.[15] In Singapore, a nationwide oral health survey conducted by the Health Promotion Board in 2003 revealed that 8.5 out of 10 adults suffered from mild to moderately severe forms of periodontal disease.[16] Another survey led by the Ministry of Community Development, Youth and Sports in 2009 reported that about one-third of community-dwelling older adults were completely toothless (edentulous)[17]—a surrogate marker for dental caries and periodontal disease, which are the main causes of tooth loss. Periodontitis commonly develops in

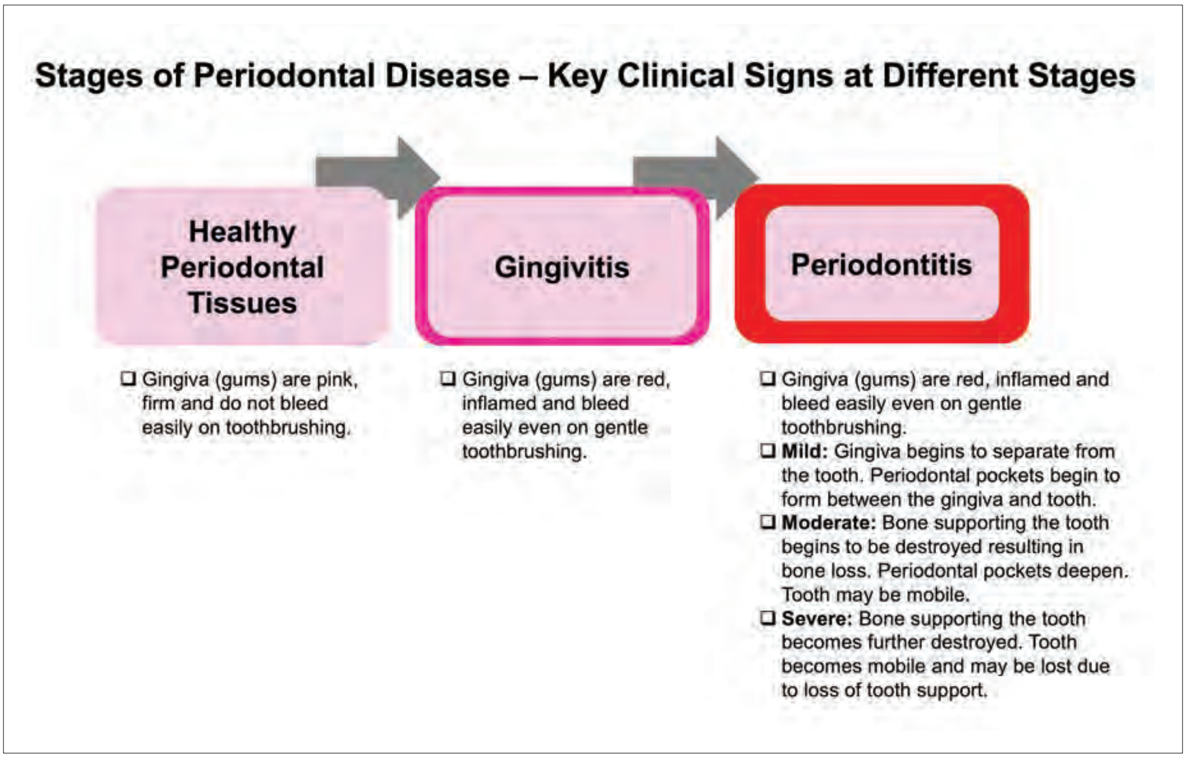

Fig. 1. Stages of periodontal disease and clinical signs.

the 4th decade of life and its prevalence increases with age. It has been projected that periodontitis will remain a salient health challenge worldwide, especially when more people are able to retain their teeth until later in life.[14]

Periodontal disease and diabetes mellitus: A bidirectional relationship

Among all possible links between oral conditions and general health, the relationship between periodontal disease and T2DM is undoubtedly the most well-established, and attracts the most scholarly and clinical attention. The link between these 2 diseases appears to be a 2-way relationship.[18] Individuals with periodontal disease exhibited poorer glycaemic control and have 19–33% higher risk of developing diabetes,[19] with the highest incidence reported in those with severe periodontal disease.[20,21] Also, presence of periodontal disease has been found to increase the risk of T2DM complications, such as macroalbuminuria, end-stage renal disease and cardiorenal mortality (ischaemic heart disease and diabetic nephropathy combined), by 2–3 times.[18] Conversely, T2DM also increases the risk of periodontal disease by 2–3 times, with a clear link between the degree of hyperglycaemia, and the onset, extent and severity of periodontal disease.[22] As such, periodontal disease has been reported as the 6th complication of T2DM, apart from the 5 known systemic complications, namely retinopathy, neuropathy, nephropathy, cardiovascular disease and peripheral vascular disease.[23]

Findings of mechanistic studies indicate that T2DM leads to a hyperinflammatory response to periodontal microbiota, and impairs resolution of inflammation and repair, which results in accelerated periodontal tissue destruction.[24] On the other hand, the effect of periodontal disease on T2DM can be partially explained by a corresponding increase in systemic pro-inflammatory mediators, which potentially exacerbates insulin resistance.[25]

Recent clinical trials in T2DM patients have shown that non-surgical periodontal therapy (for example, scaling and root planing performed by dentists) resulted in a reduction in haemoglobin A1c (HbA1c), ranging from 0.5%[26] to 1.5%[27] at 3 months—a clinical impact equivalent to adding a second drug to the pharmacological regime for diabetes.[28] Periodontal therapy has also reduced serum inflammatory markers, such as high-sensitivity C-reactive protein,[26,29,30] granulocyte colony-stimulating factor[31] and interleukin-6/tumour necrosis factor α (TNF-α),[26] at 3–6 months post-intervention. It is likely that periodontal therapy improves glycaemic control, through reduced levels of serum inflammatory markers and/or improved insulin resistance.[32] The updated evidence from these studies reaffirms that routine in-clinic periodontal treatment procedures have a direct positive clinical effect on disease prognosis of T2DM patients.[33]

Collectively, recent and consistent findings from clinical studies indicate a strong association of periodontal disease with T2DM. Possible confounders, such as sociodemographic factors and oral health behaviours, are commonly controlled in most of these reported studies. Mechanistic studies have shed light on a biological plausibility for the link between periodontal disease and T2DM, and the number of long-term (>5 years) cohort studies is increasing. This supports a temporal relationship, along with a dose-response relationship between increasing severity of periodontal disease and risk of T2DM (online Supplementary Materials, Table S1). The link between periodontal disease and T2DM is also supported by clinical trials showing positive diabetic management after periodontal therapies (online Supplementary Table S1).

Periodontal disease and cardiovascular diseases

Periodontal disease has also been identified as an independent risk factor for the development of atherosclerotic vascular disease, with systemic inflammation suggested as a potential underlying mechanism.[8,34] Pooled analysis of observational studies showed a 34% increased risk of developing cardiovascular disease in individuals with existing periodontal disease.[35] Recent large-scale cohort studies with >10 years of follow-ups in American and Korean populations reported a 2-fold increased risk of stroke (for both cardioembolic and thrombotic subtypes),[36] and increased risk of myocardial infarction and stroke in those with severe periodontal disease, respectively.[37] A recent meta-analysis has associated tooth loss, which is a common sequela of severe periodontal disease, with increased risk of cardiovascular disease and stroke, along with a dose-response relationship (i.e. every 2 subsequent teeth lost was associated with a 3% higher risk of coronary heart disease and a 3% higher risk of stroke).[38] Low-grade systemic inflammation and redox imbalance are plausible mechanisms for links between periodontal disease with hypertension and/or endothelial dysfunction,[39] with the effect mediated by inflammatory markers.[40]

Clinical trials have shown that professional dental prophylaxis and intensive periodontal therapy resulted in short-term improvement in surrogate markers of cardiovascular diseases, such as improvement in endothelial function by 1.7%[41] and 3.7%,[42] and reduction in blood pressure by 7mmHg[35,43] and 12mmHg.[44] More importantly, periodontal therapy has resulted in 10–14% reduction in the incidence of major cardiovascular events across over 10 years of follow-up period.[45-47] Encouraging patients to maintain good personal oral hygiene may be beneficial for general health, as individuals who never/rarely brushed their teeth had 70% higher incidence of coronary heart disease, compared to those who brushed frequently (twice a day).[48] Recently, frequent toothbrushing (≥3 times a day) was associated with 10% and 12% lower risk of atrial fibrillation and heart failure, respectively, in a nationwide cohort study in a Korean population.[49]

In summary, evidence from long-term (>5 years) cohort studies supports a temporal relationship between periodontal disease and development of cardiovascular disease (online Supplementary Table S2). Routine periodontal therapy has been shown to improve cardiovascular disease markers, such as increased endothelial function and decreased blood pressure (online Supplementary Table S2). Since T2DM is also an independent predictor of cerebrovascular/coronary diseases,[50] timely periodontal therapy is likely to have multiple systemic benefits in such comorbid conditions. As for possible mechanisms, it has been indicated that periodontal therapy reduces the risk of atherogenic vascular disease by improving the plasma levels of inflammatory (C-reactive protein and TNF-α) and metabolic markers (triglycerides and HbA1c), and endothelial function.[51]

Periodontal disease and adverse pregnancy outcomes

Epidemiological studies predominantly support a positive association between maternal periodontal disease and adverse pregnancy outcomes. Pregnant women with periodontal disease have exhibited a 2-fold risk of preterm birth,[52] preeclampsia[53] and low-birth-weight babies.[54] Periodontal disease is posited to affect maternal and fetal immune responses systemically, leading to premature labour, while oral bacteria may translocate directly into the pregnant uterus, causing localised inflammation and adverse pregnancy outcome.[55]

Although successful treatment of periodontal disease has improved pregnancy outcomes, such as through reduced risk of preterm birth,[56-58] the evidence still remains inconclusive as no effect was seen in some trials.[59-61] The type of periodontal treatment and its timing during pregnancy may be critical in its effect on individual pregnancy outcomes.[62] Collectively, current evidence supports that periodontal disease, especially severe forms during pregnancy, is an independent risk factor for adverse pregnancy outcomes, with timely periodontal therapy potentially useful in mitigating its deleterious effect. Additional data from future observational studies (with a temporal study design) and/or clinical trials (showing positive treatment benefits) are needed to investigate potential causal relationship.

Periodontal condition and respiratory diseases

Periodontal disease has been reported as an independent risk factor for chronic obstructive pulmonary disease (COPD), with a 2-fold increased risk of COPD in individuals with periodontal disease, after controlling for common confounders, such as smoking.[63] A recent meta-analysis of observational studies has shown a 50% increased risk of lung cancer among individuals with periodontal disease and an almost 2-fold increased risk in edentulous individuals.[64] Current evidence has also linked periodontal disease with asthma, with significant differences in periodontal parameters between asthmatic and non-asthmatic patients.[65]

Poor oral hygiene may also increase the risk of bacterial pneumonia and mortality. Higher risk of aspiration pneumonia,[66] and infectious and cardiovascular complications were observed among stroke survivors with poor oral hygiene following hospital discharge.[67] For edentulous individuals, good tongue hygiene has been shown to substantially lower the risk of developing aspiration pneumonia by almost 88%.[68] It seems imperative to incorporate oral hygiene care as part of post-stroke rehabilitation to prevent complications that could impair recovery and/or longevity.

Periodontal disease and other systemic conditions

Emerging evidence suggests that periodontal disease may be linked to various other systemic conditions. Recent meta-analyses of observational studies demonstrated increased risk of Alzheimer’s disease,[69] chronic kidney disease,[69] rheumatoid arthritis[70] and liver cirrhosis,[71] in individuals with periodontal disease, especially those with severe periodontitis.

Clinical and policy implications

Even though oral diseases are highly prevalent, affecting 3.5 billion people worldwide, they are largely neglected and rarely viewed as a part of mainstream healthcare practice and policy.[72] The emerging evidence clearly indicates that pathologic conditions in the mouth have a much greater systemic impact than many would usually expect.[73,74] This rapidly accumulating and compelling evidence has several clinical and policy implications.

Awareness and knowledge of oral health among healthcare practitioners is observed to be inadequate.[75,76] Informing practitioners about the general health impact of oral infections may assist them to develop a more holistic plan for clinical management. Such awareness about oral-systemic links would also encourage practitioners to proactively engage and educate patients to be more aware of the common signs of periodontal disease (e.g. red/swollen gums, loose teeth, etc.) and seek dental care in a timely manner.

Inter-professional collaboration and partnership are advocated for the co-management of medical and dental conditions that are linked, but currently managed by separate groups of healthcare professionals.[77,78] Closer communication, information exchange and decision support will contribute to better quality of care and optimised healthcare outcomes. Co-management of diabetes and periodontal disease, through a multidisciplinary approach, has been advocated by the International Diabetes Federation and the European Federation of Periodontology in their recent consensus report and guidelines.[79] Periodontal screening and non-surgical periodontal therapy have also been recommended as part of antenatal care, at least before the second trimester of pregnancy, to minimise the potential deleterious effects of active periodontal disease on neonatal/perinatal outcomes.[80]

Finally, policy initiatives will be the keys to success in order to catalyse positive changes in practice. There is a need to develop referral channels for patients suffering from comorbid dental and medical conditions, to enable and support care integration and care transition. Singapore has made a significant move towards integrated care by colocating dental services with medical services in the polyclinics. With this, dental prophylaxis and periodontal therapy can be integrated into primary care.[81] Strategies to incentivise holistic care, such as through subsidies for patients with complex medical needs and prioritisation of inter-professional appointments, can be explored. Evidence of oral-systemic links can be introduced to the undergraduate curriculum, postgraduate courses and continuing professional education programmes to better equip future and current practitioners for integrated patient care.[77]

CONCLUSION

The links between oral conditions and general health are multifaceted and complex. While evidence linking periodontal disease with a variety of systemic conditions continues to emerge, recent findings are pointing towards a robust relationship. Current understanding indicates that successful control of periodontal infections and dental prophylaxis improves diabetic, cardiovascular and pregnancy outcomes. The links between oral infections and major systemic diseases will likely encourage stakeholders (research, academic and clinical communities, as well as governmental organisations and civil society) to make a concerted effort towards developing a sustainable, patient-centric model for managing comorbid dental and medical conditions.

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Ann Acad Med Singap 2022;51:575-7
https://doi.org/10.47102/annals-acadmedsg.2022168

LETTER TO THE EDITOR

High burden of respiratory viral infection-associated mortality among critically ill children

Dear Editor,

Acute lower respiratory infections (ALRIs) are a leading cause of under-5 mortality globally—two-thirds could be attributable to respiratory viral infections (RVIs).[1,2] The burden of paediatric RVIs in settings of tropical climate with year-long virus circulation is relatively underreported.[3,4] Previous studies in these areas have estimated that around 8–11% of RVI-associated ALRI admission required intensive care.[5,6]

In this study, we describe the burden and epidemiology of RVI-associated mortalities among critically ill patients admitted to a paediatric intensive care unit (PICU) in Singapore.

We conducted a retrospective single-centre cohort study of children ≤18 years admitted to a 16-bedded PICU from 1 January 2010 to 31 December 2019. RVI-associated mortality was defined as any PICU mortality occurring with laboratory-confirmed RVI within 14 days prior to the certified date of mortality. Each case was reviewed and verified individually, to confirm that an RVI was either the primary cause or a significant contributor to the mortality as recorded by the clinical team in medical charts. The study team was blinded to all causes of death information at the time of data matching. Nosocomial RVI was defined as an infection with positive viral testing >72 hours of hospital admission. Pre-existing patient comorbidities were classified as complex chronic conditions (CCC) or non-complex chronic conditions (NCCC), to gauge the severity of individual comorbidities.[7]

RVI detection was by direct fluorescent antibody and/or polymerase chain reaction at the discretion of the admitting physician. The RVI-associated mortality rate (per 1,000 admissions) was calculated thus:

$$\frac{\text{no. of PICU RVI-associated mortality}}{\text{total PICU admissions}} \times 1000$$

Poisson regression was performed to determine the significance of RVI-associated mortality trends over the study period using SAS version 9.4 (SAS Institute Inc, Cary, US). A *P* value of <0.05 was considered statistically significant. This study received ethical approval from the Singapore Health Services (SingHealth CIRB Ref No. 2019/2686).

Results. A total of 6,101 paediatric patients were admitted to our PICU over the study period, with an overall PICU mortality rate of 5.6% (339/6,101). Of these, 19.8% (67/339) were determined to have an RVI-associated mortality as per our case definition above (overall rate 11 per 1,000 PICU admissions). RVI was a listed cause of death by the clinical team in 59 of the 67 (88.1%) patients. The other 8 cases had an RVI diagnosed around the time of respiratory support escalation, increased inotropic support or deterioration of their overall clinical course. The RVI-associated mortality rate increased significantly from 9.4 to 15.2 over the study period (F-test *P*=0.03) (Supplementary Fig. S1 in online Supplementary Material). Children with RVI-associated mortality had a median age of 3.5 years (interquartile range [IQR] 0.5–8), with 45/67 (67.1%) being <5 years. The median interval between RVI detection and mortality was 5 days (IQR 2–8), and the median length of hospital stay prior to death was 8 days (IQR 3–15).

Fifty-five (82.1%) of the 67 patients with RVI-associated mortality required mechanical ventilation during admission (Table 1). Forty (59.7%) patients had pre-existing comorbidities and 9 (13.4%) were palliative care patients. Of patients with pre-existing comorbidities, 39 had CCCs, under these most common categories: neuromuscular (30.6%), respiratory (20.8%), oncologic (12.5%) and cardiovascular (12.5%). A total of 23/67 (34.3%) patients were born preterm (mean birth gestation 29 weeks): 8/23 (34.8%) had chronic lung disease and 4/23 (17.4%) had cerebral palsy.

The primary documented causes of death among the patients were: infection (n=53, 79.1%), cardiovascular (n=6, 9.0%), oncologic (n=3, 4.5%), respiratory (n=2, 3.0%), neuromuscular (n=2, 3.0%) and gastrointestinal (n=1, 1.5%). Among the 53 patients with infection as a primary cause of death, 7 (13.2%) had a bacterial infection and positive blood culture within 3 days of the RVI diagnosis. The positive bacterial cultures included *Pseudomonas aeruginosa* (n=3), *Streptococcus pneumoniae* (n=1), *Staphylococcus aureus* (n=1), *Klebsiella pneumoniae* (n=1) and *Mycobacterium bovis* (n=1).

Influenza (22.7%), adenovirus (17.3%), respiratory syncytial virus (RSV) (16.0%) and rhinovirus (16.0%), accounted for 72.0% of all RVIs detected. Eight patients (11.9%) had virus coinfection, with rhinovirus (n=6, 37.5%) and bocavirus (n=3, 18.8%) the most common viruses isolated in these cases. Twenty-one

Table 1. Characteristics of patients with respiratory viral infection-associated mortalities

Characteristics	**No. (%) N=67**
Male sex	38 (56.7)
Preterm birth (<37 weeks gestation)	23 (34.3)
Age at time of infection	
≤30 days	1 (1.5)
30 days – 1 year	23 (34.3)
2–5 years	21 (31.3)
6–10 years	10 (14.9)
11–18 years	12 (17.9)
Mechanical ventilation during admission	55 (82.1)
Presence of pre-existing comorbidities	40 (59.7)
1 condition	11 (16.4)
2 conditions	10 (14.9)
>2 conditions	19 (28.4)
Palliative care	9 (13.4)
Nosocomial infection	21 (31.3)
Types of complex chronic condition	22 (30.6)
Neuromuscular	15 (20.8)
Respiratory	9 (12.5)
Cardiovascular	9 (12.5)
Oncologic	8 (11.1)
Genetic	5 (6.9)
Gastrointestinal	1 (1.4)
Metabolic	1 (1.4)
Immunologic	1 (1.4)
Haematologic	1 (1.4)
Endocrinology	

patients (31.3%) had nosocomial RVI, predominantly with adenovirus (33.3%), RSV (19.0%) and rhinovirus (19.0%). When stratified by the most common infecting RVI pathogen, the median age of infection was: influenza (6 years, IQR 3–12), adenovirus (4.5 years, IQR 2–9), RSV (0.9 year, IQR 0.5–3) and rhinovirus (2 years, IQR 1–6). Among those who were born premature (n=23), the most common RVI pathogens were influenza (n=6, 26.1%), adenovirus (n=6, 26.1%) and RSV (n=4, 17.4%).

Discussion. The burden of RVI-associated mortality among critically ill children in our setting was high, accounting for up to 20% of all PICU mortality. A significant proportion of these patients were born preterm (34.3%) and had comorbid conditions (60.0%). The overall PICU RVI-associated mortality rate of 1.1% in our study is at the lower end of previously reported rates of 0.3–17%.[5,6,8,9] The predominance of influenza (22.7%), adenovirus (17.3%) and rhinovirus (16.0%) in our cohort differs from previous reports that described a predominance of RSV infections (38–49.0%).[6,7] Almost all previous reports on the incidence of RVI-associated mortalities were from facilities located in regions with temperate or subtropical climes. Additionally, differences in viral distribution between studies could be attributed to differences in the study population (exclusion of children with comorbidities), climate[3] and vaccination rates.[7] Although seasonal influenza vaccination is recommended for pregnant mothers and children aged 6–59 months in Singapore, studies have found that the uptake was only about 10% and 15%, respectively.[10] Additionally, the local rates of palivizumab vaccination among eligible preterm infants have been reported to range from 17–39% annually.[11]

The median age of RVI-associated mortality among children with influenza and RSV in our cohort was 5.7 years and 0.9 year, respectively, which is similar to previous studies.[6,12] In a study of 49 children in Hong Kong, the reported age of RVI-associated mortality was 5.6 years and 1.2 years for influenza and RSV, respectively.[6] Neuromuscular conditions were the most prevalent comorbidity seen in this cohort of RVI-associated mortalities. Patients with neuromuscular weakness may have respiratory muscle involvement, resulting in suboptimal pulmonary mechanics and a weaker cough reflex, leading to a higher predisposition to atelectasis, aspiration pneumonia and respiratory failure.

The small sample size, retrospective study design, lack of data on the usage of antiviral medications or vaccinations, and the limited granular clinical details limit the overall generalisability and the ability to delineate the risk factors associated with such mortalities. However, the 10-year duration of this study from the largest PICU in Singapore provides a reasonable estimate of the mortality burden among critically ill children living in a tropical climate with year-long transmission of such viruses. The high RVI burden from RSV and influenza in this population of patients could potentially be mitigated by improved influenza vaccination rates and the effective use of monoclonal antibodies such as palivizumab against RSV.

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Ann Acad Med Singap 2022;51:578-9
https://doi.org/10.47102/annals-acadmedsg.2022148

Employers' attitudes towards employing people with mental health conditions

Dear Editor,

The advantages of employment for young people with mental health conditions (PMHC) are well known and documented,[1] but many remain unemployed. Besides offering monetary benefits, employment provides a better self and social identity, helps the person gain a sense of personal achievement, and enhances mental well-being. Being unemployed is a crucial risk factor for individuals' poor mental health. Several studies have explored employers' attitudes towards hiring PMHC,[2,3] with most studies reporting negative attitudes. Compared to Western employers, employers from Asian countries perceived PMHC as less loyal and having poorer work ethics.

Studies conducted in Singapore have found that stigma and discrimination were among the most mentioned employment concerns for young people with mental health conditions, and only 1 in 2 adults surveyed was willing to live nearby or work with a person with a mental health condition.[4] Singapore's unemployment rate was 3.8% in 2021, which is lower than other developed countries, such as the US' 5.4%.[4] Nevertheless, unemployment rates among PMHC remain higher than in those without mental health conditions.[3] PMHC felt discriminated by the requirement for declaration of their psychiatric history during job interviews and believed that they were procedurally removed from consideration. Employment support specialists in Singapore found that limited career options due to perceived stigma and high-performance expectations by employers often posed significant challenges for PMHC seeking employment as well as in sustaining their jobs.[5]

This was a cross-sectional study using convenience sampling to examine the attitudes among employers in Singapore towards hiring PMHC, and we explored sociodemographic and organisational correlates of these attitudes among employers. A 13-item questionnaire was adapted from the Shaw Trust Employment Survey[6] from the UK to examine the attitudes and a total of 151 respondents gave consent and completed the online structured questionnaire.

The majority of respondents were female (n=89, 58.9%), Chinese (n=122, 80.8%), married (n=119, 78.8%), and had tertiary education (n=116, 76.8%). The mean age of the sample was 42.1 (±10.4) with a range of 24 to 76 years.

Factor analysis revealed that a 2-factor solution was most optimal, for the scale. The 2 factors were named as negative attitudes and supportive workplace. Levels of agreement with each of the questionnaire statements are provided in Table 1. Results of the linear regression analyses revealed that compared to those who had close associates (work colleagues, clients) with mental health conditions compared to those who did not have close associates were associated with lower scores on the negative attitude factor (B = -2.5, 95% confidence interval [CI] -4.9 to -0.2, *P*=0.035). While compared to females, males were associated with higher scores on the supportive workplace factor (B=1.5, 95% CI 0.004 –2.9, *P*=0.049), and compared to those with tertiary education, those without tertiary education were associated with higher scores on the supportive workplace factor (B=1.7, 95% CI 0.1–3.4, *P*=0.039).

Our study found that most employers in Singapore remained neutral (41.3%) when asked if organisations provided adequate support for managers dealing with staff who have mental health conditions. This suggests that despite multitudinous employment support programmes in Singapore, few catered for supporting employers to hire people with mental health conditions. About half of employers in the Singapore study sample disagreed (versus 10.6% agree) that managers/staff in their organisation have a good understanding of mental health conditions, whereas only 15% of UK employers disagreed (vs 63% agree)[6] with the statement. These findings reflect that there is ample room to increase efforts aimed at mental health education in workplaces in Singapore.

The study found a significant association between employers' negative attitudes towards PMHC and their experiences of working/interacting with colleagues/clients who had mental health conditions. Existing Singapore literature has found that educational programmes incorporating personal contact with PMHC effectively reduce personally held stigmatising beliefs and attitudes.[7] However, personal encounters with more severe mental health conditions may result in negative attitudes. Certain conditions need to be in place for practical contact-based learning experiences. Some of the requirements include the credibility of the speaker, relevance to the audience, and disclosure of personal struggles and successes in the area of employment.

Males, compared to females, were more supportive of individuals with mental health conditions in the workplace. They felt more comfortable talking about mental health at the workplace with employees as well as in interviews with applicants. There is mixed literature on sex differences in attitudes towards mental health conditions. On the one hand, there is no association between sex and attitudes towards mental health conditions.[8] On the other, more negative attitudes are found among male managers than in female managers.[9] The study also found that employers without tertiary education were more supportive of individuals with mental health conditions at the workplace than employers with tertiary education. This contradicts a Singapore study,[10] which found that people with lower educational backgrounds tend to have more negative attitudes towards people with mental health problems. More research is needed to investigate the determinants of such a relationship.

The current study employed convenience sampling; thus, it is not representative, and the results cannot be generalised. In addition, there might be a social desirability bias, wherein the employers provided favourable answers.

The study findings provide evidence to policy and decision-makers when planning interventional programmes for stigma reduction. Incorporating contact with PHMC would be effective in reconstructing people's cognitive understanding and help de-stigmatisation. Tailoring the programmes to different sociodemographic groups should also be considered. Organisations should also be more proactive in engaging their employers with mental health wellness programmes (e.g. improving mental health literacy, and mental health first aid for staff) available in Singapore to make the working environment more conducive for PHMC.

Funding

This study was supported by funding from the National Council of Social Service, Singapore.

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Ann Acad Med Singap 2022;51:580-2
https://doi.org/10.47102/annals-acadmedsg.202282

LETTER TO THE EDITOR

Safety and efficacy of combined antiplatelet and low-dose rivaroxaban in patients with chronic limb threatening ischaemia in Singapore

Dear Editor,

Peripheral artery disease (PAD) is characterised by the debilitating atherosclerotic occlusion of arteries in the lower extremities, with chronic limb threatening ischaemia (CLTI) representing the most advanced stage of this disease process. Left untreated, these sequelae will invariably progress to major lower extremity amputation (LEA) and premature death. In Singapore, the rate of major LEA from vascular causes is 2- to 3-fold higher than in Western countries, ranking it one of the highest in the world.[1]

The high prevalence of diabetes mellitus among PAD patients in Singapore probably accounts for the exceptionally high rate of major LEA. A recent large prospective cohort study revealed that diabetes is associated with the highest estimated risk for developing severe CLTI, conferring more than a 10-fold increase in CLTI-associated major LEA.[2] The tissue ulceration and wound infections that commonly plague diabetic patients likely contribute to this elevated risk. Peripheral arterial occlusive disease in diabetics preferentially affects the distal small vessels, with a high proportion of patients harbouring multilevel or long-segment femoropopliteal-tibial lesions.[3] Open or endovascular revascularisation is offered to these patients with the aim of preventing or limiting tissue loss. Unfortunately, their disease morphology often poses a significant technical challenge, thus limiting the therapeutic benefit achieved by surgical intervention.[3] Even with successful revascularisation, these patients remain at a higher risk for subsequent vascular complications, such as an increased risk of acute limb ischaemia, and consequently, prolonged hospitalisation with a higher incidence of limb loss and death. There is therefore an urgent need for strategies to reduce the risk of major LEA and PAD-associated mortality in patients with severe CLTI.

Successful risk modification of acute limb ischaemia in patients with PAD was first demonstrated by the Cardiovascular Outcomes for People Using Anticoagulation Strategies (COMPASS) trial.[4] Through the addition of low-dose rivaroxaban (2.5mg twice daily) to aspirin, ischaemic risk—including the risk of major adverse limb events—was lowered in a population with chronic stable PAD. Thereafter, the Vascular Outcomes Study of Acetylsalicylic Acid (ASA) Along with Rivaroxaban in Endovascular or Surgical Limb Revascularization for PAD (VOYAGER PAD) trial tested the effect of combined antiplatelet and antithrombotic drug treatment on cardiovascular risk modification in patients with symptomatic PAD post-revascularisation.[5] The study demonstrated that low-dose rivaroxaban plus aspirin significantly lowered the incidence of the composite primary endpoint of myocardial ischaemia, ischaemic stroke, major amputation and cardiovascular mortality when compared to aspirin alone. This significant reduction of 15% was heavily influenced by the reduction of acute limb ischaemia. Crucially, the primary safety outcome of major bleeding was not significantly different between the 2 study arms.

The landmark study showed medical therapy improved the outcomes of post-revascularisation PAD patients. However, in contrast to our Singapore population of PAD patients, the trial recruited mostly instead of claudicants, which is not a common term, in which there was also a lower prevalence of diabetes (40% versus 80%) and chronic renal failure (27% vs 50%).[6] Given these marked differences, we sought to validate the applicability of the VOYAGER PAD dual-drug regimen in our Asian population with different disease-related histories and pharmaco-genomic profiles.

In a joint collaborative effort, 37 patients with PAD were recruited post-revascularisation from 2 tertiary vascular centres in Singapore (Singapore General Hospital and National University Hospital) and followed up for a median of 11.7±4.1 months until November 2021. The patients' baseline demographics are shown in Table 1. Of note, nearly 90% of patients were diabetic, of whom nearly half were insulin-dependent. The average wound, ischaemia, and foot infection (WIfI) score in our cohort was 3.41±2.13, with a median score of 3 (interquartile range 2–5). Twenty patients (54.1%) underwent revascularisation for multilevel disease, where the average lesion length was 175.9±142.1mm. The overall mortality rate over the study period was 8.1%. Amputation-free survival (AFS) was 86.5% with an average time interval of 6.1 months to major amputation in 5 patients. Of note, this was much lower than the estimated 3-year AFS of 97.9% of the intervention arm of the VOYAGER cohort. Freedom from target lesion recurrence was 70.2% with an

Table 1. Baseline demographics

Characteristics	No. of patients (%) N=37
Age, mean±SD, years	67±8.3
BMI, mean±SD, kg/m^2	23.8±4.2
Male sex	30 (81.1)
Ethnic group	
Chinese	25 (67.8)
Malay	1 (2.7)
Indian	11 (29.7)
Smoking status	
Smoker	10 (27.0)
Non-smoker	11 (29.7)
Ex-smoker	16 (43.2)
Comorbidities	
Diabetes	33 (89.2)
Hypercholesterolaemia	31 (83.8)
Hypertension	32 (86.5)
Cerebrovascular accident	5 (13.5)
Myocardial infarction	13 (35.1)
End-stage renal failure	2 (5.4)
Medication history	
Insulin	14 (37.8)
Oral diabetes mellitus medications	23 (62.2)
Angiotensin receptor blockers	10 (27.0)
Angiotensin-converting enzyme inhibitors	11 (29.7)
Statins	31 (83.8)
Beta-blockers	19 (51.4)
Calcium channel blockers	15 (40.5)
Diuretics	9 (24.3)
Nitrates	10 (27.0)
Aspirin	27 (73.0)
Clopidogrel	18 (48.6)
Rutherford classification	
2 (moderate claudication)	4 (10.8)
3 (severe claudication)	10 (27.0)
4 (ischaemic rest pain)	6 (16.2)
5 (minor tissue loss)	12 (32.4)
6 (major tissue loss)	5 (13.5)

average time interval of 5.4 months to revascularisation in 11 patients. There was a substantial improvement in the mean Rutherford score from 4.11 to 2.81, with 56.3% of patients showing an improvement of ≥1 Rutherford class.

Serial evidence has suggested an increased risk of bleeding with novel oral anticoagulants (NOACs) in Asians compared to non-Asians.[7] However, there were no major bleeding events reported in this study. Anaemia was noted in 2 patients who were initiated on the VOYAGER regimen; however, no definite sources of bleeding were identified. Despite the lack of bleeding events reported, rivaroxaban was stopped in favour of a single antiplatelet regimen of aspirin in 5 patients, and switched to clopidogrel in 3 patients. The treatment amendments probably reflect the perceived increase in bleeding risk associated with this dual-drug regimen.

Recently published data from the Singapore chapter of the Society for Vascular Surgery Vascular Quality Initiative database found that only 1.9% of patients were placed on the low-dose rivaroxaban regimen following revascularisation.[8] Lack of awareness of the VOYAGER regimen, coupled with apprehension regarding its side effects are likely contributing factors to the limited uptake by local physicians thus far. In the small population of patients in which rivaroxaban is initiated, accessibility and affordability remain key issues in patients' adherence to treatment.[8,9]

We report the early data from the first Asian series of 37 patients, demonstrating the application of the VOYAGER regimen in post-revascularisation PAD patients. Our Singapore data suggest that the addition of low-dose rivaroxaban to aspirin is safe, with a minimal bleeding risk and provides an acceptable improvement in disease severity and AFS despite the prevalence of more severe comorbidities and complex pathology. Moving forward, we aim to undertake a propensity-matched analysis comparing CLTI patients who do not receive anticoagulation (i.e. aspirin alone) after revascularisation with those who do, in order to interrogate the true benefit of low-dose NOACs in this challenging population of patients.

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LETTER TO THE EDITOR

Ann Acad Med Singap 2022;51:583-5
https://doi.org/10.47102/annals-acadmedsg.2022163

Prevalence of perceived weight-based stigmatisation in a multiethnic Asian population

Dear Editor,

People with obesity contend with obesity-related stigmas, in addition to health complications.[1] In contrast to the West, literature documenting the prevalence of such stigmas in Asia is sparse. We report the prevalence of perceived weight-based stigmatisation in Singapore.

An anonymised questionnaire was administered to 101 consecutive patients presenting to a multidisciplinary weight management clinic in a single centre in Singapore (Table 1). It was based on the questionnaire by the UK All-Party Parliamentary Group on Obesity in 2018.[2] The questionnaire comprised demographic information, and responder's perceived stigmatisation in self (perception), social and workplace, or educational domains. A subgroup analysis was performed by segregating respondents into class I (27.5–34.9), class II (35.0–39.9) and class III (≥40.0) obesity, in accordance with the World Health Organization body mass index (BMI) cut-off points for determining overweight and obesity, but modified to the interventional thresholds recommended for Asian populations.[3]

The median age of the respondents was 39 years (interquartile range [IQR] 31.3–48.8), and the median BMI was 39.3kg/m^2 (IQR 34.3–46.3). The majority were middle-aged adults from the 31–40 (34%) and 41–50-years-old (23%) age groups, with a slight female predominance (56.4%). The highest educational qualification attained was post-secondary (non-tertiary) qualification (44.6%), and the majority of respondents were in the low-income group (64.4%). The majority of respondents were working individuals, with 10 respondents being unemployed or retired (9.9%), and 3 respondents who were homemakers (3.0%). For our population, job industries had no significant impact on income level (*P*=0.843).

More than half (54.5%) of respondents considered obesity a disease. Most respondents surveyed felt that their weight is their own responsibility (76.2%), and blamed themselves for their own weight issues (74.3%). In total, 60.4% of respondents reported that they have felt stigmatised, criticised or abused as a direct result of their weight. However, only about one-third of respondents (33.7%) reported that they have been blamed by others for their weight issues. Among respondents who felt stigmatised, the most common consequence was an affected level of confidence and sense of self-worth (86.9%). The majority of the respondents have discussed their weight issues with a healthcare provider in the past 5 years (68.3%), and most respondents were comfortable discussing their weight issues in the primary care setting (85.1%). Most respondents have not felt stigmatised in the healthcare setting. Only 21.6% reported that they were not treated with dignity and respect by healthcare professionals, or felt discouraged to discuss their weight problems with them.

There were a disproportionately larger number of Malays and Indians in the higher BMI categories compared to Chinese respondents (*P*=0.018), consistent with Singapore literature.[4] There was a larger proportion of respondents with secondary school and post-secondary school qualifications who were class III obese compared to university graduates or postgraduates (*P*=0.038). Most respondents with class III obesity belonged to the low- and middle-income groups (*P*=0.041).

One limitation of this study is the lack of representation of individuals who were not obese, as a comparison control group. In the self (perception) domain, class II obesity respondents were less likely to report that an individual's weight was solely their own responsibility (prevalence rate ratio [PRR] 0.25, 95% confidence interval [CI] 0.07–0.93, *P*=0.04) compared with class I obesity respondents. However, this was not observed in class III obesity respondents (PRR 0.95, 95% CI 0.26–3.55, *P*=0.94). A subgroup analysis revealed that 19 of the 24 (79.2%) class I obesity respondents who believed that weight is their sole responsibility have attempted weight loss, compared with only 14 of the 27 (51.9%) class II obesity respondents. This finding highlights that weight loss efforts should be targeted towards individuals in the class II obesity group to prevent them from progressing to class III obesity.

In the social domain, class III obesity respondents were more likely to report consuming unhealthy food or partaking in less exercise because of stigmatisation (PRR 10.80, 95% CI 2.36–49.46, *P*<0.01). A similar observation of a smaller extent was observed in class II obesity respondents (PRR 3.54, 95% CI 0.78–16.03, *P*=0.10). After accounting for social and demographic baseline differences, the perceived degree of stigmatisation was more pronounced in class III obesity respondents (PRR 24.94, 95% CI 3.61–172.41, *P*<0.01).

Table 1. Unadjusted and propensity score-adjusted analysis[1] on perceived stigmatisation reported by respondents across different weight categories

	Class I obesity BMI 27.5–34.9	Class II obesity BMI 35–39.9 (unadjusted)	Class III obesity BMI ≥40 (unadjusted)	Class II obesity BMI 35–39.9 (adjusted)	Class III obesity BMI ≥40 (adjusted)
	PRR (95% CI)	**PRR (95% CI)**	**PRR (95% CI)**	**PRR (95% CI)**	**PRR (95% CI)**
Self (perception) domain					
1. Do you consider obesity a disease?	1	0.79 (0.26–2.37)	1.10 (0.41–2.97)	0.84 (0.28–2.57)	0.92 (0.32–2.62)
2. Do you believe that your weight is solely your own responsibility?	1	**0.25 (0.07–0.93)**	0.95 (0.26–3.55)	**0.23 (0.06–0.87)**	0.85 (0.22–3.33)
3. Do you believe that pressures (out of your control) have affected how you manage your weight?	1	0.34 (0.09–1.28)	0.82 (0.23–3.01)	0.31 (0.08–1.20)	0.62 (0.16–2.43)
4. Do you blame yourself for your weight issues?	1	0.49 (0.15–1.61)	1.58 (0.48–5.25)	0.52 (0.15–1.79)	1.36 (0.38–4.89)
Social domain					
1. Have you ever been stigmatised, criticised, or abused as a direct result of your weight?	1	1.69 (0.55–5.26)	1.44 (0.53–3.93)	1.60 (0.51–5.03)	1.14 (0.40–3.31)
2. Has this (stigmatisation) affected your motivation to gain better health by healthy diet and exercise?	1	0.50 (0.12–2.14)	2.40 (0.57–10.05)	0.31 (0.06–1.56)	4.66 (0.86–25.38)
3. Has this (stigmatisation) led you to consume unhealthy food, overconsume food or partake in less exercise?	1	3.54 (0.78–16.03)	**10.80 (2.36–49.47)**	2.54 (0.48–13.41)	**24.94 (3.61–172.41)**
4. Has this (stigmatisation) affected your overall confidence level and sense of self-worth?	1	0.64 (0.10–4.14)	2.46 (0.31–19.68)	0.95 (0.13–7.01)	3.23 (0.31–34.31)
5. Has this (stigmatisation) caused you to have low mood or feel depressed?	1	0.38 (0.08–1.84)	1.44 (0.29–7.21)	0.46 (0.09–2.37)	1.48 (0.27–8.13)
6. Have you ever been blamed by others for your weight issues?	1	0.35 (0.09–1.35)	1.29 (0.46–3.62)	0.34 (0.08–1.37)	0.94 (0.31–2.87)
Healthcare domain					
1. Have you discussed being overweight or losing weight with a healthcare provider over the last 5 years?	1	0.40 (0.11–1.53)	0.34 (0.10–1.17)	0.38 (0.10–1.44)	0.32 (0.09–1.15)
2. Do you feel comfortable discussing your weight problems at the polyclinic?	1	0.19 (0.02–1.77)	0.18 (0.02–1.51)	0.18 (0.02–1.69)	0.24 (0.03–2.10)
3. Have you ever felt that you were not treated with dignity and respect by healthcare professionals, or discouraged to discuss your weight problems?	1	0.63 (0.13–3.13)	2.19 (0.63–7.59)	0.65 (0.13–3.27)	1.85 (0.49–6.91)
Workplace or education domain					
1. Have you ever been bullied at school because of your weight?	1	1.77 (0.53–5.92)	1.76 (0.59–5.29)	1.88 (0.55–6.40)	1.33 (0.41–4.27)
2. Have you ever missed out on jobs, overlooked for job promotions, or retrenched because of your weight?	1	3.14 (0.57–17.35)	**7.74 (1.62–36.91)**	3.34 (0.60–18.72)	**5.73 (1.16–28.47)**

BMI: body mass index; CI: confidence interval; PRR: prevalence rate ratio
[1] Propensity score was computed to adjust for all sociodemographic parameters, which include age, sex, ethnicity, education and income level. BMI 27.5–34.9 (class I obesity) was taken as the reference category.
Values in bold are statistically significant

This eating behaviour has been previously described[5] and postulated to be due to a dopamine-based reward mechanism to diminish the negative impact of such stigmatisation.[6] In addition to further weight gain, these maladaptive eating behaviours put obese individuals at increased risk of eating disorders involving bulimia, binge eating episodes and overeating,[7] as well as mental health conditions such as depression and low self-esteem.[7,8] Such weight-related prejudice may also worsen body image disturbances,[8] resulting in avoidance of exercise for fear of further stigmatisation. Ultimately, this results in a triple detriment—the first being their initial obesity; the second being their maladaptive eating and exercise behaviours that compound further weight gain; and the third the subsequent medical complications associated with further weight gain.

In the education and workplace domains, a significantly higher number of respondents with class III obesity reported missing out on jobs, being overlooked for job promotions or being retrenched, as a direct result of their weight on the unadjusted analysis (PRR 7.74, 95% CI 1.62–36.91, P=0.01). This finding persisted even after adjusting for social and demographic parameters (PRR 5.73, 95% CI 1.16–28.47, P=0.03). The perceived prevalence of stigmatisation appeared to be present among respondents with class II obesity, although it did not reach statistical significance. Since the 18th century, stereotypes of obese individuals as being lazy have been ingrained and perpetuated.[9] Such discriminatory practices at the workplace are detrimental to an individual's mental health,[10] as well as income. Individuals with lower income will resort to the consumption of inexpensive calorie-dense foods, thus worsening weight gain and further fuelling employers' stereotypes.

In conclusion, the findings suggest that obesity stigmatisation remains prevalent in Asia. Individuals with higher BMIs were more likely to report perceived workplace stigmatisation. They also had negative adaptive responses to diet and exercise in response to weight-based discrimination, independent of socioeconomic status.

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Ann Acad Med Singap 2022;51:586-8
https://doi.org/10.47102/annals-acadmedsg.202288

LETTER TO THE EDITOR

Antiphospholipid and other autoantibodies in COVID-19 patients: A Singapore series

Dear Editor,

Thrombosis is an unexpected complication of COVID-19 initially reported in 3 patients from China.[1] These patients tested positive for immunoglobulin (Ig) A anticardiolipin (ACA), IgG anti-β2-glycoprotein I antibodies (aβ2GPI) and IgA aβ2GPI, though not for the lupus anticoagulant (LAC).

In a Singapore study comprising 47,527 patients, 19 (0.04%) developed acute cerebral arterial and 4 (0.01%) developed venous thrombosis.[2] Only 3 patients in the former group and 1 in the latter group were found to have LAC, ACA or aβ2GPI (personal communication). In a meta-analysis of 28 studies, among 2,928 intensive-care COVID-19 patients, deep venous thrombosis occurred in 16.1% and pulmonary embolism in 12.6%.[3]

We sought to identify autoantibodies (antinuclear antibody [ANA], rheumatoid factor [RF], ACA and aβ2GPI) in the serum of COVID-19 patients admitted to our hospital from 21 April to 2 September 2020. During this period, the original virus strain was prevalent and all COVID-19 patients were managed in the hospital. Leftover serum samples from completed routine tests in the laboratory were used. This work is approved by the institutional review board (DSRB 2020/00741).

Healthy control sera had been collected before the pandemic for our biobank. These were from 100 volunteers (80% men) comprising Filipinos (50%), Chinese (30%), Malays (10%) and Indians (10%).

The ANA, IgA and IgM RF, and IgG and IgA aβ2GPI kits were obtained from EUROIMMUN Medizinische Labordiagnostika AG (Lübeck, Germany). The IgG and IgA ACA kits were from Inova Diagnostics Inc (San Diego, US). The method for detection was indirect immunofluorescence for ANA, and enzyme-linked immunosorbent assay for the rest. Reference values were: ANA <1/80 titre; IgA and IgM RF, IgG and IgA ACA, and IgG and IgA aβ2GPI, <20 units/mL.

There were 52 COVID-19 patients (92.3% men). The mean age was 43.8±13.3 years, ranging 22.5–95.5 years. There were 16 Bangladeshis, 24 Indians, 9 Chinese, 2 Malays and 1 Burmese. Based on clinical record charting and chest imaging, we categorised the severity of COVID-19 infection into 3 categories: asymptomatic, mid/moderate and severe/critical. For symptomatic patients, the interval between the first symptoms and blood draw was 14.3±18.6 days (range 3–93 days, 95% confidence interval 8.1–20.4).

Twenty-one patients experienced no respiratory symptoms (including 1 hospitalised for aortic thrombus), 17 developed upper respiratory tract infection, and 14 developed pneumonia. One patient died of pneumonia. Four patients (3 with pneumonia and 1 otherwise asymptomatic) were considered to have COVID-19-associated coagulopathy, based on emerging literature at the time.[4]

There is statistically significant higher prevalence of IgA RF, IgG ACA, IgA ACA, IgG aβ2GPI and IgA aβ2GPI in our COVID-19 patients compared with healthy controls (Table 1). The odds ratios are highest for IgA aβ2GPI, IgG ACA and IgG aβ2GPI. There is no difference in the prevalence of ANA and IgM RF. Almost two-thirds of the patients (63.4%) and 11% of the controls developed at least ACA or aβ2GPI antibodies. There was no association between disease severity and presence or the concentration of any autoantibodies (Table 1).

Four patients developed arterial thrombosis—2 with cerebral infarcts, 1 with right suprarenal aortic thrombosis, and 1 with abdominal aorta and right external iliac artery thrombosis. Separately, 1 patient developed pulmonary embolism. These occurred acutely, apart from the cerebral infarcts that developed 1- and 3-month post-recovery. Per the aforementioned sequence, the first patient tested positive for IgA ACA; the second IgA RF; the third IgG ACA, IgG aβ2GPI and IgA aβ2GPI; and the fourth IgA ACA, IgG aβ2GPI, IgA aβ2GPI and IgA RF. The patient with pulmonary embolism tested positive for ANA and IgA aβ2GPI. Four of the 5 patients tested positive for ≥1 antiphospholipid antibodies.

This controlled study refines our understanding of antiphospholipid antibodies in COVID-19. We showed that COVID-19 patients are highly likely to develop antiphospholipid antibodies compared with healthy controls. Autoantibodies were not generated across the board as the prevalence of ANA and RF IgM positivity was no different between patients and controls.

The lack of association between disease severity and the development of autoantibodies is consistent with

Table 1. Frequency of the autoantibodies in COVID-19 patients and healthy controls

	COVID-19 patients				Controls (n=100)	OR (95% CI) of presence of antibody in patients of all severity compared with controls	*P* value
	Asymptomatic (n=21)	Mild and moderate (n=17)	Severe and critical (n=14)	Total (n=52)			
Antinuclear antibody, no. (%)	2 (9.5)	2 (11.8)	3 (21.4)	7 (13.5)	13 (13)	1.04 (0.4–2.8)	0.936
IgA rheumatoid factor, no. (%)	9 (42.9)	6 (35.3)	6 (42.9)	21 (40.4)	10 (10)	6.10 (2.6–14.4)	<0.001
IgM rheumatoid factor, no. (%)	0	2 (11.8)	1 (7.1)	3 (5.8)	15 (15)	0.35 (0.1–1.3)	0.095
IgG anticardiolipin antibody, no. (%)	8 (38.1)	6 (35.3)	4 (28.6)	18 (34.6)	0	108 (6.3–1837)	<0.001
IgA anticardiolipin antibody, no. (%)	10 (47.6)	8 (47.1)	8 (57.1)	26 (50)	9 (9)	10.1 (4.2–24.2)	<0.001
IgG anti–β2-glycoprotein I, no. (%)	11 (52.4)	6 (35.3)	6 (42.9)	23 (44.2)	0	160 (9.4–2716)	<0.001
IgA anti–β2-glycoprotein I, no. (%)	12 (57.1)	8 (47.1)	11 (78.6)	31 (59.6)	2 (2)	72.3 (16.0–326)	<0.001

CI: confidence interval; IgA: immunoglobulin A; IgG: immunoglobulin G; IgM: immunoglobulin M; OR: odds ratio
Chi-square test was carried out for each comparison

some reports[5] and contrasts with others.[6] A meta-analysis of 21 studies completed in January 2021 concluded that the presence of ACA (IgM or IgG) and anti-β2GPI (IgM or IgG) was significantly more prevalent in critically ill COVID-19 patients, although a source of bias could be that non-critically ill patients were included in only 3 studies.[7]

Viral infections in the acute stage are associated with the generation of autoantibodies; these antibodies tend to be transient and do not cause pathology. The relative risk of developing ACA was 10.5% in individuals with human immunodeficiency virus, 6.3% with hepatitis C (HCV), 4.2% with hepatitis B (HBV) and 10.9% with Epstein-Barr virus infection. Only HCV infection was associated with aβ2GPI antibodies. Thrombosis occurs in HBV and HCV patients only.[8] Severe acute respiratory syndrome, caused by the closely related SARS-CoV virus, is also known to be associated with autoantibodies.[9] A review suggested that although antiphospholipid antibodies may be found in COVID-19 patients, they are not closely related to thrombotic events.[10]

The strengths of our study are the classification of patients by disease severity, and comparison with healthy controls. The weaknesses are the small number of patients in our convenience sample, which may have contributed to bias. The use of anticoagulation in our patients could have reduced the incidence of clinically detected thrombosis. Our findings may not be generalisable to infection by subsequent variants, such as the Delta and Omicron strains.

In conclusion, almost two-thirds of the COVID-19 patients in our cohort developed antiphospholipid autoantibodies regardless of the disease severity. These autoantibodies are not associated with thrombosis in COVID-19.

Acknowledgement

This work was supported by grants from the Tan Tock Seng Hospital Community Fund and from the Department of Rheumatology, Allergy and Immunology of the same hospital.

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Ann Acad Med Singap 2022;51:589-90
https://doi.org/10.47102/annals-acadmedsg.202298

TB or not TB? The axillary lump question

An 81-year-old woman of healthy weight presented with a 2-week history of a painless right axillary lump. Physical examination revealed a 2cm firm nodule with a central keratinous plug in the right axilla (Fig. 1). The surrounding skin was pigmented, non-tender and indurated. Sonography of the nodule demonstrated an underlying ill-defined cystic collection containing mobile echoes with surrounding skin thickening (Fig. 2). There were a few other small right axillary lymph nodes with prominent cortices in the vicinity (not shown). The patient was otherwise well and asymptomatic. Breast clinical examination, bilateral mammography and bilateral breast ultrasound were unremarkable.

What is your diagnosis?

A. Cutaneous or nodal metastasis from primary breast malignancy
B. Hidradenitis suppurativa
C. Amelanotic/hypomelanotic melanoma
D. Keratoacanthoma
E. Tuberculous scrofuloderma

Fig. 1. The painless right axillary umbilicated skin nodule with central keratin plug.

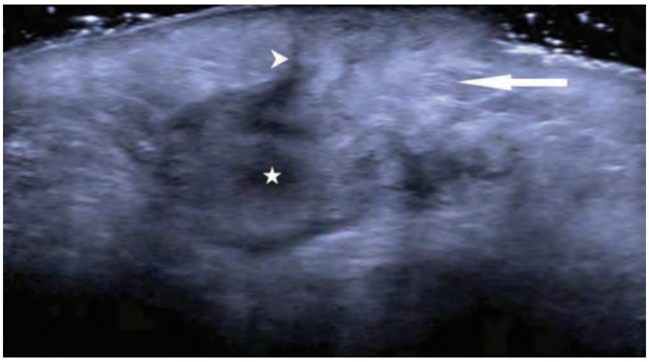

Fig. 2. Ultrasound scan over the skin nodule showing loss of skin and soft tissue planes, with echogenic thickened subcutaneous fat (arrow). An underlying 21mm ovoid cystic collection containing mobile internal echoes (star) with posterior acoustic enhancement and perilesional echogenicity is located 25mm deep from the nodule's skin surface. A thin hypoechoic track (arrowhead) communicating from the anterior aspect of the collection to the skin surface represents a sinus track, akin to a volcanic vent rising to the top. The sonographic area encompassing the inflamed, oedematous tissue is 35mm wide.

Diagnosis. An incision biopsy of the skin nodule was performed and a small amount of pus was seen on excision. Histopathological examination revealed necrotising granulomatous inflammation with the presence of *Mycobacterium tuberculosis* DNA complex. On further review, the patient had no pulmonary or systemic signs of tuberculosis (TB) and she was not immunocompromised. She was commenced on anti-TB treatment, and her recovery was uneventful.

Discussion. Scrofuloderma is a rare skin manifestation of an underlying tuberculous focus such as a lymph node, testicle, joint or bone. It forms when a cold abscess progresses to a painless skin nodule, which may break to form an undermined ulcer with discharging fistulous tracks. On healing, it tends to leave retracted and puckered skin scars. The majority of scrofuloderma is caused by *M. tuberculosis* and the rest is caused by non-tuberculous mycobacteria. The face and neck are the most common sites of manifestation.[1] However, isolated axillary scrofuloderma is rare and may not present with constitutional symptoms or associated chest infection,[2] thereby potentially causing diagnostic confusion. TB continues to be endemic in Singapore and occasionally, there may be uncommon skin presentations such as scrofuloderma, even in immunocompetent patients. It is therefore important to recognise the clinical and radiological signs so that the proper diagnosis can be made for appropriate management.

The physical finding of a non-tender, raised nodule with surrounding pigmented and indurated skin suggests an underlying chronic inflammatory or infiltrative condition. Ultrasound assessment of the nodule (Fig. 2) showed echogenic thickened subcutaneous fat. There was an underlying semi-liquefied cystic collection with mobile echoes that communicated via a thin sinus tract to the skin surface. These findings are consistent with a partially liquefied immature abscess, with differentials being a discharging, caseating and/or necrotic lymph

Answer: E

node. Not shown in the picture were a few small, non-matted axillary lymph nodes with prominent cortices, which were likely reactive in nature.

Fig. 2 showed ultrasound details that were consistent with inflammation and/or infection with an area of liquefaction that represented an immature abscess.

In metastatic nodal disease from breast cancer or other malignancies involving the skin, it is common to observe large abnormal nodes in the axillae, which were not seen in this case. There was no clinical or radiological evidence of primary breast malignancy to support this option. Finally, it would be unusual for cutaneous and nodal metastases to present with an underlying abscess collection, as shown on the ultrasound image in this case.

Hidradenitis suppurativa (HS) is a chronic inflammatory skin condition related to underlying follicular occlusion that most commonly affects the axilla.[3] It has a female predominance with typical onset in the post-pubertal age group, and presentation after menopause is rare.[3] There is a strong association with smoking and obesity.[3,4] Early HS is characterised by tender subcutaneous nodules that may rupture with foul-smelling purulent discharge.[3] With recurrence, these superficial abscesses coalesce to develop deeper dermal abscesses with intercommunicating tracts.[3] In the indolent phase, there is fibrosis, skin induration and cord-like keloidal scarring.[3] The patient who is in her 80s, did not present with significant pain and purulent discharge—this would be atypical of HS.

Amelanotic and hypomelanotic melanomas are uncommon subtypes of melanomas that contain little to no pigment, resulting in frequent misdiagnosis of these skin-coloured or erythematous lesions. Risk factors include increasing age and cumulative sun exposure.[5] The ABCD criteria (asymmetry, border irregularity, colour variegation, diameter >6mm) and 3 Rs (red, raised [i.e. papule], recent change) aid recognition and diagnosis of such melanomas.[5] While difficult to disregard melanoma based solely on the lesion's appearance, in this case, its 2-week history in a non-sun-exposed region would be highly atypical for a melanoma.

Keratoacanthoma is a rapidly growing, locally destructive skin tumour that can be difficult to distinguish from well-differentiated squamous cell carcinomas clinically. Hence, the general recommendation is to surgically excise it.[6] The typical keratoacanthoma is a solitary nodule with sharply demarcated and skin-coloured or erythematous borders, and a classic keratotic centre, giving rise to a crateriform architecture.[6] They usually occur on sun-exposed skin of the face or upper limbs, and may grow up to 1–2cm within a few weeks.[6] The clinical features of the lesion in our patient showed a central umbilication with keratinisation and in addition to its short clinical history, typified that of a keratoacanthoma. However, its axillary location and sonographic appearance that showed an underlying abscess was not characteristic of keratoacanthoma.

Another possible differential is mycosis fungoides, the most common type of cutaneous T-cell lymphoma, which presents with polymorphic patches, plaques and focal tumours.[7] Such tumours may ulcerate and become necrotic.[7] They have an insidious onset and typically occur on non-sun-exposed regions.[7] However, the patient's history of acute onset of a raised skin nodule was not in keeping with the usual presentation of mycosis fungoides.

Conclusion. TB scrofuloderma should be considered in a painless, indurated axillary skin nodule with the sonographic finding of an underlying abscess collection, even in an immunocompetent patient. The diagnosis of extrapulmonary TB must be considered and the appropriate microbiological tests should be performed for confirmation.

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Acknowledgement

The Editorial Board of the *Annals*, Academy of Medicine, Singapore
gratefully acknowledges the generous support of

The Lee Foundation

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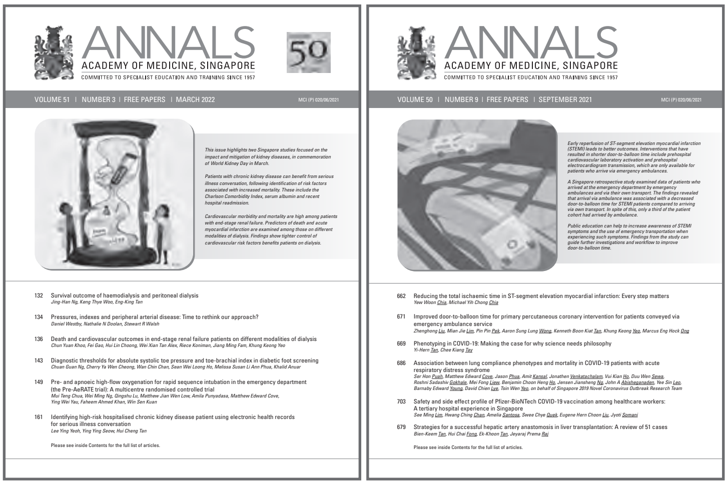

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